



# Clinical Researcher

**The Authority in Ethical, Responsible Clinical Research**

**August 2022 (Volume 36, Issue 4)**



**We're All in This Boat Together: Patients, Professionals, and Promising  
Solutions for Keeping Study Sites Afloat**

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## Clinical Researcher

### Association of Clinical Research Professionals

#### Editor-in-Chief

**James Michael Causey**  
[mcausey@acrpnnet.org](mailto:mcausey@acrpnnet.org)  
(703) 253-6274

#### Managing Editor

**Gary W. Cramer**  
[gcramer@acrpnnet.org](mailto:gcramer@acrpnnet.org)  
(703) 258-3504

#### Director, Advertising & Exhibition Sales

**Tammy B. Myers, CEM**  
[tammy.myers@acrpnnet.org](mailto:tammy.myers@acrpnnet.org)  
(703) 254-8112

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For membership questions, contact ACRP at [support@acrpnnet.org](mailto:support@acrpnnet.org) or (703) 254-8100.

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**Six issues of *Clinical Researcher* will be published on a bimonthly schedule in 2022. The Home Study tests will grant 3 Continuing Education Credits.**

#### Editorial Advisors for This Issue

**Suheila Abdul-Karrim, CCRT, CCRA, ACRP-MDP, FACRP**  
(Freelancer)

#### Victor Chen, MSc

(Kaiser Permanente/The CK Clinical Group)

**Jerry Stein, PhD, ACRP-CP, ACRP-MDP, FACRP**  
(Summer Creek Consulting, LLC)

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## **Clinical Researcher—August 2022 (Volume 36, Issue 4)**

### **CHAIR’S MESSAGE**

### **Sharing the Who, What, Why, and How of Clinical Research Careers**

David J. Morin, MD, FACP, CPI, FACRP, 2022 Chair of the Association Board of Trustees for ACRP



We all know our industry faces a critical workforce shortage. It’s disconcerting to think about potential treatments and cures that are stalled now because we simply don’t have enough skilled clinical trial professionals to run vital trials.

We must find ways to increase the diversity of the clinical trial workforce. At the same time, we must find ways to grow the clinical trial workforce.

Your Association is committed to meeting both challenges head on. Last year, we worked with a variety of enthusiastic and committed figures to develop a [Diversity Advisory Council](#) (DAC). The members of this esteemed group of thought leaders serve as volunteers supporting ACRP’s efforts to advance the important work of diversity, equity, and inclusion in the clinical research enterprise.

Further, in July, ACRP launched a powerful new campaign, “[Ready, Set, Clinical Research!](#)™” It’s a multi-layered program designed to spread the word about the amazing career opportunities in clinical research—especially to audiences whose members may not have been exposed to our wonderful profession yet.

This campaign's innovative toolkit is designed for flexible use by career advisors, recruiters, employers, and other stakeholders with a vested interest in the growth and diversification of the clinical research workforce. Developed with support from [ACRP's Partners Advancing the Clinical Research Workforce™](#), this new toolkit showcases the “who,” “what,” “why,” and “how” of a career in clinical research.

Using carefully crafted, impactful messaging intended to influence both hearts and minds in your community, the toolkit features emotive, personal stories from patients and clinical research professionals to emphasize the people-centered nature of clinical research, while the bold, eye-catching, contemporary design aims to foster a sense of excitement, inspiration, and curiosity.

I encourage you to check these new resources out for yourself, and especially to share them with people you may know outside our field. We all know what a rewarding career clinical research offers. We all know how important the work is, and how it is prolonging life and alleviating suffering every day.

Now it's time to share our passion with others, for the betterment of everyone.



*In addition to his volunteer duties with ACRP, Morin provides patient care and serves as the Director of Research at Holston Medical Group, a multispecialty practice in Tennessee and Virginia, and is Director of the High-Risk Disease Prevention program for a Fortune 100 company.*

PEER REVIEWED

## **Racial and Ethnic Disparities Among the Clinical Research Workforce: Insights and Opportunities**

Emily Botto, BA; Maria Florez, MA; Adrelia Allen, PharmD; Ruma Bhagat, MD, MPH; Ellyn Getz, MPH; Kenneth Getz, MBA



Clinical trial participant diversity has been a key topic in the pharmaceutical industry for decades. The subject first entered the literature following the National Institutes of Health's (NIH's) Revitalization Act of 1993 and was further propelled into the spotlight by the African American Heart Failure Trial in 2004.<sup>{1}</sup> Research conducted following these landmark documents has shown that racial and ethnic diversity in clinical trial participant populations can help identify variations in treatment outcome, thereby increasing the accuracy and safety of results across populations. Despite mounting evidence of the importance of participant diversity in the drug development process and an increasing number of initiatives to promote it, low representation of Black, Indigenous, and People of Color (BIPOC) among the global clinical trial participant population persists.<sup>{2,3}</sup>

As the issues surrounding participant diversity become better understood globally, driven in part by new guidance from the U.S. Food and Drug Administration (FDA)<sup>{4}</sup> and publication requirements from peer-reviewed journals,<sup>{5}</sup> more eyes are turning to the next frontier in drug development diversity, equity, and inclusion (DEI): the clinical research workforce.<sup>{6–8}</sup> Studies regarding the effect of diverse healthcare professional (HCP) staff in improving outcomes for BIPOC patient populations indicate that addressing established racial and ethnic disparities in the global clinical research workforce may be an important element in promoting participant diversity.<sup>{9,10}</sup>

This study is an expansion and update of a study conducted by the Tufts Center for the Study of Drug Development (CSDD) at Tufts University in 2008 among 1,376 U.S.-based principal investigators, which found that significant racial and ethnic disparities exist among clinical investigators despite a comparable interest in clinical research involvement.{ 11 } The authors also proposed that physician race or ethnicity may influence the race or ethnicity of clinical trial volunteers—a conclusion supported by other recently published manuscripts.{ 8 } Although the 2008 study was limited to U.S. respondents, due to the increasingly global nature of the clinical research enterprise, as well as evidence of the need for both environmental and racial and ethnic diversity in the global clinical trial participant population, the research team felt that it was important to consider global perspectives in this follow-up initiative.{ 12–14 }

This updated study includes responses from nurses and other allied health professionals in addition to those of physicians. Individuals from this demographic, like physicians, interact with patients on a regular basis and are crucial to patient care in both clinical care and clinical trial settings. Additionally, non-physician allied health professionals have been shown to experience barriers in terms of racial and ethnic disparities, and their perspective is critical to promoting diversity among entire clinical trial teams.{ 15 }

Understanding how HCPs are motivated to get involved in clinical research, as well as perceived barriers to involvement, is an important step to providing opportunities for HCPs from all backgrounds to contribute their expertise to the clinical research workforce.

## **Study Methodology**

Survey design and analysis planning were conducted and reviewed by a large working group of 24 organizations between December 2020 and March 2021. Following review and approval by the European General Data Protection Regulation (GDPR) committee and ethical review board at Tufts CSDD, the survey was distributed to a global audience between April and July 2021. Survey distribution was conducted through collaborations with a number of professional associations in addition to purchased lists.

Racial and ethnic identities were defined within the survey instrument and are provided in Table 1 as seen by respondents. These categories are consistent with those reported in a recent COVID-

19 study{ 16} and informed by classifications recommended or used by United Nations and the U.S. Census Bureau, among others.{ 17–21}

**Table 1: Race and Ethnicity Definitions as Seen by Respondents**

Race and Ethnicity	
Asian	Persons having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam.
Black (or of African Descent)	Persons having origins in any of the black racial groups of Africa.
LatinX (Spanish Origin, Hispanic, or Latino)	Persons of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race.
White	Persons having origins in any of the original peoples of Europe.
Other	Includes* “American Indian” (A person having origins in any of the original peoples of North and South America, including Central America), and who maintains tribal affiliation or community attachment); “Pacific Islander” (those having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands); “Other” (some other race, ethnicity, or origin); and any respondent selecting two or more of the available options.

*\*Racial and ethnic identities collapsed into the “Other” category were defined separately within the survey instrument.*

Raw data were stored in Microsoft Excel and data cleaning and analysis were conducted in SAS version 9.4. Analyses performed included descriptive statistics, frequency comparisons, coefficients of variation (defined as the ratio of standard deviation to the mean), comparisons of mean overall and subgroup response values, significance testing, and correlations. Subgroups were created based on white or non-white racial and ethnic identities as well as highest degree earned by respondent, with MD/PhD compared as a subgroup to overall respondents. Analyses were conducted on nursing subgroups as well; however, certain questions were only shown to half of respondents. In these areas, the white/non-white subgroup sample of nursing respondents was insufficient for meaningful analyses.



## Results

Respondents to the survey by region reflected the proportion of invitations sent to North American vs. Outside-North American HCPs. In addition to 34,552\* purchased list e-mail addresses receiving the invitation, 10 professional associations distributed the survey to their members via e-mail or social media pages. Of these, 611 respondents consented to participate in the online survey, with 54% of respondents from North America (U.S. or Canada) and 46% from outside North America. Respondent characteristics are summarized in Table 2.

**Table 2: Respondent Characteristics**

	N	Percent of Total Overall	Percent of Total North America	Percent of Total Outside- North America
<b>Highest Degree Earned</b>				
Medical or doctoral degree	295	62%	53%	72%
Nursing degree	115	24%	32%	16%
Other	66	14%	15%	12%
<b>Sex</b>				
Female	207	56%	61%	50%
Male	162	44%	39%	50%
<b>Race &amp; Ethnicity</b>				
White	253	68%	71%	64%
LatinX	16	4%	3%	6%
Asian	56	15%	12%	18%
Black	12	3%	4%	2%
Other (including mixed race)	37	10%	10%	10%

*\*The number of additional invitations sent by professional associations are not available, therefore, response rate can only be estimated (~2%).*

This survey was open to both HCPs with and without clinical research experience, and the data show a fair balance between the two backgrounds, with 56% of respondents reporting having been on study staff (i.e., part of a clinical research team) in the past (see Table 3).

**Table 3: Clinical Research Experience by Subgroup**

	<b>Total</b> <b>N = 366</b>	<b>Overall</b> <b>Non-White</b>	<b>Overall</b> <b>White</b>	<b>MD/PhD</b> <b>Non-White</b>	<b>MD/PhD</b> <b>White</b>	<b>Nurse</b> <b>Non-White</b>	<b>Nurse</b> <b>White</b>
Without Clinical Research Experience	<b>44.2%</b>	<b>45.4%</b>	<b>45.1%</b>	<b>35%</b>	<b>30.9%</b>	<b>55%</b>	<b>68.5%</b>
With Clinical Research Experience	<b>55.8%</b>	<b>54.6%</b>	<b>54.9%</b>	<b>65%</b>	<b>69.1%</b>	<b>45%</b>	<b>31.5%</b>

Overall, white and non-white respondents reported similar levels of clinical research experience. Given the options of “extremely interested,” “somewhat interested,” and “not at all interested,” non-white respondents—both overall and within the MD/PhD subgroup—selected “extremely interested” in higher proportions. In North America, non-white MD/PhDs were significantly more likely ( $\alpha = 0.001$ ) to be “extremely interested” in clinical research work (see Table 4).

**Table 4: Percent of Respondents Without Clinical Research Experience Reporting “Extreme Interest” in Clinical Research by Subgroup**

	<b>Total</b> <b>N = 133</b>	<b>Overall</b> <b>Non-White</b>	<b>Overall</b> <b>White</b>	<b>MD/PhD</b> <b>Non-White</b>	<b>MD/PhD</b> <b>White</b>
All Regions	27.9%	35.7%	24.7%	50.0%	29.7%
North America	25%	40%	20.3%	87.5% $\alpha$	22.7%
Ex-North America	33.3%	31.8%	34.5%	28.6%	40%

$\alpha$  = p-value < 0.05 in chi-square testing between white and non-white respondents in given subgroup.

## Respondents with No Clinical Research Experience

Respondents with no work experience in clinical research were asked to rate a variety of barriers to clinical research involvement as “very important,” “somewhat important,” or “not at all important.” The percentages of total respondents in the given subgroup who chose “very important” for each barrier are reported in Table 5.

**Table 5: Percent of Respondents with No Clinical Research Experience Reporting “Very Important” Barriers to Involvement by Subgroup**

	<b>Total</b> <b>N = 197</b>	<b>Overall</b> <b>Non-White</b>	<b>Overall</b> <b>White</b>	<b>MD/PhD</b> <b>Non-White</b>	<b>MD/PhD</b> <b>White</b>
Time constraints	48.6%	47.8%	48.9%	54.2%	50%
Lack of access to clinical trials	39.7%	55.6% $\alpha$	30.9%	54.2%	42.1%
Personnel needs	32.6%	37.8%	29.7%	47.8%	32.4%
Infrastructural needs	29.5%	37.8% $\alpha$	26.1%	52.2%	29.7%
Lack of patient interest	21.2%	30.2% $\alpha$	15.2%	23.8% $\alpha$	8.1%
Complexity of the study	18%	18.2% $\alpha$	16.1%	22.7%	16.2%
Lack of potential personal benefit	16.9%	31.8% $\alpha$	10%	31.8% $\alpha$	2.8%

$\alpha$  = *p*-value < 0.05 in chi-square testing between white and non-white respondents in given subgroup.

A higher proportion of non-white MD/PhDs indicated that a variety of barriers were “very important” to their decision not to participate than did white MD/PhDs. Chi-square testing showed significant differences in white and non-white MD/PhDs in lack of patient interest ( $\alpha$  = 0.04) and lack of potential personal benefit ( $\alpha$  = 0.008). Overall, non-white respondents also reported most barriers as “very important” to their decision not to become involved in clinical research in higher proportion than white respondents, except for “time constraints,” which was the highest reported barrier overall. Statistically significant differences were seen between white and non-white respondents in “lack of access to clinical trials” ( $\alpha$  = 0.01), “infrastructural needs” ( $\alpha$  = 0.009), “lack of patient interest” ( $\alpha$  = 0.006), “study complexity” ( $\alpha$  = 0.0008), and “lack of potential personal benefit” ( $\alpha$  = 0.004).

The North American subgroup saw similar results among overall respondents, with non-white North American respondents also reporting “lack of access to clinical trials” as a “very important” barrier to clinical research work in significantly higher proportion than white respondents from this region ( $\alpha = 0.013$ ).

These data indicate that higher interest shown by non-white respondents, and particularly non-white doctors (Table 4) is accompanied by higher barriers to entry (Table 5).

When asked which trial sponsor would make the respondent “more likely,” “less likely,” or would not change their attitude (“neutral”) toward becoming a clinical researcher, government and academic institutions were chosen as “more likely” at the highest rate, with industry selected at the lowest rate. The percentage of total respondents in the given subgroup who chose “more likely” for each type of trial sponsor are reported in Table 6.

**Table 6: Percent of Respondents with No Clinical Research Experience Reporting Which Institutions Funding Clinical Trials Would Make Them “More Likely” to Become a Clinical Researcher**

	<b>Total</b> <b>N = 101</b>	<b>Overall</b> <b>Non-White</b>	<b>Overall</b> <b>White</b>	<b>MD/PhD</b> <b>Non-White</b>	<b>MD/PhD</b> <b>White</b>
Government	72.3%	58.1% $\alpha$	78.6%	66.7%	81.5%
Academic	67.3%	58.1%	71.6%	80%	84%
Non-profit	51%	53.3%	50%	57.1%	46.2%
Industry	22.4%	30%	19.1%	28.6%	26.9%

$\alpha = p\text{-value} < 0.05$  in chi-square testing between white and non-white respondents in given subgroup.

