

Clinical Researcher

June 2018

HOME STUDY TEST

Principal Investigator Concerns

Earn 2.0 Continuing Education Credits

Two articles from the May 2018 issue of *Clinical Researcher* have been selected as the basis for a Home Study test that contains 20 questions. For your convenience, the selected articles and test questions are combined and posted in the form of this printable PDF at <https://www.acrnet.org/professional-development/training/home-study/>, where the test may be purchased. *The test will be active until June 30, 2019.* This activity is anticipated to take two hours. **Answers must be submitted using the electronic answer form online (members \$30; non-members \$50).** Those who answer 80% or more of the questions correctly will receive an electronic statement of credit by e-mail within 24 hours. Those who do not pass can retake the test for no additional fee.

The *Clinical Researcher* archive is at <https://www.acrnet.org/resources/clinical-researcher/>.

CONTINUING EDUCATION INFORMATION

The Association of Clinical Research Professionals (ACRP) is an approved provider of nursing and clinical research continuing education credits.

Contact Hours

The Association of Clinical Research Professionals (ACRP) provides 2.0 contact hours for the completion of this educational activity. These contact hours can be used to meet the maintenance requirements for certification programs of the Academy of Clinical Research Professionals. (ACRP-2018-HMS-006)

Continuing Nursing Education

The California Board of Registered Nursing (Provider Number 11147) approves the Association of Clinical Research Professionals (ACRP) as a provider of continuing nursing education. This activity provides 2.0 nursing education credits. (Program Number 11147-2018-HMS-006)

ACRP DISCLOSURE STATEMENT

The Association of Clinical Research Professionals (ACRP) requires everyone who is in a position to control the planning or content of an education activity to disclose all relevant financial relationships with any commercial interest. Financial relationships in any amount, occurring within the past 12 months of the activity, including financial relationships of a spouse or life partner, that could create a conflict of interest are requested for disclosure. The intent of this policy is not to prevent individuals with relevant financial relationships from participating; it is intended that such relationships be identified openly so that the audience may form their own judgments about the presentation and the presence of commercial bias with full disclosure of the facts. It remains for the audience to determine whether an individual's outside interests may reflect a possible bias in either the exposition or the conclusions presented.

ACRP EDITORIAL ADVISORY BOARD

Jerry Stein, PhD (*Chair*)
Paula Smailes, RN, MSN, CCRC, CCRP (*Vice Chair*)
Suheila Abdul-Karim, CCRA, CCRT (*Training and Development Liaison*)
Victor Chen
Fraser Gibson, CCRA, CCRP
Gregory Hale, MD, CPI
Stefanie La Manna, PhD, ARNP, FNP-C
Christina Nance, PhD, CPI
Ernest Prentice, PhD (*Association Board of Trustees Liaison*)
Shirley Trainor-Thomas, MHSA
Heather Wright, BS, BA:
Nothing to Disclose

ACRP STAFF/VOLUNTEERS

James Michael Causey (*Editor-in-Chief*)
Gary W. Cramer (*Managing Editor*)
Karen Bachman
Jan Kiszko, MD
Jo Northcutt
Deepti Patki, MS, CCRC
Barbara van der Schalie
Christine Streaker:
Nothing to Disclose

PEER REVIEWED

Opinion: Approaches to Set Up Principal Investigators for Success

Molly Downhour, MHA, BSN, NEA-BC, OCN, CCRC

[DOI: 10.14524/CR-18-0002]

Show of hands—how many people believe that principal investigators (PIs) are not currently set up for success? Odds are that not many hands would go up with confidence after that question.

As the perception of this role in the drug and device development industry currently stands, it is not surprising that the number of active PIs continues to decline.^{1} This can gut enthusiasm for opportunities in the field, which is a shame, because being a clinical research investigator used to be a coveted role. What happened, and how can we turn the tide to encourage young clinicians to seek out opportunities to lead clinical research?

What is the Problem?

