Introduction to the Clinical Trials Transformation Initiative

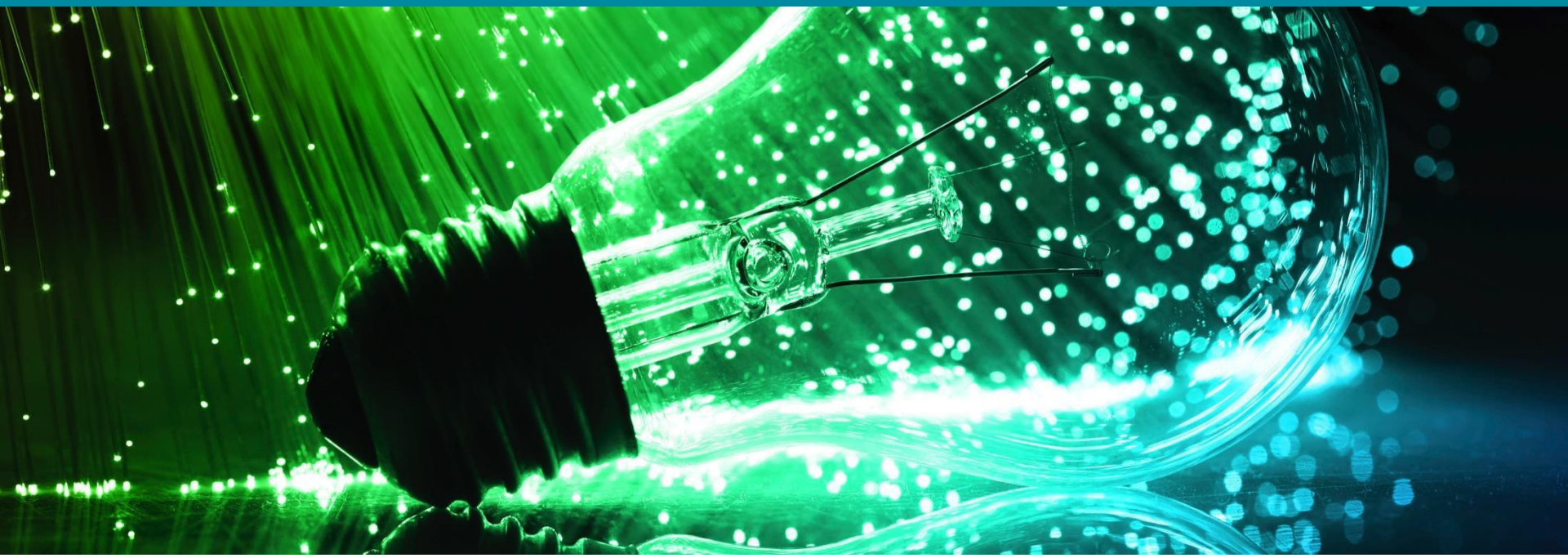
Pamela Tenaerts, MD, MBA
Executive Director
CTTI

May 19, 2016

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

Agenda

- **Welcome and Introduction to the Clinical Trials Transformation Initiative**
  - Pamela Tenaerts, CTTI
- **Project Overview**
  - Jonca Bull, FDA
- **Project Recommendations and Tools**
  - Beth Mahon, Janssen R&D
- **Discussion**



Disclaimer

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

One of the presenters is an employee of Duke University. Salary support comes from pooled membership fees of the Clinical Trials Transformation Initiative and from an FDA Cooperative Agreement.

Clinical trials in crisis

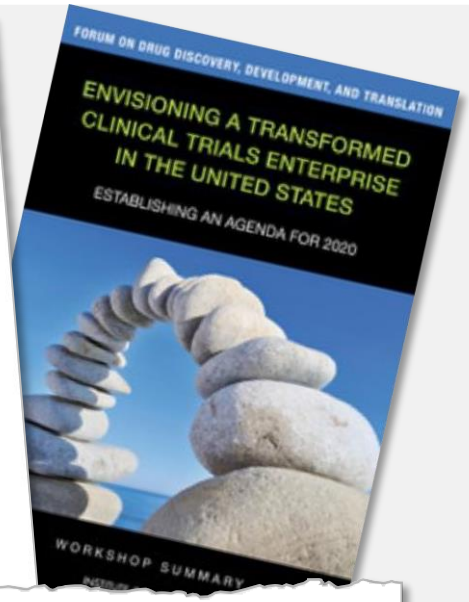
REPORT TO THE PRESIDENT

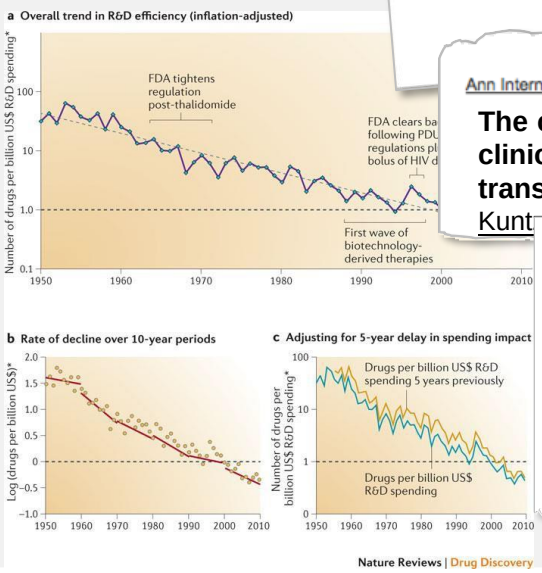
TRANSFORMATION AND OPPORTUNITY: THE FUTURE OF THE U.S. RESEARCH ENTERPRISE

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

Addressing This Need

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

To identify and drive adoption of practices that will
increase the quality and efficiency
of clinical trials

Public-Private Partnership
Co-Founded by FDA and Duke
involving all stakeholders
70+ members

