FOCUSED ON YOUR HEALTH
ADDICTION AND BEHAVIORAL HEALTH CLINICAL TRIALS IN YOUR COMMUNITY

Dr. Otto Dueno
Medical Director, Midwest Clinical Research Center
• Before one can initiate testing in human beings, they must conduct extensive pre-clinical or laboratory research.

• Research usually involves years of experiments in animal and human cells.

• If this stage of testing is successful, the sponsor then provides this data to the FDA requesting approval to being testing in humans. This is called an Investigational New Drug Application (IND)

• If approved by the FDA, testing in humans begins. This is done through a formally written and approved protocol.
• A study plan on which all clinical trials are based.

• Carefully designed to protect the health of participants

• Describes what types of people may participate in the trial (inclusion and exclusion criteria)

• Gives detailed schedule of tests, procedures, medications, dosages, and length of the study.

• Principal Investigator is responsible for assuring that the protocol is strictly followed for each participant
• Physicians
• Medical Institutions
• Foundations
• Voluntary Groups
• Pharmaceutical Companies
• Federal Agencies (cooperative group research)
  • NIH
  • NCI (ACRIN is funded through the NCI as a cooperative group)
  • DOD
  • VA
The most commonly performed clinical trials evaluate new drugs, medical devices, biologics, or other interventions on patients in strictly scientifically controlled settings, and are required for regulatory authority approval of new therapies. NIH organizes trials into 5 different categories.

- **Treatment Trials** - test experimental treatments, new combinations of drugs, or new approaches to surgery or radiology/radiation therapy.
- **Prevention Trials** - look for better ways to prevent disease in people who have never had them or prevent them from returning.
- **Diagnostic Trials** - conducted to find better tests or procedures for diagnosing a particular disease or condition.
- **Screening Trials** - test the best way to detect certain diseases or health conditions.
- **Quality of Life** - explore ways to improve comfort and the quality of life for individuals with chronic illness.
PHASES

Pre-clinical studies

Phase 0

Phase I

Phase II

Phase III

Phase IV
PRE-CLINICAL

- Involve *in vitro* (test tube or laboratory) studies and trials on animal populations.

- Wide ranging dosages of the compounds are introduced to the animal subjects or to an *in vitro* substrate.

- Obtain preliminary efficacy and pharmacokinetic information.

- Decisions are made during this phase regarding further development of the test compound, test item, or test article.
PHASE 0

• Recent designation for exploratory, first-in-human trials conducted in accordance with the FDA’s 2006 Guidance on Exploratory Investigational New Drug (IND) Studies.

• Designed to expedite the development of promising therapeutic or imaging agents

• Involve the administration of single sub therapeutic doses to a small number of subjects (10-15).

• Gather preliminary data on the pharmacokinetic and pharmacodynamic properties and mechanism of action.
PHASE I

• First step in testing in humans.

• Researchers look for safety and potentially harmful side effects.

• Usually include only a limited number of human subjects (20-80).

• This phase of testing usually takes several months.

• Three different kinds of Phase I trials include:
  • SAD - single ascending dose studies
  • MAD - multiple ascending dose studies
  • Food Effect - investigates differences in absorption caused by eating pre-dose
PHASE II

• Once a drug has shown to be safe, then it must be tested for efficacy.

• This phase may last from several months to two years.

• Usually involves several hundred patients

• Most of these trials are randomized trials

• Only about 1/3 of these studies successfully complete both phase I and phase II due to poor patient activity or toxic effects.
PHASE III

- Randomized control trials on large patient groups (300-3000).

- Compare the results of the patients on the experimental trial to those patients utilizing standard diagnostic studies or treatment

- Studies move into this phase only after a diagnostic agent, modality, or treatments have shown promise in phase I and II trials.

- These trials are typically *multi-center* trials.

- Many phase III trials are *randomized* and *blinded*.
PHASE IV

• Pre-approval, post-launch

• Involve safety surveillance and ongoing technical support of a drug.

• Sometimes mandated by the FDA for additional testing including interactions with other drugs and testing on certain populations.

• Adverse effects detected by Phase IV trials may result in withdrawal or restriction of a drug - recent examples include Vioxx.
# Regulations & Research Approval

<table>
<thead>
<tr>
<th>Phaze</th>
<th>Goal</th>
<th>Subjects</th>
</tr>
</thead>
</table>
| I     | Initial safety and tolerability (pharmacology)  
      | Determine safe dosage range (MAD, SAD)  
      | Identify side effects | 20 - 80 |
| II    | Effectiveness (therapeutic exploratory)  
      | Dose response  
      | Further evaluation of safety | 100 - 300 |
| III   | Effectiveness (therapeutic confirmatory)  
      | Monitor side effects  
      | Compare to commonly used treatments  
      | Collect information that will allow the drug or treatment to be used safely | 1,000 – 5,000 |
| IV    | Postmarketing (therapeutic use)  
      | Effectiveness in the general population  
      | Optimising drug use | Patient population sample |

*Dr. Stephen's understanding of randomisation wasn't quite up to scratch...*
HUMAN SUBJECT PROTECTION GUIDELINES

- Belmont Report
  - Ethical Principals in Human Subjects Review
  - Respect, Beneficence, Justice

- International Conference of Harmonization (ICH)
  - Brings together the regulatory authorities of Europe, Japan, and the US to discuss scientific aspects of human research.

- Good Clinical Practices (GCP)
  - Defines the roles and responsibilities of clinical trial sponsors, investigators, and monitors.

