

US public investment in development of mRNA covid-19 vaccines: retrospective cohort study

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Abstract

Objective To estimate US public investment in the development of mRNA covid-19 vaccines.

Design Retrospective cohort study.

Setting Publicly funded science from January 1985 to March 2022.

Data sources National Institutes of Health (NIH) Report Portfolio Online Reporting Tool Expenditures and Results (RePORTER) and other public databases. Government funded grants were scored as directly, indirectly, or not likely related to four key innovations underlying mRNA covid-19 vaccines—lipid nanoparticle, mRNA synthesis or modification, prefusion spike protein structure, and mRNA vaccine biotechnology—on the basis of principal investigator, project title, and abstract.

Main outcome measure Direct public investment in research and vaccine development, stratified by the rationale, government funding agency, and pre-pandemic (1985-2019) versus pandemic (1 January 2020 to 31 March 2022).

Results 34 NIH funded research grants that were directly related to mRNA covid-19 vaccines were identified. These grants combined with other identified US government grants and contracts totaled \$31.9bn (£26.3bn; €29.7bn), of which \$337m was invested pre-pandemic. Pre-pandemic, the NIH invested \$116m (35%) in basic and translational science related to mRNA vaccine technology, and the Biomedical Advanced Research and

Development Authority (BARDA) (\$148m; 44%) and the Department of Defense (\$72m; 21%) invested in vaccine development. After the pandemic started, \$29.2bn (92%) of US public funds purchased vaccines, \$2.2bn (7%) supported clinical trials, and \$108m (<1%) supported manufacturing plus basic and translational science.

Conclusions The US government invested at least \$31.9bn to develop, produce, and purchase mRNA covid-19 vaccines, including sizeable investments in the three decades before the pandemic through March 2022. These public investments translated into millions of lives saved and were crucial in developing the mRNA vaccine technology that also has the potential to tackle future pandemics and to treat diseases beyond covid-19. To maximize overall health impact, policy makers should ensure equitable global access to publicly funded health technologies.

Introduction

One of the greatest public health successes to come out of the covid-19 pandemic was the development of safe and effective mRNA vaccines against SARS-CoV-2.¹²³⁴ Approximately 92% of fully vaccinated Americans received an mRNA based vaccine, marking the first time that this vaccine delivery system has been used at scale.⁵ In the first year alone, all covid-19 vaccines are estimated to have collectively prevented 20 million deaths globally, including preventing 1.1 million deaths in the US.⁵⁶

The success of mRNA vaccines against SARS-CoV-2 was possible because of scientific ingenuity and biotechnological advances over the previous 30 years, including substantial funding from the US and foreign governments. After the pandemic began in early 2020, the US made historic financial investments in completing clinical trials and provided advance purchase guarantees for hundreds of millions of doses of vaccines even before their safety and efficacy were fully demonstrated. This accelerated development and reduced the risk for vaccine developers.⁷⁸ Every new drug marketed in the US from 2010 to 2016 was related to some previous National Institutes of Health (NIH) supported research, and a quarter of new drugs are linked to late stage public funding through an academic research center or one of its private spin-off companies.⁹¹⁰¹¹¹²¹³¹⁴

Estimates of the extent of public investment for covid-19 vaccines vary widely. For example, the Biomedical Advanced Research and Development Authority (BARDA) reported that it spent \$40bn (£33bn; €37bn) on vaccines through 2021.¹⁵ Meanwhile, one report estimates that the government invested \$900m in pre-clinical research for multiple candidate vaccines.¹⁶ Other authors have noted that the \$15bn spent on HIV vaccine research informed the development of coronavirus vaccines.¹⁷ How much the US government directly invested specifically in mRNA covid-19 vaccines remains unclear. To better understand US public funding supporting this unprecedented health technology development, we sought to quantify and classify the public investments made by the US government in the development of mRNA covid-19 vaccines before and during the first two years of the pandemic.

Methods

We identified public funding through three primary data sources—the NIH Research Portfolio Online Reporting Tool Expenditures and Results (RePORTER), the Department of Defense Contracts database, and BARDA's Medical Countermeasures Portfolio.¹⁸192021 We reviewed the scientific literature describing the history of mRNA covid-19 vaccine development and focused on four categories of indispensable inventions²²: development of lipid nanoparticles as a drug delivery system, synthesis and modification of mRNA and small interfering ribonucleic acid (siRNA), definition of the prefusion “spike” protein structure of SARS-CoV-2, and the development of RNA vaccine biotechnology for use in humans.

Search strategy

We used a published patent network analysis of mRNA covid-19 vaccines that identified 88 key patented inventions and linkages with organizations licensing the technology.²³ That analysis omitted patents related to the structure of the prefusion spike protein, so we identified 33 additional patents after reviewing the websites of mRNA vaccine manufacturers and searching Google Patents for scientists identified in our scientific review.²⁴ We identified all inventors listed on these 121 patents (n=177) and supplemented the list with other researchers we identified from published accounts of the history of mRNA vaccine development (n=17) and from news reports and press releases (n=8).²³ The complete list of patents reviewed and scientists identified are available in the supplementary material (eTable 1 and eTable 2).

After reviewing the patents and attributions in the literature, two authors (HSL and SN) independently assigned the contributions of each scientist to one or more of the four critical inventions. All potential inventions were included to maintain a broad search strategy.

