Patient Engagement Frameworks Analysis
Conclusions, Learnings, Identified Needs
Developed in September 2016
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This analysis is presented in the PFMD whitepaper “Research on patient engagement (PE) - A Literature Review and Framework Analysis”.
For more information, please access the whitepaper [here](#).

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1. Main Objectives

With FDA’s emphasis on patient focused drug development (PFDD) and patient engagement (PE) in translational research, CTTI has put forth a set of recommendations to improve PG participation in the work of clinical trial sponsors (pharma and academia), which includes meaningful engagement of patients in the development of therapeutic products from study endpoint selection, recruitment and retention, and post-marketing safety.

2. Key Learnings

Recommendations included but were not limited to:

2.1. For All stakeholders

- Inclusion of PG from beginning of R&D which allows for better understanding of unmet need, burden, indication expansion opportunity, improved targets, better design, selection of optimal subjects, endpoints, clinical sites, better recruitment, lower costs, and meaningful endpoints.

- Delineation of partnership roles, expectations, resource commitment, and program objectives.

- Understanding that research sponsors must balance PG input with scientific understanding and business/regulatory needs, thus research sponsors reserve right to make final decisions unless clearly defined at outset of collaboration (e.g. PG-funded study)

- Expectations of mutual transparency and confidentiality.

- Diversity in expertise and ability to partner with more than one group for both PGs and sponsors.

- Conflict of Interest Management Procedures.
2.2. For Research Sponsors-Industry & Academia

- Need for internal culture change to build awareness around impact of PG engagement on clinical drug development and need to identify single point of contact internally as a champion and appropriate resourcing for continuous engagement.
- Continuous and ongoing engagement of PG throughout lifecycle.
- Establishment of best practices for engaging with PGs.
- Creation of standard metrics to assess partnership effectiveness.

2.3. For Patient Groups

- Provide connectivity among partners by amplifying patient voice in disease area.
- Promotion of value as a partner, expertise and assets (skills they bring) through R&D process.

3. Pending Questions

- Although standard metrics were suggested to evaluate PG collaboration on research sponsor side, is there an opportunity to measure collaboration effectiveness on both sides?
- Will these tools be used for research sponsor internal purposes only or will tools be shared/compared?
- Will sponsors share completed tool with PGs so that they can better understand strengths/weaknesses?
- How have PGs, pharma, academia used these tools in practice?
- Although CTTI guidance provides the WHAT, need for clarification on what PGs and sponsors are using for the HOW. What best practices can be aggregated across each phase by understanding specific experiences?

4. Tools being developed

- Organizational Expertise & Assets Evaluation Tool (to support selection of appropriate PG for collaboration)
- Assessment of PG Internal Aspects
- Assessment of PG External Relationships

5. Potential Initiatives/Tools to be Developed

- Creation of standard engagement models (e.g. service providers, charitable giving, collaborators) that can be adopted as a standard across the industry.
- Standard best practices for engaging with PGs (UCB has published a framework that can potentially be adopted across industry).
- Although standard metrics were suggested to evaluate PG collaboration on research sponsor side, is there an opportunity to measure collaboration effectiveness on both sides?
- Creation of key principles document regarding collaboration around research and development programs.
- Capacity building for PGs around each of the phases.
- HOW behind the WHAT defined in recommendations within each phase of the lifecycle based on specific experiences. For instance, how did PGs collect input on the research question from their patient community? What was the process they used to determine unmet needs?
**University of Maryland - CERSI PE Framework**  
M-CERSI Conference on PFDD

<table>
<thead>
<tr>
<th>Pre-Discovery</th>
<th>Research Questions</th>
<th>Pre-clinical Development</th>
<th>Clinical Development</th>
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<th>Post Approval Surveillance</th>
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<td>Communication</td>
<td></td>
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</table>
| • Understand disease/condition from patient perspective, patient journey, outcome preference  
  • Patient Registries 
  • Identify unmet need  
  • Patient/community/researcher training on effective partnership  
  • Assess current treatment effectiveness/sub-populations | • Develop research question based on patient interests  
  • Patients prioritize research questions  
  • Patients provide feedback on potential indications | • Gather/develop study tools (PROs, ClinRos, PerfOs, ObsROs)  
  • Patients identify potential barriers for study recruitment/participation  
  • Plan for who, when and how patients will be engaged  
  • Patient feedback on study endpoints | • Patients help with recruitment & provide feedback on experiences as participants  
  • Patients serve on data safety monitoring board | • Patients serve on advisory committees, contribute to benefit/risk discussion, and as patient reps | • Patients provide input on Risk Evaluation and Mitigation Strategies (REMS)  
  • Patients provide feedback on Phase IV studies  
  • Patients understand how to report adverse events | • Patients provide context for economic information under FDAMA 114  
  • Patients provide feedback on patient counseling information, MED guides, Package inserts, instructions for use |

*Proposed PFDD Conceptual Framework. Adapted from CTI’s Patient Groups & CT Expert Meeting Summary, NHC’s Dialogue/Advancing Meaningful Patient Engagement in Drug Research, Development & Approval, and model proposed by Perfetto et al. This was based on previously proposed models and meeting discussion.

Link to the source document

PROs = Patient-reported outcomes  
ClinRos = Clinician-reported outcomes  
PerfOs = Performance outcomes  
ObsROs = Observer-reported outcomes

1. **Main Objectives**

Provide a forum for patient groups, FDA, biopharmaceutical industry, payer and other organizations to voice views, challenges, activities and aspirations for PFDD, as well as future direction and opportunity for collaboration. Through a day-long conference on March 9, 2015, the University Center of Excellence in Regulatory Science and Innovation (M-CERSI) held the “M-CERSI Conference on PFDD and outputs included a suggested definition, rubric and framework for PFDD.

2. **Key Learnings**

PFDD Definition:

- A formal process by which drug developers and regulatory form a partnership with patients to enhance drug development, research, regulatory, and reimbursement processes with the patient voice. This partnership engages patients to obtain, as critical input, their views, experiences, and preferences throughout a product’s lifecycle.

- Does not end with product approval and extends beyond drugs to all treatments and diagnostics. Patients play key role in ensuring access, defining value, and informing disease management and adherence programs.
2.1. For All stakeholders

- **Patients as Partners**: Patients, caregivers, and other relevant groups (i.e., those at risk for the disease, but currently disease-free) are recognized as partners in the drug development process throughout the product **life cycle**

<table>
<thead>
<tr>
<th>Patient Role</th>
<th>Examples</th>
<th>Engagement Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partnership</td>
<td>Continuous consultation on outcomes of importance, study design; Paid investigators/consultants; Governance role, “seat at table”</td>
<td>High</td>
</tr>
<tr>
<td>Advisor</td>
<td>Advisory Committee Members; Priori consult on outcomes of importance and study design but no leadership role/governance authority.</td>
<td>Moderate</td>
</tr>
<tr>
<td>Reactor</td>
<td>Input collected distally through surveys, focus groups, interviews but patients not consulted directly or a priori on issues such as study design &amp; outcomes of importance; patients asked to react to what has been put before them rather than at the origin of concepts of interest.</td>
<td>Low</td>
</tr>
<tr>
<td>Study Subject</td>
<td>Patients recruited or enrolled as study subjects, but not asked for input consultation or reaction.</td>
<td>None</td>
</tr>
</tbody>
</table>

- **Continuous PE**: PE is continuous, throughout drug development process and product lifecycle - not a one-time or sporadic event

<table>
<thead>
<tr>
<th>Engagement Continuity</th>
<th>Examples</th>
<th>Engagement Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous</td>
<td>Engaged in various ways throughout all phases of research planning, implementation, analysis, write up and dissemination stages of life cycle.</td>
<td>High</td>
</tr>
<tr>
<td>Sporadic</td>
<td>Asked for input into research planning, study design or outcomes of importance at several points in time w/o coordination or meaningful continuity.</td>
<td>Moderate</td>
</tr>
<tr>
<td>One-Time</td>
<td>Asked for input into research planning, study design or outcomes of importance at one point in time (e.g. early planning, late dissemination) and study /program proceeds without further patient consultation.</td>
<td>Low</td>
</tr>
<tr>
<td>No Engagement</td>
<td>Not asked for input into aspects such as research planning, study design or outcomes of importance.</td>
<td>None</td>
</tr>
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</table>

- **Meaningful PE**: PE must be real interaction and dialogue, not a check box exercise. Patient input should come from thoughtful dialogue and they should be able to see how the input they provide is used in the specific studies/aspects or processes.