The problem is the lack of PI oversight and engagement in clinical research. Over the last decade, the number one cause of Form FDA 483s (Inspection Observations) leading to Warning Letters from the U.S. Food and Drug Administration to PIs was protocol compliance issues, such that “an investigation was not conducted in accordance with the signed statement of the investigator.”^{2}

By signing Form FDA 1572, PIs agree to take on full oversight of the clinical trial, including the investigator agreement, adherence to the protocol and investigational plan, and ensuring the rights, safety, and welfare of all clinical trial participants. This is a daunting task,

considering most PIs are *not* directly responsible for the hiring, training, and allocation of available resources for the research team members within their oversight who are delegated to complete various clinical research tasks.

The conundrum is the incongruence between the government regulations requiring full responsibility of oversight to be owned by the PI, versus the operational practice most often owned by a healthcare administrator. To be honest, I prefer the PI to be the scientific and medical expert on the clinical trial and leave administrative functions to the professionals with expertise in that area.

Let's not forget that the list of additional stressors on the economic healthcare landscape contributing to the decline in investigator oversight and engagement includes:

- Decreased National Institutes of Health grant funding available to support academic careers.{3}
- Increased regulatory requirements regarding adherence to International Council for Harmonization guidelines, the U.S. Health Insurance Portability and Accountability Act mandates, and U.S. government Meaningful Use standards for using electronic health records.{4}
- Study budgets have remained static, despite trends of greater study complexity and requirements, including exponential increases in terms of electronic data capture systems each requiring lengthy training and unique logins.{4}
- Lack of adequate supporting research staff.{5}
- Lack of dedicated time for research activities.{6}
- Lack of financial incentives and/or recognitions.{6}
- Lack of PI orientation or training for the responsibilities for clinical research, despite those in this role having the most responsibility for complete oversight of the clinical trial activities per the 1572.{6}

In summary, as an investigator, you're faced with less funding, less time available, fewer resources, lack of training on clinical trials operations, and 100% responsibility of oversight on a team you with many members whom you neither hired nor trained. Sign me up!

However, there are obviously sites full of professionals that conduct clinical trials very well, indeed. These sites have institutional support to ensure the above issues are addressed in their organizational infrastructure.

With severe limitations in the availability of grant funds, site administrators have the difficult job of balancing their clinical trial portfolios amongst industry-sponsored, grant-funded, investigator-initiated, and cooperative group trials, all while meeting the community needs for innovative treatment options. These site administrators dig deep to find their true costs of running trials, and justify the amounts in their study budgets.

Truly thoughtful administrators will turn down trials with inverse expense to revenue ratio if the trial provides no other value to their sites. These site leaders understand the need to operate like a business; not accepting revenue losses simply because it is research. The culture and expectation at these sites is that adequate investigator time and resources are given for research and, in return, the sites meet research and accreditation standards. Standout sites include Duke Clinical Research Institute, clinical trials units at such other academic medical centers as the ones based out of Northwestern University and Baylor University, the Sarah Cannon Research Institute, and the HonorHealth system in Arizona.

How to Make the PI Role Attractive Again

Sharing Success Stories

The first thing I would do is highlight successful investigators in a variety of therapeutic areas and share their success stories. What are the common denominators that they share? My educated guess is that these PIs have been influenced by great mentors, have dedicated time for clinical research activities, and are part of a site that invests in the infrastructure required to execute clinical trials well, instead of demanding to financially break even on day one.

All of the above-mentioned qualities allow exceptional PIs to focus on their research and practice responsibilities, instead of on the types of administrative duties that can be handled by non-physicians on site. Further, both new and ongoing PIs who want to reach and remain

on the leading edge of trials will seek out other successful investigators and network with them at industry events or other opportune moments.

An example of a defined and successful mentoring program is HonorHealth's Drug Development Scholar program. This program recruits young oncologists and hematologists with a passion for drug development. The one- to two-year program focuses on early-phase clinical trial development, patient recruitment and follow up, statistical analysis, bioinformatics and regulatory affairs.

The scholar functions as a specialist physician, performing duties involving direct care of patients with advanced malignancies and those receiving treatment on clinical trials, evaluating new patients, and formulating treatment plan under supervision of the assigned faculty member.^{7} The Drug Development Scholars are fully immersed in the program, with interaction with all of the research staff.