### **Respondents with Clinical Research Experience**

The research team also surveyed those HCPs familiar with clinical research to deduce how they became involved and analyzed the differences in experience between subgroups. As seen in Table 7, the most reported catalysts to involvement in clinical research included applying for a job or grant and being asked by a mentor or peer to join the study. “Other” was selected by 17%

of respondents with clinical research experience, which warrants further investigation into other catalysts to clinical research involvement.

**Table 7: Types of First Involvement (Overall) for Respondents with Clinical Research Experience Responding to Survey Question**

	<b>Total</b> <b>N = 197</b>	<b>Overall</b> <b>Non-White</b>	<b>Overall</b> <b>White</b>	<b>MD/PhD</b> <b>Non-White</b>	<b>MD/PhD</b> <b>White</b>
<b>Mentor (included in Mentor or Peer)</b>	<b>23.4%</b>	<b>16.7%</b>	<b>26.8%</b>	<b>18.8%</b>	<b>29.6%</b>
Mentor or Peer	38.6%	30%	41.7%	33.3%	44.9%
Applied for Job/Grant	24.4%	28.3%	23.6%	27.1%	20.4%
Proactive	8.1%	13.3%	6.3%	10.4%	7.1%
Recruited/Referred*	11.7%	11.7%	11%	10.4%	14.3%
Other	17.3%	16.7%	17.3%	18.8%	13.3%

*\*Includes recruitment by industry sponsor, academic institution, contract research organization, or site management organization, as well as referral via institutional office or site network.*

This survey found that, out of those respondents with direct clinical trial experience, both overall white respondents and white MD/PhDs were more likely to have had a mentor or peer help them get involved in clinical research. Of those respondents with mentors, 93% agreed that mentors made them more comfortable with the clinical trial process, 91% agreed that mentors made them more comfortable with referring and screening patients for clinical trials, and 87% agreed that mentors helped them find greater access to clinical trials. Additionally, 100% of non-white mentored respondents agreed that mentors made them more likely to continue to get involved in clinical trials after their first trial, compared to 88% of white respondents.

In North America, non-white respondents were similarly less likely to have had a mentor get them involved in clinical research (see Table 8). North American results also revealed that non-white respondents were more likely to have acted proactively to get involved in clinical trials (contacting a pharma/biotech company, requesting a peer to include respondent in the study).

Although this was true for the overall dataset as well, the gap was larger among North American respondents. “Proactive” means of involvement in clinical research require expressed interest in the field and more effort from the individual, further highlighting the gap in access and opportunities readily available to this subgroup (Table 5).

**Table 8: Types of First Involvement (North America) for Respondents with Clinical Research Experience**

	<b>North America Total N = 102</b>	<b>North America Non-White</b>	<b>North America White</b>
<b>Mentor (included in mentor or peer)</b>	<b>16.8%</b>	<b>8.6%</b>	<b>20.9%</b>
Mentor or Peer	34.3%	25.7%	38.8%
Applied for job or grant	22.5%	22.9%	22.4%
Proactive	10.8%	20%	6%
Recruited/Referred	10.8%	11.4%	10.4%
Other	21.6%	20%	22.4%

These findings imply that white candidates have more access to mentorship opportunities both globally and within the North American region.

## Conclusions

Tufts CSDD’s 2008 publication exposed the disparities that exist in the race and ethnicity of principal investigators in the U.S. by identifying a trend of non-white investigators conducting and initiating fewer trials annually despite similar levels of interest.<sup>{ 11 }</sup> This study, 14 years later, shows that although the incidence of non-white MD/PhD respondents in clinical research is still lower than white MD/PhDs, “extreme interest” in participation as a clinical researcher is higher among non-white MD/PhD respondents, particularly in North America (Table 4).

By analyzing the root of these disparities at a global level and across allied health professions, the research team not only identified similar disparities in incidence of BIPOC healthcare professional involvement to the 2008 study, but also found that BIPOC healthcare professionals perceive higher barriers to clinical research involvement in access, infrastructural needs, lack of patient interest, complexity of the study, and lack of potential personal benefit. This report of higher barriers—particularly in access—among both global and North American non-white respondents was consistent with a lower proportion of this subgroup reporting having a mentor or peer ask them to join their first trial compared to white respondents.

This element is important to address, as mentorship has been found to be a more effective tool in diverse recruitment than other DEI initiatives such as mandatory diversity training, job tests, and grievance systems.{22} This is supported by perspectives from respondents to this survey, who reported overwhelmingly that having a mentor had a positive impact on their clinical research experience, as well as increased their likelihood to refer patients and to continue working in clinical research after their first trial.

Emphasizing these barriers to access for BIPOC-allied health professionals and taking steps to mitigate their effect, such as instituting mentorship and educational programs among allied health students from diverse backgrounds, could contribute to decreasing disparities in the clinical research workforce. Although these programs do exist within the U.S., wider adoption of them—both outside the U.S. and across a larger proportion of U.S. sites— is an essential element in promoting diversity in the clinical research workforce, as is the availability of early intervention programs to promote clinical research education.

Existing programs are led by various organization types, including universities,{23} government agencies,{24} and professional associations.{7,25} Some industry sponsors have mentorship programs focused on postdoctoral candidates,{26} however these are not specifically dedicated to diversity and are limited in their target audience. Implementing more diversity-targeted programs within sponsor companies, as well as encouraging their development among sites and potentially sponsoring associated costs, are promising ways that industry can directly contribute to enabling more HCPs from a broader range of backgrounds to enter the clinical research workforce.

## Study Limitations

The methodology in this study had several limitations. The original distribution plan was to reach out to professional organizations for collaboration, which was the strategy for Tufts CSDD's comparable 2008 study. However, heavy burdens due to surges in COVID-19 infections and deaths during the distribution of this survey may have affected both the willingness of professional associations to distribute the survey as well as the willingness—or bandwidth—of HCPs to contribute time to fill out the survey. Additionally, the increased number of surveys from other sources targeting HCPs during this time exacerbated survey fatigue.<sup>{27}</sup> Survey completion rates could have also been affected by these elements, as well as the length of the survey instrument. Bias may have been introduced with these recruitment methods, as the predominant demographics of members of professional associations collaborating in study distribution may have been more heavily represented than those of associations that did not respond to requests to collaborate.

Other limitations included the low awareness of DEI research from organizations outside the U.S. Some organizations, in addition to low awareness of the topic, did not perceive DEI as applicable to their region, further complicating this method of recruitment. Lack of familiarity and consideration for ethnic and racial diversity initiatives in clinical research outside the U.S. is a separate topic that requires further research and advocacy, as drug development is a global process that impacts patients worldwide. Due to these limitations, purchased e-mail lists were used.

Finally, a low number of non-white respondents made it difficult to avoid a white/non-white dichotomy. In a global study featuring a variety of geographic areas, each with varying racial and ethnic majorities, this subgroup approach may not fully account for the variations in experience among non-white respondents. Tufts CSDD is interested in following up on this study to expand the dataset and allow deeper subgroup analyses, particularly during a time when the COVID-19 pandemic does not restrict availability and enhance survey fatigue among HCPs.



Despite these limitations, these results can provide important insight into the barriers and experiences of the global clinical research workforce and introduce the subject of workforce diversity on a global scale.

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**Emily Botto, BA**, ([emily.botto@tufts.edu](mailto:emily.botto@tufts.edu)) is a Research Analyst at the Tufts Center for the Study of Drug Development in Boston, Mass.



**Maria Florez, MA**, is a Research Consultant at the Tufts Center for the Study of Drug Development.



**Adrelia Allen, PharmD**, is the Senior Director of Clinical Trial Patient Diversity at Merck.



**Ruma Bhagat, MD, MPH**, is Principal Science Leader for Health Equity and Population Science, Product Development, at Genentech, a member of the Roche group.



**Ellyn Getz, MPH**, is the Director of R&D Patient Partnerships at CSL Behring.



**Kenneth Getz, MBA**, is the Executive Director and Research Professor at the Tufts Center for the Study of Drug Development.

PEER REVIEWED

## **Findings from a Long-Term Patient Engagement Model**

Annick de Bruin, MBA; Shalome Sine, MPH; Lieven Van Vijnckt, PharmD;  
Alyson Gregg, MBA; Catherine Cole



Government agencies, pharmaceutical companies, and patient advocacy groups increasingly involve patient and caregiver feedback at various checkpoints throughout the clinical trial process to develop research protocols with greater benefit and less burden to participants and their families.<sup>{1}</sup> Involving patients and their support network in the protocol development process can take several forms, including patient advisory boards, surveys, and interviews. However, best practices and standardized processes for developing patient-centric trials have not yet been widely established.<sup>{1,2}</sup>

In recent years, several organizations and initiatives have emerged with the intention of advancing patient engagement in drug development and/or research, including the Patient-Centered Outcomes Research Institute (PCORI),<sup>{3}</sup> the Clinical Trials Transformation Initiative (CTTI),<sup>{4}</sup> the U.S. Food and Drug Administration's (FDA's) Patient Engagement Collaborative with CTTI,<sup>{5}</sup> the FDA's Patient-Focused Drug Development (PFDD) program,<sup>{6}</sup> and the not-for-profit Patient Focused Medicines Development (PFMD)<sup>{7}</sup> organization. All seek to increase patient involvement across the lifecycle of medical product development, including through the phases of research, and to improve trials in terms of quality, efficiency, safety, and ethical conduct, as well as in engaging all stakeholders as equal partners. The current trajectory toward greater patient involvement represents an opportunity to develop and conduct more effective research via outcomes such as realistic inclusion and exclusion criteria, lower participant burden, and patient-relevant endpoints.<sup>{8}</sup>

To create meaningful impacts, patient engagement strategies need to be put into place that result in substantive feedback and turn communication into actionable change.{9} Numerous types of patient engagement approaches exist, including community advisory boards, patient advisory boards, individual interviews, and surveys (see Table 1). Tools for implementing these models have been provided by the FDA, PFMD, the PARADIGM (Patients Active in Research And Dialogues for an Improved Generation of Medicines){10} initiative in Europe, and other organizations committed to furthering patient engagement across the lifecycle of medical product development.{11-14} For example, PFMD has published a series of toolkits, resources, and “how-to” guides for quality and effective patient engagement.{12,13}

**Table 1: Exemplar Models of Patient Engagement with Industry-Sponsored Research**

Method to seek patient input						
	Community Advisory Board	Traditional Patient Advisory Board	Patient Journey Workshops	Individual Interviews	Surveys	
Member Profile	<ul style="list-style-type: none"><li>• n=8-10</li><li>• Variety of conditions within a therapeutic area (e.g., immunology)</li><li>• Experienced patients with advocacy experience and strong community ties</li><li>• Global</li></ul>	<ul style="list-style-type: none"><li>• n=8-10</li><li>• Condition-specific</li><li>• Both naïve and experienced patients may mirror desired population for a proposed trial</li></ul>	<ul style="list-style-type: none"><li>• n=8-10</li><li>• Condition-specific</li><li>• Both naïve and experienced patients may mirror desired population for a proposed trial</li></ul>	<ul style="list-style-type: none"><li>• n=4-15</li><li>• Condition-specific</li><li>• Both naïve and experienced patients may mirror desired population for a proposed trial</li></ul>	<ul style="list-style-type: none"><li>• n=30-100+</li><li>• Condition-specific</li><li>• Responses may be solicited among those who have and/or haven’t participated in a clinical trial</li><li>• Global or region/country-specific</li></ul>	
	Engagement Frequency	<ul style="list-style-type: none"><li>• Engaged routinely in a series of meetings and activities</li><li>• Ongoing resource</li></ul>	<ul style="list-style-type: none"><li>• Typically a one-time meeting</li></ul>	<ul style="list-style-type: none"><li>• Typically a one-time meeting</li></ul>	<ul style="list-style-type: none"><li>• A one-time interview of 60-90 minutes</li></ul>	<ul style="list-style-type: none"><li>• One-time, online, 10-to-15-minute questionnaire</li></ul>
Member Tasks, Activities	<ul style="list-style-type: none"><li>• Advise on universal protocol elements across treatment area portfolio</li><li>• Provide insights on general patient-facing material</li><li>• Contribute input on new patient-centric initiatives</li><li>• Help develop patient engagement best</li></ul>	<ul style="list-style-type: none"><li>• Share specific experiences from being diagnosed with and living with a specific condition</li><li>• Provide thoughts on condition-specific treatments and specific protocol feedback</li></ul>	<ul style="list-style-type: none"><li>• Use hands-on activities (e.g., collages, journey mapping) to explore patient experiences being diagnosed with and living with a condition</li><li>• Brainstorm ideal participation experiences for clinical trials</li></ul>	<ul style="list-style-type: none"><li>• Share individual patient experiences in a 1-on-1 interview setting</li><li>• Provide thoughts on condition-specific treatments and specific protocol feedback</li></ul>	<ul style="list-style-type: none"><li>• Answer specific, focused questions about certain aspects of the patient experience</li><li>• Indicate receptivity to clinical trial participation and protocol design elements</li></ul>	



Key Outcomes	practices and principles					
	<ul style="list-style-type: none"><li>• <b>Best practices for patient engagement</b> across the therapeutic area</li><li>• <b>Strong, established relationships</b> with patients and extended patient communities</li><li>• <b>New, patient-centric initiatives</b> across the larger pharmaceutical organization</li></ul>	<ul style="list-style-type: none"><li>• <b>Deeper understanding of the patient experience living with a particular condition</b> and how that population perceives clinical trials</li><li>• Direct patient feedback on <b>unique elements of a proposed clinical trial</b></li></ul>	<ul style="list-style-type: none"><li>• <b>Deeper understanding of the patient experience living with a particular condition</b> and how that population perceives clinical trials</li><li>• <b>Visual representation</b> of the patient experience and ideal clinical trial journey</li></ul>	<ul style="list-style-type: none"><li>• <b>Deeper understanding of individual patient experiences</b></li><li>• Direct patient feedback on <b>unique elements of a proposed clinical trial</b></li></ul>	<ul style="list-style-type: none"><li>• <b>Surface-level understanding from a larger number of patients</b> of the patient experience</li><li>• <b>Feedback on perceptions, preferences, and receptivity from a larger group of respondents</b></li></ul>	

Among the wide range of available tools and engagement strategies, one approach Janssen utilized was to implement a long-term, recurring global community advisory board. While one-time market research activities such as interviews and surveys can and do yield actionable insights, single touchpoint projects can also limit the amount and type of data obtained and usually solicit patient feedback only on a single protocol. In contrast, the community advisory board model’s long-term focus provides the opportunity to establish a long-term partnership with patients based on trust, knowledge-building, and the reciprocity of true dialogue.

