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The relationship between trust in federal oversight of vaccine safety and willingness to participate in COVID-19 clinical trials: a repeated measures study of Philadelphia residents (September 2021 – March 2023)

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Abstract

Background The Coronavirus Disease 2019 (COVID-19) pandemic precipitated an urgent need for clinical trials to discover safe and efficacious treatments. We examined how COVID-19 experiences, clinical trial awareness, and trust in the vaccine safety process were associated with willingness to participate in COVID-19 clinical trials. The objective was to investigate the relationship between trust in federal oversight of vaccine safety and willingness to participate in clinical trials for COVID-19 treatment across four distinct time points over an 18-month period during the COVID-19 pandemic.

Methods We used four waves of data collected from September 2021 to March 2023 among 582 Philadelphia residents (with a missing data rate of 0.9%). Generalized estimating equations estimated the association between willingness to participate in COVID-19 clinical trials and participants' trust in the federal government's oversight of COVID-19 vaccine safety, COVID-19-related variables (COVID-19 related health challenges, history of COVID-19 infection), awareness of clinical trials and how to enroll in them, and sociodemographic characteristics (age, race/ethnicity, sexual orientation, gender, parental status, education, and insurance).

Results On average, willingness to participate in a COVID-19 clinical trial was positively associated with greater trust in the federal government's oversight of vaccine safety [$\beta = 0.34$, 95% confidence interval (CI): 0.15–0.53], having COVID-19 ($\beta = 0.40$, 95% CI: 0.08–0.73), awareness of clinical trials ($\beta = 0.38$, 95% CI: 0.04–0.73), and knowledge of how to enroll ($\beta = 0.83$, 95% CI: 0.44–1.23). Among sociodemographic characteristics, race/ethnicity ($p = 0.001$) and gender ($p = 0.018$) were identified as predictors for COVID-19 trial willingness.

Conclusion Willingness to participate in clinical trials may be bolstered by strengthening the public's trust in the federal government's role within vaccine safety oversight, increasing the perceived relevance of clinical trials to

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individuals' health and well-being, and offering tailored information to educate diverse communities about ongoing trials and how to enroll in them.

Keywords Clinical trial participation, COVID-19 pandemic, Trust, Federal oversight, Government regulation

Background

The Coronavirus Disease 2019 (COVID-19) pandemic, instigated by the novel coronavirus SARS-CoV-2, has posed an unparalleled global health crisis, as evidenced by its profound and far-reaching impacts [1, 2]. With the rapid spread of the virus and the severity of its impact on population health and national economies, the quest for efficacious treatments via rigorous clinical trials has become imperative [3]. In response to this challenge, clinical trials on COVID-19 treatments have emerged as a critical priority [4, 5].

Clinical trials for COVID-19 treatments have allowed for a scientifically rigorous evaluation of potential treatment options aimed at alleviating symptoms, mitigating disease severity, and reducing mortality [6, 7]. They have not only informed the development of treatment modalities for acute COVID-19 infection during the pandemic such as dexamethasone for hospitalized patients [8] and nirmatrelvir-ritonavir [Paxlovid] for non-hospitalized patients [9], but have also paved the way for ongoing exploration of therapies targeting long COVID. For example, studies are underway to evaluate the longer-term efficacy of Paxlovid in treating long COVID [10, 11]. However, the success of clinical trials is contingent upon individuals' willingness to participate, underscoring the critical role that public engagement plays in advancing science and addressing pressing public health challenges.

Various barriers impede individuals' willingness to participate in such trials. These obstacles include logistical challenges such as limited access to trial sites, transportation issues, and time constraints [12–15]. Moreover, concerns regarding the potential risks and side effects of experimental treatments, as well as the fear of being subjected to placebo or receiving inferior care, along with COVID-19-related stigma, can act as significant deterrents [12–17]. A lack of awareness or understanding about clinical trials, coupled with cultural or linguistic barriers, can further impede participation rates across diverse demographic groups [12, 13]. Within this landscape of barriers, the role of trust emerges as a critical determinant of individuals' willingness to participate in clinical trials. Skepticism or distrust stemming from historical injustices, ethical breaches, or experiences of discrimination can erode confidence in the research process and deter individuals from engaging in clinical trials [18, 19].

