Original Research

Assessing Biopharmaceutical Company Experience with Patient-centric Initiatives

Debra L. Michaels, MS, RDN[1]; Mary Jo Lamberti, PhD[2]; Yaritza Peña, BS[2]; Barbara Lopez Kunz, MSc[1]; and Kenneth Getz, MBA[2]

[1]*Drug Information Association, Washington, DC, USA; and* [2]*Center for the Study of Drug Development, Tufts University, Boston, MA, USA*

ABSTRACT

Purpose: A growing number of biopharmaceutical companies have been implementing patient-centric initiatives (PCIs). The Drug Information Association (DIA) and the Tufts Center for the Study of Drug Development (CSDD) collaborated on a study to gather data on the usage and impact of these PCIs to characterize company experience and impact.

Methods: DIA and Tufts CSDD collaborated with 17 organizations to define PCIs used in clinical research and development and to quantify their use, and to define metrics in use to document impact and return on engagement (ROE) for these PCIs. The study used a mixed methods approach that consisted of an online survey, in-depth interviews, and literature review.

Findings: Twenty-two unique companies responded to an on-line survey on the use of 23 PCIs identified by the study working group. PCIs most frequently implemented included patient organization landscape analysis, support of patient advocacy groups, use of patient advisory boards, and use of home nursing networks. Seven additional PCIs were found through a literature search and included in the group of PCIs for which impact measures were assessed. A total of 121 cases of use of the 30 PCIs and associated impact measures and impact data were gathered through literature review, in-depth interviews with the study companies, and in-depth interviews with organizations identified in the literature as having experience with patient engagement in clinical research as well as with patients who had participated in clinical trials. Analysis of the 121 case studies resulted in a list of 666 measures of impact (metrics) in use for 13 of the PCIs. Assessment of overall ROE for these PCIs found that PCIs such as support of patient advocacy groups and use of patient advisory boards indicated the greatest ROE, whereas costlier, more complex PCIs such as digital medicine and gaming indicated relatively low ROE.

Implications: Activity around PCIs among the companies studied was widespread, with initiatives more frequently planned and piloted than implemented at the time of this study. Measures of impact have been identified and can be used to assess ROE, providing insights to facilitate the adoption of PCIs of highest impact for patients and biopharmaceutical research organizations. (*Clin Ther*. 2019;41:1427–1438) © 2019 Published by Elsevier Inc.

Key words: impact, patient-centric clinical trials, patient centricity, patient engagement.

PURPOSE

During the past 7 years, there has been a proliferation of patient-centric initiatives (PCIs) across many stakeholder groups in the drug development enterprise.[1] PCIs include a wide variety of activities that are conducted with the ultimate goal of establishing "engagement among patients and their healthcare support network and to engender in them a sense of connection and ownership in the success of efforts to develop new medical treatments."[2] This represents a major shift and a fundamental and profound change to a ≥50-year-old product-centric research and development (R&D) paradigm that is now plagued with delays, inefficiencies, and high failure rates.[3]

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According to Hoos et al,[4] involving patients in the R&D process can potentially make medicine development faster and more efficient. Improvements may result from better coordination of the process, reduced duplication of effort, and more efficient use of resources. With patient input informing R&D and regulatory decision-making processes, the end result can be better outcomes for patients and ultimately a more productive process. Hoos et al[4] go on to state that "Although only few studies have attempted to measure the impact of patient involvement, alongside anecdotal reports, there is evidence in the literature to support these claims."[4]

The shift toward research and development centered on patient needs and experience has been encouraged and amplified by a number of public, private, and academic initiatives. Although varied in focus and approach, these efforts are based on the common underlying principles of meaningful engagement of patients, that is, the direct and constructive interaction with patients in various roles at all appropriate points within the medical product life cycle to ensure the best possible alignment between patient needs and products and services that improve health outcomes for patients.[4,5] Such interaction enables practices and actions that are based on patient perspectives and have a higher likelihood of resulting in outcomes that meet patient and industry needs.[5] Frameworks, such as the Clinical Trials Transformation Initiative framework for patient engagement along the R&D continuum for pharmaceuticals, have helped to clearly define when the patient voice can have an impact on drug development outcomes.[6] The Patient-Centered Outcomes Research Institute has established a detailed rubric for meaningful patient engagement in health research and requires that all its funded investigators partner with patients from the beginning of the application process through completion of the study and dissemination of its results.[7] The Food and Drug Administration (FDA), through its Patient-Focused Drug Development Initiative and resulting "Voice of the Patient" reports, has signaled its aim to more systematically obtain the patient perspective on specific diseases and their treatments to help inform the agency's decisions and oversight during both drug development and the agency review of a marketing application.[8] The Medical Device Innovation Consortium, a public–private partnership between FDA's Center for Devices and Radiological Health and Medical Alley, Inc, a Minnesota-based trade association, has published a framework for incorporating patient input on benefit–risk preferences into the regulatory assessment of new technology, including a "Catalog of Methods for Assessing Patient Preferences for Benefits and Harms of Medical Technologies."[9]

Frameworks such as these help to establish a set of core principles around meaningful patient involvement, but they are conceptual and not well harmonized at this time. With the exception of the Medical Device Innovation Consortium catalog of methods, they stop short of providing practical details about how the frameworks can be applied to best facilitate patient involvement that has a positive impact on objectives for patients and other stakeholders.