We developed search terms by pairing each scientist's name with a standardized term describing the invention(s) associated with the researcher. In addition to the four categories of inventions, we added a fifth category to identify any research specifically related to coronaviruses. We optimized the search terms by reviewing the number of publications retrieved in PubMed, to be as inclusive as possible. The five complete search terms were: [Name of scientist] AND [lipid or nanoparticle or lipid nanoparticle]; [name of scientist] AND [mRNA OR siRNA]; [name of scientist] AND [prefusion OR spike]; [name of scientist] AND [vaccin* OR immune*]; [name of scientist] AND [coronavirus OR COVID-19 OR SARS-CoV-2].

NIH RePORTER

This electronic database includes all NIH funded research grants since 1985, including grants outside and within government agencies such as the Centers for Disease Control and Prevention, Agency for Healthcare Research and Quality, Health Resources and Services Administration, Administration for Children and Family, and the US Department of Veterans Affairs.¹⁸ We searched the PubMed identification number for each article in the NIH RePORTER to identify research grants and extracted key details, including principal investigator, title, year, government agency, and funding amount. By convention, each entry in the NIH RePORTER covers one fiscal year; grants are often funded for consecutive fiscal years. We removed and consolidated all duplicate grants, including sub-projects, into a category of NIH funded grants.

Two authors (HSL and SN) independently scored each NIH funded grant to determine whether it was related to a critical scientific invention in covid-19 vaccine development, adapting previously described methods.¹²¹³¹⁴ They assigned one point if the principal investigator(s) was one of the 205 researchers identified in the search described above and a second point if the project title and project abstract included reference to any of the four categories of inventions studied or to covid-19. These NIH grants were categorized as directly related (receiving two points), indirectly related (one point), or not related (zero points) to mRNA covid-19 vaccine development. For all NIH grants receiving two points, two authors (HSL and SN) independently reviewed and scored the grant abstracts for relevance to a critical scientific invention in mRNA covid-19 vaccine development. Inter-rater disagreements in scoring were adjudicated by a blinded third author (ASK).

Department of Defense

We searched the electronic Department of Defense contract database by using the five complete PubMed search terms mentioned above to identify issued contracts and extracted the amount and rationale for funding.²⁴ This database documents contracts since 2017, with previous contracts stored on GitHub (personal communication from Jared Adams, Defense Advanced Research Projects Agency (DARPA), 4 October 2021). To account for funding issued before 2017, we reviewed USASpending.gov and reviewed press releases, reports, and fact sheets from DARPA, as the agency within the Department of Defense responsible for investing in emerging technologies.²⁵

Biomedical Advanced Research and Development Authority

We reviewed BARDA's portfolio of mRNA vaccine investments made by the Department of Health and Human Services as part of Operation Warp Speed and extracted funding awarded to Pfizer-BioNTech and Moderna, including the size, date, and rationale for each grant.¹⁹ We verified all grants with announcements such as news releases. We also

reviewed funding from programs and organizations collaborating with BARDA and the Department of Defense, including the Joint Program Executive Office for Chemical, Biological, Radiological, and Nuclear Defense, since BARDA's creation in 2006.²⁶

Statistical analysis

On the basis of these findings, we tabulated the direct public investment by the US government in mRNA covid-19 vaccines. We stratified results by pre-pandemic (1985-2019) versus pandemic periods (1 January 2020 through 31 March 2022), the governmental agency providing the funding, and the specific purpose of the funding: supporting basic and translational science, clinical trials, vaccine development (including vaccine formulation, laboratory testing, and clinical trial support), manufacturing capacity, and purchasing vaccine supply for domestic use and global donations. We converted all values to 2022 US dollars by using the Consumer Price Index for all Urban Consumers.²⁷

Patient and public involvement

We held focus groups with patient advocacy organizations to understand which aspects of this study had the greatest short term and long term importance to patients and the general public. We discussed strategies to disseminate our results publicly to reach a broad audience. We used these learnings to develop materials for the lay public. Owing to technical nature of the research, patients were not directly involved in the study design or data collection process.

Results

We identified 205 researchers and completed 449 PubMed searches of their work, yielding 4627 papers. These articles were linked to 20 825 NIH funded fiscal years in RePORTER and then consolidated to 2676 distinct NIH funded grants (fig 1). Of these, we identified 34 NIH research grants (covering 165 fiscal years), with \$692m in total funding, that were directly related to one of the four critical inventions within mRNA covid-19 vaccines, including \$116m in pre-pandemic NIH research funding covering 165 fiscal years (table 1). A complete list of all NIH grants is available in the supplementary materials (eTable 3). We identified an additional 603 indirectly related NIH grants with \$5.9bn in funding (grant abstracts not reviewed).

