BUILDING CLINICAL TRIAL AND HEALTH RESEARCH ACCESS

for People of Color via Community Health Centers (CHCs)

GRANTEE:

neighborhood HEALTHCARE

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ALTURA

Made possible by a Health Equity and Diversity Grant from Genentech, a member of the Roche Group

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The toolkit will be available in January 2024 and can be requested at info@alturastudies.com.

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Executive Summary

The *Building Clinical Trial and Health Research Access for People of Color via Community Health Centers* grant examined barriers to clinical study participation among executive leaders, providers, and medical staff at community health centers (CHCs) nationally. Neighborhood Healthcare, the CHC grantee, and Altura, the project manager and lead advisor, collaborated to initiate and execute this project.

The lack of racially and ethnically diverse populations (REPs) representation in clinical trial participants has long been a challenge in medical research. Based on U.S. census data, about 40% of the U.S. population is racially and ethnically diverse. However, less than 25% of clinical trial participants fit into this category.[1]

The core premise of this project is that REPs highly value and trust people who provide healthcare and health information in their communities. It therefore hypothesizes that CHCs could be valuable contributors, either directly or indirectly, for all types of clinical studies, thereby improving on the lack of diversity that has plagued clinical research historically.

For this project, the term "clinical studies" refers to a spectrum, ranging from basic observational studies to clinical trials involving investigational medications subject to FDA review. This range includes a wide array of non-investigational intervention clinical studies (e.g., behavioral, educational services and technology) that reside between these extremes. Given that clinical trials of investigational medications exhibit the largest diversity gap, are the most challenging to conduct, and have the greatest impact on equity in innovation, this publication will predominantly focus on this type of clinical study.

[1] U.S. Food and Drug Administration [FDA], 2021, *Drug Trials Snapshots Summary Report*. [Jul; 2021]; https://www.fda.gov/media/145718/download 2021 2:2021.

For this project, the term "people of color" refers to any persons who identify as non-white/Caucasian, such as Black/African American, Asian, Hispanic/Latino, Native Hawaiian/Pacific Islander, American Indian/Alaskan Native, or another race. This population is also collectively referred to as "racially and ethnically diverse populations" or "REPs". Throughout this white paper, the term "people of color" will be used interchangeably with the term REPs.

When REPs are inadequately represented in studies, the research findings may not be generalizable to them. Healthcare practitioners who treat REPs may be left without key information concerning the effectiveness of various treatments or other interventions for their patients.

> ***"If the [clinical trial] that showed this improvement … isn't generalizable … to [my patients], then … I'm conjecturing on whether this is going to be beneficial or not. When I look at my patient and say, 'Hey, you should do this,' I'm actually tempering my own skepticism about whether this is the right move or not because [the trials are] not based in populations that look like the patient in front of me or did not have a representative sample there." — Medical provider***

This study answered three fundamental questions to help determine a path for CHCs to appropriately support diversity in clinical studies, either directly or indirectly:

1. Do CHCs feel it is important to involve people of color in clinical trials? (Figure 16)

TAKEAWAY: Overwhelmingly, yes as 91% of respondents felt it was very important to involve REPs in clinical trials. This result is highly encouraging and highlights that CHCs are aware of the lack of representation of these populations in clinical studies. More importantly, it underlines the everyday impact this gap has on the care they provide to their patients daily. Furthermore, this result supports a strong alignment between the intent of this grant and the objectives of CHC stakeholders to provide more resources and options to the patients they serve, specifically REPs.

2. To what extent should CHCs be involved in clinical studies? (Figures 9 and 10)

TAKEAWAY: Most CHCs believe they should be involved in some way across the spectrum of clinical studies. An overwhelming majority (86.5%) noted that their CHC should be involved in a mix of observational studies and clinical trials, while among this number, most favored more involvement with observational studies. Although there is a desire for clinical trials within CHCs, in practice, their role is

restricted, primarily due to limited access to studies, inadequate resources, and/or a lack of expertise. A large majority thought that CHCs should at least let their patients know about clinical trials so they have an option to pursue them if interested. A total of 54.1% said that they could discuss clinical trial options with their patients, which is a straightforward approach with low resource investment required. Only 2% believe that CHCs should not be involved with clinical trials in any way. In addition, 37.8% felt that they could refer patients to a study site, which is also a lower-effort option for CHCs.

3. How can CHCs overcome barriers to clinical study participation? (Figure 13)

TAKEAWAY: Many barriers exist for CHCs to build a research infrastructure with the right staff and resources. Fortunately, many of these barriers can be overcome by selecting the appropriate studies and level of engagement for each CHC's specific organization. Building and operating a dedicated research site within a CHC requires significant human and financial resources. However, CHCs can establish relationships with local or regional study sites to facilitate patient referrals. Given that some patient groups may face transportation or scheduling challenges, online and virtual studies are viable alternatives. Any clinical study that seeks to understand the impact of medical or health-related interventions on REPs will help inform providers of better care options in the future.

Considering that CHCs are rarely involved in clinical trials, respondents expressed a strong belief in the benefits of such trials. 81.7% of respondents felt that clinical trials are needed for medical innovation (Figure 8). Of particular interest, many felt the proper safety precautions were in place to mitigate risks.

Engaging CHCs will mobilize a major component of the healthcare delivery model that serves over 32 million patients, mostly REPs. This will foster the trust and connections necessary to support local, regional, and national clinical studies.

A current participant in a phase III clinical trial, an African American member of Neighborhood Healthcare, stated:

> ***"It made a difference knowing that I had a link to the study center since it was being done at Neighborhood Healthcare. When considering the clinical trial, that made the study 'more legitimate.'"***

Call to Action: CHCs

CHCs are each called to take their own appropriate next step to support clinical studies. How this is done is of secondary importance, as long as it aligns both with patient care needs and with the CHC's available resources (e.g., expertise, resources, time, funds). Special consideration should be given to supporting any clinical study that directly aims to expand diversity and representation of REPs.

Options for CHCs to Participate in Clinical Studies of All Types

Source: Altura

Call to Action: Life Science and Research Organizations

Life Science and Research Organizations are called to engage CHCs in some capacity in order to increase the study participation of REPs. For any clinical study collaboration with CHCs, a long-term perspective is advised, for which the roles and interests of the parties are aligned. Below are some options for engaging CHCs:

- Conduct retrospective reviews of medical data (e.g., EHR, data warehouse, lab, claims, Rx data) for a medical condition or intervention
- Participate in observational studies
- Serve as a source for prescreened patients for clinical trials
- Serve as a satellite site for clinical trials (delegated roles to main study site)
- Serve as a main or primary site for clinical trials

The findings of this study affirm that CHCs, which provide care for a large proportion of REPs, offer a meaningful and underutilized resource to help address the lack of diversity in clinical studies. This white paper is intended to provide CHCs, CHC trade organizations, research institutions, life science companies, and other stakeholders with information to support the involvement of CHCs in clinical studies and thereby increase the participation of REPs in these studies.

A related toolkit will be made available to serve as a guide and will include information on how to organize resources and become involved with clinical studies of all types, how to distinguish participation options and study types, and how CHCs can be directly and indirectly involved with clinical trials. The toolkit will be available in January 2024 and can be requested at info@alturastudies.com.

Introduction

Neighborhood Healthcare, a Federally Qualified Health Center (FQHC) based in Escondido, California, received a grant from Genentech's Health Equity Fund to study and increase the diversity of clinical study populations. Altura served as lead advisor and project manager for the grant, *Building Clinical Trial and Health Research Access for People of Color via Community Health Centers*.

A national survey of 246 respondents (executive leaders, medical providers, and medical staff) from 41 CHCs uncovered a wide range of perspectives, issues, needs, and opportunities. These findings are highlighted in this white paper. Additionally, a CHC-specific toolkit is available to inform and guide CHCs on how to support patient participation in clinical and health studies of all types.

For this project, the term "**people of color**" refers to any person or group of people who identify as non-white/Caucasian, such as Black/African American, Asian, Hispanic/Latino, Native Hawaiian/Pacific Islander, American Indian/Alaskan Native, or another race. This population is also collectively referred to as "racially and ethnically diverse populations" or "REPs". Throughout this white paper, the term "people of color" will be used interchangeably with the term REPs.

The term "**community health center**" (CHC) generally refers to any type of grant-funded health center, such as a Federally Qualified Health Centers (FQHC) and FQHC Look-Alikes in any type of setting (e.g., rural, urban).

Clinical studies involve collecting data about patient experiences and outcomes, as well as the safety and efficacy of medical interventions. For this project, the term "clinical studies" refers to a spectrum, ranging from basic observational studies to clinical trials involving investigational medications subject to FDA review. Each category is defined as follows:

- **OBSERVATIONAL STUDIES:** This type involves observing and/or surveying of patient volunteers in natural care settings. Observational studies are the most common and are typically funded by government or healthcare foundation grants that seek knowledge about a specific medical condition, health service, or patient population.
- **CLINICAL TRIALS:** This type involves investigational medical interventions to determine if a treatment or medication is safe and effective. It requires oversight and approval by a governmental agency (e.g., Food and Drug Administration, or FDA) and an Institutional Review Board (IRB).

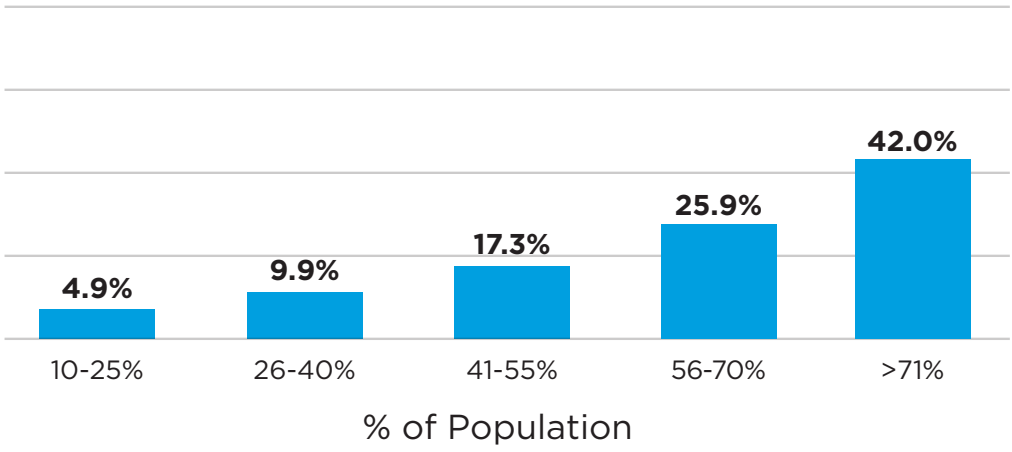
This range includes a wide array of non-investigational intervention clinical studies (e.g., behavioral, educational services and technology) which should be considered as study options for CHCs.

The Challenge

The lack of representation of racially and ethnically diverse populations (REPs) in clinical trial participants has long been a challenge. According to U.S. census data, approximately 40% of the U.S. population is racially and ethnically diverse. However, less than 25% of clinical trial participants fall within this category.[2]

The underrepresentation of diverse populations in clinical studies deepens health disparities. Critical information may be overlooked, such as genetics, risk factors, and differences in disease presentation. Without adequate data about the safety and efficacy of new and existing interventions for REPs, these populations cannot fully benefit from medical advances.

Figure 1. Approximately what percentage of your patient population are people of color?

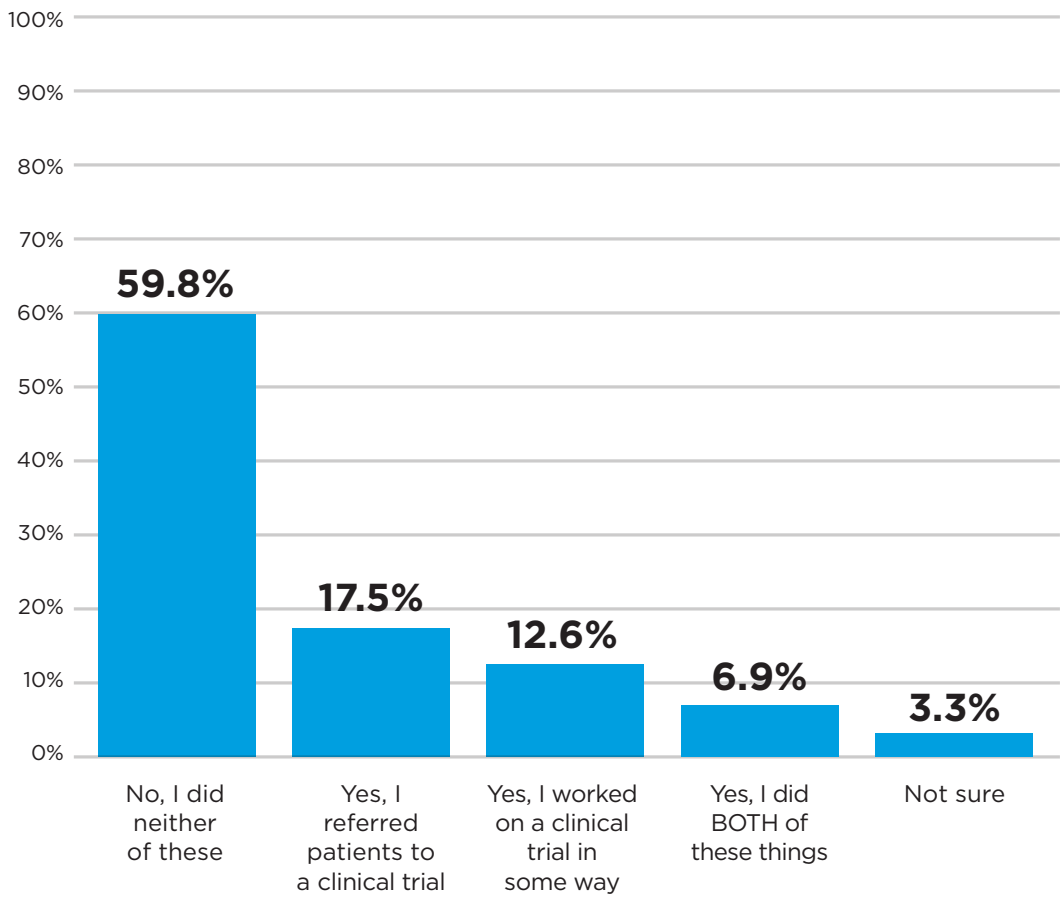


Respondents: executive leader cohort, *n* = 81.

More than half of patients served by CHCs nationally are racially and ethnically diverse. For CHCs in this survey, REPs represented the majority of patients (Figure 1). Yet the vast majority of CHCs do not participate as clinical study sites and rarely refer patients to studies (Figure 2).

[2] U.S. Food and Drug Administration [FDA], 2021, *Drug Trials Snapshots Summary Report*. [Jul; 2021]; https://www.fda.gov/media/145718/download 2021 2:2021.

Figure 2. In your current or past roles at a CHC, have you ever worked on a clinical trial in some way or referred patients to a clinical trial?



