

US COVID-19 vaccination preference (CVP) study

08 November 2020

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Introduction

Background and rationale

The COVID-19 pandemic has affected daily lives around the world. As described by Mello and colleagues, “bringing a vaccine to market is only half the challenge; also critical is ensuring a high enough vaccination rate to achieve herd immunity.” (Mello, Silverman et al. 2020) The rationale for this health preference study is to understand the effects of the vaccination attributes on its uptake among US adults generally. It is doubtful that the “Six Trigger Criteria” put forth by Mello and colleagues will be sufficient to achieve the critical uptake rate because they do not account for vaccination preferences. Furthermore, this study will be contributed for use as a worked example for a forthcoming book, *Methods for Health Preference Research*, published by Oxford University press.

Between 14 and 18 May 2020, the Associated Press and the National Opinion Research Center (NORC) at the University of Chicago conducted 1,056 telephone or online interviews using a probability-based panel of adults in the United States (US). (AP-NORC 2020) The survey asked, “If a vaccine against the coronavirus becomes available, do you plan to get vaccinated, or not?” According to their results, roughly half of American adults (49%) reported that they would get a coronavirus disease 2019 (COVID-19) vaccine if scientists working to produce one succeed. Apart from these, 20% of those surveyed would refuse the vaccine, while 31% were not sure if they would get vaccinated. Of the 174 respondents who say they will not receive the vaccine, 70 (40%) indicate concerns about the vaccine side effects. Since this study, a several studies in health preference research (HPR) have been published, but no study has identified determinants of COVID-19 vaccination uptake in the United States. (Dong, Xu et al. , Weinstein and Nguyen , Chorus, Sandorf et al. 2020, Compton, Sarraf-Yazdi et al. 2020, Farber, Ort et al. 2020, García and Cerda 2020, Grover, McClelland et al. 2020, Jonker, de Bekker-Grob et al. 2020, Liao, Ng et al. 2020)

When a COVID-19 vaccine is approved by the Centers for Disease Control and Prevention (CDC), it will likely be recommended for all US adults as part of its adult immunization schedule. Its distribution may initially be limited, targeting those at high risk and essential workers (Phase 1); however, wider uptake will be necessary to achieve herd immunity. Based on the May 2020 poll results, support for COVID-19 vaccination is far from unanimous among the US general population, particularly among those at low risk. Currently, there is no private or public organization actively coordinating the pre-launch research on vaccination uptake, which represents a major gap in the field. This study is an initial examination, asking a national sample of US adults about what might influence their uptake of a potential COVID-19 vaccine once available to the general population.

COVID-19 HPR Roundtables

To better understand how to design this study, Benjamin M. Craig (PI) hosted a series of open roundtable discussions with over 30 scientists from around the world (see acknowledgements). On 17 June 2020, they began by discussing the eighteen health preference studies related to COVID-19 that were currently under review or ongoing (including this one). (Craig, Sepúlveda et al. 2020) Like this

study, each of the seventeen other studies focused on stated preferences, specifically testing the causal relationships between attributes and preferential choice behaviors related to COVID-19. These are not single questions studies, like the NORC-AP poll; instead, they provide an in-depth understanding of health preferences related to COVID-19.

Given that COVID-19 is a new topic in health preference research (HPR), it was remarkable to hear about so many independent studies from Australia, Canada, China, France, Germany, New Zealand, The Netherlands, UK, and USA. Most sought to study preferences of the general population on alternative policies and the tradeoffs involved, either in a single country or in multiple countries. Others focused on individual health interventions (like this protocol), attempting to predict uptake of COVID-19 vaccines and of contact-tracing apps. Many topics remain untouched, such as clinical trial participation, labor decisions, testing, and long-term care. COVID-19 has affected nearly all aspects of our daily lives, and COVID-19 HPR will likely expand immensely over the coming months with little risk of duplication. During the roundtable, the teams emphasized lessons that are particularly relevant when conducting a COVID-19 HPR study.

The first lesson is that perspectives regarding COVID-19 are evolving. In practical terms, starting and finishing a study quickly, such as within 30 days, may be exciting and expeditious, but in retrospect, early evidence may age more quickly. A once perfectly valid instrument may be out-of-date two weeks later when preparing the results for dissemination. Although these rapid-cycle studies could provide near real-time information for policy decisions, traditional peer-review timelines limit their potential. Nevertheless, the publication of these studies can provide important snapshots of the public's preferences and inform the design of sequential studies. Study teams may be wise to consider pairing their objectives with dissemination plans to avoid the potential obsolescence of preference evidence due to changes in the context or as respondents gain greater firsthand experience with COVID-19.

The second lesson is that nearly all epidemiologic interventions and their social impacts are legitimately complex, which makes them challenging to convey to the general population in a health preference study. Trading off among their attributes often presents a moral dilemma, calling for the interpretation of a philosopher as much as an economist. For example, choosing to wait for a more effective vaccine may imply time preferences, but also has distributional consequences within the population. In most countries, the burden of COVID-19 in terms of health and employment has been far from uniform.