Although numerous frameworks and guidelines are now available, and a study on the conceptual impact of PCIs on the expected net present value of a development program has been conducted,[10] data are limited that indicate the extent of adoption or the actual impact of PCIs.[2] Some PCIs may deliver sufficient and consistent impact to affirm their becoming standard practice in drug development, but others may prove costly with limited to no measurable benefit. Metrics, especially quantitative measures of the relative value of PCIs in specific applications, are needed to inform decision making around the PCIs that will have the most positive impact on outcomes for the patient and for the drug development process.

In response, the Drug Information Association (DIA), a nonprofit membership organization, and the Tufts Center for the Study of Drug Development (CSDD), an independent, academic group, conducted a study to address the limited data on the adoption and impact of patient engagement in drug development among biopharmaceutical companies. The study had the following 4 primary objectives: (1) to assess the current and planned adoption rate of PCIs implemented, piloted, or planned by biopharmaceutical companies; (2) to define, collect, and measure the impact of these PCIs on drug development and patients by biopharmaceutical case studies and real examples of PCI use; (3) to identify organizational structures and mechanisms for managing and continuously improving PCIs; and (4) to assess the availability of regulatory policy documents and guidelines for PCIs: what is available, what is coming, and what may be missing.

Results of our assessments for objectives 1, 2, and 4 have been published elsewhere. DIA and Tufts CSDD found that companies have a varied approach to the adoption and implementation of PCIs and that most companies are piloting initiatives.[11–13] As a result, adoption data are anecdotal and case study based. This article presents a synthesis of data and insights from objectives 1 and 2 of this largely qualitative study.

METHODS

This study used a mixed methods approach,[14] combining quantitative and qualitative methods to address the scope of the study objectives and to provide a broader perspective for contextualizing the data. This section describes the formation of a study working group, the methods used to assess adoption rates of PCIs (objective 1), and the methods used to define, collect, and measure the impact of these PCIs on drug development and on patients (objective 2).

Formation of a Study Working Group

In early 2015, a list of companies that had implemented at least 1 PCI was drawn to form a pool of candidates for study participation. The companies were identified through a comprehensive and systematic review of the literature, including published sources, conference proceedings, company case studies, and anecdotal reports. Additional candidates were identified by culling through extensive proprietary information available to DIA and Tufts CSDD, such as members of known working groups, functional area or practice communities, and clinical trial or patient engagement networks, survey respondents, conference presentations, articles, and press releases to form the list of 58 eligible biopharmaceutical companies and contract research organizations (CROs) that met the criterion. We invited them to participate in this retrospective study. A total of 17 sponsors, CROs, and other organizations agreed to participate in the study working group, including AstraZeneca, Bayer Pharmaceuticals, Biogen, Clinical Trials Transformation Initiative, EMD Serono, HealthiVibe LLC, Horizon Pharma, ICON plc, INC Research, Janssen Pharmaceuticals, Merck, MK&A, Novartis Pharmaceuticals, Pfizer, Purdue Pharma, Quintiles IMS (now IQVIA), and UCB.

The working group was organized into 4 subcommittees, each assigned task that related primarily to 1 objective of the study. For the PCI and impact measures objectives, the working group subcommittees were asked to (1) compile a complete list of PCIs that have been implemented, piloted, planned, or not considered at their organization; (2) co-create a survey to assess the importance of and ease of implementing the PCIs and collecting data (metrics) to measure their impact; (3) participate in the survey; and (4) provide case studies that indicate the impact of PCIs used in clinical development.

Assessing Adoption Rates of PCIs

With the use of the working definition of a PCI provided by Getz[2] and previously described in the Purpose section of this article, a subcommittee of the working group identified and defined PCIs that were in use or development in biopharmaceutical organizations. Detailed descriptions of the 23 PCIs identified through this process have been published.[11] The working group developed a web-based survey to gather metrics on the various stages of adoption of these PCIs (implementing, planning, piloting, or not considering). Built in Qualtrics, a survey software, included 26 questions and asked respondents to evaluate the status of the 23 PCIs within clinical research at their organizations as implemented, in the planning or piloting stages, or not being considered. The survey also examined respondent demographic characteristics (including job role and title, years in current role, company's R&D spending, therapeutic area focus), organizational structure and function established to support PCIs, specific management approaches adopted, and corporate drivers that support patient centricity. The survey included both forced-choice and free text items.

