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Article

Research Staff COVID-19 Pandemic Survey-Results from the Prevention and Early Treatment of Acute Lung Injury (PETAL) Network

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Abstract: Objectives: There is a lack of knowledge about the challenges of researchers who continued in-person research during the early phases of the COVID-19 pandemic. Design: Electronic survey assessing work-related exposure to COVID-19, logistical challenges, and procedural changes during the first year of the COVID-19 pandemic on clinical research. Setting: National Heart, Lung, and Blood Institute-sponsored Prevention and Early Treatment of Acute Lung Injury Clinical Trial Network Centers. Subjects: Research staff at research Network Sites. Measurements and Main Results: The 37-question survey was completed by 277 individuals from 24 states between 29 September 2020, and 12 December 2020, yielding a response rate of 37.7%. Most respondents (91.5%) indicated that non-COVID-19 research was affected by COVID-19 research studies. In response to the COVID-19 pandemic, 20% of respondents were reassigned to different roles at their institution. Many survey takers were exposed to COVID-19 (56%), with more than 50% of researchers requiring a COVID-19 test and 8% testing positive. The fear of infection was 2.7-times higher compared to pre-COVID-19 times. Shortages of personal protective equipment were encountered by 34% of respondents, primarily due to lack of access to N95 masks, followed by gowns and protective eyewear. Personal protective equipment reallocation from research to clinical use was reported by 31% of respondents. Most of the respondents (88.5%), despite these logistical challenges, indicated their willingness to enroll COVID-19 patients. Conclusions: During the first year of the COVID-19 pandemic, members of the research network were engaged in COVID-19 research despite logistical challenges, limited access to personal protective equipment, and fear of exposure. The research network's survey experience can inform ongoing policy discussions to create research enterprises that can dexterously refocus research to address the knowledge gaps associated with novel public health emergencies while mitigating the effect of pandemics on existing research projects and research personnel.

Keywords: coronavirus disease 2019; research staff; critical care; pandemic response

1. Introduction

COVID-19 is an acute respiratory infectious illness caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which emerged in 2019 in the Wuhan region of China and rapidly spread to various parts of Europe and the United States in early 2020 [1,2].

The initial response of most research institutions in the United States varied and was focused on infection control and prevention measures as well as expansion of clinical services, leading to the suspension of research activities at institutions with high COVID-19 caseloads [3]. The understanding of COVID-19 disease pathogenesis and treatment modalities was limited. Research teams faced numerous challenges, including work-from-home orders and limited access to COVID-19 patients based on the recommendations of the Center for Disease Control and the World Health Organization [4–8]. Other aspects of COVID-19 challenges on medical education and training have been investigated [9–11] and have shown significant strain on medical professionals regardless of location or profession. A systematic review by Sathian et al. [12] published in 2020 indicated that clinical trials experienced delays or complete halt of operations.

There is a paucity of data on continuing in-person clinical research during the initial phases of the COVID-19 pandemic, specifically research concerning COVID-19 clinical trials. While studies have evaluated the effect of COVID-19 on researcher's work efficiency and mental health [13,14], career progression [15], and at-home work [16], these studies have primarily focused on remote or significantly reduced-contact research. Internationally, there have been reports detailing the significant effect of COVID-19 on in-person clinical research projects [12,17]. One single-center American study examined an institution's experience with continuing in-person clinical research during the COVID-19 pandemic, and its focus was largely centered on the perceptions of the transition to more remote, reduced-direct-contact research [18].

Given this knowledge gap, we initiated a survey that was sent throughout the United States to a group of investigators and research coordinators who continued to pursue direct-contact clinical research during the COVID-19 pandemic. This survey was meant to better understand the pandemic research landscape, including pandemic-specific barriers and facilitators. This research network funded by the National Heart, Lung, and Blood Institute (NHLBI) is called the "Prevention and Early Treatment of Acute Lung Injury" (PETAL) network. The focus of the network is to develop and conduct randomized controlled clinical trials to prevent, treat and improve the outcomes of patients with or at risk for the development of acute lung injury and acute respiratory distress syndrome [19]. Prior to the start of the COVID-19 pandemic, this network had successfully enrolled more than 8000 patients into clinical trials, often patients with critical illness in need of critical care unit admissions with respiratory illness, such as the ROSE [20] and VIOLET studies [21]. The PETAL network not only responded quickly to address research questions related to the COVID-19 pandemic with initiation of trials such as ORCHID [22,23] and CORAL [24], but also aligned itself with other international networks to participate in the worldwide research response efforts with the ACTIV [25–29] research projects while continuing some one of the ongoing research projects with the CLOVERS study [30,31].

Due to our own exposure to challenges conducting research during the initial response to the COVID-19 pandemic within a well-established nationwide research network, we aimed to evaluate aspects of research infrastructure and processes that would be helpful for conducting research with minimal interruption during a pandemic while concurrently assuring the safety of the research personnel.