CTTI Strategic Plan

MISSION STATEMENT

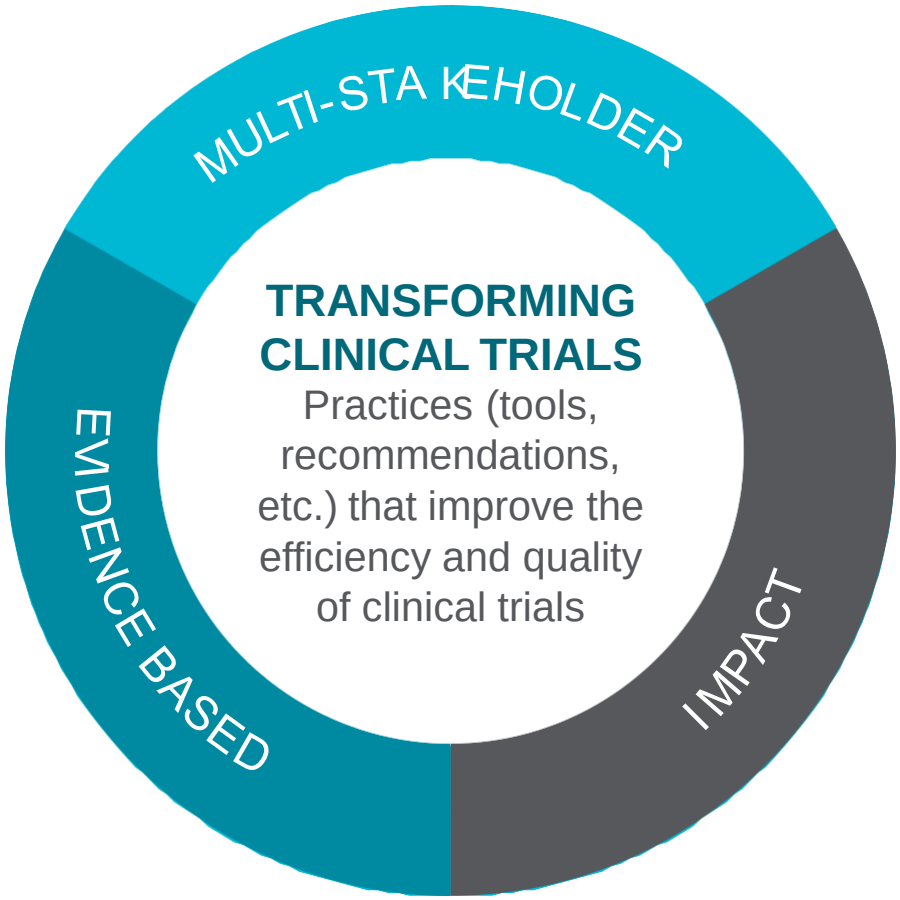
To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials

GOALS

Create recs & tools	Make data publicly available	Communicate broadly	Demonstrate impact	Characterize clinical trial landscape

AREAS OF STRATEGIC FOCUS

CTTI'S UNIQUE APPROACH



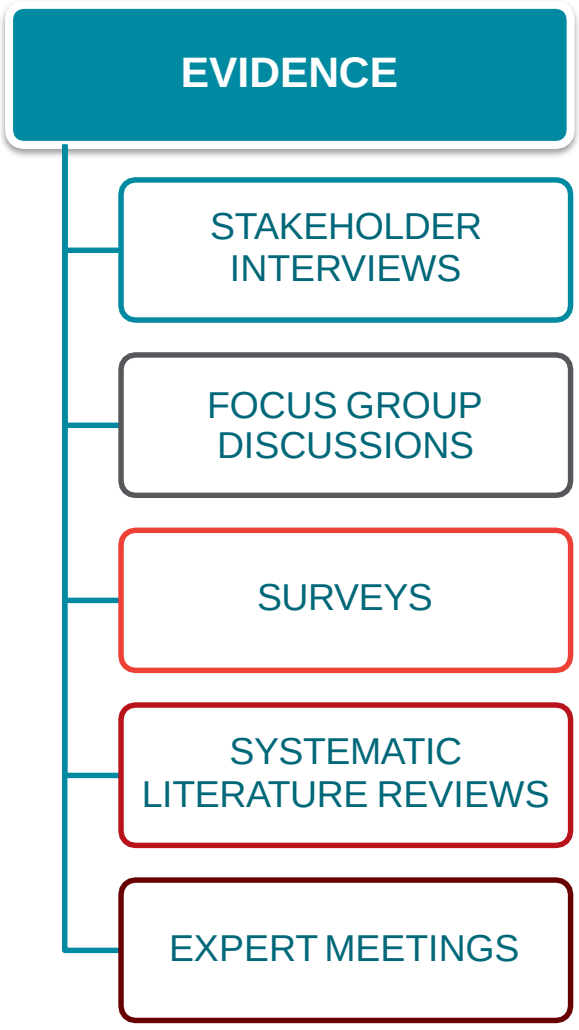
Collaboration Towards Solutions

CTTI Membership

Methodology

Evidence guides the journey to solutions

- We use quantitative & qualitative research methods, selecting those best aligned with each project's objectives, to:
  - Identify/describe "what is going on" to gain a better understanding of a particular phenomenon
  - Move beyond individual views to a more complete and objective understanding of the disincentives and motivators for change
- Equipped with data, we then challenge assumptions, identify roadblocks, build tools and develop recommendations to change the way people think about and conduct clinical trials.