An e-mail invitation to complete the survey was sent to members of the study working group and to the nonparticipating companies on the original list of 58 study candidates. A single survey link was sent to each potential respondent, but access by multiple individuals within the same organization was permitted to facilitate the most complete responses possible.

Data collected from the survey were tabulated in Excel (Microsoft, Redman, Wash) to determine the frequency of implementation, piloting activities, planning, or no consideration among the survey respondents for each PCI.

The literature review that was conducted to address objective 2 of the study (define, collect, and measure

the impact of PCIs on drug development and patients) is described in the section Defining and Collecting Impact Measures and Measuring Impact of PCIs. Conducted simultaneously with the PCI on-line survey, the search also identified additional PCIs that may not have been in use at or were unknown to the study working group at the time of the survey development. These additionally discovered PCIs were not included in the on-line survey but were added to the group of PCIs for which impact measures were collected if the working group deemed them potentially valuable to drug development or to patients.

Similarly, data from the in-depth interviews that were conducted with the study companies and others, described in the section Defining and Collecting Impact Measures and Measuring Impact of PCIs, were used to augment the survey results with additional insights and a more granular level of detail about PCIs, in accordance with the mixed methods design of the study.

Defining and Collecting Impact Measures and Measuring Impact of PCIs

A schematic summary of the mixed methods used to define and collect PCI impact measures and to collect case studies that indicate impact is shown in Figure 1.

A subcommittee of the study working group collaborated to identify impact measures for the 23 PCIs identified by the PCI subcommittee. Under the initial study plan, all data on methods of measuring the impact of PCIs and quantitative impact results were to be gathered from the experience of the working group companies. Impact measures were defined as any type of measure, whether qualitative or quantitative, used for the purpose of evaluating the effect of an implemented PCI on process, quality, outcome, or return on resources invested for patients or for biopharmaceutical development. The subcommittee and the DIA–Tufts team co-created a survey that assessed the ease of implementing the identified PCIs and the importance and ease of collecting metrics to measure their impact. The study working group, as well as the nonworking group companies that had responded to the PCI survey, were asked to complete the survey.

The full study working group was also tasked with providing case studies from their organizations with data to indicate the impact of implemented PCIs. A case study was defined as a description of an implemented PCI and of one or more metric to measure the impact of the PCI, as well as data showing the results of the implemented PCI. Cases were collected by the DIA–Tufts CSDD team by in-depth interviews with the working group members; the interviews also probed for a more granular level of detail about the use of PCIs and impact measures at these organizations.

A preliminary review of both the impact measures (metrics) and the case data gathered indicated that the quantity of the data collected from the study companies was not sufficient to obtain meaningful

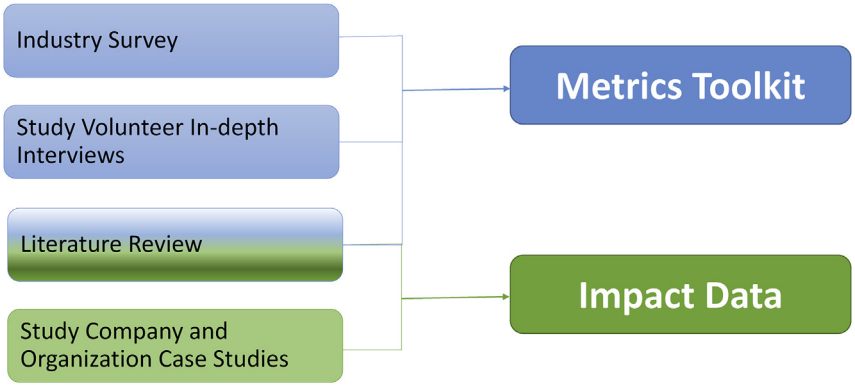


Figure 1. Mixed methods for defining and collecting impact measures and measuring impact of patient-centric initiatives (PCIs).

