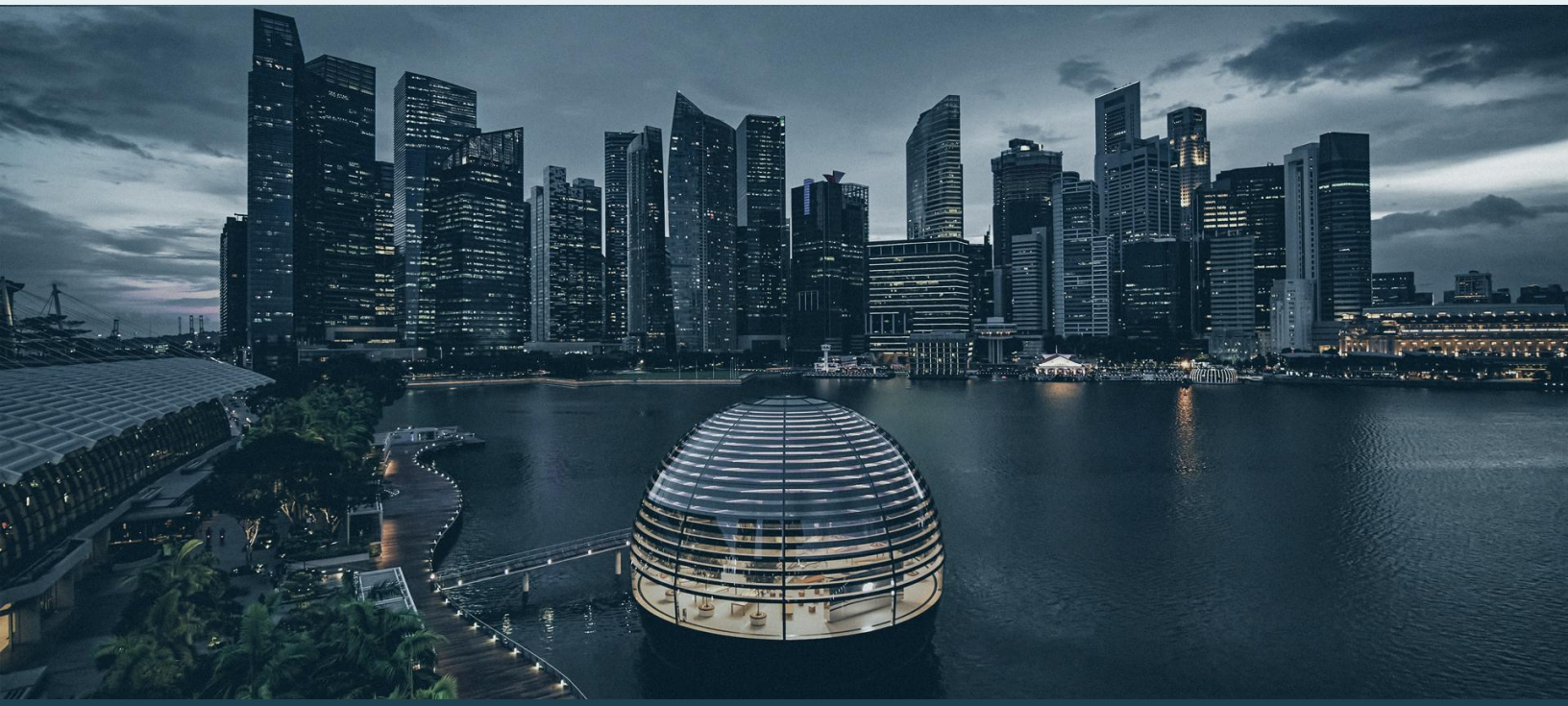
Bloomberg New Economy Forum



Bloomberg New Economy Health Council

Readings to frame the discussion

Knowledge Partner

McKinsey & Company

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Dear New Economy Forum delegates:

I'm delighted we will once again be able to "press the flesh" in Singapore, even as we keep the hand sanitizer nearby! The Bloomberg New Economy Forum is one of the first in-person global gatherings since the pandemic began. For the past 20 months, COVID-19 has dominated the global health and life-sciences agenda, while many other issues (e.g., mental health, the importance of preventative care, cancer) remain as urgent as ever. As we come together in Singapore to discuss global public health, we have a renewed opportunity to put our heads together and make progress.

To inform this unique moment, we have gathered McKinsey's most recent and relevant materials, to illuminate four urgent tasks in our collective COVID-19 response, and five other health issues that cannot remain on the back burner.

First, **we must vaccinate the world.** None are safe until all are safe. High-income countries have achieved great progress, but in low- and middle-income countries (LMICs), the situation looks quite different. Many have reached only a single-digit percentage of their populations.

A second and related point: **addressing vaccine hesitancy is essential.** Tactics will differ in high-income countries and LMICs.

Third, **we must learn to live with endemic COVID.** A world that has been fervently hoping for a clean break with the COVID-19 pandemic may be disappointed. The shift from pandemic to endemic will entail a number of actions for public-health leaders, and a new mindset.

Finally, **the world must prepare for the next pandemic.** COVID-19 was not the first pandemic, and it won't be the last. If there's any silver lining to the tragedies of 2020-21, it is that we're now aware of weaknesses in the world's infectious-disease-surveillance and -response capabilities. Fixing them won't be easy, but now is the time to act.

In our laser-like focus on COVID-19, it's important to also keep an eye on other urgent issues.

First, **mental health** - a largely under-addressed issue before the pandemic – has been exacerbated by COVID-19 and the isolation that we have imposed on ourselves. It must be addressed. Today, almost one billion people have a mental-health or substance-use disorder. Undoing the stigma of these conditions and providing appropriate affordable care are essential next steps.

The world must also shift towards **preventative care to improve health outcomes and lower costs.** COVID again shone a spotlight on this imperative: we have seen distinctly different outcomes for those who were in good health vs. those who were obese, diabetic, or suffering from other chronic conditions. As we reimagine public health for the post-COVID era, we have a singular opportunity to dramatically advance broad-based health and prosperity, and to explore an integrated view of physical, mental, social, and spiritual health.

Gene therapy has great potential; what will it take to unleash it? The successes and setbacks to date suggest that several technological challenges must still be overcome. But the wealth of innovative solutions now under investigation by academia and biotech, pharma, and contract development and manufacturing organizations indicate that viral-vector gene therapies, among others, are here to stay.

More broadly, advances in biological science and the accelerating development of computing, automation, and artificial intelligence are fueling a new wave of innovation. This **Bio Revolution** could have significant impact on economies and our lives, from health and agriculture to consumer goods, and energy and materials.

Finally, cancer is still squarely in our sights. Now, **advanced analytics has the potential to transform cancer care,** improve health outcomes, and create value for companies in research & development, manufacturing, and distribution. To realize the potential, companies will need to overcome their suspicions about the kind of experimentation inherent in developing advanced-analytics capabilities.

We hope these articles will usefully inform our discussions about health (and wealth) at the 2021 Bloomberg New Economy Forum. We'll have more to share with you in Singapore and beyond, and we look forward to the conversations.

Sincerely,

Matt Wilson
Senior Partner, McKinsey & Company
New York

Bloomberg New Economy Forum

Vaccination

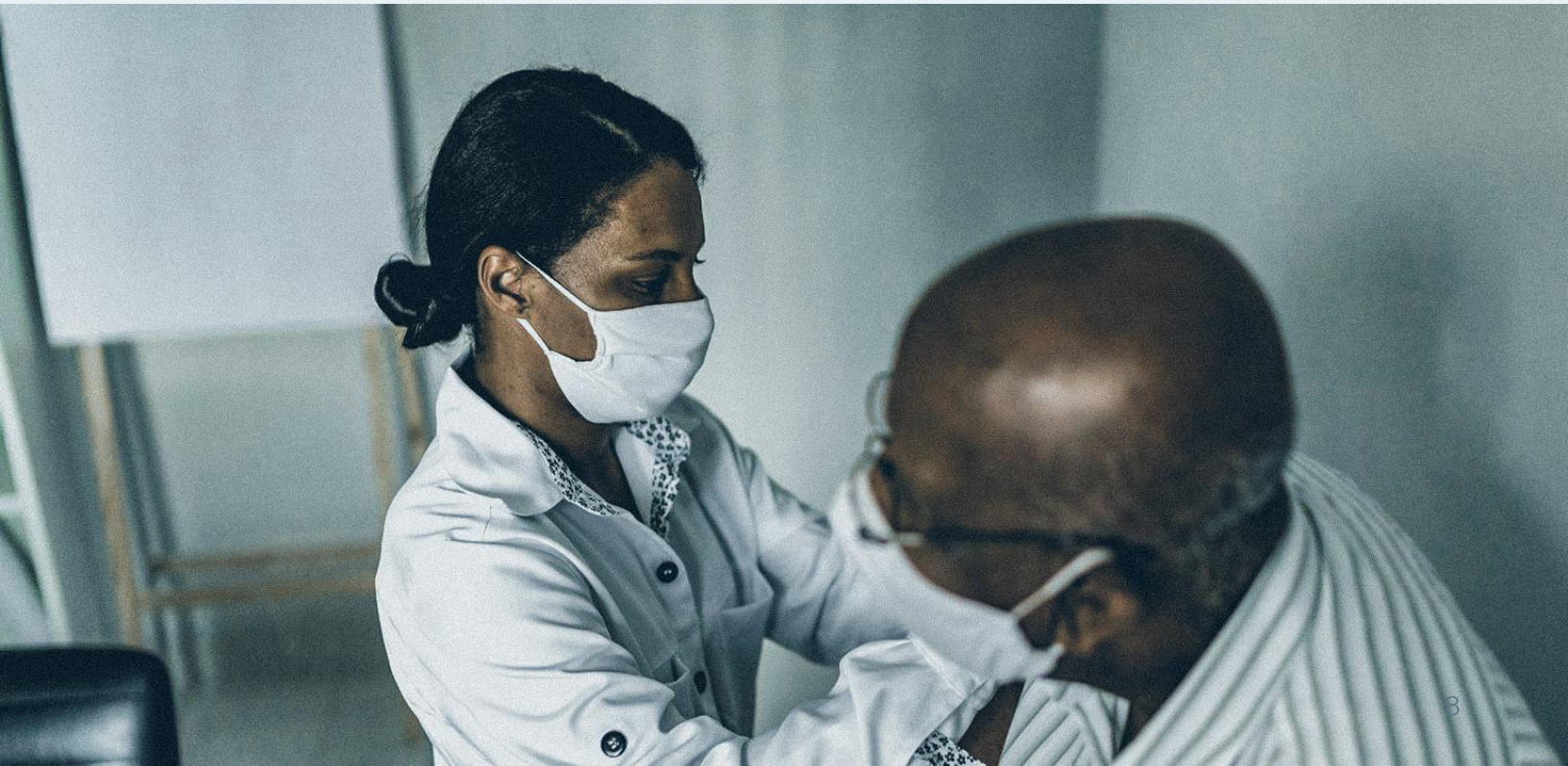
Knowledge Partner

McKinsey & Company

‘None Are Safe Until All Are Safe’: Covid-19 Vaccine Rollout in Low- and Middle-Income Countries

McKinsey

23 April, 2021



Despite persistent supply issues, in-country delivery and demand for COVID-19 vaccines is likely to be the next challenge for LMICs.

Despite persistent supply issues, in-country delivery and demand for COVID-19 vaccines is likely to be the next challenge for LMICs.

High-income countries (HICs) around the world have been deploying mass COVID-19 vaccination programs at varying speeds since December 2020. As of April 19, 2021, more than 500 million people worldwide had received at least one dose, a majority of HICs had administered at least one dose to over 20 percent of their populations, and a few outliers had provided at least one dose to well over 50 percent.

But in low- and middle-income countries (LMICs), the situation looks quite different. A large number of LMICs were yet to administer an initial dose to 1 percent of their populations as of April 19, presenting a risk not only to their residents but also to global progress in preventing the spread of potential variants. As the global initiative on COVID-19 Vaccines Global Access (COVAX) stated: “With a fast-moving pandemic, no one is safe, unless everyone is safe.”

In early March, COVAX announced the expectation to make some 1.8 billion doses available to Advanced Market Commitment countries by the end of 2021, corresponding to coverage of roughly 28 percent of those countries’ populations. Outside of COVAX, some LMIC regions and countries have secured additional doses through agreements with specific manufacturers. Now, the challenge is how to scale access, manage uncertainty amid new streams of information (for example, vaccine efficacy against variants or evolving safety profiles), and ensure vaccines distributed can effectively reach their target populations.

Globally, sizable attention has been paid to supply challenges for LMICs. Much less time and resources have been dedicated to in-country delivery of and demand for vaccines, which may quickly become the bottleneck as supply ramps up. Five critical factors LMICs can consider when designing rollout programs for COVID-19 vaccination include:

1. Robust and efficient central nerve centers are critical to drive target-setting made by policy makers, scenario planning, roadmap development, and decision making; oversee implementation; manage uncertainty; and conduct performance management of in-country vaccine rollout.

2. Specific and robust in-country delivery strategies can drive effective rollout, taking into account unique challenges and opportunities to ensure the availability, administration, accessibility, acceptability, and affordability of the vaccines, as well as the system's accountability for rollout effectiveness.

3. Agile strategies can adapt to evolving (and sometimes unpredictable) supply and demand dynamics. Even though the idea of having significant supply in LMICs may seem like a remote scenario in the near term, countries need to actively plan for scaled supply so that their absorptive capacity does not become the bottleneck.

4. LMICs may be able to leverage existing strengths from past experiences with immunization campaigns and outbreak response, while being mindful of ways in which COVID-19 vaccine rollout strategies could potentially disrupt ongoing immunization programs. LMICs are facing a secondary health crisis, compounded by the pandemic, having seen major disruptions in routine immunization (with 2020 coverage levels dropping to those not seen since the 1990s) as well as in other health services (with increasing health burdens and excess deaths across major disease categories throughout the pandemic, in many cases exceeding deaths from COVID-19).

5. COVID-19 vaccination strategies can go beyond a one-time, siloed approach. Efforts can intentionally build health system capacity and resiliency, strengthening traditional immunization efforts or other health services, such as through investments in delivery infrastructure, demand-creation activities, and new digital systems.

National and global healthcare stakeholders considering these five factors can develop actions to help more citizens receive the COVID-19 vaccine more effectively.

Critical strategic decisions for LMIC rollout of COVID-19 vaccines

Large amounts of funding are being dedicated to the procurement of COVID-19 vaccines for LMICs (although doses procured to date are still not sufficient to cover LMIC populations), but far less is being invested in planning for and implementing in-country roll-out. COVAX's recent reports indicate a cost for in-country vaccine rollout of roughly $1.5 per dose in order to deliver vaccines to cover the first 20 percent of populations, not including the cost of the healthcare workforce. Of this, COVAX has estimated that approximately $1 per dose would need to come from sources other than COVAX (for example, domestic, bilateral, or multilateral sources) at an estimated total of $1.3 billion.8 COVAX already expects to provide more than 20 percent population coverage by the end of 2021, and many LMICs have sourced additional doses through regional and bilateral deals, so the total roll-out funding requirement for 2021 alone could be substantially higher than this. Although the World Bank's $12 billion lending programs could theoretically be leveraged for vaccine delivery activities, it is yet unknown whether countries will choose to use this financing mechanism.

LMICs tend to have less well-resourced vaccination delivery systems to begin with, with more limited access to warehousing, cold-chain equipment, distribution capacity, dedicated staff, and needed information technology systems. Furthermore, LMICs will need to reach uniquely hard-to-serve populations, which can include:

+ Informal economies. Large portions of LMIC economies are informal, including many workers with high exposure risk (for example, street vendors) or those employed by small and medium-size enterprises. These workers can be much more challenging to reach than those who work for larger, more formal employers in HICs.
+ Rural communities. Many LMICs have substantial rural populations (LMIC urbanization rates are around 51 percent, and only 33 percent in low-income countries, compared with 66 percent in upper-middle income countries (UMICs) and 81 percent in HICs). Rural populations can be much harder to reach (both logistically—limited infrastructure, transportation difficulties—and because of poor health coverage) and present serious efficiency obstacles for a mass vaccination program, including limited ability to host a single vaccination site that can reach a substantial population, vaccine utilization problems for multidose vials that need to be fully used in a short period of time, and follow-up challenges for those requiring a second dose. These challenges may require more labor-intensive vaccination outreach, which can be problematic for multidose vials that need to be fully used in a short period of time. Vaccine administration may be harder in rural communities, especially to ensure second dose provision.
+ Transient populations and humanitarian situations. LMICs tend to face greater numbers of transient and hard-to-identify populations in humanitarian contexts, whether refugees, migrants, or mobile workers. These groups may be challenging to identify and access outside of formal settings (for example, in refugee camps).

The ACT-Accelerator and its partners have developed tools for country diagnostics and planning. As a compliment to that, we focus on major design considerations for national programs for COVID-19 vaccine rollout.

Setting up robust and effective central nerve centers

Given the complexity and challenges associated with these components, countries have seen benefits from developing nerve centers to set a singular strategy and manage across activities. Countries across income bands have faced challenges with a lack of role coordination between multiple government entities and other stakeholders. As a result, these countries may experience a duplication of efforts as well as a failure to consider the holistic set of activities and resources required. Given the complexity and challenges associated with vaccine rollout, many countries have seen benefits from developing nerve centers to set a singular strategy and manage across activities. As a result, these countries may experience a duplication of efforts as well as a failure to consider the holistic set of activities and resources required.

LMICs can look to successful emergency operations center (EOC) examples, such as those developed in Nigeria to combat polio. In “Eradicating Polio in Nigeria” we describe one such effort, highlighting critical success factors for high-performing EOCs, including taking a “command center” approach that drives extensive collaboration; leveraging dedicated cross-functional talent; consistently iterating the approach based on regular synthesis of fast-paced analytics; ensuring extensive and early buy-in with senior stakeholders to enable rapid decision making; and conducting intensive program management with clear targets, debottlenecking processes, and rigorous tracking and monitoring.

Some LMICs may already have such structures that can be leveraged for COVID-19 vaccination rollout. Others may find it critical to rapidly develop EOCs, and can take comfort knowing how valuable they may be beyond the COVID-19 response: a previous report, “Acting now to strengthen Africa’s health systems” details how EOCs, once set up, have been effectively used to pivot and respond to new outbreaks in real time in sub-Saharan Africa.

In addition to centrally directed planning and coordination, locally driven approaches can also be effective. A microplanning model has been deployed in a number of countries, where a central body, such as a Ministry of Health, sets eligibility principles and makes allocation decisions while outsourcing other decision making (for example, site identification, demand generation) to regional or local stakeholders. Local knowledge may be invaluable to inform decision making in centralized systems; how much decision making itself is devolved may depend on how much new infrastructure (which may be allocated and funded centrally) is required for effective rollout.

Developing an end-to-end tactical rollout plan across delivery components

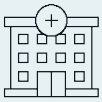
Overall, COVID-19 vaccine delivery should consider the following components:

To date, the bulk of attention and support has been focused on vaccine *access*; ultimately, the bottleneck to coverage may come from *in-country delivery*.

Requirements and critical considerations for effective vaccine roll-out

AVAILABLE
Vaccine is approved and in sufficient supply to reach population
- Technology portfolio and access
- Technology transfer and drug substance manufacturing
- Upstream/downstream sourcing and manufacturing
- Public policy planning

→ **How might LMICs access additional vaccines** given current limitations?



ADMINISTRABLE
Appropriate individuals can receive vaccination at convenient locations
- Population segmentation
- Vaccination dispensing strategy

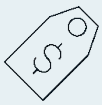
→ **How can LMICs develop the right network of vaccination points** given limited data or existing networks and hard-to-reach populations?

ACCESSIBLE
Vaccine is distributed and stored for use
- Ordering
- Logistics, transport, and warehousing

→ **How can LMICs effectively deliver COVID-19 vaccines** given limited existing infra-structure and already-disrupted health/routine immunization services?

ACCEPTABLE
Consumers have accurate information they trust and choose to be vaccinated
- Public communications, messaging, and education
- Healthcare workforce edaucation

→ **How do LMICs ensure indivi-duals make informed choices about vaccination** given limited demand intelligence and unique demand drivers?



AFFORDABLE
Costs of vaccination and administration are amenable to both payers and consumers
- Funding
- Reimbursement strategy

→ **How can LMICs alleviate transaction costs of getting vaccinated**, especially for the most vulnerable?

ACCOUNTABLE
Patients receive full course; monitoring in place on post-launch outcomes
- IT infrastructure and interoperability
- Ongoing monitoring and reporting

→ **How might LMICs develop performance management systems** to enable continuous improvement given existing paper-based systems?

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A number of critical factors can be considered for each component of the rollout strategy, with specific implications for LMICs:

Availability

LMICs are considering multiple potential levers to access additional doses. Countries will need to determine which levers to pursue, with what speed, and in what proportion. Each source has different considerations, including financing (some are at least partially funded, others require countries to self-finance), access to diverse products, availability of sophisticated intermediaries to pool/negotiate on a country's behalf, and expected timing of procurement tranches. In all likelihood, many LMICs will take a portfolio approach, combining levers to suit their needs. These levers include:

+ Additional COVAX doses. It is possible (but not certain) that the COVAX mechanism will increase the volumes it can secure for LMICs beyond the current allocation announcement. It is not yet clear how likely this is to occur or by when, or how much LMICs would be asked to co-fund.

+ Regionally coordinated pooled procurement. In a few cases, regional bodies have secured large volumes of doses to support the countries in their remit. For example, in March 2021, the African Union announced that it had secured up to 400 million doses.

+ Bilateral deals. Countries, including some LMICs, have already begun bilateral deals directly with manufacturers. Additional capacity for LMICs may become available over time, potentially driven by increasing demand saturation in HICs, deployment of new COVID-19 manufacturing facilities to ramp up supply (which may include manufacturing in LMIC regions, such as Aspen in South Africa), and potential approval of new COVID-19 vaccines.

+ Donations from over-supplied countries. Although most HICs are still limiting vaccination eligibility as supply (and delivery infrastructure) continues to increase, HICs overall appear to have secured more doses than they might ultimately need, under current manufacturing expectations. Some have already indicated that they plan to contribute excess doses to LMICs, through COVAX or directly, although realizing these donations may take some time.

As described above, countries may benefit from preparing for a range of supply scenarios. This is likely to include ensuring the proper regulatory steps are taken to approve proven products; some countries have aligned national COVID-19 vaccine decision making with either stringent regulatory authority approvals or regional reliance frameworks that can enable efficient and high-quality regulatory decisions. As availability may change over time, countries could theoretically develop a phased scale-up approach to their distribution strategies based on an availability forecast. In reality, vaccine shipments may be uncertain and unpredictable, necessitating a more agile approach that can allow for successful implementation despite changing availability.

Administration

Administering an initial wave of vaccinations focused on healthcare workers (the approach most governments have taken) can be straightforward, as this group can be easier to identify, inform, and ensure access to a vaccination than the broader population. Many LMICs have not yet needed to deploy new vaccination sites and the limited vaccine volumes available are often being administered through the traditional healthcare system and its facilities. Ramping up thereafter—especially in an equitable way—can be challenging. In many HICs, this ramp-up has usually begun with existing points of care (hospitals, followed by general practitioner/primary care physician offices). HICs have often started by adding new vaccination points in densely populated areas (such as mass vaccination in stadiums or

schools). They have then segued to mobile or smaller sites to reach specific or underserved populations. Although this approach has had some equity implications, it has allowed HICs to reach increasing numbers of target populations.

Countries will likely benefit from deploying multiple vaccination channel approaches to successfully reach target populations, balancing the need for efficiency and equity. Some LMICs have strengths to leverage in developing their approach: many have significant experience with campaign-based vaccination programs, (for example, polio) that can be brought to bear. To develop these strategies, countries may deploy the following approaches:

+ Mapping populations to existing infrastructure, leveraging local expertise. Many countries have complemented official sources (for example, census or other public records) by devolving efforts to local community leaders who can identify the strength of existing facilities as well as the size and location of population clusters for each target group (for example, municipal government staff in Brazil and the healthcare workforce in Costa Rica have driven such efforts). More innovative data sources may also be available, such as mobile data or household geotagging.

+ Designing a temporal network. Countries can choose to develop best-estimate forecasts of vaccination point capacity required over time, based on when vaccines are expected to arrive and the target populations they are intended for. Combining this with the mapping of populations and existing vaccination points, countries would help identify where different scaled vaccination points are most likely to be required, balancing efficiency (including cost implications) and equity (ensuring vulnerable populations that may be harder to access are reached).

+ Identifying solutions for each area with unmet need. Countries can select the specific types and locations of sites to be fit-for-purpose with population needs. Many UMICs are also leveraging local community leaders to self-select vaccination points based on specific community contexts and preferences.

Even if an appropriate mix of vaccination sites is developed, HIC experience has shown challenges in managing throughput capacity at these sites, balancing demand across sites, and minimizing waste; LMICs will need to develop systems and processes to address these challenges.

Accessibility

Multiple components are involved in an effective logistics system (various partners have collaborated on comprehensive checklists, as mentioned above). Three major elements of vaccine distribution logistics may prove especially challenging for LMICs:

+ IT/data systems for appointment-making, to track stock levels of all relevant products, for vaccination points to place new orders, and for allocation approvals and rebalancing decisions to be made. As HICs have begun COVID-19 vaccine rollout, challenges with the quality and reliability of these systems have arisen, as they are often overloaded by demand or have not built in the decision-making processes required for proper utilization. Furthermore, some HICs have struggled to optimally manage second dose administration, including ensuring stock and appointments are available and that people actually return for their second dose at the appropriate time. LMICs can work to identify common flaws and incorporating solutions based on forecasts.

+ Distributors, warehousing, and storage often involve multiple supply chain layers, depending on the country's size and complexity. Cold-chain equipment (CCE) may be especially difficult for LMICs.

+ COVID-19 vaccines to date require some level of refrigeration, with some requiring ultra-cold-chain (UCC) storage temperatures. Most LMICs have limited ordinary cold-chain capacity for storage or distribution, let alone UCC capacity. At the last mile, cold-chain capacity can be even more limited (in terms of the lack of available equipment, outdated technology, and limited power for non-solar CCE), creating a problem for vaccine storage at vaccination points.

+ Trained staff to administer vaccines and vaccination points. As mentioned earlier, existing vaccinator staff may not be able to conduct all COVID-19 vaccination activities without disrupting other critical services. LMICs can develop strategies to maximize the number of staff that are qualified by ensuring that healthcare workers who can administer vaccines are working at the top of their license (that is, ensuring lower-skilled staff handle non-administration steps), and exploring task shifting if appropriate.

Many LMICs have experience with vaccination delivery processes and logistics, with varying degrees (and sophistication) of ordering, tracking, transportation, warehousing, cold-chain, and staffing infrastructure. However, multiple factors are expected to make COVID-19 vaccination logistics far more complex than routine immunization programs (see sidebar, “Why are COVID-19 vaccines different?”), and a recent World Bank report notes that having a well-functioning child immunization system has not thus far been a strong predictor of readiness to roll out COVID-19 vaccines. Furthermore, simply deploying existing vaccination infrastructure for COVID-19 vaccination efforts may be considered with care, given the potential to impact the already high levels of disruption of routine immunization efforts.

In HICs, vaccine delivery activities are often outsourced to the private sector, both before and during COVID-19, from leveraging third-party logistics providers to transport and store vaccines, to contracting private developers for IT systems to track vaccination rollout, to utilizing private

pharmacies and healthcare centers to administer vaccines. When managed properly, private involvement in vaccine delivery can improve quality and accountability. Such practices—especially for distribution—are relatively rare in LMICs, often because of cost concerns, reluctance to commit to sustained funding for third-party contractors, a lack of appropriate procurement frameworks (for example, public-private partnership [PPP] frameworks), insufficient capacity to manage private contracts, or low confidence that outsourcing processes will be fair and transparent. Some LMICs have been supported in supply chain outsourcing, with a few examples in Nigeria (where Lagos State outsources its vaccine supply chain) and Senegal (where multiple third-party logistics providers have been contracted to manage delivery of a variety of public health products).

Some countries may explore outsourcing options, which could lead to broader vaccine supply chain innovation, provided the right conditions are met. Some LMICs can be supported through the strengthening of PPP frameworks, affordability costing, efforts to ensure the process is (and is seen as) transparent and justly managed, and procurement/contract management capability-building (including support for performance management). If successful, private sector engagement developed for COVID-19 vaccine delivery could be expanded for broader immunization programs. On the other hand, countries with limited PPP capabilities, private sector options, or support may find it unwieldy to undertake such a transition during an already complex COVID-19 vaccine rollout.

Acceptability

Consumer confidence in COVID-19 vaccines varies by geography and, within countries, by population segments. In LMICs, limited data exists on COVID-19 vaccine acceptability, with even less information on demographic differences, trends over time, or root causes of hesitancy. This stands in sharp contrast to some HICs, where regular surveys are

done that allow for micropattern detection.

A survey of more than 15,000 adults in 15 African countries conducted between August and December 2020 indicated that willingness to take COVID-19 vaccines varied from 94 percent in Ethiopia to 59 percent in the Democratic Republic of the Congo. Primary respondent reasons for vaccine hesitancy included a lack of trust in the safety of vaccines and a belief that the COVID-19 threat is exaggerated. Some people in LMICs have a long-standing mistrust of adult vaccinations as a result of problematic clinical trial programs in the past, although vaccine acceptability has generally been stronger for pediatric vaccines. Promisingly, some HICs saw decreases in vaccine hesitancy as COVID-19 vaccinations expanded.

A recent World Bank report notes that less than 30 percent of countries have developed demand-generation strategies to encourage COVID-19 vaccine uptake. LMICs may be able to leverage existing strengths in community engagement and demand generation from previous public health efforts (for example, HIV prevention), including from immunization programs specifically, where strategies have often leveraged deep engagement with trusted local leaders to directly address misinformation, build awareness, and provide information about how to get vaccinated. For example, in India's polio vaccination efforts, a thousands-strong "Social Mobilization Network" (SMNet) was created to communicate to underprivileged communities, engaging local officials and religious leaders, running campaigns in a highly iterative fashion to respond to community needs. SMNet's success was subsequently leveraged to expand its impact to other health areas. For COVID-19, some LMICs (for example, Morocco) have deployed local government staff or local organizations, who have gone door-to-door to inform eligible populations, answer questions, address concerns, and support appointment-making or location-finding efforts. Proper safety protocols should be applied to any in-person community outreach efforts.

LMICs may want to consider how COVID-19 vaccination efforts can be leveraged to increase acceptance and utilization of a broader set of health services, especially for vulnerable groups (for example, to ensure continued childhood immunization) or demographics that historically engage less with the health system (for example, adult men, older generations). Additionally, countries can consider providing information about primary care, or even rapid testing services, while individuals wait in line to be vaccinated.

Affordability

Today, LMIC populations are largely not expecting to be charged for COVID-19 vaccinations. As countries continue vaccination programs (which may include self-financed procurement), it is not yet known whether this will remain the case. For example, some countries might charge more affluent segments, but keep vaccines free of charge for lower-income populations.

LMIC residents can face meaningful opportunity costs and indirect costs to getting vaccinated, such as taking time off from work, securing and paying for transportation to and from vaccination points, waiting in line, and managing childcare. Many may need to take time (and put themselves at some exposure risk) to help relatives and friends get vaccinated. Countries may consider how to reduce personal disruption or cost, such as by encouraging employers to allow employees to “take time” to get vaccinated.

Accountability

The COVID-19 vaccination rollout will need to be closely monitored to ensure the best use of scarce resources; rapidly adapt to changing supply, demand, logistical, and epidemiological circumstances; and continuously improve the approach. The need to ensure that populations

requiring a second dose actually receive that second dose further complicates tracking efforts. Today, vaccination tracking and monitoring systems in many LMICs are highly manual—leveraging paper-based ledgers and reports—and delayed, often only reporting centrally every month or every quarter. These manual systems are likely to be insufficient to deal with the rapidly changing supply and demand dynamics of COVID-19 vaccines, which may require frequent load-balancing, reevaluation of site location and infrastructure strategies, and careful monitoring of wastage to inform reduction efforts. Countries may consider a range of system improvements, including lower-tech and lower-cost approaches (for example, simple mobile apps).

Where do we go from here?

Without minimizing the challenge of COVID-19 vaccines for LMICs, stakeholders can also reflect on bright spots. The last time a mass vaccination program was needed in response to a major pandemic was in 2009, with H1N1. Then, the first vaccines arrived in Africa more than 20 weeks after the first (higher-income) countries started vaccinating. By contrast, although most LMICs are receiving COVID-19 vaccines more slowly than HICs, shipments to LMICs have taken place within 12 weeks of introduction in the first HICs. The COVAX Facility has helped to move LMICs closer to parity with HICs, with initial vaccine shipments reaching 100 countries 42 days after its first international shipment.

As LMICs access larger volumes of doses over time, in-country delivery activities become more critical—and more challenging—as capacity can become stretched, making the next sets of target populations harder to reach. Furthermore, the future may only get more complex: unfolding epidemiological realities (for example, expanded or new variants) may preset novel challenges, and the need for LMICs to vaccinate younger populations to achieve herd immunity means that large new groups will need to be reached once effective pediatric vaccines are approved.

As approaches are developed, LMICs can identify opportunities to strengthen their broader health systems. Agile and robust nerve center capabilities can support response to future outbreaks. Private sector engagement and improved logistics/data systems can help expand supply chain capacity and effectiveness. Novel demand-generation approaches can bring new demographics into the healthcare system and support catch-up efforts for others. Even longer-term strategies, including broader pandemic preparedness tactics or local vaccine manufacturing, can help drive health security for the future. Such strategies can serve the dual purpose of bolstering existing service provision while also improving LMICs' ability to respond to the next public health crisis.

Who's Left? Engaging The Remaining Hesitant Consumers On Covid-19 Vaccine Adoption

McKinsey

28 September, 2021

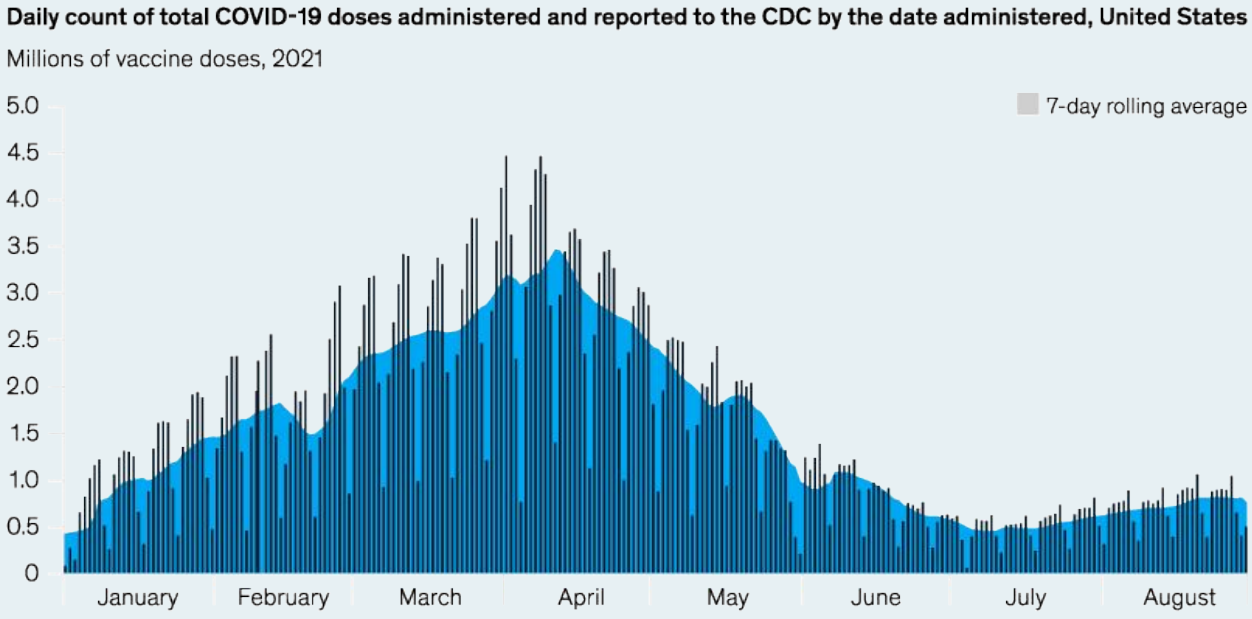
While more Americans receive and show openness to receiving the COVID-19 vaccine, concerns persist among guardians of children and other cautious segments.

More than 63 percent of the US population have received at least one dose of a COVID-19 vaccine, and more than 54 percent have been fully vaccinated, as of September 16, 2021, according to the Centers for Disease Control and Prevention. Approximate thresholds for herd immunity are benchmarked from 80 to 90 percent, which would require a minimum of roughly 80 million additional individuals to be vaccinated in the next few months.

Despite strong demand for COVID-19 vaccines in early 2021, by the end of May daily administration rates dropped to a third of their mid-April peak, reflecting waning consumer demand. While daily administration rates climbed moderately at the end of August, as of September 10, around 567,000 doses were being administered daily, compared with nearly six times that in April. At the same time, the United States continues to experience regional outbreaks, in part due to new variants such as Delta. As new variants with potentially greater severity and transmissibility continue to emerge, the effectiveness of existing vaccines or strength of immune response against these will be crucial to consider. This concern about emerging variants could potentially underscore the criticality of all eligible persons receiving the vaccine (Exhibit 1).

Exhibit 1

The daily administration rates of the COVID-19 vaccine in the United States.



Source: COVID-19 vaccinations in the United States, Centers for Disease Control and Prevention, September 1, 2021, covid.cdc.gov

McKinsey & Company

Many stakeholders are therefore evaluating how to reinvigorate vaccination rates, especially in light of potential federal requirements. Experts have sought to understand consumer decision making for adoption of COVID-19 vaccines. McKinsey consumer research, beginning in the summer of 2020, has understood consumer segments defined by their self-identified plans to receive a COVID-19 vaccine. These include four categories of consumers: 'Unlikely' (stated plans not to receive a COVID-19 vaccine), 'Cautious' (those who are uncertain whether to receive a COVID-19 vaccine), 'Interested' (those who have already scheduled or are planning to schedule their COVID-19 vaccination appointments), and 'Already vaccinated.'

The COVID-19 vaccination rollout has been unprecedented, with more than 300 million COVID-19 vaccine doses already administered so far in the United States. Some of the unique factors that enabled this effort have been the setup of mass vaccination clinics, the proliferation of drive-through and mobile clinics, and the ability of pharmacies to administer shots. Stakeholders, including state governments, employers, and providers, are already taking meaningful actions to address vaccine hesitancy. In addition to the options detailed in this article, stakeholders may consider making fundamental shifts in their approach as the United States enters this next phase of COVID-19 vaccine rollout:

+ Expanded stakeholder engagement in driving adoption with a broader set of incentives. To date, governments have helped lead community vaccination efforts with the support of providers, pharmacies, and other stakeholders. Moving forward, other stakeholders may decide to play an even larger role. This role could include businesses requiring patrons to be vaccinated where warranted, providers and pharmacists engaging in patient discussions regarding the vaccine, and insurers building in value-based care incentives for providers to deliver against vaccine adoption targets, for example. As of September 9, the Biden administration has made vaccination mandatory for federal employees, removing the option for testing weekly. The administration has also recommended that the Department of Labor's Occupational Safety and Health Administration develop a new rule regarding vaccination. This rule could require all employers of more than 100 people to either ensure 100 percent vaccination of their workforce or perform testing on a weekly basis to unvaccinated individuals. This recommendation has yet to play out, but could have a potential impact and lift on adoption of vaccination if enacted as recommended.

+ Personalized messaging and targeted engagement to address person-specific needs. Marketing to consumers remains largely broad-based and through more traditional channels. The ability to tailor messages and engagement approaches to consumer segments could have outsized impact in informing consumers. Additionally, data reflects barriers and reservations consumers have to getting the vaccine. Messages can vary. For example, those concerned about safety or side effects value information from trusted sources that speak directly to specific concerns (for example, fertility). Some consumers are focused on the freedom to make their own choice. Others may consider the vaccine if it affects those they care about.

+ Agile approach to rapidly test, learn, and adapt approaches quickly. Several vaccine campaigns have been launched, but there may be room for improvement in how quickly these are tried, learned from, and modified. Best-in-class campaigns adjust on a daily basis, learning and adapting in real time to what marketers discover. Agile programs can adapt to the changing environment, learn what works and what doesn't, leading to greater effectiveness of spend while improving outcomes.

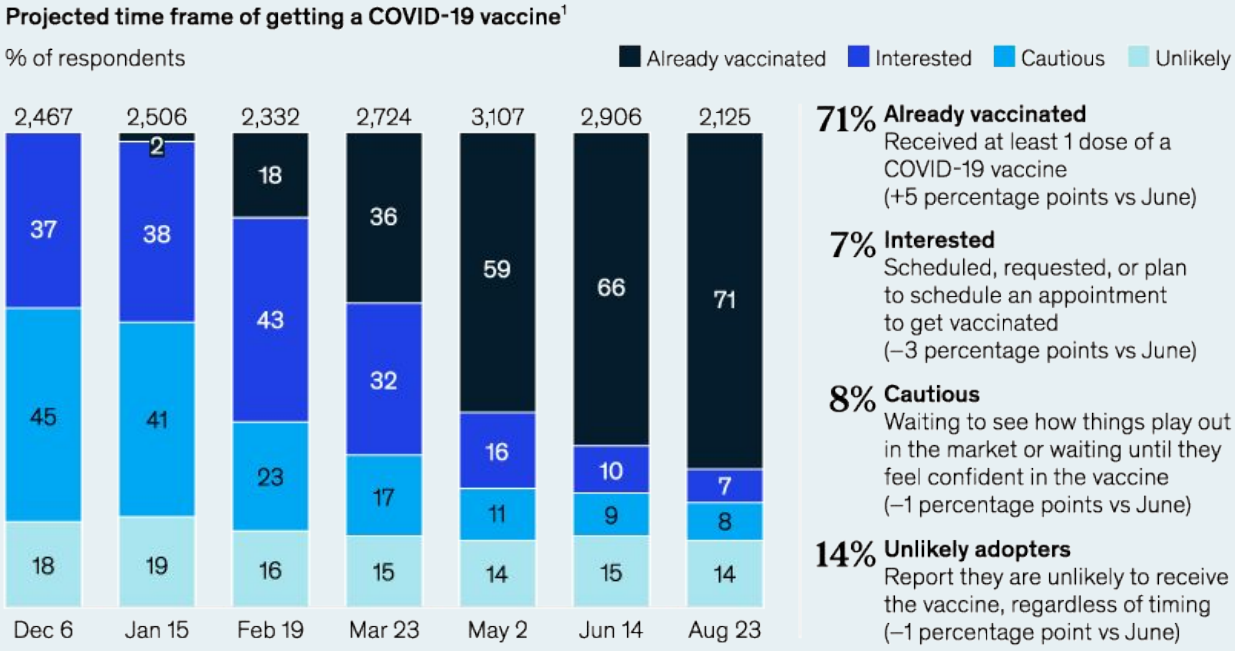
Here, we detail trends among the remaining unvaccinated, and discuss specific actions that could address the drivers of hesitancy within these populations.

Given the minimal movement in 'Unlikely' vaccinators over time, we choose to focus on the 'Cautious' segment here. Since December 2020, this segment has shrunk from 45 percent to 8 percent of respondents (Exhibit 2). Addressing the questions or concerns of even half of the 'Cautious' individuals and moving them to 'Interested' and eventually 'Vaccinated' status could translate to more than ten million Americans protected against severe COVID-19. A part of the 'Cautious' group represents decision makers for minors, and will strongly influence

whether their children receive a vaccine. Across the ‘Cautious’ and ‘Unlikely’ groups, an opportunity exists to address potential barriers, including communication from trusted advisers, improved convenience, and the reduction or elimination of direct and indirect costs associated with getting the COVID-19 vaccine.

Exhibit 2

COVID-19 vaccination: The ‘Cautious’ segment continues to decline and the ‘Unlikely’ segment is steady.



QVAX1b. Under which timeframe of COVID-19 vaccine availability would you be most likely to get vaccinated?
[1] Prior to February 2021, adoption segments were defined as: Interested: a. I would volunteer to get a vaccine as a participant in a clinical trial, b. I would get the first vaccine available under an Emergency Use Authorization (EUA), c. I would get the first vaccine available as soon as clinical trials are completed; Cautious: d. I would wait to get a vaccine until it has been on the market for 3–12 months, e. I would wait until I was confident that it has been proven to be safe; and Unlikely: f. I'm unlikely to get vaccinated. Beginning in February 2021, adoption segments are defined as: Already vaccinated: a. I have been vaccinated with 2 doses of a 2-dose vaccine, b. I have been vaccinated with 1 dose of a 1-dose, c. I have been vaccinated with 1 dose of a 2-dose vaccine, and have scheduled the second dose, d. I have been vaccinated with 1 dose of a 2-dose vaccine, and I am waiting for the appointment for the second dose to be scheduled, e. I have been vaccinated with 1 dose of a 2-dose vaccine, and I will not schedule the second dose; Interested: f. I scheduled an appointment for the first dose of a vaccine, but have not had the vaccination yet, g. I requested to schedule the first dose of a vaccine, and I am waiting for the appointment to be scheduled, h. I am planning to get a vaccine, but have not attempted to schedule an appointment to get vaccinated; Cautious: i. I will wait to get a vaccine until it has been on the market for more time, j. I will wait until I am confident that it has been proven to be safe; and Unlikely: k. I'm unlikely to get vaccinated.
Source: McKinsey Consumer Health Insights-COVID-19 Survey, 9/7/2020, 10/26/2020, 12/7/2020, 1/15/2021, 3/26/2021, 5/02/2021, 6/14/2021, 8/23/2021

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Demand trends

Further enabling decreasing hesitancy among the 'Cautious'

Certain population segments and demographics are disproportionally represented in the 'Cautious' segment. 'Cautious' adopters are more likely to identify themselves in our survey as women, to be in a household with less than $25,000 total annual income, and live in a rural area compared with all respondents.