The third lesson concerns the inelastic demand for goods and services, such as masks, apps, and vaccines. Some persons are nontraders who are implacably in favor of or against a good or service (e.g., anti-vaxxers), regardless of the attributes. (Tversky 1972, Reichman 1974) Such persons absolutely will or will not comply with public health recommendations. Knowing the proportion of nontraders is required to accurately predict uptake; however, surveying their preferences on alternatives is uninformative. Some researchers have argued that stated preference surveys are bad at predicting uptake but good at quantifying rates of substitution. The ideal approach may be to pool stated and revealed preference evidence to identify both rates of substitution and predicted uptake. In any case, it is important to acknowledge the limits of preference evidence when capturing the factors that drive real-world behaviors (e.g., working to support a household).

Some characteristics of nontraders make health preference researchers feel uneasy. Nontraders can have nuanced reasoning or be willfully ignorant. Others have distinct political views that are well outside the mainstream. Each country has its own aberrant sub-populations. Such eccentric views on the burden

of disease or the risks may be scientifically valid or unfounded, but, if a preference study attempts to change them, the study will fail to predict real-world behavior. By altering respondents' perspectives, study teams switch from positive economics (i.e., describing what is) to normative economics (what should be).

The last lesson is to recognize that the world is at the start of a pandemic like no other in terms of infectious spread and media attention. Understanding what drives uptake and other health-related behaviors is critically important for nearly every country. Capturing preference evidence now on tradeoffs and priorities can provide an evidentiary basis for health system reforms in the near and long term. Some researchers are using this moment to develop innovative prioritization tools (e.g., ventilator allocation) that may have applications across multiple future areas. Even when we overcome this challenge, there will likely be another someday with similar traits. The attendees expressed unanimous support for COVID-19 HPR, and hope to see these exciting studies published in the coming months. As such, Benjamin M. Craig plans to host the COVID-19 HPR Roundtable monthly during the pandemic.

Vaccination Preference Research (VPR)

The COVID-19 pandemic has further solidified the relevance of **vaccination preference research (VPR)** as the subfield of HPR dedicated to vaccination studies, including the value of vaccines, their delivery, their outcome and supporting systems. In this study, **uptake** refers to the utilization of a vaccination services (either as a stated or revealed preference), namely choosing vaccination over no vaccination. In VPR, **reluctance** is a negative increment in preference intensity driving this choice and **hesitance** is the likelihood of hesitating, which is a behavioral precursor to a choice. Reluctance is one of multiple causes of hesitance, such as uncertainty about perception, trust, and other behavioral contributors. Likewise, hesitance is one of multiple barriers to vaccination uptake.

In VPR, it is often easier to describe uptake than **opt-out**. After choosing to forgo vaccination, a person may change their mind the following hour, day, week, or month. In this study, the opt-out is “no vaccination for six months,” which is a realistic alternative that cannot be enforced in practice. The purpose of VPR is to understand vaccination preference recognizing that it is only one factor that may influence uptake (e.g., required to be vaccinated by an employer).

In the primary analysis of this study, all individuals are described by the likelihood of belonging to one of two groups (**grade-of-membership**): individuals who are unwilling to be vaccinated (a.k.a., **non-traders**, stayers) and individuals who may be willing to be vaccinated (a.k.a., **traders**, movers). Among those willing, some may consistently choose to not be vaccinated, because every vaccination offered was below their acceptance threshold. Likewise, some may consistently choose to be vaccinated, because every vaccination offered was above their acceptance threshold. Some in the popular literature refer to “anti-vaxxers” as persons who are non-traders; however, this term is imprecise, ignoring the heterogeneity among non-traders (e.g., some may be willing to be vaccinated against other infectious diseases). Furthermore, unwillingness to be vaccinated may be behavioral, such as a fear of needles, and unrelated to COVID-19 or its vaccines. Secondary analysis will further explore latent classes and random parameters.

Objectives

The US COVID-19 vaccination preference (CVP) study will elicit the vaccination preferences of US adults. Following economic theory, the differences between persons willing and unwilling to be vaccinated

defines the market size for COVID-19 vaccination and the effects of vaccination attributes on its uptake define their value (i.e., choice defines value) among those willing to be vaccinated. The objective of this study is to understand the observable differences between traders and non-traders and the effects of the vaccination attributes on its uptake among US adults generally.

Primary aims include:

1. To identify the observable differences between persons willing and unwilling to be vaccinated against COVID-19.
2. To test the effects of five attributes on the choice between alternative COVID-19 vaccinations and no vaccination for six months among those willing to be vaccinated.
3. To predict the uptake of COVID-19 vaccination given respondent characteristics and vaccination attributes.

These primary aims will be achieved using responses from US adults to eight non-adaptive choice tasks with three vaccination alternatives and an opt-out. We hypothesize that

1. Willingness to be vaccinated is associated with respondent characteristics, namely demographic, SES, risk perception, COVID-19 experience, health, influenza vaccination and political views.
2. Each attribute level causes a significant change in the value of COVID-19 vaccination, modifying its uptake.
3. The predicted uptake will range from 10% to 90%, depending on the respondent characteristics and vaccination attributes.

Apart from these primary aims, analyses for the secondary aims will explore methodological questions:

1. To evaluate the association between response behavior and instrument features (task sequence, attribute order, and object position)
2. To compare the preference evidence between the non-adaptive and adaptive tasks
3. To compare the preference evidence between experimental designs and blocks
4. To compare alternative cumulative density functions (CDF) in terms of goodness-of-fit,
5. To assess preference heterogeneity using latent effect and scale classes

In addition to the eight non-adaptive choice tasks, respondents will complete three adaptive choice tasks (known as triage tasks) and a qualitative task, where respondents write novel reasons for choosing the opt-out. Apart from these twelve tasks, the instrument includes a series of singleton preference questions (e.g., do you plan to be vaccinated in a community or medical setting?). Screenshots of the survey instrument are provided in the appendix.

