PATIENT-CENTERED CLINICAL TRIALS

Campbell Pharmaceutical Seminar Series 2014 at Rutgers Business School

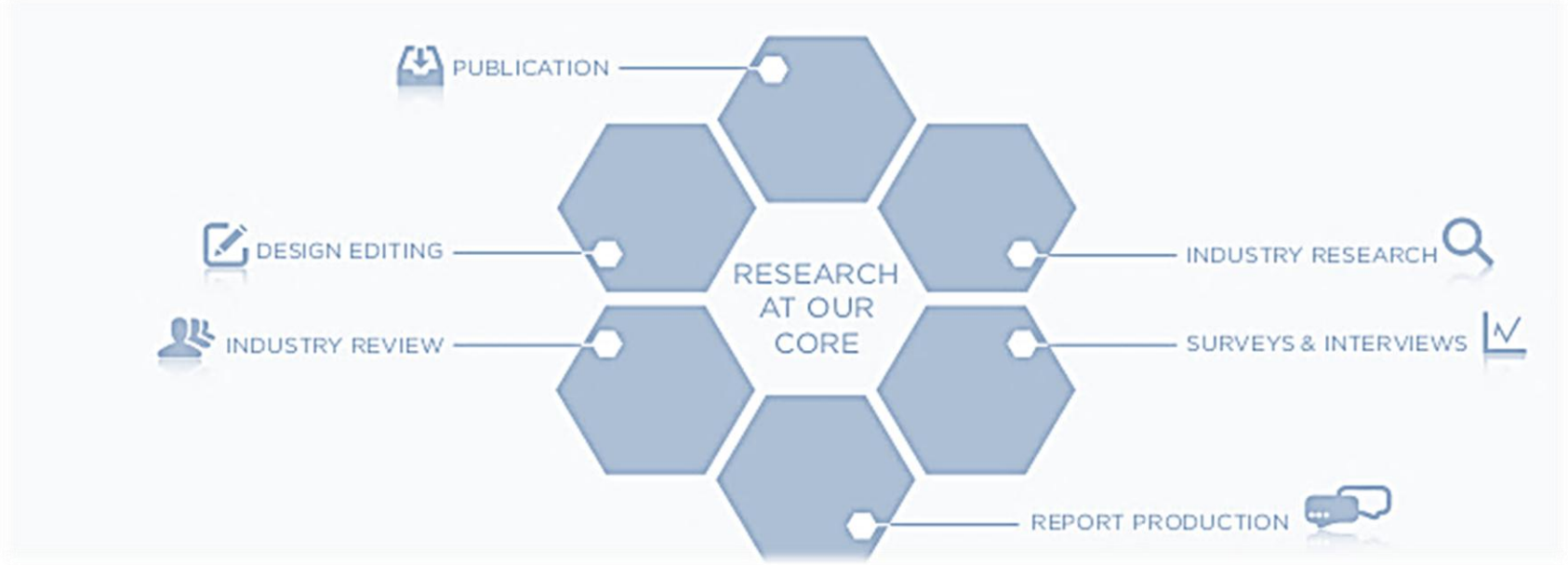
eye for pharma

TRANSFORMING THE CLINICAL TRIAL ENTERPRISE

What does eyeforpharma do?

- Global provider of **pharmaceutical business intelligence**
- Draw subject experts and decision-makers **out of their silos**
- Provide trusted hub for pharma leaders to exchange ideas and **stay up-to-date with shifting practices** within industry
- Help senior-level executives define future strategy and direction and provide them with the **insights and relationships to shape innovation** and encounter disruptive industry trends

Research-based Client Engagement



How we Broker Knowledge

Conversations and Strategic Consultations > Continous involvement with the industry through series of semi-structured in-depth interviews, systematic coding and analysis

Competitive Screening > Benchmarking studies, direct comparisons with a peer group of companies, internal gap analyses

Case Studies > Sharing of best practises and innovative pilots from leaders in the field

Survey Research > Various scales, cross-industry to customized with key job titles

Focus Groups and Faciliation > Measurement of perceptions, opinions, and attitudes

Policy Research and Regulatory Analysis

Leadership Panels, Executive Symposia, or large Industry Summits

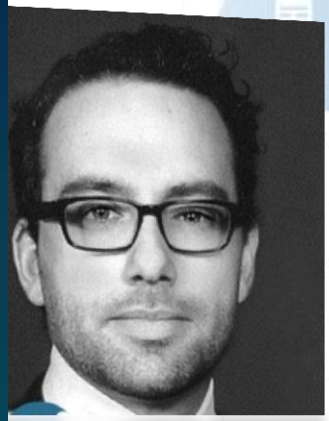
FC Business Intelligence

Part of UK-based FC BI Group

INSIDER · Decomworld · Renewable Waste INTELLIGENCE · TIDAL TODAY · NUCLEARENERGY INSIDER

Telematics UPDATE · openmobilemedia · VGI VIDEO GAMES INTELLIGENCE · eyeforpharma · WIND ENERGY update

eyefortransport · eyefortravel · Ethical CORPORATION · INCITE · USM useful social media · CSP today BUSINESS INTELLIGENCE



Ulrich B. Neumann B.A., B.Sc., M.A., M.Sc.

Global Project Director at eyeforpharma, US Office

- Leads cross-industry research and strategic projects within the biopharma sector, also manages portfolio of executive forums as well as key vendor accounts
- Successfully launched eyeforpharma's clinical trials division, currently responsible for global brand positioning and growth strategy
- Previously held Roger Silverstone Fellowship at University of Southern California
- Past client consulting work in market entry, communications, and political strategy. Former accounts include a cloud/ telco infrastructure provider, a national cancer trial foundation, a multinational energy firm, a US aircraft manufacturer as well as an industry group of bottled water brands in Europe.

eyeforpharma

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PCCT Project Milestones

- 8 months market research, incl. 95 executive interviews ✓
- 2 cross-industry surveys on the business rationale for PCCT ✓
- Executive Symposium, 100 senior representatives ✓
- 2 focus group discussions with patient advocates ✓
- Ongoing working group with key pharma leaders
- Production of interactive global seminar

- Publication of 1st white paper on Patient-Centered Innovation ✓
- Discussion in trade press: i.a. International Clinical Trials Magazine, Applied Clincial Trials, CenterWatch ✓
- Publication of book of ideas: 10 Thought Leaders speak out ✓
- Publication of 2nd white paper: PCCT Compass for the Industry
- Publication of thought paper: Patients at Heart of the Organization

Participating Industry Leaders

Mike Collins, Vice President - Global Clinical Operations, ***Alexion Pharmaceuticals***

Marie Eckerd, Feasibility & Recruitment Partner, ***AstraZeneca***

Bonnie Brescia, Principal, ***BBK Worldwide***

Sharon Hanlon, Director - Clinical Trial Partnerships, ***Bristol - Myers Squibb***

Paul Ivsin, Director, , ***IMS***

Bray Patrick-Lake, Director - Stakeholder Engagement, ***Clinical Trials Transformation Initiative***

Thomas Krohn, Business Lead of Lilly Clinical Open Innovation Team, ***Eli Lilly & Co.***

Paulo Moreira, Vice President - GCO & Head - External Innovation, ***EMD Serono***

James O'Leary, Chief Innovation Officer, ***Genetic Alliance***

Barbara Bierer, Faculty Co-Director, ***Harvard Medical School***

David Vulcano, AVP & Responsible Executive for Clinical Research, ***Hospital Corporation of America***

Andreas Koester, Vice President - Clinical Trial Innovation & External Alliances, ***Janssen***

Laura Lee, Special Assistant to the DDCC - Patient Safety and Clinical Quality, ***NIH Clinical Center***

Jeanne Regnante, Executive Director - Office of the Chief Medical Officer, ***Merck***

Colin Scott, Clinical Trial Leader, ***Novartis***

Susan Sheridan, Director Patient Engagement, ***Patient-Centered Outcomes Research Institute***

Roslyn Schneider, Global Patient Affairs Lead ***Pfizer***

Christine Pierre, President, ***The Society for Clinical Research Sites***

Tomasz Sablinski, CEO, ***Transparency Life Sciences***

Ken Getz, Director - Sponsored Programs, ***Tufts Center for the Study of Drug Development***

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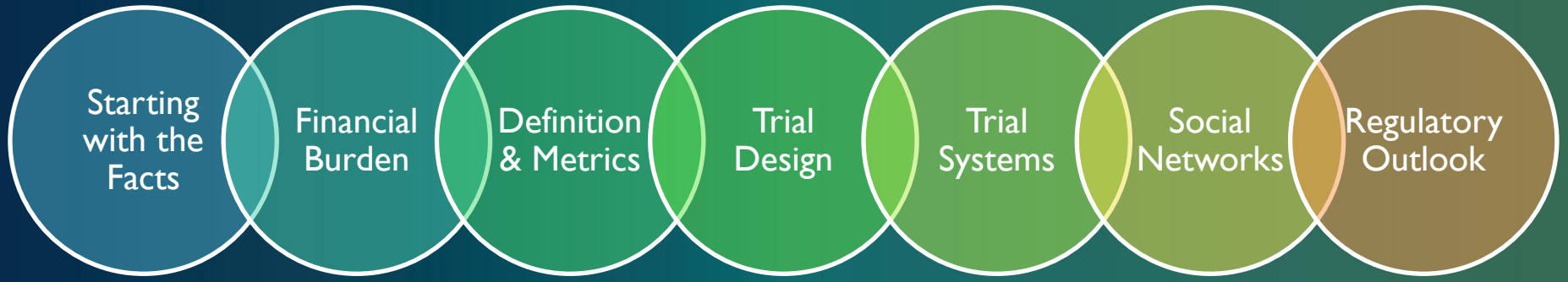
#pcct

Outline of today's presentation



- Material for this presentation has solely been selected by the presenter for educational purposes without involvement, financial, promotional or otherwise, of any of the industry organizations, individuals or initiatives mentioned.
- Statements, facts and opinions stated are attributable to the presenter and must only be interpreted in context with the oral presentation. They may not necessarily reflect opinion of Rutgers School of Business, eyeforpharma, or any of the organizations involved in their meetings.

Starting with the Facts

* Get the latest research figures where the clinical industry stands on trial challenges, patient recruitment and retention

Share of Americans who think it is very important that the USA are a global leader in medical research — **75%**

Share of Americans who say they have little to no knowledge about medical research and the participation process — **75%**

Share of Americans who say they would consider getting involved in an appropriate clinical trial if asked — **77%**

Share of Americans who say their doctor told them about the opportunity to participate in a clinical trial — **7%**

Source: Research America (2007), Society for Women's Health Research (2008), CISCRP

Are clinical trials even safe?

- **17%** generally believe clinical research studies are **very safe**
- **51%** believe them to be **somewhat safe**

- **11%** believe them to be **not very safe**
- **7%** believe them to be **not safe at all**

- **14%** say they don't have any knowledge

1/3 of people believe clinical trials are not safe or don't know that they are

So, who get's involved?

- **2% of the US population**
- **4% of physicians in the US**

Source: CISCRP Survey 2008, n=1000, Eli Lilly Presentation (2014)

Share of research sites in a given clinical trial that typically under-enroll patients	**37%**
Share of research sites in a given clinical trial that typically fail to enroll even a single patient	**11%**
Average extension of the original study timelines necessary to meet enrollment levels across all therapeutic areas (2013)	**+100%**

Source: Tufts Center for the Study of Drug Development (2013). Impact Report, Vol. 15, No.1, Jan/Feb 2013

Clinical Trials: Rising Complexity

Study Design Elements	2000–2003	2004–2007	2008–2011
Unique procedures per protocol **(median units)**	20.5	28.2	30.4
Total procedures per protocol **(median units)**	105.9	158.1	166.6
Total investigative site work burden **(median units)**	28.9	44.6	47.5
Total eligibility criteria	31	49	
number of case report form pages per protocol **(median units)**	55	180	

Average increase of trial per patient cost since 2008 **+70%**

Source: Tufts CSDD, Cutting Edge Information (2011)

Share of later stage clinical trails procedures solely conducted to collect extraneous data **20%**

Average cost of these procedures per trial **> $1 million**

A Typical Phase III Protocol	2002	2012
Total Number of Endpoints	7	13
Total Number of Procedures	106	167
Total Number of Eligibility Criteria	31	50
Total Number of Countries	11	34
Total Number of Investigative sites	124	196
Total Number of Patients Randomized	729	597
Proportion of Phase III data collected that is 'Non-Core'		31%
Total Number of Data Points Collected*		929,203

Source: Tufts (2012). Impact Report, Vol. 14, Medidata

Dangers of protocol non-adherence

Significant study delays – recruitment will have to be prolonged to maintain an adequate sample size to power the study

Increased costs – due to extended resource utilization of medicine, labs, personnel and processing

Failure to win approval – missing data may call into question reported results, as drug safety may be overestimated while risks, adverse effects as well as medication effectiveness could be underestimated

Average Trial Retention Rates

69% in 2003

48% in 2006

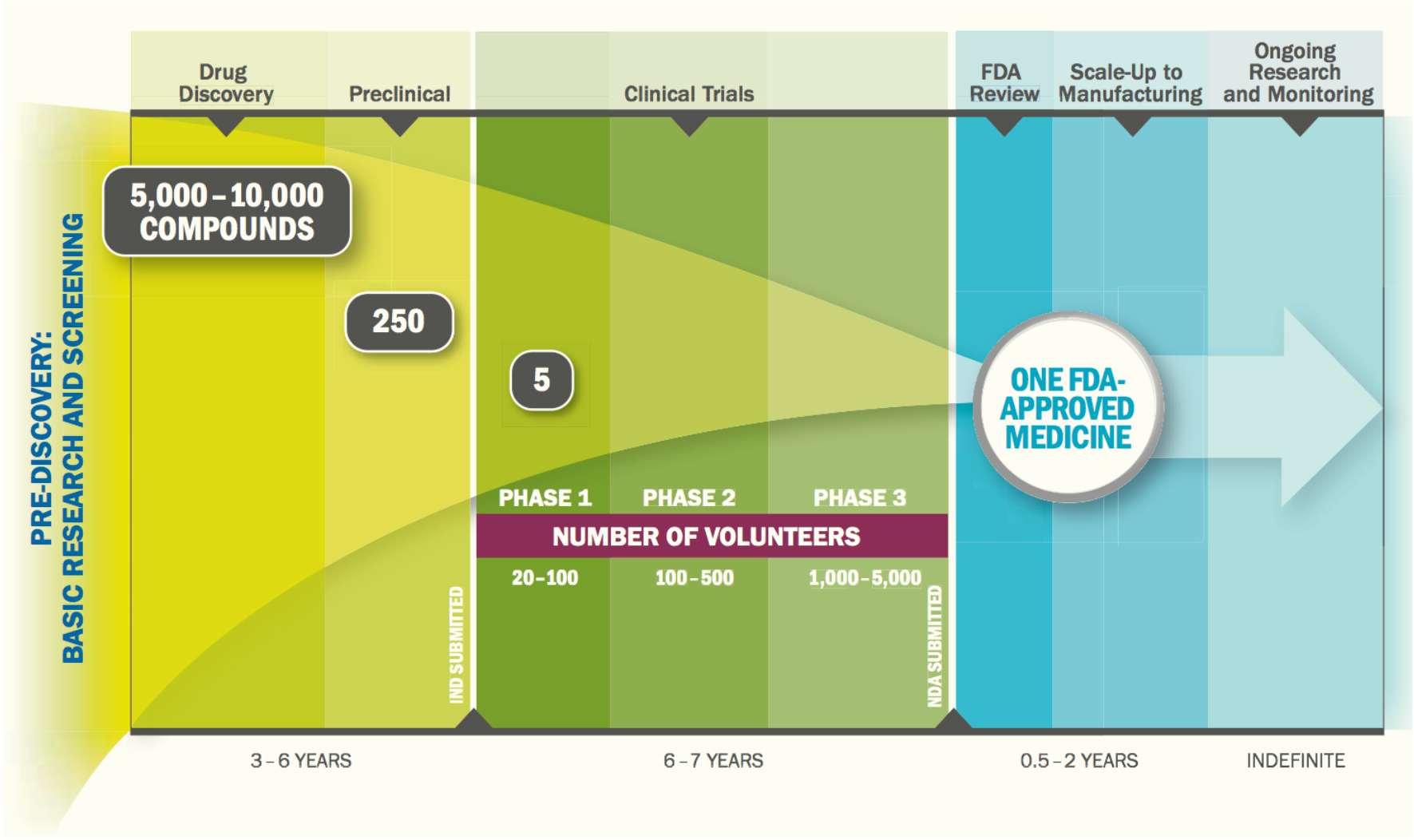
30%* in 2013

Drop in patient *enrollment* rates for clinical trials conducted between 2000 and 2006 **-16%**

Drop in patient retention rates for clinical trials conducted between 2000 and 2006 **-21%**

Drop in patient retention rates for clinical trials conducted between 2003 and 2013 **-56%***

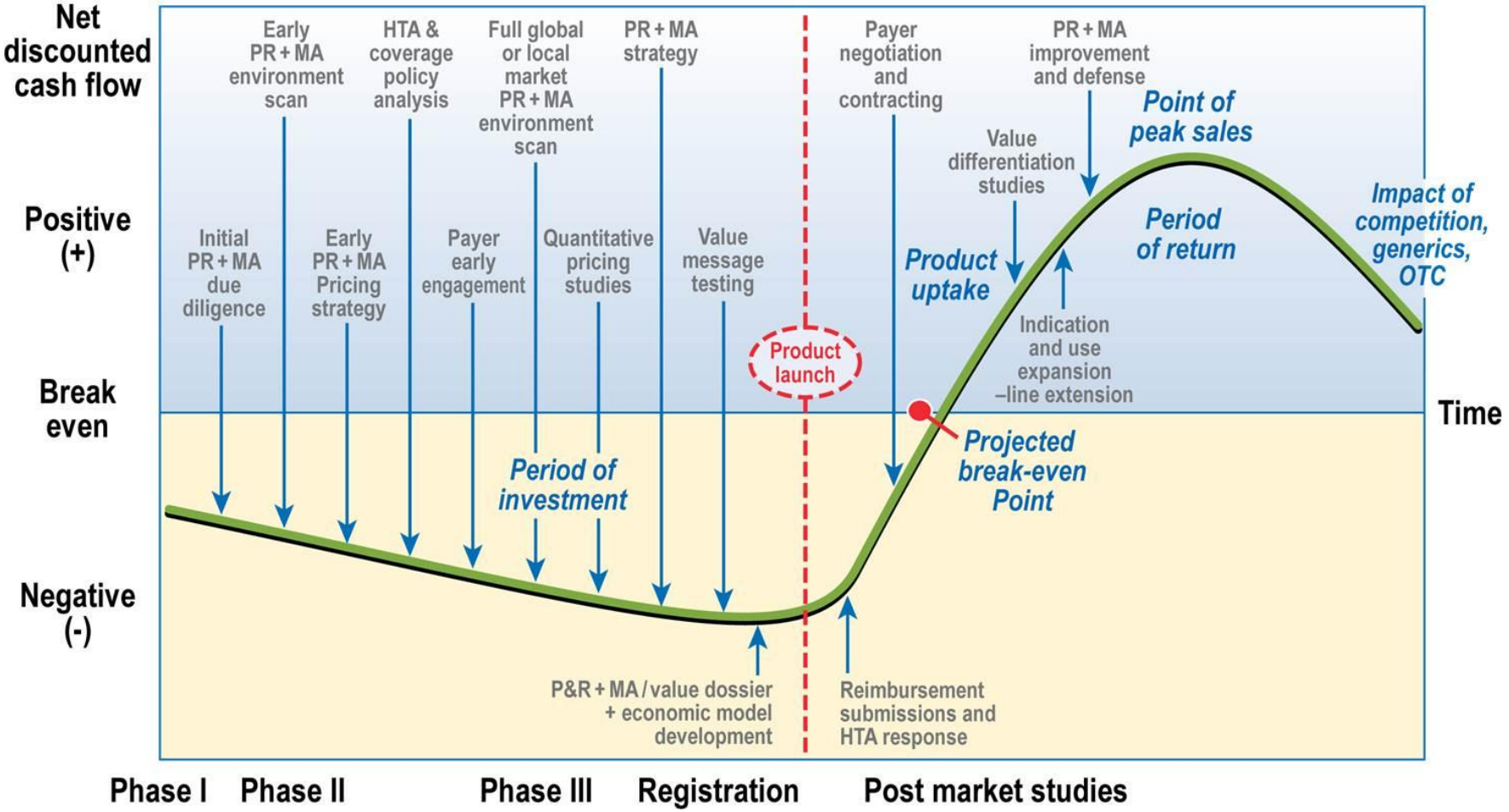
*Source: Getz K. A. 2011. Public Confidence and Trust Today: CISCRP, Tufts , "Growing Protocol Design Complexity Stresses Investigators, Volunteers" Impact Report 2008, * Patients 2 Trials (P2T) Consortium , 2014 Meeting*