Among the 'Cautious,' the most common remaining concerns lie around safety and side effects, with nearly half of these respondents concerned about long-term side effects. Twenty-eight percent of these respondents have indicated that they received the flu shot in the 2020–21 flu season, demonstrating openness to vaccination once their concerns are addressed.

Multiple factors influence the likelihood of receiving a COVID-19 vaccine. As detailed in the article "COVID-19 vaccines meet 100 million uncertain Americans," a combination of at least three highly interrelated conditions is required for broad adoption: "conviction" (desire to receive the vaccine), "convenience" (ability to access end-to-end vaccine processes without hassle), and "costlessness" (ability to take time away from work in order to get the vaccine).

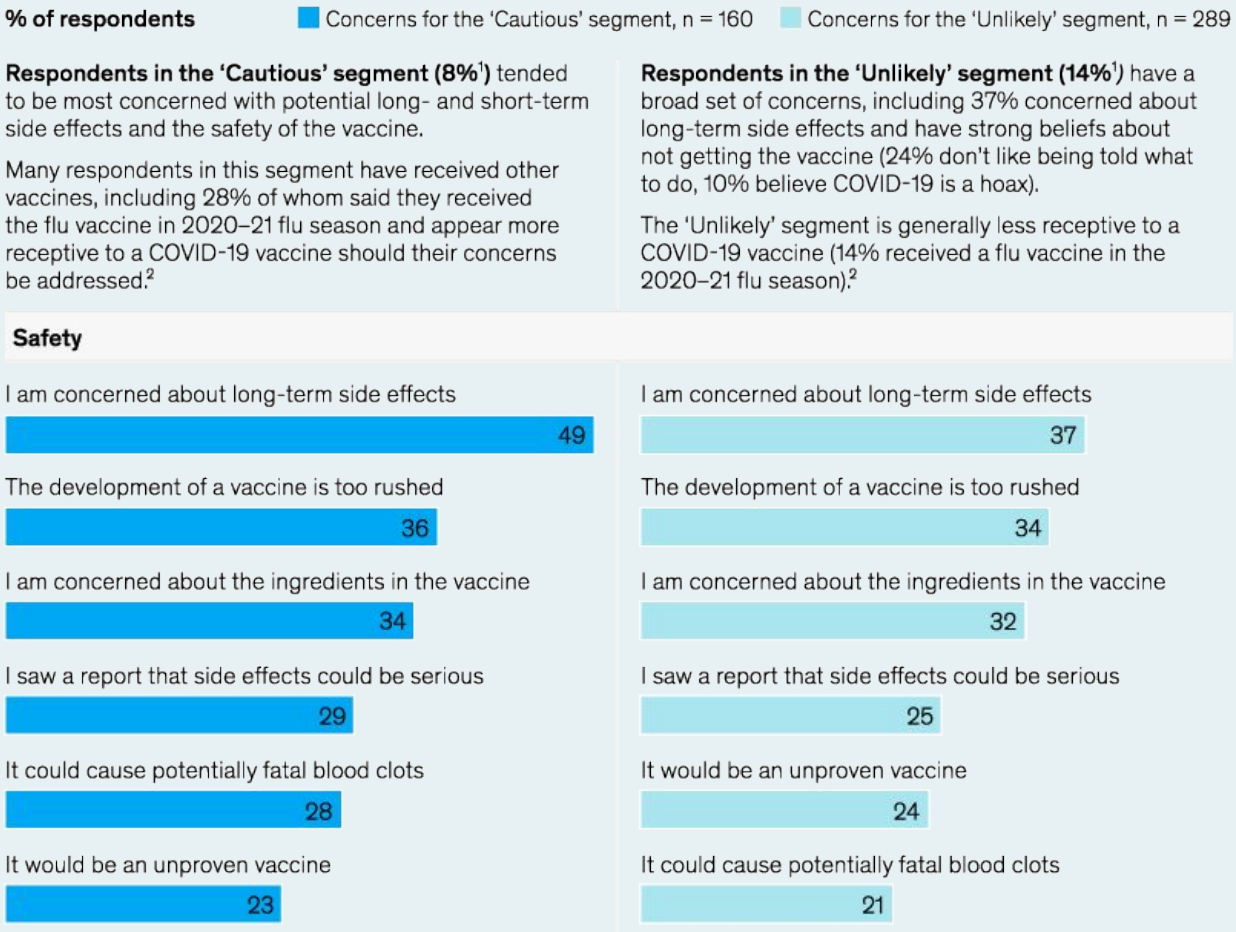
Examining respondents in May who identified as 'Cautious' but received the vaccine later can offer clarity on motivation

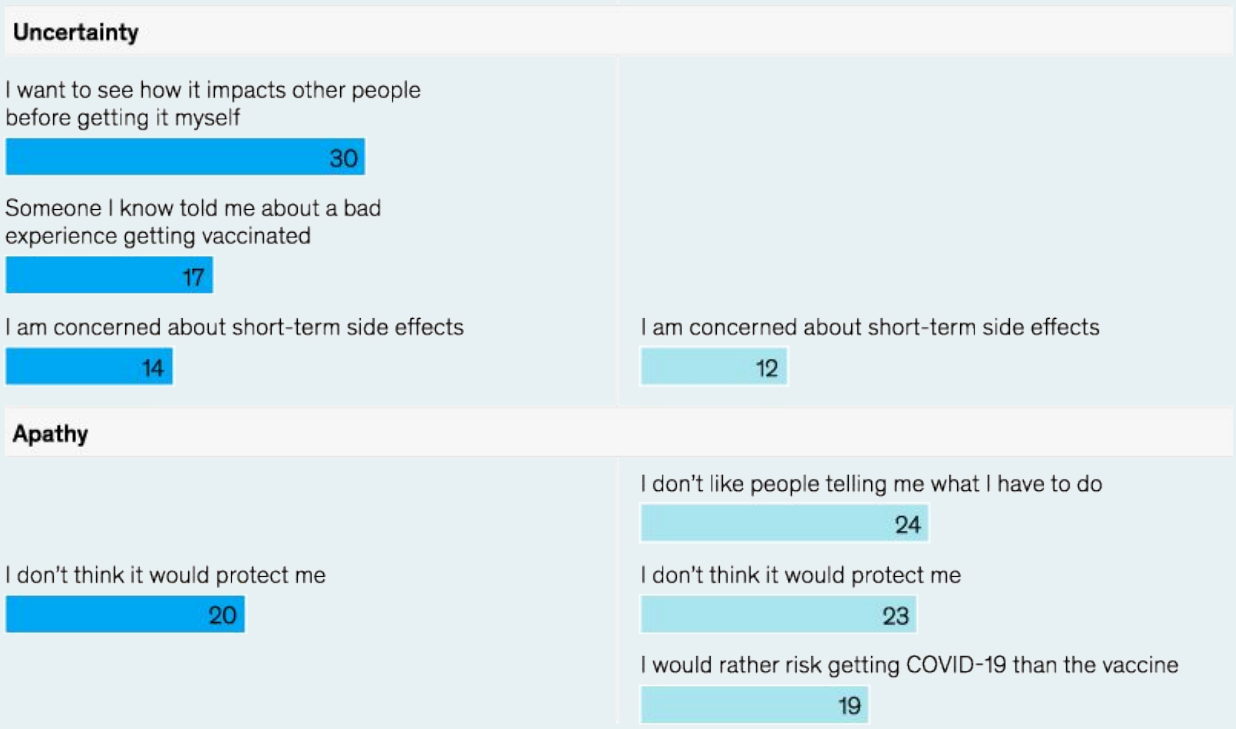
The top reasons these respondents waited before becoming vaccinated was to see how it impacted other people before getting it themselves (17 percent), difficulty getting an appointment (15 percent), and concern about long-term side effects (14 percent) (Exhibit 3). Correspondingly, ability for walk-in appointments and ability to pick the brand of vaccine they received were identified among the top influencers that resonated with them to receive a vaccine. Further, when asked why they ultimately

chose to get the vaccine, the top reasons included that they thought it was the right or responsible thing to do (12 percent), it would protect them (13 percent), or that they ultimately didn't want to risk getting COVID-19 (13 percent).

Exhibit 3

Concerns 'Cautious' and 'Unlikely' segments may have about the COVID-19 vaccine.





[1] Percent of respondents who identify themselves as either 'Cautious" or "Unlikely' out of all respondents.
[2] Survey respondents answered each survey question individually across different topics such as how COVID-19 is affecting consumers' daily activities, ability to receive healthcare, their mental health and well-being, their COVID-19 testing behavior, and COVID-19 vaccination history, perceptions, and attitudes.
Source: McKinsey Consumer Health Insights 6/14/2021

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Considering the 'Unlikely'

In contrast with the 'Cautious,' survey respondents in the 'Unlikely' segment have shown minimal movement over the past eight months, remaining relatively steady at about 15 percent of respondents. This group has historically indicated hesitancy toward vaccination in general. Only 14 percent indicated that they received a flu vaccine in the 2020–21 flu season, and just 11 percent intend to get one for the upcoming 2021–22 flu season. Nonetheless, they indicated some interest in receiving a COVID-19 vaccine with incentives, particularly cash rewards or raffles for cash prizes (13 percent and 9 percent responding positively, respectively).

Attitudes of the unvaccinated are further complicating vaccination efforts. The unvaccinated have indicated pressure to get vaccinated has either little or an opposite effect on their willingness to do so. Almost a quarter (24 percent) of 'Unlikely' respondents state that they are less likely to get the COVID-19 vaccine because they do not like being told what to do. The 'Unlikely' are more extreme in this view than the 'Cautious' or 'Interested.' The unvaccinated also deny that their actions are contributing to the rise and spread of Delta, with only 8 percent of the 'Unlikely' agreeing with the statement that "The current spread of COVID-19 is being caused primarily from the people who won't get vaccinated."

If this population continues to remain unlikely to receive a COVID-19 vaccine, a higher burden will exist to vaccinate nearly all or most 'Cautious' and 'Interested' respondents to reach herd immunity. Likewise, because conviction-driven hesitancy may be difficult to address, stakeholders may want to focus on achieving full or near-full adoption of populations with cost or convenience-based constraints. This concern is especially becoming critical as infections and deaths remain disproportionately high among the unvaccinated, with more than 99 percent of COVID-19-related deaths in June 2021 occurring among unvaccinated individuals.6 While there is an increased incidence of breakthrough infections with the Delta variant, the rate of infection and hospitalization for the vaccinated is respectively at one in 5,000 and one in a million per day.

Addressing hesitancy in decision makers for minors

The big question on the mind of vaccinated parents is: How do I decide whether and when to vaccinate my children for COVID-19? In May 2021, the FDA authorized the use of the Pfizer/BioNTech vaccine in adolescents aged 12–15 years. At the time of this article, most states

require parental consent to receive COVID-19 vaccination for children under the age of 18. Parents and guardians are critical decision makers who will influence rates of vaccination among adolescent and pediatric populations.

Parents who expressed hesitancy about vaccinating their children largely align with those who have concerns about receiving the vaccine themselves. Sixty-six percent of respondents who already received their vaccine are planning to vaccinate their children, compared with 9 percent of respondents in the 'Unlikely' segment. Around 45 percent of parents with children under age four said they planned to have them vaccinated once doses are approved for that age group and are available; this number climbs to around 53 percent when looking at children of all ages.

Approximately 20 percent of parents or guardians with children in the household said they are not likely to vaccinate their children. The primary reasons for this decision given by parents or guardians included a concern about potential vaccine long-term side effects (31 percent), a feeling that the development was too rushed (19 percent), that the vaccine is unproven (21 percent), that side effects could be serious (21 percent), and concern about ingredients (15 percent). Therefore, engaging parents and guardians in a meaningful way could have outsized impact on overall vaccination rates.

Actions for stakeholders to consider

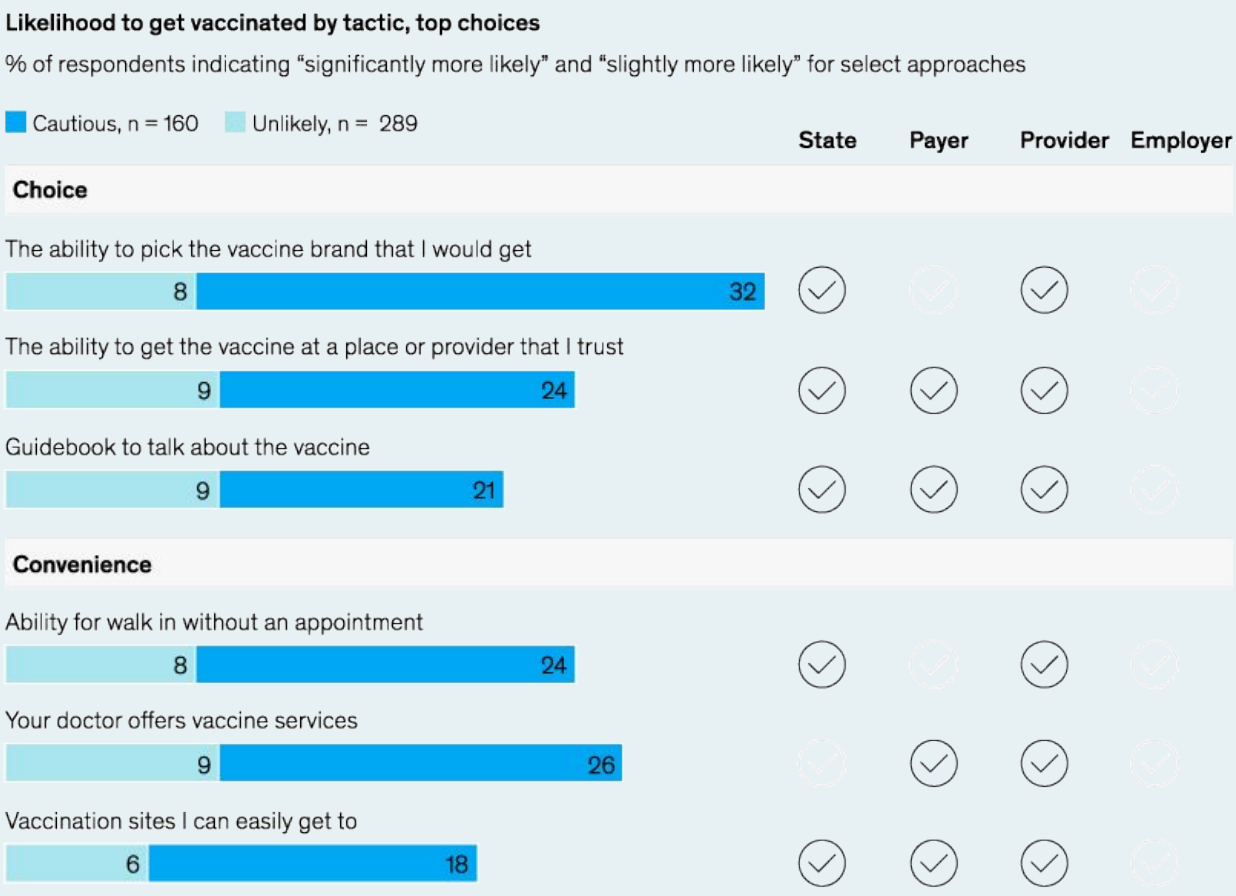
Addressing barriers to adoption will require joint mobilization across public and private stakeholders. States, healthcare providers, payers, pharmacies, and employers may each be positioned to take different approaches, but together can take actions that matter to consumers to increase the likelihood of receiving the vaccine.

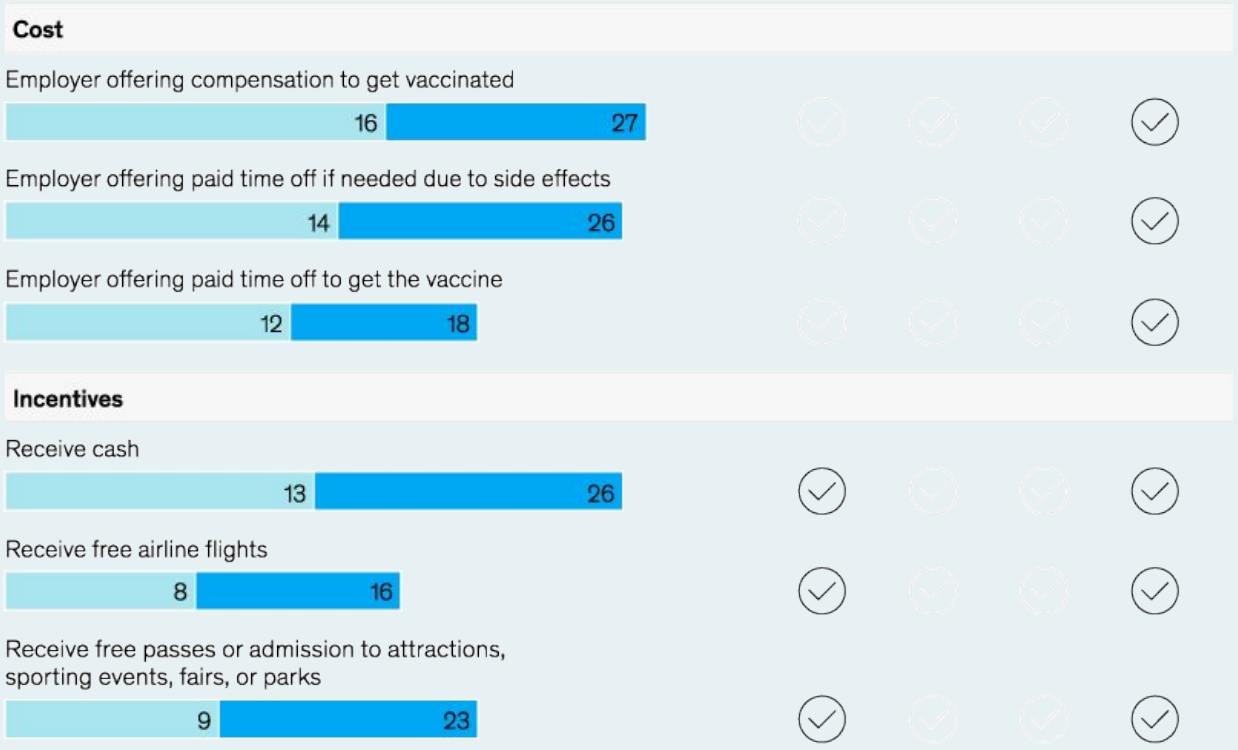
Conviction

Many consumers either are unmotivated to get the vaccine or have unaddressed concerns. For example, some would rather take the risk of getting COVID-19 (17 percent), do not like needles (10 percent), or assume that they would only get mild symptoms from COVID-19 if they were to become infected (4 percent) (Exhibit 4).

Exhibit 4

Potential approaches to take to help 'Cautious' and 'Unlikely' respondents become interested in receiving a COVID-19 vaccine.





QVAX_LIKELIHOOD: How would each of the following affect your likelihood to get a vaccination for COVID-19? Scale of 1 (significantly more likely) to 5 (significantly less likely).
Source: McKinsey Consumer Health Insights 6/14/2021

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Choice of vaccine brand was the highest reported driver of increased likelihood to receive the vaccine among the 'Cautious' and 'Unlikely' groups, with 32 percent 'Cautious' and nearly 8 percent 'Unlikely' saying that brand choice would increase their likelihood to receive the vaccine. States may want to consider allowing consumers the choice of vaccine when they schedule appointments, or help them find locations that offer their vaccine preference.

Providers can lean on their existing relationships and trust with patients to engage in a meaningful fact-based dialogue in order to address concerns or unanswered questions, thereby increasing conviction. A

large portion (27 percent) of the ‘Cautious’ look to their physician for information regarding the COVID-19 vaccine. Pediatricians play a particularly important role in influencing likelihood of vaccination with parents of adolescents and children. Most parents in the ‘Cautious’ and ‘Unlikely’ groups have said they would prefer their children to be vaccinated at a hospital or doctor’s office.

This preference may be due to higher levels of comfort and trust fostered over the length of the physician-patient relationship, which would potentially allow individuals anxious about receiving the vaccine to get their questions answered in a more relaxed setting, rather than at large vaccination sites.

However, it is important for physicians to leverage this trust to provide recommendations that can influence the ‘Cautious’ and ‘Unlikely.’ Currently, many healthcare providers are not doing so, with 22 percent providing no recommendation about the COVID-19 vaccine, and more than 11 percent advising patients against receiving the vaccine.

Additionally, pediatricians are the most preferred source of advice for deciding whether to vaccinate their children. However, this finding decreases from 20 percent overall to only 8 percent for the ‘Unlikely’ parents or guardians, indicating a widening chasm in the level of trust toward physicians within this population.

Healthcare provider sites that already offer the vaccine may consider various approaches to building trust with new and existing patients. For example, providers may engage in novel approaches to share information with patients, such as holding virtual ‘office hours,’ and leveraging digital tools and communication materials in order to answer patients’ questions. Physicians may also consider building upon vaccine services (for example, being able to schedule appointments directly with the doctor, getting follow-ups post-vaccination), which ‘Cautious’ respondents noted would increase their likelihood to receive the vaccine.

Convenience

Many consumers cited hurdles, including concerns about missing work due to vaccine side effects, lack of transportation, not wanting to wait in line for the vaccine, or finding it difficult to make an appointment. Addressing these issues can help provide vaccine access to those in the 'Cautious' and 'Unlikely' groups who see value in getting the vaccine but are unable or unlikely to do so at the moment.

+ Walk-in opportunities and appointment scheduling assistance may address some needs. Among initiatives targeting convenience, 24 percent of 'Cautious' and 8 percent of 'Unlikely' respondents report that having available walk-in appointments would increase their likelihood to be vaccinated, and a similar proportion would respond positively to the ability to schedule a vaccine appointment by phone.

+ Employers and school systems can each separately help increase access to vaccines by setting up on-site clinics, conducting drives, and encouraging family vaccination days. Survey respondents reacted positively to such tactics. Twenty-four percent of 'Cautious' and 9 percent of 'Unlikely' individuals said vaccination at their doorstep would make them more likely to get the vaccine, while a similar percentage said they would be more likely to get the vaccine if they had vaccination sites they could easily access or were able to schedule a family appointment. Mobile clinics may help address these needs and expand access to those with difficulties traveling to vaccination sites. Around 21 percent of 'Cautious' and 10 percent of 'Unlikely' respondents said they would be more likely to get the vaccine if they had the ability to do so at their workplace.

+ Another potential cause of inconvenience is travel to and from vaccination sites. States and cities may consider alleviating some of this inconvenience by arranging mobile clinics or temporary vaccination sites near rural health providers or grocery stores. Some cities, such as Philadelphia, have offered community shuttles and rideshares for individuals or groups trying to access vaccination sites. North Carolina is offering cash cards to individuals who help drive others to vaccine sites.

Costlessness

Further, some respondents indicated hesitation about getting the vaccine due to cost considerations (for example, not knowing whether they would be able to afford the vaccine) and several said they would be more likely to get the vaccine if their employer were to offer time off to get the vaccine or cope with the side effects.

+ Employers may have an opportunity to support their employees in the next phase of vaccine uptake, as discussed in "Getting to work: Employers' role in COVID-19 vaccination." Twenty-five percent of 'Cautious' respondents said they would have increased likelihood of getting vaccinated if their employers offered compensation (such as a cash reward).

+ Employers may also consider paid time off or flexibility in order to receive the vaccine and recover from any potential side effects. For example, retailers such as Trader Joe's and Target are offering hourly employees two hours of pay per vaccine dose taken, and companies such as Lidl are offering a payment of $200 per employee in order to cover any costs associated with vaccine administration. These costs include travel and childcare.

+ States may consider incentives in cash or in kind in order to encourage vaccination. States like North Carolina have provided various incentives, such as cash cards, to those receiving first doses, and other states such as West Virginia, Minnesota, and New York are offering various prizes, including hunting or fishing licenses, state park passes, scholarships, and vacations.

Stakeholder enablement

These actions may not directly engage consumers, but can improve consumer conviction, convenience, or costlessness indirectly.

+ Respondents who are covered under Medicaid indicated they are unvaccinated in greater proportions than other groups, with 50 percent unvaccinated compared with 29 percent unvaccinated overall. Medicaid providers have direct access to their patients and information about them and are thus well positioned to enact interventions. For example, managed care organizations can contact patients who may benefit from vaccination and share information regarding the vaccine.

+ Payers could consider higher reimbursement rates for vaccination. The Centers for Medicare & Medicaid Services announced an increase in the Medicare payment amount to approximately $80, from $45, for the administration of vaccines requiring two doses, and $40, from $28, for the administration of vaccines requiring one dose each.

+ Payers may also use their networks to facilitate vaccine education among member populations and partner with nongovernmental organizations and health systems to expand their reach. The Blue Cross Blue Shield Association is one such example, collaborating with Feeding America® to access a population of 40 million through their network of food banks and share materials on topics related to the COVID-19 vaccine.

+ Federal and state governments can help normalize COVID-19 vaccination and lower barriers to access by integrating this information into the routine well-child workflows, similar to other pediatric vaccinations. An example of this routinization is the inclusion of mental health screenings in primary care settings, which led to improved quality of life for patients and lowered costs, among other benefits.

As the United States plans to prepare for an uncertain winter, many residents wonder what's next, and how to keep themselves and their families safe. Effective stakeholder actions to boost COVID-19 vaccination rates addressing the 'Cautious' and 'Unlikely' could help protect millions against COVID-19. Even as many return to in-person work and activities, the lack of ability for children to be vaccinated, and the issues facing 'Cautious' and 'Unlikely' vaccine adopters, coupled with the urgency created by emerging variants of concern, should remind policy, business, and healthcare stakeholders that several hurdles remain to reach potential herd immunity levels. By considering joint mobilization of public and private sector entities to address vaccine accessibility concerns, the United States can protect more of its residents from infection and help reduce deaths due to COVID-19.

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Port to patient: Improving country cold chains for COVID-19 vaccines

McKinsey

14 September, 2021

In many developing countries, limitations of existing cold chains will provide challenges for COVID-19-vaccine distribution. Strategic distribution planning and targeted investment can help.

More than 63 percent of the US population have received at least one dose of a COVID-19 vaccine, and more than 54 percent have been fully vaccinated, as of September 16, 2021, according to the Centers for Disease Control and Prevention. Approximate thresholds for herd immunity are benchmarked from 80 to 90 percent, which would require a minimum of roughly 80 million additional individuals to be vaccinated in the next few months.

Despite strong demand for COVID-19 vaccines in early 2021, by the end of May daily administration rates dropped to a third of their mid-April peak, reflecting waning consumer demand. While daily administration rates climbed moderately at the end of August, as of September 10, around 567,000 doses were being administered daily, compared with nearly six times that in April. At the same time, the United States continues to experience regional outbreaks, in part due to new variants such as Delta. As new variants with potentially greater severity and transmissibility continue to emerge, the effectiveness of existing vaccines or strength of immune response against these will be crucial to consider. This concern about emerging variants could potentially underscore the criticality of all eligible persons receiving the vaccine (Exhibit 1).

The global response to the COVID-19 pandemic involves the largest ever single vaccination effort. As of August 22, 2021, there have been approximately 4.9 billion worldwide COVID-19-vaccine doses administered and 34 million are being administered globally every day. Yet there are still many more doses that need to be procured and administered: only 1.4 percent of people in low-income countries have received at least one dose.

There has been a global commitment by world leaders to ensure equitable distribution of vaccines through the likes of the African Vaccine Acquisition Trust (AVAT), the COVAX mechanism, and other multilateral deals. However, vaccine inequality is evident around the world, with high- and upper-middle-income countries having secured around 6.0 billion of the 8.6 billion vaccine doses available. In Africa, the African Vaccine Acquisition Task Team of the African Union and the COVAX consortium are hoping to secure 720 million doses of COVID-19 vaccines to achieve 60 percent coverage in Africa by June 2022.

WHO has so far granted an emergency-use listing for six COVID-19-vaccine products (those by China National Pharmaceutical [Sinopharm], the Pfizer and BioNTech collaboration [Pfizer–BioNTech], Janssen Global Services [pharmaceuticals arm of Johnson & Johnson], Moderna, Sinovac Biotech, and the University of Oxford and AstraZeneca collaboration [Oxford–AstraZeneca]), with an additional seven products undergoing dossier review by WHO as of August 19, 2021. Many countries also have local regulatory approval to use other vaccines that are not yet approved by WHO or a stringent regulatory authority (SRA).

Each of the COVID-19 vaccines has a different profile, but they all have one thing in common: the need for cold-chain storage, ranging from around –70°C (–94°F) during specialized shipping to around 2 to 8°C (36 to 46°F) when administered (Exhibit 1). In some cases, manufacturers are working on more thermostable versions of their vaccines, but for now, countries are having to consider how best to plan for distribution to their

citizens based on existing thermal-stability profiles and available supply-chain solutions.

Exhibit 1

Each of the COVID-19 vaccines has a maximum storage duration based on temperature.

		Maximum storage durations based on temperature		
Vaccine type	**Manufacturer**	**−80 to −60°C**	**−25 to −15°C**	**2 to 8°C**
mRNA	Pfizer–BioNTech	Until expiration	2 weeks	31 days
	Moderna	n/a	Until expiration	30 days
Viral vector	Johnson & Johnson	n/a	n/a	Until expiration
	Oxford–AstraZeneca	n/a	n/a	Until expiration
Inactivated	Sinopharm	n/a	n/a	Until expiration
	Sinovac	n/a	n/a	Until expiration

Source: Centers for Disease Control and Prevention product profiles; WHO News

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Broadly speaking, developing countries have less mature cold-chain systems than do high-income economies, with various degrees of maturity within them. Thus, they may want to consider how best to ensure that their cold-chain systems can support their COVID-19-vaccination goals, such as vaccinating 20 percent of the total eligible population in 2021.

In a previous article, our colleagues discussed the challenges of getting the vaccines from manufacturing plants to countries' receiving ports. In this article, we seek to provide visibility on four areas:

+ The pathway that vaccines will likely follow from port to patient, and the specific cold-chain requirements, within developing countries

+ The specific challenges related to the cold chain and cold-chain equipment (CCE) within developing countries
+ The steps that countries may wish to consider to improve their cold-chain systems and their distribution planning, with a resulting improvement in the effectiveness of their COVID-19-vaccination programs
+ How investments in cold chains for COVID-19 vaccines could be made through the lens of longer-term sustainability of the immunization system

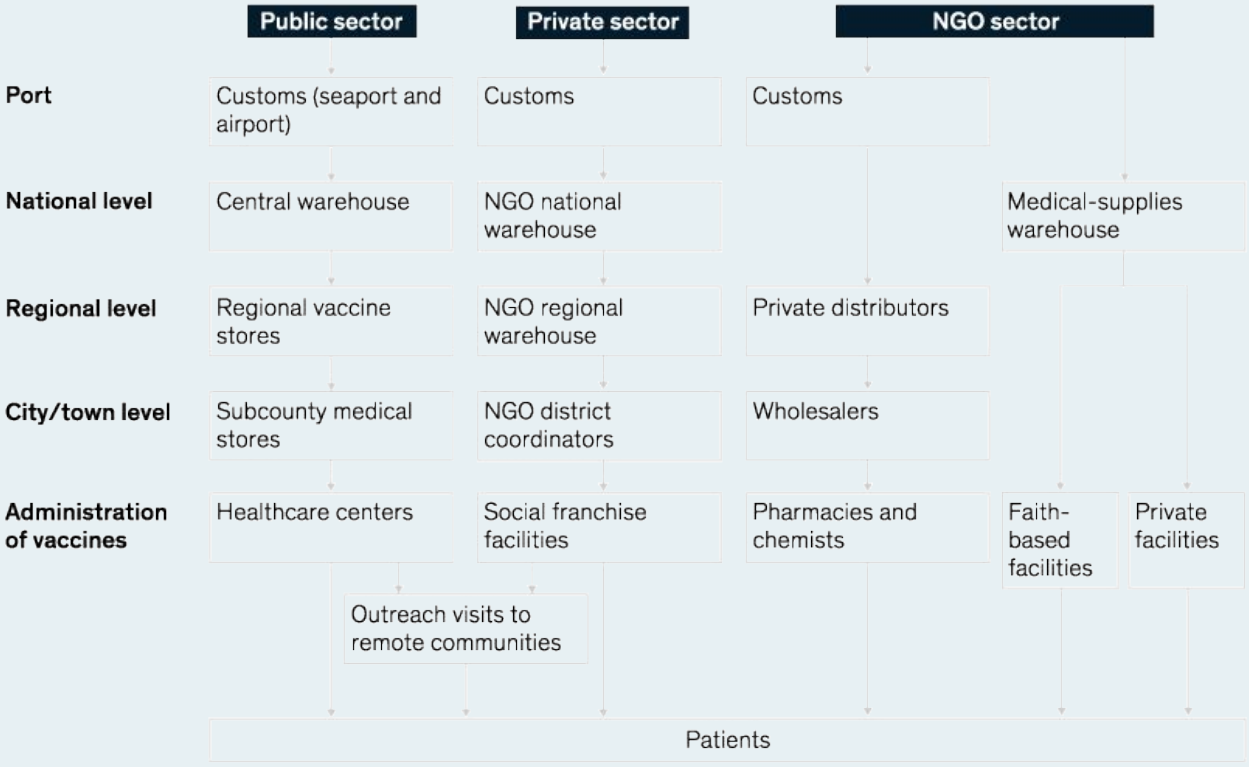
Visibility into what happens from port to patient and cold-chain requirements

The vaccine supply chain in most developing countries is complex and fragmented, with many different configurations, levels of supply-chain maturity and performance, and degrees of private-sector involvement. Exhibit 2 shows three typical supply-chain models that vary based on whether the procurer is the government, a nongovernmental organization, or the private sector. Regardless of the procurer model, in most countries, the government plays a major role in the planning, operations, and monitoring of the COVID-19-vaccine supply chain.

Exhibit 2

In-country supply-chain models for getting vaccines to patients vary based on different procurers.

Supply-chain models the government can follow, by procurement channel



Source: McKinsey analysis

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Most vaccines will travel the following logistics step in the supply-chain pathway (Exhibit 3):

1. Vaccines arrive at the port of entry by air, land, or sea in specialized cooling containers as packaged by manufacturers.

2. Vaccines are processed and then cleared by port authorities, as well as health and quality regulatory bodies. This can take one to 14 days, depending on the local approval process.

3. Trucks transport the vaccines in their original packaging to a central medical warehouse, which is usually near the port of entry:

+ Ideally, the trucks are refrigerator or freezer trucks with their own temperature-control capability. But in many countries, such specialized vehicles are not available, and standard large-haulage trucks are used instead.

+ This can take one to three days, depending on the bulk and number of available trucks.

4. At the central medical warehouse, the regulators perform additional quality checks, and the logisticians “break bulk,” or split the packaging into units that can be transported to specific regions of the country:

+ A best practice is for the splits to be done by trained warehouse staff wearing special cold-storage clothing and within specialized freezers or cold rooms that maintain the required temperature and preserve the cold chain.

+ The methodology for the split of the vaccine packages is typically based on a preprepared allocation plan indicating how many vaccine doses should go to specific areas of the country.

+ The process can take one to five days, depending on the amount of vaccine doses and the availability of trained personnel and equipment.

+ Usually, the vaccine units may be kept in the manufacturers' subpackaging, thus preserving the cold chain. However, if the manufacturer's packaging is broken and vaccine vials are exposed outside of the packaging, the appropriate cold-chain temperature (in some cases as low as –70°C) still needs to be preserved.

5. Trucks move the products to the cold rooms at district, state, or regional warehouses:

+ Ideally, specialized refrigerated trucks are used, but in developing countries, regular-haulage trucks transporting vaccines in specialized storage containers are usually used.

+ The trucks may also carry the syringes required to administer vaccine doses, or those can be transported separately.

+ Transport usually takes one to five days for a one-way trip, depending on the distance to be covered.

+ Different trucks are usually needed, subject to the volumes to be transported and terrain. The trucks required for this segment of the journey are typically smaller than the trucks required for transportation from the port to the central warehouse.

6. At the subdistrict, district, state, or regional warehouse (depending on the complexity of the supply-chain architecture in the country), another break-bulk step usually occurs to split the doses into the volumes required by individual healthcare facilities, healthcare posts, or vaccination centers (a hospital, healthcare facility, or specially arranged venue):

+ Generally, the process is not well defined, and some rationing may take place per the prerogative of the immunization officer in the region.

+ The overall process can take one to 14 days.

+ In the warehouse at this level, some developing countries have specialized freezers, but most do not. This is the step when the manufacturer's packaging is most likely to be broken, with dose vials exposed outside of the packaging and stored at 2 to 8°C in vaccine refrigerators. It is at that moment that the "clock begins to tick," as many vaccines have a limited time period when they can be stored at the standard refrigerated temperature (Moderna for 30 days, Pfizer–BioNTech for 31 days, Johnson & Johnson for three months, and Oxford–AstraZeneca for six months).

7. Transportation to the vaccination center is the final step, usually referred to as the "last mile," and is when the most common challenges in the cold chain are encountered:

+ The vaccines are transported to vaccination centers in cold boxes with ice packs or other cooling agents. The boxes can keep the vaccine temperature below 10°C for around two to seven days if using ice packs.8

+ Once at a vaccination center, the vaccines can be refrigerated. If the site does not have a refrigerator, the administration of the vaccines to patients must occur rapidly to avoid heat exposure.9

+ Once vials are taken out of cold storage, opened, and made ready for immunizing patients, they cannot be placed back in storage. At the end of each day (or after six hours), any unused doses remaining in open vials are no longer viable and should be discarded. Such wasted doses can be planned for in advance when considering dose demand.

In some circumstances, a healthcare facility may perform immunization-outreach visits to remote villages by motorbike or car using a small quantity of vaccines in a vaccine carrier with ice packs or other cooling agents.

+

Exhibit 3

Most vaccines travel a typical in-country supply-chain pathway.

Source: McKinsey analysis

McKinsey & Company

Challenges of CCE and the cold-chain system

There could be a myriad of challenges related to supply-chain logistics in developing countries, typically in the areas of operational efficiency, planning, talent availability, transportation, and warehousing infrastructure, as well as data systems and governance models. This

article will focus on the CCE-related challenges, as our colleagues have previously written about the broader challenges.

The CCE challenges are highly limited capacity in ultra-cold-chain (UCC) and freezer storage, limited capacity in cold-chain storage, outdated storage technology, and limited transportation capacity.

Highly limited capacity in UCC and traditional freezer storage

Existing cold-chain capacity within developing countries is largely geared for the 2 to 8°C temperatures required for most routine immunization vaccines. However, UCC freezer capacity at –70°C and traditional freezer capacity at –20°C may be required for specific vaccines. For example, the Pfizer–BioNTech vaccine requires UCC capacity for storage longer than about six weeks,10 and the Moderna vaccine requires traditional freezer capacity for storage longer than about one month.

Minor storage volumes may be available at –20°C at national and state stores, typically in those countries still using an oral polio vaccine. However, UCC storage at –70°C is typically extremely limited and exists only for specialist applications, such as storage of Ebola vaccines and diagnostic laboratories' biological samples. Adding fixed UCC and traditional freezer capacity may be problematic for several reasons: it can require significant funding; the ability for multiple countries to procure sufficient freezers simultaneously may be limited by global manufacturer capacity and lead times; it would require significant expertise to install correctly and conduct capability building in operations staff to ensure proper and safe handling; and the equipment (UCC freezers, in particular) may have limited application after the COVID-19 pandemic unless mRNA vaccines become more common in the future.

An alternative approach to adding fixed capacity could be to use dry ice. Some infrastructure for dry ice (for example, at carbonated beverage bottlers) typically already exists in each country, but it would need to be

expanded for healthcare-system use and may have many of the same challenges as adding fixed-freezer capacity would. Specialized training would also be required for dry-ice handling.

Limited capacity in cold-chain storage

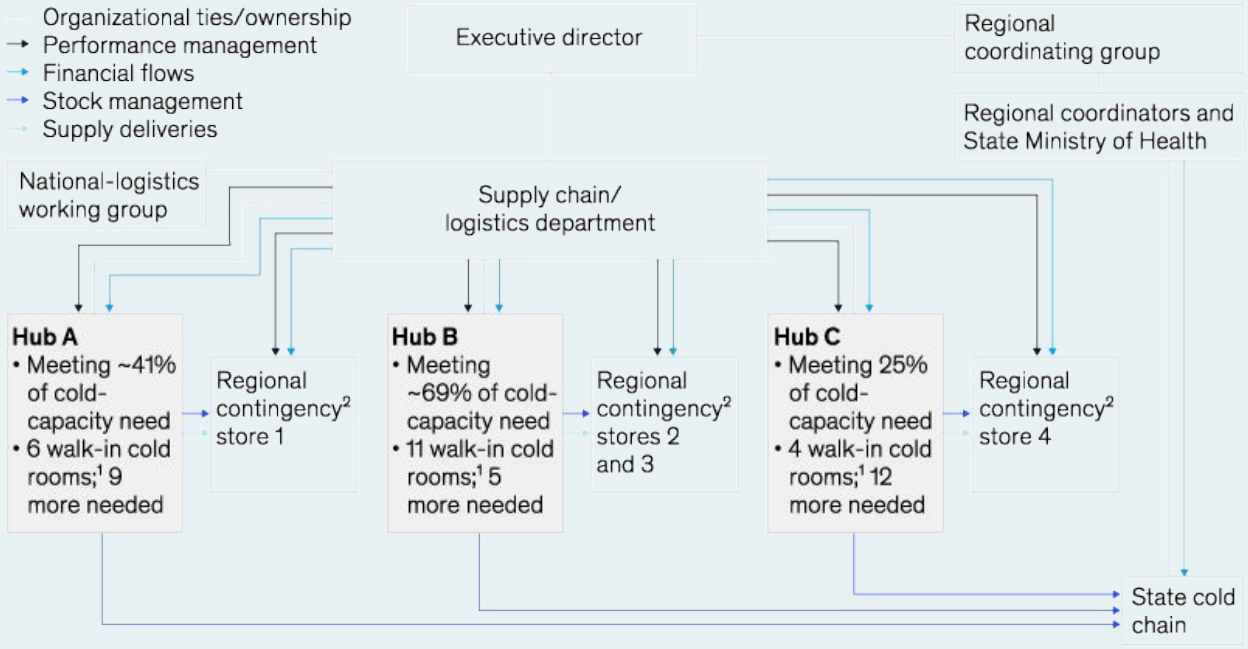
At central or national and subnational storage warehouses across most countries, there may be inadequate amounts of cold rooms and specialized protective and handling equipment. In most developing countries, there are only a small number of specialized cold rooms, and they are usually stocked with other vaccines that are part of other national immunization programs.

The sufficiency of cold-chain capacity to handle both routine- and COVID-19-vaccine volumes may depend on COVID-19-vaccine coverage targets and the number of shipments that the vaccine supply is spread across. UNICEF Supply Division estimates that for a typical country with vaccines received in two to four deliveries, an additional 4,200 liters of storage (roughly one cold room or one freezer room), on average, would be required at the national level if the COVID-19-immunization target is 3 percent of the population. The additional storage need rises to an average of 15,000–35,000 liters (roughly three to seven cold rooms or freezer rooms) if the immunization target is 20 percent of the population.

Exhibit 4 illustrates the summary of such analysis at a national level for a country in sub-Saharan Africa. The lack of storage infrastructure at this level is the most basic challenge. Apart from limiting the quantity of vaccines that can be stored, it can make it more difficult to break bulk packages into the allocation packets needed for states, districts, or regions efficiently, since that is an operation that should take place within a cold room or freezer room. Overall capacity and speed of operations are also influenced by a country's digitalization levels (for example, electronic logistics-management systems) and communication technologies that allow for tracing and tracking.

Exhibit 4

Analysis of one sub-Saharan African country illustrates the national cold-chain capacity for that country.



[1] Size of walk-in cold room is 40 cubic meters.
[2] Contingency zonal stores may occasionally deliver directly to states (not displayed).
Source: McKinsey analysis

McKinsey & Company

At the last mile, the challenges may be starker. Limited CCE at a healthcare facility is a major challenge in many countries. Historically, up to 20 percent of vaccination centers and healthcare facilities have not had a refrigerator to store routine vaccines,4 and many that do, do not have enough storage space to add COVID-19 vaccines. Temperature excursions occur most commonly at the local levels of the supply chain, especially at district stores, at healthcare facilities, and during outreach sessions. Poor maintenance also has a limiting effect on installed

capacity. Historically, roughly 15–20 percent of the currently installed cold-chain devices at the last mile have been nonfunctional, although this number may be dropping as ministries of health deploy new equipment with long-term warranty agreements.

Outdated storage technology

Over the past 15 years, vaccine-refrigerator technology has improved in both reliability and temperature control. In particular, for healthcare facilities that have inconsistent power-grid access or are completely off grid, advances in solar-powered refrigerators have significantly improved storage reliability. The latest-generation technology is the solar-direct-drive (SDD) refrigerator, which significantly improves reliability compared with prior-generation solar-battery refrigerators and older gas or kerosene fridges. However, challenges remain, as the currently installed SDD capacity is less than 20 to 30 percent of requirements.

