Patient-centricity in the Biopharmaceutical Industry: Are We Nearly There Yet?

A collection of perspectives from researchers, approvers and patients

Collated and edited by Dr. Matthew Reaney

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Table of Contents

1 Patient-centricity in the biopharmaceutical industry: Are we nearly there yet? Why are you even asking this question? Page 6

Matt Reaney (IQVIA)

An introduction to this collection of perspectives on patient-centricity in the biopharmaceutical industry

2 Patient-centricity in drug development: Past milestones, present state and future opportunities from the regulatory professional's perspective Page 10

Nick Langevin, Stephanie Sommer (Boehringer Ingelheim)

A summary of patient-focused regulatory guidance and recommendations in the United States and Europe

3 The center of focus Page 24

Selena Daniels (U.S. Food and Drug Administration – FDA)

A poem from a regulator that captures the essence of patient-centricity in drug development

4 From participants to partners: Elevating the patient voice in modern drug development Page 27

Jai Patel, Sarb Shergill (Imbria Pharmaceuticals)

An industry perspective on the growing influence of patients in drug development: progress, challenges and opportunities for patient-centric innovation

5 Will we ever achieve sustainable adoption of patient engaged planning and execution? Page 32

Ken Getz (Tufts Center for the Study of Drug Development)

A frank acknowledgement of the challenges to embracing patient-centricity and suggestions for achieving broad long-term adoption

6 From minor to major impact, how patients are increasingly shaping the world of industry drug development Page 38

Daniel J. O'Connor (Association of the British Pharmaceutical Industry – ABPI)

An introduction to evolving approaches and frameworks to help biopharmaceutical companies increase their patient-centricity

7 Patient-centricity now: People, action and culture Page 42

Anthony J. Yanni (Astellas)

An impassioned plea from a patient-centricity professional to involve patients in intervention development and routine clinical care

8 Patient-centricity: When you are all-in-one Page 47

Zsuzsanna Devecseri (Novartis)

A fictional personal discussion between a potential patient, a caregiver, a doctor and a drug developer about patient-focused decision-making in oncology; and imagining a situation when they are all-in-one

9 The full-court press: Advancing patient experience data in oncology Page 54

Rohini Sen (Abbvie)

From sidelines to center court: Personal reflections on patient experience data (PED) in oncology intervention development

10 Patient-centric treatment tolerability: Past, present and future Page 62

John Devin Peipert, Melanie Calvert, Lee Aiyegbusi (University of Birmingham); Jessica Roydhouse (University of Tasmania)

A summary of the how patient-reported tolerability is emerging as an important outcome in patient-focused intervention development

11 A decade in: Reflections from the field Page 70

Chi Pakarinen (MediPaCe)

Observations and experiences of a patient experience data (PED) researcher working across the biopharmaceutical space

12 The state of patient-centricity in drug development is strong and getting stronger! But we all have work yet to do... Page 76

Ashley F. Slagle (Aspen Consulting)

Reflections on how the United States Food and Drug Administration (FDA) has shaped patient experience data (PED) research

13 Why patient-centricity is not fit for purpose: Mutual investment, the new people-centric model for research and advocacy Page 83

Amelia Hursey (Parkinson's Europe)

A suggested approach from a patient advocate for fully integrating patient insights throughout drug development

14 United in purpose and founded in trust: Transforming clinical research through grassroots initiatives Page 87

Sarah McKeown-Cannon, Angela Radcliffe (Heartbeat); Vicky DiBiaso (Sanofi)

The story behind the creation of Reflections and Heartbeat; initiatives hoping to reshape how clinical research engages communities

15 Voices of experience: Enhancing clinical trials through patient and site engagement Page 93

Deirdre BeVard (CSL)

Perspectives from a pharmaceutical executive and patient advocates who inspire her, on the importance of site and patient insights to improve clinical trials

16 The missing voice: Why patient perspectives must drive MS drug development Page 101

Sara Loud, Hollie Schmidt (Accelerated Cure Project)

Perspectives gained from the Accelerated Cure Project's support of people with multiple sclerosis in shaping biopharmaceutical research

17 The road to co-creation: Patients and pharma shaping the future of clinical research Page 106

Jayne Spink (Prostate Cancer Research – PCR)

A historical view of the role of medical charities and patient organizations in supporting drug development

18 Patient advocacy group and pharmaceutical industry collaboration to drive patient-centric practices and accelerate the development of new medicines Page 113

Patricia B. Davidson (Tufts Center for the Study of Drug Development; PALADIN)

Introducing the PALADIN Consortium to transform the collaboration between patient advocacy groups and biopharmaceutical companies

19 Cautious optimism: My experience in pushing the patient-first narrative throughout biopharma Page 120

Ingolf Griebsch (Ferring Pharmaceuticals)

A view of an outcomes researcher about how various patient-focused initiatives should be explored when developing novel oncology treatments

20 It's the economy, stupid: Drug developers will invest in patient-centricity when the R&D economics are clear Page 123

Paul SJ Miller (Miller Economics Ltd.)

The economist view on the cost-effectiveness of patient-centered drug development

21 Patient-centricity: Reflections from a former academic, consultant, regulator and now patient representative Page 131

Bellinda King-Kallimanis (LUNGevity Foundation)

A reflection on four careers in intervention development woven together by a laser focus on the patient and caregivers

22 Peering beyond the slogans and assumptions: Are companies sincere about the patient voice in drug development? Page 139

Mark Gibson (Gibson Research Consultancy)

A critical appraisal of biopharmaceutical tokenism in the field of "patient-centricity" in intervention development

23 Patient experience of what? Page 145

Jean Paty (IQVIA)

A reflection of four decades generating PED and an appreciation of the benefits of mixed-methods PED research

24 A reality check on patient-centricity: The good, the bad and the ugly Page 150

Alexandra Lauer (Boehringer Ingelheim)

A perspective on how a combination of robust qualitative and quantitative data is needed to understand patient experience in intervention development

25 The luminous science of us: Healing beyond the algorithm Page 156

Angela Radcliffe (Author and advocate)

A fictional dystopian story of how artificial intelligence (AI) can help, and hinder, patient-centric drug development

26 Editorial: Moving from “patient-centricity” to “patient partnerships” to serve intervention development Page 161

Matt Reaney (IQVIA)

A reflection on the contributions to this collection and a discussion on the six key themes from across the essays

CHAPTER 1

Patient-centricity in the biopharmaceutical industry: Are we nearly there yet?

Why are you even asking this question?

MATT REANEY

I have been working in and around the biopharmaceutical industry for more than 20 years. I was lucky enough to begin my career just as questions about "treatment satisfaction" and "quality of life" were starting to be routinely asked by executives who were making investment decisions. They wanted to understand whether new interventions were able both to increase life expectancy *and* maximize people's health and well-being. This may have been a response to a slurry of product launches which were scientifically groundbreaking, but which did not sell well. For example, an inhaled insulin — Exubera — should have been a blockbuster drug given its promise to eliminate subcutaneous insulin delivery among people with diabetes.[1] But uptake was poor,[2] and because Exubera "failed to gain the acceptance of patients and physicians,"[3] it was discontinued barely a year after launch. Whilst there may be many reasons for the failure of Exubera, the large device required for delivery was a real problem for patients who often state discretion as a priority in the management of their diabetes.[4,5] This is not an isolated example, but one I am familiar with due to my personal connection with diabetes.

Whatever the reason, as a scientific researcher and practitioner Health Psychologist, the shift in focus from biopharmaceutical executives was exciting — it promised a move from conducting research "on" or "about" patients, to conducting research "with" patients. I assumed that the industry would soon enough be investing *only* in developing interventions that were consistent with patients' priorities, needs and preferences; that these would be tested in trials awash with patient-reported outcome questionnaires to ascertain how patients feel and function while receiving interventions; and that shared-decision making focused on individual patients' goals would become a normal part of clinical practice. I hoped that all newly qualifying Health Psychologists like me would want to come and work in the biopharmaceutical industry, and that patients would be queuing up — either to enroll in research, or to express their gratitude for what the industry has done for them. It seems that I was too optimistic.

Although the industry has been using terms like "patient-centricity" and "patient focus" to guide its investment decisions since I joined it in the early 2000s, it fumbled around for many years on how to define and operationalize it. The first formal definition of patient-centricity in intervention development was not published until 2017,[6] and even then the disconnect between the idea of patient-centricity and associated actions within the industry was evident, with Yeoman and Silva remarking "in organizations of 50–100,000 people, one will struggle to find anyone tasked with understanding the needs of... the patient."[7] Other articles have equally questioned the patient-centric nature of the biopharmaceutical industry, suggesting that adherence and persistence problems with drugs are in part a function of poor product experience, which are in turn a function of the industry

discounting the patient perspective during intervention development.[8-10] In 2020, a survey of more than a thousand patients from the UK and Ireland showed that the biopharmaceutical industry is regarded as one of the least trusted industries.[11] One reason was because people didn't believe that patients were at the heart of what the pharmaceutical companies do, but rather that their approach and priorities were driven by profits.

A 2020 survey of more than a thousand patients from the UK and Ireland showed that the biopharmaceutical industry is regarded as one of the least trusted industries.

Yet most people I know in the biopharmaceutical industry are passionate about getting life-changing medicines to patients, and in recent years I have witnessed companies actually start walking the walk. Indeed I have seen (and been part of) various initiatives, consortia and collaborations which have shown an increasing focus in the biopharmaceutical industry on maximizing patients' health and well-being.[12] Some of these have been a direct consequence of increasingly active patient advocacy organizations as well as new demands from governments, insurers and healthcare systems to define value using patient-centric approaches. Company mission statements now include terms like "focusing on accelerating the delivery of life-changing medicines that create enduring value for patients and society" (AstraZeneca) and "chase[ing] the miracles of science to improve people's lives" (Sanofi),[13] and this isn't just rhetoric; the industry is making this a real focus. However, some critics of the biopharmaceutical industry think it is still smoke and mirrors — that profits will always come before patients — and that the industry is not truly embracing the principles of patient-centricity, but rather skirting around it by initiating some highly visible initiatives without weaving it into the fabric of the organization.

Further reflection and discussion is therefore needed.

I asked more than 30 people who work in and around the biopharmaceutical industry for their thoughts on patient-centric intervention development — where we are today, what improvements are still to be made, and whether patient-centricity offers a genuine shift for the future of healthcare. Specifically, I posed five questions (see Box 1) to various pharmaceutical company executives, small biotechnology manufacturers, patient representatives / patient advocacy organizations with lived experiences, patient experience data (PED) researchers, regulatory representatives and payer and health technology agency (HTA) advisors. I invited them to answer the questions in a way that made sense to them — through a personal narrative, a review of the research, a poem, or a series of drawings. Whatever they wanted. Each contribution is presented as a chapter in this collection. Only stylistic editing has been applied to their musings and the views presented are therefore somewhat unfiltered and honest, grounded in the authors' own experiences, knowledge of and/or participation in research, and hopes for the future. In collecting these perspectives, I have been able to take a broad snapshot of patient-centricity in the biopharmaceutical industry in 2025. I present this in an editorial in Chapter 26.

Using this collection I hope that we can re-ground ourselves as an industry and look to realize the future I envisaged when I started in this field more than 20 years ago.

Box 1: Questions asked to the authors of the commentaries in this book

1. How important do you believe the patient perspective is in pharmaceutical drug development and decision-making in 2024; and how has your perspective on this changed over time?
2. How has the pharmaceutical industry involved patients during drug development, how has this changed in your career, and how should it change in future drug development?
3. What opportunities have there been, and are there now, for patients to share their stories to inform pharmaceutical drug development and decision-making?
4. What have been, and are, the challenges to "patient-centricity" in the pharmaceutical drug development and decision-making around drug development?
5. What do you think should (or must) happen in the future to ensure that new drugs are developed in line with patient priorities, preferences and needs?

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CHAPTER 2

Patient-centricity in drug development: Past milestones, present state and future opportunities from the regulatory professional's perspective

NICK LANGEVIN, STEPHANIE SOMMER

Introduction

Coming up in the laboratory in the 1990s to early 2000s, far away from a direct interface with patients, it was easy to get lost in the science and remain distant from thinking about how the medical products we worked to develop could help change the lives of people waiting for new therapeutic options.

How bold, even pretentious, we were in thinking we could sit at our desks and develop a therapy that looks, feels and functions to the expectations of people with lived experience, while we were isolated from those with this experience who would use the medical product. Could we imagine that a company like Apple would market a new product or release a new software version without starting, iterating and ending with product usability and satisfaction surveys? Should medical product development be any different?

Today, a growing body of literature demonstrates that perspectives of people with lived experience differ from those of other stakeholders in the healthcare ecosystem,[1] including in the ratings of symptom severity and impact,[2] benefit/risk trade-offs and tolerances,[3] preferences for "sooner/smaller" vs. "larger/later" outcomes,[4] and choice between different interventions.[5] With this in mind, it is important that stakeholders involved in medical product development and regulatory and access decision-making have a patient-centric mindset and seek to include people with lived experience directly into these processes. We are not fooled, however, into thinking this is an easy task to accomplish — it is easier to say than to do.

In fact, the needs and requirements of people with lived experience, just as people in general, are diverse and may (need to) be addressed by more than one approach to treatment. For example, while there may be a preference for oral administration of a drug, alternative routes may be acceptable if the novel drug provides a sufficiently large improvement on impactful signs and symptoms of the medical condition. And while one particular symptom may be perceived as the most bothersome, it may not be enough to exclusively address that one particular symptom without a more holistic approach to improving people's lives.

Data show that involving patients early and often will speed enrollment in trials, increase retention, reduce amendments, and enable relatable patient-facing materials.[6-8]

History shows we have made progress in this regard, and at present we are in a better place than we were in decades past. We now move toward a bright future with growing consensus, discussions abuzz, and a growing realization that we can do even better to co-create therapeutic options to improve lives.

In this brief essay from our roles as regulatory professionals working in medical product development, we offer a rapid review of select *past* and *present* milestones in the rise of patient-centric medical product development, with a focus on the United States (U.S.) and Europe, and describe opportunities for continued progress in the *future*.

The past

United States

The Federal Food, Drug, and Cosmetics Act (FDCA) became law in the U.S. in 1938, requiring evidence of safety prior to approval and marketing of new drugs.[9] In 1962, the Kefauver-Harris amendment to the FDCA added a similar requirement for proving efficacy of new drugs.[10] Although these necessary and foundational laws set the U.S. as a global leader in high standards for new drug approval, they also resulted in a significant decline in the number of new drugs reaching the hands of prescribers and patients in the succeeding years.[11-12] The authors see the next 30 years, until 1992, as the beginning of an era of increased focus on and involvement by patients in medical product development and regulatory decision-making. We highlight two milestones in this period which were only possible after substantial activism on the part of patients: the Orphan Drug Act (ODA) and the Accelerated Approval regulations.

