

Clinical Trials Basics and Barriers to Recruiting African American Patients into Clinical Trials

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Welcome to the Materials to Increase Minority Involvement in Clinical Trials (MIMICT) module –Clinical Trials Basics and Barriers to Recruiting African American Patients into Clinical Trials

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By the end of this module, you will be able to: (1) explain basic information about clinical trials and the phases; (2) understand the importance of clinical trials to providers, patients, and the medical field; and (3) communicate the differences between provider-side and patient-side barriers to clinical trial recruitment.

Introduction



Learning Objectives

By the end of this module, you will be able to:

- Discuss lupus symptoms and lupus-related health disparities.
- Discuss health disparities in clinical trial participation and their importance.

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Specifically, this course will cover: the importance of clinical trials, the basics of clinical trials, and the barriers and facilitators to clinical trial recruitment.

Course Overview



- Importance of clinical trials
- Basics of clinical trials
- Barriers and facilitators to clinical trial recruitment
- Steps to learn more about clinical trials

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Clinical trials benefit the medical community, individual providers, and individual patients in the present and future. Sometimes the insight gained during current clinical trials may not have an immediate benefit, but clinical trials still inform future medicines and clinical care.

Clinical trials help advance medicine. These studies investigate new and improved ways to detect, prevent, and treat diseases. These studies also help the medical community understand the side effects of treatments, as well as potential treatment interactions.

Trials are also useful to individual provider practices. Providers may resort to clinical trial opportunities when they've reached the limits of their standard treatment options with patients that have treatment-resistant conditions.

Individual patients may be interested in clinical trials for various reasons. Healthy volunteers may simply want to help advance medical innovation. For some patients, participation in a clinical trial offers hope when standard treatment has not been effective. Patients may experience therapeutic benefits by receiving the treatment being investigated or may also have feelings of altruism from participating in a trial that helps a larger community.

All clinical trials come with risk of potential harm. Providers and patients should weigh risks of harms resulting from participating in the study with the risks of potential harm occurring from any other treatment, including the current medical standard of care.

Importance of Clinical Trials

Clinical trials provide present and future benefits to:

- The medical community
- Individual providers
- Individual patients

However, clinical trials come with a balance of benefits and risks.

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There are three essential things to know about clinical trials: people involved in clinical trials, trial phases, and general eligibility considerations. This information will serve as a solid base from which providers can explain clinical trials during a patient referral.

Things to Know About Clinical Trials

- People involved in clinical trials
- Trial phases
- General eligibility considerations



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Key people involved in conducting a clinical trial include: the patient's primary providers, sponsors, the principal investigator, the clinical research coordinator, healthy volunteers, patient volunteers with active disease, nurses, administrative assistants, and clerical staff. In the patient community, clinical trial participants are often called "volunteers"

People Involved in Clinical Trials

- The primary providers
- Sponsors
- Principal investigator
- Clinical research coordinator
- Healthy volunteers
- Patient volunteers with active disease
- Nurses
- Administrative assistants
- Clerical staff

Clinical trials don't always mean the patient will be absent from their usual provider's care. For some clinical trials, patients continue to see their usual provider while they are enrolled in a clinical trial. Thus, providers can play a significant role in referring patients into clinical trials and providing care throughout. We discuss this in more detail in the module called "Referring Patients to Clinical Trials."

Sponsors are typically the pharmaceutical company funding and monitoring the research studies.

The principal investigator (and other research scientists on the team) design and implement ethical research that protects the rights and health of participants, obtain informed consent from patients, report any adverse events or unanticipated issues that involve the patient, and maintain patient health records. For lupus clinical trials, the principal investigator is usually a practicing rheumatologist.

The composition of healthy volunteers and patient volunteers varies by clinical trial phase.

Nurses, administrative assistants, and clerical staff all participate in carrying out the logistics of clinical trials.

All of these key players are present during the clinical trial phases.

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An investigation into a new drug or treatment regimen may involve multiple clinical trial phases. There are five clinical trial phases, but not every trial goes through all five phases. Clinical trial research most commonly involves Phases I, II, and III.

Phase 0 (zero) studies are optional and explore if the drugs work as intended. Volunteers during Phase 0 stand no direct benefit from the drug.