Source: PhRMA

The Financial Implications

* Realize the economic burden of the lack of patient centricity in drug development and understand why it must be seen as a revenue driver



Source: RTI Health Solutions, www.rtihs.org/sites/default/files/attachments/FS_MarketAccess_0.pdf

The bottom-line

Average yearly cost spent on patient recruitment by clinical study sponsors, investigators and their partners — **$2-3b**

Approximate average cost spent on recruitment and retention in a clinical trial, per enrolled subject — **$7,600**

Estimated loss of a sponsor's sales revenue due to the delay of a drug in clinical trials, per month — **$40m**

Source: Tufts (2011, April 26), Mintz, C., (2010). Beasley, D. (2006)

Opportunity costs

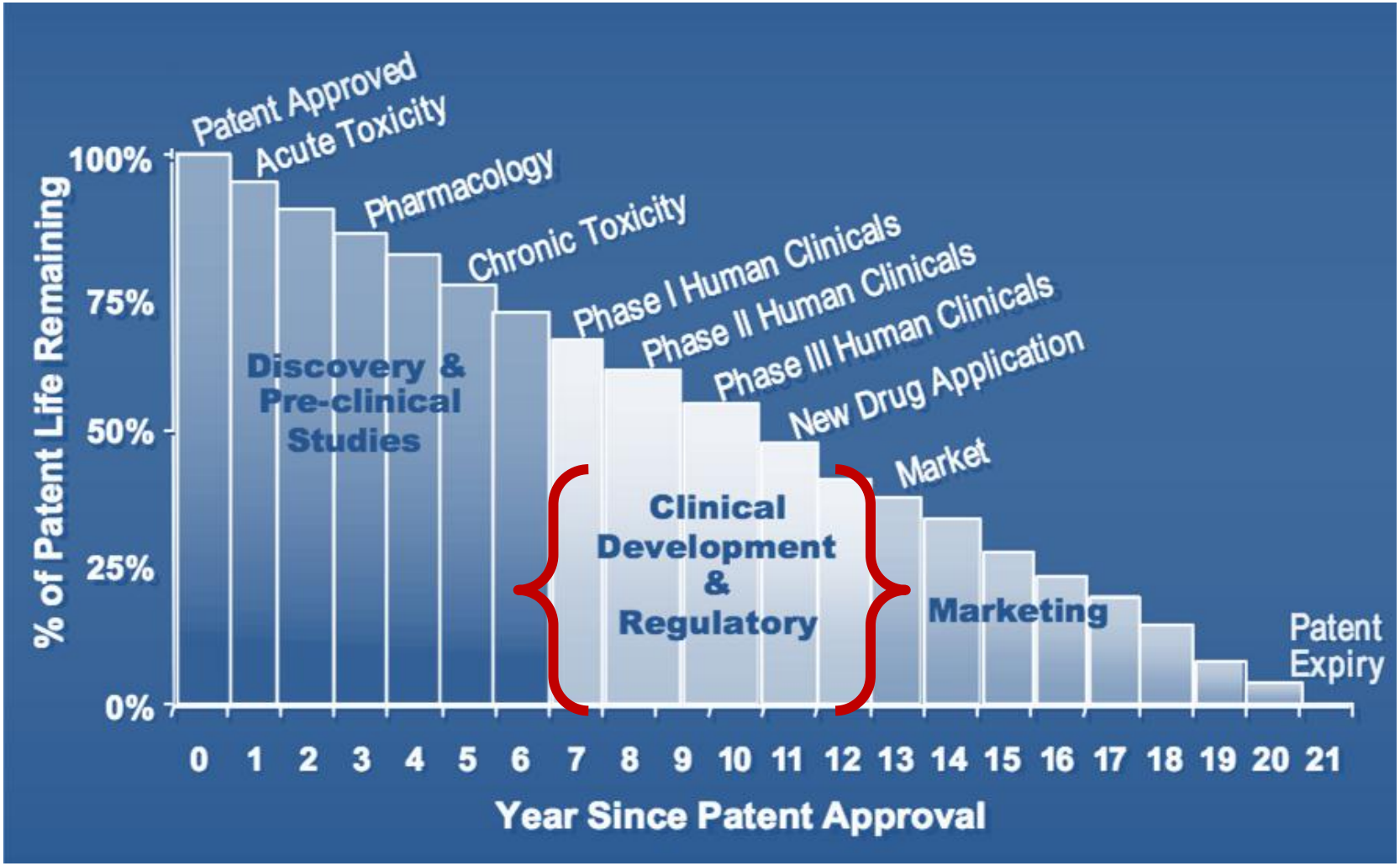
Estimated time a sponsor loses due to enrollment delays on average per trial

4.6 months

Estimated cumulative yearly time loss for a sponsor due to enrollment delays across all trials:

26 years

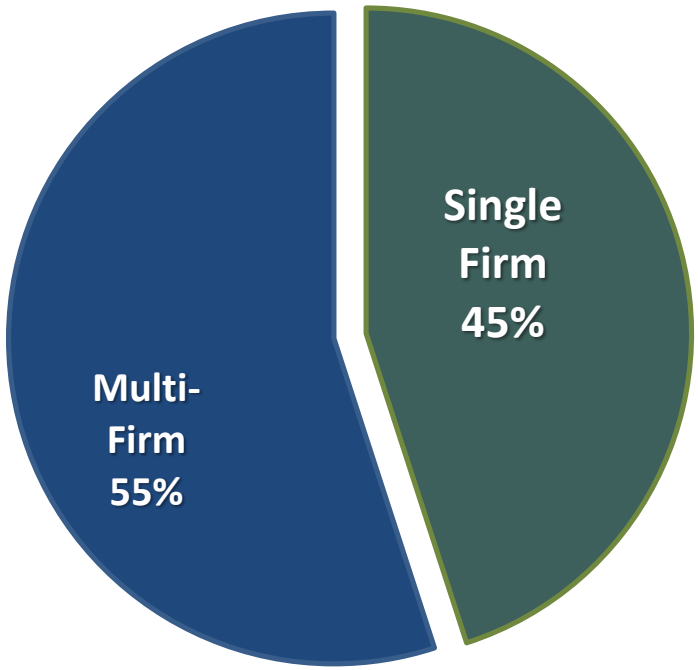
Source: Tufts (2011, April 26), Mintz, C., (2010). Beasley, D. (2006)


Patent Approved
Acute Toxicity
Pharmacology
Chronic Toxicity
Phase I Human Clinicals
Phase II Human Clinicals
Phase III Human Clinicals
New Drug Application
Market
Patent Expiry
Discovery & Pre-clinical Studies
Clinical Development & Regulatory
Marketing
% of Patent Life Remaining
100%
75%
50%
25%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Year Since Patent Approval

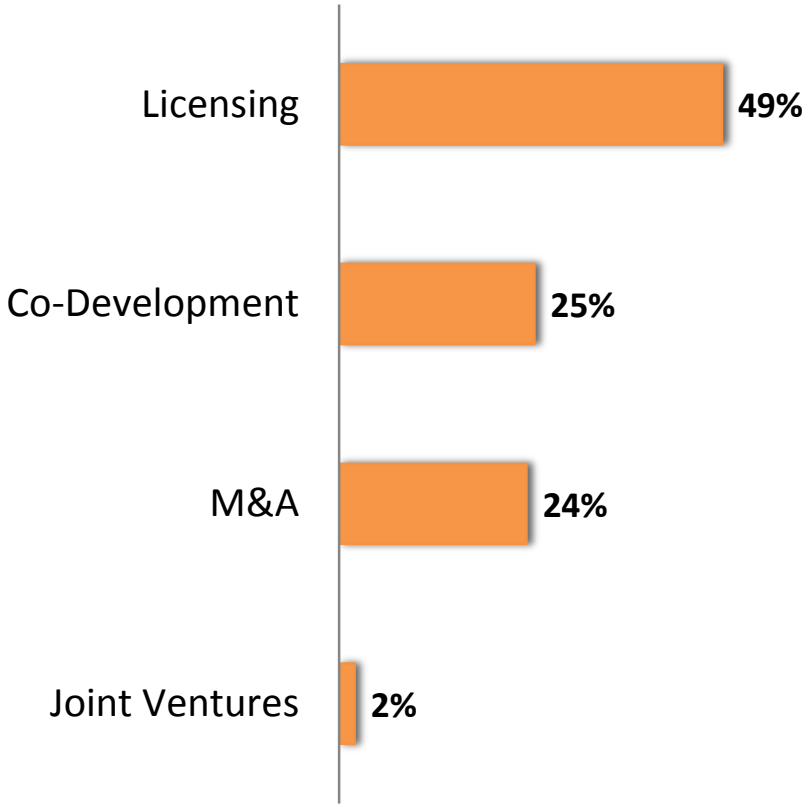
Collaborations to Spread Risk

(2000-2011)

Share of New Drugs Approved

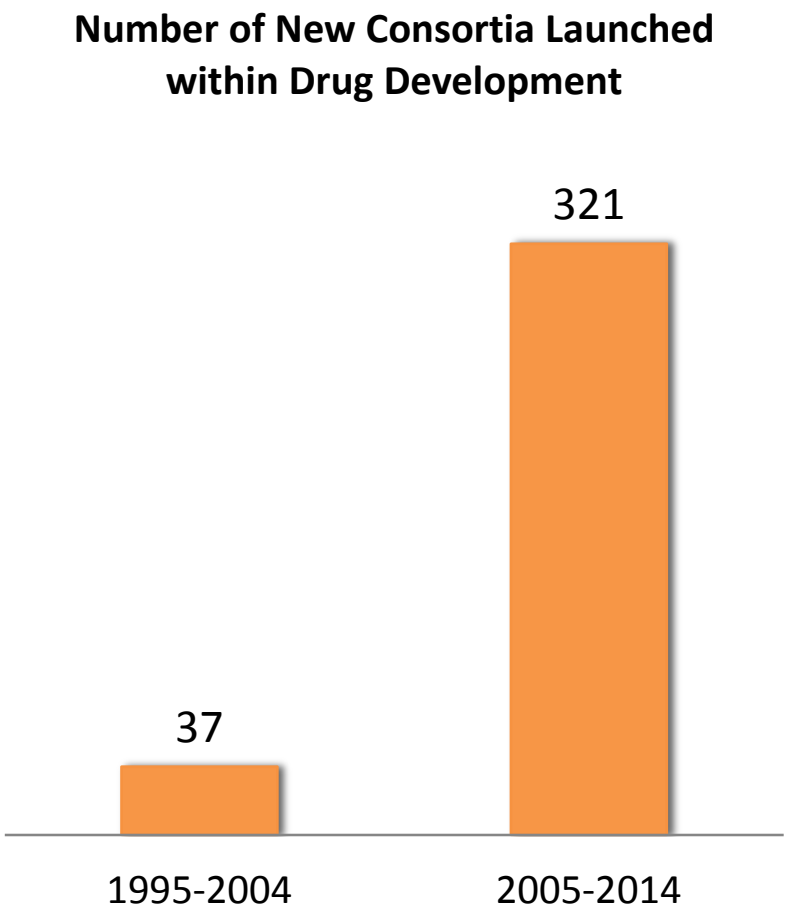


Type of Collaboration



Source: Tufts CSDD 2013

Proliferation Pre-Competitive Alliances



- Integration of research professionals from multiple sectors who have historically been 'competitors'
- Shared mission and operating plan that can be used by each stakeholder jointly or independently
- Shared governance and risk
- Leverage each participant's resources, knowledge and expertise

Ken Getz, Tufts CSDD, 2014, Source: FasterCures Consortiapedia

Definition & Measurement

* Hear definitions of patient centricity and explore how to measure the concept for clinical quality management

A paradigm shift

Established Trial Model	Patient-Centered Clinical Trial
• Linear, sequential	• Multi-directional, interactive
• Compartmentalized	• Open
• Insular	• Integrated
• Vertical ownership and centralized risk	• Horizontal ownership and shared risk
• Rigid, transactional, reactive	• Flexible, adaptive, proactive
• Proprietary clinical data at the core	• Patient experience at core
• Focus on great science	• Focus on great and feasible science
• Participant as study subject	• Participant as partner, lead customer

From Ken Getz, Tufts CSDD, 2014

What is your working definition?

IOM – Institute of Medicine (2001) Crossing the Quality Chasm: A New Health System For the 21st Century.

"providing care that is respectful of and responsive to individual patient preferences, needs, and values, and ensuring that patient values guide all clinical decisions ."

What is your working definition?

Sue Sheridan

Director of Patient Engagement,
Patient-Centered Outcomes Research Institute (PCORI)

pcori

*"There are two areas of focus regarding patient centricity in research: patient centeredness and patient engagement. **Patient centeredness** is defined as research that is based on **outcomes** that are important to patients. **Patient engagement** in research is the **active participation of patients throughout the entire research process** – the planning, the conduct and the dissemination. Patient engagement is the means to the patient centeredness."*

What is your working definition?

Tomasz Sablinski

transparency life sciences

Founder and CEO,
Transparency Life Sciences

*"A trial that measures **outcomes that patients care about**. It needs to measure or collect outcomes, broadly speaking, in a way that's least intrusive to **patients' daily lives**.*

If you can accomplish both of those things it's going to be a quantum leap compared with where we are today."

What is your working definition?

James O'Leary

James C. O'Leary, Chief Innovation Officer,
Genetic Alliance

In its purest form, patient-centricity is the creation of a direct link between the goals of clinical trials and the needs of patients on an individual and global scale. It is not simply designing trials to meet the needs of participants, but rather creating systems and tools that allow participants to inform and influence the trials themselves."

What is your working definition?

Jeremy Gilbert

patientslikeme™

VP, Product and Strategy, **PatientsLikeMe**

"Measuring what matters to the patient in the trial itself, and designing the trial as much as possible to accommodate the impact on the patient's life."

What is your working definition?

Rhonda Kost

Clinical Research Officer,
The Rockefeller University Center for Clinical and Translational Science

"Designed with the patient's experience and priorities in mind (having asked real patients, and NOT having presumed to know their experiences/priorities). Those priorities might include convenience, expense, pain, risk, benefit, etc."

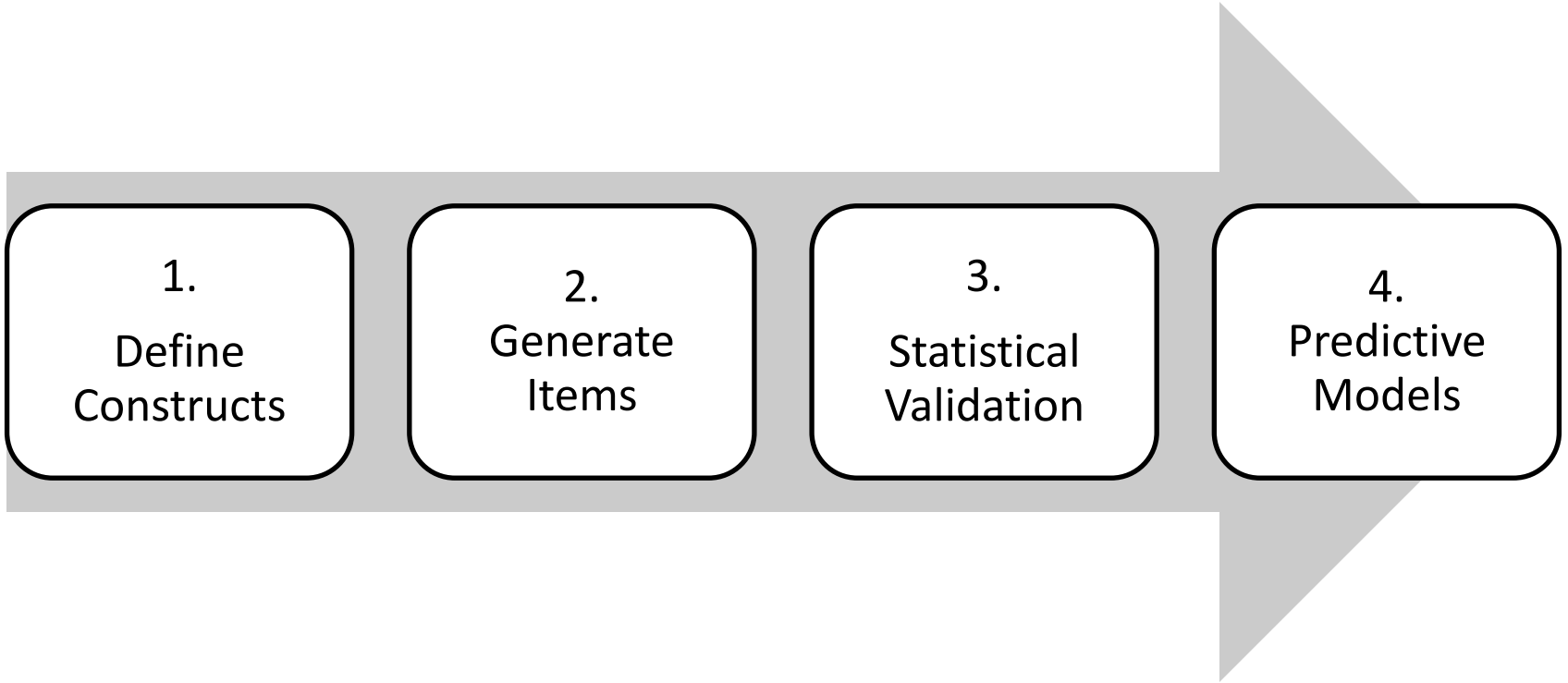
What is your working definition?

"Patient centricity is a dynamic process through which the patient regulates the flow of information through multiple pathways to exercise choices consistent with his/her preferences, values and beliefs.