<table>
<thead>
<tr>
<th>Engagement Meaningfulness</th>
<th>Examples</th>
<th>Engagement Level</th>
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<tbody>
<tr>
<td>Meaningful</td>
<td>Plan for interaction/dialogue is outlined with clear objectives, why /how dialogue will take place, information sought, how it will be used, how patients will be kept informed throughout; range of engagement methods.</td>
<td>High</td>
</tr>
<tr>
<td>Partial</td>
<td>Specific activities for meaningful dialogue undertaken but not comprehensive or well coordinated; PE methods used but may not be appropriate for circumstance.</td>
<td>Moderate</td>
</tr>
<tr>
<td>Superficial</td>
<td>Informal conversations with patients take place where input and views sought but no interactive dialogue, formal process or plan to use info.</td>
<td>Low</td>
</tr>
<tr>
<td>No Interaction</td>
<td>No interaction or dialogue is initiated.</td>
<td>None</td>
</tr>
</tbody>
</table>
**Right Patients are Engaged:** The affected patient population is well represented, and other relevant populations are considered for engagement (throughout process).

<table>
<thead>
<tr>
<th>Right Patients</th>
<th>Examples</th>
<th>Engagement Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comprehensive</td>
<td>Thoughtful effort to engage range of patients/caregivers (e.g. patients with disease, cured, at risk); Patients &amp; advocacy groups engaged; Range of patients afflicted represented (e.g. age, gender, race, geography, socioeconomic status).</td>
<td>High</td>
</tr>
<tr>
<td>Representative</td>
<td>Representative sample of patients engaged but may be limited by demographics, region.</td>
<td>Moderate</td>
</tr>
<tr>
<td>Limited</td>
<td>Small number of homogenous patients are engaged; convenience sample.</td>
<td>Low</td>
</tr>
<tr>
<td>No Patients</td>
<td>No patients included.</td>
<td>None</td>
</tr>
</tbody>
</table>

**Right Time to Engage:** Engagement happens at appropriate time(s) throughout process.

<table>
<thead>
<tr>
<th>Temporality</th>
<th>Examples</th>
<th>Engagement Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appropriate</td>
<td>Clear rationale is provided for timing of patient engagement efforts through life cycle.</td>
<td>High</td>
</tr>
<tr>
<td>Acceptable</td>
<td>Timing of engagement is well planned based on characteristics of condition, engagement goals, other documented rationale.</td>
<td>Moderate</td>
</tr>
<tr>
<td>Poor</td>
<td>Unclear rationale/temporality; no clear plan for engagement timing.</td>
<td>Low</td>
</tr>
<tr>
<td>Inappropriate</td>
<td>Timing not appropriate given condition, study design or other factors.</td>
<td>None</td>
</tr>
</tbody>
</table>

### 2.2. Background Information & Key Challenges to PFDD

- Movement in US and Europe to include patient voice in research/decision making.
  - Examples: In US, PCORI established under ACA. PCOR seeks to aid individuals/caregivers to communicate and make informed healthcare decisions by requiring patients and researchers to work together to formulate/complete studies. In Europe, patient-identified priorities have become prominent in HTA for medical products. Regional HTA bodies such as NICE, IQWiG engage patients in review/pilot projects. There is emphasis on understanding patient experience data.
  - PFDD is part of 5-year initiative conducted by FDA to more systematically obtain patient perspective on certain diseases/treatments.
  - PFDD research is one branch of PCORI.
  - PhRMA & NHC have identified PFDD as top priority for next reauthorization of PDUFA VI and 21st Century Cures legislation.

#### 2.2.1. FDA Activities and goals

- FDA PFDD meetings completed to date demonstrate great patient interest in having insights documented.
  - Opportunity for externally led PFDD meetings where patient orgs can identify/organize patient focused collaborations to generate public input on other disease areas using process established through FDA’s PFDD initiative (e.g. public meetings, web only meetings).
  - Value in engaging wider community of patient stakeholders, clinicians & social science researchers to identify approaches to collect patient input on experience of living w/particular disease and incorporating
this into benefit risk assessment and product labeling.

○ Challenge is that there is no formal policy on how externally-led PFDD meetings will take place.

• FDA Patient Representative Program - Organizes opportunity for patient rep. to sit on FDA advisory committee. Program involves 200 patient reps across 120 diseases.

• FDA Patient Consultant Program - established to fulfill obligations under Section 1137 of FDASIA to incorporate patient participation in medical product discussions in collaboration with FDA scientific review staff.

• FDA Patient Network - opportunities for PE through webinars, in-person meetings, bi-weekly newsletter w/info on e.g. new product approvals, labeling changes, safety warnings.

• Role of Patients in Health Outcomes Assessment.
  ○ Use of Clinical Outcome Assessments (COA), including PROs in clinical trials is most visible means of incorporating patient input into drug development.
  ○ Purpose of OA is to determine whether drug has been shown to provide benefit to patients. Important aspect of DD is how treatment benefit is measured. Qualitative research (focus groups, patient interviews) can be used to develop/select COA for use in clinical trials.
  ○ “FDA PRO Guidance” describes good measurement principles to consider when developing/selecting PRO assessments with recommendations on how to incorporate patient input into process.
  ○ Other COA includes performance outcomes, clinical reported outcomes and observer-reported outcomes.
  ○ “FDA Roadmap to Patient Focused Outcome Measurement in Clinical Trials” - useful in selecting/developing pathway for COA.

2.2.2. FDA Activities and goals

• Role of patient advocacy orgs is expanding including collecting info from patient community.

• Patients want opportunities to participate in accelerated approval process.

• Patient organizations are collaborating to transition lessons learned through their own PFDD meetings into operational framework for conducting PFDD. PPMD conducted its own externally-led PFDD meeting and submitted draft guidance for drug development in Duchenne Muscular Dystrophy to FDA.

• Harmonization among patient groups needed to avoid duplication/inefficiency.

• Key Themes for Overcoming Barriers to Meaningful PFDD:
  ○ Clear signals/transparency across stakeholders
  ○ Regulatory action to set guard rails
  ○ Methods/Tools to systematically engage patients
  ○ Communication tactics targeted to patients
  ○ Coordinated/strategic dissemination efforts
  ○ Infrastructure for sharing best practices
  ○ Org culture shifts
  ○ Systematic changes to incentivize PE

2.2.3. Industry Activities/ Plans

• Shift from “Why should patients be involved in drug development?” to “How do we ensure patients are at core of drug development process?”

• Core values for patient centeredness should be transparency, partnership, continuous learning and improvement, and focus on outcomes & impact.
2.2.4. Payers

- Payers under-represented in patient centric drug development initiatives.
- Payers are key decision makers in determining access.
- Payers can contribute to model to determine when PFDD would be useful in drug development process to ensure PFDD will be useful in real world decision-making. (e.g. assessment of real world tolerability through benefit-risk assessment so payers can better determine how likely patient population will tolerate an intervention).
- Managed care issues with methods to quantify tolerance of risk, balancing benefit/risk, operationalizing electronic medical record (EMR) in way that patient preferences can mirror prescribing patterns, payment/reimbursement, PFDD process.
- Through PFDD process, payers may have access to info regarding heterogeneity of treatment effects in certain subgroups.