The benefits are more for future patients. These studies are typically very small and this phase is not required by the FDA for testing new drugs.

Phase I studies determine a drug's safety at different doses. In Phase I, researchers try to tease out a dose that minimizes adverse side effects in a group of healthy participants. Some patients do benefit from Phase I trials, but the goal of these studies is not to confirm whether the new treatment is effective at treating the disease.

Once the drug has shown to be safe, Phase II studies investigate how well a drug works and seek more information about a drug's safety. Phase II studies typically last two years. If the drug performs well in Phase II, the drug will likely continue to a Phase III study.

Phase III studies compare how well the new drug performs in relation to the current standard of treatment. In Phase III, researchers seek to understand the extent to which the new drug performs better than the current best available treatment. For comparison criteria, Phase III studies consider the drug's ability to treat the disease and the associated side effects. Sometimes, there are no standard treatments available. In that case, the new drug is compared to no intervention.

Phase IV studies monitor the drug's widespread use after it receives approval to be sold and mass-distributed. In Phase IV, researchers observe the long-term effects of the drug in the real world. Studies in this phase last at least two years.

Clinical Trial Phases

- Phase 0 (zero) studies are optional and explore if the drugs work as intended.
- Phase I studies determine a drug's safety at different doses.
- Phase II studies investigate how well a drug works and seek more information about a drug's safety.
- Phase III studies compare how well the new drug performs in relation to the current standard treatment.
- Phase IV studies monitor the drug's widespread use after it receives approval to be sold and mass-distributed.

(National Institutes of Health, 2017; Clinicaltrials.gov, 2008)

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Placebos and the standard of care are related concepts. Placebos are a major point of confusion for providers and patients. A placebo is defined as substance or treatment that is used as a control in the research experiment.

Many people think that if they receive a placebo, they will be harmed because they equate receiving a placebo with receiving no treatment or therapeutic benefit at all. This is not always true in clinical trial research.

The patients in the control group receive a placebo, which is usually the current available standard of care, especially in Phase III trials. Placebos are important because they provide a reference point for comparison to see if a new treatment works or not.

Patient outcomes among those who receive the current standard of care (the placebo) are then compared to patient outcomes among those who receive the experimental treatment being tested in the trial.

If there is no current medical standard of care, then volunteers in the control condition do not receive any treatment since there is none currently established in the medical community.

Additionally, clinical trial studies are either “single-blinded” or “double-blinded” with regard to the way in which patients are assigned to receive either the treatment or placebo.

Single-blinding means that the patients do not know if they’re receiving the experimental treatment or placebo condition until the end of the study.

Double-blinding means that neither the researchers nor the volunteers know who is assigned to receive the experimental treatment or placebo until the study is over. The assignments are given at random in the beginning, without any input from the researchers conducting the study.

Placebos and Standard of Care

About placebos

- A placebo is a substance or treatment used as a control in research experiment.
- Placebos are important because they provide a reference point for comparison to see if a new treatment works or not.
- Placebo does not always mean no therapeutic benefit.

About standard of care

- Clinical trials investigate whether a new treatment is better than the current standard of care.
- Patients in the control group usually continue receiving the current treatment standard.

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Each trial sets its own inclusion criteria, but there are several general eligibility considerations common across nearly all clinical trials.

All lupus patients may not qualify to participate in a clinical trial. These general eligibility considerations represent the factors clinical trial sites consider to ensure patient safety and meaningful research findings.

General Eligibility Considerations

- Age
- Disease severity
- Medical history
- Other health conditions
- Gender
- Current health status



Generally, clinical trial sites consider a patient's age, medical history, other health conditions, gender, and current health status to evaluate potential clinical trial participants. Remember, that providers do not determine eligibility during the referral process.

Clinical trial sites realize that evaluating eligibility may be time consuming and burdensome for providers. In addition, providers may also incorrectly evaluate a patient's eligibility. Therefore, this responsibility is typically left to the clinical trial staff.

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Making clinical trial referrals is not always easy. Providers and patients may experience challenges, or barriers, that hinder recruiting African American patients into clinical trials.

