Clinical Trial Recruitment & Retention: The Toughest Job You'll Ever Love!

Mark R. Burge, MD
Professor of Medicine

Why Perform Clinical Trials?

- Clinical trials are the principle scientific method for answering treatment questions and determining what works and what doesn't work in Medicine.
- Clinical trials can involve medical, surgical, or behavioral interventions, or devices.
- They are the primary way that researchers find out if a new treatment or device is safe and effective in people.
- Often a clinical trial is used to learn if a new treatment is more or less effective than the standard treatment.

How Much do Clinical Trials Cost?

- Bringing a new drug to market typically costs $2-3 B.
- A pivotal clinical trial in support of a new drug costs an average of $19 M.
- In 2013, the U.S. pharmaceutical industry sponsored 6,199 clinical trials of medicines involving a total of 1.1 million participants.
- The total cost of these trials in 2013 was $10 Billion.
- Approximately 14% of FDA applications for new drugs are approved each year.

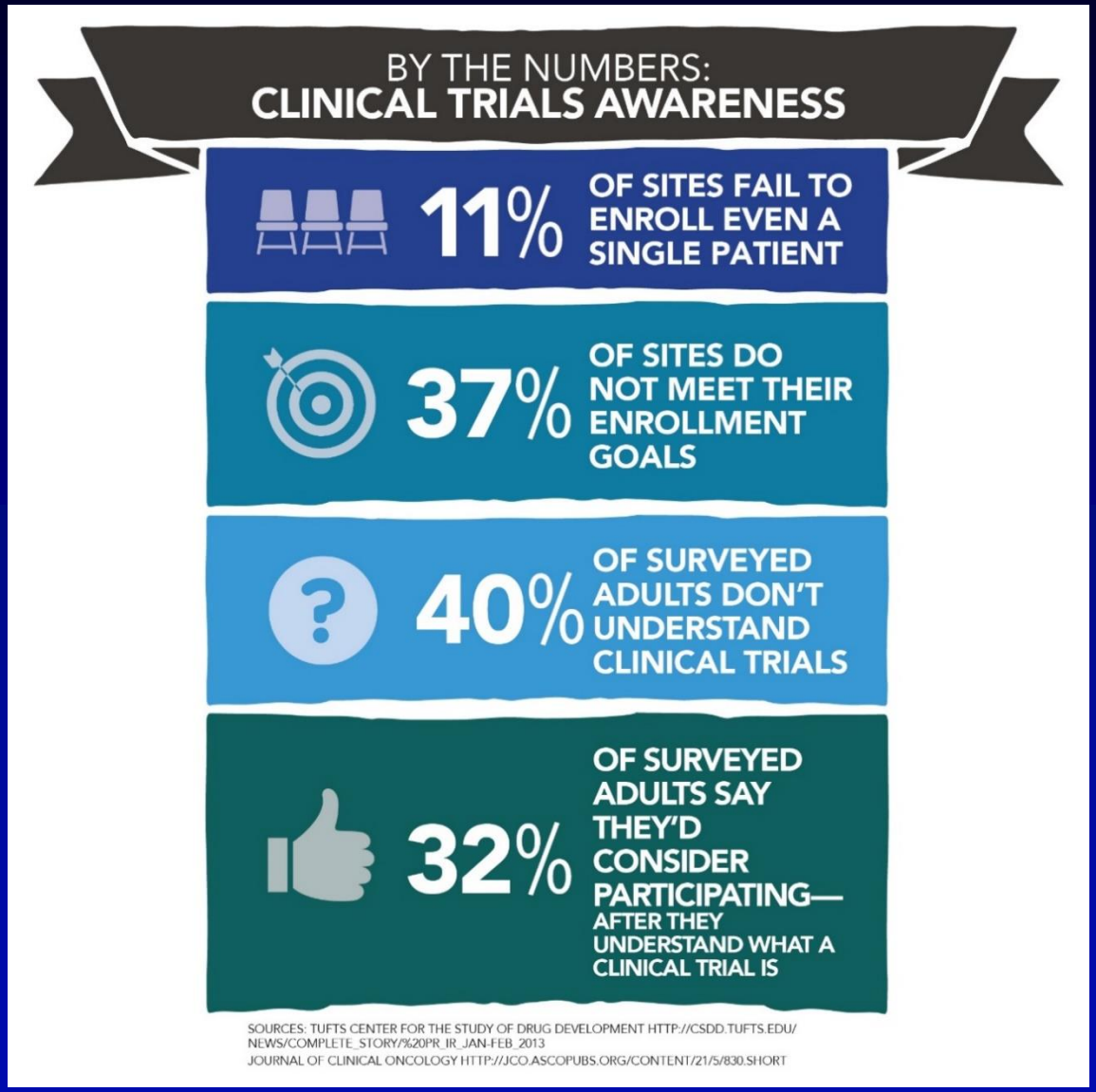
https://www.outsourcing-pharma.com/Article/2018/09/26/Clinical-trial-cost-is-a-fraction-of-the-drug-development-bill