How CTTI Works

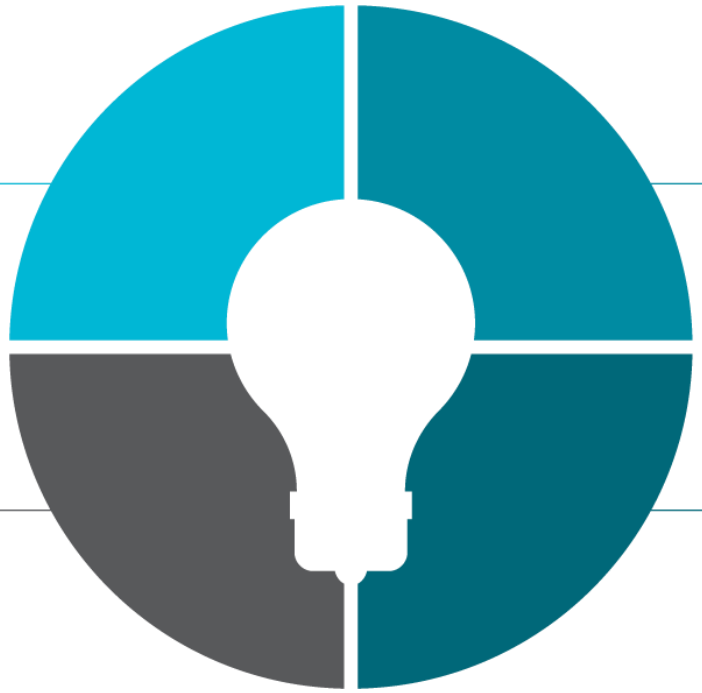
- ***Engage & value*** all stakeholders equally
- ***Understand incentives*** to maintain non-value added activities and have solutions that are mindful of those incentives
- ***Plant the seeds for change*** throughout all phases of a project
- ***Develop actionable***, evidence-based, consensus driven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

CTTI Recommendations

- CTTI projects focus on streamlining and accelerating clinical trials, while ensuring the highest standards of quality and human subjects protection. We provide **actionable**, **evidence-based**, **consensus-driven** **recommendations designed to:**

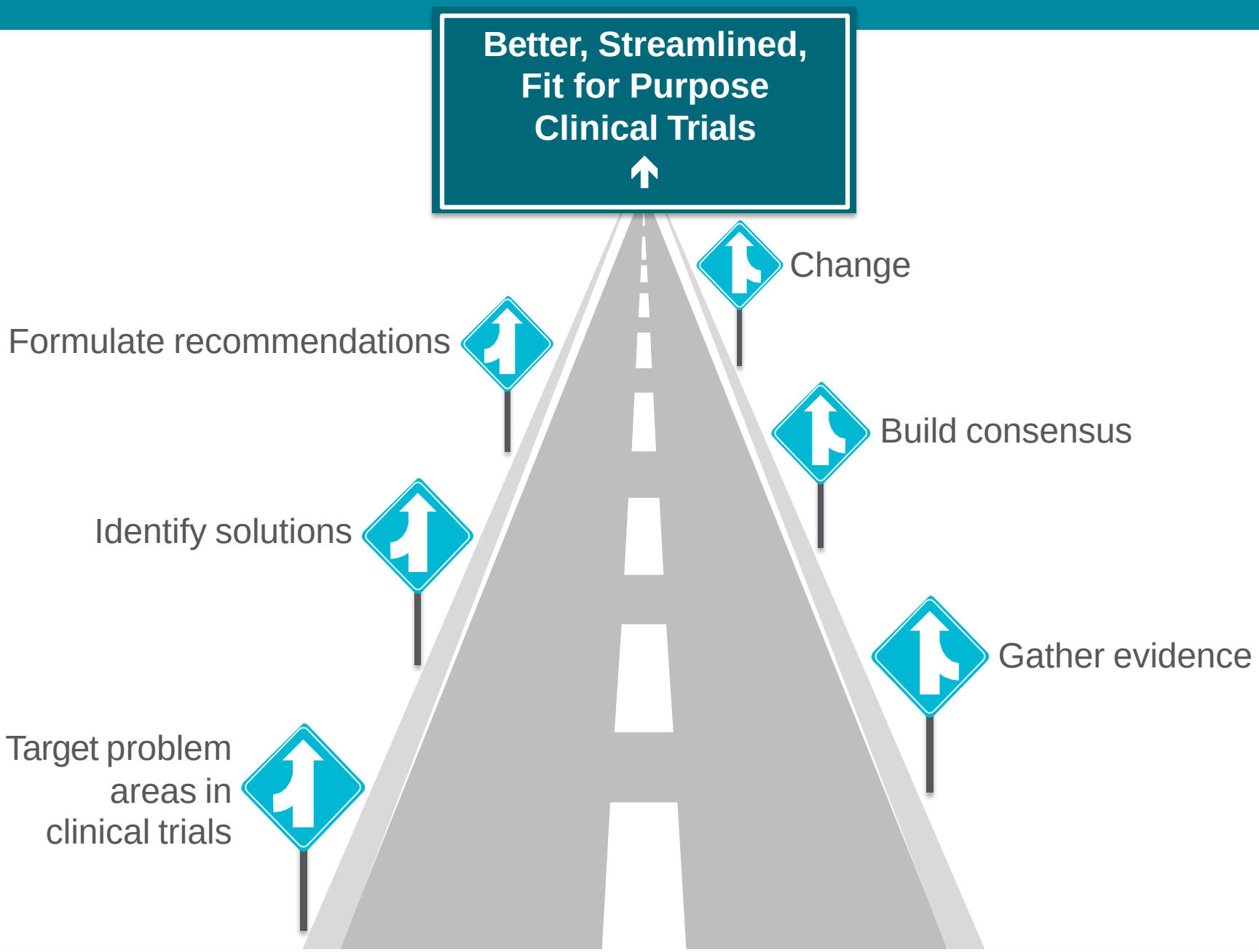
Accelerate study start-up times & streamline protocols

Enhance the quality of clinical trials without adding undue burden



Leverage new technologies to improve efficiency of clinical trials

Identify streamlined strategies while meeting regulatory requirements


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

Portfolio of CTTI Projects

	Investigational plan	Study start up	Study conduct	Analysis and dissemination	Specialty areas
Completed projects	• Large simple trials • Uses of electronic data	• Central IRB • Site metrics			

Recruitment Project Team Members

Team Leaders

- Jonca Bull (FDA)
- Elizabeth Mahon (Johnson & Johnson)
- Patricia Furlong (Parent Project Muscular Dystrophy)