Respondents: all cohorts n = 246

This lack of involvement leads to underrepresentation in studies and to data that is biased and potentially not relevant to CHCs' patient populations. Engaging CHCs in clinical studies presents a unique opportunity to increase representation and improve the validity of clinical evidence for REPs.

Project Premise and Goals

The core premise of this project is that REPs highly value and trust people who provide their primary healthcare or healthcare information in their communities. It therefore hypothesizes that CHCs could be valuable contributors, either directly or indirectly, for all types of clinical and health research. Engaging CHCs will mobilize a major component of the healthcare delivery model that serves over 32 million patients, mostly REPs. This will foster the trust and connections necessary to support local, regional, and national clinical studies.

The goals of this project were to improve clinical study access for REPs and advance diversity by:

1. **Identifying and analyzing real and perceived barriers to CHC participation in clinical studies.**
2. **Developing a framework for CHC participation in broad areas of research interest.**
3. **Expanding CHC participation in clinical studies, whether directly as study sites, or indirectly by referring patients for clinical trials and health studies.**
4. **Building interest among life science companies, academic centers, and other study sites in partnering with CHCs and supporting their involvement.**

National CHC Survey Results

METHODS: Survey Development

This project involved a cross-sectional study of clinical study perceptions among CHC executive leaders, medical providers and medical staff. The survey included both single-choice and multiple-choice questions, with some questions allowing respondents to provide free-text responses using the option "Other - Please describe". Altura developed the survey and interview protocol with feedback from Neighborhood Healthcare, the project's advisory panel, and Health Assessment and Research for Communities (HARC). HARC conducted a literature search to validate the survey, as well as a final review to confirm statistical integrity. The project's advisory panel approved the final survey questions and methods. Lastly, using the exemption review process, an IRB determined that the study qualified for an exemption from the need for IRB review in accordance with 45 CFR 46.104(d)(2(ii)).

METHODS: Data Collection and Analyses

Altura's study team administered the survey online to CHCs beginning in early April 2023 and concluded data collection in July 2023. Descriptive statistics were performed for all questions of the survey (e.g., percentages of all response options). Additionally, the study examined statistically significant differences between executive leaders, medical providers, and medical staff regarding CHC involvement in clinical trials. A comparative chi-square analysis was performed for these groups, with a p-value less than .05 considered statistically significant.

CHCs nationally were invited to participate in the project regardless of size or location. Altura's study team contacted CHCs from every state through publicly available records, and many state CHC and primary care associations invited their members to join via email and announcements at membership meetings. A deadline was given, and the first 40 CHCs to respond were included in the survey (note: the final total was 41). The only factor considered for participation, due to the grant's focus, was that the CHC's racially and ethnically diverse population was 15% or greater. Participating CHCs were each asked to invite two executives (C-suite, leaders), two medical providers (doctors, nurse practitioners, physician assistants) and two medical staff (medical assistants, registered nurses, licensed vocational nurses).

Figure 3.

What type of CHC are you considered?

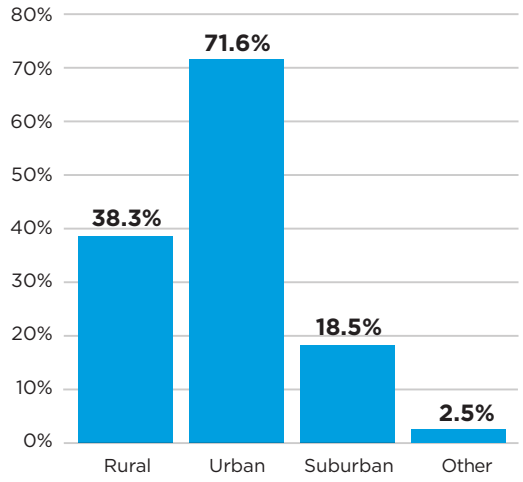
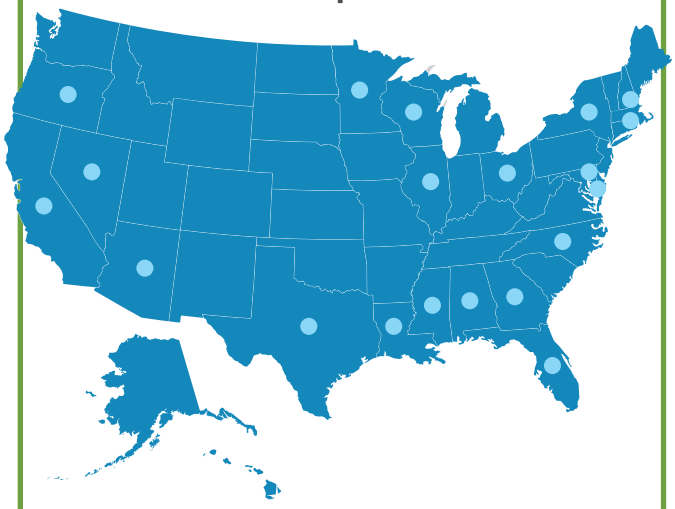


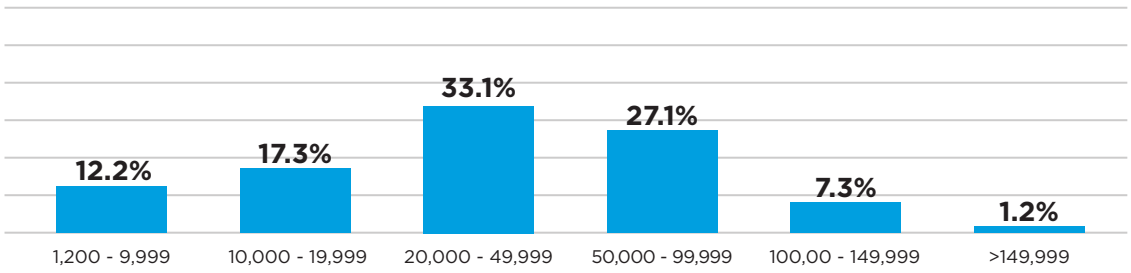
Figure 4.

States Represented



Respondents: executive leader cohort, *n* = 81.

Figure 5. Approximately how many total unique active patients does your CHC care for?



Respondents: executive leader cohort, *n* = 81.

The survey included 246 respondents, comprising 32.8% executive leaders, 34.0% medical providers, and 33.2% medical staff from 41 CHCs representing 20 states as well as various types and sizes of CHCs (Figures 3, 4, and 5).

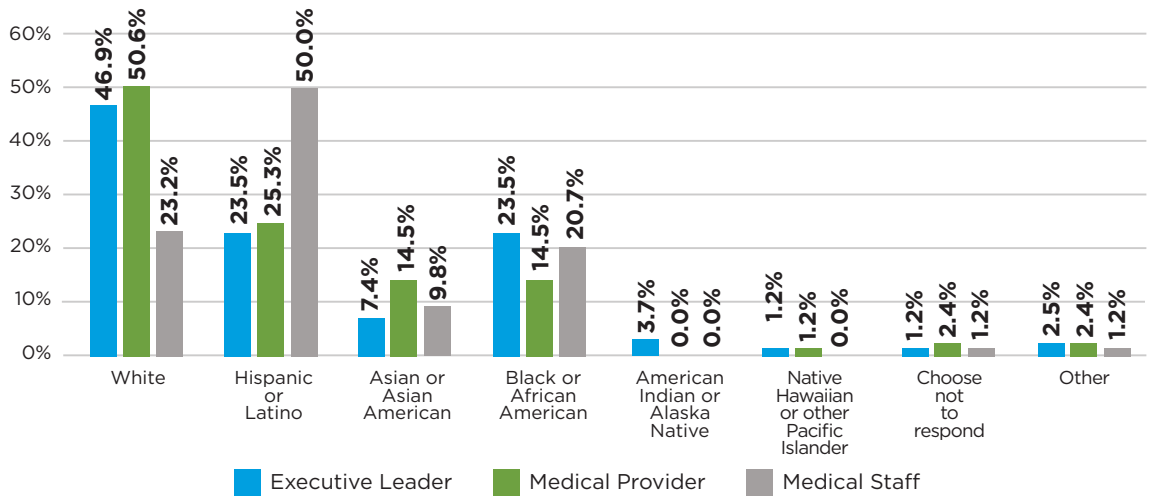
The study team also conducted phone and video interviews with 20 CHC staff members from 10 states (Arizona, California, Florida, Illinois, Louisiana, Massachusetts, Minnesota, North Carolina, Ohio, and Texas) and the District of Columbia. Seven interviewees were executive leaders, six were medical staff members, and seven were medical providers. The semi-structured interviews more deeply explored clinical study views in the CHC setting, with responses mirroring the survey results and adding other insights. Interviewees were encouraged to expand on topics or introduce new ones. Interviews were audio-recorded and the transcripts analyzed to identify common themes.

Key Findings

Among all respondents, the top three roles were physician (18.3%), registered nurse (13.0%), and medical assistant (13.0%). The average number of years worked at any CHC was 9.2, ranging from less than 1 year to 40 years.

Related to age, most respondents were in their 30s (30.0%), 40s (28.7%), or 50s (21.1%). More than two-thirds of respondents (69.1%) identified as female, 30.1% as male, and 0.8% as transgender.

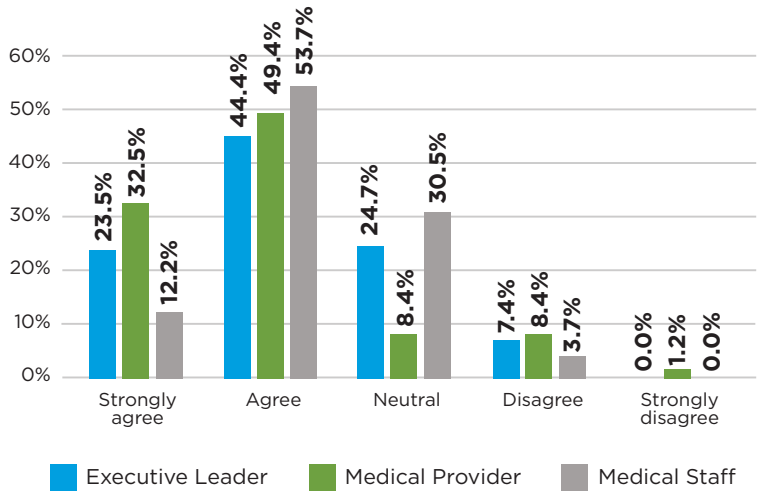
Figure 6. With what ethnicity or race do you identify?



Respondents: all cohorts n = 246

In response to the question about their self-identified ethnicity or race, 40.2% of respondents identified as White, 32.9% as Hispanic or Latino, 19.5% as Black/African American, and 10.6% as Asian or Asian American. Respondents who selected "Other" (2.0%) identified as South Asian, Hmong, Central Asian and Cape Verdean (Figure 6).

Figure 7. How do you feel about this statement: I am very knowledgeable about observational studies and clinical trials and their differences.



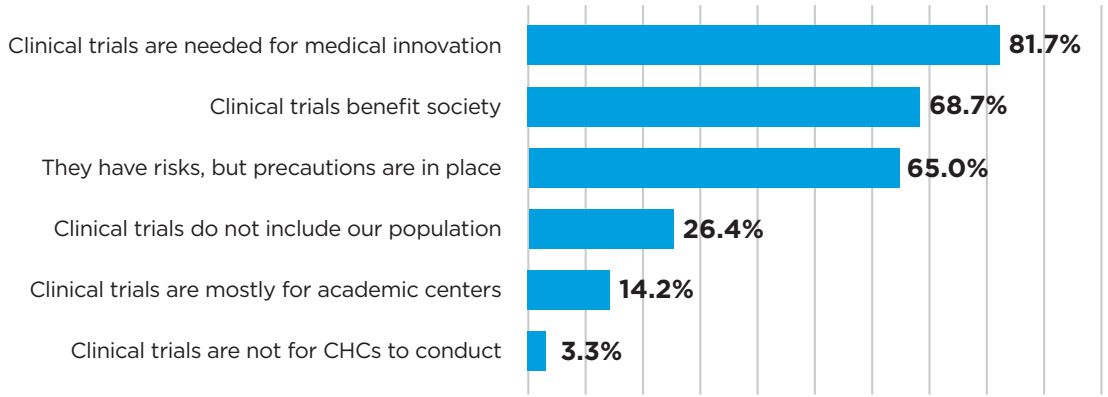
Respondents: all cohorts n = 246

Most respondents indicated they had a good understanding about observational studies, clinical trials, and their differences. (Figure 7).

It should be noted, based on the interviews conducted, that clear understanding about the different types of clinical studies, especially clinical trials, may be overstated in the survey results. Interviewees had limited experience with clinical trials. Only one executive leader reported such experience, and several others mentioned experience with observational studies or other non-clinical trial research.

Like the executives, only one staff member and one medical provider reported clinical trial experience. Several providers mentioned past experience with conducting observational studies as residents or medical or doctoral students, but not in their current practice.

Figure 8. What are your general impressions of clinical trials?



Respondents: all cohorts n = 246. Selected all that apply.

All respondents were asked about their general impressions of clinical trials and could select any statements that applied (Figure 8). The overall response was positive and very few (3.3%) felt that clinical trials were "not for CHCs to conduct." While many felt confident that safety precautions are in place to mitigate risks, additional education and awareness about the oversight and systems in place could further enhance trust.

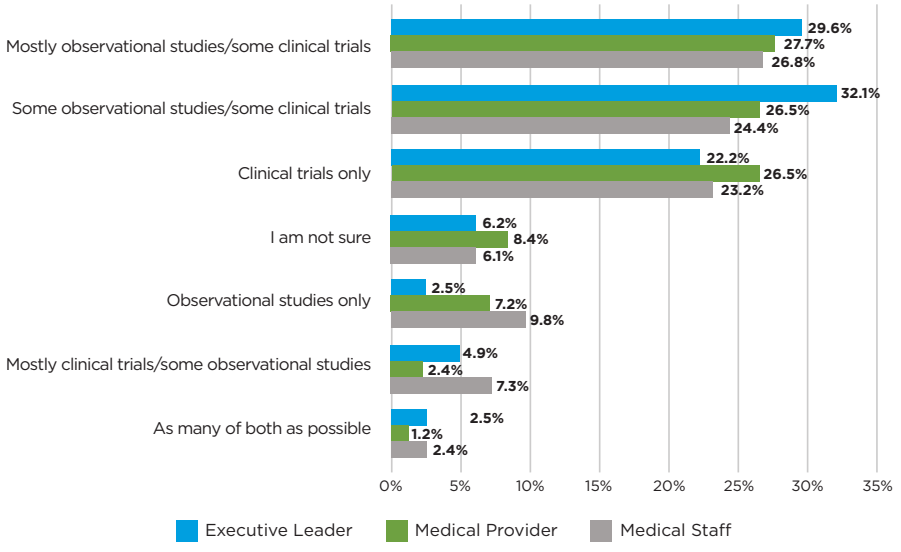
The 20 interviewees were not explicitly asked about their impressions of clinical trials, but nonetheless shared their general thoughts throughout the interviews. Executive leaders and medical providers discussed the importance of studies for patients and medical science. Several medical staff members also emphasized their benefits for underrepresented communities.

