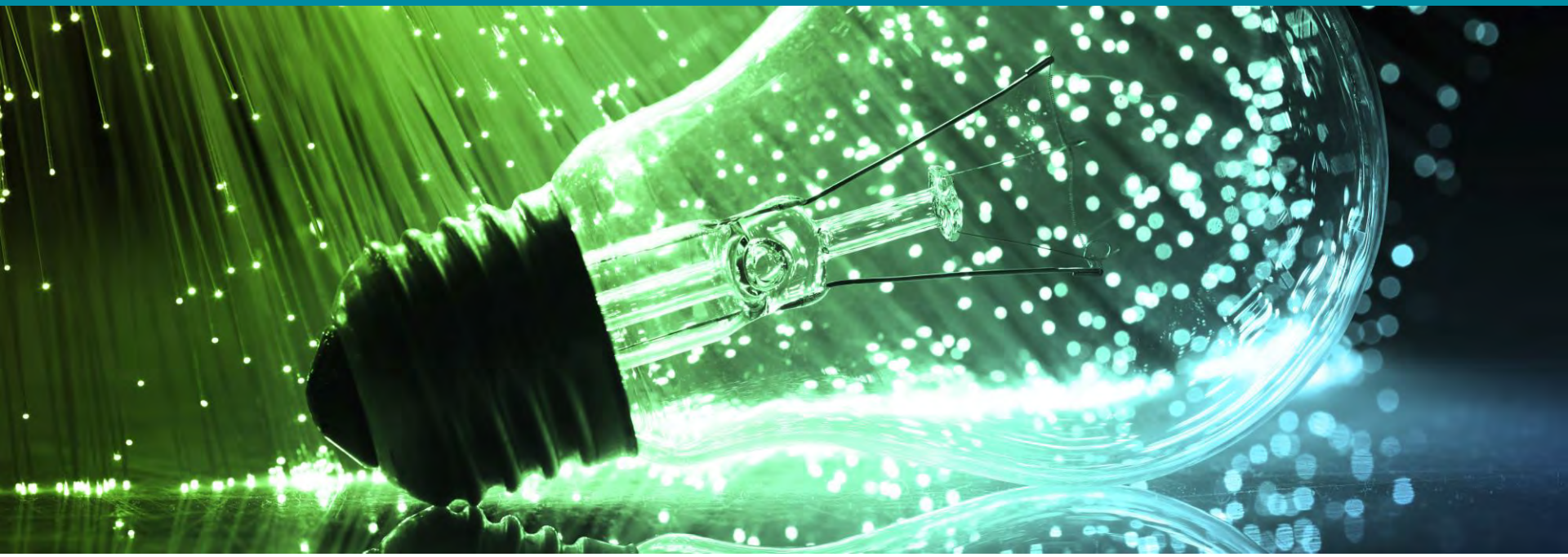
CTTI Recruitment Project Expert Meeting Welcome and Overview

Jamie Roberts, MA, MPH, Senior Clinical Project Manager
Pamela Tenaerts, MD, MBA, Executive Director

November 9, 2015

CLINICAL
TRIALS
TRANSFORMATION
INITIATIVE



Disclaimer

The views and opinions expressed in this presentation are those of the individual presenter and do not necessarily reflect the views of the Clinical Trials Transformation Initiative.

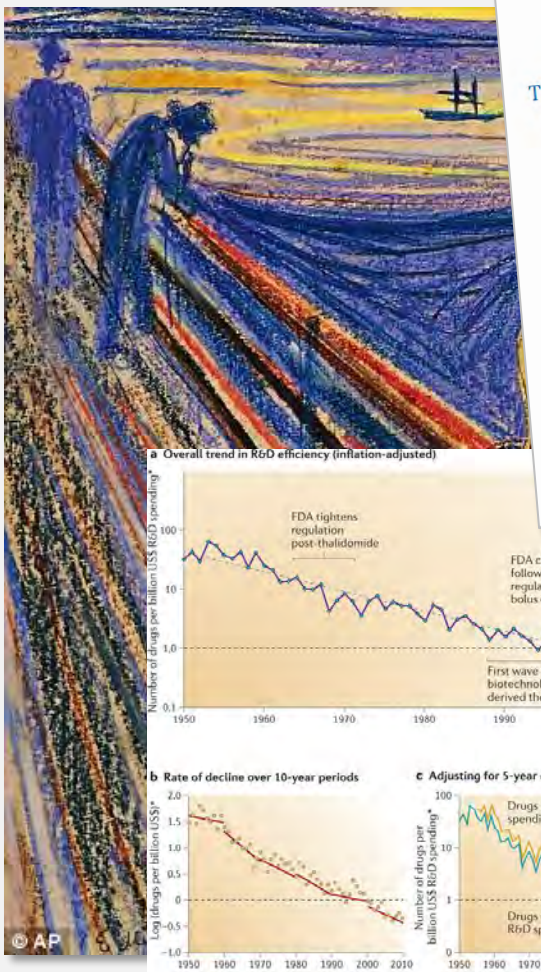
The presenter is an Employee of Duke University. Salary support comes from pooled membership fees of the Clinical Trials Transformation Initiative and from FDA Cooperative agreement.

CTTI

Meeting Goals & Objectives

- Present findings from our evidence gathering
- Obtain your perspectives and critical feedback
- Develop consensus on mechanisms for moving strategic recruitment planning upstream
- Identify implementation challenges and brainstorm solutions

Why CTTI?
Crisis in Clinical Trials



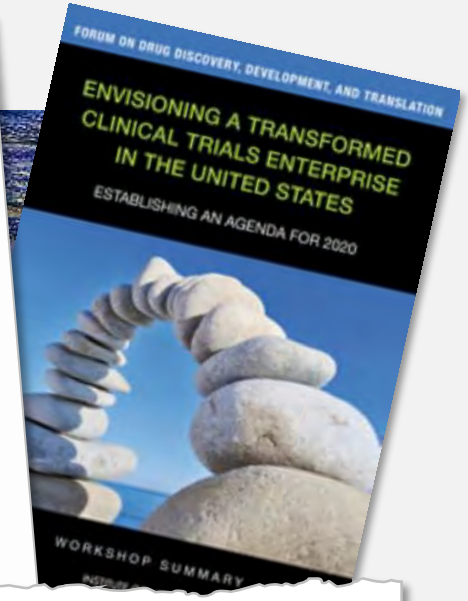
REPORT TO THE PRESIDENT

TRANSFORMATION AND OPPORTUNITY: THE FUTURE OF THE U.S. RESEARCH ENTERPRISE

Executive Office of the President

President's Council of Advisors on Science and Technology

NOVEMBER 2012



Ann Intern Med. 2013 Jun 18;158(12):914-5. doi: 10.7326/0003-4819-158-12-201306180-00011.

The changing structure of industry-sponsored clinical research: pioneering data sharing and transparency.

Kunt

BROOKINGS

RESEARCH | EVENTS | EXPERTS | ABOUT

MAR 5

PAST EVENT

Biomedical Innovation: Identifying Challenges and Prioritizing Needs

Addressing This Need

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

To identify and promote practices that will *increase the quality and efficiency* of clinical trials

Public-Private Partnership
co-founded by FDA and Duke
involving all stakeholders
60+ members

CTTI

Collaboration Towards Solutions

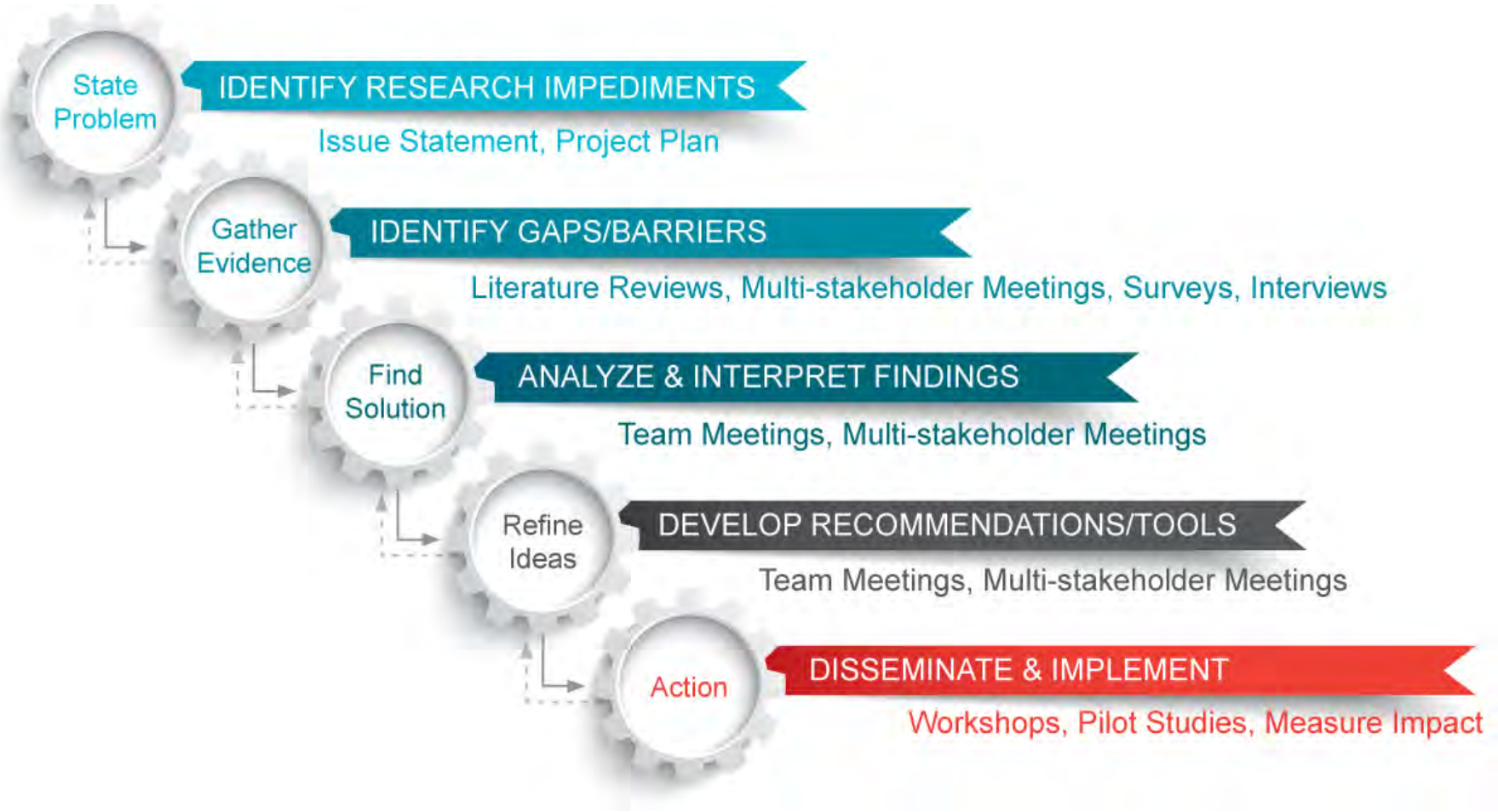
CTTI


ACI CLINICAL
ALEXION
AMGEN
AstraZeneca
BARD
Celgene
cempra
EMD Serono
Genentech
A Member of the Roche Group
gsk
GlaxoSmithKline
Johnson & Johnson
Lilly
MERCK
Pfizer
PURDUE
ST. JUDE MEDICAL
Target Health Inc
Medtronic
THE MEDICINES COMPANY
AHRQ
CDC
CMS
FDA
NIH
OHRP
Department of Veterans Affairs
ACRO
ACRP
AdvaMed
Bio
BRANY
CDISC
CHESAPEAKE IRB
cirb
CITI PROGRAM
DIA
Greenleaf Health LLC
KING & SPALDING
MedStar Health Research Institute
MK&A
PALO ALTO INVESTORS
PMG Research
Quorum REVIEW IRB
SCT
SCRS
wcg
Alliance for Lupus Research
FOUNDATION FOR PRADER-WILLI RESEARCH
FRIENDS of CANCER RESEARCH
JDRF
The Life Raft Group
Melanoma Research Alliance
MPN RESEARCH FOUNDATION
NORD
Parent Project Muscular Dystrophy
Parkinson's Disease Foundation
Pulmonary Fibrosis Foundation
susan g. komen.
C5Research
DANA-FARBER CANCER INSTITUTE
DukeMedicine
The Feinstein Institute for Medical Research
THE GEORGE INSTITUTE for Global Health
KU MEDICAL CENTER
The University of Kansas
JULIUS CLINICAL
PHRI
Health Through Knowledge
School of Medicine
University of Missouri Health System
UNC
THE NORTH CAROLINA TRANSLATIONAL & CLINICAL SCIENCES INSTITUTE
UNIVERSITY OF OXFORD
UNIVERSITY of ROCHESTER MEDICAL CENTER
THE UNIVERSITY OF SYDNEY
NYU Langone MEDICAL CENTER
UW Health

How CTTI Works

- Engage & value all stakeholders equally
- Understand incentives to maintain non-value added activities and have solutions that are mindful of those incentives
- **Plant the seeds for change throughout all phases of a project**
- **Develop actionable, evidence-based, consensus driven recommendations**
- Create and share knowledge, tools & resources to facilitate change that improves clinical trials

CTTI Methodology



Portfolio of CTTI Projects

	Investigational Plan	Study Start-up	Study Conduct	Analysis & Dissemination	Specialty Areas
Closed Projects	• Large simple trials • Uses of electronic data	• Central IRB • Site metrics • Central IRB advancement • GCP training	• Adverse event reporting • IND safety • Monitoring		• Long-term opioid data
Ongoing Projects	• Mobile clinical trials (program) • ***Patient groups & clinical trials**** • Pregnancy testing • ***QbD**** • Trials based on registries • Uses of electronic data application	• Informed consent • Investigator turnover • **Recruitment**	• IND safety advancement • Safety case studies	• State of clinical trials • DMCs	• Pediatric antibiotic trials • *Streamlining HABP/VABP trials* • Unmet need in antibiotic development • ABDD pilot

Recently approved **recommendations released*

CTTI

Recruitment Project Team

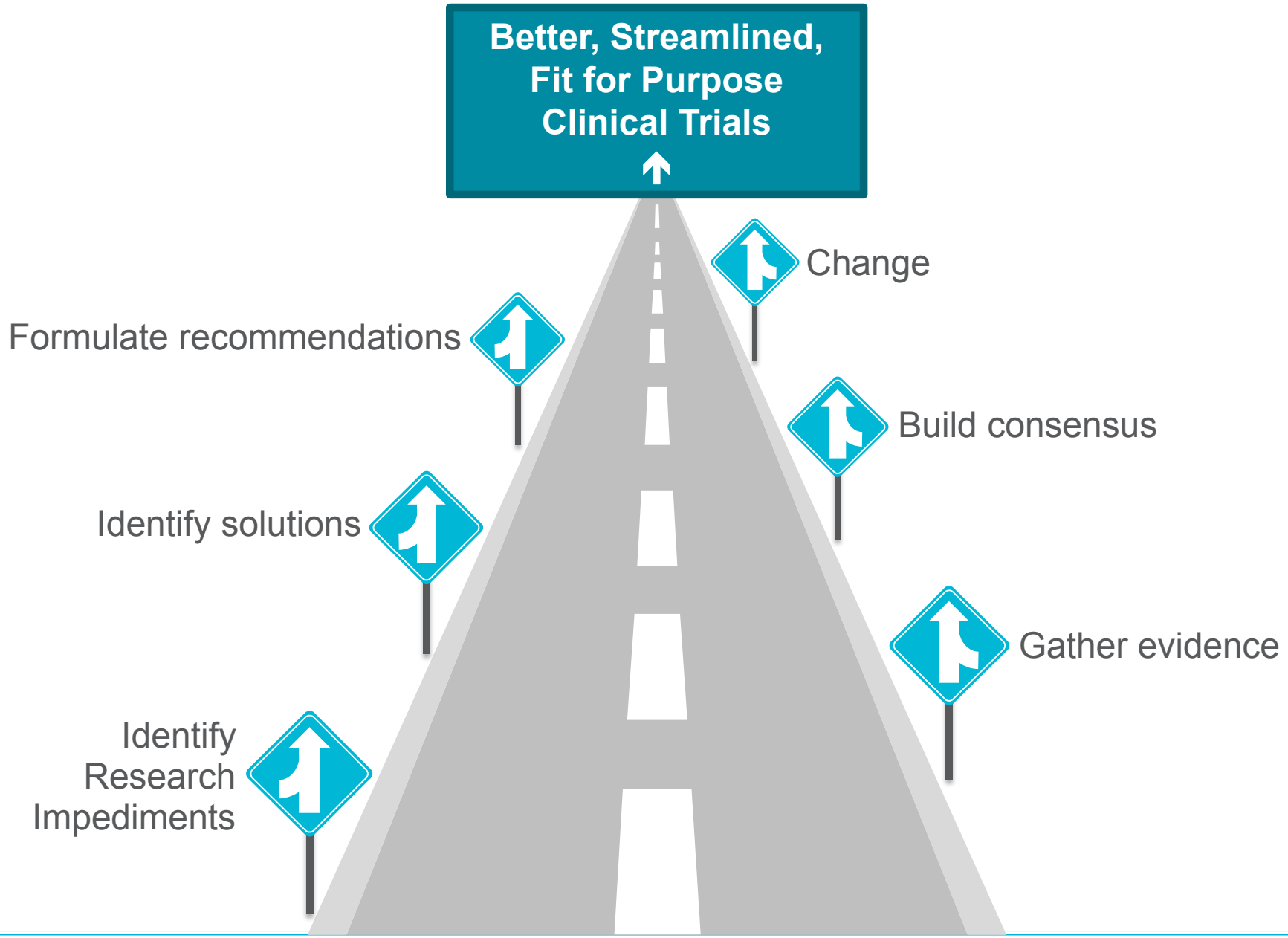
Team Leads

- Jonca Bull, MD (FDA)
- Beth Mahon, JD (Janssen)
- Pat Furlong, BSN (PPMD)

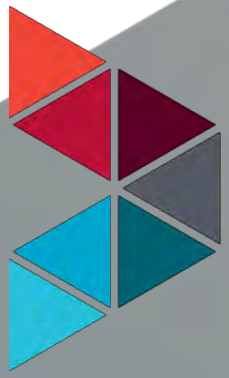
- **CTTI Support Staff**
  - Matthew Harker
  - Kelly Kilibarda
  - Jamie Roberts
  - Diane Willis
  - Kimberley Smith

Team Members

- David Ciavarella, MD (Bard)
- Beth Harper (CPP, Inc.)
- Grant Huang (VA)
- Adwoa Hughes-Morley (U. Manchester)
- Leslie Kelly (Duke)
- Jim Kremidas (ACRP)
- Barbara LeStage (Pt. Adv., CTTI SC)
- Holly Massett (NCI)
- Kelly McKee (Merck)
- Claire Meunier (MJFF)
- Ashish Oza (St. Jude Medical)
- Anuja Rastogi (FDA)


Better, Streamlined, Fit for Purpose Clinical Trials
Change
Formulate recommendations
Build consensus
Identify solutions
Gather evidence
Identify Research Impediments

Thank you.



CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

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919 695 5626

RESEARCH!AMERICA

AN ALLIANCE FOR DISCOVERIES IN HEALTH®

An Imperative for Action: Patients Are Waiting

Mary Woolley, President, Research!America

November 9, 2015

CTTI – Recruitment Project Expert Meeting
Silver Spring, MD

Overview of Presentation

- Key challenges
- Congressional & media attention
- What the public says about clinical trials: implications
- Recommendations for Action

"Nothing About Us Without Us"*

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**A slogan originating with the South African disability movement in the early 1990's*

Persistent Challenges in clinical trials

- Recruitment and retention difficulties
- Uncoordinated trial conduct—across federal agencies; across universities; globally
- Expensive, redundant data collection
- Researchers, physicians and patients interests' not well aligned
- Physicians rarely talk about research
- Failure to include patients every step of the way—from decision to study to report-out

Very little has changed in decades

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IOM Clinical Research Roundtable

"Doctors' recommendations, awareness in the community and association with people who have participated in research were identified by workshop participants as important factors that promote participant enrollment in clinical research…[in addition], many physicians are unaware of available clinical trials."

Source: Institute of Medicine of the National Academies. (2003). Exploring Challenges, Progress, and New Models for Engaging the Public in the Clinical Research Enterprise: Clinical Research Roundtable Workshop Summary.

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NIH Council of Public Representatives

Clinical trial researchers 'tend to disregard the perspective of the community and the public at large.'

(The NIH Director's Council of Public Representatives in 2005) recommended '*change in the culture of the scientific community* to ensure that medical research is viewed in the context of a long-term commitment to the community, not a one-time research study.'

- Robinson, D., & Williams, G. (2009). *Clinical and Translational Science: Principles of Human Research*. Updated chapter by Mary Woolley, submitted for publication

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My View

INTRODUCTION

This chapter examines the public and political contexts in which clinical research takes place, and the role the science community plays in shaping public and policymaker discourse and decision-making. Gaining an understanding of the links between science and the body politic, including the increasing demands for transparency and accountability, is fundamental to the long term success of science.

- Mary Woolley, "*Clinical Research in the Public Eye*"

Robinson, D., & Williams, G. (2009). *Clinical and Translational Science: Principles of Human Research*. Chapter 29

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Congressional Initiatives on Medical Progress: *Patients First*

- **House:**
  - Passed 21st Century Cures Act (HR 6) in July with bipartisan 344-77 vote
  - HR 6 includes five year Innovation Fund with $8.75B for NIH and $550M for FDA as "mandatory" funding
  - Culmination of year-long Energy & Commerce Committee effort to gather stakeholder input
- **Senate:**
  - HELP Committee is gathering stakeholder input and drafting legislation to be released soon; mandatory funding reportedly included
  - Planning mark up of legislation before end of 2015
- **End Goal:**
  - Both chambers reach a conference agreement that is signed into law ASAP

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Clinical trials a major focus of 21st Century Cures Act (HR 6)

- Extends NCATS authority for clinical trials through end of Phase IIB trials (instead of Phase IIA)
  - And extends rare disease exemption through the end of Phase III (instead of Phase IIB)
- Includes "Sense of Congress" statement supporting increased representation of underrepresented communities in clinical trials
- Requires creation of workshop on broadening age groupings in research
- Establishes a pediatric research network
- Streamlines IRB approval for multisite research
- Promotes the design of more targeted clinical trials
- Establishes clinical trial data system to foster collaboration and access to data generated in research and clinical settings

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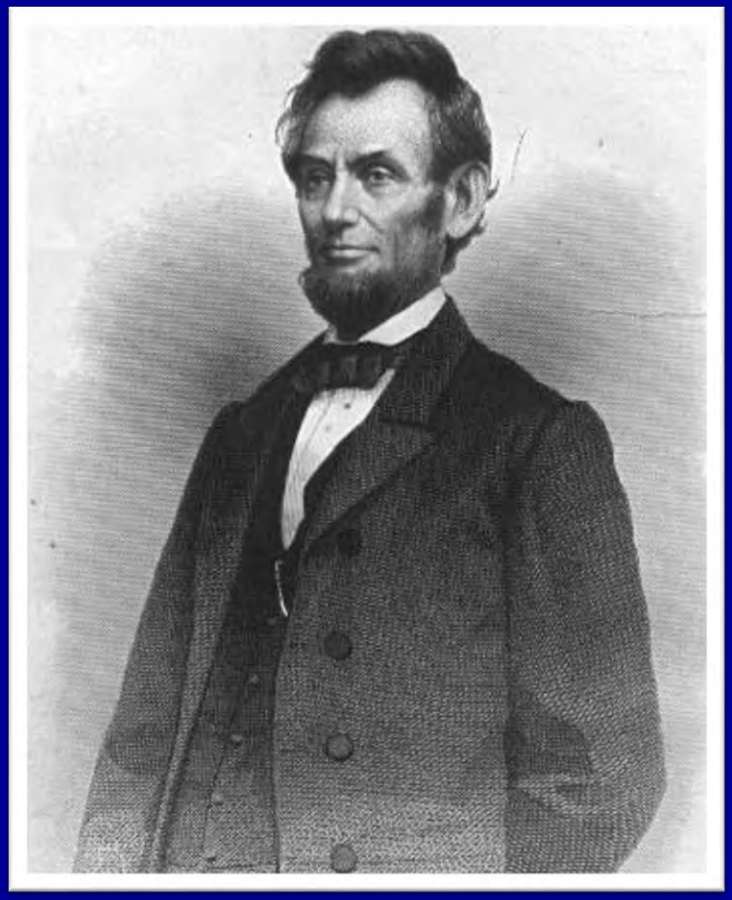
The Public is Paying Attention



"…public sentiment is everything. With public sentiment, nothing can fail; without it nothing can succeed."

President Abraham Lincoln

Media is Paying Attention

THE NEW YORKER

MEDICAL DISPATCH | JULY 21, 2014 ISSUE

ONE OF A KIND

What do you do if your child has a condition that is new to science?

BY SETH MNOOKIN

"Researchers … hesitate to share data with potential competitors, both to protect their funding and to insure that they get credit for their work … 'the current academic publication system does patients an enormous disservice.'"

—*The New Yorker*, July 21, 2014

"It isn't uncommon for studies to contradict each other, and there's no way for clinicians to know which one is right …"

—The *Washington Post*, April 15, 2014

The Washington Post

Health & Science

Scientists embark on unprecedented effort to connect millions of patient medical records

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COMMEMORATING 25 YEARS

Clinical Trial Recruitment in the News

HOME SEARCH

The New York Times

EDITORIAL
The Push for Legal Marijuana Spreads

DAVID BROOKS
Great News! We're Not Doomed to Soaring Health Care Costs

PAUL KRUGMAN
Austerity's Grim Legacy

Clinical Trials Need Cancer Patients

By STAN COLLENDER JUNE 19, 2015

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I HAVE a very rare and aggressive type of skin cancer — Merkel cell carcinoma — for which there is no approved cure, and I'm participating in a clinical trial to deal with it. If successful, the trial will show that the drug I'm being given at least manages what is now an often fatal disease.

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Health | Thu Oct 15, 2015 4:05pm EDT Relate

More evidence poor cancer patients don't join clinical trials

BY LISA RAPAPORT

Low-income cancer patients are much less likely to participate in clinical trials than their more affluent peers, a U.S. study confirms.

Even after accounting for gender, age, race, travel distance from treatment sites and

PHOTOS OF THE DAY

THE WALL STREET JOURNAL.

Home World U.S. Politics Economy Business Tech Markets Opinion Arts Life

Agricultural Giants Look to Join Forces

Disney Profit Rises

Activist Investor Bill Ackman Plays Defense

U ARE READING A PREVIEW OF A PAID ARTICLE. SUBSCRIBE NOW TO GET MORE GREAT CONTENT.

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For a Rare Disease, Drug Trials Scramble for Patients

Companies vie for enrollees amid questions that trials will siphon participants away from each other

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Polls: a Pulse on Public Opinion

- Research!America has commissioned public opinion polls on research issues for 22 years:
  - National Polls
  - State-Based Polls
  - Issue-Specific Polls
- Telephone (random-digit dialing) polls are conducted with a sample size of 800-1000 adults (age 18+) and a maximum theoretical sampling error of +/- 3.5%. Data are demographically representative of adult U.S. residents (state or national)
- Online polls are conducted with a sample size of 1000-2000 adults and sampling error of +/-3.1%. The data are weighted in two stages to ensure accurate representation of the U.S. adult population

Research!America Clinical Trial Poll

For most topics covered, no significant differences observed between general population and over-sampled populations

However,

- Altruism is more likely to be a motivating factor in trial participation among minority groups than in general population
- Minority groups are more likely to admire people who volunteer for clinical trials
- Lack of trust remains an issue among minority groups, slightly greater than the general population
- Minority populations, especially African-Americans, are more likely to say people are enrolled in clinical trials without being told

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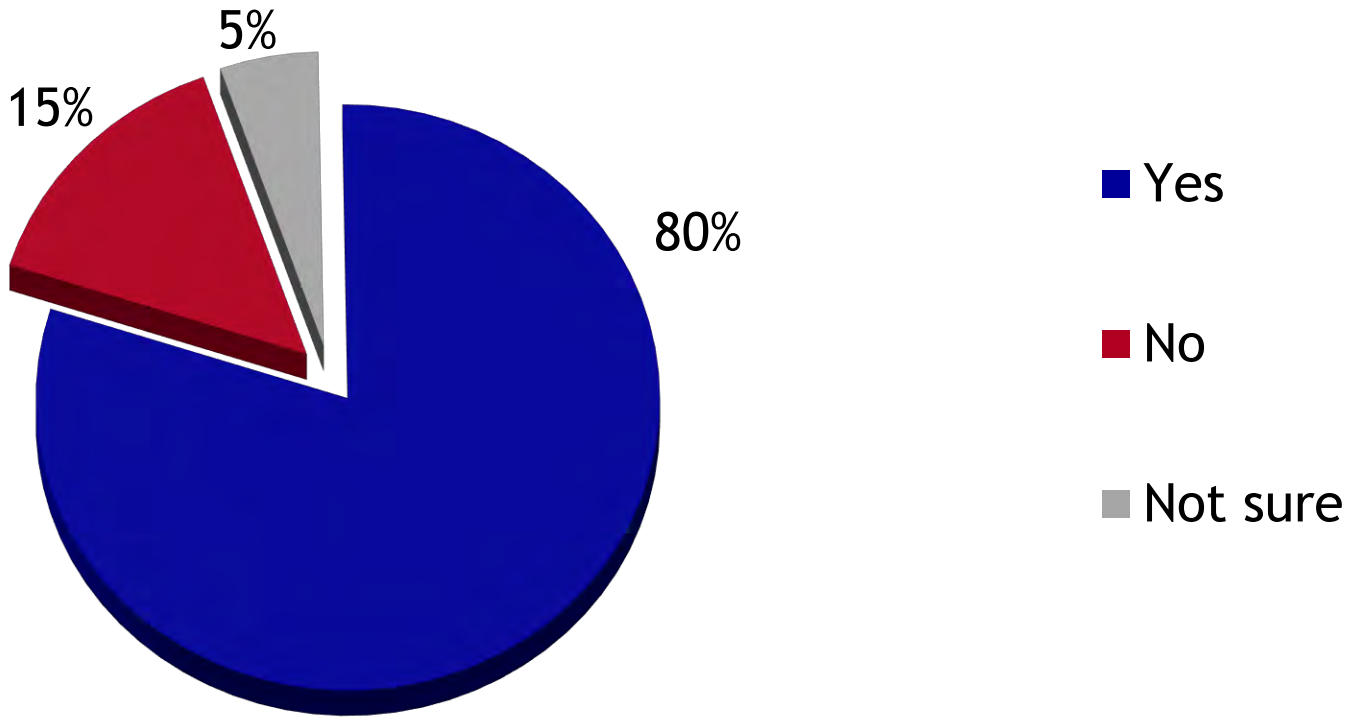
Wide Majority of Americans Have Heard of Clinical Trials

One kind of medical research is often referred to as a clinical trial. In this, volunteers choose to participate to test the safety and effectiveness of certain treatments, drugs or devices. Have you ever heard of a clinical trial?



Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

Have you or anyone in your family ever participated in clinical trials?