2.2.5. Challenges to Successful PFDD

- 10 Gaps and Need areas for PFDD (Adapted from comments by Dr. Robert Epstein):

<table>
<thead>
<tr>
<th><strong>Timing of Patient Input</strong></th>
<th>Exactly when would patient input matter? Why would it matter at these endpoints?</th>
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<tbody>
<tr>
<td><strong>Type of Patient Input</strong></td>
<td>How do we utilize quantitative input when thinking about heterogeneity of patient populations?</td>
</tr>
<tr>
<td><strong>Sampling</strong></td>
<td>How do we develop unique and innovative ways to engage large number of patients?</td>
</tr>
<tr>
<td><strong>End Points</strong></td>
<td>Do patients really care about patient-reported outcomes?</td>
</tr>
<tr>
<td><strong>Co-Morbidities</strong></td>
<td>How do we incorporate more than 1 health problem some people may have into clinical development?</td>
</tr>
<tr>
<td><strong>Addressing Other Patient Metrics</strong></td>
<td>How do you... integrate benefit/risk assessment from patient perspective? Account for patient preferences? Address gaps in data collection?</td>
</tr>
<tr>
<td><strong>Chief Complaints Ignored</strong></td>
<td>Why aren’t we doing something with chief complaints patients give to their providers?</td>
</tr>
<tr>
<td><strong>Redefining Research Question</strong></td>
<td>How should we redefine research question in patient voice?</td>
</tr>
<tr>
<td><strong>Uncertainty Measurement</strong></td>
<td>How will reducing patient uncertainty better help reduce standard deviation and help us get signal out of noise?</td>
</tr>
<tr>
<td><strong>Myth Breaking</strong></td>
<td>How do we eliminate confusion around FDA legal/compliance barriers slowing down stakeholders trying to get into conversation?</td>
</tr>
</tbody>
</table>
3. Pending Questions
How are the various stakeholders accomplishing elements of proposed framework (anecdotal, examples)?
Are there any tools to measure impact/value of elements of framework?

4. Tools to Support
- Proposed PFDD Conceptual Framework
- Rubric
- PFDD Definition

5. Potential Initiatives/Tools to be Developed
- Best practices for systematically collecting patient input on experience of living with particular disease (need to account for differences in cultures).
- Identify/test promising patient engagement methods.
- Internet and social media information from patients can be captured and used to foster engagement.
- Regulatory guidance for bio-pharmaceutical industry to understand how and when they can engage patent community.
- Methods to capture right information from appropriate patient populations and to improve use of that information in development programs and benefit-risk assessment.
- Tangible incentives (regulatory and market based) so that patients, payers and biopharmaceuticals benefit.
National Health Council (NHC) Framework

Creating Regulatory Guardrails
See full table: Prioritize development of one/series of guidance to set regulatory parameters and clarify agency thinking around topics such as: type of information to be considered by FDA, patient data endpoint selection, appropriate industry interactions, linking patient information to benefit/risk assessments

* Promoting a Culture Shift/Open Communication

 Link to the source document

1. Main Objectives
To build consensus around a vision and targeted set of actions for advancing patient engagement in drug research, development and approval.

2. Key Learnings
A multi-stakeholder group (32 attendees) convened on March 2, 2015 to discuss methods in which to transform the existing product development paradigm and come to a consensus on what it entails to meaningfully engage patients and identify key gaps and barriers in patient engagement across the research to care continuum. Many factors were discussed as it relates to designing and executing engagement strategies. A need for a set of disease/condition agnostic methods and standards to enable stakeholders to tailor and optimize engagement was identified.

- Increasingly patient centric landscape, with a greater emphasis on not only demonstrating a therapy’s safety and effectiveness, but also demonstrating how the therapy addresses patient needs and how it will improve outcomes.
- The integration of the patient voice into the early stages of R&D is being recognized as just as important as post-approval engagement.
- There is also increasing pressure to get drugs to patients faster.
- To meet this demand, stakeholders across healthcare are exploring methods to more thoroughly incorporate the patient perspective into drug research, development and approval.
- Barriers to meaningful engagement in drug discovery, research and approval fell into 3 categories: culture, communication and regulatory rules/processes.

2.1. Building a Framework for Meaningful Patient Engagement
- There is increased awareness and understanding of impact of integrating patient perspective into therapy life cycle; however, many of these efforts are transient and can be inconsistent.
- The patient perspective is not monolithic, even within a particular condition where perspectives can vary widely.
- There are limitations in generalizability of a sampling of patient perspectives and judging appropriateness of specific patients/patient groups to research aims.
- Stakeholder information needs and internal processes may vary due to culture, contexts and circumstances.
- Several methods exist to qualify whether an engagement is meaningful - reliable, valid, repeatable, authentic.
• A framework and rubric for meaningful engagement would be helpful.
• understanding patient experience data.

Definitions used by NHC were utilized in discussion and summarized below:

<table>
<thead>
<tr>
<th>Consumer</th>
<th>A generally healthy individual who moves in and out of the healthcare system as needs change over time.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>Someone dependent on the healthcare system for the rest of life after diagnosis of a medical condition/disability. Reliance on healthcare system is to feel better, have longer, healthier and more robust life. An individual patient’s views on health issues, such as benefit/risk of new treatments will vary depending on severity of condition and personal circumstances.</td>
</tr>
<tr>
<td>Patient Advocacy Organization</td>
<td>Takes a holistic view of the conditions for the patients it represents and seeks universal support from stakeholders for its mission and programs.</td>
</tr>
</tbody>
</table>

• Best practices can be identified around meaningful patient engagement to ensure that the experience is informative, constructive and mutually beneficial.
• Early stage planning is important to ensure that meaningful patient engagement is systematic.
• Patient groups should also be strategic in engagement/partnership with stakeholders.
• Feedback systems to measure impact of engagement should be established.

Questions for consideration by researchers and patients when designing, implementing and evaluating engagement approaches are summarized below:

| What are we trying to achieve? | Determine specific goals of engagement. |
| Who are we trying to engage? | Understand target population and who best to engage within specific stakeholder group. |
| When should we engage? | Identify points along given process that are optimal for engagement. |
| How should we engage? | Select methods most suitable for engagement. |
| What is the expected impact? | Develop metrics (outcomes/endpoints) that can be assessed to determine whether goals have been met. |
| What is the actual impact? | Implement frequent checkpoints during/after engagement to promote communication, data collection on outcomes/endpoints, and issue resolution. |

2.2. Key Gaps in Methods, Resources & Best Practices

• Patient engagement for every disease area and patient population will have unique challenges and best practices for engaging patients should be created to ensure consistency regardless of population size, resource, level of organization.
• Patient populations from different disease areas will vary in how well organized, informed and represented they are. For instance, rare disease populations may have limited resources/infrastructure for organized engagement.
• A toolkit or network of collaborators with common interests and goals is needed to help support efforts and build economies of scale.

• Best Practice examples for engaging patients includes:
  ○ Go to patient/relevant patient organization first, when possible.
  ○ Maximize patient participation/completion by consolidating number of steps patient must take to engage (forms, meetings, encounters, physical trips).
  ○ Understand patient environment, situation and state of mind at point of engagement and how this may impact outcomes/overall experience.
  ○ Seamlessly integrate data capture into patients’ lives.
  ○ Build capacity for patients to engage and invest in technical assistance to support.
  ○ Set clear expectations and boundaries (what’s relevant & appropriate/what’s not).
  ○ Treat patients the same as other participants (compensation for time in advisory capacity).
  ○ Need for innovative/tailored tools and methods to collect patient information and data to meet objectives and inform downstream decision-making (e.g. internal business strategies, regulatory decision-making).
  ○ Need for standards in applying validated methods.
  ○ Need to develop consensus driven tools to help guide optimal selection and use of validated methods for collecting patient information and standard methods of patient input.

2.3. Barriers to Meaningful Engagement

Traditionally patients have been narrowly engaged as clinical trial participants/subjects in the post-market and care delivery space but a dramatic shift is taking place in integrating perspectives and preferences at critical decision points along the research to care continuum.

