

Rapid Development of a Registry to Accelerate COVID-19 Vaccine Clinical Trials

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Article

Keywords:

Posted Date: June 10th, 2024

DOI: <https://doi.org/10.21203/rs.3.rs-4397271/v1>

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Additional Declarations: There is a conflict of interest JK, NFA, KM, GBB, MT, and LR declare no conflicts; RL, SS, AK, DM, SM, and JH are employed by Oracle Corporation and hold stock options.

Title: Rapid Development of a Registry to Accelerate COVID-19 Vaccine Clinical Trials

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Abstract

Background

The unprecedented scientific response to the SARS-Cov-2 pandemic in 2020 required the rapid development and activation of extensive clinical trial networks to study vaccines and therapeutics. The COVID-19 Prevention Network (CoVPN) coordinated hundreds of sites conducting phase 2 and 3 clinical trials of vaccines and antibody therapeutics. To facilitate these clinical trials, the CoVPN Volunteer Screening Registry (VSR) was created to collect volunteer information at scale, identify volunteers at risk of COVID-19 who met enrollment criteria, distribute candidates across clinical trial sites, and enable monitoring of volunteering and enrollment progress.

Methods

We developed a secure database to support three primary web-based interfaces: a national volunteer questionnaire intake form, a clinical trial site portal, and an Administrative Portal. The Site Portal supported filters based on volunteer attributes, visual analytics, enrollment status tracking, geographic search, and clinical risk prediction. The Administrative Portal supported oversight and development with pre-specified reports aggregated by geography, trial, and trial site; charts of volunteer rates over time; volunteer risk score calculation; and dynamic, user-defined reports.

Findings

Over 650,000 volunteers joined the VSR, and 1094 users were trained to utilize the system. The VSR played a key role in recruitment for the Moderna, Oxford-AstraZeneca, Janssen, and Novavax vaccine clinical trials, provided support to the Pfizer and Sanofi vaccine and prophylactic antibody clinical trials, and enhanced the diversity of trial participants. Clinical trial sites selected 166,729 volunteer records for follow-up screening, and of these 47.7% represented groups prioritized for increased enrollment. Despite the unprecedented urgency of its development, the system maintained 99.99% uptime.

Interpretation

The success of the VSR demonstrates that information tools can be rapidly yet safely developed through a public-private partnership and integrated into a distributed and accelerated clinical trial setting. We further summarize the requirements, design, and development of the system, and discuss lessons learned for future pandemic preparedness.

Funding

The US National Institute for Allergies and Infectious Diseases and the Oracle Corporation

Introduction

The domestic US plan to accelerate SARS-CoV-2 vaccine development aimed to advance multiple stages of clinical trials concurrently. The US government-funded COVID-19 Prevention Network (CoVPN) partnered with the White House and the Department of Health and Human Services (HHS) to evaluate at least two vaccine candidates from each of the three most promising vaccine platforms in tandem.¹ In addition to aligning and synchronizing clinical trial activities, CoVPN worked to coordinate activities and harmonize data and resources across clinical trials to minimize competitive practices and to increase the value of clinical and immunologic data obtained from these clinical trials. Here, we describe one such coordinated resource: a centralized clinical trial volunteer screening registry (VSR) used to support enrollment in CoVPN clinical trials.

Historically, large clinical trial networks, individual recruiting sites, and clinical research organizations (CROs) have developed and maintained independent, localized volunteer registries. With a national effort spanning several concurrent clinical trials involving over 100,000 participants, a centralized registry was envisioned to prevent redundancy and competition for volunteers. Thus, in May of 2020, we started the development and promotion of a national centralized registry.

The CoVPN VSR was designed to support multi-pronged and concurrent clinical trials, to meet requirements of private vaccine developers, and to interface with public/private clinical research networks. Additional constraints were imposed by the rapid advancement and scaling of vaccine clinical trials in the first months of the COVID-19 pandemic. Furthermore, rapidly evolving scientific evidence influenced the scope and content of screening questions, user queries, and risk estimates needed to support forthcoming clinical trials.

Existing software platforms were initially considered to support a volunteer registry. Several platforms, including customer engagement, electronic data capture (EDC), and clinical trial management systems (CTMS) were evaluated for their capacity to meet functional requirements such as connecting volunteers with clinical trial recruiters and screeners.^{2,3} Candidate systems such as REDCap^{4,5} were customizable, enabled web-based intake, and facilitated volunteer engagement. However, these systems were not designed to scale to handle millions of records and hundreds of simultaneous users. Other commercial software options included patient engagement and recruitment functions but did not meet needs of CoVPN to equitably distribute volunteers, incorporate risk scoring, or perform needed oversight functions. Building a system under an accelerated timeline allowed timely implementation of CoVPN-specific requirements including utilization metrics, scoring functions, and collaboration functions while also scaling to support national and international clinical trials. An existing COVID-19 donation agreement from Oracle Corporation (Oracle) to support HHS-related pandemic efforts enabled us to rapidly collaborate and leverage Oracle technology and development resources to create and deploy the system rapidly.

Methods

The initial scope, design, and system requirements were determined during the initial wave of the pandemic through collaboration between COVID-19 Prevention Network, HHS/NIH, Oracle, and the overall United States government (USG) operation bridging public and private sector

expertise and infrastructure. We solicited additional feedback from vaccine developers, the CDC, and clinical trial sites. The effort encompassed design of a volunteer intake questionnaire, database/user interface (UI) development, user accommodations, and development of risk and targeting algorithms.