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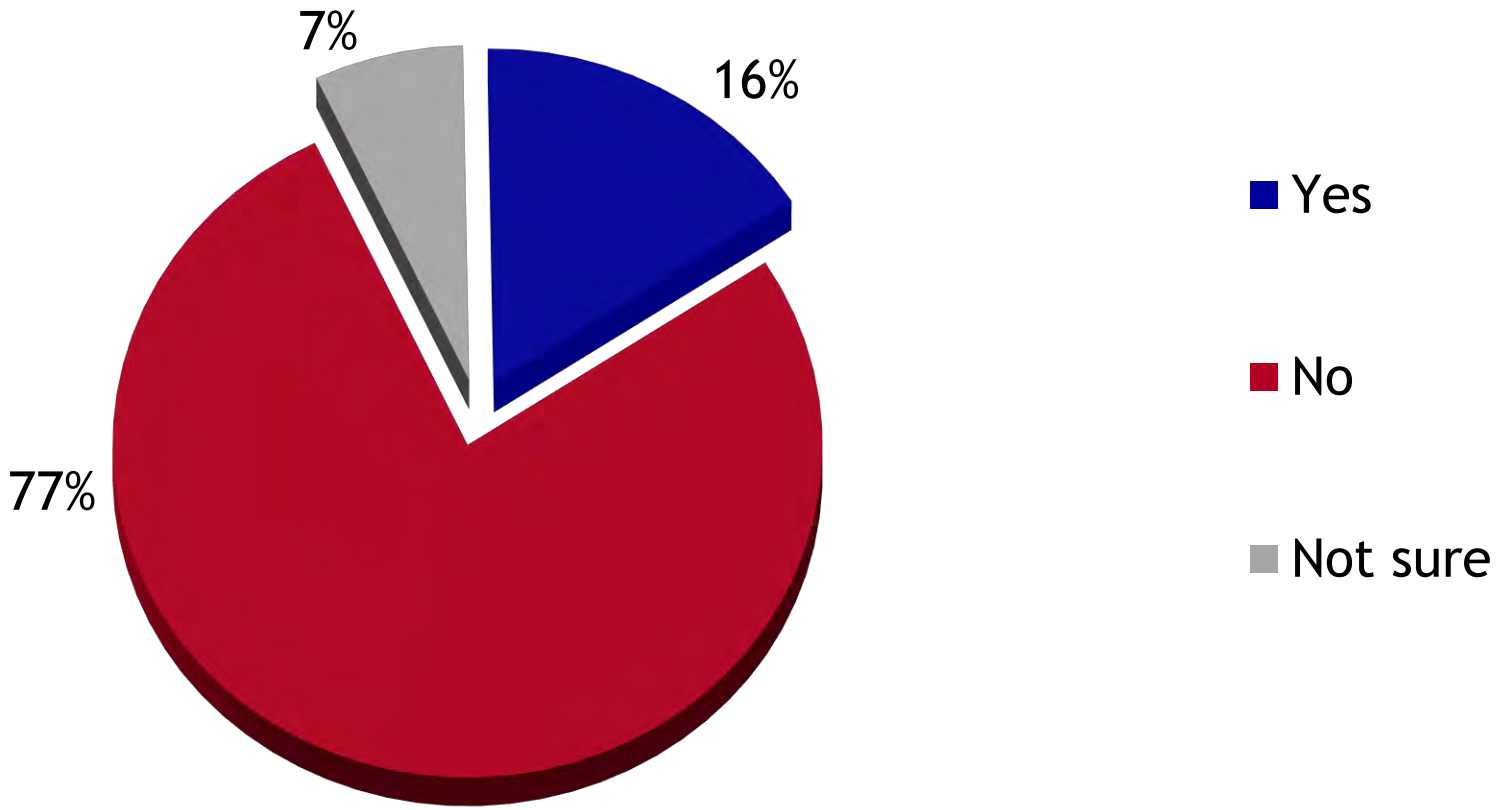
Wide Majority of Americans Have Not Participated in Trials

Have you or anyone in your family ever participated in clinical trials?



Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

Most Americans Have Not Participated in Clinical Trials

Have you or anyone in your family ever participated in clinical trials?

Zogby Analytics

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

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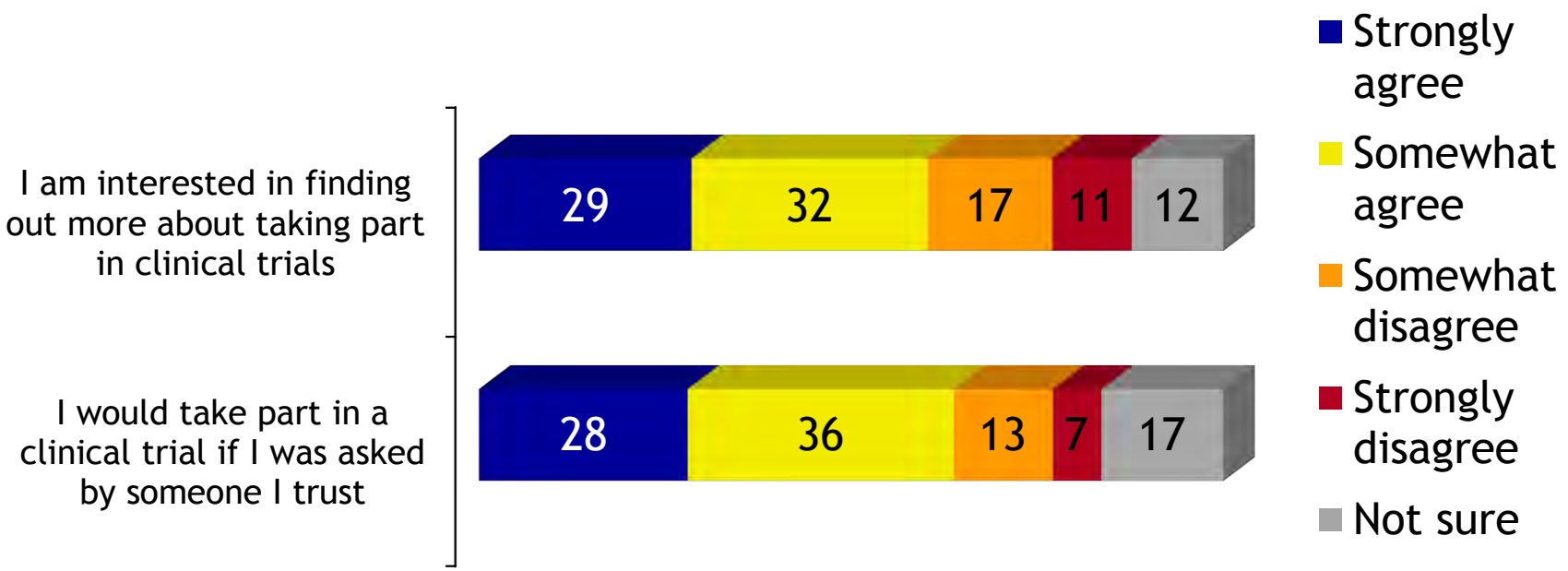
Americans are Interested in Clinical Trials

Do you agree or disagree with each of following statements?



Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

Awareness, Trust, Risk are Barriers to Better Participation

Fewer than 10% of Americans participate in clinical trials. Which of the following do you think is a reason that individuals don't participate in clinical trials? (multiple responses allowed)

Not aware/lack of information	53%
Lack of trust	53%
Too risky	51%
Adverse health outcomes	44%
Little or no monetary compensation	35%
Privacy issues	27%
Too much time	27%
Not sure	11%

Zogby Analytics

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

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Americans Willing to Share Personal Health Data for Research and Patient Care

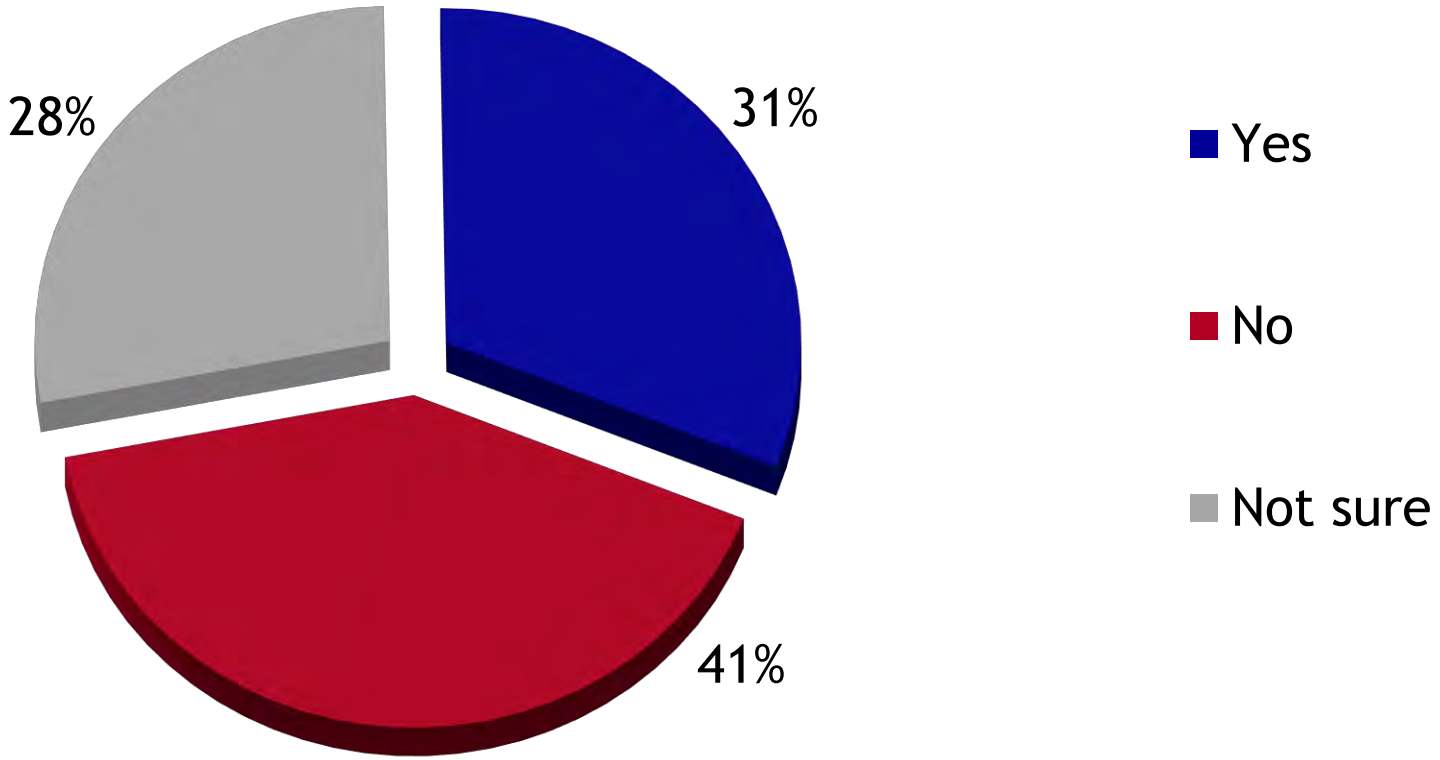
For which of the following would you be willing to share your personal health information (Choose all that apply)?

So health care providers can improve patient care	60%
To advance medical research	55%
So public health officials can better track disease and disability and the causes	46%
None	10%
Not Sure	13%

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in January 2015.

Opinions Split on Whether Patients are Enrolled Without Their Consent

Would you say that without being told, patients are sometimes included in clinical trials when they are receiving medical treatment?



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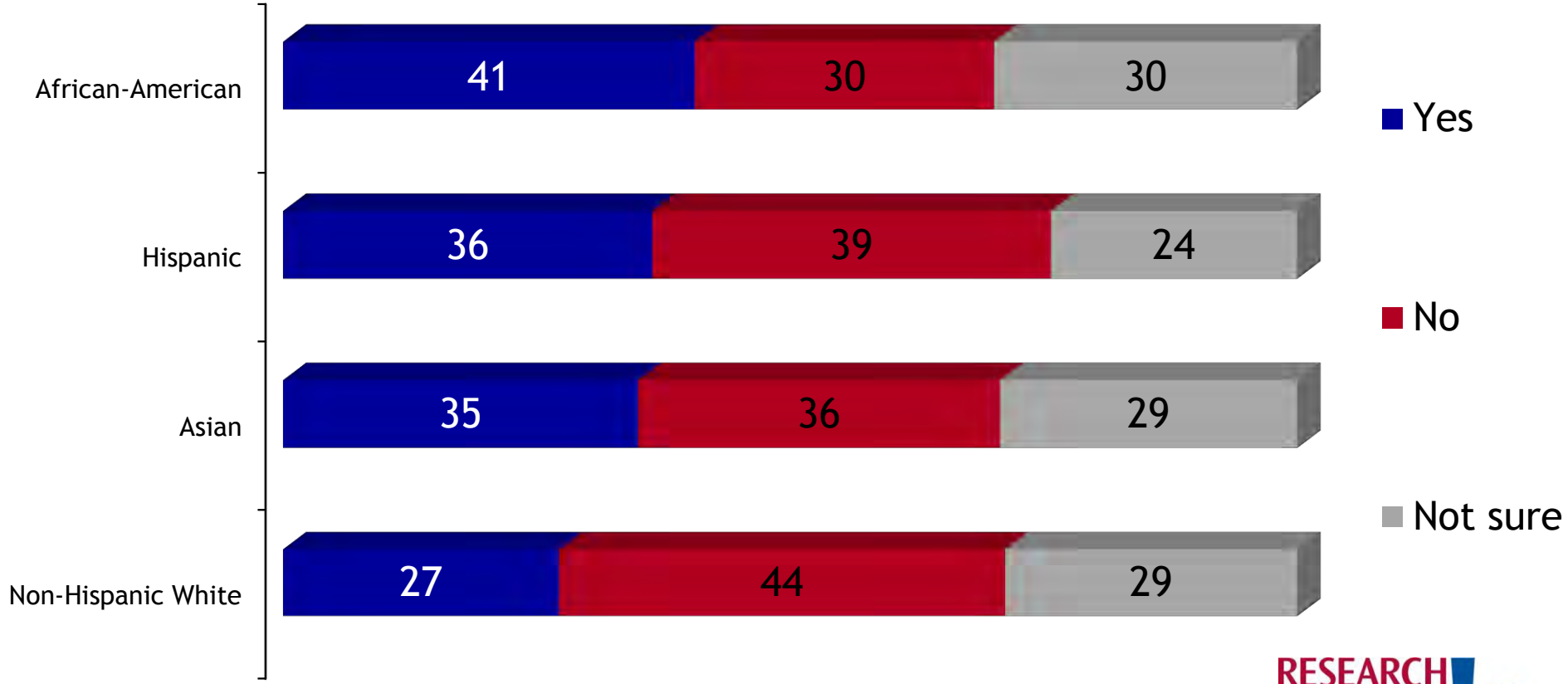
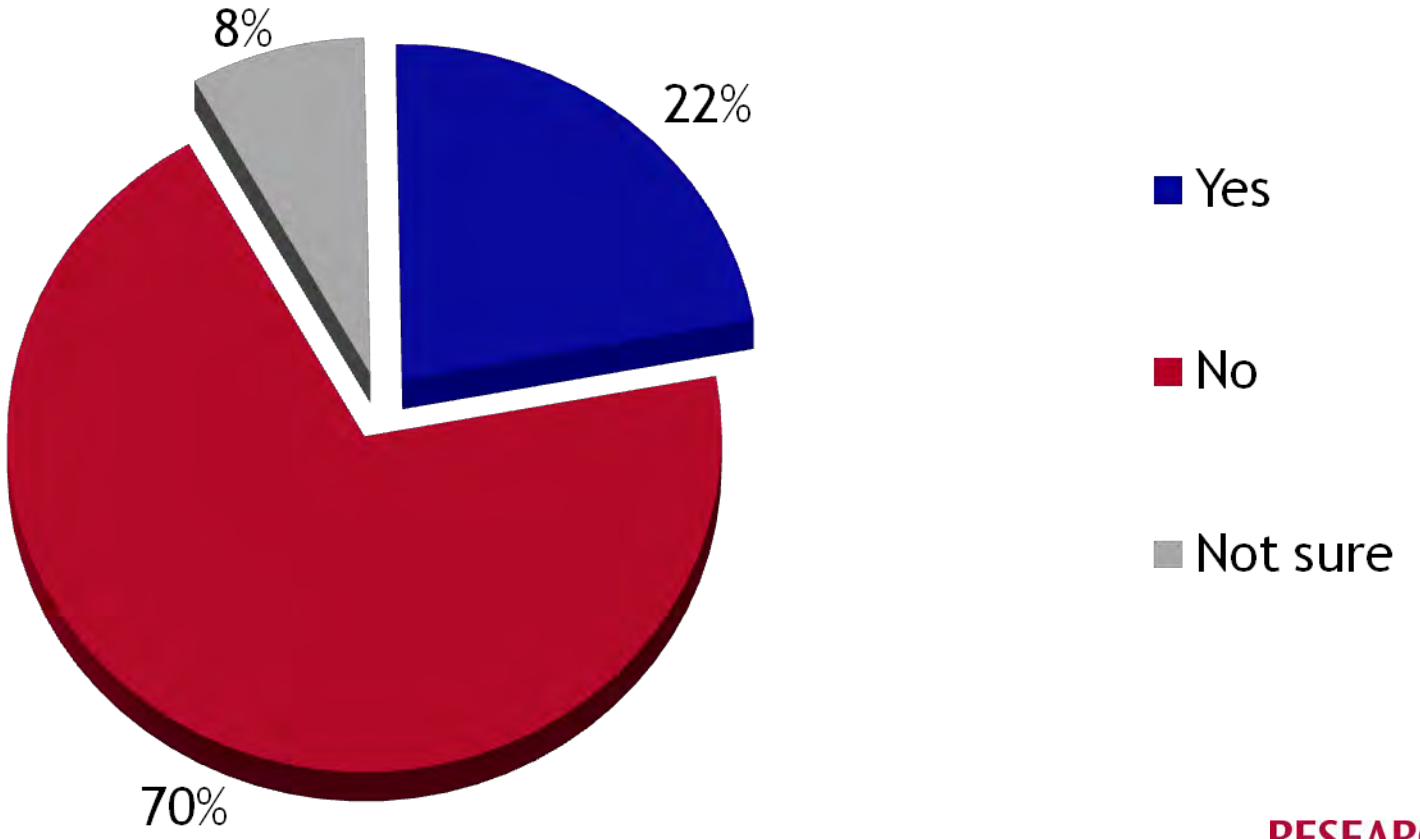


Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

Seven in 10 Say Doctors Don't Talk About Medical Research

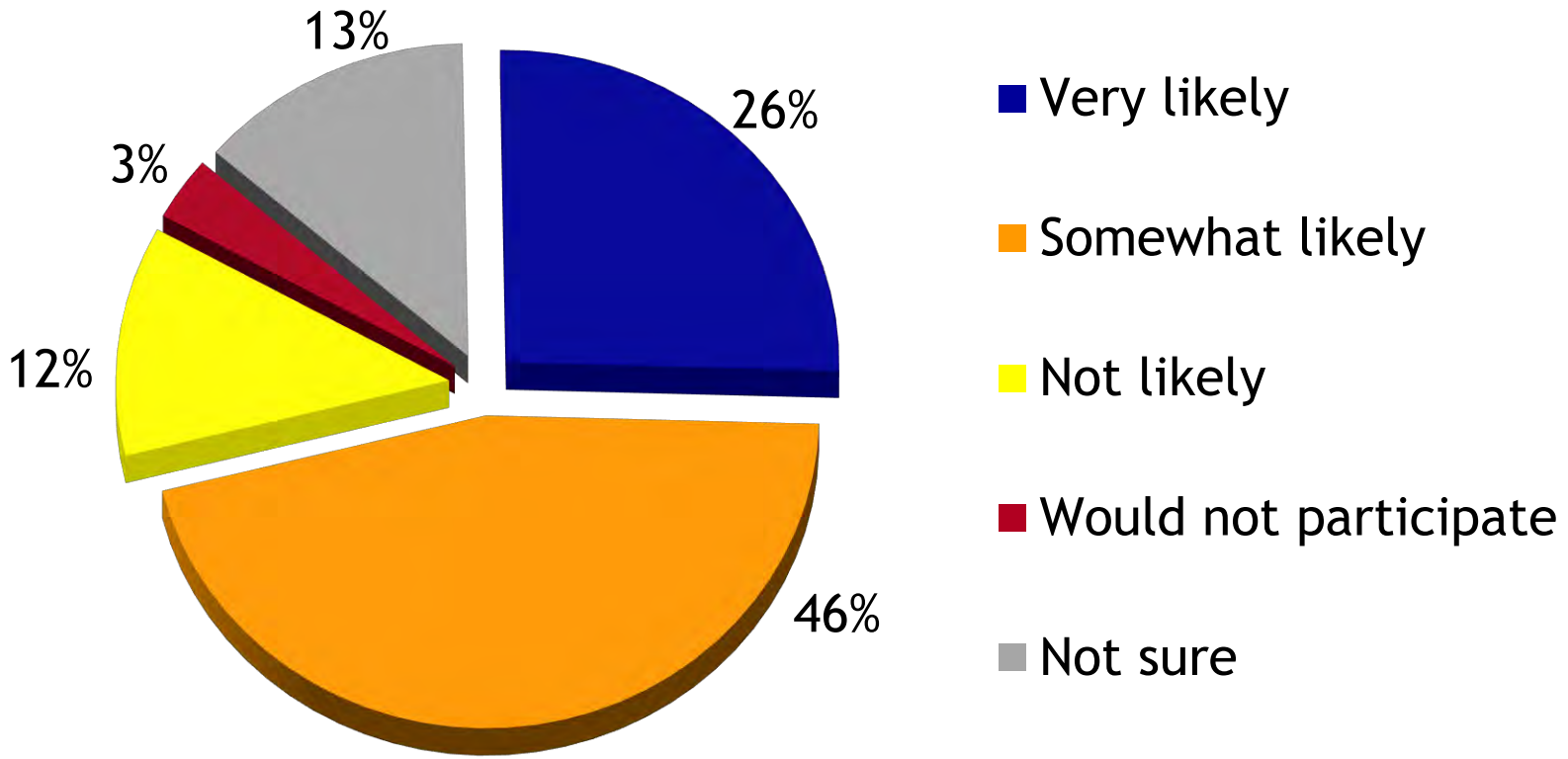
Has your doctor or other health care professional ever talked to you about medical research?



Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

Physician Recommendations Matter to Potential Participants

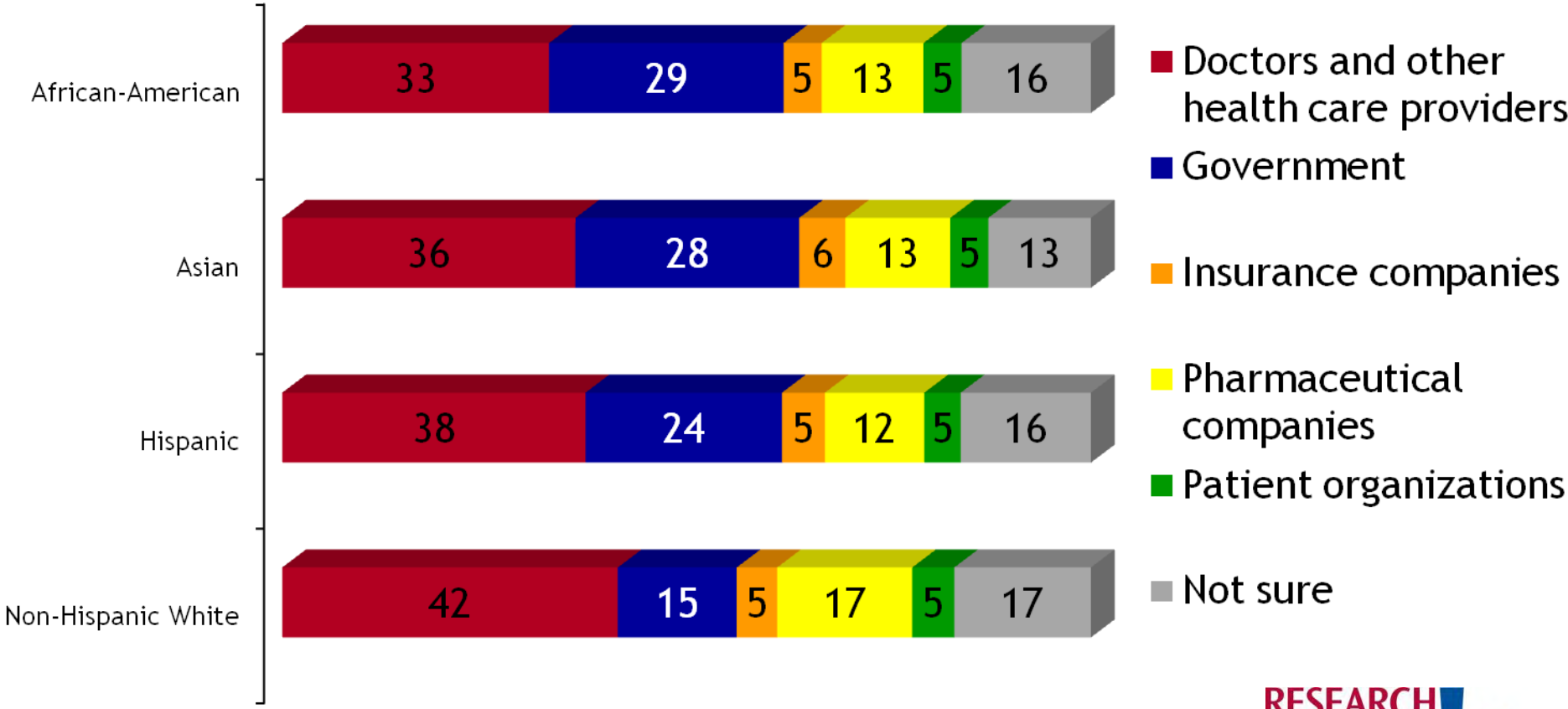
If your doctor found a clinical trial for you and recommended you join, how likely would you be to participate in a clinical trial?



Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

Doctors Should Educate the Public on Clinical Trials, Americans Say

Which organizations listed below would you say has the greatest responsibility in educating the public about clinical trials?



Zogby Analytics

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

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Why are Physicians not talking more about research?

- Don’t have time
- Aren’t aware of trials
- Aren’t being asked
- Don’t know how
- Fear of losing the patients
- Lack of incentives

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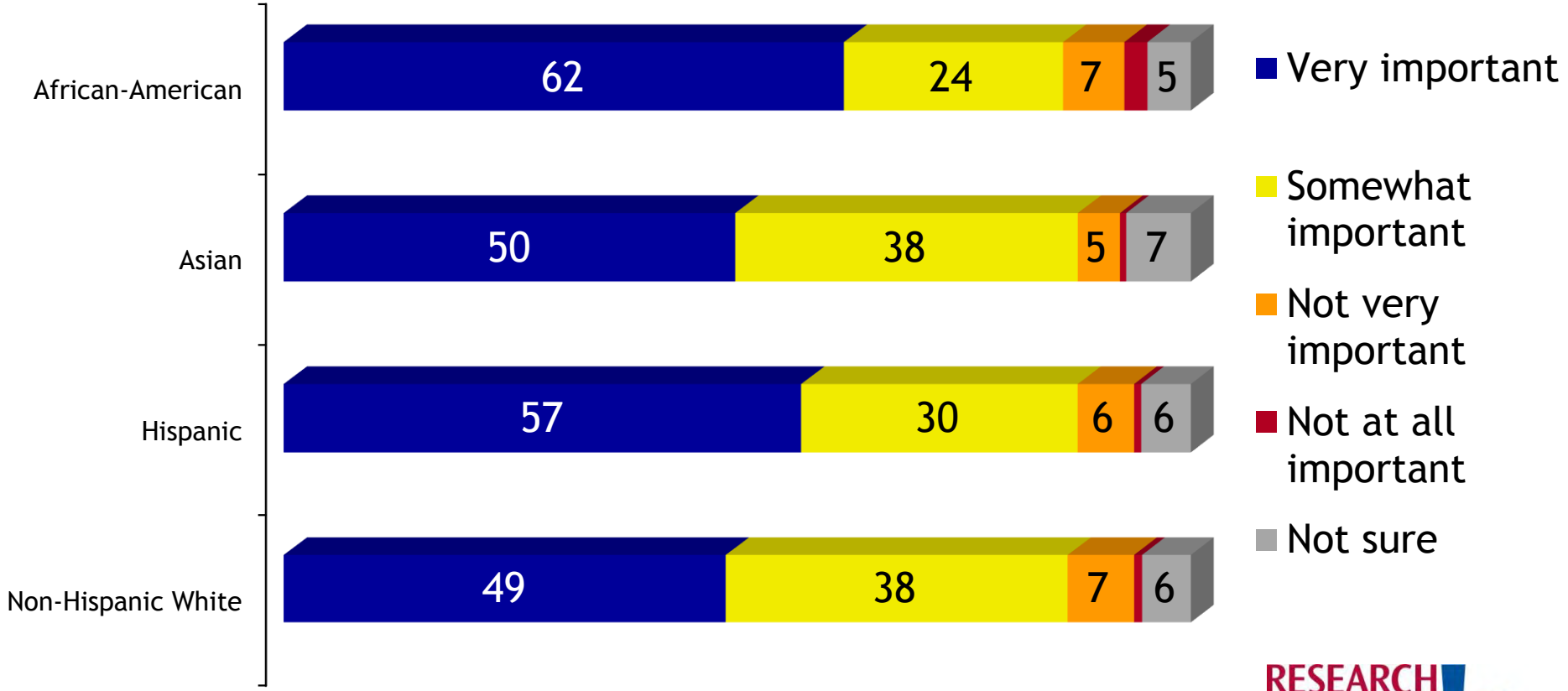
Improving Others' Health Important for Participation

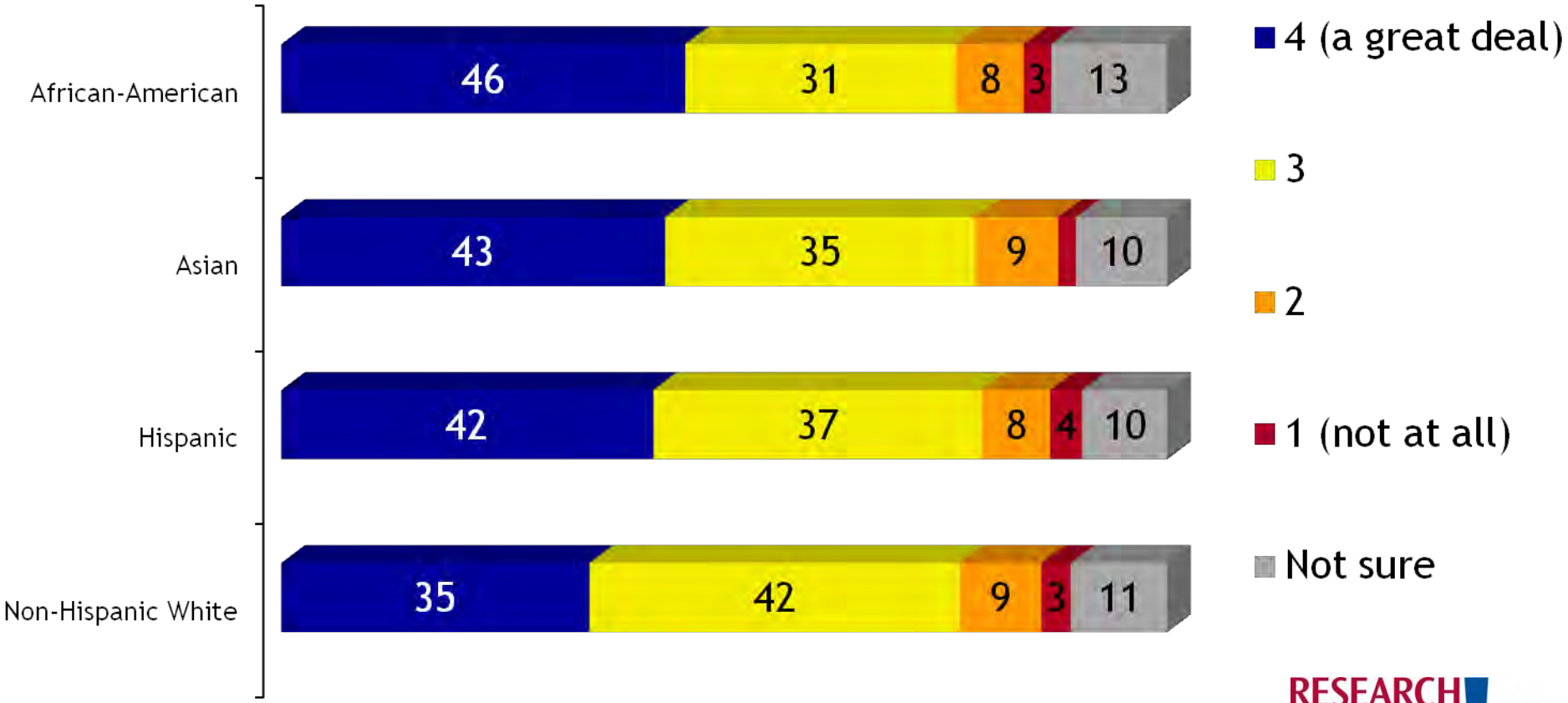
How important would the *opportunity to improve the health of others* be in your decision to participate as a volunteer in a clinical trial?



Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

Americans Admire Clinical Trial Volunteers

On a scale of 1 to 4, how much do you admire people who volunteer for clinical trials?



Zogby Analytics

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

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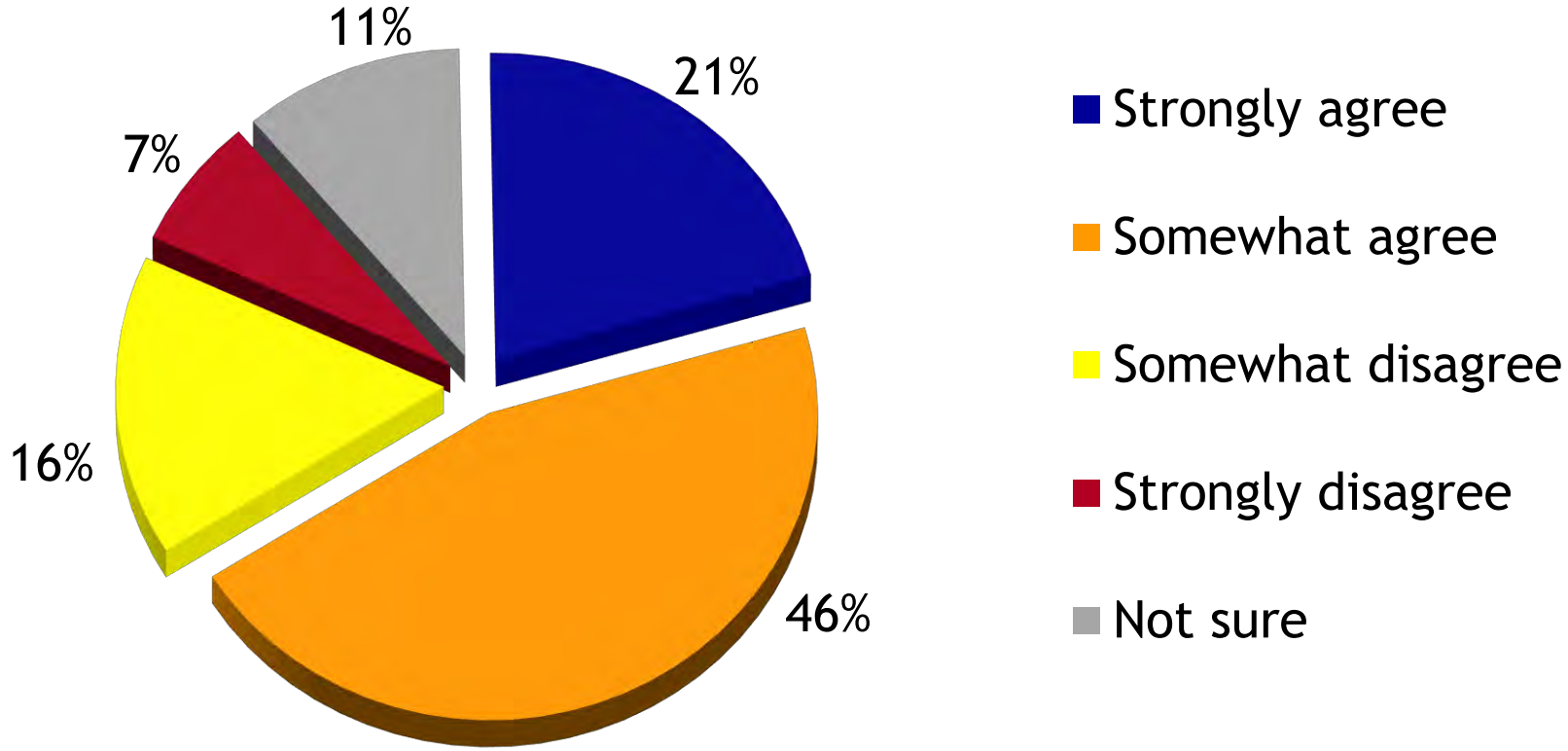
Clinical Trials are as Valuable as Giving Blood

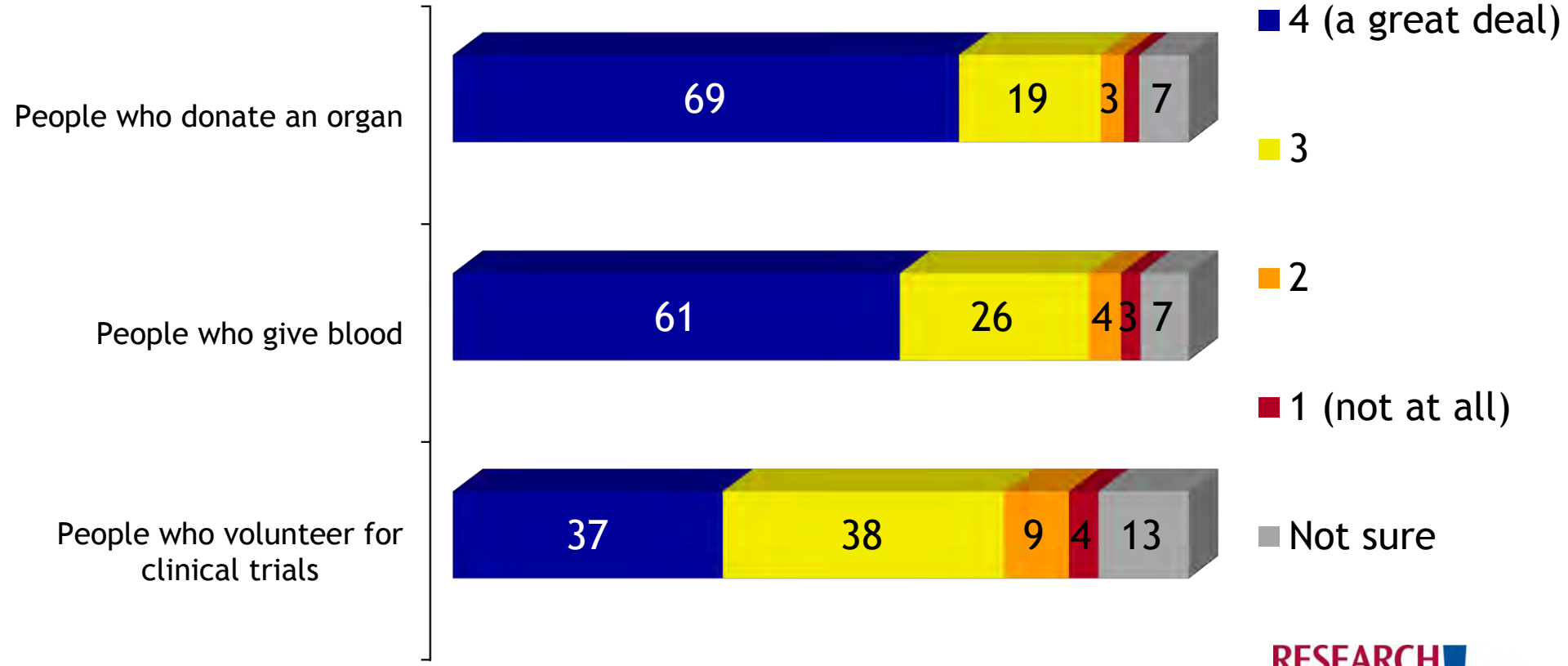
Do you agree or disagree with the following statement. Taking part in clinical trials is as valuable to our health care system as giving blood.



Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

Americans Admire Organ Donors

How much do you admire the following groups of people on a scale of 1 to 4?



Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.

BHAG*: Make volunteering for a clinical trial as valued as donating blood, organs or tissue.

Make regular participation in clinical research a new social norm and a routine ‘health behavior.’

*”Big, hairy, audacious goal” – Collins, J. & Porras J. (2004). Built to Last: Successful Habits of Visionary Companies.

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Driver's License Organ Donor Program: advocates made it happen!

- In 1969, As a result of advocacy by physicians, patients and the business community, the Tennessee Legislature passed the Anatomical Gift Act, which made it possible to donate organs.
- In 1973, Tennessee becomes first state to list organ donation as an option on a driver's license; other states followed
- By 2014, through the work of the donation and transplantation community in partnership with the DMV, 50 percent of the U.S. adult population, or 125 million people, were registered organ, eye and tissue donors.

Source: Lee, R.M.(1976). Developments in Transplantation. *AORN Journal*, 23(2), 218-226.
Tennessee Kidney Foundation, DonateLife 2015 Annual Update

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Action Recommendations (1)

- Standardize and harmonize regulations: within US and globally
- End practice of every institution having unique consent form
- Learn from other nations, e.g. UK success in doubling cancer trial enrollment
- Share more data faster—across agencies, across the research ecosystem, with patients. PCORnet provides opportunity.
- Increase reimbursements to physicians for talking about research

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Action Recommendations (2)

- Use new technology and social media to improve two-way communication:
  - 'bring clinical trials to patients, instead of patients to clinical trials'*
- Everyone involved in the conduct of research should look for opportunities to participate in research as a volunteer themselves—experience can be a great teacher, and you will be more credible, too
- Use knowledge of concerns of special populations to design better recruitment and retention
- Engage patients every step of the way!

**Corsee Sanders, Ph.D. SVP, Global Head of Development Innovation & Clinical Operations, Genentech*

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Patient Engagement is the most important component of success!

"Gone are the days when we could just say, 'We're a cloistered community of researchers, and we alone know how to do this.'"

—*geneticist Vandana Shashi*, The New Yorker, *July 21, 2014*

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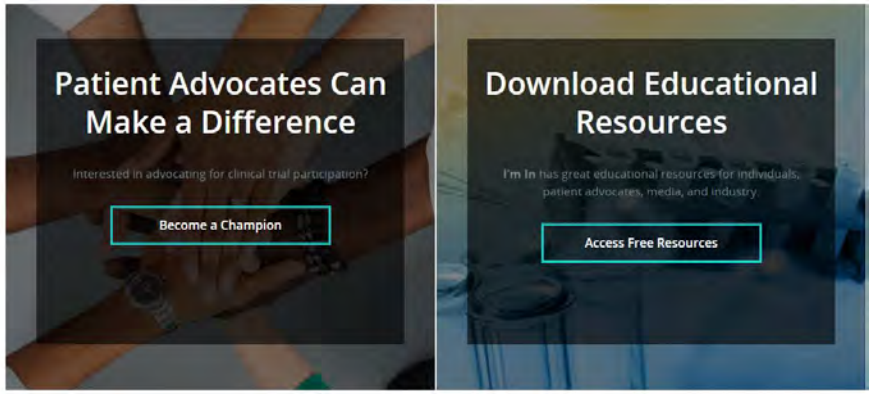
Examples of Clinical Trial Campaigns

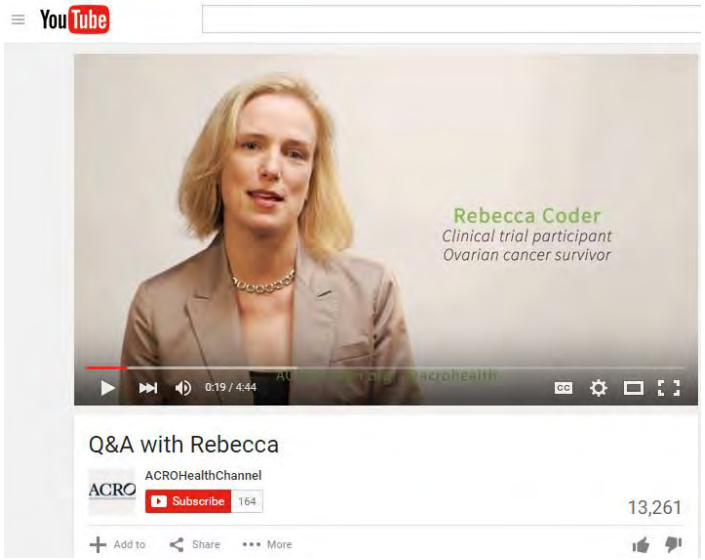
I'M IN CLINICAL TRIALS *for Better Health*

Patient Clinical Trial "Champions"



ACRO
ASSOCIATION OF CLINICAL RESEARCH ORGANIZATIONS

Patient Perspectives Video Series



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Clinical Trial Recruitment 2.0

THE WALL STREET JOURNAL

Apps to Track Exercise, Sleep Help Patients Participate in Clinical Trials
4/13/15

"Kathryn Schmitz, an epidemiologist at University of Pennsylvania and an investigator on the Share the Journey study, said it recently took her team three years, including the sending of 60,000 notices, to recruit just 351 patients for a separate conventional study about the impact of exercise on breast-cancer survivors. In the first month of recruiting for Share the Journey—which she said has less stringent enrollment criteria—nearly 2,000 patients have signed up."

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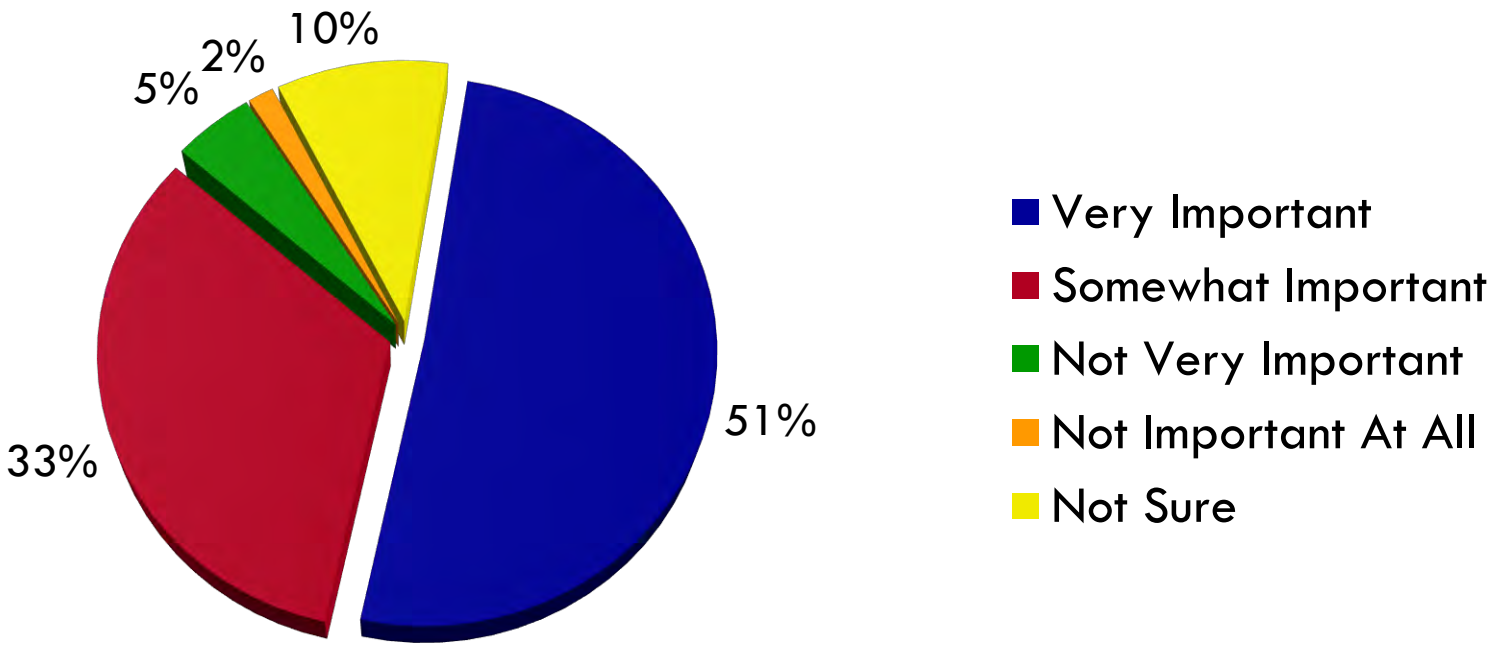
Important for Scientists to Engage with Public on Research

How important is it for scientists to inform elected officials and the public about their research and its impact on society?



Source: A Research!America and ScienceDebate.org poll of U.S. adults conducted in partnership with Zogby Analytics in September 2015.

Zogby Analytics

Science debate dot org

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Remember the most important four words a researcher can say and convey:

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“I work for you.”

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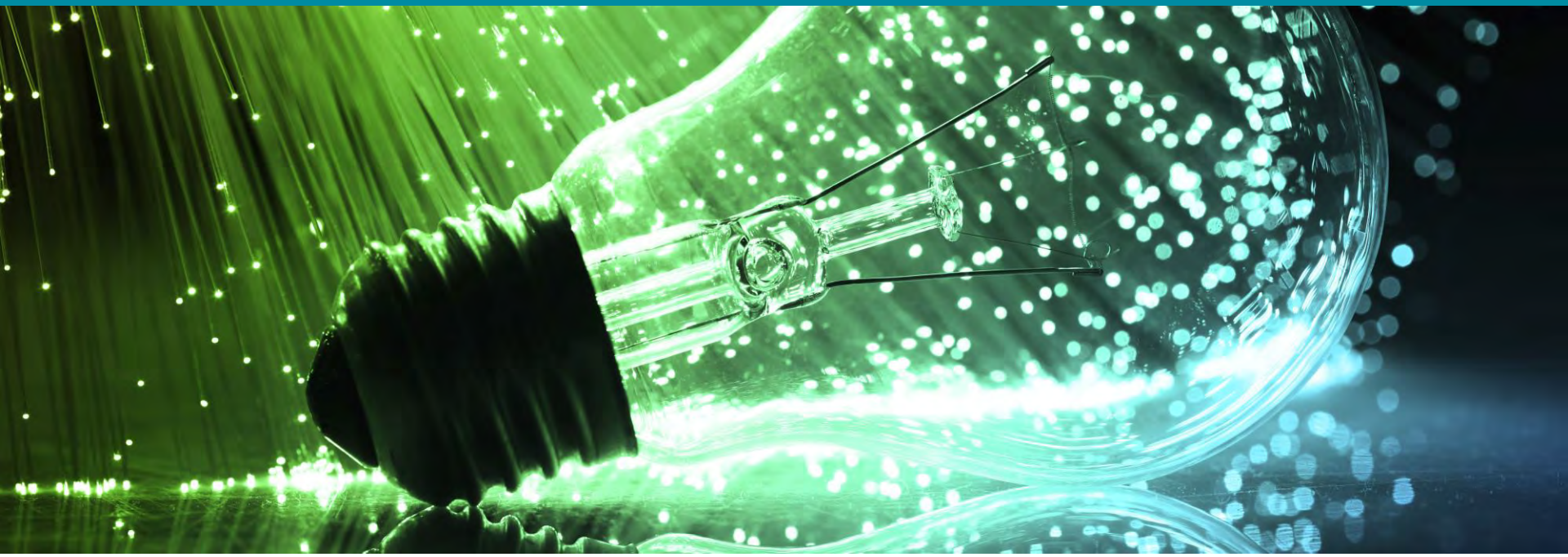
Clinical Trials Recruitment Project
Session II: Background & Findings

Jonca Bull, MD; Food and Drug Administration

November 9, 2015

CLINICAL
TRIALS
TRANSFORMATION
INITIATIVE



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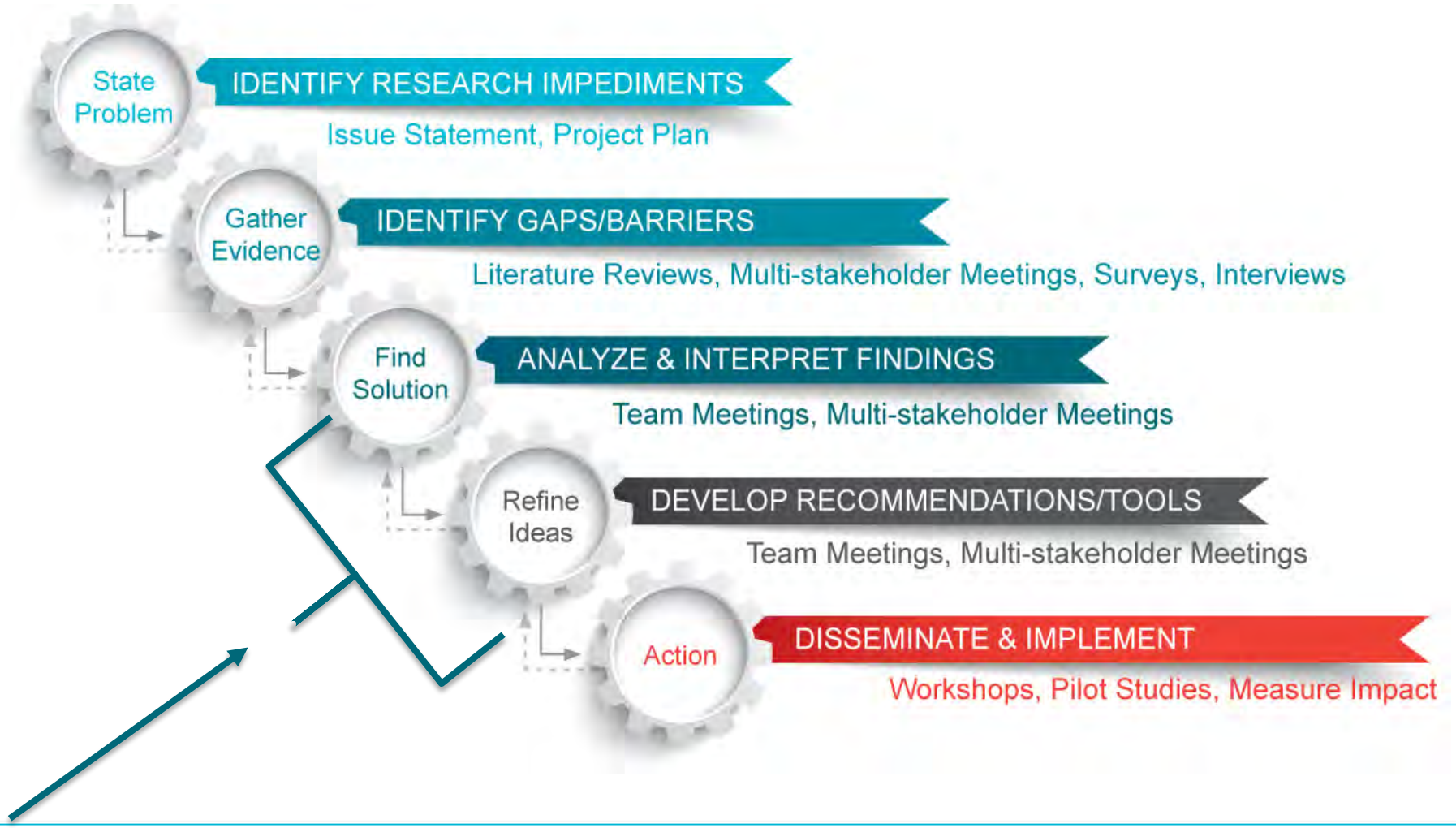
CTTI Methodology



Project Objectives: Workstream 1

Identify barriers and optimal approaches to patient recruitment

- Understand barriers and solutions for identifying, engaging and enrolling patients
- Summarize existing literature on barriers and solutions
- Survey experts representing stakeholders to obtain their perceptions of identified barriers and solutions

Project Objectives: Workstream 2

Identify methods to move recruitment planning upstream in the study development process

- **Identify and catalog current recruitment planning tools**
- **Identify key elements of recruitment plans and tools**

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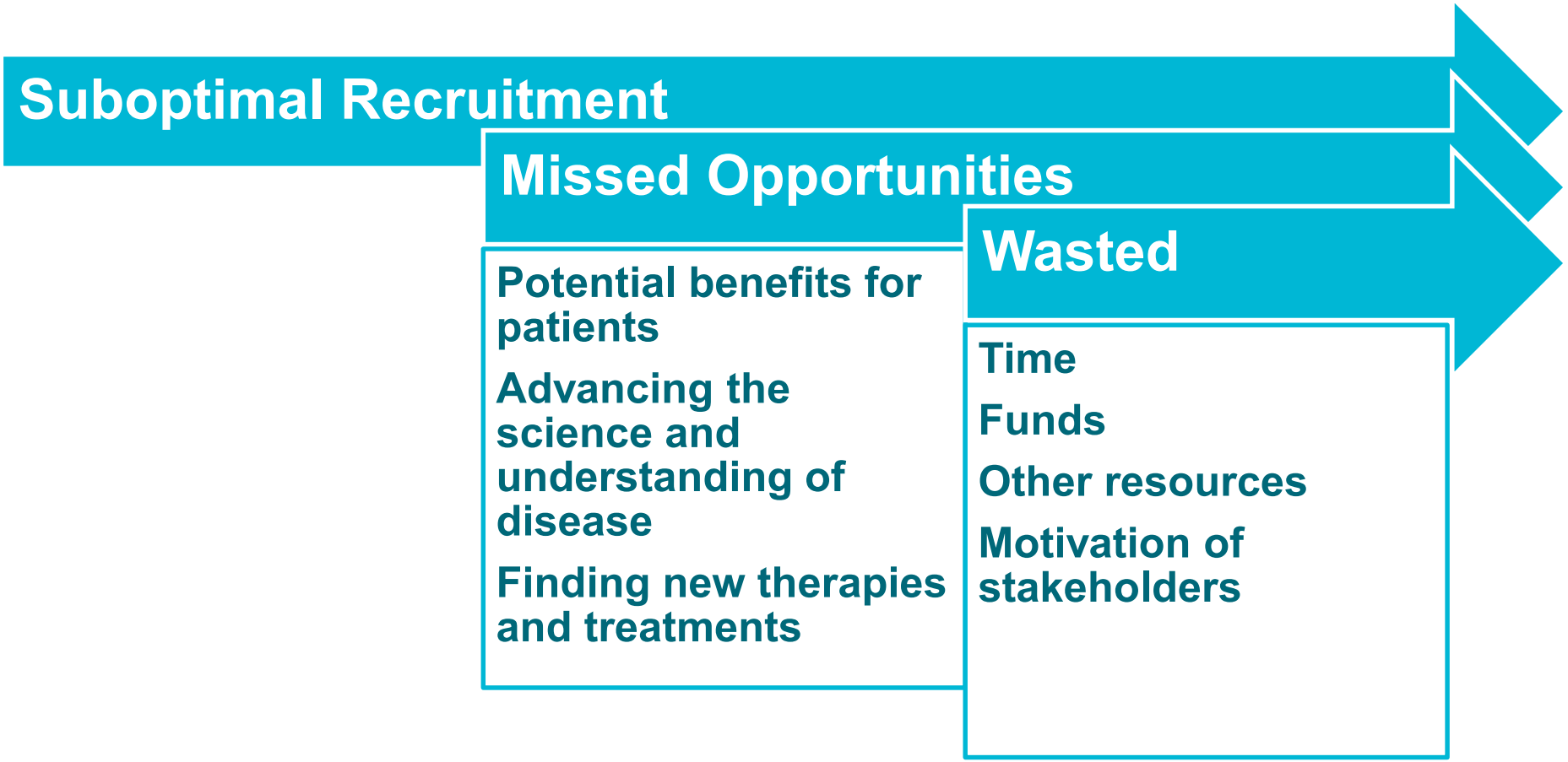
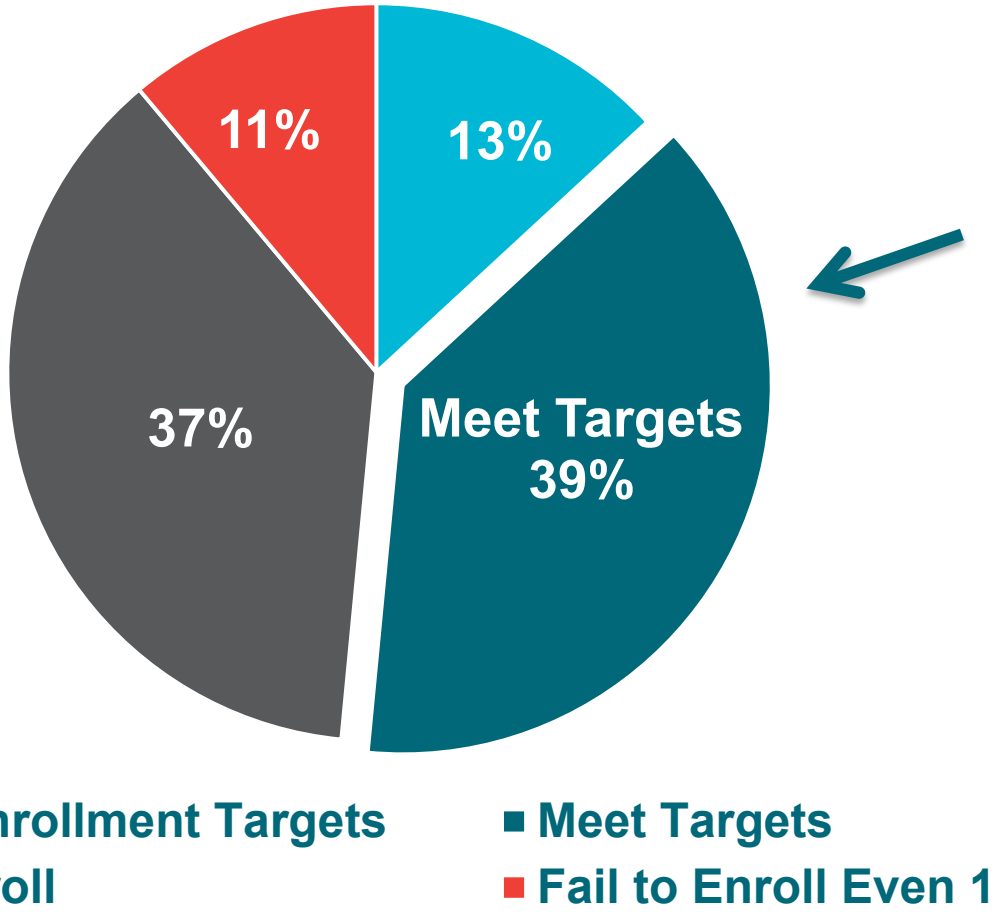
Consequences



Clinical Trials Crisis: Low Site Enrollment Rates



Adapted from Tufts Center for the Study of Drug Development, 2012

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Clinical Trials Crisis: ↑Trial Complexity = ↑ Burden on All Stakeholders

- On average, 20% of Phase II and 30% of Phase III protocols collect non-core data that are not associated with a primary or key secondary endpoint, regulatory compliance, or standard baseline assessments.

