The VA Research Enterprise: A Platform for National Partnerships Toward Evidence Building and Scientific Innovation

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Background: Within a year of the start of the COVID-19 pandemic, the US Department of Veterans Affairs (VA) was managing about 300 COVID-19–related research projects across roughly 100 facilities, which has since grown to more than 900 projects. This robust set of activities arose from an existing enterprise strategy and aimed at identifying needs for supporting the clinical care mission, more rapidly leveraging resources, and coordinating research across the VA. The VA's efforts to implement an enterprise strategy before March 2020 positioned its research community to dynamically partner with other federal agencies, academic institutions, and industry in addressing a national public health emergency.

Observations: The VA research enterprise involves a broad range of functions, scientific and clinical leaders, and organizational resources to enhance the health and care of veterans and the nation. The scope of research activities enables it to support its priorities while also partnering with others who share in mutual commitments to veteran health. Moving toward being the nation's learning health care system, the VA's leadership support, staff, patient volunteers, and partners were key contributors to a national response to COVID-19. Swift action and consistent communication helped address the complexities of the pandemic and strengthened the VA's ability to prepare and mobilize for emergencies and other potential disease outbreaks. Documenting strategies and practices can enhance future opportunities aimed at addressing the most challenging health care needs while also focusing on the primary mission to serve veterans.

Conclusions: The COVID-19 pandemic contributed to critical knowledge and lessons that enabled the VA to advance enterprise goals, particularly in the context of its health care system. Sharing these unique processes and experiences will inform current and future partnerships among research, clinical, and public health communities oriented to serve veterans and the nation through scientific innovation.

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The US Department of Veterans Affairs (VA) plays a substantial role in the nation's public health through the Veterans Health Administration (VHA). Its statutory missions of teaching, clinical care, and research enable it to serve a foundational role in the US biomedical enterprise.[1] Throughout its extensive network of VA medical centers (VAMCs) and partnering academic affiliates, thousands of clinicians and researchers have been trained to improve the lives of veterans and benefit the lives of all Americans. In supporting the largest US integrated health care system, the VA also has numerous capabilities and resources that distinctively position it to produce scientific and clinical results specifically within the context of providing care. The VA has formed partnerships with other federal agencies, industry, and nonprofit entities. Its ability to be a nexus of health care and practice, scientific discovery, and innovative ways to integrate shared interests in these areas have led to many transformative endeavors that save lives and improve the quality of care for veterans and the public.

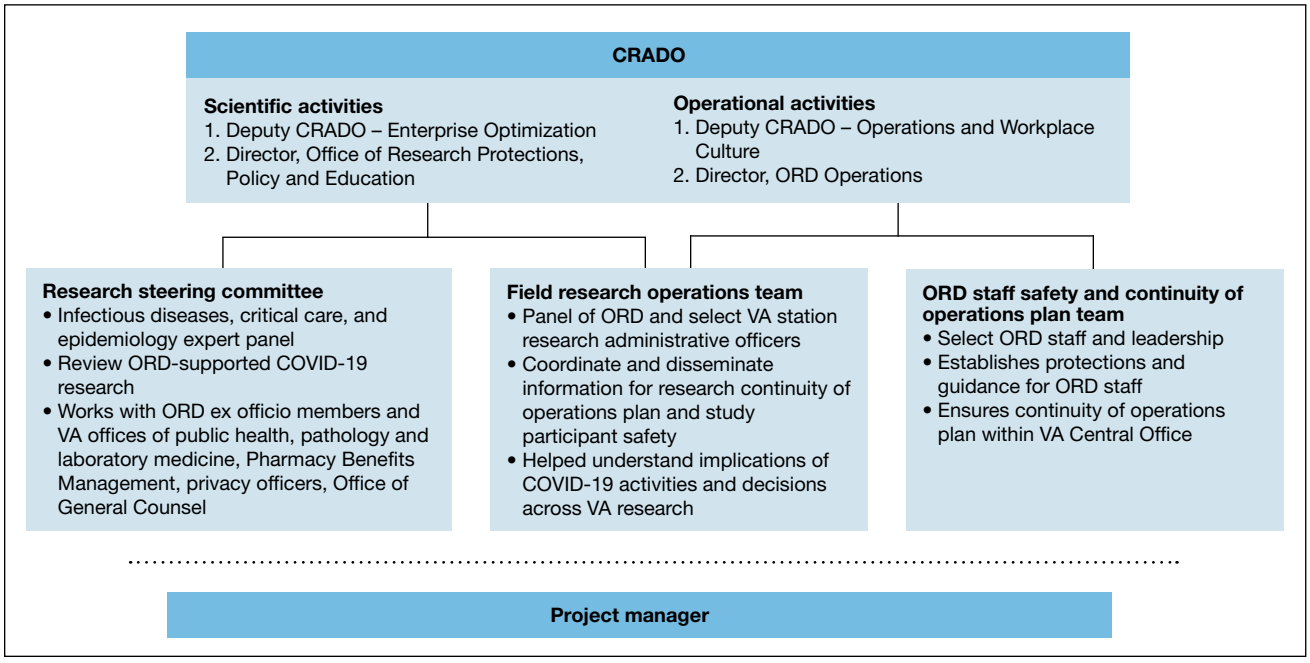
The COVID-19 pandemic triggered another mission: service in times of national emergency. Known as the Fourth Mission, the VA rapidly shifted to highlight how its health care and research enterprises could apply strengths in a unique, coordinated manner. While the Fourth Mission is typically considered in the context of clinical care, the VA's movement toward greater integration facilitated the role of research as a key component in efforts under a learning health care model.[2]