System design

The VSR system requirements encompassed the need for data scale, concurrent users, multiple client interfaces, schema flexibility, adaptability, resilience, compliance, and security. A key requirement was the ability to efficiently store, query, and/retrieve millions of associated records in order to scale to hundreds of thousands of volunteers. Given concurrent recruitment and enrollment around the country, the system was also designed to respond to hundreds of simultaneous push/pull requests. (A summary of system requirements and functions is in Supplemental Table S1.)

Due to the speed of execution, the system was planned and developed in parallel with the volunteer questionnaire and several other aspects of the clinical trial network, even as the clinical trial protocols were still being finalized. To ensure adaptability to changes of the volunteer questionnaire and downstream database use cases, the underlying database architecture was designed to allow for customizable volunteer attributes and value sets.

User interface and system design

The application UI for clinical trial sites and administrative support were created using rapid prototyping to support recruiters and CoVPN management, respectively. The primary clinical trial site UI consisted of six functions identified in consultation with HVTN and CoVPN leadership, investigators, site Principal Investigators (PIs), and informaticists. The landing page of the Site Portal was designed with simplicity in mind for ease of training, adoption, and use during recruitment (Figure 1).

The underlying relational schema contained 26 tables to support the multi-trial, multi-user nature of the system. The table structure (Suppl. Fig 1) supports various functions: Recording volunteer information (Surveys, Questions, Survey_responses, Question_values, Volunteers, Consent_forms, Risk_scores); Trial information (Trials, Trial_sites, Catchment_areas, Trial_site_zips, Site_users); Survey management (Checkout_sets, Status_codes); and System behavior (Languages, Risk_algorithms, Users, and other event logging). Survey questionnaire responses utilized an Entity-Attribute-Value model to support evolving questions/values from the survey. This approach enabled rapid and relatively seamless changes of the survey without impacting queries that supported system behavior.

Administrative functions evolved more progressively over time as additional management functions and analytics functions were identified. These included monitoring of VSR usage statistics by site, trial, and geographic area; rates and demographics of volunteer accrual; and ad hoc analytics and risk score development.

Accommodations for users and volunteers

Training materials were developed to help users navigate through the system, understand approaches to screening volunteers, and to share features and requirements of the system. Dozens of virtual training sessions were held by the developer and administrative support teams.

To ensure equitable outreach to a broader population, Spanish language versions of the VSR recruitment website, the VSR questionnaire, and other study materials were provided. A helpline was also established to facilitate registry participation for the elderly or others who faced challenges accessing the registry website.

Volunteer questionnaire design

Accelerating these clinical trials required rapidly screening volunteers and enrolling hundreds of thousands of participants to meet different study criteria. The VSR questionnaire was designed by a panel of epidemiologists, clinical trial staff, investigators, and community engagement experts to help meet these needs. Registry questions were added to represent demographics and comprehensive clinical, environmental, and behavioral risk factors identified by epidemiologic studies. When possible, questionnaire items were aligned with validated survey instruments or controlled vocabularies, clinical trial enrollment criteria, and emerging literature. The questionnaire (English and Spanish versions) and relevant skip patterns were reviewed for regulatory compliance and approved by Advarra IRB (Pro00044444). The questionnaire and UI were also pilot tested with community members and existing application review panels from different demographic groups to ensure survey comprehensibility and ease of completion. Feedback from these assessments were incorporated into the final questionnaire design.

Volunteer risk assessment

To optimize the accrual of study endpoints, we calculated risk assessments for individual volunteers. These assessments included published COVID-19 risk models as well as additional clinical and behavioral risk flags and algorithms to estimate the level of exposure, symptomatic disease, hospitalization, intensive care admission, and death. Risk predictions were used to evaluate user queries.

An evidence review was conducted to identify common variables used as inputs for available risk models early in the pandemic. (See Wynants et al. for an earlier review of COVID-19 prediction models.⁶) When possible, these variables such as age, demographics, and other emerging risk factors were included in the volunteer survey.

At the time of initial deployment, given scant published evidence, the VSR supported analytics and volunteer filtering with the COVER-H, COVER-I, and COVER-F risk scores⁷ (estimating risk of hospitalization, ICU admission, and fatality respectively). Support for additional risk models was added during the subsequent four months of VSR deployment. As additional published research on COVID-19 risk accumulated, we synthesized this evidence into additional models to predict the risk of symptomatic disease and SARS-CoV-2 exposure.

The Site Portal provided tools to support volunteer record allotment, management, and status reporting. Signed data use and confidentiality agreements were required for system access, which was further safeguarded by two-factor authentication. A non-identifying volunteer key (distinct from other patient identifiers) was provided to clinical trial sites to enable secure status updates

after volunteer contact. Each clinical trial site in the continental United States was limited to screening a fixed number of records within a local catchment area, adjusted for number of competing sites and enrollment targets of the trial. Volunteer records could be “checked out” to prevent competition for volunteers within zip codes targeted by the clinical trials. In September of 2020, queries of the VSR returned volunteer records in order of descending risk to facilitate accrual of study endpoints.

To check out new records, previously accessed records were updated with a status code indicating study enrollment, returning them to the pool of available volunteers, or otherwise removing them from the registry. The system supported a limited set of screening outcomes to simplify use of the system (Contact Not Attempted, Unable to Contact, Reconsider Later, Remove from Registry, Duplicate Record, Contacted/Not Enrolled, and Enrolled). The status codes are shown in Supplemental Table S2. Automated reminders were provided to users if the status of checked out records was not updated within two weeks.