2.4. Regulatory/Legal Uncertainty

• There is uncertainty around how the FDA will evaluate sponsor-submitted patient information during the regulatory review process and the impact data will have on therapy approval decisions.
  ○ Greater transparency from FDA will alleviate some of this uncertainty. An example of this is FDA’s benefit risk framework where guidance of the information/endpoints of interest to the FDA and clarity on how they plan to link patient preference data to the framework will provide stakeholders with what type of data/PROs to collect to inform regulatory decision-making.
  ○ There is uncertainty around what is appropriate patient engagement and actions that may be seen as violations of regulations. For instance, research-based patient interactions could be misinterpreted as promotional in nature. This uncertainty discourages stakeholders from proactively and innovatively engaging with patients.

![Diagram of Regulatory / Legal Uncertainty, Culture, and Communication](image-url)
○ Patient groups would also benefit from increased transparency so they can appropriately prepare their constituents for opportunities to further engage.

○ There is need for clearer guidance from FDA acknowledging support of patient engagement efforts to inform drug development.

2.3. Barriers to Meaningful Engagement

The lack of regulatory uncertainty has affected culture change because patient input has traditionally been difficult to gather/assess due to perceived risk. In addition, culture change has been difficult due to perception that patient information doesn’t follow science based approaches, may pose financial risk, has potential for misalignment or lack of incentives and lacks accountability.

• **Science Based Approach:** Patient perspectives are perceived as being anecdotal, emotional, and at times subjective compared to clinical outcomes data in clinical trials. Validated methods in obtaining patient perspectives exist but due to poor methodical rigor there is still a view that patient information may detract from clinical outcomes data rather than enhance the data package.

• **Financial Risk:** The business case for engagement of patients in early stages of product development rests on helping to avoid patient concerns and misalignments between a therapy and patient needs after product launch, such as types of endpoints/outcomes studied compared to what patients care about. However implementation of process and building capacity to meaningfully engage patients requires significant investment from all stakeholders.

• **Organizational Culture:** A culture that values patient engagement from organizational structure to day-to-day operations is crucial across all stakeholders. A top down approach is needed for a rapid and effective way to influence the culture of an organization with consistent messaging and leadership communication both internally and externally. Ultimately this lays the foundation for incentives to promote behavior change, accountability, and empowering employees to make strategic/operational decisions incorporating patient perspectives.

• **Proprietary Information:** Engagement with patients is often proprietary due to the competitive marketplace whereby communication and information sharing among stakeholders has been limited. Recommendations were made to distinguish information that is truly proprietary from what can/should be shared with best practices and lessons learned clearly delineated.

• **Translation & Patient Acknowledgement:** Stakeholders seldomly engage patients with continuity and engagement typically ceases after data gathering portions of a clinical trial or study. As a result, patients often don’t have a clear understanding of how input/data was used. Study outcomes are rarely communicated and shared with trial participants. The lack of a feedback system to keep patients engaged and informed is reinforcing that patient input is being collected to check a box. Translating information in a manner that’s comprehensible to the target population and acknowledges and shows the impact of their contribution can improve the quality of these patient engagements.

• **Visibility:** There is a large knowledge and information gap in patient engagement and drug development and regulatory approval with no centralized warehouse of patient engagement methods, best practices and success stories. Increased visibility of patient engagement activities or research conducted will bring awareness to a broader audience.
2.6. Next Steps

To address the barriers to meaningful patient engagement, solutions have been proposed by participants throughout the dialogue with emphasis on the group that may have a greater opportunity to operationalize (Abbreviated table below. For full list see Report).

### Creating Regulatory Guardrails

<table>
<thead>
<tr>
<th>Prioritize development of one or a series of guidances to set regulatory parameters and/or clarify agency thinking around topics such as:</th>
<th>Patient Community</th>
<th>Academia</th>
<th>Industry</th>
<th>Regulatory Agencies</th>
</tr>
</thead>
<tbody>
<tr>
<td>• What type(s) of patient information will be considered by the FDA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Patient data endpoint selection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Appropriate industry interactions with patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Incorporation of patient information or product labels</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Linking patient information to benefit/risk assessments</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Align stakeholder advocacy strategies to maximize impact</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formalize regulatory asks (FDA action) for negotiation in sixth Prescription Drug User Fee Act (PDUFA VI), as appropriate</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Generate publications or opinion pieces in high-impact clinical journals or other credible venues to heighten visibility or patient engagement, send a “signal” to broader clinical and scientific community, and enhance legitimacy of patient engagement efforts</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Create more opportunities to collect public feedback and input through public avenues such as requests for information (RFIs), town hall meetings with iterative Q&amp;A sessions, and comment opportunities</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Enhance FDA division alignment on the use of tools for evaluating patient information at the reviewer level</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Increase transparency on how information is used and incorporated in each engagement/into each decision-making step</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

### Promoting a Culture Shift

<table>
<thead>
<tr>
<th>Generate buy-in and sponsorship for patient engagement at the executive and senior leadership levels</th>
<th>Patient Community</th>
<th>Academia</th>
<th>Industry</th>
<th>Regulatory Agencies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Create accountability at all levels within an organization for collecting, understanding, and integrating patient perspectives by establishing expectations and measuring the impact</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Organize internal infrastructure and staffing to be coordinated around patient engagement activities and to prevent information silos</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Train and educate researchers on patient engagement</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Develop methods standards that can be applied across multiple disease areas</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Establish processes or models to systematically engage patients at any point in the research-to-approval continuum</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Develop and implement tools and resources that complement methods for patient engagement and facilitate implementation</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Develop and test metrics to evaluate patient engagement</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Develop a platform, repository, or system for sharing best practices, research, examples of impact (e.g., public-private partnership or “center of excellence”)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Establish a public-private partnership to serve as a central clearinghouse for patient-centered studies in the pre-market space, build capacity and infrastructure, and advance scientific methodologies for patient engagement</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Direct funds from public and private research funders through patient groups to provide patient groups with the opportunity to solicit, evaluate, prioritize, and even directly fund patient-centered studies or projects</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Facilitating Open Communication

<table>
<thead>
<tr>
<th>Activity</th>
<th>Patient Community</th>
<th>Academia</th>
<th>Industry</th>
<th>Regulatory Agencies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Translate all information provided to and communications with patients to an appropriate level such that it is comprehensible</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Create a feedback system to inform patients about how their contributions impacted decision-making and outcomes</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Manage patient expectations at the outset of each engagement through clear and transparent communications</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Consistently document the impact of patient perspective studies or other outcomes and publicize them</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Proactively conduct media and press activity to publicize successes or give periodic updates on new developments</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Publish studies and editorials in high-impact clinical and scientific journals to raise awareness among the research community and enhance credibility</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Coordinate publication strategies with other stakeholders for relevant pieces to be published at the same time or sequentially through various outlets</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Publish or make publicly available experiences, advice, best practices, lessons learned, and other resources not considered proprietary or intellectual property</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Create partnerships and collaborations among private companies that encourage and incentivize information sharing and building economies of scale to accomplish a shared goal</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Utilize the open source production model whenever possible to promote continuous refinement, improvement, and open access to an engagement “blueprint” or “design”</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

3. **Pending Questions**

A few gaps highlighted have been addressed through recent efforts and reports (e.g. PFMD, CTTI guidelines). What type of litmus test is being done to assess achievements across stakeholders in implementation (vs. guidance)?

4. **Tools being developed**

Implementation Manual: How to Operationalize the NHC’s Patient Information Tool.

5. **Potential Initiatives/Tools to be Developed**

- Feedback systems to measure impact of engagement.
- A toolkit or network of collaborators with common interests and goals to help support efforts and build economies of scale.
- Consensus driven tools to help guide optimal selection and use of validated methods for collecting patient information.
- List of Action Items in Table above.
**PCORI Engagement Rubric**
Patient Centered Outcomes Research Institute (PCORI)

**Planning the Study:**
How will patients partner in study planning and design?

**Conducting the Study:**
How will patients partner in conducting study?

**Disseminating study results:**
How will patients partner in dissemination of study findings to ensure they are understandable?

**Engagement Rubric for Applicants**

**1. Main Objectives**
To illustrate and provide guidance around how input from patients and other stakeholders can be incorporated throughout the entire research process.

**2. Key Learnings**
PCORI Engagement Principles (Reference to partners below emphasizes the patient):

- **Reciprocal Relationships:** When roles & decision-making of all research partners (including patients) are defined collaboratively and clearly.

