

Roundtable Discussion

The Ins and Outs of Incorporating Patient Centricity in Drug Development

The cost of drug R&D doubled between 2003 and 2016, according to *The Innovation Imperative: The Future of Drug Development*, a study from The Economist Intelligence Unit Committee (EIU), commissioned by Parexel (1). If the trajectory continues at the current rate, the cost of developing a drug will be \$20.5 billion by the year 2043.

To understand which new paradigms could make the drug development process more efficient, the EIU study looked at four different innovative trial types: adaptive, patient-centric, precision medicine and real-world data. Researchers covered four geographic areas—the US, the EU, China and Japan—and looked at enrollment time, likelihood of drug launch, market access, rates of adoption, barriers and enablers.

Overall, the EIU study found a dichotomy with respect to patient centricity in the drug development process. This relatively new concept is widely acknowledged as being beneficial for patients and developers alike, yet only 5.2% of the 40,000 trials examined in the study were considered to be patient-centric. Trials took place from 2012 to 2017.

Patient-centric trials are favored by payers, with the EIU study finding a 41% increase in drugs being added to the payer formulary if they have a patient-centric design. Perhaps most surprising, the drugs developed using a patient-centric approach were 90% more likely to be launched than those that were not. Across oncology, neurology and rare diseases segments, the report shows a massive increase in the likelihood of drug launch when patients were involved in the design process.

To start a discussion about these challenges and potential solutions regarding patient-centric drug development, *Pharmaceutical Executive* (in collaboration with Parexel) brought together senior leaders in the industry in a roundtable discussion about innovations in patient-centric trials that help shorten drug development timelines. Participants reflected upon the key findings of the EIU report and identified key barriers to generating more patient involvement, ways in which companies have been successful and ideas for moving forward in this area.

Important discussion points included that developers and clinical trial specialists need to innovate, invest in the workforce, collaborate and engage in multi-state formal initiatives earlier and more often.

Participants in the roundtable discussion included:

- Lisa Henderson (Moderator), Editorial Director, *Pharmaceutical Executive*
- Mathieu Boudes, PhD, European Patients' Forum, PARADIGM Coordinator
- Kristina Bowyer, Executive Director of Patient Advocacy, Ionis Pharmaceuticals
- Robyn T. Carson, MPH, Executive Director and Head, Patient-Centered Outcomes Research, Global Evidence & Value Development, Allergan
- Kenneth Getz, MBA, Director of Sponsored Research Programs and Associate Professor, Center for the Study of Drug Development, Tufts University School of Medicine
- Danya Kaye, Director of Business Development, R&D and Innovation, Inspire
- Michelle Marlborough, Chief Product Officer, AiCure
- Debra Michaels, Associate Director, Scientific Programs, DIA
- Bray Patrick-Lake, MFS, former Director of Stakeholder Engagement, Duke Clinical Research Institute
- Sy Pretorius, MD, Executive Vice President, Chief Medical & Scientific Officer, Parexel
- Steven L. Roberds, PhD, Chief Scientific Officer, Tuberous Sclerosis Alliance
- Rosamund Round, Director, Patient Innovation Center, Parexel

HOW SPONSORS ARE TAKING ON PATIENT CENTRICITY

LISA HENDERSON (*Pharmaceutical Executive*): What are the latest developments at your companies around patient-centric drug development?

ROBYN T. CARSON, MPH (*Allergan*): Two years ago, we established a cross-functional task force to evaluate current practices with respect to patient-centricity in R&D and develop a strategic plan to institutionalize patient-centricity at Allergan. As a result, we identified areas of the business that were more mature than others and created a strategic plan focused on three key areas for patient-centricity: 1) Increasing awareness and engagement; 2) Improving the patient experience; 3) Embracing new legislations.

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We identified and prioritized several patient-centric activities across these three key areas. For example, with respect to trials, we piloted protocol co-creation with patients and revamped a clinical trial website to be more patient friendly. To integrate the patient voice into our culture and keep it top of mind for employees, we have had several patients speak about their experience with their health condition and treatments at our town halls. This connection between patients and our team members is invaluable, particularly for those who do not normally have direct exposure to patients. We want to make the patient experience come alive for the entire company.