The American Association for Cancer Research and the American Society of Clinical Oncology also support an annual educational workshop on "Methods in Clinical Cancer Research." The July 2018 event is described as an "*intensive workshop in the essentials of effective clinical trial designs of therapeutic interventions in the treatment of cancer for clinical fellow and junior faculty clinical researchers in all oncology subspecialties, including radiation and surgical oncology and radiology.*"^{8}

Encouraging Nurse Practitioner Participation

My second recommendation is to encourage experienced nurse practitioners (NPs) to participate in clinical research as principal and sub-investigators. NPs are currently underutilized in clinical research, despite many of them having followed research curricula in advanced degree programs.

There is no regulation that requires PIs to be physicians. Per the *Code of Federal Regulations* in CFR 312.53 and 812.43, sponsors of clinical investigations are required to select investigators who are qualified by education and experience as appropriate experts to investigate the test article, whether investigational product or device.^{9} Not only does the

inclusion of NPs as PIs and sub-investigators increase the pool of investigators to execute trials (thus helping more patients and advancing science), it also may raise the bar on the quality of the execution of clinical trials due to their holistic training.{10}

Major pharmaceutical companies such as Celgene, Eli Lilly, Aveo, Nektar, and AbbVie have all sponsored studies run by NP PIs. Central institutional review boards such as Western IRB have and will approve qualified NPs to be PIs on industry-sponsored trials. While physician PIs are far more common than NP PIs, there is an established precedent to build upon.

Emphasizing Training

Regardless the educational background and professional licensure of investigators, they all need adequate training on the responsibilities of being a clinical investigator. Do they understand the requirements on Form FDA 1572 and the consequences of not fulfilling the relevant duties?

Clinical investigator training programs are offered by the Association of Clinical Research Professionals, the National Institutes of Health, the Collaborative Institutional Training Initiative, and academic and private organizations. Site leaders can take the training further and pay for their investigators to become certified as PIs; this demonstrates to sponsors their dedication to the role.

Sites also need a thorough investigator orientation process and competency checklist. The site orientation helps investigators understand how the site operations support their responsibilities in clinical trials oversight. An orientation should lead to routine meetings with the research staff to review and discuss research participants and documentation, and to provide guidance on reporting adverse events, updates on performance status, clinical significance of assessments, and standard operating procedures on training for new protocols and amendments.

Conversely, when taking a role at an institution, physicians and NPs should be turning the tables to ask what resources are available to be successful in the investigator role. Does the site have adequate staffing (including a low turnover rate on staff), a positive reputation in the

industry, and administrators who understand the unique needs of running clinical trials? Are financial payments designed to incentivize or de-incentivize participation in clinical trials? Investigators are obviously going to have better engagement and oversight when they choose to work at sites where the leadership understands the requirements and value of conducting clinical research.

Conclusion

Without a team effort, we will continue to see the number of investigators decline. Sites need to seek sustainability, conduct high-quality training and mentoring for new PIs, and explore expanding the talent pool with experienced NPs. Site leaders need to ensure sites are set up for success for all employees—including investigators.

References

1. Cornelius A, Pierre C, Hinkley T, Lin L, Fordyce C, Hamre G, Roe M. 2017. One and done: reasons principal investigators conduct only one FDA-regulated drug trial. *Contemp Clin Trials Comms* 31–8.
<https://www.sciencedirect.com/science/article/pii/S245186541630093X>
2. U.S. Food and Drug Administration. 2018. *Inspection Observations*.
<https://www.fda.gov/ICECI/Inspections/ucm250720.htm>
3. Lauer M. 2016. National Institutes of Health/Office of Extramural Research.
<https://nexus.od.nih.gov/all/2016/05/31/how-many-researchers/#>
4. Morgan C. 2017. Is clinical trial design complexity behind the high turnover rate for principal investigators? *MedCity News*. <http://medcitynews.com/2017/04/high-turnover-rate-for-principal-investigators/>
5. Jacobs SR, Weiner BJ, Reeve BB, Weinberger MM, Good MJ. 2014. Organizational and physician factors associated with patient enrollment in cancer clinical trials. *Clin Trials*, 565–75.

