Vaccines for Covid-19

Draft Background and Scope

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Background

In Wuhan, China in December, 2019, patients began to present with atypical pneumonia.[1] Over the next several months, the disease that would be called Covid-19 and was caused by the virus SARS-CoV-2 spread around the world as a pandemic, disrupting life in nearly every country. More than seven million people died of Covid-19 with more than 1.2 million deaths in the United States (US) alone.[2]

By early January, 2020, SARS-CoV-2 had been genetically sequenced.[1] On April 30, 2020, the first Trump Administration launched operation Warp Speed to quickly produce a vaccine for Covid-19.[1] In mid-November, 2020, vaccines using messenger RNA (mRNA) technology developed by Moderna and by Pfizer-BioNTech were found to be ~95% effective, with data published in December, 2020.[1,3,4] These and other vaccines were rolled out in early 2021 and by the end of January, 2021, more than 23 million doses were administered in the US.[1] Although these vaccines dramatically affected the course of the pandemic, by the summer of 2021 the "Delta" variant of SARS-CoV-2 became widespread and could be transmitted even by vaccinated patients.[1] Booster vaccines to address waning immunity and vaccine modifications to address viral variants were developed, and over time the vast majority of people in the US received vaccines, had experienced prior infection(s) with SARS-CoV-2, or both, creating a population that was no longer immunologically naïve. In this setting, early data from randomized trials of mRNA and other vaccines, including the highly-effective Novavax spike protein vaccine,[5] provide only limited information about the current effects of immunization in the US population.

Four vaccines for Covid-19 are currently available in the US: Spikevax (Moderna); mNEXSPIKE (Moderna); COMIRNATY (Pfizer, BioNTech); and Nuvaxovid (Sanofi). As of August 2025, the FDA labels were changed to state that the vaccines are approved for use in all individuals who are 65 years of age and older, and individuals under 64 with at least one underlying condition that puts them at risk for severe Covid-19 outcomes (minimum indicated age: six months for Spikevax, five years for COMIRNATY, and 12 years for Nuvaxovid and mNEXSPIKE).[6-9] Recent recommendations from the Advisory Committee on Immunization Practices (ACIP) generally follow the revised FDA

labels. Some professional associations and state public health departments have promulgated guidance that is more aligned with prior ACIP recommendations.[10-12]

Stakeholder Input

This draft scoping document was developed with input from diverse stakeholders, including patients and patient groups, clinicians, researchers, and manufacturers of the agents of focus in this review. This document incorporates feedback gathered during preliminary calls with stakeholders and open input submissions from the public. A revised scoping document will be posted following a three-week public comment period. ICER looks forward to continued engagement with stakeholders throughout its review and encourages comments to refine our understanding of the clinical effectiveness and value of preventive treatments.

Report Aim

This project will evaluate the health and economic outcomes of vaccines for Covid-19. The ICER value framework includes both quantitative and qualitative comparisons across treatments to ensure that the full range of benefits and harms – including those not typically captured in the clinical evidence such as innovation, public health effects, reduction in disparities, and unmet medical needs – are considered in the judgments about the clinical and economic value of the interventions.

Scope of Clinical Evidence Review

The proposed scope for this assessment is described on the following pages using the PICOTS (Population, Intervention, Comparators, Outcomes, Timing, and Settings) framework. Evidence will be abstracted from randomized controlled trials as well as high-quality systematic reviews; high-quality comparative cohort studies will be considered, particularly for long-term outcomes and uncommon adverse events and we anticipate also using such cohort studies to help evaluate updated vaccine effectiveness. Our evidence review will include input from patients and patient advocacy organizations, data from regulatory documents, information submitted by manufacturers, and other grey literature when the evidence meets ICER standards (for more information, see ICER's grey literature policy).

All relevant evidence will be synthesized qualitatively or quantitatively. Wherever possible, we will seek out head-to-head studies of the interventions and comparators of interest. Data permitting, we will also consider combined use of direct and indirect evidence in network meta-analyses of selected outcomes. Full details regarding the literature search, screening strategy, data extraction, and evidence synthesis will be provided after the revised scope in a research protocol published on the Open Science Framework website (https://osf.io/7awvd/).

Populations

The population of interest for this review is people living in the United States in 2026.

Data permitting, we will evaluate the evidence on effectiveness and harms within subpopulations defined by:

- Sociodemographic factors (e.g., sex, age, race, ethnicity)
    - We are particularly interested in specific sociodemographic subgroups including: young children; boys and young adult men; pregnant women; adults under age 65; adults ages 65 and older

- Comorbid conditions including:
    - Pulmonary conditions such as asthma and COPD
    - Cardiovascular disease
    - Immunocompromising conditions
    - Diabetes
    - Obesity

Interventions

The intervention(s) of interest of this review are:

- COMIRNATY (Covid-19 vaccine, mRNA)
- Spikevax (Covid-19 vaccine, mRNA)
- mNEXSPIKE (Covid-19 vaccine, mRNA)
- Nuvaxovid (Covid-19 vaccine, adjuvanted)

Comparators

Data permitting, we intend to compare these vaccines to each other and to not receiving an updated vaccine for Covid-19.

Outcomes

The outcomes of interest are described in the list below.

- Patient-Important Outcomes
    - Covid-19
    - Serious illness from Covid-19
    - Hospitalization
    - Mortality
    - Risk of transmitting SARS-CoV-2

    - Long Covid and permanent harms from Covid-19
    - Fetal injury from Covid-19
    - Adverse events including
        - Short-term minor adverse events including fever and malaise
        - Myocarditis and pericarditis
        - Guillain-Barre syndrome
        - Fetal injury from Covid-19 immunization
- Other Outcomes
    - Asymptomatic SARS-CoV-2 infection

Timing

Evidence on intervention effectiveness and harms will be derived from studies of any duration.