Are Clinical Trials Successful?

Nearly 80% of clinical trials fail to meet trial timelines

https://blog.covance.com/2013/02/clinical-trial-challenges.html
Kremidas J. Recruitment Roles, Applied Clinical Trials Online, 2011.

Why Do Clinical Trials Fail?



http://cctawareness.org/about-us/

Why do Clinical Trials Fail?

- Failing to demonstrate efficacy or safety.
- Lack of funding.
- Inappropriate eligibility criteria; too specific.
- Inadequate recruitment.
  - *A study of 114 trials in the UK showed that only 31% met enrollment goals.*
  - *Reduced participant interest due to fear of getting assigned to the control or placebo group.*
- Additional costs associated with recruitment. How much per enrolled participant?
- Poor recruitment, dropouts, and underpowered trials.
- Participant time and monetary investment.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6092479/

Duke Center for Living - STRRIDE 1

Advertising Method	Percent screened & enrolled	Screening Time per person (minutes)	Ad cost per person ($)
Local Newspaper	8%	148	48
Special Event Ad	26%	47	35
Flyer	16%	75	18
University Newspaper	13%	92	0
Radio	7%	180	190
TV	3%	353	205
Personal Referrals	17%	70	0
Other	2%	688	333
Total	10%	120	40

Take Home Message

RECRUITMENT AND RETENTION OF QUALIFIED PARTICIPANTS IS THE MOST DIFFICULT TASK OF ANY CLINICAL TRIAL.

Corollary Message

If you want to make your investigator happy, recruit rapidly, efficiently, accurately, and with great gusto.

Recruitment Rules

- Whatever you do to recruit participants, make sure that the IRB has been informed and approved your approach!
  - Clinic Patients, Print Ads, Radio Ads, Registry Entries, Sandwich Boards, Bulletin Board Flyers, Social Media Posts…
- Include multiple strategies with the initial IRB submission; it's much easier than adding a new approach later.
- Familiarize yourself with HIPAA rules; the fines are stiff!

Do Remuneration Rates Matter?

- Studies show it both ways; depends on the disease, the condition, and the economic status of the participant.
- Investigators must describe all recruitment methods and plans for subject payment.
- Recruitment materials and payment methods must meet IRB standards to avoid coercion.
- Include multiple recruitment methods into the initial IRB application to avoid having to go back in with a modification; use precise, verbatim language.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3601710/

Recruiting Clinic Patients

- Recruiting from an investigator's patient panel is generally allowed, since a provider-patient relationship already exists.
- Must be IRB approved and non-coercive.
- Recruiting from other clinics is more involved and requires careful planning:
  - "Dear Patient" letter from PCP
  - Reimbursement of clinic staff
  - Co-investigator status for collaborators
  - Detailing protocol to outside clinic staff
  - Possibility of multiple IRBs

Marketing & Advertising

- Newspaper
- Radio
- Television
- Bulletin Boards
- Posters
- Flyers
- Patient Information Letters
- Websites
- Social Media
- Health Fairs
- Craigslist
- Pocket cards for physicians

Do not rely on only one method!!