- **Co-Learning:** When the objective is not to turn partners (including patients) into researchers, but to help them better understand the research process. The research team will in parallel learn about patient-centeredness/engagement and integrate partners into the research process.

- **Partnerships:** When time/contributions of patient (and others) are valued and shown through fair financial compensation & reasonable time commitment expectations. Research team is committed to diversity across all activities when there are priority populations, including cultural competency and disability accommodations.

- **Transparency, Honesty, and Trust:** When major decisions are inclusive and information is openly and honestly shared with all partners.

  - “Patient partners” include those with lived experience, family members, caregivers, and organizations representative of population of interest. They are not to be confused with patient subjects (those enrolled in study as participants) and are members of the research team that are involved in planning, conduct, and dissemination of the research.

  - “Stakeholder partners” include members of constituencies based on professional experience (as opposed to personal). Example: clinicians, purchasers, payers, industry, hospitals and health systems, policy makers, and training institutions.

**2.1. Key Considerations for Planning, Conducting, and Disseminating Engaged Research**

- From original concept to implementation, identify stakeholders and patient patients who need to be included to ensure success.

- Consider budget for initiative, including compensation for patient and stakeholder partners and meeting costs, IT, facilitators of multidisciplinary work. Guidance on compensation of patient partners can be found in PCORI’s
“Compensation Framework” and budget guidance can also be found in “Budgeting for Engagement Activities”.

- Include at least one patient partner with no other role on the project. Avoid complete reliance on patient partners with dual roles on the project (e.g. stakeholders/researchers who are also patients).
- Demonstrate engagement in a research proposal, for example by asking partners to provide letters of support, bio-sketches thoroughly describing the roles/decision-making authority of partners, and clearly stating engagement activities and compensation in budget.

2.2. Guidance for Applicants Completing a PCORI Funding Announcement (PFA) Engagement Plan

Engagement Rubric is divided into: Planning, Conduct, and Dissemination.

2.2.1. Planning the Study

Description of how patients & stakeholder partners will participate in study planning and design.

Potential activities may include:

- Development of research question/relevant outcomes to be investigated, to ensure that study and results will be relevant/useful to patient and other stakeholders.
- Defining study participant characteristics, to minimize risk that certain patients may be included/excluded due to irrelevant criteria.
- Promoting study retention by designing study to minimize disruption/burden to stakeholder study participants (including patients).

Real-world examples:

- Mental health study: Patient partners and community members helped develop study name and materials to reduce potential for stigma and to reframe study goal as a movement towards emotional well-being as opposed to a mental health challenge, which may in turn improve study participant recruitment and improved community acceptance of project.
- Surgery vs. antibiotics study: > 800 patients were surveyed about treatment option preferences, which was used to shape proposal. Significant clinician input modified study inclusion criteria and logistics, as well as criteria for “failure” for one of the arms.
- Diabetes Study: A 3-arm approach was suggested after clinicians who reviewed initial study design indicated that clinical practice is variable, and study design was revised to make it more reflective of real clinical settings.
- Prescription drug for stroke patients study: Patient partners (who were stroke survivors) identified an important new outcome (that was important to them): “home-time” or number of days when a patient is living at home (e.g. not hospitalized).
- Chronic pain study: Patient partners shortened/redesigned a lengthy phone survey tool, which they felt would create a hurdle for chronic pain patient participation.
- Post-discharge care study: are actively involved in initial data run analysis, asking key questions which have helped.

2.2.2. Conducting the Study

Description of how patients & stakeholder partners will participate in conducting study.

Potential activities may include:

- Drafting/modifying study materials and protocols to ensure clinician and patient participant feasibility.
- Participating in study participant recruitment, to support viability through increased and maintenance of
• Participating in data collection/data analysis, to allow for a variation in perspective and data interpretation.
• Participating in patient/stakeholder engagement evaluation to promote authenticity and value.
• Serving as a patient representative on a data safety monitoring board to ensure patient centeredness.

Real-world examples:
• Chronic pain study: The informed consent document is created with patient partners to ensure participants can understand, which can improve recruitment.
• Chronic pain study: The patient-centeredness of the care in study to be assessed by patient partners by following participant across all aspects of study with observations to be used to improve study processes.
• Asthma study: Patients and clinicians provided guidance on who should provide the intervention, when and how to deliver it during care process.
• Falls prevention study: A caregiver of aging parents who have experienced falls is the data safety monitoring board’s patient/caregiver representative to offer interpretations of benefit, risk, and data analysis.
• Pediatric surgery study: Recruitment rates increased (after adjustments to study) when parent partners shared that they would feel more comfortable if the person discussing risks & benefits of surgery, as well as involvement in the study, was a surgeon.

2.2.3. Disseminating study results

Description of how patient and stakeholder partners will be involved in dissemination of study findings to ensure they are understandable

Potential activities may include:
• Identifying partner organizations for dissemination so that connections with end-users are meaningful.
• Planning/participating in dissemination plans, shaping study design and protocol from the start, authoring manuscripts, presenting study findings.
• Identifying unique and creative opportunities to present/share study information even while in progress.

Real-World Examples:
• Trauma study: To speed implementation of study results/findings into practice, a policy summit will be held by research team with relevant professional societies in 3rd year of study.
• Surgery vs. antibiotics study: Broad-based and diverse dissemination was demonstrated when 7 payers, 3 policymakers and 4 large employers provided letters of support and agreed to communicate results to networks.
• Chronic pain study: A continuing education will be created by physical therapists partnering in the study, where patient partners will also provide feedback on type of therapy and communication techniques that are more/less likely to be effective during acute pain episode.

3. Pending Questions
• What type of assurance/validation is being provided to ensure that patients are truly embraced as partners and brought in early during study design?
• How are patients interwoven throughout research study?
• How do we ensure patients are brought into all research meetings with information translated in a manner they can understand?
• Is there an opportunity to connect patient partners with other patients who are also participating in studies to feel empowered?
4. Tools to Support

- Financial compensation of patients, caregivers, and patient/caregiver organisations engaged in PCORI-funded research as engaged research partners.
- Budgeting for Engagement Activities.
- Sample Engagement Plans.
- Sample Engagement Plans from Methods Portfolio.
- PCORI Methodology Standards.
- Promising Practices of Meaningful Engagement in the Conduct of Research.

5. Potential Initiatives/Tools to be Developed

- No info at the time of analysis.
PERFETTO et al. Framework
When is evidence sufficient for decision making?

A framework for understanding the pace of evidence adoption
Understanding the factors that affect the pace of evidence adoption and application into routine clinical practice.

Link to the source document

1. Main Objectives
To propose a framework that examines the factors that may affect the pace of evidence adoption and application into routine clinical practice.

2. Key Learnings
The factors in framework developed include:

- **Validity, reliability and maturity of the science**: whether current understanding of disease pathophysiology, mechanism of therapeutic intervention, and measured effectiveness in improving clinical outcomes are mature enough to incorporate newly released evidence

- **Communication of the science**: whether the study results are amplified through the media or other communication vehicles

- **Applicability**: patient or provider ability to apply published scientific evidence to specific clinical needs

- **Economic drivers** that may influence adoption (for example Payment/Reimbursement model)

- **Rapid (or slow) integration** into guidelines (for example due to maturity of science.)

The framework was applied to three case studies—statins, drug eluting stents and bone marrow transplantation for breast cancer to describe impact of the factors on the speeds of evidence adoption.

These areas were selected because:

- They are well documented (clinical evidence & utilization changes).
- Demonstrate how pace of adoption into routine practice ranges from slow (>17 years) to rapid (<1 year). Pace=time interval between availability of evidence and adoption into practice.
- Include drugs, devices and procedures.
- Shed light on evidence which supports both increase and decrease in use.
- Included high quality evidence (at least in part a multiple randomized control trial).

The Institute of Medicine has advised that it takes ~17 years for new knowledge from randomized controlled trials to be incorporated into practice. In some cases, medical technologies are adopted in an absence of sufficient evidence of benefit and safety.