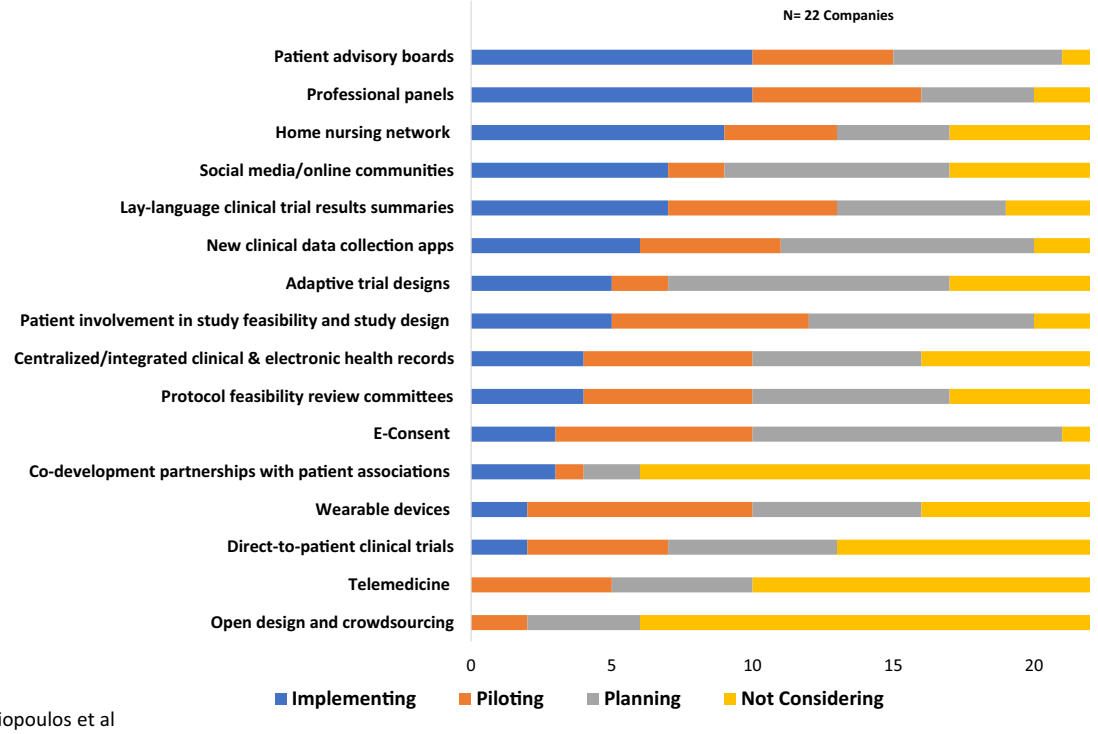
results. Literature review was added as a secondary research method to find additional PCIs, associated qualitative or quantitative impact measures, and impact data.

Organizations identified through the literature as having implemented PCIs and measured their impact were contacted with a request to participate in the same type of in-depth interview as the study companies. In addition, through a process approved by the Tufts University Institutional Review Board, the Tufts CSDD worked with the Center for the Information and Study on Clinical Research Participation to reach out to patients who had participated in clinical trials to get patient input and experience around PCIs and measures to evaluate their impact.

The qualitative and quantitative impact measures were assessed through the input and through the data on cases provided by the working group members, as well as through the literature review. The classification and organization of the impact measures into a metrics toolkit is described in Stergiopoulos et al.[13]

The case studies with impact data from the sources described (literature review, and in-depth interviews with study working group members, with patients, and with organizations identified through the literature search) were combined for the data analysis. Impact data associated with each metric were organized within the toolkit framework. All cases are cited in Stergiopoulos et al.[13]

The working group adopted a definition of return on investment specific to PCIs, labeled return on engagement (ROE).[15] ROE considers the impact of the PCI on the patient in addition to financial or operational impact on biopharmaceutical development. ROE for a specific PCI thus considered the impact on patient experience (or other desirable objective for the patient) and quality, speed, or other key performance indicator of the trial in the context of the cost and ease of conducting the PCI. The relative ROE of 13 PCIs for which metrics were



[13]PCIs defined in Stergiopoulos et al

Figure 2. Patient-centric initiatives adoption (N = 22 companies). Patient-centric initiatives are defined in Stergiopoulos et al[13].

reported was assessed within the framework of a qualitative rubric created by the study group. Metrics captured in PCI case studies differed across cases, so the data were summarized using the qualitative rubric to assess the PCIs relative to each other in terms of cost to conduct (from case data or the literature if not captured by the case), ease of conducting (from the working group co-created survey described above), and reported impact at time of study (from the case data). A simple 3-point scale was used for each assessment of cost, ease, and impact. The PCIs were then stratified into high, medium, and low impact PCIs and displayed with their relative cost and ease of conducting.

RESULTS

Assessing Adoption Rates of PCIs

A total of 22 unique companies participated in the online survey (Figure 2); 19 were pharmaceutical/biotechnology companies, and 3 were CROs. Eleven characterized themselves as large-sized companies (R&D budget >$1 billion), and 11 as mid-sized (R&D >$100 million but <$1 billion) or small companies (R&D ≤$100 million). The companies reported planned, piloted, or ongoing initiatives primarily in the United States (n = 16), United Kingdom/Northern Ireland (n = 9), Canada (n = 8), France (n = 7), and Germany (n = 7). Respondent roles varied, but most held director level or above positions and were senior-level managers within their organizations.