Orphan Drug Act (ODA) — In the late 1970s, calls from two constituents to members of the U.S. Congress served as a spark for legislative discussion around the dearth of available therapies for diseases with lower prevalence in the population.[13] In one case, a constituent was affected by Tourette syndrome for which an investigational therapy had proven effective, but was abandoned by a company because it did not prove successful in a more prevalent indication. The other of these constituents was a person living with Huntington's disease, a condition that affects fewer than five in 100,000 people.[14] The pursuant conversations led to the introduction of the ODA in 1981.[15-16] Public hearings in 1982 featured a strong voice from patient representatives and patient advocacy organizations which were beginning to establish themselves as key stakeholders in driving thought and policy change and which were crucial in seeing the ODA signed into law in 1983.[13,15,17] With clinical trial grants, tax credits and regulatory exclusivity provisions, the ODA has led by some estimates to a 10-fold increase in the number of drugs approved to treat rare conditions compared to pre-1983,[18] and orphan drug approvals have increased nearly 600% in the four decades since the ODA was enacted.[19]

Accelerated Approval — In the 1980s and 1990s, the HIV epidemic highlighted the fact that certain life-threatening conditions meant that patients were willing to take on greater risks and uncertainties for the possible benefits of extending life-expectancy and increasing quality of life. In 1992, following substantial activism on the part of patients, FDA instituted the Accelerated Approval regulations.[20] This allowed FDA to consider data from a surrogate endpoint, demonstrable on shorter timelines than previously accepted clinical outcome measures, as evidence in granting a special approval status to drugs intended to treat certain life-threatening conditions. The result was quicker delivery of medications into the therapeutic armamentarium while further confirmatory trials would be conducted to substantiate longer-term clinical benefit.[12,21] On average, confirmatory trials have resulted in approximately half of products with accelerated approval being converted to traditional approval with a median time to conversion of about three years.[22-23]

Europe

Driven by the thalidomide disaster of the late 1950s,[24-25] Council Directive 65/65 was adopted on January 26, 1965, as the first legislation on human medicines in Europe with a main focus on scientifically rigorous assessments of efficacy and safety of novel drugs before they may be put onto the market. At the time, this regulatory oversight resided exclusively with the

competent authorities of the individual European states. A decade later, Council Decision 75/320/EEC laid the foundation towards a joint European position on market authorizations through a multistate procedure and the setting up of the pharmaceutical committee. Harmonization was further enforced with Directive 87/22/EEC, which required national competent agencies to have an opinion from European level committees before authorizing innovative medicinal products. Five years later, in 1993, Council Regulation 2309/93/EEC formed the basis of the centralized procedure and the formation of the European Medicines Agency (EMA).

The mere fact that EMA was formed may already be considered a big stride towards patient-centricity, because within a year after starting its work in 1995, EMA involved people with lived experience.[26] While this involvement occurred as informal discussions initially, their contribution has become more formalized. In this section, we will look at the development in the EU until 2006 mirroring the two important pieces of legislation described in the section on the U.S.

The implementation of the ODA in the U.S. as well as legislation in Japan and Australia led to discussions in the EU to create similar legislation, and advocacy work conducted by European organizations of people with lived experience including pan-European ones, such as EURORDIS, led to the **EU Orphan Regulation (EC 141/2000)** in 2000.[27] With the implementation of the Orphan Regulation, the Committee for Orphan Medicinal Products (COMP) was formed, the first regulatory committee worldwide with representatives from people with lived experience.[28] With incentives for drug developers, such as fee reductions and 10 years of market exclusivity, the Orphan Drug Regulation also led to an increase in numbers of drugs approved for orphan indications in the EU (63 for 46 diseases in the first decade[29] and 192 in the time of 2010–2022[30]), albeit to a lesser extent compared to the U.S.[31]

The HIV epidemic and rising mortality due to cancer became areas of focus in the EU as well, leading to the 1994 Council Resolution 94/C 165/01 on the framework for community action in the field of public health with several priority areas, including cancer and HIV as well as other communicable diseases.[32] And in 1996, the Committee for Human Medicinal Products (CHMP) invited the European AIDS Treatment Group (EATG),[33] a patient-led non-governmental organization (NGO) founded in 1992, to share its views on the use of surrogate endpoints for future approvals of antiretrovirals. From then on, advocates for people with lived experience in HIV were invited regularly to ad hoc expert group meetings on antiretrovirals.[28] It was the shared view of people with lived experience that informed the creation of the **conditional marketing authorization** as laid out in Article 14a of Regulation (EC) No 726/2004. EMA may make use of this approach to grant marketing authorizations for drugs intended for seriously debilitating or life-threatening diseases, as well as in public health emergencies (such as the recent COVID-19 pandemic), based on data suggesting that the benefit of immediate availability of the medicine outweighs the risk inherent in the fact that additional data are still required.[34] As with accelerated approval in the U.S., conditional marketing authorization in the EU leads to faster approval of novel drugs when data from confirmatory trials are not available (yet). In the time of 2006–2022, a total of 80 conditional marketing authorizations were granted, of which 33 were converted into a standard marketing authorization (with one of them withdrawn after conversion) and three withdrawn, while 35 were still in conditional marketing authorization.[35]

The present

United States

The first two decades of the 2000s saw significant advancements in patient-centric medical product development in the U.S. Here we highlight three major

milestones: the issuance of FDA's patient-reported outcome (PRO) guidance, the institution of a benefit-risk framework for regulatory decision-making, and the rise of the patient focused drug development (PFDD) meeting.

FDA PRO Guidance — In 2006, the U.S. FDA published draft guidance on development and use of PRO instruments.[36-37] In preceding years, it was considered a success if a PRO instrument was included in a clinical trial, regardless of whether that outcome measure was actually sensitive and specific in the condition being studied. It was felt that in doing so we had satisfied the requirement to assess patient perspective, to hear the patient voice, to understand impact to activities of daily living and health-related quality of life — we had checked the box. But the PRO guidance, finalized in 2009,[38] led to an increase in the systematic development and use of PRO instruments. It highlighted the need to identify concepts of importance by directly engaging the patient community and put forward a basic set of parameters that would prove the instrument was reliable in the context for which it was to be used. While formally, this guidance has been superseded, we are including it in the "present" since current industry approaches for inclusion of the voice of people with lived experience are largely based on this guidance.

The enactment of the 21st Century Cures Act (CCA)[39] in 2016 expanded the best practices described in the 2009 PRO Guidance in two key regards. Firstly, it broadened the applicability of patient-centric processes for development, use and interpretation of outcome measures to also include other types of measures, such as clinician- and observer-reported as well as performance-based outcome measures. Secondly, the 21st CCA set the stage for more holistic, end-to-end inclusion of the patient perspective in medical product development and regulatory decision-making.[40] The development of a series of PFDD guidance documents aimed to satisfy the 21st CCA requirements and brought stakeholders from the pharmaceutical industry, patient advocates, regulators and academia together to discuss key considerations toward more systematic inclusion of the patient voice starting in early product development and extending to and through the regulatory approval process.[41]

Benefit-Risk Framework — During this same timeframe, the FDA began public conversation aimed at making the regulatory decision-making process more systematic and transparent. By 2013, as part of the fifth reauthorization of the Prescription Drug User Fee Act (PDUFA V), the FDA published a framework for benefit-risk (BR) assessment which would become fundamental to the medical product review and approval process.[42-43] This BR framework led regulators to consider both qualitative and quantitative evidence to determine the impact of the condition on patients, the current treatments available to patients, and to weigh the benefits and risks of an investigational product in arriving at a conclusion for regulatory action. Consideration of unmet need and seriousness of a condition had become a formalized consideration in the decision-making process. The 2023 FDA Guidance on BR assessment makes it clear that patient experience data is integral to the elements of the BR framework.[42]

Drugs are more likely to launch when trials are co-designed with patients.[44]

PFDD Meetings — In 2012, the U.S. FDA Prescription Drug User Fee Act was reauthorized for the fifth time (PDUFA V).[45] With it came a congressional mandate for more systematic gathering of patient perspectives to inform medical product development. As a result, the FDA set a performance goal of organizing disease-specific "patient-focused drug development" (PFDD) meetings where stakeholders could gather and hear directly from those with lived experience.

We thought this was a paradigm shift in itself: investment in organizing and hearing directly from patients in 20 diverse disease states with an audience of medical product developers, regulators and others gathered to hear firsthand what it is like to live with or

care for someone with various conditions. But in the next 12 years, expectations would be exceeded. There would be a mass endorsement and enthusiasm for these PFDD meetings. FDA organized at least 34 such PFDD meetings. In addition, patient advocacy groups began to organize PFDD meetings and in just over a decade would conduct more than 100 such "externally led PFDD meetings."[46]

Europe

The active participation of people with lived experience and their representatives in activities of the COMP (described above) as well as in protocol assistance procedures was soon recognized to be of high value to the EMA.[28,47] As a result, people with lived experience became more and more involved and are an integral part throughout the entire drug development process at EMA today.[44] In addition to their joining the COMP in 2000, the following milestones mark further increase of their involvement with EMA regulatory activities[48]:

- 2005: Framework of interaction with people with lived experience and their organizations
- 2006: Forming of the Patient and Consumer Working Party (PCWP)
- 2014: Creation of EMA's Public Engagement Department
- 2017: Public hearings involving young people
- 2020: Patient engagement in crisis management in the context of COVID-19

Collaboration with EMA throughout the drug development lifecycle — Today, people with lived experience participate in virtually all EMA activities[49]: pre-submission by providing input to designation and classification decisions, scientific advice procedures as well as agreements on Paediatric Investigational Plans; during the marketing authorization application (MAA) evaluation by providing input to COMP, CHMP, Committee for Advanced Therapies (CAT), Pharmacovigilance Risk Assessment Committee (PRAC) and Scientific Advice Group (SAG) discussions as well as review of information for public release (including summaries of opinion and product information); and post-approval in the pharmacovigilance space again as contributors to COMP, PRAC and SAGs and as reviewers of public information.

Contribution to scientific advice procedures — Involvement of people with lived experience in scientific advice procedures was initially limited to their participation in protocol assistance procedures for orphan drugs, which started in 2008. Following successful completion of the pilot for orphan drugs, starting from 2013 they were increasingly consulted in scientific advice procedures for non-orphan drugs as well as parallel EMA-Health Technology Assessment (HTA) scientific advice procedures.[47] To enable people with lived experience as participants in the regulatory assessments, EMA hosts trainings for those organizations and individuals who are interested in such participation.[50]

Contribution to marketing authorization application reviews — Similarly, consultation of patients during MAA review, the so-called CHMP early contact, started with a pilot in 2021–2022 for orphan drugs only. Due to the value perceived by rapporteurs, 2022, the pilot was extended to non-orphan indications.[51]

Guidelines — While EMA, in contrast to FDA, has not developed standalone guidelines on PFDD, it is actively building on public-private consortia aimed at a better bearing on appropriate methodology for the generation and use of data from people with lived experience, such as the PARADIGM Toolbox that enables structured, effective, meaningful, ethical, innovative and sustainable patient engagement[52] and SISAQOL-IMI (Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life Endpoints in Cancer Clinical Trials – IMI).[53] SISAQOL-IMI is an international multidisciplinary consortium to generate recommendations to standardize the use,

analysis and interpretation of patient-reported outcome (PRO) data in cancer clinical trials, which were released publicly in December 2024.[54] Of note is the Innovative Medicines Initiative – Patient Preferences in Benefit-Risk Assessments during the Drug Life Cycle (IMI-PREFER), which aimed to find out when and how patients' treatment preferences can be used in medical product development.[55] The 2022 IMI-PREFER recommendations have received a positive EMA qualification opinion.[56]

Future focus areas — While involvement of people with lived experience in scientific advice procedures as well as in topic- or disease-specific workshops on, e.g., policies or research projects (with an increase of three instances in 2009 to 125 in 2014), has been highlighted as particular success,[28,50] patient-centricity has been identified as a major focus area in the EMA Regulatory Science to 2025.[57]

A multistakeholder workshop convened by EMA on September 21, 2022, identified the following amongst the needs for the future: improved alignment amongst decision-makers (e.g., HTA bodies in the EU), further EMA guidance on an EU approach to generate patient experience data (PED; currently envisioned by EMA in form of a reflection paper), and transparency on how PED are being used by regulators, as well as the need for resources and technical expertise.[58-59]

The future

Now we switch our focus from a review of historical milestones to a set of recommendations for sustaining our industry's momentum in patient-focused drug development.

Avoid using patient engagement as a façade — The concept of exploiting patients' hope has been discussed by prior authors.[60] We run this risk as an industry if we do not engage those with lived experience early enough to take meaningful action on the insights we gather. For example, we must avoid engaging patients only at the end of product development as a confirmatory exercise or to find insights that fit our pre-conceived narrative. We should embark on clinical research only after a disease conceptual model is available, built upon insights directly from those with lived experience and from which we can identify concepts likely to be affected by the product under study. This disease conceptual model should also inform the target product profile — avoiding the chance that we consider *only* the needs of other stakeholders such as healthcare professionals, regulators and payers. We should seek input into protocol design from patients early enough to be able to meaningfully incorporate insights. Doing so can identify opportunities to reduce participant burden, avoid assessment fatigue, and ensure the selected measures of efficacy and safety yield results that are interpretable and meaningful to patients.

Select outcome measures co-created with those having lived experience — In conditions where treatment efficacy is best measured by *subjective* reporting, use assessment instruments co-created with patients. Ensure there is empirical evidence to support that the assessment instrument is founded in concepts that are relevant and encompassing of what matters to patients. In conditions where treatment is best measured by *objective* measures such as laboratory values or anatomical images, include fit-for-purpose PRO assessments to help contextualize the results. Doing so will highlight what impact on everyday life a patient may expect by choosing to use the medical product, a message that can be lost if we rely only on laboratory values to define treatment success. Development and communication of data obtained with fit-for-purpose instruments will only be possible if there is alignment on what is required to support their use. And while both FDA and EMA offer qualification procedures for novel methodologies,[61-62] there may be opportunities for increased collaboration of both agencies or consideration of "mutual recognition" of outcomes of qualification procedures to avoid duplication of efforts.

Take an evergreen approach to patient engagement — In therapeutic focus areas, maintain patient advisors and councils that can be routinely consulted to aid in product development, clinical design plans, and interpretation of results. This will help ensure ready access to advice from those with lived experience and enable reciprocal sharing of information between medical product developers and the patient community. When patients receive results and understand how their contribution to a program/trial made a difference, we will strengthen relationships.

Don't hold patient insights in isolation — Avoid assigning patient engagement to a single function within an organization. Rather, ensure there are patient engagement champions who can work with project teams to ensure awareness of available insights, design patient engagement activities to fill knowledge gaps across disciplines, and ensure project decisions are rooted in consideration of lived experience of the condition under study. Providing insight into the lived experience of the condition under study can be a powerful workplace motivator and help project teams to develop empathy. Where possible and appropriate, ensure pre-competitive sharing of patient insights. This will avoid redundant work by industry with the patient community and allow each interaction with the community to further the conversation and understanding of lived experience, rather than repeating established insights.

Work towards global approaches to generation and utility of data that matters to people with lived experience — While it is acknowledged that some degree of exchange on this important topic already occurs between regulatory agencies, such as FDA and EMA in form of the Patient Engagement Cluster established in 2016,[51] more is still left to be desired. In spite of this long-standing exchange, FDA and EMA have taken quite different approaches to patient-centricity, with FDA both hosting public meetings and issuing guidance to industry, whereas EMA is increasingly involving people with lived experience as advisors and discussants in their regulatory work and has deliberately chosen a case-to-case approach rather than issuing formal guidance to date.[58] Lack of EMA guidance was highlighted by industry at the 2022 EMA workshop on PED in EU medicines development and regulatory decision-making.[58] It would, for example, be helpful for drug developers to understand whether data generated in line with the U.S. PFDD guidances, e.g., for the development of a novel PRO for use as primary efficacy endpoint, were acceptable by EMA as well.

Financial models indicate significant time and cost savings from patient feedback.[63]

The 2021 International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) reflection paper on "Proposed ICH Guideline Work to Advance Patient Focused Drug Development"[64] as well as the book *Patient Involvement in the Development, Regulation and Safe Use of Medicines* published by the Council for International Organizations of Medical Sciences (CIOMS) Working Group IX in 2022[65] are steps in the right direction of global harmonization. And while this essay focuses on regulatory aspects of patient-centricity in medical product development, we would like to use the opportunity to highlight the need for further alignment of requirements in the context of PFDD not only amongst regulators, but also amongst those entities taking decisions on the reimbursement, and hence accessibility, of novel drugs that have received regulatory approval based on data obtained with measures that matter to people with lived experience.