2. Materials and Methods

An anonymous survey of research staff at the hospitals participating in the NHLBI-sponsored PETAL Clinical Trials Network was created with the aim to obtain data regarding the logistical challenges and personal experiences faced by research staff during the ongoing COVID-19 pandemic. The PETAL Network focuses on developing and conducting

randomized controlled clinical trials to prevent, treat, and/or improve the outcomes of patients who have, or who are at risk for, acute lung injury (ALI) or acute respiratory distress syndrome (ARDS), the precise condition seen in the most severe forms of COVID-19 [32]. It is composed of one clinical coordinating center and 12 clinical centers, with more than 40 hospitals throughout the United States [33]. During the early stages of the pandemic, the network pivoted to commence clinical trials focused on treatments for COVID-19. Participating centers and hospitals can be found via reference link [33]. The network and participating hospitals focus on the treatment of adults and enrolled only subjects older than 18 years of age. Researchers of the network do not have interactions with infants, children, and adolescents younger than 18 years of age.

The online survey was conducted utilizing the Research Electronic Data Capture (REDCap) platform. The Vanderbilt University Medical Center Institutional Review Board (IRB), which acts as the central IRB for the PETAL Network, determined that this study was not human subject research (IRB201768). In alignment with PETAL network regulatory requirements, the local IRB at Henry Ford Health System also reviewed and provided a determination of non-human subject research (IRB16574).

2.1. Study Design

At the time of the creation of the survey, literature on the effect of the COVID-19 pandemic on clinical research was scant. Therefore, the initial survey was developed based on consensus from the study investigators and feedback from local public health experts. The survey was piloted among two local public health science staff members as well as the study investigators and coordinators involved in the development of the survey. The survey received independent feedback from the PETAL Network's Natural History Committee before it was brought online. It focused on the following domains: (1) member demographics and hospital characteristics; (2) research staff and institutional research status; (3) COVID-19 exposure and personal protective equipment (PPE); (4) collection and processing of COVID-19 biospecimens; and (5) research obligations and institutional support. The survey was conceptualized during the initial phase of the pandemic, starting in March, and completed in June 2020, focusing on the initial impact of COVID-19 on research (Figure 1).
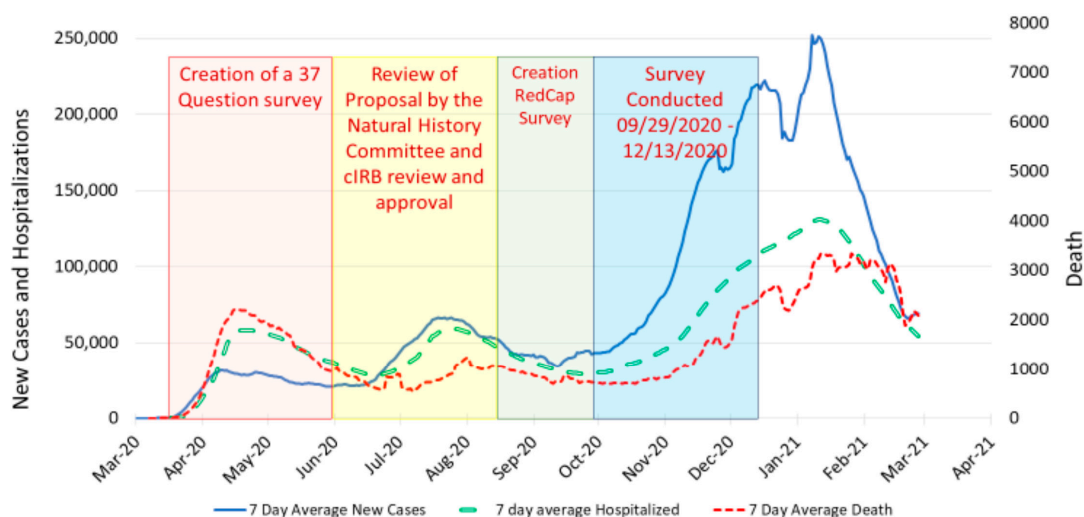

Figure 1. COVID-19 Case load and Overlapping Survey Activity.

The final survey included 37 questions (Supplement Table S2) and was distributed by the PETAL Network's Clinical Coordinating Center via email with individualized REDCap links from 29 September 2020 through 12 December 2020. All research personnel that were listed as active within the PETAL network were included. To be listed as active members of the network, regulatory documentation regarding research training, resume, and familiar-

ity with the network studies needed to be provided. An active PETAL network member would have an e-mail address stored within the network directory. Members of the PETAL network include but are not limited to research staff (i.e., research coordinators, research assistants, and research associates), investigators (i.e., principal investigators, sub-principal investigators, and co-principal investigators), and other ancillary staff (pharmacists, regulatory coordinators, and statisticians) with a target population of n= 740 (Supplemental Table S3). The survey was kept anonymous without a link between the e-mail addresses and the completed responses. All PETAL Network site staff were encouraged via weekly Friday newsletters, weekly reminder emails each subsequent Monday, and announcements at the PETAL Steering Committee meetings to complete the survey. Study data were collected and managed using REDCap at Henry Ford Hospital. REDCap was set up so that the survey could only be completed once, but incomplete surveys could be saved for later completion, and incomplete responses were also analyzed.