Through the *Patient Voice* in clinical trials program, Janssen routinely obtains patient and caregiver feedback into clinical trial design across all therapeutic areas. Because many learnings apply to more than one clinical trial, and because of a desire to build on insights in an iterative manner, the Janssen Clinical Insights and Experience team collaborated with an independent third party—the nonprofit Center for Information and Study on Clinical Research Participation (CISCRP){ 15}—to create a standing Global Community Advisory Board (GCAB) for the immunology therapeutic area. The GCAB consisted of patient advocates with a variety of immunological conditions. The main objectives of the GCAB were to obtain feedback on strategies and solutions intended for patients, with a primary focus on clinical trial design; establish a strong working relationship between patients and Janssen; establish lines of communication with the broader community of patients with immunologic conditions that Janssen could connect with, both regularly and on an *ad hoc* basis; and ensure that patient-centric practices and principles are incorporated into clinical trials sponsored by Janssen.



This approach to engaging with patients aligns with industry recommendations and frameworks. It was formed to be a standing, long-term advisory panel consisting mainly of patients from around the world, and was facilitated by an independent third party (both CISCRP and Janssen personnel were active panel members). This model focused on the broader therapeutic area of immunology to promote a long-term, more impactful engagement. Thus, the GCAB provided the opportunity to explore a host of questions about Janssen's clinical trials development and engagement strategies with a group of patient advocates in an atmosphere intended to build openness, trust, and mutual respect. The transparency and sense of trust built over time through this model were found to benefit both sides of the patient-sponsor equation.

## **Patients and Methods**

### *Formation of the Immunology GCAB*

Through relationships with patient advocacy groups and its own participant community, CISCRP identified a group of 11 individuals (eight women and three men) with various immunological conditions who expressed a willingness to serve on the GCAB. Some, but not all patients were familiar with the clinical trial process. Because of their experience in community and patient support groups, even GCAB members who were mostly unfamiliar with clinical trials had some knowledge about clinical research. The decision to convene an international advisory board resulted in a population of patient-advocates from seven countries across three global regions: North America (United States), Europe (Czechia, Denmark, Estonia, United Kingdom), and Asia-Pacific (India, Taiwan). Each patient advocate had a keen understanding of the specific challenges of his or her country of origin. CISCRP and Janssen intended for the GCAB to be a standing, long-term advisory panel with greater flexibility than the traditional, single touchpoint patient advisory board model. The Janssen team consisted of members in clinical research and operations roles, as well as members in patient engagement roles. Additional personnel from across the business also joined certain GCAB meetings as needed.

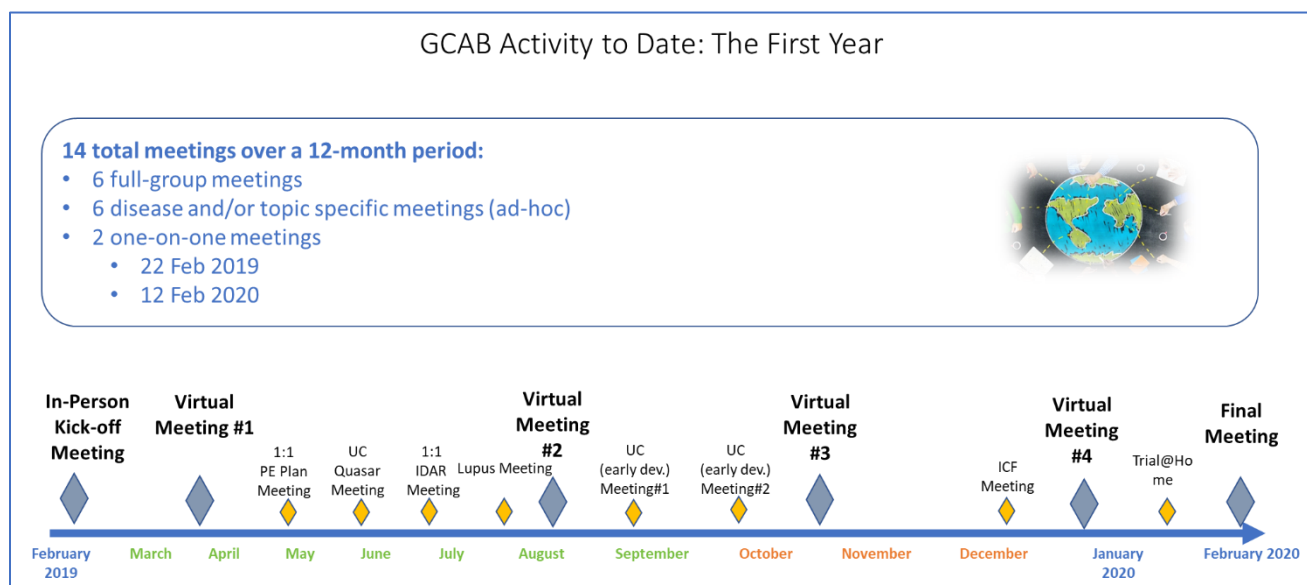
### *GCAB Activities*

Over the course of one year, two in-person GCAB meetings were held: a kick-off meeting in February 2019 and a year-end review meeting in February 2020. In between, there were four

GCAB virtual meetings held via an online platform. GCAB members also engaged in *ad hoc* communications throughout the year, both to provide feedback on questions that arose between meetings and as they desired to support one another.

In addition to the six full-group meetings, a further six virtual condition/topic-specific meetings were held. Furthermore, one-on-one feedback was solicited from GCAB members during in-person meetings (see Figure 1).

**Figure 1: Immunology Global Community Advisory Board (GCAB) Meeting Schedule.**



GCAB members also completed surveys and reflection exercises for Janssen to address areas of interest. These included general questions, such as the perception of clinical trials among patient groups, and specific questions that assessed the effectiveness of trial information materials, receptivity to trial-related technologies, inclusion/exclusion criteria, and planned clinical trial assessments that could increase or decrease participation.

## Results

### *Impact on Janssen Programs*

For Janssen, the opportunity to seek patient feedback on various projects over time resulted in several operational and protocol changes to clinical trial study designs that fulfilled the original aim of the GCAB. The willingness of GCAB members to respond to study materials in conversation with staff and researchers has changed some of the baseline assumptions of the trial design process. This enabled a greater focus on patient-relevant outcomes, which procedures are truly necessary to achieve the desired results, and how to inform and empower patients using materials that respect their experience of living with a condition. The decision to involve patients with a broad range of immunologic conditions—rather than any specific one—presented the opportunity to gather feedback and discuss problems consistently, without the need to pause a trial or to complete work based on a specific protocol’s schedule. This efficiency enabled changes to be implemented as quickly as possible, which further built trust among GCAB members.

Seeking feedback from GCAB members on proposed trials resulted in several straightforward actions intended to increase enrollment and retention. For example, a proposed trial involved regular trial visits for bloodwork and medical photography, as well as required patients to wear an actigraphy device to monitor adherence and physical activity. GCAB members highlighted the time burden involved in short repeat visits to a study site would limit participation by those with unreliable transportation and/or a long travel distance. Numerous concerns also arose regarding the invasiveness of the actigraphy device, as well as regarding data security (the latter particularly from European members). Ultimately, investigators chose to remove these requirements from the study.

### *GCAB Feedback Additionally Supported and Informed Patient Engagement Strategies*

In addition to gathering and acting on clinical trial design feedback, Janssen obtained insights from GCAB members to help shape MyTrialCommunity, a website for engaging with patients enrolled in Janssen clinical trials. Member feedback was integral to the development of this initiative. They recommended the site name and suggested changing logos and adding

testimonial videos from patients to explain the trial process in a non-threatening environment. In one example, a GCAB member shared personal experiences with the life-altering diagnosis of inflammatory bowel disease (IBD), as well as a video from a patient advocacy group about the day-to-day challenges of dealing with IBD. Janssen staff were moved by these patient stories and experiences and appreciated the opportunity for open dialogue about the impact of an IBD diagnosis, as well as the impact of living with the condition on people's lives. The Research and Development team disseminated the video throughout the research group, to drive home the real-world impacts of their work.

### *Trust, Awareness, and Advocacy Strengthened among GCAB Members*

This integration of GCAB feedback led GCAB members to feel empowered and enhanced their engagement in the advisory board process. GCAB members expressed surprise that their input affected the trial design, as some previous patient engagement experiences had not resulted in the same level of transparency and change. As a result, GCAB members reported a resulting sense of empowerment and engagement in the advisory board process, as they could observe the impact of their feedback and how it was genuinely valued.

Overall, GCAB members reported having a positive engagement experience and gaining a greater understanding of clinical trials as well as pharmaceutical companies in general. Before joining the GCAB, some believed clinical trials to be a last-resort option where patients were treated as “just a statistic.” Their perceptions evolved as members learned more about how clinical trials work, the level of effort and care pharmaceutical companies use to implement responsible trials, and the role of clinical trials in finding new treatments for their condition. Thus, GCAB members now understood that not only were clinical trials a viable treatment option for a wide range of patients, but they were an essential component in advancing the causes and objectives of their patient community.

These paradigm shifts among GCAB members highlight the success of the GCAB model in providing a collaborative, supportive environment where GCAB members could become more engaged in and educated about clinical trials. This enhanced the quality and actionability of

insights, as well as greater understanding of things that could not be changed in clinical trial design.

### *Consistent Communication and Transparency are Important*

For many patients with chronic inflammatory conditions, barriers to research can be present from the onset of their condition journey, which can ultimately influence patients' perception and willingness to participate or engage with clinical research. GCAB members reported difficulties obtaining a diagnosis, and once diagnosed, still dealt with feelings of shame and isolation brought on by their symptoms and the knowledge that they may never “get better.”

Outside the United States, patients reported greater difficulty obtaining information about clinical trials. This was particularly the case for smaller European countries without a robust patient organization network. Patients were frustrated by a lack of information about available trials on the part of their physicians and/or a perceived lack of interest from physicians who would not personally participate in the trial. Even when they searched online, barriers to information included a lack of clarity about where trials are available, limited country-specific public information about ongoing clinical trials, and engagement materials being available only in English.

Further barriers included an overuse of technical language by researchers. The era of molecular diagnostics (e.g., biomarkers) and treatment has added new layers of complexity to the research process, and this area of research remains too difficult for many patients to understand. GCAB members requested an in-depth, accessible explanation of what biomarkers are and how targeted therapy works.

A lack of transparency about what data will be collected from patients, how it will be used, and the risks and benefits of experimental interventions was also cited frequently. Long lists of potential adverse events can intimidate potential trial participants, especially when not accompanied by clear explanations of their true risk and prevalence. Further, patients consistently mentioned their discomfort with joining trials where they would never find out the results, whether their own or the overall trial outcomes, including not knowing whether they had been randomized to the active treatment or placebo arm of a study. The need for trial documents

in plain language was another item identified by GCAB patients as an important barrier to overcome in building trust and ensuring patients are truly informed before they consent to clinical trial participation.

### *Meaningful Communication is a Key Component of True Patient Engagement*

Meaningful communication, as identified by the GCAB, was that which either resulted in actionable strategies (e.g., adjusting inclusion/exclusion criteria, changing ads to increase diversity/representation) or clarified the parts of a clinical trial that remain difficult for most patients to understand. One such opportunity is the regulatory and informed consent process—giving patients information about the importance and function of regulatory requirements in place to protect participant safety was repeatedly reported by the patients as increasing their sense of trust as well as their willingness to engage with a lengthy consent process. Additionally, many patients were unaware of the many “moving parts” of a clinical trial that are not patient-facing, so educating patients about the time constraints for things such as data analysis and regulatory approval can increase trust in the timeline of therapeutic development. Ensuring that patients will have access to results of a study—and thus an understanding of how their time and effort contributed to the study—is also advantageous to building trust.

One unexpected outcome of this engagement model was that, by educating and empowering patients, they become more comfortable with and supportive of the clinical trial process in general. Several GCAB members reported that their new understanding of safety measures for Phase I and II trials removed their fear of being “lab rats.”

On the sponsor side, in response to GCAB member feedback, Janssen took steps in several areas. For example, a patient brochure was substantially modified to provide more comprehensive data about the purpose and conduct of clinical trials. A patient testimonial video was also modified to increase a sense of inclusivity by starting with definitive statements instead of questions.

A meeting addressing topics of digital health brought up questions about data collection and security. There was a division between GCAB members on this topic, with European GCAB members expressing greater skepticism about providing digital information about themselves than Asian and U.S. members. In response, Janssen put in place measures to increase

transparency about what trial data would be collected and how the data would be stored and used. Discussion from yet another meeting spurred the development of patient educational materials to more clearly describe the benefits and purpose of early-stage clinical trials and the potential long-term benefits of these trials to patient health.

### *Best Practices and Learnings for Future Engagement Models*

To ensure that meetings were structured, had pre-planned agendas and moderator guides, and were facilitated by an independent third party, Janssen partnered with CISCRP to implement the GCAB model. As a neutral party and liaison between patients and the pharmaceutical company, CISCRP helped establish a baseline of trust for both advisory board members and sponsor personnel. Because of its extensive experience in patient engagement initiatives such as community advisory boards, CISCRP was also able to manage the logistical coordination of GCAB meetings, ensure that the project progressed according to determined timelines, and accommodate GCAB member needs and questions in a timely manner.

Despite favorable responses about the GCAB and the approach taken, there were some limitations reported by GCAB members across several broad categories. These included: respect for patients' time, organization of activities, information overload, burdens to patients caused by holding several meetings, a focus on English language, and a general U.S.-centric focus on materials. Although non-U.S. GCAB members had excellent English-language skills, several non-native speakers expressed discomfort with the speed of presentations, calling for a greater level of comfort with written communication to ensure that non-English native speakers are not excluded or discriminated against. Non-U.S. patients remarked that, especially in smaller countries, pathways to information about clinical trials are lacking. This presents an opportunity to explore enrollment opportunities via non-U.S. patient advocacy and physician networks.

Regardless of language of origin, patients reiterated the need for materials and presentations to be given in plain language and in easily digestible amounts. Adequate discussion was a key factor leading to patient engagement and trust in the process. Patients frequently noted the need to keep meetings—both online and in-person—organized and on a schedule that respected patients' time constraints.

## Discussion

A growing focus on patient-centered outcomes by sponsors and regulatory agencies is an opportunity to establish practices that mutually benefit patients and pharmaceutical companies and other stakeholders. The year-long experience with the GCAB provided rich, actionable insights that could not have been obtained from other stakeholders, and demonstrated that a key component tying the GCAB's feedback together was the sense of trust built by consistent, two-way dialogue.

The opportunities for trust-building among stakeholders occur across the spectrum of clinical research. Education is a foundation of this process—issues surrounding control groups, informed consent, and the potential that results will never be published are sources of potential opacity that can be overcome by presenting clear, patient-focused information.<sup>{16,17}</sup> GCAB members consistently reported that as their knowledge increased over the course of the initiative, so did their sense of engagement, ability to provide relevant feedback, and determination to help their patient and community networks come to a greater understanding of the importance of trial participation.

Two overall themes became clear during the data review of the GCAB's first year in operation. First, patients want more information and transparency. Throughout meeting sessions, patients wanted to know more about the purpose of clinical trials, the thinking behind different trial procedures, data collected, and inclusion/exclusion criteria. They wanted to know that results would be communicated to trial participants, and how their personal information would be used for the purposes of the clinical trial. To this end, Janssen has taken steps, such as creating educational materials about drug-development trials, with the aim of lessening the stigma of these studies as a “last resort.”