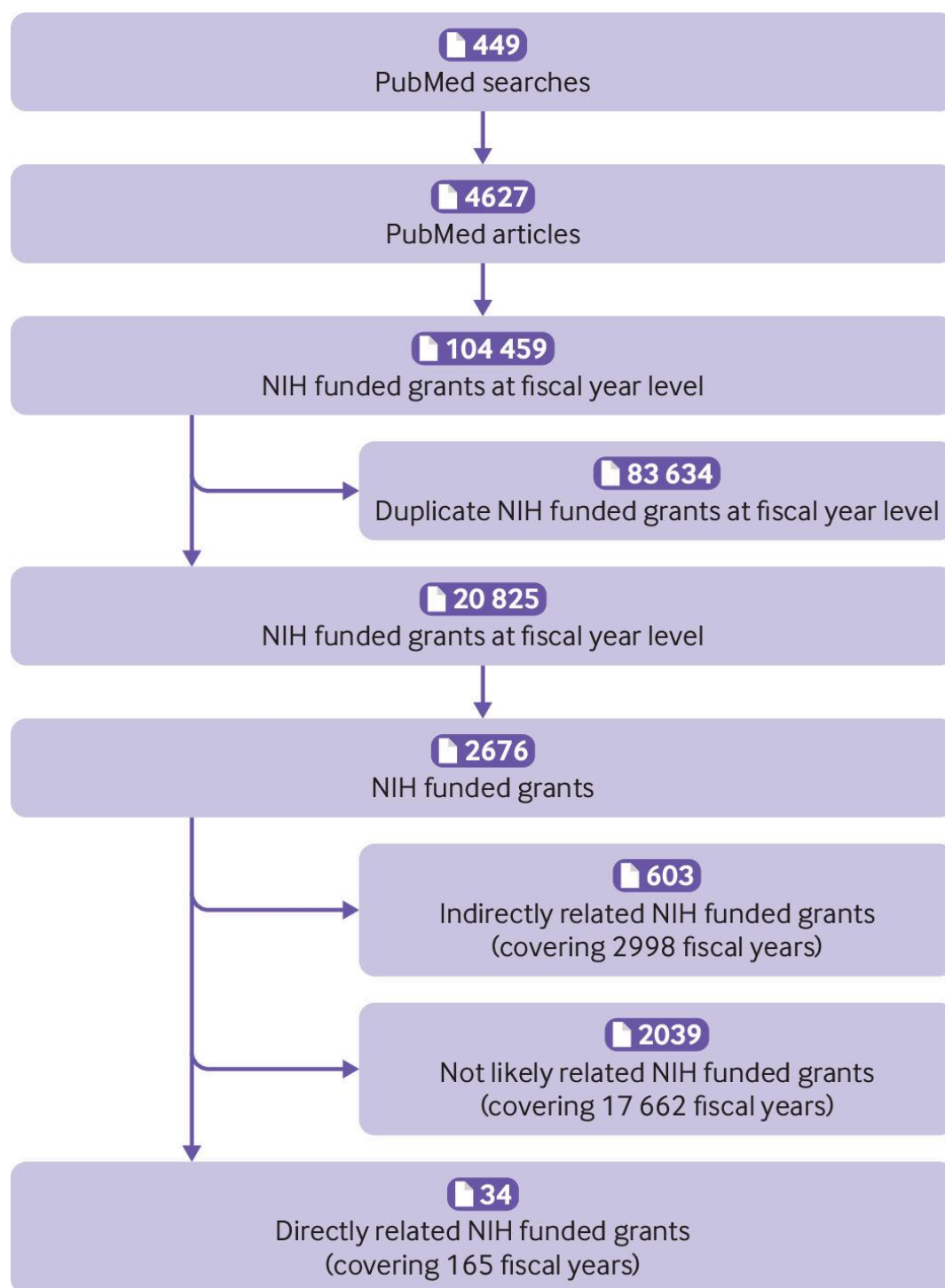


Fig 1

NIH RePORTER search strategy to identify US government funded research for mRNA covid-19 vaccines. Figure outlines PubMed search strategy and analytic method to identify National Institutes of Health (NIH) funded research grants that were directly related to key inventions in mRNA covid-19 vaccines. By convention, NIH funded grants are listed in NIH RePORTER per fiscal year as core projects and subprojects. These NIH grants often receive consecutive years of funding, so NIH funded grants at fiscal year level (n=20 825) were consolidated into distinct NIH funded grants (n=2676) by matching grant title, principal

investigator(s), and organization name. Duplicate NIH funded grants were removed. These duplicates include grants that were listed in more than one published research article in PubMed and subgrants (or subprojects), which are encompassed within grants at fiscal year level

Table 1
Categorization of US public investment in mRNA covid-19 vaccines. Values are millions of US dollars*

- View popup
- View inline

Additional investments by the Department of Defense and BARDA brought the total US public investment in pre-pandemic research and development to \$337m, and a total contribution of \$31.9bn from 1985 through March 2022, including research, development, and vaccine supply expenditures (table 1).

Pre-pandemic funding

Of the \$337m in pre-pandemic investments in research and development, \$116m (35%) was from the NIH, \$148m (44%) from BARDA, and \$72m (21%) from the Department of Defense (table 1). The number of NIH funded fiscal years increased from one between 1985 and 2001 to 21 in 2019, with a corresponding increase in NIH funding from less than \$1m to more than \$10m (fig 2). The NIH awarded \$99m (85% of grants) through the National Institute of Allergy and Infectious Diseases. BARDA and the Department of Defense primarily funded vaccine development. The Department of Defense funded CureVac and Moderna, whereas BARDA invested in basic and translational science, clinical trials, and manufacturing capacity of the mRNA Zika vaccine with Moderna (table 1).

