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Perspective

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Averting Future Vaccine Injustice

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Both rapid innovation and equitable access to vaccines are necessary to protect the world from viral pandemics. Today, however, we face gross inequities in global access to Covid-19 vaccines. As high-income countries, such as the United States and European countries, have secured a majority of the world's vaccine supply (more than twice the volumes needed to cover their populations[1]), many low-income countries have barely begun the immunization process. It will take political courage to end such vaccine injustice now and political vision to negotiate the binding international rules needed to avert similar inequities in the future.

In the immediate term, countries that share vaccines with those facing shortages can save the lives of frontline workers and vulnerable groups, helping to end the pandemic and reducing the risk of emergence of new and dangerous variants, while generating an additional $9 trillion for the global economy with trade, travel, and work fully restored everywhere.[2]

At the same time, governments need to boost and diversify vaccine production capacity to Latin America, Africa, and Asia by transferring technology and ensuring that intellectual property (IP) protections such as patents do not pose legal barriers to manufacturing.[3] The global supply of Covid vaccines is currently insufficient and uncertain. Restrictions on exports of both raw materials and finished vaccines from key vaccine-producing regions, including the United States, Europe, and India, have exacerbated shortages worldwide and highlighted the risks of relying on just a few manufacturers. To increase both the volume and the security of the supply, more than 100 countries have called for the temporary suspension of international IP rules on Covid-19 countermeasures (including vaccines, drugs, diagnostics, and other medical equipment). Such a suspension would strengthen legal certainty for producers, allowing them to start manufacturing quickly, and expand scientists' freedom to develop better, more appropriately adapted vaccines. Expanded production may take months to bear fruit, but it would be worthwhile, given the likelihood that SARS-CoV-2 will be circulating for years to come.

In the medium term, governments can negotiate international rules for access to countermeasures in future pandemics and invest in the scientific and industrial capacity that give such rules teeth. At the World Health Assembly meeting in May, member countries agreed to lay the groundwork for a potential "pandemic treaty." Access to countermeasures is among the thorniest issues to untangle, but evidence from Covid-19 vaccines clarifies what a treaty must do.

First, we believe that governments should legally commit to increasing long-term public investment in both research and technology development and should condition those investments on global public interest safeguards such as contract transparency and open sharing of data, know-how, and IP. Covid-19 has demonstrated that decades of publicly funded basic research — $17.2 billion between 2000 and 2019 from the

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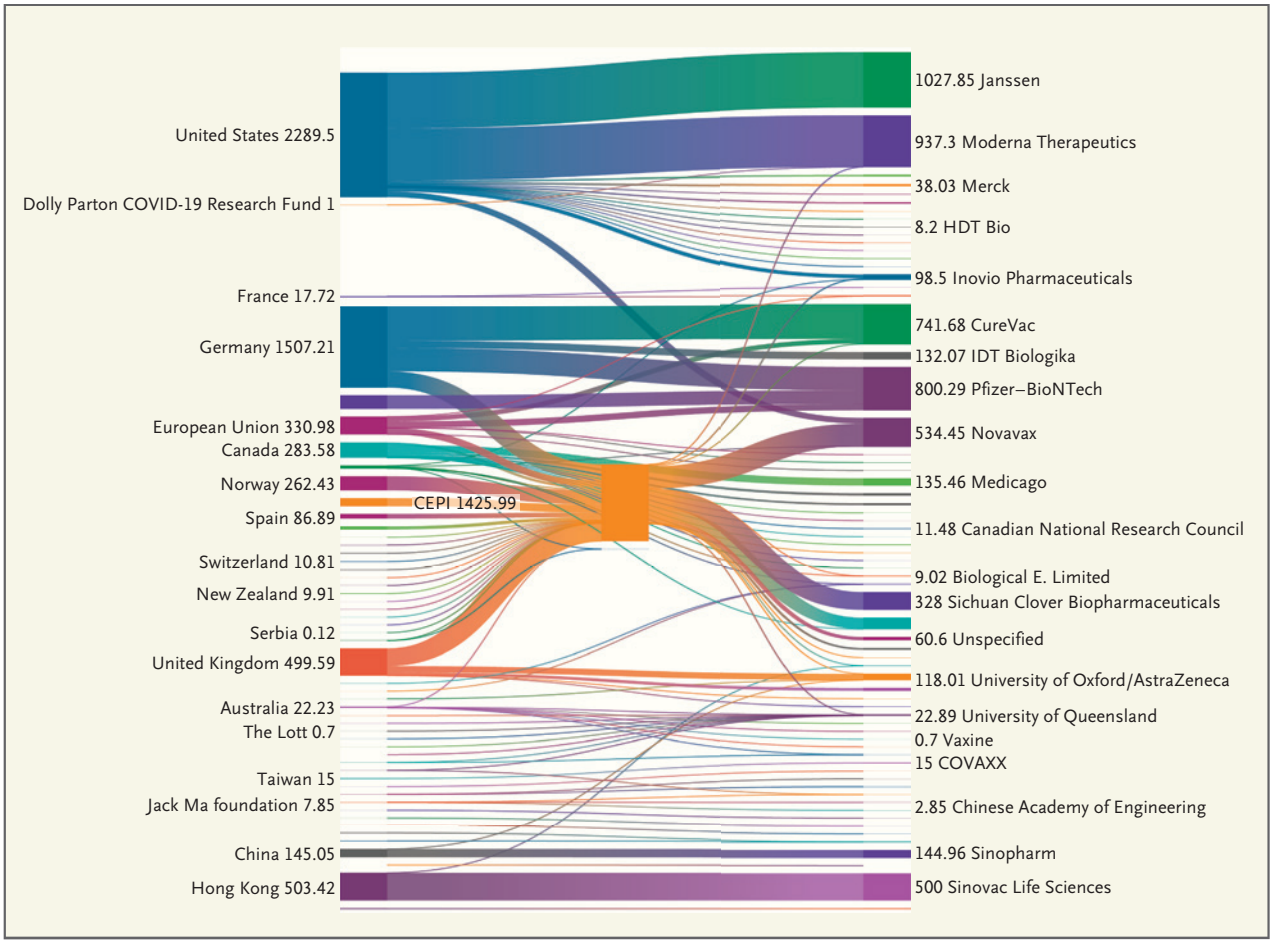