- Declaration of Helsinki
  - Developed by the World Medical Association (WMA), as a set of ethical principles for the medical community regarding human experimentation

- Nuremberg Code
  - Set of principles for human experimentation set as a result of the Nuremberg Trials at the end of the second world war. Specifically, they were in response to the inhumane Nazi human experimentation carried out during the war by individuals such as Dr. Josef Mengele.
INSTITUTIONAL REVIEW BOARD

• A group of scientists, doctors, clergy, and consumers

• All clinical trials must be reviewed and approved by your local Institutional Review Board (IRB). The IRB reviews the protocol and patient consent to make sure the study is conducted fairly and participants are not likely to be harmed.

• The IRB also decides how often to review the trial once it has begun. They also decide whether the trial should continue as initially planned and what changes should be made.

• An IRB can stop a clinical trial if there are safety concerns, inappropriate trial oversight, or if evidence becomes available that a new intervention is effective, in order to make it widely available.
WHO IS ON THE IRB?

FDA Requirements

• Must have at least 5 members
• If studies include vulnerable populations, the IRB should have members who are familiar with these groups.
• Should include both men and women.
• Members should NOT be all of the same profession.
• Must include at least one scientist and one non-scientist
• Must include at least one person who is not affiliated with the institution, sometimes called “community members”.
• Members may not vote on their own projects.
• Only actual IRB members may vote (consultant may be used but cannot vote).
INFORMED CONSENT

• The process in which a patient learns key facts about a research study and then voluntarily agrees to take part or decides against it.

• Informed consent must be documented by the use of a written consent form approved by the IRB for all ACRIN studies.

• Consent forms must be signed by the subject or the subject’s legally authorized representative.

• A copy shall be given to the person signing the form.
CONSENT FORM REQUIREMENTS

• The consent form MUST include the following:
  • Statement that the study involves research
  • Explanation of the purposes
  • Expected duration of the subject’s participation
  • Description of the procedures involved in the study
  • Identification of any procedures that are experimental
  • Risks or discomforts
  • Benefits
  • Alternatives to the research study
  • Statement of confidentiality
  • Statement about medical care and compensation should injury occur
  • Contact information for patients with concerns or questions
  • Statement that participation is voluntary and study withdrawal may take place at any time
RESEARCH STUDIES PRESENT DAY

- Treatment Resistant Depression
- Tardive Dyskinesia
- Binge Eating Disorder
- Opiate Addiction
- Attention Deficit Disorder
- Fibromyalgia
AWARENESS CHANGES ATTITUDES

First step is to regularly have the public think about participating and consider how they can help advance medical discovery.

One of the major barriers to recruitment to clinical research trials is a lack of awareness of the opportunity to participate both by the patient and the physician.

- 32% of adults indicate they would be very willing to participate in a clinical trial if asked (1).

- 28% indicated they would consider it, but had some reservations (1).

- Focus groups found that many lack familiarity with clinical trials. They generally expressed negative attitudes about participation. These attitudes significantly changed after learned more (2).

Comis, 2003, NIH FG report 2011
Approximately 3.5 million people in the United States are diagnosed with schizophrenia and schizoaffective disorder.
DEPRESSION

“You can live well with a mental illness. It may take time, but it’s worth it. You deserve to live a happy and healthy life.”

-Demi Lovato
"At times, being bipolar can be an all-consuming challenge, requiring a lot of stamina and even more courage, so if you’re living with this illness and functioning at all, it’s something to be proud of, not ashamed of." - Carrie Fisher

"Mental illness is nothing to be ashamed of, but stigma and bias shame us all."

BILL CLINTON
"I'm a recovering drug addict and know that drug addiction is an illness, it's a disease, so by criminalizing that you criminalize a huge percentage of the population. You malign them and stigmatize them, you generate more crime, you create a criminal culture, and speaking from the perspective of a sufferer it's simply not helpful."

Russell Brand

"There are peaks, there are valleys. But they're all kind of carved and smoothed out, and it feels like a low level of despair you live in. Where you're not getting any answers, but you're living OK. And you can smile at the office. You know? But it's a low level of despair."
RESEARCH TRIALS AS A COMMUNITY RESOURCE
RESEARCH TRIALS AS A COMMUNITY RESOURCE

- Estimates suggest that upwards of 80% of clinical research studies struggle with the need to find more participants \(^3\)
- Up to 20% of some clinical trials close due to lack of participation \(^4\)
- Groundbreaking medical advances will only happen through clinical research participation
- Recent national reports have strongly urged the NIH to engage the public in support of clinical research

CISCRP.org, Chang, 2011
• 75% of patients will enroll in a trial when asked to by their health care provider

• 32% of patients in clinical trials said that their health care provider took the time to answer all their questions

• Participating patients were more likely to have first learned about a clinical trial through their health care provider
RESOURCES

- www.clinicaltrials.gov
- https://www.nih.gov/health-information/nih-clinical-research-trials-you
- www.centerwatch.com
- http://thestarr.org/
- https://www.researchmatch.org/
- https://www.nih.gov/health-information/nih-clinical-research-trials-you/personal-stories
CONTACT INFORMATION

Otto Dueno, MD
Medical Director, Midwest Clinical Research Center
Odueno@midwestclinical.com
937.424.1050

Stefanie Hreha
Community Engagement Manager
Shreha@midwestclinical.com
937.863.3436

www.joinaresearchstudy.com  | 1 Elizabeth place suite G3 Dayton O.  | 937.424.1050
SOURCES


• 2. Pretesting NIH clinical trial awareness messages: A focus study with patients, caregivers, and the general public. Bethesda, MD: National Institutes of Health, April, 2011

• 3. Center for Information and Study of Clinical Research Promotion (CISCRP) website: CISCRP.org