Barriers to Recruiting African American Patients into Clinical Trials

- Provider-side barriers
- Patient-side barriers
- Impact of unethical medical research

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Providers may face several barriers to speaking with their patients about clinical trials that ultimately dissuade them from making clinical trial referrals. There are three categories of provider-side barriers: awareness and knowledge barriers, attitude barriers, and logistical barriers. We will discuss each of these barriers in detail.

Provider-Side Barriers

There are three categories of provider-side barriers:

- Awareness and knowledge barriers
- Attitude barriers
- Logistical barriers

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Awareness and knowledge barriers may stem from a provider's lack of access to information about clinical trials, lack of familiarity with clinical trial sites and principal investigators, lack of knowledge about the clinical trial protocol, or mismatch between the provider's assessment of the patient's eligibility and the patient's actual eligibility.

Providers refer less than one percent of the patients they serve every year to clinical trials and almost half of providers report not knowing where to refer patients for clinical trials.

Providers may also not be familiar with the local principal investigators, clinical trial staff, or their specific protocols.

Provider Awareness and Knowledge Barriers

- Lack of access to information about clinical trials
- Lack of familiarity with clinical trial sites and principal investigators
- Lack of knowledge about the clinical trial protocol

(Koriet, 2016) Local Trials Basics and Barriers to Recruiting African American Patients into Clinical Trials

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Providers who are confident in their local principal investigators or clinical trial site and are familiar with the site's protocol are much more likely to refer patients (Korieth, 2016).

Providers may be apprehensive about referring patients to clinical trials due to beliefs that clinical trials may be unsafe or feels coercive; that clinical trials could strain the provider-patient relationship; and that minority patients may not be able to understand and adhere to specific protocols.

Providers' safety concerns may stem, in part, from unfamiliarity with the clinical trial site staff and the staff's reputation with ethnical and safe research practices. Providers' role is to introduce clinical trials as a potential option to their patients. It's important to remember that, ultimately, the patient decides to participate or not participate in a clinical trial. Clinical trial site staff understand that providers are invested in their patient's safety, so the staff aim to maintain clear communication with providers to help eliminate these concerns.

Providers may also worry that referring patients to a clinical trial may strain their relationships with patients or that patients may permanently leave their care after enrolling in a trial. Establishing a point-of-contact at the clinical trial site to communicate with before, during, and after a clinical trial opens a channel of communication and makes for a less stressful clinical trial referral. See Referring Patient to Clinical Trials for more information about making clinical trial referrals.

Lastly, providers may be concerned about their patient's ability to understand or adhere to the trial protocols, especially for minority patients. These internal biases can affect one's willingness to make a referral. For example, reports show that providers tend to hold less positive attitudes toward minority patients, such as viewing them as less educated and less likely to comply with treatments than their non-Hispanic white patients (Van Ryn and Burke, 2000). This may result in fewer clinical trial referrals, even if the patients may be receptive to information about clinical trials (Crawley, 2000).

Provider Attitude Barriers

- Belief that the clinical trial is unsafe or coercive
- Belief that the clinical trial could have a negative impact on the provider/patient relationship
- Providers' misperceptions about patients' ability to understand and adhere to specific protocols, especially minority patients

(Van Ryn and Burke, 2000; Mills et al., 2006)

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MIMICT provides materials to help facilitate provider communication with clinical trial sites and patients to address these issues related to referring patients to clinical trials.

Common logistical barriers providers may face when making clinical trial referrals include a lack of time to talk to patients and to learn about clinical trials, a lack of connection with the clinical trial site or principal investigator, and a lack of clinical trials in close proximity to the provider's office.

More than half of providers report that they don't have enough time to learn more about clinical trials

Provider Logistical Barriers

- Lack of time to talk to patients and to learn about clinical trials
- Lack of connection with the clinical trial site or principal investigator
- Lack of clinical trials in close proximity to the provider's office



(Korieth, 2016)

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or discuss clinical trials with their patients (Korieth, 2016). But, a referral can be a very brief, informal add-on to regular patient conversations, supplemented with more detailed materials about clinical trials that patients can browse on their own.

Patients face several barriers related

Patient-side Barriers

There are four categories of patient-side barriers:

- Opportunity
- Health literacy
- Access
- Attitudes

Barriers prevent patients from taking the steps to consider and enroll in clinical trials.