Activity around PCIs among the companies studied was widespread, with most companies implementing, piloting, and planning multiple initiatives at the time of the survey. Figure 1 shows the distribution of activity for specific types of PCIs, which are defined in previous publications from this study.[11,13] The most implemented initiatives (blue bars) were patient organization landscape analysis tools (10 of 22 companies), patient advisory boards (10 of 22), and professional panels (10 of 22). Use of home nursing networks (9 of 22), community conversations (7 of 22), innovative patient data collection/analytics (7 of 22), and lay summaries of clinical trial results (7 of 22) were also relatively widely used. The PCIs less frequently implemented included use of patient wearable devices (2 of 22), direct-to-patient clinical

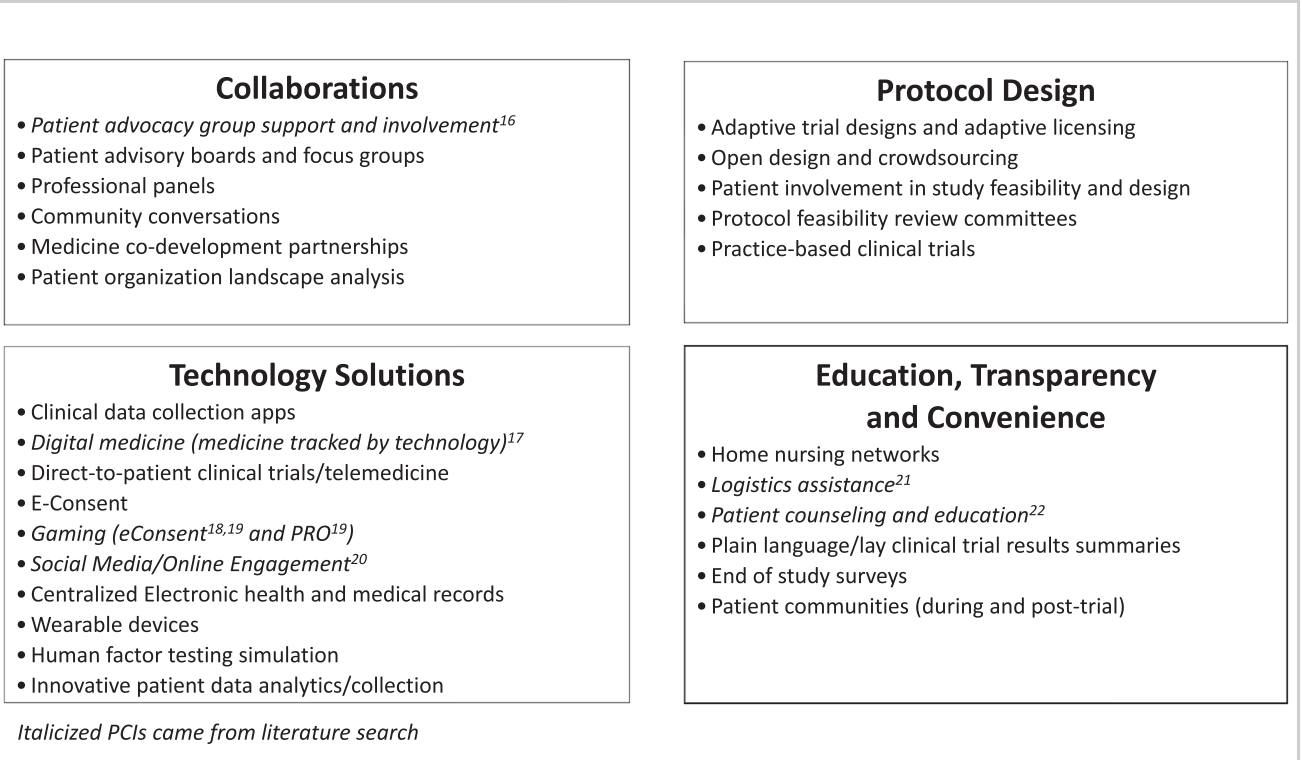


Figure 3. Patient-centric initiatives (PCIs) by category. Italicized PCIs came from literature search.

trials (2 of 22), medicine co-development partnerships (3 of 22), end of study surveys (3 of 22), and eConsent (3 of 22). No notable differences were found when size of company by patient-centric activity was examined.