Print Ads

Are you healthy

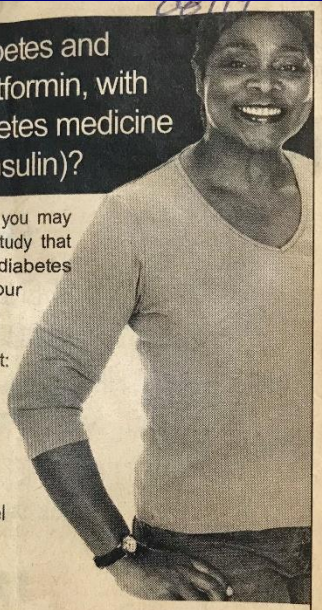
and free of thyroid disease?

If you are, you may qualify for a 6 week research study at the University of New Mexico Hospital to determine the metabolic effects on daily dietary kelp supplementation. Study volunteers will be compensated for time and expenses.

The University of New Mexico • Health Sciences Center
SCHOOL OF MEDICINE

For more information, please call
Olan Bassett at 272-1077 or **Mark R. Burge M.D.,** at 272-4658

Do you have type 2 diabetes and are currently taking metformin, with or without another diabetes medicine (including long acting insulin)?



If you are at least 18 years of age, you may qualify to participate in a clinical study that compares an investigational anti-diabetes medication in combination with your existing diabetes medicine to your existing therapy alone.
If eligible, you will receive at no cost:

- Study-related medical examinations
- Study-related investigational medication
- Diabetes testing supplies
- Compensation for time and travel (where permitted).
- Diet and lifestyle counseling

For more information, or to find out if you qualify, please contact:

UNM CTSC study team at (505) 272-8136 LixiLan-O

3/99

The University of New Mexico
HEALTH SCIENCES CENTER

Do You Have Diabetes?

If you have Type 1 or Type 2 diabetes you may be eligible for a new study involving inhaled insulin. Type 2 diabetes patients should currently be on little or no medication.

You will be compensated for time and expenses.

If interested, please call the
University of New Mexico Health Sciences Center Clinical Trials Center
(505) 272-2836

Effective & Compliant Advertising

- **Because advertising is part of the informed consent and subject selection process, all direct advertising must:**
  - Not imply certainty of favorable outcome
  - Not over-promote compensation or benefits
  - Not be misleading
  - Not include claims of safety, efficacy, equivalence or superiority
  - Not be termed “new” drug or device
  - Include the word “investigational”

Be Creative!


UNIVERSITY OF NEW MEXICO
LOOKING FOR:
Type 2 Diabetics using insulin
Ages 50-75
5-NIGHT DIABETES RESEARCH STUDY AT UNM.
PARTICIPANTS WILL BE COMPENSATED.
272-4338

Patient Registries

- Websites where participants can register if they are interested in research.
- Local Registry: *https://hsc.unm.edu/research/ctsc/participant-clinical-interactions/participant-recruitment-service/index.html*
- The UNM CTSC Clinical Research Volunteer Registry (CRVR) currently has 756 individuals listed with various conditions.
- National Registry: Research Match (CTSA-supported) *https://www.researchmatch.org/*

The UNM CRCR Registry

Clinical Research Volunteer Registry

Thank you for your interest in volunteering for research studies at the University of New Mexico's Clinical and Translational Science Center. Fill out and submit this form to volunteer for possible participation in any research study, now or in the future.

Filling out this form in no way obligates you to participate in any study. It informs researchers of your interest and provides them necessary information to match your profile with the needs of a particular study. The researchers will then contact you directly by phone or e-mail assessing your interest and suitability for a particular study. Participation in clinical research studies is voluntary, and requires visits to the University of New Mexico's Clinical and Translational Science Center in Albuquerque, New Mexico.

