

A Town Hall Meeting – Who is Accountable for Site Selection and Patient Recruitment?

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Genzyme Corporation



46th Annual Meeting
Washington, DC - 2010



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Learning Objectives

- Identify the elements in protocol design that impact execution
- Define factors that impact selecting sites that will meet your performance expectations
- Define “Patient Recruitment” and the key drivers necessary to ensure successful enrollment of a trial
- Explain the importance of having well defined responsibilities and accountabilities for enrollment performance

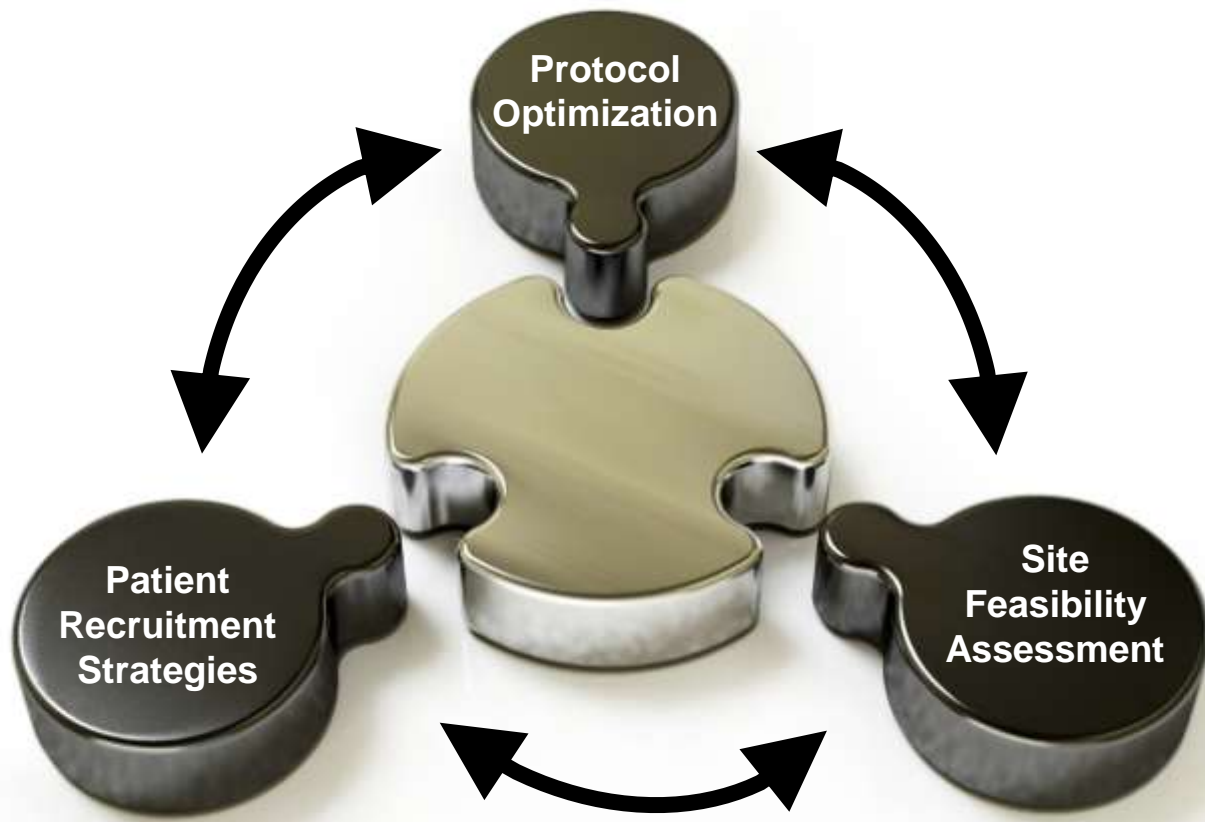


Panelists

- Jim Kremidas
 - VP Global Head of Patient Recruitment
 - Quintiles, Inc.
- Vicky DiBiaso
 - Director, Feasibility and Patient Recruitment
 - Genzyme Corporation

