Address for correspondence:
V. Hoyo, PhD, Northwestern University Clinical and Translational Sciences Institute (NUCATS), Northwestern University, Chicago, IL, USA.
Email: veronica.hoyo@northwestern.edu

Integrating special and underserved populations in translational research: Environmental scan of adaptive capacity and preparedness of Clinical and Translational Science Award (CTSA) program hubs

Verónica Hoyo[1,2] ⓘ, Raj C. Shah[3,4,5], Gaurav Dave[6,7] ⓘ and Boris B. Volkov[8,9] ⓘ

[1]Northwestern University Clinical and Translational Sciences Institute (NUCATS), Northwestern University, Chicago, IL, USA; [2]Clinical and Translational Research Institute, University of California, San Diego, La Jolla, CA, USA; [3]Institute for Translational Medicine, The University of Chicago, Rush University Medical Center, Chicago, IL, USA; [4]Department of Family Medicine, Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, IL, USA; [5]Center for Community Health Equity, Rush University, DePaul University, Chicago, IL, USA; [6]Department of Medicine, University of North Carolina, Chapel Hill, NC, USA; [7]North Carolina Translational and Clinical Sciences Institute, University of North Carolina, Chapel Hill, NC, USA; [8]University of Minnesota Clinical and Translational Science Institute, Minneapolis, MN, USA and [9]Institute for Health Informatics and Division of Epidemiology and Community Health, University of Minnesota, Minneapolis, MN, USA

Abstract

The COVID-19 pandemic has exacerbated health disparities and rendered them acutely more visible. Special and underrepresented populations need to be fully integrated into the translational research process from the very beginning and all the way through. This article presents findings and rapid analysis mini-case studies from the Environmental Scan (E-Scan) of adaptive capacity and preparedness of Clinical and Translational Science Award hubs, specific to the goal of integrating special and vulnerable populations in different institutional research settings. In our discussion of the findings and case studies, we flexibly apply local adaptive capacity framework concepts and characteristics, and, whenever possible, we present ideas on how to enhance capacity in those areas, based on the challenges and practices identified through the E-Scan. Although the past year has recorded incredible achievements in vaccine development, clinical trials, diagnostics, and overall biomedical research, these successes continue to be hampered by our inability to turn them into achievements equally available and accessible to all populations.

Introduction and Background

Interactions between human and environmental components of an emergency or crisis such as the coronavirus pandemic need to be better understood. However, in the Anthropocene era, humans have created social environment rules and engagements that generate or accelerate more disasters than the physical environment itself does. Sirleaf and Clark [1] articulated it precisely:

> "COVID-19 has been a pandemic of inequality, exacerbated between and within countries, with the impact being particularly severe on people who are already marginalized and disadvantaged. Inequality has been a determining factor in explaining why the COVID-19 pandemic has had such differential impacts on peoples' lives and livelihoods."

One of the recent goals of the Clinical and Translational Science Award (CTSA) Program is to "promote the integration of special and underserved populations (SUPs) in translational research across the human lifespan" [2]. Adaptive capacity in the face of a short or long-term emergency requires an understanding of the critical components of the program goal and their foundations in non-emergency situations. It involves understanding the current translational research across the human lifespan and defining special and underserved populations. It affects how CTSAs promote and foster their integration.

It is important to define two key elements in this CTSA goal: integration and SUPs. The Merriam-Webster dictionary defines integration as "the process of forming, coordinating, or blending into a functioning or unified whole" [3]. While there are no clear boundaries and no "official single definition" on record, the CTSA Consortium uses the umbrella phrase of "special and underserved populations," which needs to be integrated in research, to include any rural populations, minorities, vulnerable populations experiencing health disparities or affected by rare diseases, pediatric and geriatric segments of the lifespan, and persons with disabilities [3]. This deliberately abstract approach to SUPs offers both opportunities and challenges.

On the one hand, it is inclusive and general enough to accommodate any new population groups or segments of the lifespan that may at critical times become vulnerable or require greater attention to solve specific problems. For example, healthcare workers at the onset of the COVID-19 pandemic or the healthcare needs of imprisoned individuals. On the other hand, not having clear delimiters of who falls within the range of "special and underserved" populations may make it challenging to address their needs since their level of access, information and, at times, even a long-standing history of mistrust toward the research enterprise work as structurally embedded determinants of their exclusion [4].

Health disparities predated the COVID-19 pandemic but they have undoubtedly been exacerbated during its course. Racial, ethnic, gender minority groups, communities that experience historic, structural, and systemic oppressions, and all other vulnerable populations have been disproportionately impacted by the COVID-19 pandemic, regardless of how we define and measure "impact" (e.g., infections, death rate, long-COVID, access to healthcare services, vaccine intake). The Centers for Disease Control and Prevention (CDC), the National Health Institutes (NIH), and public health authorities at the federal, state, and local level have all renewed efforts to tackle health disparities more consciously. The CTSA Consortium also has tried to do its part.

The CTSA program has witnessed, studied, and experienced the hurdles and structural constraints when it comes to recruiting [5], engaging [6], collaborating, and facilitating access for SUPs in translational research [7, 8]. Accordingly, the CTSA network has a history of focused efforts to address constraints that result in health disparities across the lifespan [9]. The COVID-19 pandemic has proven to be fertile ground to truly test the scope, reach, and impact of current initiatives, as well as the hurdles (pre-existing, new, and anticipated) that CTSA institutions still need to address in future years.