> ***"I like the idea [of CHCs taking part in studies]. It's just something where all the pieces have to come together.... [It] needs to be win, win, win all across for the underrepresented groups.... It should benefit the clinic, it should benefit the drug company, it should be structured so that everyone benefits. As long as [that] happens, I'm all for it." — Medical staff member***

Interviewees expressed some reservations about clinical trials, such as the challenge of obtaining informed consent and ensuring appropriate compensation. Overall, however, they saw clinical trials as important for both the medical community and the patient population.

Figure 9.

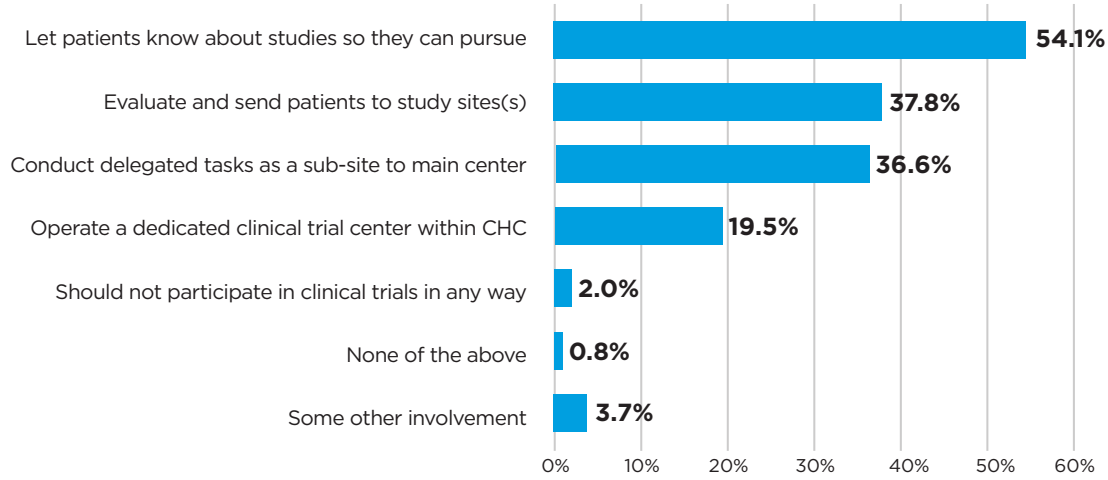
Which type or mix of clinical studies do you believe CHCs should participate in?



Respondents: all cohorts n = 246

Respondents held varying opinions on the types of clinical studies CHCs should participate in, but generally agreed that some combination of clinical trials and observational studies is appropriate. While there were some slight differences based on the respondents' roles, these were not significant (Figure 9).

Figure 10. To what extent do you feel your CHC could be involved with clinical trials?



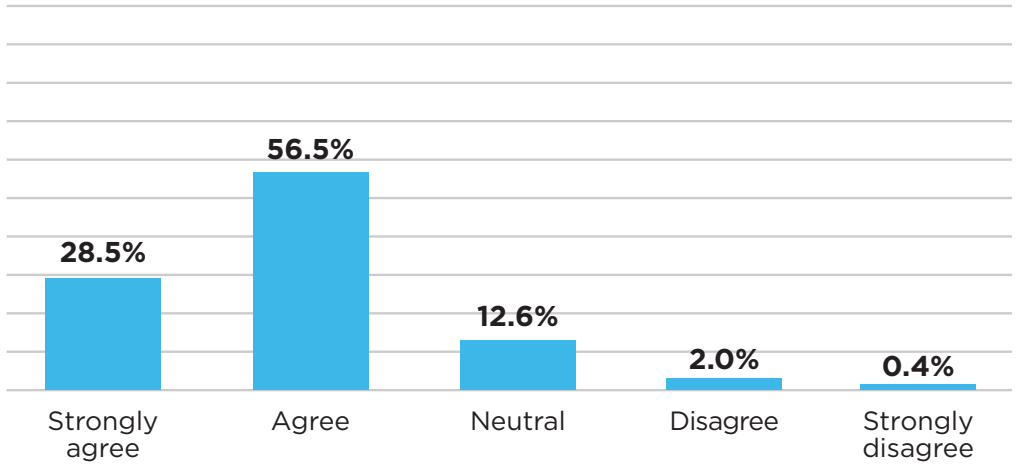
Respondents: all cohorts, n = 246. Selected all that apply.

When asked to what extent they felt their CHC could be involved with clinical trials (Figure 10), a majority (54.1%) indicated that the CHC should let its patients know about studies. This would work very well for CHCs that do not have the time and resources to be directly involved in trials.

CHCs are willing to participate directly as either a main or sub-site but, as previously discussed regarding barriers, they would need funds, guidance and training. CHCs are encouraged to start by addressing the basics, such as discussing study opportunities with patients and/or evaluating patients for participation. From there, they may progress to more direct participation as a main or sub-site.

"I would think that there would have to be some sort of physician champion, some sort of physician drive … this, and some interest from them to say, 'We believe this is beneficial to our patients because we believe this fits within the care that we give.'" — Executive leader

Figure 11. Please rate your agreement with the following statement: CHCs should provide the option for their patients to participate in clinical trials.

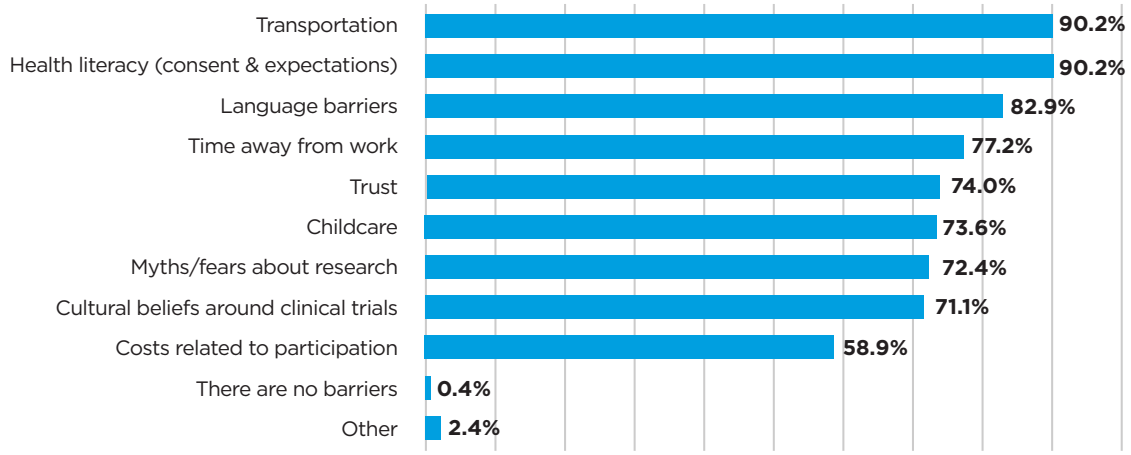


Respondents: all cohorts n = 246

Eighty-five percent of respondents either strongly agreed or agreed that CHCs should provide the option for patients to participate in clinical trials (Figure 11). Thirty-five respondents provided explanations for their agreement ratings, with selected comments including:

> ***"It is important to include CHC population in research so that data gathered can represent the patients we serve."***
> ***— Medical provider***

Figure 12. What barriers might your patients encounter when considering participation in a clinical trial?



Respondents: all cohorts n = 246. Selected all that apply.

In interviews about barriers to patient participation in clinical trials, most responses referred to people of color, while some applied to CHC patients in general. Barriers discussed included transportation, language barriers, continuity of care, and mistrust of medical research among some communities (Figure 12).

> ***"When you're asking folks to leave their home to participate in [clinical trials] … if it's not … their priority, if [they] are working two jobs and … if it's not going to fit within the [available] time that they have that week — They're just not going to go. It's why they don't come to their appointments sometimes. I feel like we just don't make it easy for them to participate." — Executive leader***

Several interviewees mentioned the infamous Tuskegee Syphilis Study[3] as an example of why African American and other communities might view clinical studies with suspicion. Interviewees also discussed the extraordinary barriers patients already face in accessing basic medical care, such as the difficulty of attending appointments due to inflexible work schedules. Figure 8 above indicates that healthcare professionals feel that safety precautions have improved for clinical trials. For this reason, it is important for CHCs to be directly or indirectly involved to foster trust within the communities they serve.

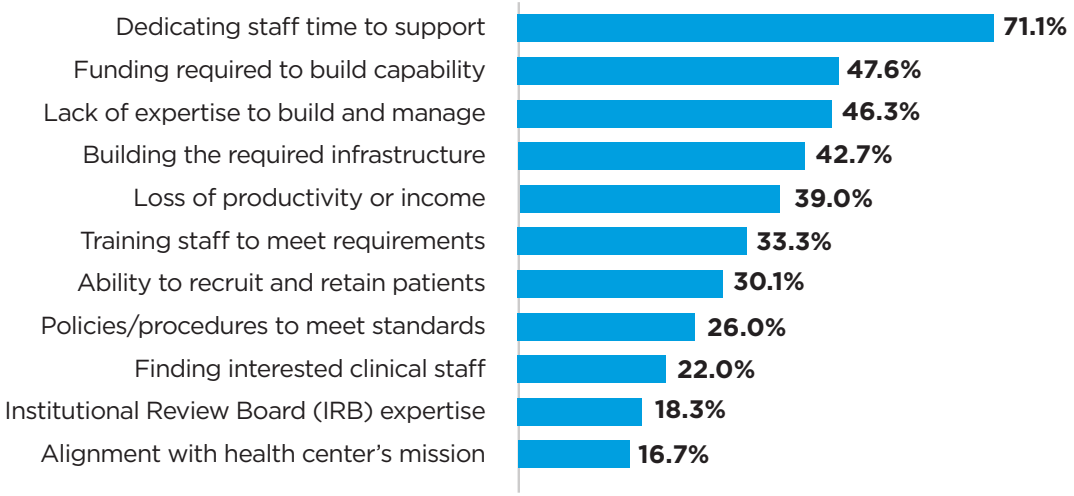
[3] As one journalist has written, the Tuskegee Syphilis Study is "perhaps the most enduring wound in American health science" (Newkirk, 2016).

Some topics mentioned during the interviews require additional clarification due to misconceptions. These include the ability to offer high patient payments or stipends (level of inducement must be considered and be governed by an Institutional Review Board or IRB), insurance coverage (not required unless standard of care is involved) and the necessity for CHCs to operate their own IRB (not required as central IRBs are available).

Patient costs related to clinical studies were mentioned as a concern; however, it should be noted that most, if not all, studies cover the expenses associated with visits and procedures for clinical trials. Additionally, to encourage clinical study participation, the Clinical Treatment Act contains provisions to cover specific costs related to clinical studies, particularly for standard-of-care components included in a protocol.

Figure 13.

What are the main barriers to CHCs in conducting clinical trials?



Respondents: all cohorts, n = 246. Selected all that apply.

CHCs face many barriers when considering direct participation in clinical trials (Figure 13). The most pressing barriers are associated with staff, expertise, and the funds required to build and operate a suitable research function.

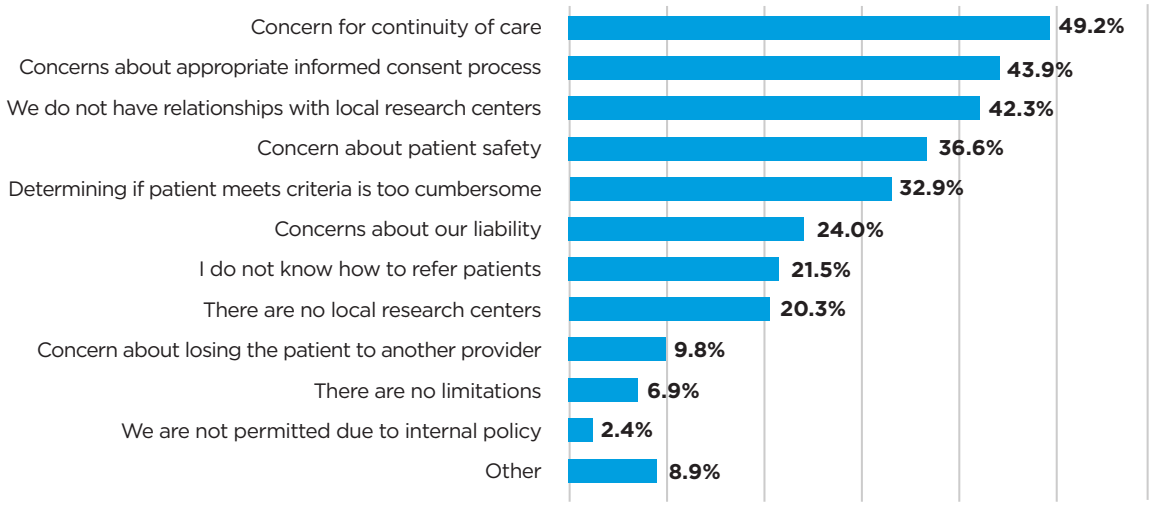
Interviewees elaborated on these concerns, citing a shortage of research experience/expertise and resources, a need for staff

"A community health center is based on reimbursement and quality metrics... Certain luxuries of increased time, increased funding aren't in the equation, and especially right now after the pandemic and with staffing shortages. Getting the manpower to assist with [clinical trials] is difficult."
— Medical provider

training, and a need for more staff. Some executive leaders expressed a desire for expert outside guidance to set up clinical trial programs. Several medical providers stressed that, given the chronic underfunding and understaffing of CHCs, there is a need for more financial and personnel resources. Some medical staff mentioned the need for assistance in educating patients about clinical trials.

> ***"What we probably want to do is find ... somebody who runs clinical trials and have them guide us through the process. What do you need, what do you have to have, what does the infrastructure look like? How do you scale the resources based on what? Based on number of participants? The time of the ... trial? How extensive or how limited it is? [We] would need, first of all, to start with somebody that would help guide and structure at least the beginnings of what would be a clinical trials department." — Executive leader***

Figure 14. Which of the following are limitations to sending patients to a research center for a clinical trial?