		Phase II	Phase III
Endpoints	Primary	14.8%	9.4%
	Key Secondary	38.3%	34.8%
	Tertiary	27.8%	29.7%
	Exploratory	19.1%	26.1%
Procedures	Core	64.9%	58.6%
	Required	4.6%	3.7%
	Standard	9.7%	7.1%
	Non-core	**20.7%**	**30.6%**

Adapted from Tufts CSDD Impact Report Vol 16, No 5, Sep/Oct 2014

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Evidence Gathering

Evidence Gathering: Literature Review

- **Goal**
  - ID barriers to successful, effective R & R
  - Catalog & analyze strategies
- **Search Methodology**
  - Systematic, comprehensive review on recruitment and retention in clinical trials
    - PubMed®
    - Embase®
    - National Cancer Institute's AccrualNet™
  - Publication date within the last 10 years
- **Results**
  - 2,069 unique citations
    - 45 articles represented a total of 38 reviews
      - 34 articles – barriers/promoters of recruitment/retention
      - 13 articles – comparative evaluation of recruitment strategies
      - **0 articles – comparative evaluation of retention strategies**
  - Validated quality controls at each step

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Literature Review: Takeaways

- ***Limited data*** regarding how successful or unsuccessful trialists have been in overcoming barriers or how barriers have affected the outcome of trials
- Most strategies investigated were supported by only one or two studies
- Paucity of literature on retention barriers, strategies and promoters

Literature Review: Conclusions

- **Recruitment barriers tend to fall into one of several areas:**
  - Design Issues
  - Trust / Communication Issues
  - Logistic / Pragmatic Issues
  - Institutional (including funding and resource) Issues

Many authors cautioned that they were not able to provide specific guidance on what works for whom or under what circumstances

Notably

Most authors emphasized the need for future trials to include randomized comparisons of different recruitment and retention interventions as part of the basic RCT design in order to increase the evidence base for these interventions.

Survey Development

- CTTI staff and project team leaders (PTLs) developed an extensive draft survey based on the lists of barriers and promoters identified in the lit review
- RTI, in collaboration with CTTI staff and TLs, pared the survey down to one that could be completed in 15 minutes
- Focus on:
  - Rating various barriers
    - Free text response regarding solutions for those rated very or somewhat significant
  - Solutions (rating and experience)
    - Free text response regarding methods to improve recruitment

Survey Methods

- 6/27/2014: RTI International sent an email announcing the upcoming web survey
- Announcements were sent to 300 individuals:
  - 90 patient advocates
  - 90 sites
  - 45 global investigators
  - 45 investigators
  - 30 sponsors
- Survey data were collected from July 15 to August 15, 2014
- **Findings reported here are based on 90 completed surveys**

Survey Results: Respondent Organizations

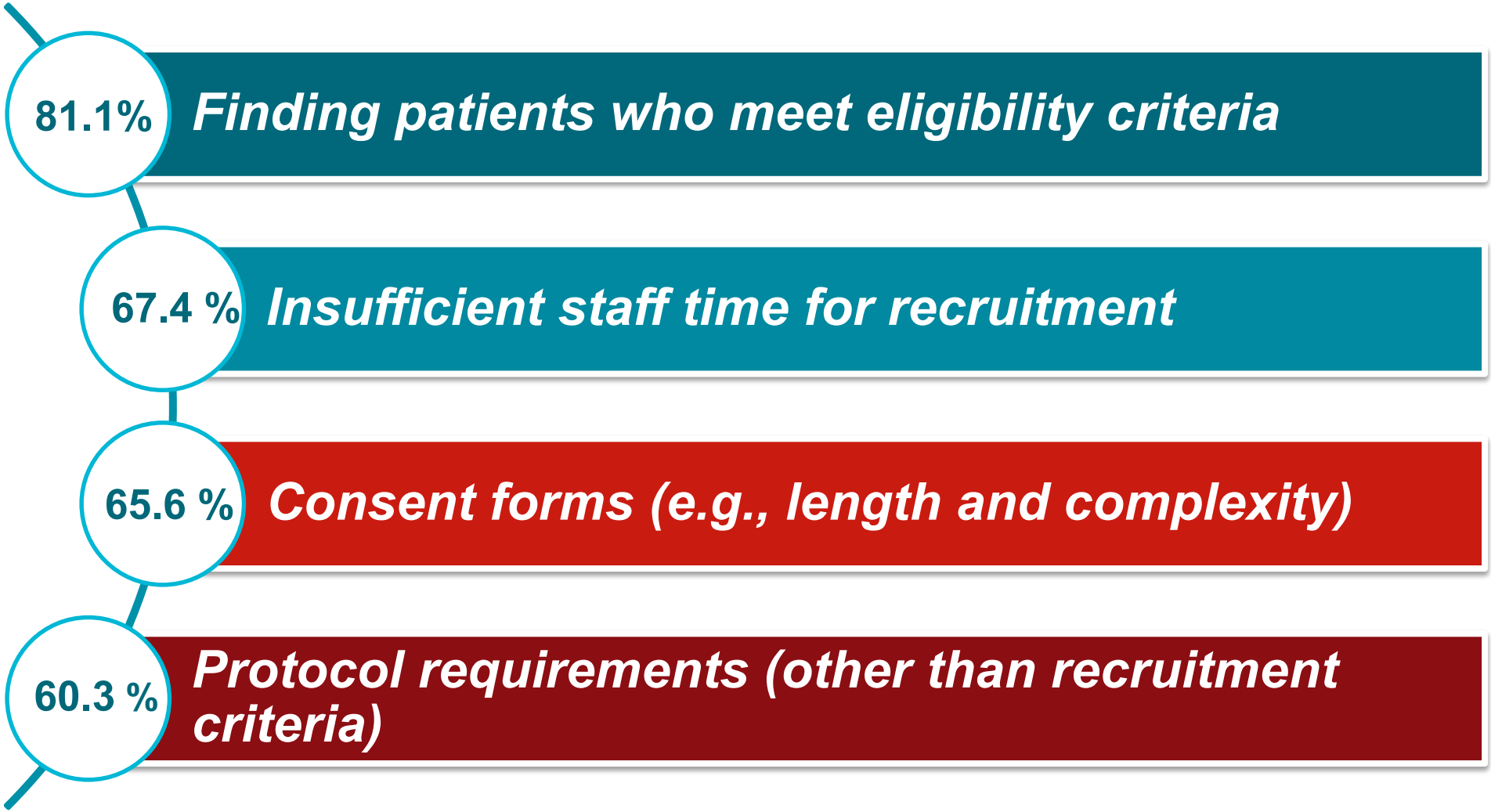
Organization Type	Percent (N)
Academic research organization	26.7 (24)
Industry: pharmaceuticals	18.9 (17)
Patient advocacy, no sponsorship of trials	15.6 (14)
Clinical research organization	13.3 (12)
Patient advocacy, including sponsorship of trials	7.8 (7)
Federal government: research (NIH, VA)	6.7 (6)
Clinical research site	2.2 (2)
Industry: biotechnology	2.2 (2)
Federal government: regulatory (FDA)	1.1 (1)
Industry: medical devices	1.1 (1)
Something else	4.4 (4)

Respondent Characteristics

- Most were executives or senior staff with 10+ years experience in clinical trials
- Most worked for organizations that had 10+ years experience in clinical trials
- 70% claimed “significant influence in determining recruitment strategies” for trials they lead or manage
- ~71% conduct business outside the US
- Broad variety of therapeutic areas, bulk in oncology

Most Significant Barriers

Results:
Perceived Barriers to Recruitment



Rated very/somewhat significant (by more than 50% of respondents)

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Categorizing The Most Common Perceived Barriers By Respondent Type

Barrier	Sponsor (Fed)	Sponsor (Industry)	CROs	Sites	Pt. Advoc	Other
Finding Pts Who Meet I/E Criteria	94.7%	92.1%	100%	77.8%	77.8%	78.6%
Insufficient Staff Time for Recruitment	73.7%	81.6%	79%	63%	73.1%	57.1%
Length & Complexity of CFs	68.5%	57.8%	63.1%	62.9%	74.1%	50%
Protocol Requirements (visits, procedures)	50.3%	64.8%	63.1%	42.3%	63%	64.3%

- % identified as significant or very significant

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Free Text Solutions to Most Common Barrier (by themes)

Identifying Eligible Patients❖ (88.81%)

❖ *This barrier was considered the most significant by 41% and somewhat significant by 40%*

- **Engage in effective study planning (37)***
- **Improve eligibility criteria (20)**
- **Using effective recruitment methods / technologies (20)**
- **Education about research (specific trials) (14)**
- **Partnering (13)**
- **Education about research (general) (6)**
- **Assisting patients with specific aspects of study (3)**
- **Design less burdensome protocols (2)**

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Barrier: Identifying Eligible Patients

Solution: Engage in effective study planning (37)

Free Text Response Themes

- Identify appropriate patient populations (2)
- Develop recruitment strategies prior to trial initiation (3)
- Establish realistic timelines (2)
- Involve site PIs in study planning / investigator engagement (2)
- *Include patient input in study design (4)*
- Communicate expectations for site (1)
- *Identify appropriate study sites (23)*

Barrier: Identifying Eligible Patients

Solution: Engage in effective study planning (37)
***By identifying appropriate sites* (23)**

Free Text Response Themes

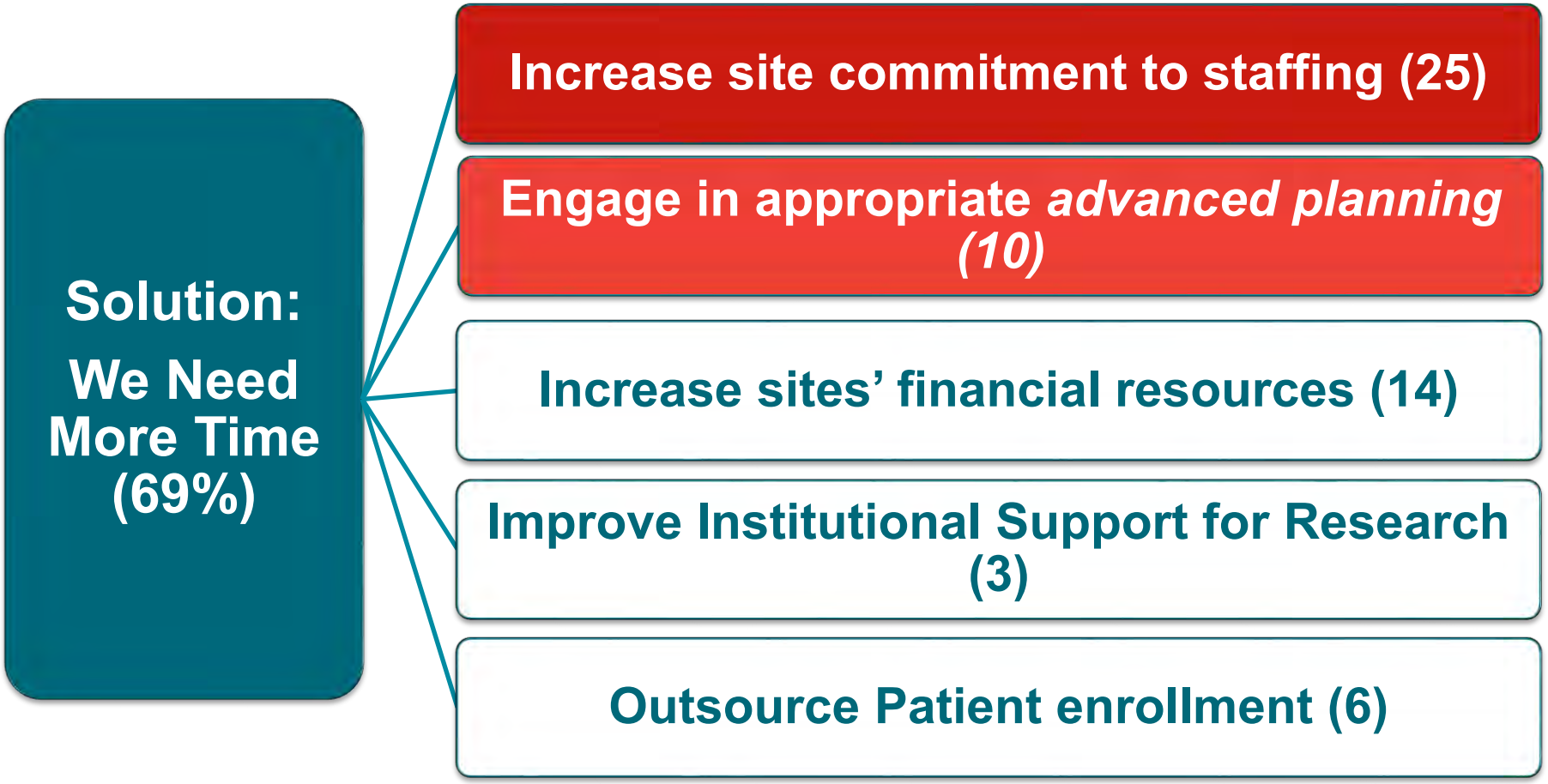
- **Site Feasibility Studies (2)**
- **Site Location (6)**
- **Document availability of potential study participants (11)**
- **Use electronic data mining (5)**

"…in an attempt to have a very specific population and make sure all possible safety issues are addressed, the ***inclusion / inclusion [sic] criteria are needlessly narrow, to the point of making few subjects eligible, even if we have many subjects with the disease available.***

"Trials are usually looking for the ideal patient with limited comorbid conditions. ***We should have trials that are more representative of the patient population, allowing patients with multiple comorbid conditions.***

Barrier:
Insufficient Staff Time for Recruitment

Free Text Response Themes



69% significant
23% very significant

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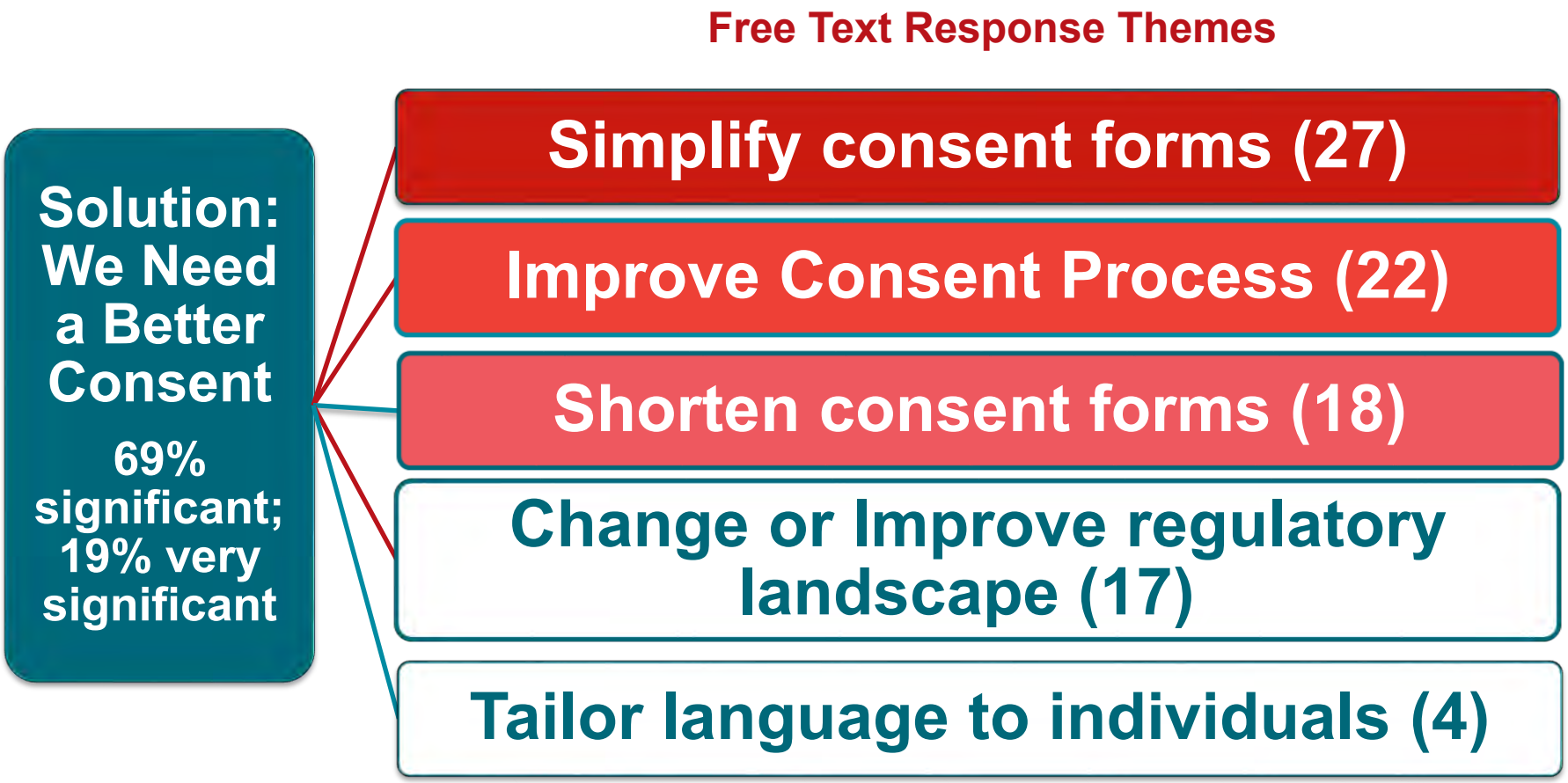
> Research staff should be realistic about the time required to achieve adequate recruitment.

> Carefully assessing site workload and resources and making the commitment to not taking on trials if there is not sufficient staff to implement them!

Barrier: Consent



These issues have been addressed by a separate CTTI Project, which has just recently released formal recommendations that you can find on the CTTI website

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Improve consent process (22)
Simplify/Shorten Consent Forms (45)

"ICFs should be short and concise and easy to understand, but I believe it is still "who" is delivering the consent and "how" it is presented.

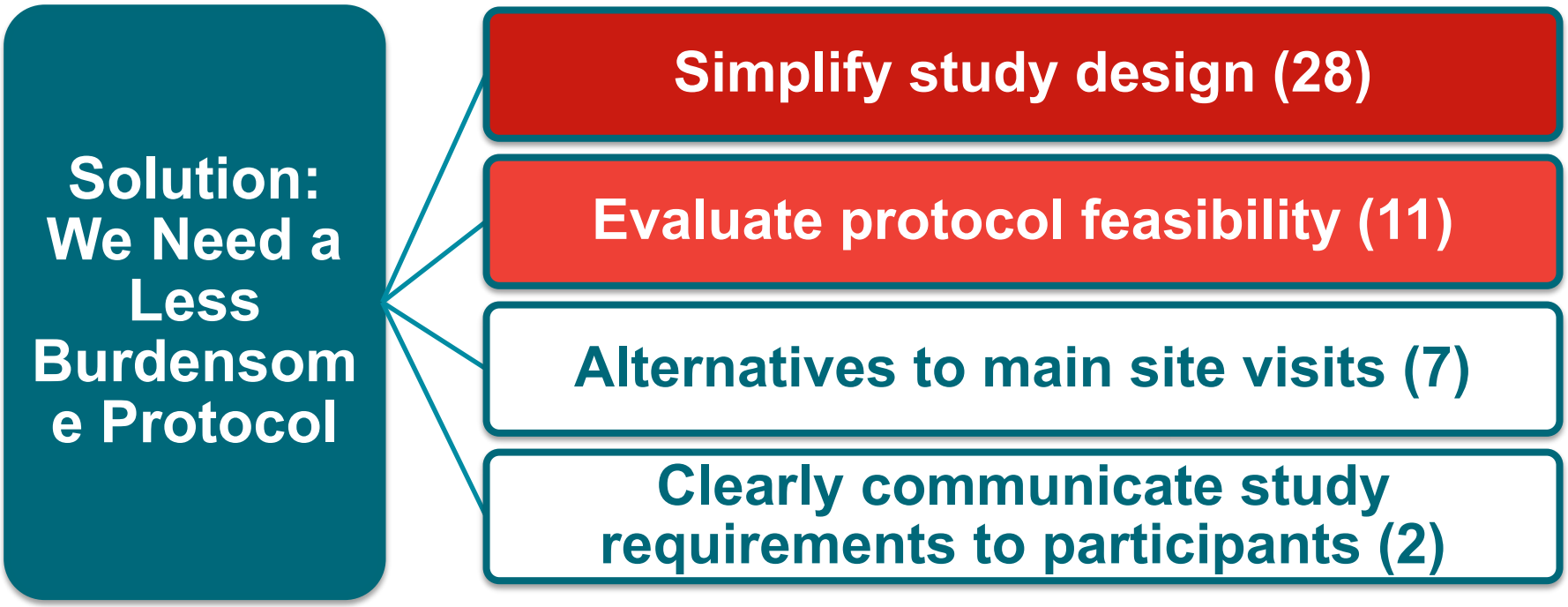
"The IRB should adapt a short form which has the most significant points (synopsis) and then a long form for the patient who wants every single detail.

"Informed consent forms should separate out study information from legal information.

"…unnecessary information in the consent that does not contribute to a participant's ability to make an informed decision.

Barrier: Protocol Requirements

Free Text Response Themes



61% significant; 17% very significant

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Eliminate visits and procedures not essential to study objectives (22)
Improve inclusion-exclusion criteria (1)

> *…Protocols need to be streamlined so that only that information necessary to answer the primary research questions are requested.*

> **Stop putting nice-to-have data requests/procedures into the protocols; *all data/procedure results should have an explanation as to how the data will be utilized within the Statistical Analysis Plan.***

Evaluate protocol feasibility (11)
By Engaging All Stakeholders

> “***Protocol feasibility measures need to include feedback from all parties that will be impacted***, not just key investigators or study coordinators, but importantly patients and caregivers.”

CTTI Recruitment Project 2014 Survey Respondents

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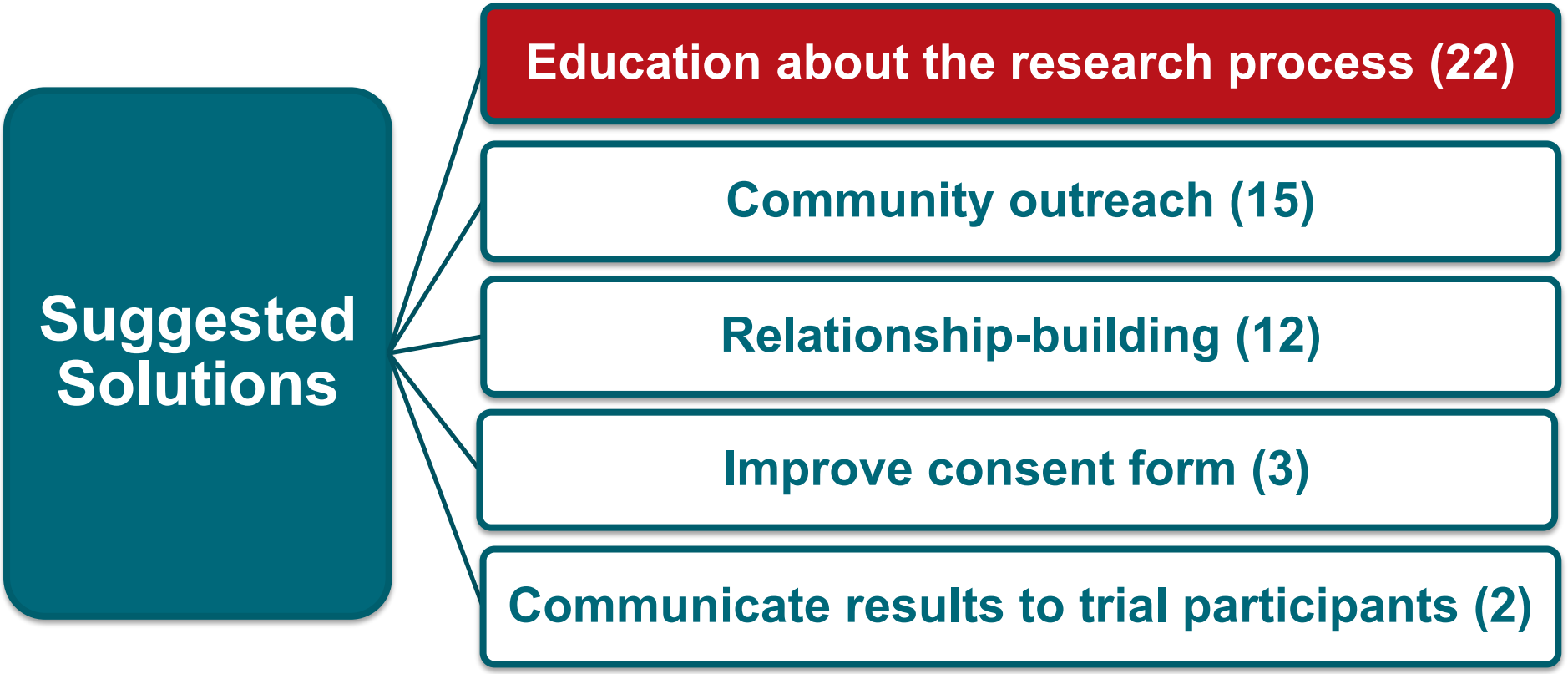
Moderately Significant Barriers

Barrier: Patient Mistrust of Research

- *Negative attitudes of patients and providers towards research were considered a moderately significant barrier*



47% endorsed as significant

8% endorsed as **very significant**

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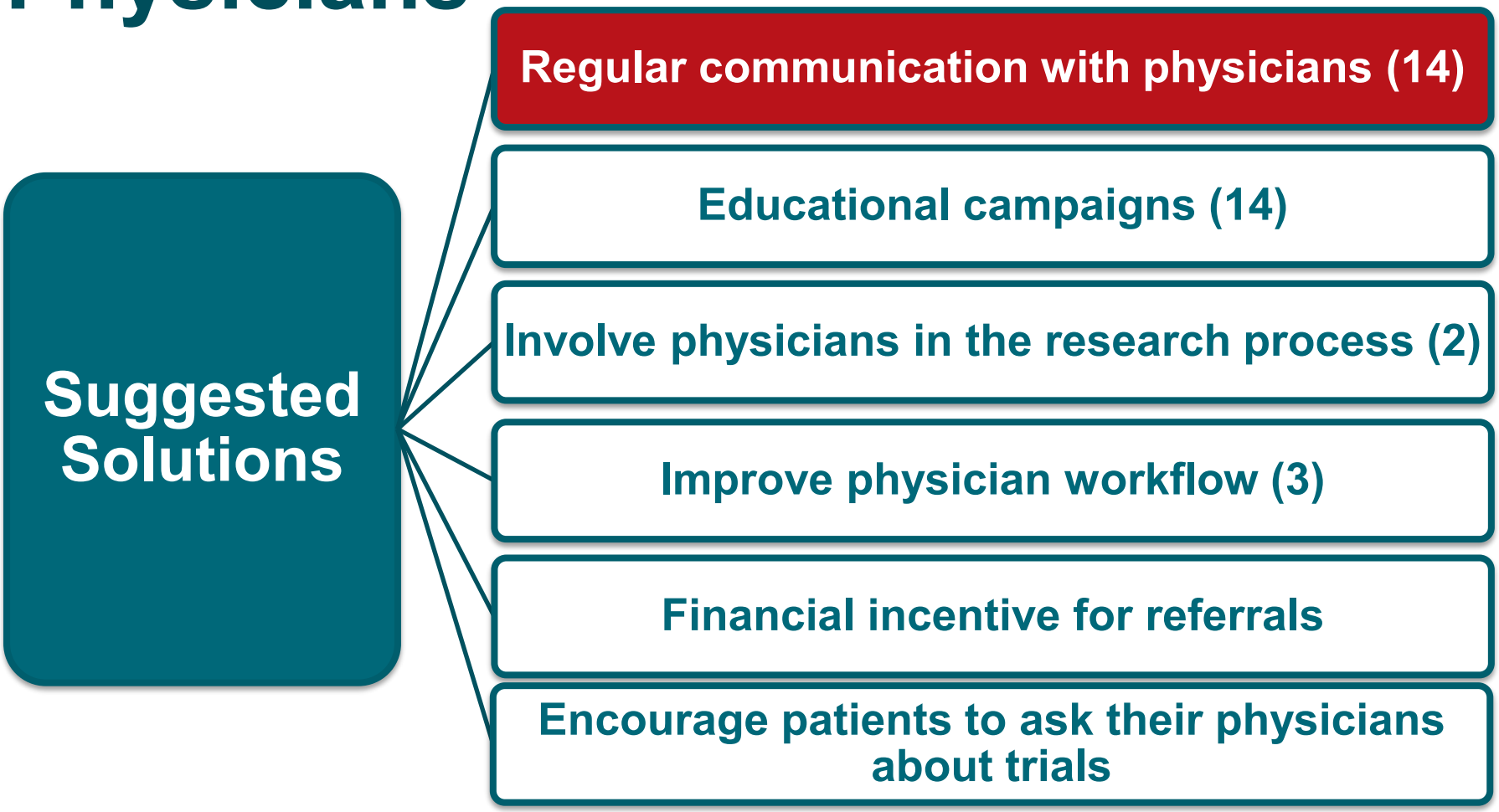
Barrier: Negative Attitudes Among Physicians



