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.
Team & Meeting Background

We are: Multistakeholder, including FDA, industry, academia, patient advocacy

This is our opportunity:
- For a reality check –
- To make sure we’ve thought of everything
- To make sure we’ve appropriately interpreted the evidence we’ve gathered
- To learn whether we need to take any deeper dives
- To let you help us understand what’s transformative and actionable in what we’ve learned and
- To help us identify where’s the REAL INNOVATION that will change the way studies recruit.
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

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

Kuntz RE.
Addressing This Need

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
Collaboration Towards Solutions

Better Streamlined Fit for purpose Clinical Trials

- Government and regulatory agencies
- Industry: pharma bio device CRO
- IRBs
- Clinical investigators
- Patients / Patient advocacy groups
- Academia
- Industry trade / Professional organizations
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

1. **State Problem**
   - Issue Statement, Project Plan

2. **Gather Evidence**
   - Literature Reviews, Multi-stakeholder Meetings, Surveys, Interviews

3. **Find Solution**
   - Team Meetings, Multi-stakeholder Meetings

4. **Refine Ideas**
   - Team Meetings, Multi-stakeholder Meetings

5. **Develop Recommendations/Tools**
   - Team Meetings, Multi-stakeholder Meetings

6. **Disseminate & Implement**
   - Workshops, Pilot Studies, Measure Impact
## Portfolio of CTTI Projects

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<th>Study Conduct</th>
<th>Analysis &amp; Dissemination</th>
<th>Specialty Areas</th>
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<td>• Central IRB&lt;br&gt;• Site metrics&lt;br&gt;• Central IRB advancement&lt;br&gt;• GCP training</td>
<td>• Adverse event reporting&lt;br&gt;• IND safety&lt;br&gt;• Monitoring</td>
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<td>• Long-term opioid data</td>
</tr>
<tr>
<td><strong>Ongoing Projects</strong></td>
<td>• Mobile clinical trials (program)&lt;br&gt;<strong>Patient groups &amp; clinical trials</strong>&lt;sup&gt;<em>&lt;/sup&gt;&lt;br&gt;• Pregnancy testing&lt;br&gt;• QbD&lt;sup&gt;</em>&lt;/sup&gt;&lt;br&gt;• Trials based on registries&lt;br&gt;• Uses of electronic data application</td>
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<td>• Pediatric antibiotic trials&lt;br&gt;<strong>Streamlining HABP/VABP trials</strong>&lt;br&gt;• Unmet need in antibiotic development&lt;br&gt;• ABDD pilot</td>
</tr>
</tbody>
</table>

*Recently approved recommendations released
Recruitment Project Team

**Team Leads**
- 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)

**Team Members**

**CTTI Support Staff**
- Matthew Harker
- Kelly Kilibarda
- Jamie Roberts
- Diane Willis
- Kimberley Smith
Better, Streamlined, Fit for Purpose Clinical Trials

- Identify Research Impediments
- Identify solutions
- Formulate recommendations
- Gather evidence
- Build consensus
- Change
Thank you.

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919 695 5626
An Imperative for Action: Patients Are Waiting

Mary Woolley, President, Research!America
Overview of Presentation

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

“Nothing About Us Without Us”*

*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
“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.”

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.’

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”

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
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
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

“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

“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
Clinical Trial Recruitment in the News

Clinical Trials Need Cancer Patients

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.

More evidence poor cancer patients don’t join clinical trials

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

For a Rare Disease, Drug Trials Scramble for Patients

Companies vie for enrollees amid questions that trials will siphon participants away from each other.
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
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
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?
Wide Majority of Americans Have Not Participated in Trials

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

- Yes: 16%
- No: 77%
- Not sure: 7%

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?

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.
Do you agree or disagree with each of following statements?

- I am interested in finding out more about taking part in clinical trials
  - Strongly agree: 29
  - Somewhat agree: 32
  - Somewhat disagree: 17
  - Strongly disagree: 11
  - Not sure: 12

- I would take part in a clinical trial if I was asked by someone I trust
  - Strongly agree: 28
  - Somewhat agree: 36
  - Somewhat disagree: 13
  - Strongly disagree: 7
  - Not sure: 17

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%

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

- Yes: 31%
- No: 41%
- Not sure: 28%

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.
Would you say that without being told, patients are sometimes included in clinical trials when they are receiving medical treatment?