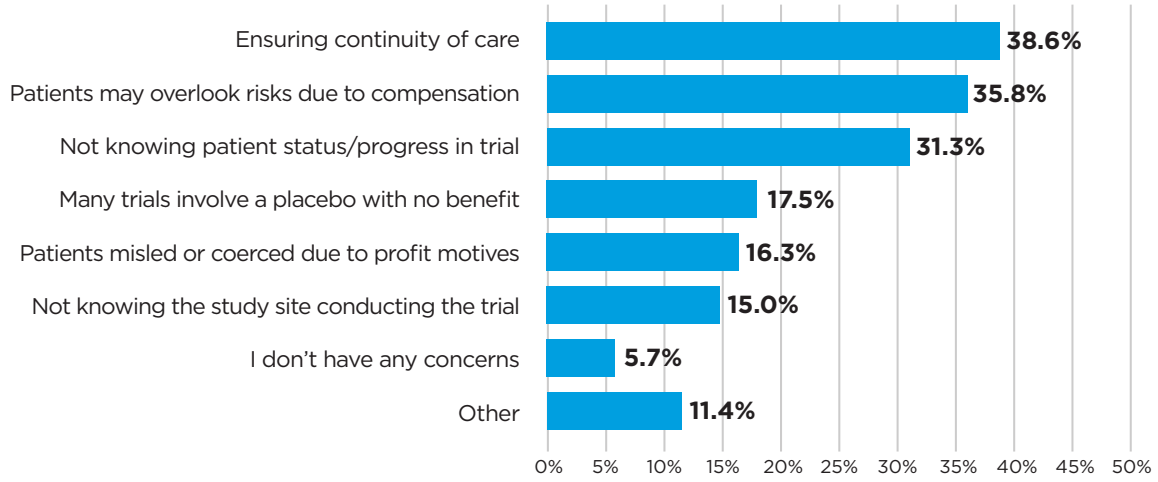
Respondents: all cohorts n = 246. Selected all that apply

When CHCs cannot directly conduct clinical trials, they must rely on external, local, or regional study sites. However, the majority of respondents noted either the lack of an established relationship with study sites or concerns about patient safety and continuity of care. This is important because CHCs are responsible for managing their patients' chronic and acute medical conditions, which could potentially interfere

with the conduct of the study (Figure 14). Receiving information about the patient's progress during the clinical trial supports continuity of care. For example, understanding which medications are prohibited during the study not only ensures patient safety but also promotes protocol compliance. Addressing these concerns will be paramount to encouraging clinical trial participation.

Concerns raised during the interviews included ensuring continuity of care post-trial, the difficulty of explaining clinical trials to CHC patients, and the barriers to low-income patients participating in clinical trials. Medical providers also noted the unequal power dynamic between themselves and patients, highlighting the need to consider this dynamic when designing study recruitment plans.

Figure 15. What would be your primary concerns with suggesting clinical trials for your patients?



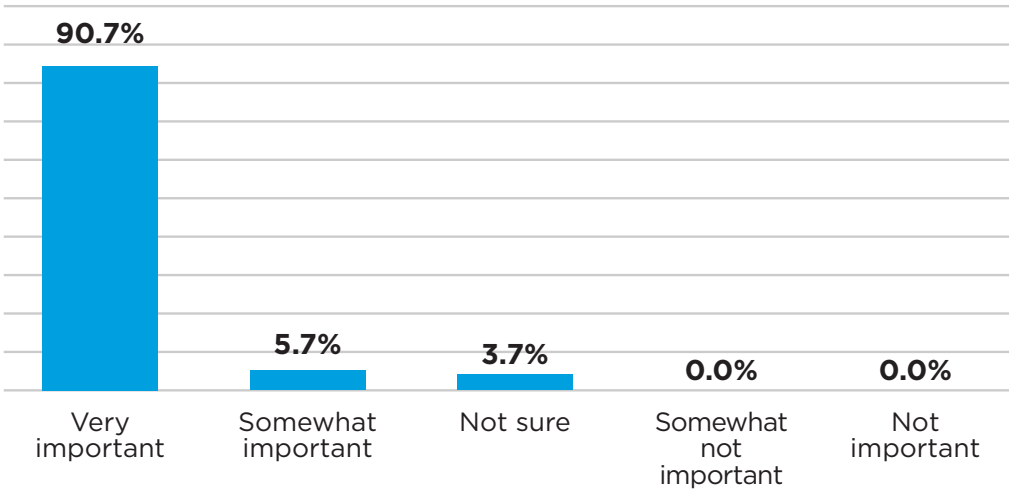
Respondents: all cohorts n = 246. Selected all that apply.

"As a provider, I owe it to my patients to ensure their safety. That should ALWAYS be the top priority." — Medical Provider

As shown in Figure 15, more than a third of all respondents (38.6%) expressed that their primary concern when recommending clinical trials to patients was ensuring the continuity of care. This concern influences their willingness to talk to patients about clinical trials and to refer patients to studies being conducted outside of the CHC.

Interviewees expressed some reservations about some aspects of clinical trials, such as the challenges associated with obtaining informed consent and ensuring appropriate compensation. It is important to note that regulations mandate that trained and professional clinical study sites obtain and document proper informed consent. IRBs govern the ethical conduct of research and the safety of study participants. Participant compensation, often referred to as stipends, is reviewed to ensure an appropriate payment level in order to minimize the potential for undue influence that may arise with higher payments.

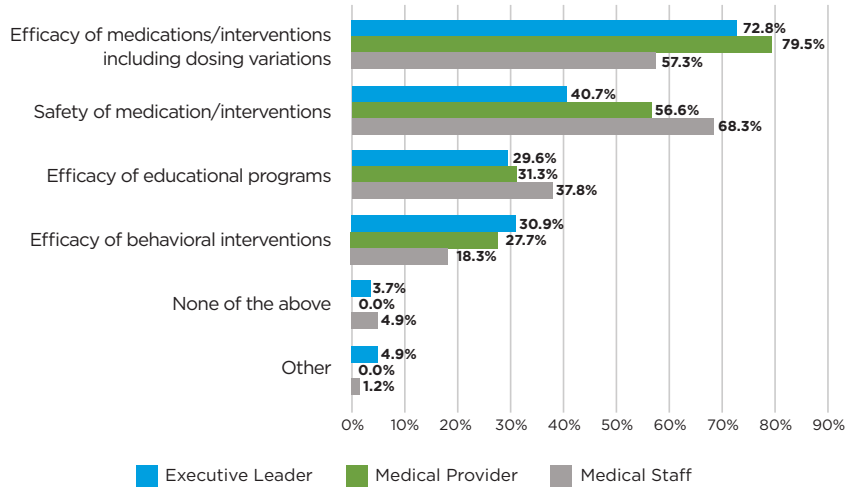
Figure 16. How Important is it to Involve People of Color in Clinical Trials?



Respondents: all cohorts, n = 246.

It was imperative to understand whether CHCs considered that involving REPs in clinical trials was important given the multitude of pressing issues within the healthcare system and with their primary focus on providing medical care with limited financial and human resources. The majority of respondents (90.7%) stated that involving people of color in clinical trials is very important (Figure 16).

Figure 17. Which areas of clinical study focus do you believe are most important for people of color to be involved in?

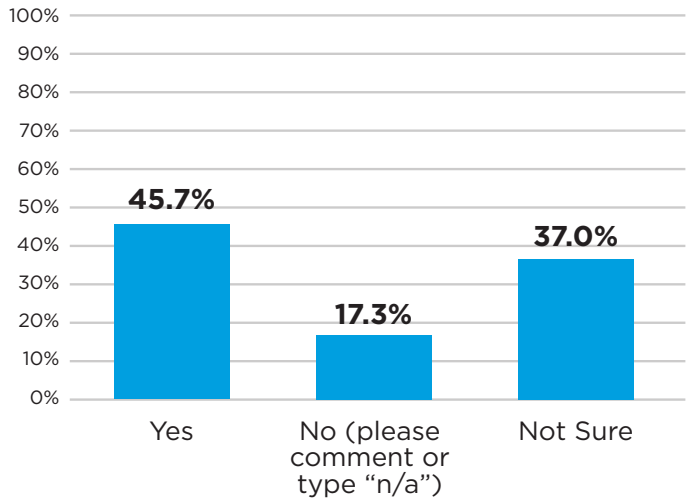


Respondents: all cohorts n = 246. Selected up to 2 options.

Respondents believed that more studies and data are needed related to how well interventions work and how safe they are in REPs (Figure 17). Providers felt more strongly about the data needed on efficacy, while medical staff were more focused on safety.

When asked whether involvement in clinical trials could be considered a part of their CHC's core mission and strategy, almost half (45.7%) of the CHC executive leadership cohort responded yes (Figure 18). This is encouraging, as currently a very small percentage of CHCs actively participate in clinical trials. This underlines the gap between the CHCs' objectives and their ability to provide clinical trials as an option for patients.

Figure 18. Would you consider direct or indirect involvement in clinical trials a part of your organization's mission or strategy?

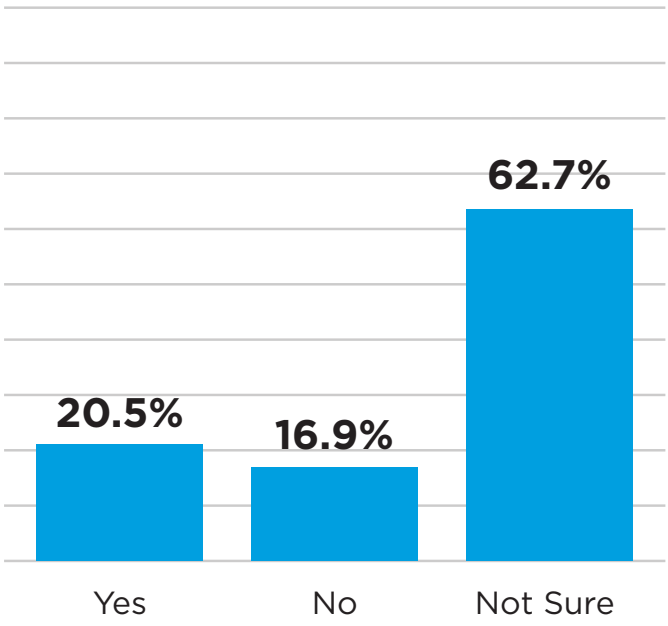


Respondents: executive leader cohort, *n* = 81.

"As far as community health centers [are concerned], if you want to get to a population of color, you have to be in their neighborhood. You have to be in their [backyard]. You have to make it easy for them to participate in these things because expecting them to travel, expecting them to travel consistently and compliantly is a challenge." — Executive leader

As illustrated in Figure 19 below, nearly two-thirds of providers (62.7%) were unsure whether they could trust external research parties to ensure continuity of care, and only 20.5% responded affirmatively to this question.

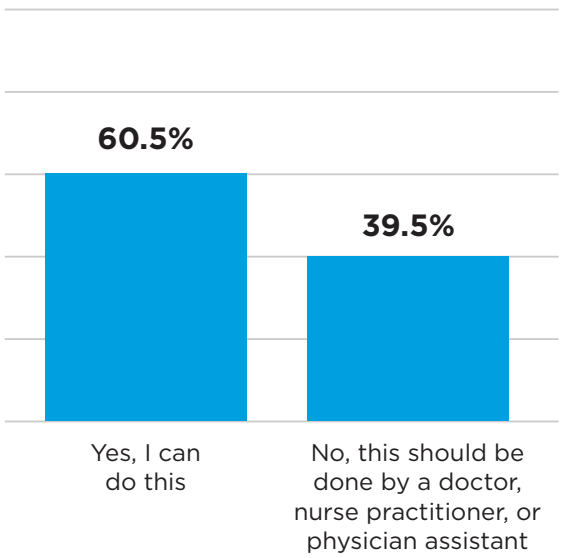
Figure 19. Can external research parties be trusted to ensure continuity of care for patients?



Respondents: medical provider cohort, *n* = 83.

In order for the majority of CHCs to either initiate or maintain a basic level of support for clinical studies—which would benefit patients and improve diversity—addressing concerns about continuity of care must be done locally and on a study-by-study basis. Providers are treating and prescribing medication for overall medical care and must be assured that gaps in care will not occur during or after a clinical study.

Figure 20. Do you feel in your role that you can share information about clinical trials with patients?

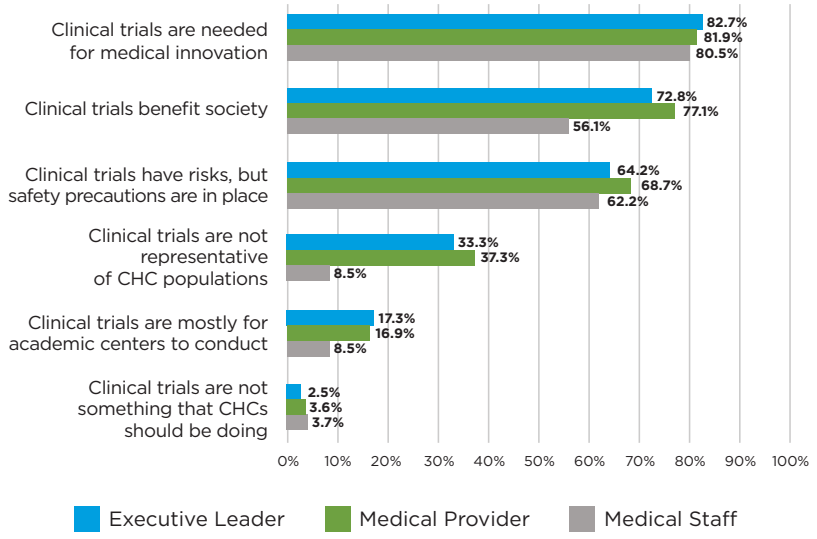


Respondents: medical staff cohort, *n* = 81.

As shown in Figure 20, the majority of medical staff (60.5%) believe that they can share clinical study information with patients. This is an important option considering that providers are often pressed for time, and most CHCs will not be direct contributors as either a main or sub-site. Medical staff may be sufficiently acquainted with the patient and have their trust, such that sharing appropriate study options can be part of the care process.

"Whether that's the doctor explaining [the drug] or the pharmacist, I think sometimes people need to hear it multiple times, maybe from different places, because sometimes the doctor's busy or the doctor's intimidating.... On a new drug, we can go over everything [with the patient] the first go-around, but maybe they'll only retain 40%, and then maybe they'll call us in the pharmacy a week later and be like, 'Hey, what am I supposed to do again?' or 'I'm experiencing this, is this from the drug or something else?' Then over time, they can build their competency." — Medical staff member

Figure 21. What are your general impressions of clinical trials?



Respondents: all cohorts n = 246. Selected all that apply.

One objective of this survey was to assess statistically significant differences in views between executive leaders, medical providers, and medical staff regarding the involvement of CHCs in clinical trials. These cohorts did not significantly vary in their responses as to how CHCs could be involved in clinical trials or in their primary concerns about suggesting clinical trials.

However, the groups did vary significantly in their general impressions of clinical trials. Specifically (Figure 21), executive leaders (33.3%) and medical providers (37.3%) were significantly more likely to state that clinical trials are not representative of their patient population, in contrast to medical staff (8.5%). Furthermore, medical providers (77.1%) were much more likely to state that clinical trials benefit society, compared with medical staff (56.1%).

> ***"I've had patients that were like, 'Oh, I've been in a community where we were experimented on before.' I think there's a really long history in the United States healthcare system of experimentation [on] underrepresented or marginalized groups. The Puerto Rican contraception study[4] is one to think about, or even the Tuskegee Syphilis Study. These are things that are in the minds of some of our patients and we have to work to rebuild [trust] before thinking about reaching out in community settings. — Executive leader***

[4] The first large-scale human trial of oral contraception was conducted in Puerto Rico before the drug was approved for safe use by U.S. authorities.