[It entails] more than just the patient's voice; it involves the patient's thoughts, values, preferences, strengths and shortcomings"

Source: Robbins DA, Curro FA and Fox CH, Defining patient-centricity opportunities, challenges and implications for clinical care and research, DIA Therapeutic Innovation & Regulatory Science 47(3): pp. 349-355, 2013

How to measure the construct



From Howley, Michael, Associate Clinical Professor, LeBow College of Business, Drexel University

How to measure the construct

Patients participate in:

- Formulating research questions
  - Assess patient participation in:
    - Identifying the RQ
    - Designing the intervention
    - Identifying the goals & outcomes
    - Describe the qualifications of subjects
- Study design
- Trial conduct
- Disseminating study results

From Howley, Michael, Associate Clinical Professor, LeBow College of Business, Drexel University

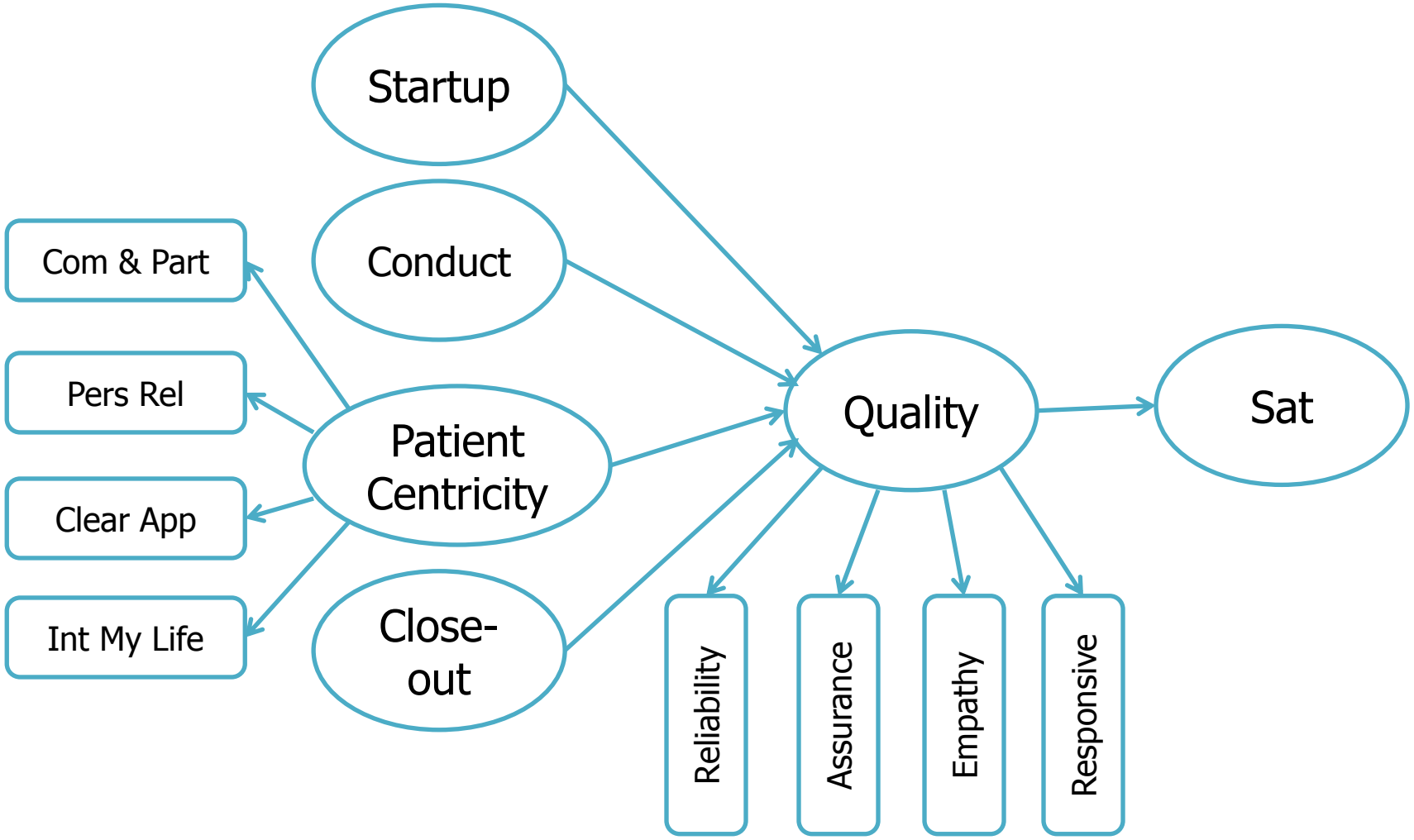
Established Measures: SERVQUAL

Rate your agreement with the following statements (1-10)

- **R**eliability
  - "When they said they would do something, they always did it."
  - "There were no mistakes in the care I received."
- **A**ssurance
  - "They were very knowledgeable."
  - "They gave me confidence by the way they provided my care."
- **T**angibles
- **E**mpathy
  - "They gave me individual attention."
  - "The treated me as a person."
- **R**esponsiveness
  - "When I requested a change, they were able to accommodate."
  - "When something went wrong, they quickly made it right."

Parasuraman, Berry, Zeithaml (1988), "SERVQUAL: A Multiple-Item Scale for Measuring Consumer Perceptions of Service Quality," Journal of Retailing, 64(1), 12-40.

A Model for Measurement



From Howley, Michael, Associate Clinical Professor, LeBow College of Business, Drexel University

Metrics to measure the construct

- Focus groups, surveys and retention rates
- Study metrics and quality measures
- Referred to randomized conversion rates
- Data quality and patient reported outcomes
- Satisfaction with care scores, level of site support
- Patient advocate feedback
- Investigative site feedback
- Social media monitoring
- Share of voice, perception
- Enrollment timelines

"We currently don't employ a reliable way of measuring it"

Customer-Centered Approaches

* Explore customer-centered approaches for informing and engaging patients

Participant Demographics

Your average trial subject

- Non-Hispanic White
- Married
- Male
- Middle Aged
- **Middle Class**

→

Common Attributes

1. Health insurance
2. Have their own physician
3. Interested in personal health
4. Medically literate

Source: Colin Scott, Novartis, 2014 Presentation, at eyeforpharma PCCT

Participant's Real Concerns

Comments Rank Ordered by Frequency of Reporting

5. I don't have insurance
4. I don't have a doctor
3. I don't have the time or money to go to doctor
2. I think clinical trials are dangerous
1. **What's in it for me?**

Source: Colin Scott, Novartis, 2014 Presentation, at eyeforpharma PCCT

Underserved Patients

1. Community Clinic in the 'Barrio' in San Antonio

2. Mario's Independent Pharmacy in the 'Barrio'

3. Social Work Departments in the Medical Center

TEXAS Department of State Health Services

DEPARTMENT OF SOCIAL WORK SERVICES

Source: Colin Scott, Novartis, 2014 Presentation, at eyeforpharma PCCT

Some Practical Findings

Achieving the highest potential of clinical trials depends on the incorporation of clinical research into the broad scope of practice of health care delivery

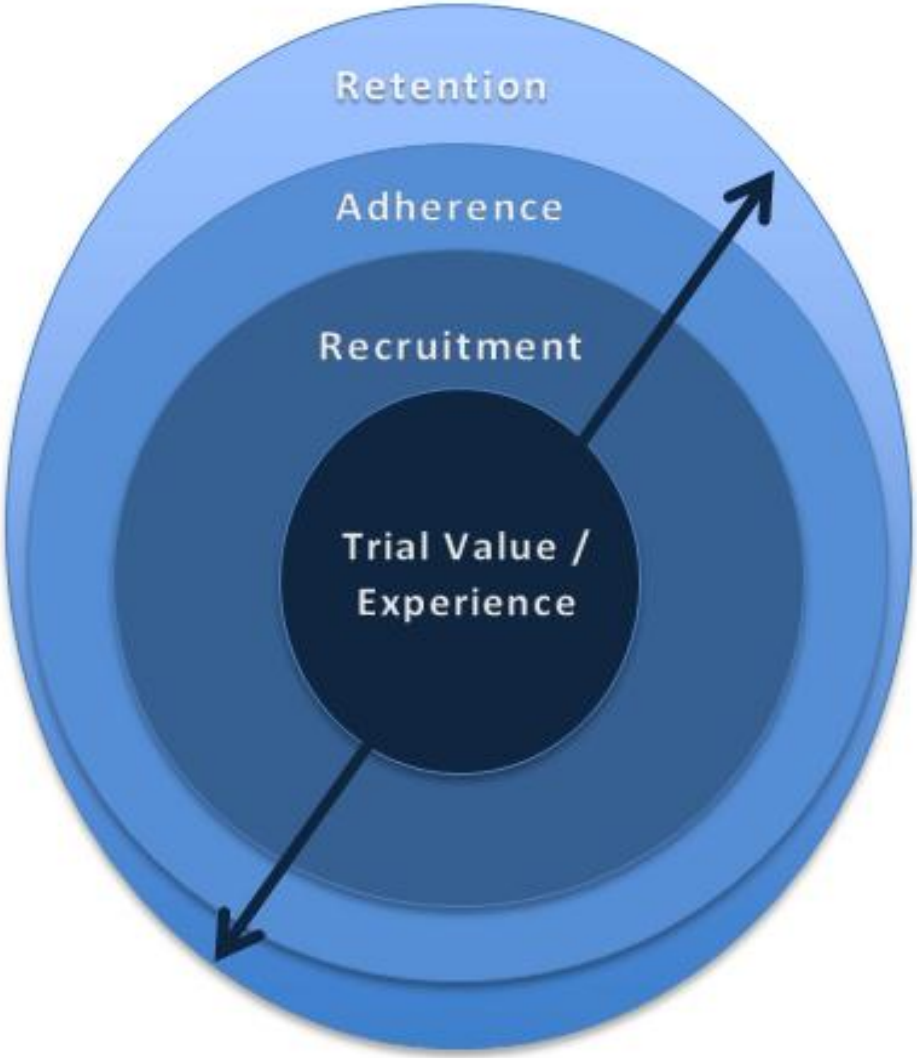
- Participation is a drain on time without obvious short term benefit
  → **Provide short term benefit: Financial incentive**

- Management of chronic health problem is not a priority

→ **Intensive medical management 'trains' patient why and how to be well**

Source: Colin Scott, Novartis, 2014 Presentation, at eyeforpharma PCCT

Customer experience as the core



Alternative methods of recruitment

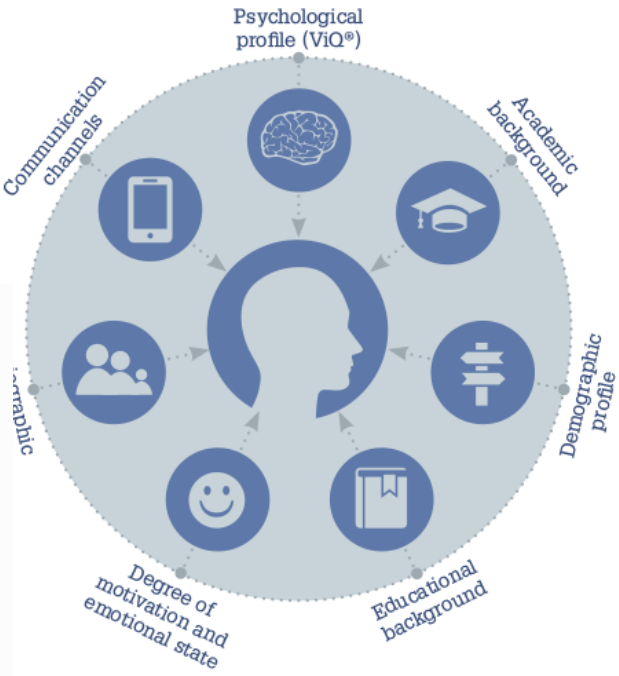
- Leveraging **Commercial Market Research Insights**
- **Extensive Surveying and Data Analysis**
- Drawing on **Psychological Profiling**
  - Methods to allow for the classification of patients along their intrinsic behavior patterns. Segmentation to provide a prediction of anticipated compliance issues that can be addressed via personalized interventions

- **STRATUM™** by MassineBoecker Personalized Population Management

Window into the Future?

- **STRATUM™** method

MASSINEBOECKER
Personalized Population Management

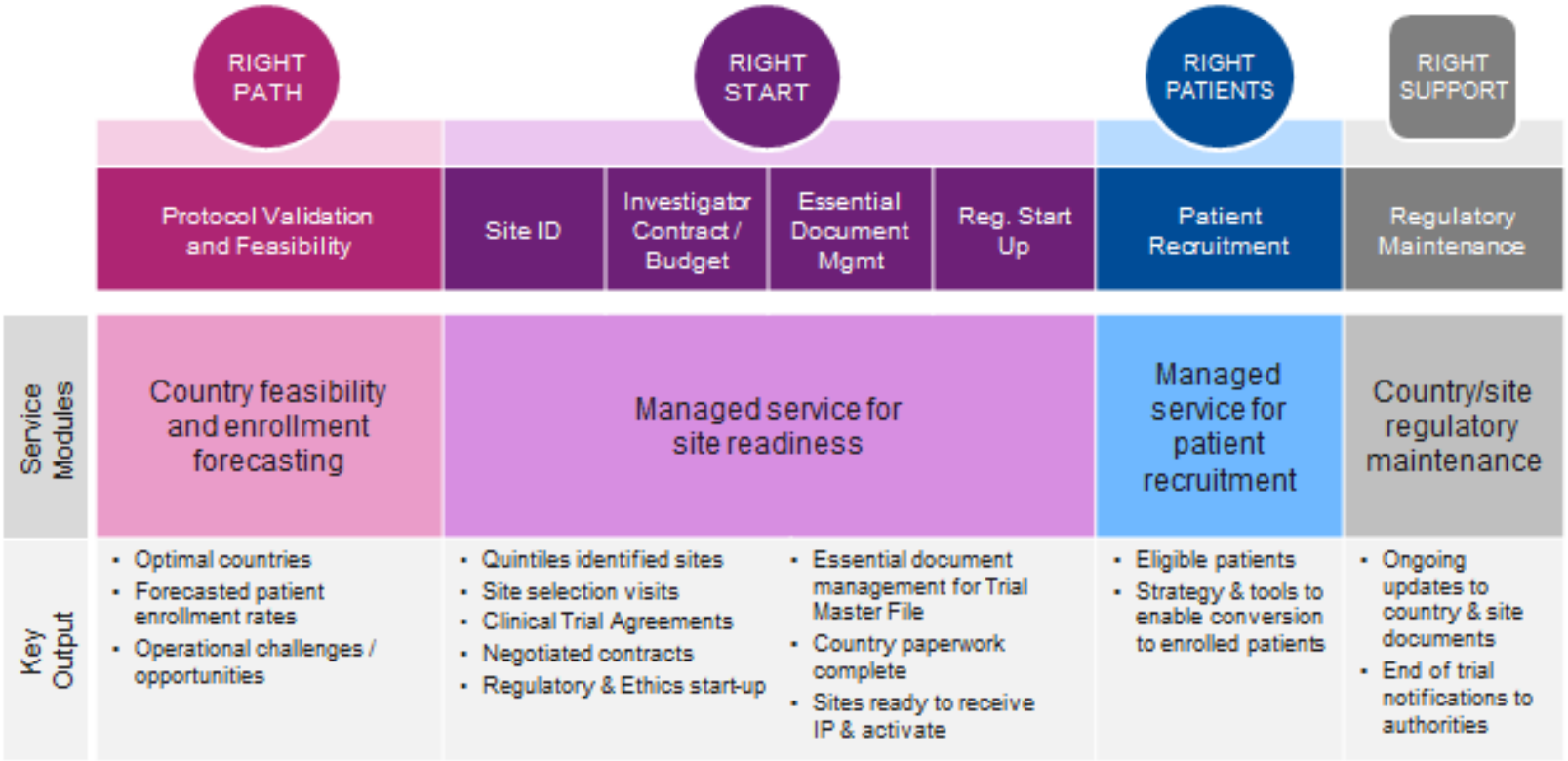


Our science has the ability to reveal:

- The **positively motivated patient** who takes responsibility and sees himself as a proactive manager of his own health
- The **resigned patient** characterized by sadness, who often exhibits low competence levels and shows little responsibility (=learned helplessness)
- The **defensive patient** (fearful, aggressive) who is often competent, but fails to take responsibility for herself and her condition
- The **submissive, serving patient**, characterized by a lack of self-confidence, who demonstrates a high degree of compliance but little self-determination

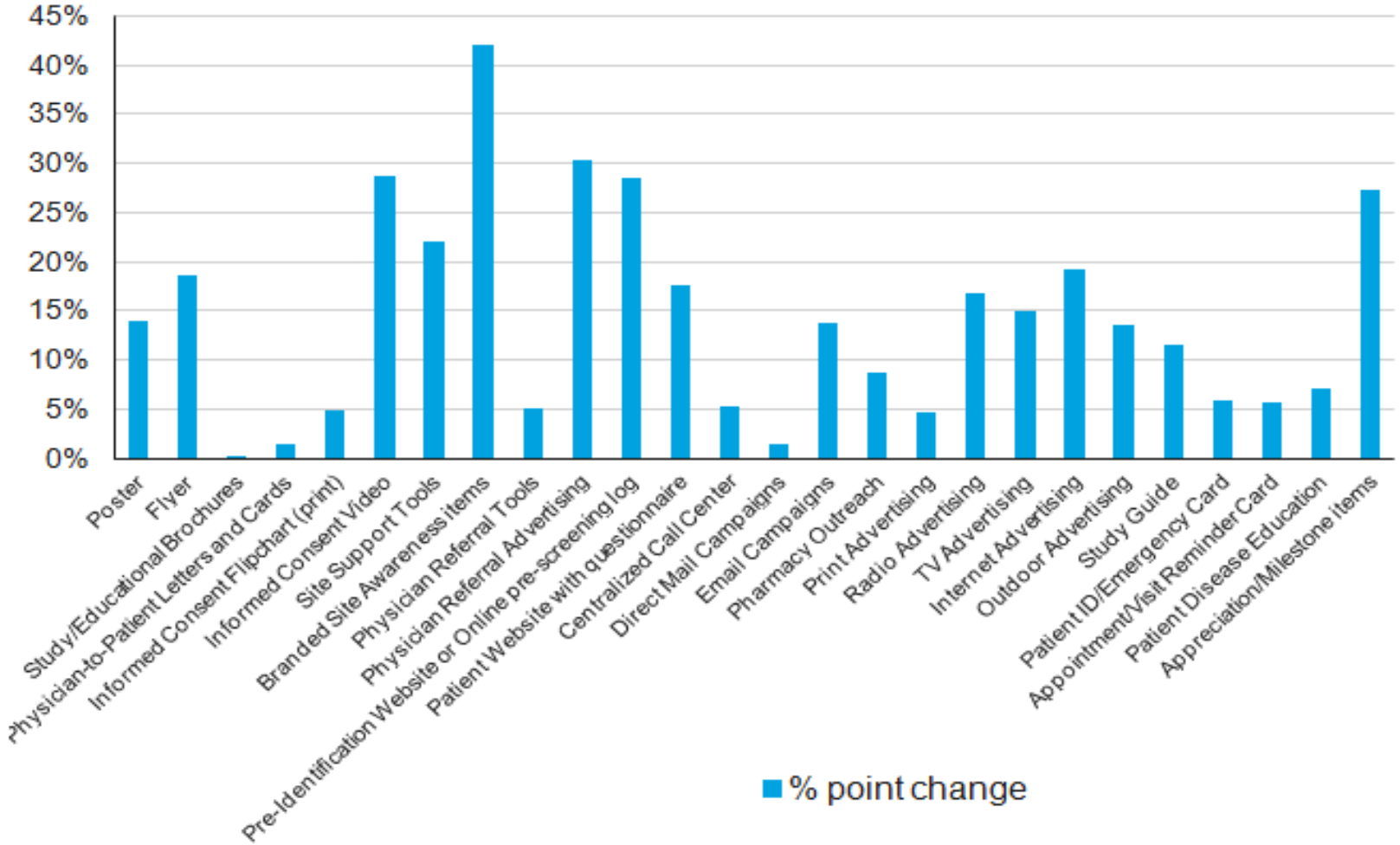
Massie Boecker, Exhibition at eyeforpharma PCCT

Regionally varied recruitment



QUINTILES®

Regionally varied recruitment



Source: Quintiles Research Presentation, at eyeforpharma PCCT

Patients 2 Trials Consortium

- Using electronic health records (EHRs), the aim is to devise a target health profile for each clinical trial that is machine-readable, so that software can match patients to specific inclusion criteria.
- Patients can search for trials using their own Blue Button data
  - A patient creates an account on a patient portal, sets up a direct address and receives a secure copy of her Continuity of Care Document and then uses our platform to search for clinical trials based on individual health record.