VA OFFICE OF RESEARCH AND DEVELOPMENT

Within the VHA, the Office of Research and Development (ORD) develops research policy and oversees interdisciplinary efforts focused on generating evidence to improve veteran health.[3] These activities span at least 100 of 171 VAMCs and include thousands of investigators and staff across all major health research disciplines. Many of these investigators are also clinicians who provide patient care and are experts in the prevention, diagnosis, and treatment of diseases and disorders affecting veterans.

The ORD has invested in a range of scientific, operational, regulatory, and technological assets and infrastructure as part of its enterprise. These strengths come from a nearly 100-year history originating as part of a set of hospital-based medical studies. This established the model for a culture of cooperative research within the VA and with external groups who benefit from the VA's foundational role in multisite clinical trials.[2,4,5] Today, the VA prioritizes bench-to-bedside research covering a broad spectrum of investigations, which are integrated with clinical operations and systems that deliver care.[3] The VA supports an extensive range of work that covers core areas in preclinical and clinical studies to health services research, rehabilitation and implementation science, establishing expertise in

FIGURE ORD COVID-19 Response Team Structure and Activities Organization



Abbreviations: CRADO, Chief Research and Development Officer; ORD, Office of Research and Development; VA, US Department of Veterans Affairs.

genomic and data sciences, and more recent activities in artificial intelligence.

In 2017, the ORD began a focused strategy to transform into a national enterprise that capitalized on its place within the VA and its particular ability to translate and implement scientific findings into real impact for veteran health and care through 5 initiatives: (1) enhancing veteran access to high-quality clinical trials; (2) increasing the substantial real-world impact of VA Research; (3) putting VA data to work for veteran health; (4) promoting diversity, equity, and inclusion within our sphere of influence; and (5) building community through research. These activities are interrelated and, where possible, the ORD works with other VA clinical and operational offices to accomplish multiple goals and coordinate within the health care system. As such, the VA continually seeks to increase efficiencies and improve abilities that provide veterans with best-in-class health care. While still in its early stages, this strategy and its initiatives established a path for the ORD response to the pandemic.

Within 2 weeks of the World Health Organization and the US declaring a COVID-19 pandemic, the ORD began to address the developing needs and challenges of the yet unknown emerging public health threat. This included outreach to and contact from federal, academic, and industry partners. At the same time, the ORD maintained its focus and energy to support its ongoing veteran-centric research portfolio and VHA health care system needs across its broad scope of activities.

This article discusses how the pandemic accelerated the VA's research enterprise strategy and enacted a response, highlighting the advantages and strengths of this direction. We demonstrate how this evolving strategy enabled the VA to quickly leverage partnerships during a health emergency. While the ORD and VA Research have been used interchangeably, we will attempt to distinguish between the office that serves as headquarters for the national enterprise—the ORD—and the components of that enterprise composed of scientific personnel, equipment, operational units, and partners—VA Research. Finally, we present lessons from this experience toward a broader, post–COVID-19, enterprise-wide approach that the VA has for providing evidence-based care. These experiences may enrich our understanding of postpandemic future research opportunities with the VA as a leader and partner who leverages its commitment to veterans to improve the nation's health.