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• Aday & Andersen proposed a framework (1974) to study healthcare access based upon assumption that healthcare utilization is a function of individual, societal and health system determinants. The model has four factors that directly/indirectly influence use, which include health policy, characteristics of the healthcare system and population, as well as consumer satisfaction. This model of access & utilization doesn’t capture influences from communication vehicles (e.g. media) and ignores service attributes (e.g. innovation or strength of evidence behind it).
• The Rogers’ model of diffusion of innovation provides additional insights using four diffusion elements: an innovation, communicated through certain channels, over time among members of a social system. Rogers recognized the role of KOLs, social networks, media & other communication forms in innovation diffusion.

As an extension of previous work and given that multiple stakeholders influence evidence adoption, various sectors (public, private and academic) congregated to discuss an approach that considers healthcare access and utilization along with diffusion of innovation.

• The goal was to also explore whether a conceptual framework might shed light on why adoption may lag at times.
• As funding for comparative effectiveness research increases, it’s crucial to minimize delays in dissemination of evidence so that it can be used in clinical care.
• To further understand why the speed of evidence adoption varies, a framework was proposed and factors applied to 3 case studies where findings rapidly (e.g. BMT for breast cancer), moderately (e.g. drug-eluting stents) and slowly (e.g. statins) impacted care.

### Conceptual factors applied to case examples

<table>
<thead>
<tr>
<th>Conceptual factor</th>
<th>Statins</th>
<th>Drug-eluting stents</th>
<th>Bone marrow transplantation for breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validity, reliability and maturity of the science</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Communication of the science</td>
<td>+</td>
<td></td>
<td>+++</td>
</tr>
<tr>
<td>Ability to apply published findings</td>
<td>0</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Economic drivers</td>
<td>-</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Rapid (or slow) adoption into practice guidelines</td>
<td>-</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

- Retarded evidence adoption; +: Modestly increased evidence adoption; ++: Strongly increased evidence adoption; +++: Very strongly increased evidence adoption; 0: No discernible relationship; NA: Not applicable.

### 2.1. Validity, reliability, maturity of science

• For years, statins showed beneficial effects on cholesterol levels, but proof of effects on cardiovascular conditions and mortality and who this actually impacted lagged in development.
• Despite high quality studies, dramatic changes in clinical understanding did not result, thus statins remained second-line therapy until the science matured and proof emerged.
• In contrast, swift reductions in use of bone marrow transplants for breast cancer manifested from the availability of results of multiple randomized controlled trials. In this case, the science was mature, the risks were clear, but the benefits needed validation from reliable studies, which became available at ASCO.
• When drug-eluting stents were introduced, bare metal stents were already the norm in percutaneous coronary intervention procedures. Two randomized studies substantiated the benefits of the new drug device combination and provided the needed evidence to rapidly shift the market away from BMS to the newer types.

2.2. Communication of the Science
• The presentation of compelling bone marrow transplant results at an international conference provided a communication vehicle to KOLs and providers with several newspaper reports leading up to the release as well as trial findings released after.
• A journal editorial advised that the bone marrow transplant should be abandoned for this use.
• In contrast, there were no landmark research results for statins and no headline communications that impacted adoption immediately after.
• Communication about drug eluting stents may have positively impacted utilization because it was an innovation in therapy.
• New findings about potential harm, such as bone marrow transplants when it showed no benefit, unexpected vessel closures in drug-eluting stents, and muscle damage from statins may obtain more attention and be rapidly integrated into patient doctor decisions than potential benefits.
• If evidence level is high the findings can be interpreted, better understood by the population, and the media can help influence speed of adoption. Newspaper articles, social media presence and talk show segments may lead to more rapid awareness of new evidence to drive adoption and change.

2.3. Ability to apply published scientific findings
• For patients, adoption of new therapies/tests requires they: search online to learn about options, but they need assistance from clinicians to translate the evidence, especially when considering initiating a new therapy.
• In contrast, discontinuing a therapy or deciding not to proceed with one can be more readily applied.
• For bone marrow transplants, enthusiasm from patients and pressure from patient groups abated when new evidence emerged. Since patients typically need referrals for a bone marrow transplant, the new information they learned from the media may have greater likelihood on impact of discussion about bone marrow transplant referral. However discontinuing therapy doesn’t always occur quickly with new and unsupportive data.

2.4. Economic Drivers
• Studies have shown that financial incentives can influence evidence adoption.
• Although bone marrow transplants for breast cancer were reimbursed at the time of ASCO, this rapidly ceased due to changes in payor unwillingness to pay for the procedure.
• Hospital payment increased when patients received drug-eluting stents, reimbursing for the increased cost of the new stent. Additionally, many device manufacturers promoted stents to cardiologists and patients as well.
• Economic factors did not influence the slow rate of adoption in statins.

2.5. Practice Guidelines
• Guidelines were likely a retarding influence on the uptake of statins.
• Unresolved questions about efficacy and who might benefit likely slowed statin adoption as first-line therapy in guidelines.
• Drug eluting stent benefits resulted in a major shift to this therapy in advance of changes in guidelines.
• The framework combines prior work on healthcare access and diffusion of innovation, building upon it by considering characteristics of the evidence, incorporation into guidelines and financial drivers.
• The case studies were selected as they represent different types of therapy (medication, surgery and devices) and a convenience sample to illustrate the usefulness of the framework.
• With a limited sample, number of publications, conference presentations and commentaries were not explored related to speed of adoption (except for the BMT case study).
• A focus on surrogate end points (e.g. cholesterol levels rather than PROs) and complexity of science may play an important role.

3. Pending Questions
• How can we apply theories presented to a broader and randomly selected set of cases?
• What role does interpersonal communication with peers and social networks play in persuading clinicians to change practice?
• How can Patient Reported outcomes be incorporated?

4. Tools being developed
TBD

5. Potential Initiatives/Tools to be Developed
Additional validation across initiatives needed.
1. Main Objectives

To determine gaps in assessing value of treatment options and create a patient perspective value framework.

2. Key Learnings

Growing concern about increased healthcare spending and clear need to assess value of treatment options based on criteria that is important to patients. Several organizations have developed/are developing frameworks to assess value of individual therapies/healthcare services.

<table>
<thead>
<tr>
<th>Table 1: Summary of Current Value Framework Approaches</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCO Value Framework</td>
</tr>
<tr>
<td><strong>Output</strong></td>
</tr>
<tr>
<td><strong>Inclusion of patient perspective</strong></td>
</tr>
</tbody>
</table>

Healthcare system needs new tools/frameworks to:

- Help providers & patients assess value of different therapy options based on perspectives/needs.
- Allow public/private purchasers to better guide patients to right health plans/services.
- Aid pharma/medical device companies to appropriately target and price therapies.
Workshop held at FasterCures “Partnering for Cures” identified challenges:

- Patient voice lacking from current value frameworks and patient perspective on value is critical.
- Value considerations need to be better assessed.
- All major stakeholders must be involved.

Four value frameworks have been assessed (Table 1)

2.1. American Society of Clinical Oncology (ASCO) Value Framework

ASCO’s framework was developed to support decision making regarding the comparative value of new cancer therapies to standard regimens within randomized controlled trials (RCTs). The value of a new therapy—or its “net health benefit score”—is analyzed based on three factors: its clinical benefit, toxicity and additional benefits such as improvements in the palliation of symptoms compared to a standard regimen.

- Net health benefit score is calculated based on:
  - Therapy’s clinical benefit score which can add up to 80 points and drawn from changes in overall survival, progression-free survival or response rate compared to standard regimen.
  - Therapy’s toxicity which can add/detract 20 points from net health benefit score when compared to toxicity/tolerability of standard regimen.
  - Therapy’s additional benefits, compared to standard regimen, where a therapy can gain 30 bonus points (e.g. improvements in palliation of symptoms and treatment-free intervals.
  - Framework is intended to provide oncologists with information to supplement shared decision-making (SDM) process but doesn’t have a patient-facing tool.
  - Unclear how well patient perspective was captured (patient advocate input was provided) in the creation of the framework.
  - Does not allow for comparison across/beyond individual RCTs.