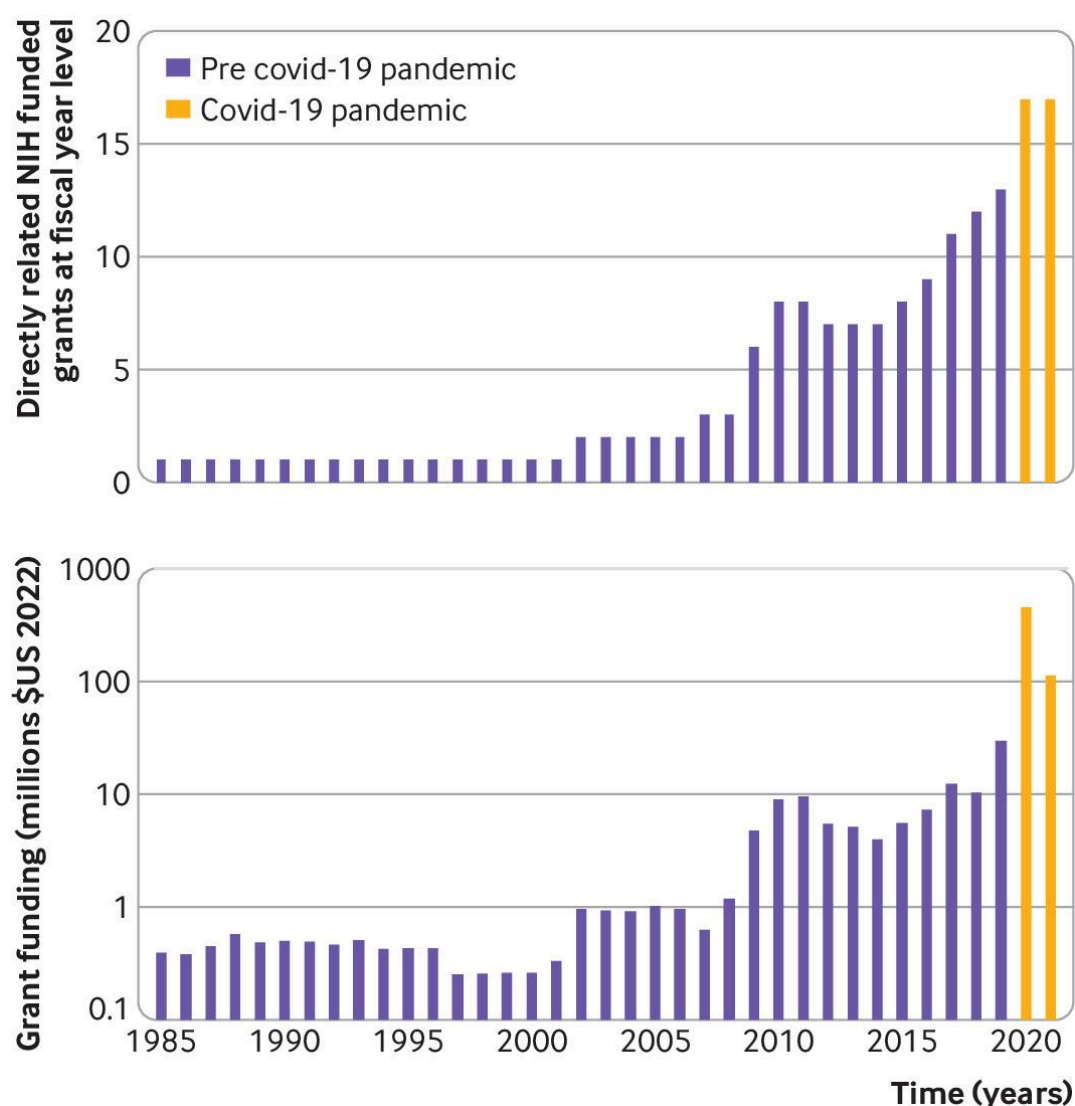


Fig 2

National Institutes of Health (NIH) grants (top) and grant funding (bottom) at fiscal year level directly related to mRNA covid-19 vaccine development from 1985 to 2021 (top). Data obtained from NIH RePORTER analysis stratified by pre-pandemic (1985-2019) and pandemic (1 January 2020 to 31 March 2022). All directly related NIH funded grants at fiscal year level were included (n=165). This corresponds to 34 NIH funded grants after consolidation of fiscal years per grant. Two NIH grants in 2022 were excluded from figure, as study analysis period ended on 31 March 2022, and additional grants had not yet been awarded. This analysis does not include grants offered by Department of Defense or Biomedical Advanced Research and Development Authority

Pandemic funding

The US federal government invested at least \$2.3bn in research and development of the mRNA covid-19 vaccines after the pandemic began in 2020 through March 2022. BARDA supported clinical trials for Moderna (\$1.7bn), the NIH funded separate clinical trials