Looking at the top piloted and planned initiatives, end of study surveys (9 of 22) and use of patient wearables (8 of 22) were the PCIs most often piloted, and e-consent (11 of 22) was among the top planned initiatives. Other top planned initiatives included adaptive trial designs and adaptive licensing (10 of 22) and establishing patient communities during and after clinical trials (10 of 22). Overall, there were more organizational patient-centric activities in the planning stages than those being implemented or piloted.

Among PCIs that companies were not considering adopting were medicine co-development partnerships with patient organizations (16 of 22) and use of open design and crowdsourcing for trials (16 of 22). More than half of the study companies (12 of 22) were not considering adoption of telemedicine at the time of the survey (Figure 3).

The research team determined that the PCIs from the primary survey fell into 4 categories based on the study domain influenced or affected by the PCI: collaborations; protocol design; technology solutions; and education, transparency, and convenience. Figure 2 shows the number of identified PCIs by category.

In addition to the 23 PCIs identified by the study working group and incorporated into the online survey, the literature search identified 7 PCIs that the working group saw as having potential value to biopharmaceutical companies and to patients. These were also grouped into the 4 study domain categories and are listed in Figure 2 in italics. Four of the 7 related to technology, including digitally tracked medicines,[17] social media and online engagement of patients,[20] and applications (apps) of gaming to eConsent[18,19] and patient-reported outcome data collection.[19]

Impact Measures Associated with PCIs

In all, 121 discrete cases of PCI use with associated impact measures were identified: 33 were gathered from the in-depth interviews with companies and with patients. The remaining 88 cases were from the literature and are described in detail in a previous publication.[13]

Figure 4 provides a breakdown of the number of cases found for specific PCIs within the 4 categories. Advocacy group support and involvement was found

	Total Cases Identified	Number of Quantitative Measures Gathered	Number of Qualitative Measures Gathered
Patient Advocacy Support	42	42	191
Direct to Patient Clinical Trials	21	55	70
Clinical Data Collection Solutions	16	50	65
Patient Advisory Panels	11	40	12
Social Media/Online Engagement	8	33	6
Patient Education	5	10	20
Crowdsourcing Design	3	11	12
Adaptive designs	7	9	6
Home Nursing Networks	2	6	8
E-Consent	1	2	0
Gaming PRO	1	1	0
Digital Medicine	1	1	0
"Patient Centricity" (General)	3	2	14

Figure 4. Metrics collected for case examples. PRO: Patient reported outcome.

in 42 cases, direct-to-patient clinical trials in 21, apps for clinical data collection in 16, patient advisory panels and focus groups in 11, social media/online engagement in 8, patient counseling and education in 5, open design and crowdsourcing in 3, adaptive trial designs in 7, home nursing networks and logistics in 2, E-Consent in 1, gaming in 1, digital medicine in 1, and general patient centricity in 3.

The case studies were also analyzed for the numbers and types of metrics used to measure the impact of each PCI[13] (Figure 4). Quantitative measures made up 39% of the metrics observed, whereas qualitative measures made up 61%. Qualitative measures can be broken down by those that measured benefits of the PCI (37%) and those that measured challenges associated with the PCI (24%). Among the 121 cases, 15 cases used cost metrics, 118 cases used return metrics (508 metrics total, both qualitative and quantitative), and 58 cases used metrics that measured challenges (158 total).

Collaborations (53 of 121 cases)

The most frequently reported category from the case studies, these PCIs include involving and supporting patient advocacy groups, as well using patient advisory boards and focus groups. Observed measures of the impact of innovative partnership initiatives include PCI cost (eg, total cost, cost per trial, percentage of overall trial cost, cost per evaluable patient, cost per submission program), overall development timelines (includes time to go/no-go decisions, comparisons to traditional trial timelines), and overall program success rate relative to portfolio benchmark.

Protocol Design (10 of 121 cases)

Adaptive trial design and licensing as well as open trial design, in which both patients and researchers are fully aware of treatment versus placebo, emerged as PCIs for which metrics have been used to measure impact. Crowdsourcing of trial data and protocol design feedback, still in early development, were identified as implemented PCIs with associated metrics, including cost of trial, outreach to both patient and investigator communities, number of changes to protocol design, and study conduct cycle time.

Technology Solutions (48 of 121 cases)

The second most frequently reported, this category included a rich source of potential metrics as technology advances are rapidly developing. PCIs included the use of apps to collect clinical data, patient-direct telemedicine and telemetry collection, the use of social media, and volunteer enrollment using e-consent. To determine their impact, measures such as study cost, study enrollment and retention rates, and patient feedback were observed. Some organizations measured efficiency between e-consent and traditional methods of study volunteer consent during enrollment.