Trust in diverse contexts has emerged as a pivotal determinant shaping individuals' willingness to participate in clinical trials in previous studies. A systematic review investigating predictors influencing participation in both cancer and non-cancer clinical trials highlighted the pivotal role of trust or mistrust in entities such as research institutions, researchers, healthcare providers, institutions, and pharmaceutical companies as significant contributors influencing individuals' participation [12, 13]. A study focusing on predictors influencing engagement in COVID-19-specific clinical trials reaffirms the central role of trust [20–22].

Despite the convergence of evidence underscoring the importance of trust, there remains a paucity of research examining the potential association between trust in federal oversight of vaccine safety, which reflects individuals' confidence or belief in the monitoring and regulation conducted by the federal government to ensure vaccine safety [23–25], and individuals' willingness to participate in COVID-19 clinical trials. Understanding this relationship is crucial during public health crises like the COVID-19 pandemic, where rapid deployment of medical interventions is vital. Moreover, trust in federal oversight is intricately intertwined with public confidence in the healthcare system and broader public health response efforts [22, 26]. Investigating this relationship can inform strategies to enhance trust-building efforts and bolster public health resilience. Consequently, this can fortify overall public health resilience and response capacity in the face of future health crises.

While trust in federal oversight has been shown to positively influence individuals' willingness to adopt recommended behaviors during pandemics, including vaccine acceptance [27, 28], its impact on clinical trial participation remains underexplored, as clinical trials differ from the adoption of recommended behaviors. Given the pivotal role of government in fostering trust and confidence among the public regarding the necessity and conduct of clinical trials [29], trust in federal oversight of vaccine safety may significantly influence willingness to participate in COVID-19 clinical trials. Robust government oversight may reassure individuals about safety protocols in clinical trials, while lower trust levels may lead to hesitancy due to concerns about safety and efficacy. Therefore, exploring the role of trust in federal oversight is essential for shaping willingness to participate in COVID-19 clinical trials.

The purpose of the study was to investigate the relationship between trust in federal oversight of vaccine safety and willingness to participate in clinical trials for COVID-19 treatment across four distinct time points over an 18-month period during the COVID-19

pandemic. Our aim was to provide a comprehensive understanding of the dynamics between trust in federal oversight and willingness to participate in COVID-19 clinical trials over time during a public health crisis. We hypothesize that, on average, participants with higher levels of trust in federal oversight of vaccine safety will exhibit greater willingness to participate in COVID-19 clinical trials, even after accounting for potential confounding variables such as awareness of clinical trials, sociodemographic characteristics, and experiences related to COVID-19.

Methods

Procedure

The study was conducted within the Philadelphia CEAL (Community Engagement Alliance) initiative [30], aiming to identify and address the disparities in COVID-19 testing, vaccine acceptance, and involvement in clinical trials in Philadelphia.

Within this initiative, we conducted longitudinal data collection through a series of online surveys for one year 1 and three waves of year 2 surveys. The online surveys were specifically designed for CEAL initiatives and included questions that formed part of a standardized set of metrics developed collaboratively by CEAL teams across the county and collaborators from the National Institutes of Health. The detailed information about the questionnaire has been published elsewhere [30]. The inclusion criteria for year 1 targeted individuals aged 13 and above residing in Philadelphia County in 2021. Participants were excluded if they did not complete the entire survey or did not provide a residential zip code matching one of the 48 zip codes of Philadelphia County. Participants were recruited online through social media channels. A real-time fraud detection protocol, developed and implemented for this study, was utilized during participant recruitment. Details of the fraud detection process employed in this study have been published elsewhere [31]. Our online survey for year 1 garnered responses from 2,870 participants between September 2021 and February 2022.

For the three waves of year 2 surveys, we utilized stratified sampling based on race/ethnicity and neighborhood, proportionate to census estimates in Philadelphia neighborhoods, from the initial pool of 2,870 participants. Based on this sampling scheme, we invited 582 participants to complete three waves of surveys, each spaced three months apart. Participants invited could complete the survey once for each wave, but participation in one wave did not exclude participation in subsequent waves. We sent invitations via emails and certified mail, each containing a unique QR code linking to a survey for the participant, a copy of the consent form, and details regarding the purpose of the study. Of those 582 participants, 343 completed at least one wave for waves 1, 2, and 3. Online surveys were conducted in August 2022 for Wave 1, resulting in responses from 194 participants. Wave 2 surveys, conducted in November 2022, garnered responses from 214 participants. Wave 3 surveys were carried out in February 2023 and received responses from 297 participants. We spaced each wave three months apart to strike a balance between capturing longitudinal trends amidst the pandemic, minimizing the burden on respondents, and maintaining flexibility to adapt and implement any necessary adjustments or refinements to the survey instrument or recruitment strategy based on feedback or emerging trends from previous waves (Fig. 1).