This paper is part of the Environmental Scan of Adaptive Capacity and Preparedness (AC&P) of CTSA Hubs [10], implemented by a special AC&P Working Group approved by the CTSA Steering Committee in 2021. The specific purpose of the AC&P Working Group and this scan was not to evaluate, test, generalize, quantify, or validate any hypotheses, approaches, or interventions, but rather to identify, curate, analyze, and share examples of practices, challenges, and lessons learned related to how CTSA hubs have used their expertise, resources, and collaborations to advance clinical and translational research during emergency. Data sources included: scientific publications and white papers on CTSAs' (and other) AC&P-related activities; a diverse sample of CTSA hubs' websites: public stories, news, highlights, measures; NCATS and other clinical and translational science organizations' websites; select CTSA hub Research Performance Progress Reports (RPPRs) de-identified information; and feedback of CTSA expert/community reviewers and other stakeholders [10]. Local adaptive capacity for disaster preparedness was considered through the lens of five core domains of the Local Adaptive Capacity (LAC) framework [10, 11]: asset base (key assets that allow hubs to respond to evolving circumstances); institutions and entitlements (an appropriate and evolving institutional environment that allows fair access to key assets and capitals); knowledge, information, learning (the ability to collect, analyze, and disseminate knowledge and information to learn in support of adaptation activities); innovation (an enabling environment to foster innovation, experimentation, and the ability to explore pragmatic solutions and opportunities); and flexible forward-looking decision-making and governance (the ability to anticipate and respond to changes

with regards to its decision-making, governance and operational structures). These domains do not work as separate and independent features but overlap and interact to create an emergent holistic panorama of disaster preparedness, response, mitigation, and recovery functions. The following sections will highlight challenges, successful practices to address them, and other lessons learned from the CTSAs' efforts to respond, learn from, adapt to, and identify continuing hurdles.

In the first section, we summarize findings from an environmental scan of the initiatives, programs and research conducted by CTSA hubs in relation to SUPs. Some LAC domains that we considered had much richer information than others, which is, in itself, telling of the areas where more work is needed. The second section offers a more holistic application of the LAC framework by focusing on what health disparities-driven research can look like through the discussion of two case studies: the effects of the pandemic on healthcare workers (a "functional special population") and the case of a SUP (birthing/breastfeeding parents) whose needs became the main drivers of research. In our discussion of the case studies, we flexibly apply the LAC characteristics, and, whenever possible, present ideas on how to enhance capacity in those areas. The final section, Implications and Conclusion, discusses findings of the scan and offers suggestions for future directions.

Asset Base

An emergency can help crystallize the need for focused engagement by reducing the "noise" factor for competing interests. However, when people are the most vulnerable to co-create knowledge, trust may be the hardest to develop unless affiliations and communications already exist. Lack of trust toward medical research, particularly regarding clinical trials, has historically been a significant barrier for recruitment, adoption of new therapeutics, etc., particularly among most underserved populations [12]. Although the CTSA consortium has made efforts to reach all communities and enhance active participation [13], the existence of historical mistrust may lead to "fast and furious" decision-making by those in power situations for the "benefit" of those traditionally overlooked. As one of the underrepresented community members candidly shared with this paper's authors, "Many times people feel tolerated, not valued. Often, engagement with the community only comes when the research community needs their input. As a community member, I recognized the importance of bi-directional conversations, even when no study is planned" (Community member, email communication, January 27, 2022).

While not necessarily uniform throughout all CTSA institutions, clinical and translational research teams at some CTSA institutions have established location-specific relationships with representatives of SUPs, either independently or through Community Advisory Boards and the Community Clusters collaborations. Some CTSAs were able to adapt and pivot key resources and essential activities during the COVID-19 pandemic to better reach SUPs in times of most need. For example, to address communication gaps in vulnerable and minority populations during the COVID-19 pandemic, community and academic partners from Rochester Healthy Community Partnership (RHCP) developed a "risk communication framework" for public health messages for diverse audiences, with concise and factual information regarding COVID-19 prevention, testing, and pandemic socioeconomic impact, in six languages across nine electronic platforms to around 1,000 individuals within their social networks. This bi-directional (from and back to the community) communication

effort at leveraging community resources and partnerships with academic experts built upon existing assets and demonstrated the community's own capacity building through prior experience [14]. Lessons learned from this experience can inform CTSAs' strategies to bring the integration of SUPs in clinical and translational research to the next level. More coordinated efforts are most likely needed on a national scale to improve the utility of the SUP community connection assets in the future to reduce the likelihood of incomplete actions to best integrate SUPs into long-term decision-making efforts.

Although "best practices" on how to leverage CTSA resources, mostly in terms of data sharing and accessing bio- and data repositories, have been developed and disseminated since the onset of the pandemic [15], there is a need to establish a central, comprehensive, easily accessible repository across the CTSA consortium that may be used routinely rather than as a response to particular crisis.

Institutions and Entitlements

National (NIH, NCATS) and local CTSA hub/institutional environments allowed access to key assets needed to respond and adapt to the COVID-19 challenges. For example, Patrick Nana-Sinkman and his collaborators wrote an informative overview of new research initiatives (e.g., N3C, National Covid Cohort Collaborative) or pre-existing partnerships which experienced greater CTSA participation, even if they were not under the CTSA Consortium purview [16]. Such NIH partnerships like the Community Engagement Alliance (CEAL) against COVID-19 Disparities and the Rapid Acceleration of Diagnostics in Underserved Populations (RADx-UP) coordinated initiatives to set a precedent for enhanced collaborations and the creation of infrastructure for engagement of vulnerable populations in the problem-solving process. Although neither of these initiatives were founded at the CTSA Consortium, both of them utilized the resources and infrastructure of the CTSA network, especially in terms of community engagement and recruitment programs, education, and training initiatives. Despite their many accomplishments, these national initiatives reiterated well-known issues and challenges for SUPs but struggled to incorporate vulnerable populations as co-creators, designers, or implementers of the projects.

Lack of diversity in clinical trials stems from minority communities' long-standing distrust, exacerbated by cost (fuel, parking, meals, lodging, etc.), lack of health literacy and information, language challenges, lack of accessibility, tacit biases, as well as the lack of PI diversity that could help decrease bias in participant recruitment of underrepresented populations. Dr. Young [17] summarizes this serious challenge for translational science:

> "Important clinical and translational research is being conducted to improve COVID outcomes, but are we bringing that innovation to special populations that are disproportionately impacted? It's those populations that suffer from health disparities and need help the most."