41% endorsed as significant

13% endorsed as **very significant**

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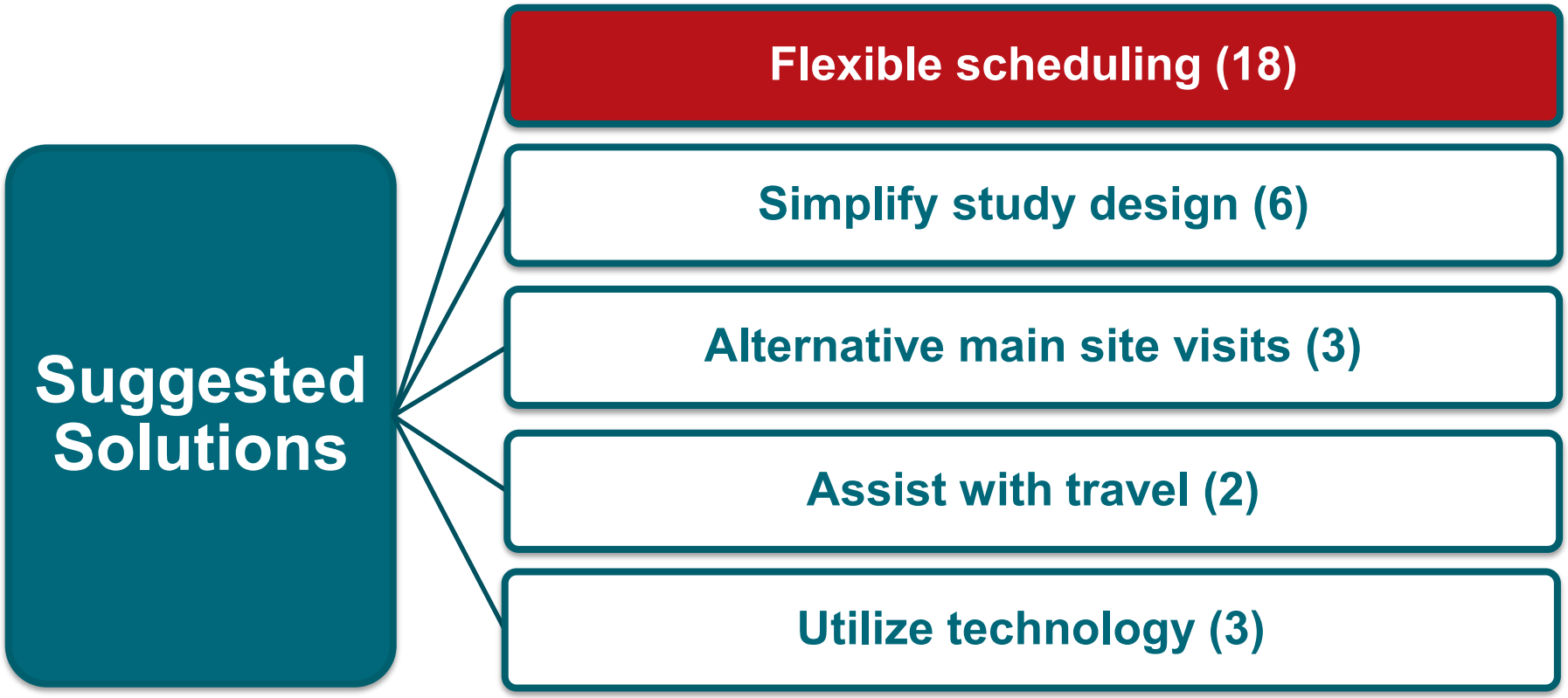
Barrier: Burden of Participation: Difficulty Scheduling Trial Visits

- *Burdens on trial participants were considered a moderately significant barrier*



39 % endorsed as significant

8 % endorsed as **very significant**

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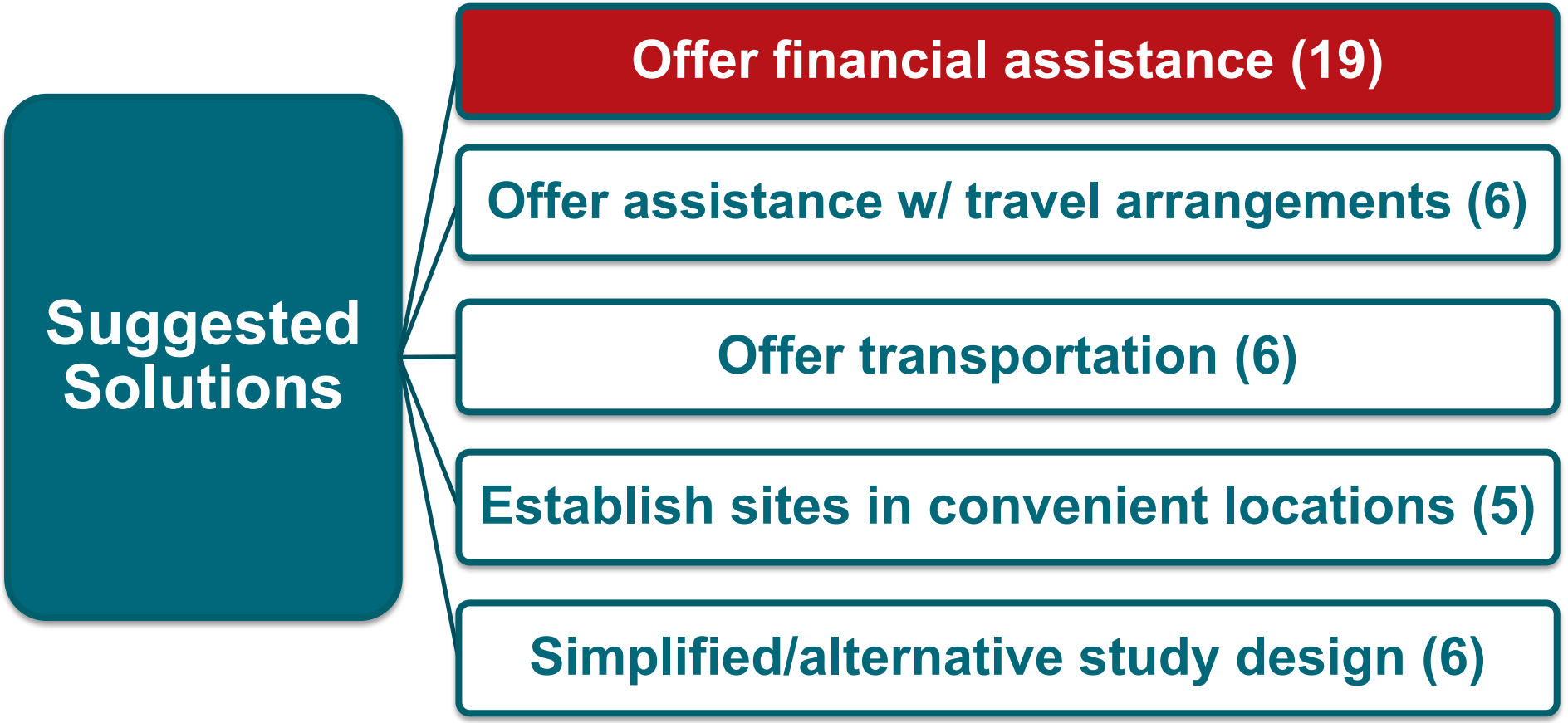
Barrier: Burden of Participation: Transportation



45 % endorsed as significant

13 % endorsed as **very significant**

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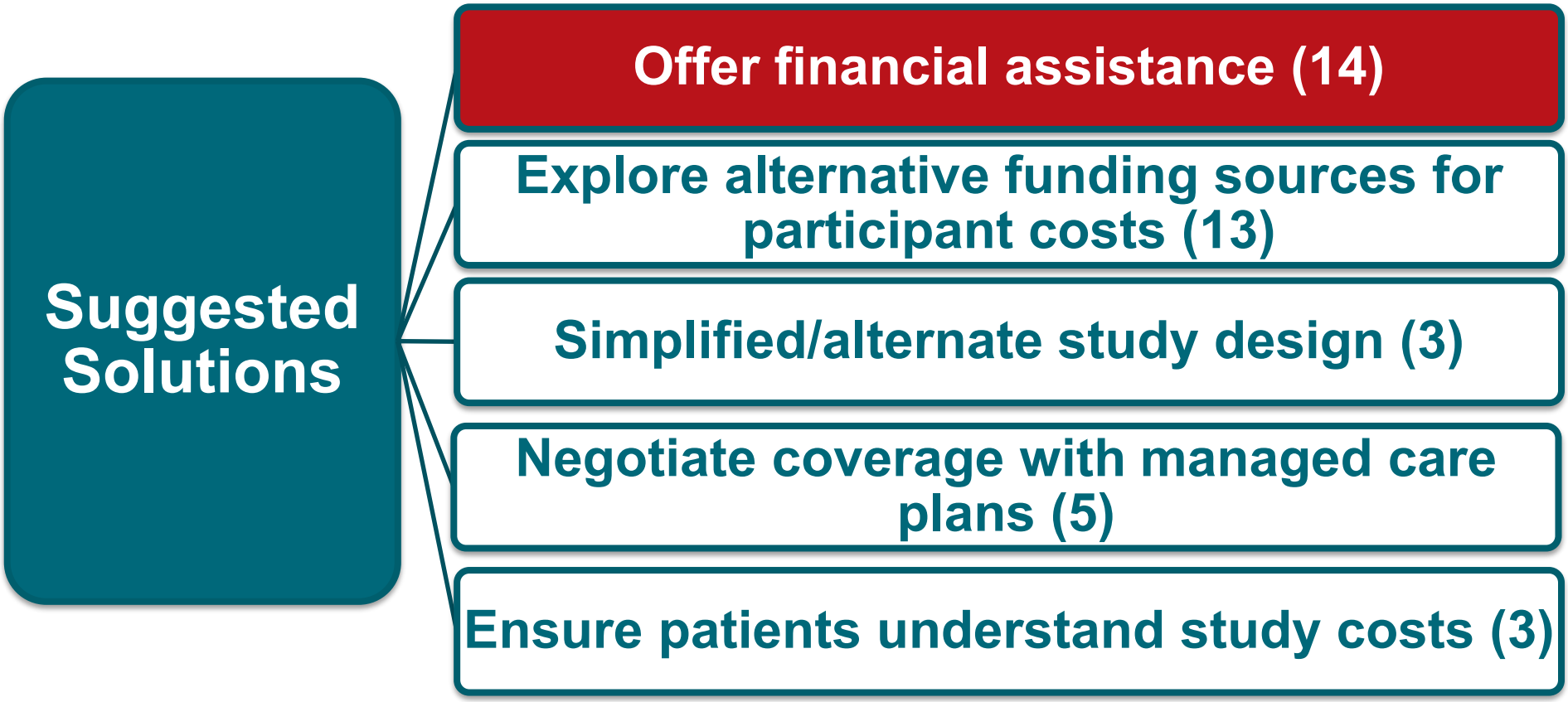
Barrier: Burden of Participation: Out of Pocket Costs



43 % endorsed as significant

12 % endorsed as **very significant**

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Less Significant Barriers

Safety (34%*)

- Commonly Suggested Solutions:
  - Educate patients about oversight and safety procedures (9)
  - Improve the Consent Process (8)

Study Design (38%*)

- Commonly Suggested Solutions:
  - Educate patients about randomization / placebo / standard of care (17)
  - Consider alternate study designs (5)

** Percent endorsed as significant*

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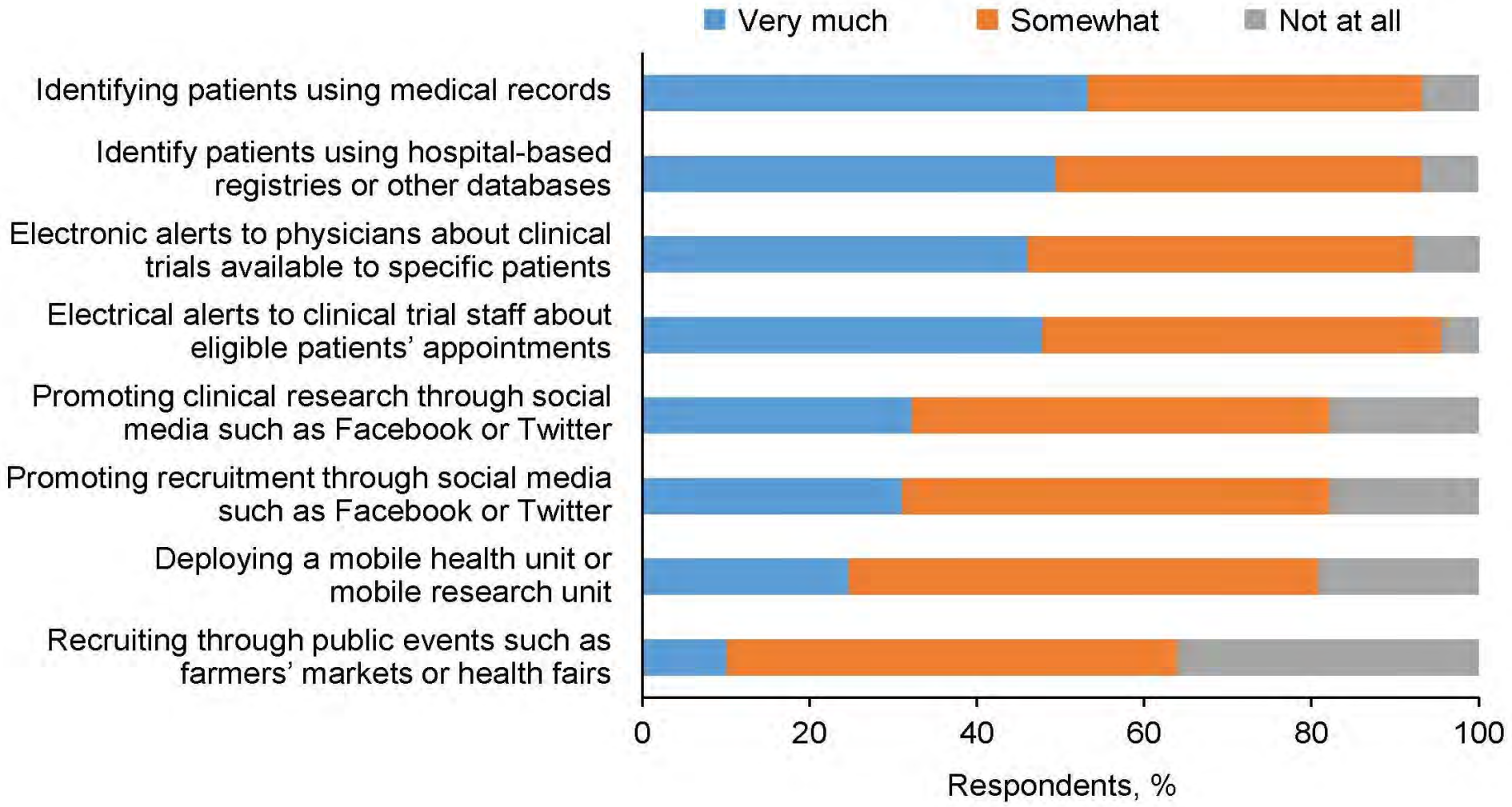
Perceptions of Specific Methods to Improve Recruitment



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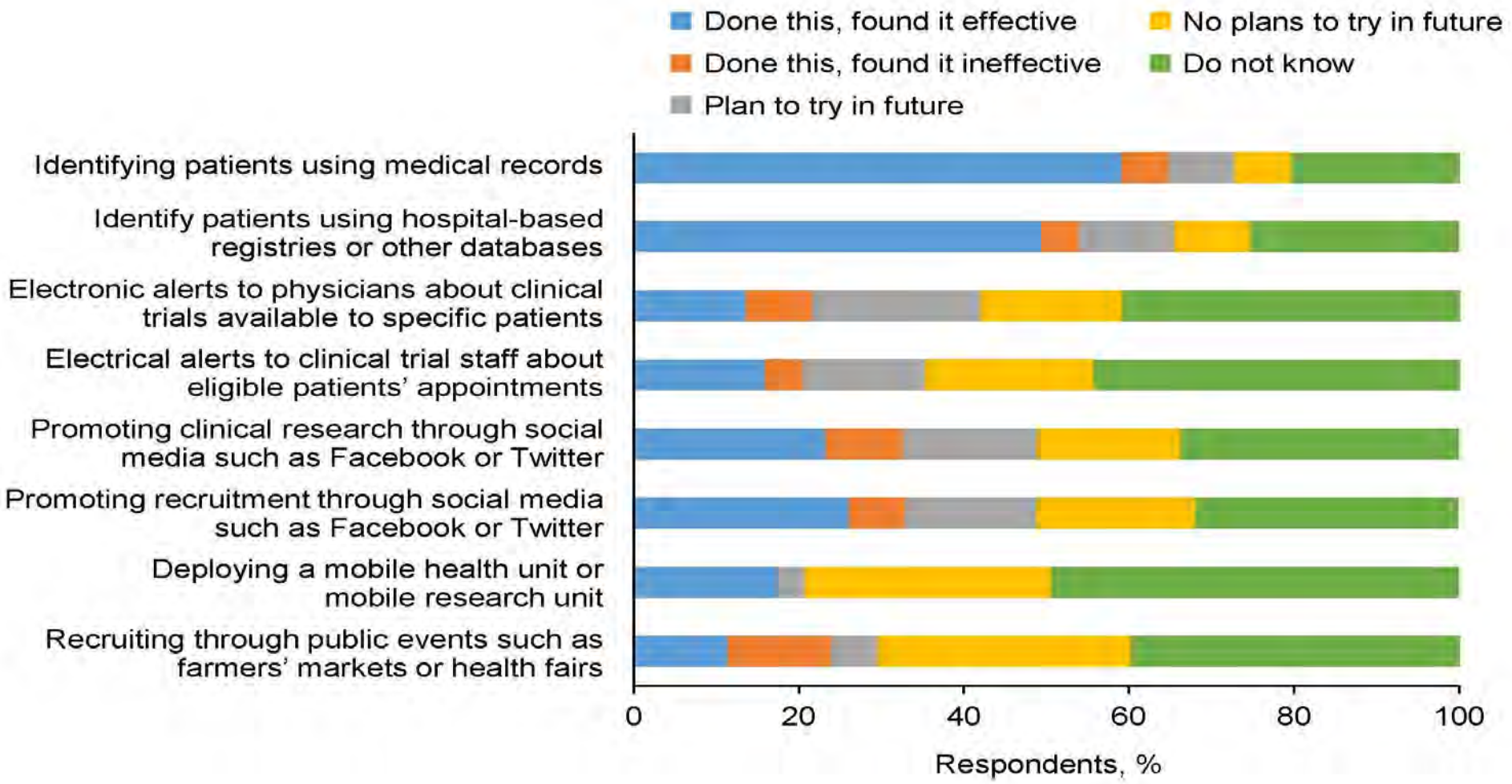
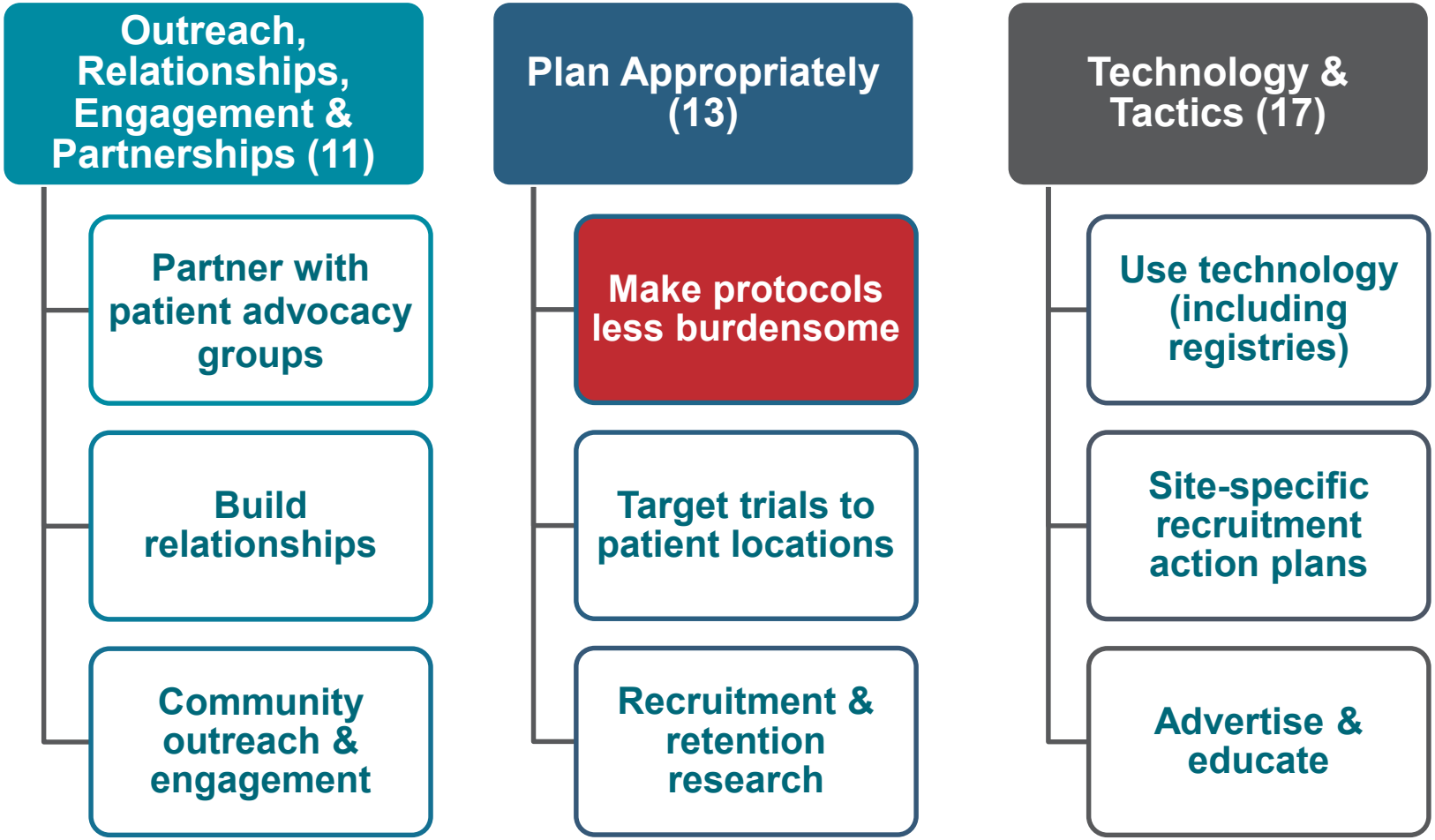
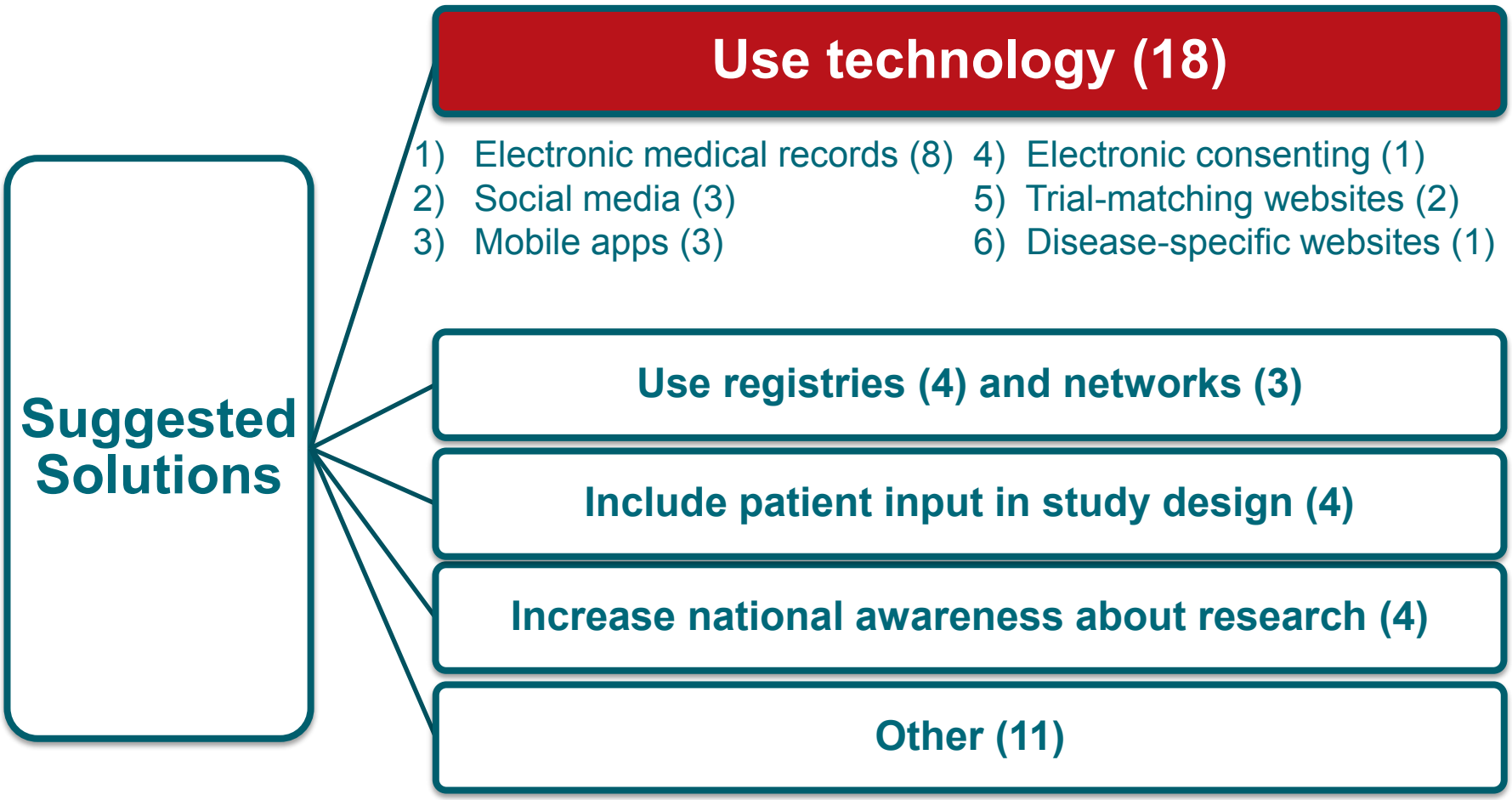
Experience with Specific Methods to Improve Recruitment



Free Text Suggestions of Methods to Increase Clinical Trial Enrollment



Emerging Recruitment Methods for National Trials



Sectors Selected as *Most Effective Partners to Increase Nat'l CT Recruitment Rates*

Sector	% (N)
Patient advocates	82.2 (74)
Sponsors	71.1 (64)
Researchers	67.8 (61)
Professional societies	44.4 (40)
Government regulators	37.8 (34)
Trade organizations	7.8 (7)
Other	4.4 (4)

NOTE: Respondents could select multiple sectors.

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Top 6 Sector Combinations Reported as *Most Effective Partners to Increase Nat'l CT Recruitment Rates*

Sectors	N
Patient Advocates, Researchers	**9**
Patient Advocates, Government Regulators, Researchers, Sponsors, Professional Societies	**9**
Researchers, Sponsors	7
Patient Advocates, Researchers, Sponsors, Professional Societies	7
Patient Advocates, Sponsors, Professional Societies	7
Patient Advocates, Researchers, Sponsors	6

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Major Take-Aways

- ***Barriers*** most often reported as problematic:
  - ***Eligibility criteria***
  - ***Insufficient staff time for recruitment***
  - ***Protocol requirements (other than I/E criteria)***
  - ***Complexity of consent forms***
- Barriers least often reported as problematic:
  - Patient concerns about trial safety
  - Social stigma associated with disease/condition
- **Patients offer a valuable perspective to overcoming recruitment barriers.**
- **A comprehensive recruitment strategy, rather than a single tool or solution, will be required to address the range of significant recruitment barriers identified**

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***The key is making sure the trial is worth doing, that it asks an important question and that the endpoints are significant*… After that, we can work on all kinds of recruitment strategies."**

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Summary of Key Findings, cont'd

- Many organizations used medical records or hospital-based registries to identify patients and found them effective.
- Respondents reported interest in and plans for trying new technology-based recruitment methods (tactics vs. strategies):
  - **E-alerts to physicians about specific patients who might be eligible** for clinical trials
  - **E-alerts** to clinical trial staff **about upcoming appointments**
  - ***Promoting clinical research*** generally ***through social media***

Summary of Key Findings, cont'd

- **Most effective partners** for promoting clinical recruitment:
  - Patient advocates
  - Sponsors
  - Researchers
- Outlook:
  - Respondents were more positive about the prospects for clinical recruitment over next 10 years, compared to next 5 years

Discussion

- Industry: variable and siloed approaches to the development of recruitment plans
  - Sponsors are the primary owners of the recruitment problem
    - Hence, efforts should start centrally with study design
  - Tactics to enhance recruitment are often developed too late in the process of a clinical trial
    - Frequently reactive rather than proactive
    - Often to rescue
- Inference:
  - ***Need for a culture shift toward developing a recruitment plan from the earliest stages of clinical trial development***

But…

- What ***is*** a recruitment plan?
- What are the necessary components and key features?
- What ***tools*** are being used to create them?
- ***Who*** is creating them?

Landscape Scan by Team Members

- Gathered recruitment planning tools from wherever we could find them
- Major themes:
  - Recruitment plans are illusive, typically study specific and tactic based
  - Recruitment planning tools are likely abundant but often proprietary
  - No single framework for planning recruitment as part of planning a study
- Inference: ***Need for a systematic framework for thinking about recruitment planning in parallel with trial design & development***
  - Planning concerns fall into 3 areas
    - Trial design & development
    - Trial feasibility and site selection
    - Communications

Clinical Trial Recruitment Planning Continuum

Study Question Development:
- Engage all stakeholders
- Addressing an unmet need
- Meaningful & relevant

Trial Feasibility Analysis
- Disease prevalence
- Market data
- Patient Pathway Mapping
- Modeling & Metrics

Recrutiment Communication Planning
- Engage stakeholders, partners, audience(s)
- Have a mission & vision

Plan Implementation
- Pilot test
- Deploy multiple tactics over time
- Monitor their effect
- Return to stakeholders for advice

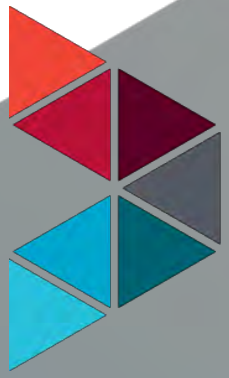
Protocol Design & Complexity
- Broaden I/E criteria
- Minimize burden
- Data parsimony

Site Selection
- Evidence-based
- Performance & Efficiency metrics
- Competing trials
- Location in relation to pts

Budgeting
- Determine trade-offs between time & costs
- Determine what resources will be needed & when

Process & Performance Evaluation
- Define success metrics
- Analyze & monitor for impact
- Test & share results & best practices

Thank you.



CLINICAL
TRIALS
TRANSFORMATION
INITIATIVE

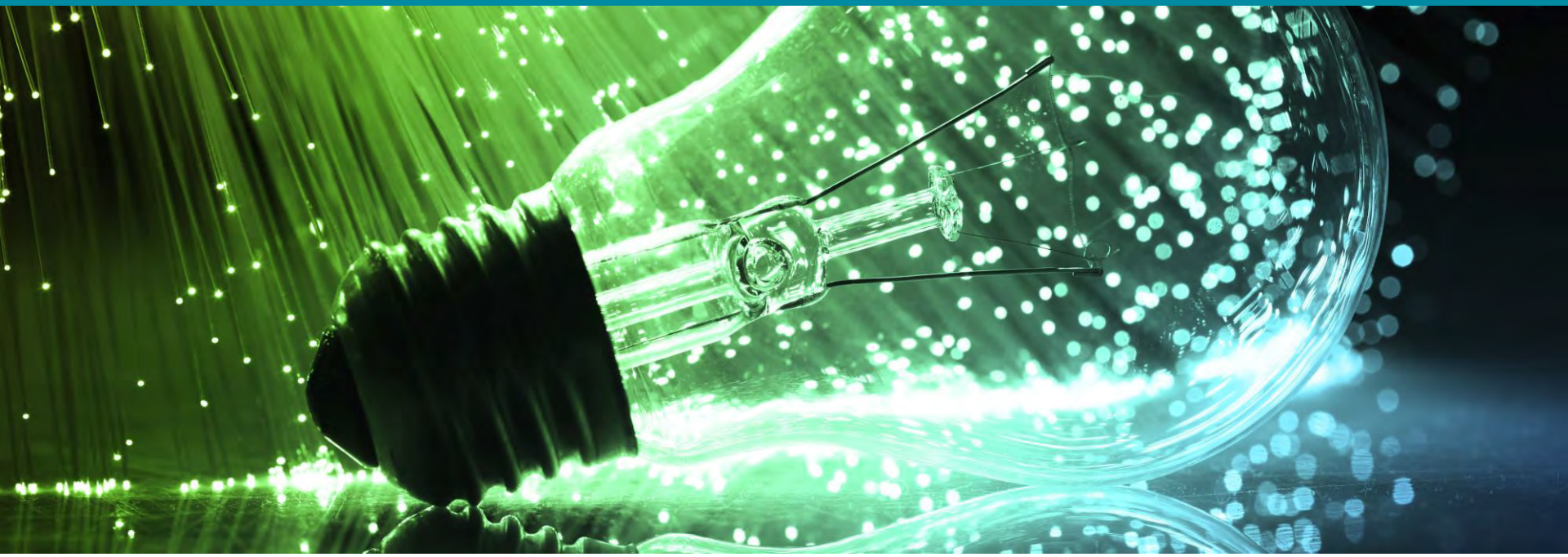
Jonca Bull, MD

Session III: Presentation of Draft Considerations

Jamie Roberts
Beth Mahon
Beth Harper
James Kremidas

November 9, 2015

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE



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The views and opinions expressed in this presentation are those of the individual presenter and do not necessarily reflect the views of the Clinical Trials Transformation Initiative.