GCAB feedback highlights the importance of engaging patients in the clinical trial design process. Effective communication about how patients are centered in the conduct of a study can increase retention through trust and transparency. Patient engagement can allow researchers and sponsors to ask questions such as:



- Are there opportunities to reduce the number of procedures, especially those which are highly burdensome for patients (for example, invasive and painful procedures like biopsies, endoscopies, and blood draws)?
- How can visits and data collection be grouped to minimize travel and time burdens on participants and their support networks?
- Which interventions, either additive (such as patient comfort kits for procedure days) or subtractive (for example, requiring fewer blood draws), have the greatest impact on the participant's trial experience?

These types of practical questions can help researchers design protocols focused on greater efficiency, minimized invasiveness, and respect for the people taking part, while still enabling the collection of necessary evidence. The actions Janssen took in response to GCAB feedback resulted in increased engagement by both research teams and GCAB members.

It is beyond the scope of this article to delve into the financial metrics of this type of partnership, but involving patients as partners is a pragmatic strategy to increase transparency of the research process and overcome disparities in health research.{ 18} Other groups have assessed the financial benefit to sponsors and found significant potential for savings in terms of efficiency and retention.{ 19} One such potential is to troubleshoot trials before they even start. Not only does this potentially increase enrollment and retention, but it can prevent costly protocol amendments. The investment in time and educational materials in this new type of engagement model was well worth the outcomes in terms of engagement and trust.

## Conclusions

A meaningful partnership among the various stakeholders in any clinical trial depends on defining goals, choosing the right partners, and investing the time to ensure that all voices are heard.{ 20} By engaging an advisory board consisting of knowledgeable patient advocates, we were able to present and receive valuable feedback on numerous projects and scenarios, including educational materials, inclusion/exclusion criteria and other protocol elements, and regulatory and consent documents. In doing so, the sponsor received actionable takeaways, which resulted in changes to different elements of several protocols. Engaging a neutral third

party to serve as primary contact for patients, ensure well-planned meeting objectives and agendas, and collate feedback helped achieve quality engagements and effectively summarize feedback.

Further, the opportunity to make changes and demonstrate them to the GCAB was a powerful motivator for Janssen staff and researchers, as was the increased understanding of the real-world, daily experiences of patients living with immunological conditions. Because the GCAB was convened as a long-term advisory body, we were able to demonstrate to GCAB members the actions Janssen took in response to their recommendations. This investment in time and evidence proved to be key in the trust-building process and was cited by all GCAB members as a major factor in their overall positive reaction to this initiative and their views on clinical research in general.

## **Acknowledgements**

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**Annick de Bruin, MBA**, is Senior Director of Research Services, Center for Information and Study on Clinical Research Participation, in Boston, Mass.



**Shalome Sine, MPH**, is Project Manager for Research Services, Center for Information and Study on Clinical Research Participation, in Boston, Mass.



**Lieven Van Vijnckt, PharmD**, works in Investigator and Patient Engagement as TA Head (IMM – ID&V), Janssen Pharmaceutica NV, in Beerse, Belgium.



**Alyson Gregg, MBA**, is Director of Patient Insights, Janssen Pharmaceutical Companies of Johnson & Johnson (Janssen), in Titusville, N.J.



**Catherine Cole** is Program Team Leader for Investigator and Patient Engagement, Janssen Pharmaceutical Companies of Johnson & Johnson (Janssen), in High Wycombe, UK.

GOOD MANAGEMENT PRACTICE

## Build a DCT Ecosystem to Keep Pipelines Flowing Despite Growing Staff Shortages

LaQuinta Jernigan



The so-called “Great Resignation” has compounded staffing challenges in the clinical trials space, hampering the sector’s ability to develop the life-changing new medicines patients are desperately waiting for.

The solution is taking as much pressure off sites as possible.

That means building a robust clinical trials ecosystem that provides consistent access to high-quality healthcare professionals and the most appropriate physical and technological infrastructure, while ensuring that every precious recruit stays engaged, on track, and on protocol throughout the lifecycle of the study.

### Short Staffed

Over the last year, vast swathes of employees have resigned their positions in search of new opportunities and a greater work/life balance. In a trend compounded by the impact of the COVID-19 pandemic, millions have realigned their priorities, with a “if not now, when” attitude. Current figures show 4.5 million people in the United States and 391,000 in the United Kingdom quit their jobs in November 2021 alone.{ 1 }

Dubbed the “Great Resignation” by commentators, the movement has affected all sectors, including clinical trial professionals. In fact, the 2022 Society for Clinical Research Sites [Staff Turnover Survey](#) found the current turnover of patient-facing staff had almost doubled, from up to 37% before the pandemic to up to 61% last year.

Of course, this is not wholly a new problem. As far back as 2016, [a blog](#) submitted to the Association of Clinical Research Professionals was pointing to a “bidding war” for monitors and clinical research associates (CRAs).

This matters to sponsors because staff shortages impact on site effectiveness. Not having the right people in place can delay study start, extend study timelines, and delay approvals. All this costs money and, more importantly, restricts patient access to new medicines.

As such, it makes both business and moral sense for sponsors and contract research organizations (CROs) to do everything in their power to support sites to support their programs.

### **Remote Challenges**

The recent shift from wholly site-based studies to decentralized clinical trials (DCTs) and the hybrid (onsite/offsite) model has been mooted as a solution to many of researchers’ most pressing challenges.

By expanding the pool of eligible participants, the model can increase access and contribute to greater cohort diversity. In addition, by removing the need for frequent site visits, the model can reduce patient burden, boosting recruitment and retention.

For it to work effectively, however, the DCT/hybrid approach must be supported by the right infrastructure, including the right healthcare professionals (HCPs) for remote visits, the right backend systems, and the right patient support.

HCPs conducting home visits need the right skillset, not only in terms of therapy areas and examination experience, but also with regard to interpersonal skills. It is crucial, for example, that people are able to trust the professionals they invite into their homes. This trust then becomes the foundation for the strong rapport necessary to facilitate open and honest conversations about health and wellbeing.

However, high caliber HCPs are in high demand, and many companies are finding it challenging to recruit into the specialist roles needed to conduct clinical research.

It's also important to note that the move from onsite to remote offices and trials is placing additional pressures on site staff.

Despite its many advantages, the DCT/hybrid model brings with it a multitude of additional administrative tasks, such as making payments, liaising with the remote HCPs, and coordinating everything from visits to equipment and supplies procurement and delivery. All this is happening at a time when sites are already short staffed, further contributing to burnout and increasing staff turnover.

The right patient support is also crucial to the success of remote or partially remote clinical trials. One of the oft-cited benefits of DCTs is that they reduce burden on patients, boosting recruitment and retention rates. However, they also have the potential to weaken the all-important relationship between participant and site, meaning sponsors and CROs have to look for alternative engagement strategies.

## **Ecosystem Approach**

Luckily, many commentators and organizations are talking about these issues and high-quality solutions are becoming increasingly available.

In terms of staffing, for example, specialist HCP resourcing agencies can provide a bespoke, fully trained clinical team that meets the needs of the trial and the patient cohort at hand.

Specialist backend solutions can provide the physical and technical infrastructure needed to help reduce pressure on sites. Elements such as visit schedule systems and international distribution center networks, for instance, can make sites more efficient in how they conduct studies on behalf of their sponsor and CRO partners.

Further, we all know that dropouts delay the already lengthy drug development timelines, and that the re-recruitment process is as expensive as it is time-consuming and resource-hungry for site staff. The good news is that concierge-style patient support services, including taxis to and from site visits, automated expense payments, and convenient, tech-enabled communication with



the clinical team, can bridge the gap between site and patient. This helps to drive up engagement, minimizing dropouts.

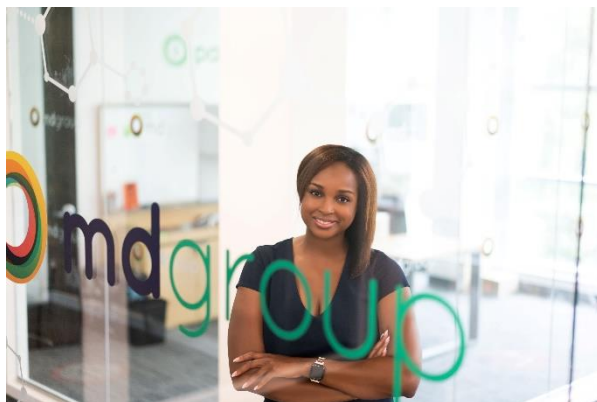
Yet while such approaches hold real efficiency-driving value, sponsors and CROs tend to implement them in a piecemeal fashion. This results in staff being asked to be trained on, and then switch between, multiple systems and interfaces, which only serves to increase pressure on already under resourced sites.

Instead, sponsors and CROs should be thinking systemwide. Using the same trusted partner for all elements of DCT support means all parts of the ecosystem can “talk” to each other. It allows, for example, remote HCPs to communicate directly with distribution centers, and for HCPs to act as a valued liaison between site and patients.

All of this eases burdens on sites, increasing job satisfaction and reducing the sense of being overwhelmed among staff, thus boosting staff retention and, ultimately, making clinical trials run as cost-efficiently as possible.

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**LaQuinta Jernigan** is Chief Operating Officer with **mdgroup**, a global digital and patient health services company that provides a patient-first approach to clinical trial recruitment, retention, diversity, and accessibility. She advocates both at work and outside work for diversity in clinical trials, and is passionate about addressing the many disparities that exist in healthcare for people of color. She previously wrote for *Clinical Researcher* in [December 2021](#).

## **A Life Raft for Clinical Research: How Sponsors, CROs, and Vendors Can Buoy Sites Drowning in DCT Technology**

Mary Costello; Brad Hightower, CCRC



Talk to nearly any clinical research site professional today and you'll likely hear their mounting struggles adopting and managing new technology. Site staff are treading water as wave after wave of technology complexity crash over their heads. They need a life raft before they drown.

While many professionals working in drug development were fortunate to have the option of working remotely during the height of the pandemic, clinical site staff such as healthcare workers were on the front lines. They were the unsung heroes of COVID-19. The unprecedented speed with which COVID vaccines were developed was thanks to the incredible commitment of clinical site teams worldwide—that, and the sudden adoption of a modern clinical research model called decentralized clinical trials (DCTs).

Hybrid (onsite/offsite) and fully remote DCTs have proven to provide reliable options for trials during unprecedented events like a pandemic lockdown, as well as the potential to solve some of the industry's most deep-seated problems. For instance, DCT-related technology can add flexibility, expand access, and even improve population representation. However, as with all major innovations, the industry now faces the challenges of implementation at scale—and clinical research sites are shouldering a disproportionate burden.

The most recent Society for Clinical Research Sites (SCRS) annual survey reveals that technology is adding an average of 17.5 hours in training per study per site per month among the

nearly 500 respondents—one principal investigator (PI) reported having more than 300 unique passwords and logins.{ 1 } Further, PIs aren’t the only ones facing tech-related overload—Hightower Clinical’s clinical research coordinators (CRCs), for example, often must use eight or more systems for each study assigned.

On top of this heavy burden, sites are experiencing a concomitant set of challenges not unlike the rest of the industry. The backdrop of rapid DCT adoption comes at a time when turnover rates for clinical research professionals now [hover around 30%](#) amidst America’s “great resignation.”{ 2 } If the [1.7 million healthcare workers](#) who quit their jobs already in 2022 is any indication, clinical research is also experiencing higher-than-normal turnover as site staff suffer from burnout.{ 3 } Not to mention, sites are operating at ever thinning margins—higher costs coupled with [stagnant study budgets](#) are resulting in less revenue and profit.{ 4 }

All in all, sites are underwater. The DCT model has provided a blueprint for the future, but even as the industry makes progress following that blueprint, it’s time to take a scrupulous look at whether technology is reducing burden or adding to it along the way. As an industry, we must reassess the current state of deployment and intervene to ensure that there is a clear path for sites and all stakeholders to deliver on the promise of modern technology. Here are six ways to buoy sites up, while at the same time improve trials.

## **1. Take time to understand the site perspective.**

Sites have been struggling for years, but these struggles have not resulted in any wholesale change. [Tufts Center for the Study of Drug Development](#) has tracked the rise in trial complexity, which translates into a rise in procedures heaped onto site staff, with Phase II and III protocols now involving an average of 263 procedures per patient supporting approximately 20 endpoints.{ 5 } At the same time, study budgets have largely remained flat. While the industry has invested in capturing the patient perspective, there has been little focus on understanding the potential problems being inadvertently created for sites.

Paradoxically, as the patient’s voice has been amplified, the site’s voice was muted—in the same SCRS survey, one-third (32%) of sites report being treated as “less than a partner” by sponsors and contract research organizations (CROs) over the last two years.{ 1 }

One step industry can take to prevent sites from sinking under this heavy weight is to invest more time to listen carefully to the site leaders and staff who are largely responsible for implementing the technology. They are at the center of the action and have valuable feedback to provide that can help ease technology implementation and speed adoption with less friction for all stakeholders.

Even governing bodies have awoken to this problem, addressing it directly in the first [revision of ICH E8](#) from the International Council for Harmonization since it was adopted in 1997 (in effect as of April 2022). It now encourages engaging with all the stakeholders, including PIs, CRCs, other site staff, and patients/patient organizations.{6}

While gathering this experiential information, sponsors and CROs should look back in history to understand how sites have gotten to this point. For instance, the site community has been rewarded for pinpoint consistency for decades. Suddenly, they are being told to do things in a new way, often without receiving proper education as to how. We need to listen and learn—then re-invent how we support sites’ needs.

## **2. Start, and end, with a site focus group.**

Research needs to be consistent, iterative, and reproducible. In contrast, the varied interpretations of ICH guidelines by sponsors and CROs over-complicate the process that sites must follow.

Sites know their patient populations better than anyone, but are rarely consulted about them before starting a trial. Most sponsors and CROs dictate the patient engagement strategy without ever seeking insights from other sources, even from the professionals who have the greatest knowledge of their patients. Are sponsors and CROs asking sites what flexibility options for patients will have the biggest impact?

Take the time to ask sites what will be most effective. This small, simple step can speed a trial and prevent misstarts. Not only will sites appreciate being asked and treated as a true partner in the trial, but they will also provide sponsors and CROs with valuable information—something everyone needs as we continue learning about the DCT model and its many facets.

**3. Provide the right training at the right time in the right format.** *Hint: it's unlikely to be "one size fits all."*

With increasing amounts of new technology added to studies, sponsors require extra technology training, and that means a bigger time commitment for site personnel. Worse, sites selected for a trial may not discover the extent of the required technical training until it's too late to account for this extra effort in their contract.

An additional challenge is the quality of the required training. Many sponsors and CROs have not taken an inventory of their training modules in years, and often default to online PowerPoint templates. Not only are most training programs limited, but they are also poorly administered online. For instance, a common complaint is for a training course to prematurely "time out" and reset to the beginning if the trainee steps away momentarily. It sounds minor, but it can waste hours of valuable time and frustrate already overwhelmed staff who would better serve the protocol if they were spending that time with patients.

One way to help alleviate this pervasive issue is to provide sites with an overview of all the technologies up front. Clearly outline all the systems that will be (or could be) involved in the trial, when they will be used, and how they all fit together in alignment with the protocol. Provide a concise, flow chart-style resource so site managers can budget the time and costs for the extra training from the start—preventing underestimations of timelines and ensuring they are rightfully compensated.