This study adhered to stringent ethical guidelines to ensure the protection and respect of all participants involved. Informed consent was obtained from each participant, with full disclosure about the study's purpose, the nature of the questions, and the voluntary nature of their participation. Confidentiality was maintained by de-identifying data and analyzing responses in aggregate form [32]. The study procedures received approval from the University of Pennsylvania Institutional Review Board (#848650), ensuring it met ethical standards for research involving human subjects. Transparency was prioritized by informing participants about data usage and their right to withdraw at any time. The study was inclusive and non-discriminatory, ensuring a diverse and representative sample from the Philadelphia population.

Measures

Predictor variable

Trust in federal oversight of COVID-19 vaccine safety for the public was assessed by a single item: "How much do you trust the federal government to ensure the COVID-19 vaccine is safe for the public?" This question formed part of a set of standardized metrics developed through an iterative process involving CEAL teams nationwide and collaborators from the National Institutes of Health [30]. Responses were recorded on a four-point Likert scale, with options including '1=fully trust,' '2=mostly trust,' '3=somewhat trust,' and '4=do not trust.' To facilitate analysis, these responses were reverse-coded, with higher scores indicating greater trust in the oversight of COVID-19 vaccine safety by the federal government.

Outcome variable

Participants' willingness to participate in a clinical trial for COVID-19 treatment was assessed using a single-item question: "If you get COVID-19, how willing would you be to sign up for a clinical trial for a COVID-19 treatment?" Participants provided their responses on a seven-point Likert scale, spanning from '1=not at all willing' to '7=very willing.'