Greater integration of SUP from the beginning (and enough knowledge about how to do it effectively) would have been a step forward to more effectively dealing with the disparate effects of the pandemic from an institutional (CTSA Consortium-wide) perspective. Notwithstanding, in terms of institutional adaptive capacity, the CTSA Consortium had recognized, prior to the pandemic, the need to make faculty and staff investments in domain task forces, programs, and centers to create toolkits (e.g., the Life Course Research Visual Toolkit by CTSA Program National Center for Data to Health) [18] and channel common resources

to engage in greater, deeper research on Life Course and Vulnerable populations. As shown below in the case studies (see Box #2), the existence of prior connections with the underrepresented communities (in the second case study, pregnant and lactating parents) was a way to rapidly mobilize research participants into emerging COVID-19 clinical trials and observational studies.

Knowledge, Information, and Learning

Data gaps concerning significant disparities in COVID-19 community disease burden were observed and documented from the pandemic start [19–22]. Eder *et al.* [22] led and analyzed discussions between (and written reports from) Community Engagement hub leaders from eighteen CTSA institutions on their activities pertaining to six key community engagement response themes. Two themes were focused on special populations: collecting data to understand the impact of COVID-19 on distinct communities and groups; and engaging hubs and underrepresented populations in COVID-19 research.

The following are some examples of collecting data to understand how COVID-19 impacted local communities and groups. Stanford Medicine Office of Community Engagement developed a COVID-19 Community Outcomes Survey in four languages to ascertain and share information about unmet needs in distinct minority communities [23]. University of California – LA conducted COVID-19 focus groups with community members experiencing the harshest COVID-19 impact (based on race/ethnicity, age, income). Special COVID-19 related items were also added to the survey on social determinants of health, administered by the University of Minnesota [22]. Similarly, a recent mixed-methods study to ascertain the scale and scope of the COVID-19 pandemic's impact on refugee communities representing 18 countries found that refugee families struggled to adapt to an online learning environment; experienced stigma around communicable diseases as a barrier to accessing testing and treatment; were confused regarding medical systems, lacked trust in technology and privacy concerns; and endured overcrowded living conditions, financial stressors and high emotional toll derived from all the new challenges. The study findings were used to inform San Diego County's relief efforts [24].

Further strengthening the foundation of trust as an indispensable asset for successful adaptation, the Institute for Translational Sciences (ITS) at the University of Texas Medical Branch (UTMB) worked on addressing the needs of SUPs during the COVID-19 pandemic by employing available resources to provide trustworthy information, facilitate communication, increase medical response, and access to public health outreach. They focused on translating information to multiple audiences and enhancing patients' voice to guide research by developing infographics, media notices and educational materials related to preventions, testing, and appropriate use of personal protective equipment. Dissemination efforts included reaching out to nontraditional communication venues (e.g., regional newspapers and social media networks). In addition, ITS organized community meetings where trainees (doctoral and MPH) participated in and supported contact tracing efforts. This initiative led to community-based interventions and further research, which eventually translated into an NIH proposal where ITS collaborated with 11 community organizations to increase testing and reduce vaccine hesitancy [25].

Unless specific actions are taken, our historical implicit biases and limited contextual understanding may continue to result in

sub-optimal solutions, especially if we do not pay attention to the lessons from last year. For instance, successful pivoting to online recruitment and enrollment of research participants (an issue which has been extensively addressed in this thematic issue) is to be commended. However, we must go beyond lauding the technology and think how much of these innovative approaches exacerbated the limited access, potentially widened informational gaps, and continued under-serving of SUPs. For instance, the HOPE Registry [26] deliberately sought to engage patients and community stakeholders in all phases of the registry's development, implementation, and evaluation. By listening to the needs and preferences of the different SUP communities (related to awareness of research opportunities, outreach messages, consent language, etc.), the research team was able to increase the local community's knowledge about and access to available COVID prevention and therapeutic trials, even if recruitment success rates were not homogenous among SUP groups and Johns Hopkins healthcare workers were overrepresented.

Future efforts need to focus on understanding the modifiable risk factors for vulnerability and developing an underlying framework to pivot as new challenges arise. If learning from prior experiences is truly an institutional goal, consider disaster drills to stress-test the translational research enterprise to maintain some residual memory of past events and build command structures similar to what health systems have to do in response to natural and unnatural disasters. The CTSA consortium and, by its extension, NCATS can accomplish it as suggested in the Institute of Medicine 2017 report on creating a resilient biomedical enterprise recommendation [27]. In the report, one suggestion was that the academic biomedical enterprise participates in broader National and State Disaster Preparedness exercises. Intentional redundancies can be created so that a nodal network of biomedical research can still function even when the disaster impacts one region.

Innovation

Sometimes, "innovation" and "niche solution" mean that you have to go back to the use of traditional methods and mix relatively new and old approaches for better and more equitable impact. With electronic medical records (EMR) becoming omnipresent in health care and electronic-based recruitment methods used widely to boost participation in clinical trials, there is a concern that an overreliance on electronic/online technology may diminish access for eligible and interested underrepresented participant populations. In the research funded by the Johns Hopkins Institute for Clinical and Translational Research, a hybrid outreach strategy combining use of EMRs with postal mailings demonstrated enhanced cost-effectiveness and participation of under-represented groups, including Black participants and women [28].

In an attempt to leverage prior successes with recruitment registries, the Johns Hopkins Institute for Clinical and Translational Research (ICTR) sought to respond to the crisis by developing a COVID-19 registry (*HOPE Registry*) [26] to help study teams in expediting access to study participants and achieving their recruitment goals. The registry also sought to become an information tool (in terms of eligibility and convenience of access, especially remotely) for populations who may have otherwise felt "overwhelmed by outreach from multiple study teams" [26].

Although there are other well-known and available recruitment registries (such as ResearchMatch and Pitt+Me), this group opted

to tailor their creation to the specific needs of the Baltimore community and their research institution in particular. Since the HOPE Registry is still operational and actively recruiting, outcome metrics are still being collected. However, since its inception and until March 2021, 4600 matches have been made for 11 study teams that have used this particular recruitment tool. Despite the obvious successes of this initiative, the recruitment of minorities continues to be challenging: despite a 64% Black or African-American population in Baltimore City, only 9% of the HOPE registry enrollees are Black/African American. The HOPE team acknowledged that pivoting to remote activities due to the COVID-19 restrictions was beneficial in reaching large numbers of people without potentially risky in-person encounters. However, it also meant that the digital divide became greater: "individuals without access to computers or the internet" were further discriminated against, albeit unintentionally.