This "tech cheat sheet" could be made available in any number of formats—from a one-page printed piece to an interactive webpage that also includes a one-click "help" button and diagrams. Providing sites with an informative resource that offers both a holistic view and a drilled down explanation not only lessens the training burden, but also reduces the number of calls back to the sponsor's help desk.

#### **4. Provide a single sign-on.**

Sponsors need to find a way to seamlessly integrate platforms on the back end so that users like CRCs can simply log in to their desktops or devices with a single sign-on and access all the information they need via one interface. Enough said.

#### **5. Invest in a trial site liaison.**

One of the more interesting approaches some sponsors have taken to improve site partnerships has been to provide a bonus resource—a personal site liaison—to site staff in addition to the standard clinical research associate (CRA). This liaison is deeply trained in the individual protocol, and therefore can provide reliable, full-bodied answers to more specific questions both technology-related and protocol-related. Rather than being a third party tied to specific sites, liaisons can be implemented with a broader regional responsibility. Early reviews from sites of this investment have been very positive.

While CRAs also act as internal problem solvers, they don't always have a holistic view of trial execution or know how all the technologies connect. A site liaison could augment the role of the CRA and personally partner with site staff as a respected colleague, checking in weekly to provide more collaborative support. Technology providers, too, could work closely with a site liaison to help facilitate change management and user adoption of new systems.

Hightower Clinical, for instance, worked with a small sponsor that supplemented its CRA with a dedicated liaison who understood every aspect of the trial, including the technologies, and was very effective. In turn, the liaison listened to the site's ongoing feedback leading to a high-performance trial.

Alternatively, sponsors could provide extra technology training to CRAs, or even a select subset of technology specialist CRAs, so they are well versed in the technology included in a study and can provide faster and more comprehensive site support. CRAs are often the first point of help for sites, so creating a reliable framework within which site teams can consolidate their questions and funnel them to a single point of contact is extremely efficient, when it works.

## **6. Offer optionality for sites as well as patients.**

When designing the study itself, consider how much can be performed by the site. Often, sponsors work with the same site for multiple trials and have come to trust and rely on them for their high-quality work. Out of respect for that relationship, consider the damage that could be done by outsourcing a part of the trial to a third party and diverting funds from your long-time site partner.

Before implementing a study-wide solution using a third-party provider, ask whether the site would be willing to undertake responsibility for some of the challenges at hand, such as home healthcare and direct-to-patient drug deliveries, and if standard operating procedures already exist to support those tasks. If sponsors or CROs are concerned that the necessary skill sets do not exist uniformly across sites, would they be willing to give support or an upskilling program for key sites to allow them the chance to retain revenue, gain new capabilities, and retain tighter oversight? What, too, are the legal, insurance, and oversight considerations with a third-party vendor? How can sites be expected to retain control?

Remember if the site isn't doing a task, it isn't getting paid. Asking sites to handle trials with shifting parameters is not only disrespectful, but also cuts the sites out of the equation. Many clinical sites function on 90 days of operating cash or less. Consider the impact of moving the tasks to a separate organization—not just on the patient, but also on the site.

### **Show Respect, Offer a Life Raft...and Reap DCTs' Great Promise**

Drug development is part of a complex ecosystem; consequently, implementing any major innovation industrywide will take time and creative execution to perfect. Open dialogue and ongoing feedback are crucial to ensuring the innovation reaches its potential.

DCTs hold great promise, but to maximize their benefits the industry must identify its pain points for all stakeholders, especially sites that are on the front lines of research and working directly with patients. Sponsors, technology providers, and patients most of all have the most to gain from DCTs, so it behooves us to formalize tactics for helping sites evolve in a way that honors their efforts both financially and intellectually.

We cannot let sites drown under each wave of new technology. The organizations that invest the time and resources to ease this transition to the modern clinical trial model will see the greatest success.

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**Mary Costello** ([mary.costello@medable.com](mailto:mary.costello@medable.com)) spent more than 30 years in leadership roles in the healthcare and clinical research fields with large organizations such as Covance and Thermo Fisher, and, more recently, with eClinical Solutions and Elligo Health Research. Costello is a founder and board member of BioAustin. At Medable, she serves as Head of the Site and Investigator Network.



**Brad Hightower**, CCRC, has worked with clinical research sites for almost 15 years and is the former Executive Director of the Oklahoma Heart Hospital Research Foundation. Most recently, he founded the integrated site network, Hightower Clinical, and hosts the *Note to File* podcast on clinical research site topics.



ETHICS IN ACTION

## Finding Ways to Alleviate the Impact of War on Patients and Clinical Research

Thomas Dobmeyer, MD



After nearly six months of war, life for patients in Ukraine continues to get harder. The World Health Organization (WHO) has reported that people's health has been imperiled by difficulty in accessing emergency care and essential medicines.

Dr. Hans Henri P. Kluge, WHO Regional Director for Europe, [noted](#) that there had been more than 260 verified attacks on healthcare in Ukraine by early June, resulting in some health facilities being destroyed and others struggling to cope with

people seeking care from trauma and injuries.

The war has also made it extremely difficult for patients with chronic conditions, such as diabetes, to access the medicines they require. While pharmaceutical companies remain committed to ensuring patients everywhere receive life-saving products, some pharmaceutical companies [have suspended operations](#) in Russia for non-essential medications, which has the potential to further exacerbate supply chain bottlenecks.

Manufacturing and the supply of finished medicines, as well as raw materials in the region, have also been severely affected. Many insurance companies implemented tougher requirements to cover Ukraine supply contracts, which restricted cooperation with international suppliers. Fortunately, local manufacturers been able to use their expertise to step in and negotiate new terms to ensure the supply of active pharmaceutical ingredients, excipients, packaging materials, and other raw materials. However, managing the supply routes of medicines and raw materials in Ukraine has been challenging due to ongoing attacks and the closure of airports and seaports. In response, suppliers have had to quickly adjust routes.

## Effects on Clinical Trials

Further, the war has stopped many clinical trials in the region, with GlobalData's Clinical Trials Database [claiming](#) that by April, eight Phase II and Phase III trials had been disrupted and another eight trials were in jeopardy as sponsors were forced to suspend enrollment in Russia and Ukraine.

The impact is likely to be more extensive, with the U.S. Food and Drug Administration [noting](#) that around 250 drugs and devices were undergoing clinical trials in Ukraine. Trials in Russia [have also been impacted](#), with Moscow State Medical University noting that international pharmaceutical companies have halted recruitment of new patients to its 120 ongoing trials.

## Mitigating the Harm of War on Patients

There are steps that compassionate leaders within sponsors, contract research organizations, and study sites can take to ease this crisis with clinical trials and, wherever possible, ensure patients keep participating. A priority should be to maintain ongoing follow-up with patients and doctors involved in the trials, do what they can to track where patients are located, and, where possible, enable them to continue to participate in other parts of the world.

Clinical trial data should also be accessible via online channels, from when treatment starts to when it is completed, while of course doing whatever is needed to prevent unblinding of participants. To achieve that objective, companies should put in place processes to safeguard those data, such as implementing data provenance, data privacy, traceability, and auditability. Another important step will be to provide emergency contact details to patients who have been displaced by the war so they can get the care they need.

Experiences from previous wars offer examples of mitigation steps that can help to ensure patients get the care they need. However, the most valuable lessons may be from the COVID-19 pandemic, which required companies to quickly pivot in order to ensure business continuity. In particular, technology and digital enablement came to the fore during the pandemic. Clinical trials are becoming increasingly decentralized and healthcare providers are turning more and more to telehealth or digital health to connect with patients.

These innovative processes are now being used to provide virtual care to patients in need. As an example, the nonprofit organization [Health Tech Without Borders](#) (HTWB) was founded in 2022 in response to the war in Ukraine and acts as a hub to connect digital innovation with medical care. HTWB's Ukraine Telehealth Relief aims to help hospitals cope with the rapid increase in patients, provide psychological help to those affected by the conflict, and support Ukrainian refugees across Europe.

## **Taking a Stand**

As providers and consultants in the healthcare industry, we are committed to using our expertise to help pharmaceutical clients, for example through the establishment of a network, or advisory alliance. This alliance is working across the industry and with nongovernment organizations and healthcare providers to identify unmet needs, urgent priorities, and vital solutions and recommendations to support patients in impacted regions.

Among the steps we have been taking internally is outreach to colleagues who have been affected, ensuring they are protected and giving them the flexibility that they might need to do their jobs. We are both proud and supportive of our colleagues in Poland and Ukraine who are doing what they can to support refugees and provide humanitarian aid. For example, many of our staff members in Poland are hosting Ukrainian families. Money raised by colleagues globally has been used to ensure refugees are properly fed, but also to bring some joy to children affected by war, such as with a trip to the zoo.

For all of us in healthcare and the life sciences, mitigating the suffering of patients has to remain our primary concern.



**Thomas Dobmeyer, MD**, is CEO of PharmaLex, with more than 20 years of experience in late-stage clinical development, medical affairs, and pharmacovigilance for a variety of therapeutic areas. He is a physician by training, as well as a researcher and investigator in immunology, haematology, and infectious diseases.

NEW E-R-A IN PROJECT MANAGEMENT

## **Leading Intelligently with Heart: Emotional Intelligence as a Key Differentiator for Outstanding Leadership by Female Project Managers**

Zoran M. Pavlovic, MD



In 2016, a report from the Davos International Economic Forum on “The Future of Jobs” identified emotional intelligence (EI) as the essential and vital leadership attribute within the “soft skill” armamentarium. {1} The next report from 2018 on reskilling in the workplace stated that by 2022, no less than 54% of all employees would require significant re- and upskilling. Of these, about 35% were expected to require additional training of up to six months, 9% would require reskilling lasting six to 12 months, and 10% would require additional skills

training of more than a year. {2} According to this report, skills continuing to grow in prominence by 2022 were EI, leadership competence, social influence, and service orientation. In the latest “The Future of Jobs” survey from 2020, EI is ranked among the top 15 skills for 2025. {3}

### **EI and Leading Remotely in a Time of Crisis**

New research from The University of Toledo by Professor Wittmer and Hopkins conducted during the pandemic and published in a special issue of the *Journal of Leadership and Organizational Studies*, found that individuals with higher levels of EI experienced lower levels of concern for leading remotely during the crisis. At the time of the survey, 82% reported that their current leadership was 100% remote, and 85% of them stated that during the COVID-19 pandemic was the first time they led remotely. The capacity to understand oneself and regulate one's emotions, as judged by the self-perception and stress management scales of EI, were the two most important components contributing to leading remotely in a crisis. {4}

## **EI Definitions**

In 1990, Mayer and Salovey defined EI as “organized responses inter-linked with many peripheral psychological systems, including physiological, knowledge, motivation and trial systems.”{5} In 1993, the two researchers expanded their definition of EI and considered it “a form of social intelligence which includes the ability to perceive the emotions of the individual and others, to distinguish between them, and to use the emotional information to direct the thinking and actions of the individual.”{6} In 1997, Mayer, Caruso, and Salovey proposed a new definition that “EI indicates the ability to recognize the meanings of the emotional patterns, and cognitive analysis of this based on which problems are then solved.”{7}

In 1995, Goleman described EI as a set of abilities and competencies that enable an individual to detect their own and other people’s feelings, as well as to motivate themselves, control their emotions, and effectively manage their relationships with others. These competencies and skills include five areas: self-awareness, management of emotions, self-motivation, empathy, and dealing with others or social skills. He explained each of these five categories and believed self-awareness to be the key to EI since it is tied to emotional understanding.{8}

In 2017, Allothman stated that EI is “the ability to be aware and note emotions and own feelings, to understand and be able to clearly articulate these feelings, and to regulate these feelings based on observation and a good awareness of the emotions and feelings of others, to be able to engage with them in positive social and emotional relationships which would enhance individual’s capacity for mental, emotional and professional development, and to acquire an increasing amount of positive life skills.”{9}

Meanwhile, in 2007, Semadoni argued that EI is a type of social intelligence that represents the capacity to comprehend one's own inner emotions and sensations as well as the emotional states of others,{10} and in 2003, Nasif presented three frameworks within which most of the EI theories converge.{11}

## EI Models

Four EI models currently dominate the scientific field of emotion perception and regulation. The first, from 1988, is Bar-On's model of what he calls "emotional and social intelligence."

According to his research, these personal attributes include the ability to be aware of, comprehend, and express oneself; the ability to be aware of, understand, and relate to others; the ability to deal with strong emotions and control one's impulses; and the ability to adapt to change and to solve problems of a personal or social nature.{ 12 }

Another major EI model is based on the 1997 work of Mayer, Salovey, and Caruso.{ 7 } They see their model as a "mental ability" or "information-processing" approach, and measurements based on it have a higher correlation with cognitive ability tests than with personality tests. The four components (or branches) of their model are: the ability to perceive emotions, the ability to use emotions to facilitate thought, the ability to understand emotions, and the ability to manage emotions.

A third model is based on the 2004 work of Boyatzis and Sala.{ 13 } Although their approach was influenced by the earlier work of Mayer, Salovey, and Caruso, it was meant to include the social and emotional abilities associated with great job performance. The model consists of numerous specific competencies organized into four basic clusters: self-awareness, self-management, social awareness, and relationship management.

The most recent model to emerge comes from work in 2007 by Petrides, Pita, and Kokkinaki, and is known as "trait EI." { 14 } This model might be called second-generation because it integrates many of the personal characteristics seen in earlier generations. It is based on a content analysis of early EI measures and is meant to include all "personality facets that are specifically related to affect." The model consists of four components: well-being (which includes self-confidence, happiness, and optimism), sociability (social competence, assertiveness, and emotion management of others), self-control (stress management, emotion regulation, and low impulsiveness), and emotionality (emotional perception of self and others, emotion expression, and empathy).

## **EI and Gender**

According to the Athena Doctrine, our future is female (or should be female), and the worldwide consistent beliefs we have toward what is called “feminine” features are the ones that will promote economic development and sustainability in the 21st century. We live in a more social, interconnected, and transparent society, and feminine values are thriving. Powered by, among other things, collaboration, communication, nurturing, and inclusivity, it appears that institutions, corporations, and individuals are breaking free from traditional male structures and mindsets to become more flexible, collaborative, and compassionate, as noted by Gerzema and D’Antonio in 2013.{15}

In 2011, Broadbridge and Simpson proposed that the “future is female,” indicating that EI can be a key differentiator of the individual to distinguish his/her effectiveness in the implementation of important human abilities or behaviors during the various phases of the project.{16} The comparison of masculine and feminine features (emotional control, rational, quantifiable use of emotions for performance, talking about emotion, empathy, and caring) reveals sociologically established and biased gender-linked disparities.

With empathy, collaboration, conscientiousness, reliability, patience, and honesty skewing toward women and high emotional quotient, a change toward a more “feminine” leadership style may be on the horizon, and it may be just what our future workforce needs to flourish and prosper in our ever-changing world. Just as one consideration, females are more adept in guiding and managing emotions, both their own and those of others. They also occasionally outperform males in emotional attentiveness and empathy, although males outperform females in emotion control, according to 2006 studies by Bindu and Thomas and by Goldenberg, Matheson, and Mantler.{17}

## **EI and Project Success**

Over the last two decades, the “human face” of project management has become widely recognized as a vital component of the project manager’s (PM) position linked with success, as noted by Cooke-Davies in 2002.{18} According to Keeling et Branco in 2012, to succeed in the projects, the PM, in addition to having a good understanding and skills in applying tools and

management techniques, must have personal skills.{19} These refer to management and interpersonal skills (i.e., the ability to lead and communicate with project stakeholders). The PM must have specific personal characteristics such as courage, steadfastness, tenacity, self-respect, and the ability to deal with one's own emotions and those of his/her colleagues, thus creating a more productive working environment.