2.2. Statistical Analysis

Categorical variables are reported as absolute counts and percentages, whereas continuous variables are reported as means and standard deviations with medians also included to account for distributional non-normality. The chi-square test, Fisher's exact test, and Wilcoxon rank sum test were used. Statistical analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC, USA).

3. Results
3.1. Demographics

A total of 740 emails with survey links were sent out to the PETAL members (Figure 2). While 14 e-mails were returned, local sites identified 8 additional possible participants that were added to the survey, leading to a survey audience reached of 734. Of these, 305 PETAL members opened the survey link, and 277 members completed the survey, yielding a survey completion response rate of 37.7% (Figure 2). Most of the respondents identified as female (58.9%). Respondent age ranged from 18 to 75 years (mean 40).

Most of the respondents (76.8%) worked in hospitals with more than 500 beds, with 84.3% of survey takers working at teaching university hospitals and only 6.5% working at teaching non-university hospitals (Table 1). Graduate and professional degrees were held by 64.5% of survey takers, 31.3% had a college degree, and 1.4% were medical students. Most of the respondents (38.6%) were research coordinators, followed by investigators (36.2%) and research staff (8.5%). Other ancillary staff (16.7%) comprised the remainder of respondents. Clinical background varied from physician (37.2%) to emergency medical technicians (EMTs)/paramedics (4.8%) (Supplemental Table S1). Survey respondents had from 0 to 50 years of experience in the medical field and 0 to 42 years of experience in research trials.

Responses were received from most of the PETAL Network clinical sites. Clinical sites in California, Michigan, and Massachusetts had the highest response rates of 10.5%, 9.4% and 7.0%, respectively (Supplemental Table S2). Results were included from both partially and fully completed surveys. The conduct of the survey overlapped with the second wave of the pandemic in the United States (Figure 1). Some questions allowed for multiple responses from survey takers, and some questions did not have to be completed if the questions were not applicable to the survey taker.

Table 1. Demographics.

Characteristics of Survey Audience	n (%)
Research personal contacted	734
Number of complete responses	277 (37.7)
Number of partial responses	28 (0.03)
Female survey responders	169 (58.9)
Male survey responders	118 (41.1)
Age, years	
18–25	27 (9.3)
26–35	67 (23.2)
36–45	75 (25.9)
46–55	79 (27.3)
56–65	31 (10.7)
66–75	10 (3.5)
Ethnic groups	
Hispanic/Latino	23 (8.1)
Non-Hispanic/Non-Latino	260 (91.9)
Race	
White	226 (79.9)
Black	15 (5.3)
Hawaiian or Pacific Island	2 (0.7)
Asian	39 (13.8)
Others	7 (2.5)
Highest education level	
High school graduate/GED	1 (0.3)
Some college, no degree	7 (2.4)
College degree	91 (31.3)
Medical student	4 (1.4)
Graduate/professional degree	188 (64.6)
Hospital size	
101 to 200 beds	3 (1.1)
210 to 500 beds	59 (22.1)
More than 500 beds	205 (76.8)
Hospital type	
Community hospital	18 (6.1)
Public hospital	32 (10.9)
Private-for-profit hospital	7 (2.4)
Private non-profit hospital	33 (11.3)
Rural hospital	1 (0.3)
Urban hospital	42 (14.3)
Teaching university hospital	247 (84.3)
Teaching non-university hospital	19 (6.5)

Table 1. *Cont.*

Characteristics of Survey Audience	n (%)
Research title	
Research assistant/research associate	25 (8.5)
Research coordinator	113 (38.6)
Investigators	106 (36.2)
Other	49 (16.7)
Clinical background	
EMT/paramedic	14 (4.8)
Registered nurse	45 (15.4)
Medical assistant	8 (2.7)
Respiratory therapist	2 (0.7)
Advanced practice practitioner	5 (1.7)
Pharmacist	28 (9.6)
Physician (MD/DO)	109 (37.2)
Other	82 (27.9)
Years working in the medical field, means ±SD	16 ± 10.9
Year working research trials, mean ± SD	9.8 ± 8.1

DO: doctor of osteopathic medicine, EMT: emergency medical technician: MD: doctor of medicine, SD: standard deviation.