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?

- 22% Yes
- 70% No
- 8% Not sure

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.
If your doctor found a clinical trial for you and recommended you join, how likely would you be to participate in a clinical trial?

- Very likely: 26%
- Somewhat likely: 46%
- Not likely: 12%
- Would not participate: 3%
- Not sure: 13%

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?

- Doctors and other health care providers
- Government
- Insurance companies
- Pharmaceutical companies
- Patient organizations
- Not sure

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.
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
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.
On a scale of 1 to 4, how much do you admire people who volunteer for clinical trials?

Americans Admire Clinical Trial Volunteers

- **African-American**
  - 4 (a great deal): 46
  - 3: 31
  - 2: 8
  - 1 (not at all): 3
  - Not sure: 13

- **Asian**
  - 4 (a great deal): 43
  - 3: 35
  - 2: 9
  - 1 (not at all): 10
  - Not sure: 10

- **Hispanic**
  - 4 (a great deal): 42
  - 3: 37
  - 2: 8
  - 1 (not at all): 4
  - Not sure: 10

- **Non-Hispanic White**
  - 4 (a great deal): 35
  - 3: 42
  - 2: 9
  - 1 (not at all): 3
  - Not sure: 11

Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in May 2013.
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.
How much do you admire the following groups of people on a scale of 1 to 4?

- People who volunteer for clinical trials: 37 (4), 38 (3), 9 (2), 4 (1), 13 (Not sure)
- People who give blood: 61 (4), 26 (3), 43 (2), 7 (1), 7 (Not sure)
- People who donate an organ: 69 (4), 19 (3), 3 (2), 7 (1), 3 (Not sure)

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.’

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.

Tennessee Kidney Foundation, DonateLife 2015 Annual Update
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
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
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.’”

Examples of Clinical Trial Campaigns

Patient Clinical Trial “Champions”

Patient Perspectives Video Series
“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.”
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.
Remember the most important four words a researcher can say and convey:
“I work for you.”
Connect With Us

www.researchamerica.org/blog
www.researchamerica.org/facebook
www.twitter.com/researchamerica
www.youtube.com/researchamerica
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CTTI Methodology

1. **State Problem**
   - Issue Statement, Project Plan

2. **Gather Evidence**
   - Literature Reviews, Multi-stakeholder Meetings, Surveys, Interviews

3. **Identify Gaps/Barriers**
   - Team Meetings, Multi-stakeholder Meetings

4. **Find Solution**
   - Team Meetings, Multi-stakeholder Meetings

5. **Refine Ideas**

6. **Analyze & Interpret Findings**
   - Team Meetings, Multi-stakeholder Meetings

7. **Develop Recommendations/Tools**
   - Team Meetings, Multi-stakeholder Meetings

8. **Action**
   - Workshops, Pilot Studies, Measure Impact

9. **Disseminate & Implement**
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
Consequences

Suboptimal Recruitment

Missed Opportunities
- Potential benefits for patients
- Advancing the science and understanding of disease
- Finding new therapies and treatments

Wasted
- Time
- Funds
- Other resources
- Motivation of stakeholders
Clinical Trials Crisis: Low Site Enrollment Rates

- Exceed Enrollment Targets
- Meet Targets
- Under Enroll
- Fail to Enroll Even 1