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KRISTINA BOWYER (Ionis Pharmaceuticals): We're a smaller biotech company, with just under 500 employees. We don't have a commercial component. We partner all our programs with external commercial expertise and we are a platform technology and therefore, very target-specific in our disease focus.

We are patient-focused at various levels of the company but even at a small company, groups can get siloed. Over the past few years, we have implemented a continuum approach with a focus on the patients for each target.

We hold R2D (research through development) meetings that include the entire team, from bench research scientist all the way through to the development team and include every department that will play a role in the development of that drug (e.g., regulatory, manufacturing, etc.). Projects are required to include advocacy and the patient focus on the disease; even research programs incorporate the patient perspective. We also create a pathway for all of the relevant patient related data that we capture to be published.

Our programs have a higher success rate because of the combination of our technology and these initiatives.

MATHIEU BOUDES, PhD (European Patients' Forum [EPF]): In the patient engagement community, there is a need for more data showing that the impact and the relevance—businesswise—of patient engagement in medicines R&D and access. No matter the current momentum around patient engagement, advocacy is still very much needed and therefore our evidence-based advocacy work will now take into account the results coming from the report. Up to now and until this report, few data were available to back the idea that patient engagement is a smart thing to do when developing medicines. Indeed, the only publication that supported the previous statement was about the expected net present

value associated with investment in patient engagement activities in clinical trials.

So, now there is a growing body of evidence showing that all stakeholders must be more prepared to meaningfully take on the challenging of systematically engaging patients in the processes of developing new treatments and to bring them to the market.

At EPF, by leading the PARADIGM consortium—composed of 34 partners including 18 pharmaceutical companies, four patient advocacy groups and academics—we are working to develop a monitoring and evaluation framework aiming to support the collection of data when engaging with patients to demonstrate the wide impact that those activities have. It will be ready by mid-2020. Also, to support the movement of patient engagement, we do believe in empowering the patient community through training and, since 2012, the program EUPATI (standing for European Patient Training Academy on Therapeutic Innovation) to trigger a major rethink in the way patients and the public understand the medicines development process and their own involvement therein. Armed with a deeper understanding, patient experts and advocates will be empowered to work effectively with the relevant authorities, healthcare professionals and industry to influence the medicines development process for the benefit of patients. This has not only been a tremendous success so far and a breakthrough for the patient community, but also—and more interestingly—far beyond. The current trend is also to train the professional on how to best engage with the patients in the context of medicines development.

PATIENTS AS KOLS

HENDERSON: Can we drill down a bit and talk about the patients themselves?

STEVEN ROBERDS, PhD (Tuberous Sclerosis Alliance): I led at least one project that was pre-IND. It was a common disorder: renal failure in chronic kidney disease. One key lesson for me, moving from outside pharma and into patient advocacy, was

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—Rosamund Round, Parexel

not to waste the opportunity to learn about what patients really need. The patients are a different kind of KOL. At the start of project, when you talk to scientific or medical KOLs, add the patient group or individual patients to get that conversation started early. Doing it in parallel saves time.

BOWYER: I agree. Sometimes, KOLs are looking at what they can treat, which may be something entirely different from what the patients want relief of. The disconnect is that researchers are focused on academic collaborations and KOL relationships, and even clinical development is very focused on KOLs.

Another issue is that cultural differences make patient centrality challenging in some areas of the world. For example, we have almost no experience in China.

SY PRETORIUS, MD (Parexel): We had a patient-centricity workshop in China with representatives from the regulator, general industry and academia for that reason. The key takeaway was they are very keen to use China as a “living laboratory” because there is limited patient information available about trials. An interesting idea that came out of that discussion was to leverage social media platforms like WeChat, which is popular in China, for patient engagement. How do we create the patient-advocacy infrastructure?

HENDERSON: That’s an interesting point. What role does budget play in developing patient-centric protocols?

DANYA KAYE (Inspire): Budget can be a big challenge, along with time. Many times, a sponsor organization says, “I don’t have the time to do research with patients,” even though Inspire can turn around a program in a week or two. They note that even if Inspire did do patient research, they wouldn’t have time to make any changes on the protocol design based on patient feedback. We had one situation where the sponsor was measuring the reduction of tremors as an endpoint, but through research, we uncovered that the outcome the patient really cared about was forgetfulness. So, their research was not focused on the endpoint that mattered most to patients.