3.2. COVID-19 Impact on Research

COVID-19 affected nearly all of the active non-COVID-19 studies (91.5%), with 25% of respondents reporting reassignment to another role at their institution in response to COVID-19. These roles varied from visitor screening and COVID-19 testing to additional clinical and research responsibilities.

Reassigned researchers were significantly more likely than the non-reassigned researchers to be older than 35 years ($p = 0.028$) and more frequently were investigators (27.4%) rather than other research staff (18.1%, $p = 0.085$). The primary areas of clinical responsibility among respondents included the intensive care unit (49.1%), emergency department (32.2%), and general practice unit (8.0%), with 10.7% working in another clinical domain.

Due to infection control concerns, modifications to the consent process were implemented. These changes enacted by institutions for researcher's safety varied and included telephone consent (68.6%), email consent (52.4%), text message consent (13.7%), video consent (54.2%), and electronic consenting (86.9%). The use of tablets for consenting and of photographs of signed consent documents were reported by 65.7% and 69.3% of the respondents, respectively (Table S1).

When asked if the respondent's coworkers were willing to share the procedural workload of COVID-19 patient enrollment, a majority indicated willingness to help. On a scale of 0 to 10 (0 meaning not willing to help and 10 meaning extreme willingness to help), the mean response was 8.6 (standard deviation [SD] 2.5). Only 11.6% of the respondents indicated that they utilized the option to refuse to approach a possible COVID-19 patient for enrollment.

Respondents stated that various support measures had been implemented at their institution during the ongoing COVID-19 pandemic, including emotional support services, enhanced ability to work from home, time off for suspected or confirmed COVID-19 infection, a pay enhancement/incentive program, and quarantine accommodations (Table S1).

The survey questionnaire also evaluated how satisfied survey takers were with their respective organizations' clinical and research responses to the COVID-19 pandemic. On

a scale of 0 to 10 (0 meaning extremely dissatisfied, 5 meaning neutral, and 10 meaning extremely satisfied), the mean response was 7.6 (SD 1.9) and 6.8 (SD 2.6) for clinical and research response, respectively.
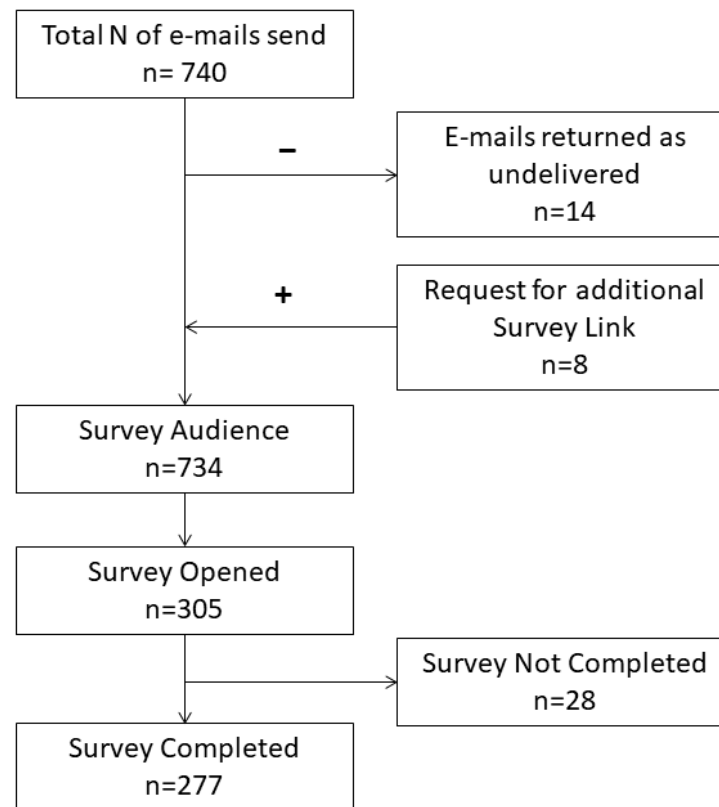

Figure 2. Survey Response Rate.

3.3. Medical Supplies

The evaluation of fear versus comfort of processing COVID-19 related biospecimens indicated some degree of comfort, with a mean response of 7.4 (SD 3.0). For COVID-19 biospecimen processing, 92.9% of the respondents stated that their institution had a standard research procedure for COVID-19 biospecimen processing; 86.3% of respondent's institutions had a negative pressure room or flow hood, and 79.6% researchers reported having access to these resources.

While only 15.8% of the respondents reported that their institution could not provide adequate PPE during the pandemic, 38.5% responded that a PPE shortage had affected their ability to conduct research at their institution (Table 2). Given lack of data linking individual respondents with specific hospitals, further analysis of this result could not be performed.

N95 masks were the least available PPE during the pandemic (Supplemental Figure S1); 30.6% of the respondents reported re-allocation of PPE from research to clinical use at their institution. To meet the research needs for PPE, 91% of the respondents felt that PPE should be budgeted into research grants.