Education, Transparency, and Convenience (7 of 121 cases)

In traditional trials, poor access to trial sites can lead to low enrollment and dropout. Techniques such as logistical support in getting patients to sites, collecting data by a clinician visit, or remote telemetry can positively influence trial success. However, only 7 of the 121 cases reported this type of PCI, including patient counseling and education initiatives and home nursing networks/logistical assistance. Examples of metrics for study volunteer education, transparency, and convenience PCIs included use of patient activation measure (PAM) scores,[23] patient enrollment and retention, number of investigative sites opened, and cost of the trial.

Classification of Impact Measures

Biopharmaceutical companies used a variety of metrics to measure usage and impact of PCIs, including measures of cost, speed, quality, and impact on the study volunteer. DIA and Tufts CSDD have compiled the identified metrics, both long-term and short-term in nature, into a toolkit (https://www.diaglobal.org/en/resources/areas-of-interest/patient-engagement)[24] organized within the framework described by Getz.[2]

ROE for PCIs

The results of assessing the relative ROE for 13 PCIs using the qualitative rubric are shown in Figure 5.[16,21,22]

Within each level of PCI impact, there was a range of associated cost and ease of conducting the PCI. Looking across the impact levels, the study team found that the cost or ease of implementing a PCI

PCI Case Studies	Relative Cost to Conduct	Relative Effort to Conduct	Relative Reported Impact
Advocacy Group Involvement	Low	Low	High
Patient Advisory Panels & Focus Groups	Low	Low	High
Social Media/Online Engagement	Low	Low	High
Plain language results summaries	Low	Low	High
Patient Counseling and Education	Low	Medium	High
Adaptive Trial Designs	Medium	High	High
Open Design and Crowdsourcing	Low	Medium	Medium
Direct-To-Patient Clinical Trials / Telemedicine	Medium	Low	Medium
Home Nursing Networks	Medium	Medium	Medium
Apps For Clinical Data Collection	High	High	Medium
E-Consent	Medium	Medium	Low
Digital Medicine	High	High	Low
Gaming	High	High	Low

N= 121 Case Examples

Figure 5. Case study-based return on engagement assessment (N = 121 case examples). PCI = patient-centric initiative.

did not necessarily correlate with its impact. In fact, primary and secondary research found that lower cost PCIs generally had higher impact. For example, the research found that advocacy group support/involvement and patient advisory panels and focus group PCIs indicated a relatively high level of reported impact at relatively low cost of time and effort.

The cost of working with patient advocacy groups/patient advisory boards was minimal: ≤$100 K in donations, approximately $100 to $250 per in-depth patient interview, and $1 K to $40 K for focus group sessions. Social media/online engagement PCIs lead to a relatively high median randomization rate (number of study volunteers randomized per number referred) of 20%, also at relatively low costs. Another finding was that study volunteers had significantly higher PAM scores in PCIs that include patient counseling and education. Adaptive trial design/adaptive licensing was the second highest PCI in terms of planned initiatives, reported in 10 of the 22 surveyed companies. Although these PCIs are expected to have a high impact for patient and trial benefits, they are complex to implement and higher in initial cost.

For PCIs that indicated relative medium impact, the research found that among companies using open or crowdsourcing designs, 67% of respondents reported lessening of numbers of protocol amendments, 53% reported reduction in site work burden, and 44% reported improvements in study conduct cycle time. Open and crowdsourcing designs have also been reported to strengthen reach to both patients and study sites. In this stratum, however, the costs of conducting the PCIs can be relatively high. For example, telemedicine apps can cost >$1000 per study volunteer. Development of apps for clinical data collection can be relatively expensive, with the cost varied by sophistication of the app and wearable device. A simple app can cost ~$30 K to develop, plus $100 to $250 per wearable device, and positive patient feedback varies with the type of wearable device. Cost and complexity of conduct can thus have a dampening effect on the ROE of the medium impact PCI.

Among PCIs with a lower relative impact, the research found that, at the time of the survey, digital medicine and gaming were viewed as costly with higher difficulty to conduct, resulting in a lower expected ROE and fewer companies considering adoption.