Another challenge comes from the fact that patient engagement groups are usually not fully integrated within organizations and often don’t own any budget for these sorts of patient-centric activities. Often, the budget for these initiatives come from the study teams that perceive these efforts to be additional work, time and money. And sometimes, nobody knows who owns the budget for developing patient-centric protocols and patient centrality efforts in general. Although a handful of organizations are making real progress in developing patient-centric protocols, it’s also a lot of talk about this being very important, with not enough adoption and implementation because nobody’s accountable for making it happen.

ROSAMUND ROUND (Parexel): I also see that disparity among many of our pharma and sponsors that were saying yes, developing patient-centric protocols is really important at the senior level. On an individual, study-by-study basis, however, there may be no budget for such work. So, we actually started going to the executive steering committees with our sponsors saying, “Let’s have a core set of materials that will be patient-centric on every study, and this is just the way that we do business now.”

They know that every time they work with us, we’ll do a protocol review. We need to get that patient input as soon as possible and we have a quick and cost-effective process that we can use to accomplish that goal from the draft protocol synopsis to the protocol finalization.

BOWYER: I’ve been fighting for a budget under this department for eight years, and it has been a painful process because we don’t have the right metrics.

BRAY PATRICK-LAKE, MFS (Duke Clinical Research Institute): Patient-centric development is viewed as an add-on, or it gets pulled out as a per-head recruitment fee in some way that never works because the dollars don’t flow. It’s not an actual integrated part of most programs.

BOWYER: I have to do some creative maneuvering with budgets. But the recognition of the benefits of patient centrality is happening now, starting at the top with our CEO all the way down through the organization. It’s as though all of a sudden, the spotlight is on patient centrality. The budget process will always be painful, but I think the value is more tangible now and the metrics are a little bit more available to show management.

THE ROLE OF CROs IN PATIENT-CENTRIC TRIALS

HENDERSON: What is the role of the CRO?

BOWYER: We’re bombarded by CROs who say that they do patient-centric research, but that’s not their specialty. For example, a CRO may say they have a new capability for rare diseases, but they really have no experience in this area, they have no patient relationships and they have no knowledge of rare disease. It can be difficult to determine what’s a marketing gimmick and what’s the honest truth.

KENNETH GETZ, MBA, (Tufts University School of Medicine): I think rare disease is a unique environment. If you’re looking at traditional diseases, with large patient populations, we view the CROs as better positioned to support a truly integrated patient-centric or patient-engagement model. Some organizations have found ways of integrating the analytics. That’s been a big eye opener for us. They’re positioned to guide a lot of companies, integrating so many fragmented and siloed functions within their organizations. And, I think that collaboration is key between the sponsor and the CRO to make that happen.

A lot of what’s being done by major sponsors and smaller companies has been insular to some extent. It’s very pilot-oriented, but it rarely reaches a point where you’re truly able to collaborate with other parties that are supporting your research activity. I think that helps explain why so many CROs are also trying to innovate in this area. We’re all trying to do what we can within our organizations to change the

culture, but we're not interacting with other organizations to move in the same direction. That's been a real challenge for us and one reason why we're not seeing more adoption.

PATRICK-LAKE: We recently had one product where the sponsor was using a CRO. The process was not even close to the standard that we would say is legitimate engagement. We use bi-directional relationships, which means patients actually have some input, some influence, and they get something back. It's got to create some kind of value for the patient group that helps us co-design.

KAYE: I believe things are changing. The FDA has been helping encourage and advance the thinking around patient-focused drug development. Inspire has had ongoing contact with the FDA for the last two years to discuss patient-focused drug development and the patient voice, and understand what sort of research methodologies they're comfortable with, and applying these in our current work with them to incorporate patient and caregiver insights, such as by leveraging social media as a data source to better understand the patient experience. I think we've come a long way.

CHALLENGES AND OPPORTUNITIES

HENDERSON: What challenges do you face in becoming more patient-centric?