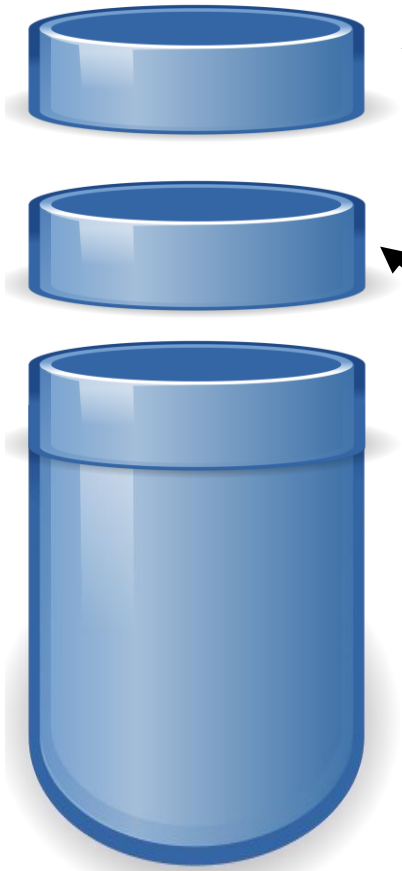
- Platform has been tested with a number of different clinical research studies sponsored by Lilly, Novartis and Pfizer, using a database of anonymized patient health records.

Proposed Approach

"Target Profile" for automated filtering

"Augmented Content" for additional patient centric content

Clinicaltrials.gov as foundation

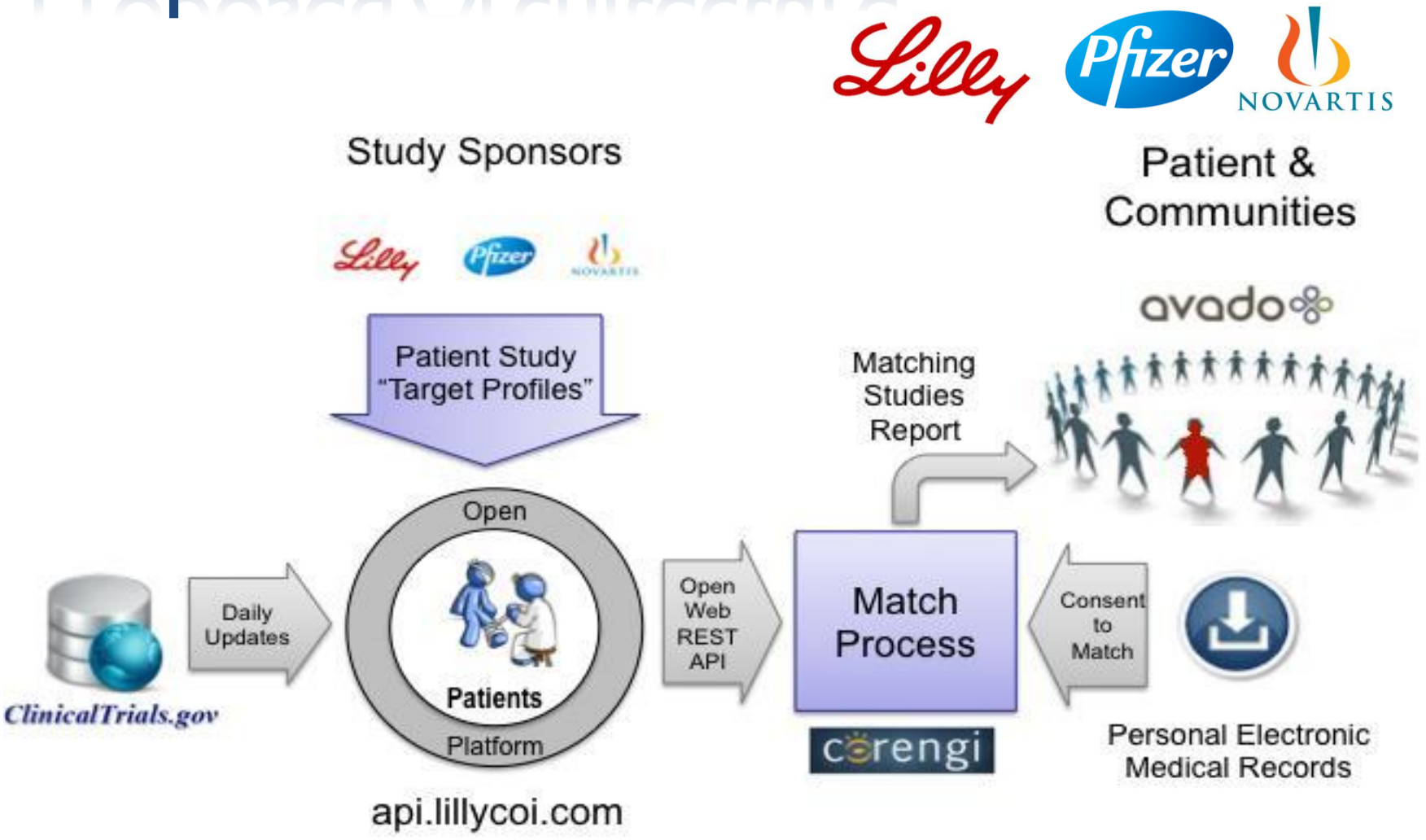


- What studies do I qualify for?
- What does the study do?
- How often will I have to take off from work to participate to this study?

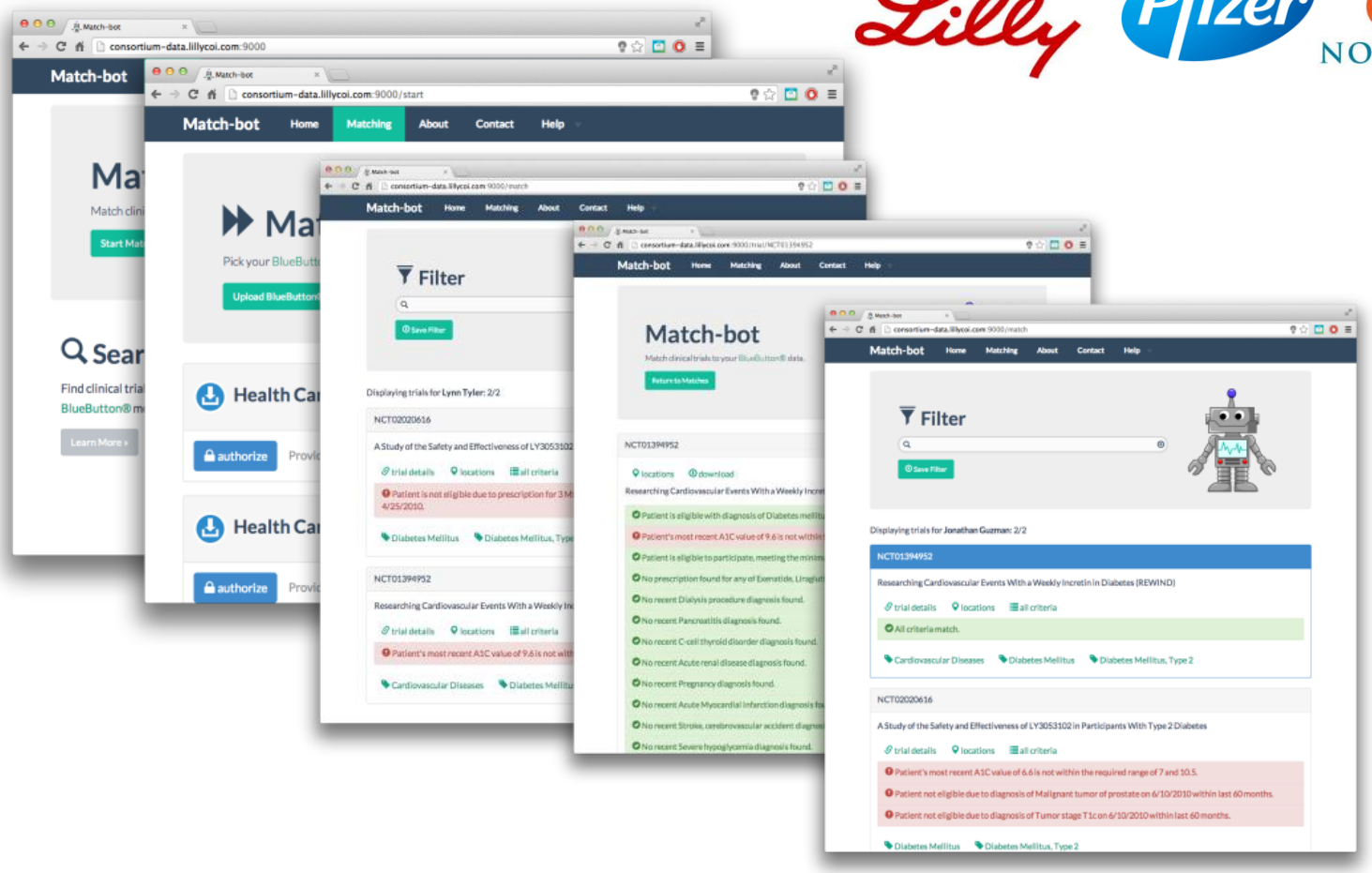
Proposed approach - detail

- The Target Profile is a machine readable query, that can be executed against an electronic file (or "record") with patient health data – such as an Electronic Health Record (EHR), an Electronic Medical Record (EMR) or Personally Controlled Health Record (PCHR)
- Augmented Content is public, IRB approved information about the study that has not been published on clinicaltrials.gov, and that is shared with / targeted for patients with a matching Target Profile.

Proposed Architecture



Patient App Prototype

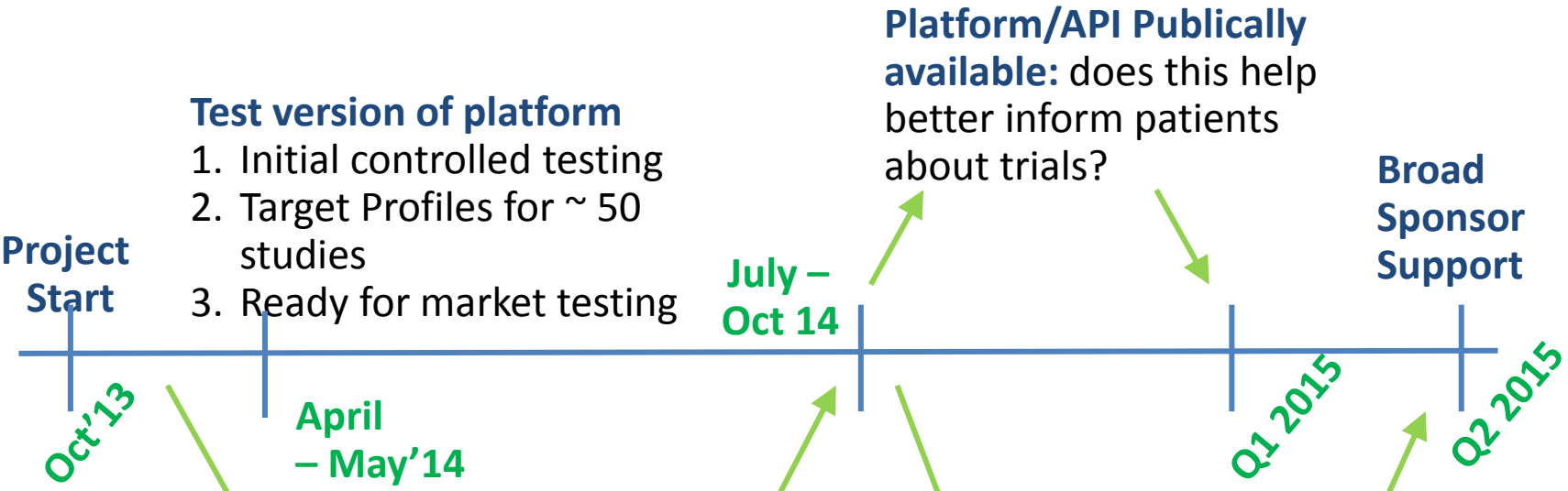


Proposed End State

- An open platform, where:

1. Study sponsors can login, and upload Target Profile, Augmented Content for their research studies
2. Public matching services are available, to which patients or organizations can send de-identified electronic health data and find matching studies
3. Open standards for those who wish to develop their own matching services against the Target Profiles

Timelines



Identify partner organizations and test drive the platform.

- Does it work for them?
- Does it help them match patients to trials?
- How can we improve the platform?

Long Term Sustainable Model Development

- Who will host?
- Who will pay?
- Content governance?

Experiences to date

"**Not all Eligibility Criteria are created equal**":

We are finding there are different types of eligibility criteria, e.g.

1. Things that the patient knows
2. Things that the doctor knows (and you could expect to find in the patient electronic health record)
3. Things that are assessed during screening

So our process for developing Target Profile, is to:

1. Sit down with the Study Responsible Physicians
2. Find out which of the eligibility criteria are in category 2
3. Discuss whether and how criteria from the other categories can be replaced or approximated by additional criteria in category 2

Trial Design

* Realize why trial design is becoming a competitive differentiator for succesfull enrollment and trial management

Approach to recruitment feasibility

- Objective: Forecasting and managing the probable randomization rate for a specific protocol, determine realistic parameters for site enrollment months
- Involves planning how each group of study stakeholders would respond to the protocol – **regulators**, **investigators**, **coordinators**, **project managers**, **monitors**, and **patients**
  - In what way would protocol measures be off-putting to one or more of these groups? Can it be afforded to prioritze one stakeholder over the other?
- Established feasibility planning sequence is **country > sites> patients** while it is rare that sponsors consistenly ask patients directly for input. Mostly relying on investigators, KOLs, country heads as surrogates

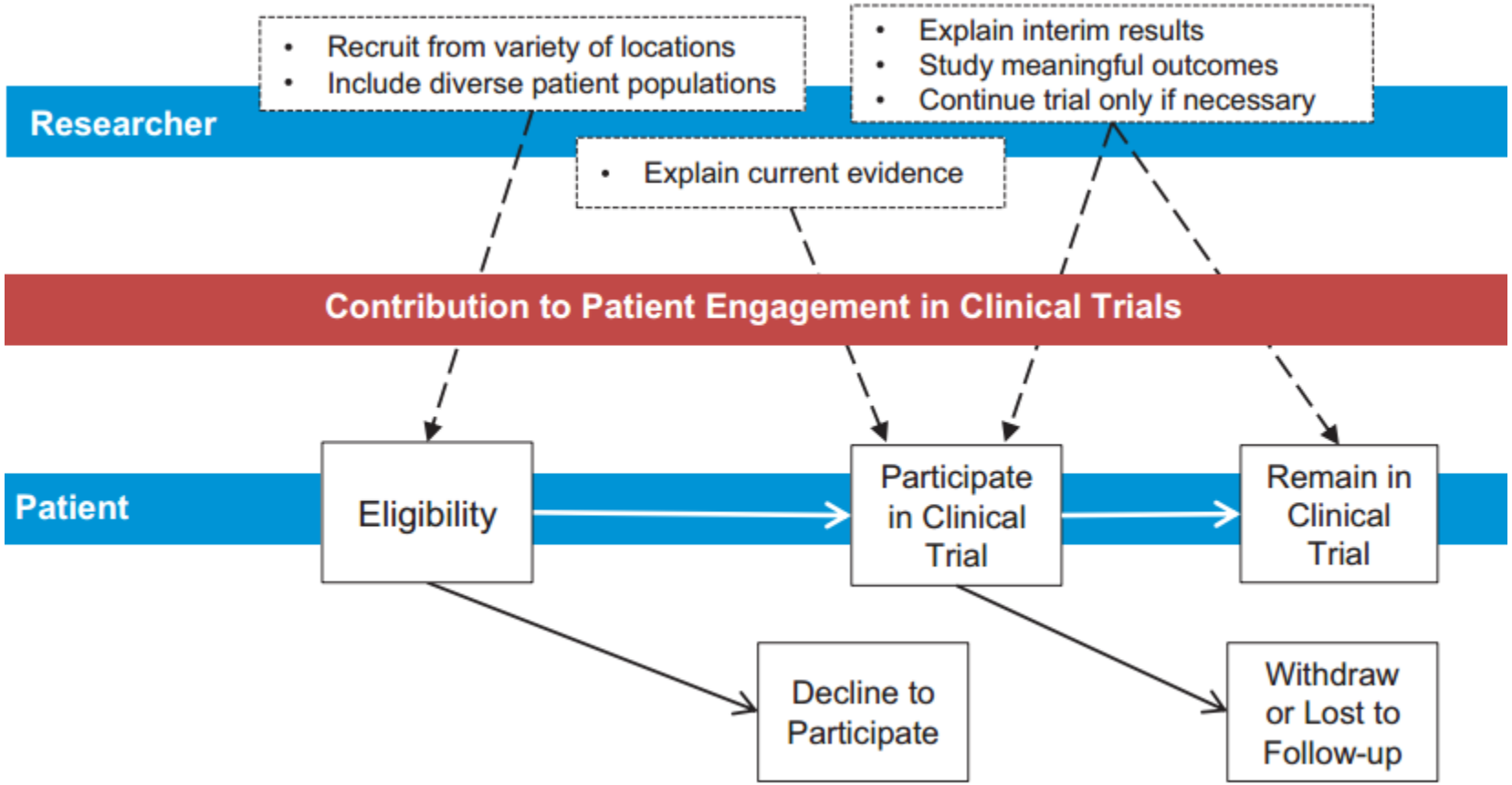
Alternative Trial Designs

Lack of patient-centeredness in clinical trials can be partially addressed through innovative study designs

- **Pragmatic Trial Design** to evaluate the effectiveness of interventions in real-life routine practice conditions
- **Bayesian Statistics** use available patient-outcome information, including biomarkers that accumulating data indicate might be related to clinical outcome. They also allow for the use of historical patient data for synthesizing results of relevant trials.
- **Adaptive Trial Design** allow features of the trial to change while in progress, allowing for evaluation of comperative effectiveness, especially useful in long-running rare disease trials

Source: Mullins, C.D. et al (2014). Patient-Centeredness in the Design of Clinical Trials. Value in Health (in press)