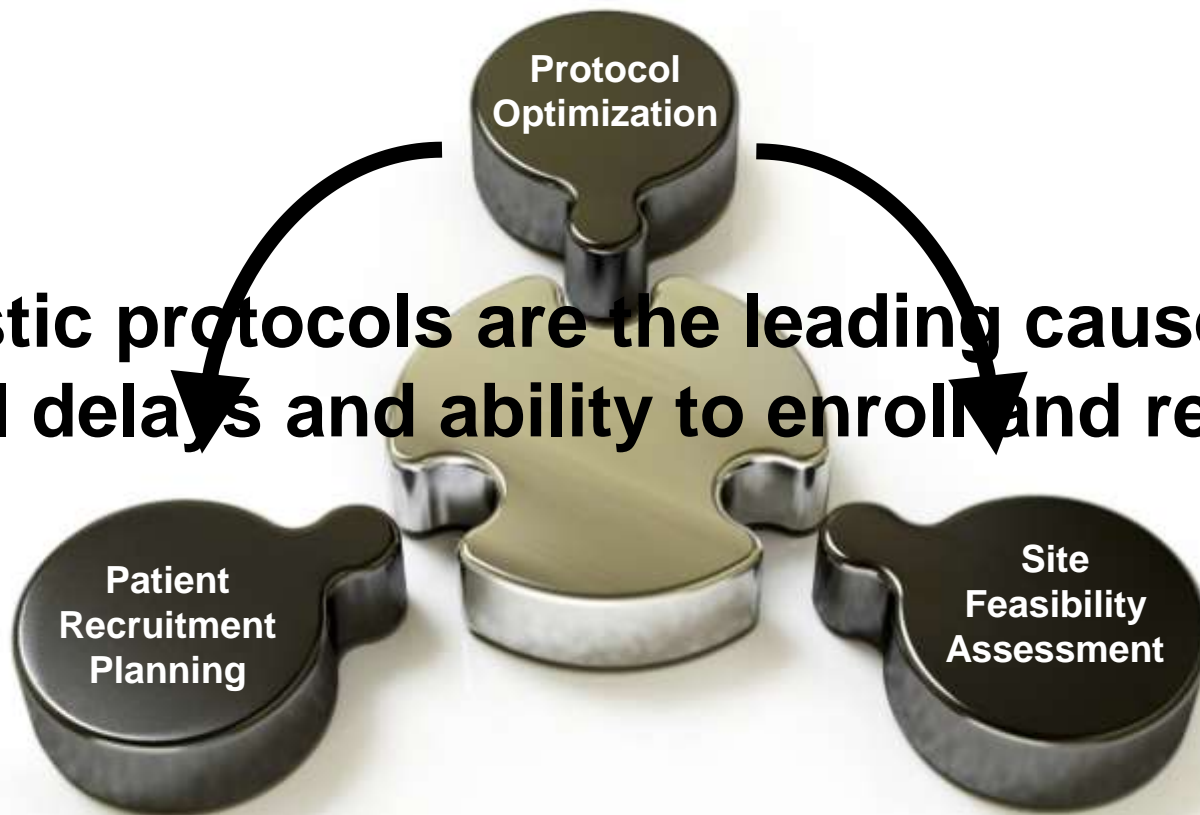


The Three Challenges to Your Study's Success



Protocol Optimization

Unrealistic protocols are the leading cause of protocol delays and ability to enroll and retain patients



Current State

- The cost of a protocol Amendment = >\$500,000
- 80% of our patients come from 20% of your sites
 - Cost \$15,000 to set-up and initiate a site
 - Cost \$25,000/site management
- Cost for poor performing sites \$5-15M



The Current State

- Lot of stakeholders to satisfy - locally and internationally
 - Internal Management
 - Regulators
 - Insurers
 - Policy Makers
 - Investigators
 - Patients