Apart from the three primary hypotheses, we hypothesize that

1. Ordinality in effectiveness, duration, and risk of side effects.
2. An interaction between duration of immunity and effectiveness;
3. An interaction between proof of vaccination and duration;
4. Non-linearity in the side-effects attribute levels;
5. No design, block, task sequence, object position or attribute order effects;
6. No association between respondent characteristics and response quality (e.g., drop-out);
7. Independence from irrelevant alternatives (IIA) based on the non-adaptive responses;
8. An association between timing (e.g., time of day, completion and response times) and the grade of membership for scale classes, enhancing the identification of effect heterogeneity.

Although the primary analysis estimates the main effects without constraints or interactions, the results are expected to fail to reject ordinality and two interactions but reject linearity in the side-effect attribute levels.

Overall, the analysis will test for lexicographic preferences, main effects, and predict behavior under hypothetical scenarios as well as explore secondary aims. To enhance internal and external validity of the evidence, quota sampling will be applied during recruitment. Sampling weights may be included on demographic response in a sensitivity analysis, if deemed necessary.

Study design

The preference elicitation component of the survey contains a series of choice tasks, where subjects are presented with a hypothetical scenario and asked to choose between alternatives (e.g., which do you choose?).

Methods

Study setting

The online survey requires an internet browser on a tablet or computer with sufficient internet connectivity to complete the survey. (Hartman and Craig 2019) The panel company excluded persons accessing the survey via smartphones.

Eligibility criteria

The eligibility criteria of the US CVP study limit the target population to US adults.

Inclusion criteria include:

1. Connected to the internet in the 50 US states or Washington, DC.
2. Has access to a device and browser compatible with the survey software.
3. Eighteen years of age or older.
4. Can read English text and respond using their device.

Exclusion criteria include:

1. Persons who drop out of the survey prior to its completion.
2. Persons who request to be excluded from the study.
3. Persons in Nebraska or Alabama who are less than nineteen years of age.
4. Persons in Mississippi who are less than twenty-one years of age.

The last two exclusion criteria were recommended by the institutional review board due to differences in the age threshold of adulthood by US state.

Descriptive framework

The descriptive framework for the CVP study is largely taken from the published literature on influenza vaccination and expert consultations. It starts with a hypothetical scenario based on the CDC Vaccination Program Interim Playbook for Jurisdiction Operations version 2.0 which was published on 29 October 2020. (US Centers for Disease Control and Prevention (CDC) 2020)

Under the base scenario, the COVID-19 pandemic persists in 2021, many people across the United States are at risk of becoming newly infected, and new cases and preventable deaths are being reported each day. In this hypothetical scenario, multiple injectable COVID-19 vaccines have been approved by the US

Food and Drug Administration (FDA) and Centers of Disease Control and Prevention (CDC). While other vaccines are under development, no other vaccines are expected to be approved and available within six months. The first-generation vaccines were in limited supply for a short period (**Phase 1**). Initial doses were distributed in a limited manner, focusing on critical populations as defined by the US Centers for Disease Control and Prevention (CDC).

In this hypothetical scenario, all critical populations were vaccinated during Phase 1, but the respondent has not been vaccinated. Now, the first-generation vaccines are widely available and free for the general population (**Phase 2**). The US Centers for Disease Control and Prevention (CDC) recommends that all US adults be vaccinated (two injections, one month apart).

This scenario implies that multiple vaccines have been approved in Phase 2. Some of their attributes may be modified to account for patient preferences and enhance take-up. To better understand the value of alternative vaccinations, each respondent is asked to choose between alternative vaccinations as well as opt-out (i.e., no vaccination for six months). Before attempting the choice tasks, the respondent is asked to confirm four statements:

1. I will tell the truth and always provide honest answers.
2. In this hypothetical scenario, each injection of a COVID-19 vaccine is similar to a flu shot and is free.
3. Understanding the vaccination preferences of persons like me may reduce the spread of COVID-19 and help save lives and livelihoods.
4. Selecting no vaccination increases my risk of infection potentially causing short- and long-term consequences for my health.

Each vaccination is described using five attributes:

1. Proof of vaccination (two nominal levels): No vaccination card; Vaccination card

After COVID-19 vaccination, each person may be given a **vaccination card**, listing the person's name, provider information, vaccine, and dates. (US Centers for Disease Control and Prevention (CDC) 2020) Using this card, a person can demonstrate vaccination status quickly by scanning its code. These cards are also useful as a reference, particularly when a person returns for a second dose or booster. A person may request their **full vaccination records**, but this documentation can take a few days to assemble.

Today, most healthcare workers are required to get an annual flu vaccine to protect their patients, many of whom already have weakened immune systems. Vaccination is also compulsory for US immigrants, active duty military, and many occupations, such as commercial pilots, firefighters, and police officers. Vaccinations are required for travel to some countries (e.g., yellow fever) to mitigate the potential burden on the local healthcare system. US students are typically required to be vaccinated to attend a daycare, school or university. Some employers may require that all employees be vaccinated to deter outbreaks within their companies (e.g., restaurants, meat packing plants).