Role of funding source

Representatives of the funding source (US government) were involved in review of the VSR survey and websites, as well as in site selection, timelines, and protocols for specific CoVPN clinical trials. However, the funding source did not contribute to the analyses or conclusions.

Results

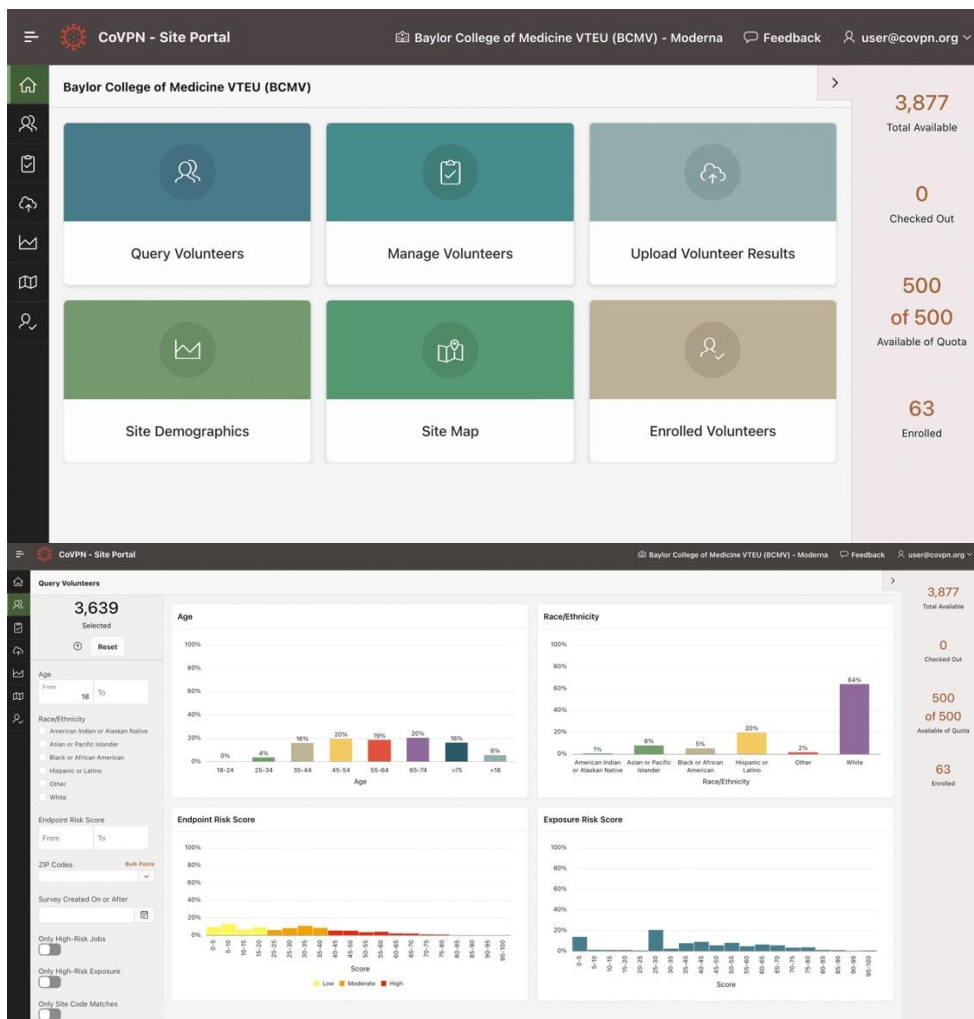
System implementation

The CoVPN VSR consisted of distinct user interfaces: the Volunteer Questionnaire; the clinical trial Site Portal for screening volunteers; and an Administrative Portal for oversight of volunteer records, analytics, and site monitoring.

The Volunteer Questionnaire was tested and designed in May-June of 2020 to support varied, projected needs of clinical trials that might hinge on volunteer risk factors, exposures, symptoms, as well as evolving inclusion/exclusion criteria of clinical trials still under active development. This was a challenging task due to the unclear etiology of COVID-19 disease, the contributions of intrinsic versus behavioral risk factors, and the unfolding requirements of each clinical trial. The final components of the questionnaire included *Contact info*, *Demographics*, *Occupation*, *Residence*, *Community interactions*, *COVID-19 risks and testing*, and *Symptoms and health risks*. These records supported volunteer screening and prioritization for multiple clinical trials (the full survey is provided in Supplemental Materials).

The Site Portal was developed as an interface for clinical trial site staff and principal investigators to characterize, query, and access volunteer records for the purpose of volunteer contact. The portal provided six ways of interacting with volunteer records:

- Query volunteers - Selection of tailored subsets of volunteer records
- Manage volunteers - In-browser tools to set volunteer record statuses or return records
- Upload volunteer results - De-identified record status updates via file upload
- Site demographics - Descriptive statistics of volunteers within a site’s catchment area
- Site map - Interactive map and selection tools to identify volunteers within target areas
- Enrolled volunteers - Overview of volunteers marked as enrolled by a site



CoVPN - Site Portal

Baylor College of Medicine VTEU (BCM) - Moderna

Feedback

user@covpn.org

Query Volunteers

3,639
Selected

Reset

Age
From 18 To

Race/Ethnicity
☐ American Indian or Alaskan Native
☐ Asian or Pacific Islander
☐ Black or African American
☐ Hispanic or Latino
☐ Other
☐ White