Settings

All relevant settings will be considered, with a focus on outpatient settings in the United States.

Benefits Beyond Health and Special Ethical Priorities

Our reviews seek to provide information on benefits beyond health and special ethical priorities offered by the intervention to the individual patient, caregivers, the delivery system, other patients, or the public that would not have been considered as part of the evidence on comparative clinical effectiveness. These general elements (i.e., not specific to a given disease) are listed in the table below.

Table 1.1. Benefits Beyond Health and Special Ethical Priorities

Benefits Beyond Health and Special Ethical Priorities*
There is substantial unmet need despite currently available treatments.
This condition is of substantial relevance for people from a racial/ethnic group that have not been equitably served by the healthcare system.
The treatment is likely to produce substantial improvement in caregivers' quality of life and/or ability to pursue their own education, work, and family life.
The treatment offers a substantial opportunity to improve access to effective treatment by means of its mechanism of action or method of delivery.

*Benefits beyond health and special ethical priorities shape to some extent how the value of any effective treatments for a particular condition will be judged and are meant to reflect the broader effects of a specific treatment on patients, caregivers, and society. For additional information, please see the ICER Value Assessment Framework.

ICER encourages stakeholders to provide input on these elements in their public comment submissions.

Scope of Comparative Value Analyses

A detailed economic model analysis plan with proposed methodology, model structure, model parameters, model inputs, and model assumptions will be published on February 13, 2026. This scoping document provides early thoughts about the overall model structure.

As a complement to the evidence review, we will develop an economic model to assess the lifetime cost-effectiveness of vaccines for Covid-19 (i.e., Spikevax (Moderna); mNEXSPIKE (Moderna); COMIRNATY (Pfizer, BioNTech); and Nuvaxovid (Sanofi) compared to each other and to not receiving a vaccine. The model structure will be based in part on a literature review of prior published models of vaccines for Covid-19. Analyses will be conducted from the health care system perspective and the modified societal perspective. The base case analysis will take a health care system perspective (i.e., focus on direct medical care costs only). Societal impacts (e.g., patient and caregiver productivity) and other indirect costs will be considered in a separate modified societal perspective analysis. This analysis will be considered as a co-base case when (a) direct data on indirect costs are available, (b) the societal costs of care are large relative to direct health care costs, and (c) the impact of treatment on these costs is substantial. This will most often occur in cases where the incremental cost-effectiveness ratio changes by greater than 20%, greater than $200,000 per QALY or evLY, and/or when the result crosses the threshold of $100,000-$150,000 per QALY or evLY gained. If direct data are lacking on patient and/or caregiver productivity, we will implement a method to capture the potential impacts of vaccines for Covid-19 on productivity (patient and caregiver) as well as certain other impacts (e.g., patient time seeking care).

The target population will consist of individuals living in the United States. The model will differentiate between uninfected individuals, those experiencing mild, severe, or critical Covid-19 illness, and those with post-acute outcomes such as long Covid, long-term complications, or death. Additionally, short-term adverse events following vaccination will be included. We anticipate using a decision tree to capture short-term outcomes, and a Markov model to capture long-term events and survival. A cohort of patients will transition between states during predetermined cycles over a lifetime time horizon, modeling patients from vaccination until death. In addition, cost-effectiveness will be estimated for shorter time horizons (e.g., five years).

Key model inputs will include clinical probabilities, quality of life values, and health care costs. Probabilities, costs, and other inputs will differ to reflect varying effectiveness between vaccine types. Treatment effectiveness will be estimated using clinical trials and observational studies.

Health outcomes and costs will be dependent on time spent in each health state, clinical events, adverse events (AEs), and direct medical costs. The health outcome of each intervention will be evaluated in terms of hospitalization, need for ventilation, long Covid, deaths, life-years gained, quality-adjusted life years (QALYs) gained, and equal value of life years gained (evLY). Quality of life weights will be applied to each health state, including quality of life decrements for serious adverse

events. The model will include direct medical costs, including but not limited to costs related to vaccination, Covid-19-related treatment costs, condition-related care, and serious adverse events. In addition, patient and caregiver productivity changes and other indirect costs will be included in a separate analysis, as available data allow. Relevant pairwise comparisons will be made between treatments, and results will be expressed in terms of the marginal cost per QALY gained, cost per evLY gained, cost per life-year gained, and separate estimates for cost per hospitalization, ventilation, and cases of long Covid averted. We plan to explore subgroup analyses by relevant demographic and clinical characteristics, data permitting.

In separate analyses, we will explore the potential health care system budgetary impact of vaccination over a five-year time horizon, utilizing published or otherwise publicly-available information on the potential population eligible for treatment and results from the economic model for treatment costs and cost offsets. This budgetary impact analysis will indicate the relation between treatment prices and level of use for a given potential budget impact, and will allow assessment of any need for managing the cost of such interventions. More information on ICER's methods for estimating potential budget impact can be found here.

Identification of Low-Value Services

ICER includes in its reports information on wasteful or lower-value services in the same clinical area that could be reduced or eliminated to create additional resources in health care budgets for higher-value innovative services (for more information, see ICER's Value Assessment Framework). These services are ones that would not be directly affected by vaccines for Covid-19 (e.g., intensive care unit (ICU) admission for Covid-19), as these services will be captured in the economic model. Rather, we are seeking services used in the current management of Covid-19 beyond the potential offsets that arise from a new intervention. ICER encourages all stakeholders to suggest services (including treatments and mechanisms of care) that could be reduced, eliminated, or made more efficient.

References

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