Build patient insights into the benefit-risk framework and improve transparency on their use for regulatory decision-making — We raised the topic of the BR framework and the lack of transparent communication on how insights from people with lived experience contribute to it earlier and it is appropriate to close with it here. We

would be remiss if we failed to realize the obvious fact that those with lived experience should inform every decision factor in the BR framework and that their contribution should be clearly spelled out in regulatory documents, such as the FDA review documents and the European Public Assessment Report (EPAR):

- Analysis of condition: who better than people with lived experience to tell us what it is like to live with a condition and which outcomes are priority?
- Current treatment options: who better than people with lived experience to tell us what is good about an existing therapy; what can be improved; and in the absence of an available treatment, how one should look, feel and function?
- Benefit: who better than people with lived experience to help us understand the benefit of a treatment in terms of effect on daily life and function? Who better than people with lived experience to help us understand whether a treatment effect is actually meaningful?
- Risk: who better than people with lived experience to tell us whether they are willing to take on certain risks given the potential benefit they may gain?

FDA's Benefit-Risk Framework for New Drug Review[42,66]

DIMENSION	EVIDENCE AND UNCERTAINTIES	CONCLUSIONS AND REASONS
Analysis of Condition		
Current Treatment Options		
Benefit		
Risk and Risk Management		
Conclusions Regarding Benefit-Risk		

Concluding remarks

It is our hope that the milestone accomplishments we have described in the endeavor for patient-centricity in medical product development have provided encouragement that progress has been made. Regardless, the job of ensuring true patient-centricity is an ongoing and ever-improving effort. So likewise, we hope the recommendations for an even better future state sparked some enthusiasm and ideas for how we can instill a patient-focused culture within our organizations and project teams as well amongst all the external stakeholders around the globe who ensure novel treatments become available that truly address the needs of people with lived experience and make them drive regulatory decision-making.

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Nick Langevin is a regulatory affairs strategy leader with more than 25 years' experience in medical device and pharmaceutical product development. At Boehringer Ingelheim, Nick works with cross-functional teams to bring new therapeutic options to those living with ophthalmology and mental health conditions.

Nick's past roles include United States region regulatory lead and several positions within toxicology, project management, manufacturing and quality assurance. He holds a MS in Biology, is an alumnus of the University of California San Francisco Regulatory Sciences program, and is certified as a regulatory professional by the Regulatory Affairs Professional Society and as a project manager by the Project Management Institute.

In terms of patient-centric medical development, there have been many career-shaping influences for Nick. Starting in the 2010s, the rise of the PFDD meeting series from FDA and Advocacy Groups represented a true shift in thinking. Upon joining Boehringer Ingelheim in 2020, seeing patient focus segments at the beginning of project and departmental meetings provided motivation and purpose to his work. Attending a Patients as Partners meeting in 2022, hearing Jen Horenjeff speak about patient-centeredness with such energy and passion only fueled his fire more. Colleagues such as Keri Yale have had a significant impact on realizing how we (medical product developers) can truly think with the patient in mind throughout the product lifecycle, actively listening to them and actually incorporating what we hear into the project and the product.

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Dr. Stephanie Sommer is a regulatory affairs strategy leader with approximately 25 years' experience in pharmaceutical product development of both novel chemical and biological entities. At Boehringer Ingelheim, Stephanie works with cross-functional teams to bring new therapeutic options to those living with mental health conditions.

Stephanie's past roles include medical writing and global regulatory lead for various projects at pharmaceutical companies in Germany and Denmark. She holds a Ph.D. in Biology from Luebeck University and an M.Sc. in Drug Regulatory Affairs from Bonn University.

Stephanie's interest in patient-focused drug development has been kindled mainly by personal encounters of people with lived experience making it clear that each person's experience is unique. These diverse and unique experiences have made Stephanie realize how limited we are in capturing these with many clinical outcome assessment measures available to date. This has spurred her interest in exploring more how best to ensure drug developers understand better what matters most as early during drug development as possible.

Disclaimer: The views, opinions and statements made in this presentation are solely those of Nick Langevin and Stephanie Sommer and may not reflect the views of Boehringer Ingelheim Pharmaceuticals, Inc. or its affiliates.

CHAPTER 3

The center of focus

SELENA DANIELS

In drug development, the patients' journey should take center stage. Each patient's journey is unique and reflects their individual path of experience(s). Often times, the spotlight is not placed on their specific feelings, perceptions and needs along their journey. The intent behind patient-focused drug development (PFDD) is to capture the patient's voice and incorporate it into drug development and evaluation to better understand and enhance the patient experience, as well as improve patient outcomes (as prioritized by the patient voice). The underlying mechanism of PFDD is listening or tuning in to patients. We need to see their journey through their lens to align our strategies with patients' needs and expectations — refocus the spotlight to let patients shine.

Tune In

How can you know what one should consume?
Without hearing their truth
Without walking in their shoes

How can one make a choice?
Without contributing their voice
Without having a view to hoist

How can one partake?
Without having a stake
In a place where decisions are made

To be at the center
Patients have to be at the forefront
To understand their battlefront

Putting patients first
Becoming tuned in and versed
In all aspects of their cares

That's what it means
When it comes to patient-centricity
Listening to patients implicitly, explicitly

They are the star in the spotlight
Experts in their own right
The truth of the matter, it is their life

Little by little, more and more
Patient inclusion is being explored
Their voice emerging, no longer being spoken for

But this should be addressed
Without a request
A natural integration — seamless

Actions speak louder than words
It takes a village for the patients' voice to be heard
Patients, caregivers, sponsors, payers, and regulators

A true collaboration
The basis for foundation
While a challenge, it's the start to causation

Patients' stories shared without an agenda
An open extension and communication
Via meetings and listening sessions

An opportunity to be deeply invested in
Incorporating patient input into multiple elements
Throughout the life cycle of drug development

Maintaining patient-centricity
May not come easy
But it comes with great responsibility

Hearing from various patient populations
Not just one view, but a gradation
Representative of the affliction

Moving forward, to make more gains
We may have to switch lanes
To make a lasting change

A commitment
No halfway or in between
For the outcome we want manifested

To know what one should consume
Hear their truth
Walk in their shoes

For one to make a choice
Let them contribute their voice
Express a view to hoist

For one to partake
Let them have a stake
A place where decisions are made

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Dr. Selena Daniels serves as the Deputy Division Director in the Division of Clinical Outcome Assessment at the FDA. She provides direction, oversight and leadership to a team of expert analysts who provide consultation and advice on clinical outcome assessment (COA) endpoint development and validation, including considerations for clinical trial design, conduct, analysis, interpretation and reporting for regulatory determinations of medical product benefit.

Prior to joining the FDA in 2015, Selena worked in the Health Economic and Outcomes Research (HEOR) group at Allergan, Inc (now Abbvie), where she developed and executed HEOR strategies, as well as developed and implemented innovative COA strategies and endpoints for clinical trials. Selena received her Doctor of Philosophy degree in Education at Nova Southeastern University and Doctor of Pharmacy degree at Loma Linda University.

While she is a regulator and healthcare professional (pharmacist), Selena has been on the other side as a patient, as a caregiver and advocate for a parent with metastatic neuroendocrine cancer, and as a mother of a child who had to spend time in the neonatal intensive care unit. Having to wear all these different hats, she understands how important the patient voice is in drug development and how critical it is to amplify it so it can be heard to improve patient care and experience. This is why patient-focused drug development is her passion and why she will continue to promote it.

Disclaimer: The views, opinions and statements made in this presentation are solely those of Selena Daniels and may not reflect the views of the U.S. Food and Drug Administration (FDA) or its affiliates.

CHAPTER 4

From participants to partners: Elevating the patient voice in modern drug development

JAI PATEL, SARB SHERGILL

How important do you believe the patient perspective is in pharmaceutical drug development and decision-making in 2024; and how has your perspective on this changed over time?

The patient perspective is increasingly important and is no longer a "nice to have" but an important and critical part of current drug development. Patients are increasingly involved in their own care decisions. By understanding what matters to them — be it symptom relief, fewer side effects, or ease of use — pharmaceutical companies can design drugs that fit into shared decision-making models.

Patients can provide perspectives on unmet medical needs in different disease areas to help drive investment in drug development. For example, in the 1980s HIV patients helped to increase investment in HIV research. Similarly, patients have driven significant interest and early research in Parkinson's disease and other central nervous system (CNS) disorders.

Patients are often hesitant to participate in clinical trials due to concerns about time commitments, discomfort, or disruptions to their daily lives. Proactively addressing these challenges through trial design can help make trials more accessible and attractive to potential participants.

During the COVID-19 pandemic, the public gained unprecedented insight into the drug development process and its critical role in safeguarding public health. This heightened awareness has empowered patients to advocate for a more active role in the design of clinical studies. Patients are increasingly demanding a "seat at the table," urging sponsors to incorporate their perspectives to ensure that studies align with their needs. This includes ensuring an acceptable risk/benefit profile, manageable adverse events, user-friendly dose formulations and administration methods, and clinical endpoints that address the aspects of their condition most important to them. This shift underscores the growing recognition of patients as essential stakeholders in drug development.

When studies focus on outcomes that matter most to patients, such as symptom improvement or quality of life, participants are more likely to feel their involvement is valued and meaningful. This alignment with patient priorities fosters a sense of relevance and can significantly enhance compliance and engagement throughout the study.

We are also seeing an important role that patient advocacy groups are playing in advocating for more research in their disease and/or lobbying regulators to approve drugs. The approval of Exondys 51 (eteplirsen) for Duchenne muscular dystrophy by the FDA was heavily influenced by input from patient advocacy groups and families.

Regulatory agencies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have increasingly prioritized the integration of patient perspectives into drug development and approval processes. This emphasis

extends to incorporating patient-reported outcomes, preferences and experiences in clinical trial designs, regulatory submissions and labeling claims.

How has the pharmaceutical industry involved patients during drug development, how has this changed in your career, and how should it change in future drug development?

Over the past decade, the pharmaceutical industry has made remarkable progress in integrating patient perspectives, shifting from passive observation to active collaboration.

Earlier drug development efforts historically included little or no patient voice in either study design or execution. Pharmaceutical companies and researchers primarily focused on scientific and clinical endpoints they deemed critical, often without consulting patients about what mattered most to them. Study protocols were typically designed around convenience for researchers rather than participants, leading to trials that were sometimes misaligned with patients' real-world experiences, preferences and needs.

Over the past decade, however, there has been a growing recognition of the vital role that patient perspectives play in the successful development of new therapies, especially in the rare disease and oncology areas. Regulatory agencies, advocacy groups and industry leaders have increasingly acknowledged that engaging patients early and throughout the drug development lifecycle can result in treatments that better address patients' priorities, improve adherence, and ultimately achieve better health outcomes.

By embedding the patient perspective throughout the drug development lifecycle, the industry is moving closer to its ultimate goal: delivering treatments that are not only effective but also meaningful and accessible to the patients they aim to serve.

Advocacy groups representing patients with specific conditions have played a critical role in pushing for their voices to be heard. These organizations have educated stakeholders about the challenges and unmet needs faced by patients, leading to greater involvement in trial planning.

Over time, the pharmaceutical industry has increasingly integrated patient insights into many stages of solution development. These insights inform the creation of meaningful clinical endpoints, guide CMC development (chemistry, manufacturing and controls) to optimize features such as injection device usability (including human factor usability testing), and address sustainability considerations for medical devices. Additionally, patient input has driven the adoption of innovative digital tools, such as continuous glucose monitors (CGMs), to enhance drug monitoring and improve the overall patient experience. This patient-centered approach ensures that solutions are both effective and aligned with real-world needs.

Looking ahead, digital health technologies (DHTs), including wearable devices and mobile apps, are poised to play a crucial role in drug development. These technologies enable the collection and sharing of real-time data, such as vital signs, physical activity and behavioral patterns, providing researchers with a wealth of information that extends beyond traditional clinic visits during a clinical trial. Additionally, real-time data availability allows clinicians and researchers to remotely monitor patients, improve adherence to trial protocols, and identify individuals who may benefit from participation in a new clinical trial. Platforms like Medable further enhance this approach by utilizing digital tools to support decentralized trials, allowing participants to contribute data remotely and seamlessly.

What opportunities have there been, and are there now, for patients to share their stories to inform pharmaceutical drug development and decision-making?

Opportunities for patients to share their experiences and influence pharmaceutical drug development and decision-making have grown significantly in recent years. These avenues enable patients to contribute valuable insights into their needs, priorities and challenges, helping to shape therapies that are more closely aligned with real-world conditions and expectations. Examples include:

- **Patient advocacy organizations** act as a bridge between patients and pharmaceutical companies, organizing forums, focus groups and surveys to gather patient input.
- **FDA's Patient-Focused Drug Development (PFDD) initiative** organizes public meetings on specific diseases, where patients and caregivers share their experiences and priorities, generating reports and guidance that shape trial design and regulatory reviews.
- Many pharmaceutical companies now form **patient advisory boards,** enabling patients and caregivers to offer continuous input at every stage of the drug development process.
- Online platforms such as **PatientsLikeMe** and social media groups provide patients with avenues to share their experiences and data directly with researchers.
- Patients contribute to **real world evidence** studies by sharing data through registries, mobile apps, or wearable devices.
- **Patients testify before regulatory bodies, legislatures and health organizations**, influencing drug approval processes and access decisions.
- Companies increasingly use **patient narratives in marketing, education and training materials** to create messaging that reflects real-world experiences.

Patients can share valuable information in various ways, such as recounting how the disease impacts their daily lives. For example, they may highlight the most limiting symptoms and how these affect their quality of life. These real-life anecdotes put a "human face" on the disease, making it more relatable to researchers. They also serve to inspire and reinforce the purpose behind the researchers' efforts to develop new treatments. In other instances, when patients share their data, it helps researchers better understand the disease's progression and identify the most appropriate endpoints for clinical trials, ultimately aiming to improve patient outcomes. Both personal stories and shared data play critical roles in shaping how patients' perspectives can influence and drive drug development.

What have been, and are, the challenges to "patient-centricity" in the pharmaceutical drug development and decision-making around drug development?

While significant progress has been made in incorporating the patient voice into pharmaceutical drug development, achieving true "patient-centricity" remains challenging. Some of the major factors include:

- **Lack of standardized processes:** Many organizations lack standardized frameworks for integrating patient input consistently across all stages of drug development.

- **Resource limitations:** Engaging patients effectively requires significant resources, including time, funding and trained personnel. Smaller companies, in particular, may struggle to allocate sufficient resources to patient engagement initiatives.
- **Regulatory constraints:** While regulatory agencies support patient-centric approaches, their guidance is often broad and leaves room for interpretation.
- **Traditional industry mindset:** Shifting this mindset to prioritize patient input as equally important can be slow and requires cultural change within organizations.
- **Patient diversity:** Patients have diverse experiences, needs and preferences influenced by factors such as demographics, disease severity and cultural backgrounds. Ensuring equitable representation and capturing this diversity remains a significant challenge in drug development.
- **Methodological challenges:** Balancing patient-centric endpoints, such as quality of life, with traditional clinical endpoints, like biomarkers, often creates challenges in trial design. Reconciling these priorities demands innovative methodologies, which can be complex and difficult to implement effectively.

What do you think should (or must) happen in the future to ensure that new drugs are developed in line with patient priorities, preferences and needs?