In this hypothetical scenario, you will be asked for **proof of vaccination** when attending schools or universities; visiting a nursing home or hospital; traveling to Hawaii or Europe; working in health or long-term care; or working around others without a mask. As a precaution, other similar activities may require proof of vaccination, fulfilled by showing either a vaccination card or full vaccination records.

To some respondents, proof of vaccination may be an alternative to wearing a mask, evidence of civic duty, or a symbolic return to normalcy. Proof of vaccination may become as common as proof of age

when purchasing alcohol or a driver’s license when renting a car. Respondents may not value the vaccine, but choose to be vaccinated to acquire the vaccination card alone. Others may not want the card due to the potential loss of privacy or burden of carrying an additional card with them.

- 2. Vaccination setting (two nominal levels): medical setting; community setting (e.g., pharmacy, store, work)

COVID-19 vaccinations may be delivered in a medical setting or a community setting. Medical settings are doctor’s offices, hospitals, emergency departments, clinics, and health centers or departments. Community settings include pharmacies or drugstores, local supermarkets or grocery stores, workplaces, or other non-medical settings.

According to the CDC, 57.7% of influenza vaccinations were delivered in medical settings. Within the community setting, vaccinations occur in pharmacy/store (22.2%), workplace (15.5%) and other nonmedical settings (4.6%). (Zhai, Santibanez et al. 2018)

Vaccination setting is a nominal attribute: some respondents may prefer the medical setting due to its perceived safety and other may prefer the convenience of the community setting.

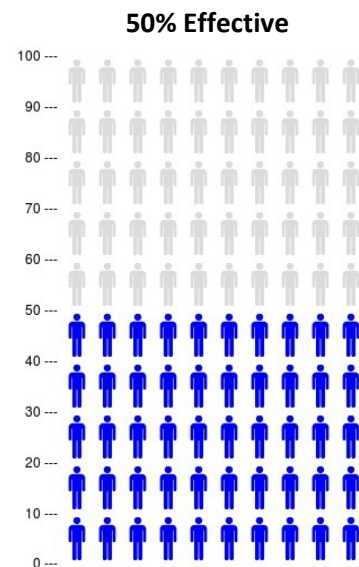
- 3. Vaccine effectiveness (two ordinal levels): 50%; 70%

At this time, the effectiveness of the COVID-19 vaccine is uncertain. However, in this hypothetical scenario, vaccine effectiveness is known and expressed as a proportion.

According to the CDC, the effectiveness of the influenza vaccine ranges from 40% to 60%, depending on the flu season. (US Centers for Disease Control and Prevention (CDC 2013) However, the US FDA defines 50% as the minimum threshold of effectiveness.

To help communicate effectiveness, we will use icon arrays based on 100 person icons and numeric statements (right). (Risk Science Center and Center for Bioethics and Social Sciences in Medicine 2020) In complement to the icon arrays, we will include an information box based on a recent study by de Bekker-Grob and colleagues (de Bekker-Grob, Donkers et al. 2020):

Suppose that all 100 people had the vaccination, the number of people who become infected depends on the effectiveness of the flu vaccination. The effectiveness differs per vaccination and may, for example, have the following level: 60%. This means that of all 100 people who would be infected, 60 people will NOT be infected anymore, while 40 people will still get infected.



Vaccine effectiveness may modify the value of duration of immunity, because duration is zero if the vaccine is not effective (i.e., potential interaction).

- 4. Duration of immunity (two ordinal levels): 3 months; 6 months

At this time, how long the COVID-19 vaccines will last is uncertain. However, in this hypothetical scenario, the duration of immunity is known and expressed in months.

For example, a five-month duration implies that the vaccine's immunity lasts for five months after the second injection. In five months, you may choose to be vaccinated again with the same or different vaccine.

According to the CDC, the duration of the influenza vaccine ranges between six to eight months in younger populations, depending on the flu season. (US Centers for Disease Control and Prevention (CDC 2013)

The duration of immunity also implies the rate of boosters needed and the expiry of the vaccination card (i.e., potential interaction).

- 5. Risk of severe side-effects (four ordinal levels): 1 per 1,000,000 (city); 1 per 100,000 (large town), 1 per 10,000 (small town), 1 per 1,000 (village).

At this time, the risks of side effects are uncertain for the COVID-19 vaccines. In the hypothetical scenario, the risks of side effects are known.

The risk of mild side effects is the same as a flu shot, namely soreness, redness, and/or swelling from the shot; headache; fever; nausea; muscle aches; and fainting.

Every vaccine has a risk of severe side effects, such as a life-threatening allergic reaction, requiring hospitalization. For example, suppose that everyone was vaccinated for each of these infectious diseases, a moderate risk of severe side effects may be expressed by group size, such as 1 side effect in 1,000 persons vaccinated (i.e., a village).

According to the CDC, the likelihood of severe side-effects from the influenza vaccine is approximately 1 in 1,000,000. However, the influenza vaccine has undergone years of development and refinement, and the COVID-19 vaccine will be recently approved.