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

<table>
<thead>
<tr>
<th></th>
<th>Phase II</th>
<th>Phase III</th>
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</thead>
<tbody>
<tr>
<td><strong>Endpoints</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>14.8%</td>
<td>9.4%</td>
</tr>
<tr>
<td>Key Secondary</td>
<td>38.3%</td>
<td>34.8%</td>
</tr>
<tr>
<td>Tertiary</td>
<td>27.8%</td>
<td>29.7%</td>
</tr>
<tr>
<td>Exploratory</td>
<td>19.1%</td>
<td>26.1%</td>
</tr>
<tr>
<td><strong>Procedures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Core</td>
<td>64.9%</td>
<td>58.6%</td>
</tr>
<tr>
<td>Required</td>
<td>4.6%</td>
<td>3.7%</td>
</tr>
<tr>
<td>Standard</td>
<td>9.7%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Non-core</td>
<td>20.7%</td>
<td>30.6%</td>
</tr>
</tbody>
</table>

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

2013
- Literature Review

2014
- Stakeholder Survey

2015
- Landscape Scan
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
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
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

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

- Finding patients who meet eligibility criteria: 81.1%
- Insufficient staff time for recruitment: 67.4%
- Consent forms (e.g., length and complexity): 65.6%
- Protocol requirements (other than recruitment criteria): 60.3%

Rated very/somewhat significant (by more than 50% of respondents)
Categorizing The Most Common Perceived Barriers By Respondent Type

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

% identified as significant or very significant
### Free Text Solutions to Most Common Barrier (by themes)

<table>
<thead>
<tr>
<th>Identify Eligible Patients (88.81%)</th>
<th>Engage in effective study planning (37)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Improve eligibility criteria (20)</td>
</tr>
<tr>
<td></td>
<td>Using effective recruitment methods / technologies (20)</td>
</tr>
<tr>
<td></td>
<td>Education about research (specific trials) (14)</td>
</tr>
<tr>
<td></td>
<td>Partnering (13)</td>
</tr>
<tr>
<td></td>
<td>Education about research (general) (6)</td>
</tr>
<tr>
<td></td>
<td>Assisting patients with specific aspects of study (3)</td>
</tr>
<tr>
<td></td>
<td>Design less burdensome protocols (2)</td>
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</tbody>
</table>

*This barrier was considered the most significant by 41% and somewhat significant by 40%*
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)
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."

...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."
Barrier: Insufficient Staff Time for Recruitment

Solution: We Need More Time (69%)

Free Text Response Themes

- Increase site commitment to staffing (25)
- Engage in appropriate advanced planning (10)
- Increase sites’ financial resources (14)
- Improve Institutional Support for Research (3)
- Outsource Patient enrollment (6)

69% significant
23% very significant
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!
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.
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.

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

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.

...unnecessary information in the consent that does not contribute to a participant's ability to make an informed decision.
Barrier: Protocol Requirements

Solution: We Need a Less Burdensome Protocol

- Simplify study design (28)
- Evaluate protocol feasibility (11)
- Alternatives to main site visits (7)
- Clearly communicate study requirements to participants (2)

61% significant; 17% very significant
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.”
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.”
Moderately Significant Barriers
Barrier: Patient Mistrust of Research

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

**Suggested Solutions**

- Education about the research process (22)
  - Community outreach (15)
  - Relationship-building (12)
  - Improve consent form (3)
  - Communicate results to trial participants (2)

47% endorsed as significant

8% endorsed as very significant
Barrier: Negative Attitudes Among Physicians

Suggested Solutions

- Regular communication with physicians (14)
- Educational campaigns (14)
- Involve physicians in the research process (2)
- Improve physician workflow (3)
- Financial incentive for referrals
- Encourage patients to ask their physicians about trials

41% endorsed as significant 13% endorsed as very significant
Barrier: Burden of Participation: Difficulty Scheduling Trial Visits

- Burdens on trial participants were considered a moderately significant barrier

Suggested Solutions

- Flexible scheduling (18)
- Simplify study design (6)
- Alternative main site visits (3)
- Assist with travel (2)
- Utilize technology (3)

39% endorsed as significant
8% endorsed as very significant
Barrier: Burden of Participation: Transportation

Suggested Solutions

- Offer financial assistance (19)
  - Offer assistance w/ travel arrangements (6)
  - Offer transportation (6)
  - Establish sites in convenient locations (5)
  - Simplified/alternative study design (6)

45% endorsed as significant
13% endorsed as very significant
Barrier: Burden of Participation: Out of Pocket Costs