To align new drug development with patient priorities, preferences and needs, the pharmaceutical industry, regulators and other stakeholders must adopt systemic and cultural changes throughout the drug development ecosystem. Key steps include the following:

- **Embed patient-centricity as a core value:** Pharmaceutical companies must embed patient-centricity as a core value, driven by leadership commitment and a patient-first mindset across all phases of drug development.
- **Standardize patient involvement across all stages of development:** By standardizing patient involvement at every stage, stakeholders can create a more inclusive, effective and patient-focused drug development process.
- **Patient diversity:** Develop strategies to engage underrepresented populations, ensuring diversity in patient input and clinical trial participation.
- **Prioritize meaningful patient outcomes:** Shift the focus from traditional clinical endpoints to outcomes that matter most to patients, such as quality of life, functional status and symptom relief.
- **Stronger regulatory frameworks:** Regulatory agencies must provide detailed, *actionable* guidelines for incorporating patient input throughout the drug development lifecycle.
- **Global regulatory harmonization:** Align patient engagement standards across regulatory bodies, such as the FDA, EMA and other global agencies, to create a consistent framework.

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Dr. Jai Patel has been in the pharmaceutical industry for over 30 years and is currently the Chief Medical Officer at Imbria Pharmaceuticals, whose mission is to develop innovative medicines for the treatment of heart diseases, including heart failure and hypertrophic cardiomyopathy, conditions that are closely linked to impaired cardiac energy generation. His role is centered on advancing therapies that address the underlying pathophysiology of these diseases to improve patient outcomes and quality of life.

Jai is a passionate about patient-focused medicines development because it places the needs and experiences of patients at the heart of the innovation process. Understanding how diseases impact patients' daily lives and incorporating their perspectives into drug development not only humanizes the process but also ensures that the treatments developed address the outcomes that matter most to patients. Jai believes that by actively involving patients, the pharmaceutical industry can create therapies that improve not just clinical metrics but also quality of life, fostering a stronger connection between science and the people it serves.

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Dr. Sarb Shergill is an accomplished and strategic biopharmaceutical executive with over 30 years of experience in global clinical development operations in biotech and pharmaceutical companies. Renowned for a patient-centric approach and ensuring the patient perspective is included in all phases of drug development, she has successfully led integrated drug development initiatives through regulatory approval and commercialization from early clinical phases. Sarb's expertise spans a diverse range of modalities, including siRNA, gene therapy and biologics, across multiple therapeutic areas. She is dedicated to driving innovation in clinical research.

Sarb is passionate about including the patient's voice and perspective in all phases of drug development. Working with several patient organizations and advocacy groups over her career, she has had the privilege of learning from patients how their diseases impact them. She has also seen how much difference, when new therapies are approved, they can make to patients in terms of managing their disease. This is especially true in diseases where there are no current treatments.

As a patient herself and someone who works in the pharmaceutical industry, Sarb knows first-hand that when patients are equal partners in the drug development process, the pharmaceutical industry benefits from the insights and perspectives patients share and ensures that the medicines and tools they develop empower the patient and put them in charge of managing their disease together with their clinicians.

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CHAPTER 5

Will we ever achieve sustainable adoption of patient engaged planning and execution?

KEN GETZ

Patient engagement still feels relatively new, in its nascent stages, yet it has been around for more than fifteen years. Most transformative changes that have received enterprise-wide adoption touch a single or a small number of functions. The patient engagement movement is unusual in that all stakeholder groups and functions participating in the drug development process are impacted: patients, patient advocacy groups, research sponsors, clinical research professionals, regulatory and health authorities, bioethicists, healthcare providers and payers. Without exception, each of these stakeholders recognizes the importance and conceptual promise of patient engagement. But something fundamental is lacking.

To date it has been easier to develop conceptual frameworks and guidelines to inform HOW to support patient engagement. What we are lacking is a credible and evidence-based value proposition — the WHY — to compel the drug development enterprise to embrace and incorporate patient engagement into standard operating practices and processes. As a result, the patient engagement movement has remained largely experimental and optional, in the pilot phase of adoption. Regulatory requirements play a key role in compelling organizations to adopt new practice. Economic incentives and a measurable return on investment (ROI) are also needed to move patient engagement into mainstream clinical research planning, execution and reporting.

Progress in how to deploy patient engagement

Between 2006 and 2012, organizations created and promoted frameworks and guidelines in earnest to inform and shape patient engagement policy and practice.[1] The European Medicines Agency (EMA) formed its Patients' and Consumers' Working Party (PCWP) in 2006, for example, giving patient groups a platform for providing information about real-life experiences and for making recommendations on regulatory matters related to investigational and commercially available medicines. The U.S. Food and Drug Administration's (FDA's) Plain Writing Act in 2010 mandated that all agency communications be provided in lay language. That same year the FDA issued guidance encouraging solicitation of patient input into endpoint measurement for patient-reported outcomes (PROs). Shortly thereafter, the Patient-Centered Outcomes Research Institute (PCORI), established through the Affordable Care Act, produced guidance, tools and incentives to encourage researchers to engage with patients and caregivers as study partners.

The FDA's Patient-Focused Drug Development (PFDD) initiative, established as part of the fifth reauthorization of the Prescription Drug User Fee Act (PDUFA) in 2012, was initiated to systematically obtain patient perspective on select diseases and their treatment — for typically rare and ultra-rare medical conditions — to more effectively inform the agency's evaluation of risks and benefits for new therapies. Since then, regulatory

agencies and advocacy groups have continued to solicit patient input to understand relevant and meaningful clinical outcomes.

Between 2014 and 2022, the Clinical Trials Transformation Initiative (CTTI) and the Medical Device Innovation Consortium (MDIC) developed frameworks and resources to help identify stages in the R&D continuum where patient engagement practices might enhance development outcomes. Other groups produced guidelines, frameworks and resources informing patient engagement policy and practice during this time period include the European Patients' Academy for Therapeutic Innovation (EUPATI), a public-private partnership project of the EU Innovative Medicines Initiative (IMI); the National Health Council (NHC); the National Institute for Health Research (part of the UK's National Health Service (NHS)); and TransCelerate BioPharma, a pre-competitive consortium of major global pharmaceutical companies.

Since 2008, the Center for Information and Study on Clinical Research Participation (CISCRP), an independent nonprofit patient education and advocacy organization, has been providing and refining services to assist organizations in soliciting patient input into draft protocol designs and in returning plain language communications — protocol synopses, informed consent forms and trial results summaries — to clinical trial volunteers.

The European Union's Clinical Trial Regulation (EU CTR) No. 536/2014, went into effect in January 2022, and requires that sponsors make plain language clinical trial results summaries publicly available for all clinical trials conducted in at least one EU member country. And in June 2024, the FDA issued draft guidance encouraging the enrollment of historically underrepresented patient communities in clinical trials.

Yet patient engagement adoption has languished

Table 1 presents the results of a study conducted in 2022 by the Tufts Center for the Study of Drug Development (Tufts CSDD) among 225 pharmaceutical and biotechnology companies.[2] The results of this in-depth assessment provide insight into the key challenges hindering enterprise-wide adoption of patient engagement practices.

Table 1: Top reported challenges to achieving enterprise-wide adoption of innovations supporting clinical research planning and execution

INITIATION TO INNOVATION EVALUATION	"GO" DECISION TO FULL IMPLEMENTATION
• Poor cross-functional coordination, alignment and support • Financial constraints • Poor pilot design and execution • Difficulty comparing providers • Low senior management involvement	• Insufficient "evidence"/ inability to determine ROI • Poor change management planning and execution • Provider uncertainty and volatility • Poor cross-functional support • Insufficient long-term investment • Internal champion turnover • Low senior management involvement

Source: Tufts CSDD 2022. (n=225 pharmaceutical and biotechnology companies)

Pharmaceutical and biotechnology companies initially approached the patient engagement movement by creating internal teams and committees made up of staff from multi-functional areas including clinical and clinical operations. Some sponsor companies established dedicated functions often led by heads of medical affairs

functions, innovation groups and senior-level patient officers. Among the primary responsibilities given to these individuals and functions were to facilitate culture change; create new operating policies, procedures and tools; and share effective practices.[3]

Sponsor companies devoted energy and investment in translating patient and community engagement into patient-centric practices. Early on, the most widely piloted patient engagement initiatives focused on clinical trial design and planning. Companies piloted the use of patient advisory boards and professional panels to react to endpoint definition and selection, eligibility criteria, visit schedules and durations, and the number of procedures performed per visit. These advisory panels could be set up easily and quickly at minimal cost, making their perceived impact and potential return on investment high. Sponsor companies also piloted initiatives to improve participation convenience (e.g., virtual and remote components, transportation and compensation assistance) and simplify data collection.[4]

Despite early exuberance, and well-intentioned commitment and investment, for the vast majority of companies patient engagement initiatives have remained in exploratory and pilot stages.[5] Typically, these initiatives have fallen under the responsibility of small internal patient engagement groups or innovation teams siloed or partitioned from line functions. As such, it is difficult to gather and access reasonable and realistic measures and there is limited awareness among clinical teams and the broader organization. Piloted initiatives are given relatively small budgets with little to no plans or funding beyond the pilot stage.

And more recently, among larger pharmaceutical companies, patient engagement staff have been dispersed into clinical operations (e.g., patient recruitment) functions, giving clinical teams and associated functions the option to support patient engagement activity if they expect improvement in timelines and enrollment effectiveness, and if their budgets permit investment. In some instances, sponsor companies have downsized patient engagement departments and staff to rein in development spending.

Empirical evidence on the adoption maturity of patient engagement initiatives among sponsor companies has been disappointing. A 2023 Tufts CSDD survey among several hundred sponsor companies found that only 27% are routinely soliciting patient input into protocol design decisions.[6] Despite high and rising protocol design complexity and the ensuing burden placed on patient participation, less than 10% of study volunteers report receiving any convenience-enhancing support according to a 2024 study of 4,558 participants completed by the CISCRP. In that same study, CISCRP found that only 35% of clinical trial volunteers report receiving a formal verbal or written “thank you” for their participation and less than 30% report receiving any information about the results of their clinical trial after participation has ended.[7]

And, in a robust assessment of racial and ethnic diversity in pivotal trials supporting drugs and biologics approved between 2007 and 2021, Tufts CSDD found little evidence of progress made in reducing long-standing and widespread demographic disparities. Based on disease prevalence, Tufts CSDD found that the overrepresentation of White participants had only modestly decreased during this 14-year time horizon. High levels of underrepresentation were observed among other racial and ethnic communities though some improvement in the proportional representation of Black participants occurred between 2017 and 2022.[8]

Several factors have delayed adoption and contributed to this protracted piloting stage. Many have pointed to the challenge of modifying legacy practices, and the perception that new initiatives will be too time-consuming or expensive. Others point to the lack of

vision, insufficient authority to drive cross-functional support and implementation, highly risk-averse cultures, concerns about job security, and a lack of clear evidence demonstrating impact and value.

To inform the latter, in 2017 the Clinical Trials Transformation Initiative (CTTI) in collaboration with Tufts CSDD and Janssen quantified the net financial value of patient engagement using standard risk-adjusted financial modeling techniques for a typical oncology development program entering Phase II or III testing. Assuming a modest $100,000 (USD) investment in patient engagement that resulted in avoiding one substantial protocol amendment and improved recruitment and retention timelines, program development costs decreased in the model by $0.56 million (USD) and $2.1 million (USD) for Phase II and III oncology programs, respectively. The model also showed that the expected net present value (eNPV) of a development program is equivalent to accelerating a pre-Phase II product launch by 30 months and a pre-Phase III project by 18 months.[9] Although the drug development enterprise welcomed this assessment, it had limited impact. It was viewed as largely conceptual, based primarily on assumptions and not actual experience.

Moving the bar — Getting a deeper answer to the WHY

As the predominant sector funding 90% of clinical trials of medical interventions, it is critical that pharmaceutical and biotechnology companies embrace patient engagement as a core tenet driving drug development planning and execution. Broad sustainable adoption requires moving from “nice to have” to “must have.” Five primary operating conditions need to be addressed:

1. Lack of senior corporate leadership and cross-functional senior management support
2. Poorly designed and executed pilots that have failed to gather sufficient evidence to assess and compare innovations, and to demonstrate return on investment (ROI)
3. Inadequate post-pilot investment resulting in insufficient continuity to drive implementation momentum
4. Absence or delayed preparation of a comprehensive change management plan to guide implementation
5. Misaligned incentives dissuading personnel and functions from committing to transform legacy processes and practices and support sustained implementation

The tipping point in addressing these conditions rests with broad, industry-wide efforts to share (i.e., publish and present) hard evidence on actual experiences with patient engagement practices and their impact. The aggregation and analysis of collective evidence to derive benchmarks and measure demonstrated value in drug development and clinical care will be essential to this effort including quantifying the net financial benefit of deploying patient engagement practices on the lifecycle value of a commercialized therapy.

Tufts CSDD is eager to support this effort and is taking steps to constitute a new consortium in 2025 to gather and share empirical data. Through this effort, and others, we hope to meaningfully and sustainably move patient engagement into the fabric of mainstream drug development.

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Throughout his 35-year career in the drug development enterprise, Ken has been passionate about educating and advocating for patients and their families as partners in the clinical research process. After all, their courageous decision to participate in clinical trials typically offers no personal benefit but has a profound impact on public health and the advancement of new medical knowledge and treatments.

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CHAPTER 6

From minor to major impact, how patients are increasingly shaping the world of industry drug development

DANIEL J. O'CONNOR

Introduction

Patient-centric drug development can be defined as the systematic approach to incorporate the patient's perspectives and preferences into the design, assessment and production of a therapeutic product. Over the last decade or so, there has been progressively universal agreement across different stakeholders that involving the patient voice in the development of medical technology is not only desirable but essential. By involving the end user, it is recognized that these products will more likely meet patient, regulator and payer needs. However, despite the growing consensus of the need to incorporate the patient's perspectives and preferences, doing this well and ensuring that the patient voice is both meaningful and impactful is still an evolving science and practice. In particular, the degree to which a development program can be considered or recognized to be "patient-centric" is challenging and not widely agreed upon.

The pharmaceutical industry plays a critical role in the development of innovative technologies and new medicines that can address patients' unmet medical needs and support public health agendas. The types of activities that industry may be involved in that can be considered to contribute to a patient-centric approach are diverse and growing. These include interactions or instruments such as:

- Engaging individual and groups of patient representatives during the lifecycle of a drug's development for a variety of reasons, but with a common theme that the patient has a legitimate and special experience or view that should be captured and taken into account.
- Identifying feasible patient-centered outcomes at structured scientific advice meetings between drug developers and regulatory agencies.
- Involving patients and patient views in health technology assessment (HTA) and payer aspects.
- Including patient-reported outcomes (PROs) in clinical development programs and eventually in drug labels, supporting the benefit-risk assessment and helping patients and prescribers with therapeutic decision-making.