Trial designers can affect the patient

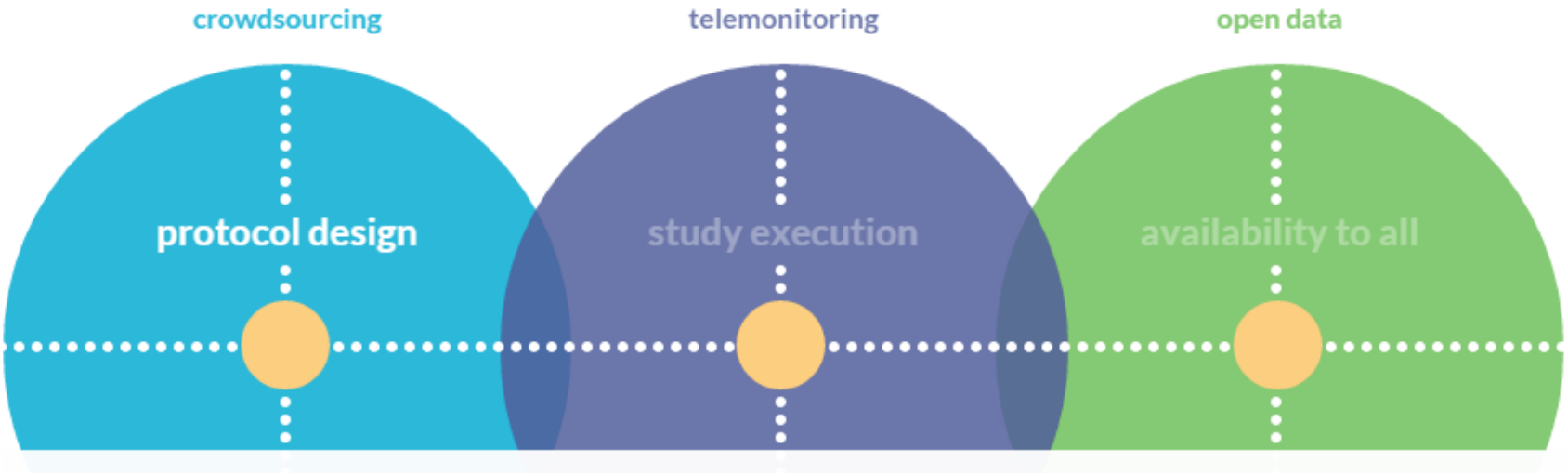


Source: Mullins, C.D. et al (2014). Patient-Centeredness in the Design of Clinical Trials. Value in Health (in press)

Crowdsourcing the protocol

transparency life sciences

The world's first drug development platform based on open innovation

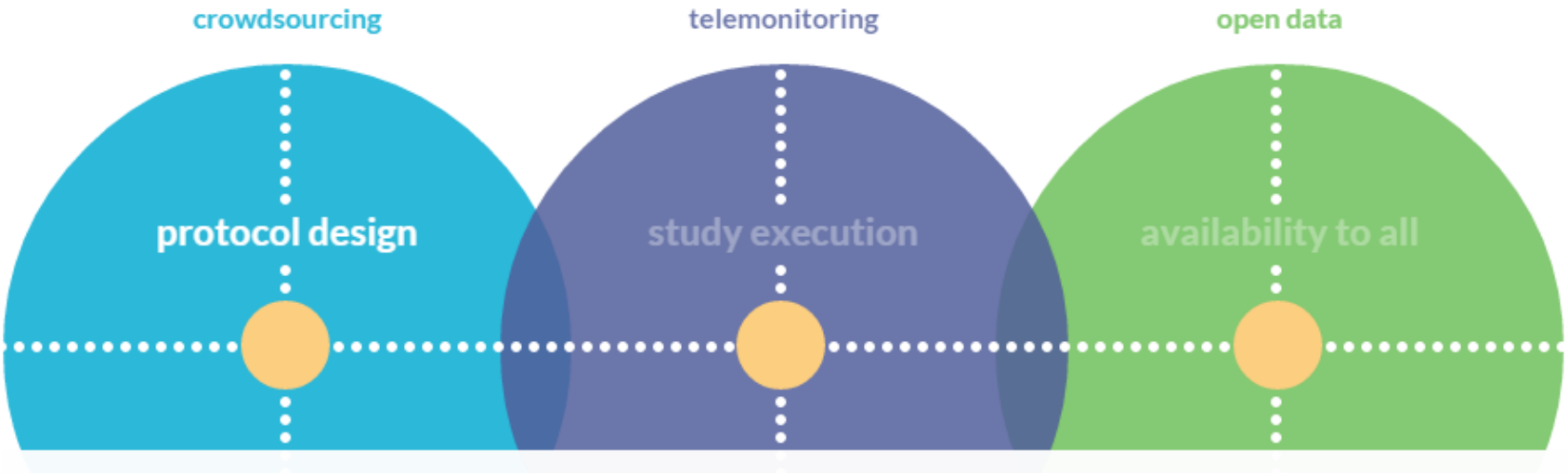


- **Protocol Builder** is TLS's crowdsourcing survey tool to help develop our clinical protocols
- **Indication Finder** is a crowdsourcing tool that invites participants to identify potential new applications for stalled compounds.

Excute through remote monitoring

transparency life sciences

The world's first drug development platform based on open innovation

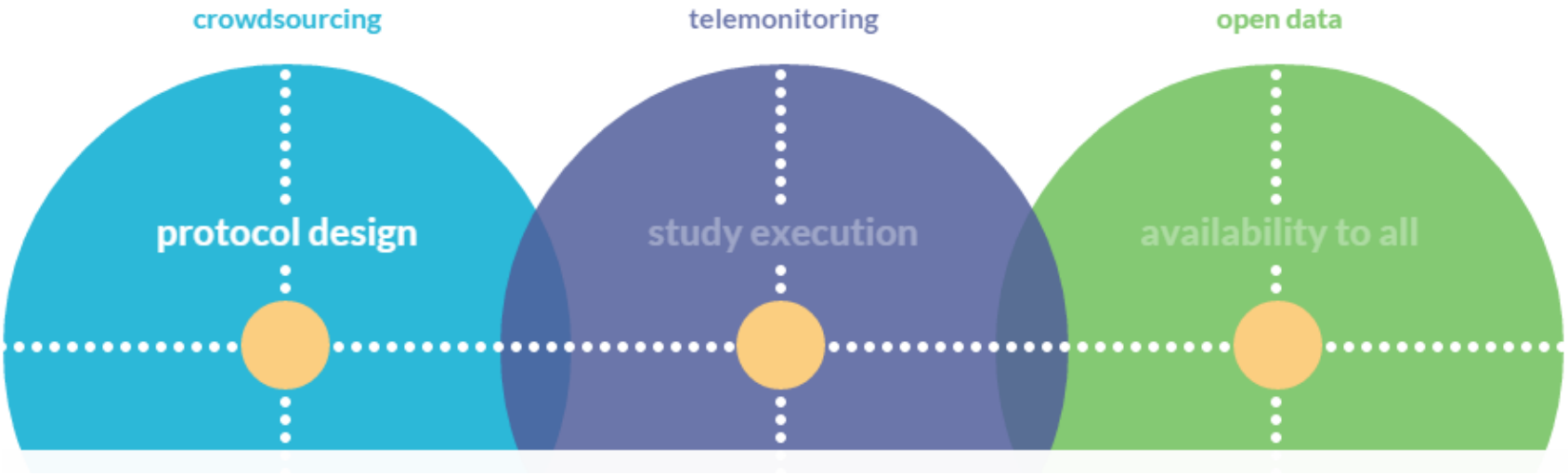


- **Remote monitoring and mobile health** allow for decentralized trials, improved data collection and reduce costs by 50%
- **Pilot study with Genentech** on the effectiveness and ease-of-use of telemonitoring technology in patients with inflammatory bowel disease

Share data with all

transparency life sciences

The world's first drug development platform based on open innovation



- **Awarded $1.4 Million NCATS/ NIH Grant** to conduct innovative trial of Lisinopril in Multiple Sclerosis with Mount Sinai
- Protocol developed with with **crowdsourced input from MS researchers, physicians and patients**

Pioneers: LillyCOI

Lilly
Answers That Matter.

Informing through Patient-Centric Study Websites

What if…

We decoupled Informed from Consent?

A focus on "Informed"

1. Make CT information (clinicaltrials.gov) easier to access
2. Enabled real-time pre-screening for patients
3. Provide clear, patient-centric information to patients BEFORE they have to travel to the site

App Lab: labs.lillycoi.com (sample apps)
Twitter: @Lilly_COI

Digitally Informed Consent

Transformation

From…	To…
Sponsor Centric	Patient Centric
Paper	Multi-media dig
Poor patient comprehension	Focus on patie comprehensio
Lengthy and difficult to understand	Shorter, simplif content

Next Steps

- Pilot eConsent on 3-4 trials in 2014 using existing content – start with limited sites and then expand the scope
- Gather input from patients and sites to improve the multi-media experience
- Then focus on improving the content to enhance patient comprehension and compliance
- The transformation continues today with gathering your feedback…

Patients at the Center of Clinical Trials Workshop:
portal.lillycoi.com/paccr/

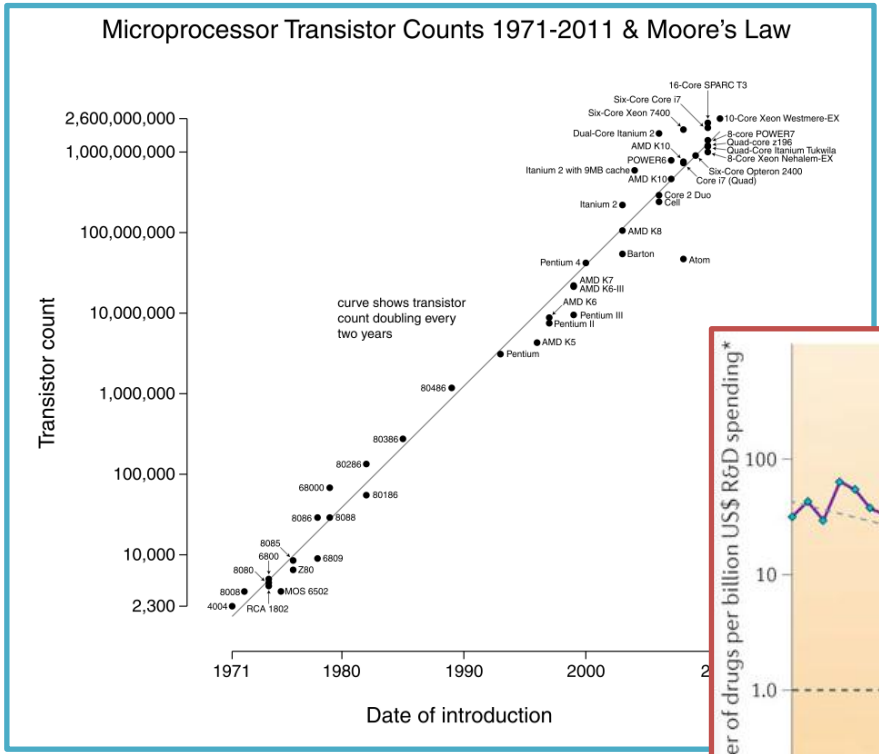
eyeforpharma

Patient-Centered Systems

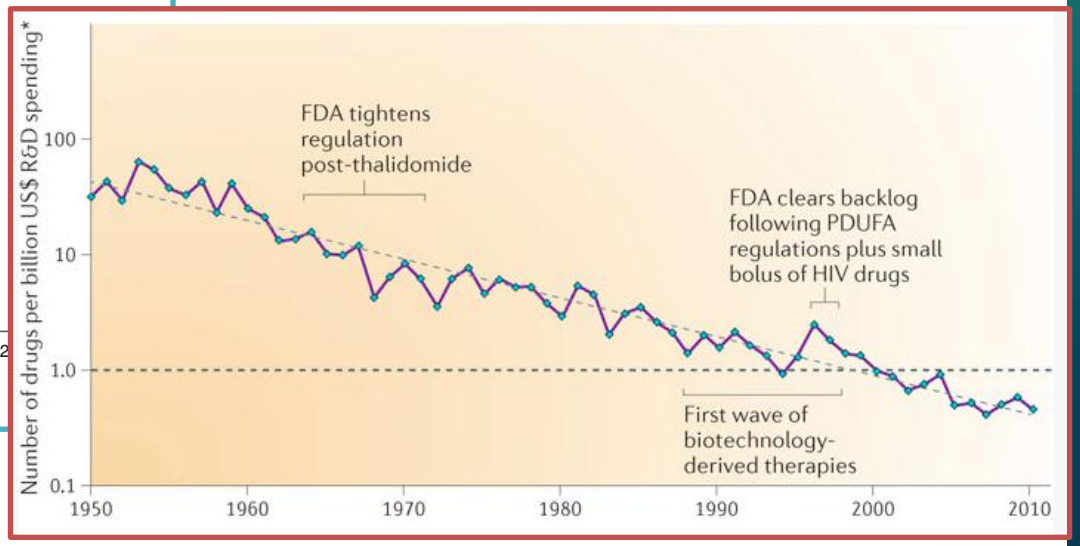
* Learn about innovative patient-centered trial management, systems and technology that lie at the operational heart of effective patient engagement

PATIENT-CENTERED DRUG DEVELOPMENT
REVENUE DRIVER AND PARADIGM SHIFT?

Moore's vs. Eroom's Law



Source: Wikipedia



Source: Nature

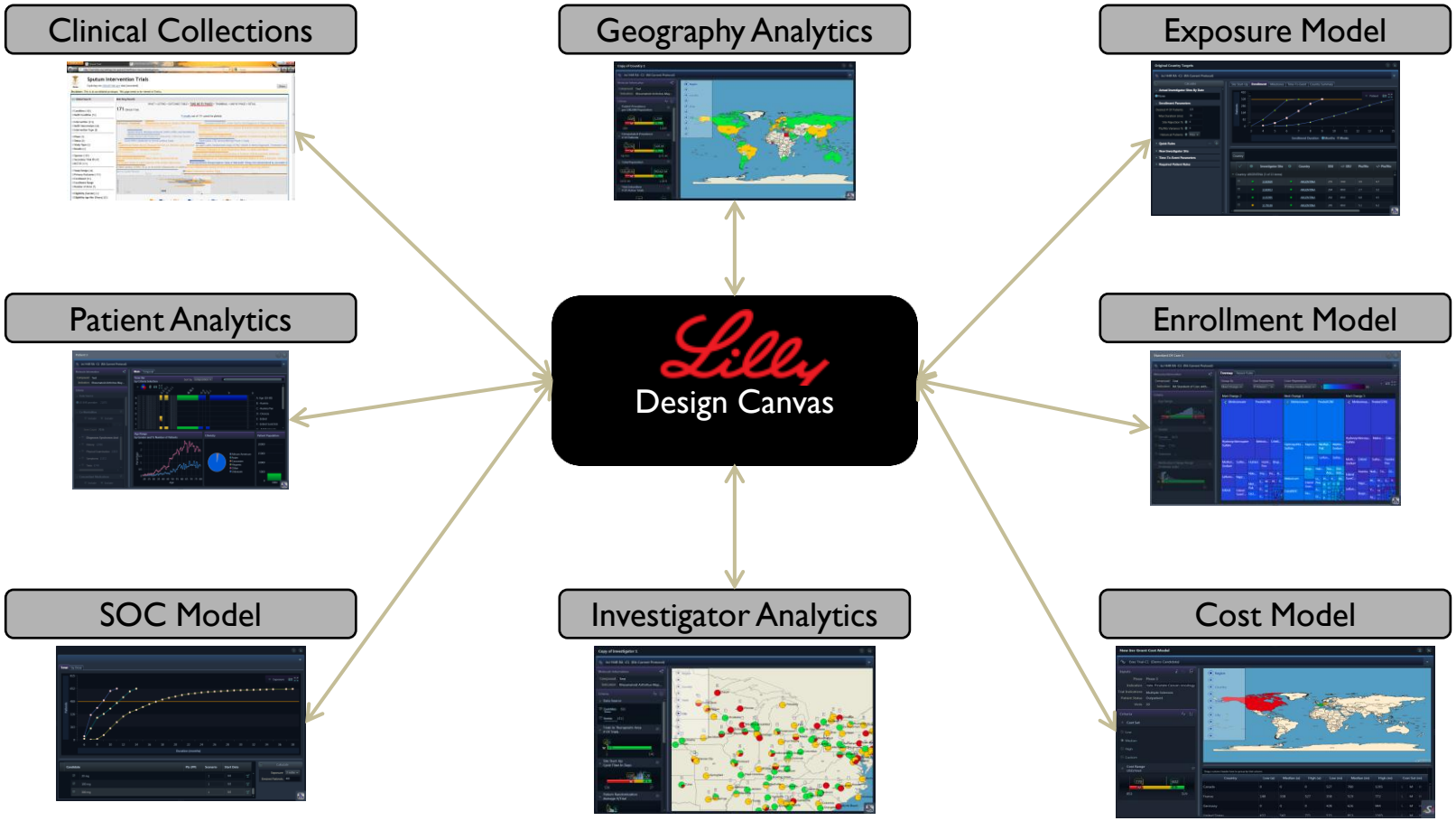
Lilly's Innovative Study Design Platform

- **Platform that digitizes the entire study design process**
- **Fully integrated Clinical Plan functionality**
- **User-Centered Design**
- **Engaging internal and external stakeholders**

- Once the data is categorized, Lilly initiates 'Interactive Jam Sessions'
  - Internal stakeholders from different groups (i.e., project management, drug safety, data monitoring committee, etc.) convene in a virtual room, where Lilly facilitators assist internal stakeholders with strategizing and organizing their thoughts on designing robust studies.