In 2008, Rudolph et al. reported that the behavioral component of project management, which includes communication, engagement, motivation, and conflict detection, is crucial to project success.{20} Along the same lines, Druskat et Druskat in 2006 suggested that the concept of EI can be a key differentiator for the individual to distinguish his/her effectiveness in the implementation of important human abilities or behaviors during the various phases of the project.{21} In the same context, Mersino in 2009 reported that this kind of intelligence can assist the PM in the development of one's relations with stakeholders, the anticipation of eventual interpersonal conflicts, increasing his/her assertiveness in making decisions and effective communication, and facilitating team engagement to fulfill the promised scope of the project.{22}

In 2011, Davis showed that EI can help PMs to assume leadership roles, causing them to act efficiently by, for example, performing feedback through constructive criticism, allowing the development of the team members, dealing with negative behaviors, and effectively understanding communications and accountabilities of all stakeholders.{23} Finally, an accurate understanding of what motivates team members by the PM facilitates the process of their redirection toward the achievement of the project objectives, according to Oliveira in 2011.{24}

According to the PMI Survey from 2012 overall, 93% of the professional agree that EI impact the success of the project; 56% agreed with the statement that the emotions, present in routine work, when unrecognized or poorly managed directly impact the outcome of the project; 68% felt it is important to understand the emotions of those involved and this helps to manage the project to success.{25} Also in this line, 78% believe that keeping the positive emotional climate of the team also contributes to the project's success. Mount in 2006 assessed the skills related to the success of PMs in 74 international petroleum corporations and found that, of all the skills that contributed to PM's success, 69% were the emotional competencies (self-confidence, influence,



achievement orientation, teamwork, and coordination); 31% were business expertise, whereas there was none (0%) in the area of cognitive skills, such as conceptual or analytical thinking.{26}

Based on the findings of a variety of studies, it has become clear that personality and organizational culture influence the way the PM conducts the project because their EI allows self-knowledge, which is dependent on the personal characteristics of each PM and determines his/her way of leading and managing people. It is understood that everything starts with “knowing yourself” to be able to understand the aspirations and achievements of others and lead them in achieving common goals, thus satisfying the goals and corporate strategies.

Another highlighted issue is the level of emotional involvement that the PM should have with the project. Sharing of existing problems with team members should be dosed just to be enough to motivate them. Experienced PMs have greater discernment between one’s feelings and those of their team members, thereby demonstrating an equalization of thought and conduct related to a certain project activity.

### **Transformational Leadership**

Transformational leadership (TL) is characterized as one that raises collective awareness and interests, builds group and individual confidence, and strives to focus subordinates' priorities on development and success rather than simply survival, according to Gardner and Stough in 2002.{27} In their 2000 study, Barling, Slater, and Kelloway examined the EI and leadership styles of 49 PMs.{28} They found that EI highly correlated with TL, with the highest correlation being between inspirational motivation (a component of TL) and EI.

Gardner and Stough investigated whether EI predicted the leadership styles of 110 senior-level managers and found a strong correlation between TL style and EI.{27} Further, Leban and Zulauf in 2004 reported on their study of 24 PMs and their related projects in six different organizations from varying industries to examine the relationship between leadership in projects and EI. They found that EI scores and the ability to understand emotions were found in significant relation to inspirational motivation (a dimension of TL).{29} They concluded that a

PM's TL behavior has a positive impact on project performance; in other words, EI abilities contribute to a PM's TL and subsequent actual project performance.

According to research, the rise of feminization in the workplace has impacted an increase in the desire for “feminine” attributes in employees and leaders, such as warmth, connection, openness, and empathy, wrote Thory in 2012.{30} These characteristics are associated with TL, focus on interpersonal relations, and work satisfaction from interpersonal warmth, which are more likely associated with female leaders. TL is preferred over transactional and *laissez-faire* leadership in our modern economy due to its emphasis on “high organizational involvement” that focuses on open communication channels and decentralized management, which is seen as more democratic and customer-centric. Therefore, female leaders are considered more transformational than male leaders, noted Powell and Butterfield in 2011.{31}

### **Can We Train EI?**

One of the more appealing theories in the EI training approach is that the observed EI-related gains after training reflect the plasticity in the cognitive-neural system underpinning EI. The evidence for this came from neuroimaging studies of EI by Krueger et al. in 2009{32} and Barbey et al. in 2014.{33}

It appears that, to increase knowledge transfer regarding emotional concepts, moods, and social expressions, the training content should be provided and practiced over multiple spaced sessions. Kotsou et al. in 2019{34} and Hodzic et al. in 2018{35} reported on data indicating that EI could be improved through training and that one possible reason is that the neuro-cognitive system supporting EI is malleable to a considerable degree.

### **EI Training for Female PMs**

A study of South African Women Leaders from 2017 by Mayer et al. showed that women leaders need to improve their awareness of emotional quotient dimensions related to independence, stress tolerance, flexibility, and optimism. They should also explore the importance of these functions on a deeper level, as they might strengthen their independence in

decision-making and networking, increase levels of stress tolerance, and enhance flexibility to plan and organize their working and private lives.{36}

Findings by Nicholas Clarke in 2010 suggest that EI ability related to understanding emotions can be developed in PMs as a result of a two-day training intervention.{37} The study also found statistically significant improvements in the self-assessed project management competencies of teamwork and managing conflict. The ability to understand emotions enables individuals to identify what circumstances cause different emotional responses and how more simple emotions blend to cause more complex emotional states. This knowledge is thought to be important in enabling individuals to understand why they may be experiencing particular feelings, which is a prerequisite for considering how these feelings are best managed or controlled.

Understanding how events in projects can trigger specific emotional responses that then impact performance can assist PMs in planning, setting, and communicating tasks, Jordan et al. noted in 2002.{38} Knowledge of how different emotions are generated and how they can influence attitudes and behaviors is also likely to offer PMs distinct advantages within contexts where they are dependent on building commitment and trust rapidly for individuals to work effectively together within projects, reported Burgess and Turner{39} as well as Hartman in 2000.{40}

Beyond project effectiveness, it would seem likely that there may well be other major gains that could be made from PMs attending EI training, in terms of wider health and well-being aspects, as the improvements in self- and social awareness abilities may moderate the levels of emotional distress that PMs are experiencing. The findings from Clarke's study suggest that, certainly as far as developing the EI ability of understanding emotions, organizations wishing to develop this particular EI competence of their PMs might achieve similar positive results if they adopt the following strategies when designing the training program:{37}

- Taking advantage of opportunities for participating in structured practice sessions that require participants to consider how emotional abilities may be used in their roles as PMs.
- Practicing EI-associated behaviors and then receiving feedback.
- Observing others during role plays and simulations.

Clarke also suggested that initial improvement in EI abilities is unlikely to be achieved within short periods after the training, and that findings from the few empirical studies to date point to periods of two months or more as being necessary.{37} The results indicate then that the impact of training on this ability is unlikely to be seen immediately, requiring some months before any improvements can be detected. This suggests that, although training can provide an initial self-awareness of the importance of emotions, the actual processes associated with the development of this EI ability continue taking place after training, possibly through on-the-job learning mechanisms.

### **Calculate Your Leadership EI**

A self-assessment questionnaire designed to measure the various aspects of EI associated with your leadership competencies [is available here](#) from the National Health Service in the United Kingdom.{41}

*In the next issue of Clinical Researcher, we will focus on daily practices that you can use to self-improve your EI in the long-term, so stay tuned for more information on this vital soft skills topic.*

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## Key Takeaways

- EI is ranked among the top 15 skills for 2025 by the World Economic Forum.
- EI is a key differentiator and predictor of a PM's effectiveness and one of the main components associated with project success.
- Attributes with strong links to TL, success, pleasure, and morality which are considered primarily “feminine” are also traits associated with high emotional quotient.
- Female PMs are more interested and motivated for EI training than males, as they typically underestimate their current emotional quotient skills.
- EI training for female PMs should focus on improvement of their inherently less developed EI competencies, which include self-perception (self-regard), self-expression (independence), emotion regulation, and stress management (stress tolerance) skills.



**Zoran M. Pavlovic, MD,** ([heruka.innovations@gmail.com](mailto:heruka.innovations@gmail.com)) is a psychiatrist, psychotherapist, and executive coach for life science leaders on agile, entrepreneurial, and mindful leadership with Heruka Lifescience and Health Innovations. He is also a creator of 4-H SWELL (States of Wellness) Leader and Employee® Self-Care and HELO (Heruka Employee, Leader and Organization) Resilience™ training.

**ON THE JOB**

**Site Origins and the Joy of Self-Promotion**

Elizabeth Weeks-Rowe, LVN, CCRA



Investigational site models are as diverse as the infrastructure and personnel that embody their missions. Yet, they all share a compelling origin story; the seedling idea, steps, and struggles that wrought their inception to this field. The story of how an inspired individual or an entire investigational team worked to create a research company/site and overcome the challenges involved (finances, staffing, strategic relationships, logistics) provides insight into their sustainability, and sometimes, success. The most

memorable stories do not necessarily involve extraordinary physician/entrepreneurs, but regular individuals with an extraordinary passion for clinical research.

In the following real-world stories of a few such individuals, the workplace details are accurate, but their names have been changed to protect their privacy.

**From Study Coordinator to Research Company Owner**

Several years ago, I was tasked to evaluate an investigational site for a diabetes study. The feasibility questionnaire identified the site's principal investigator (PI) as an internal medicine physician, and as a PI with a research department in their medical practice was a common site model, I assumed the study coordinators worked for the PI.

The site evaluation visit was quickly scheduled by a responsive coordinator and I was looking forward to the assessment process. The day of the visit arrived, and as the receptionist escorted



me to the coordinator's work area, I noted the research area shared space with the PI's main clinic area. However, in speaking with the coordinator I discovered how wrong I had been with my initial presumption; the research site may have been in the PI's practice, but the coordinators absolutely did not work for the PI. Rather, the primary coordinator owned the research company with which investigators contracted to conduct their clinical trials. That provided just a hint as to how inspirational the company's origin story was when I heard all the details.

Linda, the primary study coordinator/owner, had worked at a dedicated research site for many years. During her tenure she had become close friends with another coordinator named Mary. They were both medical assistants by training, extensively experienced with the clinical responsibilities of the study coordinator role. They also developed research administrative skills with their involvement in contracts/budgets while working at the research site.

Eventually, the site was purchased by a large healthcare organization and the mission changed with the ownership. There was much more emphasis placed on financial incentives/study acquisition than patient safety/credible data, and the change made Linda vastly uncomfortable. She had entered the field of clinical research to participate in drug development, which included upholding those critical tenets. She could no longer work for an institutional model that did not align with her convictions, and thus the idea for her company began.

Linda had met several coordinators/site owners at investigator meetings over the years, but did not have the first idea about how to go about forming a research company. She spent a year researching and preparing for the change. She spoke with banks about small business loans and research financing. She spoke with attorneys about clinical trial agreements and budgets. She had always performed well on her studies and maintained strong relationships with her monitors, so the critical relationships required for study leads were established.

She then began to reconnect with previous investigators with whom she had worked for the possibility of partnerships. She knew she could not afford to lease the appropriate working space, so she decided the best option would be to lease space in an investigator's already-established practice. Through networking she was ultimately connected to an experienced sub-investigator

with extra clinic space, and who was looking to move into the PI role. He provided infrastructure and she provided knowledge, personnel, and trial contracts.

When all the required financial, clinical, and logistical components were in place—and especially once the partners had secured their first potential study—Linda gave notice at the site she had come to feel out of place at and never looked back.

It had been a daunting process of balancing the books to ensure their seed money lasted long enough for them to begin qualifying for studies that would keep the bills paid after the early funding ran out. Though the struggle was sometimes nearly overwhelming, she persevered until they were profitable, and they were able to hire a second coordinator, her friend Mary.

Linda never dreamed that her commitment to research integrity would lead her to site ownership and the discretion to make the kinds of decisions that would truly serve the best interests of her patients.

### **Finance Guy Becomes Research Director**

Approximately two years ago I was involved with site selection for a cardiology study and was asked to conduct an evaluation visit in Southern Florida. The site was added at the last minute due to its extreme persistence and the sponsor's need for investigators with access to the unique population of patients available in that area. The potential cardiologist PI was new to clinical research, but had a large patient database and was working with a dedicated research site.

The research site director had doggedly pursued the study lead until the sponsor yielded (it was typically hesitant about any new investigator) and allowed the evaluation visit. An inexperienced investigator required a more complex assessment process, so I made sure I was adequately prepared.

When I arrived at the site, the research director met me in the lobby and introduced himself as David. The research site was adjacent to a clinic that David explained was the medical practice of his business partner, Michael, who was a primary care physician and experienced PI.

Michael and David co-owned the research site, and had been acquainted with one another long before striking up the business partnership—since high school, in fact. David was refreshingly transparent as he explained the story of their collaboration, noting how Michael was a primary care physician and an experienced investigator, having served as a sub-investigator on other cardiology studies (which lent credibility to their idea that Michael would support the new cardiologist investigator they had enlisted to serve as a potential PI on the cardiology study for which they were being evaluated). In earlier days, they had often discussed starting a business, but as they grew older so did the gap in their career interests, leaving the idea of a shared business adrift for the time being.

While David pursued a business degree and worked in finance, Michael attended medical school and started a thriving medical practice. They corresponded by e-mail, but had not spoken in several years until Michael contacted David about starting a clinical research site—he had the clinical experience, but needed David’s business and legal acumen for the research site administration. David had never let go of the idea of starting his own business, but had not found a business model that piqued his interest until Michael contacted him, so their childhood dream finally moved forward to fruition.

They secured financing from personal and family investments. They leased additional space next to Michael’s practice and organized their site. David learned all aspects of clinical research administration while hiring two experienced study coordinators and a research assistant. It took almost six months to obtain and start their first study, and my evaluation visit was for what would only be their second study.

David was extremely enthusiastic and determined to succeed, which was evident in his presentation to me. Before I opened my laptop, he provided me a notebook filled with staff training certificates and site standard operating procedures. They had given their chosen PI for the new study additional regulatory guidances to review in preparation for the investigator role. David explained that Michael was going to be a sub-investigator and work with the PI on the first several screening visits to assure his familiarity and compliance.

Their study coordinators were adequately experienced, and their site was organized and well equipped. Their PI was professional and came prepared to discuss the protocol design as well as his access to the study population. They had completed due diligence in preparing for the evaluation visit and the various support methods to accommodate their new investigator. They had worked tirelessly to open their site and the diligence continued in the preparatory efforts to obtain studies.

## Conclusion

These stories serve as just two examples of how research sites might spring to life and how, sometimes, it takes promoting yourself into a new position to get the job done. They also go to show how successful research partnerships start where science and business intersect for ethical study conduct.



**Elizabeth Weeks-Rowe, LVN, CCRA,** ([elizabethwrowe@gmail.com](mailto:elizabethwrowe@gmail.com)) is a former clinical research coordinator who now works in site selection and education in the contract research organization industry. She last wrote for *Clinical Researcher* in December 2021 (“[A Chance Encounter: When CRAs and Study Patients Meet](#)”).