Suggested Solutions

- **Offer financial assistance (14)**
- Explore alternative funding sources for participant costs (13)
- Simplified/alternate study design (3)
- Negotiate coverage with managed care plans (5)
- Ensure patients understand study costs (3)

43% endorsed as significant  12% endorsed as very significant
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
Perceptions of Specific Methods to Improve Recruitment

Identifying patients using medical records

Identify patients using hospital-based registries or other databases

Electronic alerts to physicians about clinical trials available to specific patients

Electrical alerts to clinical trial staff about eligible patients’ appointments

Promoting clinical research through social media such as Facebook or Twitter

Promoting recruitment through social media such as Facebook or Twitter

Deploying a mobile health unit or mobile research unit

Recruiting through public events such as farmers’ markets or health fairs

Respondents, %
Experience with Specific Methods to Improve Recruitment

- Identifying patients using medical records
- Identify patients using hospital-based registries or other databases
- Electronic alerts to physicians about clinical trials available to specific patients
- Electrical alerts to clinical trial staff about eligible patients’ appointments
- Promoting clinical research through social media such as Facebook or Twitter
- Promoting recruitment through social media such as Facebook or Twitter
- Deploying a mobile health unit or mobile research unit
- Recruiting through public events such as farmers’ markets or health fairs
Free Text Suggestions of Methods to Increase Clinical Trial Enrollment

Outreach, Relationships, Engagement & Partnerships (11)
- Partner with patient advocacy groups
- Build relationships
- Community outreach & engagement

Plan Appropriately (13)
- Make protocols less burdensome
- Target trials to patient locations
- Recruitment & retention research

Technology & Tactics (17)
- Use technology (including registries)
- Site-specific recruitment action plans
- Advertise & educate
Emerging Recruitment Methods for National Trials

Suggested Solutions

Use technology (18)
1) Electronic medical records (8) 4) Electronic consenting (1)
2) Social media (3) 5) Trial-matching websites (2)
3) Mobile apps (3) 6) Disease-specific websites (1)

Use registries (4) and networks (3)

Include patient input in study design (4)

Increase national awareness about research (4)

Other (11)
Sectors Selected as *Most Effective Partners* to Increase Nat’l CT Recruitment Rates

<table>
<thead>
<tr>
<th>Sector</th>
<th>%</th>
<th>(N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient advocates</td>
<td>82.2</td>
<td>(74)</td>
</tr>
<tr>
<td>Sponsors</td>
<td>71.1</td>
<td>(64)</td>
</tr>
<tr>
<td>Researchers</td>
<td>67.8</td>
<td>(61)</td>
</tr>
<tr>
<td>Professional societies</td>
<td>44.4</td>
<td>(40)</td>
</tr>
<tr>
<td>Government regulators</td>
<td>37.8</td>
<td>(34)</td>
</tr>
<tr>
<td>Trade organizations</td>
<td>7.8</td>
<td>(7)</td>
</tr>
<tr>
<td>Other</td>
<td>4.4</td>
<td>(4)</td>
</tr>
</tbody>
</table>

NOTE: Respondents could select multiple sectors.
Top 6 Sector Combinations Reported as *Most Effective Partners to Increase Nat’l CT Recruitment Rates*

<table>
<thead>
<tr>
<th>Sectors</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Advocates, Researchers</td>
<td>9</td>
</tr>
<tr>
<td>Patient Advocates, Government Regulators, Researchers, Sponsors,</td>
<td>9</td>
</tr>
<tr>
<td>Professional Societies</td>
<td></td>
</tr>
<tr>
<td>Researchers, Sponsors</td>
<td>7</td>
</tr>
<tr>
<td>Patient Advocates, Researchers, Sponsors, Professional Societies</td>
<td>7</td>
</tr>
<tr>
<td>Patient Advocates, Sponsors, Professional Societies</td>
<td>7</td>
</tr>
<tr>
<td>Patient Advocates, Researchers, Sponsors</td>
<td>6</td>
</tr>
</tbody>
</table>
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.
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.”
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?
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

**Recruitment 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

*Draft*
Thank you.