The Current State

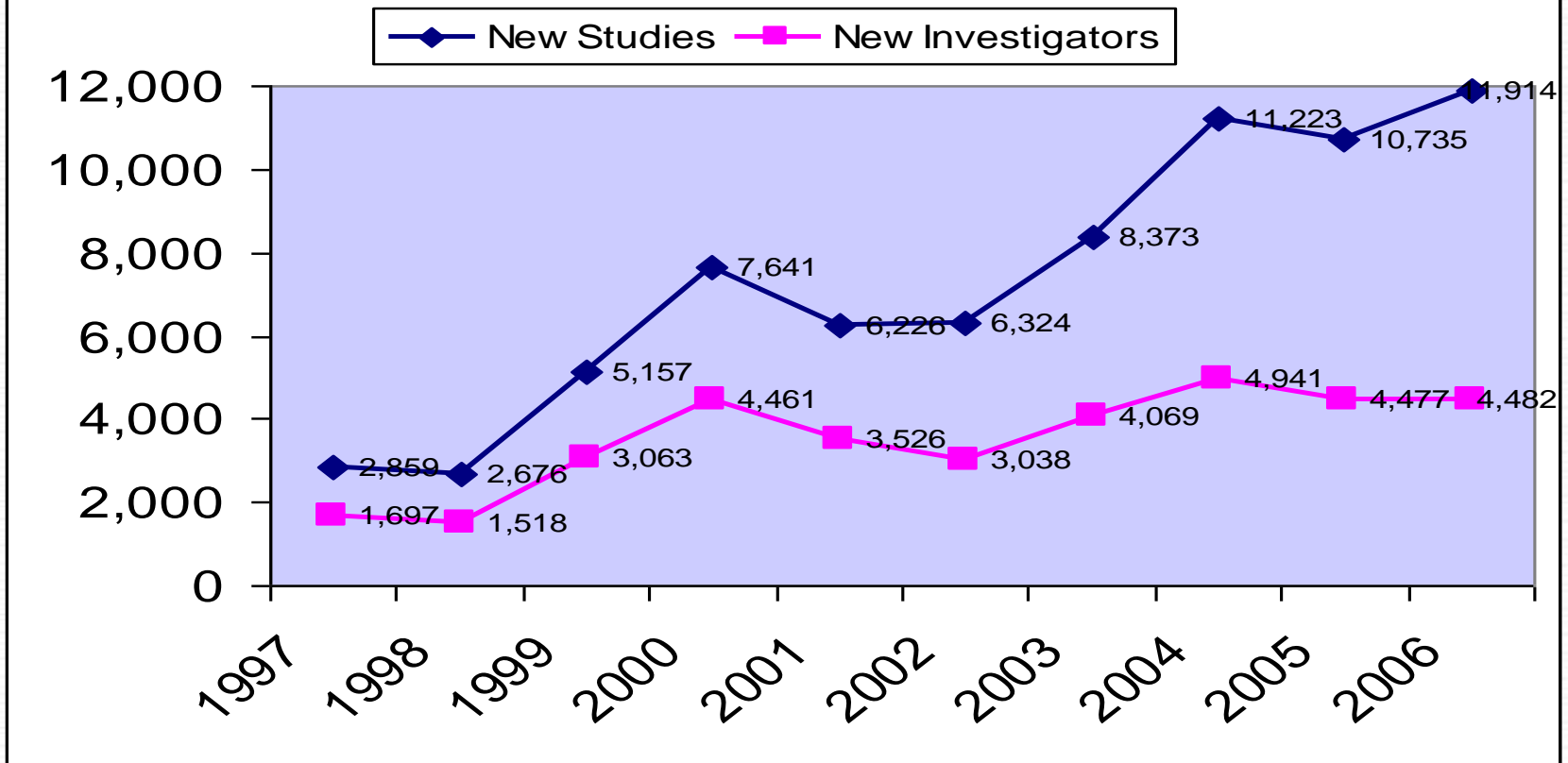
- Protocols too complex
 - Between 1999 – 2005 annual growth rate in number of procedures per protocol increased 6.5%
 - In this same time period CRF pages rose from 55 to 180 per subject
 - Annual Growth rate in procedural frequency increased by 8.7%
 - 3 fold increase in number of inclusion criteria
 - Significant increase in the use of PRO
 - Inclusion of biomarkers and efficacy signals earlier

Source – Tufts CSDD



The Current Status

More Investigators, Lots More Studies Non-US Investigators



Source: CenterWatch Analysis, FDA, 2008. Published in "State of the Clinical Trials Industry" CenterWatch, 2008

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What are we to do?

- **Protocol Optimization**
 - Investigator and clinical coordinator review early design parameters
 - Critical review of advanced draft by investigators, coordinators, Providers, internal management
- **Study Procedures**
 - In pivotal trials avoid exploratory endpoints
 - Understand how the patient will move through your study and ensure your assessments maximize the site coordinator and patient convenience
 - Specify only relevant body systems for examination
 - Objectively assess the need for each inclusion and exclusion criteria



What are we to do?

- Study Procedures – Inclusion/exclusion
 - Avoid arbitrary numerical ranges for entry criteria (e.g. age ranges, history of symptoms, time since diagnosis, periods of clinical stability) if other medical criteria or definition adequately describe the relevant patient population
 - Impact on ability to enroll patients
- Study Assessments
 - Be flexible in how time windows are assigned
 - Minimize the number of study visits

What else do we need to do....what do you do?