To help communicate the risk of side-effects, this study uses group sizes and five skyline graphics (below) representing the community cluster classification system of risk communication along with proportional statements based on the size of a group where 1 person experiences the side effect. (Calman and Royston 1997) These pictures are based on a study by Johnson and colleagues (Poulos, Johnson et al. 2015) and re-enforce the difference in risk using skyline graphics:



Overall, the effectiveness and side effect risk attributes express risk and include graphics and adjectival statements. The proof, place, and duration attributes have only adjectival statements. To promote

familiarity, each of the attributes is introduced with a separate task drawing attention of its levels. For example, the risk attribute will be introduced using a serious game (a game designed for a primary purpose other than pure entertainment). In this game, the respondent will guess the incidence of three infectious diseases based on group size. The skyline graphics are not used for infection risks, because cities are associated with greater transmission and their use confuses respondents. After being shown the CDC estimates of infection risk, the respondents can re-assess their own risk perception as a means of self-calibrating their interpretation of the risk levels (see the screenshots for more details).

Preference elicitation

The primary outcomes are preferential choice behaviors. At the start of the survey, subjects will be asked three singleton preference questions:

- “If a vaccine against the coronavirus becomes available, do you plan to get vaccinated, or not?”
- “In the case that you decide to be vaccinated, do you prefer to get a vaccination card, or not?”
- “In the case that you decide to be vaccinated, do you prefer to be vaccinated in a medical setting or a community setting?”

The first question was taken from the NORC-AP poll and its results will be compared to its May 2020 results. This question serves as a baseline before the introduction of the descriptive framework, which may influence the subject’s preferences. The second and third questions define the ordinality of the attribute levels from the perspective of the respondent, and define the pivoted profile using the adapter choice tasks.

Eight non-adaptive choice tasks

The primary method of preference elicitation is the eight non-adaptive choice tasks with four alternatives, starting with a warm-up task. A choice between four alternatives (e.g., ABCD) implies three inequality statements (AB, AC, AD), resolving ambiguity.




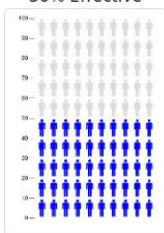
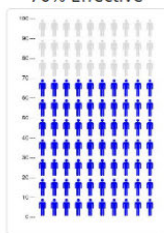
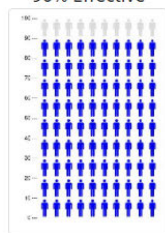
Each task asks a respondent to choose between three COVID-19 vaccinations and no vaccination for six months. The respondent is instructed that “selecting no vaccination means that you will not be vaccinated for six months, increasing your risk of infection and potentially causing short and long-term consequences for your health.” The Figure 1 shows the warm-up task with a vaccination that dominates the two other vaccinations.

Three adaptive choice tasks

The secondary method of preference elicitation is three adaptive choice tasks, starting with a warm-up task. It includes choices between two alternatives (e.g., AB), five alternatives, four alternative, three alternatives, and two alternatives. Each task implies eleven inequality statements, resolving ambiguity. In comparison, one adaptive task has a similar amount of preference evidence as four non-adaptive tasks.

Each adaptive task breaks down the choice into three steps: 1. Choose between vaccination and no vaccination (select a column). 2. Improve the vaccination by making three changes (select three rows, starting with the potential change you want most). 3. Choose between the *improved* vaccination or no vaccination (select a column). The task advances automatically to the next step after each response. Given the novelty of the task, the evidence is largely exploratory.

Figure 1. Warm-up for the non-adaptive tasks

Warm-up task:	Vaccination A	Vaccination B	Vaccination C	No vaccination for six months
Duration of immunity	Three months	Three months	Six months	
Proof of vaccination	Vaccination card	Vaccination card	Vaccination card	
Vaccination setting	Medical setting	Medical setting	Medical setting	
Risk of severe side effects	Low risk: 1 side effect in 10,000 	Very low risk: 1 side effect in 100,000 	Lowest risk: 1 side effect in 1,000,000 	
Vaccine effectiveness	50% Effective 	70% Effective 	90% Effective 	
Which do you choose?	Vaccination A	Vaccination B	Vaccination C	No vaccination for six months

Qualitative task

Apart from the singleton questions and non-adaptive and adaptive tasks, the final tasks ask respondents “Why might you choose no vaccination for six months? Please list three potential reasons excluding the risk of severe side effects and those shown previously.” This qualitative evidence may assist with understanding the limitations of the descriptive framework for future research. Additional outcomes include survey feedback (e.g., task difficulty, open comments) and paradata (e.g., survey duration, time to response, changed response).

Participant timeline

Upon notification of recruitment from the panel, subjects will accept the invitation and be directed to the survey instrument. Each participant will have up to one hour to complete this 15-minute survey. After its completion, the participant will be re-directed to the panel website, which credits the panelist’s account for their participation.

Sample size

A minimum of 1050 subjects will be recruited.

Recruitment

The recruitment is similar to past US health preference studies. (Craig, Reeve et al. 2014, Craig, Reeve et al. 2014, Craig, Brown et al. 2015, Craig, Brown et al. 2016, Craig, Greiner et al. 2016, Craig and Rand 2018, Craig, Rand et al. 2018) The 1050 subjects will be recruited for a pre-existing panel of US adults based on their demographic characteristics. Recruitment will fill 18 demographic quotas (Table 1):

(female, other) x (Hispanic, non-Hispanic Black, non-Hispanic other) x (18 to 34, 35 to 54, 55 and older). For example, each subject-specific series of choice sets will have at least one response from a young, Hispanic woman. These quotas are identical to past studies and described further in the allocation sections.