The presenter is an Employee of Duke University. Salary support comes from pooled membership fees of the Clinical Trials Transformation Initiative and from FDA Cooperative agreement.

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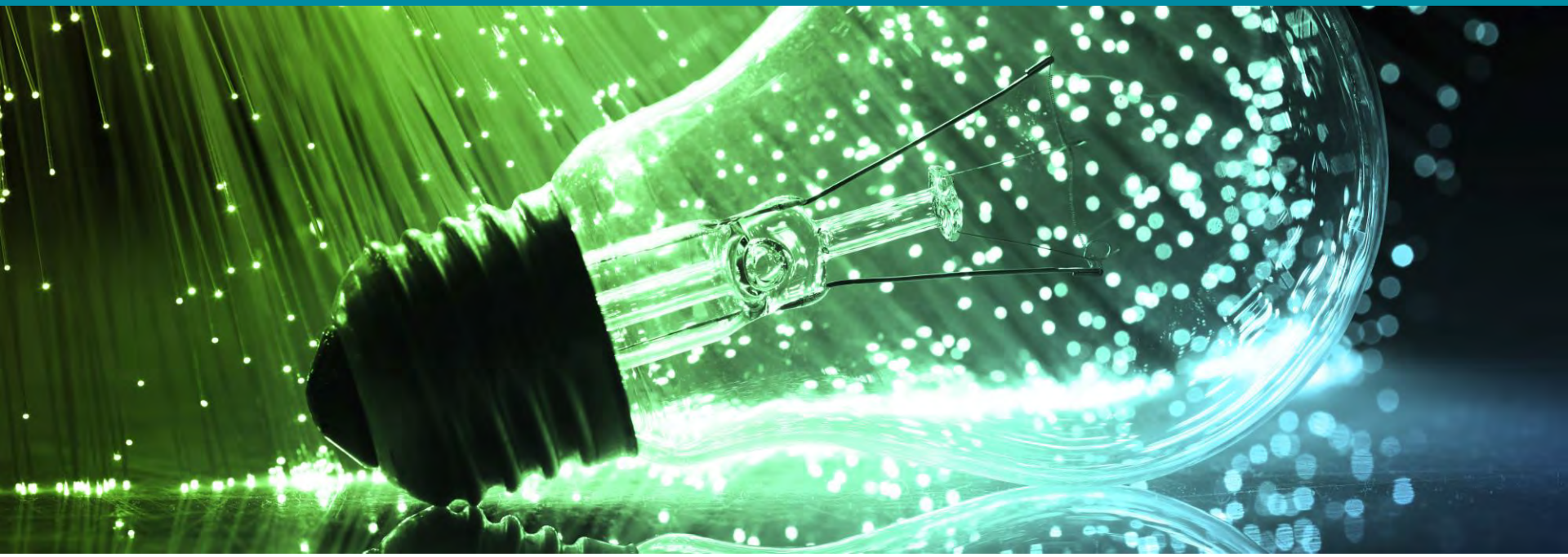
Key Assumptions

- ***First***, it is recognized that all clinical trials are unique. Therefore, a "one-size-fits-all" approach to recruitment is likely not possible.
- ***Second***, context is important.
- ***Third***, recruitment is an iterative process that involves multiple stakeholders in developing and reviewing plans.
- ***Fourth***, better recruitment planning should, in turn, lead to improved retention
- ***Finally***, the CTTI Recruitment Project Team believes that there is a critical need to look at all phases of the drug and device development continuum through a patient-centered lens and to incorporate the needs, preferences, and values of patients into the design of trial questions, development of clinical protocols, and dissemination of results.



Session III: Trial Design & Protocol Development

Beth Mahon (Janssen)

Disclaimer:
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Trial Design and Protocol Development

Points of Consideration for Improving Recruitment Through Effective Trial Design and Protocol Development

Clinical Trial Recruitment Planning Continuum

Study Question Development:
- Engage all stakeholders
- Addressing an unmet need
- Meaningful & relevant

Trial Feasibility Analysis
- Disease prevalence
- Market data
- Patient Pathway Mapping
- Modeling & Metrics

Recrutiment Communication Planning
- Engage stakeholders, partners, audience(s)
- Have a mission & vision

Plan Implementation
- Pilot test
- Deploy multiple tactics over time
- Monitor their effect
- Return to stakeholders for advice

Protocol Design & Complexity
- Broaden I/E criteria
- Minimize burden
- Data parsimony

Site Selection
- Evidence-based
- Performance & Efficiency metrics
- Competing trials
- Location in relation to pts

Budgeting
- Determine trade-offs between time & costs
- Determine what resources will be needed & when

Process & Performance Evaluation
- Define success metrics
- Analyze & monitor for impact
- Test & share results & best practices

The Rationale

- CTTI's Quality By Design Recommendations
  - Determine which study activities are key to maintaining subject safety while providing credible study results
  - Consider elimination of non-essential activities to simplify conduct, improve efficiency, and better target resources.
- Well designed effectively planned study trial arises from
  - Sound medical and biostatistical principles
  - Appropriate site selection
  - ***Effective recruitment planning***

Engage *all* stakeholders as real partners in the process

- Obtain and incorporate input and feedback on ***all*** of the following steps. Include patients, investigators, sponsors/funders, sites, key opinion leaders, and providers on your advisory/concept/steering committee.

Ensure the Relevance of the Scientific Question

- Jointly determine the relevance of the scientific question, including whether there is an unmet need, the endpoints and outcomes are relevant to the patients living with the disease and the providers who treat them and whether the question is broad enough to be generalizable to a wider population (when appropriate). Confirm that the scientific question is relevant outside of the study team.

Optimize Protocol Design & Limit Complexity

- Limit procedures and visits to those necessary to answer the scientific question and protect the safety of participants; consider the impact of the invasiveness and risk of procedures and the length and frequency of visits on recruitment. Limit exploratory endpoints that may impact enrollment and the regulatory and logistical burden on sites.

Develop Realistic Eligibility Criteria

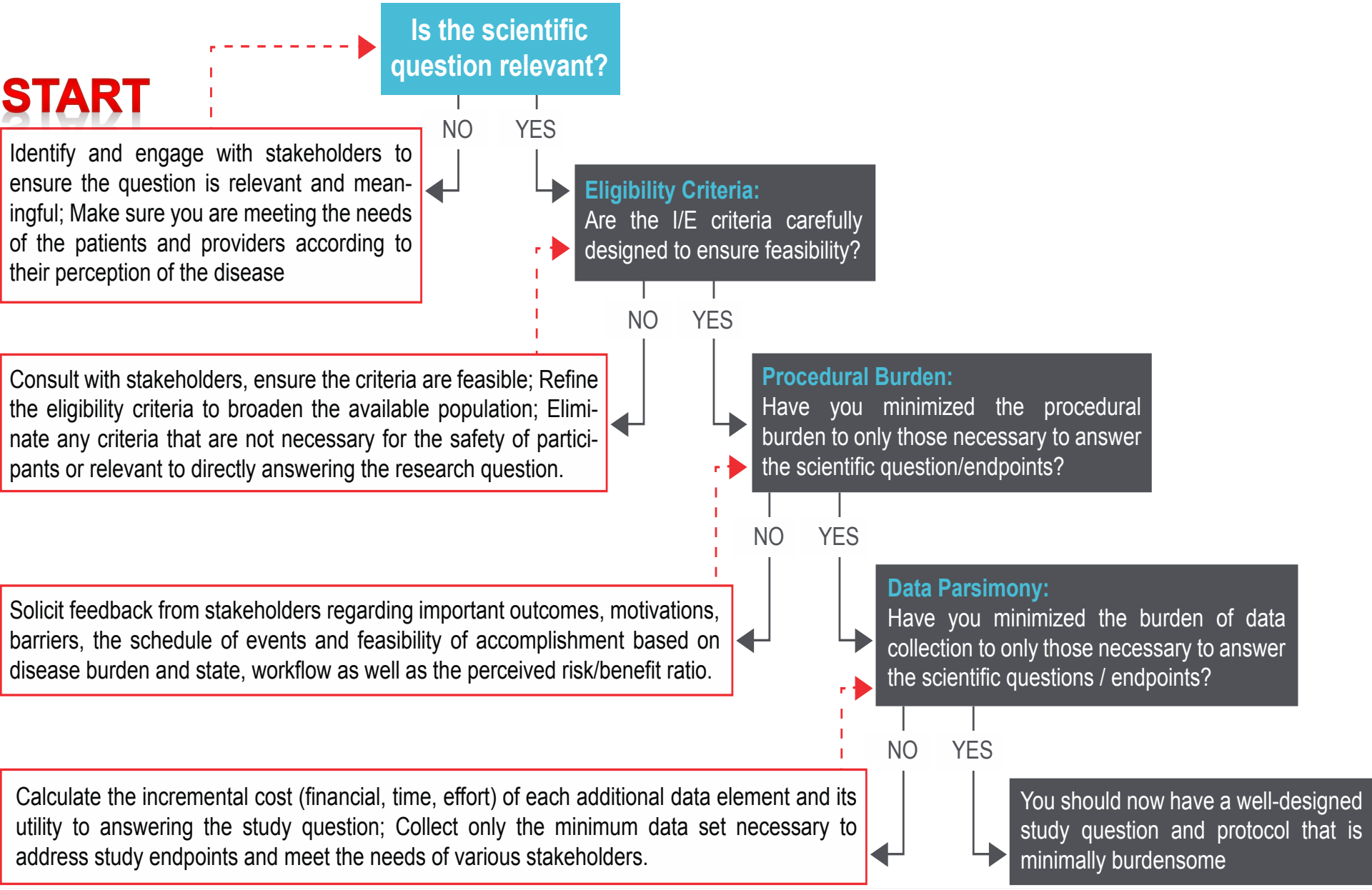
- Eliminate any criteria that are not necessary for the safety of participants or directly relevant to answering the research question. Consider the enrollment impact of various criteria including age restrictions, time since diagnosis, previous lines of therapy/treatment, comorbidities and current medications.

Minimize Procedural Burden

- Minimize study procedures to only those necessary to maintain participant safety and answer the research question / endpoints. Eliminate any procedures that are not essential to safety or study objectives and consider alternatives to main site visits (remote visits, telehealth, phone or home visits).

Optimize Data Collection (Data Parsimony)

- Identify the data points necessary to address the primary and secondary objectives and which are exploratory only. Collect only those data points necessary to maintain participant safety and answer the scientific question / endpoints.


START
Is the scientific question relevant?
NO
YES
Identify and engage with stakeholders to ensure the question is relevant and meaningful; Make sure you are meeting the needs of the patients and providers according to their perception of the disease
Eligibility Criteria:
Are the I/E criteria carefully designed to ensure feasibility?
NO
YES
Consult with stakeholders, ensure the criteria are feasible; Refine the eligibility criteria to broaden the available population; Eliminate any criteria that are not necessary for the safety of participants or relevant to directly answering the research question.
Procedural Burden:
Have you minimized the procedural burden to only those necessary to answer the scientific question/endpoints?
NO
YES
Solicit feedback from stakeholders regarding important outcomes, motivations, barriers, the schedule of events and feasibility of accomplishment based on disease burden and state, workflow as well as the perceived risk/benefit ratio.
Data Parsimony:
Have you minimized the burden of data collection to only those necessary to answer the scientific questions / endpoints?
NO
YES
Calculate the incremental cost (financial, time, effort) of each additional data element and its utility to answering the study question; Collect only the minimum data set necessary to address study endpoints and meet the needs of various stakeholders.
You should now have a well-designed study question and protocol that is minimally burdensome

Thank you.

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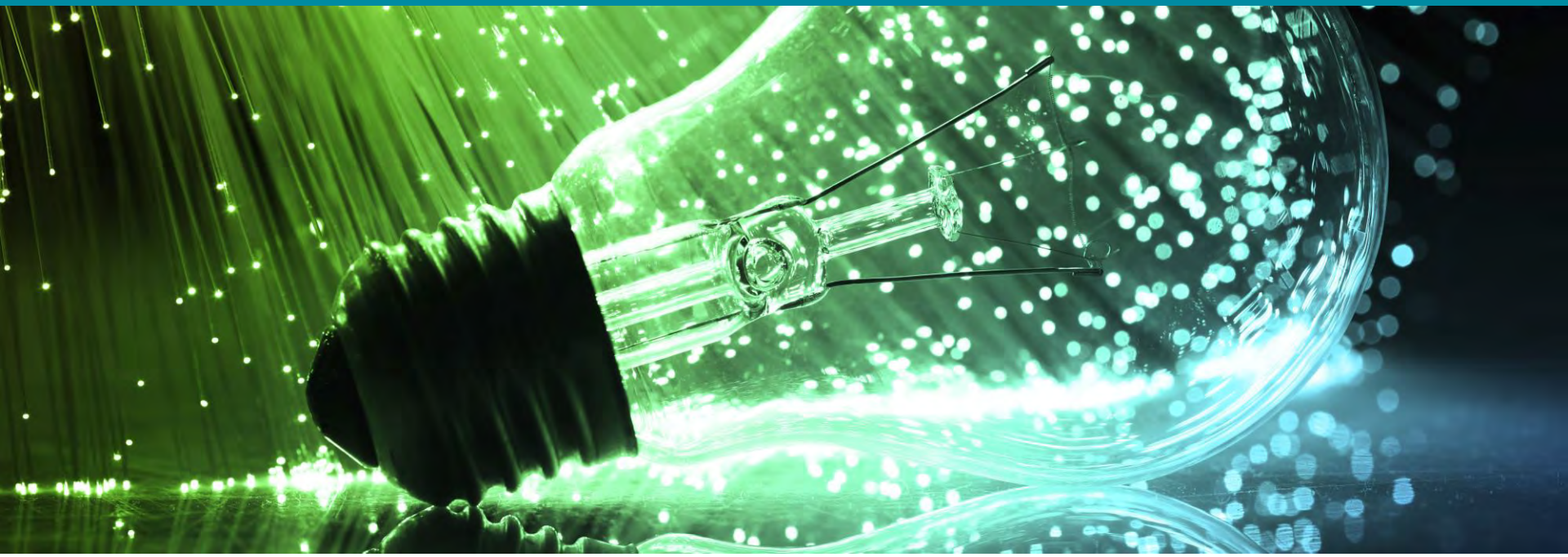
Elizabeth Mahon, JD

Janssen



Session III: Trial Feasibility & Site Selection

Beth Harper (Clinical Performance Partners, Inc.)

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Trial Feasibility & Site Selection

Points of Consideration for Improving Recruitment Through Effective Trial Feasibility & Site Selection Planning

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Three Keys to Successful Recruitment

- Realistic, data-driven feasibility assessments
- Thoughtful selection of sites
- Setting clear expectations with ongoing performance monitoring
- Mechanisms to provide appropriate feedback

Clinical Trial Recruitment Planning Continuum

Study Question Development:
- Engage all stakeholders
- Addressing an unmet need
- Meaningful & relevant

Trial Feasibility Analysis
- Disease prevalence
- Market data
- Patient Pathway Mapping
- Modeling & Metrics

Recrutiment Communication Planning
- Engage stakeholders, partners, audience(s)
- Have a mission & vision

Plan Implementation
- Pilot test
- Deploy multiple tactics over time
- Monitor their effect
- Return to stakeholders for advice

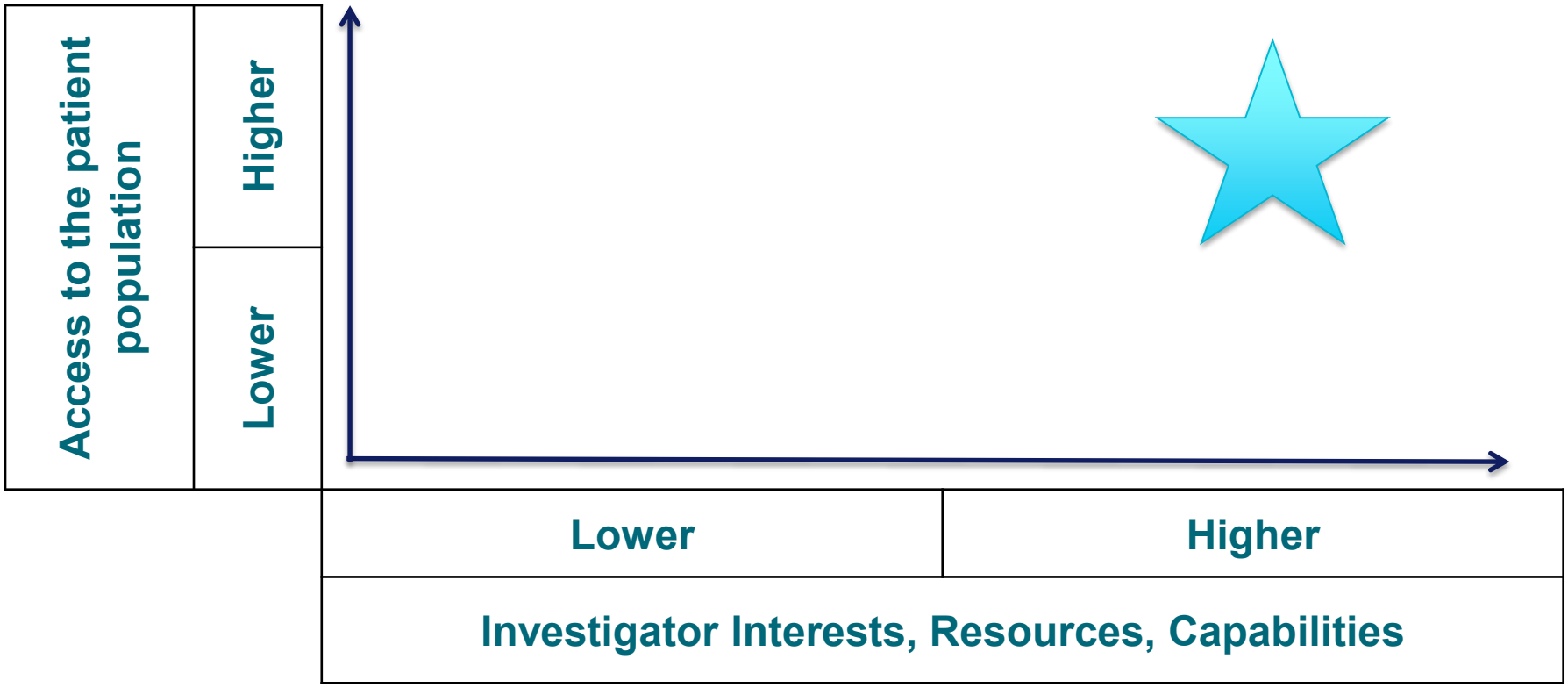
Protocol Design & Complexity
- Broaden I/E criteria
- Minimize burden
- Data parsimony

Site Selection
- Evidence-based
- Performance & Efficiency metrics
- Competing trials
- Location in relation to pts

Budgeting
- Determine trade-offs between time & costs
- Determine what resources will be needed & when

Process & Performance Evaluation
- Define success metrics
- Analyze & monitor for impact
- Test & share results & best practices

The Rationale



Identifying sites that are able to meet the trial's enrollment goals is critical to successful recruitment.

Critical Success Factors for Site Selection & Enrollment Management

The Recommendations - Overview

- **Proactively considering trial feasibility and site selection issues early in development and as a crucial part of recruitment planning will alleviate downstream recruitment and retention challenges**
- **5 Core recommendations**
  - Conduct an Evidence-Based Trial Feasibility Analysis
  - Establish Realistic Metrics and Milestones
  - Develop an Adequate Budget and Resources
  - Ensure Appropriate Site Selection
  - Engage in Suitable Site Performance Monitoring

Conduct an Evidence-Based Trial Feasibility Analysis

- Conduct formative research to ensure the logistical, motivational and behavioral barriers to participation for patients, their caregivers and providers/investigators are understood.
- Environmental scan / SWOT analysis to ensure understanding of how the environment (competition, policy, seasonal fluctuations, awareness, disease stage and rarity, and economic concerns) will impact enrollment.

Establish Realistic Metrics & Milestones

- Set realistic expectations for completing enrollment to the study by anticipating key factors that will influence site activation, screening, and enrollment trajectories.
- Early, and well-researched, development of these scenarios will also inform what resources will be necessary to ensure the development of an adequate recruitment budget.
- Map out anticipated events, even if estimations are rough, to help planners identify potential pitfalls and bottlenecks.

Develop an Adequate Budget & Resources

- An initial recruitment budget should, at minimum, address the following: assuring the necessary time, resources and funds for efficient implementation of any recruitment strategies or tactics, with specific attention paid to site activation timelines and the projected (*realistic*) enrollment period)

Ensure Appropriate Site Selection

- Develop an ideal site profile that describes the necessary investigator experience and capabilities, site infrastructure and institutional resources, as well as access to the relevant target population.
- This will help sites identify appropriate studies in which they should participate, as well as identify appropriate sites to participate in your study.

Engage in Suitable Site Performance Monitoring

- Plan to meet with sites at regular intervals in order to discuss progress and develop and share specific, realistic and transparent expectations of performance.
- Engage with sites to determine what they need to support efficient and effective recruitment.

Discussion

- General thoughts, observations or questions about the proposed recommendations before we go into the panel discussion?

Thank you.

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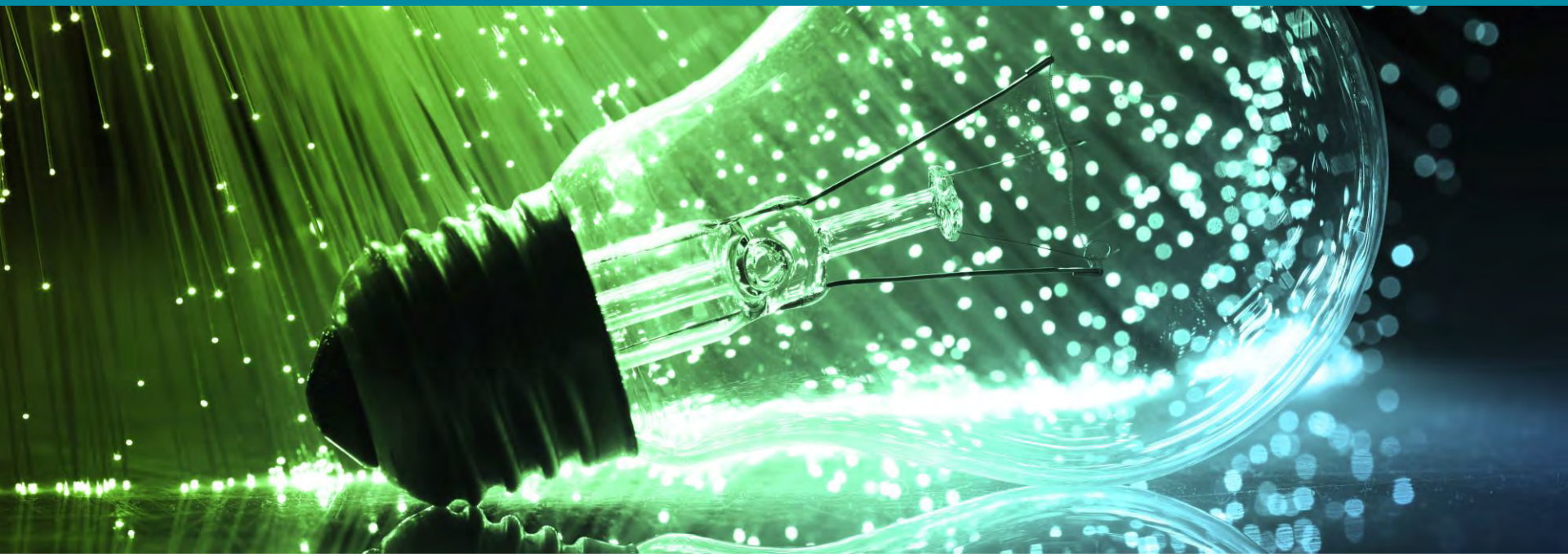
Beth Harper

Clinical Performance Partners, Inc.



Session III: Recruitment Communication Planning

James Kremidas (ACRP)

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Recruitment Communication Planning

Points of Consideration for Improving Recruitment Through Effective Recruitment Communication Planning

Clinical Trial Recruitment Planning Continuum

Study Question Development:
- Engage all stakeholders
- Addressing an unmet need
- Meaningful & relevant

Trial Feasibility Analysis
- Disease prevalence
- Market data
- Patient Pathway Mapping
- Modeling & Metrics

Recrutiment Communication Planning
- Engage stakeholders, partners, audience(s)
- Have a mission & vision

Plan Implementation
- Pilot test
- Deploy multiple tactics over time
- Monitor their effect
- Return to stakeholders for advice

Protocol Design & Complexity
- Broaden I/E criteria
- Minimize burden
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Site Selection
- Evidence-based
- Performance & Efficiency metrics
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Budgeting
- Determine trade-offs between time & costs
- Determine what resources will be needed & when

Process & Performance Evaluation
- Define success metrics
- Analyze & monitor for impact
- Test & share results & best practices

The Background

- Four key factors that drive the decision to participate in a clinical trial
  - ***Practical***
  - ***Emotional***
  - ***Environmental***
  - ***Logistical / Financial***

Identify & Engage All Stakeholders & Partners

- Identify and prioritize who the stakeholders are with whom you will need to communicate about the study, including (but not limited to) patients and their families/caregivers, patient advocacy organizations, providers and other healthcare professionals, and investigators and site staff.

Identify the Ideal Candidate Locations

- Identify where potential participants are located, from whom they seek treatment, where they seek information and the various patient pathways into the study so that barriers and bottlenecks may be identified and resolved or addressed.

Develop a Mission, Vision & Messages

- Develop statements that convey why the trial is being done, why the research question is important, to whom the answer will matter and what the value proposition for the participant is.

Develop Material & Select Appropriate Channels for Delivery

- Identify the best channels for reaching each of the target stakeholder groups by conducting formative research such as focus groups, social listening exercises and semi-structured interviews.

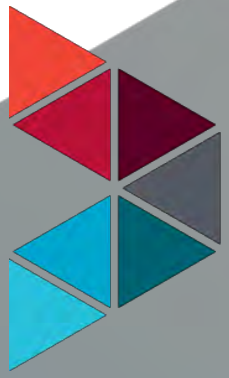
Develop a Realistic Communication Budget

- Develop budget plans early to ensure that recruitment costs are anticipated and covered. Determine the trade-off between time and costs (extra money spent on the front end of a study to ensure the communication strategy is well-researched and planned may be worth if it ensures a trial will finish on time (or early).

Monitor & Evaluate Both Process & Performance

- *Secure stakeholder buy-in*
- *Define measurable recruitment goals*
- *Identify metrics for each goal*
- *Define success for each metric*
- *Identify the required data for each metric*
- *Collect process and performance data*
- *Analyze*
- *Embed recruitment intervention studies into clinical trials and share your results* (good and bad) *and best practices*

Thank you.