Apart from the refrigerators, cold boxes are also used to transport vaccines in the last mile, but they are less efficient. There has been some use of solar-powered carrier boxes, but they have not been scaled up enough to be beneficial on a large scale for the COVID-19-pandemic response.

Limited transportation capacity

Lack of specialized refrigerated vehicles that can preserve the temperature integrity between central or regional stores and vaccination centers (and other levels in between), as well as the long duration of trips, could mean that COVID-19 vaccines are at risk of temperature excursions during each break point and each level of the journey. That can be especially true for hard-to-reach communities (for example, riverine communities typically accessed by boat).

Perspective on steps that countries can take to improve their cold-chain systems

There are a number of actions that could be considered by decisions makers to help strengthen a country's ability to overcome the cold-chain challenges and help ensure successful COVID-19-vaccination campaigns. They include new distribution approaches, more efficient shipment size and frequency, and a targeted increase in cold-chain-storage capacity.

Design distribution approaches that reduce freezer requirements

Each COVID-19 vaccine has a certain amount of time it can be stored at 2 to 8°C before patient administration must occur. When a vaccine vial's time in the distribution channel is reliably less than that amount, it can be moved into 2 to 8°C storage (the most common cold storage available—and often the only existing storage available at subnational levels). This means that reducing the end-to-end distribution time can reduce the need for UCC or –20°C freezer capacity, especially at subnational levels. Countries can plan around this and could consider the following approaches:

+ Campaign-based immunization approaches (for example, mass-immunization events and mobile immunization clinics) can greatly reduce the time taken for vaccines to be administered once they arrive at local districts. For this, countries can leverage planning expertise used in prior campaigns (for example, those for meningitis and yellow fever immunization) or emergency-operations centers, but it may need to be adapted, given the national scope and large target-population cohorts.
+ Innovative distribution techniques can shorten distribution time from national stores to local districts. For example, Ghana is making drone-based deliveries to rural clinics, allowing for same-day delivery from a few national hubs.

+ Packaging optimization is another potential approach. Countries could explore the potential of having vaccines packed in smaller UCC-packaging units. While this may be less cost efficient for shipping, it may enable distribution from national to state stores without break bulking at the national level, hence better preserving the UCC without additional equipment. This could also help reduce waste or breakage.

Optimize shipment size and frequency to limit requirements for new cold-chain capacity

The amount of new capacity needed at any node in the supply chain is determined by the largest volume of vaccine vials that must be stored at that node at any specific point in time. When taking delivery of COVID-19 vaccines from manufacturers, countries might explore the potential for large shipments to be broken into a few smaller shipments spread out over a period of a few days. Provided that each small shipment can be moved down the supply chain before the next shipment arrives (and efficiently administered once it reaches the local level), this approach would allow the amount of any new cold-chain capacity required to be significantly reduced. Subnational shipments within a country can be staggered in this fashion to alleviate capacity needs at subnational levels.

Increase cold-chain-storage capacity in a targeted way, leveraging private-sector support, especially for freezer capacity.

Even with careful planning, countries may still require additional cold-chain capacity. There could be three reasons for this: to meet any UCC or traditional freezer requirements that the existing cold chain was not designed for; to ensure the routine 2 to 8°C cold chain can handle the planned incremental volume associated with COVID-19 vaccines, including sufficient local capacity to support mass immunization events; and to provide buffer capacity in case of any unexpected delays in distribution and backup of COVID-19 vaccines at national and subnational stores.

Additional capacity could take different forms. At national and state levels, it could include the following:

+ Permanent UCC, freezer, or cold-room capacity
+ Temporary warehouse capacity rented from the private sector, such as pharmaceutical- or food-warehouse cold storage at the required temperature band

At district and clinic levels and for mass-immunization events, additional capacity could include the following:

+ Additional portable freezer, refrigerator, or cold-box storage and the associated capacity to produce ice packs
+ Mobile cold storage (freezer or reefer trucks)

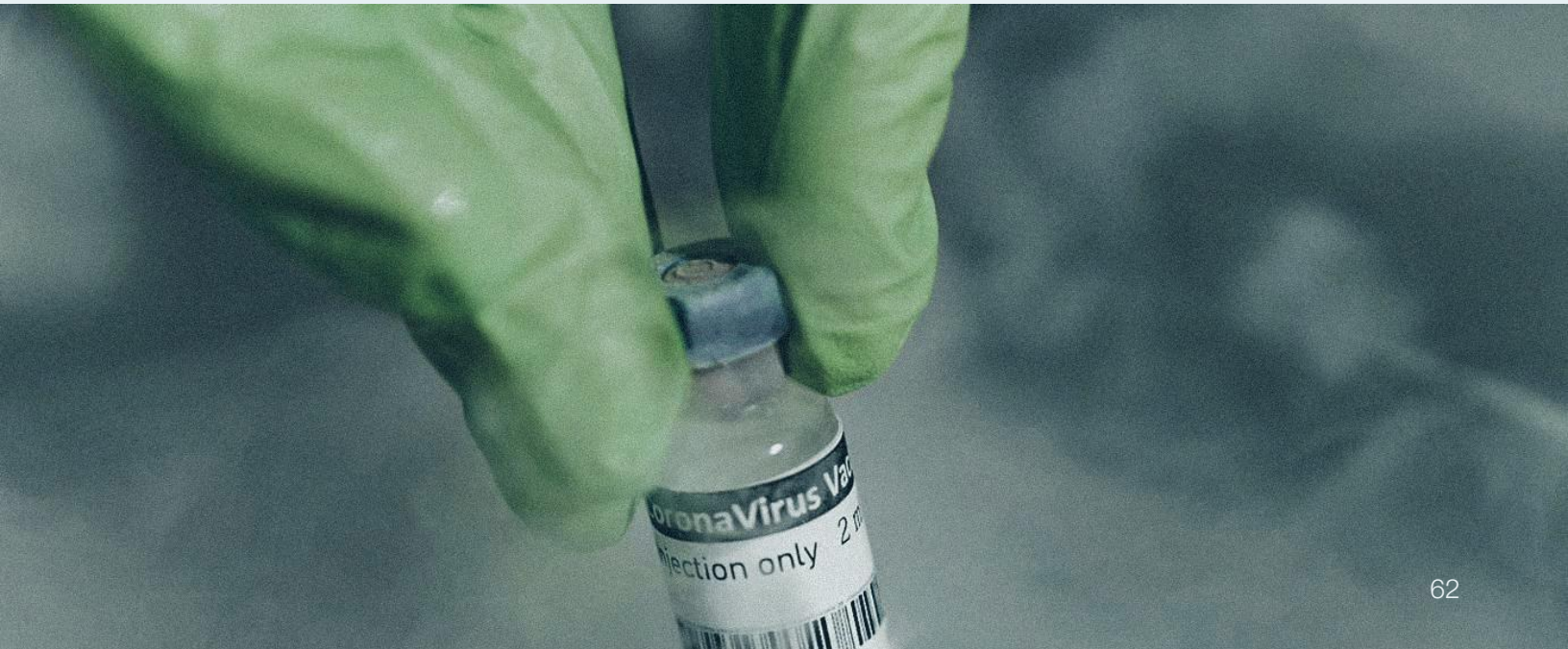
Before procuring new CCE, countries may want to determine how much of the required capacity could be met by repairing existing broken CCE, since repairs are typically more cost effective and quicker than adding all new capacity. A best practice is for CCE capacity to be backed up with emergency generators (if reliant on electrical power) and for it to be supported with proper maintenance plans to ensure that its useful life is maximized.

Designing the cold-chain-distribution plan with long-term benefit in mind

Ideally, any investment made in expanding cold-chain capacity for COVID-19 vaccines would be made in such a way that it also provided benefit to the healthcare system in the long term. For instance, any additional cold-chain storage at national and state levels could be temperature adjustable to serve the future needs of the routine immunization cold chain (for example, a new freezer room at –20°C that is easily convertible to a 2 to 8°C cold room once COVID-19-vaccine distribution is complete). Acquiring new CCE investments

for district stores that use the latest-generation technology would enable outdated or poorly functioning equipment to be retired at a suitable moment. Investments in data systems to support the campaigns could be made with future pandemics or campaigns in mind and have a clear long-term owner within the national healthcare agency (for example, an emergency operations center).

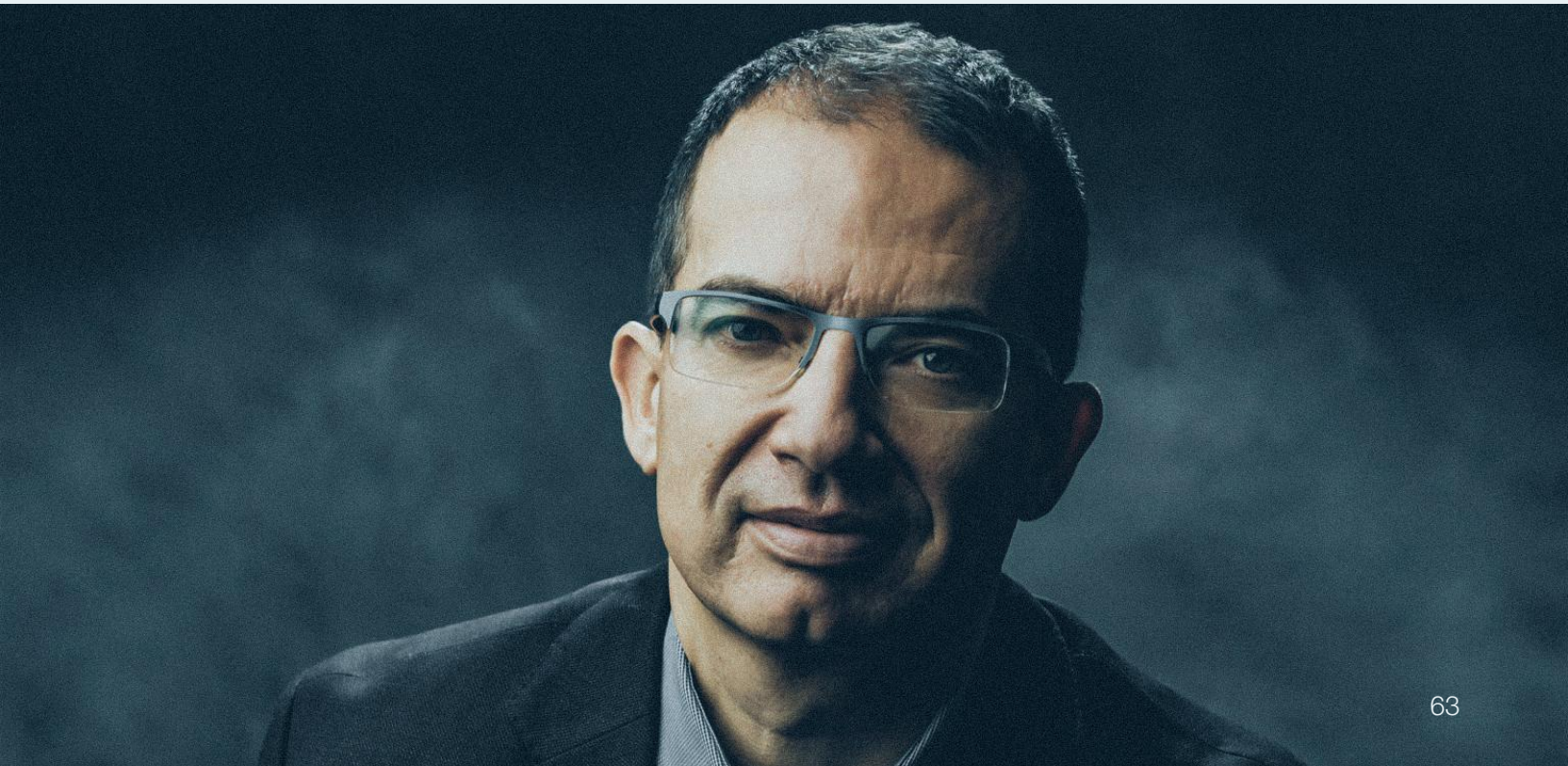
The design choices that countries make for COVID-19-vaccine distribution have the potential to greatly mitigate many of the associated CCE challenges. Careful advance preparation and investment can help countries to address the remainder of the challenges. As countries plan their CCE resources, they could seek to base their investment decisions around opportunities that not only meet immediate requirements for COVID-19-vaccine distribution but also provide long-term benefit to their healthcare systems once the pandemic is over. Given the long lead times for activities such as procuring new CCE and contracting with the private sector, countries that wish to maximize their level of success may want to start such planning immediately if they have not already done so.



Moderna’s path to vaccine innovation: A talk with CEO Stéphane Bancel

McKinsey

27 August, 2021



Moderna's delivery of a COVID-19 vaccine comes on the heels of revolutionary science that may accelerate innovation across the industry well into the future.

This interview is part of COVID-19 vaccines: The road to recovery and beyond, a series that includes a broad array of voices leading the historic global effort to develop, distribute, and provide equitable access to COVID-19 vaccines, including the Africa CDC; CEPI; Gavi, the Vaccine Alliance; Moderna; and Pfizer.

The COVID-19 pandemic has resulted in devastating public-health and economic outcomes. It also spurred one of the most promising scientific feats in the last century—the development of several highly effective vaccines authorized for emergency use by the US Food and Drug Administration (FDA) in less than one year.

This achievement required unprecedented mobilization and the cooperation of a broad set of global stakeholders in both the public and private sectors, including governments, vaccine developers, and public-health organizations. Building on deep scientific knowledge gained from years of experience working with viruses, such as MERS, SARS, influenza, HIV, and Hepatitis C, the medical industry's private sector has made immense progress in advancing potential treatments and vaccines to help address COVID-19.1 Looking ahead, the breakthroughs stemming from COVID-19 hold vast potential for the broader vaccines industry with the emergence of ground-breaking innovation, more public engagement, and increased focus from health officials.

Making inroads in the fight against COVID-19 is Massachusetts-based biotech company Moderna, which has been looking to innovate approaches to vaccine development since the company's start in 2010. Before COVID-19, Moderna already had a new class of vaccines in the works that use messenger ribonucleic acid, or mRNA,2 which instructs a

patient's own cells to produce the proteins needed to activate the immune system to prevent illness. "The potential implications of using mRNA as a drug are significant and far-reaching and could meaningfully improve how medicines are discovered, developed, and manufactured," says Moderna's CEO Stéphane Bancel.

Bancel spoke with McKinsey's Olivier Leclerc about why he believes his company was well positioned to respond to the COVID-19 crisis, how scientific breakthroughs with mRNA led to an effective COVID-19 vaccine, and what it takes to lead his company for long-term impact during the crisis. Below is an edited excerpt of Bancel's remarks.

Responding to COVID-19

McKinsey: Vaccine development is a long, complex process. How did Moderna step up when the pandemic was declared?

Stéphane Bancel: By March 2020, the World Health Organization [WHO] declared COVID-19 a pandemic, and we were racing against the virus every day while we still had almost 20 non-COVID-19 programs that needed to keep moving. We raised the cadence of our executive-committee meetings from once a month to once or twice a week to have a clock speed that was adapted to the situation. We also used a decentralized model, which gave the distinct teams the independence to move quickly. The pace was unprecedented, fueled by the need to respond to a pandemic situation. To deliver on our goal of 100 million doses of COVID-19 vaccines within 12 months3 and a billion doses by the end of 2021, the team worked seven days a week and, at times, pulled all-nighters. If it weren't for the extraordinary people I work with—who are selfless, mission-driven, and committed to building the best version of Moderna possible—we would not be where we are today.

McKinsey: Considering the intense pressure to develop an effective vaccine, how was interaction with the US government managed?

Stéphane Bancel: It came down to the collaboration between the pharmaceutical industry and the US federal government. The US government picked three different technologies to invest in for a diversified risk profile and then chose two pharmaceutical companies per technology. In the end, they were betting on six different companies. It was a brilliant move. The conditions of the contract included a base business of 100 million doses, with options to increase depending on the clinical data and the efficacy at the time of launch. This allowed us to take on a lot of business risk at a time when every single day mattered.

The other key part of this equation is that the FDA worked relentlessly to authorize the Moderna COVID-19 vaccine, and others, with an emergency use authorization [EUA]. Usually, you submit a question to the FDA, and they have a defined timeline for responding and engaging with clinical-trial sponsors. But they adapted to the crisis situation. During the pandemic, we could reach out to them any time—including weekends.

McKinsey: What were some difficult decisions you faced while developing the COVID-19 vaccine?

Stéphane Bancel: One tough spot we were in was deciding whether to slow down our Phase 3 clinical study. The study began on July 27, 2020, and the first few weeks were fantastic. However, we weren't enrolling enough people from diverse backgrounds into the study, especially those disproportionally affected by COVID-19, such as African Americans. We felt we were failing society if we didn't include communities most impacted by the virus. After many discussions, we decided to slow down the study, which made a big impact on our timeline. But at the end of the day, when you step back and look at the big picture, you can see that the tough decisions are well worth it.

We are now one of the first biotech companies to publish the demographic data of our clinical trials. In our Phase 3 study, we had 9.7 percent African American or Black participants, 4.7 percent Asian, 0.8 percent American Indian or Alaska Native, and 20.0 percent Hispanic participants, which reflects a greater diversity among participants than many other previous drug trials.

Delivering innovative solutions

McKinsey: What is mRNA technology? And why is it so effective against COVID-19?

Stéphane Bancel: Simply put, messenger RNA [mRNA] vaccines are a new type of medicine that trigger an immune response to protect against infectious diseases. Many other vaccines put a weakened or inactivated virus into the body to trigger that response. Instead, mRNA vaccines teach our bodies how to make a protein, or a piece of a protein, to get the same result.

Moderna's COVID-19 mRNA vaccine tells your cells to make a harmless viral protein called a spike. This stimulates your immune system to make antibodies and immune cells that counterattack the spike when they come across it. When scientists published the genetic code for the COVID-19 virus in January of 2020, we realized that the spike protein of the Middle East Respiratory Syndrome [MERS], and SARS-CoV-25 were very similar. In our previous work on the MERS virus with Dr. Anthony Fauci's team at the National Institute of Allergy and Infectious Diseases [NIAID], we determined that the best vaccine using Moderna immunotechnology was a full-length spike protein. Based on that work, and all the work we had done on vaccines before, we were hopeful that we were off to a great start.

McKinsey: How can Moderna's mRNA platform respond to new variants of coronavirus and their potential to evade the immune system?

Stéphane Bancel: Some mutations of the COVID-19 virus will likely have no impact on our vaccine's efficacy, while others might. With several mutations, there is more and more "drift" from the original SARS-CoV-2 that was sequenced. Our mRNA platform lets us create new versions of the vaccine to attach to that variant in a matter of weeks. In January 2020, it took us just 42 days to go from a sequence of the SARS-CoV-2 virus to shipping the first product for human clinical trial to the federal government. The mRNA platform also allows for multiple variant sequences to be included in one vial, which lets us respond to new mutations faster than ever.

Our team, like most scientists around the world, has been following new variants, and we continue to have clinical trials under way. One of the benefits of mRNA is the flexibility and speed to development. We have been closely monitoring how our authorized COVID-19 vaccine protects against emerging variants, and in parallel, we are advancing our booster strategy.

McKinsey: Now that mRNA technology has been proven to work for COVID-19, what role do you expect it to play in the future of medicine and healthcare?

Stéphane Bancel: At Moderna, our mission is to deliver on the promise of mRNA science to create a new generation of transformative medicines for patients. Since mRNA is an information-based platform, it works similar to a computer's operating system, letting researchers insert new genetic code from a virus—like adding an app—to create a new vaccine quickly. When COVID-19 struck, we already had nine vaccines in clinical trials using mRNA technology. The COVID-19 vaccine was our tenth. Because we had invested in building our mRNA platform, it was basically a copy and paste—inserting the new genetic code into our preexisting platform. It's this type of technology that helped Moderna develop a COVID-19 vaccine in only 11 months.

We are now in a world where mRNA as a platform has been derisked for use in vaccines and can be authorized for emergency use. Moving forward, using genetic information—either human genes or the genome of a virus—gives us more opportunities for new mRNA programs. Moderna was always built to scale up, and we plan to conduct larger trials and accelerate our clinical programs. We are studying the use of our mRNA platform to develop medicines for infections of the lung and many other organ systems where we hope mRNA may help patients.

Looking ahead at the opportunities for faster product innovation and delivery—combined with a world where the general public, healthcare professionals, and governments are more conscious of the spread of viruses and willing to invest in treatment—I think there is an opportunity with mRNA to transform infectious diseases in the next five years.

Creating impact for the long haul

McKinsey: What has helped Moderna deliver impact—not just over the past year, but also over the past ten years?

Stéphane Bancel: I'm obsessed with digitalization. At past companies, I was extremely frustrated about the time we wasted as a business not serving the customer and not pushing the envelope because we didn't have data or the data were incorrect. I remember a moment that shifted my thinking for the rest of my career. It was the year 2000, and I was fresh out of business school and working for a big pharma company. I spent a week chasing down a manufacturing lot. The internet was booming, yet I was still sending emails trying to locate a lot—information that should have been available to me from any device or computer system. Now at Moderna, we challenge ourselves daily to digitize the company better.

The process starts by being very thoughtful about technology, building our own apps, adding the right people, and then giving all employees

access to that technology. The last step is very important. Everyone at the company has access to our systems from anywhere via their company mobile device—whether they are approving an invoice or designing a drug. This digital experience is completely ingrained in our DNA.

One of the biggest challenges over the next three years for both the HR team and the digital team is to incorporate more artificial intelligence as part of our process. With all of the structured data we've gathered—through preclinical trials, research, and experiments—we've been able to build better algorithms. These algorithms are enabling us to employ machine learning and make faster decisions. For instance, we can get predictions in the clinical space that humans wouldn't be able to make in a reasonable amount of time.

McKinsey: Managing for the long haul can be hard under normal circumstances. Did you have to adjust your leadership style in response to the crisis?

Stéphane Bancel: One of the hardest things to deal with in this type of crisis is being able to go the distance. Many of us end up working more hours under stress when we are in crisis mode, which tends to come at the expense of our health and well-being. It's important to make the right lifestyle choices to avoid possible burnout. I've learned over the years that engaging in sports and getting good sleep is critical for me in managing my stress. Everyone needs to find what works best for them to maintain that type of pace, or else it's just not possible to sustain.

I also learned that fighting COVID-19 has to be a team effort. When we're juggling many decisions, it's the team that has to keep all the pieces in the air at the same time. And subsets of the team need to be able to accomplish a task or get aligned even if I'm not in the room. To do so, the team needs to be informed and have enough pieces of the puzzle to be effective and avoid any disconnects. It also takes being even clearer

than usual on our goals, articulating those goals clearly, and passing the ball when needed. Our whole team needs to be moving in the same direction.

for district stores that use the latest-generation technology would enable outdated or poorly functioning equipment to be retired at a suitable moment. Investments in data systems to support the campaigns could be made with future pandemics or campaigns in mind and have a clear long-term owner within the national healthcare agency (for example, an emergency operations center).

The design choices that countries make for COVID-19-vaccine distribution have the potential to greatly mitigate many of the associated CCE challenges. Careful advance preparation and investment can help countries to address the remainder of the challenges. As countries plan their CCE resources, they could seek to base their investment decisions around opportunities that not only meet immediate requirements for COVID-19-vaccine distribution but also provide long-term benefit to their healthcare systems once the pandemic is over. Given the long lead times for activities such as procuring new CCE and contracting with the private sector, countries that wish to maximize their level of success may want to start such planning immediately if they have not already done so.

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When will the COVID-19 pandemic end?

McKinsey

23 August, 2021

This article updates our perspectives on when the coronavirus pandemic will end to reflect the latest information on vaccine rollout, variants of concern, and disease progression. Among high-income countries, cases caused by the Delta variant reversed the transition toward normalcy first in the United Kingdom, during June and July of 2021, and subsequently in the United States and elsewhere. Our own analysis supports the view of others that the Delta variant has effectively moved overall herd immunity out of reach in most countries for the time being. The United Kingdom's experience nevertheless suggests that once a country has weathered a wave of Delta-driven cases, it may be able to resume the transition toward normalcy. Beyond that, a more realistic epidemiological endpoint might arrive not when herd immunity is achieved but when COVID-19 can be managed as an endemic disease. The biggest overall risk would likely then be the emergence of a significant new variant.

Since the March installment in this series, many countries, including the United States, Canada, and those in Western Europe, experienced a measure of relief from the COVID-19 pandemic when some locales embarked on the second-quarter transition toward normalcy that we previously discussed. This progress was enabled by rapid vaccine rollout, with most Western European countries and Canada overcoming their slower starts during the first quarter of 2021 and passing the United States in the share of the population that is fully immunized. However, even that share has been too small for them to achieve herd immunity, because of the emergence of the more transmissible and more lethal Delta variant and the persistence of vaccine hesitancy.

Among high-income countries, cases caused by the Delta variant reversed the transition toward normalcy first in the United Kingdom, where a summertime surge of cases led authorities to delay lifting public-health restrictions, and more recently in the United States and elsewhere. The Delta variant increases the short-term burden of disease, causing more cases, hospitalizations, and deaths. Delta's high transmissibility also makes herd immunity harder to achieve: a larger fraction of a given population must be immune to keep Delta from spreading within that population (see sidebar, "Understanding the Delta variant"). Our own analysis supports the view of others that the Delta variant has effectively moved herd immunity out of reach in most countries for now, although some regions may come close to it.

While the vaccines used in Western countries remain highly effective at preventing severe disease due to COVID-19, recent data from Israel, the United Kingdom, and the United States have raised new questions about the ability of these vaccines to prevent infection from the Delta variant. Serial blood tests suggest that immunity may wane relatively quickly. This has prompted some high-income countries to start offering booster doses to high-risk populations or planning for their rollout. Data from the US Centers for Disease Control and Prevention also suggest that

vaccinated people who become infected with the Delta variant may transmit it efficiently.

These events and findings have raised new questions about when the pandemic will end. The United Kingdom's experience nevertheless suggests that once a country has weathered a Delta-driven wave of cases, it may be able to relax public-health measures and resume the transition toward normalcy. Beyond that, a more realistic epidemiological endpoint might arrive not when herd immunity is achieved but when countries are able to control the burden of COVID-19 enough that it can be managed as an endemic disease. The biggest risk to a country's ability to do this would likely then be the emergence of a new variant that is more transmissible, more liable to cause hospitalizations and deaths, or more capable of infecting people who have been vaccinated.

Raising vaccination rates will be essential to achieving a transition toward normalcy. Vaccine hesitancy, however, has proven to be a persistent challenge, both to preventing the spread of the Delta variant and to reaching herd immunity. The US Food and Drug Administration has now fully approved Pfizer's COVID-19 vaccine, and other full approvals may follow soon, which could help increase vaccination rates. Vaccines are also likely to be made available to children in the coming months, making it possible to protect a group that comprises a significant share of the population in some countries.

In this article, we review developments since our March update, offer a perspective on the situation and evidence as of this writing, and present our scenario-based analysis of when a transition toward normalcy could occur.

Even without herd immunity, a transition toward normalcy is possible

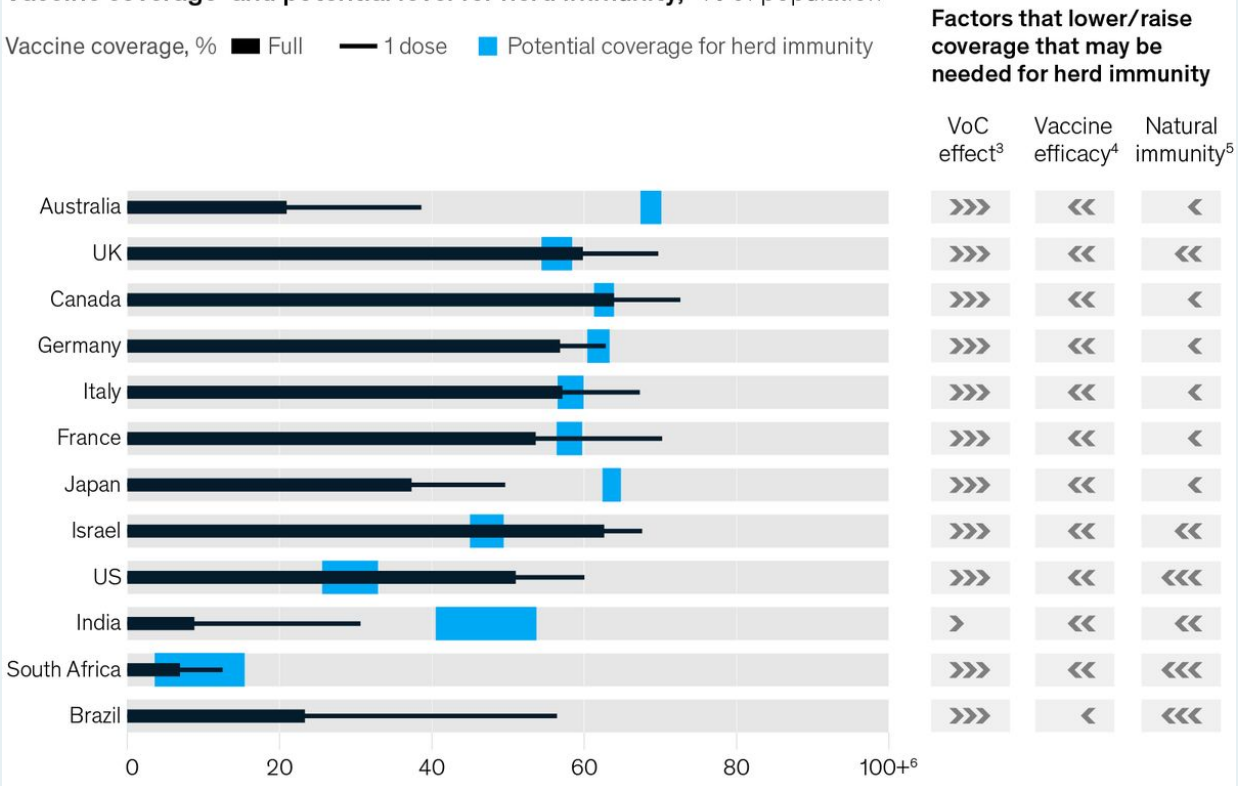
We have written previously about two endpoints for the COVID-19 pandemic: a transition toward normalcy, and herd immunity. The transition would gradually normalize aspects of social and economic life, with some public-health measures remaining in effect as people gradually resume prepandemic activities. Many high-income countries did begin such a transition toward normalcy during the second quarter of this year, only to be hit with a new wave of cases caused by the Delta variant and exacerbated by vaccine hesitancy.

Indeed, our scenario analysis suggests that the United States, Canada, and many European countries would likely have reached herd immunity by now if they had faced only the ancestral SARS-CoV-2 virus and if a high percentage of those eligible to receive the vaccine had chosen to take it. But as the more infectious Delta variant becomes more prevalent within a population, more people within that population must be vaccinated before herd immunity can be achieved (Exhibit 1).

Exhibit 1

Because of the highly transmissible Delta variant, countries may have to reach higher COVID-19 vaccination rates to achieve herd immunity.

Vaccine coverage[1] and potential level for herd immunity,[2] % of population



[1]Population that has received vaccine, independent of vaccine efficacy.
[2]Key assumptions for simplicity: no additional cases of natural infection occur, natural immunity is close to 100% effective and lasts long enough to reach herd immunity, and no new variants of concern emerge. Herd-immunity threshold calculated as 1 – (1/R0). Modeled estimates also assume that each member of a population mixes randomly with all other population members (in reality, people mix mostly with others whose patterns of interaction are similar to their own). Subpopulations with fewer interactions have lower thresholds for herd immunity than do those with more interactions. Potential range required to reach herd immunity based upon range of estimated natural immunity; this is based on available data and actual ranges may be higher or lower. Some individuals who already have natural immunity will also receive vaccinations.
[3]Variant of concern effect, based on reported mix of variants of concern in the past 28 days and published estimates of their increased transmissibility.
[4]Effective population-level vaccine immunity, based on type(s) and volume of vaccines distributed.
[5]Natural immunity estimates based on reported age-stratified deaths and age-stratified infection mortality rates.
[6]Mathematical estimates of potential vaccine-coverage levels for herd immunity may exceed 100%, because vaccines are not 100% effective.
Source: Census data; Centers for Disease Control and Prevention; Moderna; Our World in Data; Outbreak.info; Pfizer; SeroTracker; web searches

McKinsey & Company

Vaccine hesitancy makes it all the more difficult to reach the population-wide vaccination level rates that confer herd immunity. Researchers are learning more about differences among individuals' attitudes, which include both "cautious" and "unlikely to be vaccinated." Meanwhile, social tolerance for vaccination incentives and mandates appears to be growing, with more European locations adopting vaccination passes and more large employers in the United States implementing vaccine mandates.

While it now appears unlikely that large countries will reach overall herd immunity (though some areas might), developments in the United Kingdom during the past few months may help illustrate the prospects for Western countries to transition back toward normalcy. Having suffered a wave of cases caused by the Delta variant during June and the first few weeks of July, the country delayed plans to ease many public-health restrictions and eventually did so on July 19, though expansive testing and genomic surveillance remain in place. UK case counts may fluctuate and targeted public-health measures may be reinstated, but our scenario analysis suggests that the country's renewed transition toward normalcy is likely to continue unless a significant new variant emerges.

The United States, Canada, and much of the European Union are now in the throes of a Delta-driven wave of cases. While each country's situation is different, most have again enacted public-health restrictions, thus reversing their transitions toward normalcy. The trajectory of the epidemic remains uncertain, but the United Kingdom's experience and estimates of total immunity suggest that many of these countries are likely to see new cases peak late in the third quarter or early in the fourth quarter of 2021. As cases decline, our analysis suggests that the United States, Canada, and the European Union could restart the transition toward normalcy as early as the fourth quarter of 2021, provided that the vaccines used in these countries continue to be effective at preventing

severe cases of COVID-19. Allowing for the risk of another new variant and the compound societal risk of a high burden of influenza, respiratory syncytial virus, and other winter respiratory diseases, the question for these countries will be whether they manage to arrive at a different epidemiological endpoint, as we discuss next.

Endemic COVID-19 may be a more realistic endpoint than herd immunity

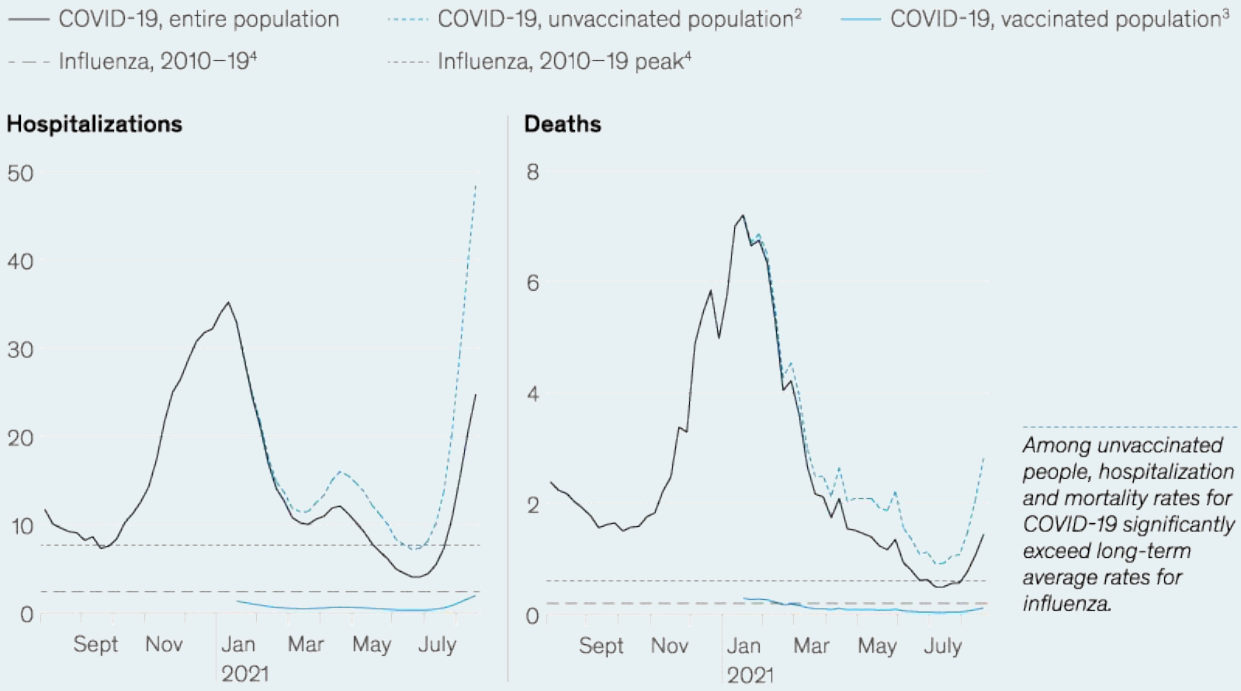
We have previously written about herd immunity as a likely epidemiological endpoint for some countries, but the Delta variant has put this out of reach in the short term. Instead, it is most likely as of now that countries will reach an alternative epidemiological endpoint, where COVID-19 becomes endemic and societies decide—much as they have with respect to influenza and other diseases—that the ongoing burden of disease is low enough that COVID-19 can be managed as a constant threat rather than an exceptional one requiring society-defining interventions. One step toward this endpoint could be shifting the focus of public-health efforts from managing case counts to managing severe illnesses and deaths. Singapore's government has announced that it will make this shift, and more countries may follow its lead.

Other authors have compared the burden of COVID-19 with that of other diseases, such as influenza, as a way to understand when endemicity might occur. In the United States, COVID-19 hospitalization and mortality rates in June and July were nearing the ten-year average rates for influenza but have since risen. Today, the burden of disease caused by COVID-19 in vaccinated people in the United States is similar to or lower than the average burden of influenza over the last decade, while the risks from COVID-19 to unvaccinated people are significantly higher (Exhibit 2). This comparison should be qualified, insofar as the burden of COVID-19 is dynamic, currently increasing, and uneven geographically. It nevertheless helps illustrate the relative threat posed by the two diseases.

Exhibit 2

In the United States, incidence of COVID-19 cases in June and July was similar to long-term incidence of influenza cases, but now exceeds it.

Weekly incidence of COVID-19 and influenza cases,[1] rate per 100,000



[1]Estimates for recent seasons are preliminary and may change as data are finalized.
[2]Following Centers for Disease Control and Prevention (CDC) methodology, rate in unvaccinated = combined rate / ((1 - fully vaccinated coverage) + (1 - vaccine effectiveness) * fully vaccinated coverage).
[3]Following CDC methodology, rate in fully vaccinated = (1 - vaccine effectiveness) * rate in unvaccinated. At ~50% fully vaccinated with vaccine effectiveness rates of 87%/96%/96% at preventing symptomatic infection/hospitalization/death.
[4]Influenza incidence rates are based on data from 2010–19; peak rates assume that all cases, hospitalizations, and deaths occur over a 4-month time period.
Source: CDC; Our World in Data; Stowe et al., "Effectiveness of COVID-19 vaccines against hospital admission with the Delta (B.1.617.2) variant," preprint not certified by peer review, Public Health England, June 2021; USAFacts

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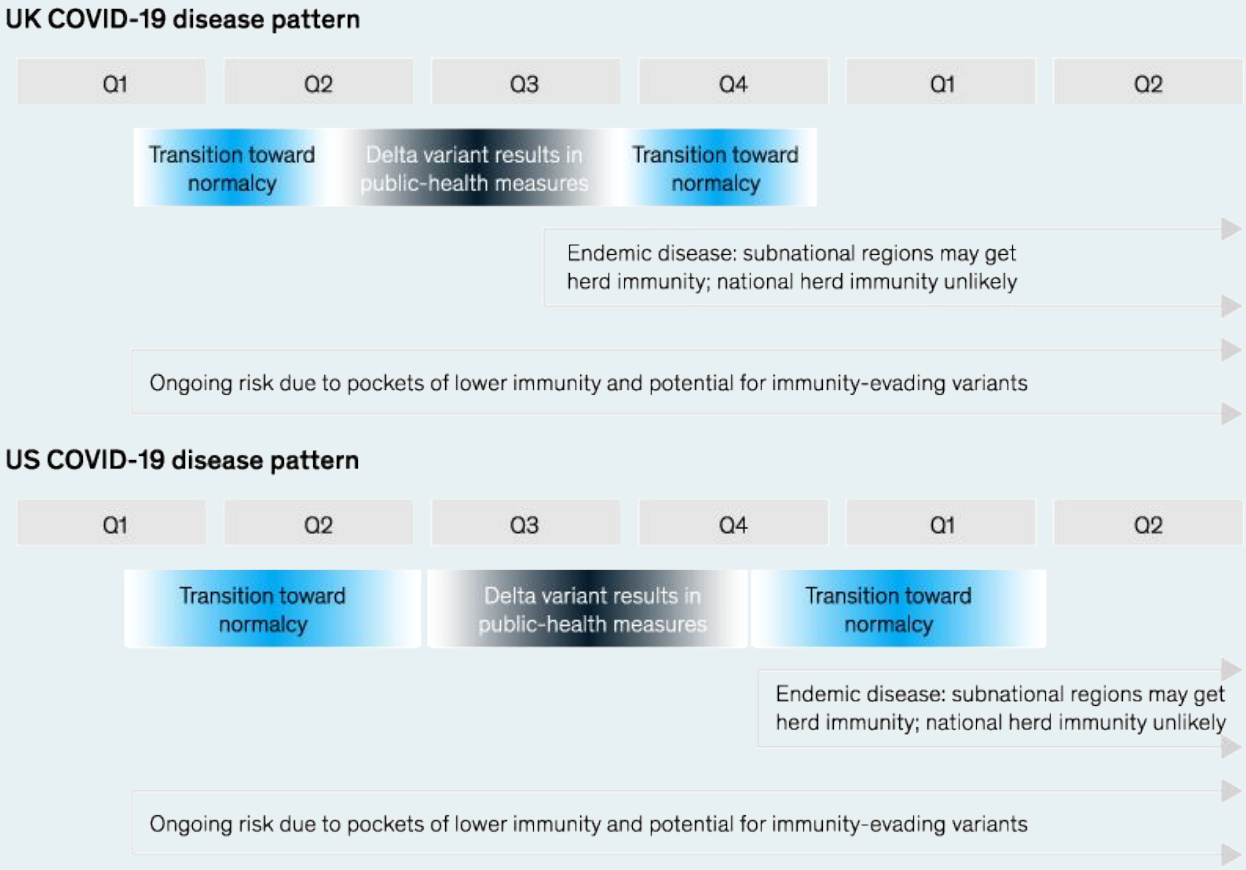
Countries experiencing a Delta-driven wave of cases may be more likely to begin managing COVID-19 as an endemic disease after cases go into decline. The United Kingdom appears to be making this shift now (though cases there were increasing as of this writing). For the United States and the European Union, scenario analysis suggests that the shift may begin in the fourth quarter of 2021 and continue into early 2022 (Exhibit 3). As it progresses, countries would likely achieve high levels of

protection against hospitalization and death as a result of further vaccination efforts (which may be accelerated by fear of the Delta variant) and natural immunity from prior infection. In addition, boosters, full approval of vaccines (rather than emergency-use authorization), authorization of vaccines for children, and a continuation of the trend toward employer and government mandates and incentives for vaccination are all likely to increase immunity

Exhibit 3

Some countries could resume a transition to normalcy and begin managing COVID-19 as an endemic disease after the recent wave of Delta-variant cases.



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Our scenario modeling suggests that although the resulting level of population immunity may not be high enough to achieve herd protection, it would still protect a substantial portion of the population. Most serious cases of COVID-19 would occur in unvaccinated people. Flare-ups and localized epidemics would happen while COVID-19 is managed as an endemic disease, but scenario modeling suggests that these may have less of an effect on the whole of society than the waves seen to date. Booster vaccinations will be important in maintaining immunity levels over time. A new variant that substantially evades existing immunity would remain the biggest overall risk.

Countries have varying prospects for reaching the end of the pandemic

Here, we offer a broader geographic view, comparing the current state as of the time of publishing in countries around the world. Our analysis suggests that countries fall into three general groups (within which national conditions can vary to some extent):

1. High-vaccination countries. These countries, primarily in North America and Western Europe, are the ones discussed above.
2. Case controllers. This group includes countries such as Singapore that have been most successful in limiting mortality associated with COVID-19 to date. They have typically maintained tight border restrictions and a strong public-health response to imported cases. Their residents have mostly enjoyed long periods of relative normalcy without public-health restrictions, aside from limits on international travel. Some countries in this group, such as Australia, have recently faced a Delta-driven surge in cases, but in absolute terms the burden of disease remains low relative to other countries. Unless these countries choose to maintain their border restrictions (such as hotel-based quarantine) indefinitely, they might accept the risk of endemic COVID-19 after governments determine that a sufficient

portion of the population is vaccinated. The pace of vaccine rollout varies among the countries, but in many cases reopening of borders may not begin until 2022, dependent in part on public-health outcomes for countries in other groups. The shift from a zero-COVID-19 goal to an endemic, low-burden goal may be challenging for some countries.

3. At-risk countries. Mainly comprising most lower-income and many middle-income countries, this is a group of nations that have not yet gained access to enough vaccine doses to cover a large portion of their populations. Estimates of their overall immunity remain low enough that there is still a risk of significant waves of disease. Recent projections suggest that it is likely to take until late 2022 or early 2023 for these countries to achieve high vaccine coverage. The possible time frame for them to manage COVID-19 as an endemic disease is less clear.