Site Selection

Vicki DiBiaso, Senior Director,
Feasibility and Patient Recruitment

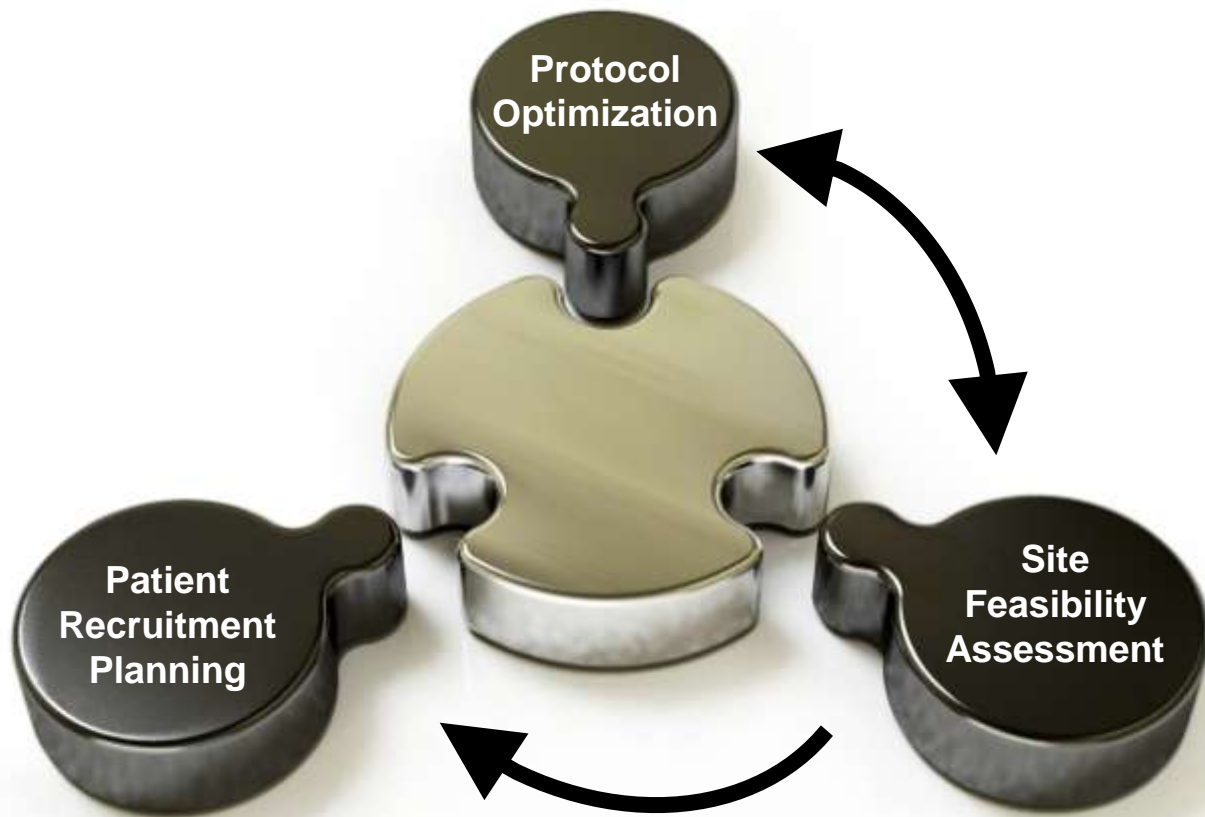


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Site Feasibility Assessment



Site Selection / Feasibility Assessment Challenges



Protocol-specific “Must Have” site characteristics are not defined and communicated to all parties



The “wrong” questions are asked of the “wrong” people in the “wrong” way







Enrollment validation activities are not performed



Site selection decisions are not “evidence-based”

What Type of Site Are We Looking For – In General?

		Investigator Interest , Capability & Willingness	
		High	Low
Availability & Enrollability of Patient Population	High	Dr. Smith Dr. Gonzales Dr. Abrams	Dr. Cassidy Dr. Williams
	Low	Dr. Ellis Dr. Garcia Dr. Robinson	Dr. Jones Dr. Armstrong

-  Higher likelihood of success
-  May be able to support with training, resources, recruitment assistance, etc.
-  Will be harder to engage but may be able to leverage available patients
-  All the resources, motivational efforts, and support will likely not yield expected results



Defining the “Must Have” Criteria: Protocol Specific

Criteria	Criticality	Can Be Determined by	Category
A minimum of 1500 patients in their own database	Must Have	Enrollment Validation Exercise	Patient Availability & Enrollability
Availability of PI at least 2.5 hours for close patient monitoring during invasive screening procedure (visit 1)	Must Have	Site Contact: Visit	Willingness / Commitment
Access to (specialty equipment) and at least 2 certified technicians	Must Have	Investigator Data Base	Capabilities
Standard of care practice which allows for concurrent treatment with Drug X	Must Have	Site Contact: Phone	Patient Availability & Enrollability
IRB / EC which accepts patient stipend of ~\$250.00 per each visit with invasive procedure	Nice to Have	Site Contact: Survey	Patient Availability & Enrollability
Electronic medical record system for efficient pre-screening	Nice to Have	Site Contact: Survey	Patient Availability & Enrollability