2.2. Institute for Clinical & Economic Review (ICER) Value Assessment Framework

Framework created to assess value of medical services, including drugs, devices and procedures based on care value, potential budget impact, and provisional value to health system. ICER produces a value based price benchmark for each service.

- Care Value is determined based on:
  1. Comparative clinical effectiveness: reflects therapy’s comparative net health benefit and level of uncertainty in evidence.
  2. Incremental cost per outcomes achieved: reflects cost per quality-adjusted life year.
  3. Benefits/Advantages: not included in clinical effectiveness (e.g. whether method of administration encourages adherence).
  4. Contextual Considerations: includes ethical, legal issues, etc. that affect relative priority of illness and therapies, such as whether other acceptable treatments exist.
- Therapy’s potential budget impact is calculated based on estimated net change in total in healthcare costs over initial 5-year period.
- Intervention’s provisional health system value is assessed based on whether it can treat a population with reasonable long term value and short term costs that wouldn’t exceed growth in national economy.
- ICER convened a Value Assessment Development Group. Families USA= only consumer advocacy org in group of 16 stakeholders.
- ICER’s framework and data not intended for patient audience and does not include patient-facing tool.
2.3. Memorial Sloan Kettering (MSK) Cancer Center’s DrugAbacus

This tool provides cost benefit analysis for 54 cancer drugs approved by FDA between 2001-2015.

- Drug Abacus measures value according to:
  - **Value of life year** according to overall survival improvement.
  - **Toxicity** based on number and severity of side effects vs. side effects experiences if not on drug.
  - **Treatment novelty** based on whether treatment has a novel mechanism of action/delivery.
  - **R&D costs** according to number of subjects enrolled in approval trials.
  - **Rarity** of targeted cancer based on projected incidence.
  - **Population health burden** based on estimated years of life lost due to cancer in US.

- Tool suggests it was not intended for patient audience - created for healthcare providers (HCP). Patient (advocate involvement) in development unclear.

2.4. National Comprehensive Cancer Network’s (NCCN) Evidence Blocks

NCCN’s Evidence Blocks was created by panels of expert clinicians to assess the value of the regimens in its 66 cancer treatment guidelines according to **efficacy, safety, quality and quantity of evidence, consistency of evidence and affordability**. The Evidence Blocks measure:

- **Efficacy** according to prolonged life, lack of disease progression and reduced symptoms.
- **Safety** according to side effect likelihood.
- **Quantity/Quality of Evidence** related to an intervention based on the number of existing relevant trials.
- **Evidence consistency**: based on trial results.
- **Affordability** including drug cost, supportive care and hospital care.

2.5. Workshop Results

Focus on five key patient perspective value considerations:

- **Value of treatment to patient** - assessment of clinical, functional and quality of life (QOL) benefits/harm of treatment long term:
  - Value may vary depending on condition specific vs. general that cuts across conditions.
  - For chronic illness there is need to consider long-term effects and how it will fit into complex treatment regimen.
  - Current value framework landscape too focused on end of life and cancer care. Need for more disease agnostic framework.
  - Whole person value–how treatment fits into overall patient experience (e.g. symptoms alleviated, method/side of administration, support services).

- **Cost of Treatment** - including out of pocket spending and dependent on coverage/plan benefits:
  - Need to incorporate current prices of treatments into existing value frameworks.
  - Include additional costs such as imaging, rehab, and supportive care.
  - Consider potential opportunity costs-lost wages, transportation costs.
  - Need to explore how HCPs assess what is considered affordable to patient since time of year relative to out of pocket maximum, type of coverage and changing formulary inclusions/exclusions may change.

- **Evidence Strength**:
  - How can value frameworks better assess evidence for how treatment may affect individual vs. heterogeneity in patient population (different disease experience and variability in responses)?
  - Need to explore how same treatment affects different age groups or may be used differently in daily practice.
Can patients test different treatments and rely on relationship with HCP to parse out different responses?

**SDM & Information Usability**
- Future value frameworks need to ensure costs and quality info is accessible and usable to patients.
- Significant gap in market for patient facing tools and strategies that help inform patients on therapy value and those for HCPS to drive conversations with patients and aid in decision making.

### 2.6. Next Steps

- **One-year action plan to develop patient-perspective value framework:**
  - Two Multi-Stakeholder Workgroups
    - 8-10 organizations to engage in framework development, 15-20 orgs on steering committee (SC).
  - Input from Stakeholder Groups on Current State of Activities, patient value considerations, concerns, challenges, key framework features/considerations, use cases for piloting. Draft framework components to be created by workgroup and vetted through SC.
  - Drafting/Pressure Testing: Leveraging existing work and conducting background research to draft patient perspective value framework in public facing report. Draft framework to be refined by workgroup and pressure tested with SC.
  - Promotion & Outreach - to be presented at November 2016 Partnering for Cures meeting for feedback. Draft framework to be released for feedback. Strategy to be developed for piloting final framework.

### 3. Pending Questions

- Will generic tools suffice or will there be a need to test in disease populations?
- Is this US specific? All frameworks evaluated were US in scope.
- What type of patient input will be included in creation?

### 4. Tools being developed

### 5. Potential Initiatives/Tools to be Developed

- Patient-Perspective Value Framework
- Patient Facing tools to assess value
## Overview - Shared Conclusions

### 1. Overview and Timeline

Frameworks analysed:
1. CTTI
2. M-CERSI
3. National Health Council NHC
4. PCORI
5. Perfetto
6. FasterCures

**Timeline**

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
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<tbody>
<tr>
<td>Perfetto Framework</td>
<td>2013</td>
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<tr>
<td>M-CERSI Conference on PFDD</td>
<td>03/2015</td>
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<tr>
<td>PFMD Meeting</td>
<td>09/2015</td>
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<tr>
<td>PCORI Framework</td>
<td>10/2015</td>
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<tr>
<td>FasterCures Value Framework Published</td>
<td>03/2016</td>
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<tr>
<td>NHC / Genetic Alliance</td>
<td>06/2016</td>
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<tr>
<td>FasterCures Value Framework</td>
<td>11/2016</td>
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### Table of Pre-Discovery, Research Questions, Pre-clinical Development, Clinical Development, FDA Approval, Post Approval Surveillance, and Evidence Communication

<table>
<thead>
<tr>
<th>Framework</th>
<th>Pre-Discovery</th>
<th>Research Questions</th>
<th>Pre-clinical Development</th>
<th>Clinical Development</th>
<th>FDA Approval</th>
<th>Post Approval Surveillance</th>
<th>Evidence Communication</th>
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<tbody>
<tr>
<td>CTTI - Clinical Trials Transformation Initiative</td>
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<td>Dialogue/Advancing Meaningful Patient Engagement in R&amp;D and Review of Drugs, NHC &amp; Genetic Alliance</td>
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<tr>
<td>Patient Centered Outcomes Research Institute (PCORI) Engagement Rubric</td>
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<tr>
<td>Perfetto et al Framework</td>
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<td>FasterCures - Integrating the Patient Perspective into the Development of Value Frameworks</td>
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1.1. Objectives

| CTTI - Clinical Trials Transformation Initiative | With FDA's emphasis on patient focused drug development and patient engagement in translational research, CTTI has put forth a set of recommendations to improve Patient Group (PG) participation in the work of clinical trial sponsors (pharma and academia), which includes meaningful engagement of patients in the development of therapeutic products from study endpoint selection, recruitment and retention, and post-marketing safety. |
| M-CERSI Conference on PFDD | Provide a forum for patient groups, FDA, biopharmaceutical industry, payer and other organizations to voice views, challenges, activities and aspirations for patient focused drug development, as well as future direction and opportunity for collaboration. Through a day-long conference on March 9, 2015, the University Center of Excellence in Regulatory Science and Innovation (M-CERSI) held the “M-CERSI Conference on PFDD” and outputs included a suggested definition, rubric and framework for PFDD. |
| Dialogue/Advancing Meaningful Patient Engagement in R&D and Review of Drugs, NHC & Genetic Alliance | To build consensus around a vision and targeted set of actions for advancing patient engagement in drug research, development and approval. |
| Patient Centered Outcomes Research Institute (PCORI) Engagement Rubric | To illustrate and provide guidance around how input from patients and other stakeholders can be incorporated throughout the entire research process. |
| Perfetto et al Framework | To illustrate and provide guidance around how input from patients and other stakeholders can be incorporated throughout the entire research process. |
| FasterCures - Integrating the Patient Perspective into the Development of Value Frameworks | To determine gaps in assessing value of treatment options and create a patient perspective value framework. |