Globally and nationally, the epidemiological and public-health situation remains dynamic, and the prospects for each country group are subject to uncertainty. Factors that could influence actual outcomes include:

+ The potential for new variants to emerge (for example, a variant that evades vaccine-mediated immunity to the extent that it frequently causes severe disease in the vaccinated and spreads widely would likely have the most significant effect on any country's prospects for reaching the end of the pandemic)
+ Further evidence of waning natural and vaccine-mediated immunity over time, and challenges with rolling out vaccine boosters quickly enough to maintain immunity
+ Further challenges with vaccine manufacturing or global rollout
+ Changes in the ways that countries define an acceptable burden of disease (for example, setting different targets for disease burden in vaccinated and unvaccinated populations)

The surge of COVID-19 cases resulting from the spread of the Delta variant and from vaccine hesitancy brought a sudden, tragic end to the transition toward normalcy that some countries had begun to make. But the United Kingdom's experience indicates that a transition toward normalcy may yet be possible before long, at least in countries where the vaccine rollout is well under way. Their task will be determining what burden of disease is low enough to warrant lifting of public-health restrictions, and how to manage the public-health impacts of endemic COVID-19. In countries where vaccination rates remain low, the prospects for ending the pandemic remain largely tied to the availability and administration of additional doses. Expanding the international vaccine rollout remains essential to achieving a postpandemic sense of normalcy worldwide.

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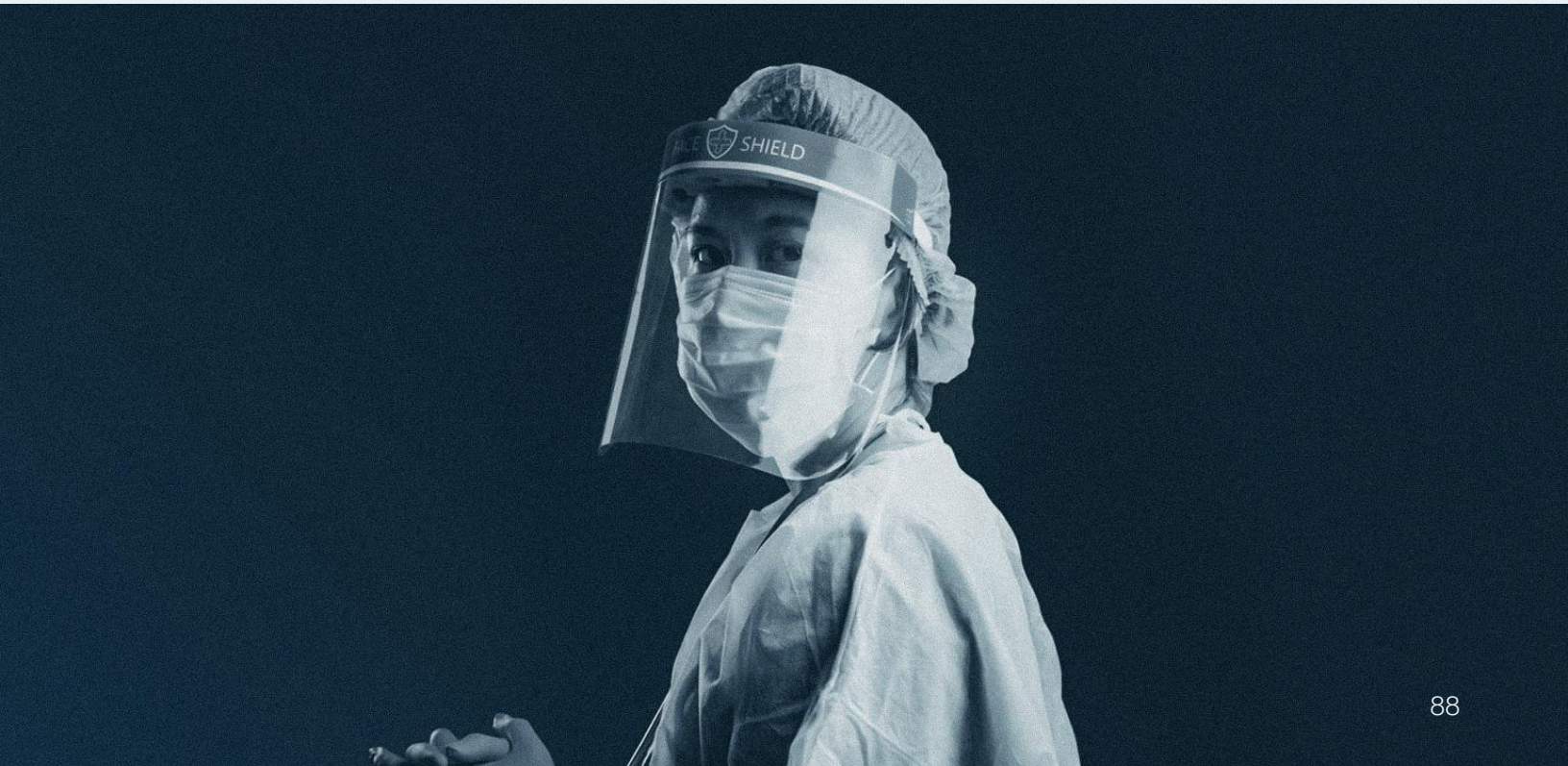
Not the last pandemic: Investing now to reimagine public-health systems

McKinsey

21 May, 2021



The COVID-19 crisis reminds us how underprepared the world was to detect and respond to emerging infectious diseases. Smart investments of as little as $5 per person per year globally can help ensure far better preparation for future pandemics.

This article was originally published in July 2020 to make an economic case for investments in infectious-disease surveillance and preparedness. The overall message remains as clear now as it was a year ago: the returns from smart investments in preparedness and response are likely to be large multiples of their costs. We have refined the article with three updates that build on our prior work:

+ We sharpened some cost estimates based on further analysis and new information that has become available over the past year. For example, the importance of genomic sequencing, “ever warm” vaccine manufacturing capacity, and R&D platforms has been made ever clearer by the trajectory of the COVID-19 pandemic.
+ We have included more detail on our line-item cost estimates (see appendix) and a deep dive on surveillance costing (see research preview).
+ We have included new cost analyses, including cost per capita and the share of spend at the global, regional, and country levels.

The COVID-19 pandemic has exposed overlooked weaknesses in the world’s infectious-disease-surveillance and -response capabilities—weaknesses that have persisted in spite of the obvious harm they caused during prior outbreaks. Many countries, including some thought to have strong response capabilities, failed to detect or

respond decisively to the early signs of SARS-CoV-2 outbreaks. That meant they started to fight the virus's spread after transmission was well established. Once they did mobilize, some nations struggled to ramp up public communications, testing, contact tracing, critical-care capacity, and other systems for containing infectious diseases. Ill-defined or overlapping roles at various levels of government or between the public and private sectors resulted in further setbacks. And the challenges, including difficulties with vaccine rollouts, lingering vaccine hesitancy, and difficulties in managing second and third surges, have continued as the pandemic has entered its second year.

Correcting these weaknesses won't be easy. Government leaders remain focused on navigating the current crisis, but making smart investments now can both enhance the ongoing COVID-19 response and strengthen public-health systems to reduce the chance of future pandemics. Investments in public health and other public goods are sorely undervalued; investments in preventive measures, whose success is invisible, even more so. Many such investments would have to be made in countries that cannot afford them.

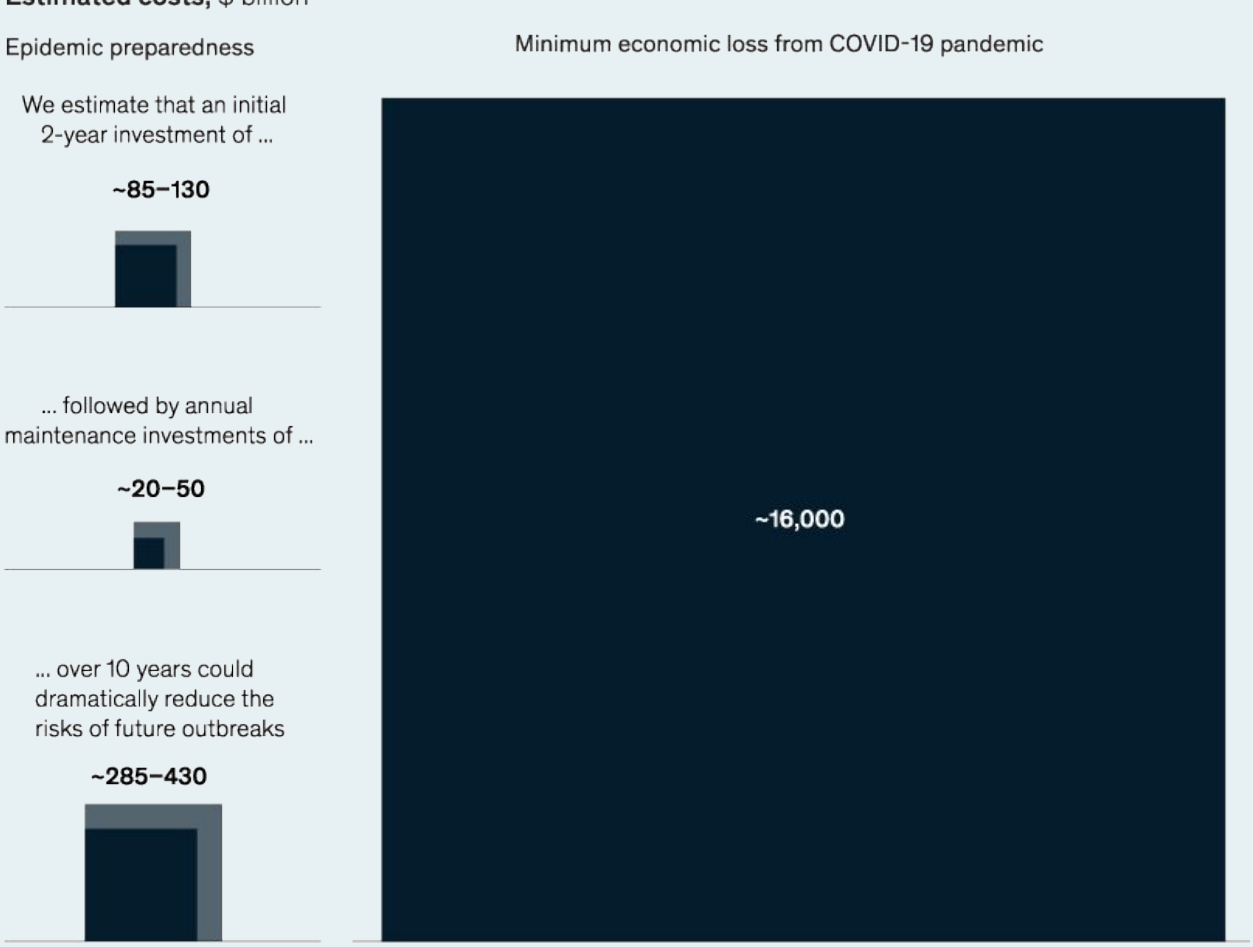
Nevertheless, now is the moment to act. The world has seen repeated instances of what former World Bank president Jim Kim has called a cycle of "panic, neglect, panic, neglect," whereby the terror created by a disease outbreak recedes, attention shifts, and we let our vital outbreak-fighting mechanisms atrophy. The Independent Panel for Pandemic Preparedness and Response published its findings in May 2021, describing the COVID-19 pandemic as the 21st century's "Chernobyl moment" and making clear that if investment doesn't occur now, "we will condemn the world to successive catastrophes."

While some are calling the COVID-19 crisis a 100-year event, we might come to see the current pandemic as a test run for a pandemic that arrives soon, with even more serious consequences. Imagine a disease that transmits as readily as COVID-19 but kills 25 percent of those infected and disproportionately harms children.

The business case for strengthening the world's pandemic-response capacity at the global, national, and local levels is compelling. The economic disruption caused by the COVID-19 pandemic could cost more than $16 trillion—many times more than the projected cost of preventing future pandemics. We have estimated that spending approximately $85 billion to $130 billion over the next two years and approximately $20 billion to $50 billion annually after that could substantially reduce the likelihood of future pandemics (Exhibit 1). This equates to an average of about $5 per person per year for the world's population. Approximately 27 percent of this spend would take place at the global and regional levels, and about 73 percent would take place at the country level (8 percent in high-income countries and 65 percent in middle- and low- income countries).

Exhibit 1

Assuming a COVID-19-scale epidemic is a 50-year event, the return on preparedness investment is clear, even if it only partly mitigates the damage.



These are high-level estimates with wide error bars. They include pandemic-specific strengthening of health systems but not the full health-system-strengthening agenda. Cost estimates will continue to evolve as new information emerges. We hope the overall message is clear: infectious diseases will continue to emerge, and a vigorous program of capacity building will prepare the world to respond better than we have so far to the COVID-19 pandemic.

In this article, we describe and estimate the cost of five areas that such a program might cover: building “always on” response systems, strengthening mechanisms for detecting infectious diseases, integrating efforts to prevent outbreaks, developing healthcare systems that can handle surges while maintaining the provision of essential services, and accelerating R&D for diagnostics, therapeutics, and vaccines (Exhibit 2). Details of the costing analysis are available for download (see appendix).

Exhibit 2

Five shifts in healthcare systems can help reduce the chance of future pandemics.

	From	To	Rationale
	“Break glass in case of emergency” response systems	“Always on” systems and partnerships that can scale rapidly during epidemics	Outbreak response is most effective when it uses regularly applied mechanisms
	Uneven disease surveillance	Strengthened global, national, and local mechanisms for detecting infectious diseases	Effective detection capacity is needed at all levels
	Waiting for outbreaks	Integrated epidemic-prevention agenda	Targeted interventions can reduce pandemic risk
	Scramble for healthcare capacity	Systems ready to surge while maintaining essential services	Epidemic management requires ability to divert healthcare capacity quickly without lessening core services
	Underinvestment in R&D for emerging infectious diseases	Renaissance in infectious-disease R&D	Response to COVID-19 pandemic has shown speed possible in moving against infectious diseases when motivated

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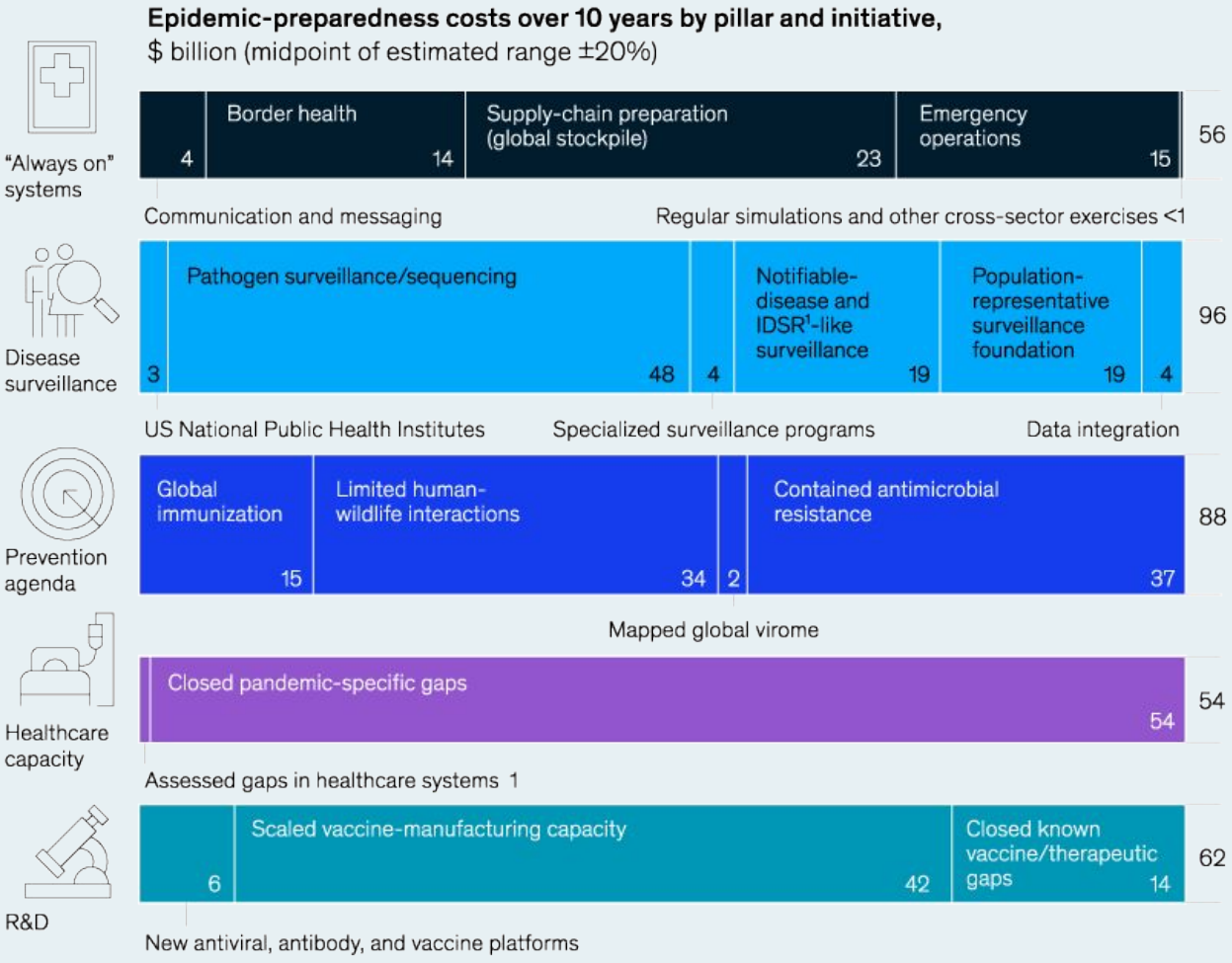
We estimate that these five pillars of preparedness can be achieved at a total cost of $357 billion over 10 years (Exhibit 3).

Exhibit 3

Five pillars of preparedness can be built for $357 billion, in our estimate.



Note: Figures may not sum to listed totals, because of rounding.
[1]Integrated Disease Surveillance and Response (framework from US Centers for Disease Control and Prevention).

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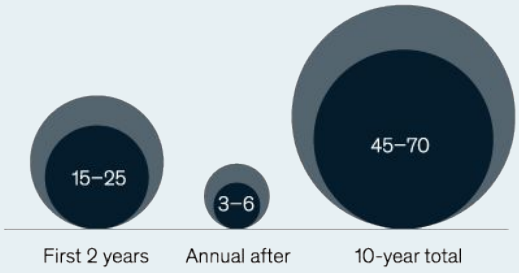
From ‘break glass in case of emergency’ response systems to always-on systems and partnerships that can scale rapidly during pandemics

Responding to outbreaks of infectious diseases involves different norms, processes, and structures from those used when delivering regular healthcare services. Decision making needs to be streamlined; leaders must make no-regrets decisions in the face of uncertainty. But much of our present epidemic-management system goes unused until outbreaks happen, in a “break glass in case of emergency” model. It is difficult to switch on those latent response capabilities suddenly and unrealistic to expect them to work right away.

Building ‘always on’ epidemic-management systems means they are ready as soon as outbreaks start.

Summary of estimated epidemic-preparedness initiatives and investments, $ billion



- Support epidemiological-response capacity
- Maintain robust medical-supply stockpiles and emergency supply-chain mechanisms
- Conduct regular outbreak simulations and cross-sector preparedness activities
- Improve communications and messaging
- Implement effective public-health responses at points of entry

Source: Gavi, the Vaccine Alliance; Georgetown University; Global Virome Project; National Academy of Medicine; *Nature*; *The Lancet*; US Centers for Disease Control and Prevention; World Bank; World Health Organization; World Organisation for Animal Health

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A better system might be founded on a principle of active preparedness and constructed out of mechanisms that can be consistently used and fine-tuned so they are ready to go when outbreaks start (Exhibit 4). We see several means of instituting such an always-on system. One is to use the same mechanisms that we need for fast-moving outbreaks (such as COVID-19) to address slow-moving outbreaks (such as HIV and tuberculosis) and antimicrobial-resistant pathogens. Case investigation and contact tracing are skills familiar to specialists who manage HIV and tuberculosis. But few areas have

deployed their experts effectively in responding to the COVID-19 pandemic.

Both the public and private sectors have played major roles in the response to the COVID-19 crisis, but collaboration has not always been as smooth as it might have been if collaboration channels had been preestablished. There have been notable exceptions, including collaborations to increase access to ventilators.

The principle of active preparedness might also lead governments to strengthen other aspects of pandemic response. For example, the past year has highlighted gaps in the manufacturing and stockpiling of personal protective equipment, the sharing of information with the public through risk-communication systems, and the different stakeholders' capability of maintaining border health at points of entry. Predefining response roles for different stakeholders at the global, national, and local levels is also an important part of active preparedness, since well-defined roles prevent delays and confusion when an outbreak occurs.

Last, governments can keep outbreak preparedness on the public agenda. Iceland offers an example of how to do that effectively. Since 2004, the country has been testing and revising its plans for responding to global pandemics. Authorities there also encourage the public to take part in preparing for natural disasters. The government's efforts to heighten public awareness of the threat posed by infectious diseases and to engage the public in the necessary response measures aided the country's successful always-on early-response systems to the COVID-19 pandemic.

To build always-on systems around the world, an up-front two-year investment of $15 billion to $25 billion and ensuing annual investments of $3 billion to $6 billion (for a ten-year total of $45 billion to $70 billion) would go into the following areas:

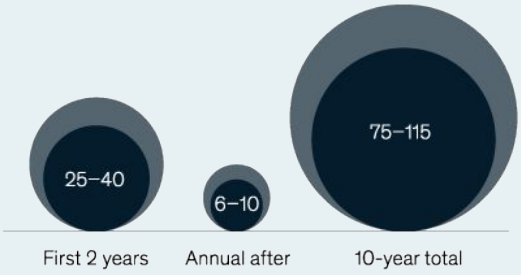
+ Supporting epidemiological-response capacity with emergency operations centers (EOCs) that function during all types of major crises
+ Maintaining robust stockpiles of medical supplies and emergency supply-chain mechanisms at the subnational, national, or regional levels (depending on the setting)
+ Conducting regular outbreak simulations and other cross-sectoral preparedness activities
+ Strengthening communications and messaging through established risk-communication systems, internal and partner communication and coordination, public communication and engagement with affected communities, dynamic listening, and rumor management
+ Ensuring national border health by establishing routine capabilities and effective public-health responses at points of entry

From uneven disease surveillance to strengthened global, national, and local mechanisms to detect infectious diseases

Retrospective analysis shows that SARS-CoV-2 was circulating in a number of countries well before it was first recognized. Failures to detect the disease meant that chains of transmission had been firmly established before countries began to respond. Such problems occur in part because disease surveillance is often based on old-fashioned practices: frontline health workers noticing unusual patterns of symptoms and reporting them through analog channels. Most countries are far from realizing the potential of data integration and advanced analytics to

Strong disease-surveillance mechanisms help stop chains of transmission sooner.

Summary of estimated epidemic-preparedness initiatives and investments, $ billion



- Close gaps in foundational surveillance
- Build and maintain high-quality outbreak-investigation capacity
- Increase IDSR[1]-like surveillance of notifiable diseases
- Develop strong pathogen surveillance
- Support serosurveillance
- Strengthen data integration and analysis

[1]Integrated Disease Surveillance and Response (framework from US Centers for Disease Control and Prevention).
Source: Gavi, the Vaccine Alliance; Georgetown University; Global Virome Project; National Academy of Medicine; *Nature*; *The Lancet*; US Centers for Disease Control and Prevention; World Bank; World Health Organization; World Organisation for Animal Health

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supplement traditional event-based surveillance in identifying infectious disease risks so that authorities can initiate efforts to stop individual chains of transmission. Data fragmentation has hindered the efforts to respond to the COVID-19 pandemic in many parts of the world (Exhibit 5). The past year has also highlighted the critical role that genomic sequencing can play in the management of outbreaks.

Stopping individual chains of transmission requires strong detection and response capabilities at the national and local levels. Those capabilities are important to have in place across the globe, especially in parts of the world where frequent human–wildlife interactions make zoonotic events (transmission of pathogens from animals to people) more likely. Many developing countries will need external funding and support to build up their disease-surveillance systems. Donor countries might think of their investments in those systems as investments in their own safety.

Recognizing that one country's infectious-disease threat is a threat to all nations—a lesson reinforced by outbreaks of SARS in Toronto, cholera in Haiti, MERS in South Korea, and Zika across the Americas—previous generations created the International Health Regulations (IHR) to promote cooperation and coordination on outbreak response. However, compliance with the IHR has been imperfect because countries may be reluctant to suffer the economic consequences of admitting to a major

outbreak. Weak cooperation efforts were identified as a factor in the slow initial response to the West Africa Ebola outbreak. As the COVID-19 crisis continues, leaders are finding reasons to renew their commitments to global and regional mechanisms for coordinating outbreak responses—for example, through the proposed new international pandemic treaty, currently under discussion.

Such an agenda might include closing gaps in population-representative foundational surveillance; strengthening notifiable disease, lab-based, and pathogen surveillance; and improving data integration and the use of data. More data are available here (see research preview). An investment program of $25 billion to $40 billion for the first two years and $6 billion to $10 billion per year thereafter (for a ten-year total of $75 billion to $115 billion) would pay for the following:

+ Closing the gaps in foundational surveillance, such as through civil-registration and vital statistics, sample registration systems, and mortality surveillance
+ Building and maintaining high-quality, flexible outbreak-investigation capacity in all geographies: most countries have a field-epidemiology-training program of some kind, but many of them are underfunded and place their graduates onto uncertain career pathways; strengthening such programs is likely to be one of the most effective investments that a country can make in developing its outbreak-investigation capacity
+ Increasing the use of notifiable disease surveillance, such as the US Centers for Disease Control and Prevention's Integrated Disease Surveillance and Response framework
+ Developing strong pathogen surveillance, including through genomic sequencing
+ Supporting serosurveillance and vaccine-effectiveness monitoring

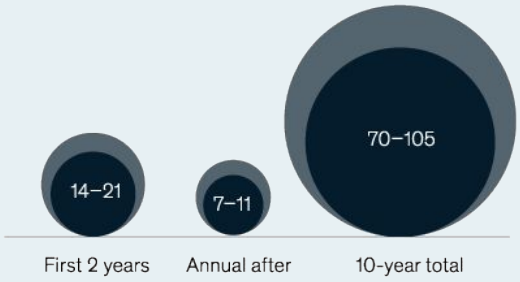
+ Strengthening data integration and analysis, such as by US National Public Health Institutes

From waiting for outbreaks to an integrated epidemic-prevention agenda

While we cannot prevent all epidemics, we can use all the tools in our arsenal to prevent those we can. Four approaches to doing so stand out: reducing the risk of zoonotic events by discovering unknown viral threats, reducing the risk of zoonotic events by limiting human and wildlife interactions, limiting antimicrobial resistance (AMR), and administering vaccines more widely (Exhibit 6).

Outbreak prevention calls for new approaches to zoonosis, antimicrobial resistance, and immunization.

Summary of estimated epidemic-preparedness initiatives and investments, $ billion



- Reduce human–wildlife interactions
- Discover unknown zoonotic viral threats, including mapping global virome
- Limit antimicrobial resistance
- Close the global immunization gap

Source: Gavi, the Vaccine Alliance; Georgetown University; Global Virome Project; National Academy of Medicine; *Nature*; *The Lancet*; US Centers for Disease Control and Prevention; World Bank; World Health Organization; World Organisation for Animal Health

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Zoonotic events, in which infectious diseases make the jump from an animal to a human, touched off some of the most dangerous recent epidemics, including of COVID-19, Ebola, MERS, and SARS. Zoonosis can't be eliminated, but their occurrence can be reduced. Areas with high biodiversity and places where humans frequently encounter wildlife present the greatest risk of zoonotic events and therefore require special attention to and investment in research. Another root cause is ecosystem degradation, which makes zoonotic events more likely by increasing interactions between humans and wildlife. Scientists have estimated that a

large portion of zoonotic-disease outbreaks can be linked to changes in agriculture, land use, and wildlife hunting over the past 80 years. Economic incentives, legal changes, and public education can lessen contact between humans and wildlife and help protect forests and wilderness areas, thereby decreasing the likelihood of zoonosis. There is also much more to learn about the threats we face through wider mapping of the viruses that exist in animal populations.

Limiting AMR—the evolution of pathogens to be less susceptible to antimicrobial agents—is another important way to prevent epidemics. AMR is a public-health crisis to be managed in its own right. It is also a potential accelerant of future outbreaks: as pathogens become resistant, diseases that are currently controllable can spread more widely. Conveniently, managing AMR requires many of the same tools and techniques that support responses to acute outbreaks, including surveillance, case investigation, information sharing, and special protocols for healthcare settings. Efforts to improve AMR management, therefore, not only strengthen outbreak-response capabilities but also help prevent outbreaks in the first place.

Finally, the unprecedented R&D effort that has been launched to develop a vaccine against COVID-19 serves as a reminder that we are not realizing the full benefit of existing vaccines. Recent outbreaks of measles, for example, show that places with lower vaccination rates are more susceptible to diseases that vaccines can prevent. Achieving full global coverage of all of the vaccines in our arsenal would save millions of lives over the coming decades. It will be especially important to jump-start immunization efforts after the current pandemic with catch-up campaigns for children who have missed scheduled vaccines.

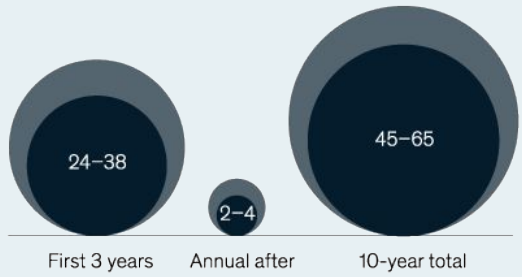
The approaches we have described represent important steps toward preventing outbreaks. We estimate that it would cost approximately $14

billion to $21 billion for two years and then $7 billion to $11 billion per year thereafter (for a ten-year total of $70 billion to $105 billion) to limit human exposure to wild animals, map more of the global virome, slow the spread of AMR, and close the global immunization gap.

From a scramble for healthcare capacity to systems ready to surge while maintaining essential services

Local healthcare systems can be made ready to handle surges in demand while still delivering essential services.

Summary of estimated epidemic-preparedness initiatives and investments, $ billion



- Conduct assessments to highlight gaps in healthcare systems
- Target strengthening of health systems to address largest gaps

Source: Gavi, the Vaccine Alliance; Georgetown University; Global Virome Project; National Academy of Medicine; *Nature*; *The Lancet*; US Centers for Disease Control and Prevention; World Bank; World Health Organization; World Organisation for Animal Health

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Exponential case growth during some phases of the COVID-19 pandemic has compelled officials in some countries to rapidly redirect much of their healthcare capacity to treating patients with COVID-19. The current challenges in India and elsewhere highlight the need to ensure that healthcare systems are prepared to respond to demand surges (Exhibit 7). Some gaps, such as the need for ad hoc conversions of spaces to care for patients with highly contagious diseases, have been common across many countries. Others, such as a lack of oxygen concentrators, have been especially acute in low- and lower-middle-income countries.

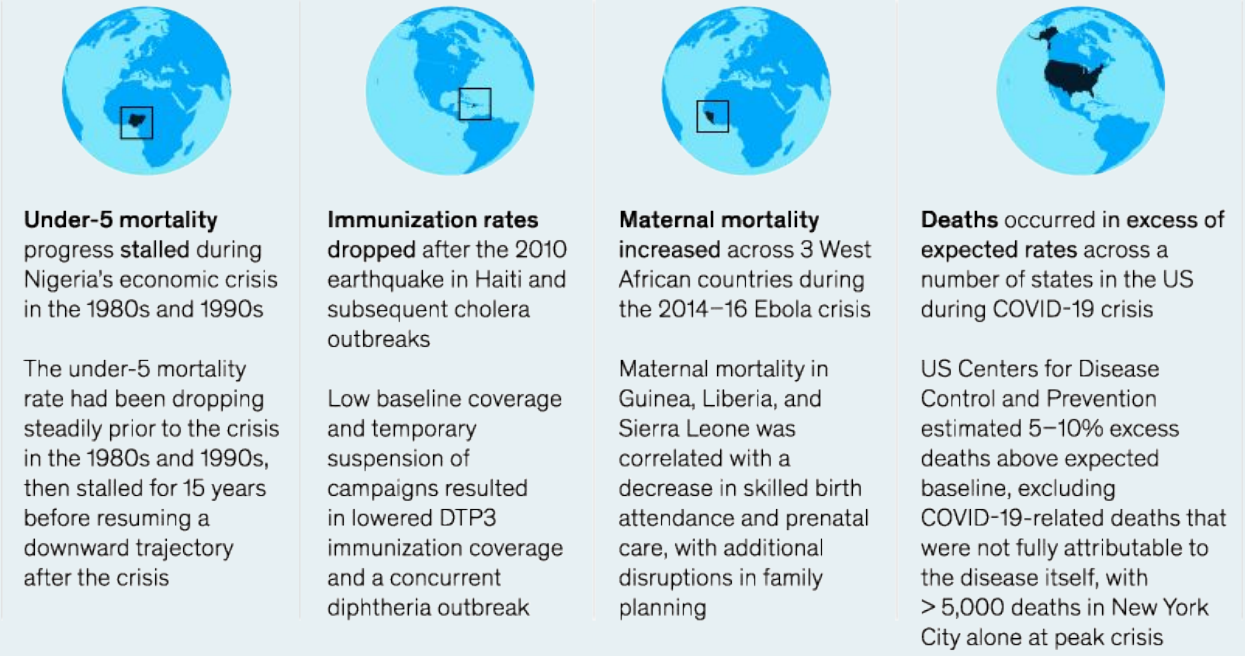
To prepare, health systems can establish plans detailing how capacity can be diverted to pandemic management and how additional capacity can be added quickly (for example, by converting nonmedical facilities to temporary healthcare facilities and by establishing field hospitals). Some places used existing plans of that type to respond to the COVID-19 pandemic; others created emergency plans during the outbreak. More can be done to codify and improve such plans. While universal healthcare is an important long-term goal, we consider only the portion of health-system-strengthening costs that are most relevant to pandemic preparedness. Tools such as Service Availability and Readiness Assessment (SARA) and joint external evaluations (JEEs) can help assess overall system readiness and identify the highest-priority needs for pandemic preparedness.

Surge-capacity plans for pandemics should account for the need to maintain essential healthcare services (Exhibit 8). It is becoming increasingly clear that the secondary impacts of the COVID-19 pandemic on population health are of a similar magnitude to those directly attributable to the disease. This is caused by crowded-out urgent-care resources for other conditions, delayed screening and health maintenance, and increased burden on mental health.

Exhibit 8

To mitigate the secondary health effects of public-health crises, health systems need to plan for surges and continuation of essential services.

Example secondary health effects of health crises



Source: Academic articles; expert/field interviews; ministries of health; news reports; US Centers for Disease Control and Prevention; World Bank data sets; World Health Organization

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Certain investments can help prepare healthcare systems to handle surges while delivering essential and routine services. An initial three-year outlay of $24 billion to $38 billion and yearly spending of $2 billion to $4 billion thereafter (for a ten-year total of $45 billion to $65 billion) would pay for the following actions:

+ Conducting relevant assessments (such as SARA and JEEs) to highlight gaps and address the challenges identified in scaling healthcare capacity

+ Strengthening health systems in targeted ways to prepare for future pandemics: while building resilient health systems around the world is a multidecade agenda, closing the largest gaps in care capacity offers disproportionate benefit (the total cost of building high-quality, resilient health systems will be far higher than the cost of closing capacity gaps and goes beyond the scope of the analysis presented in this article)

From underinvestment in R&D for emerging infectious diseases to a renaissance

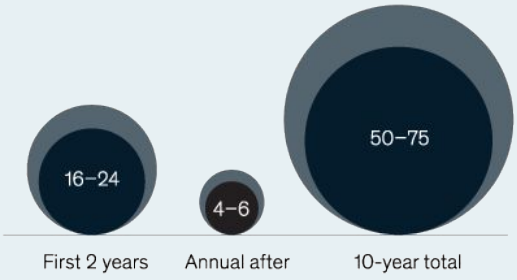
Humans have done more to overcome the threat posed by infectious diseases in the past 100 years than during the previous 10,000. The widespread availability of antibiotics allows us to manage most bacterial infections. HIV remains a serious condition, but it isn't usually an immediately life-threatening one for people with access to antiretroviral therapy, thanks to the innovations of the past 35 years. And the past decade has seen remarkable progress in our ability to cure hepatitis C.

However, important gaps remain. Public-health leaders have frequently called attention to the threat posed by emerging infectious diseases. Even before the COVID-19 outbreak, the pandemic threat posed by known pathogens such as influenza and by an unknown "pathogen X" was well understood. The pace of innovation in antibiotics is not keeping pace with the increases in antimicrobial resistance. Current regulatory and incentive structures fail to reward innovations that can help counteract emerging infectious diseases or resistant bacteria. It is difficult for companies to project the financial returns from interventions for diseases that emerge sporadically and may be controlled before clinical trials are complete (as happened during the West Africa Ebola outbreak). That is especially true of interventions for diseases that mainly affect people in low-income countries. R&D efforts in response to the

COVID-19 pandemic have been unprecedented. Vaccine-development records have been smashed, both for time to market and for the number of candidates advanced in a short period of time. The bar for vaccine development during a crisis has been raised: CEPI (Coalition for Epidemic Preparedness Innovations) has suggested that for a future pandemic, it may be possible to develop a vaccine within 100 days.7 On a less positive note, the limits of what can be achieved through drug repurposing have become clearer. No one expects that we will go back to the prepandemic R&D model, but it will be important to ensure that the product-development lessons of the pandemic are fully internalized.

The efforts behind the COVID-19 response may start a renaissance in infectious-disease R&D.

Summary of estimated epidemic-preparedness initiatives and investments, $ billion



- Accelerate development of diagnostics, therapeutics, and vaccines against known threats
- Scale vaccine-manufacturing capabilities
- Invest in new vaccine, antibody, antiviral, and therapeutic platforms

Source: Gavi, the Vaccine Alliance; Georgetown University; Global Virome Project; National Academy of Medicine; *Nature*; *The Lancet*; US Centers for Disease Control and Prevention; World Bank; World Health Organization; World Organisation for Animal Health

McKinsey & Company

Building on the momentum created by COVID-19-related R&D, there is potential to spark a renaissance in infectious-disease R&D (Exhibit 9). The renaissance might focus on several necessities that the response to the COVID-19 pandemic has highlighted. One necessity is closing gaps in the tool kit to respond to known threats, such as influenza. A second is maintaining platforms that will allow us to respond rapidly to newly discovered diseases (as mRNA has done for SARS-CoV-2, for example). A third is sustaining the ability to manufacture billions of vaccine doses quickly to ensure equitable access to the fruits of innovation.

Delivering such necessities will require building on the early success of initiatives such as CEPI to reimagine product-development pathways, from funding models and collaboration platforms to regulatory review and access agreements. Spending $16 billion to $24 billion in the first two years and $4 billion to $6 billion per year thereafter (for a ten-year total of $50 billion to $75 billion)would fund these activities:

+ Closing gaps in vaccine and therapeutic arsenals against known threats, including influenza, for which effective R&D might yield significant advances
+ Scaling vaccine-manufacturing capabilities to produce 15 billion doses in a six-month period to provide sufficient coverage to immunize the global population
+ Investing in the development of new vaccine, antibody, antiviral, and therapeutic platforms against emerging infectious diseases

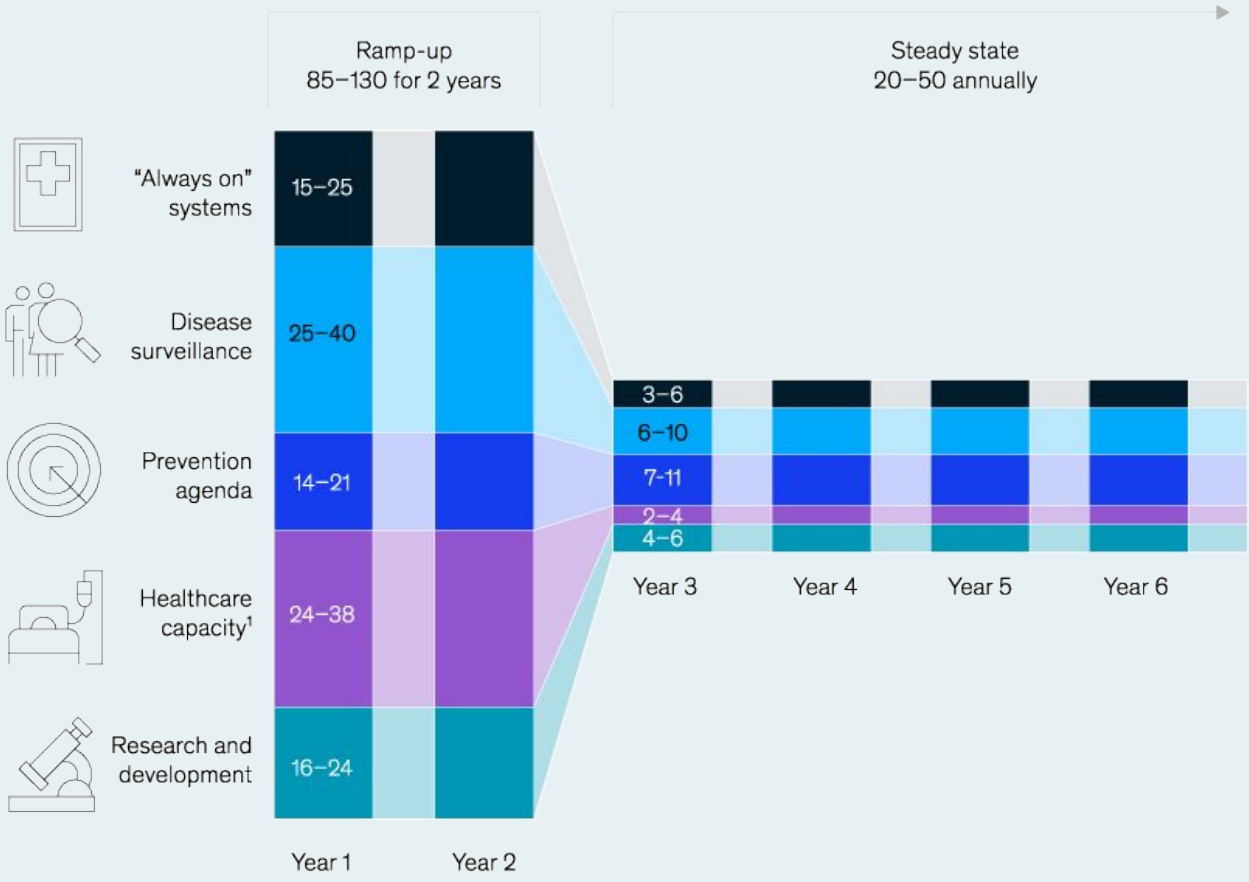
Bringing it all together

As we continue to respond to the COVID-19 pandemic, countries should make deliberate investments to reduce the chance of such a crisis happening again. We estimate that an initial global investment of $85 billion to $130 billion over the next two years ($40 billion to $65 billion per year), followed by an investment of $20 billion to $50 billion per year to maintain always-on systems, would significantly reduce the chance of a future pandemic. Those figures, totaling $285 billion to $430 billion over the next decade, include spending at the global, country, and subnational levels (Exhibit 10).

Exhibit 10

Funding for epidemic preparedness requires an up-front investment to close current gaps.

Illustrative funding needed to invest in epidemic preparedness, $ billion



[1]Initial investment in healthcare capacity takes place over 3 years.

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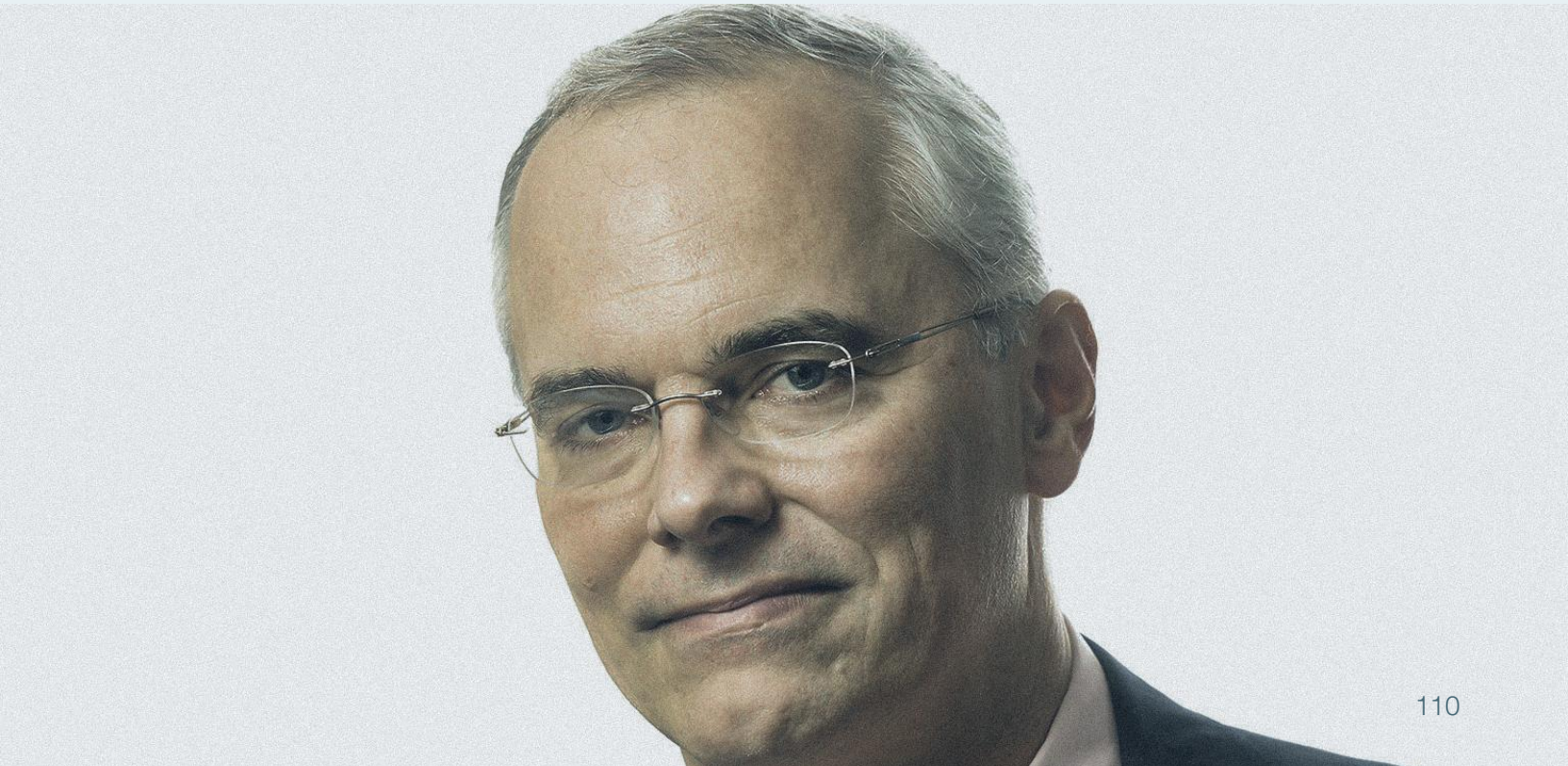
We have spent too much time behaving as though another deadly pathogen won't emerge.