Limitations

While this grant, its findings, and the toolkit are transformative, further research is required, as potential limitations may exist:

- CHCs that chose to participate may be more forward-thinking than others that did not.
- CHCs were responsible for selecting the individual respondents from their teams: these respondents may have had a more positive view of clinical studies than others.
- Even after a detailed explanation, respondents could still be confused about the difference between clinical trials and observational studies.
- Respondents may have provided answers they believed to be socially acceptable or aligned with expectations of their roles (e.g., within healthcare roles).
- This study focuses on people of color/racially and ethnically diverse populations. However, other populations are also underrepresented and could be included in future research (e.g., disabled, older adults, LGBTQ+ communities, those who are uninsured or low-income, etc.).

It is important to note that, while other underrepresented populations (e.g., disabilities, age, gender, income, location) were not the focus of this grant (see above limitations), the results and tools generated from this project have the potential to benefit many people in addition to REPs, given the diversity of populations served by CHCs.

Call to Action for CHCs and Related Stakeholders

The *Building Clinical Trial and Health Research Access for People of Color via Community Health Centers* project aimed to identify clinical study participation barriers, misconceptions, and knowledge gaps among CHC executive leaders, medical providers, and medical staff.

Overall, these health professionals articulated a clear-eyed view of the small- and large-scale challenges to clinical study diversity — the kinds of challenges that CHCs face every day in providing equitable, quality care to patients of all backgrounds.

CHCs are each called to take their own appropriate next step to promote the participation of REPs in clinical studies. The level of engagement is of secondary importance, as long as it aligns both with patient care needs and with the CHC's available resources (e.g., time, people, funds). Special consideration should be given to supporting any clinical study that directly aims to expand diversity and representation of REPs.

It should be noted that CHCs have autonomy in determining their level of support for clinical studies and can choose study types based on study objectives, interventions, and/or disease states of interest. Participation options range from indirect (basic), such as referring patients to a local research center, to direct (complex), such as operating a dedicated research site. In addition, CHCs can be involved in various clinical studies with a combination of indirect and direct roles (direct with basic observational studies and indirect with clinical trials).

Options for CHCs to Participate in Clinical Studies of All Types

Source: Altura

Below is a summary of options for CHCs to consider based on their current involvement with clinical studies. It is imperative that all levels of the organizations are aware and educated on their CHC's direction and resources related to clinical studies.

CHCs with limited resources and/or clinical study experience should consider:

- Connecting patients with online or virtual clinical studies.
- Connecting patients with local, vetted study sites conducting in-person studies.

CHCs that occasionally conduct basic observational studies should consider:

- More observational studies or additional non-investigational intervention studies.
- Connecting patients with online or virtual clinical studies.
- Connecting patients with local, vetted study sites conducting in-person studies.

CHCs that regularly conduct observational and non-investigational clinical studies should consider:

- Being a satellite site for a clinical trial or building infrastructure to conduct clinical trials as a primary site.
- Grants for investigator-initiated clinical studies.
- Connecting patients with online or virtual clinical studies.
- Connecting patients with local, vetted study sites conducting in-person studies.

CHCs that conduct clinical trials should consider:

- Adding Principal Investigators (PIs) and expanding therapeutic areas for clinical trials.
- Grants for investigator-initiated clinical studies.
- Connecting patients with online or virtual clinical studies.
- Connecting patients with local, vetted study sites conducting in-person studies.

Virtual or online clinical studies are defined as any study for which in-person visits are not required. These clinical studies are non-investigational in nature and provide an easy way for patients to participate in either observational clinical studies or interventional studies that are designed and approved to be conducted remotely (e.g. home, online). They also require less time and effort from CHCs. The Michael J. Fox Foundation's Parkinson's Progression Markers Initiative (PPMI) study is an example.

"I think the biggest barrier is resources, not just for the patients, but for the clinics themselves. We are often struggling to just get the basic operational things down, getting the patients processed, getting the charts completed and the billing completed. It works, but those basic things are often challenging.... I think having clinical trials now added on is a whole other, not even a department, but a whole other sector that would need to be investigated and figured out how that would be managed within the things that are mandated of the clinic itself."
— Executive leader

It is important to note that CHCs are not required to build or have an IRB. IRBs play a crucial role in providing initial approval and ongoing reviews of clinical studies to ensure regulatory compliance and to safeguard participant safety and privacy. Fortunately, there are viable IRB options for CHCs. Many research organizations have internal IRBs that review studies. Additionally, independent external IRBs are available to support research organizations and CHCs.

CHCs express concern about study safeguards for their diverse and often vulnerable patient populations. The Common Rule defines vulnerable people as "people who are vulnerable to coercion or undue influence." Specifically, it identifies categories such as "children, prisoners, individuals with impaired decision-making capacity, and economically or educationally disadvantaged persons." When such populations are involved, additional safeguards can be recommended by IRBs. Ultimately, safeguards would be implemented by the research organizations conducting the study, so it is important that CHCs choose their partners carefully.

Generally speaking, CHCs with residency programs are likely to be good candidates for direct involvement in all types of studies. Residency training requirements, such as with Family Medicine, require scholarly activity among faculty and residents, and clinical study participation can help achieve this requirement. Grant options exist for CHCs that can write proposals or partner with organizations that support writing and implementation. Grants can help with education, training, research structure development, patient outreach, or clinical study development and implementation.

CHCs that are considering participating in clinical studies feel that continuity of care and ensuring the proper situation for the patients are imperative. CHCs have total autonomy in the process, as they can choose which studies to participate in, how to participate, and who to partner with.

Given the options and the ability to support patients in their healthcare journeys, CHCs clearly have a path toward supporting the participation of REPs in clinical studies of all types.

A separate survey in September 2023 asked 2,704 Neighborhood Healthcare patients what they considered important in learning about a clinical study, and if they would consider a study at a location other than their CHC (Figures 22 & 23).

This project's advisory panel included a patient representative who is a Neighborhood Healthcare member, a phase III clinical trial participant, and an African American. He says,

> ***"It made a difference knowing that I had a link to the study center since it was being done at Neighborhood Healthcare. When considering the clinical trial, that made the study 'more legitimate.'"***

Figure 22. Which of the following is important to you when considering joining a clinical study?

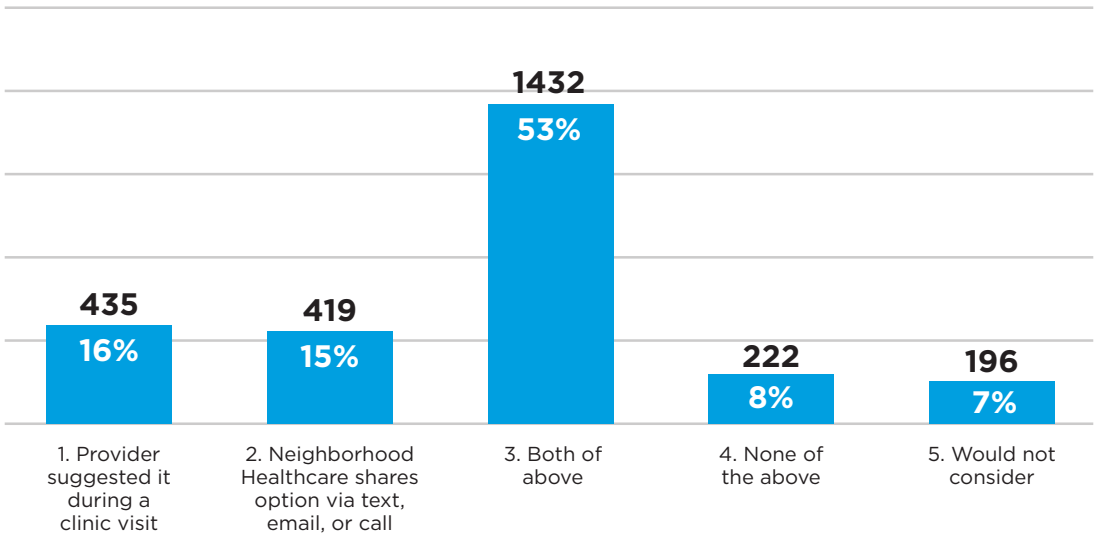
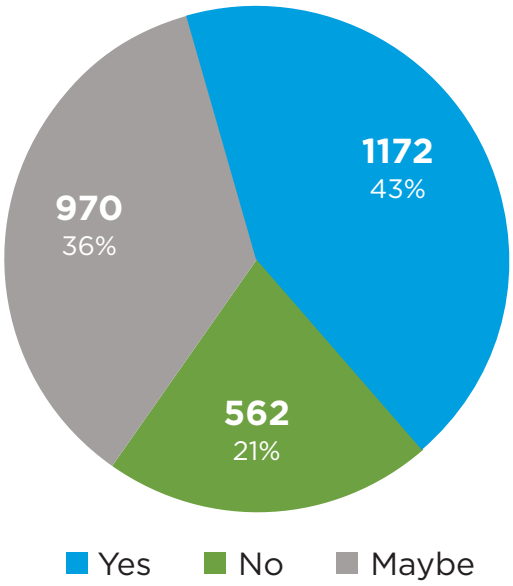


Figure 23. If your provider or Neighborhood Healthcare suggested a clinical study at another location, would you participate?



Trust is important for any decision related to healthcare, and even more so when a patient considers clinical study participation. Based on the results of this project, Neighborhood Healthcare's patient survey results, and the advisory panel's experience supporting REPs with their healthcare and/or clinical study participation, it is very important for patients to have studies vetted and recommended by their CHC. It is even better if a CHC is directly involved with a clinical study.

This project's related toolkit will provide participation use cases for the various clinical study types: patient triage to study sites for clinical trials, observational studies, interventional studies (behavioral interventions, control group studies for education and technology), and clinical trials. The toolkit will be available in January 2024 and can be requested at info@alturastudies.com.

Call to Action for Life Science and Research Organizations

The clinical research industry is vast and complex with various segments that can overlap when the research required involves the participation of people ("human subjects" in regulatory terms). This call to action will focus on two stakeholders that drive study enrollment and execution: sponsors and study sites.

For the purpose of this section, the term "sponsors" includes any organization that develops and funds clinical studies of investigational or approved interventions, such as medications, biologics, medical devices, and medical software. These would include biotech, pharmaceutical, medical device, and medical software companies, as well as government agencies, health-related foundations and independent researchers. At times, these organizations include relevant service providers, such as contract research organizations (CROs) that are tasked with providing some or all of the required clinical study operations.

For the purpose of this section, the term "study sites" refers to academic centers, dedicated research centers, research centers within health systems and medical practices, site management organizations (SMOs), and other entities that implement and enroll patients for sponsors, regardless of funding source and type of study.

Community Health Centers (CHCs), also called Federally Qualified Health Centers (FQHCs), as well as FQHC Look-Alikes, are community-based and patient-directed primary care centers. By mission and design, CHCs exist to serve those who have limited access to healthcare via 1,500 health centers and 15,000 locations nationally in any type of setting (e.g., rural, urban). CHCs care for over 32 million patients, of which over 60% are REPs.

Too often in clinical trials, the need for collaboration arises only after a trial starts and REPs enrollment is lower than expected or behind projections. The ensuing outreach by study sites and patient recruitment vendors is often viewed as insincere and short-term focused, without the patients' best interest in mind. Unfortunately, this approach has led to mistrust and misconceptions about clinical trials and other types of studies.

It is important to note that many CHCs will not have the time, interest, and/or resources to conduct any type of clinical study, or they may be able to support a basic observational study and nothing more complex. In these cases, CHCs can be a source of patients; however, this likely will only work with a long-term view and if patient continuity-of-care issues are resolved. Continuity of care was consistently mentioned as a barrier to referring patients to clinical trials.

These types of issues revolve around:

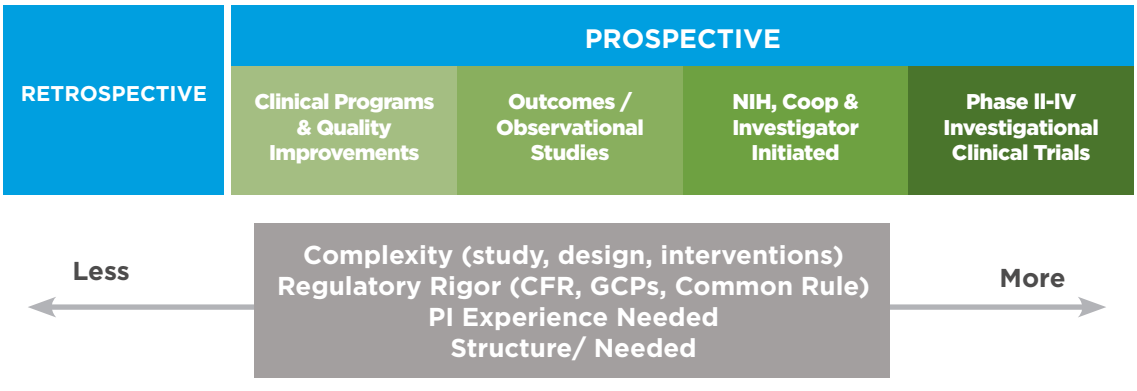
- transparency of patient status during the entire study process (e.g. screen fail, enrolled, dropped, completed)
- medications discontinued or added
- awareness of abnormal labs and exams
- study completion to coordinate any transition back to standard of care (e.g. Rx).

It is important to note that CHCs and their medical providers maintain healthcare responsibility for patients' chronic and acute medical conditions before, during, and after a clinical study. Awareness of the role of the CHC and the importance of ensuring continuity of care is paramount to engaging CHCs in the clinical trial process. This was reinforced throughout the survey as one of the primary limitations impacting the medical providers' willingness to discuss clinical trial opportunities with their patients or refer them to clinical trials being conducted outside of the CHC.

The following are options for sponsors and study sites to engage CHCs in order to increase REP study participation.

- Conduct retrospective review of healthcare data related to interventions or medical conditions of mutual interest (e.g. EHR, data warehouse, lab, claims, Rx data).
- Conduct observational and health outcome studies.
- Serve as a source of patients for clinical trials (triage to existing study sites).
- Participate as a satellite site for clinical trials (delegated roles to main study site).
- Participate as a main site for clinical trials.

CHC Clinical Study Spectrum



Source: Altura

For any clinical study collaboration with CHCs, a long-term perspective is advised, for which the roles and interests of the parties are aligned. Sponsors often lack understanding of the CHC environment and mission, and their approach may be short-term and acute in nature.

Clinical trial sponsors should also consider incorporating CHCs as satellite sites to their main study sites, allowing CHC medical providers to acquire experience as investigators. Additionally, sponsors should consider providing study sites with a budget to engage CHCs as a source of patients. These funds could be utilized by CHCs to conduct specific database queries, patient identification, evaluations, and triage to support study enrollment.

CHCs not only have access to their patient population, but they are also uniquely positioned for community outreach and engagement, given their profile of active involvement in their communities and support for healthcare screenings.