Endpoint Risk Score
From To

ZIP Codes Bulk Paste

Survey Created On or After

☐ Only High-Risk Jobs

☐ Only High-Risk Exposure

☐ Only Site Code Matches

Age

Age Range	Percentage
18-24	0%
25-34	4%
35-44	16%
45-54	20%
55-64	19%
65-74	25%
>75	16%
<18	9%

Race/Ethnicity

Race/Ethnicity	Percentage
American Indian or Alaskan Native	1%
Asian or Pacific Islander	8%
Black or African American	5%
Hispanic or Latino	20%
Other	2%
White	64%

Endpoint Risk Score

Score Range	Percentage
0-10	20%
10-20	15%
20-30	10%
30-40	10%
40-50	10%
50-60	10%
60-70	10%
70-80	10%
80-90	10%
90-100	10%

Exposure Risk Score

Score Range	Percentage
0-10	20%
10-20	15%
20-30	10%
30-40	10%
40-50	10%
50-60	10%
60-70	10%
70-80	10%
80-90	10%
90-100	10%

3,877
Total Available

0
Checked Out

500
of 500
Available of Quota

63
Enrolled

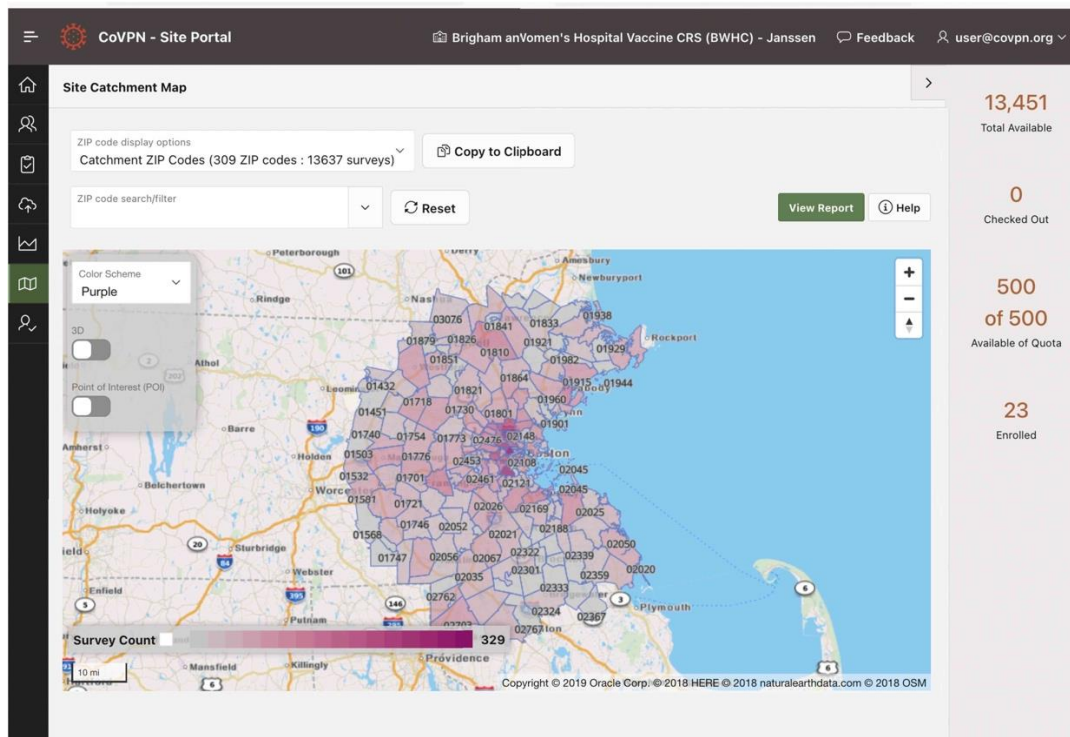


Figure 1. Site Portal. A) Landing page showing six core functions; B) Query volunteers function showing interactive filtering, descriptive statistics of volunteer demographics, and risk scores. C) Interactive map of a site catchment area and volunteer density that enabled selection of volunteers from target regions.

Registry Administration

The Administrative Portal utilized an activity dashboard, and provided standardized reports that facilitated survey response monitoring, site administration, and risk algorithm administration (Figure 2). Several reports were customized to provide survey statistics and site-specific and trial-specific monitoring. The system also supported all functions from the Site Portal at the site level, as well as the ability to pose ad hoc queries, reports, and data visualizations.