Source: Eli Lilly Case Study 2014, at eyeforpharma PCCT

Integrated Study Design Canvas

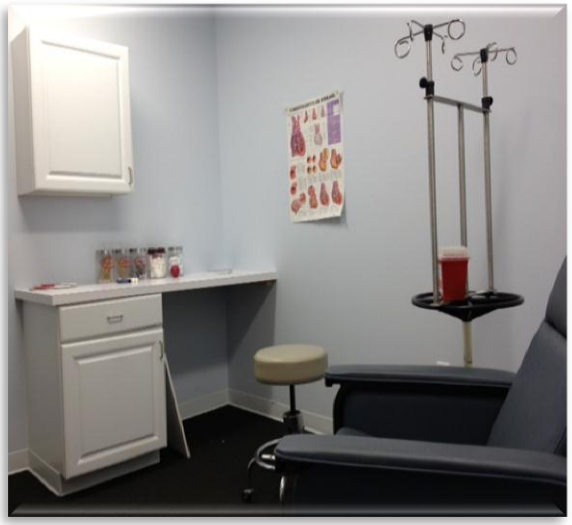


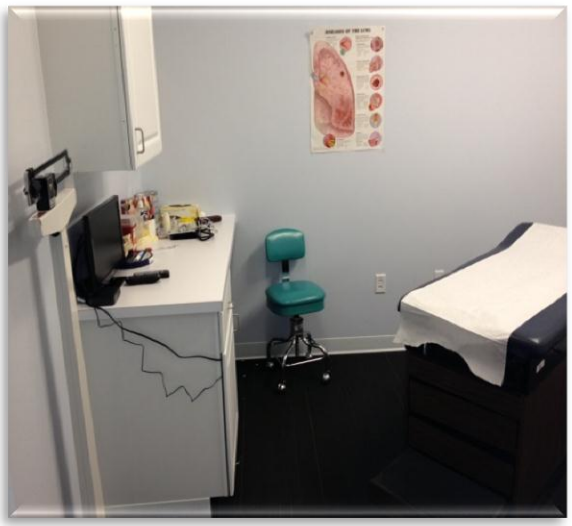
Source: Eli Lilly Case Study 2014, at eyeforpharma PCCT

Interactive & Virtual Collaboration

Source: Eli Lilly Case Study 2014, at eyeforpharma PCCT

Simulating the Site





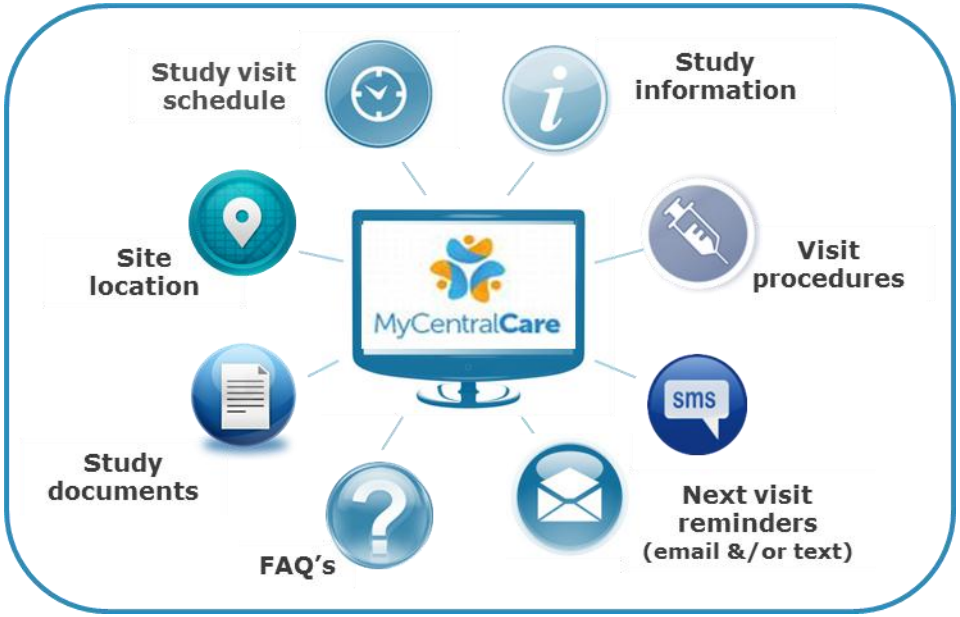
- Lilly's performance mandates now require study teams to build protocols using the innovative digital approach

Source: Eli Lilly Case Study 2014, at eyeforpharma PCCT

Proof Of Concept: Patient Portal

MyCentralCare

janssen

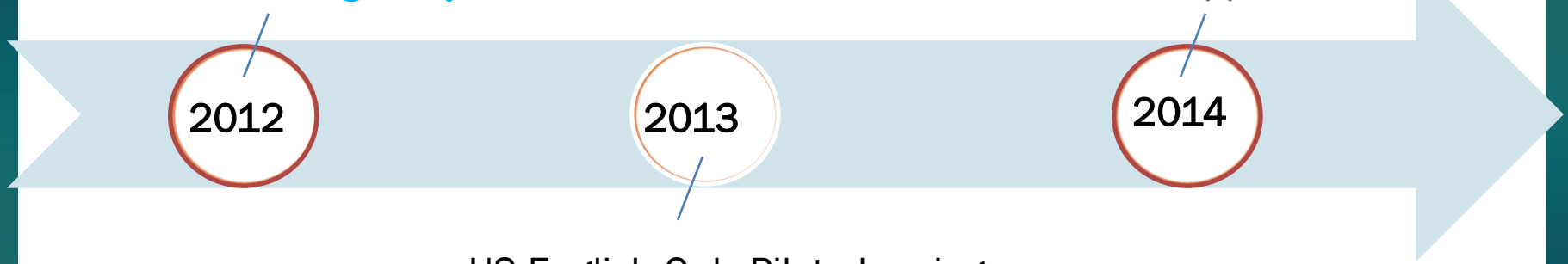


Source: From Janssen Case Study 2014 , at eyeforpharma PCCT

Making the idea reality

- Top idea for pt. engagement innovation
- Used Creative Design Lab to ideate website
- Internal focus group - features, design
- No one doing this yet

- Finalized website
- IRB approved
- Ready for FPI
- Mobile apps on market



- US English-Only Pilot planning
- Application development & eDC integration
- Patient panel & media consultant input
- External landscape has evolved:
  - One generic portal now on market
  - 2 other pharma's exploring this

janssen

Source: From Janssen Case Study 2014 , at eyeforpharma PCCT

Lessons learned to date

- Patient-Facing Innovation Takes Time
  - Ensure adequate time for stakeholder review & approval
- Internally developed & hosted website
  - Pro: cheaper, 100% control
  - Con: burden of ownership
- Central IRB + local IRB approval
  - Good preparation pays off – no IRB objection or changes
- Timelines of pilot depend on timelines of trial
  - If trial is delayed, so is the pilot (ours delayed 9 months)

janssen

Source: From Janssen Case Study 2014 , at eyeforpharma PCCT

New Frontiers for Patient Portals

- Live communication?
- 1-way communication → 2-way?
- Site ← → Patient communication (e.g. 1:1 "chat hours" with study nurse or investigator; webinar with PI)
  - Challenges – unsolicited safety reporting, security, privacy, site staff burden
- Patient to patient communication
  - Worst nightmares: bias, un-blinding, sharing of signs and symptoms, speculation of treatment assignment, drop outs, unsolicited safety reporting, privacy violations ….

janssen

Source: From Janssen Case Study 2014 , at eyeforpharma PCCT

But what if they talk to each other...

- Participants talking to each other about their experiences within a trial might accidentally unblind them.
- "We needed to find a way to help patients talk safely about their clinical hopes and experiences" Joe Kim, Shire
- Shire partnered with UK agency Langland and CISCRP to create "***Speak out, but speak smart***"

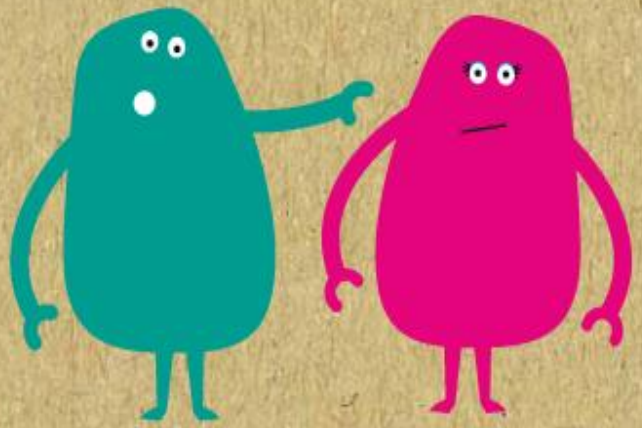
Shire langland CISCRP

SPEAK OUT, BUT SPEAK SMART.

ABOUT US

ABOUT CLINICAL TRIALS IN GENERAL

LINKS



SMART TALKING ABOUT CLINICAL STUDIES

VIDEO GALLERY

Social Media/ Networks

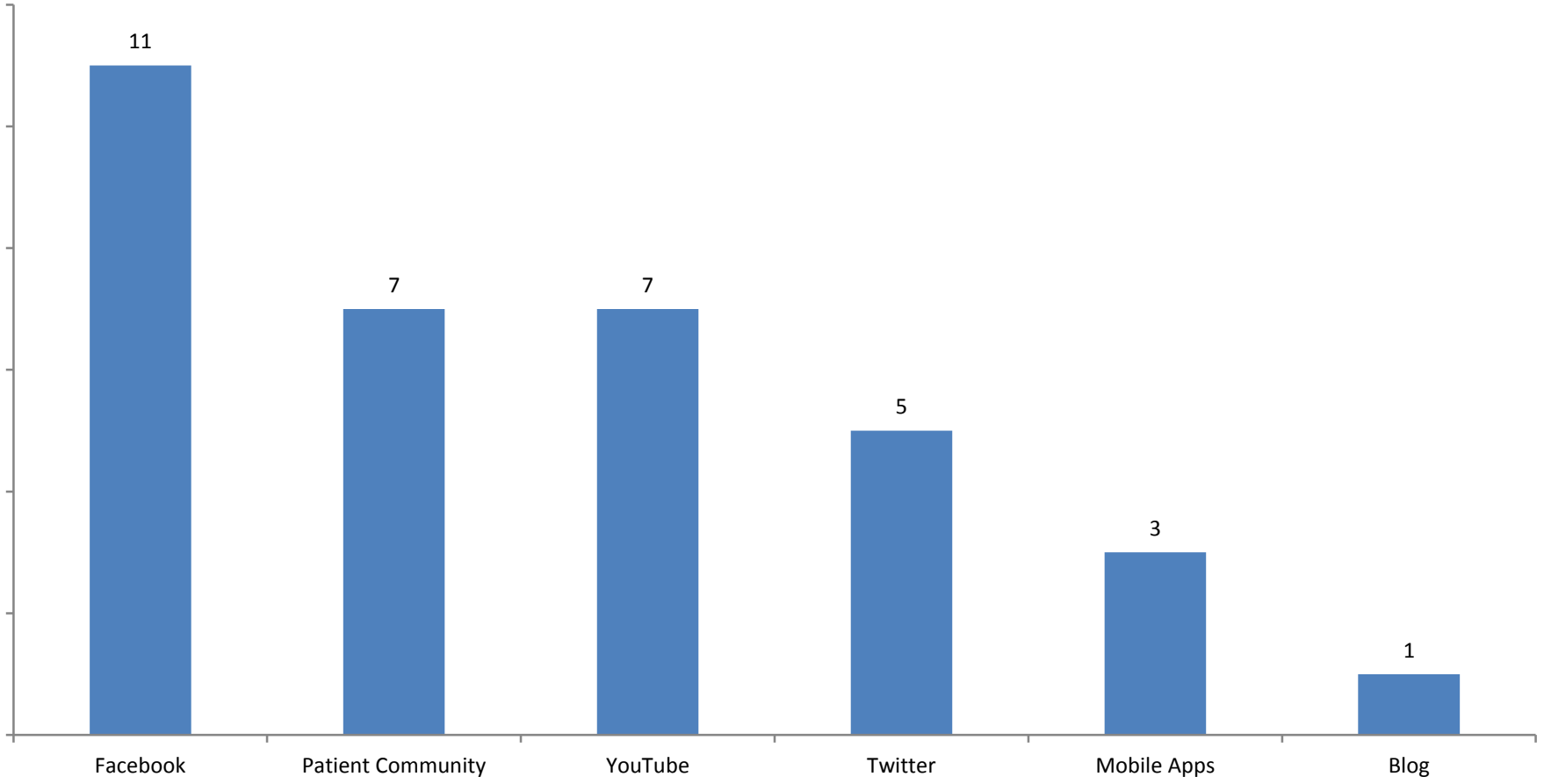
* Get cross-industry data on the usage of social media in trials, as well as insights from particular networks on how to engage trial participants and capture data to recruit volunteers.

Tufts Working Group on Social Media

- **Limited FDA guidance on use of social media in clinical research**
  - FDA draft guidance released in January 2014 – focus on postmarketing submissions
  - FDA draft guidance released in June 2014 – Two documents concerning company behavior on social media platforms like Twitter and when correcting misinformation on third-party sites
- **Among Tufts working group companies, social media (including ad placement) is on average being used in ~11% of trials**
- While 14/15 companies have posted ads on social media websites, only 3/13 biopharmaceutical companies and 2/2 CROs have used it to "interactively" engage patients.

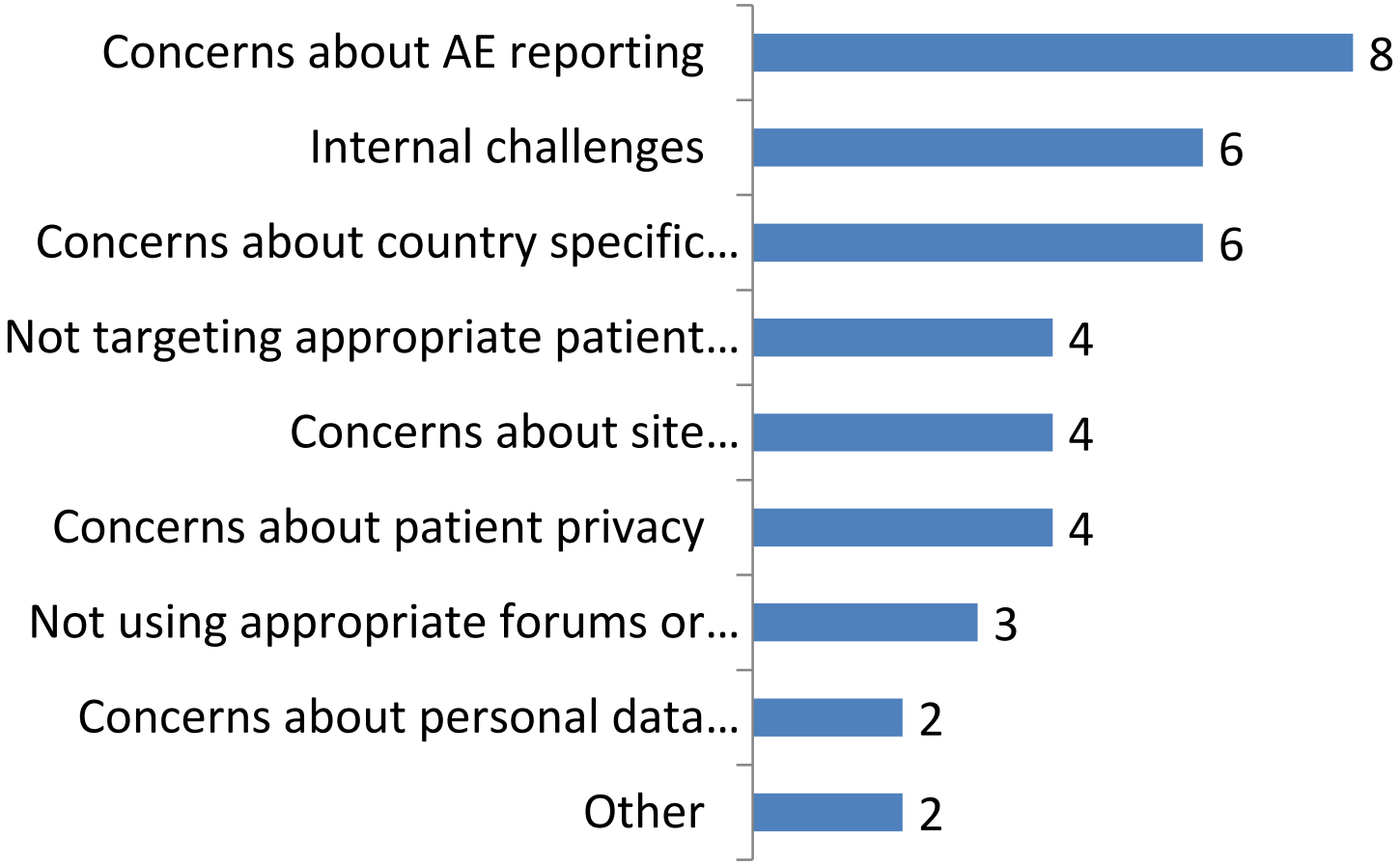
From Tufts CSDD Briefing, at eyeforpharma PCCT

Platforms Used for Recruitment



From Tufts CSDD Briefing, at eyeforpharma PCCT, n=14

Top Challenges in Using Social Media



From Tufts CSDD Briefing, at eyeforpharma PCCT

Legal and Regulatory Challenges

- Lack of clear guidance from FDA makes internal reviews/approvals more difficult
- Concerns over AE reporting and safety issues/pharmacovigilance
- Concerns about unblinding patients to their treatments or sites/sponsors to patients' treatments
- Concerns over intellectual property
- Not being able to effectively monitor/moderate when a site is set-up for 2-way communication
- Lack of organizational experience or alignment
- Off-label marketing

From Tufts CSDD Briefing, at eyeforpharma PCCT

MyHealthTeams and Biogen Idec

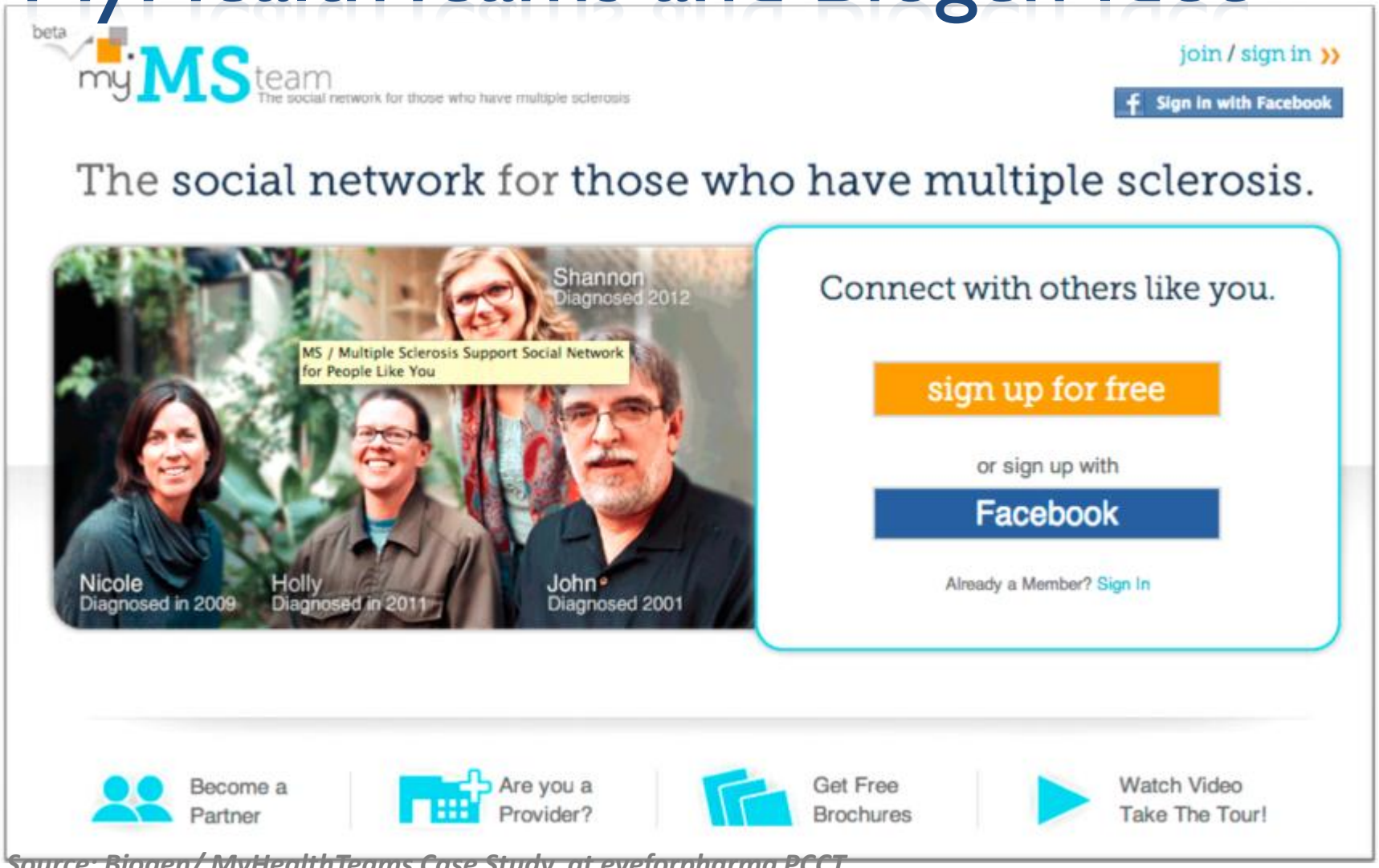
- Social networks are the best way to reach niche audiences
- Narrowing inclusion criteria requires targeted outreach
- The most engaged patients are on social networks, not patient registries, databases, Google, or health sites
- Communication through the social network, not directly to its members
- Thinking beyond just patient recruitment