For late-stage and less complex clinical trials, sponsors may consider adding CHCs as sites if they have the appropriate clinical trial infrastructure and training, even without a prior history of clinical trial participation. Sponsors should also consider protocol design when possible, especially for phase IV or sub-studies in phase III clinical trials. Consideration should be given to relaxing inclusion criteria to reflect real-world conditions, reducing the number of study visits to lessen the burden, offering virtual or home visits for better participant retention, and allocating an appropriate budget for CHCs to ensure successful study execution and enrollment.

> ***"Even the funding to have the additional support staff [for] educating your patients on the trials [would be needed]. Obviously, [patients are] going to have questions. That would definitely be something that I always think of is [that] I would want someone to be a specialist... Or [have] access to someone that we could direct questions to, or be a constant support for us... A source of information or contact if we had questions." — Medical staff member***

Below is a checklist of questions for sponsors and study sites when considering collaborating with CHCs for clinical studies:

QUESTIONS FOR CHC COLLABORATION	IMPORTANCE / CONSIDERATIONS
What type of clinical studies has the CHC supported or conducted in the past? Does your clinical study align with this history/ experience?	Recognizing that few CHCs will have in-depth clinical study experience, what investments are you willing to make to ensure the CHC is adequately trained and prepared to support specific aspects of the study(ies)?
Can you take a long-term view on a collaboration that will involve many types of clinical studies?	Recognize that CHCs are not available on-demand to simply refer patients without funding, infrastructure, and resource support, and without trusted relationships with experienced researchers. To what extent is your organization willing to support and make such investments?
Are you able to provide long-term resources as well as short-term, study-specific support to fill CHC gaps?	See above
Does the clinical study include a budget to cover CHC-related costs for database access, prescreening, training, patient identification and triage (e.g., referrals), and patient monitoring?	Regardless of the role the CHC will play (patient identification, satellite, or main site); ensure that there are sufficient funds to compensate the CHC for their time and resources to support the trial.
Is a process in place to notify the CHC when patients are enrolled, active, or completing a clinical study to ensure continuity of care?	This addresses the continuity of care and safety concerns of CHCs and their providers. Transparency is key for the long-term.
Is a process in place to notify the CHC provider of any adverse events, lab anomalies, or patient safety concerns to ensure continuity of care?	See above
Is a plan in place to share clinical study results so that CHCs can learn and/or apply relevant findings to their healthcare practices?	In an evolving value-based healthcare environment, CHCs will view clinical studies as a way to improve care for patients.

> ***"Let's say if you're [a physician] in a trial, you're giving medication… to a patient, but that's all you're really doing. You're [just] recording the results… You are kind of like at the tail end [or] almost like at the frontlines of the clinical trial, but you're not necessarily involved… in the analysis… You're just that conduit to hand out medications and/or placebos [or] whatnot… You don't own a lot of the stuff that happens with the data, with the results, with any of that stuff. I guess the question would be, if we're expected to run a clinical trial, are we involved in all of it or are we simply just that end user, end-result conduit…?"***
> ***— Executive leader***

The traditional approach to selecting sites and recruiting patients falls short in establishing trust with healthcare systems and providers, particularly CHCs. Sponsors have a vast, yet untapped opportunity to expand diversity in clinical studies and engage the over 32 million patients within CHCs. This can be achieved by thinking outside of the box and building long-lasting CHC engagement, either directly or through the study sites that conduct their clinical trials.

To support CHC involvement in clinical studies, sponsors and study sites are welcome to distribute this white paper and related toolkit as needed. The toolkit will be available in January 2024 and can be requested at info@alturastudies.com.

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BUILDING CLINICAL TRIAL AND HEALTH RESEARCH ACCESS

for People of Color via Community Health Centers (CHCs)

TOOL KIT

GRANTEE:

neighborhood HEALTHCARE

LEAD ADVISOR AND PROJECT MANAGER:

ALTURA

Made possible by a Health Equity and Diversity Grant from Genentech, a member of the Roche Group

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A special thanks to the research leadership at Desert Oasis Healthcare (DOHC), a primary care medical group based in Palm Springs, CA. For the past 20 years, DOHC has conducted clinical trials and been a leader in expanding research access to minority populations while employing a diverse study team that includes bilingual staff.

The toolkit is provided as a supplement to a white paper that presents the findings, perceptions, and feedback from a nationwide survey of CHC executive leaders, providers, and medical staff. It is available for review and can be requested at info@alturastudies.com.

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Made possible by a Health Equity and Diversity Grant from Genentech, a member of the Roche Group

Section 1: Introduction

Background

The Building Clinical Trial and Health Research Access for People of Color via Community Health Centers grant examined barriers to clinical study participation among executive leaders, providers, and medical staff at community health centers (CHCs) nationally. Neighborhood Healthcare, the CHC grantee, and Altura, the project manager and lead advisor, collaborated to initiate and execute this project.

The lack of racially and ethnically diverse populations (REPs) representation among clinical trial participants has long been a challenge in medical research. Based on U.S. census data, about 40% of the U.S. population is racially and ethnically diverse. However, less than 25% of clinical trial participants fit into this category.

The core premise of this project is that REPs highly value and trust people who provide healthcare and health information in their communities. It therefore hypothesizes that CHCs could be valuable contributors, either directly or indirectly, for all types of clinical studies, thereby improving on the lack of diversity that has plagued clinical research historically.

For this project, the term "clinical studies" refers to a spectrum, ranging from basic observational studies to clinical trials involving investigational medications subject to FDA review. This range includes a wide array of non-investigational intervention clinical studies (e.g., behavioral, educational services, and technology) that reside between these extremes. Given that clinical trials of investigational medications exhibit the largest diversity gap, are the most challenging to conduct, and have the greatest impact on equity in innovation, this publication will predominantly focus on this type of clinical study.

There are many benefits for CHCs to support or conduct clinical studies. These include:

- Providing options for patients to be involved with research and innovation
- Contributing to the diversity and applicability of evidence-based medicine with learnings and results from underserved and under-studied patient populations
- Creating a new funding stream and business diversification strategy
- Enabling another pathway for staff development, retention and recruitment
- Expanding CHC capabilities in terms of resources and expertise
- Generating name recognition, reputation/prestige, and brand—driving towards "provider of choice"

Purpose

This toolkit is provided as a supplement to a white paper entitled, "*Building Clinical Trial and Health Research Access for People of Color via Community Health Centers*." The white paper presents the findings, perceptions, and feedback from a nationwide survey of CHC executive leaders, providers, and medical staff. It is available for review and can be requested at info@alturastudies.com.

The toolkit's purpose is to provide CHCs with an overview of study options and guidance on how to participate in a variety of studies, either directly or indirectly. The aim is to demonstrate CHCs' potential to engage at any desired level in clinical studies of all types.

The simplest way for a CHC to participate is to support patients by referring them to studies that may be at a local research center, online, or home-based. This type of involvement would not require any financial investment, infrastructure or direct oversight responsibility; and CHC may be provided compensation for their time and effort.

At the other end of the research spectrum is developing a research structure to conduct investigational clinical trials that are governed by federal agencies, such as the Food and Drug Administration (FDA). This would require an investment of time and financial resources by a CHC.

In between these two extremes lie many options for CHCs to be involved, directly or indirectly, with a variety of studies that could ultimately benefit patients and improve diversity in health studies of all types. The CHC self-assessment in Section 2 can help organizations determine their preferred path to supporting research access and diversity.

Options for CHCs to Participate in Clinical Studies of All Types

Source: Altura

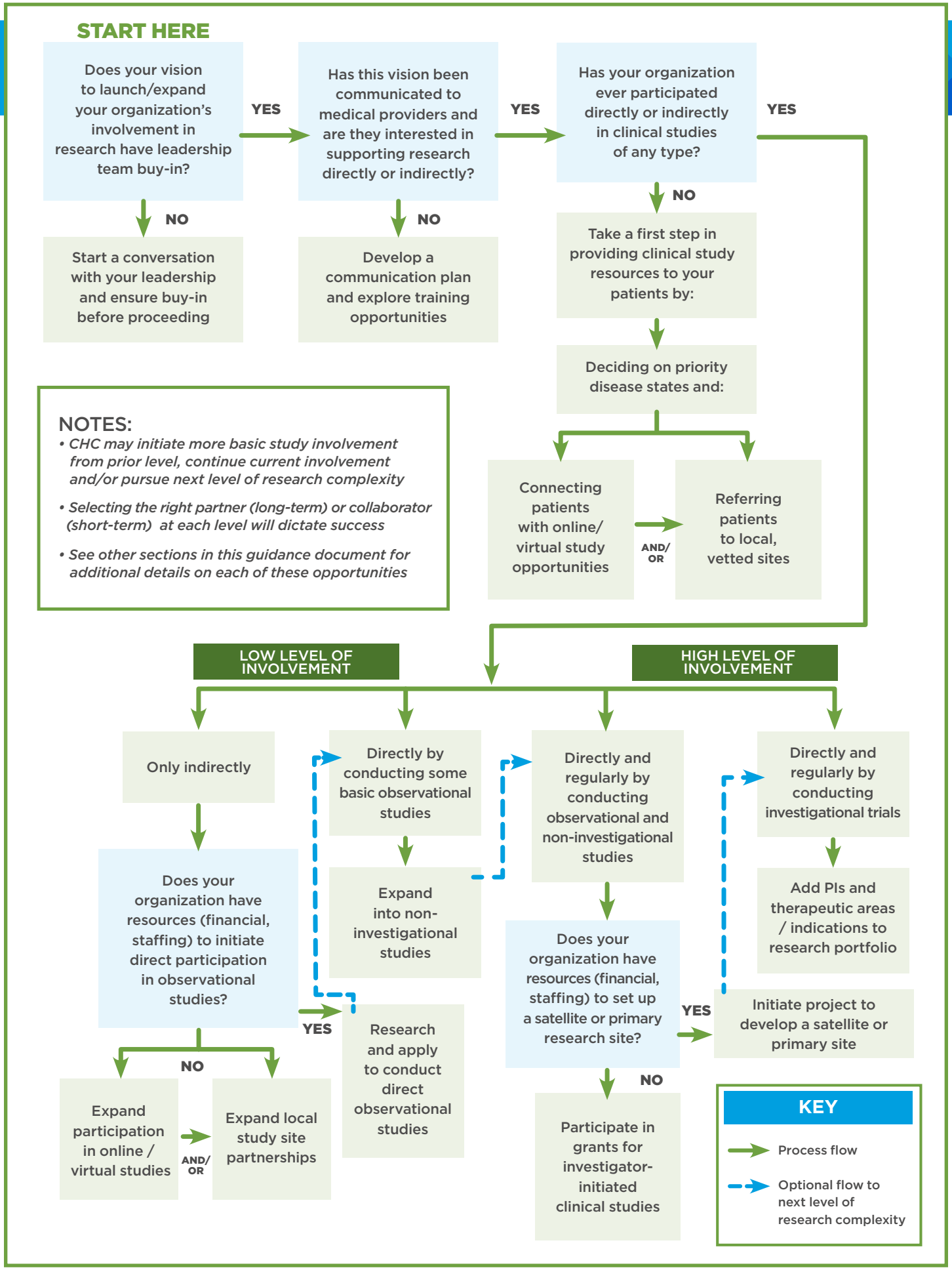
How To Use

It is important for CHCs to keep in mind that they can support patients on their healthcare journey via clinical studies of all types, without prior research experience or infrastructure. For CHCs interested in exploring this possibility without making a large upfront investment, we suggest selecting a study type with requirements that are already in line with your CHC's existing capabilities. Most chronic or acute medical conditions are included at every study level, and CHCs can select studies that focus on one or more priority conditions for each CHC's patient population. Section 2 provides a decision tree to help CHCs think through a starting point or next step in the clinical study evolution, and Section 3 provides more information on each study type.

Over time CHCs can move along the spectrum for more direct involvement in studies, based on local interests and needs. Refer to the Resource and FAQ sections to access additional information sources and tools which can help your CHC start or expand its involvement in clinical studies.

Section 2: CHC Self-Assessment & Clinical Research Participation Decision Tree

Below is a framework for CHCs to consider as they assess their readiness and the appropriate research participation options. Keep in mind, the goal is to take a first step towards supporting clinical studies and providing more options for patients. As your organization becomes more familiar with clinical studies and their requirements, your team can review this checklist and reassess as needed. Additionally, while the flowchart is linear according to the next most intensive option, CHCs that are willing and able to invest the resources and enter into the appropriate partnerships can make the jump to any study level desired.


START HERE
Does your vision to launch/expand your organization's involvement in research have leadership team buy-in?
YES
Has this vision been communicated to medical providers and are they interested in supporting research directly or indirectly?
YES
Has your organization ever participated directly or indirectly in clinical studies of any type?
YES
NO
Start a conversation with your leadership and ensure buy-in before proceeding
NO
Develop a communication plan and explore training opportunities
NO
Take a first step in providing clinical study resources to your patients by:
Deciding on priority disease states and:
Connecting patients with online/ virtual study opportunities
AND/ OR
Referring patients to local, vetted sites
NOTES:
• CHC may initiate more basic study involvement from prior level, continue current involvement and/or pursue next level of research complexity
• Selecting the right partner (long-term) or collaborator (short-term) at each level will dictate success
• See other sections in this guidance document for additional details on each of these opportunities
LOW LEVEL OF INVOLVEMENT
HIGH LEVEL OF INVOLVEMENT
Only indirectly
Directly by conducting some basic observational studies
Directly and regularly by conducting observational and non-investigational studies
Directly and regularly by conducting investigational trials
Does your organization have resources (financial, staffing) to initiate direct participation in observational studies?
Expand into non-investigational studies
Add PIs and therapeutic areas / indications to research portfolio
YES
Research and apply to conduct direct observational studies
Does your organization have resources (financial, staffing) to set up a satellite or primary research site?
YES
Initiate project to develop a satellite or primary site
NO
NO
Expand participation in online / virtual studies
AND/ OR
Expand local study site partnerships
Participate in grants for investigator-initiated clinical studies
KEY
Process flow
Optional flow to next level of research complexity

Section 3: Clinical Study Types

Below is a review of the types of clinical studies available to CHCs. Level of involvement will vary based on your organization's capabilities and interest. These fundamental questions should be considered when evaluating participation in a clinical study:

- Are the objectives of interest and/or important to our CHC and patients?
- Does our CHC have the type of patient needed for this study?
- Do we have the resources to do the required CHC tasks (see section 4)?
- Is the partnering organization trustworthy related to conducting the study, enrolling REPs and ensuring a positive experience for REPs (see section 5)?