CTTI Staff

- Jamie Roberts
- Diane Willis
- Kimberley Smith

Team Members

- David Ciavarella (CR Bard)
- Beth Harper (Clinical Performance Partners)
- Grant Huang (VA)
- Leslie Kelly (Duke)
- Jim Kremidas (ACRP)
- Barbara LeStage (Patient Advocate)
- Claire Meunier (Michael J. Fox Foundation)
- Holly Massett (NIH)
- Kelly McKee (Lilly)
- Ashish Oza (St. Jude Medical)
- Anuja Rastogi (FDA)

Recommendations for Recruitment: Moving Recruitment Planning Upstream To Reduce Barriers to Participation

CTTI Recruitment Project Team
Jonca Bull, Food and Drug Administration
Beth Mahon, Janssen R&D

May 19, 2016

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

Framing the Issue: Lackluster Recruitment to Clinical Trials

Jonca Bull, MD
Director, Office of Minority Health, Food and Drug Administration

May 19, 2016

CLINICAL
TRIALS
TRANSFORMATION
INITIATIVE

Critical Issues in Recruitment to CTs

LACKLUSTER RECRUITMENT

A staggering number of clinical trials fail to meet recruitment goals, leading to delays, early trial termination, or inability to draw conclusions at trial completion due to loss of statistical power.

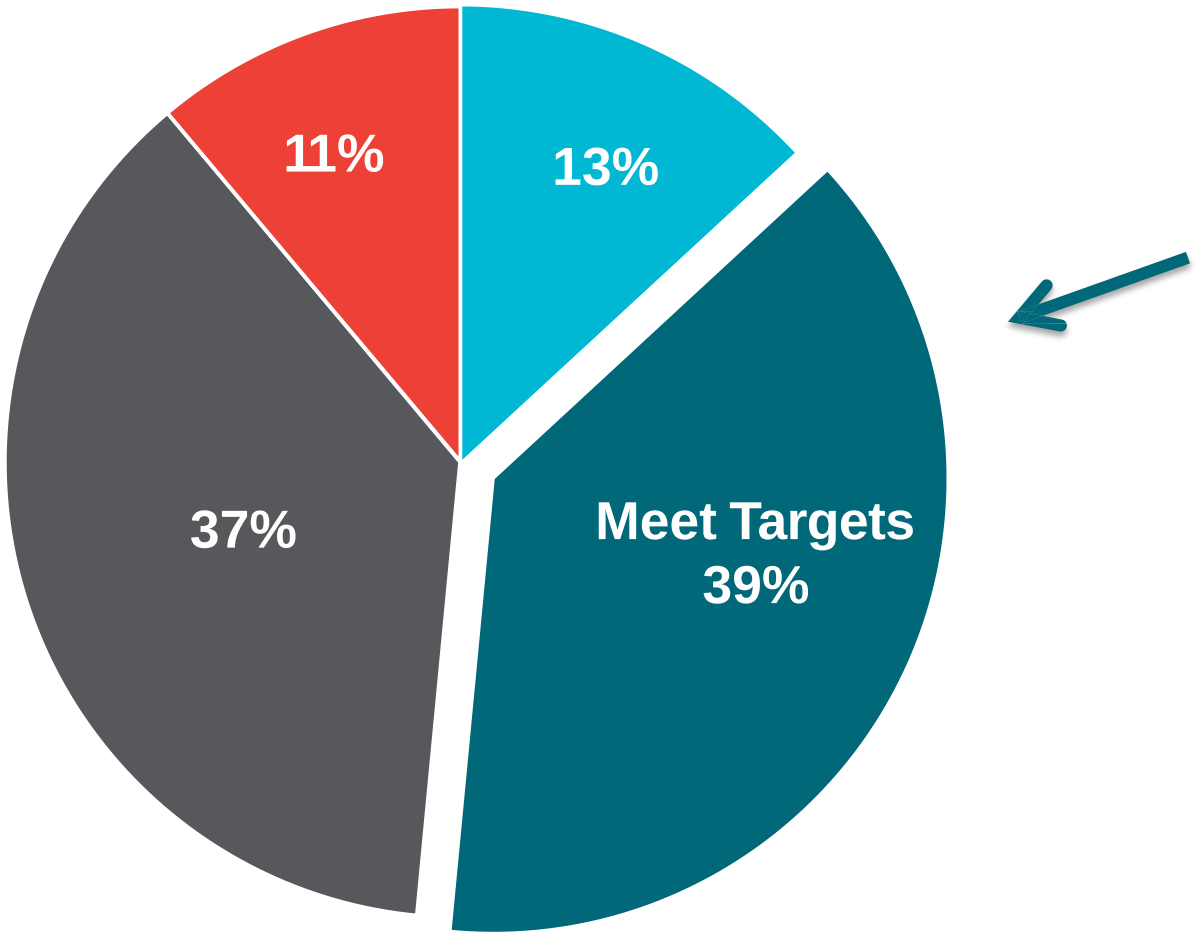
INADEQUATE SOLUTIONS

Many explanations have been offered including poor study design, lack of patient engagement, insufficient staff time, inadequate attention to determine and identify available patients who meet eligibility criteria, and inadequate centralized site support.

NEW PARADIGM NEEDED

Solution ➔ CTTI project to identify recruitment challenges and develop actionable recommendations