Also, looking elsewhere may provide us with a path forward in terms of novel approaches and tools. The revised UNAIDS/WHO Ethical Guidance for HIV Prevention Trials may be a good model for integrating special and underserved populations in translational research across the human lifespan. A newly revised guidance document, Ethical Considerations in HIV Prevention Trials [29], was released by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) in January 2021. A 12-month collaborative process included "representatives of communities with an increased risk of acquiring HIV infection, regulatory authorities, manufacturers, prevention researchers, trial designers, trial sponsors, relevant funders, biostatisticians, and ethicists." In the revised document, the second guidance highlights the "importance of equal partnerships among research teams, trial sponsors, and key populations, potential participants and community members who live in settings where trials are taking place." Increased recognition of community advisory boards and involvement of people directly affected by the challenges of HIV prevention enhanced the ethical design and implementation of trials.

Guidance also considered fair and inclusive selection of study populations, recommending that "arbitrary exclusion of individuals and populations based on characteristics such as age, pregnancy, and gender identity must be avoided." A guidance point on vulnerability emphasized that "persons and groups should not be labeled as vulnerable but rather the emphasis should be on the social or political contexts in which people live that may render persons or groups vulnerable" and that people may live in more than one context of vulnerability. In addition, the document "emphasizes the need to mitigate harms and to balance specific protections against potential overprotection."

Older adults—the most vulnerable and the hardest hit by COVID-19 [30]—have long been excluded from clinical trials due to institutional and sociocultural barriers: a historical lack of federal guidelines for their inclusion, lack of recruitment and retention techniques and infrastructure appropriate for this population, and ageism. The CTSA Consortium and the Research Centers Collaborative Network convened a workshop on the "Inclusion of Older Adults in Clinical Research." Its participants identified the following actions to integrate this particular population into research, which could also be applied to other SUPs: (1) engage with policy making processes to promote broader inclusion; (2) publicly disseminate existing resources to overcome biases associated with "-isms"; and (3) build institutional capacity to support age inclusion [31].

Flexible Forward-Looking Decision-Making and Governance

Adaptable, forward-looking decision-making can only be accomplished when it includes voices of its key stakeholders and community members. Some CTSA institutions have succeeded at integrating community partners in clinical research processes [22]. For example, University of California – San Francisco's (UCSF) COVID Research Patient and Community Advisory Board (COVID Research PCAB) uniquely advanced clinical and translational research by integrating stakeholders from across institutional research initiatives. This included community members from the CTSA Integrating Special Populations, and patient and community advisors from populations underrepresented in research. PCAB recommended strategies for stakeholder integration and health equity for pandemic studies and those not specifically investigating COVID-19 [32].

A number of other hubs collaborated with underrepresented populations to inform decision-making regarding COVID-19 research activities (data collection, recruitment, retention, implementation, and dissemination). An example of multi-institutional partnership of hubs engaging underrepresented minorities in emergency response and research is SOCCER (Southern California Consortium of Community Engagement Resources: University of California-Irvine, University of California – Los Angeles, University of California – San Diego, University of Southern California, Scripps Health). This collaboration integrated community expertise in developing and implementing pandemic research (e.g., COVID-19 vaccine trials). According to Eder *et al.*, community/stakeholder input integration and Patient and Community Advisory Board engagement can be considered "a best practice institutional transformation expected for a CTSA funded institution."

Hardeman *et al.* [33] recognized the need to combat racial health inequities as a fundamentally urgent task of all healthcare systems and learned through the pandemic responses that "systemic change can in fact happen overnight." Decision-makers of clinical and translational research organizations may adjust their structures, operations, and planning by learning from the five practices identified by the authors for dismantling of structural racism and improving the well-being of the black community:

1. *Divest from racial health inequities*: Racial health inequities are not indicators of a health care system malfunction but rather the by-product of that system working as intended. New health care policies and models (e.g., universal single-payer health care) may help remove barriers to equitable healthcare.
2. *Desegregate the healthcare workforce*: lack of diversity in the healthcare workforce must be eliminated and substituted with the creation of employment opportunities for all.
3. Make "*mastering the health effects of structural racism*" a professional medical competency: racism must be addressed in all medical schools and training programs. In addition, licensing, accreditation and qualifying procedures should test this knowledge.
4. *Mandate and measure equitable outcomes*: standards on how institutions address structural racism and equity outcome metrics should be required.
5. *Protect and serve*: patient and SUP advocacy must be an integral component in any health care system [33].

Translational scientists, including CTSA leaders, strive to learn from other fields and innovate by crossing boundaries and being flexible in adopting and blending promising approaches. Community Science in partnership with the Center for Neighborhood Technology (commissioned by the Barr Foundation) developed a guide with existing equity assessment tools that help public agencies, advocates, organizers, and other influencers to make and evaluate decisions that advance transportation equity [34]. The guide describes the purpose of equity tools as:

> "A structured problem solving approach that examines the benefits and burdens on communities most impacted by policies, decisions, and actions using quantitative and qualitative data from the community so that the solution:
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> ➤ Challenges any status quo or "we always did it that way" assumptions and decision-making process.
> ➤ Uses data to define the problem, racial and other disparities, and desired outcomes.
> ➤ Engages the community to identify the root cause of disparities.
> ➤ Leverages data and community knowledge to create a strategy and equity progress indicators.
> ➤ Builds evidence for new approaches to resource and improve conditions in communities of color and low-income communities" [34].

Such a comprehensive combination of characteristics and processes is a potentially impactful approach to ensure forward-looking, inclusive, and equitable decision-making in clinical and translational science. Following its tenets can help advance the integration of all populations in all aspects of decision making, design, implementation, dissemination, and beyond.