You may **modify or withdraw** your information at any time by following the directions listed on the last page of this document.

A parent or legal guardian may enter information on behalf of a minor (child less than 18 years of age). **However, all contact information** (Guardian's name, address and phone number) **must be completed with the parent or guardian's information.**

The UNM CRVR Registry

Please include participants* contact information below

FirstName:_____Middle_____

Last Name:_____

Date of Birth: Mo:_____Day:_____Yr:_____ Gender :(circle one) Male Female

Participant's Height: Feet:_____Inches:_____Participant's Weight (lbs):_____

(If completing form for a minor)
Parent/Legal Guardian's Name (first/last):_____

Street Address *:_____

City:*_____ State:*_____ Zip:*_____

Preferred Phone Number:*_____

Alternate Phone:_____Email_____

Many trials enroll healthy volunteers as 'control' subjects. Are you in good general health, with no chronic medical conditions? *

- ☐ Yes - I am in good health (without chronic medical conditions)
- ☐ No - I currently have a medical condition

Social Media

- Approximately 74% of internet users are active on social media. Of that group, nearly 80% use social platforms to seek out health-related information.
- Social Media may be transformative for Rare Disease trials.
- When campaigns are set up correctly, the outcome is typically fewer patient leads overall, but those that do come through tend to do so quickly, and to be of a much higher quality.

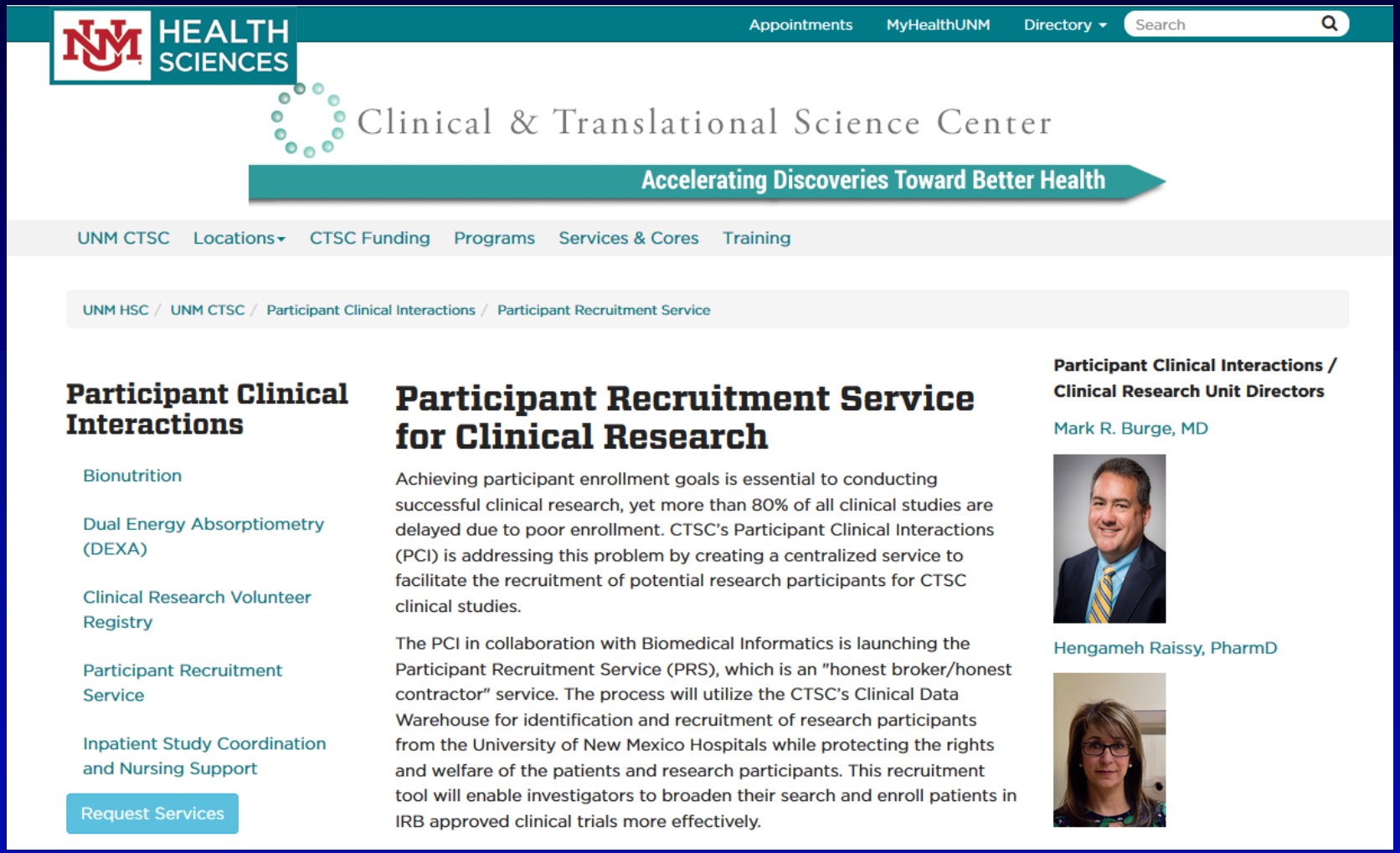
- Guidelines for Research Using Social Media
    - Social media communications include ads, online- diaries or surveys, text messages, and other info
    - All must be approved by the UNM HSC IRB)
    - Avoid use social media to collect PHI
    - Measures should be taken to ensure privacy