Jonca Bull, MD
Session III:
Presentation of Draft Considerations

Jamie Roberts
Beth Mahon
Beth Harper
James Kremidas

November 9, 2015
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.
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
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- Define success metrics
- Analyze & monitor for impact
- Test & share results & best practices

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

**DRAFT**
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.
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

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.

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.

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.

Elizabeth Mahon, JD

Janssen
Session III: Trial Feasibility & Site Selection

Beth Harper (Clinical Performance Partners, Inc.)

Disclaimer:
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Trial Feasibility & Site Selection

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

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

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

Plan Implementation
- Pilot test
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- Return to stakeholders for advice

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

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

Study Question Development

DRAFT
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

1. Thoughtful Site Selection
2. Setting clear enrollment expectations
3. Ongoing performance monitoring, feedback, and intervention
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.

Beth Harper
Clinical Performance Partners, Inc.
Session III: Recruitment Communication Planning

James Kremidas (ACRP)

Disclaimer:
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Recruitment Communication Planning

Points of Consideration for Improving Recruitment Through Effective Recruitment Communication Planning
### Clinical Trial Recruitment Planning Continuum

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<tbody>
<tr>
<td>- Engage all stakeholders</td>
<td>- Broaden I/E criteria</td>
<td>- Evidence-based</td>
<td>- Engage stakeholders, partners, audience(s)</td>
<td>- Pilot test</td>
<td>- Define success metrics</td>
</tr>
<tr>
<td>- Addressing an unmet need</td>
<td>- Minimize burden</td>
<td>- Performance &amp; Efficiency metrics</td>
<td>- Have a mission &amp; vision</td>
<td>- Deploy multiple tactics over time</td>
<td>- Analyze &amp; monitor for impact</td>
</tr>
<tr>
<td>- Meaningful &amp; relevant</td>
<td>- Data parsimony</td>
<td>- Competing trials</td>
<td></td>
<td>- Monitor their effect</td>
<td>- Test &amp; share results &amp; best practices</td>
</tr>
</tbody>
</table>

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

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

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

#### Recruitment 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

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

---

**DRAFT**
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.

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

Beth Harper
Jim Kremidas

November 9, 2015
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

**WHY?**

- We aren’t sure which or how many stakeholders to include
- We don’t know how to reach them to involve them
- Stakeholders may not understand the key considerations in study design
- The time/resources involved to have meaningful inclusion are prohibitive
- Stakeholder interests may be conflicting/competing with those of others
- Including patient perspectives is not currently an element of the design process
- We’ve never done this before
- No time to find and communicate with them
- They haven’t been part of trial design efforts previously and/or do not have needed training
- Collecting data/info requires an organized approach for potentially a number of stakeholders
- We have to launch our study & begin enrollment in a short time frame
- The value of a clinical trial differs for different stakeholders
- Their time/interests are focused on other priorities in the clinical trials process
- Varying input requires a mechanism for filtering and/or integrating as part of the protocol design
- We need to complete the trial, get product approved and earn revenues by a certain time in order to meet corporate strategic goals
- Clinical trials support a range of interests

*Focus on patient stakeholders for the purpose of this exercise*
We won’t be able to systematically analyze all barriers or factors that could limit enrollment.

- We don’t have time to do this type of analysis.
- Many barriers may not be realized until actually after the study starts.
- Site personnel may not have the time to do an in-depth analysis of their ability to do the trial.
- We don’t see much value in doing this analysis.
- We need to launch the trial soon to meet corporate timelines.
- Takes too much time, staff or money.
- New population or criteria.
- There may be no prior history to compare to.
- We’ve had limited discussions with internal & external stakeholders already.
- We already have an idea of what the barriers will be.
Creating a realistic budget will be challenging. We don't have any benchmark data or prior experience. We have very limited funds to begin with. Budgets are not built in up front for communication tools. Sites believe they can do recruitment on their own so there is not need for budget or other support.
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

![Bar Chart]

- A. 63%
- B. 2%
- C. 25%
- D. 2%
- E. 4%
- F. 4%
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