Table 1 Demographic Quotas for Series (N_s=50) and Sample (N=1050)

Demographics	Age in Years			Age in Years		
	18-34	35-54	55+	18-34	35-54	55+
Female						
Hispanic	1	1	1	21	21	21
Non-Hispanic Black	1	1	1	21	21	21
Non-Hispanic other	5	7	7	105	147	147
Male or other						
Hispanic	1	1	1	21	21	21
Non-Hispanic Black	1	1	1	21	21	21
Non-Hispanic other	5	7	7	105	147	147

An earlier version of the protocol excluded persons who were unwilling to be vaccinated (e.g., anti-vaxxers), because their responses were likely all opt-outs. According to the AP-NORC study, this criterion would have led to the removal of 20% of US adults. (AP-NORC 2020) However, counsel from the COVID-19 HPR roundtable, namely Mark Oppe and Juan Marcos González Sepúlveda, led to the elimination of this exclusion criterion and to the increase of the series-specific sample size from 30 responses to 50 responses. Instead of removing nontraders, this study will recruit them along with all other US adults, so that the study can account for their uptake in the predictions assess their preferences using the adaptive and qualitative tasks.

On similar grounds, the follow-up component of the survey instrument will identify, but not remove persons who are (1) high risk; (2) previously or currently infected; and (3) previously vaccinated due to employment. However, the potential loss of statistical efficiency motivates the compensatory increase in recruitment (from 630 to 1,050 respondents), which is almost the same number of respondents as the May 2020 AP-NORC poll (1,056).

Allocation for the non-adaptive tasks

The appendix shows the three design matrices for the non-adaptive tasks (**fractional factorial design**). Each matrix is the same size (56 sets), but used a different method for set selection. The **random design** entailed randomly selecting sets (ABC) under the assumption that any form of systematic selection may produce biased results. Such designs emphasize their versatility and tend to be inelegant and inefficient. The **generator-developed design** was built from an orthogonal array, an approach known for its mathematical elegance and symmetry. The **efficient design** was produced with the assistance of John Rose and involved selecting sets by optimizing a numerical measure of statistical efficiency under an assumed likelihood function, namely d-efficiency. All matrices were required to exclude dominated alternatives and include overlaps (i.e., attribute levels shared by alternatives).

In the appendix, each of the three design matrices has been arranged into seven subject-specific series (i.e., blocks) of eight non-adaptive tasks (3 designs x 7 series = 21 series). The 18 demographic quotas (Table 1) are applied to these 21 series such that each series is completed by a demographically similar

subsample of 50 US adults. In practical term, this implies fielding 18 nearly identical versions of the survey instrument, each with its own quota size and exclusion criteria. With 21 series and 50 respondents per series, the study has 1050 respondents. The subject matrix shows the relationship between the blocks, quotas, subjects and sets.

Allocation for the adaptive tasks

The allocation for the adaptive tasks uses a **full factorial design**. Each task requires a **single profile** such that each attribute level of the profile is inferior to another. The singleton questions on proof of vaccination and vaccination setting define which attribute level is inferior from the perspective of the respondent. Likewise, reduced effectiveness and duration of immunity is inferior for all respondents. The risk of severe side effects has three inferior levels; therefore, the allocation of each respondent includes three tasks, one for each inferior level of side-effect risk.

Data collection

The survey instrument will have five active components (consent, screener, background, choice tasks, and follow-up) and two passive components (panel recruitment and paradata). It is constructed to collect one to three responses per page and to show a progression bar with the proportion of pages remaining. The questions are numbers (1 consent, 5 screener, 10 background, 12 choice tasks, and 30 follow-up questions). Respondents will be allowed to go back pages, except between sections and tasks due to randomization and adaptive features. Respondents will not be allowed to return to the survey once the browser has been closed.

As part of the survey instrument, task sequence and attribute order are randomized at the subject level (i.e., different between subjects, same across tasks). Object position (i.e., left-right) and response option are randomized at the task level. The groups of follow-up questions were shown in random order, except that the EQ-5D instrument and political affiliations were asked last.

Data

A record is created when a subject initiates the survey instrument. All data associated with the event are indexed, including the experimental design, survey responses, and paradata. Apart from the exclusion criteria or unanticipated technical issues, no data will be dropped from the analytical file a priori.

Statistical methods

After the descriptive analyses of the respondent characteristics and survey behaviors (e.g., the duration of survey), the statistical analyses will focus on the primary and secondary aims. Multinomial models are used in economics to predict choices among alternatives that cannot be ranked from most to least preferred uniformly for all individuals. Aitchison and Bennett introduced the multinomial probit model (MNP), (Aitchison and Bennett 1970) and Hausman and Wise the multinomial logit model (MNL); (Hausman and Wise 1978) however, McFadden's conditional logit is better suited to understand the causal relationship between object attributes and choices. (McFadden 1974)

In this study, the primary specification is a main-effects conditional logit (8 parameters) with an opt-out inflation and respondent-level clusters. Multiple other models will be estimated including stratified, mixed, and latent-class analyses to assess the secondary hypotheses.