https://healthitanalytics.com/news/can-social-media-aid-clinical-trial-recruitment-disease-research

Recruiting Members of Under-Represented Groups is a Challenge

- Principles of Community Engagement are often necessary, and the process can be time consuming.
  - Build long-term relationships
  - Do "*with*," Not "*for*" or "*to*"
  - Be responsive to different priorities & perspectives
  - Emphasize mutual benefit and respect
  - Share findings with the groups that help
  - Be collaborative from start to finish

Innovative Recruiting Methods: The CTSC Participant Recruitment Service

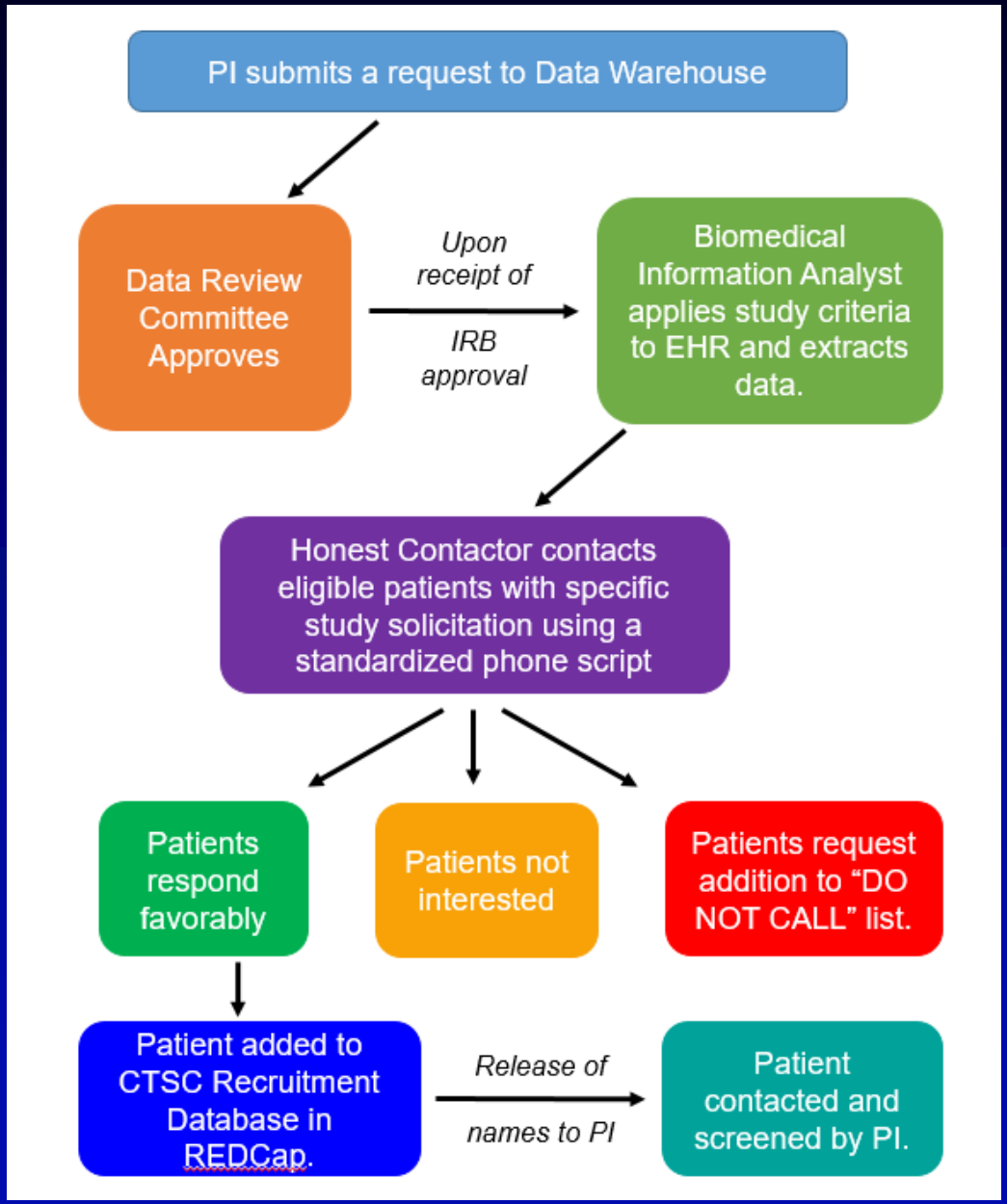


https://hsc.unm.edu/research/ctsc/participant-clinical-interactions/participant-recruitment-service/index.html

The Participant Recruitment Service

- The PRS uses the CTSC's Clinical Data Warehouse for identification and recruitment of potential research participants from UNM Hospitals while protecting the rights and welfare of the patients and research participants.
- This tool enables investigators to broaden their search and enroll patients in IRB approved clinical trials more effectively.
- The PRS assumes a large part of the recruitment burden and ensures a higher success rate for subsequent contacts by your study coordinator.
- The PRS assists investigators by identifying, contacting, and gauging determining the interest of potential volunteers for your research study.
- There's a fee! $300 for 250 contacts.