Evolving approaches and importance

Guidelines, frameworks and consensus documents that support consistent and robust approaches are key elements of practice that help ensure that the patient voice is meaningful and can be incorporated into a variety of activities. The following provide examples in different settings:

Industry interactions

One of the key areas that has matured in recent years is how direct interactions between patients and industry are structured, and many activities are defined in codes of practices which, among other things, set the standards and influence how the industry can productively and ethically engage. As an

example, Clause 27 of the Association of the British Pharmaceutical Industry (ABPI) Code of Practice for the Pharmaceutical Industry covers aspects of engaging with patient organizations ("patient organization" means an organization mainly comprising patients and/or caregivers or any user organization such as a disability organization, carer or relative organization and consumer organization that represents and/or supports the needs of patients and/or caregivers). In addition to individual pharmaceutical companies engaging with patients, the ABPI as an industry trade association set up the Patient Advisory Council, which is designed to enable ongoing full, frank and open discussions and information sharing between health charity chief executives and the ABPI Board and Executive team. The ABPI aims to consistently integrate patient insight into its decision-making, developing a mechanism to ensure the patient perspective is embedded into their strategic thinking, with meaningful engagement helping to inform policy priorities and work-plans. An example of collaborative working is the published report, *How to make sure patients get faster, more equitable access to innovative treatments,* developed by the Patient Advisory Council and the ABPI.[1]

International public private initiatives

Drug development is increasingly a global operation and international collaborations across multiple stakeholders that include patients are seen as high-value interactions. As well as collaborations, harmonization of approaches and requirements is considered to be of importance for driving efficiencies and reducing duplication. Some good examples of a platform that can facilitate such interactions and goals are projects from the Innovative Health Initiative (formerly the Innovative Medicines Initiative, IMI), an EU public-private partnership funding health research and innovation. The IHI aims to leverage a range of skills and fund projects that can address public health needs, improve patients' lives, and boost the competitiveness of Europe's health industries. Two projects that stand out in the area of patient-centricity are:

- **IMI PARADIGM:**[2] Patients Active in Research and Dialogues for an Improved Generation of Medicines: advancing meaningful patient engagement in the lifecycle of medicines for better health outcomes. This completed project developed a set of tools and guidelines to help integrate patient perspectives in the drug development process. The toolbox includes tools for assessing the impact of patient engagement-related activities, guidelines on contracts, conflicts of interest, and a code of conduct. A complete roadmap helps to ensure optimal patient engagement practices, using the tools generated in the project and elsewhere.
- **SISAQOL-IMI:**[3] Establishing international standards in the analysis of patient-reported outcomes and health-related quality of life data in cancer clinical trials. This project aims to develop recommendations on how to analyze and interpret data on health-related quality of life (HRQoL) and PROs in cancer clinical trials. The project will seek to achieve consensus internationally and across stakeholder groups on the optimal use of PROs in cancer clinical trials, and gain clarity on the research objectives for the use of PROs in trials, including the definition of "clinically meaningful change." Ultimately, the tools and resources developed should help ensure that cancer clinical trials accurately capture how patients feel or function during treatment, aiding in decision-making for regulators, health technology assessment bodies, and, crucially, improve patient satisfaction.

Regulatory frameworks

Regulators are another stakeholder who are interested in involving the patient in decision-making and opportunities for patient-regulator-industry interactions are growing. Such activities are increasingly facilitated by regulatory procedures, for example, at the European Medicines Agency (EMA) through the Scientific Advice Working Party (SAWP) and the Committee for Orphan Medicinal Products (COMP), with the additional possibility to bring patients as experts to scientific advice meetings at national authorities. The International

Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) brings together regulatory authorities and the pharmaceutical industry to discuss scientific and technical aspects of pharmaceuticals and develop ICH guidelines. In 2020, in a first for their guidelines, the ICH created a Reflection Paper on Patient-Focused Drug Development for public consultation.[4] The paper identifies key areas where incorporation of the patient's perspective could improve the quality, relevance, safety and efficiency of drug development and inform regulatory decision-making.

Patient training and education

Helping to ensure that patients are able to meaningfully engage with industry is a priority for a number of initiatives. EURORDIS[5] (Rare Diseases Europe) is a non-profit alliance of more than 1,000 rare disease patient organizations from 74 countries. Its Open Academy School on Medicines Research & Development aims to provide rare disease patient advocates with the knowledge and skills needed to become experts in medicines research and development. More than 20 experts from across all rare disease stakeholders (including from industry) deliver the training each year. The topics covered include clinical trials methodology, clinical research, ethics in medicines development, regulatory affairs, health technology assessment and marketing authorization.

To the future

There is no doubt that there is now sustained interest in accurate and well-defined methods that can rigorously capture the patient's perspective throughout the drug-development process. However, to further enhance the integration of the voice of the patient, I believe based on my experience that we need to:

- Better define what we mean by being patient-centric and identify more clearly what are the key activities and what adds most value — resources are limited and we need to focus on what is meaningful.
- Ensure better demand signaling from decision-makers who can highlight the importance of the patient views in their activities (including the value of PRO data), helping to drive the behavior of industry.
- Create policies that can help resolve patient engagement and involvement capacity issues and funding aspects, both for individual patients and patient organizations.
- Develop proportionate approaches to managing conflict of interest in the knowledge that excluding patients from particular activities due to involvement in others is likely to create unnecessary barriers.
- Support research and new methodology that can help address outstanding challenges such as how we "weight" patient data and integrate the data amongst other more traditional datasets.
- Determine how we prospective capture and combine data generated through clinical trials to real world data monitoring.

Overall, patient-centricity is embedding across the lifecycle of medicines and industry is rising to the opportunity and the challenges. With coordinated policies and improving recognition of the added value, the patient voice can be seen as being a standard (not a "nice to have"), majorly shaping the world of drug development and access.

There is no doubt that there is now sustained interest in accurate and well-defined methods that can rigorously capture the patient's perspective throughout the drug-development process.

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Dr. Dan O'Connor is medically and PhD qualified and currently the Director Regulatory and Early Access Policy at The Association of the British Pharmaceutical Industry (ABPI). He joined the ABPI from the Medicines and Healthcare products Regulatory Agency in 2023. At the MHRA he was Deputy Director of the Innovation Accelerator and Regulatory Science. Dan has special interests in drug development, rare diseases, regulatory science, health innovation, patient engagement and drug repurposing.

Although he left clinical practice many years ago, Dan did not leave or lose his interest in wanting to ensure the best opportunities for patients whilst enhancing public health goals. As such he has always gravitated towards activities that have allowed him to connect drug development and access to innovative therapies as directly as possible to the patient, helping to ensure that we move to an era where patient-centricity becomes the norm.

Dan has competed higher medical training in Pharmaceutical Medicine and is Editor-Author of the Oxford Specialist Handbook in Pharmaceutical Medicine.

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CHAPTER 7

Patient-centricity now: People, action and culture

ANTHONY J. YANNI

> ***"To be persuasive we must be believable, to be believable we must be credible, to be credible we must be truthful."***
>
> *— Edward R. Murrow*

The time is now. We can no longer travel the path well-worn in how we develop patient solutions within the halls of pharma companies, and we can no longer accept that treating illness is the same as caring for the individual. While fully well-intentioned, both the drug development space and healthcare delivery process have crept toward a place where patients are the observers — silently hoping for their expectations to be met. The journey of creating and delivering solutions we assume are impactful should be replaced with one that moves patients into an active role — from spectator to collaborator.

Patient-centricity is the vehicle to get us there… and it is the bridge that necessarily connects the development and the delivery of solutions.

So, what does a fully functional and mature patient-centricity function look like? First, it is more than patient engagement. While pharma has had positive movement toward engaging patients, the act of discussion has in some ways slowed our progress. Too often now, when patient-centricity is discussed, we hear "we're doing that." However, when the discussion goes a bit deeper, there is the scribing of information shared by patients, but no action attached to it. That is, no meaningful changes are occurring in the decision-making process in the research, development and delivery activities. This acceptance of terminology in place of results has impeded the full integration of the patient perspective into the solution development and delivery process by default. This needs to end.

To have a positive impact on patients *and* the business, specialized teams need to connect information with action, providing full support of the research, development and delivery process. Only then will decisions be influenced, and the "good business" argument made through measurement.

To have a positive impact on patients* and *the business, specialized teams need to connect information with action, providing full support of the research, development and delivery process.

For those yet skeptical, let's consider the "why." Why would we include the voice of the customer from the very beginning through delivery? This question may

be mumbled frequently in the halls of pharma and healthcare systems but has been debated and resolved for decades in nearly every other industry. Whether considering the complexity of a car dashboard interface or the simplicity of a handheld razor, customers have had a voice in how the final product is more aligned with their expectations and use before the first one is mass-produced. Why have we not had this same approach consistently in pharma and healthcare delivery? Too often we view our work as excessively complex to allow for valuable patient input. This "we know best" argument has failed. McKinsey, LEK and others have reported high launch failure rates for new treatments — some as high as 40% off market expectations. When diving deeper into why that is, many studies have found it was the lack of truly understanding the customer early enough in the process to impact decisions. Patient-centricity provides the necessary humility for life science companies and hospital delivery systems to recognize we are not omnipotent, and we need help. Strong collaborative processes with patients and patient advocacy organizations are the solution.

Broader implications of this patient-centered work extend to regulators, payers and government agencies. Regulators, for example, have long supported the idea of patient input and many have developed processes to allow voice to patients through patient panel input into the review process. One can imagine, without much effort, the expanded role of the patient in the eyes of the Big 3 mentioned above. How to utilize this information from a regulatory perspective remains opaque, but here is where advanced patient-focused systems can show, by example, the impact and the influence it has had on internal decision-making. How a patient population was chosen, their views regarding gaps in care, how a particular asset may impact that gap, the goals of treatment, and how it aligns with patient, caregiver and provider perception of value are all outcomes of patient centric processes. This information, in my view, will become increasingly important when presenting to regulators and payers the benefit of a new medicine. For certain, safety and efficacy will always be primary areas of focus, but as we begin to chart courses for difficult to treat illnesses and higher cost treatments, the "why" from patient and provider perspectives will weigh heavier on the scale.

Patient-centricity provides the necessary humility for life science companies and hospital delivery systems to recognize we are not omnipotent, and we need help. Strong collaborative processes with patients and patient advocacy organizations are the solution.

From the delivery side, we have accepted that service, in many instances, has been sacrificed for appropriate treatment and volume of care. This is quite unfortunate since care has many components beyond the delivery of appropriate medicines. Further, we are not taking advantage of our greatest strength: our people. Individuals join healthcare systems because of a passion and focus. For example, an accountant can execute their work in multiple industries; I would argue those who choose pharma and healthcare do so because of their patient focus and desire to have an impact on the lives of those waiting for solutions. When we ignore this positive selection bias, we drive high performers out of our systems.

An example of people and culture from my days in healthcare as taken from my book *A Bandana and A Bluebird: The Path to a Patient Centric Healthcare System:*[1]

The Art of Culture

SUSTAINABILITY REQUIRES A UNIFIED CULTURE

It was early evening, around 6:30 PM. I had a very long day in the office, starting at 7:30 AM and just finished seeing my 32nd patient at 6:00 when I received the call that there was a patient that required admission to the hospital. I was on call for our four-person internal medicine practice and due to the practice size, being on call would certainly mean a busy night. Feeling a little sorry for myself, I drove to the hospital. It was autumn in Pennsylvania, so it was predictably dark and cool which matched my deteriorating mood.

I had already given the order for the patient to be moved from the emergency room to a bed on a general medical floor — this one on the 9th floor of the hospital. As always, the hospital was bright with lighting and at that hour, with visitors milling about to spend time with their loved ones. The occasional IV pump alarm and somewhat frequent nurse call buzzers could be heard, as well as a few televisions from the patient rooms and some quiet conversations among the nursing staff hustling from patient to patient.

Despite the relative quiet, it was a very busy night and as usual the nurses and aids were working extremely hard. I had talked to and examined the patient I was admitting and was standing at the corner of the nurses' station, writing orders, and completing the admission paperwork. That's when it happened; I experienced the greatest example of healthcare I have ever witnessed.

As I was finishing, I could hear a nurse speaking to a patient in a room near where I was standing. The patient was elderly and clearly in poor health. My impression from what I saw, without any knowledge of the patient or his illness, was that he was near the end of life. The nurse was standing next to the bed on the right side of the patient; her left hand on his right shoulder and her right hand working the dinner tray that sat on his table over his bed. She would scoop some food and talk to him. "Ray, how about a few peas?" she said, slowly moving the food toward his mouth. Between these small bites she said "Ray, today is Thursday and it's a little cold outside. How about some mashed potatoes?" This went on for about 15 minutes, the patient remaining quiet but responding with his eyes and facial expression. This nurse, in each moment, attempted to connect with the patient, to make him feel important, to let him know he mattered to her. This despite a heavy workload and many patients to care for.

This was perfection.

We are poised to do better. Patients are waiting and processes exist that have shown to be effective in making better decisions for patients with patients.

I'll conclude with another excerpt from my book. A letter I think we all wish we could write to our patient partners; a note that can be written tomorrow if we make the changes necessary today. The time is now. Let's go!

Dear patients and caregivers waiting impatiently for new treatments,

I appreciate you spending your valuable time with me and my team last week giving us your perspective on the difficult journey you and your family have been on taking care of your child with a rare disease. I want you to know we appreciate you and heard every single word.

We also heard your frustration with the slow progress of science to help treat your baby as well as your anxiety about the future. We sensed your skepticism as to whether we were deeply committed. We heard your anger, if I may say so, about the need to repeat your story. Endlessly you are willing to share these most personal and painful feelings and experiences at the request of folks in pharma and yet you see no progress as a result. Each time, hearing your own words causes pangs of dread within you. You have conflicting feelings about wasting your time, yet maybe, just once, your words will result in action.

How can you not? You see your baby slowly weakening before your eyes. Despite every human effort to the point of exhaustion, nothing you do is slowing the decline. It is clear to us through our discussion that you have created the best environment possible, and your son is comfortable and happy. However, how his story ends will be certain should new treatments not be made available. How can you not share the story again and again, even if you don't believe anything will come of it? You must ask yourself; will my voice ever make a difference?

I'm happy to say this was the time.

Since we spoke, our CEO and leadership have endorsed a full Patient Centricity function. We will be hiring specialized team members to support our researchers, using your words and advice to help direct our program. This will not be a subtle change; it will be an earthquake.

We will also continue to support programs in the development space, and we will be connecting more closely with patients and their families to learn more about their challenges in their real-world setting. This will help us solve one of the problems you mentioned to us — an understanding of patients and their caregivers beyond the disease. We will concentrate on understanding behavior to be more inclusive to a diverse population across the world.

Remarkably, our company has doubled down on our focus on patients. We have invested in programs that will create and maintain a culture that thinks about your little boy every day, in every role. This will ensure what you have helped us achieve will be sustainable.

My promise to you is that we will transition all you have shared with us into action. Your time is not wasted. While we can never fully understand your experience or that of your son, we will work to have the best understanding possible.

We are all-in with you, committing to allocate all of our efforts to help your little boy. While there is no certainty in the results of our effort there is complete certainty in the method. We will work every day — with you — to make new solutions available. You, your family, and your son are the "why" we do what we do. We recognize the professional privilege we have working with patients, and we will be relentless in our efforts.

Thank you for your partnership.

Sincerely,

Patient Centricity Officer

References

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About the author

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Dr. Anthony Yanni, a veteran healthcare professional and pharma executive, grew up the youngest of four in a close-knit Italian family. He was exposed early in life to a child with a rare disease and saw first-hand the impact it had on the lives of everyone; the change in focus of an entire group of people. He was in awe of the healthcare workers who were able to convey difficult information in an honest and hopeful way and knew that he wanted to be part of a system that cared for patients and provided meaningful impact.

After getting his MD degree from Drexel University/Hahnemann School of Medicine, Anthony practiced medicine for 15 years, holding roles such as Chief Medical Officer and Chief of Internal Medicine in a Northeastern US health system. His clinical experience led him to recognize the significance of focusing on the patient, not just the disease.

Then he moved to industry. At Sanofi, Anthony served as Head of Patient Insights, Solutions and Outcomes, creating an industry-first process for incorporating patient and clinician perspectives into research portfolio decisions. His work brought clinical researchers closer to clinical practice by integrating the patient, their perspectives and their journey into the laboratory. And now Anthony is at Astellas Pharma as the Senior Vice President and Global Head of Patient Centricity where he has been pivotal in integrating patient perspectives and real-world needs into pharmaceutical innovation, development and delivery. He also serves on the Board of Trustees of The University of Scranton and the Astellas Global Health Foundation.