Potential Fixes

- Site selection / feasibility strategy meetings
- Approach a few sites first to find out...
 - what the key obstacles and critical success factors are
 - what the site would recommend to make the study more operationally efficient
 - what factors would make the study more easy to enroll and retain subjects
- Use this to define your “Must Have” Characteristics
- Prioritize information gathering requirements and process
- Focus site conversations and site visits on the value-added aspects that will address the “Must Have” criteria
- Ensure sites have all the information they need to answer the questions
- Validate enrollment potential
- Score sites in an objective fashion using pre-identified and agreed-up success criteria



Accountabilities & Responsibilities

Sponsors / CROs

- Be open and honest about the challenges up front
- Give sites adequate time and information
- Tell sites it's OK to decline
- Help them decline quickly

Sites

- Be proactive about alerting sponsors to the issues as well as opportunities
- Don't commit without taking the time to evaluate all aspects of study feasibility
- Just say "no"



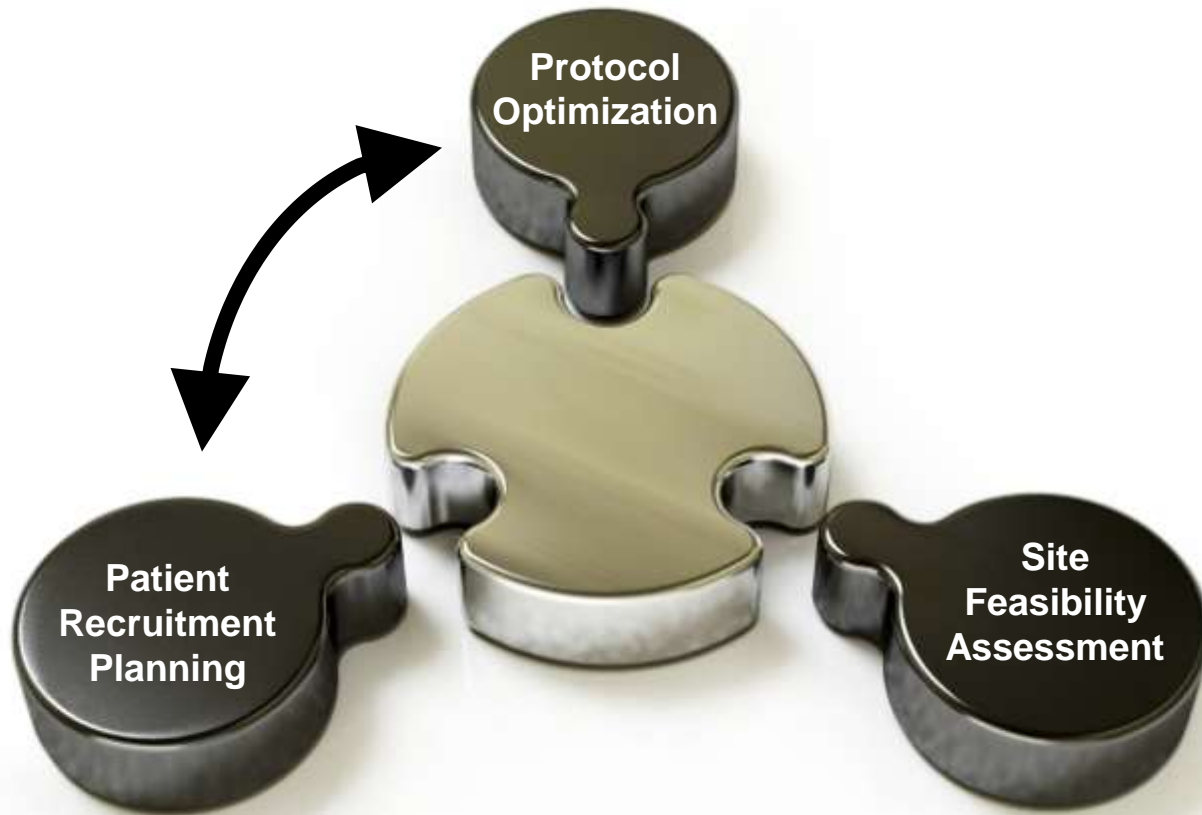
Jim Kremidas
VP Global Head of Patient
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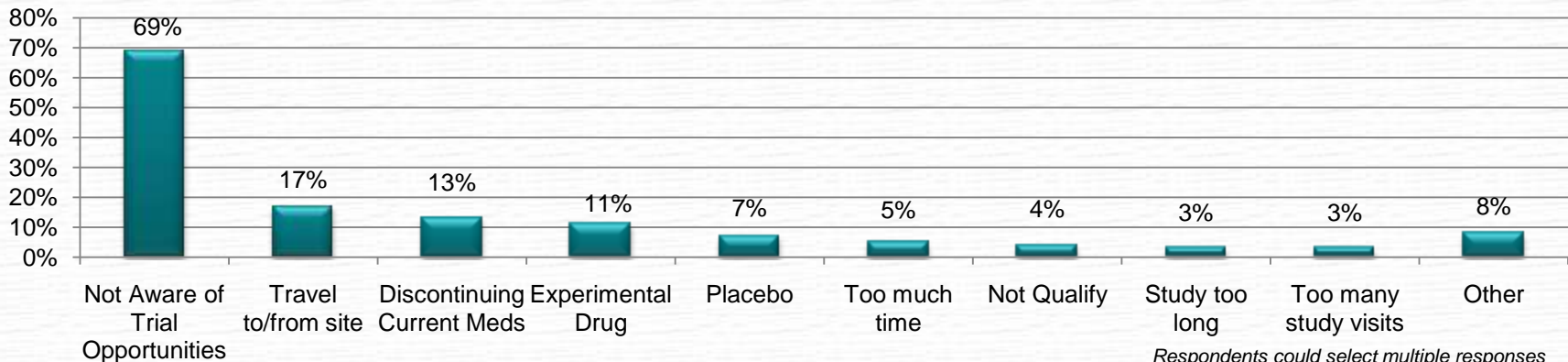