ORGANIZING THE VA COVID-19 RESEARCH RESPONSE

VA Research seeks to internally standardize and integrate collaborations with clinical and

TABLE 1 Department of Veterans Affairs Partnerships During COVID-19 Response

Internal	External
National Center for Health Promotion and Disease Prevention	Executive Office of the President, Office of Science and Technology Policy
Pharmacy Benefits Management	Biomedical Advanced Research and Development Authority
Pathology and Laboratory Medicine Services	Centers for Disease Control and Prevention
National Organization for Chiefs of Staff	COVID-19 Prevention Network
National Infectious Diseases Service	Department of Defense
VA Offices of Healthcare Innovation and Learning, Information and Technology, and General Counsel	Food and Drug Administration
	National Institutes of Health, National Institute of Allergy and Infectious Disease
VHA Offices of Finance and Operations	VA-affiliated nonprofit corporations
	Industry/pharmaceutical companies

operational partners throughout the agency. When possible, it seeks to streamline partnership efforts involving external groups less familiar with how the VA operates or its policies, as well as its capabilities. This need was more obvious during the pandemic, and the ORD assembled its COVID-19 response quickly.[6]

In early January 2020, VA offices, including the ORD, were carefully observing COVID-19. On March 4, 2020, a week before the World Health Organization declared COVID-19 a pandemic, the ORD and its National Research Advisory Council arranged a briefing from VA public health leaders to deal with reported cases of COVID-19 and VA plans. Immediately afterward, the ORD Chief Research and Development Officer gathered a team of experts in clinical research, infectious disease, and public health to strategize a broader research enterprise approach to the pandemic. This group quickly framed 3 key targets: (1) identify critical research questions to prioritize; (2) provide operational guidance to the research community; and (3) uphold VA research staff safety. This discussion led to the creation of a larger ORD COVID-19 Research Response Team that managed activities within this scope. This team included other ORD leaders and staff with operational, scientific, and regulatory expertise charged with enterprise-level planning and execution for all research activities addressing or affected by the pandemic (Figure).

Effective and timely communication was chief among key ORD responsibilities. On March 19, 2020, the Response Team informed the VA Research community about ORD plans for organizing the VA COVID-19 research response.[7] It also mobilized VA research programs and investigators to support an enterprise approach that would be coordinated centrally. We achieved communication goals by developing a dedicated website, which provided a means to distribute up-to-date notices and guidance, answer frequently asked questions, and alert investigators about research opportunities. The site enabled the field to report on its efforts, which enhanced leadership and community awareness. A working group of ORD and field personnel managed communications. Given the volume of existing non–COVID-19 research, we established a research continuity of operations plan to provide guidelines for study participant and research staff safety. The ORD issued an unprecedented full-stop administrative hold on in-person research activities after the global announcement of the pandemic. This policy provided formal protections for research programs to safeguard staff and research participants and to determine appropriate alternatives to conduct research activities within necessary social distancing, safety, and other clinical care parameters. It also aligned with guidance and requirements that local VAMCs issued for their operations and care priorities.

The Response Team also established a scientific steering committee of VA infectious disease, critical care, informatics, and epidemiology experts to prioritize research questions, identify research opportunities, and evaluate proposals using a modified expeditious scientific review process. This group also minimized duplicate scientific efforts that might be expected from a large pool of investigators simultaneously pursuing similar research questions. Committee recommendations set up a portfolio that included basic science efforts in diagnostics, clinical trials, population studies, and research infrastructure.

Leveraging Existing Infrastructure

Besides quickly organizing a central touchpoint for the VA COVID-19 research response, the ORD capitalized on its extensive nationwide infrastructure. One key component was the Cooperative Studies Program (CSP); the longstanding VA clinical research enterprise that supports the planning and conduct of large multicenter clinical trials and epidemiological studies. The CSP includes experts at 5 data and statistical coordinating centers, a clinical research pharmacy coordinating center, and 4 epidemiological resource centers.[8] CSP studies provide definitive evidence for clinical practice and care of veterans and the

nation. CSP's CONFIRM trial (CSP 577) is the largest VA interventional study with > 50,000 veterans.[9] CONFIRM followed the Trial of Varicella Zoster Vaccine for the Prevention of Herpes Zoster and Its Complications (CSP 403), which involved > 38,000 participants to evaluate a vaccine to reduce the burden of illness-associated herpes zoster (shingles). In the study, the vaccine markedly reduced the shingles burden of illness among older adults.[10] These studies highlight the CSP cohort development ability as evidenced by the Million Veteran Program.[11]