STUDY TYPES	Level of Involvement	Involvement Options	Location Options	Staff Needed	Investment Needed	Infrastructure/ Other Key Factors
OBSERVATIONAL STUDIES	Minimal to moderate	• Secure grant and operate as main site • Operate as a subsite • Refer patients	• Onsite • Remote & Online • Home-based	• CHC liaison to lead effort • Provider & staff support	• Minimal if any	• Existing space may be used • Leadership approval • Suitable patient base for study enrollment • Ability to generate reports from EMR/databases
INTERVENTIONAL NON-INVESTIGATIONAL	Minimal to moderate	• Secure grant and operate as main site • Operate as a subsite • Refer patients	• Onsite • Remote & Online • Home-based	• CHC liaison to support tasks • Provider & staff support • Trained study team	• Some time to ensure proper processes for billing and work to be conducted • Time for provider and staff training	• Leadership approval • Suitable patient base for study enrollment • Depending on enrollment volume, may need to ensure exam rooms are available as needed • Ability to generate reports from EMR/databases
CLINICAL TRIALS (PHASE II-IV)	Minimal to significant	• Operate as a main site • Operate as a subsite • Refer patients	• Onsite	• CHC liaison to support tasks • Provider & staff support • Experienced PI • Experienced research coordinator • Significant training • Relevant contracting and finance experience	• Executive and management time for set-up • Time for initial and ongoing provider and staff training (more extensive than other training) • Funds to support launch and advisors if needed and • Hiring at least one experienced research coordinator	• Leadership approval • Dedicated space for storage and visits – can be small to start • Financial support for Accounts Receivable and Accounts Payable • Contract/budget review support • Facilitate monitoring and inspections • Suitable patient base for study enrollment • Ability to generate reports from EMR/databases

Note: for definitions, see Section 7

Section 4: Examples of Clinical Studies

To provide a better understanding of the various clinical study types and what is involved with each, this section provides examples of studies. Studies in each category can vary by medical condition, design, or objectives, however, they should have the same type of structure.

Observational Studies – Opportunity to Refer Patients

The Parkinson's Progression Markers Initiative (PPMI) Study is sponsored by the Michael J. Fox Foundation (www.michaeljfox.org/ppmi).

WHAT is the study about?	WHO is eligible to participate?	WHAT is involved for the participant?	WHAT are the CHC's roles and requirements?
PPMI is a landmark observational study. It aims to gather information from >4,000 volunteers worldwide over time to learn more about how Parkinson's disease (PD) starts and changes and how to stop it. PPMI offers different ways to get started in the study.	• **Age 18+ in the U.S:** Anyone age 18 and older in the U.S. — with and without Parkinson's disease — can join the online part of PPMI.	• Surveys on health and wellness will be sent directly to your inbox every 90 days.	• CHCs invite and refer their patients for applicable studies. • No study task or work required by CHCs other than making your patients aware of the opportunities and sharing information about the study.
	• **Recently Diagnosed with Parkinson's:** Medical centers are enrolling people from diverse backgrounds (e.g., race, ethnicity) diagnosed with Parkinson's in the past two years and not yet taking PD medication.	• In-person visits to local medical centers	
	• **Age 60+ without Parkinson's:** Age is a risk factor for Parkinson's disease. So is smell loss. PPMI is asking everyone age 60 and up without Parkinson's in the U.S. and Canada to take a free scratch-and-sniff test.	• At-home smell test for anyone 60+ without PD (age and smell loss are risk factors) in the U.S. and Canada. • Smell test results may make you eligible to join the in-person part of PPMI.	

Observational Studies – CHC Conducts the Study

Social Determinants of Health (SDoH) in Women with Heart Failure: Prospective Observational Cohort Study

Source: https://www.sciencedirect.com/science/article/pii/S2667036423000171

WHAT is the study about?	WHO is eligible to participate?	WHAT is involved for the participant?	WHAT are the CHC's roles and requirements?
• Social determinants of health (SDoH) are an important contributor to health outcomes in cardiovascular disease, including heart failure. • Women have an increased risk of adverse social determinants of health in cardiovascular disease. • This study's aim was to evaluate the relationship between the baseline SDoH status of women with heart failure with subsequent all-cause and cardiovascular hospitalization.	• Women > 18 years old with a diagnosis of heart failure • No severe cognitive impairment • No ESRF on hemodialysis	• Baseline determined with completion of the Institute of Medicine Measures of Social and Behavioral Determinants of Health and the Kansas City Cardiomyopathy Questionnaire 12-item (KCCQ-12). • Monthly follow-up phone calls or in-person clinic visits from month 1 to 6, assessing medication changes, hospitalization events, primary care visits, vital status, and NYHA class and KCCQ-12. • Ad-hoc follow-up phone calls in case of hospitalization to determine cause.	• CHCs can conduct straightforward observational studies, requiring minimal time and transportation for patients • Requires minimal staff resources (EMR data analytics, patient phone outreach/ in-person visits, and statistical analytics.) • Can be carried out primarily virtually, via phone interview if space is limited and/or patients face transportation issues • Requires study approval by IRB (in this example, the institution partnered with a university IRB).

Interventional, non-investigational studies – CHC Conducts or refers patients

Dulce Digital-Project Dulce 2.0 Texting Study in High-Risk Latinos with Diabetes

Source: https://classic.clinicaltrials.gov/ct2/show/NCT01749176

WHAT is the study about?	WHO is eligible to participate?	WHAT is involved for the participant?	WHAT are the CHC's roles and requirements?
• Project Dulce 2.0 (PD 2.0) is a randomized controlled trial testing the efficacy of a text messaging intervention in a low income, low health literacy group of Latino patients with diabetes. • The study will address barriers to participation in health education classes, increasing adherence to treatment and medications and improving diabetes self-management behaviors and skills.	• Adults between 18-75 years old • T2DM diagnosis • Latino ethnicity • HbA1c >=8% • Has cellphone with texting capabilities • No severe illness precluding frequent in-person visits • Creatinine level <=3.5 • No history of alcohol or drug abuse within 12 months	• **Behavioral intervention:** Behavioral text messages will be sent at random times throughout the week regarding healthy nutrition tips, benefits of physical activity, benefits of medication adherence and requests to check blood sugar and send back results. • **Active comparator:** Participants will continue to receive their usual care in their primary care home. They will return at months 3 and 6 to conduct behavioral and laboratory assessments to compare results with the intervention group.	• CHCs can choose to refer patients to such studies or conduct directly. • To refer patients, CHCs must partner with a local primary site and determine optimal pathways to send and track patients. • To conduct an interventional non-investigational study, consider staff resources (EMR analytics, statistical analytics, behavioral message content), technology resources (mass texting). • Requires study approval by IRB.

Clinical Trials – CHC Conducts the Study

CHCs can choose to refer patients to clinical trials or conduct studies directly as a sub-site or main site. If the CHC opts to participate in clinical trials indirectly by referring patients, roles and requirements are similar to those of an observational study (cf. PPMI study in first clinical study example of this section).

A Phase 3, Randomized Double-Blind, Placebo-Controlled study to investigate the Effect of a Drug in the Reduction of Morbidity and Mortality in Adults with Obesity.

WHAT is the study about?	WHO is eligible to participate?	WHAT is involved for the participant?	WHAT are the CHC's roles and requirements?
• This study will investigate the effect of tirzepatide on the reduction of morbidity and mortality in adults living with obesity and provide additional evidence for the potential clinical benefits of tirzepatide in this population. • Overall study looking for several thousand patients. Each site expected to enroll about 12 – 15 patients.	Patient Criteria (34 total inclusion and exclusion criteria – below are top 5): • Patients with a BMI >27.0 kg/m² and >40 years old, with: - established CVD, or - patients without CVD but have documented CV risk factors • Have not had or plan to have a surgical endoscopic or device treatment for obesity. **Exception:** Liposuction or abdominoplasty. • Have not used products intended for weight loss including prescription drugs, over-the counter (OTC) drugs, and herbal preparations, within 3 months prior to screening. • Have not used a GLP-1 RA within 3 months of screening. • Have not used any agent with antihyperglycemic effect within 3 months of screening, with the exception of SGLT-2 inhibitors indicated for chronic kidney disease or heart failure.	• Each patient is seen every 4 weeks over a 28-month period (2.3 years) and then followed by visits every 3 months until the 5.5-year mark. • Visits typically include administration of medication, vitals, patient-reported outcomes, adverse event assessment, review of concomitant meds and labs. Initial/ Screening visits will have additional intake information such as medical history, documentation of disease state (inclusion criteria) and patient consenting.	• Site provides primary investigator (PI) and ancillary medical staff (e.g., nurses, medical assistant) to find, enroll, schedule, and see patients and collect necessary study data. • Site also needs exam rooms to see patients and locked storage rooms to keep medication (which may require temperature-monitored refrigerators or freezers). • Site also needs file and storage space for the required study documentation (regulatory and patient binders). • Site also has periodic visits from sponsor monitors to review the study files for completeness, correctness, and compliance with the study protocol and Good Clinical Practices (GCPs). • Site will be expected to cull suitable subjects from existing patient database, or may need to advertise or interface with community and partners to identify potential candidates. • IRB approved protocol and Informed consent (central study IRB utilized)

Section 5: Partnering for Success

Regardless of the type of study and participation option selected, partnerships are a key success factor for a CHC's path to support clinical studies and provide valuable and innovative care options for patients.

Collaborations may be established with local research sites, health systems, medical groups, medical foundations, academics centers, pharmaceutical/biotech companies, medical device companies, medical/health software companies. Below is a checklist of key items to look for in a potential partner to ensure they are aligned with your goals and understand the requirements for collaborating with CHCs.

When vetting potential partners, building trust is of utmost importance. Patients highly value and trust their relationship with their providers, especially in the CHC setting. Therefore, any partner you decide to work with must be vetted for trust, ensuring your providers and patients have confidence in the partnership and expected outcomes. Regardless of discussions prior to your engagement, ultimately trustworthiness is built over time. When possible, explore options to begin with a pilot and validate that the partner's behaviors are in line with their promises. Include trustworthiness as part of the due diligence process (see Principles of Trustworthiness in Resource section) and consider appropriate exit strategies if trust does not materialize in the partnership.

Collaborations may be short-term/transactional agreements or long-term partnerships. In many cases, especially with sponsor organizations, such as pharmaceutical, biotech, medical device, and healthcare technology companies, collaborations will tend to fit a short-term/transactional approach. While due diligence in these cases may not be as extensive as for longer-term partnerships, many of the same questions will apply to some extent. Keep in mind that CHCs already having successful partnerships can take inventory of what has worked previously and seek those qualities in new partners to ensure successful short- and long-term collaborations.

Depending on the context of the partnership or study, due diligence should revolve around one or more of these areas:

- aligned mission and values,
- commitment to building relationships and trust with communities of color,
- cultural and linguistic competencies or inclusion,
- operational mindset and integration flexibility,
- financial aspects such as fee schedule,
- revenue/cost splits and timing of payments,
- available resources and support that supplement or complement existing CHC resources,
- clinical research experience and history,
- CHC support history,

- CHC and clinical research references,
- previous results with the type of study being conducted including therapeutic area,
- data sharing requirements, and
- past FDA audit or other quality audit findings

For investigational and non-investigational intervention studies, it is important to determine the team members, such as clinical research associates (CRAs), that will provide training, support, and quality assurance as part of the study. Ensure that these individuals understand the protocol extremely well, as study sites rely on their expertise when misunderstandings occur (this is common as protocols often contain inconsistencies and/or missing information).

Partnerships can be an excellent long-term source to help identify study and training opportunities. Establishing a network will be important to receive notice of opportunities. Academic centers and research organizations in your area have a constant flow of observational studies as well as interventional and investigational studies. Keeping in touch with their clinical research teams is important. For investigational clinical trials, study sponsors often have databases that study sites can submit to (often on the R&D, pipeline or clinical trial section of their websites such as https://www.gene.com/medical-professionals/clinical-trial-information , https://trials.lilly.com/en-US/healthcare-professionals#find-a-lilly-clinical-trial or https://www.merckclinicaltrials.com/). Additionally, you can find clinical trials and contact information for most sponsors at https://www.clinicaltrials.gov/.

CHCs that aspire to conduct more complex research as a main or satellite site should consider partnering with a local study site or academic center to gain experience. Working with an experienced principal investigator (PI) and clinical research coordinators (CRCs) will build confidence and prepare for a smooth transition to being a main study site.

Since most CHCs will opt to refer patients to local or online studies, as part of the Health Equity Innovation grant, the HCP Studies™ Research Engagement Platform is available to CHCs at no cost. CHCs can leverage HCP Studies™ to streamline the patient referral process and facilitate continuity of care with external study sites. HCP Studies™ includes a healthcare provider and patient version and is available as an app (iOS and android) or desktop version https://alturastudies.com/hcp-studies-2/. CHCs can add unlimited users and gain access to local, regional, and national studies. CHCs can also add nonfunded internal studies to facilitate patient recruitment internally with CHC providers, as well as externally. Additionally, the latest health study news and research educational resources are available for users.

This table highlights different types of organizations with which CHCs may choose to develop relationships. It also outlines different considerations when evaluating these entities as potential partners and collaborators.

ORGANIZATION TYPE	DESCRIPTION OF ORGANIZATION	WHAT TO LOOK FOR
ORGANIZATIONS WHERE CHCS CAN REFER PATIENTS OR PARTNER FOR DIRECT SUPPORT		
Professional Study Sites	Investigative sites that conduct research only (i.e., do not provide health care services)	• Communication channel for patient status updates and continuity of care (e.g., adverse events, study completion) • Understanding, and processes in place for vulnerable patients • Experience & understanding related to enrolling and retaining racially and ethnically diverse populations • Ownership structure and stability • Proven history with CHCs or primary care groups • Fee schedule • Staff turnover • Study pipeline alignment and depth • Research staff provided at CHC if needed
Site Management Organizations (SMOs)	Entity that oversees a network of investigative sites and typically provides centralized services such as business development and financial support services on behalf of the site	• Same as study sites • Long term stability (e.g., are they for sale, merging) • Start-up support & funds
Academic Medical Centers	Health system typically associated with medical school that conducts clinical trials and other types of research in addition to providing patient care	• Same as study sites • Option to co-author publications • Option to co-lead on grants • Shared study design involvement • Data analysis access & support • Local IRB provided
Health Systems	Health system that conducts clinical trials and other types of research in addition to providing patient care	• Same as study sites
Research Service Providers	Entity that provides management services to support research entry, restructuring, or growth	• Same as study sites • Types of services or support provided
ORGANIZATIONS THAT CAN PROVIDE CHCS STUDIES OR FUNDS TO DEVELOP STUDIES		
Life Science Companies (aka study sponsors)	Pharma, Biotech, medical device, and health software companies that sponsor/fund the clinical trial and who have the investigational product that is being researched	• Study pipeline alignment and depth • Appropriate study contracts and budgets • Experience and support of study monitors • Central IRB provided
Contract Research Organizations (CROs)	Service provider that supports many aspects of clinical trials on behalf of the sponsor of the trial	• Same as Life Science Companies
Government Entities	Federal and state agencies that fund clinical research (e.g., National Institutes of Health, National Cancer Institute).	• Aligned grant options and deadlines • Search websites such as: National Institutes of Health (NIH) National Cancer Institute (NCI) Patient-Centered Outcomes Research Institute (PCORI)
Non-Profit Organizations	Patient foundations that fund and support research (e.g., Michael J. Fox Foundation) – typically does not involve investigational products	• Aligned grant options and deadlines • Option to co-author publications • Option to co-lead on grants • Shared study design involvement • Data analysis access and support
Practice-Based Research Networks (PBRNs)	PBRNs are groups of primary care clinicians and practices working together to answer community-based health care questions and translate research findings into practice.	• Same as Non-Profit Organizations • See Agency for Healthcare Research and Quality (AHRQ) PBRN website: https://www.ahrq.gov/ncepcr/communities/pbrn/index.html

Section 6: Resources

This section includes resources where you can learn more about regulatory requirements, IRBs, clinical research and training associations, patient resources and related publications. This table is meant to be used as a starting point and is not a comprehensive list of all resources. Please contact the study authors for more information or additional resources on a particular topic, or email info@alturastudies.com.