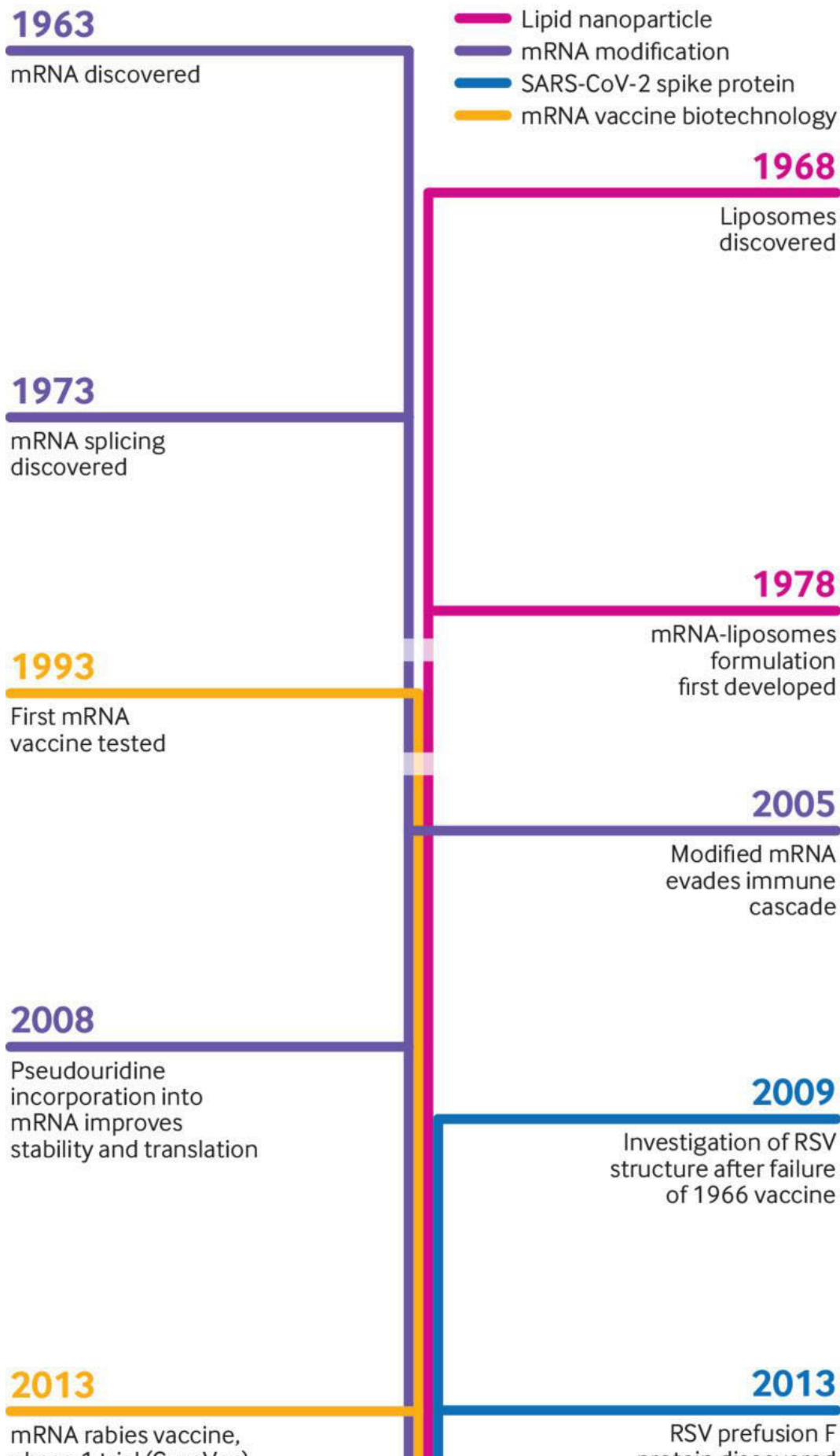
(\$490m), and investments in manufacturing and basic or translational science were made (\$108m).

An additional \$29.2bn (92%) was spent by BARDA (\$21.8bn; 75%) and the Department of Defense (\$7.4bn; 25%) for advance commitments to purchase 2 billion doses of vaccine (table 1). These advanced market commitments included doses intended to vaccinate the US population and global vaccine donations (supplementary materials, eTable 4).

Moderna received \$10.8bn, of which \$8.8bn (81%) was for vaccine supply. Pfizer-BioNTech received \$20.4bn, mostly for vaccine supply. One billion vaccine doses were purchased for international donation from Pfizer-BioNTech at a substantially reduced price compared with vaccines intended for Americans (eTable 4).

Key basic and translational scientific innovations

The basic and translational science supporting mRNA covid-19 vaccines involved at least four critical inventions. A timeline of some key events illustrates the gradual progression of research and development over time, starting with the discovery of mRNA in 1963 to emergency use authorization of two mRNA covid-19 vaccines in December 2020 (fig 3).