There was a notable difference between the completion of gowning/de-gowning training over the previous 12 months among research staff (61.6%) compared to investigators (94.3%, $p = 0.001$).

Table 2. Responses Related to Fear of Infection, PPE, and Research Conduct.

Survey Questions	Yes n (%)	No n (%)
Have COVID-19 research studies at your institution impacted non COVID-19 research studies?	268 (91.5)	25 (8.5)
At any point during the pandemic have you been redeployed or reassigned to another role at your institution in response to COVID-19?	60 (20.5)	233 (79.5)
Do you think your institution has provided adequate PPE[1] to conduct research since the beginning of the COVID-19 pandemic?	245 (84.2)	46 (15.8)
Has PPE shortage affected your ability to conduct research?	112 (38.5)	179 (61.5)
Have you completed gowning/de-gowning training in the past 12 months?		
Does your institution have standard operating procedures for bio-specimen processing of confirmed or suspected COVID-19 patients?	265 (92.9)	20 (7.0)
Does your institution have a designated negative pressure room or flow hood for research-related biological specimen processing?	245 (86.3)	39 (13.7)
Do you have access to the designated equipment for processing the biospecimens of suspected or confirmed COVID-19 patients?	195 (79.6)	50 (20.4)
If given the option, would you refuse to approach a suspected or confirmed COVID-19 patient for research enrollment?	32 (11.6)	245 (88.5)
Do you believe PPE should be budgeted for in research grants during the pandemic for studies that expose researchers to suspected or confirmed COVID-19 patients or their biological specimen?	252 (90.9)	25 (9.0)
Have you had any work-related exposure to COVID-19 patients?		
Research related COVID-19 exposure	54 (18.6)	237 (81.4)
Clinical work-related COVID-19 exposure	40 (13.7)	251 (86.3)
Both research and clinical work-related exposure	70 (24.1)	221 (75.9)
No work-related exposure	127 (43.6)	164 (56.4)
Have you been tested for COVID-19 at any time during the COVID-19 Pandemic?	146 (50.2)	145 (49.8)
Have you tested positive for COVID-19?	12 (8.2)	134 (91.8)
At any time during the pandemic have you or someone in your department:		
Quarantined due to exposure to COVID-19	122 (42.9)	162 (57.0)
Got infected and recovered from COVID-19	93 (32.8)	191 (67.3)
Been hospitalized due to COVID-19	16 (5.6)	268 (94.4)
Applied for disability benefits due to COVID-19	4 (1.4)	280 (98.6)
Died from a COVID-19 infection	1 (0.4)	283 (99.7)

[1] Personal protective equipment.

3.4. Infection and Safety

COVID-19 exposure related to research or clinical work was reported by 56.4% of the respondents. Research-related exposure to COVID-19 was slightly higher among research staff (49.3%) compared to investigators (46.2%). Naturally, investigators had greater clinical exposure to COVID-19 (77.3%) than research staff (17.4%). This contributed to the observation that investigators had higher COVID-19 testing rates (65.1%) and higher rates of COVID-19 infections (13.0%) compared to research staff (44.2% and 4.9%, respectively) (Table 3).

In all, 43% of survey takers reported someone in their department quarantining due to COVID-19 exposure at any time during the pandemic. Within their department, 32.8% of respondents reported that someone had been infected with and recovered from COVID-19, and 5.6% knew someone who had been hospitalized due to COVID-19; 1.4% of respondents knew someone in their department who had been disabled due to COVID-19, and 0.4% knew someone who had died due to COVID-19. Reported rates of hospitalization, disability, and death were all numerically higher among investigators, though only hospitalization of a colleague within a department was statistically significant, with 10.5% of investigators versus 1.5% of research staff being hospitalized ($p = 0.002$).

Researchers were asked about various aspects of subjective fear on a scale of 0 to 10 (0 indicating no fear and 10 indicating extreme fear of being infected by any infectious agent). The median fear of infection was 3.0 (interquartile range [IQR] 1–5) prior to the

pandemic, which increased to 8.0 (IQR 4–8) during the pandemic. Despite the higher rate of testing and case positivity among investigators compared to research staff, there was no statistically significant difference in fear of infection.

Table 3. Results by Research Title.