VA Research, particularly through the CSP, contributed to multiple federal actions for COVID-19. The CSP had already established partnerships with federal and industry groups in multisite clinical trials and observational studies. During COVID-19, the ORD established a COVID-19 clinical trial master protocol framework: the VA CoronavirUs Research & Efficacy Studies network.[9] The CSP also supported studies by the Coronavirus Prevention Network, the National Institute of Allergy and Infectious Disease (NIAID), and the US Food and Drug Administration (FDA). As such, the VA could translate requirements in working with an industry sponsor on the rapid execution of studies within a federal health care system. Much of the success arose when there was either earlier engagement in planning and/or existing familiarity among parties with operational and regulatory requirements.

Before the pandemic, the ORD had also been working on various external partnerships to increase opportunities for veterans in clinical trial participation, particularly for cancer, which Caroff and colleagues discuss further.[12] A newly emerging Partnered Research Program (PRP) offered a strategy for participation in the major COVID-19 vaccine efficacy clinical trials. VA Research, through PRP and CSP, rapidly engaged others and managed critical communication (Table 1). In quickly pivoting to COVID-19 clinical studies, the VA also used the Networks of Dedicated Enrollment Sites (NODES), its site-based, CSP-supported infrastructure of existing investigators and coordinators with clinical, operational, and regulatory proficiency for large trials.[13,14] Together, the CSP and PRP solidified the VA's scientific, operational, and regulatory support basis for working with industry partners and federal agencies to conduct therapeutic and vaccine trials.

Speed, Knowledge, and Safety

The scope of VA Research partnerships covers several goals but can be broadly categorized in the following ways: research aimed at evaluating the efficacy of new treatments; development of infrastructure to facilitate more rapid and innovative approaches to research; and building connections within the health care system to take an enterprise approach to research.

Activities are not limited to COVID-19. The VA partners with federal entities on research primarily through interagency agreements whose authorities are derived from the Economy Act (31 USC § 1535). For industry and nonfederal groups, the VA enters into Cooperative Research and Development Agreements that are rooted in the Federal Technology Transfer Act (15 USC § 3710). Although the VA has experience in each of these processes, COVID-19 prompted many groups, existing partners and new ones, to engage with the VA. Consequently, the ORD needed to quickly understand the complexities of how to handle such engagements on a larger scale. The VA Research enterprise strategy also focused on facilitating these processes.

As part of VA integration goals, ORD leaders engaged VA clinical leaders, especially in Public Health, Preventive Medicine, Pharmacy Benefits Management, and Pathology and Laboratory services. The ORD also worked closely with operational leaders, including those responsible for the Veterans Integrated Service Networks and VAMC chiefs of staff and network chief medical officers. The ORD's familiarity with coordinating complex activities for research further helped to organize nonresearch responses for clinical needs and resources to support the VA COVID-19 response. The Office of the Under Secretary for Health recognized VA Research's critical role as part of the VA health care system. In turn, it served as a major champion to drive success among the active research efforts, especially the partnered efforts, responding to COVID-19. Continuously communicating support and offering resources for the agency's overall COVID-19 response reinforced the positive impact of VA Research that extended beyond its traditional roles. That is, the research component of VHA was highlighted as an integral part of the COVID-19 response along with its clinical operations. This integrated approach was perhaps best demonstrated in a VHA-wide push to start and conduct the national vaccine efficacy trials.