The playwright Edward Albee once said, "I find most people spend too much time living as if they're never going to die." So it is with the global response to infectious diseases: we have spent too much time behaving as though another deadly pathogen won't emerge. Outbreaks of SARS, MERS, Ebola, and Zika led to some investments in pandemic preparedness over the past 20 years, but few of them are the lasting, systemic changes needed to detect, prevent, and treat emerging infectious diseases. And now, even with all of humanity's knowledge and resources, millions of people have been killed by a disease that was discovered less than 18 months ago. The COVID-19 pandemic won't be the last epidemic to threaten the world. By taking action and funding changes now, we can better withstand the next one.

Accelerating pandemic response efforts: An interview with CEPI's Richard Hatchett

McKinsey

5 October, 2021



Amid the COVID-19 crisis, the CEO of the Coalition for Epidemic Preparedness Innovations explains his five-year strategy that includes reducing vaccine timelines.

This interview is part of COVID-19 vaccines: The road to recovery and beyond, a series that includes a broad array of voices leading the historic global effort to develop, distribute, and provide equitable access to COVID-19 vaccines, including the Africa CDC; CEPI; Gavi, the Vaccine Alliance; Moderna; and Pfizer.

Before COVID-19 emerged, viruses of epidemic proportions had been top of mind for leaders in global public health for decades. In 2017, the concern led to the creation of the Coalition for Epidemic Preparedness Innovations, or CEPI, with the purpose of financing breakthrough independent research projects to develop vaccines before pandemics could take hold. Launched by the governments of Norway and India, the Bill & Melinda Gates Foundation, Wellcome, and the World Economic Forum (WEF), CEPI is the largest vaccine-development initiative focused on viruses that are potential epidemic threats.

The coalition, founded in the wake of the West Africa Ebola outbreak of 2014–16, funds clinical trials for vaccines against Middle East Respiratory Syndrome (MERS), Nipah virus, and Lassa fever, among other diseases. As a part of this effort, CEPI invests in innovative platform technologies—systems that can be adapted against different pathogens, such as mRNA —that can be used for rapid vaccine development.

CEO Richard Hatchett leads the global vaccine-development fund following his previous roles in the public sector, including serving as acting director of the US government's Biomedical Advanced Research and Development Authority (BARDA), a member of the US Homeland

Security Council for then-president George W. Bush, and a member of the US National Security Council for then-president Barack Obama. Under Hatchett, CEPI is championing a global effort to compress the vaccine-development process from 300 days—a huge breakthrough achieved for COVID-19—to just 100 days.3 This effort has been embraced by the G-7 summit in its report, 100 days mission to respond to future pandemic threats.4

McKinsey's Tania Holt and Lieven Van der Veken joined Hatchett to discuss the key components of CEPI's strategic five-year plan, also called CEPI 2.0, which lays out the 100-day goal, as well as the tools that could help reduce COVID-19 variants and future pandemic threats. The following is an edited excerpt of their conversation.

McKinsey: What were some of CEPI's goals pre-COVID-19, and how did they influence the pandemic response?

Richard Hatchett: We had not yet celebrated our third anniversary when the pandemic started. Our main goal before COVID-19 was to support vaccine development against emerging infectious diseases that we anticipated might have, at most, regional impact—such as Ebola in West Africa—and we were especially focused on ensuring equitable access to these vaccines, since the risk of emerging diseases is greater in lower- and middle-income countries.5 That's where all of the diseases we worked on were principally found.

Pandemic flu was not on our agenda because there is a global architecture in place directed against pandemic flu. In retrospect, I see it as shortsighted to think that the only pandemic threat was influenza. But where we weren't shortsighted was in recognizing that we might encounter new diseases where we needed to develop vaccines very rapidly. Many of us viewed coronaviruses as a particularly concerning threat, so we allocated around $140 million to developing vaccines for MERS, another infectious respiratory illness caused by a coronavirus

[MERS-CoV].6 We had also made substantial investments in rapid-response platforms, including a couple focusing on mRNA-based approaches.

When COVID-19 emerged, we were able to ask our partners who were working on MERS and rapid-response platforms to turn their attention to COVID-19 and the ignition of COVID-19 vaccine programs. Within a couple of months, it became obvious that the vaccines were going to be needed at a global scale, and we started working on vaccine accessibility as well. Our experience with COVID-19 has been an extension of commitments that we made prior to the pandemic, which allowed us to leap into the pandemic response.

McKinsey: How did CEPI respond to the pandemic, and can you describe some of the impact it has had?

Richard Hatchett: CEPI formulated the COVAX7 concept with Gavi, the Vaccine Alliance,8 early in the pandemic to address the challenges of global vaccine development, allocation, distribution, and access. The COVAX mechanism, co-led by CEPI, Gavi, and WHO, with key delivery partner UNICEF, includes philanthropic and sovereign partners, the private sector, and civil society coming together to fight the pandemic.

A term sometimes used to describe these partnerships is “networked multilateralism.” Such efforts are objective-driven or mission-focused and bring together partners from different sectors, typically for a limited time to achieve a specified end. This was at the heart of designing the COVAX concept. The pooling of investment in R&D to have an expanded portfolio provides benefits to all, particularly in an uncertain environment where it was unknown what percentage of the vaccines were going to be successful.

As part of the initiative, we made a choice early on to use our R&D investments to secure access commitments from our partners. These

investments had the potential to result in COVAX having a right of first refusal to up to three billion doses of COVID-19 vaccines—if the programs were successful. With this approach, we had hoped to provide more equitable distribution of vaccines. However, we've only been partially successful.

When the first shipments of COVID-19 vaccines went out from COVAX at the end of February 2021, we watched the footage of people in Ghana and Côte d'Ivoire receiving vaccines. It was incredible to have seen what, at that point, was nearly 14 months' worth of effort resulting in vaccines being delivered to people who didn't expect to see them that soon. It was really powerful and a vision of hope for the African continent. But subsequent deliveries were paralyzed by restrictions on the export of vaccines from one of our major suppliers. Consequently, as of September 2021, only about 3 percent of Africa's population has been fully vaccinated.9 Vaccine supplies are beginning to increase now, but we need more equitable and efficient solutions for the future. Understanding why COVAX couldn't deliver in the time frame needed will be an important lesson for designing better systems.

McKinsey: In March 2021, as part of a new initiative to tackle future pandemics, CEPI announced the ambition to develop a vaccine in under 100 days. How did this goal come about, and what will it take to make it happen?

Richard Hatchett: COVID-19 has been a catalyst for the rapid scientific and technological development of vaccines. It's changed the face of vaccines. We now have the rapid-response tools in play that we believe—if coupled with investments in preparedness and advancements in regulatory science and process—could get vaccine development down to 100 days. The 100-day goal pushes us to define and prioritize what needs to be done first and identify what, if anything, needs to change to make it possible. We can then take strides to create the necessary change. Our 100-day ambition is based on a three-pronged approach.

First, preparing a library of vaccines against prototype pathogens that can be adapted rapidly to meet new threats. Virus taxonomy is changing all the time. Depending on how you count viral families, there are between 25 and 28 that we know can cause human disease. Each viral family presents viruses with a particular structure—whether DNA or RNA, single stranded or double stranded, encapsulated or not—that poses unique challenges from a vaccinology perspective. We have vaccines for pathogens from 15 of the families, which proves at least that vaccines are possible. But only one or arguably two of them have been developed on rapid-response platforms. Our ability to pivot to respond to new threats is currently very limited. We now want to develop vaccines on rapid-response platforms against prototype pathogens from each of the families. If we can do that, we hope to be able to accomplish what we were able to with COVID-19, which was to use what we knew about developing vaccines against one coronavirus [MERS] to accelerate the development of vaccines against another [SARS-CoV-2]. To be truly prepared, we need to be able to do that for any viral threat we might face in the future

The second component is optimizing and reducing the time required at every stage of the vaccine-development process. By focusing on every element of that process, we can begin to optimize and ideally shorten development timelines. Some of the time savings may be incremental and only shave a week off here or a few days there, but some may be more impactful. In aggregate, we think we can achieve significant efficiencies.

Third, we need to work with regulators to develop risk-adapted strategies for ensuring that safety and efficacy of new-candidate vaccines are carefully evaluated.13 Time savings may come on the back end with new approaches to carefully regulating safety and efficacy while working more efficiently. These strategies can also help us anticipate the need for new provisions if we face something that is even more threatening than COVID-19.

The 100-day goal is a quantum leap over what we did in 2020, but it's not unattainable.

McKinsey: What are some approaches for the long-term management of COVID-19 and other epidemic diseases or potential future pandemics?

Richard Hatchett: COVID-19 is going to be with us for the foreseeable future, so we need to prepare ourselves for that and continue to work on COVID-19 until the world is well positioned to manage a long-term relationship with the disease.

There is still work to be done to optimize the use of the vaccines we have. The emerging issue of waning immunity and the threat posed by the evolution of the virus tell us that we need to produce broader and more enduring immune responses. We are evaluating mix-and-match dose strategies, where first and second doses could be from different manufacturers, to improve the performance, as well as fractionated, or dose-sparing strategies, to boost coverage of the vaccines we have. We also need to determine the optimal sequence for "priming"—which refers to the intervals between doses and whether two or three doses are required.

The vaccines we have now represent only the first generation of COVID-19 vaccines. They have been terrific at helping reduce the impact of the virus. But there could also be improved vaccines for the long term, ideally ones that perform equally well against most or all variants and that protect broadly against coronaviruses, such as SARS, MERS, COVID, and all their cousins. There is some exciting data emerging that suggests that developing such a vaccine may be possible, which would likely help us reduce, or even eliminate, the threat that coronaviruses present.

We also know about other epidemic diseases like Ebola and Lassa fever, which may be lesser threats but are not going away. While the epidemics they can produce won't have the kind of scale that a pandemic has, they

can still have tremendous global and economic impacts. For example, the best estimate of the Ebola epidemic in West Africa is that it created a global social burden in excess of $50 billion on top of the direct impact that it had on the economies and livelihoods in the countries that were affected. We need to continue our efforts to develop solutions for such threats, even while we prepare for unknown fast-moving pathogens that could emerge as serious infectious diseases.

We can also endeavor to create a global architecture for response that connects efforts around the world—from national efforts to regional efforts to the international efforts that CEPI will support directly. This relates to making sure that the world is connected and able to coordinate its efforts and do that very rapidly in a crisis. Collectively, we can invest in building out clinical-trial networks, lab networks, networks for performing animal-model studies, and not leaving anybody behind by making sure that we include lower-income, lower-middle-income, and upper-middle-income countries in the process.

CEPI sees itself playing an important role in helping to knit together that global collaborative effort in partnership with WHO, the major international financing institutions, and our other multilateral and regional partners. Emerging regional efforts are already showing strong potential in playing an increasingly important role in preparedness. We're seeing that in the efforts of the African Union to promote the development of manufacturing capacity in Africa and of the European Union to establish a Health Emergency Preparedness and Response Authority [HERA] modeled on BARDA. We're likely to see a lot more of these types of efforts in the future.

McKinsey: What are some of the biggest challenges in increasing pandemic preparedness?

Richard Hatchett: The biggest challenges are around vaccine manufacturing—and these are manifold. For the COVID-19 response, we

have experienced challenges around supply chains and making sure that our producers have the materials they need to make the vaccines.

As we think about manufacturing capacity for the future, we need to recognize the factors that have come together to produce the outcomes we don't like in the current response—the fact that a handful of countries and regions have dominated the vaccine supply—and take these into account as we develop solutions for the future. And whatever solutions we propose need to be sustainable. There will undoubtedly be a strong desire by many countries to have their own vaccine manufacturing facilities. But the question is, how many facilities can the world support and sustain? A facility that is built and then mothballed to wait until the next pandemic is not going to be very functional. So we have to balance across those dilemmas and find solutions that maximize our ability to scale up rapidly when necessary but that can also produce vaccines sustainably when we are not responding to a global crisis.

Also, as we think about global manufacturing capacity, we shouldn't do it with blinders on. We won't necessarily have to be able to vaccinate eight billion people every time a pandemic threat emerges. If we detect it early enough and use an empowered public-health enterprise to respond and suppress transmission—while we do the compressed-vaccine development and bring countermeasures in—maybe we only need 100 million doses. We shouldn't just focus on our productive capacity for vaccines without recognizing that we need to be able to address pandemics as efficiently as possible.

McKinsey: What has worked well in the current response efforts, and how might we need to improve our efforts moving forward?

Richard Hatchett: What's gone well is attributable to the sense of global scientific solidarity—the degree to which the global science community came together to understand the virus, to understand its epidemiology, and to develop countermeasures. That has been extraordinary. And the

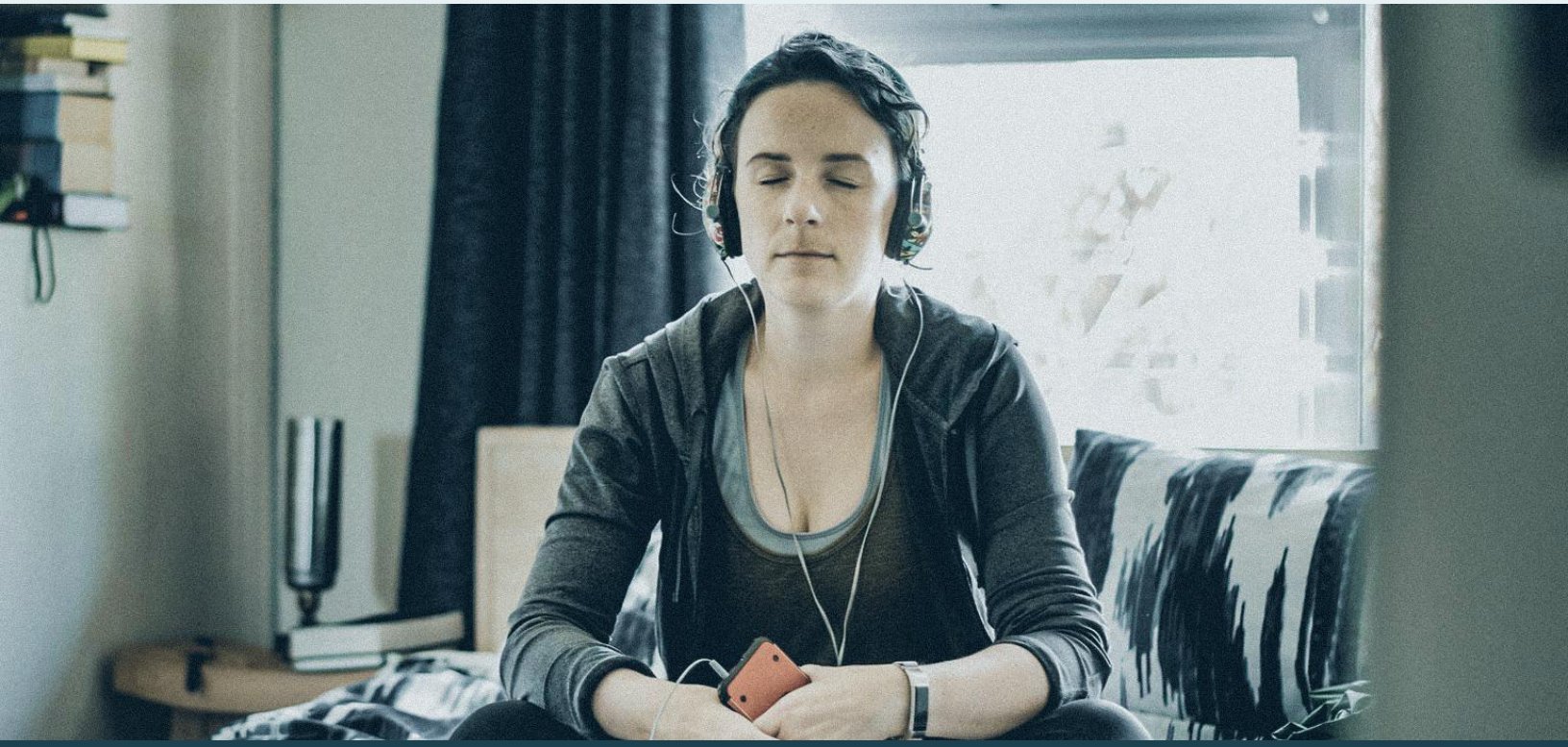
industry effort to develop vaccines, in particular, at record speeds represents a historic accomplishment.

Vaccine access and delivery have definitely been a challenge, but 18 months into the pandemic we have distributed more than five billion doses of vaccines. That's beyond the highest of high-side scenarios that we could possibly have imagined. Unfortunately, those vaccines haven't been shared equitably, but the production of vaccines at that scale is also a historic accomplishment.

Now it's time to capture the practical lessons learned. We can accomplish this by doing a credible, after-action review and being very honest and objective about anything we might have done that could have improved the response and choices that seemed rational at the time but may have contributed to a less-than-optimal outcome. We anticipated the risk of vaccine inequity and tried to hedge against it by investing in multiple technologies with manufacturing distributed across multiple geographies. And yet, we ended up in a position where some of those risks materialized, leading COVAX to experience severe and prolonged vaccine shortages. Facing these issues head on will allow us to emerge from this experience stronger and smarter.

The views and opinions expressed are those of the interviewee and are not necessarily those of McKinsey & Company. These materials are provided "as is" solely for informational purposes. The materials are not a legal, health, or safety resource, and organizations should engage their own experts to ensure compliance with applicable laws and standards. The materials are current as of the date indicated and may not incorporate the most recently available information. References or links to source materials do not imply any endorsement or recommendation by such source. McKinsey does not express an opinion or recommendation in the materials concerning COVID-19 vaccines.

Bloomberg New Economy Forum



Urgent challenges beyond COVID

Mental Health

Knowledge Partner

McKinsey & Company

How affordable is mental healthcare? The long-term impact on financial health

McKinsey

8 October, 2021

Those who report mental illness have disproportionately faced economic disadvantages and report greater financial stress.

Since the start of the COVID-19 pandemic, mental health has declined for many Americans, with more individuals reporting mental illness since 2019. Those diagnosed with mental illness have disproportionately faced economic disadvantages and report greater financial stress. Affordability barriers are compounding these challenges by limiting mental health access for many in need.

Among our findings:

+ More respondents are seeking psychotherapy, behavioral health help, and treatment at an ER for mental health needs since 2019.
+ Respondents reporting mental illness said they have greater fears around keeping their housing, especially if they have children.
+ Respondents reporting mental illness were on average 66 percent more likely to report debt across all categories.
+ Those who report having a mental health condition but have not sought treatment are 60 percent more likely to declare mental health services unaffordable.
+ Those reporting having a mental illness said they were less likely to pursue education or additional training.

The lower sense of financial security reported by those with mental illness underscores the importance of holistic care for behavioral health—not just treating mental illness symptoms but considering the broader needs an individual with mental illness may have. Holistic approaches, such as supportive housing and supportive employment,

can improve outcomes across both healthcare and broader functioning in society.

A year after the pandemic began in the United States, the portion of the population reporting signs of psychological distress increased.

Our survey found 30 percent of all respondents reported having a mental illness. Younger generations, caregivers, and LGBTQ+ respondents reported mental illness at a greater frequency.

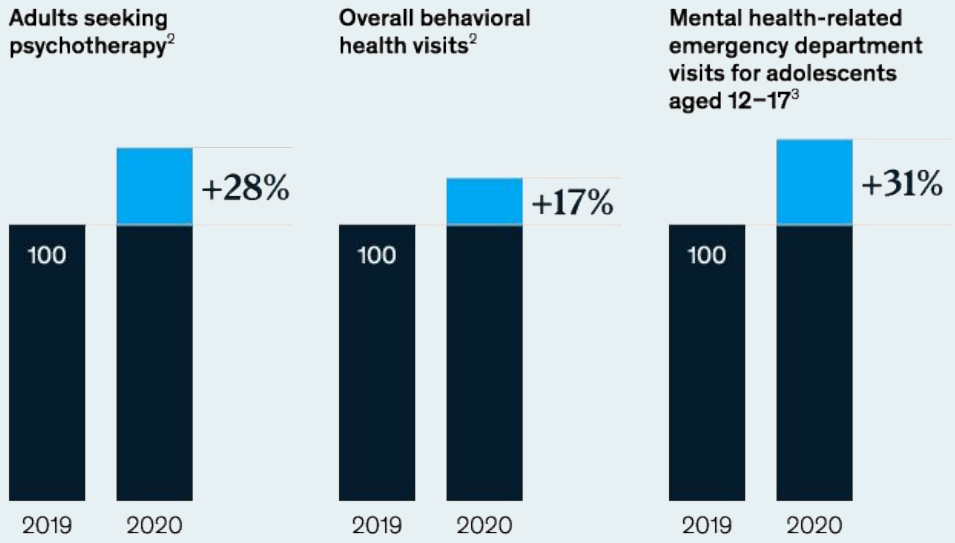
Before the pandemic…

~1 in 4
Americans were impacted by mental illness or substance use disorder in any given year[1]

Since the pandemic…

The number of Americans impacted by mental health concerns increased

Changes in mental health support needs 2019–20, % (2019 = 100)



[1] Substance Abuse and Mental Health Services Administration, Key substance use and mental health indicators in the United States: Results from the 2019 National Survey on Drug Use and Health (HHS Publication No. PEP20-07-01-001, NSDUH Series H-55), Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, 2020, samhsa.gov.
[2] McKinsey Interactive tool: Vulnerable Populations: Data Over Time.
[3] Ellen Yard et al., "Emergency department visits for suspected suicide attempts among persons aged 12–25 years before and during the COVID-19 pandemic—United States, January 2019–May 2021," *Morbidity and Mortality Weekly Report*, June 18, 2021, Volume 70, Number 24, pp. 888–94, cdc.gov.
Source: McKinsey American Opportunity Survey, March 9 and April 8, 2021

McKinsey & Company

Those with mental illness report a lower sense of financial security than those without mental illness.

Twenty percent of respondents who report mental illness disclose not being on track to meet short-term financial obligations[1] (such as rent/mortgage, groceries, transportation) compared with 12 percent of respondents who did not report mental illness. The disparity worsens when considering long-term financial goals with a 14 percentage point difference in respondents with mental illness reporting they feel off track.

Across income levels, those with mental illness are more likely to report concerns about losing their current housing, highlighting that while access to affordable treatment and treatment outcomes are worse for lower-income groups, mental illness affects individuals across socioeconomic groups.

Respondents who report a mental illness and are caregivers for children are 60 percent more likely to show concern for losing their current housing than respondents who report a mental illness condition yet are not caregivers.

Behavioral health conditions can interfere with work, family, and navigation of daily life. The lower sense of financial security reported by those with mental illness highlights the importance of holistic care in supporting mental health

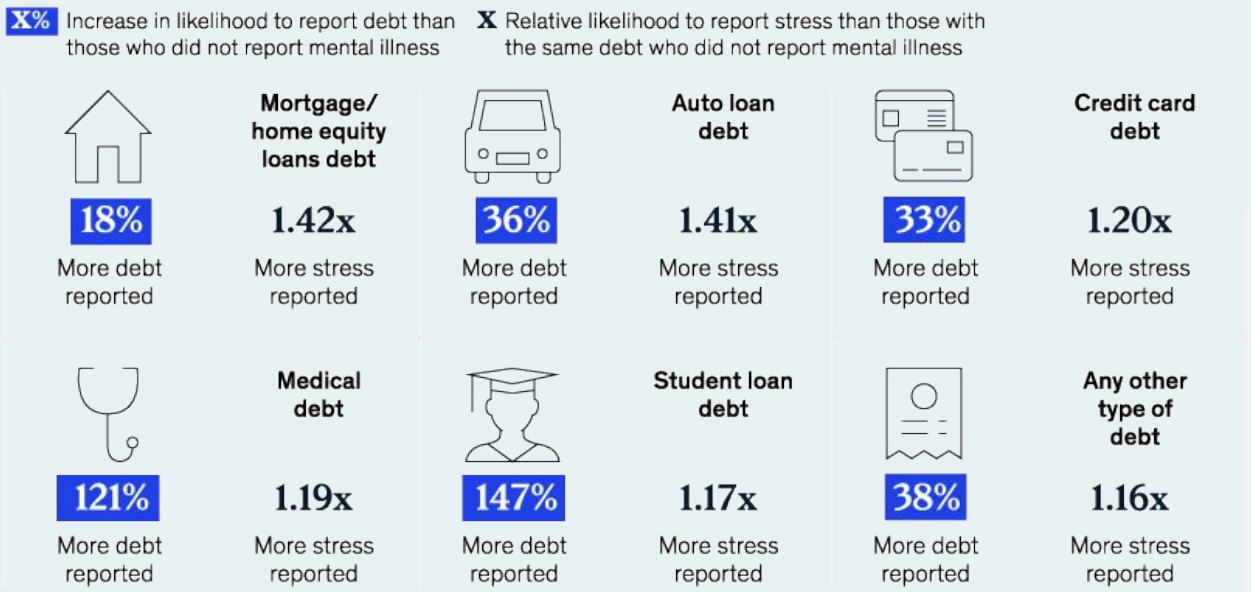
[1] Relationship exists when controlled by reported household incomes under $100K—respondents that reported MI disagreed 40 percent (less than $50K) and 30 percent ($50K–$100K) in comparison with those that did not report MI disagreeing 32 percent (less than $50K) and 23 percent ($50K–$100K).
[2] Relationship exists when controlled by employment in addition to reported household income—of fully employed respondents, those that reported MI agreed with the statement—31 percent (less than $50K), 25 percent ($50K–$100K), and 38 percent (more than $100K) in comparison with those that did not report MI agreeing with the statement—24 percent (less than $50K), 15 percent ($50K–$100K), and 11 percent (more than $100K).
[3] Less than $50K—those with MI who report concern they will lose current housing, n = 1,200, without MI, n = 1,177; $50K–$100K—those with MI who report they will lose current housing, n = 430, without MI, n = 547; greater than $50K—those with MI who report concern they will lose housing, n = 349, without MI, n = 288.
Source: McKinsey American Opportunity Survey, March 9 and April 8, 2021

McKinsey & Company

Further investigation could help better understand the bi-directional relationship between debt and mental illness.

Respondents who report mental illness were on average 66 percent more likely to report debt across all categories than respondents who did not report mental illness.

An association exists between mental illness and higher levels of debt and debt-related stress. This association may arise from initial debt leading to stress and triggering an underlying susceptibility for mental illness. However, respondents reporting a mental illness also may have found it more difficult to maintain a stable job, making it more likely they would incur debt.



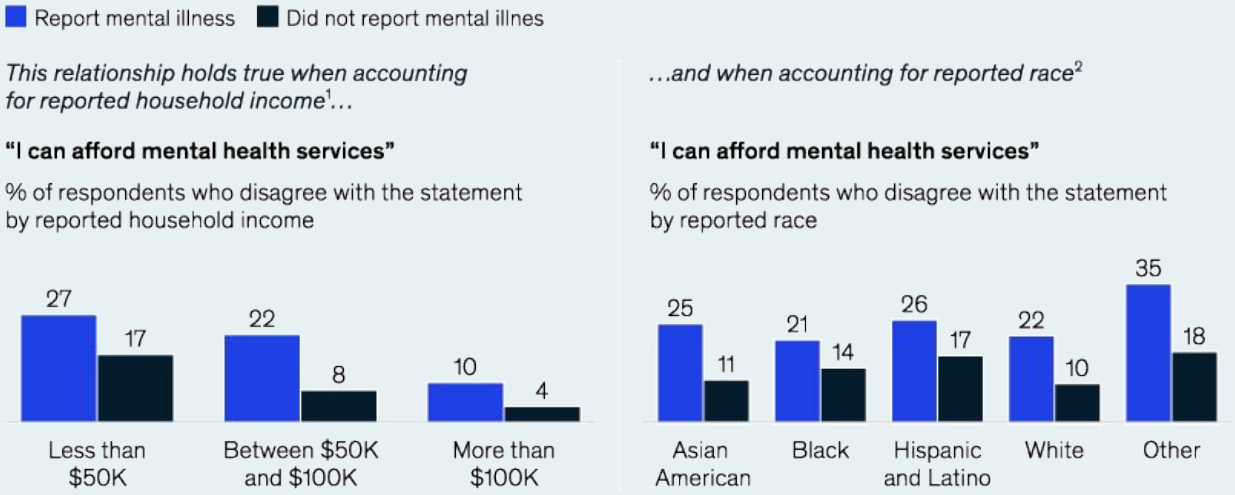
Source: McKinsey American Opportunity Survey, March 9 and April 8, 2021

McKinsey & Company

Respondents overall (including both those with and without a mental illness) report mental health services as one of the least affordable essential services.

Mental health services and childcare were listed by respondents as the least affordable among essential services (for example, nutritious food, internet, health insurance, reliable transportation). Respondents who report mental illness were two times more likely to perceive mental health services as unaffordable. Other studies have indicated that consumers are up to 40 percent less willing to pay for mental health services than services for generic physical health conditions.

Limited affordability and willingness to pay for mental health services suggests cost may be a core factor in limited access to mental health services.



[1] Less than $50K report mental illness (MI) and disagree n = 1,104, did not report MI and disagree n = 1,230; $50K–$100K report MI and disagree n = 444, did not report MI and disagree n = 473; greater than $100K report MI and disagree n = 126, did not report MI and disagree n = 146.
[2] Asian American respondents to question n = 1,404, Asian American respondents with and without reporting MI who disagree n = 180; Black respondents to question n = 2,968, Black respondents with and without reporting MI who disagree n = 457; Hispanic & Latino respondents to question n = 4,095, Hispanic & Latino respondents with and without reporting MI who disagree n = 771; White respondents to question n = 15,910, White respondents with and without reporting MI who disagree n = 2,094; Other respondents to question n = 344, Other respondents with and without reporting MI who disagree n = 80.
Source: McKinsey American Opportunity Survey, March 9 and April 8, 2021

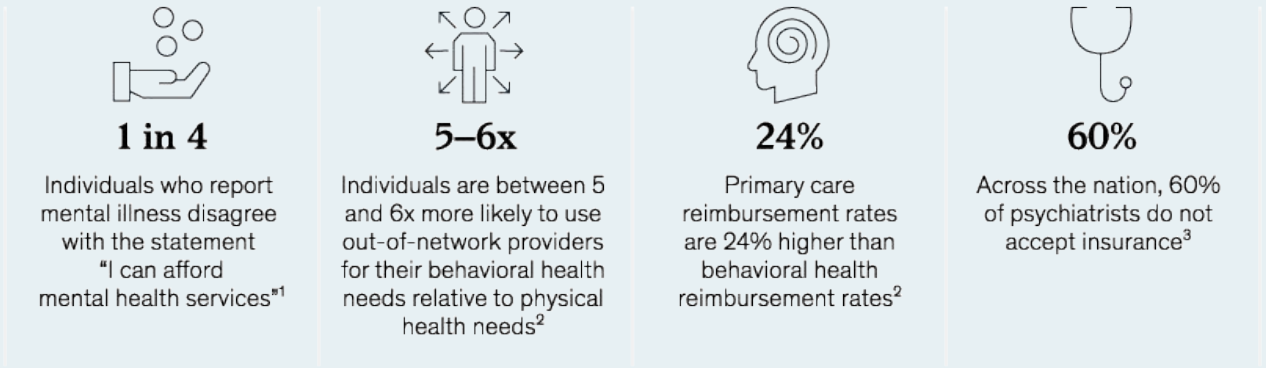
McKinsey & Company

The affordability of mental health services may be a barrier to care.

Almost a fourth of respondents reported deferring healthcare, with lack of affordable treatment ranking as the #1 reason why.

Those who report having a mental health condition but have not sought treatment for it are 60 percent more likely to declare mental health services unaffordable. This holds true when controlling for reported household income, as those who reported mental illness but have not sought treatment were still approximately 1.7 times more likely to report mental health services were unaffordable on average.

Individuals are between five and six times more likely to use out-of-network providers for their behavioral healthcare needs than for physical healthcare—which could lead to higher out-of-pocket costs. The lower-than-average in-network reimbursement rates for behavioral health providers may also lead to higher costs, with a high share of mental health providers not accepting insurance. This places more of the financial burden of mental health services on individuals.



[1] McKinsey American Opportunity Survey, March 9 and April 8, 2021.
[2] Steve Melek, Stoddard Davenport, and TJ Gray, *Addiction and mental health vs. physical health: Widening disparities in network use and provider reimbursement*, a joint report from Milliman and Mental Health Treatment and Research Institute, November 2019, milliman.com.
[3] McKinsey Vulnerable Populations Dashboard.
Source: McKinsey American Opportunity Survey, March 9 and April 8, 2021

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Untreated mental health conditions can impact people's ability to pursue education.

A study published by Mental Health America found nearly nine in ten employees report that workplace stress affects their mental health, and that nearly three in five employees feel their employer does not provide a safe environment for employees who live with mental illness, demonstrating the workplace could be a challenging setting.

Fifty-one to 54 percent of those who report mental illness disclose taking at least one day off in the last 12 months as a result of burnout or stress, as opposed to 15 to 18 percent of those who did not report mental illness.

Mental health challenges ranked prominently as barriers for pursuing educational opportunities for those with mental illness.

In going to/back to school

When asked to rank barriers to pursuing educational or training opportunities, mental health challenges ranked[1]

#3 For respondents who *did* report a mental illness

vs

#9 For respondents who *did not* report a mental illness

In entering the workforce after school

Percent of respondents who agreed that behavioral health resources impacted their decision in selecting a future employer (ie, selected very important or important), showcasing how top-of-mind behavioral health is for all employees[2]

65% For respondents who *did* report a mental illness

vs

44% For respondents who *did not* report a mental illness

[1] McKinsey American Opportunity Survey, March 9 and April 8, 2021.
[2] Behavioral Health Perceptions: Consumer Survey 2021, McKinsey.
Source: McKinsey American Opportunity Survey, March 9 and April 8, 2021

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While there are challenges, possible actions by healthcare stakeholders could help those reporting mental illness

[NOT EXHAUSTIVE]

Make care accessible

Integrate behavioral and physical health with the collaborative care model

Bolster behavioral health screening and treatment in primary care (for example, encourage measurement-based care, embed behavioral healthcare managers who provide mental health interventions—virtually or in person—as well as care management and a consulting psychiatrist)

Invest in behavioral healthcare at parity with other health conditions

Improve rate parity and network adequacy to ensure access to affordable, timely, evidence-based behavioral healthcare (for example, consider lessening the reimbursement differential[1] between behavioral healthcare and physical care, which may help bring more behavioral health providers in-network and attract more professionals to the field)

Expand equitable access to measurement-based behavioral health services

Expand provider coverage and increase access to measurement-based treatments (for example, expand provider network to include more in-network providers, support providers in understanding and using measurement-based care, offer CBT[2])

Encourage and support those who require care

Address unmet health-related basic needs

Activate home- and community-based services for a holistic approach (for example, safe housing, food, reliable transportation)

Support development of functional skills

Support efforts to equip individuals with life or functional skills (for example, financial literacy, budget management, supportive employment, supportive housing)

Strengthen community prevention

Bolster community resources toward mental health education and awareness (for example, national hotline awareness, workplace supports, mental health days)

Shift perceptions of mental illness and eliminate discriminatory behavior

Educate individuals and establish standards of inclusivity (for example, provide mental-health literacy trainings, develop guidelines for non-stigmatizing language, commit to neurodiversity)

[1] Steve Melek, Stoddard Davenport, and TJ Gray, *Addiction and mental health vs. physical health: Widening disparities in network use and provider reimbursement*, a joint report from Milliman and Mental Health Treatment and Research Institute, November 2019, milliman.com.
[2] CBT, cognitive behavioral therapy.
Source: McKinsey American Opportunity Survey, March 9 and April 8, 2021

McKinsey & Company

How employers can improve their approach to mental health at work

McKinsey

15 September, 2021

Employers benefit when they help employees to prioritize mental wellness, thereby reducing the stigma of mental-health issues, addressing disparities in their incidence and treatment, and providing support through formal structures and programs.

No one is untouched, either directly or indirectly, by mental-health issues. Even before the COVID-19 pandemic, one in four Americans over the age of 12 had a mental or substance-use disorder each year, according to the US Substance Abuse and Mental Health Services Administration. Not surprisingly, that figure has risen sharply during the long, stress-inducing COVID-19 health crisis. Our research last year found that employers had major concerns about the behavioral health and productivity of their employees. We observed many kinds of actions by employers to address this concern, and many of them are now navigating the transition back to the workplace.

In a recent webinar, Erica Coe and Kana Enomoto, coleaders of McKinsey's Center for Societal Benefit through Healthcare (CSBH), sat down with former US Surgeon General Jerome Adams, MD, and with Paul Gionfriddo, former president and CEO of Mental Health America, to discuss the current behavioral-health crisis and the imperative for employers to act on it. These leaders—all of whom have a personal connection to the topic—discuss the importance of addressing the mental health of employees, as well as the particular challenges associated first with the pandemic, and now with the return to work. The following are edited excerpts from their conversation.

Kana Enomoto: I want to start with the massive impact of COVID-19 on mental health, especially for our national workforce, as we begin transitioning back to in-person work. Our recent research on employers

shows that nine out of ten say they know that COVID-19 is having an impact on their employees by creating unprecedented anxiety and depression, and 70 percent say they're taking action. Yet our recent consumer-health survey reveals that almost half of the respondents—49 percent—anticipate that going back will have somewhat or significantly negative impacts. Going beyond the data, how have the two of you seen and thought about the mental-health implications of returning to work?

Jerome Adams: Every challenge brings with it opportunity. There are tremendous opportunities now, because of COVID-19, to rethink the workplace and the flexibility that we afford people. Awareness of mental health is the first step. The existing mental-health issues in this country were exacerbated by the pandemic and will be further amplified, for many, by the transition back to work. Employers need to take actions that make employees feel safe while also enabling them to meet their financial obligations and care for their families—two big stressors that can compound mental-health issues. Another critical step is for employers to step up because you realize not only that it's the right thing to do for your community and your employees but also that it matters to you and your economic bottom line.

And that's why I put out the first-ever surgeon general's report1 written not for a health audience but for a business audience. It points out that we are at a health disadvantage in our country: we spend more for healthcare than any other country, by far, yet get terrible results. And that's hurting us in terms of healthcare expenses, which are the number-two expense for most companies. It hurts us in terms of worker turnover. It hurts us in terms of absenteeism, decreased productivity, and workplace accidents. And you're not going to have a healthy workforce, or a healthy community to draw from, if you ignore the importance of mental health.

Paul Gionfriddo: To build on that, we know that some employees' mental health is disproportionately impacted. For example, going into

this pandemic, people believed—and continue to believe—that young people would be the most resilient and older groups would be the most fearful, but the opposite is true. Younger people are feeling the effects more deeply. As Dr. Adams pointed out, we're talking about trauma being built upon trauma being built upon other traumas. If we fail to address these successive traumas, they will continue to add up. There are countless free resources available online. Millions of people access them every year. You're not alone in looking for help and information.

Erica Coe: As our country is emerging from the pandemic, what gives you hope about our ability to overcome the challenges of mental illness and substance abuse?

Paul Gionfriddo: I see a transition taking place to something I'll just refer to as "wellness days"—the flexibility some employers are beginning to give employees to take days off when they need them, whether or not they have a diagnosable physical- or mental-health condition, and not to have those days charged against vacation time or traditional personal time. Similarly, companies have extended three-day holiday weekends to four-day weekends and given people other times off at random. What gives me hope is that employers, in particular, are recognizing that productivity can go up under those circumstances. You do not have to worry about people not working hard enough; in fact, part of the problem is people working too hard and not realizing that their productivity drops off after hour 40, 50, 70, or 80.

Everybody felt things had been so fragile this past year, and that any one of us, almost at any time, could have gotten an illness that could have killed us within a few days. It's caused people to take a few deep breaths and think about how to create work–life balance for adults and school–life balance for kids.

Jerome Adams: I have hope because, going into the pandemic, we were finally making a dent in the opioid-misuse epidemic. We created some

real momentum. We were lowering the stigma of opioid misuse and increasing the availability of naloxone. We were helping people recognize the spectrum that starts with adverse childhood experiences, early anxiety, and depression and then turns into substance misuse, which then triggers the need to connect people to treatment and then, ultimately, to long-term recovery. I'm also optimistic because COVID-19 forced a reckoning in terms of the disparate impacts that certain risk factors and diseases have on certain communities. No one can argue against that anymore, because we saw how communities of color were ravaged by COVID-19.

Telehealth visits increased from about 10,000 per week, pre-COVID-19, paid for by the Centers for Medicare & Medicaid Services [CMS], to over a million per week paid for by CMS at the peak of the pandemic. A lot of those visits were mental-health visits. We've got new tools and a new comfort level with many of those tools, and new realizations about society that I hope will be a catalyst moving forward.

Erica Coe: Stigma around mental health as compared with physical health remains a huge issue. What other perspectives can you share on this topic?

Jerome Adams: Stigma is the biggest killer out there. Stigma kills more people than cigarettes, than heroin, than any other risk factor. Because it keeps people in the shadows, it keeps people from asking for help, it keeps good people from being willing to offer help. And the way we overcome stigma is by sharing our stories as people who have mental-health issues of our own, sharing our stories as people who have overcome mental-health challenges, and sharing our stories as people who have reached out to help and embrace others who had mental-health challenges. Once we normalize mental health the way we normalize an MRI for your tweaked knee or any other medical treatment, that's when you start to see stigma come down. When you fight stigma, you can save lives.

Kana Enomoto: I want to add that Dr. Adams, as surgeon general, did so much to reduce stigma. When "the nation's doctor" is talking about mental health and addiction and substance use, it's not just a fringe issue; it's everybody's issue.

Paul Gionfriddo: Yes, when we normalize, then we address and mitigate any effects of stigma. When we leave stigma alone, it transitions quickly to discrimination, and discrimination translates quickly to lack of access and unequal services and support. That's where we have, unfortunately, too frequently allowed ourselves to go in this country and, really, in the world. And, certainly, Dr. Adams's work and Kana's work and the work of others to pull that back and move in the other direction has been essential to addressing, not so much stigma, but the way stigma lies at the heart of the dichotomy, or the dialectic, between normalization and discrimination.

Jerome Adams: There's also the question of how workplaces can support disabled employees. We know that people with disabilities of all kinds suffer higher rates of mental-health issues because of stigma that then turns into discrimination, that then turns into barriers to the ability to interact in society. Again, COVID-19 has given us an opportunity to engage people with disabilities in new ways through technology and to make the workplace more accessible to them. When we have an inclusive workplace and an inclusive society, we all benefit.

Erica Coe: Any closing thoughts on how to focus on resilience and promoting mental wellness with the goal of prevention?

Jerome Adams: For the employers that have the capacity to do this, I would encourage you to think about appointing a mental-health and wellness champion. Every single company is going to have someone who is their point person for COVID-19. And the reality is that as someone who is running an organization, you are going to be just as likely, if not more likely, to encounter problems with mental-health and wellness issues as people come back into the workplace as you are to encounter

problems with COVID-19. That's just a fact, so you should be thinking proactively about it. And if we are proactive about it at work and if we create an atmosphere where we can talk about "how can we be healthy? how can we build resilience? how can we prevent burnout?"—and not just "what do we do once someone's burned out?"—then I think we'll be in a better place.