![Bar chart showing the percentage of respondents: A: 24%, B: 24%, C: 29%, D: 18%, E: 6%]
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

- A. 12%
- B. 8%
- C. 36%
- D. 8%
- E. 20%
- F. 16%
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

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>~40 min</td>
<td>Implementation Challenge 1</td>
<td>You have been assigned to a group to provide you an opportunity to:  &lt;br&gt; - Share your expertise  &lt;br&gt; - Interact with other experts  &lt;br&gt; - Brainstorm and problem solve  &lt;br&gt; See your name tag for your group assignments</td>
</tr>
<tr>
<td>~40 min</td>
<td>Implementation Challenge 2</td>
<td></td>
</tr>
<tr>
<td>~40 min</td>
<td>Implementation Challenge 3</td>
<td></td>
</tr>
<tr>
<td>30 min</td>
<td>Report Out / Discussion</td>
<td></td>
</tr>
</tbody>
</table>

- **Trial Design and Protocol Development**
- **Trial Feasibility and Site Selection**
- **Recruitment Communication Planning**
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.
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
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.
First, some basics

Enrollment Planning

- Algebra 1
  - \( \frac{\text{# patients}}{\text{# sites}} \times \frac{\text{s}}{\text{p/s/m}} = \text{enrollment cycle time} \)
  - 100pts/5sites/2p/s/m = 10 months

- Leading indicators, dependent variables
  - Site Ready Curve
  - Sites Actively Screening
  - Screening Rate
  - Screen Failure Ratio
Mechanism of Action

Today

- Known Patient
- Unknown Patient
- Paid Media
- Earned & Paid Media
- Deactivated Patient

Diagram shows flow of patients through different stages: Known Patient, Unknown Patient, Paid Media, Earned & Paid Media, Deactivated Patient. Stages include Drop Outs, IN TRIAL, and Screen Failures. The process also includes a step for Decline Consent.
Mechanism of Action

Tomorrow

Fewer Decline Consent
Screen Failures

LPV

IN TRIAL

Fewer Drop Outs
What does it mean to be this patient?

RESEARCH ADVOCATE!
Thank you.
Highlights & Wrap-Up

Kelly McKee
Merck

November 9, 2015
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

Recruitment 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

DRAFT
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
Disclaimer

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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?

<table>
<thead>
<tr>
<th>Region</th>
<th>Somewhat willing</th>
<th>Very willing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>41%</td>
<td>39%</td>
</tr>
<tr>
<td>North America</td>
<td>40%</td>
<td>44%</td>
</tr>
<tr>
<td>South America</td>
<td>29%</td>
<td>45%</td>
</tr>
<tr>
<td>Europe</td>
<td>25%</td>
<td>44%</td>
</tr>
<tr>
<td>Asia Pacific</td>
<td>43%</td>
<td>41%</td>
</tr>
</tbody>
</table>

Base: Total (n=12,009), North America (n=6,665), South America (n=877), Europe (n=2,618), Asia Pacific (n=1,302)
General Knowledge about, and Confidence in Finding, a Clinical Research Study

**General Knowledge**

- **Not at all informed**
  - Total: 2%
  - North America: 2%
  - South America: 2%
  - Europe: 4%
  - Asia Pacific: 3%

- **Not very informed**
  - Total: 17%
  - North America: 12%
  - South America: 18%
  - Europe: 27%
  - Asia Pacific: 18%

**General Confidence**

- **Somewhat confident**
  - Total: 48%
  - North America: 48%
  - South America: 48%
  - Europe: 46%
  - Asia Pacific: 48%

- **Very confident**
  - Total: 24%
  - North America: 25%
  - South America: 35%
  - Europe: 18%
  - Asia Pacific: 23%

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

<table>
<thead>
<tr>
<th>Can You Name a Medical Research Scientist?</th>
<th>Where are Clinical Research Studies Conducted?</th>
</tr>
</thead>
<tbody>
<tr>
<td>'Yes'</td>
<td>58%</td>
</tr>
<tr>
<td>'No'</td>
<td>19%</td>
</tr>
<tr>
<td>'Not Sure'</td>
<td>23%</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: CISCRP 2013 N=5,701
And Little Recognition and Appreciation

Who makes a greater contribution to human health?