		Research Position			
		Investigators [#] **(n = 106)**	**Research Staff [€]** **(n = 138)**	**Other [$]** **(n = 49)**	***p*-Value Investigators vs. Research Staff**
Male gender		71 (67.6%)	33 (24.4%)	14 (31.1%)	<0.001(C) *
COVID-19 research at your institution has impacted non-COVID-19 studies.		98 (92.5%)	127 (92.0%)	43 (87.8%)	0.903 (C)
You have been reassigned to another role due to COVID-19.		29 (27.4%)	25 (18.1%)	6 (12.2%)	0.085 (C)
Primary clinical area of enrollment	Emergency department	29 (27.4%)	58 (42.6%)	6 (12.8%)	<0.001(C) *
	Intensive care unit	66 (62.3%)	59 (43.4%)	17 (36.2%)	
	General practice unit	10 (9.4%)	7 (5.1%)	6 (12.8%)	
	Other	1 (0.9%)	12 (8.8%)	18 (38.3%)	
Type of work-related COVID-19	Research exposure	0 (0.0%)	49 (35.5%)	5 (10.6%)	<0.001(C) *
	Clinical exposure	33 (31.1%)	5 (3.6%)	2 (4.3%)	
	Research and clinical exposure	49 (46.2%)	19 (13.8%)	2 (4.3%)	
	No work-related COVID-19 exposure	24 (22.6%)	65 (47.1%)	38 (80.9%)	
You have been tested for COVID-19 at any time.		69 (65.1%)	61 (44.2%)	16 (34.0%)	0.001 (C) *
If yes, a test result was positive.		9 (13.0%)	3 (4.9%)	0 (0.0%)	0.110 (C)
Your institution has given you adequate PPE during the pandemic.		92 (86.8%)	114 (82.6%)	39 (83.0%)	0.372 (C)
PPE shortages have affected your ability to conduct research.		37 (34.9%)	59 (42.8%)	16 (34.0%)	0.214 (C)
You have completed gowning/de-gowning training in the past 12 months.		100 (94.3%)	85 (61.6%)	27 (57.4%)	<0.001 (C) *
Scrubs are not provided.		8 (7.5%)	10 (7.2%)	1 (2.0%)	0.929 (C)
Gloves are not provided.		4 (3.8%)	6 (4.3%)	1 (2.0%)	1.000 (F)
Surgical masks are not provided.		2 (1.9%)	11 (8.0%)	2 (4.1%)	0.036 (C) *
N95 masks are not provided.		23 (21.7%)	44 (31.9%)	11 (22.4%)	0.077 (C)
Rate your highest fear of infection at work prior to the pandemic.		3.4 ± 2.7 2.5 (1–5)	3.0 ± 2.5 2(1–5)	2.8 ± 2.5 2(1–5)	0.247 (W)
Rate your highest fear of infection at work since the pandemic.		6.1 ± 3.0 7 (4–8)	5.8 ± 2.8 6 (4–8)	5.9 ± 3.0 7 (3–8)	0.407 (W)
Rate how comfortable you feel in the lab while processing possible COVID-19 samples.		6.8 ± 2.9 8 (5–9)	6.4 ± 3.0 7 (4–9)	5.6 ± 3.4 6 (2.5–8.5)	0.355 (W)
Someone in your department was hospitalized due to COVID-19.		11 (10.5%)	2 (1.5%)	3 (6.7%)	0.002 (C) *
Someone in your department was disabled due to COVID-19.		2 (1.9%)	2 (1.5%)	0 (0.0%)	1.000 (F)
Someone in your department was quarantined due to COVID-19.		46 (43.8%)	62 (46.3%)	14 (31.1%)	0.705 (C)

Table 3. *Cont.*

	Research Position			
	Investigators [#] **(n = 106)**	**Research Staff [€]** **(n = 138)**	**Other [$]** **(n = 49)**	***p*-Value Investigators vs. Research Staff**
Someone in your department got infected by and recovered from COVID.	37 (35.2%)	42 (31.3%)	14 (31.1%)	0.525 (C)
Someone in your department died from COVID-19.	1 (1.0%)	0 (0.0%)	0 (0.0%)	0.439 (F)
Rate how obligated you feel to enroll suspected/confirmed COVID-19 patients in trials.	7.2 ± 3.0 8 (5–10)	7.5 ± 3.1 9 (6–10)	6.2 ± 4.1 8 (1–10)	0.137 (W)
Rate how comfortable you feel enrolling suspected/confirmed COVID-19 patients in studies.	8.6 ± 2.1 9 (8–10)	8.0 ± 1.9 8 (7–10)	7.4 ± 2.7 8.5 (7–9)	0.001 (W) *
Rate how willing your co-workers are to share workload on possible COVID-19 patients.	7.4 ± 2.4 8 (6–10)	7.6 ± 2.5 8 (6–10)	8.2 ± 2.4 9 (7.5–10)	0.513 (W)
You would refuse to approach a possible COVID-19 patient for enrollment.	4 (3.9%)	19 (14.4%)	9 (21.4%)	0.007 (C) *
Available emotional support	73 (70.9%)	71 (53.8%)	37 (88.1%)	0.008 (C) *
Available work from home support	86 (83.5%)	112 (84.8%)	39 (92.9%)	0.777 (C)
Available time-off support	76 (73.8%)	92 (69.7%)	35 (83.3%)	0.491 (C)
Available pay incentive support	23 (22.3%)	18 (13.6%)	0 (0.0%)	0.081 (C)
Available quarantine support	46 (44.7%)	39 (29.5%)	16 (38.1%)	0.017 (C) *
Other available support	0 (0.0%)	1 (0.8%)	0 (0.0%)	1.000 (F)
Rate the clinical response to COVID-19 by your organization.	74.8 ± 18.9 77 (64–88)	77.4 ± 19.6 81 (68–95)	77.5 ± 15.6 79 (70–90)	0.242 (W)
Rate the research response to COVID-19 by your organization.	64.9 ± 27.5 72 (50–86)	68.3 ± 26.7 76 (50–92)	75.6 ± 20.7 81.5 (61–92)	0.293 (W)