DISCUSSION

The study was undertaken to examine the types of PCIs being implemented by biopharmaceutical companies, the extent of PCI adoption, and metrics that measure the impact of current PCIs implemented. The PCIs evaluated were defined as such, either through direct experience or through literature search, by the study working group according to the working definition described. Although there is growing consensus around the principles of patient centricity in the drug development process, at this time there is no commonly accepted definition.[25] Perspectives on the degree of patient-centeredness of the specific PCIs chosen by the working group may differ even within a stakeholder group. This is indicative of the landscape at the time the study was conducted but is a limitation of the study. Numerous PCIs were found to have been implemented, planned, and piloted by the 22 companies completing the online survey. The possibility of selection bias exists and must be considered before generalizing the observed levels of PCI adoption to the wider industry; the companies invited to participate were known to have some interest in patient-centric drug development. They and companies that opted to participate in the study or one of its components were potentially farther along in their planning and execution of initiatives. Thus, the adoption rates observed in this group are possibly higher than among the industry as a whole. For PCIs, metrics, and ROE assessments identified through the literature, publication bias may have limited our access to negative results, again skewing the view of activity levels to the positive. A number of data sources were anecdotal or from non–peer-reviewed publications. Further, because some cases were real-world examples conducted in applied settings, there was no opportunity to review methods, assumptions, confounding factors, or to view verification of the results. The study was also a point in time, and we have no ability to predict future efforts from the data. Nonetheless, the level and scope of activity around PCI implementation are greater than levels observed $\geq$4 years ago.[26]

PCIs implemented by the 22 companies responding to the PCI adoption survey could be grouped into 4 categories based on the study domain affected: collaborations, protocol design, technology solutions, and education, transparency & convenience for the patient (study volunteer ease). Several PCIs were observed within each category, but the most widely implemented fell within the innovative partnerships and study volunteer ease categories. Although protocol design-related PCIs have the potential for highest impact on reducing trial length and cost, they were among the least reported. Within collaborations, 10 of the 22 companies implemented assessments of the patient organization landscape, signaling desire or intent to engage with appropriate patient groups. Involvement with patient advocacy groups (10 of 22 companies) and use of patient professional panels (10 of 22) rounded out the most frequently implemented PCIs. Within education, transparency, and convenience, use of home nursing networks (9 of 22) and lay-language clinical trial results summaries (7 of 22) were also among the top implemented PCIs. Frequently reported planning and piloting of PCIs within this category supports the expression of strong interest by the interviewed companies in promoting transparency and a positive patient experience: 10 of 22 companies were establishing patient communities (during and after clinical trials), and 9 of 22 were piloting end of trial surveys.

The study companies were found to be developing and gathering some metrics around the impact of implemented PCIs, but the quantity of data collected for these metrics was not sufficient to obtain meaningful results. Aggregated across the companies surveyed, the metrics were broad and not generalizable across PCIs.

Collection and analysis of case studies yielded additional data on measures of PCI impact. Because these metrics were not uniformly gathered by companies, even the expanded data were not sufficient to provide comparative analytic data to support specific methods of patient-centric practice. However, a few broad trends were observed, and some return assessments found long-term drug development portfolio improvement that allowed companies to save substantial costs with relatively

small investment of resources. Overall, PCIs showing the highest benefit tended to be the lowest in cost: when companies engaged patients, particularly patient advocacy groups, trial performance improved as evidenced by faster planning, institutional review board and FDA approval, and study enrollment, and by fewer protocol amendments. In addition, study volunteer feedback was more positive, and PAM scores,[23] which measure patient self-efficacy and activation in managing their own health and health care, were higher. Viewed as a tool to measure changes in patient ability to engage, some clinical researchers have reported using PAM scores to gauge the impact of PCIs, especially those involving education and counseling, on the patient.

PCIs involving technology found mixed ROE results, in part because of the range of costs associated with their implementation but also to a relative lack of metrics for some PCIs such as e-consent and use of social media. Internal and external reach improved, particularly with use of technology such as telemedicine, mHealth, and social media. High cost digital medicine and gaming indicated lower ROE, possibly because of high early adoption costs and implementation complexities. E-Consent was an interesting outlier. Qualitative research found that the reported impact was expected to be low, and the ease and cost to conduct were moderate, but that e-consent had the highest number of planned initiatives (11 of 22 study companies). Of the 22 surveyed companies, 18 were planning or piloting the use of e-consent, indicating considerable interest in this PCI. The development of impact measures looking across the drug development domains would be of value for these higher cost and more complex initiatives.

The impact of PCIs is influenced by many factors, including the variability of circumstances in which they may be implemented, the unique objectives of different stakeholders in the drug development process, and the quality of implementation. The use of standardized metrics for measuring the impact of PCIs would provide valuable data for continuous improvement of patient-centric practices and ultimately of patient outcomes. The results of this study provide a framework for assessing the impact of PCIs across several domains of the drug development process, and a preliminary set of metrics positioned within indicate how and when such measures may provide valuable information for planning and implementing particular PCIs.

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CONFLICTS OF INTEREST

The authors have indicated that they have no other conflicts of interest regarding the content of this article.

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Address correspondence to: Debra L. Michaels, MS, RDN, Drug Information Association, 21 Dupont Circle NW, Suite 300, Washington, DC 20036, USA. E-mail: debra.michaels@diaglobal.org