6. Rahman S, Azim MA, Shaban SF, Rahman N, Ahmed M, Bin Abdulrahman K, D'Souza UJ. 2011. Physician participation in clinical research and trials: issues and approaches. *Advances Med Ed Pract*, 85–93.
7. HonorHealth. 2018. <https://www.linkedin.com/jobs/view/physician-drug-development-scholar-at-honorhealth-544505968/>
8. AACR/ASCO. 2018. *Methods in Clinical Cancer Research*.
<http://vailworkshop.org/Pages/AboutWorkshop.aspx>
9. U. S. Food and Drug Administration. 2018. *Title 21 Food and Drugs*.
<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.53>
10. Hersher R. 2012. Nurses on trial. *Nature Med*, 1165–7.

Molly Downhour, MHA, BSN, NEA-BC, OCN, CCRC, (mdownhour@medixteam.com) is a Clinical Research Strategy Executive at Medix.

Embedding Clinical Research into the Continuum of Care

Jennifer J. Byrne; Jane M. Shen, PharmD; Amanda W. Wright

[DOI: 10.14524/CR-18-0004]

Clinical research is the frontline of medical innovation. Through research projects, scientists and physicians make medical breakthroughs that directly impact the lives of patients and their families. However, what many patients and physicians don't realize is that when clinical research is integrated into the continuum of patient care, it represents a valuable care option.

When patient volunteers participate in clinical research, they get access to leading-edge research treatments or devices, generally at no cost, and a network of healthcare providers who are focused on making sure their overall experience is positive, and meets the highest quality medical standards. Such care excellence is a critical component of the clinical research experience for a patient volunteer. Study leaders are deeply invested in each participant, and go to great lengths to ensure trial volunteers adhere to strict care protocols. That translates to greater adherence, and often results in patients, as healthcare consumers, being more educated and invested in their care.

Such dedication to patient care doesn't just benefit the researchers. Patient engagement has become an increasingly important measure of success in the healthcare space. Mounting evidence confirms the influence of patient engagement on improved health outcomes and on reduced costs.^{1} This directly drives the coveted value-based healthcare delivery of improving the patient experience of care, improving overall population health, and reducing the per-capita cost of healthcare.

Participation as a Positive Experience

A recent study shows that people can be far more engaged in their care when participating in a clinical trial, perhaps because they see the connection between their participation and the greater good of the patient community. In this 2015 study, a series of phone surveys were conducted with 42 diabetic patients participating in an ongoing diabetes clinical trial. The results showed a surprisingly high level of patient engagement and satisfaction with their treatment.

Overall, the surveys show positive experience across all dimensions for clinical research participants, with significantly higher levels of satisfaction in many patient-important dimensions, such as access to care, efficiencies in care delivery, and qualities of care received from the research team. Fully 100% of respondents said participating in clinical research reduced the overall cost of their healthcare compared to traditional treatment options; and 95% agreed that adding clinical research improved their overall quality of care. These data points validate what we've long known—that patient volunteers generally have an overwhelmingly positive experience when participating in clinical trials.

Even more intriguing, all participants said that participating in clinical research improved their interest and/or involvement in their overall healthcare. In the free-text response, many respondents said they found that the trial experience motivated them to be more engaged in their care, and prompted them to educate themselves about their disease. They also felt the research team more closely monitored their status, and that the experience inspired them to be more focused on their health.

In an era in which treatment adherence is a significant challenge, these results should excite physicians, other providers, healthcare systems, and payers. Non-adherence is associated with higher rates of hospital admissions, suboptimal health outcomes, increased morbidity and mortality, and increased healthcare costs, according to the U.S. Centers for Disease Control and Prevention.{2}

Looking ahead, further research is needed to quantify the influence of integrated clinical research on adherence, along with patient satisfaction, population health, and cost. However,

this and other studies{3,4} suggest that participation in trials can have a positive impact on adherence, and thus perhaps reduce the negative effect of this trend. Data from patients across several therapeutic categories at several value-based healthcare systems could generate further evidence supporting meaningful integration of clinical research as a care option.

Physicians and Research: A Collaborative Approach

The care delivery model, embedded within a patient volunteer's clinical trial journey, brings tremendous shared value—not just for biopharma companies in collecting data, but in the outcome, experience, and cost to the healthcare consumer.

Despite these benefits, healthcare organizations have often ignored the value of integrating clinical research into the overall continuum of care—and that's a problem. Low clinical trial participation exponentially increases cost of drug development and, more importantly, delays new solutions coming to market to meet unmet medical needs.