How the PRS Works



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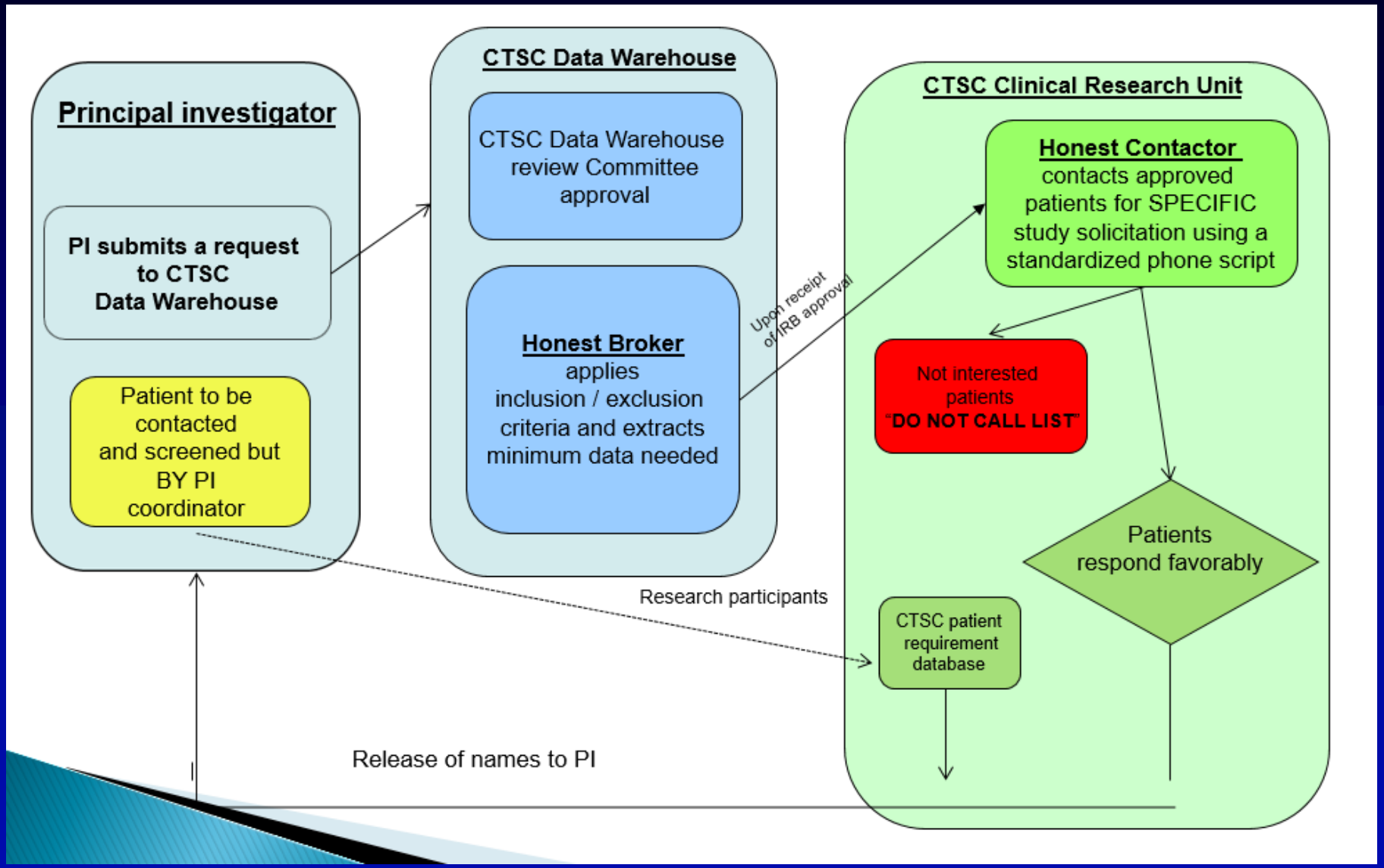

Does the PRS Work?

Grant Year (Calendar Year)	6 (2015)	7 (2016)	8 (2017)
# Protocols Using PRS	2	5	4
# Calls Made	1663	1542	7887
# Contacts Made (% of those called)	539 (32%)	374 (24%)	834 (11%)
# Patients Assenting (% of contacted)	398 (74%)	235 (63%)	672 (81%)
# Enrolled (% of Assenting)	31 (8%)	7 (3%)	41 (6%)
# “Do Not Call” Requests (Cumulative)	73	91	170

We Are Proud of the PRS!

The University of New Mexico

Implementing an Innovative Patient Recruitment Service that Employs an Honest Contactor to Make "Cold-Calls" in a Compliant Manner for the Purposes of Clinical Research Recruitment

Mark R. Burge, MD, Hengameh Hedarian-Raissy, PharmD
University of New Mexico HSC Clinical and Translational Science Center, Albuquerque, NM

The University of New Mexico

Abstract:

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Mark R. Burge, MD, Hengameh Hedarian-Raissy, PharmD
University of New Mexico HSC Clinical and Translational Science Center
Category: Recruitment and Retention