MICHELLE MARLBOROUGH (AiCure): At AiCure, our role, through our technology platform, is to establish the link between patients, disease and treatment. We do this by quite literally engaging patients through a smartphone application to confirm medication ingestion. The challenge is that access to patients through the sponsor or CRO (ahead of our deployment) can be extremely limited, as is the availability of any patient information. While we hope to achieve access to patient information in advance, we are, at a minimum, typically one step removed. At times, the sponsor or CRO will take technology to a patient board, but rarely we will be invited to engage with patients direct in the room to discuss about the technology.

PATRICK-LAKE: At Duke, we have a team working on the patient-centric model, including pricing models. We've had pushback from some sponsors that either don't want to pay for it or think we should just do it. They have the attitude that if this is so important, then Duke should just do it for free.

ROUND: We have been in discussions at various executive committee meetings, to talk about the value of patient centrality and the related budget. It's so important. We need agreement at the top level that this is how we do business together; this is how we work.

GETZ: Is the ultimate burden on pharma and biotech? We mostly talk about waiting for research sponsors to drive this process. Is that how patient-centric activity will ultimately be adopted?

BOWYER: I think so. For all the money that pharma spends on patient involvement, they really believe they have better ways to spend it. In the recent study we did on amyloidosis, we were able to work with the Amyloidosis Research Consortium and fund aspects of our patient centrality work.

What are patient-centric trials?

Patient centrality has no universal definition. For the purposes of this discussion, *patient-centric trials* are trials designed (or co-designed with patients) around patient needs and patient-relevant outcomes. The goal is to make it easier and more relevant for patients to be involved in trials. Patient-centric trials incorporate participants' needs, reviews and experiences into the trial design. On average, recruitment times can be reduced by half or more, and more participants are being recruited when the patient-centric approach is incorporated.

GETZ: With Duchene's, cystic fibrosis and Parkinson's disease, advocacy groups co-fund the development. Those are interesting models where I think the level of patient engagement is much higher than is typical.

BOWYER: What's missing is that industry doesn't understand the value of empowering the patient group. You have to empower patient advocacy groups so that they have the tools they need to support their patient community. And most of the funding we provide has been focused on empowering patient groups to conduct projects focused on the support that they need to develop their community so they can interact and support their community with industry. It's the beginning of a long transparent relationship.

CARSON: One of the challenges we face in industry is that we need to think about multiple stakeholders, and we're in an environment with constrained resources. I was really excited to hear that there are some established metrics now because when we are making decisions about allocating resources, we need to balance what is important to patients with the needs of other stakeholder groups. Another barrier for internal adoption is the need for pure education—not everyone understands patient centrality and how to implement this within R&D medical product development.

Also, you don't get meaningful engagement with patients if you haven't directly engaged with them. We've been doing a lot of exit interviews with patients, asking about their experience in the trial and their experience with a new, innovative technology platform. These insights inform future trials. The earlier you can do that work and engagement, whether it's Phase I or Phase II, the more chance you have to align solutions with those insights and meet requirements of the varied stakeholders.

GETZ: The challenge we've seen with pilots is they're never compared with a representative program that will convince the rest of the teams that it's worthwhile. The pilot becomes compartmentalized or siloed itself. That's a huge issue.

DEBRA MICHAELS (DIA): We've talked about surveying the internal landscape and understanding what is going on within the organization that might need improvement. Then, you have to make sure you've got your leadership—or a champion—behind you, because it really takes that support to integrate it into the wider organization. There are so many places where touch points with patients can be meaningful and make a difference.

MARLBOROUGH: We need to remember that clinical trial sites are mission critical to the advancement of a patient-centric model. Being that study sites are ground zero, how many of our colleagues in the industry have ever set foot in a site? How many have observed and engaged a patient being identified, screened, recruited, or participating in a trial? This experience should be a non-negotiable entry requirement for anyone to work in any position in our industry. It's one of the things I did early on in my career, and it was eye opening to share in a moment with these patients hoping to embark on the clinical trial process.

BOWYER: Working with operations can be challenging. They don't want to know the patient. They collect data, and they're not supposed to know the patient. That was the hardest group for me to embed myself in.

I form relationships with all the sites, study coordinators and physicians so that when there is an issue, the first point of contact when they need help is relationship based.