Other COVID-19 research supported by the ORD included participation in the Mayo Clinic–led convalescent plasma expanded access treatment protocol, which had emerged as a potential therapeutic option.[15] The ORD provided centralized regulatory support to nearly 100 VAMCs, helping to reduce inconsistencies in protocol approval processes for what was hoped to be a

TABLE 2 Major COVID-19 Studies Undertaken by VA Using Centralized Support[a,12]

Trial sponsor/name	Study type	Participating sites, No.	Centralized support resources
VA ORD/EPIC3	Observational	15	Cooperative Studies Program
VA ORD/Nasal Swab Objective and Statistical Evaluation (NOSE) Study	Diagnostic	5	Rehabilitation Research and Development
Pharma/other government agency	Vaccine	17	PRP, NODES
Pharma/other government agency	Vaccine	2	PRP, NODES
Nonprofit/Expanded Access Program for Convalescent Plasma	Therapeutic	90	ORD
Other government agency/ACTIV-2	Therapeutic	8	International Coordinating Center
Other government agency/ACTIV-3	Therapeutic	24	International Coordinating Center
Other government agency/ACTIV-4a	Therapeutic	9	CoronavirUs Research & Efficacy Studies (CURES)
Other government agency/STRIVE	Therapeutic	21	International Coordinating Center

Abbreviations: ACTIV, Accelerating COVID-19 Therapeutic Interventions and Vaccination; EPIC3, Epidemiology, Immunology and Clinical Characteristics of COVID-19 Within the Veterans Health Administration; NODES, Network of Dedicated Enrollment Sites; ORD, Office of Research and Development; PRP, Partnered Research Program; STRIVE, Strategies and Treatments for Respiratory Infections & Viral Emergencies; VA, US Department of Veterans Affairs.
[a]Adapted from: Caroff K, Davey V, Smyth M, et al. VA lessons from partnering in COVID-19 clinical trials. *Fed Pract*. 2023;40(suppl 5):S18-S22. doi:10.12788/fp.0415

promising treatment for COVID-19.[16] This rapid approach to address a real-time treatment option demonstrated the VA Research capability for swift mobilization in an emergency.

The ORD also coordinated with other federal agencies. For example, it collaborated with the US Department of Defense to begin a parallel observational study on COVID-19 infections and potential severe outcomes. The study enrolled > 3000 veterans who are being followed for up to 2 years to better understand the natural history and course of COVID-19.[17] Other interagency efforts focused on vaccine and therapeutic trials, including Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) with the National Institutes of Health. In these activities, VA Research helped increase recruitment, particularly of a more diverse patient population, in helping to assess promising treatments.[10]

Motivated by its expanding portfolio of COVID-19 intervention studies, the VA also created a COVID-19 research registry for all VA investigators. This registry included almost 59,000 veterans who indicated a willingness to volunteer for clinical studies. This registry exemplified a long-standing tradition of veterans willing to serve their nation again in a time of need. Iaquinto and colleagues showcased how VHA programs (eg, Office of Healthcare Innovation and Learning) collaborated by expediting a study on 3D-printed swabs to address supply chain shortages. The study, which involved the FDA, showed that the printed swabs were as effective as commercially available ones.[18] It provided evidence supporting the production and dissemination of a greater number of testing swabs to the public while also reducing the cost and time requirements (Table 2).

Altogether, these collaborative efforts advanced a transformative approach within the VA that was already happening but was accelerated by the pandemic. Such activities enabled greater understanding throughout the VA for how research is not merely complementary but an integrated part of how veterans receive health care. By giving opportunities to veterans to participate in studies, especially clinical studies, the VA created a path in which such expectations, understanding, and operations were more fluid.

Future Directions

The VA continues to work for veterans by emphasizing its strategic goals and strengths in clinical, data science, and other pioneering activities at an enterprise level to provide the highest quality evidence for care. These capabilities perpetuate a scientific and learning environment that also builds toward the future by giving junior investigators and others opportunities to work within a national health care setting. In turn, this provides a more focused perspective on endeavors that align with the VA mission through ORD-supported career development, merit review (independent investigator submissions), and CSP.[19] Preclinical, health services, genomic, and implementation research were given

insights into more effective operational and methodological partnerships to help inform the health care system. The pandemic also served to strengthen our ability to mobilize and prepare even faster for emergencies and other potential disease outbreaks, including newer pandemic concerns (eg, mpox, Ebola) from research and public health perspectives.

CONCLUSIONS

Throughout its 100-year history, VA Research has been a critical, enduring institution within the national medical landscape. The ability to collaborate with partners has helped us to design and create even better processes, optimize and maximize our infrastructure, and learn more about common research interests that can be even more responsive to national health care needs. As an enterprise, VA Research also aims to continually learn and expand on these valuable lessons gained from internal, interagency, and industry collaborations to effectively meet and exceed our mission to serve our veterans.

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Disclaimer

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Ethics and consent

Not applicable.

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