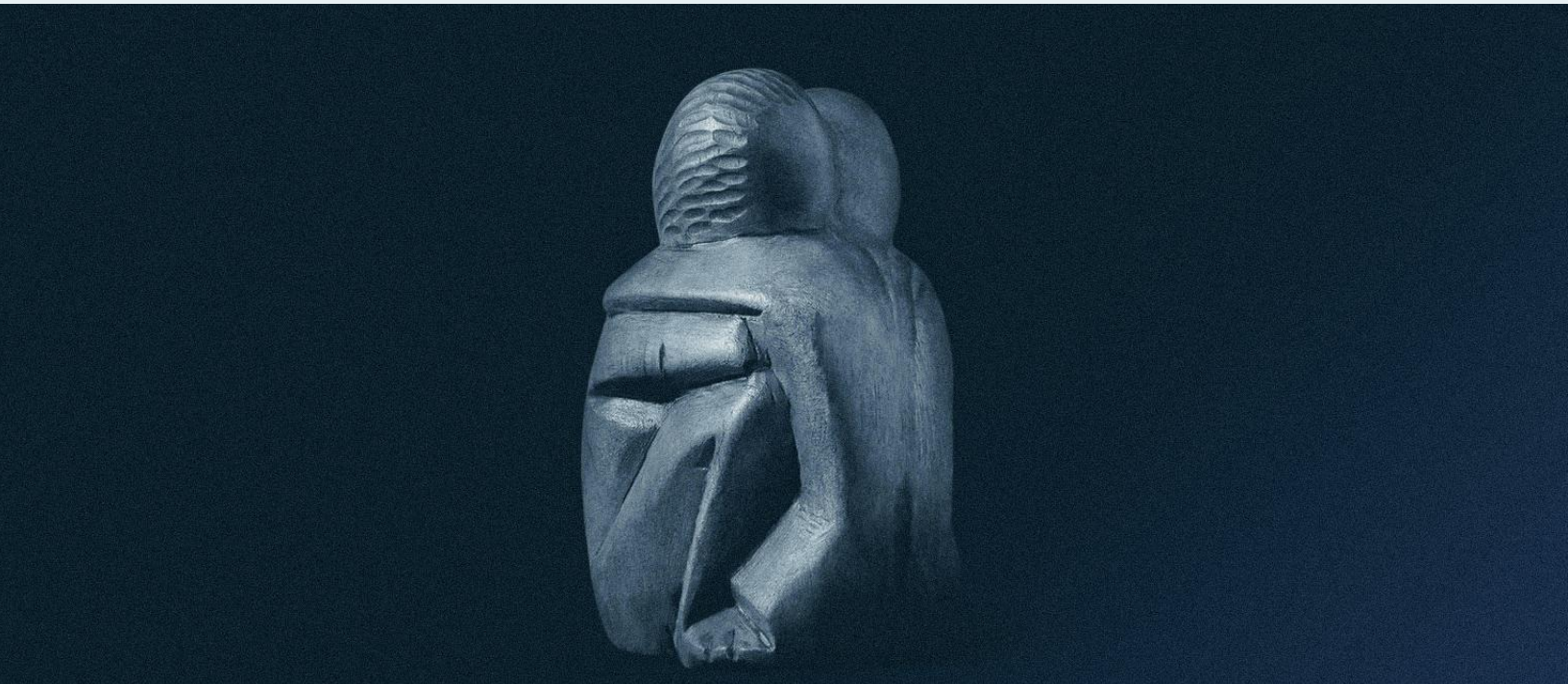
Paul Gionfriddo: If we understand that rather than one in four, this past year it was probably one in two people that had a diagnosable mental-health condition—so this is everybody's concern, this is everybody's matter, this is everybody's lives—hopefully, we will be able to move as far upstream as we can and recognize that mental health is the goal, just as overall health is the goal. There's no such thing as overall health without mental health

And so I'm hopeful that people will not wait till stage IV. We've spent too many years, too many generations, waiting till crises have occurred to say, "OK, now we need to address our mental-health challenges and our challenges to mental health." And I do think we have the opportunity here because we have the attention of the public, we have the attention of the media, we have the attention of policy makers. We need to make use of that and drive change right now because this is our opportunity.

Overcoming stigma: Three strategies toward better mental health in the workplace

McKinsey

23 July, 2021



Employees are worried about their mental health as they return to the workplace after the COVID-19 pandemic. Stigma can exacerbate their concerns, but employers can thwart its impact.

The COVID-19 pandemic has taken a heavy toll on the global psyche. Today, as the world moves toward the end of the pandemic, almost one billion people have a mental-health or substance-use disorder —collectively referred to as behavioral-health conditions. As companies prepare for a postpandemic return to the workplace, identifying behavioral-health conditions and offering the necessary support for employees affected by them should be a top C-suite priority.

While most employers report that they are serious about employees' mental health, many haven't confronted one critical challenge: stigma. Using data from two recent US surveys conducted by McKinsey's Center for Societal Benefit through Healthcare, this article takes a deep look at stigma in the workplace and its role in exacerbating behavioral-health conditions and driving down an employee's self-worth and productivity. This is a widespread problem with serious implications. The good news is that employers are in a unique position to address stigma—especially during the short postpandemic window when many organizations are evolving their operations for the new reality of hybrid work.

Stigma and its impact

In behavioral health, "stigma" is defined as a level of shame, prejudice, or discrimination toward people with mental-health or substance-use conditions. Because of stigma, such conditions are often viewed and treated differently from other chronic conditions, despite being largely rooted in genetics and biology. Stigma affects everything from interpersonal interactions to social norms to organizational structures, including access to treatment and reimbursement for costs.

The National Academy of Medicine defines three primary forms of stigma, each of which can have far-reaching and harmful effects:

+ Self-stigma occurs when individuals internalize and accept negative stereotypes. It turns a "whole" person into someone who feels "broken." As one employee told us, "Depression can be a terrible illness. It makes you feel worthless and without a purpose."
+ Public stigma (which is sometimes referred to as social stigma) is the negative attitude of society toward a particular group of people. In the case of behavioral-health conditions, it creates an environment in which those with such conditions are discredited, feared, and isolated. As an employee explained, "There is such a stigma against mental-health disorders. But if you don't talk about it, you suffer alone."
+ Structural stigma (including workplace stigma) refers to system-level discrimination—such as cultural norms, institutional practices, and healthcare policies not at parity with other health conditions—that constrains resources and opportunities and therefore impairs well-being. "The number-one challenge I face is finding [healthcare] providers," one employee told us. "It's a problem for me, for my wife, and for my kids."

The impact of stigma can be profound. At a time when people are at their most vulnerable and most in need of help, stigma prevents them from reaching out. This terrible paradox can deepen an illness that is often invisible to others. Evidence-based, effective treatments that allow people with behavioral-health conditions to live productive and fulfilling lives exist. Stigma creates a cloud of shame and uncertainty that obscures what could be a clear path to recovery

Our analysis of our two surveys substantiates that impact. For example, many employees with a behavioral-health condition indicated that they would avoid treatment because they didn't want people finding out about their mental illness (37 percent) or substance-use disorder (52 percent).

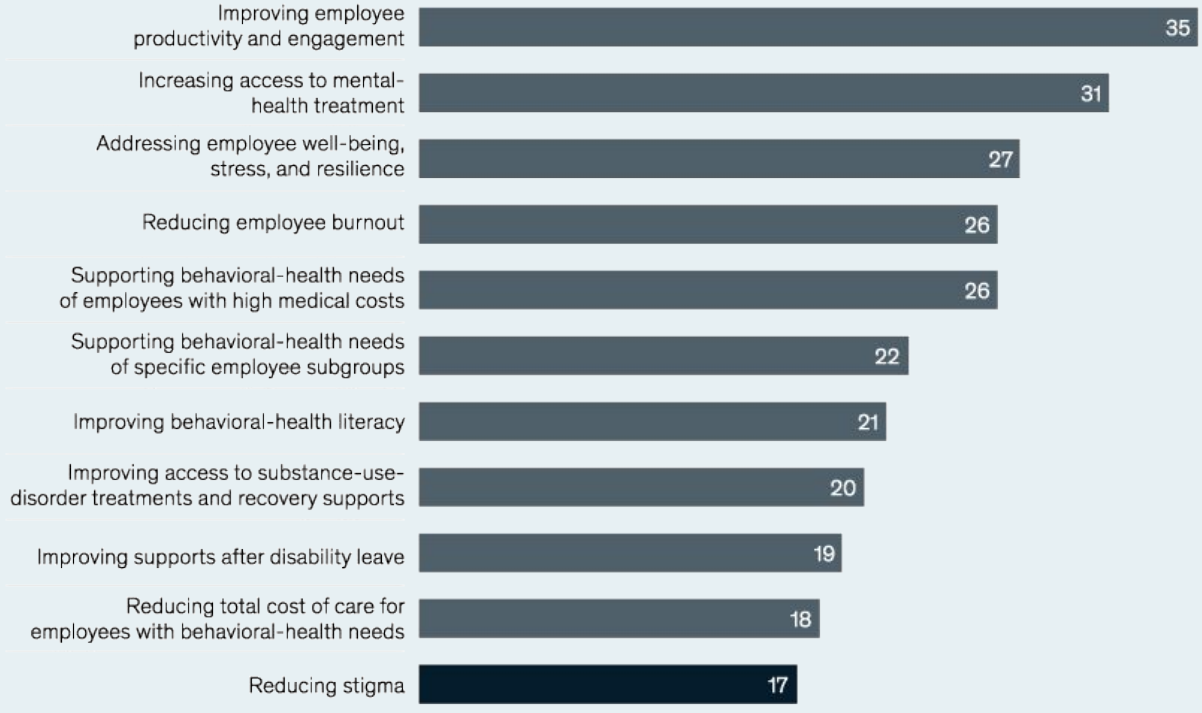
Stigma was also associated with lower workforce productivity. Close to seven in ten respondents with high self-stigma levels reported missing at least a day of work because of burnout or stress.

Opportunity for employers to address stigma

There is a pronounced disconnect between employer and employee perspectives on stigma in the workplace. While some 80 percent of the full-time-employed individuals we queried indicated that they believed that an antistigma or awareness campaign would be useful, only 23 percent of employers reported having implemented such a program. Further, when employers were asked to prioritize 11 potential behavioral-health-focused initiatives, they ranked stigma reduction last (Exhibit 1).

Stigma ranks last when employers list their top mental-health priorities.

Top behavioral-health priorities,[1] % of respondents indicating as a top 3 priority (n = 289)



[1]Question: Respondents selected their organization's top 3 behavioral-health priorities for 2021 from the list above.
Source: McKinsey Health Employer Survey, 2020

McKinsey & Company

Yet 75 percent of the same employers acknowledged the presence of stigma in their workplaces. They know that their employees are afraid to speak up about behavioral-health needs. In fact, many leaders admit that they themselves may not be comfortable asking for help. So why aren't they acting on what they know?

While companies may shy away from stigma because they imagine that it is too abstract to address, they are, in fact, missing an enormous opportunity. Employers can't solve every aspect of substance-use disorders and mental illnesses in their workplaces. But stigma is something that they actually can change. Taking the right kind of actions can shift the dialogue from stigma to support.

The short window of time when organizations are evolving their operations for post-pandemic life is the perfect moment to act. Understanding, prioritizing, and planning for employees' postpandemic mental health should be part of every company's strategy for returning to the workplace. An inclusive culture and equitable benefits can lead to earlier, more effective intervention and support for people with behavioral-health conditions. Addressing stigma as a collective responsibility across three levels—organizational systems, leaders, and peers and teammates —will make those plans far more effective and help ensure the long-term health and commitment of the workforce.

Strategies for reducing stigma in the workplace

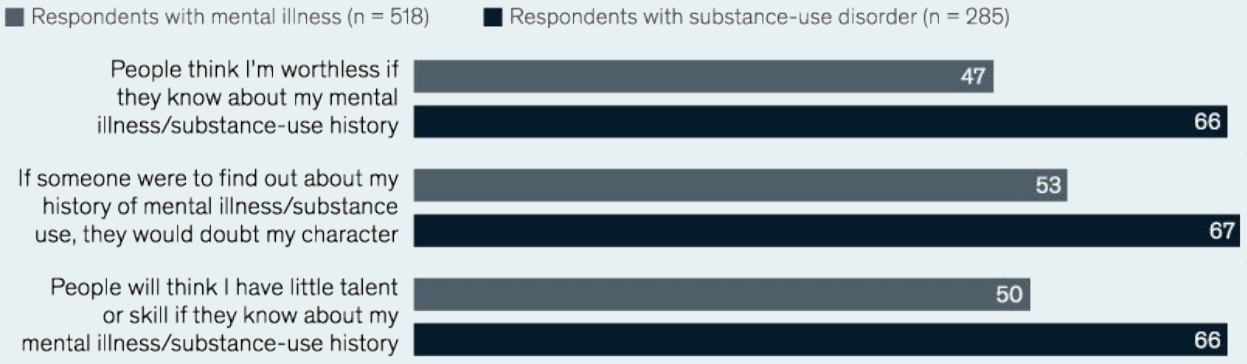
We understand that stigma can seem like a vague concept and an insurmountable challenge for employers. We also know that attitudes toward stigma can vary by demographics and other factors, making it harder to address effectively without a tailored approach. Nevertheless, those employers that have addressed stigma have modeled approaches that can work across a variety of populations. Blending their experiences and the lessons from our research, here are three overarching strategies that can help dismantle the stigma associated with behavioral-health conditions in the workplace.

Shift the perception of mental illness and addiction

For starters, employers can change the misperception that a behavioral-health condition is a moral failing. These conditions are treatable diseases like other medical conditions. In our survey, a significant percentage of employees with behavioral-health conditions reported feeling “ashamed” or “out of place in the world” because of their conditions. Many respondents expressed worry that people would think they were worthless, or had serious character flaws, if their behavioral-health condition was known (Exhibit 2). As one employee told us, “I had a strong sense of shame, and upper management did not talk to me at all. They acted as if nothing had happened, even though the reason I had to take a leave from work was because of work-driven anxiety.” Many respondents were also concerned that colleagues who knew about their illness would doubt their talents or skills.

People with behavioral-health issues believe they are stigmatized by colleagues.

Perceptions reported by employees with behavioral-health conditions, by condition type, % of respondents agreeing with statement[1]



[1]Respondents who answered “agree strongly” or “agree slightly.” Respondents who answered “disagree strongly,” “disagree slightly,” “neither agree nor disagree,” “don’t know/not sure,” or “prefer not to say” are not shown.
Source: McKinsey Mental Health Consumer Survey, 2020

McKinsey & Company

Companies can't shift perceptions of mental illness by fiat. Instead, they need targeted programs that educate people and promote supportive teams. These direct actions can mitigate harmful sentiments across the company:

+ Provide mental-health-literacy training to all employees. Programs such as Mental Health First Aid or Just Five can help people recognize and respond to behavioral-health challenges in the workplace. This kind of training spreads the message that mental and substance-use disorders are treatable conditions for which prevention, early-intervention, treatment, and recovery support can allow people to live healthy and fulfilling lives.

+ Train leaders and managers to recognize signs of distress. If team leaders are educated to understand behavioral-health issues, they will be able to spot problems early and connect colleagues with available and appropriate supports. This kind of tangible support can reduce the stigma that may inhibit colleagues from asking for help.

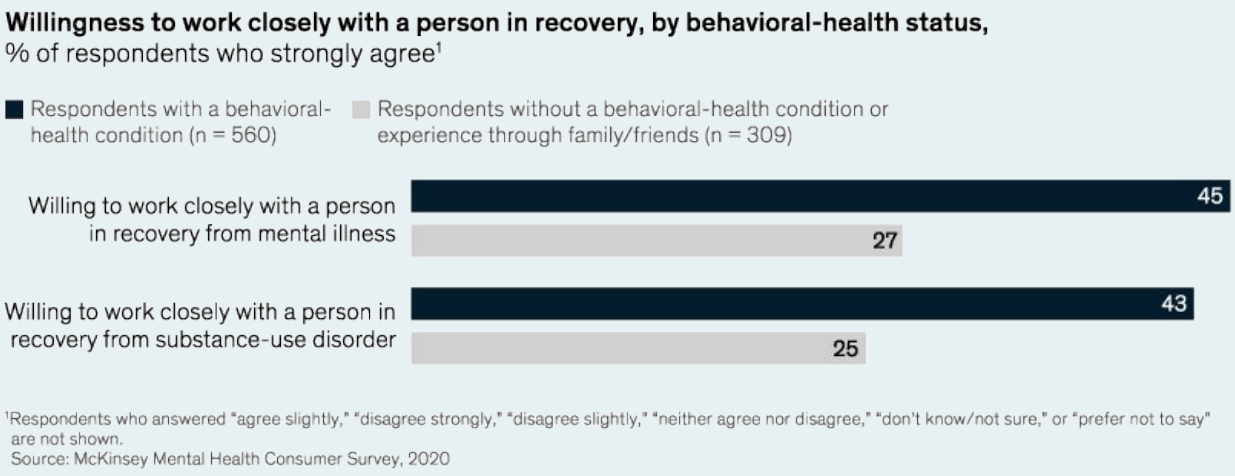
+ Use contact-based-education strategies. An evidence-based approach to education allows individuals with stigmatized conditions to humanize them by sharing their stories. Encourage leaders to share their experiences with behavioral-health challenges. This often-undertapped channel (only 24 percent of employers reported using their C-suites to communicate about mental health) can have a powerful impact across a company.

Eliminate discriminatory behavior

Not surprisingly, most employers agree that behavioral-health conditions should be treated with the same urgency, skill, and compassion as other medical conditions (for example, diabetes) are. Yet many employees still face prejudice in the workplace. "At my employer, there is a stigma associated with seeking out help and speaking about mental illness,"

said one employee. “Maybe that’s because many workplace practices here are the reason many people feel anxious, stressed, and depressed.” Among our survey respondents, the great majority with mental illness (65 percent) or substance-use disorders (85 percent) perceive stigma in the workplace—and for good reason. Respondents who had little experience with behavioral-health conditions were far less likely to be strongly willing to work with a person in recovery compared with individuals with a mental or substance-use disorder (Exhibit 3). However, over a third of respondents who had little experience with behavioral-health conditions reported being somewhat willing, indicating a potential opportunity to reduce stigma among a substantial part of the workforce.

Few employees want to work closely with someone who has had behavioral-health issues.



[1]Respondents who answered “agree slightly,” “disagree strongly,” “disagree slightly,” “neither agree nor disagree,” “don’t know/not sure,” or “prefer not to say” are not shown.
Source: McKinsey Mental Health Consumer Survey, 2020

McKinsey & Company

Policies and practices to create a culture free from discrimination are now considered “table stakes.” Employers should look closely at their workplace cultures, and many may well need to take concrete steps to ensure that their workplaces are inclusive and supportive environments as they commit to treating people with mental-health and substance-use

disorders with dignity and respect. Here are some potential actions they can take to curtail discriminatory behavior:

+ Commit to using nonstigmatizing language across internal and external communications. For example, using person-first language that emphasizes a person's humanity reduces stereotypes. Making the effort to call someone a "person with a substance-use disorder" instead of an "addict" replaces a negative stereotype with acceptance.
+ Include neurodiversity (including behavioral-health conditions) as part of an expanded diversity, equity, and inclusion agenda. Creating a supportive workplace with widely available flexibility and customization is a significant way to help people with behavioral-health conditions—disclosed or undisclosed—overcome barriers.
+ Promote a psychologically safe culture. Think about rewarding an athlete mindset instead of instilling some kind of hero complex. Prioritize mental wellness as critical for peak performance instead of rewarding overwork at the expense of rest and renewal.

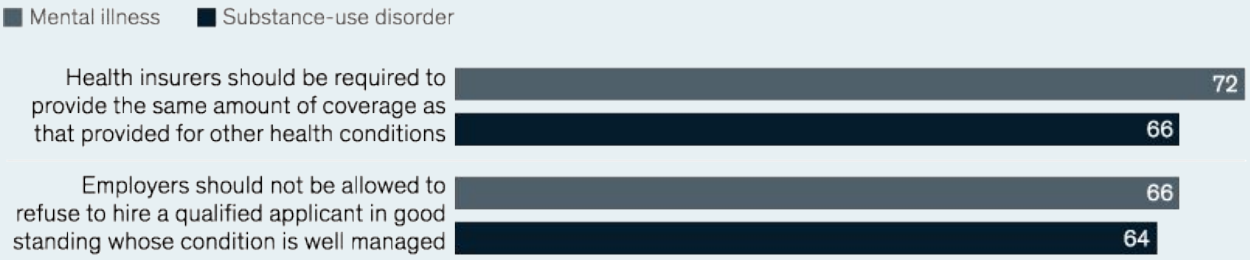
Strive to ensure parity among the mental- and physical-health benefits offered

The majority of employees want their employers to ensure parity in the health plans, employee-assistance programs, and other support programs offered (Exhibit 4). Making it happen wouldn't just be a symbolic move by employers. It would be, in fact, one of the most tangible things they could do for their workforces. As one employee reported, "Getting behavioral-health services can be incredibly challenging. It leaves me feeling very alone."

Exhibit 4

Most employees support equitable benefits and hiring practices for people with behavioral-health issues.

Sentiments on parity for employees with behavioral-health conditions, by condition type, % of respondents who agree[1] (n = 988)



[1]Respondents who answered "agree strongly" or "agree." Respondents who answered "disagree strongly," "disagree," "neither agree nor disagree," "don't know/not sure," or "prefer not to say" are not shown.
Source: McKinsey Mental Health Consumer Survey, 2020

McKinsey & Company

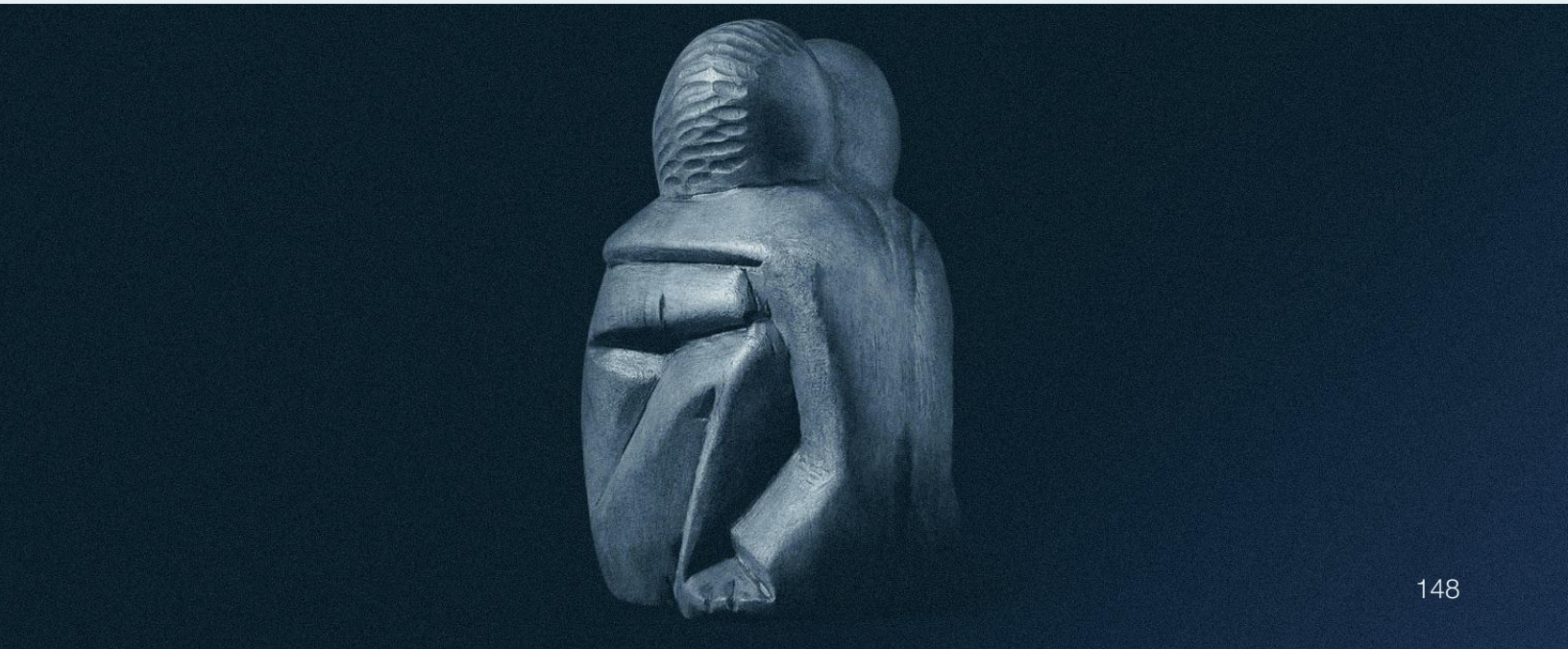
Offering true parity in employee-support programs takes work. Companies have to check regularly to make sure that they are actually offering what they say they offer. Stigma makes the issue even more important. It takes a lot of confidence for a person to be willing to even ask for help in the first place. If they come across barriers to access, their perceptions of stigma may drive them to simply give up rather than press harder for help. One employee told us, “I got a referral for my mental illness through my employee-assistance program back in February, but the provider they referred me to was not accepting new clients. It took a lot to seek that referral, and I haven’t taken the time to request another one.”

Here are some potential actions employers can take to drive the parity of mental- and physical-health benefits they offer:

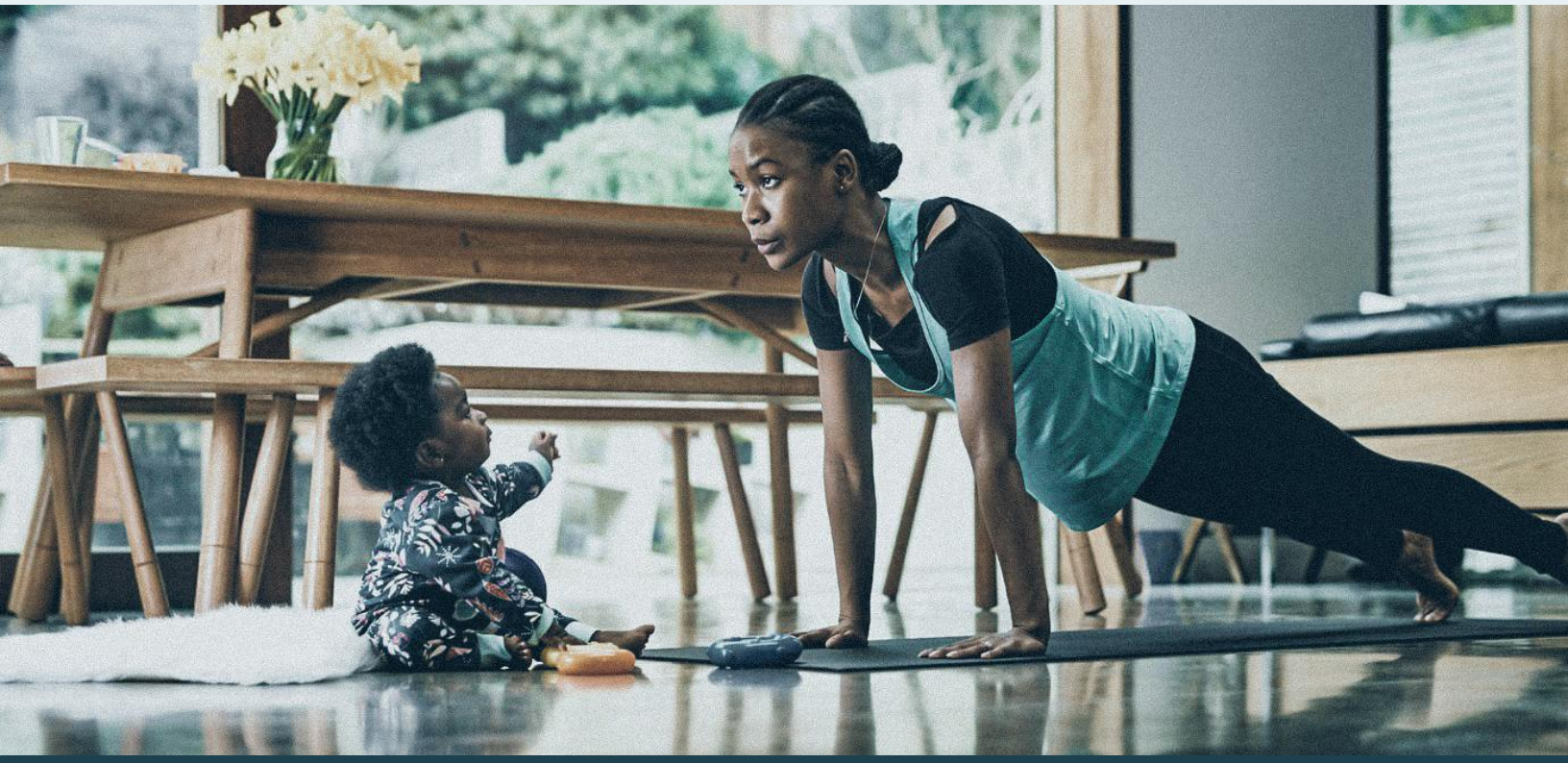
+ Guarantee and widely communicate on parity. Employers can instill parity in policies (for example, return-to-work policies for individuals with behavioral-health conditions), benefits (for example, access to care and lower out-of-pocket costs), and workplace programs. They can triple-check that policies and benefits regarding behavioral-health conditions are fully aligned and then amplify and explain their availability. Parity assessments help employers benchmark the current state of their benefits and identify areas for improvement.
+ Ensure equity in leadership priorities. Employers can designate and empower leaders to make mental health a priority throughout their organizations. Our survey results suggest that only 39 percent of organizations have appointed an executive-level leader who is responsible for overseeing the organization's behavioral-health portfolio. Employers can also deepen measurement and accountability for behavioral-health outcomes, as they would for any other organizational priority. Less than half of employers reporting that they hoped to improve mental-health outcomes said they were actually measuring results.

Fewer than one in ten employees describe their workplace as free of stigma on mental or substance-use disorders. As anxious employees return to the workplace and organizations adjust to new realities after the COVID-19 pandemic, organizational systems and behaviors of leaders and employees need to change. Companies have a unique opportunity to replace negative attitudes and discriminatory policies with healthier attitudes and policies that can improve the well-being of their people.

Promoting behavioral-health literacy, creating an inclusive culture, and making mental health a clear organizational priority are no-regret moves, especially at a time when the battle for talent is getting tougher. By reducing stigma and increasing support, employers can mitigate the human, organizational, and economic costs of the pandemic-driven rise in mental illnesses and substance-use disorders



Bloomberg New Economy Forum



Prioritizing Health

Knowledge Partner

McKinsey & Company

Prioritizing health: A prescription for prosperity

McKinsey

8 July, 2021

Could 65 be the new 55? Each year, poor health takes a heavy societal and economic toll. Improving the health of the world's population would add 10 healthy years in midlife—and much more.

The COVID-19 pandemic is an unwelcome reminder of just how much health matters for individuals, society, and the global economy. For the past century or more, health improvements from vaccines, antibiotics, sanitation, and nutrition, among others, have saved millions of lives and been a powerful catalyst for economic growth. Better health promotes economic growth by expanding the labor force and by boosting productivity while also delivering immense social benefits. However, in recent years, a focus on rising healthcare costs, especially in mature economies, has dominated the policy debate, whereas health as an investment for economic return has largely been absent from the discussion.

As the whole world reimagines public health and rebuilds its economy, we have a unique opportunity not merely to restore the past but to dramatically advance broad-based health and prosperity.

In Prioritizing health: A prescription for prosperity, we measure the potential to reduce the burden of disease globally through the application of proven interventions across the human lifespan over two decades. By intervention, we mean actions aimed at improving the health of an individual. These range from public sanitation programs to surgical procedures and adherence to medication and encompass interventions recommended by leading institutions like the World Health Organization or national medical associations. We also examine the potential to reduce the disease burden from innovations over the same period.

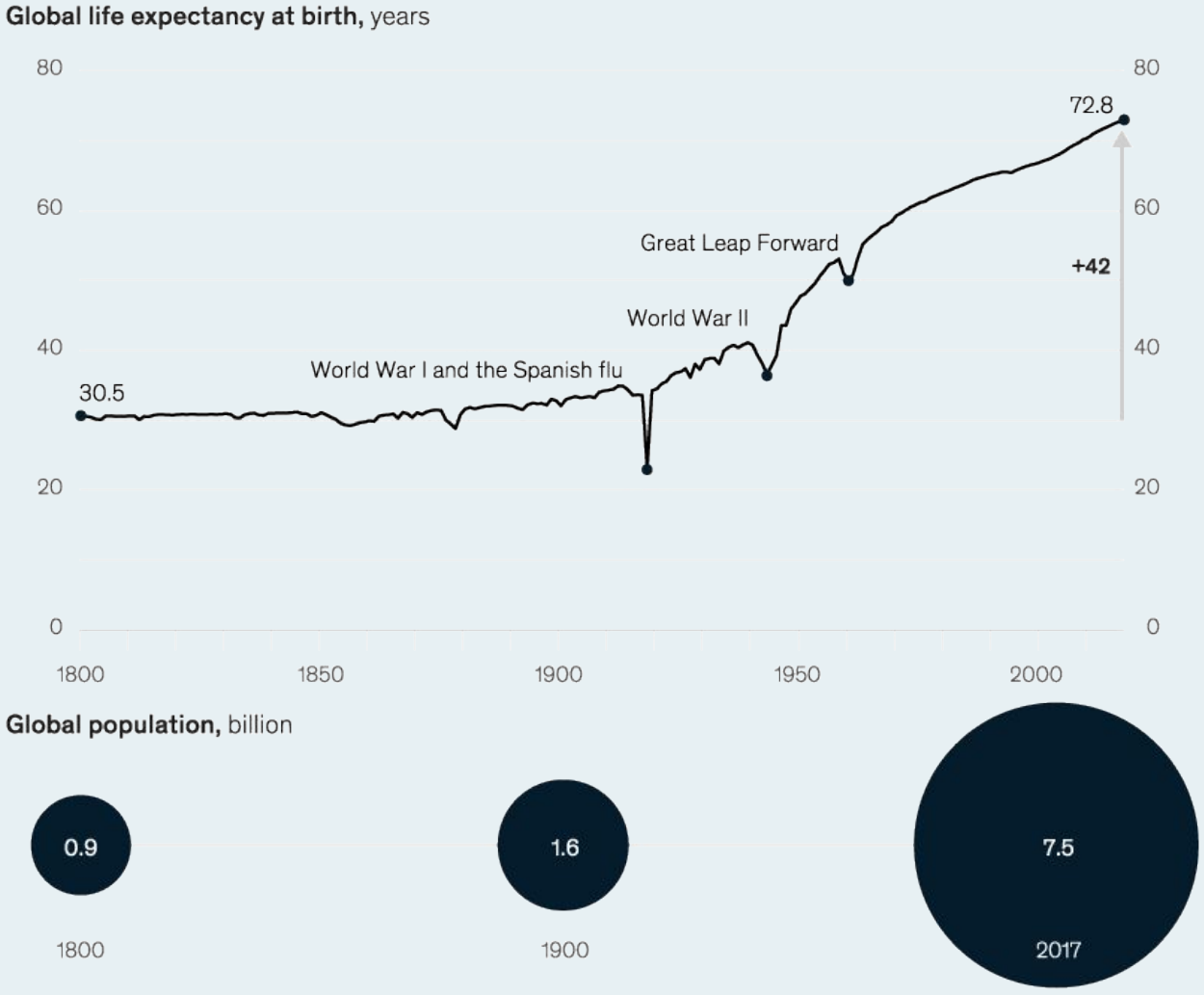
We then determine the impact the disease burden reduction could have on population health, the economy, and wider welfare over the period to 2040 (see sidebar, “Our research methodology”). We conduct our analysis for almost 200 countries; our global, regional, and income-level analyses are aggregated from the country-level analysis.

Throughout this report, we often use short hand to refer to the disease burden reduction potential as the healthy growth scenario. This scenario is an aspirational yet realistic assessment of the range of interventions that could lead to meaningful health improvement at the population level and boost long-term global economic growth.

Health as a catalyst for growth

Over the past century, improved hygiene, better nutrition, antibiotics, vaccines, and new technologies have contributed to tremendous progress in global health (Exhibit 1). Recent innovations have led to dramatic improvements in survival rates for people with certain types of cancer, heart disease, and stroke in many countries. Improvements in health have extended lives and improved quality of life, contributing to the rapid expansion of the labor force and labor productivity in the second half of the 20th century, which were key factors behind strong economic growth over that period. As countries grew richer, they invested in better food and safer environments, creating a virtuous cycle of improved health and higher incomes. Economists estimate that about one-third of economic growth in advanced economies in the past century could be attributed to improvements in the health of global populations. Research focused on more recent years has found that health contributed almost as much to income growth as education.

As health improved in the 20th century, life expectancy more than doubled and the global labor force expanded.



Source: Gapminder.org; McKinsey Global Institute analysis

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Despite the progress of the past century, in a typical year, poor health and health inequity continue to limit economic prosperity. This plays out in two ways. First, premature deaths limit growth by reducing the size of the potential labor force. Over 17 million people lost their lives prematurely in 2017. Second, poor health or morbidity makes it hard for those suffering from health conditions to be economically active and

realize their full productive potential. For example, a total of 580 million person-years was lost to poor health among those aged 15 and 64 in 2017, leading them to be absent from work or quit employment altogether.

Overall, we estimate that the cost of ill health was more than $12 trillion in 2017, about 15 percent of global real GDP. Health shocks such as the COVID-19 pandemic, H1N1 influenza, and SARS can result in additional humanitarian and economic costs. The COVID-19 pandemic and its repercussions, such as the shelter in place measures to control the spread of the virus, are forecast to reduce global GDP by 3 to 8 percent in 2020.

Health has not typically been part of economic-growth discussions, especially in developed countries where the recent debate has primarily focused on the cost of healthcare. But a number of trends suggest that health may well matter more for growth in coming decades. First, improving health can counter the drag on growth that result from slowing population growth. Labor force growth globally is expected to slow from an annual rate of 1.8 percent over the past 50 years to 0.3 percent in the next 50 years. At the same time, the demand for highly skilled knowledge workers is increasing.

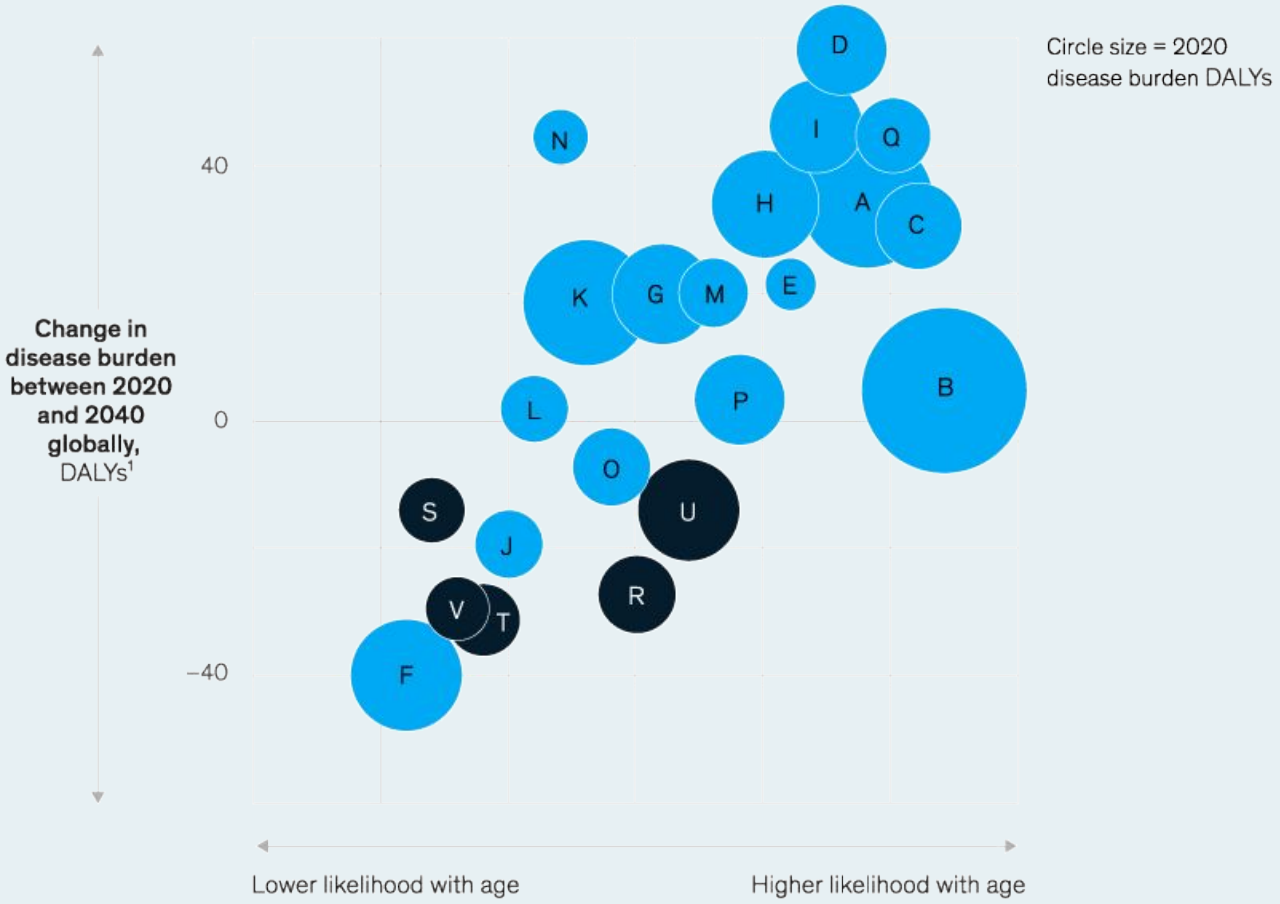
Improved health can help counter these longer-term headwinds by extending healthy lifespan for workers of prime working age and older, and by developing the physical and cognitive ability of children, the future labor force of the world. Second, health is no longer improving in all regions because obesity-related conditions and mental health challenges are burdening people of all ages, including those of prime working age. In addition, persistent and in many cases growing health inequity creates a gap in health outcomes between rich and poor within societies. Third, healthier populations are more resilient in the face of new infectious diseases, like COVID-19, that can often present higher risks to people with existing health conditions.

What would it take to improve the world's health?

The Institute for Health Metrics and Evaluation (IHME), the institution that maintains the leading database on the global disease burden, projects that the global disease burden (measured in disability adjusted life years known as DALYs) will decline at a slower rate that in the past. This particularly applies to mature economies where the population is aging and faces more age and income-related health conditions as diabetes, cardiovascular disease, and some cancers. However, greater health gains are expected in low-income countries, many of which lag behind higher-income countries in life expectancy and other measures of health, mainly from preventable and treatable causes such as diarrhea and malaria, nutritional disorders, and poor child and maternal health (Exhibit 2).

Looking ahead, incidence of age- and lifestyle-related diseases is expected to rise while many infectious diseases could decrease significantly.

Global baseline disease burden forecast



- Other diseases
  - A Cancers
  - B Cardiovascular disease
  - C Chronic respiratory disease
  - D Diabetes and kidney disease
  - E Digestive disease
  - F Maternal and neonatal disorders
  - G Mental-health disorders
  - H Musculoskeletal disorders
  - I Neurological disorders
  - J Nutritional deficiencies
  - K Other noncommunicable diseases
  - L Self-harm and interpersonal violence
  - M Skin and subcutaneous disease
  - N Substance-use disorders
  - O Transportation injuries
  - P Unintentional injuries
  - Q Vision and hearing loss
- Infectious diseases
  - R Diarrhea and intestinal infections
  - S HIV/AIDS and sexually transmitted diseases
  - T Neglected tropical disease and malaria
  - U Respiratory infections and tuberculosis
  - V Other infectious diseases

[1]DALY = disability-adjusted life year.
Source: Global Burden of Disease Database 2016, Institute for Health Metrics and Evaluation, used with permission, all rights reserved; McKinsey Global Institute analysis

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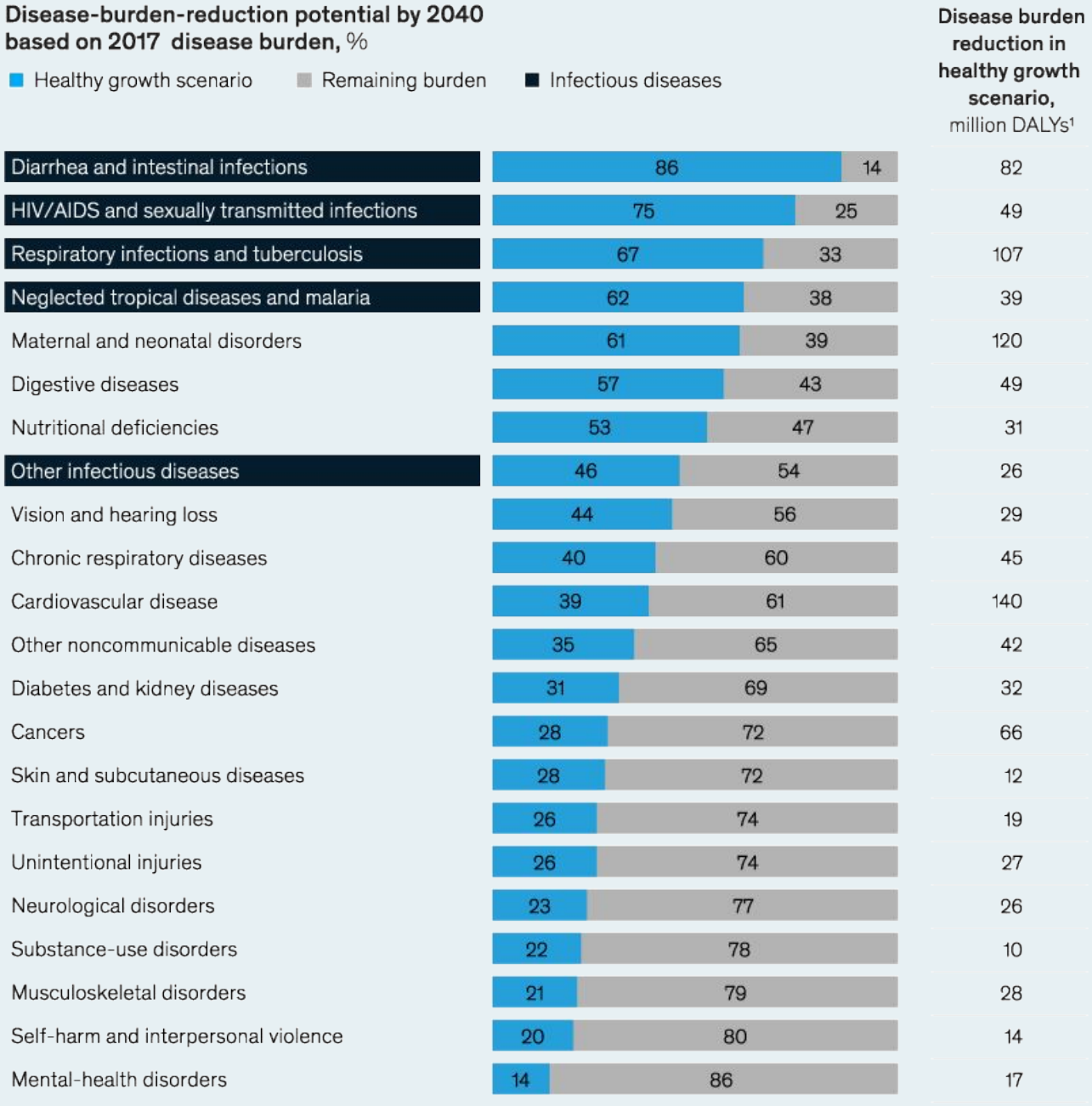
We estimate that the global disease burden could be reduced by about 40 percent by applying known interventions in broader segments of populations and with closer adherence to the most effective tools available.