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to learning about and participating in clinical trials. There are four categories of patient-side barriers: access, opportunity, attitudes, and health literacy. Such barriers prevent patients from taking the steps to consider and enroll in clinical trials.

Patient opportunity barriers include lack of awareness about clinical trials; a general lack of referral by all providers; and a lack of minority providers who are engaged in clinical trial research due to challenges with infrastructure support, especially providers who practice outside of academic medical centers.

A majority of patients are not aware of clinical trials, even for diseases like cancer, but more than three-fourths state they would have been willing to participate if presented with the opportunity (NCI, 1997). Some patients may seek information about clinical trials on their own and return to their primary providers to discuss further questions about clinical trials.

Patient Opportunity Barriers

- Lack of awareness of clinical trials
- Lack of referral by providers
- Lack of minority providers who are engaged in clinical trial research

(Ford et al., 2008; Westat, 2004; National Cancer Institute, 1997)

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Essentially, providers and clinical trial sites need to work in parallel efforts to explain what a clinical trial is, raise awareness, and introduce clinical trial opportunities to increase minority patient involvement in clinical trials.

Health literacy barriers to clinical trial participation include a lack of disease education, misunderstanding of study group randomization, and/or difficulty understanding the informed consent process; belief that the clinical trial has little or no benefits; and challenges understanding study documentation written at too high a reading level.

Providers can educate patients about clinical trials and provide information written at accessible reading levels. Patients tend to prefer learning about clinical trials from their trusted providers. Visits with patients are already short and quick, so there may only be enough time to briefly introduce patients to the idea of clinical trials.

Patient Health Literacy Barriers

- Lack of disease education, misunderstanding of study group randomization, and difficulty understanding the informed consent process
- Belief that the clinical trial has little or no benefits
- Challenges understanding study documentation written at too high a reading level

(The Society for Women's Health Research, 2011; Ford, et al., 2008; Agre, et al.,1996; Lidz, et al.,1983; Davis, et al.,1998)

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The MIMICT toolkit includes patient materials that assist with patient education. Providers with limited time to explain details about clinical trials to patients, then provide them with MIMICT's patient materials or simply direct them to MIMICT's online resources to learn more.

Access barriers tend to be structural and difficult for patients to overcome by themselves. Some examples of patient access barriers include lack of transportation, lack of childcare, lack of health insurance, and lack of access to nearby rheumatologists.

Sponsors of clinical trials, the pharmaceutical companies funding the research, may make special accommodations for clinical trial participants. Sponsors often fund participant travel, lodging, and even childcare to make it easier to participate in a trial.

Patient Access Barriers

- Lack of transportation
- Lack of access to childcare
- Limited or no health insurance
- Lack of access to rheumatologists

(Fitzgerald et al., 2013; Mills et al., 2006; NCI, 1997; Guadagnolo et al., 2009)

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Providers should inform patients that clinical trial sites may be able to help them overcome access barriers. Be sure to encourage patients to inquire about what accommodations may be available to allow them to participate in a clinical trial.

Attitude barriers include patients' feelings of uncertainty and anxiety towards medical research and fear of not satisfying the eligibility criteria for a clinical trial they had hoped to join.

Many minority patients fear a negative impact on quality of life through loss of autonomy and side effects from participating in the clinical trial. They may also be uncomfortable with feeling like a "guinea pig" in an experiment and lack trust in the medical community. Many of these fears and distrust stem from unethical medical research, which we will discuss in greater detail.

Providers should remind patients that no one knows, with certainty, if the experimental drug will work or not. This is why researchers conduct controlled clinical trials. The MIMICT online materials include a provider response chart that has sample language to phrase this important point and answer common patient questions when making a referral.

Providers may also find that patients experience anxiety for reasons other than distrust in research. Patients who hope to enter a clinical trial because they believe that a new treatment will work for them may feel dismayed if they don't meet the trial's eligibility criteria.

Feelings of rejection may discourage patients from seeking other clinical trials for which they do qualify. Inclusion and exclusion criteria may seem arbitrary, but they serve two very important purposes in medical research.