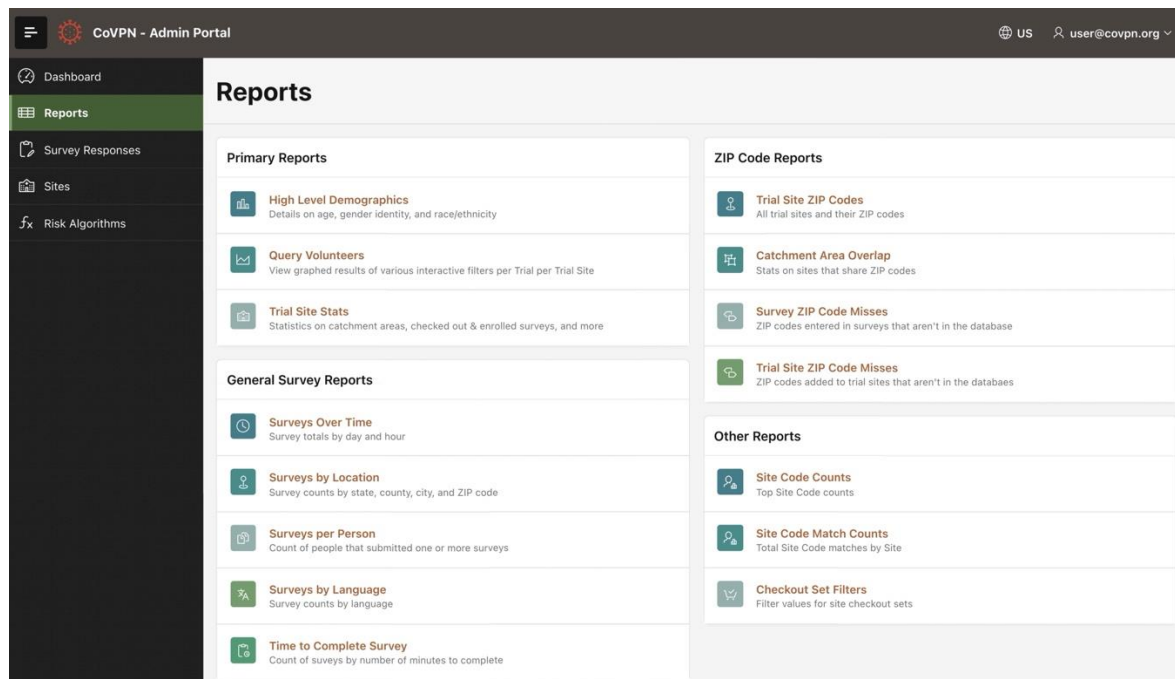


Figure 2. Administrative Portal. A variety of live reports from the database supported periodic monitoring of volunteering, site utilization, and enrollment according to time, geography, or clinical trial.

Volunteer and site usage statistics

The registry was launched to the public on July 8, 2020, seven weeks after the announcement of federal vaccine development plans.⁸ With 657,750 volunteers in total, the VSR was highly effective; 50% of these volunteers signed up within the first 36 days. Volunteer registrations also increased in concert with public service announcements during August and September (see Figure 3). Participation was also increased using site-specific registration codes, which enabled recruiters to utilize the VSR in concert with volunteer campaigns and events.

The Site Portal was subsequently launched on August 4, 2020. In the US, 455 unique clinical research sites, accessed a total of 168,015 volunteer records for recruitment and enrollment into six phase 3 COVID-19 vaccine clinical trials. These volunteers were drawn from catchment areas that included 22,201 US zip codes. Supplemental Table S3 shows the number of sites involved per clinical trial.

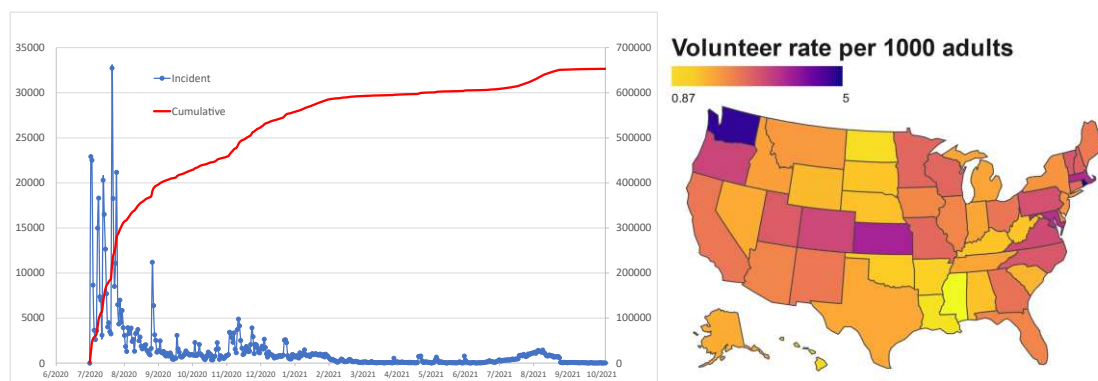


Figure 3. Volunteer registrations over time and geography. Over 300,000 volunteers registered in the system within the first month. The map shows the volunteering rate per 1000 adults in each state (mean = 2.23 / 1000 US adults).

Evaluation and feedback

The rapid development and deployment of the system limited intensive user-centered design or system evaluations. However, the VSR was publicly credited with advancing the clinical trials. Although the emergency circumstances prevented a formal evaluation, we detail below steps taken to respond to volunteer and user system requirements.

The median time to complete a survey was 5 minutes. The completion rate of the VSR questionnaire was 95.3%.

The VSR survey and Site Portal both allowed submission of comments to the development team. Volunteer feedback on the survey was reviewed weekly to identify any logical errors, omissions, usability concerns, or confusing questions. For a summary of user feedback, see Supplemental Table S4. Site Portal users also requested some functions including support for site- and campaign-specific recruitment codes for volunteers, additional query filters, and the ability to save and retrieve query results. These features were incorporated into updated versions of the system. Thrice-weekly development team meetings and task management software were used to prioritize any bugs or feature requests.

Stage 2 and 3 clinical trials for each vaccine launched on different dates. Therefore, some clinical trials were able to access more diverse and recent volunteers than other clinical trials.