Can a social network recruit MS patients for Phase III trial (37 sites)?

myHealthTeams
biogen idec

Source: Biogen/ MyHealthTeams Case Study, at eyeforpharma PCCT

MyHealthTeams and Biogen Idec



Source: Biogen/ MyHealthTeams Case Study, at eyeforpharma PCCT

MyMSTeam's: Patient Recruitment

1. Target the Right People

- ❑ RRMS
- ❑ Interferon beta 1a/1b
- ❑ City
- ❑ Age

2. Notify Them of the Trial

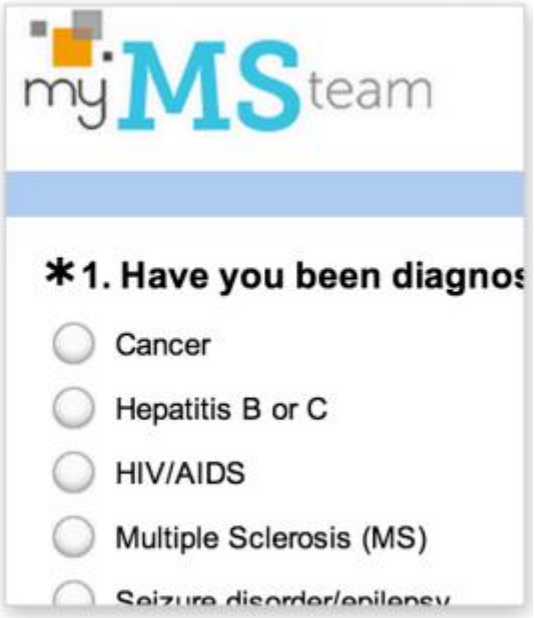
Dear Eric,

Many members of MyMSTeam have urg
relevant MS clinical trials as they arise.
to share news of the ALLOW study whic
MS who are currently taking a standard
AVONEX® (interferon beta 1b), BETASI
(interferon beta 1a).

find out if you are eligible

People living near any of the study c
eligible and choose to participate in this

3. Qualify with Screener & Pass to Site



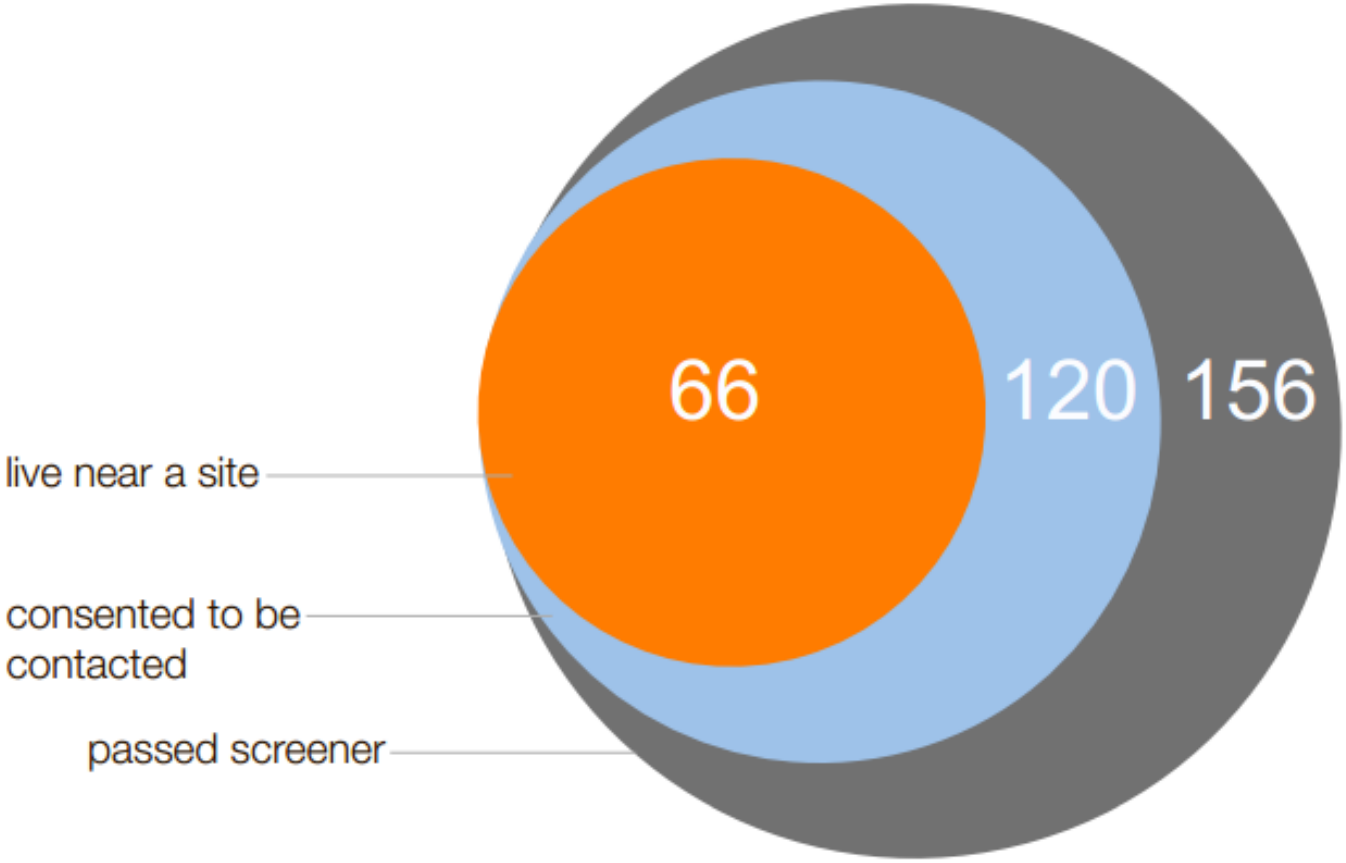
myHealthTeams

biogen idec

Source: Biogen/ MyHealthTeams Case Study, at eyeforpharma PCCT

Results After Two Weeks…

798 screeners taken, 66 people passed who live near a site and asked to be contacted.



myHealthTeams
biogen idec

Source: Biogen/ MyHealthTeams Case Study, at eyeforpharma PCCT

MyHealthTeams and Biogen Idec

Lessons Learnt

- Partner with a social network focused on your therapeutic area
- Coordinate with sites and CRO to ensure buy-in & site readiness before launching social
- Submit patient recruitment materials to IRB early
- Consider your patient value proposition
- Discover quickly why leads drop out
- Recruit qualified patients quickly and cost-effectively
- Identify locations that could be opened

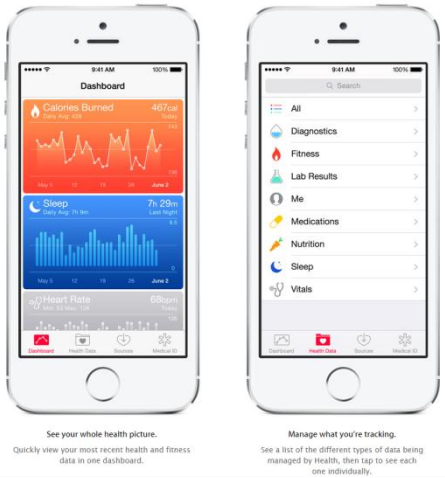
myHealthTeams
biogen idec®

Source: Biogen/ MyHealthTeams Case Study, at eyeforpharma PCCT

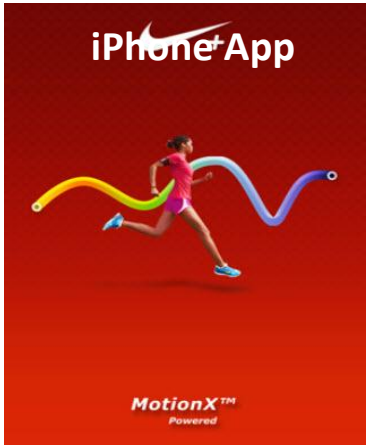
Our Data are everywhere…

23andMe

Microsoft HealthVault

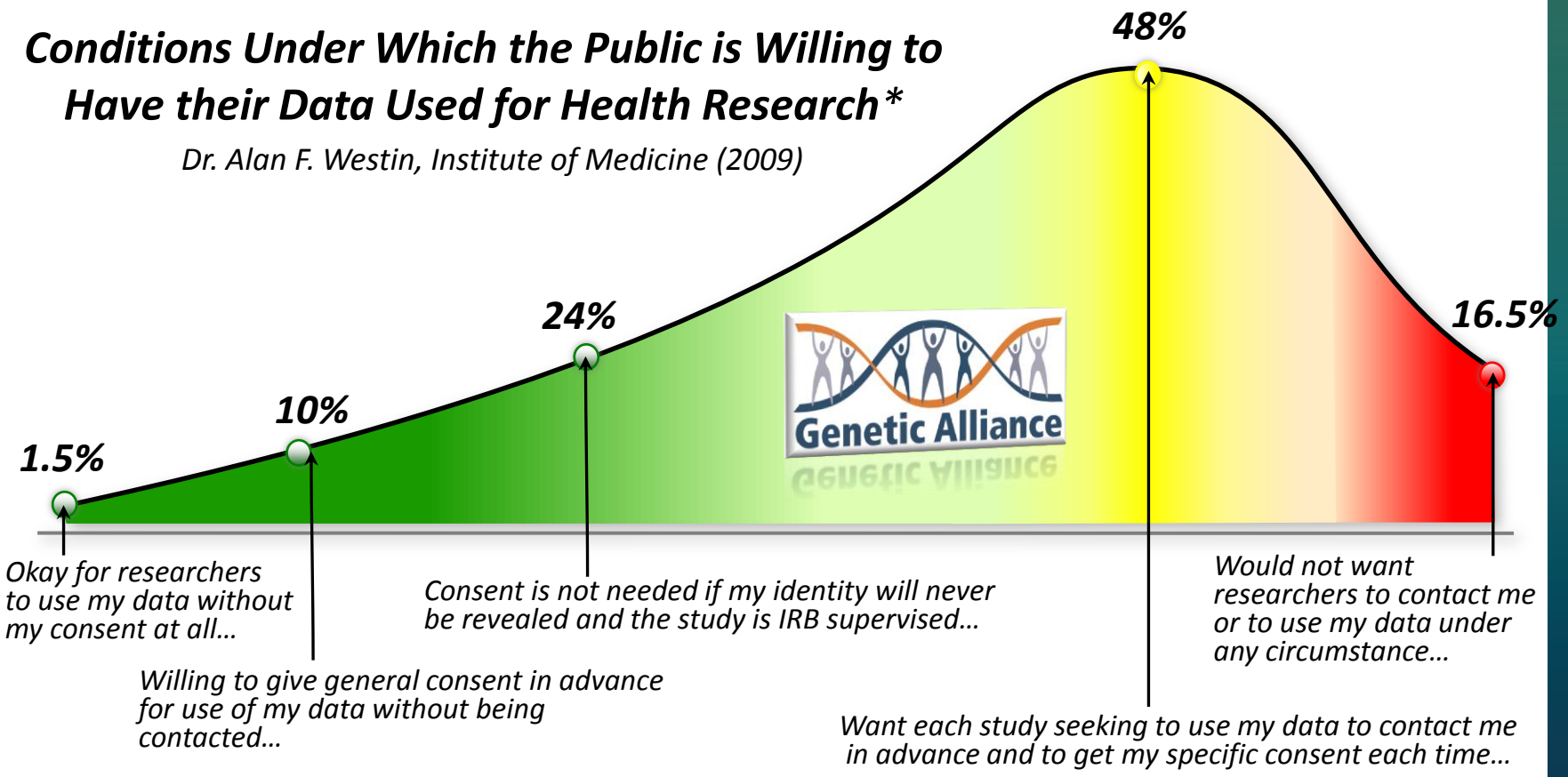


FitBit ®



Source: Genetic Alliance Case Study 2014, at eyeforpharma PCCT

"How can we share the clinical and genetic data of millions of individuals and still respect their diverse wishes?"



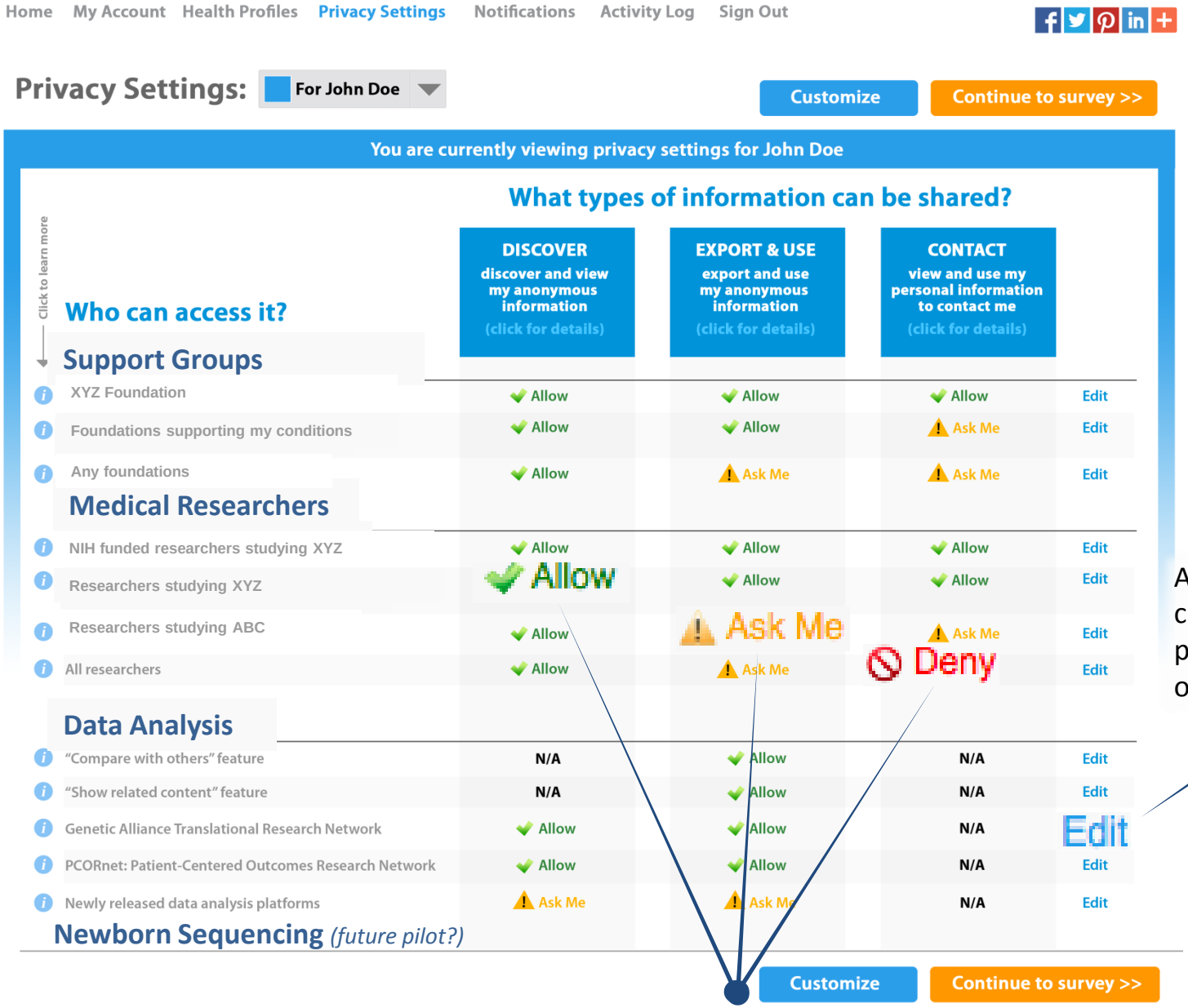
* Percentages shown reflect the views of those persons expressing an opinion. An additional 20% of the persons surveyed indicated that they were "Not sure."

Source: Genetic Alliance Case Study 2014, at eyeforpharma PCCT

Platform for Engaging Everyone Responsibly (PEER)

- launched in 2014 as a major effort to give individuals a powerful way to contribute to translational and participant-centered outcomes research
- committed to accelerating research through access to health information that remains in the control of the participants.
- Currently in development for a wide range of organizations and uses, including a **PCORI funded project** and **Patient Powered Drug Development projects** associated with the FDA mandate to engage a number of communities.