Clinical Trials Crisis: Low Site Enrollment Rates



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

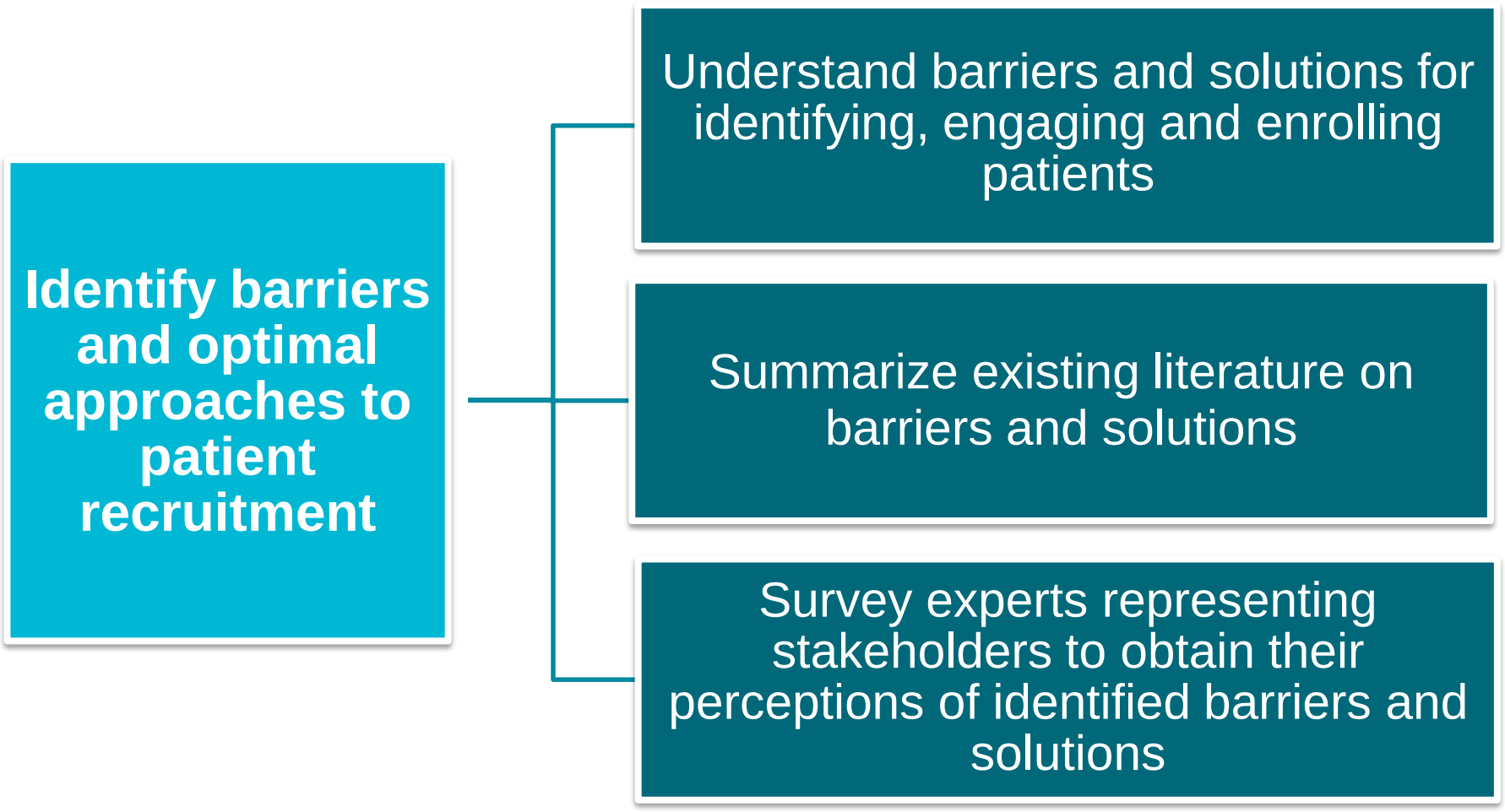
- On average, 20% of Phase II and 30% of Phase III protocols collect non-core data that are not associated with a primary or key secondary endpoint, regulatory compliance, or standard baseline assessments.

		Phase II	Phase III
Endpoints	Primary	14.8%	9.4%
	Tertiary	27.8%	29.7%
Procedures	Core	64.9%	58.6%
	Standard	9.7%	7.1%