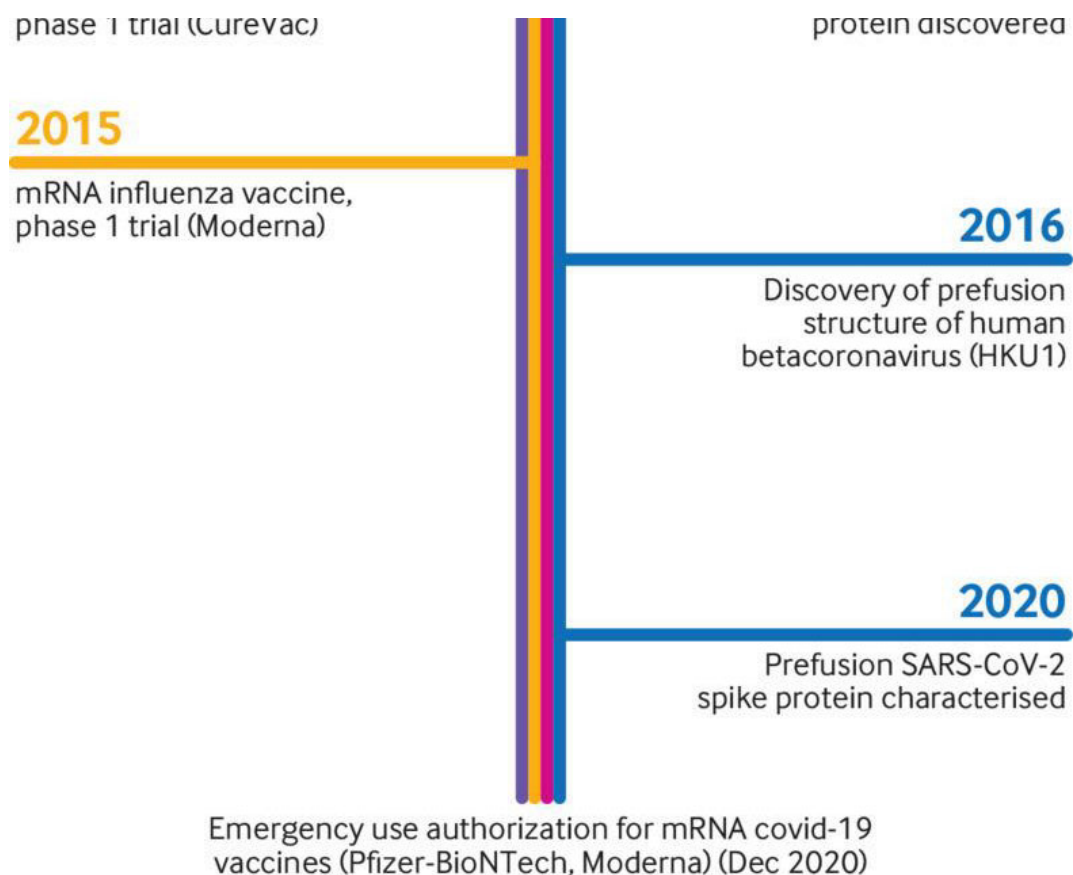


Fig 3

Timeline of selected key events in research and development of mRNA covid-19 vaccines. Summary of certain key events that led to invention of mRNA covid-19 vaccines based on analysis of government funded grants awarded by National Institutes of Health, Department of Defense, and Biomedical Advanced Research and Development Authority and adapted from historical literature review. RSV=respiratory syncytial virus

Lipid nanoparticles evolved from the discovery of liposomes in the 1960s, with the capacity to provide a strong architectural backbone to stabilize and transport negatively charged nucleic acids, protecting them from degradation and enhancing delivery of drug to the target cell. Pieter Cullis and colleagues from the University of British Columbia pioneered the innovation with significant funding from the Canadian government.³⁰³¹

Modification of mRNA synthesized in the laboratory and avoidance of immune detection was a key breakthrough led by Katalin Karikó and Drew Weissman of the University of Pennsylvania. In 2005, after more than a decade of work, they succeeded in synthesizing mRNA without initiating a vigorous inflammatory cellular response to a foreign material. In 2008 they successfully modified pseudouridine, an isomer of the nucleoside uridine, enhancing RNA stability, altering RNA-protein interactions to affect gene expression, and decreasing the inflammatory response further.²²³²³³

Discovery of the structure and effectiveness of targeting prefusion coronavirus proteins was based on decades of research on the failed respiratory syncytial virus vaccine of 1966. Identification of the respiratory syncytial virus prefusion F protein in 2013 led to the understanding that prefusion proteins were a superior target to post-fusion proteins. In 2016 the prefusion structure of the human betacoronavirus, a genera of coronaviruses, was discovered. This technology was used to characterize the structure of the prefusion SARS-CoV-2 “spike” protein within weeks after the pandemic began in early 2020.³⁴ This research was led by Barney Graham beginning at Vanderbilt University. He moved to the NIH in 2000, where he worked with Kizzmekia Corbett (NIH) and collaborated with Jason McLellan at the University of Texas and Andrew Ward at the Scripps Institute.

Development of the RNA vaccine biotechnology was necessary to safely and effectively elicit an immune response to lipid nanoparticles and modified mRNA. The first mRNA vaccine was tested in mice in 1993, and the first human trial began in 2013 with a rabies vaccine after the Department of Defense funded CureVac, a German biopharmaceutical company. The Department of Defense also funded scientists working on developing mRNA vaccines for other infectious diseases, such as Chikungunya, Zika, and HIV.

Discussion

In the 35 years before the covid-19 pandemic, the US government directly invested more than \$330m in research and development that made the development, testing, and rapid production of mRNA covid-19 vaccines possible. During the pandemic through 31 March 2022, the US government contributed an additional \$30bn, primarily through BARDA and the Department of Defense, to support clinical trials and vaccine manufacturing and to purchase vaccines in advance, even before their efficacy and safety were fully defined.

Strengths and limitations of study

This study is the first to systematically catalog the direct pre-pandemic US public investments in mRNA covid-19 vaccines by using an established public investment method.¹²¹³¹⁴ Our analyses use data from three federal agencies—NIH, BARDA, and Department of Defense—and collectively pool and categorize the rationale for these investments. We identified 121 key patented inventions in the mRNA covid-19 vaccine and 34 NIH funded grants covering 165 fiscal years that directly contributed to these inventions (eTable 3).

Our focus, however, was limited to direct public investment by the US government in the first generation mRNA covid-19 vaccines, and we did not evaluate public funding for other covid-19 vaccine candidates, mucosal vaccines, or the next generation pan-coronavirus vaccines.³⁵ Our estimation of NIH funding is limited by research published in the literature. We also excluded investments made by private companies (for example, pharmaceutical,

biotechnology, venture capital), other nations (for example, Canada, Germany), and private foundations (for example, Bill & Melinda Gates Foundation) because we could not evaluate them systematically.³⁶³⁷³⁸

Our estimate of \$337m is likely a substantial underestimate of the total pre-pandemic investment of public funds. We were intentionally conservative in classifying funding as directly related to these vaccines; an additional \$5.9bn was deemed indirectly related. Furthermore, we were unable to include data from the National Science Foundation because they were inaccessible and incomplete.