Adaptive Capacity and Preparedness and Special/Underrepresented Populations: Rapid-Analysis Case Studies

Integration is a higher-level function. It has proven difficult even in non-pandemic situations to achieve the CTSA goal of "promoting the integration of special and underserved populations in translational research across the human lifespan" [3]. It may be pragmatic to consider a reframing of the goal. We propose that the CTSA goal should be to "promote the integration of translational research in achieving the health and well-being needs of special and underserved populations across the human lifespan." In fact, the federal understanding of this important issue seems to be moving in the right direction since the most recent CTSA FOA presents one of its programmatic goals as "3) creating, providing, and disseminating innovative research programs and partnerships across institutions and communities to address health disparities and deliver the benefits of translational science to all" [9].

By joining spaces where special and underserved populations across the human lifespan already have power, the translational research enterprise can become a resource for addressing the needs of the broader group. The translational research enterprise, while significant, is on scales of magnitude lower than the constituents of various special and underserved populations. As a result, CTSAs can be more flexible and targeted in defining and adapting their capacities. Such a change in the narrative could flip the issue of trust where the translational research enterprise essentially is deemed trustworthy and of utility by how well it finds solutions to the needs of special and underserved populations across the lifespan. It would promote the "nothing about us without us" mantra that defines patient-centered and community partnered research.

By bridging the gap between a reductionist, usually single and mutually exclusive categorization of populations of interest from

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Box 1. Vignette #1: Adaptive Capacity and "Functional Special Populations"

The COVID-19 pandemic has highlighted the disparities among special populations by their employment and functional role in society. Often called "frontline or essential workers," this label includes a very diverse set of professionals, employees, and workers including but not exclusive to healthcare personnel, food and agriculture workers, government, transportation, and commercial facilities sector employees, communications, and IT professionals, etc. Given their functional designation, the group brings together individuals from all races, ethnicities, genders, socioeconomic statuses, geographic locations, origins, etc. This heterogeneity creates an added layer of complexity when seeking to address any problem or issue that results from their occupation and role.

Problem:

As early as July 2020, researchers reported COVID19-related suicide among hospital nurses [36]. A June-September 2020 survey conducted by community-based mental health non-profit organization revealed healthcare workers were stretched too thin: 93% experiencing stress, 86% anxiety, 77% frustrated, 76% felt exhausted and burnout, and 75% were overwhelmed. KFF/Washington Post Frontline Health Care workers survey confirmed the adverse effect COVID19 has had on this special population (62% worried that the pandemic had hurt their mental health). However, 76% of frontline health care workers felt "hopeful" about going to work these days (April 2021). As recently as June 2021, a survey of nurses and nursing students led by a private workforce consultant firm in partnership with Florida Atlantic University, showed a dramatic decrease in job satisfaction, only 32% of nurses manifested being very/completely satisfied with their job (as compared to 52% prior to the pandemic). In addition, 66% of nurses considered leaving their profession, and 37% claimed to be burned out, stressed or overworked. These data suggest that healthcare management, government agencies, and workplaces for essential workers need to identify new models of mental health care and other support services for their employees.

Solution:

Adapt and use current institutional resources to provide an outlet for frontline workers to release their workplace-induced stress. For example, The Johns Hopkins Hospital quickly acknowledged during the COVID-19 lockdown that their interactive gaming room (originally intended to accelerate stroke patient recovery) was not getting used. The therapist and neurologists in charge of the room decided to make it available to healthcare workers treating COVID-19 to decompress. Anecdotal evidence reported by Dr. Mona Bahouth, medical director of the Brain Rescue Unit and early stroke recovery group, suggests that people who have experienced the immersive gaming room have felt their blood pressure drop in response to spending time in there.

Lessons learned:

- The Johns Hopkins example constitutes an excellent case study in the application of local adaptive capacity concepts, namely: Domain 1. Asset Base: immersive treatment room which was devoid of "patients"; Domain 2. Institutions and Entitlement: hospital management identifying a low-cost, immediate solution to provide mental care options for their frontline workers; and Domain 4. Innovation: a creative, niche solution to a two-fold problem: healthcare/frontline worker job related stress and the lack of use of available resources.

- Like all special, underrepresented, and vulnerable populations, many more issues currently affect frontline workers. CTSAs can develop and implement an agile, thorough, and innovative adaptive capacity response in the immediate future to foster the provision of COVID-19 vaccine boosters for essential workers, especially those with least visibility such as agricultural, factory workers, and transit employees. Although healthcare workers were among the first to be offered a COVID-19 vaccine given their risk of exposure at their workplace and the need for them to continue the "functioning of society," see CDC's Phased Allocation decisions, their early vaccination now seems to be putting them at greater risk of infection given waning vaccine effectiveness with the most recent Sars-cov2 variants (e.g. Delta and Omicron) [37]. It will not be the first time that all institutions are required to choose how to phase out vaccine distribution. They all did it less than a year ago, and it is perhaps an excellent starting point for applying some of the AC&P lessons learned thus far.

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the biomedical research community and the more diverse, fluid, and complex current sociodemographic composition of our country with intersectionality as an analytical framework, we can start to reshape the healthcare and health-related research infrastructure to adapt to our current challenges [35]. We highlight an example of broadening our definition of special and vulnerable populations by applying the lens of intersectionality in a rapid-analysis case study below (Box 1).

We continue to explore the LAC application in a rapid-analysis case study from another CTSA hub: UC San Diego (see Box 2, Vignette #2).

Implications and Conclusion

In many ways, the special and underserved populations are a subset of "patients and communities" referenced in another one of the CTSA program goals. Traditional groupings such as those used in the current definition of SUPs tend to focus on a unique affiliation to a single group or subgroup. However, these groups are heterogenous and multidimensional, where most persons have a constellation of identities that creates *intersectionality*. Bowleg [40] defines intersectionality as a "theoretical framework for understanding how multiple social identities such as race, gender, sexual orientation, SES and disability intersect at the micro-level of individual experience to reflect interlocking systems of privilege and oppression (i.e., racism, sexism, heterosexism, classism) at the macro social-structural level." The medical, public health, and translational science fields seldom embrace the concept of intersectionality fully in research and practice. This critical omission of overlapping identities hinders our comprehension of the work that we need to do to further the mission, enhance the scope, and deepen the reach of the CTSAs to those who are the most vulnerable.