PATRICK-LAKE: I used to work as the director of stakeholder engagement for CTTI on the patient engagement work. It's clear to me now that we need more than one group to support multiple interests and resourcing models. We used to get DIA, PCORI, CTTI and TransCelerate together for regular meetings and exchange ideas on what's working and how we could share without duplicating.

BOUDES: At EPF, we are a co-founder of Patient-Focused Medicine Development (PFMD), that was established in October 2015 as an open, independent global coalition of health stakeholders. PFMD aims to transform the way in which we understand, engage, and partner with patients globally in the design and conducting of research and development of medicines by focusing on unmet patient needs. It brings together relevant experts and synergizing disparate but complementary efforts that integrate the voice of the *patient* across the lifecycle of medicine. PFMD is driving the culture change and co-producing tools needed to make systematic patient engagement happen.

We try hard to work together because we feel that that's been missing. As it is clear that the patient engagement is fragmented and there is a call from all stakeholders to reduce this fragmentation, the three initiatives PARADIGM that I mentioned earlier, PFMD and EUPATI will co-power in the coming months, an Patient Engagement Open Forum, a two-day event where we will explore patient engagement beyond aspirations and work in a multi-stakeholder context to make it happen. The Forum aims to provide a holistic perspective of patient engagement, the landscape and actors, and foster collaboration and co-creation while breaking down fragmentation and silos that are often present in-patient engagement work. The agenda offers a deep dive into some ongoing patient engagement work done by many collaborative initiatives. Topics range from tools and recommendations for effective patient engagement, methods for monitoring and evaluation of impact and outcomes in patient engagement activities, and fair market compensation for patient input to interactive sessions on assessing good practices in patient engagement and more.

PATRICK-LAKE (DIA): It would be powerful if the current leaders in this landscape could develop a standard for patient engagement. The industry, including the DIA, has initiatives in place to create such standards.

MICHAELS: Something useful that might come out of this is a validated evaluation instrument, which at the least could be used for self-assessment. This would seem very straightforward, but there are a lot of challenges even in just completing that assessment.

PATIENT INVOLVEMENT IN CLINICAL TRIALS: A CHANGING LANDSCAPE

HENDERSON: How has patient involvement changed?

KAYE: We did research across 10,000 of our members and found that patients will proactively bring a clinical trial option to their doctor more often than their doctor will bring it to the patient (21% of the time vs. 19%, respectively). Patients are becoming a lot more knowledgeable. I think patients are looking for clinical trial options.

GETZ: Many trials on rare diseases are being pushed out to physicians who have never conducted a clinical trial. They're so inexperienced, and the patient turnover rate is much higher with this community as well, so they never achieve a good level of experience.

MARLBOROUGH: What Robyn mentioned is very important. The only way this becomes the future of the industry is if it becomes normal practice. You can't achieve this as a standard by only having one individual in an organization and having that person address every inquiry. This needs to be deeply embedded into every part of an organization. To ensure that these techniques are consistently communicated and adopted as a core component, we need to establish a set of metrics or performance indicators to achieve efficiency, quality output, and uniformity of performance.

Developing informational snippets, addressing these teachable moments, or drafting basic talking points can be among the gold standard of things to think about. If your demographic looks like this, then you should consider what may be going on in their lives. We should agree to an acceptable set of standards and move to get these data and recommendations published—this could be a recipe for success in the making.

Henderson: What are you doing to support patients' involvement in clinical trials?

BOWYER: Virtual assessments are becoming more important, but I need a tool so that I'm not burdening the patient family with monthly visits to a web site, which may not be easy for them. Creating apps with clear, simple directions is important so patients can do a short assessment at home and capture it on video is one of the things that we're looking at.

KAYE: It's important to help patients feel connected during a study. When I was in a clinical trial, I asked my oncologist if I could talk to another patient that had gone through the trial or was going through the trial. I was unable to be connected to anyone. Patients want to connect with other patients, and the industry doesn't really facilitate that. There's a fear of legal ramifications. If the industry can do a better job of facilitating that need and really helping patients connect with each other during the clinical trial and afterwards, that would be doing a big service to improving the patient experience during and after a clinical trial.

PATRICK-LAKE: You can use technology to take data or you can use technology to create value and enhance that high-touch participant experience. We need to think about opportunities to give to patients, rather than just taking. Some will really enjoy the experience of high touch that technology can give them.