Discussion

Due to COVID-19 lockdowns and limitations on in-person collaboration, clinical and research teams responding to the pandemic faced unprecedented challenges. In our case, the CoVPN VSR development and administrative teams assembled and collaborated remotely during every phase of the project, encompassing system design, development, documentation, training, technical support, and evaluation. In addition to remote collaboration tools such as Zoom and Microsoft Teams, the team utilized telephone, email, Slack, and web-based office productivity, scheduling, project management, and survey applications to support information sharing and coordination. Team members' experience with these platforms varied according to institutional licensing for specific technologies, which required compromise as the team formed new work processes.

The network of clinical trial sites engaged for each study was selected through a collaborative process that involved stakeholders from HHS, vaccine developers, CoVPN, and CROs. Because each trial included sites from pre-existing vaccine trial networks as well as newly appointed CRO sites, it was necessary to position the VSR for accessibility and generality instead of specializing for a more uniform user base or the needs of a single developer. To achieve adoption, dozens of training sessions were held with hundreds of recruiters and investigators from different clinical trial sites. Individual sites often employed specialized recruitment procedures or utilized additional digital platforms mandated by vaccine developers or CROs. Future efforts to coordinate clinical trial networks may benefit from establishing plans for secure, standards-based, bidirectional information sharing akin to electronic medical record exchange.

The CoVPN VSR quickly accrued volunteers upon its introduction, reaching over 300,000 within the first month. However, despite ongoing advertising, volunteering rates slowed after the initial few months of availability. Vaccine misinformation and fears were already circulating during this time before the clinical trials were even complete. It is possible that this misinformation affected volunteering rates as well as subsequent recruitment efforts. To combat these efforts, the CoVPN website included information about vaccine science, individual clinical trials, the study process, and frequently asked questions in both English and Spanish.

One chief concern raised from VSR data was the inclusion of potentially sensitive identifying information and health conditions among survey responses. Such data were required to identify volunteers potentially at risk of severe COVID-19 outcomes, to ensure participants could be reached, and to ensure equitable recruitment. The need to collect and store this data might have been obviated by a national health identifier or linkage to electronic health records. Having collected this information, our user interface, training, and data use policy were crafted to promote retention of such data within the VSR system. Collection and use of the data were approved through an Institutional Review Board.

Several alternative COVID-19 clinical trial volunteer registries were developed in the initial months of the pandemic by both commercial and non-profit entities.⁹⁻¹² For example, some registries leveraged electronic health records to identify patients for COVID-19 therapeutic clinical trials, following the clinical cohort-driven model adopted by Clinical and Translational Science Award sites through the Accrual to Clinical Trials initiative (CTSA ACT).^{13,14} This recruitment model was not appropriate for prospective vaccine clinical trials that required healthy volunteers.

Other approaches included vaccine developer-specific, site-specific, region-specific^{12,15,16}, or comorbidity-specific^{11,17-19} volunteer registries. Though beneficial for specific recruiting organizations, this approach had the drawback of locking volunteers into one or a small subset of clinical trials for which they might be eligible. Two NIH initiatives provide prior examples of attempts to recruit a broader population of healthy volunteers. ResearchMatch.org is a general volunteer registry to connect eligible volunteers with clinical trials.²⁰ In its 12-year history, this CTSA project has accrued 166,289 volunteers. Another NIH program, the Clinical Research Volunteer Program, is designed to support local clinical trials run by the NIH.²¹

Enabling technologies

The rapid design and implementation of the CoVPN VSR was facilitated by Oracle Application Express (APEX, a low-code application development platform), application programming interfaces, web-based visualization tools, and the Oracle Database (all hosted in Oracle's Government Cloud). Use of an Entity-Attribute-Value²² data definition for questionnaire intake data allowed for mid-flight schema updates which could be quickly passed through to updated user interfaces. This prevented the need for major architecture changes as new COVID-19 risk data and clinical trial priorities became available in the last months of 2020. Web-based project management, video conferencing, chat, file-sharing, and email facilitated rapid collaboration and establishment of new cross-organization teams.

CoVPN Voluntary Screening Registry impact

Although the full impact of the registry on final clinical trial enrollment is currently unknown, we estimate that it increased enrollment up to 20% in some clinical trials. Given the difficulties commercial CROs had in recruiting diverse participants, adoption of the VSR unquestionably accelerated accrual into clinical trials and increased participation of more diverse populations.²³⁻²⁵

In addition to expediting enrollment, the VSR thus served as a crucial recruiting platform to ensure representation of diverse populations in study findings. Moreover, it improved recruitment efficiency by enabling sites to reach volunteers who met preliminary eligibility criteria.

Finally, by achieving an unprecedented geographic coverage in record time, the VSR mitigated the risk of alternative epidemic scenarios or unfavorable clinical trial outcomes, which could have required highly targeted or continuous enrollment.

Lessons for the next pandemic

Open communication and flexibility were key to rapidly organizing a functional development team and meeting the unique needs of these accelerated clinical trials. The use of specialized teams to focus on system requirements, architecture, rapid iterative design-and-build process, administration, and training allowed the efficient division of labor.