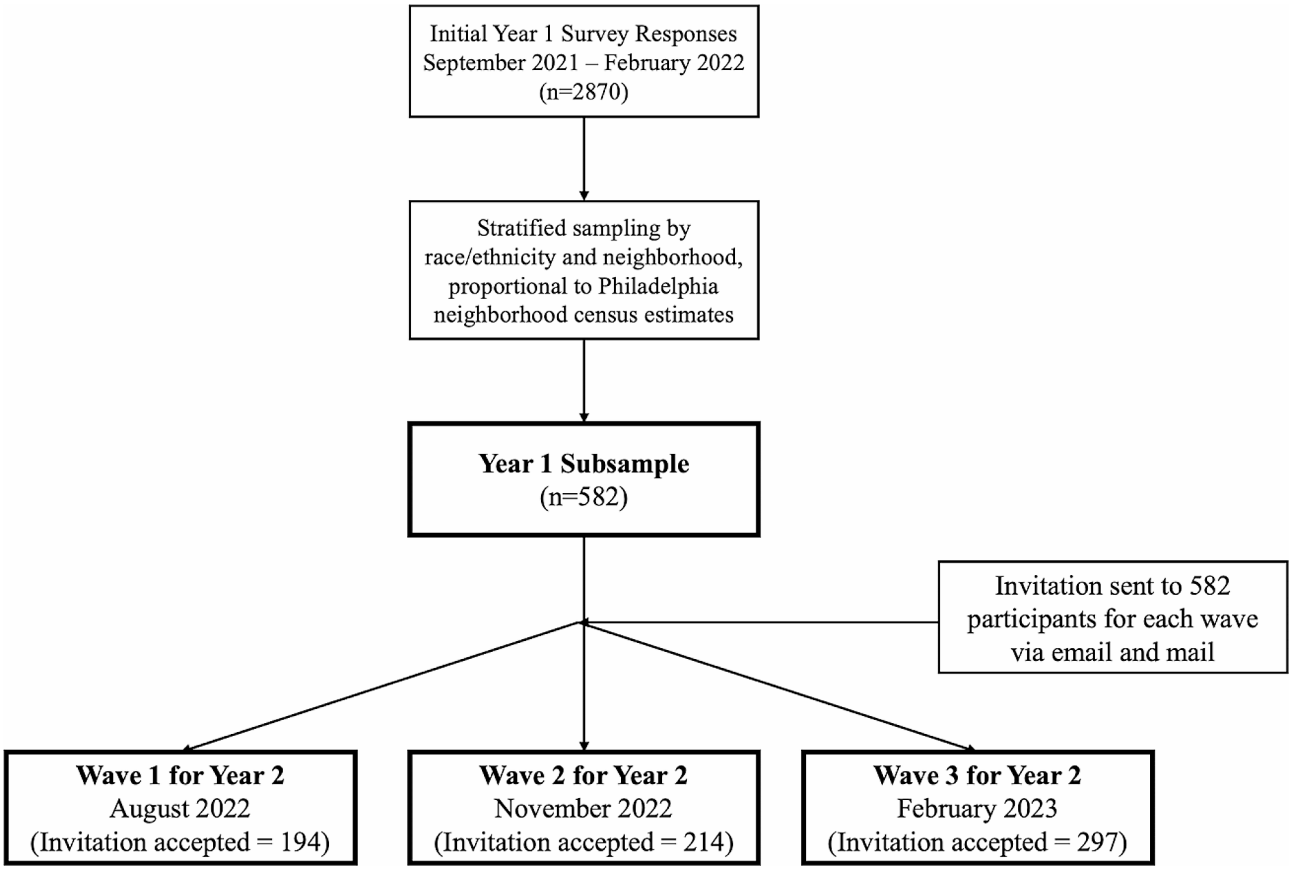

Fig. 1 Sampling diagram

Covariates

In our analysis, we incorporated various sociodemographic characteristics that have previously been associated with either trust in the government or individuals' willingness to participate in clinical trials. These characteristics were identified based on prior research and conceptual frameworks outlining the determinants of clinical trial participation [33, 34]. By including these covariates in our analysis, we aimed to account for potential confounding variables and better understand the relationship between trust in federal oversight and willingness to participate in COVID-19 clinical trials.

Time-invariant covariates in our analysis included a range of demographic characteristics that remained constant throughout the study. These included race and ethnicity [35–37], age [33, 35], educational attainment [26, 33], parental status [38] and gender [20, 39]. Given the underrepresentation of sexual and gender minority patients in clinical trials [40], we included sexual orientation as a variable of interest to investigate potential disparities in willingness to participate in COVID-19 clinical trials among this demographic group. Additionally, we included baseline awareness of COVID-19 clinical trials and knowledge about the logistics involved in participating in such trials [33, 41, 42]. Awareness of COVID-19 clinical trials at baseline was assessed using a single binary question: "Are you aware of COVID-19 clinical trials that are being done?" Similarly, knowledge about the logistics involved in participating in these trials was evaluated using another binary question: "Do you know what to do to sign up for a COVID-19 clinical trial in your area?" Given the relatively short interval between waves of data collection, variables such as participants' age, parental status, and education level served as time-invariant covariates, providing a stable basis for comparison across different time points.

Time-varying covariates captured variables that might change over time or across different waves of data collection. These included the wave of data collection, insurance status [43], history of positive COVID-19 test results, and COVID-19-related challenges. Challenges resulting from COVID-19 were operationalized as the sum total of participants' reported difficulties arising from the COVID-19 pandemic, including various aspects such as accessing necessary healthcare, securing adequate housing and food, ensuring access to clean water, obtaining required medications, and fulfilling transportation needs. The sum score ranged from 0 to 6, with a higher score indicating a higher level of challenge

experienced by participants. For the insurance and history of positive COVID-19 test results variables, given the exceedingly few instances of "don't know" responses in our dataset, we decided to combine them with the "no" responses. This approach was adopted to ensure an adequate sample size for robust statistical analysis. We calculated generalized variance inflation factors for each independent variable to assess multicollinearity. The results indicated low generalized variance inflation factor values for all variables.

Statistical analysis

We used Stata version 17 to explore the average relationship between participants' trust in federal oversight of COVID-19 vaccine safety and their willingness to participate in a clinical trial for a COVID-19 treatment within the longitudinal data. To accommodate the repeated measures collected over four distinct time points and control for both time-invariant and time-varying covariates, we employed a generalized estimating equation model [44, 45]. The generalized estimating equation is a statistical technique frequently employed for analyzing longitudinal data, where measurements are taken repeatedly over time from the same individuals or units. It addresses within-subject correlation and unequal spacing between measurements. The generalized estimating equation is capable of accommodating changes in respondent composition across waves while still yielding reliable parameter estimates over time. Additionally, the generalized estimating equation does not necessitate complete panel data, making it adept at handling missing waves from participants [44, 45].