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

CTTI

Project Objective 1

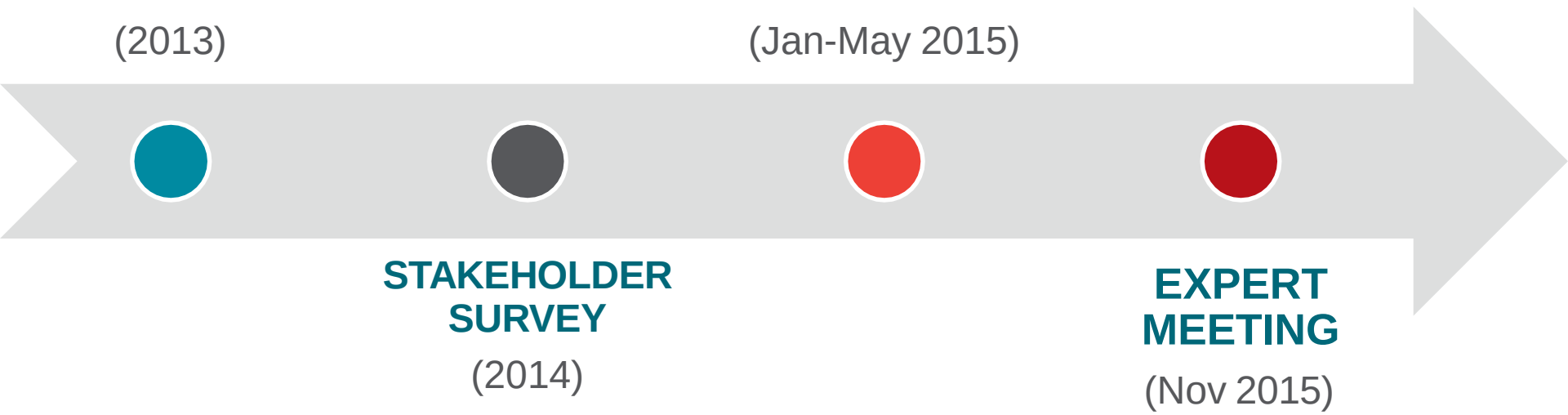


Project Objective 2

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

Evidence Gathering



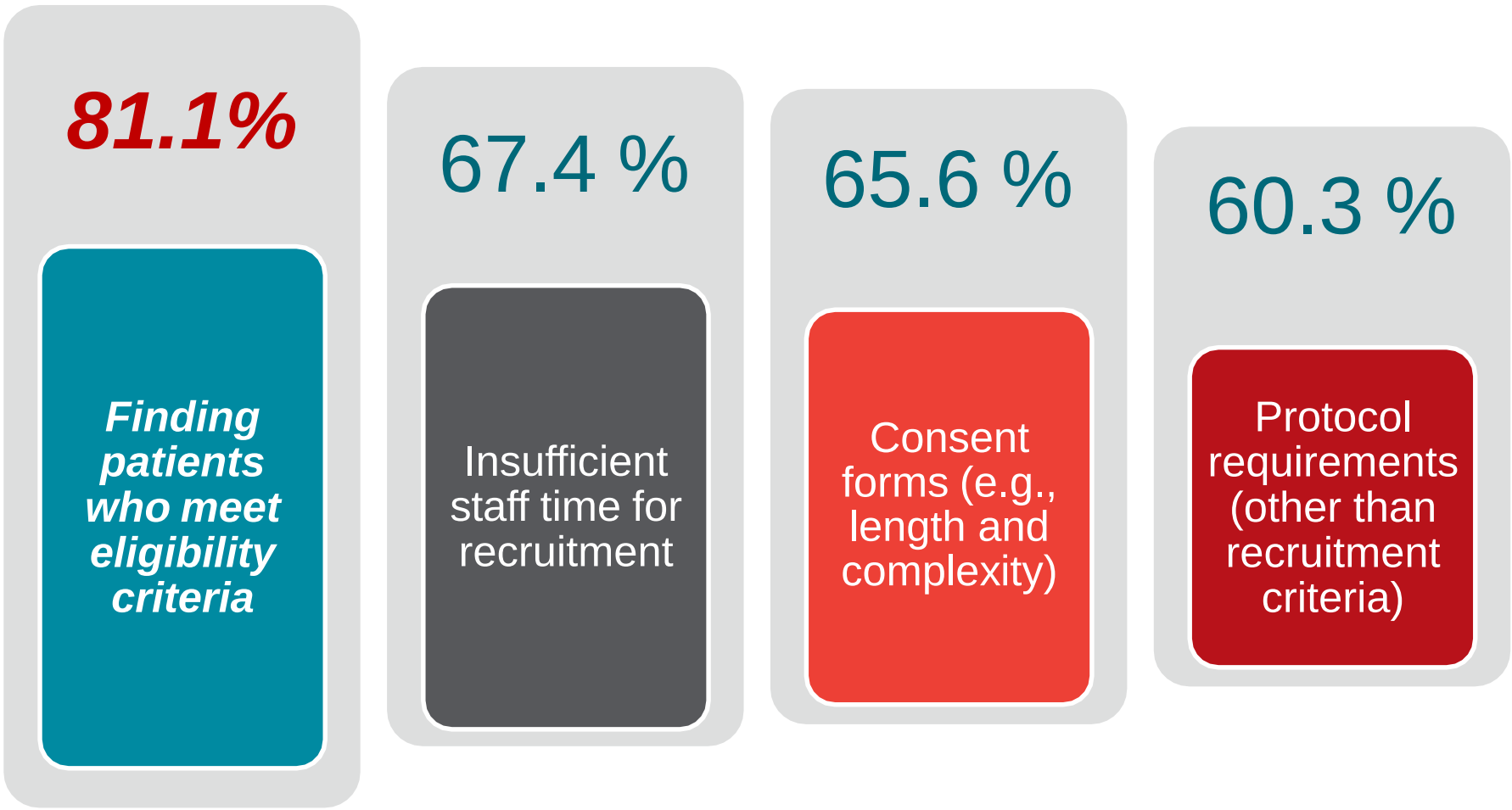
Literature Review: Takeaways

Limited data **regarding how successful or unsuccessful trialists have been in overcoming barriers or how barriers have affected the outcome of trials**

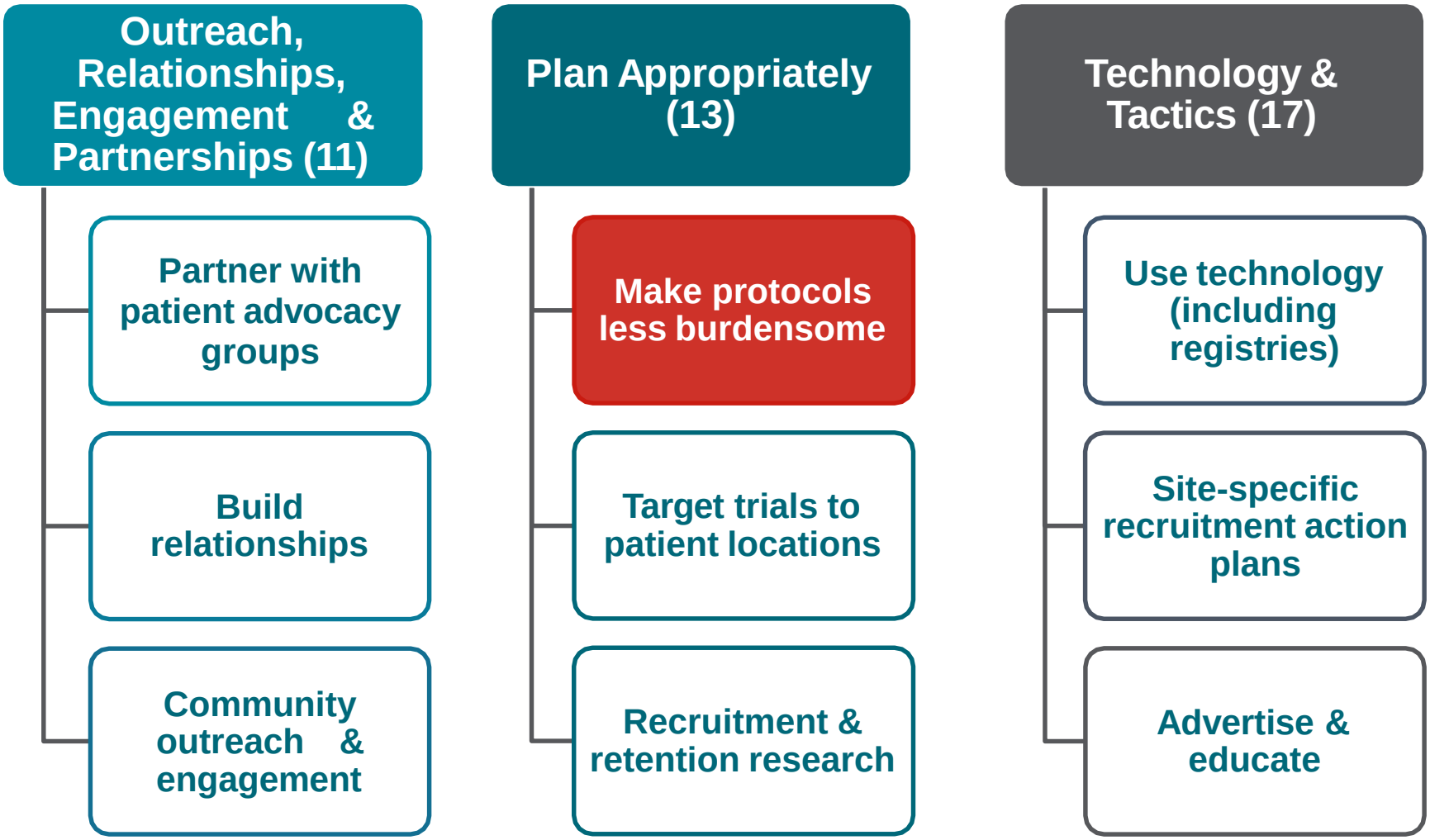
Most strategies investigated were supported by only one or two studies