But it goes beyond increasing patient or community voices in translational science. Intersectionality involves proper *integration* (i.e., fully involving and actively giving equitable decision-making power to special and vulnerable populations (see Agenor [41] for recommendations). We must strive to integrate SUPs in the biomedical and mainly translational science workforce [42] as

> **Box 2. Vignette #2: Adaptive Capacity and Pregnant, Birthing, and Lactating People**
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> **Problem:**
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> COVID-19 pandemic onset had a critical impact on pregnant and lactating people due to a lack of information about the transmissibility of the SARS-CoV2 virus and the potential effects of an infected birthing person in the life of an unborn child. There was no official guideline or public health advice on the safety of breastfeeding, especially in the case of infected birthing parents. The pandemic immediately affected institutional management and support of breastfeeding practices as some hospitals discouraged direct breastfeeding and even prohibited skin-to-skin care and rooming-in [38].
>
> **Solution:**
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> Use CTSA's assets (Biobanking), institutions (UCSD-Center for Lifecourse and Vulnerable Populations Research, CLVR), Knowledge (CTSA hub expertise and dissemination of findings, also in non-traditional/academic outlets), and self-advocacy and agency (inclusiveness of infected mothers willing to donate breastmilk samples) to engage in research immediately. Namely, the UCSD CTSA hub conducted a study of 64 samples of breast-milk collected from 18 women across the US infected with severe acute SARS-CoV-2 which found that the virus was unable to replicate and breast milk was deemed not likely to be a source of infection for the infant. By rapidly responding to a societal need for scientific evidence to guide their action, these findings were able to fill a serious data void that was severely impacting this vulnerable population [39].
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> **Lessons learned:**
>
> - UCSD-CLVR example demonstrates the LAC characteristics in the following ways: Domain 1: Asset Base: The translational researchers involved in the study have developed longitudinal community engagement with representatives of special and underrepresented populations either independently or through efforts such as through Community Advisory Boards and the Community Clusters of CTSAs. CTSAs can leverage these relationships to the next level of integration. Biorepositories and data repositories with samples and information from lactating parents existed previously and they facilitated the project. Domain 2: Institutions and Entitlements: CTSA institutions already have made faculty and staff investments in programming (Center for Lifecourse and Vulnerable Populations). Consented women had already been engaging with the institution pre-disaster. Domain 3: Knowledge: Persons already felt able to raise questions with investigators about what to do regarding breastfeeding during COVID infection. Information conduits for dissemination were already present. Domain 4: Innovation: Ability to rapidly add testing of specimens of breast milk to address participant questions. Domain 5: Flexible/Forward-Looking Decision Making: Investigators being open to suggestions and issues raised by constituents, expeditiously translating the study of breastmilk into practice and impact of COVID-19 vaccine's response; as well as the creating an "open call" to breastfeeding people to join as study participants of new and potential areas of research related to COVID-19 and, consequently, new research agendas and peer-reviewed publications of findings.
> - Lack of current information and clear healthcare guidelines for immediate decision-making during a crisis may be more detrimental for an already vulnerable population (breastfeeding parents and their infants), especially in a national context where breastfeeding practices need to be supported (Breastfeeding report card 2020).
> - Timely research that provides initial, actionable evidence to counteract the lack of misinformation will immediately impact health outcomes and create further research opportunities for confirmation of initial findings. Although identifying connections between research findings and policy changes is extremely hard, the research dissemination impact of the initial breast milk analysis is tangible. One way to explore the translational impact of this research on breastmilk is to look at the study's [39] "Altmetrics" (metrics of research reach and influence that are complementary to traditional, citation-based metrics). The article's "attention score" is in the top 5% of all research outputs scored by Altmetric, and 87% of the people who have accessed the study are "members of the public" (in contrast with 6% of scientists and 6% of practitioners). New research agendas can evolve from integrating special and underrepresented populations in the translational spectrum. The same research team mentioned above has continued expanding the scope of their work and are now analyzing vaccine immune response, health of birthing person and child and mRNA vaccination impact in breastfeeding parents.

mentors, healthcare professionals, CTSA leaders, and national decision-making/public health authorities. For instance, community-academic collaborations are critical assets to integrating historically marginalized and underserved populations, and although they exist throughout the CTSA Consortium, in the form of Community-Academic Pilot Awards, they still face many gaps (funding) and barriers (administrative) that prevent them from garnering the attention that the purely scholarly, traditional Pilot awards counterparts do [43].

So, what would the implications be for the local adaptive capacity core concepts for the translational research enterprise to achieve such a naturally integrative goal for the CTSA network? In the area of building its *Asset Base*, CTSA programs should invest more resources that fund the translational research enterprise and leverage federal and non-federal funding to foster integration and promote the health and well-being of underrepresented and special communities across the lifespan.

When it comes to the *Institutions and Entitlements*, CTSA hubs should prioritize community integration initiatives that support the translational research enterprise's ability to promote resilience in underrepresented and special populations. CTSA resources and infrastructure need to be optimized for engagement of vulnerable populations in the problem-solving process and as co-creators, designers, implementers, or reviewers of the projects.

To optimize its *Knowledge, Information, and Learning*, the translational research enterprise's knowledge and data science tools need to be designed for accessibility for learning in underrepresented and special populations across the human lifespan. Oversight for any new data science tools by the translational research enterprise has to include underrepresented and special populations across the human lifespan explicitly. The translational science enterprise must be agile enough to create generalizable knowledge from mixed qualitative and quantitative research methods that best align with the knowledge generation mechanisms of underrepresented and special populations across the human lifespan.