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James Kremidas

ACRP

Session IV: Anticipated Implementation Challenges, Root Cause Analyses and Prioritization

Beth Harper
Jim Kremidas

November 9, 2015

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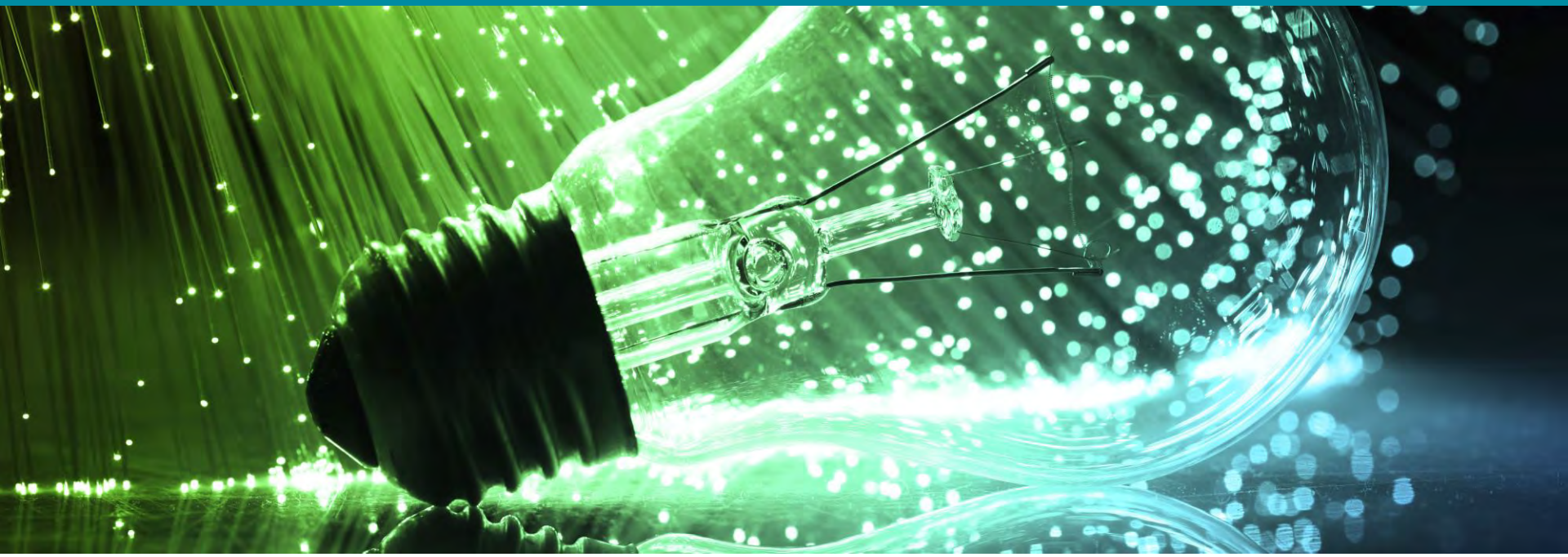

An Interactive Presentation and Discussion

Beth Harper (Clinical Performance Partners)
James Kremidas (ACRP)

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Overview

- Explore the potential challenges with implementing the recommendations
- Outline the key root causes contributing to difficulty implementing the recommendations
  - Introduction only…for further exploration tomorrow
- Solicit your input on the implementation challenges and prioritize these for Day 2 brainstorming
- Review process and expectations for Day 2

Re-Cap of The Draft Considerations

Trial Design and Protocol Development

- Engage *all* stakeholders as real partners in the process
- Ensure the Relevance of the Scientific Question
- Optimize Protocol Design and Limit Complexity
- Develop Realistic Eligibility Criteria
- Minimize Procedural Burden
- Optimize Data Collection

Trial Feasibility and Site Selection

- Conduct an Evidence-Based Trial Feasibility Analysis
- Establish Realistic Metrics and Milestones
- Develop an Adequate Budget and Resources
- Ensure Appropriate Site Selection
- Engage in Suitable Site Performance Monitoring

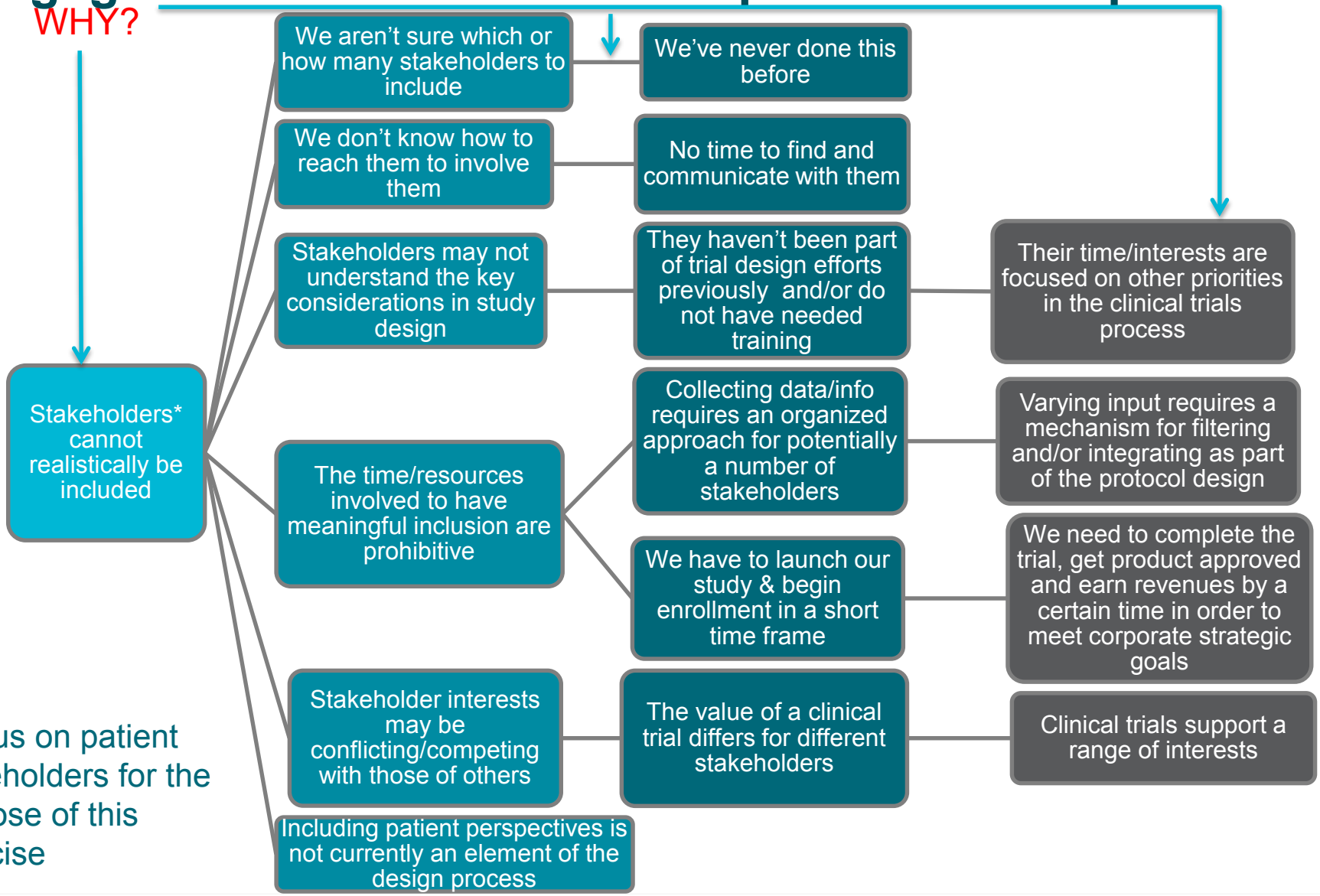
Recruitment Communication Planning

- Identify All Stakeholders and Partners
- Identify the Ideal Candidate Profile
- Identify the Ideal Candidate Locations
- Develop a Mission, Vision and Messages
- Develop Material and Select Appropriate Channels for Delivery
- Develop a Realistic Communication Budget
- Monitor and Evaluate both Process and Performance

Why Might Implementation Be Difficult?

- 5-Why's Methodology was used to conduct initial root cause analysis
- A number of potential challenges were identified for each recommendation…likely there are more to uncover as well
- Illustrative examples

Engage *all* stakeholders as real partners in the process



*Focus on patient stakeholders for the purpose of this exercise

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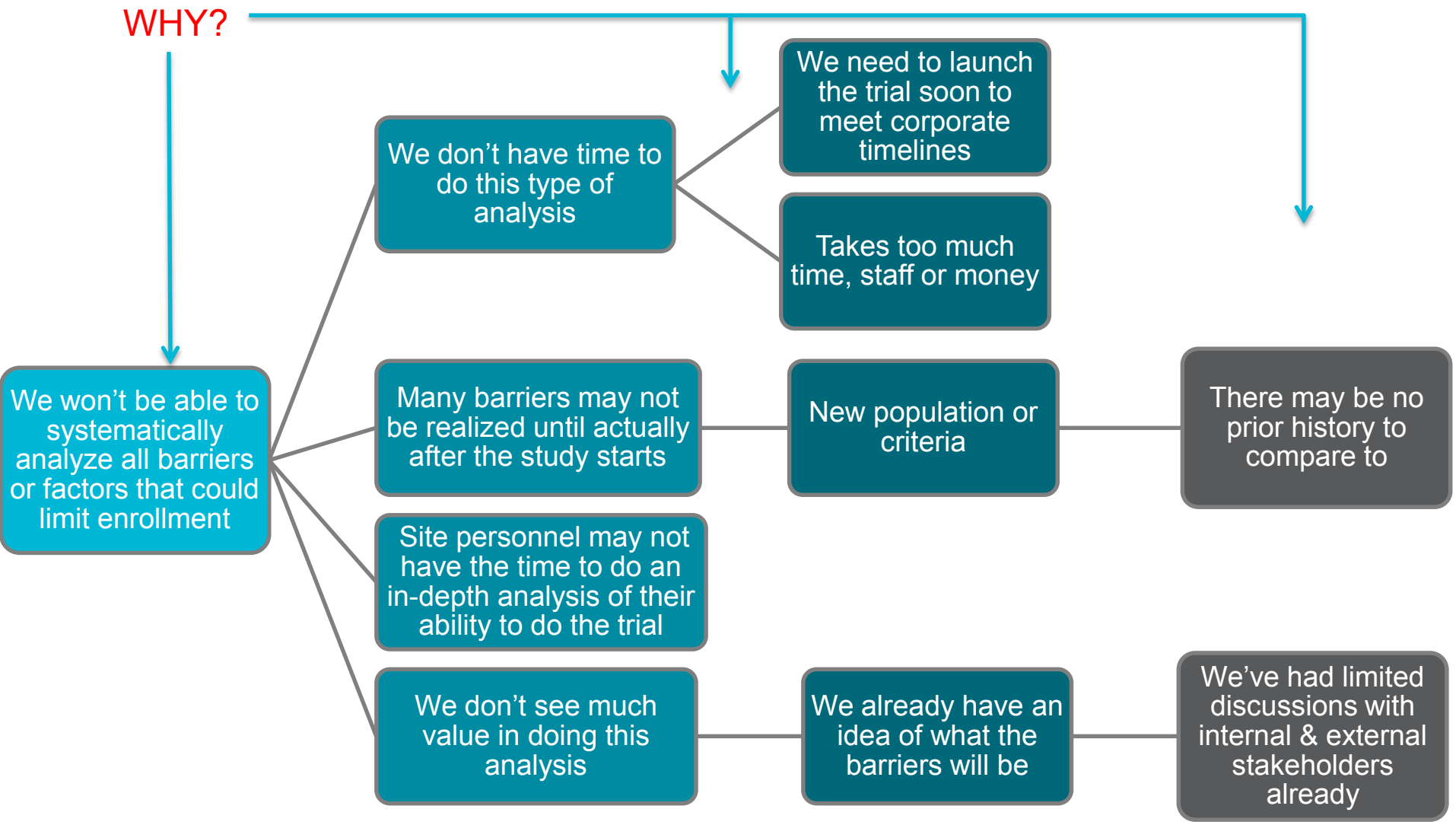
Conduct an Evidence-Based Trial Feasibility Analysis



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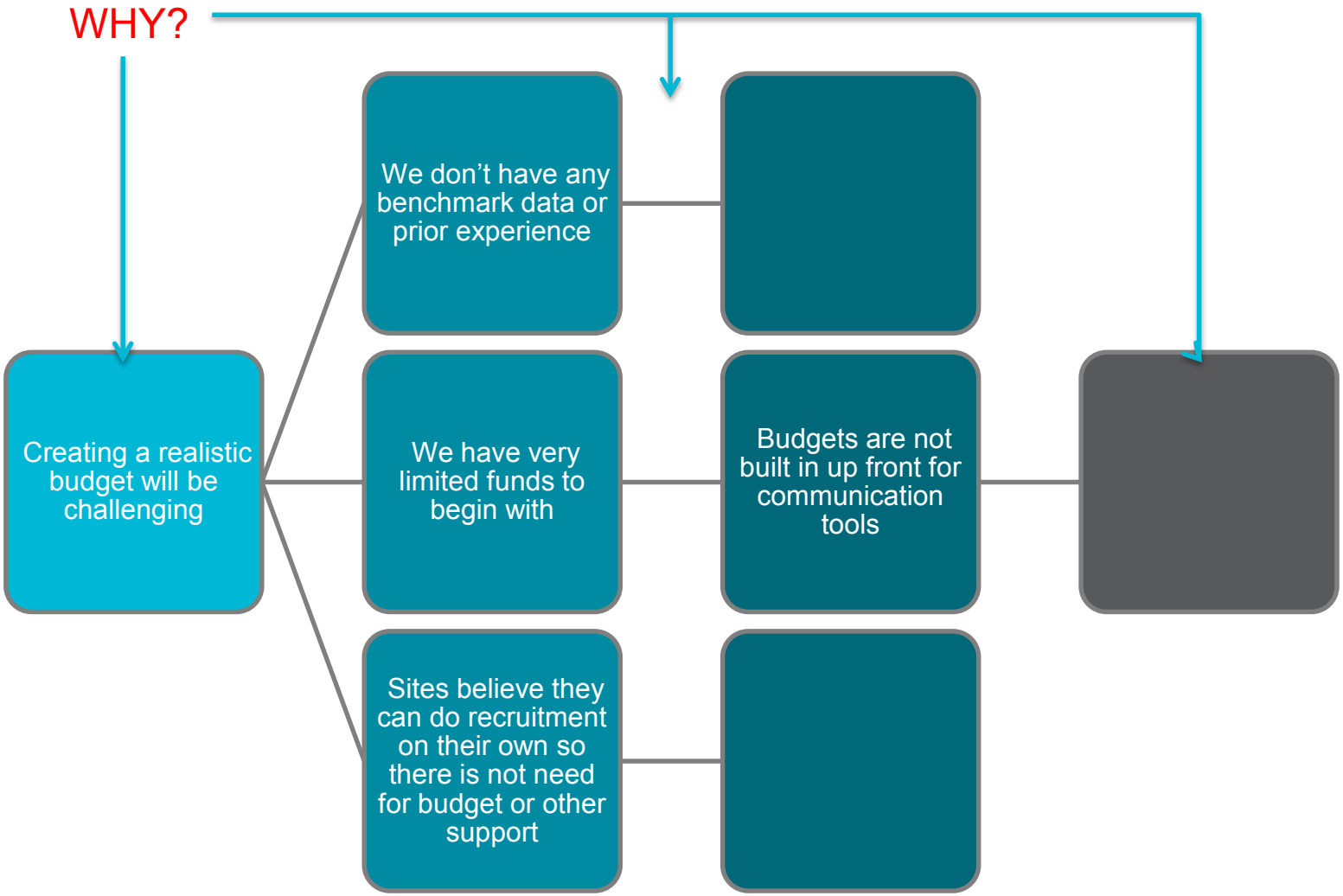
Develop a Realistic Communication Budget



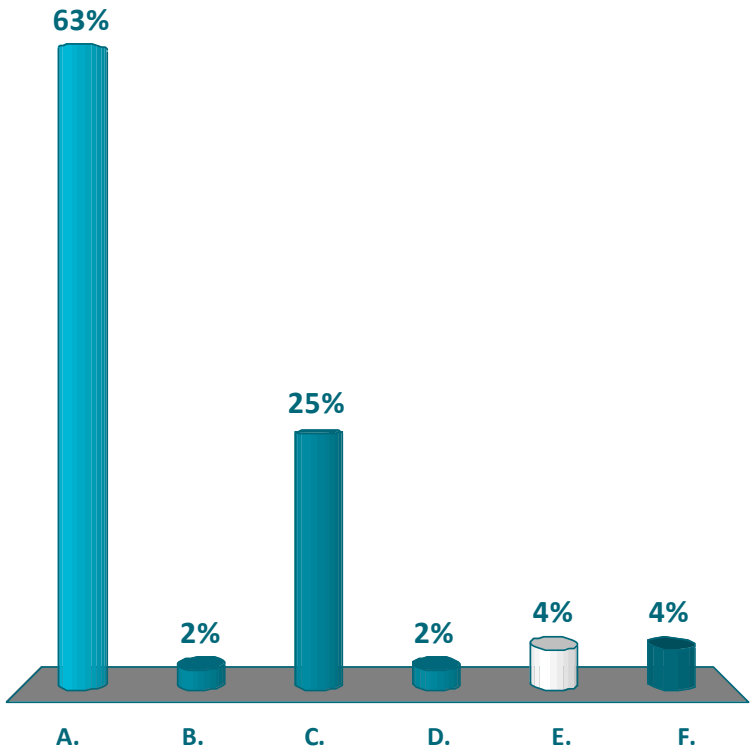
We Need Your Input!

- Audience Response Polling
- We will present the recommendations and ask you to indicate which will be the most challenging to implement
- We will take the top 2-3 challenges from each category and use these for our interactive problem solving session tomorrow

Trial Design and Protocol Development

Using your keypad please indicate which of the following recommendations you believe will be the MOST challenging to implement:

A. Engage all stakeholders as real partners in the process
B. Ensure the Relevance of the Scientific Question
C. Optimize Protocol Design and Limit Complexity
D. Develop Realistic Eligibility Criteria
E. Minimize Procedural Burden
F. Optimize Data Collection



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Survey Says…

- The 2 top recommendations that will be most difficult to implement are…

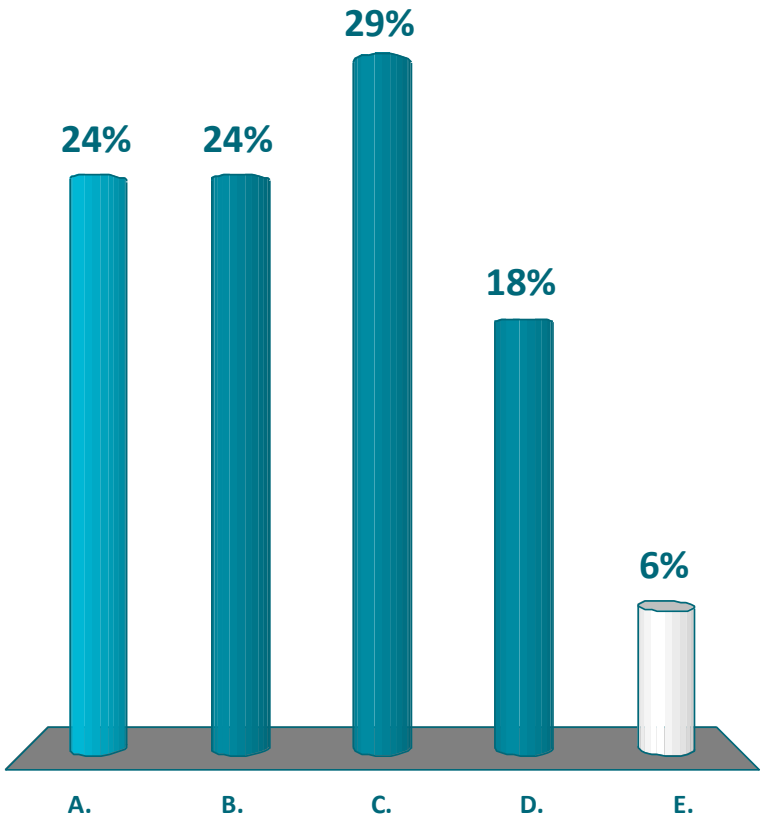
Engage *all* stakeholders as real partners in the process

Optimize Data Collection

Trial Feasibility and Site Selection

Using your keypad please indicate which of the following recommendations you believe will be the MOST challenging to implement:

A. Conduct an Evidence-Based Trial Feasibility Analysis
B. Establish Realistic Metrics and Milestones
C. Develop an Adequate Budget and Resources
D. Ensure Appropriate Site Selection
E. Engage in Suitable Site Performance Monitoring



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Survey Says…

- The 3 recommendations that will be most difficult to implement are…

Conduct an Evidence-Based Trial Feasibility Analysis

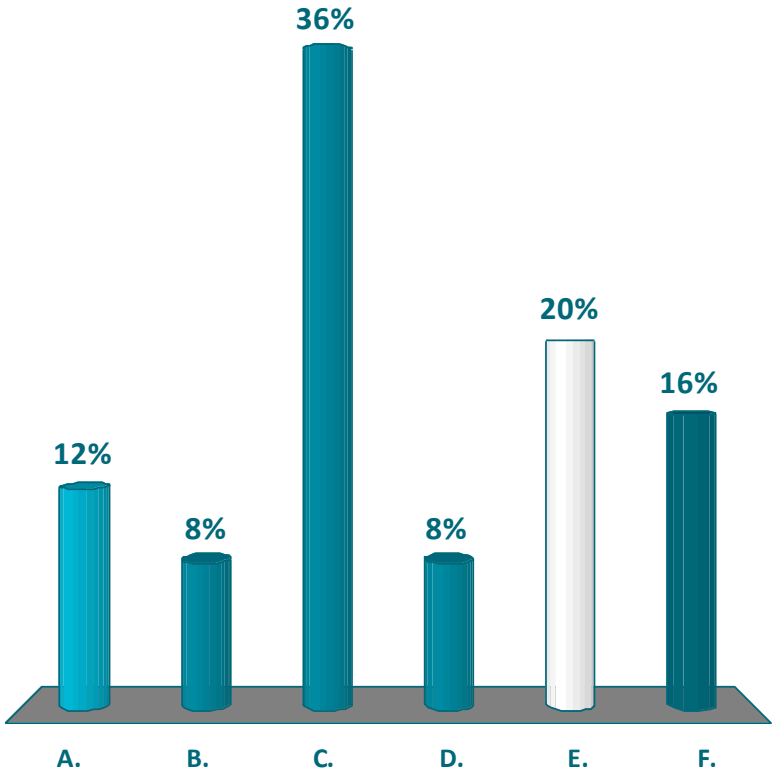
Establish Realistic Metrics and Milestones

Develop an Adequate Budget and Resources

Recruitment Communication Planning

Using your keypad please indicate which of the following recommendations you believe will be the MOST challenging to implement:

A. Identify All Stakeholders and Partners
B. Identify the Ideal Candidate Locations
C. Develop a Mission, Vision and Messages
D. Develop Material and Select Appropriate Channels for Delivery
E. Develop a Realistic Communication Budget
F. Monitor and Evaluate both Process and Performance



CTTI

Survey Says…

- The 3 recommendations that will be most difficult to implement are…

Develop a Mission, Vision and Messages

Develop a Realistic Communication Budget

Monitor and Evaluate both Process and Performance

Road Map for Day 2 Interactive Problem Solving

		Trial Design and Protocol Development	Trial Feasibility and Site Selection	Recruitment Communication Planning
~40 min	Implementation Challenge 1			
~40 min.	Implementation Challenge 2			
~40 min	Implementation Challenge 3			
	Report Out / Discussion	30 min.	30 min.	30 min.

You have been assigned to a group to provide you an opportunity to:

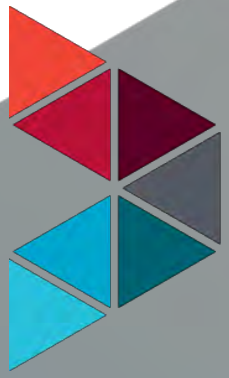
- Share your expertise
- Interact with other experts
- Brainstorm and problem solve

See you name tag for your group assignments

Discussion

- Are there any other thoughts or observations about the potential implementation challenges?
- Are there any questions related to the focus for the interactive problem solving sessions tomorrow?
- NOTE: We will remind you of your group assignments and the rotation schedule tomorrow!

Thank you.



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A New Framework for Innovation: Trial Recruitment as a Mechanism of Action

Joseph Kim

Sr. Advisor, Clinical Innovation, Eli Lilly and Company

November 9, 2015

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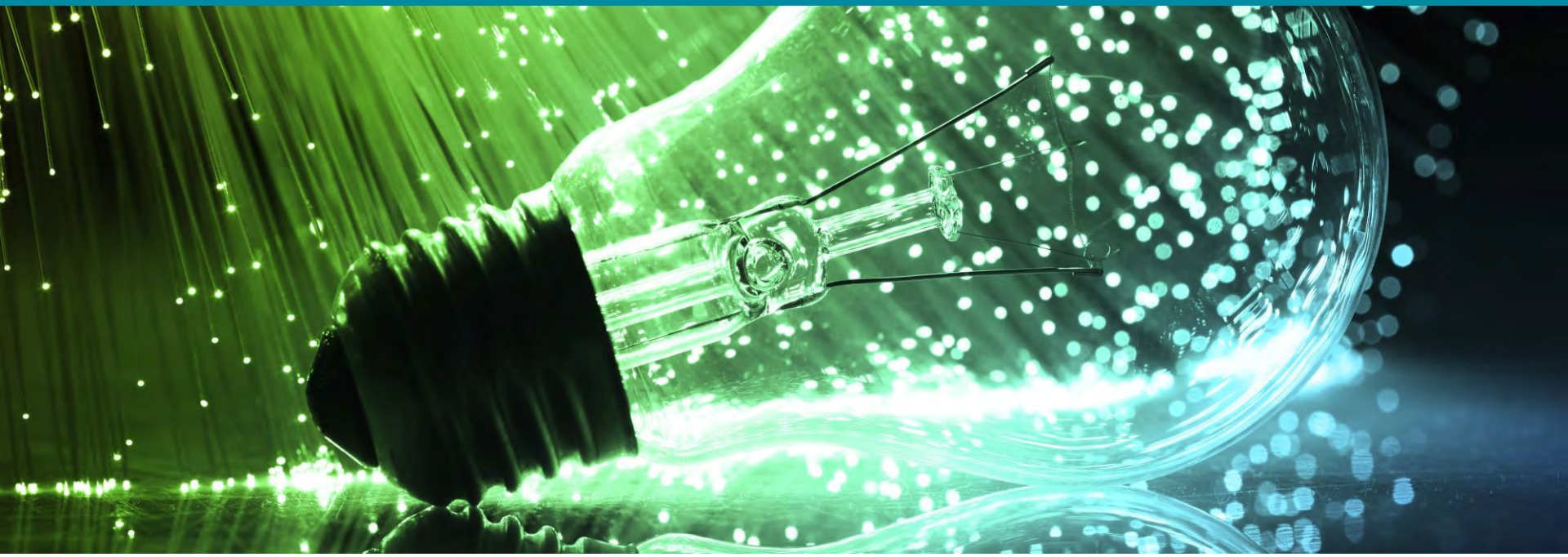

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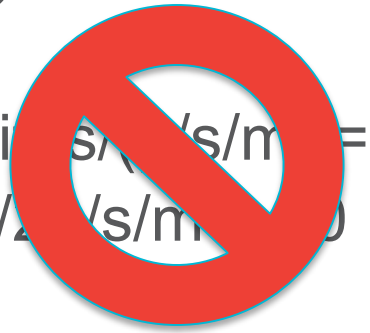
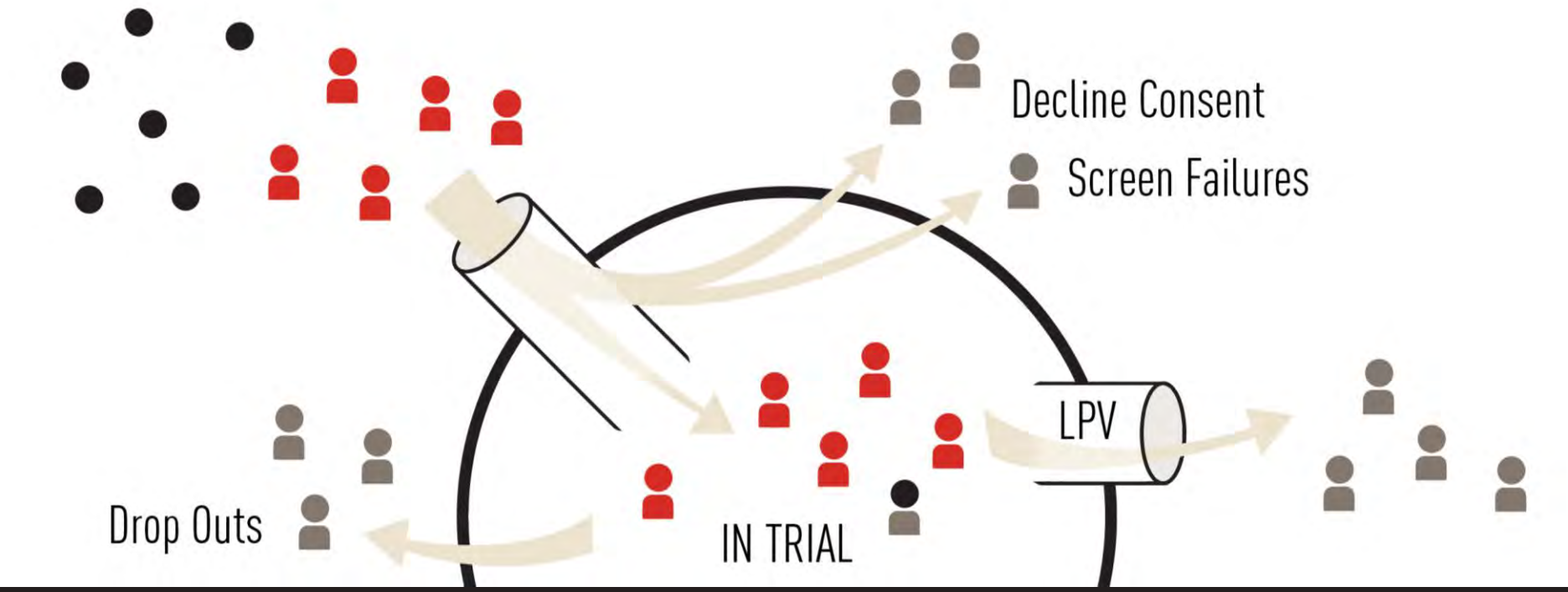
First, some basics

- Enrollment Planning
  - Algebra 1
    - # patients/# si[illegible]s/[illegible]/s/m[illegible] = enrollment cycle time
    - 100pts/5sites/[illegible]/s/m[illegible] months
  - Leading indicators, dependent variables
    - Site Ready Curve
    - Sites Actively Screening
    - Screening Rate
    - Screen Failure Ratio



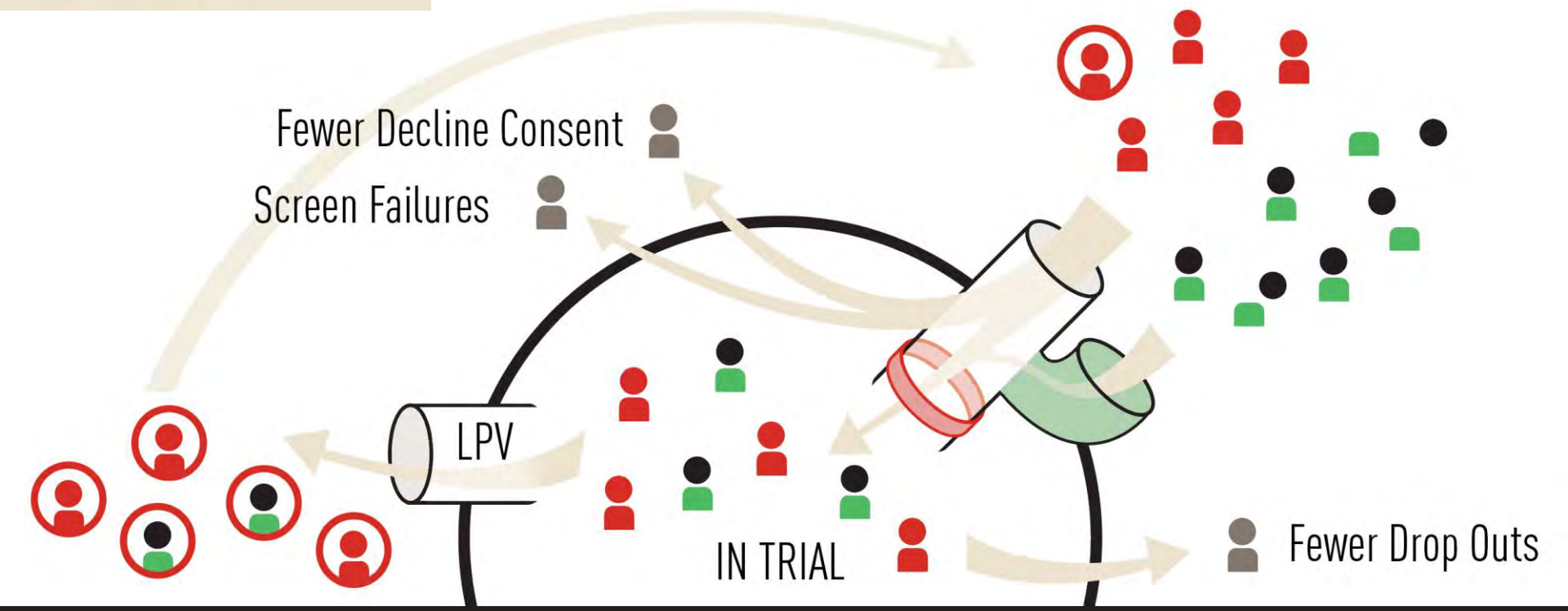
Mechanism of Action

Today



Mechanism of Action

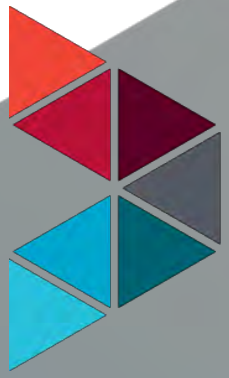
Tomorrow



What does it mean to be this patient?

RESEARCH ADVOCATE!

Thank you.