Patient Attitude Barriers

- Feelings of uncertainty and anxiety towards medical research
 - Side effects may negatively impact quality of life
 - Uncomfortable with feeling like a "guinea pig" in an experiment
 - Lack of provider-patient trust and trust in the medical community
- Fear of not satisfying the eligibility criteria for a clinical trial

(Ford et al., 2008; Westat, 2004; Mills et al., 2006)

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Reinforce to patients that the criteria not only define the target study population, but the criteria also ensure patient safety by excluding certain patients who may be harmed because of potential drug interactions. Reassure discouraged patients by emphasizing that, in some cases, it's better to be excluded from a clinical trial than be harmed.

Lack of trust contributes to lower

Unethical Medical Research and the Impact on Trust

- Lack of trust is one of several barriers that contributes to lower African American patient participation in clinical trials.
- Discrimination and a history of unethical medical research contribute to strained trust in the provider-patient relationship.
- African American patient experiences and perceptions are influenced by the history of slavery, structural discrimination, and unethical medical research.

(Northington Gamble, 2005 ; Satcher, Pamies, and Woefl, 2005)

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African American patient recruitment and participation in clinical trials. Discrimination and a history of unethical medical research contribute to lack of trust in the provider-patient relationship. African American patient experiences and perceptions are influenced by the history of slavery, structural discrimination, and unethical medical research.

There are numerous examples of unethical medical research prior to National Research Act of 1974.

Many people cite the Tuskegee Syphilis study as a primary source of mistrust among African American patients. However, structural racism and discrimination against minority communities within U.S. medical research predate (and continued after) this historical event.

Here, we provide a timeline with four examples of unethical medical research within the African American community. Click on each example for more information.

In the 1840s, Dr. J. Marion Sims' performed gynecological experiments on African American female slaves who were unable to freely assert their consent to the surgeries and post-operative care.

During the 1880s, the bodies of southern African American slaves were stolen from graveyards and sold to anatomy professors to be used as instructional cadavers in medical schools.

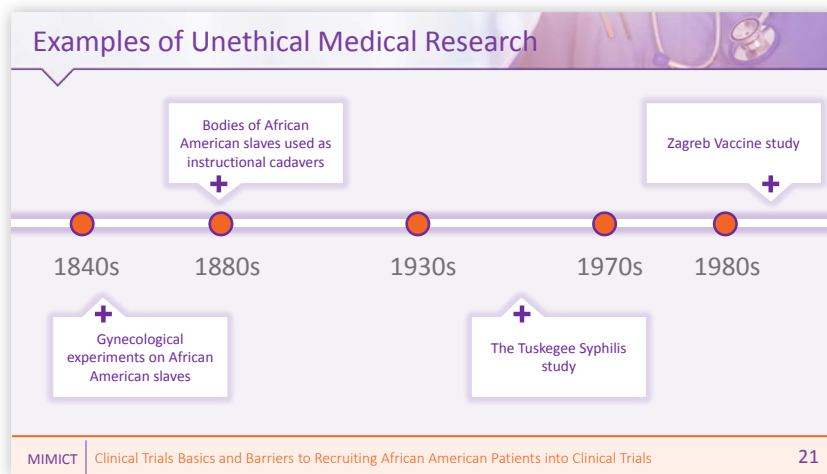
From 1930s-1970s, during the Tuskegee Syphilis study, African American men living with syphilis were not fully informed about the purpose of the study, offered the choice to leave the study, or to receive treatment, even after treatment became widely accepted in the medical community. Researchers misled participants and failed to present all the facts, therefore participants could provide informed consent.

Even more recently in the 1980s, the U.S. government sponsored an experimental clinical trial of two measles vaccines among 1,500 African American and Latino children. One of the vaccines was the Edmonston-Zagreb vaccine which was still experimental, unlicensed, and not approved for widespread use. The parents of the children in the clinical trial were not informed that their children might be receiving an experimental drug.

Each of these examples involved researchers who did not fully inform participants of the research protocol, withheld information on the potential risk, did not adequately protect the participants against harm, and did not provide opportunities for participants to assert their consent. These are topics we discuss in more detail Patient Safety and Protections.

Still, the Tuskegee study, and the public response to it, remain vivid parts of collective memory of many African American patients.

(Northington Gamble, 2005; Halperin, 2007; Satcher, Pamies, and Woefl, 2005)



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