Comparison with other studies

Compared with previous studies of public investment in covid-19 vaccines, our results are more systematic and specific to the mRNA vaccines. For example, one study focused on BARDA funding given to six covid-19 vaccine candidates.³⁹ Meanwhile, a recent study found that the NIH invested \$17.2bn in research on all vaccine technologies before 2020. Of this, \$943m was for mRNA vaccines, a higher estimate than ours.⁴⁰ Another analysis found that the NIH had invested \$700m in coronavirus research and development since the severe acute respiratory syndrome outbreak of 2003.⁴¹ However, the PubMed and NIH RePORTER search terms used in the last two studies were broad and did not emphasize patented inventions or factor the relevance of each grant. Finally, the covid-19 mapping project evaluated funding for vaccines, therapeutics, and diagnostics combined.⁴²

We included the most pivotal research in HIV and oncology that directly contributed to mRNA covid-19 vaccine development, but one study quantified the repeated setbacks of the HIV vaccine from 2000 to 2019, 80% of which were funded by the US federal government, and discussed how the \$15bn invested laid the groundwork for the covid-19 vaccine.¹⁷ All of these studies provide evidence that our calculation of direct NIH research funding is a low estimate of the total pre-pandemic US public investment.

Findings in context

Public financing of key scientific discoveries is a longstanding practice. The US is the largest funder of biomedical research in the world, and this has led to many vitally important breakthroughs.⁴³ These breakthroughs are the result of both public and private funding. An important spur to such investment was the Bayh-Dole Act of 1980, which encouraged universities to work with industry to commercialize federally funded research.⁴⁴ When DARPA started investing in nucleic acid vaccines in 2011 under the Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) program to support military personnel against infectious diseases, it sent a strong guiding signal that the US government believed that this biotechnology was worthy of investment. Similarly, in 2016, DARPA launched the

Pandemic Prevention Platform (P3) program to discover and manufacture antibody treatments using influenza, Zika, and Middle East respiratory syndrome, and it led to great early success. These efforts were redirected toward SARS-CoV-2 in early 2020.²⁸

The NIH's partnership and direct involvement in developing the covid-19 vaccine marketed by Moderna was so substantial that three NIH researchers (Barney Graham, John Mascola, and Kizzmekia Corbett) were initially listed on the patents for this product. The company later disputed the importance of their involvement, leading to a protracted legal dispute.⁴⁵ Moderna has thus far not patented the key genetic sequence in the vaccine.⁴⁶

The US government was not alone in publicly funding basic and translational science underlying mRNA covid-19 vaccines before the pandemic. Canada made significant investments in the lipid nanoparticle invention, and Germany invested in mRNA synthesis and modification by funding, for example, Ozlem Tureci and Ugur Sahin starting in the late 1990s.²²⁴⁷

Our results document the extent to which public funding supported all aspects of covid-19 mRNA vaccine development. Although the public funding supporting Moderna is widely recognized, Pfizer-BioNTech executives have claimed that the company did not accept any US government support to develop its vaccine. However, Pfizer-BioNTech would not have been able to develop an mRNA covid-19 vaccine without the licensed technologies emerging from research funded by US taxpayers.²³ Additionally, BioNTech was awarded \$445m from the German government to accelerate covid-19 vaccine development and to expand manufacturing capacity.³⁶ The private investment contributions made by Moderna or Pfizer-BioNTech to this work are likely substantial, but their scale is unknown and not specifically disclosed on public filings with the US Securities and Exchange Commission.

During the pandemic, the public investment in the mRNA covid-19 vaccine products via Operation Warp Speed was far more extensive than for any previous public product development.¹⁰¹¹ For example, the NIH invested \$220m in research for an Ebola vaccine from 2004 to 2013 and about \$1.1bn in 2015 for Ebola countermeasures via BARDA, the Department of Defense, and the NIH. From 2014 to 2021, the NIH invested \$369m toward a tuberculosis vaccine and \$439m toward a malaria vaccine.⁴⁸⁴⁹ Total public funding previously estimated for other key pharmaceuticals included \$62m for buprenorphine, \$60.9m for sofosbuvir, \$13.8m for pregabalin, and \$85m for paclitaxel.¹²¹³¹⁴⁵⁰

In this case, BARDA and the Department of Defense co-developed the mRNA vaccine marketed by Moderna throughout its development, eventually investing more than \$18bn, including guaranteed vaccine purchases. By committing to purchase hundreds of millions of mRNA vaccine doses in advance and directly funding clinical trials and manufacturing capacity for the Moderna vaccine, the US government substantially de-risked the vaccine development process.

Policy implications: access, equity, and pricing

The extensive US public investment in covid-19 vaccine technology and products over 35 years has led to questions about the return that the US public should expect on their investment. Traditionally, public research grants, including those from the NIH, BARDA, and the Department of Defense, do not include provisions to safeguard public access or affordability of future inventions. They also do not typically include provisions for equitable global access for inventions of public health significance.⁵⁰ Instead, US technology transfer policy has allowed recipients of public funding, such as academic research centers, to manage any intellectual property and licensing arrangements directly with commercial partners. As a result, products developed with public funding are often sold at high prices both in the US and around the world. For example, the antiretroviral combination of emtricitabine/tenofovir (Truvada) was shown to be effective in preventing HIV via the use of \$50m in federal grants, and yet it was priced at \$2100 per month by its manufacturer, sparking a 2019 congressional oversight investigation.⁵¹⁵²

Inequities in access to global vaccines have persisted through the first two years of the pandemic. Fewer than 35% of Africans have received at least one dose of any covid-19 vaccine, and 51% of vaccine doses were purchased in advance by high income countries representing just 14% of the world population.⁵³⁵⁴⁵⁵ One reason for this is the lack of access to intellectual property, although other factors contributed as well.⁵⁶⁵⁷ Although the US licensed some of its technology to the World Health Organization's Covid-19 Technology Access Pool (C-TAP) 17 months after emergency use authorization was granted in the US, no mRNA patents were shared.⁵⁸⁵⁹ Instead, the American strategy for global vaccine equity has been focused primarily on vaccine donations, with more than 1.2 billion doses promised by 2023 and about 500 million delivered to more than 110 countries as of March 2022.⁶⁰⁶¹