Patient Recruitment Planning



Supporting Sites to Reach their Recruitment Goals

- Develop trial level recruitment/retention **communication** strategy
 - **Site Support Materials**
 - Site staff “top of mind” (differentiate trial)
 - Communication tools to facilitate patient / staff discussions
 - **Direct to Patient Outreach programs**
 - Use appropriate tools based on protocol, healthcare market and patient type
 - **Retention**
- Integrate the recruitment **communication** plan into the “**holistic**” recruitment plan
- Track results and capture knowledge/data to drive **process improvement**



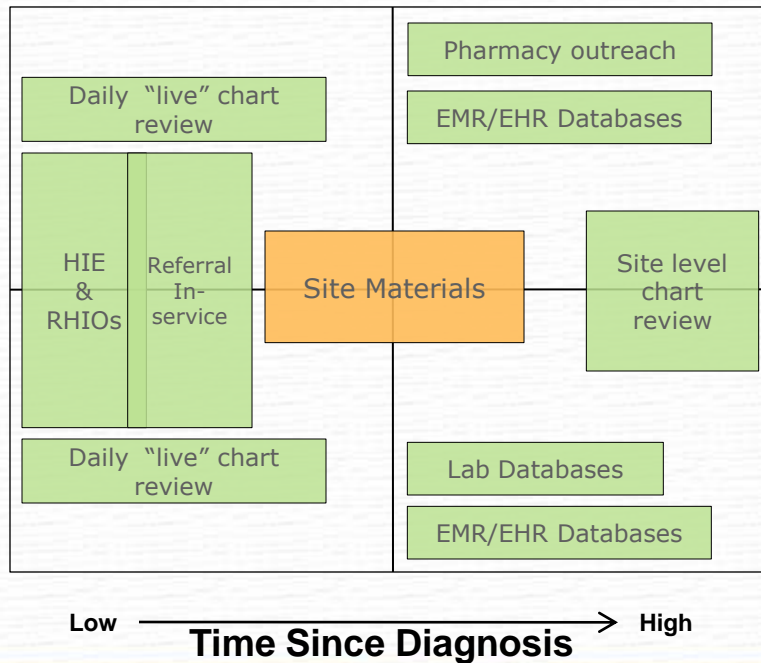
Respondents could select multiple responses
Source: iGuard.org 2009



