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

ACKNOWLEDGEMENTS

This toolkit is dedicated to the healthcare professionals nationally that are seeking to support expanding clinical trial and health research access and diversity. We would like to thank all who have contributed to the development of this toolkit.

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.

Core Project Team: Thank you to the Core Project Team for the development of this resource. Their time, expertise and dedication contributed significantly to the vision and content of this publication.

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Other Contributors and Acknowledgments: Thank you to the many primary care associations across the country who supported identification of survey participants. In addition, the authors also thank the following professionals who dedicated their time and expertise to provide valuable feedback and support:

Rakesh Patel MD, Joseph Risser MD, Alyssa McNees, Beth Harper, Tamara Salvio, Tim O'Connor PharmD, and **Pat Ticknor.**

Funding: This research and resulting white paper and toolkit would not have been possible without the generous support of Genentech, a member of the Roche Group, and its Health Equity and Diversity Grant.

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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

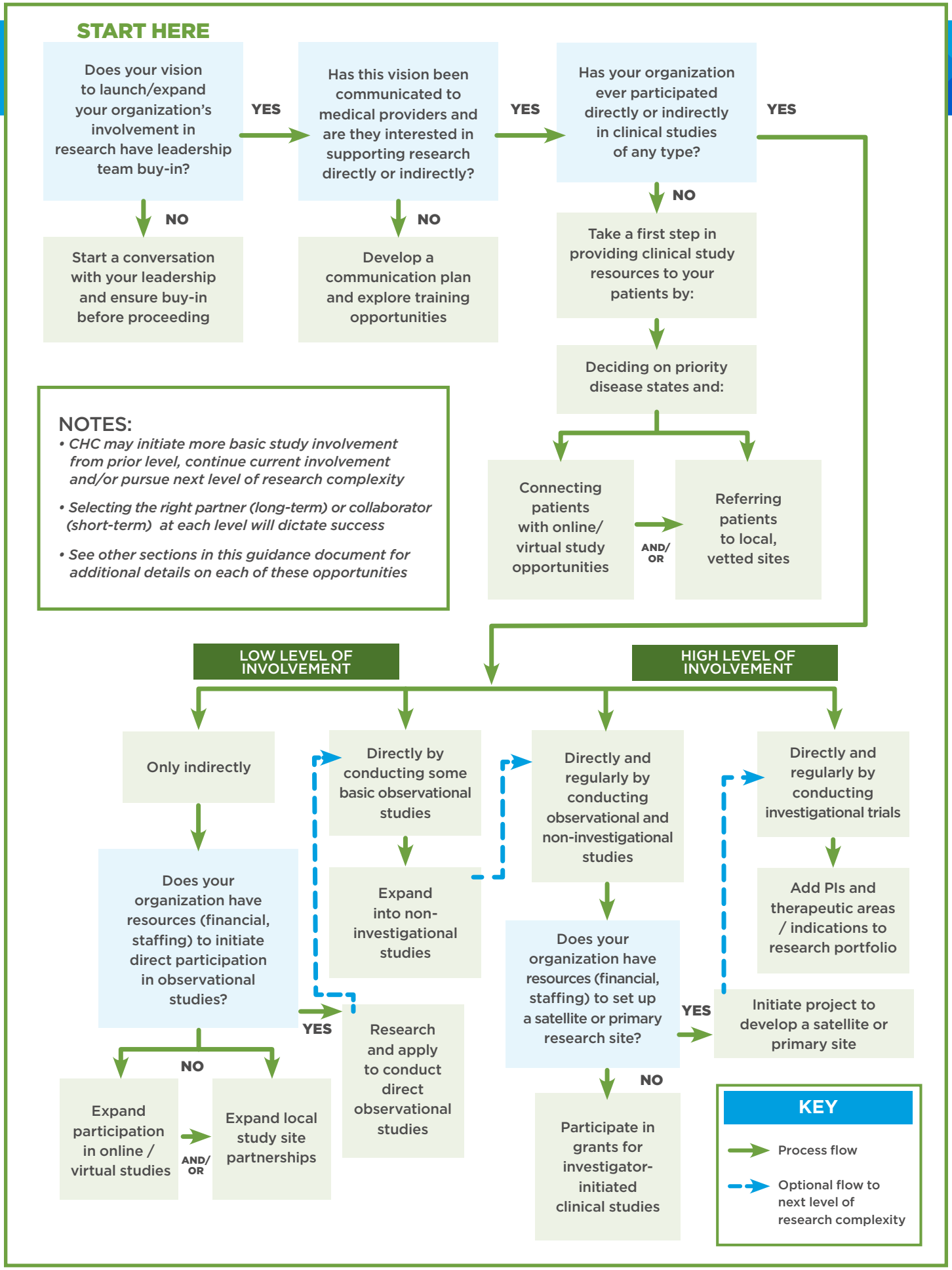
How To Use

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.