POLICY & PROCEDURE

## Highlighting the Growing Importance of Institutional Biosafety Committees in Clinical Research

Daniel Kavanagh, PhD, RAC



Institutional biosafety committees (IBCs) play a critical role in ensuring the safe and responsible conduct of research involving genetically modified products, infectious agents, and biological toxins. For clinical research involving genetically engineered products, IBCs review protocols and procedures to minimize risks to clinical staff, visitors, the general public, and the environment. In doing so, IBCs enhance and promote clinical research and scientific discovery.

Many aspects of human health and disease are controlled by information encoded in our DNA. To make proteins—the building blocks of cells, tissues, and organs—information from the genetic code is transcribed from DNA into mRNA and translated from mRNA in proteins. Chemically, DNA and RNA are classified as nucleic acids. With modern synthetic technology it is relatively straightforward to synthesize nucleic acids encoding any desired sequence and programmed to alter biological functions. Genetically engineered nucleic acids are being incorporated into an increasing array of medical products designed to treat or prevent disease.

The promise of genetic engineering and synthetic biology has already been demonstrated by more than a dozen gene transfer products—including biologic drugs and vaccines—that have U.S. Food and Drug Administration (FDA) marketing approval. These include cancer-curing chimeric antigen receptor T cell (CAR-T) therapies and mRNA vaccines to prevent infectious disease, among others.

For many of these products, the genetically modified components only persist for a short time in the human body. However, some gene transfer products have a built-in capacity to *replicate* themselves in a human research participant, and some gene transfer products have the capacity to *integrate* into chromosomes and make permanent changes in the DNA of affected cells. In some cases, the gene transfer products are living microbes derived from naturally occurring infectious agents.

Assessing potential risks associated with various genetically modified products requires expert knowledge of microbiology, molecular biology, environmental health and safety, and related disciplines. Biosafety is the field of practice dedicated to managing the risks of accidental exposure to genetically modified products and infectious agents in clinical and nonclinical research.

To promote proper oversight of research with genetically modified products, the National Institutes of Health (NIH) published the first version of the current *NIH Guidelines for Research Involving Recombinant and Synthetic Nucleic Acids (NIH Guidelines)*{1} in 1976, which include instructions defining the purpose, responsibilities, and composition of IBCs. Clinical research subject to the *NIH Guidelines* must be approved by an IBC prior to initiation.

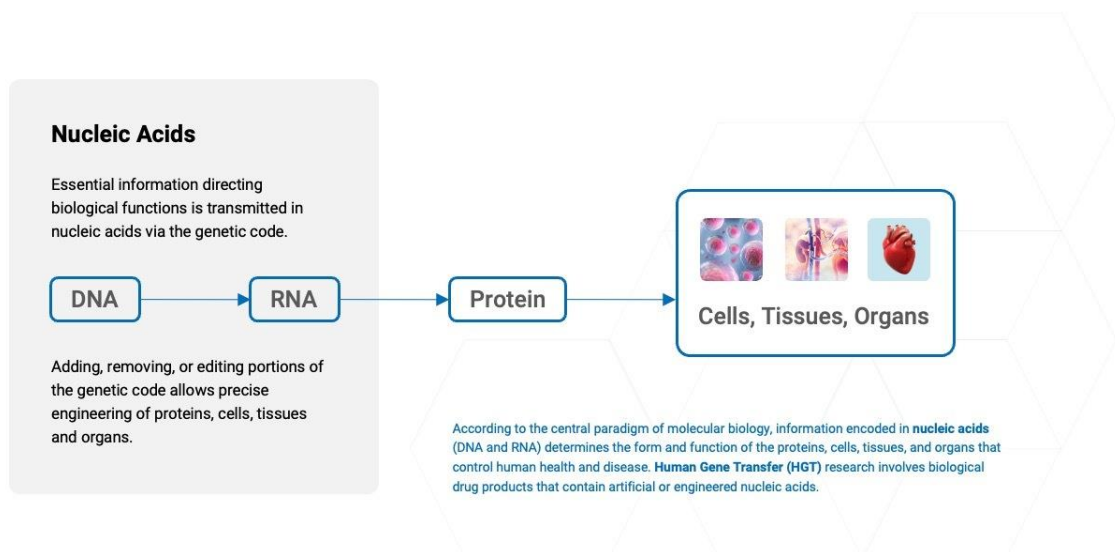
For clinical research, IBC membership should include experts in domains such as microbiology, biosafety, and genetic engineering. In addition, each IBC must include two community members who are unaffiliated with the research site, who live or work nearby, and who can represent community interests and values on the IBC. Each IBC must be registered with the NIH, and each registration applies to one specific institution. There are currently more than 2,700 IBCs registered with the NIH.

## **IBCs in Clinical Trials**

Under the *NIH Guidelines*, IBC review is required for many kinds of basic science and translational research, as well as clinical trials; this column focuses on oversight of clinical research. Clinical trials requiring IBC review fall into the category of human gene transfer (HGT) research. A technical definition of HGT research is provided in the *NIH Guidelines* Section III-C, but essentially HGT research is the introduction into a human research participant

of a product containing genetically engineered or artificially modified DNA or RNA (with certain exceptions for molecules that are very small and incapable of inducing lasting molecular changes in the cell).

### The Central Paradigm of Molecular Biology



Examples of HGT products include: an mRNA or DNA vaccine; a gene therapy delivered by an engineered “viral vector”; a lymphocyte engineered to kill cancer (e.g., CAR-T or CAR-NK therapies); and a bacterial strain genetically modified to express a therapeutic protein in the human gut. Under the *NIH Guidelines*, IBC approval of HGT research is required when certain types of NIH funding apply to the study. This includes funding for product development, funding to the research sponsor, and/or funding to the research site (including for unrelated research). In addition, the *NIH Guidelines* recommend IBC oversight of HGT research even when not required due to funding (“voluntary compliance”).

Interventional clinical trials in the United States require approval by an institutional review board (IRB). Clinical trials subject to the *NIH Guidelines* require review by an IBC in addition to IRB review. IRB review is focused on protection of human research participants, while IBC review is focused on protection of staff, visitors, the general public, and the environment at a clinical trial site.

In the past, there was significant overlap in what was reviewed by IRBs and IBCs with respect to human research participant protection, but under the most recent amendment to the *NIH Guidelines*, the separation of IRB and IBC responsibilities is much more clearly delineated. Notably, IBCs are no longer required to review informed consent or other participant-facing documents. Nevertheless, IRBs and human research participant-protection departments often rely on the expertise of IBC members to address complex risks in gene transfer trials.

Approval by both the IRB and IBC is required prior to initiation of clinical research subject to the *NIH Guidelines*. IRB and IBC review may be conducted sequentially or simultaneously according to the policy of the institution or committee administrator.

As mentioned above, each IBC must be registered with the NIH. In the past, each IBC was usually registered and administered locally by the respective research institution. Today, many institutions have IBCs that are registered and administered centrally by a commercial service provider. Centrally administered IBC services are especially critical for research sites that lack the scientific and administrative expertise and personnel to manage their own IBC. In addition, many universities and academic research centers find it useful to have an auxiliary IBC administered by a central service provider for clinical trials, alongside a locally administered IBC for basic science and other research.

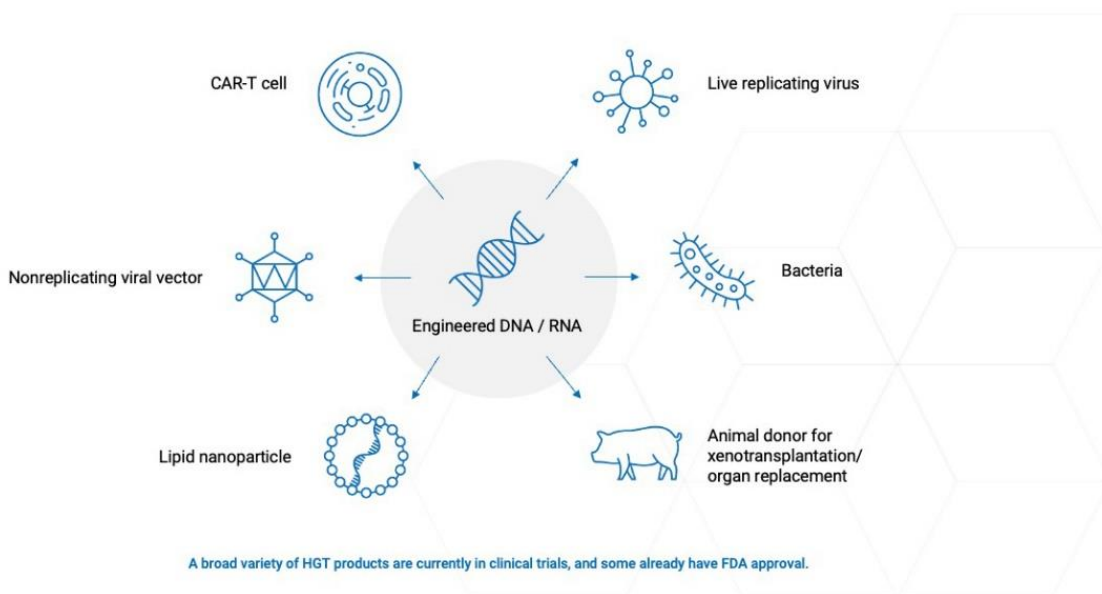
When reviewing an HGT trial, an IBC will focus on specific questions mandated by NIH or recommended by the Centers for Disease Control (CDC).{2} These include, for example:

- What is the appropriate biological safety level (BSL) for this research? IBCs must approve research at BSL-1, -2, -3, or -4; clinical trials are generally approved at BSL-1 or BSL-2. The BSL designation helps inform the selection of equipment and procedures suitable for safe handling of investigational products.
- What infectious agents or biological toxins may be contained in or produced by the test article/drug product? What measures are in place at the research site to contain these agents and factors?
- Does the site propose to use appropriate equipment? For some trials, a biological safety cabinet is recommended and the site must show that the cabinet is inspected and certified for proper function.
- How are hazardous spills deactivated/disinfected? IBCs ensure that appropriate disinfectants for specific categories of agents are selected from approved lists published by the Environmental Protection Agency.



- How is biohazardous waste disposed of? Biohazardous waste must be appropriately segregated from nonhazardous waste and deactivated or transferred to a qualified waste hauler.
- What measures are in place to minimize the risk of needlestick exposures to experimental drug products? Needlestick injuries are a frequent cause of accidental exposures—the risk of such exposures can be mitigated with appropriate equipment and training.
- How are staff trained and informed on standard operating procedures and emergency response?

Importantly, new developments in fields such as genetic engineering, synthetic biology, and xenotransplantation are constantly raising challenging new questions, so it's important that IBC members and advisors stay abreast of rapidly progressing discoveries and techniques.



## Getting Started with Gene Transfer Research

Gene transfer research represents a rapidly growing sector of clinical drug development in a diverse array of therapeutic areas. Research sites interested in getting involved may download and study the relevant NIH and CDC guidances required to staff, register, and operate a locally administered IBC. On the other hand, commercial services staffed by dedicated biosafety professionals and compliance experts are also readily available to provide IBC oversight services

to research sites. In many cases, all costs associated with these services are borne by the commercial clinical trial sponsors. Clinical research sites planning new construction or opening new clinics or pharmacies should engage with their IBC or with a professional biosafety consultant in advance to assess what type of facilities and equipment will best enable engagement with cutting-edge clinical trials.

## Conclusion

Many of the most exciting new developments in clinical drug development in the coming years will involve gene transfer research. Contract research organizations, clinical research sites, and investigators can enhance their capabilities and help ensure the safe conduct of research by engaging with a registered IBC and partnering with biosafety experts before, during, and after each new HGT trial.

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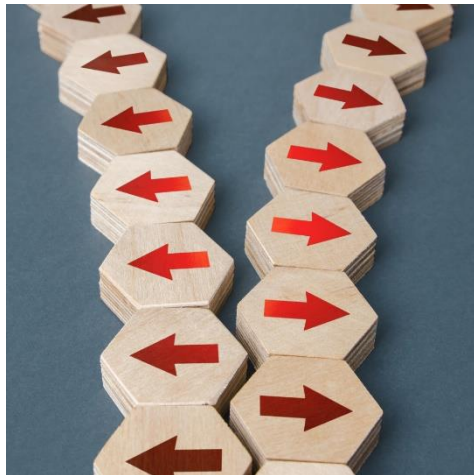


**Daniel Kavanagh, PhD, RAC,**  
([dkavanagh@wgcclinical.com](mailto:dkavanagh@wgcclinical.com)) is Senior Scientific Advisor, Gene Therapy, at WCG and serves as scientific lead in WCG's IBC Services division.

PRESCRIPTIONS FOR BUSINESS

## Leveraging Registries and Natural History Studies to Drive Rare Disease Drug Development

Kris O'Brien



Drug development success is driven by a deep understanding of the disease of interest—its etiology, epidemiology, presentation, manifestations, and progression. For rare diseases, where patient populations are small and historical data collection is inconsistent and dispersed across treating physicians in diverse geographies, much of this information may be unknown. Therefore, sponsors seeking to design reliable clinical trials with relevant, clinically meaningful outcome

measures may rely on patient registries and natural history studies as valuable sources of rare disease information.

In this column, we explore the distinctions between registries and natural history studies, highlighting the potential value of each in informing and shaping clinical development in rare diseases.

### Challenges of Rare Disease Development

In rare diseases, developing a comprehensive understanding of the disease of interest is hampered by: { 1 }

- Inherently small populations
- Frequent lack of timely diagnosis
- Scarce, incomplete, or inconsistent data

- Disease heterogeneity, which complicates diagnosis, categorization, and data collection
- Lack of precedents
- Scarcity of validated methods for assessing disease-specific conditions
- Need for more careful, more extensive planning

Observational studies play a critical role in addressing these challenges and filling in knowledge gaps, creating a solid foundation of disease knowledge to support product development.

## **Types of Observational Studies**

Unlike clinical trials, where patients receive interventions according to a well-defined protocol, observational studies do not assign participants to specific interventions and do not attempt to affect the outcome.

Observational studies are divided into two categories:

1. **Registry studies**, which may include a broad collection of defined data
2. **Natural history studies**, which are used for controlled, detailed collection of data that may be subject to review by a regulatory agency

While the terms registry study and natural history study are often used interchangeably, they differ in definition and application.

## **The Role of Patient Registries**

A patient registry is an organized system for collecting, storing, retrieving, analyzing, and distributing information on individuals who have one of the following:

- A disease of interest
- A condition or risk factor that predisposes them to a health-related event
- Prior exposure to substances that are known or suspected to cause adverse health effects

A subset of patient registries is designed for a specific purpose—for example, collecting particular demographic, epidemiological, efficacy, cost-effectiveness, quality of life, or care

pattern data. However, most registries are less restrictive and less structured and can be set up to collect data, including patient communications and post-marketing data.

Since registries are typically broad in scope, registry studies may be useful throughout drug development. Common applications of patient registries include:

- Collection of disease information
- Study of the standard of care or best practices
- Recruitment for clinical trials
- Observation or identification of population behavior patterns
- Monitoring of long-term outcomes

If a drug product is included in a registry study, that product must be approved, commercially available, and used in accordance with the approved labeling.