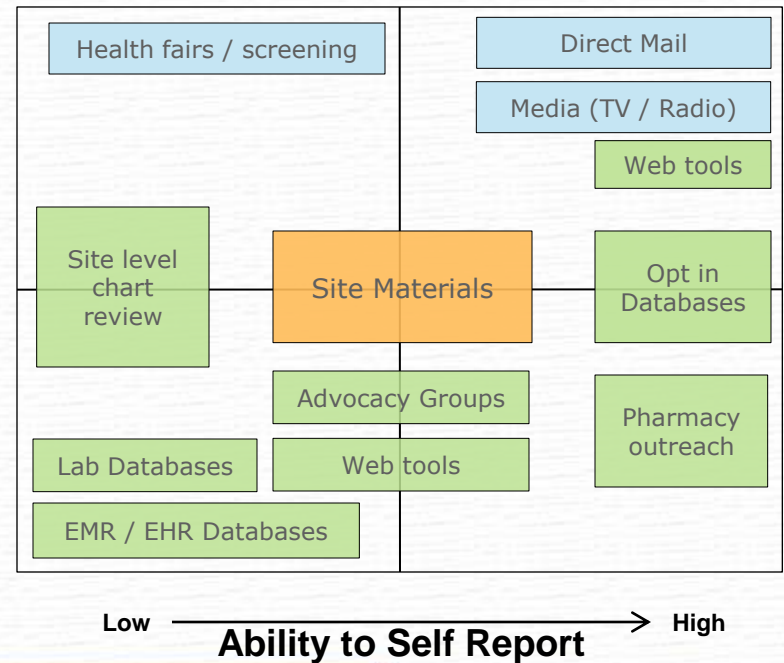
Recruitment Tool Strategic Framework

- Understanding and classification of each protocol helps to determine appropriate tool selection, recognizing each study is unique
- Although a hammer is a great tool.... it functions poorly as a saw....

Acute / Oncology Indications



Chronic Indications



Logistical and emotional barriers to clinical trial participation.

Logistical Barriers

- Most logistical issues revolve around **time and flexibility**
 - Study visits not compatible with patients' work schedules.
 - Key follow-up events perceived to be fixed on the calendar.
- **Transportation issues** are significant problems
 - Key issue with elderly patients.
 - Major problem in areas where patients travel long distances for care or where weather affects ability to travel.
 - Travel costs becoming greater issue.
- Patients more likely to be interested in trials due to lack of adequate insurance are often the least likely to be able to afford to take time from work for follow-up visits.
- Logistical burden is especially **hard to rationalize if patient may be on placebo.**

Emotional Barriers

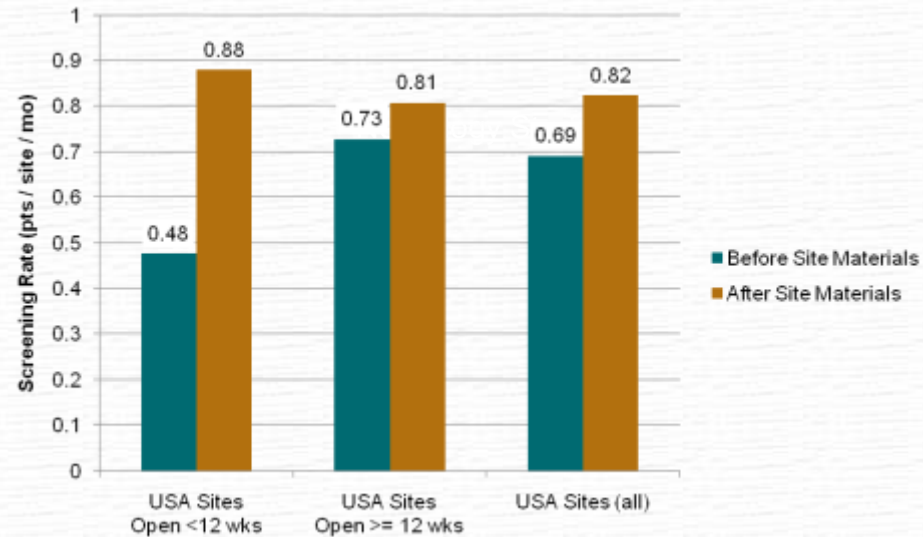
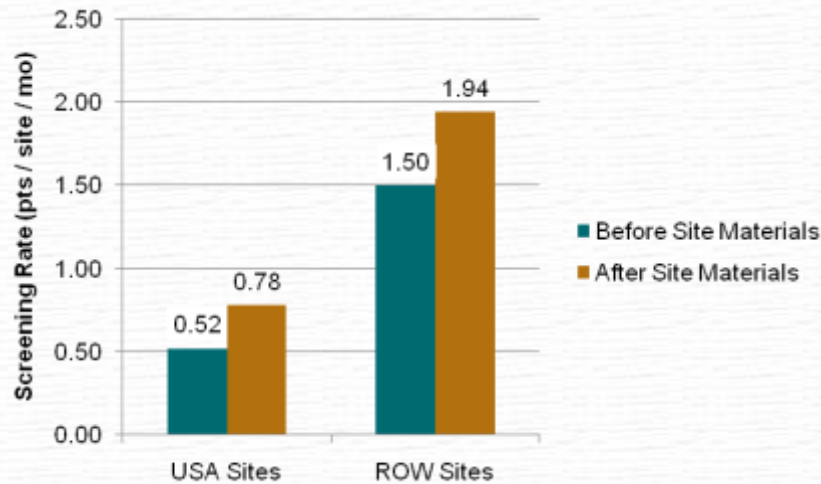
- **Control issues** are significant barriers for patients who are seriously ill. This emotional barrier is often part of the "guinea pig" fear.
- **Inability to "forget" your disease.** Additional office visits after course of therapy has ended are often very negative for cancer patients. They want to leave the cancer behind them.
- More **extensive monitoring sometimes communicates greater risk** for trial participants.
- **Fear of delaying initiation of therapy** in order to complete enrollment and screening process. This is especially problematic in oncology studies. By the time patients get diagnosed, they want to be treated immediately.