In an emergency situation, competing priorities among stakeholders require compromises in the design and implementation of digital health systems. Public health experts have widely discussed the need for increased surveillance capacity, sustained investments in the public health infrastructure, and investments in data standardization and the health care system to better prepare and respond to pandemics. To support this, such investments must encompass the infrastructure for clinical trials and research IT. Additional facilitators of efficient and coordinated clinical trials include:

- Access to updated data standards, survey instruments, and other artifacts²⁶
- Surge capacity among clinical and IT experts
- Harmonized record sharing across EMR, CTMS, laboratory, and other clinical sources
- Flexible funding streams to support partnerships between domain experts and private enterprise

Conclusion

Through a public-private partnership, remote teamwork, and nimble development, we overcame barriers to collaboration imposed by the pandemic to connect hundreds of thousands of study volunteers to vaccine and antibody clinical trials. Emergency circumstances required balancing different priorities of the US government, sponsors, vaccine and antibody developers, research partners, and the public. Preparedness for future public health emergencies will benefit from continued investments in cross-institutional collaboration tools, data standardization, digital health data linkage, and platforms for public health communication.

Data sharing statement

Deidentified summary data of volunteer survey completion rates and CoVPN site statistics are available upon email request to the corresponding author upon publication. Data representing enrollment status, geography, demographics will be considered on a case-by-case basis.

Acknowledgements

The registry and clinical trials would not have been possible without the participation of many selfless volunteers. Funding for the system was provided by NIAID grants UM1AI068614 and UM1AI068635. Oracle Corporation provided a rapid build development team that supported the project, often under tight deadlines and outside business hours, as a pro-bono effort in response to the pandemic. Partners at HHS, NIAID, NHLBI, and the White House assisted in the national implementation, maintenance, and promotion of the registry website. We would also like to thank the clinical trial site PIs and staff who provided useful feedback about the system design.

Contributors

JK acquired funding. NFA, RL, KM, GBB, and JK administered the project; NFA, RL, SS, AK, MA, and JK provided supervision. NFA, MT, GBB, RL, DM, SS, and JK participated in conceptualization. NFA, KM, MT, LR, GBB, MA, RL, and JK developed the methodology. NFA, KM, DM, SS, SM, AK, JH, and JK provided data curation. NFA, KM, RL, DM, SS, SM, AK, and JH provided validation, visualization, and resources. NFA conducted the formal analysis. NFA and JK wrote the original manuscript. All authors participated in study investigation, manuscript review, and editing.

Declaration of interests

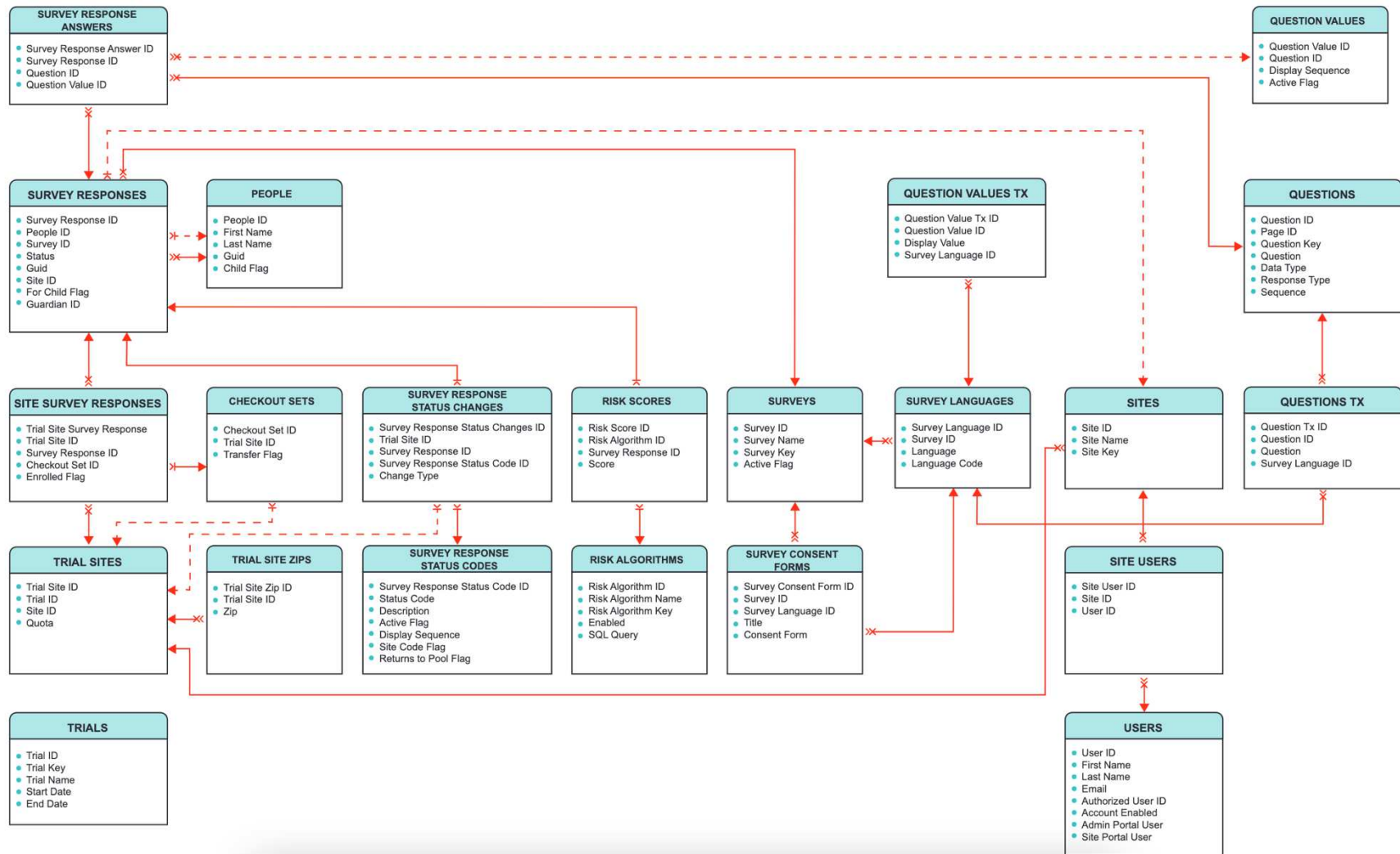
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Supplemental Figure 1. CoVPN Registry database schema.