As mentioned in Section 5, the HCP Studies™ Research Engagement Platform is available to CHCs at no cost. HCP Studies™ includes healthcare provider and patient versions and is available as an app (iOS and android) or desktop version https://alturastudies.com/hcp-studies-2/. CHCs can add unlimited users and gain access to local, regional, and national studies. CHCs can also add nonfunded internal studies to facilitate patient recruitment internally with CHC providers as well as externally.

REGULATORY RELATED RESOURCES	
Clinicaltrials.gov https://clinicaltrials.gov/	ClinicalTrials.gov is a registry of clinical trials. It is run by the United States National Library of Medicine (NLM) at the National Institutes of Health, and holds registrations from over 444,000 trials from 221 countries.
Code of Federal Regulations (CFR)	These are the general and permanent regulations established by the executive departments and agencies of the federal government. The FDA and NIH are agencies included in this umbrella and their regulations on how research is conducted are found in the CFR. Here are some general references to sections of the CFR. • CFR regarding obligations of the Site investigator https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-312/subpart-D/section-312.60 • CFR regarding obligations of the IRB https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-56 • CFR regarding obligations of the sponsor https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-312/subpart-D/section-312.50
Food and Drug Administration (FDA) https://www.fda.gov/patients/clinical-trials-what-patients-need-know/basics-about-clinical-trials	The FDA is a federal agency within the U.S. Department of Health and Human Services that regulates human and veterinary drugs, vaccines, medical devices, food, cosmetics, dietary supplements, and products that emit radiation. The FDA aims to protect public health by ensuring the safety, effectiveness, and quality of these products, and by providing the public with accurate, science-based information.
National Institutes of Health https://www.nih.gov/	The National Institutes of Health (NIH), a part of the U.S. Department of Health and Human Services, is the nation's medical research agency — making important discoveries that improve health and save lives.

INSTITUTIONAL REVIEW BOARDS (IRBS) AND PATIENT SAFEGUARDS	
The Federal Policy For the Protection of Human Research Subjects (or "the Common Rule") https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html FDA's regulations on human subject protection (21 CFR part 50) and Institutional Review Boards (IRBs; 21 CFR part 56) (cf. Code of Federal Regulations links above)	Safety precautions and ethical conduct of clinical studies of all types have made substantial progress during the past few decades. The research diversity white paper results indicated that the majority felt that while clinical studies may have risks, appropriate oversight and safety precautions are now in place. Historically CHCs have not been involved in clinical studies and may have refrained from suggesting studies to their patients due to concerns with safety and continuity of care. Since CHCs are a safety net for underserved populations, some patients may fit under the category of "vulnerable" groups. The Common Rule describes vulnerable people as "people who are vulnerable to coercion or undue influence" (45 CFR §46.107(a)). They mention "children, prisoners and individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons." When such populations are involved, additional safeguards can be recommended by the IRB or research organizations. According to 45 CFR §46.111, the IRB must determine that additional safeguards to protect the rights and welfare of subjects who are likely to be vulnerable are included in the study under review. To make this determination, the IRB—and before the study is submitted for IRB review, the investigators—might be advised to consider two questions: (1) Is inclusion necessary? and (2) If so, are safeguards adequate? Besides ensuring that proper IRB approval and review is in place, CHCs should confirm that the adequate determination and safeguards for vulnerable groups are in place with their research organization partners.
PROFESSIONAL ASSOCIATIONS / TRAINING ORGANIZATIONS	
Association of Clinical Research Professionals (ACRP) https://acrpnet.org/	With more than 16,500 members, the ACRP is the only non-profit organization solely dedicated to representing, supporting, and advocating for clinical research professionals. ACRP supports individuals and life science organizations globally by providing community, education, and credentialing programs. Founded in 1976, ACRP is a registered 501(c)(3) charitable organization whose mission is to promote excellence in clinical research and whose vision is that clinical research is performed ethically, responsibly, and professionally everywhere in the world.
The Society for Clinical Research Sites (SCRS) https://myscrs.org/	SCRS was founded in response to the growing need for a global organization advocating for the needs of clinical research sites globally. SCRS is an influential voice for sites and an active partner in industry-wide initiatives and dialogues with a focus on unifying the voice of the global clinical research site community for site sustainability. Representing more than 10,000 research sites in 47 countries, SCRS provides sites with a community dedicated to advocacy, education, mentorship, and connectivity.
Collaborative Institutional Training Initiative (CITI) (https://about.citiprogram.org/)	The CITI Program is an online training platform that provides courses and series on research, ethics, compliance, and safety topics for various learners and organizations
PATIENT EDUCATION AND OTHER RESOURCES	
Principles of Trustworthiness	AAMC toolkit outlining 10 principles of engaging with the community and building trust
The Center for Information and Study on Clinical Research Participation (www.ciscrp.org)	Non-profit organization that provides educational materials about clinical trial participation (including multi-lingual resources)
WHITE PAPERS /PUBLICATIONS ON CLINICAL RESEARCH, DIVERSITY, EQUITY AND INCLUSION	
The Building Clinical Trial and Health Research Access for People of Color via Community Health Centers white paper	Request a copy through info@alturastudies.com or visit https://alturastudies.com/research-ecosystems/#researchdiversitywhitepaper
Broadening research participation through community engagement (NACHC/Deloitte)	Community-based clinical trials | Deloitte Insights https://www2.deloitte.com/us/en/insights/industry/health-care/community-based-inclusive-and-equitable-clinical-trials.html
Clinical Trial Diversity (FDA)	https://www.fda.gov/consumers/minority-health-and-health-equity/clinical-trial-diversity

Section 7: Terms and Definitions

TERM	DEFINITION / DESCRIPTION
Blinding	Single blind – patient does not know which treatment was assigned. Double blind – neither patients nor study team are aware of assigned treatment.
Clinical Research Coordinator (CRC)	A Clinical Research Coordinator (CRC) is a healthcare professional who manages and conducts the day-to-day activities of a clinical trial at a study site. The Principal Investigator (PI) determines the CRC's specific responsibilities and works closely with the CRC.
Good Clinical Practices (GCPs)	Good Clinical Practice (GCP) is an international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials. It also serves to protect the rights, integrity and confidentiality of trial subjects
Human subjects	A living individual about whom an investigator (whether professional or student) conducting research: • Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or • Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
Informed Consent	The process for patients to read, understand and agree to join a study. Must occur before any treatment can begin.
Institutional Review Boards (IRBs)	IRB is a generic term used by the Food and Drug Administration (FDA) and Department of Health and Human Services (HHS) to refer to a group whose function is to review research to assure the protection of the rights and welfare of the human subjects. Institutions may use different names, but the purpose of IRB review is to assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in the research. To accomplish this purpose, IRBs use a group process to review research protocols and related materials (e.g., informed consent documents and investigator brochures) to ensure protection of the rights and welfare of human subjects of research. IRBs must comply with HHS and FDA regulations in 45 CFR part 46 and 21 CFR parts 50 and 56, respectively, when reviewing research subject to those regulations. Both the HHS regulations at 45 CFR 46.103(b)(4) and (5) and the FDA regulations at 21 CFR 56.108(a) and (b) state that IRBs must follow written procedures for various functions and operations.
Investigational / non-investigational study	An investigational intervention (which may be a drug or medical device) has not been approved by regulatory authorities for use in humans or for the condition in which it is being studied. In these studies, the intervention is evaluated for safety and effectiveness in treating a disease or medical condition. A non-investigational clinical trial is a clinical trial that uses interventions that have already been approved by regulatory authorities for use in humans, or do not require regulatory approval for use.
Investigator-Initiated Trials	A clinical trial in which the investigator conceives the research, develops the protocol, and serves as sponsor-investigator. The sponsor-investigator initiates and conducts a clinical trial alone or with a team. The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator: creating, coordinating, and conducting the study.

TERM	DEFINITION / DESCRIPTION
Observational Studies	An observational clinical study is a type of clinical research in which investigators observe individuals without manipulating or intervening in their routine medical care or lifestyle. These studies can be retrospective or prospective in nature.
Phase I Clinical Trial	The initial introduction of an investigational new drug into humans. These studies are typically closely monitored and may be conducted in patients or normal volunteers. The primary objectives of Phase I studies are to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. Often Phase I studies are conducted in dedicated laboratories or specialized study sites and not typically placed in medical practices.
Phase II Clinical Trial	The FDA defines Phase II studies as controlled investigational clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study, and to determine the common short-term side effects and risks associated with the drug.
Phase III Clinical Trial	These clinical trials are large-scale investigational studies that involve several hundred to several thousand participants. These trials are designed to confirm the effectiveness of a new drug or treatment, monitor side effects, compare it to commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely.
Phase IV Clinical Trial	Phase IV studies are post-marketing studies that are imposed upon a pharmaceutical firm as a condition for drug approval. These studies are designed to provide additional information about the drug's risks, benefits, and best use.
Principal and Sub Investigators (PI & SI)	A Principal Investigator (PI) is the researcher, usually a doctor or other medical professional, who leads the clinical research team and, along with the other members of the research team, regularly monitors study participants' health to determine the study's safety and effectiveness. A PI is primarily responsible for the preparation, conduct, and administration of a research grant, cooperative agreement, or other sponsored project in compliance with applicable laws and regulations and institutional policy governing the conduct of clinical research. The Sub-Investigator (SI) is a medical professional who is under the supervision of the Principal Investigator and is responsible for performing some study–related procedures and /or to make important study-related decisions, but they do not accept primary responsibility for the research study.
Protocol and synopsis	The study protocol is a document that describes how a study will be conducted (the objective(s), design, methodology, statistical considerations and organization of a clinical trial), and ensures the safety of the trial subjects and integrity of the data collected. The synopsis is an overview/summary of the protocol.
Randomization	The process by which patients are randomly assigned to a treatment. It can be placebo, or it can be an active comparator such as a product already approved to treat the condition, at 1:1 or some other ratio.
Sponsor	A sponsor is a person or entity who takes responsibility for and initiates a clinical investigation of a new drug. The sponsor is also the applicant who applies to FDA for approval to market a drug product in the United States. The sponsor is responsible for compliance with applicable provisions of the Federal Food, Drug, and Cosmetic Act and related regulations.
Study Site	A location where one or more clinical trials are conducted (i.e., patient participants are recruited, treated, and monitored). These sites are usually universities, medical centers, clinics, hospitals, and standalone/independent centers. The sponsor of the clinical trial determines which study sites are selected for a study.

Section 8: Frequently Asked Questions

CLINICAL TRIAL DESIGN QUESTIONS	
Is a placebo always involved for clinical trials?	Investigational clinical trials always include a comparator arm that may or may not be placebo. Often an active comparator is utilized, but it can be a placebo alone or placebo added to the current prescribed treatment. Randomization ratios can vary, but 1:1 is typical.
What kinds of tests and treatments are involved? Length of trial?	The tests and treatments will vary by study type and medical condition. Always ask for a protocol, or at least the synopsis, when considering a study. The length of the study will also vary depending on its objectives.
PATIENT PARTICIPATION QUESTIONS	
Are patients reluctant to participate in clinical trials?	Patients are more likely to consider clinical trials if their healthcare provider or CHC is suggesting the option. Experience with CHCs conducting clinical trials indicates patients are very willing to consider clinical trials. During the informed consent process patients have the option to ask questions and determine their obligations in the trial which could include stopping medications and involvement of placebo and other treatments. Patients always have the option to join a study or stop it at any time.
Can patients remain on investigational drugs after the trial ends?	No, unless the study has an extended phase. Extension phases are typically open label and not blinded.
Is the clinical trial a good option based on patient's current treatment for their condition?	The protocol design will determine if a patient is able to remain on their current treatment or if some type of discontinuation is required. A patient's current medical status is a factor in this decision and should be made in conjunction with the patient's primary care provider. The Principal Investigator also has the option to exclude a patient from a study, based on their assessment of the patient's health status.
Who qualifies to join clinical trials?	Each clinical trial has a very specific set of inclusion and exclusion criteria. The various types of clinical studies impact who qualifies. Observational studies tend to be more open, while the investigational clinical trials tend to be very specific with the populations permitted to enroll.

CHC PARTICIPATION QUESTIONS	
Does a CHC need to operate an internal IRB?	No. Studies involving human subjects or that are supported by HHS or governed by FDA require IRB approval and oversight, but CHCs are not required to operate such IRBs. IRBs require significant resources, and often the research organizations sponsoring or partnering on trials operate an IRB or contract with an independent IRB for all required services. CHCs should consult with an IRB to confirm if IRB review, or exemption from review, is required when considering studies not overseen by FDA or HHS.
To be a main site for any type of study, how big is the time and financial investment upfront?	The cost and time required to build an internal research center varies based on the resources and experience available within the CHC. CHCs can consider a cost-effective slower growth strategy for which a basic structure is created and incremental growth occurs as more studies are contracted. The time frame can be anywhere from six months to one year to build a basic research structure which could include starting the first trial. The cost could vary significantly depending on the partnership model or external support that the CHC will acquire.
Who pays for clinical studies?	An investigational phase II-III clinical trial is paid for by the study sponsor. Other types of interventional studies could be funded via grants by government agencies or foundations.
How much time is involved with the different participation options?	Involvement is dictated by the type of study a CHC is involved with (see Section 3 – Clinical Study Types). The time range varies considerably by study type and level of involvement.
How do we know if a clinical study is beneficial for our patients and community?	The study feasibility process is important and involves a few factors to consider. First, there should be a review to determine whether the interventions and study design are appropriate. Each CHC may have its own requirements or priorities related to the medical conditions and types of interventions they would like to offer to their patients. Second, the schedule of events for the study should be considered to determine the impact on patient participation and retention. Lastly, it is important to ensure that a reputable organization is sponsoring the study or serving as a main site if required. Factors such as appropriate informed consent and continuity of care should be explored and confirmed.
What type of qualifications are required for PI, Sub-Investigator and Clinical Research Coordinators?	For investigational clinical trials, sponsors seek study sites that have staff with previous clinical trial experience. There are exceptions, and subsites may include research team members that have no experience but can be trained to help execute the study. Typically, Good Clinical Practice (GCP) training is required as a baseline. Most of the time the principal investigator is a primary care or specialty physician, depending on the need. Sub-investigators can be physicians, nurse practitioners or physician assistants. Clinical research coordinators (CRCs) can be RNs, LVNs, or MAs, although there is usually no specific requirement.