The generalized estimating equation model was specified using a Gaussian family, which is suitable for continuous and symmetrically distributed outcome variables such as willingness to participate in clinical trials. We utilized an identity link function, which is appropriate for modeling associations without any transformation on the outcome scale. Additionally, to capture any potential correlations between repeated measures, we implemented an independent correlation structure. After fitting the model, we assessed the assumption of normality of residuals, confirming that no violation occurred. To ensure the reliability of our estimates, we employed robust standard errors, which are robust to heteroscedasticity and other violations of the classical assumptions of regression analysis. This comprehensive approach allowed us to rigorously assess the association of interest while effectively accounting for the longitudinal nature of the data and controlling for potential confounding variables.

Our missingness rate stands at 11 cases out of 1,287 observations (0.9%). A sensitivity analysis comparing results derived from data with listwise deletion and imputed data showed no significant differences. Due to the small proportion of missing data, we chose to utilize the data with listwise deletion instead of imputed data. This decision is based on the understanding that listwise deletion, resulting in the removal of only a small percentage of participants, may not lead to a significant loss of information or biased estimates [46, 47].

Results

Table 1 shows the sociodemographic characteristics of participants who participated and did not participate in the year 2 survey. Statistically significant differences were observed in gender, education, history of positive COVID-19 results, awareness of COVID-19 treatment clinical trials, and knowledge of the logistics of clinical trials between participants who participated in the year 2 survey and those who did not.

The coefficients and confidence intervals (CI) of the predictor variables and covariates are outlined in Table 2. As trust in how COVID-19 vaccines are monitored by the government increases, individuals are more likely to be willing to participate in clinical trials for COVID-19 treatment. On average, a one-point increase in trust was associated with a 0.34-point increase in willingness to participate in a clinical trial for a COVID-19 treatment ($p<0.001$, 95% CI: 0.15–0.53). Compared to participants with a history of positive COVID-19 results, those without such history showed a decrease in willingness of 0.4 points ($p=0.016$, 95% CI: -0.73 – -0.08), and participants who had never tested reported a decrease in willingness of 0.65 points ($p=0.013$, 95% CI: -1.16 – -0.14). Those aware of COVID-19 treatment clinical trials at baseline reported a 0.38-point increase in willingness compared to the unaware ($p=0.031$, 95% CI: 0.04–0.73). Similarly, participants with knowledge of clinical trial logistics at baseline reported a 0.83-point increase in willingness compared to those without ($p<0.001$, 95% CI: 0.44–1.23).

Additionally, race ($\chi^2=18.78$, $p=0.001$) and gender ($\chi^2=10.08$, $p=0.018$) emerged as a significant predictor. Compared to non-Hispanic White participants, Hispanic participants exhibited a 0.5-point increase in willingness ($p=0.028$, 95% CI: 0.05–0.94). Transgender or gender diverse participants showed a 1.31-point increase in willingness compared to women participants ($p=0.022$, 95% CI: 0.19–2.44), while participants who preferred not to report gender exhibited a 0.24-point decrease in willingness ($p=0.041$, 95% CI: -2.51 – -0.05). No significant associations were observed between the wave of data collection, age, insurance status, sexual orientation, parental status, education or COVID-19 related challenges and participants' willingness to participate in a clinical trial for COVID-19 treatment.

Table 1 Demographic characteristics of participants who participated and did not participate in the year 2 survey between August 2022 and March 2023 in Philadelphia