Source: Genetic Alliance Case Study 2014, at eyeforpharma PCCT



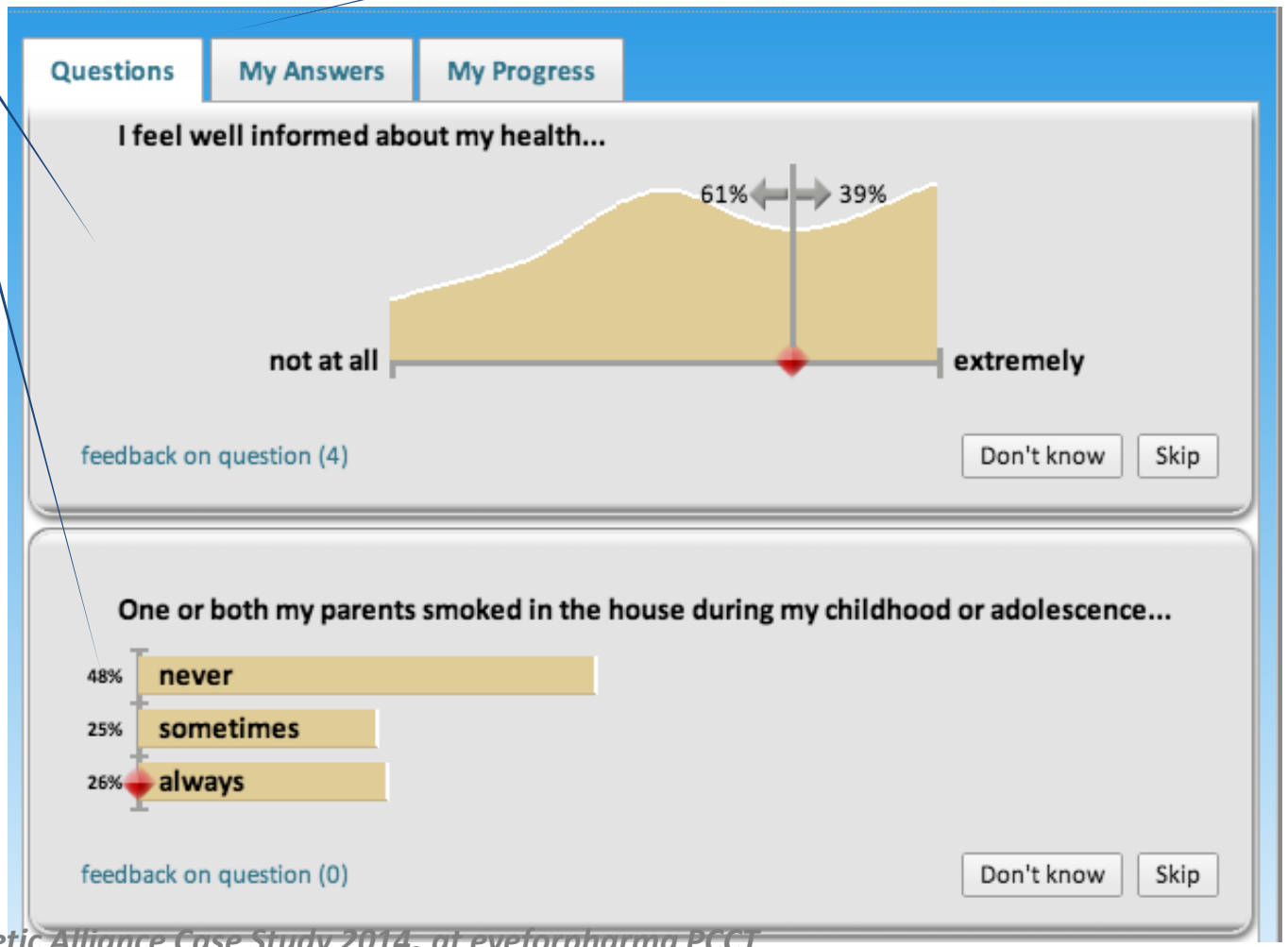
And may change these preferences over time

Source: Genetic Alliance Case Study 2014, at eyeforpharma PCCT

“Gamified” Interface for Questions and Answers

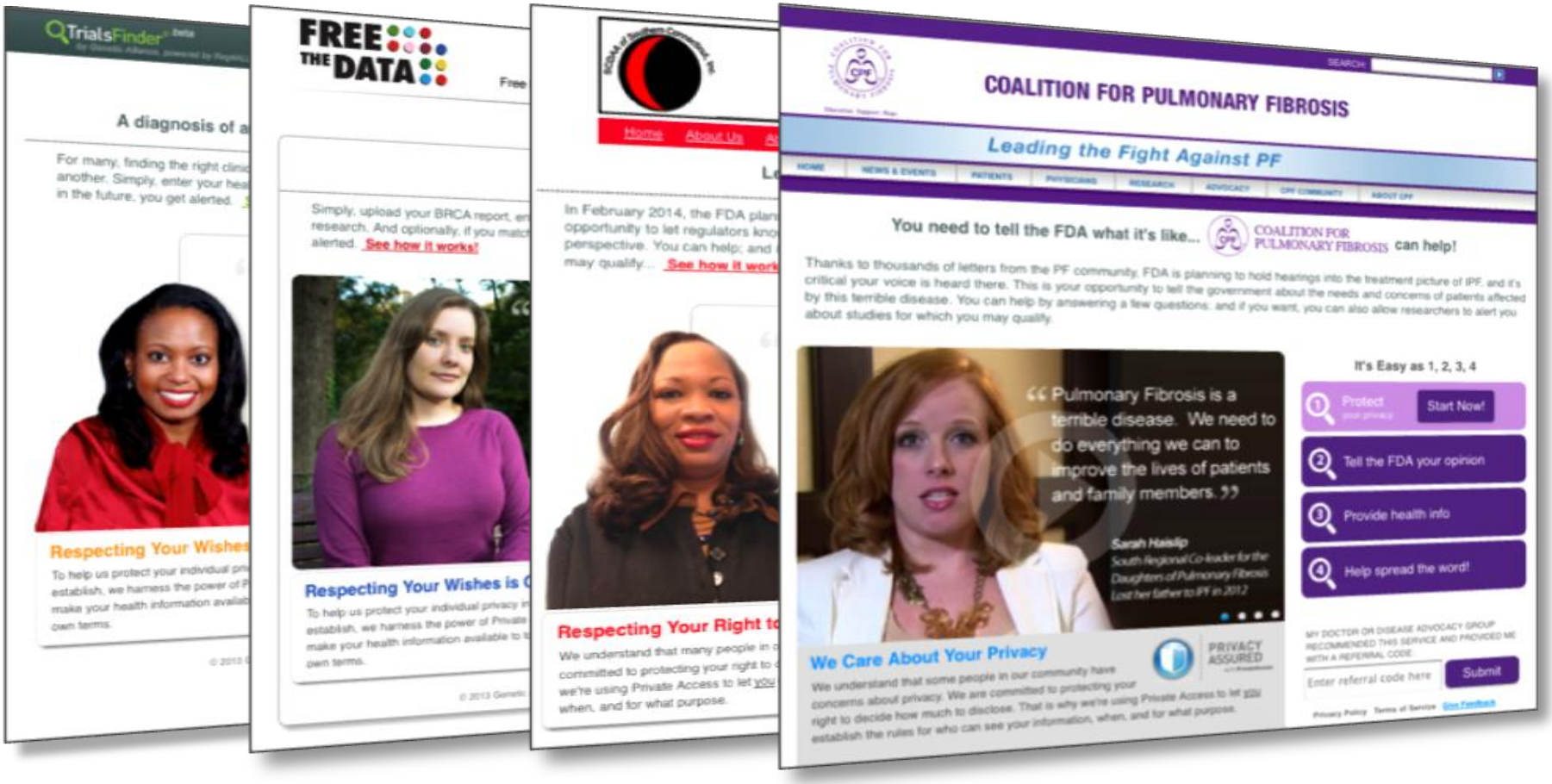
Questions appear in a dynamic user interface, and provide immediate feedback on how others responded to the same question…

Participants can review their prior answers, make updates and/or remove the data at any time.



Source: Genetic Alliance Case Study 2014, at eyeforpharma PCCT

PEER is Completely Customizable



Source: Genetic Alliance Case Study 2014, at eyeforpharma PCCT

Regulatory Players

* Review how regulatory and policy players support the patient's role in drug development

FDA

- FDA has encouraged and fostered the use of patient-reported outcome measures in clinical trials, such as impact on quality of life or pain control, to support labeling claims in medical product development.
- **FDA's Patient-Focused Drug Development initiative** is a commitment under the fifth authorization of the Prescription Drug User Fee Act (PDUFA V) that aims to more systematically gather patients' perspectives on their condition and available therapies to treat their condition.
- FDA is holding at least **20 public meetings** over the course of PDUFA V, each focused on a specific disease area.
- **Richard M. Klein** is the Director of the Patient Liaison Program

Meetings: http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm347317.htm

pcori

- Independent, non-profit health research organization authorized by the Patient Protection and Affordable Care Act of
- Funded to do comparative clinical effectiveness research on patient-centered outcomes
- PCORI's patient engagement and industry's patient engagement are parallel efforts

Patient-Centered Outcomes Research Institute

Patient and Family Engagement Rubric

Planning the Study

Conducting the Study

Disseminating the Study Results

PCOR Engagement Principles

Patient-Centered Outcomes Research Institute

Patient Engagement in Data Network Development (PCORnet)

Enrollment and diversity

- Increasing size of the network
- Increasing the diversity of the network
- Retention of network members

Governance

- The development of the network governance structure, roles and responsibilities
- Development of procedures, bylaws and policies for the network

Data collection

- The development of data collection tools
- Identification of Patient Reported Outcomes (PROs) for inclusion in database

Data sharing, privacy and

- The development of consent processes and policies
- Development of data sharing agreements
- Development of privacy policies

Concluding Thoughts

PATIENT-CENTERED DRUG DEVELOPMENT
REVENUE DRIVER AND PARADIGM SHIFT?

Reality Check: Patient Engagement

- In **prepatory phase**: setting of the research agenda, prioritization of topics and funding
- In **execution phase**: study design and procedures, recruitment, data collection, data analysis
- In **translational phase**: dissemination of results, implementation and evaluation

- Mostly convenience sampling, rarely randomization
- Engagement methods: Focus groups, interviews, surveys, study boards
- Few conceptual frameworks, poor quality of reporting
- Involvement is possible but insufficent data to evaluate positive impact

Tokenism? Scope creep? Frustration over lengthy process?

Domecq et al. BMC Health Services Research 2014, 14:89, including other systematic meta reviews

Crux of the Problem with Data

patient-centric information

- The principle of patient-centered trial data – the outcomes and evidence that are most relevant to all patients with the condition.
- more data from trials, not less.

patient-centric studies

- The principle of patient-centered trial design – re-engineering our studies to make them friendlier and more accessible to the patients who will actually enroll in them

"Our attempts to make our clinical trials more patient friendly have, for the most part, been subverted by our need to collect more comprehensive and more patient-relevant data."

Paul Ivsin, IMS

The Crucial Trial Challenges

Patient/Caregivers Education

Lack of understanding of trial procedures

Patient Engagement

Long duration of trials, patients going through personal, psychological & emotional factors leading to drop out rates

Protocol Complexity

Patients need to take multiple medications, come for multiple visit that they can miss

Focus on individual patient

Patients need a patient focused and pleasant experience

Physician Communication

Investigators have less time in person with patients. Patients cannot travel for long distances, decreasing time with investigators

Medication Adherence

Number of medications to be taken per day can influences, the adherence rates dropping to as low as 20%*

Support

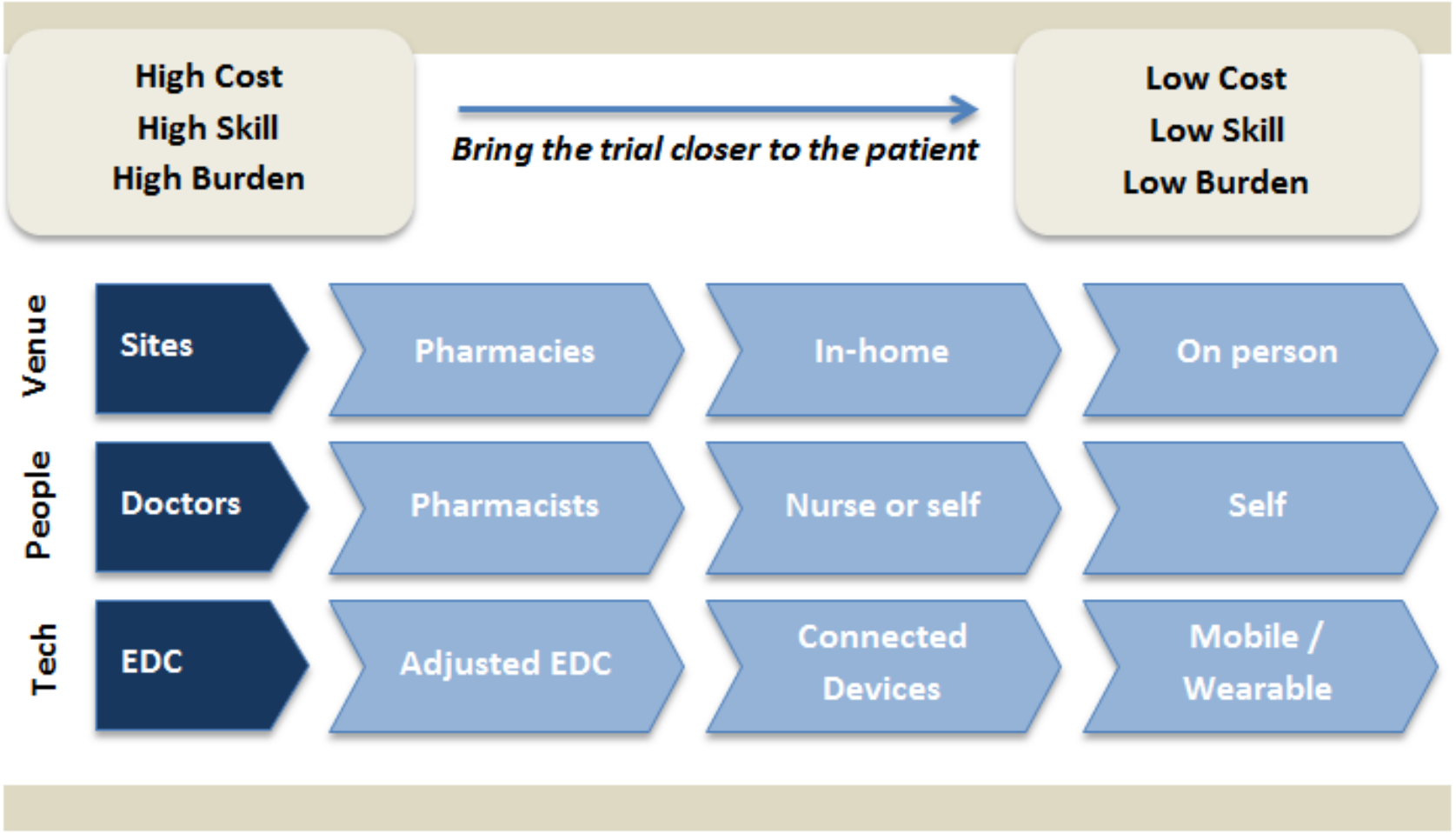
Patients need a reliable person to call to for questions about medications.

No reporting mechanism

No mechanism to report if patient has taken/not taken medications

Cognizant Life Sciences Solutions (2014)

Direct to patient, no site in sight?



Shore, E. (2013). Defining Disruptive Innovation in Clinical Trials.

Jack Whelan Video

Industry Priorities for next 2 years

1. Meaningful integration of patient reported outcomes and quality-of-life metrics
2. Emphasis on data sharing throughout the overall trial process
3. Recruitment materials that speak to the patient's health concerns
4. Systematic patient input in protocol design
5. Focus on patient friendly and patient-focused endpoints
6. Integration of healthcare-related systems with clinical research systems, leverage EMR data

Industry Priorities for next 2 years

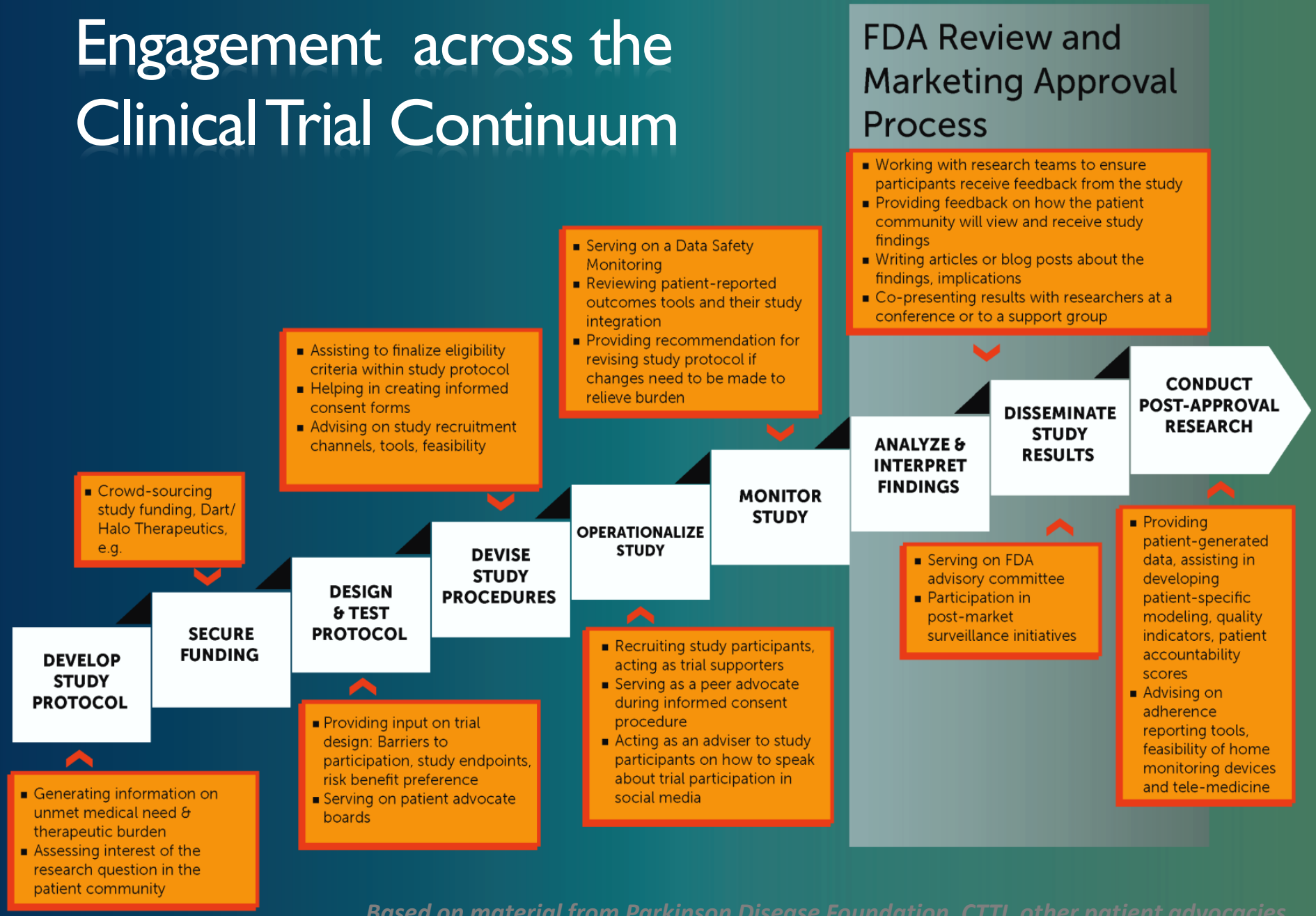
7. Cloud computing to access patient information and medical history
8. Defining patient centricity and defining framework for patient interaction
9. Industry-wide commitment to sharing patient engagement best practices
10. Placebo-controlled studies with a follow-up extension study which guarantees active study drug is a good example of study design with patient involvement in mind.
11. Easing patients' burden by making it easy to provide high quality data (i.e. using smartphones and tablets that fit into their daily lives)

Patient-Centered Trials Initiatives

Research Stage	Activities	Specific Initiatives
Study Planning and Start Up	✓ Development planning ✓ Protocol design ✓ Site identification ✓ Study start-up	✓ Patient/patient-advocacy input into research agendas, funding and participation ✓ Input into planning and protocol design ✓ Patient-willingness driven site selection
Ongoing Study Activity	✓ Patient recruitment ✓ Study conduct/data collection ✓ Informed consent form review ✓ Ongoing informed consent ✓ Interaction during participation	• Direct-to-patient clinical trial participation • Mobile device data collection and patient reported outcomes • Video and iPad informed consent • Ongoing study volunteer assessment
Study Close Out	✓ Volunteer completion ✓ Communication and disclosure	• Blue button initiative • Dissemination of trial results to study volunteers and broader publication

Adapted from Ken Getz, Tufts CSDD, 2014

Engagement across the Clinical Trial Continuum



Based on material from Parkinson Disease Foundation, CTTI, other patient advocacies

Questions & Discussion

Will there be a lesser role for clinical trial sites in the coming era of "direct-to-patient" studies and mobile technologies? Do you support it?

As SVP of Global Clinical Operations at a big pharma, which area would you prioritze for investment to become more patient-centered?

What is the impact of outsourcing clinical operations when it comes to pharma's relationship with patients? From an economic POV, would you change the current model?

References and Literature

References & Recommendations

Smart reads

Robert M Califf et al. 2012
The Clinical Trials Enterprise in the United States: A Call for Disruptive Innovation
Institutes of Medicine: Discussion Paper

Leiter, Amanda et al. 2014
Use of Crowdsourcing for Cancer Clinical Trial Development
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