[#] PI/CO-PI/SUB-PI, [€] Research coordinators/research assistants and associates, [$] Pharmacists, administrative staff (C) * Statistically significant value. Categorical or ordered data is given as frequency (column percent). Rating data is given as mean ± standard deviation and median (interquartile range). C, chi-square test; F, Fisher's exact test; W, Wilcoxon rank sum test.

When asked if the respondents felt obligated to enroll suspected or confirmed COVID-19 patients in clinical trials on a scale of 0 to 10 (0 indicating no obligation and 10 indicating extreme obligation), the median response was 9 (IQR 8–10). Respondents' reported comfort level while enrolling this patient population on the same scale yielded a median of 10 (IQR 8–10). Notably, 14.4% of research staff reported that they would refuse to approach a possible COVID-19 patient for enrollment, whereas only 3.9% of investigators reported the same.

4. Discussion

This survey of research personnel in the NHLBI's PETAL Network elucidates that the COVID-19 pandemic had major effects on clinical research teams and the conduct of both their new and existing research projects.

Launching this survey during the second surge of the COVID-19 pandemic in 2020 highlights not only the challenges and risks associated with the initial phases of the pandemic but also challenges that persisted despite 7–9 months of research adaptation. These challenges underscore the importance of preparation for future pandemics, including the stocking of PPE for both researchers and clinicians, increasing donning/doffing training for research personnel, increasing flexibility among research roles, enhancing virtual enrollment capacity, providing quarantine support, and developing measures to enhance research personnel retention.

The pandemic made it necessary to modify the processes of informed consent for participation in research studies to allow for electronic or remote consent with modifications in the signature processes along with a wider use of waivers and approaches for higher enrollments of non-English speakers and legal authorized representatives [34]. Some of these changes will also enhance enrollment for non-COVID-19 related research.

All PETAL Network sites reported significant difficulty in obtaining the necessary resources to continue to conduct safe research, primarily due to a lack of PPE and lack of access to designated equipment for processing the biospecimens of suspected or confirmed COVID-19 patients. Moreover, it appeared that even having an appropriate stock of PPE for research endeavors did not ensure an ability to continue research, as more than 30% of researchers reported reallocation of research PPE to clinical endeavors. In response, it is perhaps unsurprising that the vast majority believed that PPE should be budgeted for in future research grants that expose researchers to suspected or confirmed COVID-19 patients or their biological specimens.

Alongside the lack of PPE allocated to research personnel, the lower rate of donning and doffing training among research staff may have led to the significantly higher rate of refusal among research staff to approach a possible COVID-19 patient for enrollment compared to investigators. Additionally, lower rates of clinical exposure to and experience with COVID-19 may have heightened reluctance among research staff compared to investigators. The lower rates of reported emotional support ($p = 0.008$) and quarantine support ($p = 0.17$) among research staff compared to investigators may also have contributed to this difference. Enhanced infection control training and provision of support for those infected may reduce the reticence of research staff, who infrequently encounter such risks in their non-clinical roles, potentially also reducing research staff turnover during future pandemics.

Of note, this survey reflects a time when COVID-19 vaccines were not yet available alongside high COVID-19 transmission and hospitalization rates. It would be interesting to see if the above response has changed over time. The COVID-19 infection rate among respondents (8.2%) was similar to that reported for healthcare workers during the initial phases of the pandemic. In a meta-analysis of COVID-19 among 75,859 health care workers screened for COVID-19 using reverse transcriptase-polymerase chain reaction, the estimated pooled prevalence of SARSCoV-2 infection was 11% [35]. More importantly, the risk of morbidity and mortality among research staff was notable, with over 5% reporting hospitalization and 1.4% reporting disability due to COVID-19. Sadly, even deaths among research personnel were reported. This is consistent with other reports showing a higher risk of infection in health care workers working in large tertiary care hospitals [36–38].