	Year 1 Subsample (*n* = 582)	Year 2 Participants (*n* = 343)	Year 2 Non-Participants (*n* = 239)	*p*-value
Willingness (mean (SD))[a]	4.23 (2.1)	4.34 (2.0)	4.08 (2.2)	0.152
Trust in federal oversight of COVID-19 vaccine safety for the public (mean (SD))[b]	3.04 (0.8)	3.07 (0.8)	3.01 (0.8)	0.386
Number of COVID-19 related challenges (mean (SD))[c]	1.38 (1.6)	1.33 (1.5)	1.45 (1.7)	0.399
History of positive COVID-19 results (n (%))				0.006*
No/Don't know	405 (69.7)	225 (65.6)	180 (75.6)	
Never tested	96 (16.5)	70 (20.4)	26 (10.9)	
Yes	80 (13.8)	48 (14.0)	32 (13.4)	
Age (mean (SD))	38.8 (13.0)	38.7 (12.3)	38.9 (14.0)	0.867
Age (range)	13 to 84	15 to 84	13 to 79	
Race and ethnicity (n (%))				0.198
Hispanic/Latinx	87 (14.9)	54 (15.7)	33 (13.8)	
Non-Hispanic Asian	64 (11.0)	40 (11.7)	24 (10.0)	
Non-Hispanic Black or African American	209 (35.9)	111 (32.4)	98 (41.0)	
Non-Hispanic Multiracial/Other	46 (7.9)	25 (7.3)	21 (8.8)	
Non-Hispanic White	176 (30.2)	113 (32.9)	63 (26.4)	
Gender (n (%))				0.017*
Man	166 (28.5)	83 (24.2)	83 (34.7)	
Prefer not to answer	5 (0.9)	4 (1.2)	1 (0.4)	
Transgender or gender diverse	13 (2.2)	6 (1.7)	7 (2.9)	
Woman	398 (68.4)	250 (72.9)	148 (61.9)	
Sexual orientation (n (%))				0.619
Non-heterosexual	87 (14.9)	54 (15.7)	33 (13.8)	
Prefer not to answer	16 (2.7)	8 (2.3)	8 (3.3)	
Straight or heterosexual	479 (82.3)	281 (81.9)	198 (82.8)	
Education (n (%))				0.002*
College degree (reference)	368 (63.2)	235 (68.5)	133 (55.6)	
Non-college degree	214 (36.8)	108 (31.5)	106 (44.4)	
Insurance (n (%))				0.146
No/Don't know	32 (6.0)	16 (4.7)	19 (7.9)	
Yes	546 (94.0)	326 (95.3)	220 (92.1)	
Parental status (n (%))				0.978
Parents	276 (47.4)	162 (47.2)	125 (52.3)	
Not parents	306 (52.6)	181 (52.8)	114 (47.7)	
Awareness of COVID-19 treatment clinical trials (n (%))				0.017*
Yes	174 (29.9)	116 (33.8)	58 (24.3)	
No	408 (70.1)	227 (66.2)	181 (75.7)	
Knowledge of the logistics of clinical trials (n (%))				0.039*
Yes	83 (14.3)	58 (16.9)	25 (10.5)	
No	499 (85.7)	285 (83.1)	214 (89.5)	

Abbreviation SD = standard deviation

* $p < 0.05$

[a] Response options for willingness: '1 = not at all willing' to '7 = very willing,' with participants selecting a number between 2 and 6 to express their willingness, representing varying degrees of willingness between 1 and 7

[b] Response options for trust: '1 = fully trust,' '2 = mostly trust,' '3 = somewhat trust,' and '4 = do not trust' (The responses were reverse-coded for analysis.)

[c] COVID-19 challenges: (1) accessing necessary healthcare, (2) securing adequate housing and (3) food, (4) ensuring access to clean water, (5) obtaining required medications, and (6) fulfilling transportation needs

Discussion

The study aimed to investigate the association between trust in federal oversight of vaccine safety and willingness to participate in COVID-19 clinical trials across four time points over 18 months. The results supported our hypothesis that there would be an association between higher trust levels and greater willingness to participate in trials, even after adjusting for various

Table 2 Multivariable analysis using generalized estimating equations to predict willingness to participate in a COVID-19 clinical trial across four waves of data collection between September 2021 and March 2023 in Philadelphia ($n = 343$ unique participants with 1,276 observations over time)