The pricing of publicly funded and privately patented essential public health technologies has been controversial. The cost of manufacturing a single dose of mRNA covid-19 vaccine is estimated to be between \$1 and \$3.⁶²⁶³ However, despite the significant US public funding and advanced market commitment, the US paid Pfizer-BioNTech \$19.50 per dose in 2020, \$24 in 2021, and \$30.48 in 2022 for the bivalent booster. Meanwhile, the US paid Moderna \$15.25 per dose for the first order and \$26.36 in 2022.⁶⁴⁶⁵ In October 2022 Pfizer announced that it planned to charge health insurance plans \$110 to \$130 per dose once the US government stops buying vaccines, and Moderna followed suit in January 2023.⁶⁶⁶⁷ This represents a 650% to 800% increase in the price of vaccine compared with the initial price. Even if insured patients have zero cost sharing for the vaccine in the future, this higher commercial price will ultimately contribute to higher healthcare spending. Globally, the prices of all mRNA vaccines vary widely by country.⁶⁸

The future of mRNA based therapeutics and vaccines

With the success of the mRNA technology platform demonstrated with covid-19 vaccines, hundreds of new products incorporating this technology using mRNA synthesis and lipid nanoparticles are being tested. Actively recruiting clinical trials involve mRNA medicines ranging from common diseases such as influenza and respiratory syncytial virus to rare conditions including glycogen storage diseases and methylmalonic acidemia.⁶⁹ Some experts believe that we are entering a new era with mRNA technology and the promise of regenerative medicine and personalized cancer vaccines on the horizon.⁷⁰ For example, the first universal mRNA influenza vaccine against all known types of influenza is being tested in animals and is showing promising early results.⁷¹ In late 2022 investigators announced that an mRNA cancer vaccine (mRNA-4157/V940) might be useful in helping to treat advanced high risk melanoma.⁷²

Policy solutions

Policy makers have several options to consider that could improve equitable access to government sponsored innovations such as covid-19 vaccines.⁷³ Firstly, the US government could add conditions to public funding contracts requiring certain access, equity, and affordability benchmarks to be met for inventions that are a result of public funding. Secondly, US government funding agencies could be more proactive about following up on the technology licenses they grant to ensure that manufacturers are making the products appropriately available for the benefit of public health. Thirdly, the US and the European Union could reaffirm the Doha Declaration of 2001 on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and public health, and they could pledge to open science and freely share intellectual property licenses to essential public health inventions with the global community.⁷⁴

Conclusion

The development of mRNA covid-19 vaccines during the pandemic was a monumental scientific success. This achievement was possible, in large part, because of significant US public investment in research and development during the preceding 35 years and record setting public contributions during the pandemic to accelerate and reduce the financial risk of vaccine development. The resulting mRNA vaccines have benefitted millions of people and saved millions of lives. The substantial role played by public funding should help to justify greater efforts by the US, Canadian, and German governments to assure equitable and affordable access to this lifesaving technology in the US and globally.

What is already known on this topic

- Vaccines against covid-19 are estimated to have prevented approximately 20 million deaths globally in the first year of their use
- Government funding helped to support the development of covid-19 vaccines

What this study adds

- From 1985 to 2019, the US government invested at least \$337m into research and development that directly contributed to key inventions in the mRNA covid-19 vaccines
- During the pandemic through March 2022, the US government contributed at least \$31.6bn for clinical trials (6%), vaccine development (2%), and vaccines purchases (92%)
- These investments should inform vaccine payment policies and intellectual property assignments for essential global health technologies

Ethics statements

Ethical approval

This study was not submitted for institutional review board review because it is based on publicly available data and involved no health records (45 Code of Federal Regulations [CFR] 46.102)

Data availability statement

No additional data available.

Acknowledgments

We thank the patient advocacy organizations for sharing their expertise on the relevance and importance of this research to the lives of patients.

Footnotes

- **Contributors:** HSL, JA, and ASK conceived the study. HSL, AS, JA, ASK, and REB designed the study. HSL and SN acquired and collated the data. HSL, SN, and ASK analyzed the data. All authors contributed to and critically revised the manuscript. All authors gave final approval of the version to be published. The authors had full access to all the data in the study, and all authors shared final responsibility for the decision to submit for publication. HSL is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.
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- **Competing interests:** All authors have completed the ICMJE uniform disclosure form at <https://www.icmje.org/disclosure-of-interest/> and declare: grant support from Arnold Ventures, Commonwealth Fund, Anthem Public Policy Institute, National Institutes of Health, and Tennessee Department of Mental Health and Substance Abuse Services; HSL is a senior advisor to the Public Good Projects; AS and REB have received consulting fees from the Council for Informed Drug Spending Analysis and Alosa Health, respectively; HSL is a co-founder of ThisIsOurShot and VacunateYa, a national grassroots organization that empowers trusted messengers on social media to spread accurate health information and combat covid-19 vaccine misinformation (unpaid); no other relationships or activities that could appear to have influenced the submitted work.
- **Transparency:** The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.
- **Dissemination plans to patients and the public:** The results of this study will be shared with the public through press release, social media, and interviews.
- **Provenance and peer review:** Not commissioned; externally peer reviewed.

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