- Organ Donor: 46%
- Blood Donor: 33%
- Financial Donor: 12%
- CT Volunteer: 9%

Source: CISCRP 2013 N=5,701
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
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)

<table>
<thead>
<tr>
<th>Pre-MHs</th>
<th>1-Wk Post</th>
<th>1-Mo Post</th>
<th>2-Mo Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>22</td>
<td>14</td>
<td>4</td>
</tr>
</tbody>
</table>

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

Enrollment Rate in 12 Markets with Mass Media Recruitment Ads Only

<table>
<thead>
<tr>
<th>Enrollment Rate in 6 Markets with Mass Media Recruitment Ads in Conjunction with ‘Everyday Heroes’ Campaign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improvement in Enrollment Rates from Concurrent Ad and Outreach Campaign Use</td>
</tr>
</tbody>
</table>

| 4.0 Patient/Month | 9.6 Patients/Month | 140% |

Source: Eli Lilly & Company, 2009

Source: CISCRP, 2012
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
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

### IMPACT

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

Source: CISCRP; N=1,718 attendees
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
Thank you.

Ken Getz,
Founder and Board Chair, CISCRP
Director and Associate Professor, Tufts CSDD
617-636-3487
Kenneth.getz@tufts.edu
Game Plan: Breakout Sessions

Jamie Roberts, CTTI

November 10, 2015
## Breakout Sessions

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Room</th>
<th>Room</th>
<th>Room</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Challenge</td>
<td>Challenge</td>
<td>Challenge</td>
</tr>
<tr>
<td>2</td>
<td>Challenge</td>
<td>Challenge</td>
<td>Challenge</td>
</tr>
<tr>
<td>3</td>
<td>Challenge</td>
<td>Challenge</td>
<td>Challenge</td>
</tr>
</tbody>
</table>

**Trial Design & Development**<br>Grant Huang, Jonca Bull

**Trial Feasibility & Site Selection**<br>Beth Harper, Claire Meunier

**Recruitment Communication Planning**<br>Jim Kremidas, Kelly McKee
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.
Disseminating the Recommendations

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

November 10, 2015
A Lesson From the Business World

Be the Change you Want to See in Your Organization

Take Business Actions to Shift the Culture

Take Organization Actions to Shift the Culture

Align Culture with Business Strategy

What will be our strategy for achieving culture change?
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
<table>
<thead>
<tr>
<th>Venue</th>
<th>Mission</th>
<th>Audience</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DIA</strong> Drug Information Association</td>
<td>Education forum and convener, exhibition, knowledge exchange, networking</td>
<td>Sponsors, CROs, CRAs, researchers, more commercial than academic</td>
</tr>
<tr>
<td><strong>SCT</strong> Society for Clinical Trials</td>
<td>Education, clinical trials research methodology and member networking</td>
<td>Academics and statisticians, data managers</td>
</tr>
<tr>
<td><strong>BIO</strong> Biotechnology Organization</td>
<td>Biotechnology development, exhibition, investment, partnering, community. Includes bio other than medical</td>
<td>R&amp;D investors, sponsors, CROs, trialists</td>
</tr>
<tr>
<td><strong>PRIM&amp;R</strong> Public Responsibility in Medicine and Research</td>
<td>Education, professional development, networking</td>
<td>IRB &amp; human research protection professionals, Ethics</td>
</tr>
<tr>
<td><strong>ACRP</strong> Association of Clinical Research Professionals</td>
<td>Education forum and convener, exhibition, knowledge exchange</td>
<td>R&amp;D operations, vendors, research coordinators, CRAs, CEU focus</td>
</tr>
</tbody>
</table>

Other: ???, SCOPE, CTSA outreach
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.
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
- Build consensus
- Gather evidence
- Formulate recommendations
- Identify solutions
- 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
Thank you.

Jamie Roberts