Predictor variables and covariates	Coefficients (95% confidence interval)	*p*-value
Trust in federal oversight of COVID-19 vaccine safety for the public	0.34 (0.15–0.53)	< 0.001*
Number of COVID-19 related challenges	0.08 (-0.01–0.15)	0.050
History of positive COVID-19 results		0.020*
Yes (reference)		
No/Don't know	-0.40 (-0.73 – -0.08)	0.016*
Never tested	-0.65 (-1.16 – -0.14)	0.013*
Wave		0.831
Year 1 (reference)		
Wave 1 for Year 2	-0.06 (-0.36–0.24)	0.701
Wave 2 for Year 2	-0.01 (-0.28–0.27)	0.966
Wave 3 for Year 2	-0.10 (-0.35–0.16)	0.451
Age	0.01 (-0.002–0.03)	0.083
Awareness of COVID-19 treatment clinical trials		
No (reference)		
Yes	0.38 (0.04–0.73)	0.031*
Knowledge of the logistics of clinical trials		
No (reference)		
Yes	0.83 (0.44–1.23)	< 0.001*
Parental status		
Not parents (reference)		
Parents	-0.26 (-0.58–0.07)	0.119
Insurance		
No/Don't know (reference)		
Yes	0.13 (-0.48–0.75)	0.671
Race and ethnicity		0.001*
Non-Hispanic White (reference)		
Non-Hispanic Multiracial/Other	0.11 (-0.56–0.77)	0.749
Non-Hispanic Asian	-0.44 (-0.93–0.05)	0.081
Non-Hispanic Black or African American	-0.38 (-0.78–0.03)	0.067
Hispanic/Latinx	0.50 (0.05–0.94)	0.028*
Gender		0.018*
Woman (reference)		
Man	0.16 (-0.17–0.49)	0.331
Transgender or gender diverse	1.31 (0.19–2.44)	0.022*
Prefer not to answer	-1.28 (-2.51 – -0.05)	0.041*
Sexual orientation		0.194
Straight or heterosexual (reference)		
Non-heterosexual	-0.24 (-0.74–0.27)	0.360
Prefer not to answer	-0.73 (-0.25–1.70)	0.143
Education		
College degree (reference)		
Non-college degree	-0.16 (-0.47–0.14)	0.300

* $p < 0.05$

sociodemographic characteristics. This finding highlights the enduring influence of trust in shaping individuals' willingness to participate in clinical trials amid the uncertainties of the pandemic. While the effect size may be relatively modest, it is important to underscore the clinical significance of this association. Even subtle increases in willingness to participate in clinical trials can have profound implications for medical research, potentially leading to advancements in treatment development, improved patient outcomes, and ultimately, enhanced healthcare delivery. Additionally, as COVID-19 clinical trials continue, with a specific emphasis on understanding long COVID and developing strategies to mitigate its long-term consequences [48], the importance of understanding predictors influencing participation in these trials remains paramount.

Given the pivotal role of clinical trials in advancing our understanding of COVID-19 and developing effective interventions, addressing trust-related concerns, including doubts regarding safety regulations, assumes heightened importance [20, 26, 38, 41]. This underscores the importance of establishing transparent and effective communication channels from public health authorities [27]. Engaging community messengers is also crucial to addressing public apprehensions and fostering trust in the safety monitoring systems of clinical trials. Increasing community engagement can help build public trust, thereby facilitating greater participation in clinical trials and advancing public health initiatives [49, 50]. Additionally, targeted interventions to address barriers and raise awareness and understanding of clinical trial logistics could facilitate greater engagement in clinical research efforts during public health crises.

In addition to examining time-varying trust in federal oversight, our study identified other time-varying variables significantly associated with individuals' willingness to participate in COVID-19 clinical trials during the pandemic. Individuals who had previously tested positive for COVID-19 displayed a greater willingness to participate in such trials. This finding underscores the intricate interplay of contributors that influence participation in clinical research during times of crisis. One plausible explanation is that prior exposure to COVID-19 may heighten individuals' awareness of the severity of the disease, thus motivating them to engage in clinical trials as a means of contributing to the advancement of medical knowledge and potential treatments. Additionally, increased access to trial information through healthcare providers or public health initiatives may play a role in fostering higher participation rates among individuals with a history of COVID-19 infection [51].

The longitudinal analysis revealed that time throughout the pandemic was not significantly associated with individuals' willingness to participate in clinical trials over

the 18-month study period. This finding suggests that despite the evolving nature of the pandemic and potential shifts in public perceptions and attitudes toward clinical research, participants' willingness to participate in trials did not exhibit substantial variation, highlighting the stability of individuals' decision-making regarding clinical trial involvement amidst the dynamic and rapidly evolving context of the COVID-19 pandemic.

Despite controlling for several variables, including trust in federal oversight, sociodemographic disparities in willingness to participate in COVID-19 trials were observed. Previous studies examining willingness to participate in COVID-19 trials across different countries have identified various sociodemographic predictors, such as gender [14–17, 21, 22], race [21], and age [16, 17]. Our study highlights the significance of race and gender as a notable predictor. Specifically, Hispanic participants demonstrated heightened willingness compared to their non-Hispanic White counterparts. This finding aligns with studies on cancer clinical trials where Hispanic participants exhibited increased willingness [35]. However, contrasting results have been reported in other studies on cancer clinical trials, indicating decreased willingness or lower participation rates among Hispanic individuals [36, 37]. Additionally, this finding is inconsistent with a study on COVID-19 vaccine trials, which have shown greater rejection rates among Black participants [21]. Although our study identified gender as a predictor, it is important to note that the limited sample sizes for transgender or gender diverse participants, as well as participants who preferred not to report their gender, restrict the generalizability and robustness of our inferences. Further research with larger and more diverse samples is warranted to provide a more comprehensive understanding of the role of gender in this context.