Paucity of literature on retention barriers, strategies and promoters

Survey Results: Key Findings
Perceived Barriers to Recruitment



Free Text Suggestions of Methods to Increase Clinical Trial Enrollment



Survey Results: Key Findings & Recurrent Themes

- ***Barriers*** most often reported as problematic:
  - ***Eligibility criteria***
  - ***Insufficient staff time for recruitment***
  - ***Protocol requirements (other than I/E criteria)***
  - ***Complexity of consent forms***
- **Patients** offer a valuable perspective to overcoming recruitment barriers.

  Stakeholders are not engaged in the process
  - Barriers are often ***designed into*** protocols (and must later be amended out) at significant cost (opportunity and economic)
- A comprehensive recruitment strategy, rather than a single tool or solution, will be required to address the range of significant recruitment barriers identified

Illustrative comment from a survey respondent

> ***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.”**

- THE TRUSTED CLINICAL TRIALS BUSINESS RESOURCE -

APPLIED CLINICAL TRIALS

Barriers to Clinical Trial Recruitment and Possible Solutions: A Stakeholder Survey

Sep 03, 2015
By Elizabeth Mahon [1], Jamie Roberts [2], Pat Furlong [3], Gina Uhlenbrauck [4], Jonca Bull, MD [5]
Applied Clinical Trials

Survey Findings: Published Online September 3, 2015

Analysis & 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***

Sounds Great! But…..

What ***is*** a recruitment plan?

What are the necessary components?

What are the key features?

What ***tools*** are being used to create them?

Who is creating them?

Landscape Scan

- 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 was available 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 should touch a number of areas
    - Study question design & protocol development
    - Trial feasibility and site selection
    - Communications

Expert Meeting: Consensus

- 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
- Consensus: **We need…**
  - ***A culture shift toward developing a recruitment plan from the earliest stages of clinical trial development***
  - ***A systematic framework for thinking about recruitment planning in parallel with trial design & development***
- Planning concerns fall into 3 main areas
  1. Study design & development
  2. Trial feasibility and site selection
  3. Communications

The Recommendations

Beth Mahon, JD
Associate Director, Global Clinical Operations - US
Janssen R&D

May 19, 2016

CLINICAL
TRIALS
TRANSFORMATION
INITIATIVE

Trial Design & Development

- Identify and engage all stakeholders
- Ensure the relevance of the scientific question to stakeholders
- Limit protocol complexity to reduce the burden of participation
- Develop realistic eligibility criteria
- Optimize data collection to only what's necessary to maintain patient safety and answer the scientific question

CTTI

Trial Feasibility & 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

CTTI

Recruitment Communication Planning

- Identify ALL stakeholders and partners
- Identify participant locations based on where participants may seek treatment & relevant information
- Develop and test tailored messages
- Develop creative material and select appropriate channels for delivery
- Develop a realistic communication budget
- Monitor and evaluate both the recruitment process & performance with meaningful metrics
- Embed recruitment intervention studies into clinical trials & share the results to develop best practices

CTTI

The Tools and Resources

- CTTI website: http://www.ctti-clinicaltrials.org/
- Recommendations, Tools and Figures can be found at https://www.ctti-clinicaltrials.org/our-work/quality/recruitment-2/

Framework for Strategic Recruitment Planning

TRIAL DESIGN & PROTOCOL DEVELOPMENT

- Identify & engage all stakeholders
- Ensure the relevance of the scientific question
- Limit complexity to reduce burden
- Have realistic eligibility criteria
- Optimize data collection

TRIAL FEASIBILITY & SITE SELECTION

- Conduct evidence-based feasibility analysis
- Have realistic metrics & milestones
- Develop an adequate budget & resources
- Ensure appropriate site selection
- Engage suitable performance monitoring

RECRUITMENT COMMUNICATION PLANNING

- Identify and engage all stakeholders
- Identify where participants seek treatment & relevant information
- Develop & test tailored messages
- Develop creative material & select appropriate delivery channels
- Have a realistic budget
- Monitor & evaluate process & performance
- Embed recruitment intervention studies & share results

CLINICAL TRIALS TRANSFORMATION INITIATIVE

CTTI TOOLS FOR
EFFICIENT AND EFFECTIVE CLINICAL TRIAL RECRUITMENT PLANNING

TOOL 1. DECISION TREE FOR OPTIMIZING PROTOCOL DESIGN

START → **Is the scientmc question relevant?**

NO | YES

NO: 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

YES: **Are the I/E criteria carefully designed to ensure feasibility?**

NO | YES

NO: 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.