This attitude is exacerbated by the lack of collaboration between clinical research teams, physicians, and the broader healthcare organization. Physicians often view clinical research as transactional in nature, and not as an integrated part of a healthcare organization's care options. This often results in trials conducted by investigators unbeknownst to the healthcare institutions employing them.

The impact of this disconnect cannot be overstated. When healthcare organizations fail to integrate clinical research into their portfolio of care options, it creates an environment where physicians may be hesitant to recommend patients to trials for fear of losing track of them. As a result, unless a physician is directly involved in the research, patients who would benefit from participating in a clinical trial typically do not learn about the opportunity.

Today, less than 1% of the U.S. population participates in clinical trials, yet 72% say they would participate if recommended to do so by their doctor.{5} Conversely, large quantities of clinical research study data that could be transformed by healthcare systems into actionable information used to analyze and improve population health are ignored. This reduces the

healthcare system's ability to deliver the highest quality of care based on the most current research, and reduces the impact of research spending.

At the same time, the clinical research environment is facing increasingly complex obstacles that could be alleviated through a more collaborative approach to care. Sponsors and clinical research organizations (CROs) are increasingly looking to move clinical trials into settings that have the infrastructure and support of electronic medical records (EMRs) to drive efficiencies in trial delivery while expanding their potential patient pool.

The healthcare landscape is also changing, with a shift from physicians owning their own practices to physicians hired as full-time employees for healthcare systems. By 2020, an estimated 80% of all U.S. physicians will be employed by healthcare systems.{6}

Lastly, patients are becoming actively engaged in their healthcare, and there is increased development of new value-based payment models that emphasize higher quality at lower costs.

Spread the Word

These changes can be leveraged by taking a more collaborative and inclusive approach to clinical research as a care option; but to do that, we need to change the culture around clinical trial participation so that all the stakeholders in the healthcare continuum benefit. That begins with creating a more collaborative culture where researchers, physicians, patients, healthcare systems, and advocates have more opportunities to connect and educate each other.

One driver of change may be the Enhanced Clinical Trials Design Act, which took effect in August 2017 and strives to modernize the clinical trial process and provide more treatments and therapies to improve patients' lives as an integrated part of the care continuum. The Act intends to reduce the barriers for all stakeholders to ensure access to research and the data associated are fully utilized to the advantage of the patient. It encourages conversations between the U.S. Food and Drug Administration, National Institutes of Health, key industry stakeholders, and Americans who participate in clinical trials, and the creation of a framework to facilitate further integration of research in the continuum of care.{7}

Laws alone will not be enough. To bridge the gap between healthcare and clinical research, we need to alter the dialog around what it means to participate in a trial, and engage healthcare providers in the conversations so they feel connected to the care their patients receive.

Even simple conversations with patients about the value of clinical research can change the way they think about participation. In a recent survey conducted by Greater Gift, we asked participants that attended a Hero's Journey Art™ Project event held in Winston-Salem, N.C., if they would be willing to participate in a clinical trial. The project combined science and art to convey the importance of clinical trial participation and raise awareness of clinical research. Before the event, 25% of respondents said they were “probably not willing” or “not willing” to participate in a clinical trial and 40% said they were “somewhat willing.” After the event, the number not willing to participate dropped to 12%, and those who were somewhat willing rose to 60%.{8} Collectively, the data show increased willingness to participate following the event experience.

All of us, as healthcare consumers, need to be informed on these opportunities. That’s where healthcare industry organizations come in.

Breaking Down Walls

Healthcare organizations need to break down the barriers between clinical research and conventional treatment, and to create opportunities for physicians and their care teams to learn about and even participate in these care options. When physicians feel confident that a trial will benefit their patients, and that they can stay engaged in their care, they may be more willing to suggest clinical research within the menu of options.

Such integration can be accelerated using rapidly evolving healthcare technologies and other approaches that get at the core of infusing clinical research with everyday care:

- Predictive analytics can identify gaps in care and help guide pathways toward clinical research to fill those voids.
- Outcomes research can help chronic disease management and preventive health by leveraging continuous engagement in the community.

- Precision medicine technologies can help extract patient and clinical intelligence to guide personalized treatment via clinical research.
- Telemedicine addresses the issue of patient access and can help to fill gaps in patient care and engagement.