1.2. Gaps & Opportunities

| CTTI - Clinical Trials Transformation Initiative | PFMD has an opportunity to create standard engagement models that can be adopted as a standard across the industry. Standard best practices for engaging with patient groups.  
- Can we leverage what UCB & FDA have done and expand upon it?  
- Although standard metrics were suggested to evaluate PG collaboration on research sponsor side, is there an opportunity to measure collaboration effectiveness on both sides? PFMD can create key principles document regarding collaboration around research and development programs with Capacity Building for PGS around each of the areas.  
- Can PFMD now do a deeper dive to understand the HOW behind the WHAT defined in recommendations within each phase of the lifecycle based on specific experiences?  
- For example, how did PGs collect input on the research question from their patient community?  
- What was the process they used to determine unmet needs? |
| M-CERSI Conference on PFDD | Internet and social media information from patients can be captured and used to foster engagement. Regulatory guidance for bio-pharmaceutical industry to understand how and when they can engage patient community (FDA guidance status?). Tangible incentives (regulatory and market based) so that patients, payers and biopharmaceuticals benefit. |
| Dialogue/Advancing Meaningful Patient Engagement in R&D and Review of Drugs, NHC & Genetic Alliance | Feedback systems to measure impact of engagement—this is #1 opportunity for PFMD. Is there an opportunity for PFMD to develop consensus driven tools to help guide optimal selection and use of validated methods for collecting patient information? PFMD has opportunity to develop a measure around expectations vs. impact across sectors. PFMD also has an opportunity to develop, test and validate patient engagement measures. Can we do a retrospective assessment on a study that was completed? There is also an opportunity for us to create an ROI demonstration of patient engagement based on best practices collected to date and a deeper dive interview. Framework and engagement rubric for meaningful engagement. Need to get payors involved in conversation. |
PCORI has established an engagement framework to ensure patient partners are part of the early planning of studies.

- How can we learn from studies that have been supported by PCORI that have incorporated Engagement rubric?
- Has PCORI conducted research on best practices in applying engagement rubric?
- Can we interview PIs, patient partner authors? What type of assurance/validation is being provided to ensure that patients are truly embraced as partners and brought in early during study design?
- How are patients meaningfully interwoven throughout research study?
- How do we ensure patients are brought into all research meetings with information translated in a manner they can also understand?
- Is there an opportunity to connect patient partners with other patients who are also participating in studies to feel empowered?

**Perfetto et al Framework**

Suggest we incorporate elements into PFMD framework but also include Peer/Social network influence; Patient Reported Outcomes. It’s critical we examine how to influence adoption of therapy into clinical practice in a timelier manner.

**FasterCures - Integrating the Patient Perspective into the Development of Value Frameworks**

FasterCures is working on a patient perspective value framework to be presented at Nov 2016 meeting. All the value frameworks originally assessed were US specific.

- Will framework be US-focused and how can PFMD play a role in globalizing? Can elements be tested in our pilots?

### 1.3. Elements Applicable to PFMD Framework

<table>
<thead>
<tr>
<th><strong>CTTI - Clinical Trials Transformation Initiative</strong></th>
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<tbody>
<tr>
<td>Various elements are applicable to PFMD’s framework but this will require us to scratch beyond the surface and interview those who have attempted to implement.</td>
</tr>
<tr>
<td>• For instance, Parkinson’s model was used as a basis of CTTI’s framework. What best practices has Parkinson’s Foundation adopted to solicit input on research question?</td>
</tr>
<tr>
<td>• How are they compiling data on unmet need and therapeutic burden?</td>
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<tr>
<td>• Would any of these best practices be applicable to other disease states?</td>
</tr>
<tr>
<td>• Who else has implemented CTTI’s recommendations? What have main hurdles been?</td>
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<table>
<thead>
<tr>
<th><strong>M-CERSI Conference on PFDD</strong></th>
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<tbody>
<tr>
<td>FDA PRO Guidance &amp; Patient Focused Outcome Measurement in Clinical Trials. Rubric proposed as well as corresponding definitions are very much applicable to PFMD’s.</td>
</tr>
<tr>
<td>• Many action items listed in the report include PFMD’s remit (e.g. system for sharing best practices, establish public-private partnership to build capacity and infrastructure, train researchers on patient engagement). A good exercise before next PFMD meeting would be to go through action items with members to see what elements have been created to address points made in publication. Use 10 gaps identified as an opportunity for best practice.</td>
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<table>
<thead>
<tr>
<th><strong>Patient Centered Outcomes Research Institute (PCORI) Engagement Rubric</strong></th>
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<tbody>
<tr>
<td>PCORI Engagement Principles: Reciprocal Relationships, Co-Learning, Partnerships (value in time/contributions), Transparency/Trust.</td>
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<tr>
<td>• Definition of patient partner.</td>
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<table>
<thead>
<tr>
<th><strong>Perfetto et al Framework</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>The five factors of framework that are applicable to PFMD’s framework include: validity, reliability, maturity &amp; communication of science; applicability to apply evidence to clinical needs; economic drivers; rapid/slow integration.</td>
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<table>
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<tr>
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<tbody>
<tr>
<td>Value of treatment to patient would be good to further apply; however cost of treatment will be difficult to incorporate although this is a huge factor in US and heavily affects shared decision making which is another element that’s important. Information usability is another key element to be considered in framework.</td>
</tr>
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### 1.4. Additional Notes

| **CTTI - Clinical Trials Transformation Initiative** |  |
| **M-CERSI Conference on PFDD** |  |
| **Dialogue/Advancing Meaningful Patient Engagement in R&D and Review of Drugs, NHC & Genetic Alliance** | A set of actions were noted under Regulatory Guardrails and since then FDA has been working on Patient Engagement guidelines that have not yet been released thus there may be elements that have been addressed through this. There are a set of best practices around patient engagement that have been outlined here.  
  - What studies have applied these principles and what was return on value demonstrated from both researcher and patient perspective? Regulatory/Legal Uncertainty, Culture Shift and Communication were cited as biggest barriers.  
  - Can we obtain data from anyone who has addressed these hurdles in their studies to put a spotlight on applicability?  
  Open Communication and Culture Shift Across all phases. |
| **Patient Centered Outcomes Research Institute (PCORI) Engagement Rubric** | Planning, Dissemination & Communication of Study with Patients as Partners.  
  - *Not limited to product review/approval*  |
| **Perfetto et al Framework** | Understanding the factors that affect the pace of evidence adoption and application into routine clinical practice.  
  Requires additional validation. |
| **FasterCures - Integrating the Patient Perspective into the Development of Value Frameworks** | Value Framework to be released in November but primary focus=cost, evidence strength, usability of info & value of treatment to individual (e.g. QOL, LT, etc.) |
Bibliography

CTTI Clinical Trial Transformation Initiative
CTTI recommendations: effective engagement with patient groups around clinical trials, October 2015.

University of Maryland M-CERSI Framework
Accessible here: http://www.pharmacy.umaryland.edu/media/SOP/wwwpharmacyumaryland.edu/centers/cersievents/pfdd/mcersi-pfdd-framework-rubric.pdf

National Health Council (NHC) Framework

PCORI Patient Engagement Rubric
PCORI Funded Projects: Sample Engagement Plans From Methods Portfolio, August 6, 2014.

Perfetto et al. Framework

FasterCures Value Framework
Integrating the Patient Perspective into the Development of Value Frameworks, March 2016.
Accessible here: http://www.fastercures.org/reports/view/56