YES: **Have you minimized the procedural burden to only those necessary to answer the scientific question/endpoints?**

NO | YES

NO: Solicit feedback from stakeholders regarding important outcomes, motivations, barriers, the schedule of events and feasibimy of accomplishment based on disease burden and state, workflow as well as the perceived risk/benefit ratio.

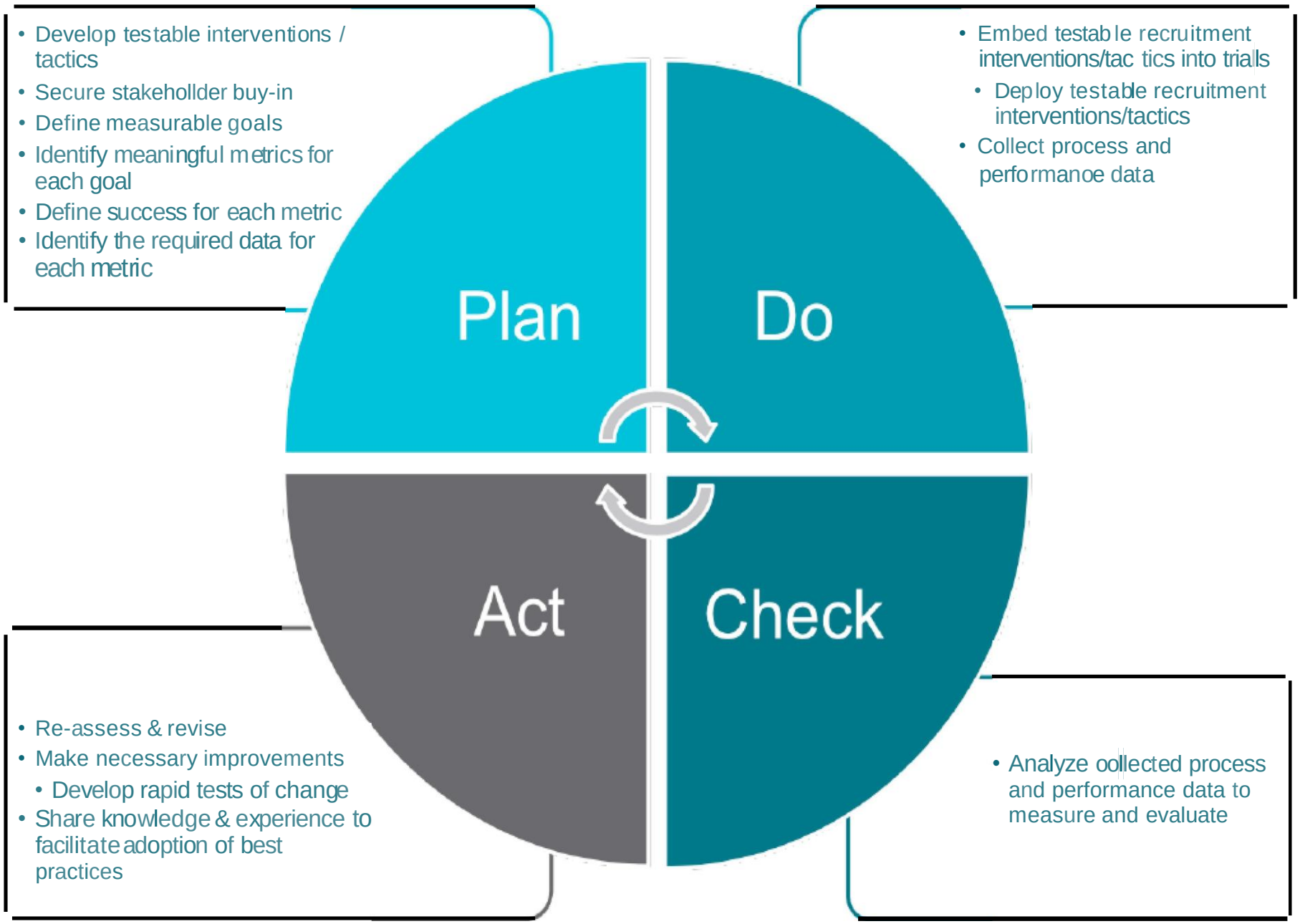
YES: **Have you minimized the burden of data collection to only those necessary to answer the scientific questions/ endpoints?**

NO | YES

NO: Calculate the incremental cost - financial, time - of each additional data element and its utimy to answering the study question; Collect only the minimum data set necessary to address study endpoints and meet the needs of various stakeholders.

YES: **Goal: a well-designed, minimally burdensome protocol that is poised to provide data to answer a meaningful scientific question**

FIGURE 2. MONITORING RECRUITMENT PROCESS AND PERFORMANCE



-Process: Did we do what we said we were going to do (e.g., deploy 3 paid ads in newspapers)?
Performance: What impact did the intervention have (e.g., increase enrollment by 10%)?

Tool #2: Stakeholder Identification and Analysis Tool

STAKEHOLDERS & RESOURCES	STRATEGY			TACTICS
Characteristic	Why this group is important to a successful trial (e.g., their role)	What do we need them to know and to do? What do we need to know about their current attitude(s) or concerns?*	How can they help us develop a viable study?**	How and when should/can/will we engage them? How frequently will we need to communicate with them to maintain their engagement?
Participants				
Patients (diagnosed)				
Patients (at risk)				
Healthy persons				
Families of patients				

CTTI Recruitment Project Conclusions

- ***Actionable solutions are needed*** since, without them, the promise of many trials will remain unfulfilled. It is time to move recruitment planning upstream and parallel to the clinical trial design process to ensure trial feasibility given the anticipated scientific, environmental, financial, time, and resource constraints
- Overall, recruitment must involve a critical level of thought that is more inclusive of ***all*** who might have influence on, or be influenced by, the development and implementation of a clinical trial.
- The development of protocol elements must be done with attention paid to upstream activities that may have a downstream impact on recruitment.

Thank you.

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

With tremendous thanks to the CTTI Recruitment Project Team for all their efforts at making these recommendations possible

Jamie Roberts, MA, MPH, CCRP
Project Manager
Jamie.Roberts@duke.edu