Participant Recruitment for clinical research remains a major challenge that is complicated by HIPAA rules and the need for protection of privacy. To address this challenge, we have devised an innovative method that allows representatives of the UNM Clinical and Translational Science Center (CTSC) to call prospective participants to gauge their interest of participating in a clinical study. Contact information is subsequently forwarded to specific study personnel for potential participants who answer in the affirmative. Development of this methodology required the efforts of the following professionals to institute protections against coercion and misrepresentation before gaining institutional approval: the Director of Clinical Trials, the HIPAA Privacy Officer for UNM Hospital, the CTSC Bioinformatics Director, the University Hospital Chief Medical Information Officer, and the Executive Chair of the UNM Human Research Protections Office (HRPO). It is also important to note that the privacy statement signed by all UNM patients states that "protected health information (PHI) may be used for research proposes." The currently operative UNM CTSC Patient Recruitment Service incorporates the following elements:

1. Data search requests are made by the Principal Investigator using an online request form that provides information regarding study inclusion and exclusion criteria and for the data to be extracted from UNM Hospital electronic medical record (EMR). The resulting aggregated data may be useful for feasibility testing, but PHI are not released to the investigator.

2. Studies are submitted to HRPO for approval as per usual. The application includes a check-box for using the "Honest Contactor" service as a method of participant recruitment.

3. Once HRPO approval is received, a list of potential patients derived from the EMR is released to the UNM CTSC Research Participant Advocate (RPA), who is specifically trained on issues relevant to HIPAA, participant rights with respect to research, and cultural sensitivity. A standardized, predetermined script specific to each study is developed and reviewed by the patient literacy division at UNM Hospital to assure that appropriate language and information is provided to patients. The intent of the initial contact is to provide only general information about the study and to obtain permission from the patient to be contacted by a study coordinator, who will provide more detailed information. Interested patients are asked to provide the best times to contact them over the next three days.

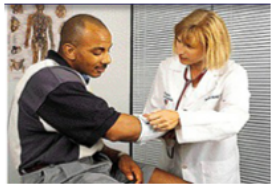
4. If a patient decides to opt out from the contact list, his or her name is added to our standing "do not call" list. This list is maintained by the RPA, allowing the CTSC to serve as the gatekeeper for this activity as the party responsible for maintaining the "do not call" list.

5. The list of patients is stored in a secure, password protected database with access limited only to trained staff and the Medical Director of CTSC Clinical Research Unit (CRU).

6. Names and contact information for interested patients are released to the PI or the study coordinator for a period of three days. The PI and/or coordinators are not allowed to save the list for future trials.

7. The UNM CTSC CRU charges for this service in minimum increments of ten hours of work.

In conclusion, the UNM CTSC has demonstrated that it is possible to query the EMR for the purposes of clinical research recruitment in a manner that is respectful of patient privacy rights and fully compliant with applicable laws. The UNM CTSC plays a critical role in assuring the safety and security of this system and in meeting the needs of investigators.



Background

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Participant Retention is a Challenge

- A *CenterWatch* report stated that dropout rates of 15%-40% are not uncommon; the average is about 25%
- Common Reasons for Drop Out:
  - Difficulty complying with the protocol:
    dosages, timelines, and/or procedures
  - Adverse Events, SAEs
  - Loss of motivation
  - Peer pressure
  - Financial constraints
  - Disease improvement or lack of improvement

Retention Strategies

- Maintain communication
- Listen
- Be convenient
- Send reminder emails, letters, calls, text messages
- Maintain a positive attitude
- “Treat ‘em like royalty”
- Know the protocol
- Optimize stipends
- Provide transportation options

Conclusions & Recruitment Pearls

- Recruitment is always harder than you first thought!
- Plan to spend lots of time on the phone.
- Call when patients are likely to pick-up: after hours, weekends.
- Use your “happy phone voice.”
- Be ready with a simple capsule explanation of the importance of the research.
- Offer flexible visit hours whenever possible.
- Provide the consent form in advance of the screening visit, if possible.
- Pre-screen inclusion and exclusion criteria on the phone.

Thank You!