The above may help explain why the COVID-19 pandemic led to increased levels anxiety among health care workers, including research staff [39,40]. In this setting, researchers in the PETAL Network reported a significantly increased fear of infection compared to their pre-pandemic work. However, they continued to display a considerable willingness to enroll COVID-19 patients and help share the workload that was altered by COVID-19. This is reflected by the PETAL Network's enrollment in COVID-19 studies, including ORCHID [23] and CORAL [41], as well as the significant enrollment contributions of the PETAL Network sites in various ongoing COVID-19 studies with other national and international research networks [23–26,41–43].

Researchers across a broad range of ages, experience, research expertise, geographic locations, and unique hospitals had to adapt to newly assigned roles during the initial phase of the COVID-19 pandemic. These reassignments were due to a combination of clinical necessity as well as concrete changes in the type or method of research that could be safely performed during the pandemic. Because quarantine requirements can strain research continuity and limit the manpower required to ensure efficient research progress, the hiring and training process for research staff should consider similar expected role revisions in the setting of future pandemics to allow for more fluid adaptation to new roles and responsibilities [44].

4.1. Limitations

Though reasonably high, the incomplete survey response rate could have introduced bias. Moreover, the survey assessed the experience of a single national clinical trial network, which may not be representative of the overall national or international experience of COVID-19′s effect on clinical research. Regarding timing, some trials were halted during the initial phases of the pandemic when this survey was circulated, which could have affected responses. Additionally, the survey was distributed at the same time to all sites, irrespective of the volume and acuity of COVID-19 cases in each location. Individual responses might have varied based on local caseloads, especially given the dynamic nature of the pandemic, its associated challenges, and continually evolving policies and responses.

Geographically, responses were recorded by state rather than research center, which did not allow for complete analysis of whether certain centers were over-represented in terms of number of responses. Similarly, no hospital-level safety data was collected, nor was data on whether one or a small number of hospitals running out of PPE might have resulted in the discrepant data showing high rates of PPE shortage affecting the ability to perform research despite a much lower rate of inadequate PPE being reported.

Questions related to competing studies, research staff burnout and research staff turnover, the role of the IRB, and local contracting issues were not included. Furthermore, the frequency of direct patient contact for research staff was not evaluated.

Limited testing ability initially might have under-represented the number of researchers testing positive. Moreover, the time to test results were initially variable, potentially affecting the results of questions pertaining to quarantine. Workflow and infection control recommendations changed several times throughout the pandemic, and this survey reflected research challenges during only a small window of time during the second national surge in COVID-19 cases.

4.2. Future Directions

Additional efforts should be made to develop a research contingency plan for continuing research uninterrupted during future pandemics. The focus should be on logistical, safety, and staffing challenges during a pandemic. This should include stockpiling of PPE for research personnel, increasing donning/doffing training for research personnel, developing provisions for biospecimen processing equipment to the researchers, enhancing the pre-existing data collection infrastructure, creating specific guidelines on consenting research subjects, increasing flexibility among research roles, enhancing virtual enrollment capacity, providing quarantine support, and developing measures to enhance research personnel retention.

Research in fields other than medicine highlights the impacts of the pandemic on logistics and supply chain processes with wide-reaching repercussions [45]. Many authors in this field have highlighted the fact that supply chain sustainability and the role of technology implementation strategies for resilience of various systems is needed [46,47]. Some translation of these logistical challenges into medical research is ongoing, with the broader use of electronic consent and electronic-built databases that allow for remote and real-time monitoring of research data that allows for faster publication and sharing of knowledge. Other challenges during a pandemic are addressed with creation of worldwide research networks such as ACTIV [29] that are conducting research worldwide. The WHO brief from May 2023 indicates that healthcare systems are starting to recover from the COVID-19 pandemic, with reductions of disrupted services with service recovery for sexual, reproductive, maternal, newborn, child, and adolescent health; nutrition; immunization; communicable diseases (including malaria, HIV, TB, and other sexually transmitted infections); neglected tropical diseases; noncommunicable diseases; management of mental, neurological, and substance use disorders; care for older people; and traditional and/or complementary care [48]. This WHO brief highlights remaining challenges to workforce strengthening, building the monitoring capacities of health services, designing primary health care-oriented models of care, governance, policy and planning, and financial plan-

ning and funding. Structured and streamlined efforts not bound by borders or resource limitations are needed to address the next pandemic. Researchers and their teams face these challenges head on and must be included in pandemic response planning.

The NHLBI PETAL network can be a role model in the development of these research contingency plans in preparation for the challenges of the current and future pandemics as shown with the rapid development and implementation of the ORCHID study [22,23].

5. Conclusions

Researchers of the NHLBI PETAL Network encountered various stressors while conducting research during the COVID-19 pandemic. These included logistical challenges, access to PPE, sample processing, and fears of exposure. In-spite of logistical challenges, the NHLBI PETAL Network was actively engaged in research throughout the early phases of the pandemic as highlighted by various publications [22–28,31,41,43].

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