Supplemental Table S1 - Overview of specialized CoVPN Registry requirements and functions

	Functional requirement	Rationale	Enabling function or Implementation
Volunteer survey	Unique volunteer & record identifiers	Enable volunteers to update surveys	Many-to-one relationship b/t volunteers and surveys
		Volunteer privacy	Redundant internal and sharable IDs
	Risk score inputs	Leverage existing evidence to identify those with high likelihood of exposure or symptomatic disease	Standardized survey instrument questions and data elements
	Validation rules	Ensure high quality of user-entered data	Browser- and internal database rules and constraints; data validation queries
	High-bandwidth and high-capacity storage and retrieval	Multiple concurrent users of registry survey (volunteers) and portal (sites) to enable rapid screening	Enterprise-grade and cloud-hosted database and web services
Clinical Trial Site Portal	View demographics and summary statistics of local volunteer population	Identify sub-populations that meet inclusion criteria and recruiting goals	Interactive charts Choropleth maps
	Filter volunteer records by demographics, risk, and geography	Enroll targeted groups more efficiently	User interfaces for filtering and selecting records based on volunteer details
	Volunteer screening tools	Quickly assess volunteer eligibility and interest and prevent redundant contact	In-browser UI for rapid status code assignment and volunteer follow-up
	Update volunteer statuses	Track enrollment progress; prevent redundant contact	Status codes and functional removal of volunteers from registry search results upon record checkout or volunteer request
	Save and reuse screening criteria	Improve ability to find new volunteers fitting established criteria	User-specific naming, reproduction, and storage of search queries
	Search for volunteers by outreach campaign	Improve follow-up of volunteers most likely to participate while providing credit to recruiters	Site- and campaign-specific recruitment codes stored with volunteer surveys and searchable in UI
Administrative Portal	Detailed reports of volunteer statistics	Monitor volunteering rates, populations, and diversity campaign results	Stored administrative queries linked to analytics and visualizations,
	Monitor site and trial record access and accrual progress	Improve site and record utilization; ensure trial enrollment progress and status codes of participants	Real-time report generation with accrual charts and statistics, broken out by targeted metrics including demographic representation
	Upload site information and catchment areas; Restrict access to volunteer information	Scope new sites/users to appropriate volunteer populations	Tables and queries return volunteer records only in site-specific local zip codes
	Add and edit pre-computed volunteer risk scores	Increase speed and efficiency of interactive tools; adapt database to new risk evidence	Score computation prototyping and validity/ security checking prior to deployment

Supplemental Table S2. Volunteer record status codes

	Meaning	Result
Code		
5	<u>Contact Not Attempted</u> : no attempt to email/call was made.	Returned to pool – others can query
10	<u>Unable to Contact</u> : contact attempted but unsuccessful. Used after all contact attempts have been made.	Returned to pool – others can query
20	<u>Contacted - Not Right Now, Consider Me Later</u> : not moving forward now, but interested in this study or another study in the future.	Returned to pool – others can query
30	<u>Contacted - Remove from Registry</u> : not interested in this or any study now or later – do not contact again.	Removed from registry
35	<u>Duplicate Record</u> : More than one survey was completed by the same person. Retain the latest record and return the other(s) with code 35.	Duplicates removed from registry, latest record retained
40	<u>Contacted - Not Enrolled</u> : contacted and may have screened, but ultimately did not enroll. May still be eligible for other studies.	Returned to pool – others can query
50	<u>Enrolled</u> : has been randomized into the study and vaccinated (per definition in the protocol).	Removed from registry

Supplemental Table S3. Number of sites utilizing the registry from each clinical trial.

	Sites participating	Records accessed
Trial		
AstraZeneca mAb (PROVENT)	39	838
AstraZeneca mAb (STORM CHASER)	54	7854
AstraZeneca Vaccine	71	59,318
CoVPN 3006 - Transmission Study	53	5117
Janssen	122	18,892
Janssen 2 Dose	2	271
Moderna	91	40165
Novavax	113	30,777
Novavax Adolescent	9	149
Pfizer	19	15
Sanofi Phase 2	9	2612
Sanofi Phase 3	122	721
Total	**	166,729

** Note that several sites participated in more than one non-concurrent trial, so this column does not sum to the total number of sites cited in the paper.

Supplemental Table S4 – Count of Individual User Feedback Items by Category.

	Count
User feedback category	
Communication and Contact	5
Inclusion, Eligibility, and Language	3
Information Accessibility	11
Location and Logistics	3
Miscellaneous	4
Protocol Questions	7
Survey Clarity and Understanding	22
Symptom Reporting and COVID-19 Awareness	2
Technical Issues	2
User-Friendly Design	7

Feedback on the VSR survey was solicited from diverse users during internal pilot testing. Sixty-six unique items of feedback were grouped into the discrete categories above, reflecting the frequency of questions or concerns raised. This feedback, as well as ongoing feedback from users of the live system, were used to iteratively improve the design and usability of the VSR.