With the necessary healthcare and research interfaced platform, implementing a clinical research program can create the infrastructure needed to better manage care coordination—thus resulting in reduced cost of care and improved treatment decision making.

New technologies and partnerships have the potential to help build integrated networks and to support value-based healthcare delivery, offering potential for innovative organizations to drive change. Such partnerships may also enhance the trust placed in clinical research by both healthcare providers{9} and the public.{5}

Further, we need to create platforms to broadcast the data, and to share individual success stories highlighting how clinical research has changed the lives of patient volunteers who participate.

Often the media only focus on negative stories about clinical research, but the industry is full of extraordinary examples of lives transformed by clinical trial participation. Consider Emily Whitehead, who had a resistant form pediatric lymphoblastic leukemia and was out of treatment options when she joined a ground-breaking CAR-T cell therapy trial in 2012. Within three weeks of participating, she was in remission and has been cancer free ever since.{10} Similarly, after Carl Walker, a hemophilia patient who at one time required thrice-weekly blood infusions, participated in a gene therapy trial in 2011, he no longer needed any infusions—either preventative or as a result of an injury.{11}

For every life-saving example, there are hundreds of other stories of research volunteers who had positive clinical research experiences, felt valued by the staff, and, because of that engagement, were more invested in their care and maintained better adherence to their treatment regimen. We need to celebrate all of these stories, and to spread the message of what it means to participate and what clinical trials entail. We can encourage our social circles

to consider participating and we can speak to our healthcare providers about potential opportunities.

Finally, the biopharma industry must do its share. For biopharma, a collaborative and integrated approach to clinical research touches on four areas of importance to the industry:

- **Population health improvement:** A common goal for all healthcare stakeholders.
- **Patient advocates for research:** With positive experiences, patient volunteers become advocates for clinical research, leading to greater acceptance and participation. Patient advocacy organizations also serve as a vitally important and influential resource, given the deeply entrenched and trusted relationships they have with their constituencies.
- **Trial effectiveness:** With the right engagement and strongly managed processes, trials become more effective.
- **Trial efficiency and cost management:** A collaborative approach to clinical trials can greatly improve the efficiency and speed of a trial while reducing costs.

Conclusion

All of the approaches touched upon in this article lead to improved patient experiences, based on high levels of engagement by all stakeholders, including physicians and organizations. Optimized support for patient volunteers and physicians and other healthcare providers, coupled with high-quality, standardized processes, allows the right physician to connect the right patient to the right trial. This improved patient volunteer matching reduces the frequency of screen failures, improves retention rates, and enables positive healthcare experiences.

Collaboration amongst all stakeholders—patient volunteers, healthcare providers, healthcare systems, drug developers, and policy makers—must be increased to better communicate the value of integrating clinical research into the overall continuum of care, and to further enhance public trust in, and patient engagement with, clinical research.

References

1. Laurance J, Henderson S, Howitt PJ, Matar M, Al Kuwari H, Edgman-Levitan S, Darzi A. 2014. Patient engagement: four case studies that highlight the potential for improved health outcomes and reduced costs. *Health Aff* 33(9):1627–34.
www.ncbi.nlm.nih.gov/pubmed/25201668
2. Neiman AB, Ruppar T, Ho M, et al. 2017. CDC grand rounds: improving medication adherence for chronic disease management—innovations and opportunities. *MMWR Morb Mortal Wkly Rep* 66. <http://dx.doi.org/10.15585/mmwr.mm6645a2>
3. van Onzenoort H, et al. 2011. Participation in a clinical trial enhances adherence and persistence to treatment: a retrospective cohort study. *Hypertension*.
<http://hyper.ahajournals.org/content/hypertensionaha/58/4/573.full.pdf>
4. Heaney L, Hicks W, Seetuthum R. 2013. Adherence in asthma: comparing clinical trials to the real-world. PPDI. www.pppdi.com/late-stage-asthma/Adherence-In-Asthma_PPD-White-Paper.pdf
5. Research!America National Poll on Clinical Research conducted in partnership with Zogby Analytics. 2013. <https://www.elsevier.com/connect/poll-majority-of-americans-wouldparticipate-in-clinical-trials-if-recommended-by-doctor>
6. CenterWatch. 2015. Integrated research partnerships build momentum. *The CenterWatch Monthly* 22(7). <https://store.centerwatch.com/p-459-july-2015-the-centerwatchmonthly.aspx>
7. S. 1048: Enhanced Clinical Trial Design Act of 2017.
<https://www.govtrack.us/congress/bills/115/s1048>
8. Causey M. 2018. Patients emerging as increasingly important clinical trial advocates. *ACRP Blog*. <https://www.acrpnet.org/2018/01/02/patients-emerging-increasingly-important-clinical-trial-advocates/>