Multinomial models of individual choices

Assume that N independent individuals make a single choice among J alternatives (i.e., cross-sectional data). Let $(y_{i1}, y_{i2}, \dots, y_{ij})$ be a set of binary random variables representing this choice, such that $y_{ij} = 1$ if and only if individual i ($i = 1, \dots, N$) chooses alternative j . Define latent variables U_{ij} ($j = 1, \dots, J$) representing gains in utility received from these choices, such that

$$U_{ij} = X_i \beta_j + \varepsilon_{ij}, \quad (1)$$

where X_i is a vector of exogenous regressors, β_j is a conformable parameter vector, and ε_{ij} is a vector of error. Then the observed choices are defined as

$$y_{ij} = \prod_{k=1}^J I_{[0, +\infty)}(U_{ij} - U_{ik}), \quad j = 1, \dots, J,$$

where $I_{[0, +\infty)}$ is the indicator function for the set $[0, +\infty)$. When subjects make multiple choices over time (i.e., panel data), the gains in utility and observed choices have three subscripts ($i = 1, \dots, N; t = 1, \dots, T; j = 1, \dots, J$). This study has 1050 subjects ($N = 1050$) and eight tasks ($T = 8$) with four objects ($J = 4$); therefore, its response matrix holds 25,200 inequality statements ($N \times T \times (J - 1) = 1050 \times 8 \times 2 = 25,200$ rows), the empirical evidence for the model estimations.

MNL, conditional, and mixed logit models

To better understand the analysis, we present the MNL, conditional logit, and random-coefficient and error-components mixed logit models:

MNL:
$$U_{ij} = X_i \beta_j + \varepsilon_{ij}$$

Unlike the MNP, the MNL model is derived under the assumption that the errors ε_{ij} are distributed as type I extreme values. In this case, X_i consists only of subject-specific attributes, and $U_{ij} = 0$ is imposed for identification.

Conditional logit:
$$U_{ij} = X_{ij} \beta + \varepsilon_{ij}$$

This is similar to the MNL except that X_{ij} consists of subject- and choice-specific attributes and β is a vector of coefficients, the same for all alternatives. In this case, there is no need to restrict U_{ij} for identification.

Random-coefficients mixed logit:
$$U_{ij} = X_{ij} \beta_i + \varepsilon_{ij}$$

This mixed logit model is similar to the conditional logit, except β_i varies with individuals, as a vector of random variables with density $f(\beta_i)$ (i.e., random coefficients). For example, β_i may vary between subjects due to the potential for systematic differences between groups (i.e., heterogeneous classes) or within groups (i.e., random utility).

Error-components mixed logit:
$$U_{ij} = X_{ij} \beta + W_{ij} \alpha_i + \varepsilon_{ij}$$

In this model, β is a vector of fixed coefficients. Unlike in the conditional logit, α_i is a vector of random variables with a mean of zero, and W_{ij} is a vector of indicator variables. These error components together with the type I extreme value errors, $W_{ij} \alpha_i + \varepsilon_{ij}$, define the stochastic portion of utility, U_{ij} .

Differences in the logit specifications affect their estimations. The MNL and conditional logit probabilities have closed-form solutions, but the mixed logit probabilities integrate over a density of parameters without a closed-form, motivating the use of maximum simulated likelihood.

$$\text{Multinomial:} \quad \Pr(y_{ij} = 1) = \frac{\exp(X_i\beta_j)}{1 + \sum_{k=1}^{J-1} \exp(X_i\beta_k)}$$

$$\text{Conditional:} \quad \Pr(y_{ij} = 1) = \frac{\exp(X_{ij}\beta)}{\sum_{k=1}^J \exp(X_{ik}\beta)}$$

$$\text{Random-coefficients:} \quad \Pr(y_{ij} = 1) = \int \frac{\exp(X_{ij}\beta_i)}{\sum_{k=1}^J \exp(X_{ik}\beta_i)} f(\beta_i) d\beta_i.$$

$$\text{Error-components:} \quad \Pr(y_{ij} = 1) = \int \frac{\exp(X_{ij}\beta + W_{ij}\alpha_i)}{\sum_{k=1}^J \exp(X_{ik}\beta + W_{ik}\alpha_i)} f(\alpha_i) d\alpha_i.$$

Although the mixed logit (random-coefficient or error-components) allows for greater heterogeneity, it does not benefit from an overarching structure that separate groups of persons by respondent characteristics or behaviors. In this study, the X_{ij} consists of only choice-specific attributes; therefore, the primary model is a conditional logit.

The latent class logit model

The latent class logit model assumes that the population can be decomposed into C distinct latent classes such that subjects of each class ($c = 1, \dots, C$) are homogeneous with respect to their class-specific parameters β_c , which differ between the classes.

To indicate that the choice probabilities depend on class membership c , the conditional logit model may be expressed as

$$\Pr(y_{ij} = 1|c) = \frac{\exp(X_{ij}\beta_c)}{\sum_{k=1}^J \exp(X_{ik}\beta_c)}$$

and, the probability of belonging to class c conditionally on additional covariates Z_i can be expressed using a separate conditional logit

$$\Pr(c) = \frac{\exp(Z_i\theta_c)}{\sum_{s=1}^C \exp(Z_i\theta_s)}$$

The latent class model puts individuals into probabilistic groups based on their likelihood of belonging in that group; therefore, the probability density associated with individual i has the following form.

$$\text{Latent class logit: } \Pr(y_{ij} = 1) = \sum_{c=1}^C \Pr(y_{ij} = 1|c)\Pr(c) = \sum_{c=1}^C \frac{\exp(X_{ij}\beta_c)}{\sum_{k=1}^J \exp(X_{ik}\beta_c)} \frac{\exp(Z_i\theta_c)}{\sum_{s=1}^C \exp(Z_i\theta_s)}$$

Unlike the mixed logit models, the latent class logit is a finite mixture model, and its probability does not integrate over a density of parameters. The two main features that differentiate the latent class from mixed logit models are its closed-form solution and its reliance on covariates Z_i for identification. The mixed logit model may also be extended to incorporate covariates Z_i into its specification, creating the conditional density $f(\beta_i|Z_i)$; however, such interactions can be difficult to interpret.