Public Funding for Covid-19 Vaccine Research and Development 2020–2021: Sources, Intermediaries, and Recipients ($U.S. millions).

Approximately $5.6 billion from public and philanthropic sources has been invested in Covid-19 vaccine research and development (R&D) since January 2020. According to publicly available data, 55 different entities (shown on the left) made up-front investments into R&D primarily with public funds; the majority of these funds went to private firms, but they also went to academic, government, and other research organizations (shown on the right). The three largest funders were the United States, Germany, and the Coalition for Epidemic Preparedness Innovations (CEPI). Most governments invested in entities within their own jurisdictions. Investments were not necessarily coordinated, and few seem to have had conditions attached to ensure global access.

U.S. National Institutes of Health alone — was necessary for and effective at building the scientific foundation on which vaccines could be rapidly developed.[4] This pandemic has also illustrated the importance of large-scale public investment for rapid product development. Starting in early 2020, dozens of governments individually and jointly (through the Coalition for Epidemic Preparedness Innovations, or CEPI) infused approximately $5.6 billion of up-front funding into academic and private-sector vaccine research and development (R&D) (see figure).

Governments also reduced the financial risk for vaccine producers by committing, even before vaccines had obtained regulatory approval, to purchase more than $45 billion worth of these products.[1,5] Such large-scale public funding is necessary for pathogens with pandemic potential, since market returns are highly uncertain at early stages and yet hesitation to invest can be fatal.

Nevertheless, it is past time to renegotiate society's contract with the pharmaceutical industry for combating pandemics: if taxpayers bear the lion's share of risks and costs, private companies should price the resulting products affordably and openly share the data, technology, and know-how that have been subsidized. Open knowledge sharing accelerates innovation by allowing scientists to build rapidly on each other's research, helps manufacturers meet global demand, and enables regulators to assess products more quickly — all critical factors in emergencies. Adequate public control over knowledge is

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essential for rapid, open sharing, given companies' strong commercial interest in withholding knowledge from competitors.

With legally binding commitments for up-front public funding of vaccine R&D, IP monopolies would not be necessary to induce innovation. Governments could make their funds go further by pooling them through regional or global vehicles such as CEPI, which is mandated to secure global access to the vaccines that result from its investments. Early in the pandemic, governments acting unilaterally largely invested in companies based in their own countries.[5] Though unsurprising, this approach generates smaller, riskier portfolios for each country and ensures neither equitable access nor adequate global supply.

In contrast, CEPI developed a geographically diverse portfolio of vaccine candidates that spread out both scientific and manufacturing risk. Some companies that received large-scale grants from CEPI (AstraZeneca and Novavax) made stronger commitments to allocate supply to developing countries, price their vaccines affordably, and transfer technology than did some other companies (Moderna and Pfizer). With funding from 17 governments, the European Union, foundations, and firms, CEPI was among the world's three largest public R&D investors (having committed over $1.4 billion, more than 90% of it public funds, primarily for R&D but also for manufacturing), alongside the United States ($2.3 billion) and Germany ($1.5 billion).[5] More in-depth evaluation of CEPI is needed to elucidate the factors that facilitated and impeded global access in this pandemic, and to provide lessons for the future. Nevertheless, it offers proof of principle that governments can invest together in vaccine R&D, up front, at risk, at scale, and for access.