9. Mainous AG 3rd, Smith DW, Geesey ME, Tilley BC. 2008. Factors influencing physician referrals of patients to clinical trials. *J Natl Med Assoc* 100(11):1298–303.

www.ncbi.nlm.nih.gov/pubmed/19024226

10. Children's Hospital of Philadelphia. Relapsed leukemia: Emily's story.

www.chop.edu/stories/relapsed-leukemia-emilys-story

11. Gallagher J. 2011. Haemophilia gene therapy shows early success. *BBC News*.

www.bbc.com/news/health-16107411

Jennifer J. Byrne (jbyrne@greatergift.org) is Founder and President of Greater Gift in Winston-Salem, N.C.

Jane M. Shen, PharmD, (jmshen@wakehealth.edu) is President of the Board of Directors at Wake Forest Healthcare Venture, a company based with the Wake Forest Baptist Medical Center in Winston-Salem, N.C.

Amanda W. Wright (awright@greatergift.org) is Executive Director of Greater Gift.

JUNE 2018 CLINICAL RESEARCHER

HOME STUDY

Principal Investigator Concerns

Opinion: Approaches to Set Up Principal Investigators for Success

LEARNING OBJECTIVE

After reading this article, participants will be able to explain the reasons for the change in the number of active principal investigators (PIs) in clinical research, including defining the problem and identifying current stressors; list several ways to make the PI role attractive again; explain the potential role of nurse practitioners in expanding the pool of active PIs; and list several ways that clinical research sites can improve the experience of PIs at their clinical research site.

DISCLOSURE

Molly Downhour, MHA, BSN, NEA-BC, OCN, CCRC: *Employee of Medix*

- 1. The number of active principal investigators (PIs) is currently:**
 - a. Stable
 - b. Increasing
 - c. Decreasing
 - d. Not tracked

- 2. According to the author, a major problem affecting the number of PIs is:**
 - a. Absence of any compensation from sponsors for research-related services
 - b. Lack of awareness of the role of clinical trials in medical breakthroughs
 - c. Insufficient opportunities to conduct clinical trials in the United States
 - d. Disinclination to take on full oversight of trials under increasing regulatory expectations

- 3. Over the last decade, the number one cause of Form FDA 483s (Inspection Observations) leading to Warning Letters from the U.S. Food and Drug Administration to PIs was:**
 - a. Lack of appropriate institutional review board (IRB) oversight
 - b. Conflict of interest
 - c. Incomplete documentation
 - d. Protocol compliance issues

- 4. PIs agree to take on full oversight of the clinical trial, including the investigator agreement, adherence to the protocol and investigational plan, and ensuring the rights, safety, and welfare of all clinical trial participants when they:**
 - a. Complete and sign Form FDA 1572
 - b. Complete the Conflict of Interest form
 - c. Enroll the first participant in a clinical trial
 - d. Agree upon their salary

5. Additional stressors in the current economic healthcare landscape that contribute to the decline in investigator oversight and engagement include:

- a. Too many highly trained clinical research staff members available causing a glut of qualified staff
- b. Decreasing regulatory requirements regarding adherence to the ICH guidelines causing confusion
- c. Increased NIH grant funding available providing increased alternatives to clinical research
- d. Lack of PI orientation/training regarding their responsibilities when conducting clinical research

6. The culture and expectations at sites at which site leaders understand the need to operate like a business include:

- a. Providing adequate time and resources for research
- b. Minimizing training for clinical staff
- c. Increasing the size of clinical trials
- d. Increasing the number of clinical trials

7. The HonorHealth's Drug Development Scholar program is a program that:

- a. Recruits mature physicians with a passion for drug development
- b. Rewards physicians for their work in clinical research
- c. Focuses on Phase IV (post-marketing) clinical trials
- d. Has been successful at mentoring young oncologists and hematologists