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Highlights & Wrap-Up

Kelly McKee
Merck

November 9, 2015

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Key Transformative Messages From Today

- We have defined the problems we face in study design, feasibility, site selection and recruitment with a very engaging group. Thank you!
- We have explored the problems identified and challenged our draft consideration, specifically in regards to emerging trends in:
  - Identifying the value proposition for sites and patients
  - Communication
  - Transparency
- We hear you! You want more:
  - Details
  - Profiles of studies, sites and patients
  - Instructions and customization

Clinical Trial Recruitment Planning Continuum

Study Question Development:
- Engage all stakeholders
- Addressing an unmet need
- Meaningful & relevant

Trial Feasibility Analysis
- Disease prevalence
- Market data
- Patient Pathway Mapping
- Modeling & Metrics

Recrutiment Communication Planning
- Engage stakeholders, partners, audience(s)
- Have a mission & vision

Plan Implementation
- Pilot test
- Deploy multiple tactics over time
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- Return to stakeholders for advice

Protocol Design & Complexity
- Broaden I/E criteria
- Minimize burden
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- Evidence-based
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Budgeting
- Determine trade-offs between time & costs
- Determine what resources will be needed & when

Process & Performance Evaluation
- Define success metrics
- Analyze & monitor for impact
- Test & share results & best practices

Game Plan for Day 2

- Root cause analyses of implementation challenges identified today
  - What if? Why not?
  - Interactive prioritizing
- Breakout sessions:
  - Brainstorming workable solutions
  - Identifying tools needed
  - Consensus building
- Dissemination Plans

- Kelly McKee
- Recruitment & Retention Team Leader
- kelly_mckee@merck.com

Establishing Engagement through Coordinated National Outreach

Ken Getz

Associate Professor, Tufts CSDD; Board Chair, CISCRP

November 10, 2015

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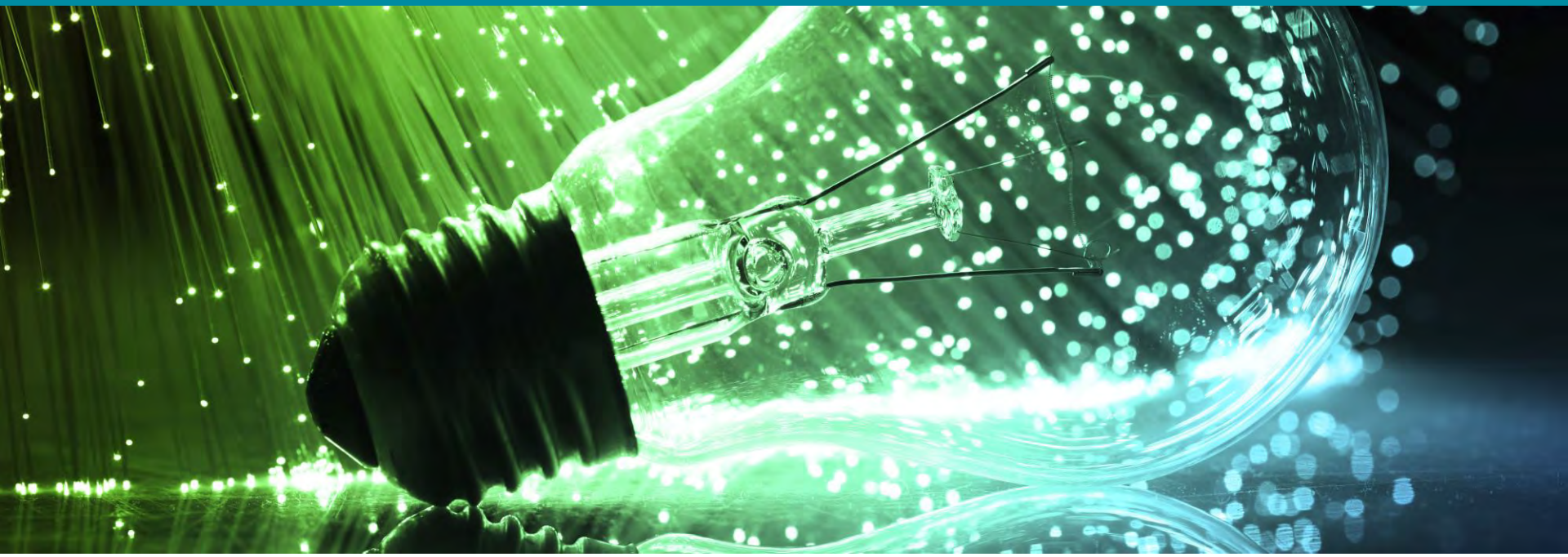

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Agenda

- A Critical Need for a National Outreach Campaign
- Positioning and Success Factors
- Concluding Remarks

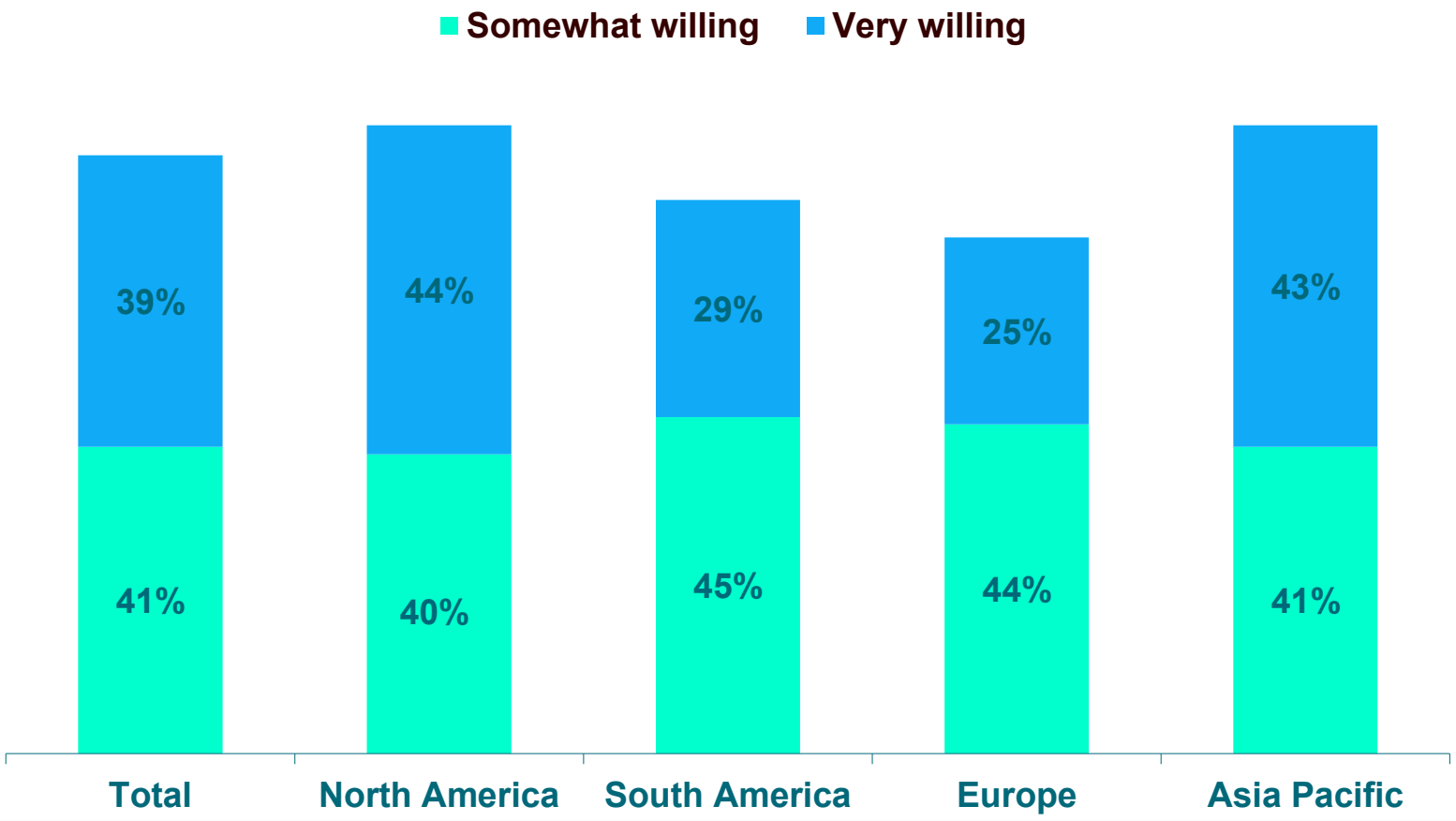
The Perennial Engagement Puzzle

High Willingness

=

Low Participation

How Willing are You to Participate in a Clinical Research Study?



Base: Total (n=12,009), North America (n=6,665), South America (n=877), Europe (n=2,618), Asia Pacific (n=1,302)

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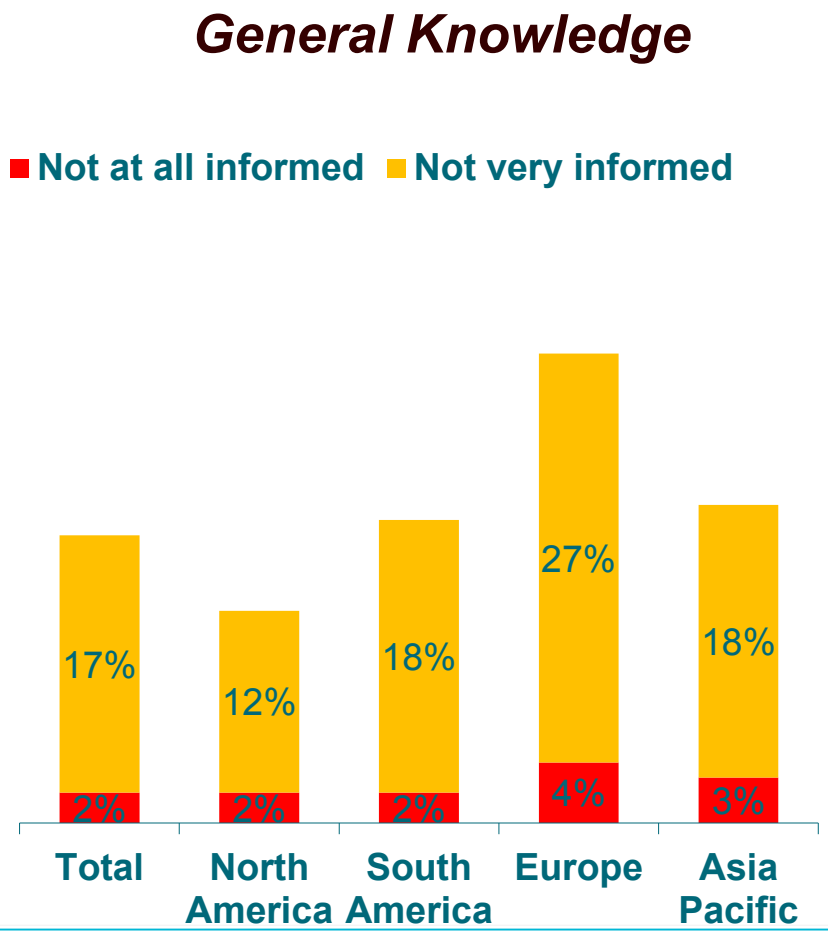
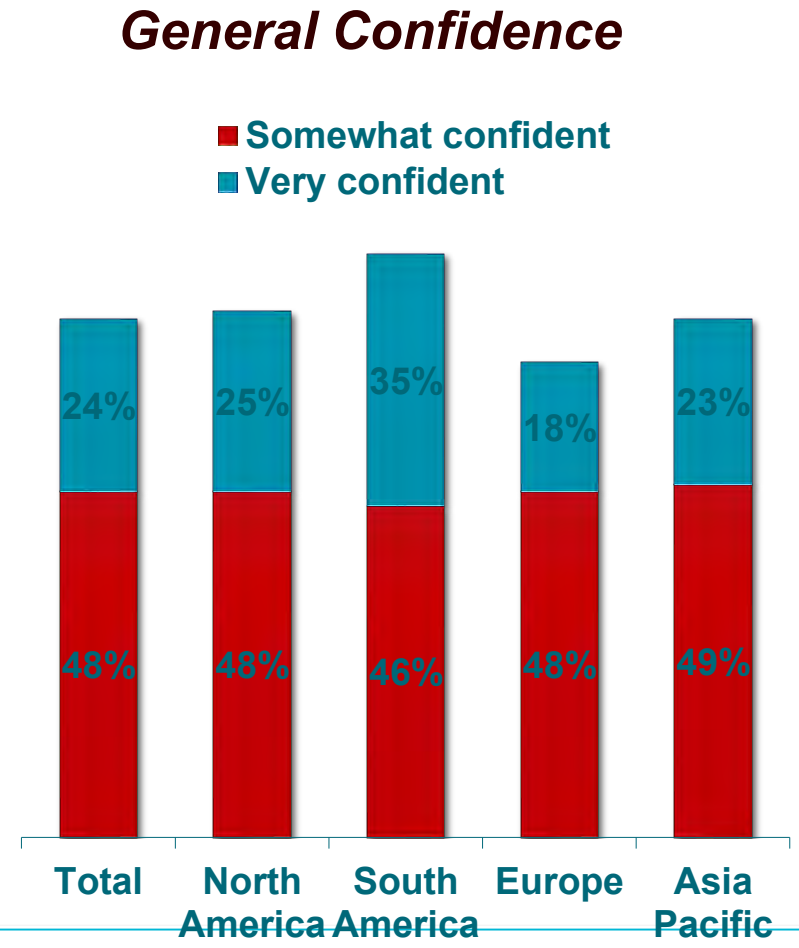
General Knowledge about, and Confidence in Finding, a Clinical Research Study





Base: All Respondents (n=12,009), North America (n=6,665), South America (n=877), Europe (n=2,618), Asia Pacific (n=1,302)

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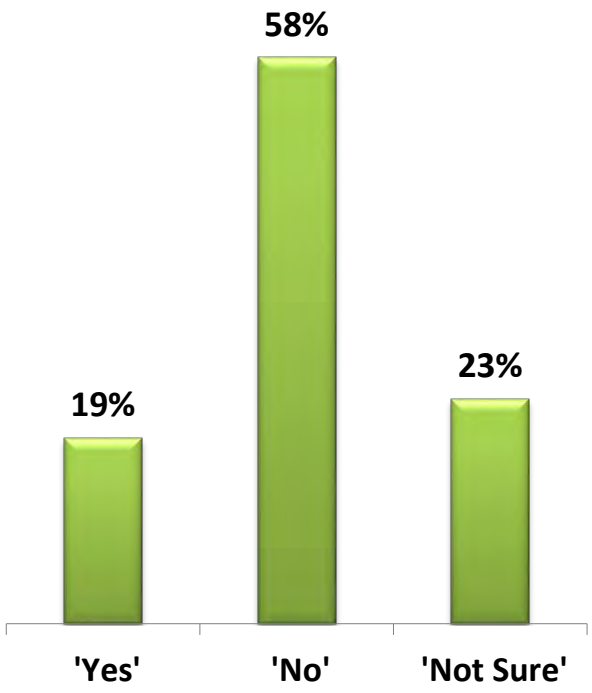
…But Limited Connection

Can You Name a Medical Research Scientist?



Where are Clinical Research Studies Conducted?

	OVERALL
Academic Medical Research Center	44%
Government Research Institute or Hospital	23%
Don't Know	26%
Private Physician's office	7%

Source: CISCRP 2013 N=5,701

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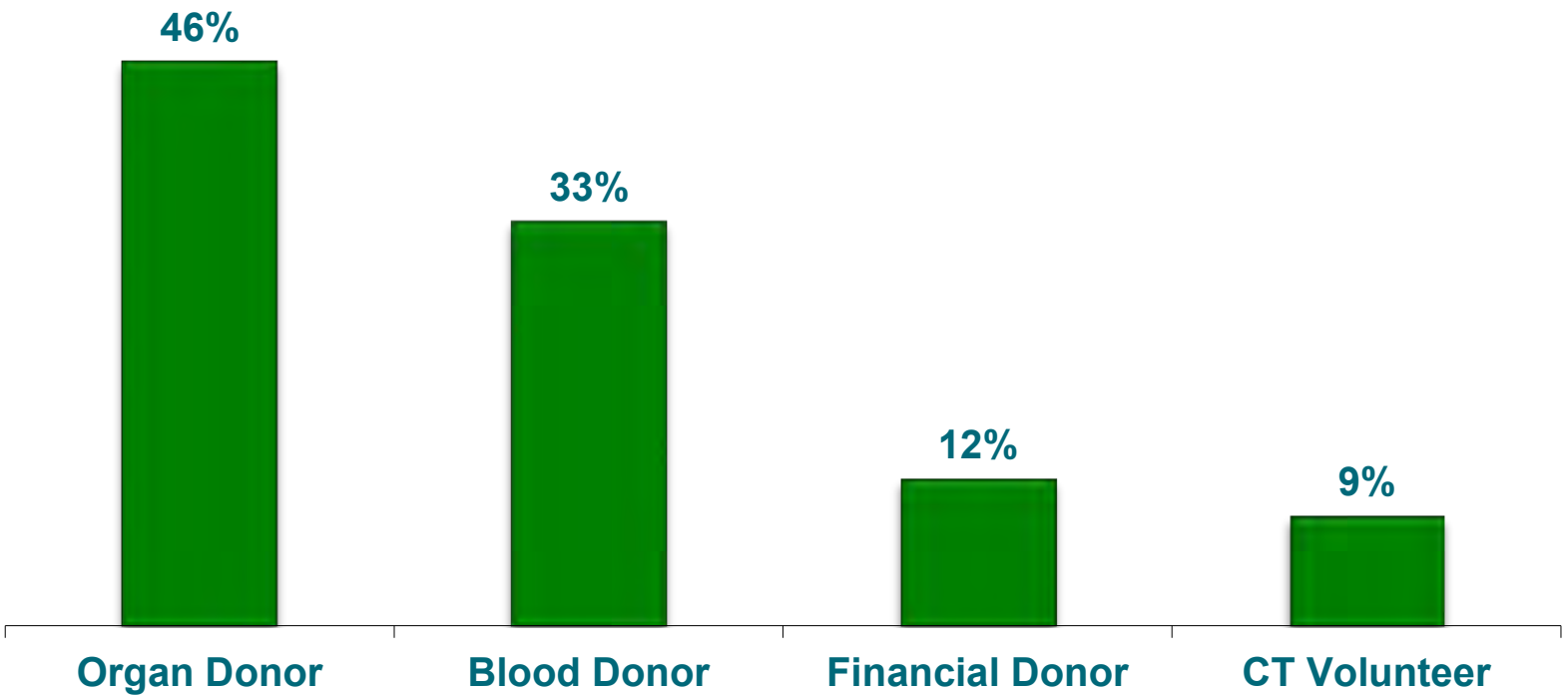
And Little Recognition and Appreciation

Who makes a greater contribution to human health?



Source: CISCRP 2013 N=5,701

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Historical National Outreach Campaigns

- Short term
- Uncoordinated
- Therapy and company specific
- Ad agency developed to support medical breakthroughs
- Not educational
- No ‘engagement’

An Early Engagement Campaign

- Multi-stakeholder developed
- Educational message designed to engender appreciation
- Relevance and Call-to-Action
- Single medium
- Limited budget

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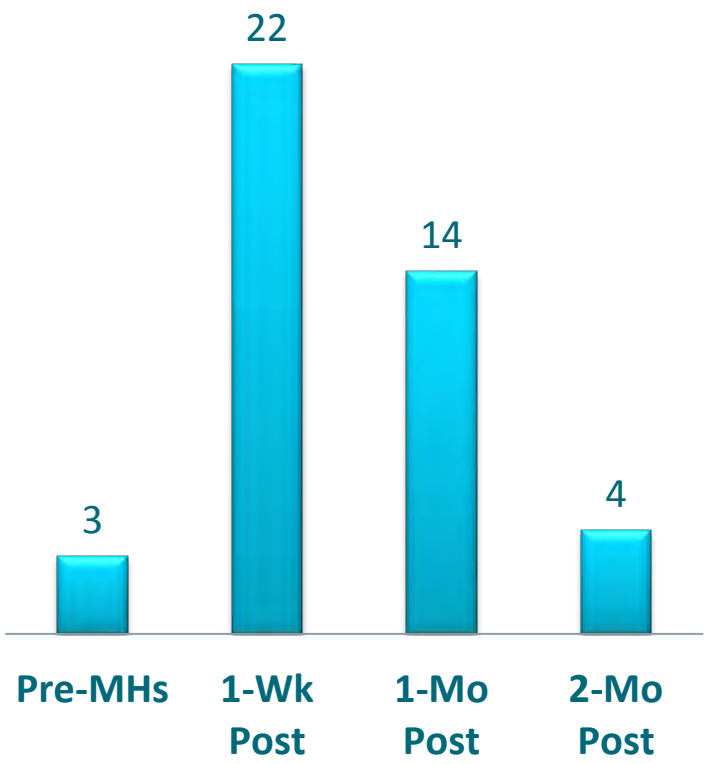
The Medical Heroes Campaign

- Multi-stakeholder Inputs
- Multimedia Formats
- Recognizable
- Continuity/Longevity
- Public education model
  - Not study specific
  - Addresses broader benefits of clinical research and the gift of participation
  - Provides a call to action
- Launched in 2007

Medical Heroes PSA IMPACT

Greater Pittsburgh Area (Ave. Number of CT Search Requests)



Pilot test involving two CNS studies; 30 sites across 18 markets throughout the US

Enrollment Rate in 12 Markets with Mass Media Patient Recruitment Ads Only	Enrollment Rate in 6 Markets with Mass Media Recruitment Ads in Conjunction with 'Everyday Heroes' Campaign	Improvement in Enrollment Rates from Concurrent Ad and Outreach Campaign Use
4.0 Patient/Month	9.6 Patients/Month	140%

Source: Eli Lilly & Company, 2009

Source: CISCRP, 2012

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Critical Success Factors

- Engagement through establishing personal relevance, connection, ownership and appreciation
- Enterprise-wide coordination
- Continuity
- Positioning cohesiveness and consistency
- Culturally sensitive and tailored educational messages

AWAREforAll

IMPACT

- Total number of AWARE events in major US cities between 2004 and 2014: 37
- Total attendees: 10,247
- Attendee Race/Ethnicity:
  - Black: 26%
  - Hispanic: 28%
  - White: 41%
- 71% Have Never Participated
- 31% of attendees follow-up with sites to learn more about participating

(Percentage who answered correctly)	Pre-Test	Post-Test
What is a clinical trial?	73%	83%
What is the role of the PI?	72%	84%
What is the role of the IRB?	36%	54%
What is the role of the FDA?	78%	86%
What is the informed consent process?	66%	80%
Why is a placebo used?	58%	87%
What is randomization?	48%	57%
What are the benefits of clinical trials?	46%	69%
What are the risks of clinical trials?	61%	89%
Where are trials conducted?	42%	91%

Source: CISCRP; N= 1,718 attendees

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Medical Heroes Science Museum Exhibit

- 1,000 sqft educational exhibit focusing on clinical research participation
- Traveling to science museums in 12 cities over three years
- Targeting elementary through high-school age children and their families
- Estimated reach: 1.1 MM visitors; 15 – 20 MM through media exposure
- Coordinated with local research and health professional communities; local school and health curricula

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Thank you.

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Founder and Board Chair, CISCRP
Director and Associate Professor, Tufts CSDD
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Kenneth.getz@tufts.edu

Game Plan: Breakout Sessions

- Jamie Roberts, CTTI

- November 10, 2015

Breakout Sessions

	Room	*Room*	*Room*
Challenge	Trial Design & Development *Grant Huang, Jonca Bull*	Trial Feasibility & Site Selection *Beth Harper, Claire Meunier*	Recruitment Communication Planning *Jim Kremidas, Kelly McKee*
1	Challenge	Challenge	Challenge
2	Challenge	Challenge	Challenge
3	Challenge	Challenge	Challenge

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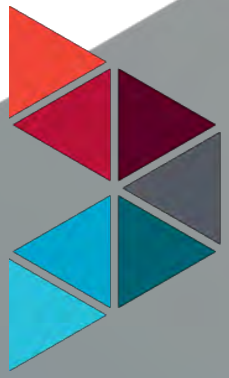
Buckminster Fuller's Challenge

You never change things by fighting the existing reality.
To change something, build a new model that makes the existing model obsolete.

Thank you.



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Disseminating the Recommendations

Matthew Harker, MPH, MBA
Associate Director of Projects, CTTI

November 10, 2015

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A Lesson From the Business World

What will be our strategy for achieving culture change?

SIGNIFICANCE

LEVEL OF EFFORT

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CTTI Dissemination Products

- Recommendations
  - Change (incremental vs. transformational)
  - Guidance/Direction (translation & consensus)
- Manuscripts & Industry Publications
- Tools (Online content) (Framework)
- Webinars (Content plus use cases)
- Website/Workshops/Packaged Materials
- Audience
  - Traditional users within the Clinical Trial Enterprise
  - Multi-stakeholder (meet in the middle)
    - Practical steps moving forward

Meetings Where CTTI Presents

Venue	Mission	Audience
DIA Drug Information Association	Education forum and convener, exhibition, knowledge exchange, networking	Sponsors, CROs, CRAs, researchers, more commercial than academic
SCT Society for Clinical Trials	Education, clinical trials research methodology and member networking	Academics and statisticians, data managers
BIO Biotechnology Organization	Biotechnology development, exhibition, investment, partnering, community. Includes bio other than medical	R&D investors, sponsors, CROs, trialists
PRIM&R Public Responsibility in Medicine and Research	Education, professional development, networking	IRB & human research protection professionals, Ethics
ACRP Association of Clinical Research Professionals	Education forum and convener, exhibition, knowledge exchange	R&D operations, vendors, research coordinators, CRAs, CEU focus

Other: ???, SCOPE, CTSA outreach

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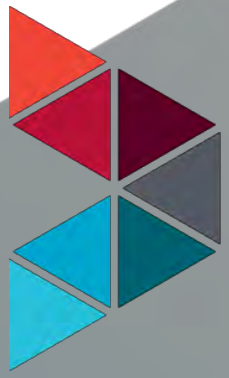
Diffusion of Information (Who, What, Where)

- Who do we need to reach?

- What are the best products to influence change?

- Where do they seek information?

Thank you.



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Taking Recruitment Planning to the Next Level: Where to from here?

Jamie Roberts, CTTI

November 10, 2015

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Change Isn't Easy

New ideas are always suspect, and usually opposed, without any other reason than because they are not already common.

John Locke

A journey of a thousand miles begins with a single step.

Lao Tzu

Being patient-focused is not limited to specific initiatives or programs for patients. ***It's a way of feeling, believing, thinking and acting****.*

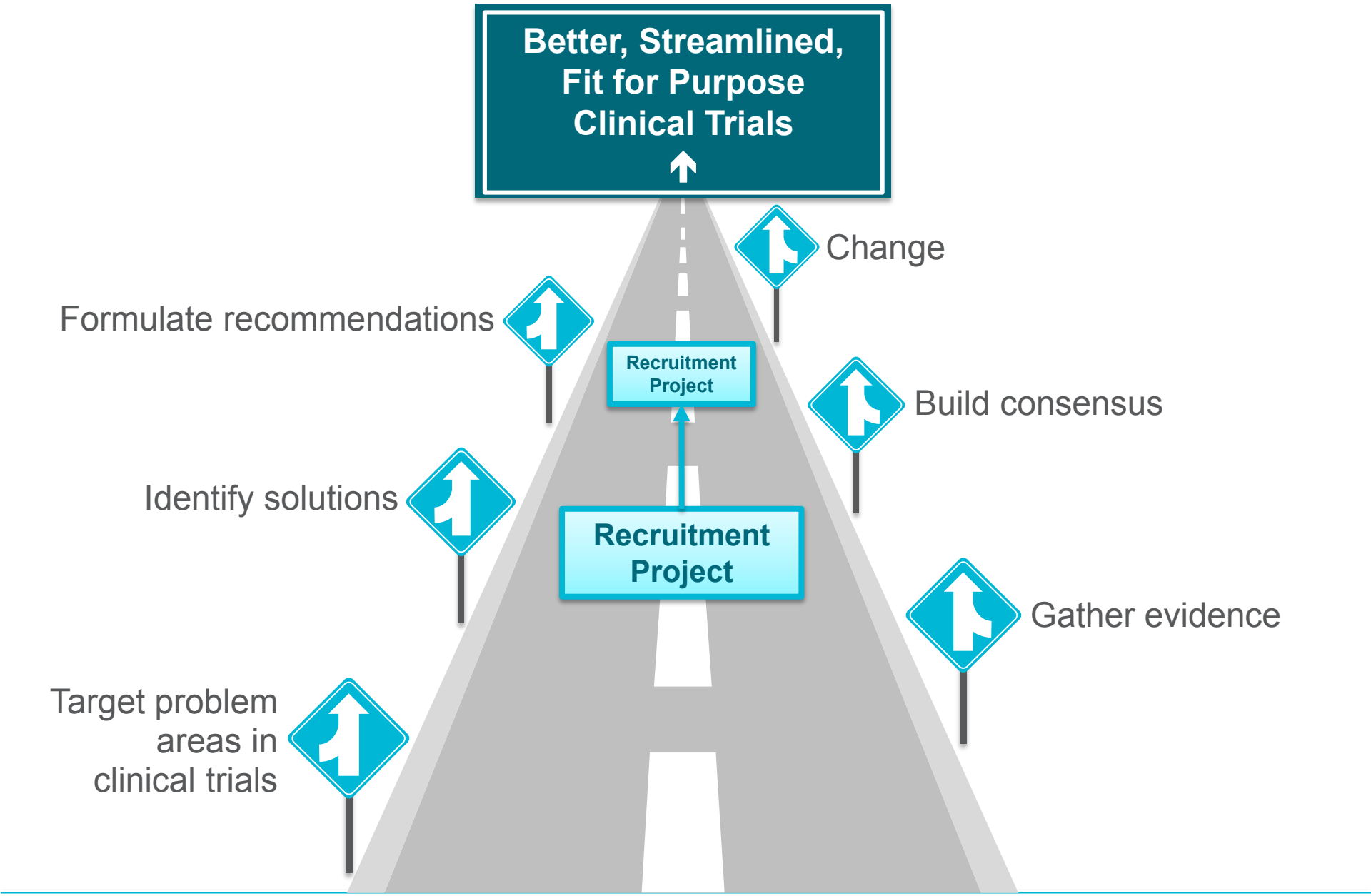
Jill Donahue

Have We Achieved Consensus?

- Key Messages
  - Identifying and engaging the ***right*** stakeholders is necessary to improved recruitment planning
  - Recruitment planning requires careful thought and consideration of the downstream effects of design elements and their burden
  - It's possible we can't afford not to spend the time and money up front to engage in appropriate recruitment planning.
    - We need to know what is the return on investment and how to demonstrate it.

Next Steps

- Review feedback
- Refine recommendations
- Build tools
- Obtain approval
- Disseminate


Better, Streamlined, Fit for Purpose Clinical Trials
Change
Formulate recommendations
Recruitment Project
Build consensus
Identify solutions
Recruitment Project
Gather evidence
Target problem areas in clinical trials

> **If patients are to be subjected to a protocol and accept the risk and burden of participation, that *protocol must be developed in partnership with patients or caregivers representative of the study population…* Additionally, to prevent recruitment and retention failures, no study or marketing application should move forward until a trial has been assessed by patients for feasibility and undergone a simulation exercise. The days of "our best guess" recruitment planning by people who've never organized and engaged a particular patient community must also come to an end. .. *Attempting to predict patients' values, preferences and comfort level with uncertainty as an intellectual or observer-reported exercise is preposterous. Patients and caregivers with lived experience must be the ones to speak for their own communities.***
>
> Bray Patrick-Lake

CTTI

Thank you.

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

Jamie Roberts