An audio interview with Dr. Moon is available at NEJM.org

In a context of geopolitical competition, however, not all governments may be willing to cooperate so closely on the sensitive security issue of pandemic vaccines. The United States, Europe, Russia, and China all rapidly developed Covid-19 vaccines that have now been deployed globally. A network of regional funds could complement a global entity like CEPI by investing in vaccine developers closer to home, while agreeing to coordinate and adopt common binding rules for transparency, pricing, and sharing of data and technology. Successful vaccine development anywhere could then mean vaccines produced and accessible everywhere.

Beyond funding, binding international rules are critical for ensuring rapid sharing of pathogen samples and related data. The sharing of genomic sequencing data on SARS-CoV-2 by scientists in China on the publicly accessible GISAID platform in January 2020 jump-started the development of diagnostics and vaccines worldwide. Rapid international sharing of genomic sequencing data has also been essential for tracking emerging variants. But such data sharing rests on soft norms of scientific cooperation and is not reliable. International sharing of physical pathogen samples is also critical but lagged behind the flow of sequencing data. An international agreement could mandate rapid, open sharing of both samples and data, contingent on guaranteed access to the resulting benefits (e.g., research results, scientific credit, training opportunities, and countermeasures) for the originating researchers and countries. The 2011 Pandemic Influenza Preparedness Framework developed by member countries of the World Health Organization (WHO) established such a quid pro quo: all countries agreed to share influenza samples with a WHO laboratory network in exchange for assured access to at least some vaccines and other technologies that companies would subsequently develop. The political bargain that this framework struck provides a foundation on which to build stronger rules covering all pathogens and data.

After vaccines are developed, there is likely to be at least an initial scarcity of global supply. Ideally, all governments would commit to consume only their fair share and to permit exports of vaccines produced in their jurisdictions. But such promises are not politically credible. A more reliable strategy is to build scientific and industrial capacity to develop and produce adequate volumes of countermeasures in all regions and to negotiate rules ensuring that knowledge and technology are globally shared, even when physical products are not. Using and expanding regional manufacturing hubs today are necessary steps toward ending the current pandemic and preparing for the next one.

In 2013, governments rejected the chance to advance a WHO treaty establishing an international public fund for medicines R&D and rules making the resulting technology openly accessible. We should not lose the opportunity now to craft international laws that would make future pandemic vaccines available to all as global public goods and avert a repeat of the ethical, epidemiologic, and economic catastrophe that is unfolding today.

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Scaling Up Covid-19 Vaccination in Africa — Lessons from the HIV Pandemic

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Concerns regarding access to Covid-19 vaccines in Africa are reminiscent of concerns raised about responding to the HIV pandemic in the mid-1990s and early 2000s, when highly active antiretroviral treatment (ART) was accessible in high-income countries but had limited availability in African countries — a disparity that resulted in many preventable deaths in these high-burden settings.[1] Funding for scaling up ART throughout Africa was not available until 2002, when the United Nations Global Fund against AIDS, Tuberculosis, and Malaria and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) began to provide it. During the Covid-19 pandemic, these programs provided a model for the World Health Organization (WHO) and global partners to rapidly establish the COVID-19 Vaccines Global Access (COVAX) initiative to bridge the vaccine gap and ensure rapid and equitable access to vaccines in both high-income countries and low- and middle-income countries.[1]

The HIV pandemic taught us that ART provision alone was insufficient to achieve global disease control. It highlighted the need to scale up health infrastructure for multiple purposes: to procure drugs, promote ART adherence and retention in care, identify key populations at risk, overcome stigma inhibiting access to care, and develop community support for HIV prevention and treatment. Another key need was obtaining robust data for efficacious HIV treatment in vulnerable populations, including children and pregnant women (see table).

In addition to access to Covid-19 vaccines and therapies, countries require sufficient infrastructure to receive and administer these interventions, which may be logistically challenging in rural and remote areas. Local resources for addressing these requirements, especially for vaccines, vary among urban and rural settings in the various African subregions. The current mRNA-based Covid-19 vaccines (developed by Moderna and Pfizer–BioNTech) require a continuous cold chain for distribution: Moderna's vaccine needs –20°C for shipping and storage before dilution, and Pfizer's vaccine must be kept at –70°C, a much greater challenge in Africa. Many health care centers in African countries lack the personnel, equipment, and stable electrical power for low-temperature vaccine storage. Innovative solutions for storage and transport are needed, such as the high-tech, insulated, reusable container developed to keep Ebola vaccines at ultracold temperatures for up to a week. The mRNA vaccines are administered as two doses separated by 3 to 4 weeks, which presents the challenge of retaining patients long enough to complete the full series. The Johnson and Johnson adenovirus-vector vaccine, which recently received emergency use authorization from the Food and Drug Administration, offers advantages for rollout in Africa, including single-dose administration and no need for ultracold storage. The Oxford–AstraZeneca vaccine can be stored and transported at normal refrigeration temperatures (2 to 8°C) for at least 6 months.

The identification of populations at high risk for HIV and the development of tailored strategies to engage them in HIV prevention and treatment has been critical for the success of nation-

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