### **The Role of Natural History Studies**

A disease's natural history refers to how a disease process progresses over time without any treatment.<sup>{2}</sup> The objective of a natural history study is to document the course of a disease, starting just before it begins and progressing through its different clinical stages until the patient is cured, chronically disabled, or deceased.

Unlike registries, natural history studies are designed with a specific purpose, such as tracking the evolution of a disease over time, identifying factors that correlate with the disease and outcomes in the absence of treatment, or informing clinical trial design. These studies may also be used for:

- Obtaining more accurate estimates of disease prevalence
- Identifying and differentiating among disease subtypes
- Identifying demographic, genetic, environmental, or other factors that affect disease prognosis
- Identifying and assessing potential serological, tissues, and imaging biomarkers
- Evaluating and validating potential clinical outcome assessments

- Assessing the background risks associated with rare untreated diseases, providing context for assessment of potential risks associated with future therapeutic interventions
- Refining protocol design, including study duration, inclusion and exclusion criteria, and appropriate endpoints

Data collected from natural history studies may also be useful for understanding the dynamics of laboratory and clinical changes that can help identify the optimal time for therapeutic intervention.<sup>{ 1 }</sup> Natural history studies may be especially valuable in rare disease research where it is not possible to include a placebo control clinical trial arm for logistical or ethical reasons. In certain situations, a natural history study can even serve as a surrogate for the control population, provided the study has been designed to meet the requirements for regulatory submission.

### **Timing of Natural History Studies**

In its draft guidance document, *Rare Diseases: Natural History Studies for Drug Development*, the U.S. Food and Drug Administration urges sponsors to carefully consider the timing of natural history studies in the development process.<sup>{ 3 }</sup> The guidance includes a discussion of the pros and cons associated with implementing natural history studies at various stages of clinical development. Generally, these studies are likely to be most useful if completed before initiating interventional studies, but they can also be performed in parallel with clinical trials.

### **Types of Natural History Studies**

There are several natural history study designs, each with advantages and disadvantages. The designs may be retrospective, focused on the present, or prospective.

Medical literature reviews are the easiest, least expensive way to begin elucidating the natural history of a disease. Still, data may be difficult to standardize, and these studies may not meet natural history study objectives. Retrospective chart reviews are also relatively inexpensive, though missing and non-standardized data may present hurdles to the research.

Prospective natural history study designs include cross-sectional and prospective longitudinal studies (see Figure 1). Cross-sectional studies collect data from a variety of patients at a single point in time. While these studies may provide insight into disease generalities, they do not provide any insight into the progression or patient experience. Meanwhile, longitudinal studies collect data over a prospectively defined period. These studies can be lengthy and costly, but may provide valuable information on how the disease progresses over time.

**Figure 1: Comparison of Prospective Natural History Study Designs**

	Prospective Cross-Sectional	Prospective Longitudinal
Description	Collection of data from a variety of patients at one point in time	Collection of data from a variety of patients over a defined period of time
Pros	<ul style="list-style-type: none"> <li>Limited duration of study</li> <li>Predefined data elements</li> <li>May provide insight into generalities about disease</li> </ul>	<ul style="list-style-type: none"> <li>Predefined data elements</li> <li>Able to assess disease progression over time</li> </ul>
Cons	<ul style="list-style-type: none"> <li>Doesn't collect patient experience in time; data is a 'snapshot'</li> <li>Doesn't provide robust data on the pace of progression of a disease state</li> <li>Difficult to extrapolate from 'snapshot' to make assumptions about disease progression on a per patient basis</li> </ul>	<ul style="list-style-type: none"> <li>Can be quite lengthy to complete, especially in diseases that progress slowly</li> <li>Can be expensive</li> <li>Need to plan for changes in measurements and SOC over time</li> <li>May require amendments to adjust for additional assessments or biomarkers over time</li> </ul>

### Natural History Study Design Considerations

Though natural history studies may collect information on therapeutic interventions, it is essential to ensure that data gathering also includes measures that assess all facets of the disease of interest. When considering what data to collect, sponsors should anticipate any questions that might arise over the course of drug development. This includes disease presentation, manifestations, morbidity, and progression. Often, natural history studies include evolving protocols that incorporate plans to refine data collection as new disease knowledge emerges.<sup>{ 1 }</sup> Ideally, the data collected should be sufficiently robust to support the development of multiple therapeutic options.

Data collection requirements, assessment type, and frequency must align with the standard of care, which may differ among providers or institutions and may even change over time. Standard

of care may help inform the selection of meaningful endpoints and appropriate assessments for measuring or monitoring disease progression. It is also critical to understand how the standard of care may impact site feasibility, study duration, and inclusion/exclusion criteria.

Due to regulatory scrutiny, data quality and monitoring are essential for any study subject. Even if the planned natural history study will not be included in regulatory submissions, it is critical to ensure high-quality data. While 100% source data verification is not mandatory, some level of monitoring is recommended.

### **Collecting and Ensuring High-Quality Data in Natural History Studies**

As with interventional clinical trials, data collection in natural history studies can be performed through either local sites or one or more central sites. With local sites, data are collected by a patient's existing provider and submitted to central data collection. While this approach limits the burden on the patient, it may introduce variability. With central sites, all study assessments are performed at a limited number of experienced sites. This approach to data collection increases consistency and helps minimize the risk of missing data or protocol deviations, but may increase the study burden if patients need to travel long distances to those central sites.

Combination models offer a hybrid approach where complex or specialized assessments are performed at central sites and routine assessments are completed at local sites. Sponsors may also opt for a patient-reported model where all assessments and data collection are performed in the patient's home. Although this approach is the most convenient for the patient, it may introduce variability and requires significant training of in-home providers. Ultimately, the most appropriate data collection model for a natural history study will depend on the overall objectives.

### **Conclusion**

Both registries and natural history studies play important but different roles in the clinical development of therapeutics for rare diseases. Therefore, understanding how—and when—each of these observational studies should be used is essential for guiding the design of successful clinical trials.



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**Kris O'Brien** is Executive Director for Program Strategy in the Rare and Pediatric Diseases area at Premier Research, and has been conducting clinical research for more than 35 years in multiple therapeutic indications, programmatic areas, and corporate leadership settings.

## **The Value of Data Diversity in Clinical Data Registries**

Mac Bonafede, PhD, MPH



Clinical patient disease registries collect information on large numbers of people in diverse clinical practices.

Diversity applies to both the types of clinical practices and the patients themselves, since researchers consider hard-to-reach patients{ 1 } as potential clinical trial participants from outside typical research recruitment settings.

With patient disease registries, life science researchers also find a pathway for deeper understanding of:

- Variations in a disease's treatment and outcomes
- Variations in care delivery, quality of care, and care effectiveness
- Safety signals and opportunities for enhanced surveillance
- Factors that influence disease prognosis and associated quality of life for patients

These registries are powerful tools{ 2 } for better understanding of distinct therapeutic areas of interest—from cardiovascular disease, diabetes, and hypertension to other chronic conditions that require longitudinal views of patient data. They also provide an efficient avenue for custom data collection or site recruitment and engagement to support pharmacovigilance and other real-world evidence (RWE) generation activities.

Incorporating data from patient disease registries in a real-world data (RWD) mix offers four impactful benefits for clinical researchers in terms of facilitating improved diversity in research, accessing hard-to-reach patients, making more-informed public policy decisions, and presenting opportunities for better health outcomes. Let's look at each of these separately in the following sections.

### **Improved Geographic and Demographic Diversity**

RWD obtained from patient disease registries allow research beyond what is possible{3} with randomized controlled trials (RCTs).

In RCTs, researchers attempt to reduce bias by a) randomizing the medical intervention delivered to each patient, and b) using strict inclusion and exclusion criteria for selection of the trial patient population. However, this reduction of bias is frequently obtained at the expense of generalizability; that is, how research findings apply to a larger population or different setting. Results in a trial patient population almost certainly represent a restricted subset of patients seen in real-world practice.{4}

For example, recent research{5} revealed patient populations enrolled in studies with the greatest impact on current heart failure treatment differ significantly from patients observed in clinical practice. Most heart failure clinical trials have been conducted in white, male patients with a mean age of 60 years. However, in most developed countries, patients affected by heart failure are typically older and more balanced between male and female.

Similarly, RCTs frequently exclude older adults.{6} Age has a clear influence on clinical outcomes. Medication efficacy and optimal dosing are often uncertain in the elderly, whose drug metabolism and clearance rates may be diminished; who may have lower drug tolerance; and in whom there is the potential for drug-drug interactions.

## **Access to Hard-to-Reach Patients**

Patient disease registries have emerged as an important means of gaining insight into the effects of medical interventions in more diverse clinical settings than can be achieved in clinical trials.

They can:

- Provide access to RWD from research naïve, geographically diverse sites, across multiple electronic health record (EHR) and practice management platforms.
- Produce results complementary to those obtained in RCTs.
- Obtain data on large numbers of patients at significantly reduced costs and with quicker timelines.

## **More-Informed Public Policy Decision Making**

Patient disease registries offer data to better understand how diverse populations with diabetes, cardiovascular disease, hypertension, and other chronic conditions responded to the virus and subsequent treatments. For example, limited access{7} to COVID-19 vaccines and treatments for hard-to-reach patients surfaced as the pandemic expanded across the globe, casting a spotlight on existing imbalances.

Care of women before, during, and after pregnancy in the U.S. presents mental and basic care challenges{8} that are often addressed inadequately or totally ignored in underserved populations, such as care provided by a regular doctor or in a regular location.

Understanding these disparities requires reported outcomes data that highlight the lack of care for women or specific patient populations. Clinical patient disease registries offer such data so that researchers can pinpoint specific population health needs. Policy makers then access those data in their effort to establish local, state, and federal health policies.

## **Opportunities for Better Health Outcomes**

The three factors addressed above—greater geographic and population diversity, improved access to hard-to-reach patients, and more-informed public policy decision making—all lead to opportunities for better health outcomes using data from patient disease registries.

Registries can fill in gaps{9} where efficacy for specific, defined RCT populations cannot be generalized to patients seen in clinical practice, making them particularly valuable for cardiovascular, cardiometabolic, and diabetes research on population health management and treatments.

## The Power of Patient Data Registries

Research across populations, geographic locations, and disease states has become even more vital to understand what treatments life sciences researchers can identify and advance. The power of data analytics coupled with advancement of interoperable data sharing{10} across digital EHR systems benefits users of clinical patient disease registries.

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**Mac Bonafede, PhD, MPH**, is Vice President of Real-World Evidence at Veradigm, an Allscripts Company, where he leads a team of data scientists, statisticians, and epidemiologists in real-world evidence generation using Veradigm’s PINNACLE and Diabetes Collaborative Registries.

OVER THE TRANSOM

## Fellow Travelers in a Mighty Small Boat: Dispatches from the Highs Seas of DEI

Edited by Gary W. Cramer ([gcramer@acrpn.net](mailto:gcramer@acrpn.net)), Managing Editor for ACRP



*“Now, now, now, we’re all sort of fellow travelers in a mighty small boat, in a mighty big ocean. And the more we quarrel, criticize, and misunderstand each other, the bigger the ocean gets and the smaller the boat.”*

—Henry Hull, playing Charles J. “Ritt” Rittenhouse Jr. in *“[Lifeboat](#)”* (1944)

### Fostering Diversity and Inclusion in the Healthcare Workforce

For U.S. health systems, valuing diversity and inclusion in the workforce is vital to serving the emerging needs of a diverse patient population. The much-aspired patient-centered care is feasible when the approach and focus are shifted to enable health systems to improve care quality and the patient experience of diverse patients.

Published in *JMIR Formative Research*, [a study](#) titled “Valuing Diversity and Inclusion in Health Care to Equip the Workforce: Survey Study and Pathway Analysis” asks the following questions:

- Can the healthcare workforce leverage the educational pipeline to fulfill diversity needs and address workforce shortages?
- How do the alternative pathways of improving, recruiting, and collaborating compare in this process?

The study finds that [improving the current workforce](#) through upskilling or returnships around diversity and inclusion needs is more effective than recruiting or collaborating with universities to find fresh talent. The findings suggest that health systems that value *only* a diversity and inclusion strategy may *not* rely on collaboration with universities to equip their workforces.

However, health systems that adopt a recruiting strategy will look externally to find new workers and seek collaboration with universities. Moreover, these pathway effects go hand in hand with a talent-improvement strategy, indicating that talent and diversity strategies must be aligned to achieve the best results for a health system.

Giving voice and committing resources to diversity and inclusion initiatives will fail unless leaders instill a process inside their organizations through education and training. Good intentions will not be enough. Just recognizing or appreciating the concept of diversity is not enough. Leaders need to implement actionable plans within their systems to improve inclusiveness.

### **Spanish-Speaking Patients Show Strong Interest in Trial Participation in the U.S.**

Writing for SubjectWell in June, Ivor Clarke [noted how](#) language barriers faced during the clinical trial process can often result in lower participation rates of non-English speakers, an unsatisfactory patient experience and, ultimately, imprecise data.

When SubjectWell fielded a U.S. survey from March to April 2022 of 438 primary English- or Spanish-speaking patients (224 and 214 people, respectively), Spanish-speaking respondents were more likely to show interest in trial participation. However, more Spanish speakers reported being “somewhat likely” to consider participation compared to English speakers, meaning interest is more prevalent, but enthusiasm is lower. Spanish-speaking respondents were also more likely to participate in a trial with bilingual staff.

Compensation motivated both groups, but was stronger for English-speaking respondents. Additionally, respondents without health insurance were more likely to be only somewhat interested (54%) and less likely to be extremely interested (12%) than those with health insurance, suggesting they may need more factors to motivate them to participate.



Despite Spanish speakers' interest in participation, Hispanics represent only [11% of trial participants](#), but make up [18.5% of the general population](#). To make up this deficit, this survey found that an inclusive study design for Spanish speakers includes both a bilingual staff and financial compensation. However, Clarke explains, the industry is still exploring the best accommodations to provide improvements in patient diversity and remove barriers to patient recruitment. Financial compensation is just one simple, but proven, way to increase interest in both Spanish- and English-speaking populations and should be considered during study design.

### **ASCO, ACCC Release Recommendations to Increase DEI in Clinical Trials**

The American Society of Clinical Oncology (ASCO) and the Association of Community Cancer Centers (ACCC) in June [jointly released recommendations](#) that address the lack of diversity, equity, and inclusion (DEI) in cancer clinical trials. Published in the *Journal of Clinical Oncology*, their recommendations detail specific actions to engage the entire cancer clinical trial ecosystem in expanding the participation of underrepresented individuals in research that advances progress against cancer.

The research statement underscores that inclusive participation in clinical trials is necessary to understand potential differences in efficacy and safety across diverse populations, mitigate racial and ethnic disparities in health outcomes, and promote equity and justice. The recommendations focus on the following key areas that address barriers to cancer clinical trials:

- Access to Clinical Trials
- Equity-Focused Design
- Partnerships Among Stakeholder Groups
- Continuous Education and Training
- Investment in Equity, Diversity, and Inclusion
- Sharing Data and Strategies

The full ASCO-ACCC Research Statement clarifies which clinical trial stakeholders would be instrumental in implementing specific recommendations, while encouraging all research stakeholders to help achieve the goal of ensuring cancer clinical trials reflect the racial and ethnic diversity of people with cancer.