Anthony is a transformative leader known for advocating and executing patient-centricity in global healthcare practices and was selected as one of 2021's 100 Most Inspiring People in the life-sciences industry by *PharmaVoice* magazine and was recognized with the 2022 Reuters Pharma Europe Patient Champion Award for having "real impact on patients, carers and international health systems." In 2024, he was recognized with the Life Sciences Voice Rising Stars Award for "innovative work shaping the future of the life science industry."

In 2024, Anthony published his first book, *A Bandana and A Bluebird: The Path to a Patient Centric Healthcare System*, in which he details, through patient vignettes and programmatic examples, the progress made toward achieving a more patient-focused system of care as well as the challenges that remain.

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CHAPTER 8

Patient-centricity: When you are all-in-one

ZSUZSANNA DEVECSERI

"All-in-One" Podcast

Zsuzsanna Devecseri, a Generation X woman (here: **Zsuzsanna, potential patient**)

Zsuzsanna Devecseri, MD, practicing oncologist (here: **Zsuzsanna, the doctor**)

Zsuzsanna Devecseri, MD, MBA, pharmaceutical executive (here: **Zsuzsanna, the drug developer**)

Zsuzsanna Devecseri, whose parents passed away young from cancer (here: **Zsuzsanna, the daughter**)

Transcript

Zsuzsanna, potential patient:

Hello all, thank you for accepting the invitation. I have an important topic to discuss that I'm thinking about a lot recently. As my parents had cancer in their sixties, I have a considerable likelihood of a cancer diagnosis at some point of my life as well. Although I live healthy and keep up with all screenings — so I do my very best on the prevention and early detection front — I still want to prepare for a potential future situation of being a cancer patient. How much would my opinion matter in the decisions made about my treatment?

Zsuzsanna, the doctor:

When we decide about certain treatments, there are multiple factors we take into consideration. A cancer diagnosis is a shocking experience. It is important to respect the patient's emotional journey, what can be discussed and when. There are also huge differences in health literacy, how much the patient knows about their own body and the disease itself. Then the science comes into the picture, how advanced the disease is and how many treatment options we have. I must admit, in the past there wasn't much shared decision-making with the patient. The approach was very paternalistic, but I see that's changing.

Zsuzsanna, the daughter:

When my father was diagnosed with prostate cancer, we had a lot of questions, but the treating physician's communication was very transactional: what test will be done and when, which treatment will be given, and what side effects we can expect. He avoided any discussions or questions about my father's expectations and preferences, and as a result my father was afraid to ask. When we asked the most important question of *"Is his disease curable?"* or *"How much time does he have left?"*, the only answer we got was that every patient is different, every cancer is different, and everybody responds to the treatments differently. It wasn't useful at all.

Zsuzsanna, the potential patient:

Considering all that has been said, it seems there are lots of psychological and communication aspects during the treatment journey. So it must be very hard for pharmaceutical companies to gather real insights, especially considering patients all around the world with different cultures,

healthcare systems and education. What has been the industry practice and is there any evolution on this front?

Zsuzsanna, the drug developer:

In the past, even earlier in my career, drug development was focused primarily on clinical study execution and regulatory success. Clinical studies were focused on the disease, primarily to ensure patient safety, and making sure that treatment outcomes were properly measured. Inclusion of patient voice typically focused on ways to ensure patient enrollment and to educate patients about the treatment to promote compliance.

It is well known that as we include more and more aspects, clinical trials are getting more complicated. Appropriate prioritization is critical, and this requires resources, time and data — and we are in short supply of many if not all of those. The more diverse the patient population is, the harder it is to define appropriate endpoints and reach statistically significant results. That's why we've heard for years that the patient population we include in trials doesn't represent real-world patients. But things have changed, and the structured patient perspective is now an integral part of the development workflow throughout the lifecycle.

Zsuzsanna, the daughter:

We have jumped a little ahead, so I would like to bring us back to the diagnosis. My father's cancer was diagnosed late, when it had spread into his bones. My mom's disease was diagnosed early, but as an incidental finding during a doctor's visit for another issue. So, we were lucky. But I still feel guilty about not catching my dad's cancer earlier.

Zsuzsanna, the doctor:

There is a limitation what the relatives can do, but knowing the screening options and encouraging parents and relatives to get tested are essential. There are multiple ways we can detect the most common cancers early. Of course the same is also true of other diseases, like diabetes, atherosclerosis, high blood pressure, etc., but as an oncologist, my focus is cancer. Generally, I can say that the health literacy even among the highly educated is very poor. The majority of people don't even know where certain organs are (for example, the prostate), and how they normally work. How can we expect them to recognize the early signs and symptoms of a disease? Screening and early detection I see as societal responsibility, with multiple stakeholders involved.

Zsuzsanna, potential patient:

All right, maybe we can discuss that topic in further detail in another podcast episode. So, back to our original topic. Let's say I'm diagnosed, ideally early. How can I be sure that those who develop the treatments know what I really need, and more importantly, what I want?

Zsuzsanna, the drug developer:

This is a critical point. For most cancers, early diagnosis and intervention (mainly surgery and pre- and post-operative treatment) can cure or provide a long life-expectancy. But with the current regulatory framework, with almost every new treatment modality, we start development in the very late stage of the disease. At that time not only the cancer is different, but the patient's needs are drastically different too. There are some regulatory initiatives to incentivize companies

to investigate new treatments in earlier stages of the disease, but in practice, we are far from reaching the actual potential. So, what we need to do is to include patient feedback in a more systematic and continuous manner. We need to ensure that their experiences, preferences and real-world needs, including their lifestyle, are taken into consideration when we identify their unmet needs, to make sure that treatment will improve health outcomes and lead to patient satisfaction.

Zsuzsanna, the daughter:

How can the late-stage patient's needs be standardized? I experienced that doctors think that patients want to live as long as possible, no matter how. I also saw with my parents at a certain point that the treatment was no longer helping, it was only a torture. Has this been taken into consideration during the drug development process? Or is it the treating physician's decision? Who should decide how to tailor treatments to individual patients and are they empowered (with data, information) to make this decision?

Zsuzsanna, the doctor:

Let me answer the first question: deciding between multiple potential treatment options should be the treating physician's and patient's shared decision. To do it right, the doctor needs to have data (from clinical studies), and the patient needs to be informed about potential benefits and risks. When we talk about patient preference, it is important to understand the underlying motivation (the "why") that can help guide our work and potentially also be valuable for those who develop new drugs. For example, there could be very different patient motivations not just in deciding between treatment options, but also in whether to participate in clinical trials or not. All the information we provide together should be easily understandable. People like visuals and infographics.

Zsuzsanna, the drug developer:

In the last decade, patient-centric principles have been developed and tested, and there is a good understanding what the most important aspects are for patients. Some of them are related to the point of care, including care coordination, patient transition between specialties, and hospital environment, which are very complex and very diverse if considered globally. There is a universal shortage of healthcare workers almost everywhere in the world. This inadequate capacity highly impacts patient experience and this trend is worsening. It is very alarming.

Other aspects — respect, information, education, emotional support — are shared responsibilities. Information is always a two-way street, and the more we learn from and about patients, the more we can improve their experience. I have seen the tangible benefits of incorporating patient perspectives into the development process in many ways. Engaging patients leads to more comprehensive clinical trial designs, improved adherence to treatment protocols, and ultimately better health outcomes.

Zsuzsanna, the potential patient:

So, we all agree that the inclusion of patient voice is critical and essential. Can we talk about the "how"? I guess it's easier when the treating physician meets individual patients during their hospital visit, than for the pharmaceutical industry, considering their focus on huge and diverse patient populations.

Zsuzsanna, the daughter:

That's not entirely true. It is very critical to highlight the essential role of the caregivers here. My personal experience is that we (speaking as caregiver) sometimes can give better information about the patient experience and needs than the patient themselves.
On many occasions, patients are too shy or embarrassed to admit that they have pain (like *"Strong men can tolerate pain!"*) or urinary difficulties, not to mention any symptom related to their sexual functioning (don't forget, prostate cancer is one of the most common cancers among men worldwide!). During the doctor's visit, patients usually don't remember all their symptoms and their frequency, as they may be nervous or tired.

Zsuzsanna, the doctor:

I fully agree with everything you just said. Patient/physician conversation can't be rushed. In real life, it is hard to provide the right environment and appropriate amount of time to understand fully what is going on in patients' lives. We learn a lot over time by experience and we do our best under pressure, but I'm sure we could do better. That's why we use all the help we can get, including technology.

There are multiple phone and tablet applications that can help registering and sharing symptoms, but most of them are not completely user-friendly. Any tool that is simple, almost effortless, would be highly desirable to gather the whole picture, not just about the treatment effects and side effects but the overall functioning of the patient.

Zsuzsanna, the drug developer:

Historically we collected patient insights from patient stories, from patient advocates, and later using questionnaires to understand factors that impact the quality of life of patients. This led to structured and validated tools that became standard practice in clinical trials. These are almost never used outside of clinical research. Why is that? First, as we discussed earlier, it is very complex, and these questionnaires are really time-consuming to fill out, and as there is no immediate impact for patients, they are not motivated to use them. Hospitals are not the ideal environment to answer these sometimes sensitive questions; we see significant differences if patients answer at the point of care or in their home.

Patient-reported outcomes (PROs) are an essential and critical part of not only drug development but also standard of care. Although they will probably never be a single primary clinical study endpoint for new treatment registration, they should be a co-primary endpoint in many diseases if not all. But we need to be better at asking the right questions and collecting and analyzing the data as well.

Zsuzsanna, the potential patient:

Let's finish this discussion with our dreams and wishes! What would you do or ask for to make sure patients are put first in their journey, that things are handled respectfully and compassionately to achieve the best experience and outcome for them and their family? Any specific ask from each other?

Zsuzsanna, the daughter:

Everybody should recognize that patients are not just end-users of medical products, it is about their lives. They need to be completely informed about their condition and prognosis to be able to make the right decisions. Healthcare providers and the pharmaceutical industry need to learn "patient language," how patients describe their conditions (I learned a couple of those terms from my parents), and they need to speak this language. It includes a lot of listening, and I hope technology like large language models as well. That would lead to self-tailored information development. For example, we could ask artificial intelligence (AI) tools (ChatGPT, Copilot, etc.) to explain a diagnosis to a 46-year-old high school history teacher or a 30-year-old chef, or input any description that would help describe things to people in their own words. Information means a lot to patients and families, and accessing reliable information is invaluable.

My ask is to all doctors: please ask patients and families their priorities and preferences repeatedly, as they can change over time, and please make sure the timing and the situation are appropriate in order to gather the right information.

Zsuzsanna, the doctor:

I would advocate for more patient-centric endpoints; the hardest oncology endpoint, overall survival, does not alone describe the full patient experience. If you ask a patient about a treatment, first thing you will hear are the side effects and not efficacy, as side effects impact their quality of life the most, especially if they are in pain. I know the therapeutic index is very well considered during the drug development, but I would like to hear more about the impact of the side effects when presenting the trials, and not just their grade.

I also hope that technology will help using a more tailored approach and we will have the opportunity to use more predictive models when deciding the treatment for patients.

And lastly, I would like to mention convenience: the drug formulation, route of administration and dosing schedule. The majority of the treatments are combinations, and we know that patient adherence to treatment is drastically decreasing over time, which is even more true if multiple treatments are involved. Taking a pill or self-administering a subcutaneous injection is always preferred over intravenous injections or infusions. That is, of course, in the event that patients take them.

My ask to the pharmaceutical industry: further and continuous support in improving our patient communication materials about clinical trial data in a way that can be shared directly during the clinical consultation.

Zsuzsanna, the drug developer:

I'm sure there will be dramatic changes in endpoints (if the regulators allow) with the evolution of wearables and digital endpoints, which will hopefully address your concern, Zsuzsanna, about patient compliance. Technology is evolving so fast, there are smart watches, rings, bracelets, belts, etc. to detect patient symptoms, side effects, early signs of disease progression (gait or mobility change, cognitive functions, speaking, elevated temperature) that will be an essential part of drug development and standard of care as well.

Technology and automatization of data collection can help alleviate the current capacity issues and we will have access to more and better real-world data to help us understand the utilization of treatments, multiple factors that can influence treatment outcomes, and individual responses and side effects.

My ask to the patients and caregivers: to make sure they seek opportunities to share their knowledge and experience with their physicians, other patients, patient advocates, and the pharmaceutical industry as well.

In my ideal world, there will be a jointly developed and sustained patient-centric ecosystem, where all stakeholders work together for one goal, the best patient experience possible.

Zsuzsanna, the potential patient:

I couldn't have wished for anything better or more fitting myself. Thank you, all, for joining me for this important conversation. It has been great having you today.

Dear listeners, you've just heard Zsuzsanna Devecseri and the "All-in-One" podcast on patient-centric drug development. If you liked it, please join us for our next episode! Take care until next time!

About the author

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Dr. Zsuzsanna Devecseri started her career as a pediatric oncologist after graduating from the Semmelweis University of Medicine in Hungary. She later obtained an MBA in Economics from Corvinus University and a certificate in Health Economics and Outcomes Research from the University of Washington in Seattle. Zsuzsanna has certification in health insurance and marketing excellence, and she is also a certified coach.

Zsuzsanna started her career in the pharmaceutical industry in 2004 and held various commercial and medical roles with increasing responsibility across multiple therapeutic areas, including, cardiometabolic, oncology and rare diseases at Abbott, Sanofi, Genzyme and recently Novartis. She has been working in global roles in Boston since 2010 and she has gained deep understanding of healthcare systems worldwide. Zsuzsanna had the opportunity to build and lead high performing engaged teams and has been a speaker at multiple medical affairs and leadership conferences.

Zsuzsanna is passionate about early diagnosis and treatment and leads projects that address diversity and inclusion in clinical trials, patient-centric drug development and use of technology and data to improve clinical care and patient experience. She is determined to witness the cure for cancer in her lifetime.

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CHAPTER 9

The full-court press: Advancing patient experience data in oncology

ROHINI SEN

Finding my voice: Advocating for patient voices in oncology

A little over a decade ago, understanding the healthcare industry seemed a distant and unfamiliar proposition, especially for an immigrant like me, adapting to a new country and its intricate systems. My journey began as a math major, immersed in numbers, equations and abstract models. Yet, over the years, life led me to a place far removed from pure theory: that of the lived experiences of patients navigating the complexities of oncology treatment in a foreign healthcare landscape. Through this journey, I have developed two abiding passions: patient experience data (PED) and basketball. While they may seem disparate, they share a fundamental commonality: both thrive on collaboration, strategy and resilience. Basketball is my lens for life, offering insights and analogies that transcend cultural and professional boundaries. Thus, when reflecting on the evolving role of PED in oncology, comparing it to basketball seemed as intuitive as the swish of a well-executed three-pointer.

For me, PED is not just data; it's the collective voice of patients, researchers, clinicians and regulators, all coming together much like a well-coordinated team. Together, these voices form a cohesive story that shapes oncology drug development. When I first entered this therapeutic area, I approached it like any researcher might: diving headfirst into the theoretical realm. I devoured the relevant literature on PED in oncology, eager to walk into asset team meetings armed with knowledge and fully prepared to contribute. But, as it turned out, no amount of reading could have prepared me for what lay ahead. The reality of being a PED advocate involves far more than theoretical understanding. It requires navigating cross-functional education in the face of understandable skepticism, self-education on evolving priorities, repeatedly reassessing my strategies — all while finding ways to bring every stakeholder along on the journey. Ultimately, it is a process of learning by doing. And the truth is, I could not have done it alone.

For me, PED is not just data; it's the collective voice of patients, researchers, clinicians and regulators, all coming together much like a well-coordinated team.