8. According to the *Code of Federal Regulations* in CFR 312.53 and 812.43, sponsors are required to select investigators who:

- a. Are qualified by education and experience as appropriate experts to investigate the test article, whether investigational product or device
- b. Are physicians
- c. Are board certified for the medical specialty in which the clinical trial is being conducted
- d. Have served on an IRB prior to conducting clinical research

9. According to the author, nurse practitioners are:

- a. Not qualified to be PIs or sub-investigators because they are not physicians
- b. Currently underutilized in clinical research
- c. Excluded from being PIs or sub-investigators by the CFR
- d. Not being approved to be PIs by central institutional review boards on industry-sponsored trials

10. Clinical investigator training:

- a. Is not necessary if the investigator has the appropriate licensure and educational background
- b. Is not the responsibility of the clinical research site and takes away valuable time from conducting clinical research
- c. Is standard across all types of clinical research and research sites so it only needs to be conducted once in a clinical investigator's career
- d. Should involve a thorough investigator orientation process and competency checklist conducted at the clinical research site

Embedding Clinical Research into the Continuum of Care

LEARNING OBJECTIVE

After reading this article, participants will be able to explain the value of the integration of clinical research into the continuum of patient care; describe the overall experience of participants in clinical research; list several ways of breaking down the walls between clinical research and conventional treatment; list several ways of spreading the word around the value of the integration of clinical research into conventional treatment; and list several ways that the biopharma industry can support the collaborative and integrated approach to clinical research.

DISCLOSURE

Jennifer J. Byrne; Jane M. Shen, PharmD; Amanda W. Wright: *Nothing to disclose*

11. People are far more engaged in their care when participating in a clinical trial because:

- a. They know they are being closely monitored and may be reported for nonadherence
- b. They don't want to be disqualified for being remunerated for their participation
- c. They are often desperate for care and have been told by doctors that a trial is their last hope
- d. They see a connection between participation and the greater good of the patient community

12. A recent study conducted with 42 diabetic patients participating in an ongoing diabetes trial found:

- a. A high level of engagement and satisfaction with their treatment
- b. A high level of engagement but low satisfaction with their treatment
- c. A low level of engagement but a high level of satisfaction with their treatment
- d. A low level of engagement and satisfaction with their treatment

13. Overall, surveys show significantly higher levels of satisfaction across which of the following dimensions of care in clinical research?

- 1. Access to care
- 2. Efficiencies of care delivery
- 3. Quality of care
- 4. Cost effectiveness of care

- a. 1, 3, and 4 only
- b. 2, 3, and 4 only
- c. 1, 2, and 4 only
- d. 1, 2, and 3 only

14. Non-adherence to treatment is associated with:

- a. Longer clinical trials
- b. Increased morbidity and mortality
- c. Decreased healthcare costs
- d. Lower rate of hospitalizations

- 15. What percentage of the U.S. population participates in clinical trials?**
- a. Less than 1%
 - b. 20%
 - c. 50%
 - d. 72%
- 16. What percentage of the U.S. population would participate if their doctor recommended it?**
- a. Less than 1%
 - b. 20%
 - c. 50%
 - d. 72%
- 17. According to the authors, healthcare organizations need to break down the barriers between:**
- a. Clinical research and conventional treatment
 - b. Clinical research and biopharmaceutical companies
 - c. Clinical research and the U.S. Food and Drug Administration (FDA)
 - d. Clinical research and contract research organizations
- 18. Predictive analytics can identify:**
- a. Potential funding sources
 - b. Gaps in care
 - c. Potential clinical research participants
 - d. Potential FDA inspection events
- 19. The Enhanced Clinical Trials Design Act:**
- a. Focuses on reducing the cost of clinical trials
 - b. Strives to modernize the clinical trial process
 - c. Focuses on minimizing the oversight of the FDA
 - d. Increases the scrutiny of data by the Centers for Disease Control and Prevention
- 20. Which of the following areas of importance to the biopharmaceutical industry involves a collaborative approach to clinical trials that can greatly improve the efficiency and speed of a trial while reducing costs?**
- a. Population health improvement
 - b. Patient advocates for research
 - c. Trial effectiveness
 - d. Trial efficiency and cost management