A reduction in the global disease burden of this magnitude would deliver significant health benefits. Child mortality could drop by 65 percent by 2040. Cancer deaths could decline by 29 percent, cardiovascular disease deaths by 39 percent, and neglected tropical diseases and malaria deaths by 62 percent. Overall, 230 million more people would be alive in 2040, half of them under the age of 70. For people at middle age, the shift could extend the number of years in good health by a decade, essentially making 65 the new 55. Every region in the world would experience an improvement in this range.

While we find that the overall potential to improve global health is substantial, known interventions vary widely in their capacity to battle specific diseases (Exhibit 3). Over 70 percent of the health gains could be achieved from prevention by creating cleaner and safer environments, encouraging healthier behaviors and addressing the social factors that lie behind these, as well as broadening access to vaccines and preventive medicine. The remaining 30 percent would come from treating disease and acute conditions with proven therapies including medication and surgery.

The potential to reduce the disease burden varies significantly by disease type; chronic conditions are more challenging to tackle.



[1]DALY = disability-adjusted life year.
Source: Global Burden of Disease Database 2017, Institute for Health Metrics and Evaluation, used with permission, all rights reserved; McKinsey Global Institute analysis

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To identify interventions with the highest health benefit at the lowest cost we use cost curves. Over all, we find that over 40 percent of health improvements can be achieved at a net cost of less than $100 for every additional healthy life year. Because the costs of delivering better health vary widely, we estimate them separately for four country income archetypes. In low-income countries, we find the most cost-effective interventions (lowest incremental cost of reducing ill health by 1 DALY) include childhood immunizations, prevention and treatment of malaria, safe childbirth, better nutrition, and cardiovascular disease prevention.

In lower-middle-income countries, we find midwife-assisted safe childbirth could deliver 1 percent of the total addressable disease burden for 0.1 percent of the total additional costs. Treatment for malaria and TB, and prevention of cardiovascular disease with support and education for lifestyle change and pharmacological prevention are also very important. In upper-middle- and high-income countries, the greatest health improvement could come from increased use of preventive strategies for cardiovascular disease and diabetes including weight management, smoking cessation, and prevention and treatment of substance-use disorders and low back pain, which includes supported behavior change and weight management.

What role does innovation play?

Today's interventions are the innovations of the past. Without them, healthy lifespans would not be as long as they are. Innovation continues to be critical to tackle diseases without a known cure as well as help us increase uptake and adherence to interventions we know work (about 60 percent of the remaining disease burden in our analysis). Leading the list of diseases without a known cure are mental health and neurological disorders, cardiovascular disease, and cancers. The good news is that innovations that completely change the lives of patients continue to emerge and prove the continuing power of innovation. One example is the nearly 70 percent reduction in premature death due to chronic

myeloid leukemia in Switzerland from 1995 to 2017.

We identify ten promising innovations in progress that could have a material impact on health by 2040. We determined these technologies by focusing on areas with the greatest combination of unmet need, biological understanding of the disease pathway, and the effort and excitement surrounding each, measured by funding. While identifying and sizing the potential scope of innovations in the pipeline is inherently difficult, we estimate that these technologies have the potential to reduce the disease burden by a further 6 to 10 percent, assuming aspirational yet realistic adoption rates by 2040, on top of the 40 percent from known interventions.

Not only could some of these innovations be fully curative for some diseases, but by tackling the underlying biology of aging, they could significantly extend healthy lifespan by postponing the onset of several age-related conditions. This contrasts with innovations of the past 30 years, many of which reduced symptoms or delayed disease progression while prevention and cures were rare. Additionally, the innovations we have identified here are more digitally-enabled than in the past. As an example, artificial intelligence (AI) systems make advances in omics and molecular technologies, such as gene editing, faster and more accurate.

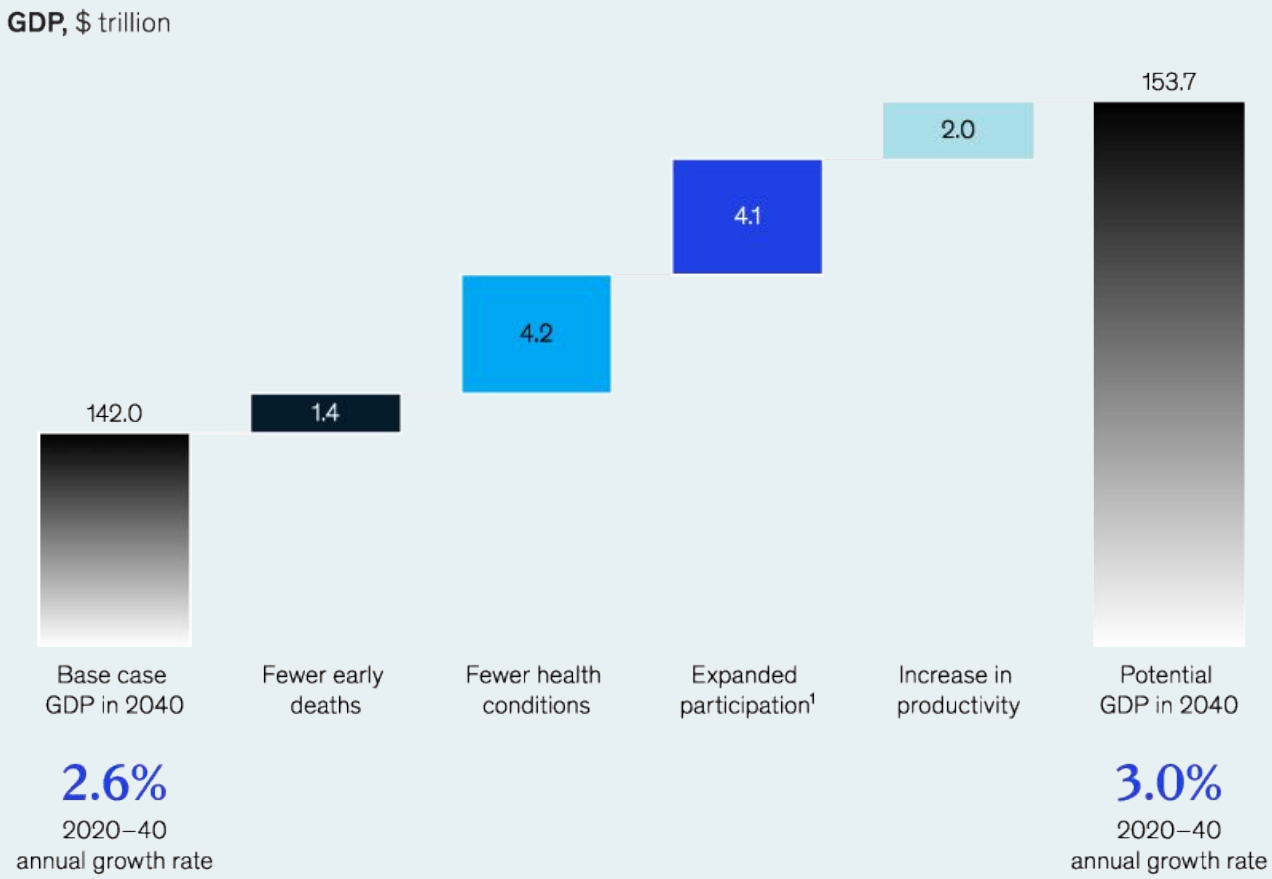
Realizing these innovations will require continual investment in research and development across pharmaceutical companies, medical and other technology companies, and academia.

How large is the economic prize?

The economic benefits from the health improvements we size are substantial enough to add $12 trillion or 8 percent to global GDP in 2040, that translates into 0.4 percent faster growth every year (Exhibit 4). These benefits arise through the labor market, both by expanding future employment through fewer early deaths, fewer health conditions, and higher labor-force participation of healthier people and through the

productivity gains achievable by workers who are physically and cognitively healthier.

Global GDP could rise by about $12 trillion in 2040, an 8 percent increase, from fewer health conditions and expanded participation in the labor force.



[1]Includes impact on older adults (only high- and upper-middle-income countries), informal caregivers (only in OECD), and people with disabilities (global).
Source: Eurostat; ILOSTAT; Institute for Health Metrics and Evaluation; National Transfer Accounts project; Oxford Economics; Organisation for Economic Co-operation and Development; McKinsey Global Institute analysis

McKinsey & Company

By 2040, 245 million more people could be employed. About 60 million of them would have avoided early death from cardiovascular disease, cancers, malaria, and other causes, adding $1.4 trillion to 2040 GDP. Addressing mental health disorders, diabetes, or other conditions would

no longer be a barrier to joining the labor force for an equivalent of about 120 million full-time workers, contributing an additional $4.2 trillion. Another $4.1 trillion could be unlocked by expanding labor-force participation among three groups: older populations for whom better health can be an opportunity to work longer (about 40 million people), informal caregivers who no longer need to care for loved ones (12 million people), and people with disabilities who can go to work because workplaces adapted to accommodate their needs (eight million people).

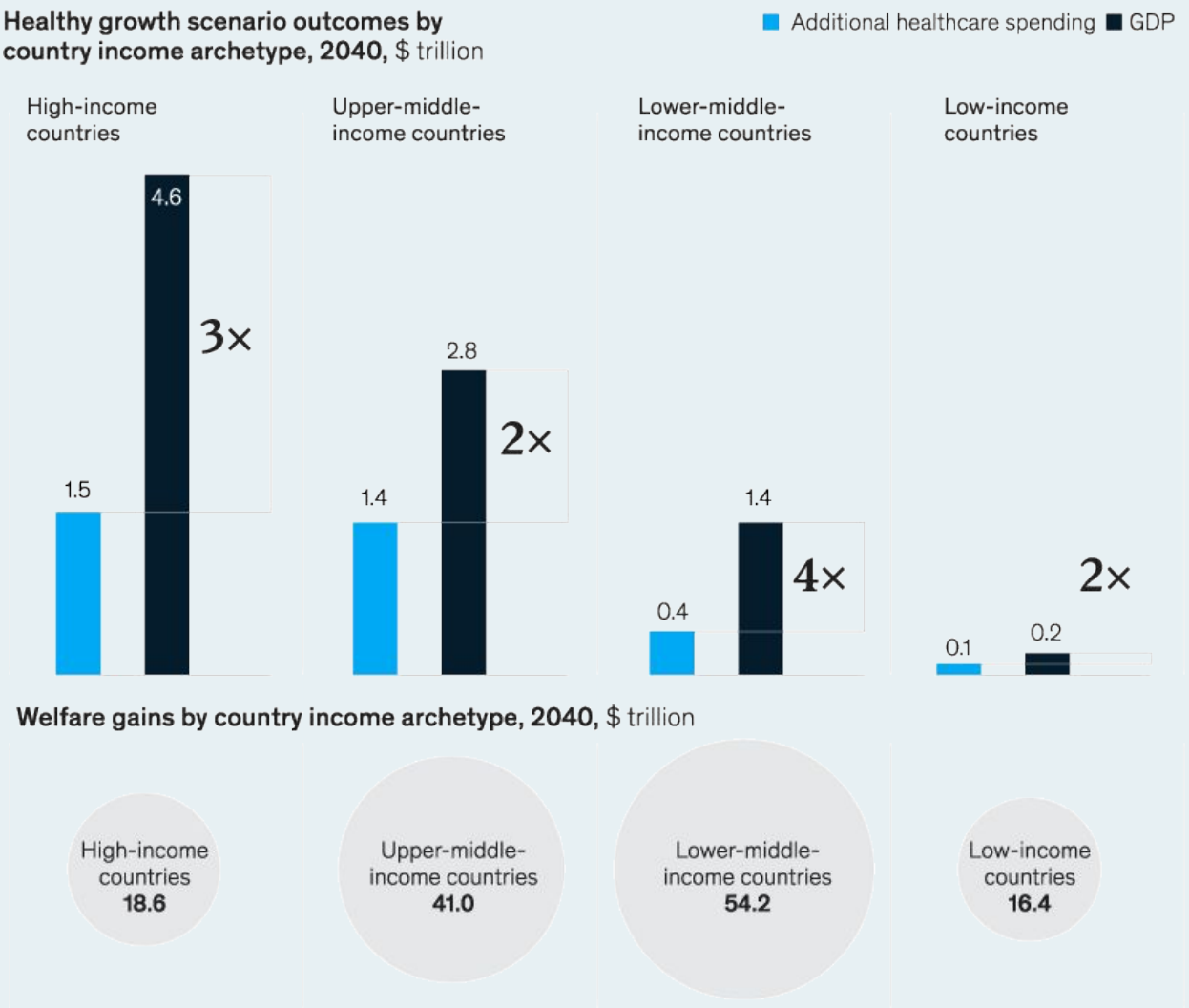
Lastly, improving health could drive up productivity and lift GDP by as much as $2.0 trillion by reducing presenteeism from chronic conditions such as low back pain, but also through investing in childhood nutrition, which improves the cognitive and physical health of the future workforce. Just addressing adolescents' mental and behavioral health issues, which affect about 60 million young people globally, could unlock $600 billion by 2040 through raising their educational attainment and earnings potential.

The expansion of the labor supply in a healthy growth scenario could add 0.3 percent to global employment growth. One-fifth of the new labor-market entrants would be in high-income economies, where this expansion could fully counter the projected slowdown in labor-force growth. The rest, 80 percent, would improve health and increase the labor force in low- and middle-income countries.

While more challenging to value in dollars, we estimate the social benefits from improved health by applying the approach used in economics to measure welfare. We estimate the total combined value of deaths averted and reduced ill health could be approximately $100 trillion without adjustments for income levels—eight times the estimated GDP benefits. This number is so high because people typically value good health above everything else. Improving health could also help narrow health disparities within countries and across countries. This in turn could also contribute to reducing income inequality within countries and strengthen the social contract.

The best part is that focusing on known health improvements could deliver an incremental economic benefit of $2 to $4 for each $1 invested (Exhibit 5).

For each $1 invested in improving health, an economic return of $2 to $4 is possible.



Note: Snapshot view of the healthy growth scenario in 2040. Additional healthcare spending, GDP impact, and welfare gains directly attributable to better health only (excluding expanded participation).
Source: *Disease Control Priorities 3 (DCP-3)*, University of Washington Department of Global Health, 2018; ILOSTAT; Institute for Health Metrics and Evaluation; National Transfer Accounts Project; Oxford Economics; Tufts Cost-Effectiveness Analysis Registry; "Updated Appendix 3 of the WHO Global NCD Action Plan 2013–2020: Technical Annex," World Health Organization, 2017; McKinsey Global Institute analysis

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Realizing the benefits would mean shifting spending to prevention. Prevention of diseases is typically less expensive than treatment and reduces the need for more expensive treatment later on, contributing to a high economic return. Shifting incremental spending to prevention would not be simple, however, because it requires substantial changes in where and how healthcare is delivered, as well as changes to communities that would help individuals grow up, work, and age in healthy ways. It is important to note that our economic analysis should not be interpreted as calling for additional funding for healthcare as currently delivered, but as an alternative approach under which health needs are addressed early, with proven, effective, typically lower-cost approaches.

Realizing the healthy growth opportunity

Capturing the benefits that we identify in this report would require dramatic changes that extend beyond what we typically think of as healthcare. That means it would necessitate change by governments and regional authorities, companies, innovators, and communities to shape environments and societies in ways that promote healthy lives and capture the societal and economic benefits we size.

The COVID-19 pandemic provides a unique moment to engage governments, companies, and communities around the world in this endeavor. The pandemic has exposed deep vulnerabilities in healthcare systems, supply chains, and social structures, and vast inequities that need to be addressed.

As societies emerge from the immediate crisis, we can aspire to do more than plug gaps and hope for recovery. We can build a better healthcare system and a stronger, more resilient global economy that delivers better health for all and shared prosperity for decades to come. To help realize that opportunity, we identify four imperatives:

1. Make healthy growth a social and economic priority

Our analysis shows that investing in health can be a critical lever for future growth and an important part of the economic policy debate. Instead of thinking of health as a cost to society, focusing on health as an investment can deliver significant social and economic returns. Governments around the world have a lead role to play and should consider developing and delivering healthy life agendas including labor market and employment policies, that deliver both health and economic benefits.

2. Keep health on everyone's agenda

The COVID-19 pandemic forced health onto the agenda of every organization and every household around the world. Keeping it there can deliver significant benefits. Long-term prevention and health promotion, which encompasses more than 70 percent of the benefits we identified, cannot simply be left to healthcare providers or healthcare systems. It is quite literally everybody's business. Advancing healthy communities and healthy and inclusive workplaces will be critical.

3. Transform healthcare systems

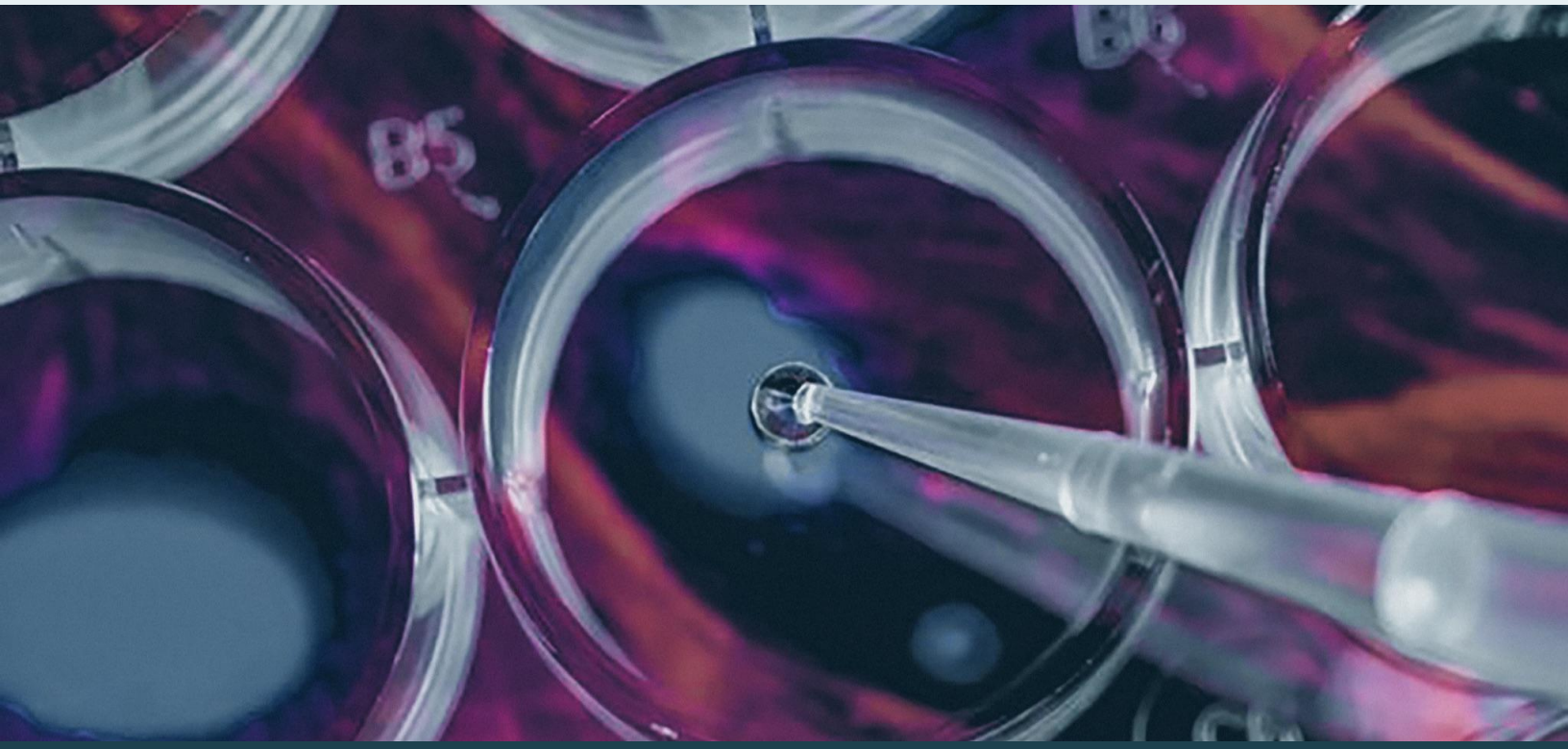
The COVID-19 pandemic has exposed vulnerabilities in healthcare systems everywhere. Taking the opportunity to strengthen and reimagine systems may not only ensure better preparation for future crises but also deliver healthcare more effectively. The challenge is making and sustaining changes that shift to preventive health while ensuring resilience and flexibility. This will involve high-quality and holistic primary care and services that address behavioral and social health needs, like housing, deploying a broader range of delivery channels to reach people when and where they are most likely to benefit. The current incentives in many healthcare systems and organizations are not sufficient to ensure this transition and require a fundamental reassessment.

4. Double down on innovation

As the world awaits a vaccine or an effective treatment for COVID-19, the vital role that innovation plays for health and the global economy could not be more evident. Innovations will continue to be critical to improving the health of the world's population. Today a little over a half of the $300 billion in global R&D spending on healthcare comes from the private sector. Promising innovations include genomics to deliver more targeted prevention and treatment; data science and AI to detect and monitor disease and enhance research; tech-enabled delivery to expand and reimagine access; and advances in the understanding of the biology of aging. However, realizing the full potential of the innovation pipeline may require shifting economic incentives to reward the areas with greatest need and highest return and building more collaborative approaches to R&D.

Realizing the healthy growth opportunity that we size in this report requires a coordinated effort by all stakeholders—governments, companies, and health institutions—to promote change within healthcare systems and beyond. But today, in the face of the COVID-19 pandemic, a unique opportunity to do just that has emerged. The benefits would be large: a $12 trillion economic opportunity, hundreds of millions of lives saved, and better health in the global population. Could there be a more important objective than making the world both healthier and more prosperous?

Bloomberg New Economy Forum



Gene Editing

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Gene-therapy innovation: Unlocking the promise of viral vectors

McKinsey

17 March, 2021

Viral-vector gene therapies show great promise, but the full extent of their clinical impact in the long term is not yet certain. Success depends on innovative solutions that remain under development.

The past year revealed both successes and setbacks for viral-vector gene therapies. The rapid development and large-scale rollout of multiple adenovirus-vector vaccines represented an unprecedented achievement that is poised to help mitigate the devastating impact of the COVID-19 pandemic. During the same period, multiple high-profile gene-therapy assets encountered challenges, with clinical trials paused because of safety concerns or failing to meet efficacy targets.

These successes and setbacks are emblematic of the current state of viral-vector gene therapy: a technology with considerable promise but with a set of challenges still ahead. As more and more gene therapies have reached the clinic, it has become clear that multiple technological challenges must still be overcome to unlock the full potential of viral-vector gene therapy.

Rising to meet these challenges, biotech and pharmaceutical companies are testing a multitude of technological advances and innovative strategies that address all aspects of viral-vector gene-therapy development. For companies prepared to keep abreast of the rapid pace of change, these innovations offer a path for ushering in the next generation of viral-vector gene therapies.

The state of viral-vector gene therapy

Viral-vector gene therapies use modified viruses as drug-delivery vehicles to introduce specific DNA sequences—encoding genes, regulatory RNAs (for example, small interfering RNAs [siRNAs]), or other therapeutic

substrates—into cells. The technology has long drawn interest for its potential advantages over traditional modalities. Many types of therapeutic agents (for example, enzymes, antibodies, and siRNAs) can be encoded in DNA sequences that can be rapidly designed and synthesized once a target is identified.

Viruses serve as powerful delivery vehicles for these sequences because of their ability to enter cells efficiently and potentially gain access to hard-to-reach, highly specific cells. In combining these features, viral-vector gene therapies can be used to modify gene expression in a programmable way, offering the flexibility to potentially treat a wide spectrum of diseases—including rare monogenic diseases by gene replacement and broad-population diseases by controlling gene expression—and help disease prevention by immunization.

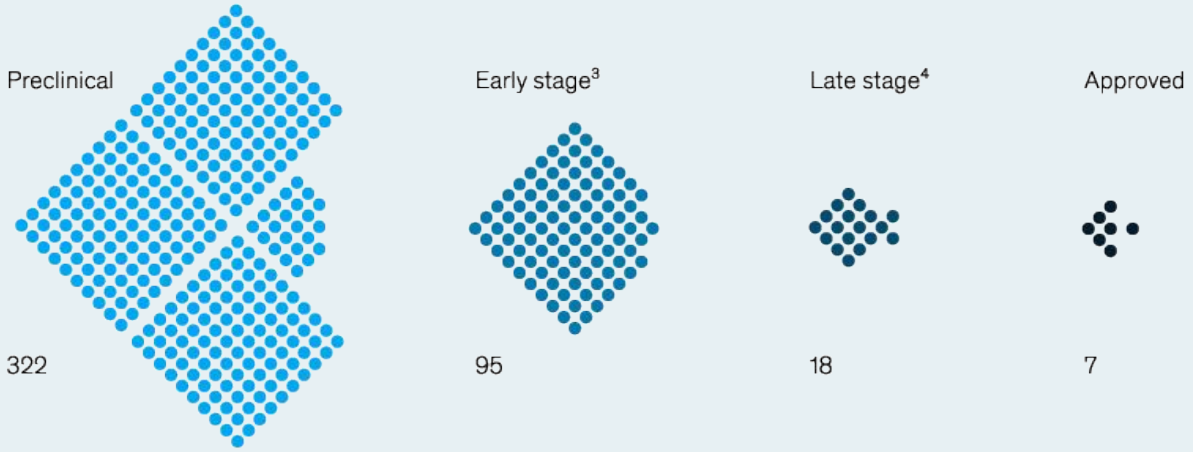
Nearly all gene therapies currently available use one of three vector types: adeno-associated-virus (AAV) vectors, adenovirus vectors, or lentivirus vectors (Exhibit 1). AAV and adenovirus vectors are typically used in gene therapies that are directly administered to patients by infusion or local administration (in vivo), with AAV being the most popular vector for areas outside of oncology and vaccines. Lentivirus vectors are typically used for ex vivo therapies, in which cells harvested from a patient are modified in the lab before retransplantation. This article primarily focuses on in vivo gene therapies; however, many of the challenges and advances discussed are applicable across both routes of administration.

Exhibit 1

The viral-vector gene-therapy pipeline comprises mostly preclinical and early-stage assets across multiple vector types.

Viral vectors used in gene therapy[1] by type, % of worldwide assets

Viral-vector gene-therapy assets by development stage, number of worldwide assets



[1]In vivo and ex vivo viral-vector gene therapies; excludes ex vivo genetic modification of cells for cancer immunotherapy (eg, chimeric antigen receptor [CAR]-T-cell therapies).
[2]Includes herpesviruses (which cause herpes simplex), rhabdoviruses (which cause vesicular stomatitis), and other viruses.
[3]Phase I, Phase I/II, and Phase II.
[4]Phase II/III and Phase III.
Source: Jote T. Bulcha et al., "Viral vector platforms within the gene therapy landscape," *Signal Transduction and Targeted Therapy*, February 2021, Volume 6, Number 53, nature.com; Evaluate; McKinsey analysis

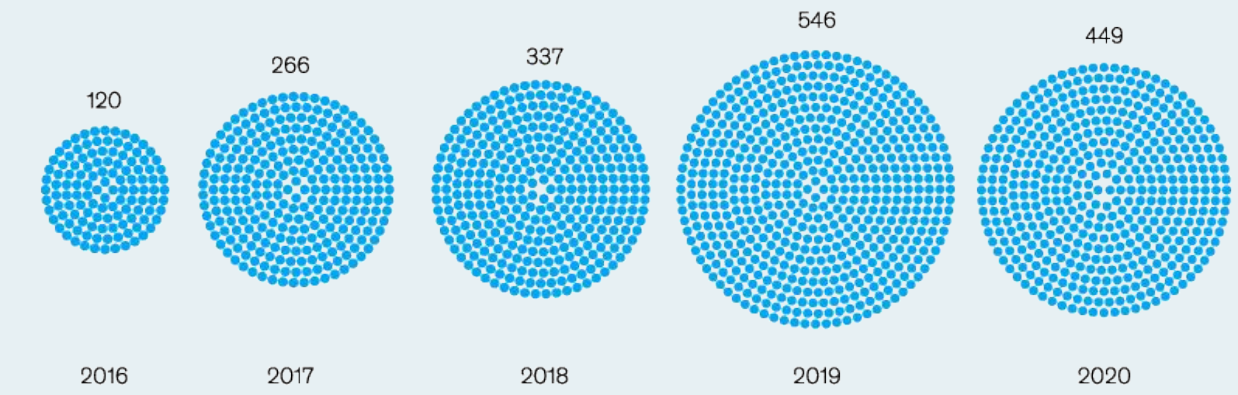
McKinsey & Company

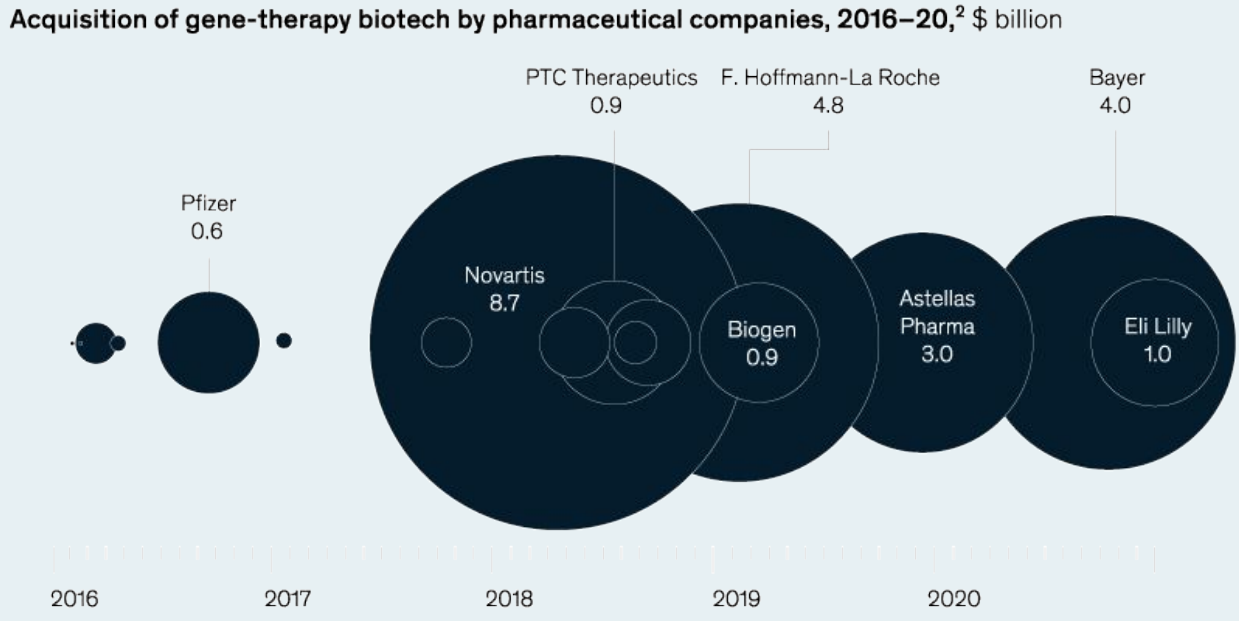
Excitement around viral-vector gene therapies is evident. While only four in vivo viral-vector gene therapies are currently on the market, more than 100 gene-therapy assets are in clinical trials as of late 2020, with a far greater number in preclinical development.

Many of these assets have emerged from the steady stream of small- and midsize biotech companies and academic labs supported by continued, high levels of venture-capital funding. Large pharma

companies have increasingly focused on the potential of viral vectors, with seven biotech-company acquisitions valued near or above $1 billion in the past two years alone (Exhibit 2).[1] Adenoviruses are being proven as a vaccine platform, with approvals for Ebola vaccines and groundbreaking COVID-19 vaccines over the past year.[2]

Strong investment in viral-vector gene therapies reflects high levels of excitement about the technology.





[1]Sum of seed-round, early-stage venture-capital, and late-stage venture-capital funding; 2020 values extrapolated to a full year based on deals in January–October 2020.
[2]Each circle represents 1 acquisition; circle size corresponds to total deal value; labels indicate acquisitions >$500 million.
Source: Evaluate; IQVIA Pharma Deals; PitchBook Data; McKinsey analysis

McKinsey & Company

While the high list-price of some gene therapies was once seen as a near insurmountable challenge to commercialization, innovative reimbursement strategies have shown that successful launches are possible, with ZOLGENSMA (treating more than 600 infants with spinal muscular atrophy in its first ten months on the market) beating analyst expectations. Worldwide sales of viral-vector gene therapies are forecast to grow at a rate of more than 50 percent year-on-year for the next five years (excluding the potential impact of COVID-19 vaccines), affecting the lives of tens of thousands of patients.

However, while there is significant momentum, there have also been multiple recent setbacks. Many of these relate to challenges previously outlined by McKinsey in its perspective on the future of gene therapy (including efficacy, durability, and manufacturing). As these therapies have sought to expand beyond the ultrarare indications they originally targeted, three technological challenges have emerged as recurrent obstacles. For viral-vector gene therapies to reach their true transformative potential—much like monoclonal-antibody technology 20 years ago—this set of technological challenges must be overcome.

Challenges to realizing the potential of viral-vector gene therapies

The current generation of viral-vector gene therapies represents the culmination of decades of biological and clinical research. As more patients have received these therapies, it has become clear that three fundamental challenges will restrict the applicability of viral vectors: getting past the immune system, lowering the dose, and controlling transgene expression. Ongoing work to address these challenges is generating technological innovations that have the potential to leapfrog current therapies and unlock the potential of viral vectors.

Getting past the immune system

The success of any viral-vector gene therapy depends on its ability to get past multiple lines of defense deployed by the human immune system. Viral capsids, viral-vector DNA, and even the transgene products themselves may be recognized as foreign, providing multiple opportunities for the immune system to clear the gene therapy from the body.

Immunity against viral capsids can limit the efficacy of a gene therapy. Because most viral-vector gene therapies today use vectors derived from harmless viruses circulating in humans, many patients (up to 60 percent) may have preexisting immunity from past exposure. CanSinoBIO, for example, reported reduced efficacy of its COVID-19 vaccine in individuals with preexisting antibodies to the adenovirus-5 (Ad5) vector it chose for drug delivery.

Although this effect depends on the vector serotype used, and the clinical impact is still unclear, many clinical-trial sponsors conservatively exclude patients from their studies if they have antibodies to the vector in question. This can come at the cost of making most patients ineligible for therapy. Acquired immunity to viral vectors poses additional challenges for viral-vector gene therapy in the long term. Patients treated with a gene therapy today may not be able to receive a second gene therapy in the future if the same viral vector is used in both contexts.

In addition, viral capsids and viral-vector DNA can actively provoke an immune response from the body. For viral-vector vaccines, this immunogenicity can be beneficial, as it reduces the need for adjuvants and increases efficacy. However, for other viral-vector gene therapies, immunogenicity can reduce efficacy, increasing the chance that the gene therapy is detected and eliminated by the immune system. Indeed, some have speculated that immunogenic vector DNA sequences are behind the limited durability of some recent gene therapies, leading to their

abandonment. More concerningly, immunogenicity can lead to safety concerns during therapeutic use, as high levels of viral capsids can cause severe immune reactions at the time of injection.

Unraveling the immune system's intertwined responses to viral-vector gene therapies remains difficult. Animal models do not recapitulate all relevant aspects of the human immune system (as immune systems behave quite differently among species). While human clinical trials offer a valuable source of insight, many gene-therapy trials are too small to confidently isolate the parameters associated with a drug's success or failure.

Lowering the dose

Current viral-vector gene therapies require the administration of large numbers of viral particles to patients, particularly for therapies aimed at treating systemic diseases. For example, recent gene therapies for Duchenne muscular dystrophy (DMD) that aim to correct mutations in muscle cells throughout the body have delivered up to approximately 10^16 (ten-thousand trillion) viral particles in a single dose (for example, a dose of 3 × 10^14 vector genomes [vg] per kilogram [kg], assuming a 30-kg child), which is multiple times the number of cells in the human body. For systemic diseases, the need to individually target and repair many cells in the body partly explains why such large doses are administered. Another explanation is the limited cell-type specificity of current viral vectors: large numbers of viral particles must be delivered to ensure that an adequate number reach clinically relevant cells.

The large doses used in current gene therapies pose two challenges. First, large doses are difficult and expensive to manufacture. Today, a typical manufacturing run of an AAV-vector therapy using high-yield cell lines and large-capacity bioreactors might only produce approximately ten doses of a systemic gene therapy from a single batch at a cost of nearly $100,000 per dose (assuming approximately 1 × 10^17 vg per

batch). Although these costs will gradually decrease as gene therapies begin to reach clinical and commercial scales, any technological advance that reduces the required dose would bring immediate benefit, as a tenfold reduction in dose might also bring about a tenfold reduction in costs.

Second, and even more critically, administering large doses of virus has been linked to adverse safety outcomes. Although investigations of four deaths in clinical trials of AAV-vector therapies in 2020 are ongoing, three deaths occurred in high-dose cohorts. Clinical-trial protocols have subsequently been revised to limit viral dosage, reflecting the tremendous importance of this issue.

Controlling transgene expression

Once a viral vector successfully delivers its therapeutic gene to the cells in question, the efficacy of the gene therapy depends on the quality of transgene expression. Specifically, the transgene must be expressed at the appropriate level (neither too low nor too high), in the appropriate cells, and for the appropriate duration to mediate the desired clinical effect. For therapeutic uses (in contrast to use for vaccines), the transgene may need to be expressed permanently if the gene therapy is to serve as a one-time cure and represent an appealing alternative for patients over current standards of care requiring repeated dosing (which may not be possible because of the challenges previously laid out). Regulators have required multiple years of follow-up data showing that gene expression is maintained. Indeed, some drugs have been abandoned when expression waned after 12 months.

To maximize chances of success, early viral-vector gene therapies have opted to include regulatory elements (DNA sequences such as promoters and enhancers that control how genes are expressed) that have been selected to drive high levels of transgene expression in all cell types. However, this approach may have significant drawbacks, particularly as

gene therapies move beyond gene replacement for monogenic rare diseases. Overexpression of the transgene or its expression in the wrong cells may contribute to inflammation and other toxicities (as was observed in recent studies of nonhuman primates). Moreover, current gene therapies, once administered, cannot be controlled or turned off by clinicians should the need ever arise.

Innovative solutions that address gene-therapy challenges from many angles

To tackle the challenges facing gene therapy, academic labs, start-ups, and established companies are generating myriad innovative solutions (Exhibit 3). Each focuses on a specific component of a gene-therapy product (for example, the viral capsid) or part of the development process (such as manufacturing). However, these innovations often address multiple core challenges, outlining multiple paths to realizing the promise of viral-vector gene therapy.

New innovations often address many core challenges facing viral-vector gene therapy.

Innovations and challenges affecting gene therapy	Getting past the immune system Critical for efficacy, redosing, and safety	Lowering the dose Critical for safety and ability to manufacture	Controlling transgene expression Critical for efficacy and safety
Improved capsids	✓	✓	✗
Improved vectors	✓	✓	✓
New types of cargo	✗	✗	✓
Improved manufacturing processes	✗	✓	✗
Improved pretreatment and conditioning regimens	✓	✗	✗

Source: Evaluate; IQVIA Pharma Deals; PitchBook Data; McKinsey analysis

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We have identified five key trends to watch.

1. Improved capsids

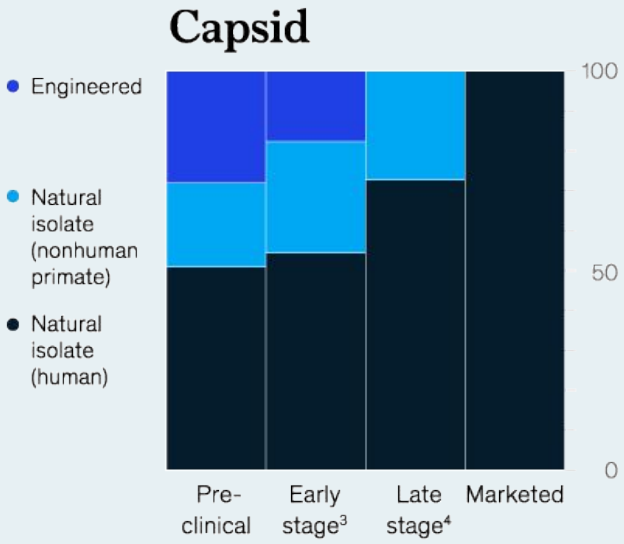
The viral capsid is a critical component of viral-vector gene therapy. It determines which cells are targeted, the efficiency of cell entry, and the probability that the gene therapy is detected and eliminated by the immune system. In addition, the capsid is largely responsible for the stability of the viral vector during the manufacturing process and can affect storage and distribution requirements.

The capsids most widely used today, including those used in on-market products, are derived from naturally occurring viruses. They have suboptimal properties, including little cell-type specificity, moderate efficiency of cell entry, and relatively high levels of preexisting immunity in humans. To address the problem of preexisting immunity, many assets use capsids from viruses found in other species. For example, the AAV8 and AAVrh74 capsids used in multiple AAV-vector gene therapies are derived from AAV serotypes isolated from macaques, and some of the COVID-19 vaccines that have been developed have used adenovirus serotypes from chimpanzees and gorillas. While this approach may limit the challenges of preexisting immunity, it largely doesn't address specificity or efficiency (particularly as these viruses have evolved to infect nonhuman species).

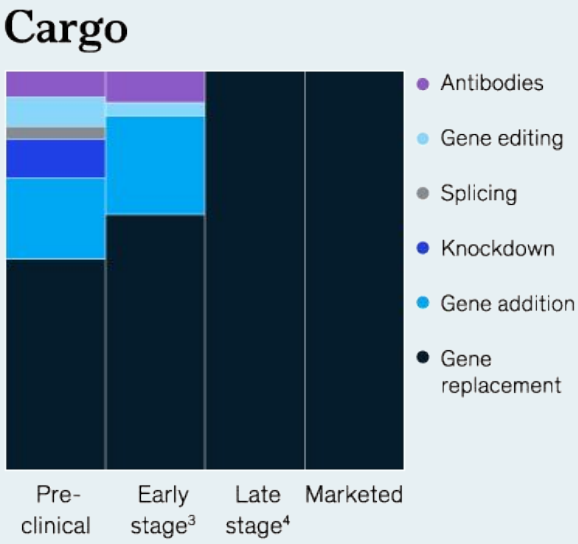
Increasingly, drug developers are turning to capsids that have been engineered in the lab and can be selected to overcome the challenges mentioned previously (Exhibit 4). These engineered capsids are identified through large-scale screening efforts in which millions of variant capsids are screened for the desired properties and iteratively refined. Capsid-engineering platforms—many of which have been spun out of academic labs to form companies—achieve these ends by leveraging advanced technologies, such as cryo-electron microscopy (cryo-EM) and artificial intelligence.

Innovative technologies are being increasingly adopted in early-stage gene-therapy assets.

Adoption of new capsids by development stage and type, % of assets[1]



Adoption of new types of cargo by development stage and type,[2] % of assets[1]



[1]Among adeno-associated-virus assets for which capsid or cargo type could be ascertained from public documents.
[2]Antibodies: delivery of vectorized antibody genes; gene editing: delivery of gene-editing enzymes or substrates; splicing: delivery of splice-modifying oligonucleotides (eg, antisense oligonucleotides); knockdown: delivery of small RNAs to reduce gene expression; gene addition: delivery of gene to increase expression or provide novel function; gene replacement: delivery of gene to compensate for loss of function of patient gene.
[3]Phase I, Phase I/II, and Phase II.
[4]Phase II/III and Phase III.

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Improving capsid properties could bring multiple immediate benefits. For example, a twofold increase in a capsid's cell-type specificity could enable a twofold decrease in the overall viral dose required, thereby improving safety and cost. It's still too early to determine the true impact of capsid engineering, as most engineered capsids are still in preclinical development. However, companies' early reports suggest that capsids with five- to tenfold improvements in multiple attributes may be entering the clinic soon.