Site Materials Lift

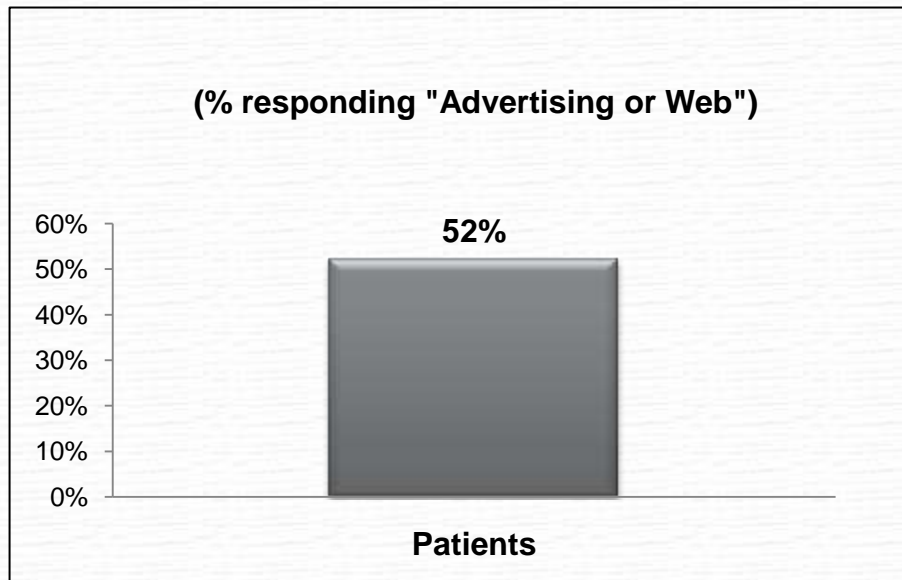
Site materials drive 20%-60% increase in screening rate

Clear benefit to early distribution of site materials

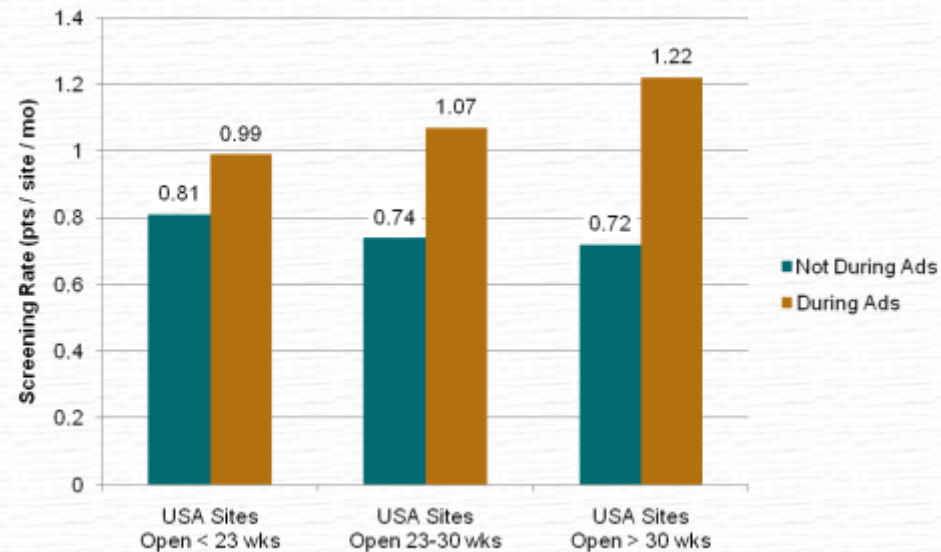


Timing / Value of Advertising

How Patients Learn about Trials



Sites open longer before advertising realize greater lift



The Three Challenges to Your Study's Success

Who is and should be responsible and accountable for these critical success factors in your organization?

How does this process work within your organization?

How can we improve the process?