So, what is it like? If I were to join the industry today and take up the role of a PED advocate in oncology, what would I have wanted to know at the start? This chapter is my earnest attempt to answer that question — not just for others, but also for myself. It serves as a reflection on what it takes to stay focused on the higher purpose of PED while navigating the complexities of oncology drug development. To my future "selves" stepping onto this court, equipped with little more than a clear vision of the goal and a willingness to observe, adapt and take all stakeholders on this journey to better serve our patients — this chapter is for you. (Please stay tuned for my final buzzer-beater conclusion imagery.)

The tip-off: The evolution of PED in oncology, a historical context

Understanding the history and key milestones of a subject is crucial when approaching anything new. In oncology, recognizing how PED has evolved over the past few decades is especially important. This awareness helps when collaborating with various teams, who may not possess the historical context of PED and its growing importance.

About a couple of decades ago, the focus in drug development, especially in oncology clinical trials, fell predominantly on endpoints like progression-free survival (PFS) and overall survival (OS), often sidelining the subjective experiences of patients.[1] This narrow focus, while instrumental in measuring the clinical efficacy of therapies, overlooked crucial dimensions of patient well-being. While tools like the EORTC QLQ-C30 have existed since 1987, they were underutilized, and patient voices were not a priority. The shift towards a more patient-centered approach was largely influenced by evolving regulatory guidance from authorities like the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), as well as growing advocacy from patients and academia. These voices highlighted the importance of incorporating quality of life and other patient-experience measures, reflecting a broader understanding that patient perspectives add crucial value to drug development beyond mere survival rates.

In terms of regulatory guidances, the FDA's guidance on patient-reported outcomes (PROs) in oncology highlights the necessity of capturing critical aspects such as treatment tolerability and symptomatic adverse events.[2] In addition, the FDA's Patient-Focused Drug Development (PFDD) guidances provide a structured framework for systematically integrating patient experience data, ensuring that clinical trials and outcomes better align with patient needs and expectations. This approach facilitates a more holistic understanding of treatment impacts, which is essential for developing therapies that effectively address patient experiences. Complementing these efforts, other initiatives and guidances, such as those from the EMA and the International Council for Harmonisation (ICH), highlight the importance of PROs and health-related quality of life in evaluating clinical benefits. The Patient-Centered Outcomes Research Institute (PCORI) and the National Comprehensive Cancer Network (NCCN) further reinforce the focus on patient-centric outcomes. Additionally, initiatives like Friends of Cancer Research (FOCR) emphasize the importance of collecting and analyzing physical functioning data alongside traditional clinical endpoints.[3]

These developments signaled a transformational shift in the clinical trial landscape: PED was no longer a "nice to have" component, but a necessary component to understanding a therapy's comprehensive impact. In oncology, this shift is exemplified by the FDA's Project Optimus initiative, which focuses on reforming dose optimization in clinical trials to ensure that treatments are effective, safe, tolerable and aligned with patient needs and experiences. As a result, PED plays a critical role in informing dosing decisions, ultimately enhancing treatment tolerability and patients' quality of life. I will further elaborate on capturing patient-reported tolerability and overall burden in clinical settings later in this chapter.

The evolution of PED in oncology aligns with a broader movement towards personalized medicine, where patient preferences and experiences can guide treatment choices effectively. As the oncology community continues to embrace and refine the use of PROs, the ultimate aim remains clear: to enhance patient care by not only prolonging life, but ensuring that extended life is lived to its fullest potential.[4]

Facing the press and passing the ball: Stakeholder management

Recognizing the importance of PED, the challenge is to effectively generate it within a trial setting. This involves navigating competing priorities such as meeting tight trial timelines, managing resource constraints, and addressing operational complexities at trial sites. Adding to this complexity, the nuanced needs of patients — such as prioritizing quality of life,[1] reducing symptom burden,[3] or addressing logistical barriers like accessibility[5] — do not always align with the standards required by sponsors and regulators, which often prioritize traditional endpoints like overall survival (OS) or progression-free survival (PFS).[6] Implementing PROs in clinical trials presents challenges across operational, medical and regulatory dimensions. Operational challenges predominantly involve site and patient burdens alongside difficulties with PRO training and monitoring. Site burdens stem from increased administrative workloads and the need for robust data collection systems, which can strain resources. Patients may face burdens due to lengthy or frequent PRO questionnaires, leading to fatigue and decreased compliance, especially if digital PRO tools present technological hurdles. Furthermore, inadequate training can compromise data standardization and quality monitoring. Standard medical costs in clinical trial implementation include recruitment, monitoring, lab tests, medical staff, patient care, technology, and data analysis. Implementing PROs necessitates significant investments in technology and personnel, contributing to increased trial costs. Additionally, integrating PRO measures with clinical endpoints to ensure they provide meaningful insights is complex and resource-intensive. From a regulatory perspective, ensuring the relevance and standardization of PROs is crucial. Regulators demand that PROs capture outcomes significant to patients, adding complexity to selecting suitable measures. Standardization is encouraged, yet challenging, due to the variability in disease states and endpoints, particularly in oncology trials. Furthermore, ensuring that PRO data is interpretable and actionable for stakeholders is essential for regulatory approval.

In summary, the effective use of PROs in clinical trials requires addressing significant operational burdens, justifying medical costs, and satisfying regulatory demands for relevance and standardization. Collaboration and investment in technology, training and methodologies are vital to overcoming these obstacles and optimizing PRO implementation in trials.

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Without deliberate effort, these patient needs risk being deprioritized. However, the key to ensuring PED integration lies in collaboration and knowledge-sharing. Through cross-functional education within the organization, stakeholders — including clinical operations, regulatory affairs, data managers and patient advocates — can be empowered to champion the value of PED.[7] Internal education equips teams to capture patient priorities alongside traditional endpoints, fostering alignment between trial protocols and lived patient experiences.

Assuming we successfully manage cross-functional stakeholders and align our strategies, what key considerations should we keep in mind in oncology? The following sections will delve into oncology-specific PED strategies to ensure success.

Executing the play

Integrating PED in early-phase trials

The integration of PROs into early-phase oncology trials represents a significant advancement in cancer research, shifting the focus from solely safety and dose optimization to a more comprehensive view that includes patient experiences. By capturing PROs early, researchers gain valuable insights into how patients tolerate treatments, allowing them to find a balance between efficacy and quality of life. This approach not only aids in selecting doses that patients can better manage but also enhances adherence and overall treatment success. However, not all PROs are created equal, and their utility in both early and late-phase clinical trials significantly relies on their capacity to measure factors that resonate with patients and satisfy the requirements of regulators and health technology assessment (HTA) bodies. To achieve this, it's crucial that the measurements are conducted using instruments that are well-defined, reliable, valid and interpretable.

Moreover, the data gathered from PROs in early phases can guide the design of later-phase trials, ensuring that the endpoints reflect what is truly important to patients, such as improvements in quality of life and symptom relief. This patient-centric focus ensures that research findings remain relevant and impactful. The relevance of early PRO integration was recently reflected in two recent approvals for new treatments in breast and thyroid cancers. For breast cancer, PROs assessed through tools like PRO-CTCAE, BPI-SF and EORTC QLQ-C30 demonstrated that most patients experienced moderate or less severe symptomatic adverse events, suggesting that inavolisib does not add additional treatment burden. The combination of inavolisib + palbociclib + fulvestrant provided sustained benefits beyond disease progression with manageable safety, supporting its establishment as a new standard of care.[8] In thyroid cancer, the FDA granted approval to selpercatinib for patients with advanced or metastatic medullary thyroid cancer, relying on PRO data that showed less severe side effect bother compared to alternative treatments, cabozantinib or vandetanib.[9] These developments underscore a shift towards recognizing the value of early PRO integration in evaluating tolerability and guiding treatment decisions in oncology.

Overcoming bias and misconceptions

While the above recent successes are encouraging, it is also important to highlight that some PROs may be more susceptible to open-label biases than others. Mouillet et al.[10] discuss how open-label biases can influence trial outcomes by causing discrepancies between measured and actual effects, potentially leading to overestimation of treatment benefits. Chakavarti et al.[11] underscore the importance of blinding and other methodological strategies to mitigate these biases, ensuring that the PROs accurately reflect the genuine impact of the intervention. Furthermore, Atkinson et al.[12] emphasize the critical role of selecting appropriate PROs and methodologies. They point out that the design of these PROs can significantly affect the magnitude of bias, thus urging careful consideration and validation of PROs in the context of open-label trials.

Only recently were claims of open-label studies inflating benefits or minimizing side effects of a treatment evaluated empirically via the Lord-Bessen et al.[13] study that investigates the potential biases in PROs associated with open-label trials in oncology. The research involved comparing PROs from ipilimumab trials for melanoma and docetaxel trials for non-small cell lung cancer (NSCLC), using individual patient data to minimize bias. Despite concerns that open-label designs might inflate patient-reported benefits or underreport adverse effects due to the lack of blinding, the study found no significant differences in the outcomes between open-label and blinded trial conditions.

Furthermore, findings showed that although differences in PROs were observed, they were not clinically significant, suggesting concerns about open-label bias may often be overstated. The study employed robust statistical methods, such as propensity score weighting, to adjust for differences in patient characteristics, ensuring the reliability of the comparisons. This investigation supports the continued use of open-label designs in certain contexts, reflecting patient realities and maintaining the relevance of PROs in understanding the broader implications of oncology treatments, particularly where blinding may not be feasible. Thus these findings reinforce the importance of including PROs, even in studies where biases may be present.[13] Advancing the field requires continuing to produce empirical evidence that validates their utility.

Leveraging the Core PRO in Cancer Clinical Trials guidance

So, how do we start putting together a PRO strategy for our oncology trials? I will not delve into the steps involved in developing a detailed PRO strategy but would like to underscore the FDA's guidance on *Core Patient-Reported Outcomes in Cancer Clinical Trials* that was recently finalized and which serves as a valuable resource for developing PRO strategies in oncology trials, especially when there is limited information about patient experiences in a particular indication. This guidance provides a framework for integrating PROs into trials, enhancing the evaluation of treatment impacts on symptoms and quality of life. It emphasizes collecting and analyzing core PROs, including disease-related symptoms, symptomatic adverse events, overall side effect impact, physical function and role function. The document offers considerations for selecting appropriate PRO instruments, ensuring they are well-defined, relevant and reliable. It also addresses trial design elements like assessment frequency and methods to mitigate missing data. Additionally, the guidance underscores labeling considerations, highlighting the need for well-designed trials and robust data to support the inclusion of PRO findings in product labeling.

Planning for and mitigation of missing data

Methodological challenges remain significant for PRO analysis in oncology. A major issue in PED, particularly in PRO analysis, is missing data. The SISAQOL-IMI Consortium defines missing data as any uncollected data crucial for a specific research objective. Thus, study protocols should specify how to handle such data, and document the extent and reasons for missing data. For instance, if only patients who feel better complete a questionnaire, it can lead to selection bias and distort results. High rates of missing data often stem from logistical challenges and the demands of implementing PRO assessments in trials, leading to deprioritization. To improve completion rates and tackle these barriers, the literature suggests strategies such as ensuring patients understand the assessment's purpose, providing clear instructions, educating physicians on PRO significance, designating a person to oversee data collection, checking questionnaire completeness, and identifying reasons for missing data. The SISAQOL-IMI Consortium has issued guidelines for managing missing data.[14]

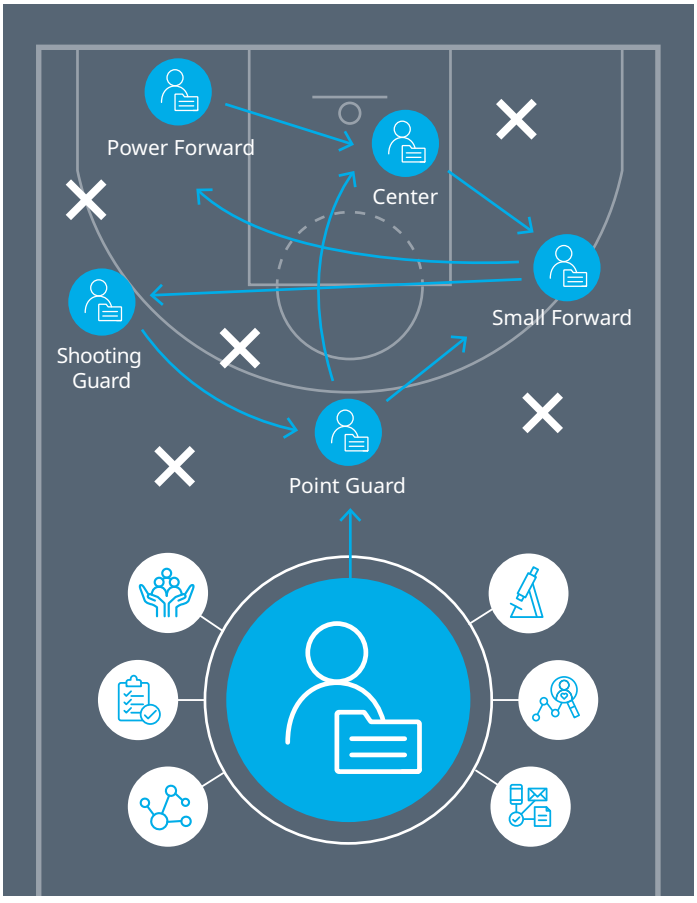
The final basket: Reflecting on progress and vision for future

The integration of PED into oncology trials has been a transformative yet challenging journey. As early-phase trials progressively normalize the inclusion of PROs, regulatory agencies are recognizing their value in assessing tolerability and quality of life. Despite these milestones, the journey is far from the final buzzer. Just as a team requires consistent execution to succeed, so too does the field of oncology need standardization of methodologies to ensure consistency across diverse regions and patient populations. Expanding PED collection into real-world settings is essential, akin to testing strategies on the home court, to capture long-term impacts and provide meaningful real-world evidence. Equally crucial is the development of culturally sensitive tools that reflect the diverse experiences of patients globally.

Throughout this chapter, I've explored the diverse responsibilities and opportunities for PED generation within pharmaceutical development. PED is not just a component — it is a guiding principle that shapes every decision and strategy. Early in my career, I found it challenging to navigate the various functions and stakeholders involved in understanding the patient's experience. Over time, I've embraced the dynamic nature of my roles, akin to the diverse positions on a basketball team, each crucial to advancing a PED-centered approach in pharma. Through collaboration with key stakeholders, I've adapted to different roles, each contributing uniquely to the collective goal. I'd like to leave my readers with a gametime visualization that weaves together these varied roles and the multifaceted aspects of PED generation, illustrating how flexibility and teamwork drive success in our shared endeavors.

- **I've played Point Guard:** The PED expert, guiding the team and ensuring patient experiences remain central to drug development.
- **I've played Shooting Guard:** The primary scorer, creating a robust PED strategy that drives measurable successes, such as PROs in labels and beyond.
- **I've played Small Forward:** The versatile player, blending scientific insight, implementation, and communication to generate meaningful data for regulators, HTA bodies, healthcare professionals, and patients by working with PRO implementation teams, biostatisticians and health economics outcomes research scientists.
- **I've played Power Forward:** The enforcer, pushing initiatives forward and demonstrating PED's value through actionable wins.
- **I've played Center:** The protector, upholding ethical practices, ensuring operational integrity, and safeguarding the molecule's strategic direction.

My hope is that by juggling between these metaphorical roles, we can effectively steer through the dynamic and fast-paced environment of drug development. This approach keeps us grounded in our commitment to a unified, patient-focused strategy, reinforcing both patient-centric values and achieving regulatory success.