The variability in findings concerning race and ethnicity, and the lack of statistical significance for other sociodemographic variables, such as parental status, insurance status, age, and education in our study, may be attributed to several factors. One explanation is the distinct nature of COVID-19 and its associated clinical trials. The urgency and global scale of the pandemic likely influenced individuals' perceptions, motivations, and decision-making processes differently than in non-COVID-19 contexts, such as cancer clinical trials. The dynamic landscape of COVID-19, marked by rapidly evolving public health recommendations, shifting government responses, and varying levels of public awareness, could also introduce complexities into decision-making regarding clinical trial participation. Additionally, the unprecedented speed at which COVID-19 vaccines and treatments were developed and authorized for emergency use may have shaped public attitudes toward COVID-19-specific clinical trials differently. Finally, unmeasured variables in previous COVID-19 clinical trial studies, such as awareness of clinical trials and knowledge about participation logistics, may have mediated the relationship between sociodemographic characteristics and willingness to participate. Sociodemographic disparities in awareness and knowledge could have driven the associations observed in other studies.

The study has several limitations that should be considered. First, our research was conducted solely among individuals residing in Philadelphia, which may limit the generalizability of the findings to other settings. Second, the potential for selection bias is another limitation, given the statistically significant differences observed in gender, education, history of positive COVID-19 results, awareness of COVID-19 treatment clinical trials, and knowledge of the logistics of clinical trials between members of the Year 1 subsample who participated in the year 2 survey and those who did not. This could impact the generalizability of our findings, as certain demographic groups and individuals with specific experiences or levels of knowledge may be overrepresented or underrepresented in the year 2 survey sample. Third, while our longitudinal design allowed for a comprehensive assessment of trust dynamics over time, the study's duration was limited to 18 months. Next, the survey was administered via an online survey platform and online outreach was a primary recruitment strategy. Therefore, study participation was limited to individuals who have access to the internet on web-enabled devices. Additionally, the study focused primarily on trust in federal oversight of vaccine safety, and did not measure other important dimensions of trust, such as trust in healthcare providers or researchers. Finally, the study did not assess participants' actual enrollment in clinical trials, relying instead on self-reported willingness to participate. Actual enrollment rates may differ from reported willingness.

Future research could investigate the interplay between different dimensions of trust and their impact on clinical trial participation. It could also explore the mechanisms by which trust in governmental safety monitoring influences participation and assess the effectiveness of different communication strategies in building this trust. Comparative studies could analyze the impact of various messaging approaches on trust levels and recruitment rates to inform evidence-based strategies to enhance public confidence and increase clinical trial participation. Additionally, future studies with larger sample sizes, longer follow-up periods, and comprehensive measures could explore the nuanced influences on clinical trial participation decisions and validate self-reported willingness with objective enrollment data. Further exploration of the underlying determinants contributing to consistent willingness to participate across phases of the pandemic may also be warranted.

Conclusions

Trust in federal COVID-19 vaccine oversight is associated with individuals' willingness to participate in clinical trials for COVID-19 treatment during the pandemic. Understanding the root causes of mistrust in federal oversight is crucial for addressing barriers to participation in COVID-19 clinical trials. Through efforts to cultivate trust and alleviate concerns regarding oversight, we can encourage greater engagement in clinical research endeavors, thereby advancing our collective response to ongoing COVID-19 challenges.

Abbreviations

COVID-19	Coronavirus Disease 2019
SD	Standard Deviation
CI	Confidence Interval
CEAL	Community Engagement Alliance

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Author contributions

HY, SB, UO, SA and JB made contributions to the conception and design of this article. HY, SB, SA, KM, AV and JB contributed to the acquisition, analysis and interpretation of data. HY drafted the manuscript. SB, UO, SA, KM, KG, AV and JB revised the manuscript. All authors approved the final manuscript.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All study procedures received approval from the University of Pennsylvania Institutional Review Board (IRB protocol number: 848650). Written informed consent was obtained from all participants after fully explaining the nature and potential consequences of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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