For tangible success in the *Innovation* domain, the Network Capacity Cluster in current CTSA programs could be re-organized

Table 1. *Challenges for special and underserved population (SUP) integration in the context of emergency and approaches to address them (derived from the AC&P E-Scan)*

Challenges in the context of emergency	Approaches for integration of SUPs in the context of emergency
History matters: SUPs mistrust of the research process is grounded on previous negative experiences.	Trust needs to be earned through effective action. Coordinated efforts to create SUP community connections at the local, state and national levels are needed. (Asset Base)
SUPs are most disproportionately affected by health disparities. Implicit biases, racism, and mistreatment of SUPs are exacerbated during crises.	Diversity in clinical trials must be a reality. Optimize access to information, data repositories, programs, centers, toolkits, and new compensation models developed to increase SUP participation and recruitment. (Institutions and Entitlements)
Rapid change, when seeking SUP integration, is very difficult. SUPs mistakenly seen as a monolith.	Successful pivoting of resources and technology solutions that work for general populations may not work for SUPs. Identify particular needs and specific methods to engage with different SUPs. (Knowledge, Information, and Learning)
Overreliance on technology and other electronic-based methods further exclude SUPs from the research process.	Look for hybrid outreach strategies that combine old and new methods to bridge the digital divide. Reach out to the SUP community for solutions. (Innovation)
Racial health inequities exist across the entire research spectrum and beyond.	Acknowledge inequities, diversify workforce, data, approaches and communication mechanisms with SUPs. (Flexible, Forward-looking Decision Making)

to focus on providing disaster-resilient human-centered design to integrate the translational research network to promote disaster-resilience in underserved and special populations across the life-span. CTSA leaders and translational researchers must develop the knowledge, attitudes, and skills to partner with and listen to community leaders and members most familiar with what communities need.

Finally, to ensure *Flexible Forward-looking Decision-making and Governance* for this program goal, the CTSA Director should report to a Board of Trustees that also includes highly informed representatives from underrepresented and special communities across the lifespan—a Board that has decision-making authority on the translational research enterprise's vision, mission, and values. A similar structure should be embedded in each of the CTSA programs in the Administrative Cores. As part of the overall biomedical research enterprise, the translational research enterprise should be engaged with the Hospital and Public Health component of the National (and State and Local) Disaster Preparedness Plan as recommended in the 2017 Institute of Medicine Report [27]. It will extend the initial concept that the biomedical research enterprise is an essential, national resource, and like the National Guard, it should be an active component for preparedness, mitigation, and recovery of human health.

Some of the challenges, lessons learned, and approaches to integrate SUPs in the translational research process—grounded in the pandemic experiences and captured by the Environmental Scan—are summarized in Table 1. In conclusion, our main tenet is rather simple: although the past year has recorded incredible achievements in vaccine development, clinical trials, diagnostics and overall biomedical research, these successes continue to be hampered by our inability to turn them into achievements for all and equally available to all. The prevalent health disparities are "direct calls to action for the research community: to interrogate the social construct of race and intervene upon the complex multicomponent drivers of outcomes" [44]. There is no time like the present to seriously think and critically evaluate how to immediately address the needs and solve the problems that afflict all special, vulnerable, and underrepresented populations that have gone ignored for such a long time.

References

1. **Kennedy D.** Clinical trials and public trust. *Science* 2004; **306**(5702): 1649.
2. **Sirleaf EJ, Clark H.** Report of the independent panel for pandemic preparedness and response: making COVID-19 the last pandemic. *The Lancet* 2021; **398**(10295): 101–103.
3. **NCATS.** *PAR-15–304*; 2015. (https://grants.nih.gov/grants/guide/pa-files/PAR-15-304.html)
4. **Merriam-Webster.com.** Integrate. *Merriam-Webster* [Internet], 2022. (https://www.merriam-webster.com/dictionary/integrate)
5. **Rhodes SD, Alonzo J, Mann-Jackson L**, *et al.* Selling the product: strategies to increase recruitment and retention of Spanish-speaking Latinos in biomedical research. *Journal of Clinical and Translational Science* 2018; **2**(3): 147–155.
6. **Matthews AK, Rak K, Anderson E**, *et al.* White paper from a CTSA workshop series on special and underserved populations: enhancing investigator readiness to conduct research involving LGBT populations. *Journal of Clinical and Translational Science* 2018; **2**(4): 193–200.
7. **Rak K, Matthews AK, Peña G**, *et al.* Priority populations toolkits: enhancing researcher readiness to work with priority populations. *Journal of Clinical and Translational Science* 2020; **4**(1): 28–35.

8. **Vizueta N, Sarkisian CA, Szilagyi PG.** A CTSA-based consultation service to advance research on special and underserved populations. *Journal of Clinical and Translational Science* 2020; **4**(4): 271–278.

9. **NCATS.** *Federal grant opportunity for clinical and translational science award (UM1 clinical trial optional) PAR-21–293*; 2021. (https://grants.nih.gov/grants/guide/pa-files/PAR-21-293.html#_Part_2._Full)

10. **Volkov BB, Ragon B, Doyle JM, Bredella MA**, *et al.* Adaptive capacity and preparedness of Clinical and Translational Science Award (CTSA) program hubs: overview of an environmental scan. *Journal of Clinical and Translational Sciences* 2022; 1–32. DOI 10.1017/cts.2022.400.

11. **Jones L, Ludi E, Levine S.** Towards a characterisation of adaptive capacity: a framework for analysing adaptive capacity at the local level. Overseas Development Institute [Interet], December 2010. (https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2782323)

12. **Cunningham-Erves J, Villalta-Gil V, Wallston KA, Boyer AP, Wilkins CH.**Racial differences in two measures of trust in biomedical research. *Journal of Clinical and Translational Science* 2019; **3**(2–3): 113–119.

13. **Holzer J, Kass N.** Understanding the supports of and challenges to community engagement in the CTSAs. *Clinical and Translational Science* 2015; **8**(2): 116–122.

14. **Wieland ML, Asiedu GB, Lantz K**, *et al.* Leveraging community engaged research partnerships for crisis and emergency risk communication to vulnerable populations in the COVID-19 pandemic. *Journal of Clinical and Translational Science* 2021; **5**(1): e6.

15. **Gewin V.** Six tips for data sharing in the age of the coronavirus. *Nature* 2020. DOI 10.1038/d41586-020-01516-0.

16. **Nana-Sinkam P, Kraschnewski J, Sacco R**, *et al.* Health disparities and equity in the era of COVID-19. *Journal of Clinical and Translational Science* 2021; **5**(1): e99.