You also have to provide the social aspect. I would consider a monthly retention event, where people get together with the site PI or whoever. You can still do that intervention if it's cheaper. These are all value tradeoffs.

COLLABORATION AND THE PATHWAY FORWARD

HENDERSON: How have collaborations helped your organization achieve your goals?

CARSON: We have a great collaboration with a group called SonarMD, where we developed a patient engagement platform for irritable bowel syndrome with diarrhea (IBS-D). We leveraged patient-reported outcome measures and put it in the hands of the patients on any platform they wanted. They logged in once a day, provided answers to a set of questions, and were provided with a disease severity score that was immediately accessible to the patients as well as their clinician and nurse manager. It created a connectivity between patient and provider between office visits, whereby, the provider can monitor them in real time and intervene if necessary.

BOWYER: I think the continuous glucose monitor, Dexcom, is the perfect example of that. Your doctor sees the patient's readings firsthand.

HENDERSON: On the other hand, one problem with collaborations is when they're not formalized, monetary relationships. That's where they can break down.

Shall we recap some of the actionable steps that we've discussed here today?

CARSON: I think it's about continuing to educate internally about what truly must happen to do meaningful patient-centered work. New innovations and process always take time to diffuse through an organization, but the changes we are making are both exciting and important.

MICHAELS: It's just not easy. It's as much a management exercise as it is about the actual patient engagement and what we're doing.

CARSON: With respect to trial design, we need to put a step in the planning process where we review whether it's convenient for the patient to participate in our research studies. Can we leverage new technologies to take a customized approach to trial participation that meets participants' needs?

PATRICK-LAKE: Workforce development is an issue. We spend a lot of time all coming from different perspectives—patients, academics and sponsors. We all sat around the table and asked, "How do we work together?" We cut CROs out of that process because we were afraid they were going to commercialize themselves. Now, I think we should have kept them in the room because it's important for them to understand what we are doing and how we are doing it.

I also am seeing, in companies, situations where people are moved from one area to another but never actually see things through the patient lens. If you've come from regulatory or medical affairs, you're not thinking from the patient's viewpoint. I'm seeing that too often really.

BOWYER: You have to meet and know the patients to be driven.

PATRICK-LAKE: Yes, you need somebody who has a lens that puts that first. Some CROs do engagement really well, but I don't know that we've all been in the same room a lot, sharing that thinking as the field grows.

ROUND: Some sponsors are still early in their patient centrality journey. Together in this room, we are obviously all huge advocates for the approach, but ideas adoption in the industry is still not yet widespread.

SUMMARY

The importance of incorporating patient centrality into the drug development process is widely acknowledged, even though the concept is relatively new. The clear message that came out of this *Pharmaceutical Executive* roundtable is that making the drug development process more patient centric can pay dividends in many areas such as higher likelihood of FDA approval, much higher likelihood of product launch and more favorable decisions from payers. These benefits are particularly important in an era where the cost of drug development is skyrocketing, in the billions of dollars.

While building patient centrality into drug development and clinical trials is an industry-wide goal, it can be a challenge to infuse new ideas and practices into an old process. Such a shift will take time as industry determines how to best use patient-centric approaches and explores ways to make patient centrality a collaborative endeavor among CROs, sponsors, those that carry out clinical trials and other stakeholders.

Such a collaborative approach among parties might include:

1. Creating a standardized model for patient engagement and a plan for generating adoption for this model,
2. Continuing to develop metrics that demonstrate the very real advantages of patient centrality and
3. Sharing the metrics and the models with everyone involved in the drug development process, including top management and those who determine budgets.

Another critical component of this plan is ensuring that patients feel they are a part of the study design planning and follow-up. Engaging with patients early on in this process may even be a matter of forging partnerships with patient groups, many of which are very interested in being part of the drug development process. Hand-in-hand with these efforts is the need to develop new, convenient tools that support patient involvement, including novel ways for those in a trial to report their experience with a drug and, if needed, receive outreach from physicians.

When all groups in the drug development process embrace a patient-centric model and become stakeholders in it, industry can expect increased success in getting new drugs to market.

REFERENCES

1. *The Innovation Imperative* <https://druginnovation.eiu.com/>