2. Improved vectors

Like the capsid, the DNA sequence of the viral vector itself affects

multiple aspects of a gene therapy's performance, but engineering the vector can often be considerably easier, cheaper, and quicker. Accordingly, vector engineering is becoming a growing focus of gene-therapy R&D. Vector engineering is often easier with adenovirus and lentivirus vectors than with AAV vectors because of AAV's inability to package large pieces of DNA. However, innovative vector elements are beginning to appear in AAV-vector designs as well.

Vector engineering broadly has two aims: reducing the immunogenicity of the viral vector and improving transgene expression. One strategy to achieve both aims is codon optimization, in which variations in the vector sequence are explored to eliminate immunogenic sequence motifs while optimizing the transgene for robust expression. Subtle changes in vector sequence achieved through codon optimization can have large effects, such as increasing expression levels and possibly extending the duration of expression for multiple years.

Transgene expression can be further programmed by engineering regulatory elements into the vector sequence. Some regulatory elements turn on transgene expression only in certain cell types or tissues—ideally, the disease-causing cells—preventing potentially toxic expression in other contexts. Such cell-type- or tissue-specific regulatory elements (for example, promoters and enhancers) have become relatively common in viral-vector gene therapies. For an additional layer of control, some viral-vector gene therapies are also incorporating regulatory elements, such as microRNA-target sites, that reduce expression in specified cells—for example, in cells that promote an immune response.

Finally, a more distant and challenging goal is to engineer vectors that are inducible, where transgene expression can be controlled using an additional signal, such as an orally administered small-molecule drug. This could allow clinicians to turn on, turn off, or otherwise adjust a gene therapy after it is administered, delivering a personalized course of treatment.

3. New types of cargo

The cargo delivered by a viral-vector gene therapy is typically a working copy of a gene that is used to replace the patient's disease-causing copy of that same gene. However, any therapeutic agent that can be encoded in DNA can theoretically be delivered by a viral vector. Researchers and drug developers are increasingly leveraging this flexibility to deliver other types of molecules with therapeutic value—alone or sometimes in combination—including regulatory RNAs (for example, short hairpin RNAs [shRNAs]), vectorized antibodies, and substrates for gene editing.

Gene editing is an intriguing potential solution for achieving long-lasting, physiologically appropriate gene expression. For patients with diseases caused by certain types of mutations, restoring the function and expression of the patient's own copy of the gene through gene editing may be simpler (and more permanent) than attempting to engineer and deliver a replacement.

4. Improved manufacturing processes

Early gene-therapy-manufacturing processes originated in academic labs and were focused on small, research-scale batches. These processes were not optimized for moderate- or large-scale production or for the delivery of systemic therapy. As gene therapies start to expand outside the treatment of ultrarare diseases, one of the many challenges being addressed is the presence of empty capsids created during the manufacturing process. These empty capsids, which have no active cargo, can create the requirement for higher doses and, accordingly, stimulate stronger immune responses.

Two approaches are being developed to reduce the ratio of empty-to-full capsids in manufacturing: developing improved methods to separate the empty from full capsids based on specific properties (for example, charge and molecular weight) and engineering cell lines that package full

capsids more efficiently. By reducing the empty-to-full ratio, these advances reduce manufacturing costs, reduce immune responses, and improve the safety of gene therapy. Indeed, regulators have used reducing the empty-to-full capsid ratio as part of the rationale for lifting clinical holds on gene-therapy products with previous safety issues

5. Improved pretreatment and conditioning regimens

Beyond engineering the capsid and vector, a separate approach for reducing the immune system's detection of viral-vector gene therapies involves coadministering the therapy with an immunosuppressive agent. Multiple such conditioning regimens are currently being tested to reduce the impact of neutralizing antibodies on the efficacy of the treatment, both of preexisting antibodies and newly generated antibodies that could prevent future redosing. Nearly all current viral-vector gene therapies use steroids to help manage the potential immune response to the viral vector; however, the type, dosage, and timing of the steroid treatment varies widely.

Some clinical trials are experimenting with more targeted immune suppression, such as the use of rituximab to reduce the creation of memory B cells. An even greater assortment of approaches is being tested in animal models to directly reduce the presence of neutralizing antibodies. These include the use of enzymes cleaving to immunoglobulin G (IgG), plasmapheresis to remove the neutralizing antibodies specific to the gene therapy, and even CRISPR-based repression of neutralizing-antibody creation. These approaches could expand the pool of eligible patients to include those with preexisting immunity. Moreover, these approaches could enable a patient to receive multiple doses of the same therapy or of different therapies using the same vector backbone.

The road ahead

Viral-vector gene therapies find themselves at another inflection point. Early successes in the treatment of rare diseases and vaccines have proven the potential of this modality, while the challenges to gaining widespread adoption—the way that monoclonal antibodies have over the past 20 years—have only become clearer. Nevertheless, the wealth of innovative solutions being explored across academia, biotech, pharma, and contract development and manufacturing organizations demonstrate that viral-vector gene therapies are here to stay.

As described previously, different solutions are emerging to address each of the core challenges. The diversity of these approaches and the complexities of gene therapy mean that no single approach is likely to "win." That situation will enable a rapid innovation cycle in which gene therapies are constantly being improved upon, which will offer new opportunities to leapfrog existing products. Even as AAV-vector-based delivery is becoming the leading technology, some prominent limitations combined with the rapid pace of innovation leave the door open for other delivery technologies to emerge.

Owners of viral-vector platforms will need to consistently look to the next set of innovations beyond their current platforms and assets. That could include investing directly to help overcome the broader challenges or buying or licensing critical technology to upgrade their platforms. Indeed, multiple new biotech companies have launched to solve one or more of the challenges outlined in this article as a service to developers of gene therapies. Staying abreast of these developments will require fastidious monitoring of scientific and technological progress on all fronts. However, since it is difficult at this early stage to place bets across all potential solutions and innovators, gene-therapy leaders will need to make their investments judiciously.

In the short to medium term—while technological challenges limit the scope of gene therapies to curative treatments for rare diseases—fast followers may find it difficult to be successful, even with improved technologies, as first entrants rapidly address prevalent populations. Gene-therapy leaders will therefore need to strike a careful balance by accelerating programs today while retaining the flexibility to adopt innovative technologies that unlock treatments for broader-population diseases and the full promise of viral-vector gene therapies in the long term.

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Cancer

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Fulfilling the promise of advanced analytics in oncology

McKinsey

23 April, 2021

Advanced analytics will transform cancer care, but companies have been slow to adopt it. Progress requires a strategy that not only builds data and talent but also embraces experimentation.

In recent years, dozens of large corporations and tech start-ups announced that they would deliver self-driving cars by 2020, thanks to the power of advanced analytics. It seemed like a daunting but plausible goal, as newer models already included semiautonomous features such as adaptive cruise control and driver-assist parking. But over time, we discovered, based on the massive amounts of data, machine-learning models, and expert engineers required, just how complex it is to build a fully autonomous vehicle. Nevertheless, while no company is producing self-driving cars on their assembly lines yet (due to the continual pushback of estimated delivery dates), it is only a matter of time.

In oncology, the story is much the same. We have read the exciting headlines predicting that big data and advanced analytics will transform cancer care and research and that all patients, thanks to machine learning, will soon receive personalized treatment plans. But progress has been arguably slower than initially envisioned.

However, without a doubt, important advances are being made. Researchers have built a model that can accurately predict molecular subtypes in head and neck cancers using radiomics, a machine-learning technique that can help identify, classify, and monitor solid tumors from CT, MRI, or PET scans, rather than relying entirely on radiographers and often-painful biopsies. Elsewhere, machine-learning models have outperformed board-certified dermatologists in identifying melanoma through image recognition

Yet most pharmaceutical companies still do not systematically apply advanced analytics to their work in oncology, even though it can deliver

value at every stage of the product life cycle, from research and early development to market access and commercialization (see sidebar, “The value of advanced analytics in oncology.”) They do not, for instance, routinely analyze real-world evidence to identify additional indications for existing therapies—analysis that could prove particularly helpful in treating rare cancers where it is difficult and time intensive to find patients for a trial. And they are unable to use data to understand the full network of a patient’s care team—specialists, primary-care providers, and sites of care. At a time when the COVID-19 pandemic has so hindered cancer care, think of the advances that might be made if companies could use such data to help oncologists keep abreast of the often-bewildering array of new combination therapies and targeted treatments, ensuring that patients receive the best standard of care based on their history, genetics, and biomarkers.

Lack of talent is one reason why pharmaceutical companies are not making more progress applying advanced analytics to oncology—data scientists with expertise in oncology are few and far between. Lack of data is also an issue. But perhaps the biggest impediment is a culture that is suspicious of the kind of experimentation inherent in developing advanced-analytics capabilities. As a result, many companies are simply postponing a steep learning curve, as advanced analytics will, without doubt, come to play a huge role in cancer research and care, as well as pharmaceutical companies’ success in oncology.

Paving the way for advanced analytics in oncology

A management-aligned technology road map that makes clear the expected impact, timeline, and investment required to deliver on priority initiatives is the starting point for any successful advanced-analytics strategy, regardless of sector. Advanced analytics can cover a range of approaches, from statistical models to artificial intelligence (AI) and the deployment of machine-learning tools such as the neural networks used for image recognition. Analytics models can be built without a clear,

strategic road map, but they won't necessarily give the business a leading edge or, of critical importance in the case of pharma companies, help patients. A strategic technology road map is the first of our six-component framework for successfully integrating digital and analytics technologies to create value, the others being talent management and planning, an agile delivery model, data-strategy and data-management capabilities, technology capabilities, and the implementation of measures to drive adoption of a new operating model (Exhibit 1).

A six-component framework can successfully transform commercial analytics.

	1	2	3	4	5	6
What is needed	**Strategic road map:** a clear vision and priorities	**Talent:** a strong team with diverse skill sets (technical and business)	**Agile delivery:** ways of working efficiently across functions to deliver value	**Technology:** architecture to enable integration and deployment	**Data:** robust, integrated data assets with defined architecture and governance	**Adoption and scaling:** pilot, show value, and drive change and adoption
Lessons from experience	In the absence of an overall strategy, it is difficult to get senior leadership to align and commit to priority efforts	Analytics talent is hard to recruit, and some roles (eg, translators) require both business and technical knowledge to unlock value, making talent even more challenging to find	Most agree on principle to agile delivery, but few put it into practice; time commitment and team empowerment are the main friction points	Failure to link the technology road map to the overall strategy creates ongoing challenges	There are no perfect data sources or universal business rules; clear governance and leadership are needed to reduce the inevitable complex and seemingly unsolvable problems	Most pilots fail due to insufficient change management, which should be incorporated as early as possible

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While all are key, we focus here on the elements that can prove particularly important in overcoming challenges in oncology, namely, building the right talent within the right organizational structure, kickstarting the program by leveraging existing data assets first, and embedding a culture that will speed adoption.

Build the right talent in the right organizational setup

Large, established pharmaceutical companies are not short of data scientists, but most of them work on commercial analytics, executing repetitious analyses such as performance reporting. If companies are to capture the full power of analytics, they will need to consider devoting specialist resources to different therapeutic areas (TAs). This is particularly important in oncology, which poses unique analytical challenges, such as integrating pharmaceutical and medical data, translating clinical markers, and building complex lines of therapy.

Finding such expertise is a tall order. It is rare to find talent with a strong technical background as well as a medical understanding of a disease area, the ability to link clinical guidelines to all manner of data in the patient journey, and the business sense to recognize and prioritize the most valuable insights.

Some companies might therefore turn to data-science companies and contractors to resource analytics projects and deliver insights fast. But if the aim is to establish a competitive advantage through advanced analytics in oncology, companies will probably need to build analytics excellence in-house. This, in turn, will require a strong talent-recruiting strategy that differentiates the cutting-edge role of analytics in the pharmaceutical industry—particularly oncology—and ensures well-defined career paths and growth opportunities.

Another question to settle is whether these new data scientists should sit in a centralized analytics center of excellence, which provides platform

services across the organization, or within the oncology division itself. Centralization versus decentralization is a much-debated design choice in all sorts of companies. Some opt for a centralized model to help ensure resources are used efficiently and data scientists learn from one another. Some prefer decentralization to keep data scientists more attuned to the needs of the business. And some strike a balance with a hybrid model. The size of the oncology portfolio could guide the choice. With a single oncology drug, the best option might be for analysts to sit within the business unit. With a larger portfolio, there could be benefits to them sitting within an oncology cell in a centralized analytics function to share and scale their knowledge.

Kick-start the program with existing data assets

Data needs for oncology use cases are more specialized than those for other TAs. For example, mapping a patient journey containing combination chemotherapies requires integrating medical, prescription, and laboratory-results data sets, while identifying later lines of therapy may require three or more years of patient-history data.

The quality, availability, and cost of oncology-specific data sets have undoubtedly improved over the past five years. Yet, there is still a long way to go. Data remain relatively sparse, and sample sizes tend to be low, particularly for biomarker data due to the collection cost, potential errors in measurements, and the risks to patients when collecting specimens such as neural tissue. Additionally, with the exception of electronic-medical-records (EMR) data, clinical data seldom include the outcomes of tests or procedures. Claims data, for example, exclude laboratory values and genomic test results.

Notwithstanding the pressing need, time should not be wasted waiting for perfect data. To kick-start the analytics program, pharmaceutical companies should identify and put to quick use as many existing data assets as possible—including those typically used for operations and

standard reporting, which often get overlooked when it comes to supporting advanced analytics. Data on rebate cards, oncology practices and cohorts, and oncologists who have participated in clinical trials could all prove valuable.

At the same time, companies should look to acquire novel external data sets, including biomarker data and even data from digital-health monitors. Ultimately, they can combine existing and new data sets to reveal even more powerful insights, notwithstanding that new data assets can take time and most companies already have data that they consider “good enough.”

As more data is incorporated and use cases proliferate, data governance becomes critical if the data are to be usable, accessible, and secure. This should include governance of top-level issues, such as who owns the overall data strategy, as well as of tactical issues, such as how to define data fields. Take the data field for physician affiliation, for example. Oncologists are often linked to several hospitals, clinics, and offices, which means the best definition of “affiliation” would depend on which question you are trying to answer: Where are oncologists seeing patients, where do sales reps interact with them, or through which entity do they order or bill for medications?

Change the culture

Even companies that build strong data-science teams and strong data assets can struggle to get new tools adopted. The problem is pervasive across sectors, but it can be more prevalent in life sciences, including pharmaceuticals, where the prevailing orthodoxy is that data and models must be perfect before being harnessed for decision making. That orthodoxy is correct when applying analytics to some areas within R&D, but there are plenty of other areas where a less-than-perfect analytical tool can be beneficial. Moreover, given how quickly standards of care can change and the complexity of different lines of therapy, companies

will struggle to get off the starting line if they wait for perfection.

Lack of transparency and training can also hamper adoption. Field teams handed a tool backed by complex models are often skeptical that it can outperform their years of institutional knowledge, particularly if the drivers of a recommendation are unclear, which is often the case with AI models. The skepticism is compounded if the tool also fails to make clear what action to take as a result of the analytics—a situation that is not uncommon.

Overcoming such issues requires a cultural change that embraces advanced analytics. Several actions can help drive one:

Change the way teams work. Tools will only be adopted if the teams that build them are integrated, putting to use the expertise of data scientists, analytics translators, and business leaders. Translators are the bridge between the technical knowledge of the data scientists and the operating expertise of business leadership. Their role is to ensure data scientists are going after the highest priority business problem and that the business will adopt new analytical tools by explaining their output and value. Teams also need to adopt agile ways of working, rapidly building solutions and testing and learning as they go, rather than striving for the perfect answer at the outset (Exhibit 2).

Identify quick wins. To build enthusiasm, start with high-priority pilots that are not overly complex to conduct but that might deliver important insights. In development, that could be identifying patients eligible for a given protocol in each hospital in a region or country. For medical affairs, it might be understanding oncologists' treatment regimens in terms of dosage and duration with a view to improving them where appropriate.

+ Standardize. Standardizing the way new projects are launched and their progress measured accelerates adoption across the organization, positioning them as continuous, ongoing efforts to build competitive advantage as opposed to one-off pilots.

Different companies will find themselves at different starting points, facing different challenges when considering an advanced-analytics strategy for oncology. Larger, established pharmaceutical companies will likely benefit from a wealth of internal data sets and more data scientists. On the other hand, they might struggle to shift a more deeply engrained, cautious culture. Smaller biotech companies are likely to be more agile and more attractive to data scientists and other technical experts. However, they will have fewer existing data assets; a smaller portfolio of products, each perhaps critical to the company's success, could also make them more averse to a new, advanced-analytics-led approach because of the perceived risk.

Scarcity of data is also a challenge for companies researching and developing treatments for rare cancers or therapies with small eligible populations. Particularly sophisticated statistical techniques will be required to derive valid insights from the data.

Whatever their circumstances, however, all pharmaceutical companies will need a strategy for applying advanced analytics to their work in oncology. Failure to establish one amounts to a decision not to participate in a technical development that is reshaping cancer care. Companies have a choice of whether to keep pace with the development or lead it, but falling behind is not an option.

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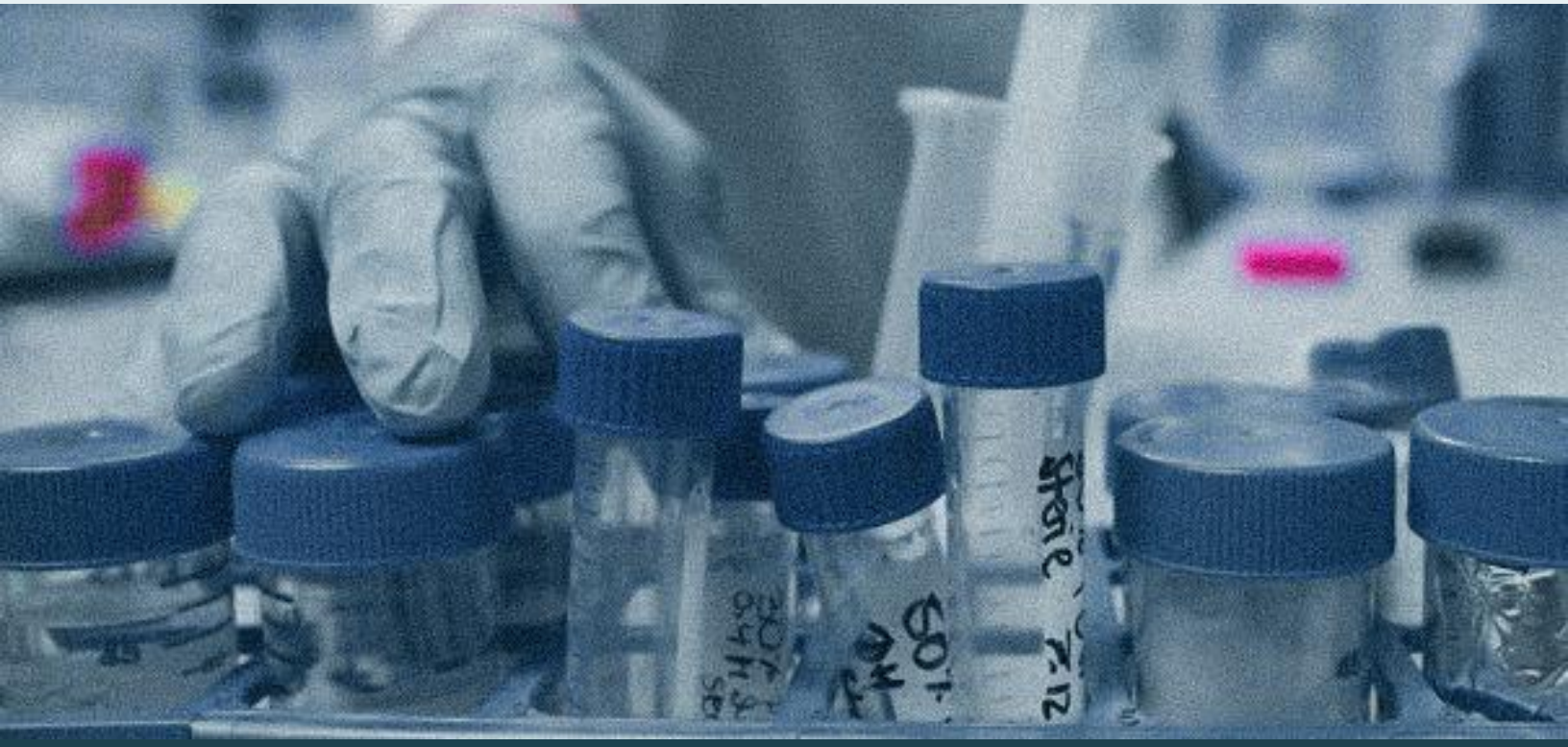

Biological Revolution

Knowledge Partner

McKinsey & Company

The Bio Revolution: Innovations transforming economies, societies, and our lives

McKinsey

13 May, 2020

Advances in biological science could transform economies and societies, helping to tackle global challenges from climate change to pandemics.

A confluence of advances in biological science and accelerating development of computing, automation, and artificial intelligence is fueling a new wave of innovation. This Bio Revolution could have significant impact on economies and our lives, from health and agriculture to consumer goods, and energy and materials.

Some innovations come with profound risks rooted in the self-sustaining, self-replicating, and interconnected nature of biology that argue for a serious and sustained debate about how this revolution should proceed. Accidents can have major consequences—and, especially if used unethically or maliciously, manipulating biology could become a Pandora's box that, once opened, unleashes lasting damage to the health of humans, ecosystems, or both. The risks are particularly acute because many of the materials and tools are relatively cheap and accessible. Moreover, tackling these risks is complicated by a multiplicity of jurisdictional and cultural value systems, which makes collaboration and coordination across countries difficult.

However, new biological applications are already improving our response to global challenges including climate change and pandemics. Global responses to the novel coronavirus—SARS-CoV-2—illustrated substantial advances in biological science in just the past few years. The speed with which scientists sequenced the virus's genome—weeks rather than months—bore witness to the new world of biology described in this research. However, sequencing is just the start: biological innovations are enabling the rapid introduction of clinical trials of vaccines, the search for effective therapies, and a deep investigation of both the origins and the transmission patterns of the virus.

As much as 60 percent of the physical inputs to the global economy could, in principle, be produced biologically—about one-third of these inputs are biological materials (wood or animals bred for food) and the remaining two-thirds are nonbiological (plastics or fuels) but could potentially be produced or substituted using biology. Therefore, it is possible that bio innovations could impact up to 60 percent of physical inputs, although attaining that full potential is a long way off. Even modest progress toward it could transform economies, societies, and our lives, including what we eat and wear, the medicines we take, the fuels we use, and how we construct our physical world. In human health, at least 45 percent of the current global disease burden could be addressed using science that is conceivable today.

A pipeline of about 400 use cases, almost all scientifically feasible today, is already visible. These applications alone could have direct economic impact of up to $4 trillion a year over the next ten to 20 years. More than half of this direct impact could be outside human health in domains such as agriculture and food, consumer products and services, and materials and energy production. Taking into account potential knock-on effects, new applications yet to emerge, and additional scientific breakthroughs, the full potential could be far larger.

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Biological innovation covers four arenas

The current innovation wave in biology has been propelled by a confluence of breakthroughs in the science itself, together with advances in computing, data analytics, machine learning, artificial intelligence (AI), and biological engineering that are enabling and accelerating the change. This revolution has been decades in the making. The $3 billion, 13-year effort to map the human genome that began in 1990 is a foundational building block, but the power of this map only began to materialize when it became cheaper and faster to sequence DNA. The cost of DNA sequencing has been decreasing at a rate faster than Moore's Law. Advances in lower-cost and high-throughput screening have helped lower the costs of entry, accelerate the pace of experimentation, and generate new forms of data—to help us better understand biology.

Innovations are grouped into four arenas: (1) biomolecules—the mapping, measuring, and engineering of molecules; (2) biosystems—the engineering of cells, tissues, and organs; (3) biomachines—the interface between biology and machines; and (4) biocomputing—the use of cells or molecules such as DNA for computation (Exhibit 1).

Exhibit 1

A confluence of breakthroughs in biological science, with the development of computing, automation, and AI, are fueling a new wave of innovation.

4 arenas of biological innovation				
Definitions	**Biomolecules**	**Biosystems**	**Biomachine interfaces**	**Biocomputing**
Mapping	Cellular processes and functions via measuring intracellular molecules (eg, DNA, RNA, proteins) in the study of "omics"[2]	Complex biological organizations and processes and interactions among cells	The structure and function of nervous systems of living organisms	Intracellular pathways or networks of cells to return outputs based on specific conditions (for computation)
Engineering[1]	Intracellular molecules (eg, via genome editing)	Cells, tissues and organs, including stem-cell technologies and transplantation	Hybrid systems that connect nervous systems of living organisms to machines	Cells and cellular components for computational processes (storing, retrieving, processing data)
Examples	Gene therapy for monogenic diseases	Cultured meat grown in a lab	Neuroprosthetics for motor control (implant or external headset) of human or robotic limb	Data storage in strands of DNA

[1]Design, de novo synthesis, or modification.
[2]"Omics" refers to technologies that allow the identification and quantification of molecules of a biological system.
Source: McKinsey Global Institute analysis

McKinsey & Company

Major breakthroughs in each of the four arenas are reinforcing one another. In biomolecules and biosystems, advances in omics and molecular technologies are enhancing our understanding of biological processes, as well as enabling us to engineer biology. The ability also exists to engineer or modify a living cell to cure or prevent disease; for example, the groundbreaking CRISPR tool allows scientists to edit genes more quickly and precisely than previous techniques. Essentially the same process is being applied to manufacturing everything from textiles to meat. Advances in biomachines and biocomputing both involve deep

interaction between biology and machines; it is becoming increasingly possible to measure neural signals and power precise neuroprosthetics. It is now also possible to store the world's wealth of data using DNA. The storage density of DNA is about one million times that of hard-disk storage. DNA. The storage density of DNA is about one million times that of hard-disk storage. density of DNA is about one million times that of hard-disk storage.

New biological capabilities could bring about meaningful change across economies and societies

New biological capabilities have the potential to bring sweeping change to economies and societies:

Biological means could be used to produce a large share of the global economy's physical materials, potentially with improved performance and sustainability. Fermentation, for centuries used to make bread and brew beer, is now being used to create fabrics such as artificial spider silk. Biology is increasingly being used to create novel materials that have unique qualities, introduce entirely new capabilities, are biodegradable, and/or produced in a way that emits significantly less carbon. Some companies are already using genetically engineered microbes to create biofuels for the aviation and marine industries.

Increased control and precision in methodology is occurring across the value chain, from delivery to development and consumption with more personalization. Advances in molecular biology have made R&D and delivery processes more precise, predictable, and deliberate—enabling rational design rather than discovery by accident. Increasing knowledge of human genomes and the links between certain genes and diseases is enabling the spread of personalized medicine and precision agriculture.

The capability to engineer and reprogram human and nonhuman organisms is increasing. Gene therapies could offer complete cures of some diseases. Crops can be genetically engineered to produce higher yields and be more heat- or drought-resistant, for instance—traits that are becoming even more important given climate change.

Technically, one kilogram of raw DNA could store the entirety of the world's data.

New methodologies using automation, machine learning, and proliferating biological data are enhancing discovery, throughput, and productivity in R&D. Biology and computing together are accelerating R&D, thereby addressing a productivity challenge. McKinsey analysis in 2017 found that the ratio of revenue to R&D spending in the biopharmaceutical industry hit a productivity nadir between 2008 and 2011. Biotech companies and research institutes are increasingly using robotic automation and sensors in labs that could increase throughput up to ten times. Advanced analytics using machine learning can provide better insights during the R&D process.

Potential is growing for interfaces between biological systems and computers. A new generation of biomachine interfaces relies on close interaction between humans and computers. Such interfaces include neuroprosthetics that restore lost sensory functions (bionic vision) or enable signals from the brain to control physical movement. Biocomputers that use biology to mimic silicon are being researched, including the use of DNA to store data. DNA is about one million times denser than hard-disk storage; technically, one kilogram of raw DNA could store the entirety of the world's data.

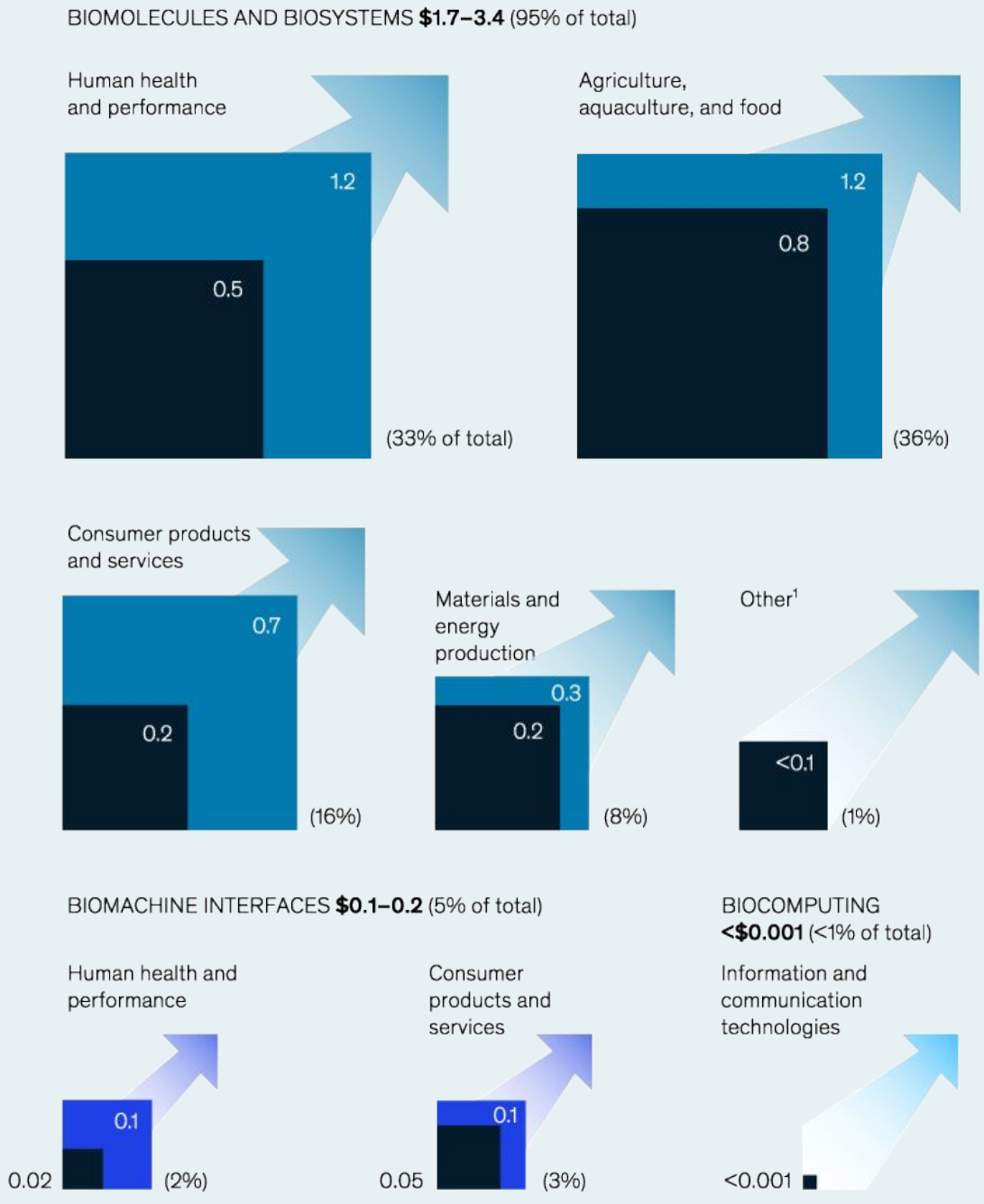
Today's pipeline of applications is a fraction of the far-reaching impacts expected ahead

For this research, a library of about 400 use cases was compiled that already constitute a visible pipeline for the years ahead. The library comprises applications that are scientifically feasible today and likely to be commercially viable by 2050. Over the next ten to 20 years these applications alone could have direct economic impact of between $2 trillion and $4 trillion globally per year.

Human health and performance has the clearest pipeline from research to commercialization. The science is advanced, and the market is generally accepting of innovations. However, more than half of the direct impact of the applications in the library over the next ten to 20 years is likely to be outside health, primarily in agriculture and consumer products (Exhibit 2).

More than half of the impact is outside of healthcare in agriculture, consumer, and other areas.

Partial estimate of range of annual potential direct economic impact by domain, 2030–40, $ trillion



Note: Figures may not sum to 100%, because of rounding. These impact estimates are not comprehensive; they include only potential direct impact of the visible pipeline of applications identified and assessed. Estimates do not represent GDP or market size (revenue), but direct economic impact; broader knock-on economic effects are not included. Estimates are relative to the 2020 economy; they do not include changes in variables such as demographics and inflation.
[1]Other applications include defense and security, undoing environmental harm, and education and talent.
Source: McKinsey Global Institute analysis

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Over this period, applications will tend to be in four key domains:

Human health and performance. Applications include cell, gene, and RNA therapies to treat or even prevent disease, a range of anti-aging treatments to extend lifespans, innovations in reproductive medicine, and improvements to drug development and delivery and new predictive modelling of human health and disease. Many more options are being explored and becoming available to treat monogenic (caused by a single gene) diseases such as sickle-cell anemia, polygenic diseases such as cardiovascular disease, and infectious diseases such as malaria. The direct annual global potential impact is estimated at $0.5 trillion to $1.3 trillion over the next ten to 20 years, or 35 percent of the total (including impact from biomachine interfaces).

Agriculture, aquaculture, and food. Applications in this domain include innovative new ways to conduct breeding of animals and plants using molecular or genetic markers that are many times quicker than established selective-breeding methods; new, more precise tools for the genetic engineering of plants; fast-developing work using the microbiome of plants, soil, animals, and water to improve the quality and productivity of agricultural production; and the development of alternative proteins including lab-grown meat. Direct annual impact could be between about $0.8 trillion and $1.2 trillion over the next ten to 20 years, or 36 percent of the total.

Consumer products and services. Opportunities are opening up to use increasing volumes of biological data to offer consumers personalized products and services based on their biological makeup. Applications in this domain include direct-to-consumer genetic testing, beauty and personal care increasingly based on increased knowledge of the microbiome as microbiome testing spreads, and innovative approaches to wellness (or fitness) not only in humans but in pets. There could be annual direct economic impact over the next ten to 20 years of $200 billion and $800 billion, or 19 percent of the total (including impact from

biomachine interfaces).

The direct annual global impact of the Bio Revolution could be $2 trillion to $4 trillion in 2030-40.

Materials, chemicals, and energy. New biological ways of making and processing materials, chemicals, and energy could transform many industries and our daily lives, although the economics are challenging. Applications in this domain include innovations related to production of materials such as improved fermentation processes, new bioroutes utilizing the ability to edit the DNA of microbes to develop novel materials with entirely new properties (self-repairing fabrics is one example), and building on advances in biofuels to innovate new forms of energy storage. Over the next ten to 20 years, the direct annual global impact could be $200 billion to $300 billion a year, or 8 percent of the total.

Biology has many other potential applications, although some of these are likely to be further in the future. It could be deployed to help the environment through biosequestration—using biological processes to capture carbon emissions from the atmosphere—and bioremediation. Impact is also emerging in biomachine interfaces and biocomputing where the science and development is at an early stage but applications are promising. Applications that have already been developed include neuroprosthetics to restore hearing and vision.

The direct potential impact of the around 400 use cases may only be a small portion of the potential scale of impact. Many other innovations are being developed in private labs or in the defense industry where developments remain confidential for commercial or national security reasons.

Eventually impact will radiate out to almost every sector of the economy with effects on societies and the environment as biological innovation transforms profit pools, value chains, and business models. In the years

ahead, if you are not using biology to make products, you will very likely be consuming them. The impact could go much further, with biology potentially being used to address some of the great challenges of our time including mitigating climate change. By 2040 to 2050, the direct applications we sized could reduce annual average man-made greenhouse-gas emissions by 7 to 9 percent from 2018 emissions levels.

Biological innovation has profound and unique risks

Profound risks accompany this surge of innovation in biology. Get it right and the benefits could be very significant; get it wrong and there could be disastrous consequences at the population level. These risks introduce a unique set of considerations which, if not managed properly, could potentially outweigh the promised benefits of a particular application:

- *Biology is self-replicating, self-sustaining, and does not respect jurisdictional boundaries*. For example, new genetically engineered gene drives applied to the vectors that spread disease (mosquitoes in the case of malaria) could have enormous health benefits, but such gene drives can be difficult to control and can potentially permanently change ecosystems.

- *The interconnected nature of biology can increase the potential for unintended consequences.* Changes to one part of the system can have cascading effects and unintended consequences across entire ecosystems or species. Gene editing could also have unintended or "off-target" effects.

    + *Low barriers to entry open the door to potential misuse with potentially fatal consequences.* Some biological technologies are relatively cheap and accessible. Commercial kits to perform CRISPR gene editing are being sold relatively cheaply on the internet.

+ *Differing value systems make it hard to forge consensus, including on life and death issues.* Technical and scientific issues, such as embryo editing, quickly become moral questions, and often, decisions across these issues are expressions of one's value system. The challenge of cooperation and coordination of value-systems across cultures and jurisdictions is no easy task, particularly when advances in these scientific domains could be seen as a unique competitive advantage for businesses or economies.

+ *Privacy and consent issues are fundamental.* Concerns about personal privacy and consent are rife, given that the cornerstone of biological advances is data mined from our bodies and brains.

+ *Unequal access could perpetuate socioeconomic disparity, with potentially regressive effects.* Biological advances and their commercial applications may not be accessible to all in equal measure, thereby exacerbating socioeconomic disparity. At a country level, developments are advancing quickest and most broadly in relatively rich countries.

These risks demand a considered response and potentially new approaches. In past waves of technological change, regulation has emerged in response to innovations; in biology, there is a strong argument for a proactive approach. Regulation will be important, but so too will oversight and monitoring of science even as it develops. The choices scientists make will help determine what kinds of technologies develop. International collaboration and coordination will be valuable as biology doesn't respect borders—as we experienced in early 2020 with the rapid spread of COVID-19.

In the journey to adoption, science is just the starting point

Risks need to be addressed, but beyond that there are many stages to negotiate as innovations move from the lab to adoption. The journey to adoption has three broad stages: scientific research; commercialization; and then diffusion. For biological applications to diffuse and deliver impact, six broad factors play a role; they determine whether adoption occurs and how long it takes:

+ *Investment in scientific research*. Funding, tools, talent, and access to data are necessary and powerful elements of the investment needed to enable scientists to be successful. It tends to take years of research and sizable investment in these capabilities to get an idea to the point at which a product or service is scientifically feasible.

+ *Four factors play a role in commercialization and diffusion.* First, a new biology-based product or service needs to compete with existing products and services not only on cost but also by offering higher quality or new properties or, indeed, by meeting a need not fulfilled by existing offerings. The second factor is whether business models are suitable for what may be a fast-changing landscape. Third, a new biology-based product and service needs to hit the right potential customers with go-to-market elements including pricing, sales, and marketing. The fourth factor is the ability to scale up operations.

+ *Risk and mechanisms governing use.* Given the profound and unique risks accompanying biological innovation, mechanisms governing use, including broad acceptance from society and regulation, are key at all stages. About 70 percent of the total potential impact could hinge on consumer, societal, and regulatory acceptance, based on an analysis of areas where regulations exist today in major economies.

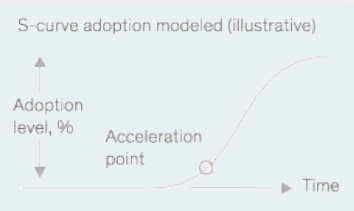
The pace and extent of adoption will vary enormously depending on the application and the domain. Some applications including using new bioroutes to manufacture drugs are already showing robust signs of early commercial adoption. Others such as CAR T-cell therapy for cancer have recently become commercially viable, adoption is early, and could increase rapidly in the near term over the coming decade. Yet others such as using genetically engineered plants to sequester CO2 show promise in scientific research but commercial viability and adoption by farmers or other buyers is likely further out (Exhibit 3).

Among applications assessed, adoption timing varies.

Example use-cases of estimated time horizon of acceleration point

The acceleration point is when adoption starts to experience rapid growth[1]

	Existing Before 2020	**Short term** 2020–30	**Medium term** 2030–40	**Long term** Beyond 2040
Human health and performance	• Carrier screening • Noninvasive prenatal testing	• CAR T-cell therapies for liquid tumors • Lipid biopsy	• Gene drives to reduce vector-borne diseases • CAR T-cell therapies for solid tumors	• Transplantable organs produced from stem cells • Embryo editing for medical purposes (eg, via CRISPR)
Agriculture, aquaculture, and food	• Marker-assisted breeding (crops and animals used for food) • Genetic tracing of food origin, safety and authenticity (eg, allergens, species, pathogens)	• Plant-based proteins • Crop microbiome diagnostics and probiotic treatments	• Cultured meat • Genetically engineered animals—faster growth	• Genetically engineered crops—faster growth through enhanced photosynthesis
Consumer products and services	• DTC genetic testing—ancestry	• Personalized meal services based on genetic and microbiome profile • DTC genetic testing—personal insights about health and lifestyle	• Biosensors for monitoring of personal health, nutrition, and fitness based on "omics"[2] data	• Gene therapy—skin aging
Materials, chemicals, and energy	• New bioroutes for drug manufacturing (eg, peptides)	• Novel materials—biopesticides/biofertilizers (eg, RNAi pesticides) • Improve existing fermentation processes—food and feed ingredients (eg, amino acids, organic acids)	• Novel materials—biopolymers (eg, PLA, PET)	• Biosolar cells and biobatteries
Other applications	• DNA sequencing for forensics		• Biosequestration of CO_2 • Bioremediation for pollution	



Note: See chapter 6 of the report for the full list of applications that we sized in these domains.
[1]The point at which adoption accelerates. We characterize this as the max of the second derivative of the adoption curve—see our technical appendix for more detail. Adoption level and timing for each use case depend on many variables, including commercial availability, regulation, and public acceptance. These estimates are not fully risk or probability adjusted. [2]"Omics" refers to technologies that allow the identification and quantification of molecules of a biological system.
Source: McKinsey Global Institute analysis

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Striking a balance that enables potential to be captured while managing risks

Given the breadth of change that likely lies ahead, innovators, businesses, governments, and individuals need to become literate in biological science in order to understand the fundamental shifts under way, seize the large potential benefits, but in a way that ensures that innovation is safe for citizens and society.

Innovators. Scientists govern their own research processes. Peer review is a powerful internal governing mechanism to ensure that research is accurate and well grounded. But scientists cannot operate in a vacuum; to an extent, they need to take into account the views of society in the research they propagate. The scientific community must play a consistent and effective oversight role.

Businesses should consider how to take advantage of biological innovation, potentially adapt strategies. The Bio Revolution could transform entire value chains, and companies in virtually every sector may need to adapt strategies. Given the uncertainty and evidently varied timing of adoption for different applications, companies should consider a portfolio-based approach toward investment. By its nature, biological innovation is cross-discipline and, as such, it is unlikely that any business that exists today can go it alone. Large companies should consider the degree to which they develop the full range of necessary capabilities in-house or “buy in” what they need through mergers and acquisitions, and partnerships. As in the Digital Revolution, some companies should consider how to use platform-based business models that can seize cross-sector opportunities, reduce marginal costs, and drive combinatorial innovation by leveraging growing biological data. Among other aspects to consider are the range of opportunities for more personalized and precise offerings enabled by growing biological data,

and innovative revenue models that could help accelerate diffusion.

The Bio Revolution could transform entire value chains, and companies in virtually every sector may need to adapt strategies.

Civil society, governments, and policy makers need to inform themselves about biological advances and respond to them effectively. Several governments including those of China, the United Kingdom, and the United States have set the tone for biological innovation with published strategic plans and goals intended to catalyze biological innovation and capture its benefits. However, innovation needs to be balanced by mechanisms to govern use and misuse, and whether existing professional and regulatory mechanisms are fit for purpose must be considered.

Individuals and consumers may be pivotal to the adoption path of biological advances. To contribute effectively to what can be controversial debates (consider embryo editing as an example), individuals need to seek to understand the benefits versus the risks. They also need to appreciate that there are personal trade-offs. DTC testing, for instance, provides individuals with potentially valuable insights into the probability of contracting certain diseases, but mining that information may compromise their privacy.

Different companies will find themselves at different starting points, facing different challenges when considering an advanced-analytics strategy for oncology. Larger, established pharmaceutical companies will likely benefit from a wealth of internal data sets and more data scientists. On the other hand, they might struggle to shift a more deeply engrained, cautious culture. Smaller biotech companies are likely to be more agile and more attractive to data scientists and other technical experts. However, they will have fewer existing data assets; a smaller portfolio of products, each perhaps critical to the company's success, could also make them more averse to a new, advanced-analytics-led approach because of the perceived risk.

Scarcity of data is also a challenge for companies researching and developing treatments for rare cancers or therapies with small eligible populations. Particularly sophisticated statistical techniques will be required to derive valid insights from the data.

Whatever their circumstances, however, all pharmaceutical companies will need a strategy for applying advanced analytics to their work in oncology. Failure to establish one amounts to a decision not to participate in a technical development that is reshaping cancer care. Companies have a choice of whether to keep pace with the development or lead it, but falling behind is not an option.

Thank you

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