The latent class model will be extended to estimate separate effect and scale classes, known as the scale-adjusted latent class (SALC) model. SALC is arguably a constrained version of a standard latent class model, but it is much easier to interpret, because characteristics related to variability (e.g., speeding through a survey) are usually distinct from differential effects (e.g., health experience).

All models of preference heterogeneity are considered exploratory analysis unless the heterogeneity is specified in advance. Currently, there is insufficient evidence to support such a confirmatory analysis.

Opt-out inflation

The opt-out inflation is similar to a latent class logit with two classes (traders and non-traders). In this model, non-traders place an infinite value on “no vaccination for six months” such that:

$$\Pr(y_i \text{ optout} = 1 | \text{nontrader}) = 1 \text{ and}$$

$$\Pr(y_{ij} = 1) = \Pr(\text{nontrader})\Pr(y_{ij} = 1 | \text{nontrader}) + \Pr(\text{trader})\Pr(y_{ij} = 1 | \text{trader})$$

Opt-out inflation increases the likelihood of choosing “no vaccination for six months” based on the respondent characteristics. Its first regression $Z_i\theta$ describes the association between respondent characteristics and the likelihood of being a non-trader (i.e., grade-of-membership). The second regression $X_{ij}\beta$ describes the causal relationship between vaccination attributes and the likelihood of between specific vaccinations and opt-out. This approach allows for heterogeneity in grade-of-membership (between-class) and homogeneity in vaccination preferences among traders (within-class).

Alternative models were considered for the primary analysis. First, random parameter models may poorly identify non-traders, because their opt-out coefficient is indefinite by construction. Second, hurdle models inherently exclude persons who consistently opt-out, which is a loss of information and changes the definition of the observable class by the block allocation. Third, sample selection models incorporate the error term from the hurdle into the choice model to adjust for sample selection bias; however, this approach may confuse the interpretation of the causal relationship (i.e., under the unrealistic scenario that traders were the same as non-traders).

Overall, the main-effects conditional logit with an opt-out inflation and respondent-level clusters seems to fit economic theory by separating out the non-traders from market and examining causal relationships solely among those who may be willing to be vaccinated.

Analysis plan

Overall, the analysis plan includes eight steps:

- (1) descriptive analysis of respondent characteristics and participatory behaviors (e.g., drop-outs).
- (2) descriptive analysis of response quality, such as lexicographic behaviors (i.e., nontraders, $Z_i\theta$) and the effects of task sequence, object position, and attribute order on the preference evidence.
- (3) primary analysis of the main effects (i.e., traders, $X_{ij}\beta$), including diagnostic tests of ordinality, linearity, pre-specified interactions, IIA, and poolability, as well as predictions of the marginal and conditional effects.
- (4) secondary analysis of the order effects and heteroskedasticity, including all two-way interactions, alternative-specific constants (ASC), and behavioral determinants of scale.

(5) secondary analysis of the experiment effects, including the influence of task, design, and blocks on the main effects.

(6) secondary analysis of the model specification, including alternative cumulative density functions (CDFs).

(7) exploratory analysis of preference heterogeneity, including mixed (random coefficients and error components) and latent class models (including SALC).

(8) exploratory analysis of respondent feedback, including qualitative evidence.

Data monitoring

Data monitoring of an online survey involves the regular download of spreadsheets from the survey platform. This is necessary to target recruitment toward quotas. No further oversight is required.

Harms

The study does not include any direct identifiers. There are no physical risks posed by this study. There may be a risk of psychological distress resulting from questions that ask respondents to evaluate alternative scenarios.

Audit

No audit process is part of the study protocol.

Ethics and dissemination

Research ethics approval and protocol amendments

On 5 November 2020, the independent review board (IRB) at Advarra determined that this research project is exempt from IRB oversight based on the Department of Health and Human Services regulations found at 45 CFR 46.104(d)(2):

Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).

Furthermore, the IRB reported that the project is not subject to requirements for continuing review.

Consent or assent

Under a double opt-in process, respondents consented when they first joined the panel. The second consent is located on the first page of the online survey, an Informed Consent page. Respondents will

click I understand/I do not understand radio buttons. Participants must consent to progress to the second page. Participants may leave the survey at any time by closing their internet browser or by leaving a comment.

Confidentiality

The study does not include any direct identifiers.

Declaration of interests

The Principal Investigator has no interests to declare.

Financial Support

Benjamin M. Craig funded this project personally and did not receive any outside financial support.

Access to data

Authorized research personnel, the independent review board, and its staff may inspect the records from this research project. A de-identified version of the final dataset will be made publicly available after the initial publications.

Dissemination policy

The results of this study will be prepared for publication in peer-reviewed journals. The statistical code and screenshots of the survey instrument will be disseminated along with these results to facilitate their interpretation.

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Appendices

1. Screenshots of the Survey Instrument
2. Experimental Design
3. Exemption determination
4. Beta testing workbook