17. **Georgia Clinical & Translational Science Alliance.** Georgia CTSA leader explores lack of diversity in COVID-19 trials [Internet], August 14, 2020. (https://georgiactsa.org/news-events/news/2020/discovery/trial-diversity/index.html)

18. **The CTSA Program National Center for Data to Health (CD2H).** Life course research visual toolkit [Internet], April 28, 2021. (https://cd2h.org/node/438)

19. **Alcendor DJ.** Racial disparities-associated COVID-19 mortality among minority populations in the US. *Journal of Clinical Medicine* 2020; **9**(8): 2442.

20. **Chen JT, Krieger N.** Revealing the unequal burden of COVID-19 by income, race/ethnicity, and household crowding: US county versus zip code analyses. *Journal of Public Health Management and Practice* 2021; **27**(1): S43–S56.

21. **Labgold K, Hamid S, Shah S**, *et al.* Estimating the unknown: greater racial and ethnic disparities in COVID-19 burden after accounting for missing race and ethnicity data. *Epidemiology* 2020; **32**(2): 157–161.

22. **Eder M, Millay T, Cottler L.** A compendium of community engagement responses to the COVID-19 pandemic. *Journal of Clinical and Translational Science* 2021; **5**(1): e133. DOI 10.1017/cts.2021.800.

23. **BACHAC – Bay Area Community Health Advisory Council.** Stanford COVID-19 Community Outcomes (COCO) survey [Internet], June 16, 2020. (https://www.bachac.org/blog/stanford-survey)

24. **San Diego Refugee Communities Coalition (SDRCC).** COVID-19 refugee community impact report [Internet], September 2020. (https://drive.google.com/file/d/1acuF7Cg6JjuMxYrwCxf46yrBndmAmJXh/view)

25. **Croisant S, Hallberg L, Prochaska J, Singleton C**, 13124 COVID-19: the urgency of engaging during crisis. Poster presented at Translational Science 2021. (https://epostersonline.com/acts2021/node/500)

26. **Peeler A, , Miller H, Ogungbe O**, *et al.* Centralized registry for COVID-19 research recruitment: design, development, implementation, and preliminary results. *Journal of Clinical and Translational Science* 2021; **5**(1): e152.

27. **National Academies of Sciences, Engineering, and Medicine.** *Strengthening the Disaster Resilience of the Academic Biomedical Research Community: Protecting the Nation's Investment*. Washington, DC: The National Academies Press, 2017.

28. **Miller HN, Charleston J, Wu B**, *et al.* Use of electronic recruitment methods in a clinical trial of adults with gout. *Clinical Trials* 2021; **18**(1): 92–103.

29. **UNAIDS.** *Ethical considerations in HIV prevention trials. UNAIDS and WHO guidance document*; 2021. (https://www.unaids.org/en/resources/documents/2021/ethical-considerations-in-hiv-prevention-trials)

30. **Powell T, Bellin E, Ehrlich AR.** Older adults and Covid-19: The most vulnerable, the hardest hit. *Hastings Center Report* 2020; **50**(3): 61–63.

31. **Petrovsky DV, Đoàn LN, Loizos M**, *et al.* Key recommendations from the 2021 "inclusion of older adults in clinical research" workshop. *Journal of Clinical and Translational Science,* 2022; **6**(1): e55. DOI 10.1017/cts.2022.1.

32. **UCSF Clinical and Translational Science Institute (CTSI).** USCF COVID research patient and community advisory board in motion & receives PCORI funding [Internet], June 9, 2022. (https://ctsi.ucsf.edu/news/ucsf-covid-research-patient-and-community-advisory-board-motion-receives-pcori-funding)

33. **Hardeman RR, Medina EM, Boyd RW.** (2020). Stolen breaths. *New England Journal of Medicine* 2020; **383**(3): 197–199.

34. **Community Science and Center for Neighborhood Technology (commissioned by the Barr Foundation).** Tools for equitable mobility [Internet], December 15, 2021. (https://barrfdn.issuelab.org/resource/tools-for-equitable-mobility.html)

35. **Hankivsky O, Doyal L, Einstein G**, *et al.* The odd couple: using biomedical and intersectional approaches to address health inequities. *Global Health Action* 2017; **10**(sup2): 1326686.

36. **Rahman A, Plummer V.** COVID-19 related suicide among hospital nurses; case study evidence from worldwide media reports. *Psychiatry Research* 2020; **291**: 113272.

37. **Keehner J, Horton LE, Binkin NJ**, *et al.* Resurgence of SARS-CoV-2 infection in a highly vaccinated health system workforce. *New England Journal of Medicine* 2021; **385**(14): 1330–1332.

38. **Perrine CG, Chiang KV, Anstey EH**, *et al.* Implementation of hospital practices supportive of breastfeeding in the context of COVID-19 — United States, July 15–August 20. *MMWR Morbidity and Mortality Weekly Report* 2020; **69**(47): 1767–1770.

39. **Chambers C, Krogstad P, Bertrand K**, *et al.* Evaluation for SARS-CoV-2 in breast milk from 18 infected women. *JAMA* 2020; **324**(13): 1347–1348.

40. **Bowleg L.** The problem with the phrase women and minorities: intersectionality – an important theoretical framework for public health. *American Journal of Public Health* 2012; **102**(7): 1267–1273.

41. **Agénor M.** Future directions for incorporating intersectionality into quantitative population health research. *American Journal of Public Health* 2020; **110**(6): 803–806.

42. **Estape ES, Quarshie A, Segarra B**, *et al.* Promoting diversity in the clinical and translational research workforce. *Journal of the National Medical Association* 2018; **110**(6): 598–605.

43. **Dunn A, Smith KL, , McClinton-Brown R, Evans JW, Goldman-Ross L, Cullen M.** Understanding the barriers, challenges, and facilitators to community-engaged research: a review of a CTSA community engagement pilot program. *Journal of Clinical and Translational Sciences* 2019; **3**(s1): 99–100.

44. **Cook NL, Lauer MS.** Biomedical research COVID-19 impact assessment: lessons learned and compelling needs. *NAM Perspectives* 2021. Discussion Paper, National Academy of Medicine, Washington, DC. DOI 10.31478/202107e