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Dr. Rohini Sen is a dedicated advocate for patient experience data (PED) with over a decade of expertise in patient-centered outcomes research, especially within oncology and rare diseases. As the Director of Patient Centered Outcomes Research (PCOR) Oncology HEOR at AbbVie, she spearheads cross-functional collaboration to weave patient insights into the oncology drug development fabric. Rohini's commitment to prioritizing patients was recently recognized with the prestigious AbbVie CAN Impact Award, celebrating her success in integrating PED early in oncology trials. She has an impressive track record of creating innovative clinical outcome assessments (COAs) that enhance patient engagement and facilitate productive FDA and EMA regulatory interactions.

As an active participant and presenter at renowned conferences such as DIA, ISOQOL and ISPOR, Rohini champions the pivotal role of PED in drug development. Her professional journey includes influential roles at Takeda Pharmaceuticals, where she served as Associate Director of Global Evidence and Outcomes for Rare Diseases and Neuroscience. She holds a Ph.D. in Psychometrics and an M.S. in Statistics from the University of Connecticut, alongside a B.S. in Mathematics from Bryn Mawr College. Her research interests span sensor-based digital endpoints, psychometrics, observational research, real-world evidence and instrument design.

Rohini's unwavering dedication focuses on advancing the generation of PED in alignment with evolving industry standards and trends.

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CHAPTER 10

Patient-centric treatment tolerability: Past, present and future

JOHN DEVIN PEIPERT, MELANIE CALVERT, JESSICA ROYDHOUSE, OLALEKAN LEE AIYEGBUSI

The role of the patient's voice in drug development has expanded rapidly over the past decade. This is evidenced nowhere better than the guidance documents issued by the United States Food and Drug Administration (FDA) around patient-focused drug development (PFDD).[1] Initial guidance issues in 2006[2] and 2009[3] was followed by updated guidance either directly or indirectly driven by the U.S.'s 21st Century Cures Act, passed and signed in 2016. Though only binding in the U.S., the Cures Act and its implementation by the FDA have had significant international impact firmly establishing PFDD as a recognized field for patient-reported outcome (PRO) researchers. On the whole, this greater emphasis from regulators on PFDD has been positive in that it has moved us closer to having patients' interests and values reflected in the evaluation and approval of treatments. In other ways, we are still at the start of a relatively new enterprise, and there is more important work to pursue. Here, we reflect on the place of treatment tolerability within PFDD and provide perspective on how to evolve to keep delivering on the promise of PFDD. The emergence of treatment tolerability within PFDD has gained attention for its potential to contribute to drug approvals and labeling claims, potentially serving as an endpoint in some trials, as well as a way to guide post-approval treatment decision-making by providing data on the patient's experience for others to review.

Historically, treatment tolerability, or the extent to which someone can remain on treatment given its toxicity,[4] has been lumped together with safety via clinician-assessed or laboratory-tested adverse event monitoring, even when the adverse events in question are symptomatic. For example, within oncology, the Common Terminology Criteria for Adverse Events (CTCAE) is used internationally in clinical trials. Summaries of CTCAE grades for key toxicities stratified by treatment arm are typically reported in a manuscript reporting the trial's primary results. If the investigational drug did not have too many high-grade events, it was considered generally well-tolerated.

Given the well-documented underreporting of adverse events by clinicians,[5] the argument emerged that symptomatic adverse events should be reported by patients directly. This argument was made throughout the scientific literature,[6-7] but it was perhaps articulated most directly in a Friends of Cancer Research position paper that offered a new definition of treatment tolerability: *"The tolerability of a medical product is the degree to which symptomatic and non-symptomatic adverse events associated with the product's administration affect the ability or desire of the patient to adhere to the dose or intensity of therapy. A complete understanding of tolerability should include direct measurement from the patient on how they are feeling and functioning while on treatment."*[4] Since this definition was published in 2018, significant momentum has built around using PROs to understand tolerability in clinical trials.

The U.S. FDA has signaled that patient input on treatment tolerability is a priority. In its *Core Patient-Reported Outcomes in Cancer Clinical Trials* Guidance for Industry,[8] it identifies five concepts as core PROs: disease-related symptoms, symptomatic adverse events, overall side effect impact summary, physical function,

and role function. Of these, symptomatic adverse events and overall side effect impact summary directly and exclusively relate to treatment tolerability, while physical and role function can be indirect indicators of tolerability. Disease-related symptoms is the only concept of the five identified that would not relate to tolerability. Two recent FDA-approved oncology drugs (involisib for HER2– metastatic breast cancer and selpercatinib for locally advanced or metastatic non-small cell lung cancer) included tolerability labeling claims assessed by PROs and further evidence of the FDA's interest and commitment to hearing and incorporating the patient's voice.[9-10] Alongside this activity, the U.S. National Cancer Institute (NCI) launched its Cancer Moonshot Tolerability Consortium,[11] which funded four projects focused on various methodological topics around use of PROs to capture treatment tolerability in cancer. This follows the NCI's sponsorship of the development, validation and stewardship of the PRO-CTCAE, which provides a PRO option for patients to directly report on symptomatic adverse events.[12] Finally, organizations such as the Friends of Cancer Research and Drug Information Association have dedicated significant attention to treatment tolerability, convening expert groups to further guide drug development.

As a result, the scientific literature over the past decade has been increasingly populated with work advancing our ability to use PROs to inform tolerability, signaling a "new era" of patient-reported tolerability, situated within the modern PFDD framework. But how new is it, really? As an example, the item GP5 from the Functional Assessment of Cancer Therapy (FACT) system, *"I am bothered by side effects of treatment,"* is the leading PRO measure used to capture overall side effect impact.[13-16] Significant attention has been paid to this item's measurement properties over the past several years, and it featured in one of the aforementioned FDA labels. However, it has been in use as part of the FACT-General measure widely in oncology trials since the early 1990s,[17] long before the terms "patient-focused drug development" or even "overall side effect impact" were in our lexicon. Similarly, the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ), which dates to 1987,[18] the FACT-G, and other early PRO measures within the FACT and EORTC systems, contain content on known cancer treatment side effects like nausea. Of course, this content was included to reflect the impact of cancer treatment, not cancer disease, on the patient's quality of life.

So, if we have been using PROs to assess symptomatic side effects and overall side effect impact, not to mention physical and role function, in trials for close to 40 years, what does the recent activity in patient-reported tolerability offer that is new? In part, we might think of historical inclusion of tolerability-related content in PROs to come from a different paradigm than the more recent focus by organizations such as FDA and NCI. The historical paradigm saw inclusion of content on side effects such as nausea and vomiting with the intention of capturing their contribution to or impact on multidimensional quality of life. With measures like the FACT-G or EORTC QLQ-c30, responses to items representing these concepts are taken together with responses to disease symptoms, physical function, emotional distress, and social functioning to generate overall scores that represent quality of life. In the newer paradigm, the goal is to be more parsimonious, attempting to isolate specific experiences with and effects of cancer treatment from effects of the disease itself, or other factors.

If we have been using PROs to assess side effects, not to mention physical and role function, in trials for close to 40 years, what does the recent activity in patient-reported tolerability offer that is new?

Certainly, there are pros and cons associated with each of these paradigms, and our goal here is not to argue for the virtue of one over the other. However, if the "new" patient-reported tolerability paradigm is to continue to evolve and grow, there are some important questions to consider. First, it is useful to consider whether the new paradigm's focus is really on tolerability or not, but instead more on side effect severity or impacts. The Friends of Cancer Research definition of tolerability not only includes adverse events or side effects but also whether those impact the patient's ability or willingness to stay on treatment. Therefore, a comprehensive assessment of tolerability would capture the extent to which a person could or would stay on treatment given the level of side effects they experience. The factors that determine whether the patient can stay on treatment may be "dispositional," like the individual's preferences around treatment (e.g., administration mode and schedule), attitudes or elements of personality, life events, family requirements, and socioeconomic status.[19] To some extent, measures like FACT GP5 and PRO-CTCAE may be tapping into these issues in as much as they capture interference in patients' daily lives; a qualitative study of GP5 found that people understand the term "bother" as used in FACT GP5 to include impact on daily functioning.[16] Additionally, measures of tolerability may need to capture the patient's considerations of trade-off between treatment efficacy and side effects. The best approach for doing so is unclear.

Next, the "new" paradigm is a fairly U.S.-centric perspective, at least in that it has largely been generated by U.S.-based organizations (FDA, NCI, Friends of Cancer Research). Less is known about the opinions of non-U.S. organizations regarding patient-reported tolerability. It is known, however, that the European Medicines Agency (EMA) places more value on, and is therefore more ready to accept, PRO measures of overall health-related quality of life, whereas this is discouraged by the U.S. FDA.[20] Does this mean that there is less need to incorporate targeted tolerability PROs for EMA submissions? Related to this, the "new" patient-reported tolerability paradigm clearly distinguishes between tolerability and safety, such that PROs only inform tolerability.[7] Is the same true outside of the U.S.? Are there cultural differences in how tolerability is perceived? This is unclear to date but will be useful for trialists to optimize PRO-related design in the future. Given that there are cultural differences in how symptoms are perceived,[21] it is indeed possible that the concept of tolerability, especially as it pertains to symptomatic adverse events, differs between cultures as well, even if in small ways. Moreover, the different demands that society places on one's daily life in different cultures may also impact individuals' perceptions of tolerability. One study of the FACT GP5 item across multiple European countries and the United States found no evidence of differential item functioning,[15] but this is a topic that should be studied further, likely with in-depth qualitative interviews.

Regardless of whether the regulatory focus is within or outside the U.S., there is greater need for cultivation of tolerability-focused PRO strategies in non-oncology clinical areas. The vast majority of PRO science around treatment tolerability has been in oncology. The FDA's Oncology Center of Excellence (OCE) has been a major catalyst in this work. In addition to its *Core Patient-Reported Outcomes in Cancer Clinical Trials* Guidance for Industry, which heavily features tolerability, personnel from the OCE have published in the scientific literature on this topic.[6-7,22-23] In addition, the Friends of Cancer Research has published multiple white papers and hosted key expert discussions at its annual conferences on tolerability over the past decade.[24] To our knowledge, other clinical areas have not embraced the use of PROs in tolerability assessment at the same level, though standard and emerging treatments with significant toxicities in other clinical areas certainly have tolerability issues that could benefit from PRO assessment.[25] One exception has been a recent call from stakeholders in solid organ transplantation to focus on tolerability as captured by PROs to support PFDD.[26] In addition, an example of implementing PROs for tolerability assessment outside oncology is seen in the POLARISE

basket trial investigating the efficacy and tolerability of a cell therapy, ORBCEL-C™ in multiple inflammatory conditions, including primary sclerosing cholangitis, rheumatoid arthritis, lupus nephritis, and Crohn's disease,[27] which has used the PRO-CTCAE and FACT GP5 to assess symptomatic adverse events and overall side effect impact, respectively. Interestingly, this trial is assessing the real-time use of PRO-CTCAE or FACT GP5 scores considered severe and/or a PRO-CTCAE™ response of "yes" to notify the clinical team, review the data and complete a CTCAE assessment as required.

Early-phase clinical trials are an area where tolerability assessment is growing quickly but is not yet fully realized. Tolerability assessment in early-phase trials is a natural connection, since the objectives of early-phase trials tend to prioritize tolerability and safety. A recent international expert consensus roundtable including patients, regulators, clinical trialists and PRO researchers convened to discuss the need and feasibility of developing a standard set of PROs for use in early-phase clinical trials, including both Phase I (dose finding) and Phase II (dose optimization).[25] This group concluded that the PRO concepts identified in the FDA's *Core Patient-Reported Outcomes in Cancer Clinical Trials* Guidance for Industry would be suitable for early-phase trials with both oncology and non-oncology patients, and they determined PROs would be largely feasible to implement around a number of different research objectives, but further refinement of the best approaches is needed. For example, participants agreed that use of PROs to inform the clinician's adverse event grading and used to inform dose decisions directly could be feasible, but it is not clear which of these is most appropriate in different trials or trials settings.

More research is needed before PROs are ready to for widespread implementation in early-phase trials to capture tolerability and, indeed, it is ongoing. For example, the Incorporating Patient-Reported Outcomes in Dose-Finding Trials – Analysis Recommendations (OPTIMISE-AR) project through the Institute of Cancer Research in the UK is working to determine PRO objectives and appropriate statistical methods for use in the context of dose finding oncology trials.[28] This builds on novel dose-finding statistical approaches seeking to formally incorporate PRO responses into dose decisions.[29-31] For dose optimization designs, recent focus on comparative tolerability hypotheses has emerged, with a set of new PRO-based tolerability endpoints recently published.[32]

There are other areas where expansion of tolerability assessment through PROs is needed. In particular, medical devices require further scrutiny and likely require a different approach to drugs. Like drugs, devices often entail a host of impactful adverse events, so their safety and tolerability are a routine part of their evaluation. There is similar need for the patient's voice in this evaluation. U.S. FDA guidance and commentary on use of PROs in device approvals incorporates their role in safety evaluation,[33-34] which would be closely related to PRO-based tolerability assessment. To date, devices have largely been left out of the patient-reported tolerability literature.

To conclude, PRO-based tolerability assessment seems to have come into its own in the past decade and still seems to be growing. The fast growth has been enabled by dedicated attention from a diverse set of stakeholders from patients to regulators. It has also been supported by a strong foundation of PRO resources already in place to address key tolerability research questions. The continued growth of this new subspecialty should continue to determine how best to bring the patient's voice into drug development in practical, impactful ways, hopefully sidestepping long methodological discourses that paralyzed other topics in PRO research. To do this, we need to remain focused on what information is needed by regulators to make decisions about the tolerability of drugs, and what information will be useful for patients to understand those decisions after they have been made.

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CHAPTER 11

A decade in: Reflections from the field

CHI PAKARINEN

Thinking about the past — If patient involvement had always been an essential part of drug development, and without evidence of it no drug could get market authorization, how advanced would healthcare be today? Would we have avoided disasters like thalidomide?

How I interpret patient involvement today — The concept and practice of involving the relevant patient community (including their families and caregivers, or people working with and/or representing those affected by the condition) and members of the public in the research, design and development of drugs, treatment and care for a specific condition.

How I hope people talk about patient involvement in the (not so far away) future — A great shift that happened in the beginning of the 21st century in how drug development was done until then: not involving the end user (patients) to inform how and what drugs should be developed or what needs they should address and whether the end user prefer them over the standard of care or alternatives — not to mention the appalling diversity in clinical studies of that era, which luckily patient involvement also helped improve.

Pre-words and a bit of background

My journey in patient involvement started around nine years ago, in 2016. As a complete newbie to the health scene, my only awareness was through doctor's appointments for myself and my family. As we've been fortunate enough to have never experienced serious illnesses, and to live in a county with a highly developed healthcare and social security system, I hadn't even thought about patient involvement at the time.

I had just completed my master's degree when I joined a small company to project-manage a global patient engagement initiative that is now a household name.

This initiative was started by a group of pharmaceutical executives who had been trying to drive more patient involvement in their own companies. With little traction gained, they joined forces with other stakeholders and called for this collaborative program to help accelerate patient involvement in drug development. Thinking back, it should be acknowledged that there was probably a wide variety of motivations for members joining. Back then, when it was unknown territory, those venturing into it did so at their own risk. However, even with this context, all the initial 10–12 members of this group were already united behind a common understanding that, if done right, patient involvement and engagement could help improve healthcare for all in the future.

The earliest aims of the initiative were to try and increase awareness of patient involvement, "legitimize" the thinking that patient involvement should be done because it was the "right thing to do," as well as create information, guidance and instructions on how to deliver involvement activities. Through baseline research, we demonstrated that the kind of **systematic patient involvement** we talk about today did not exist yet. Instead, there were groups and individuals in various organizations who tried to advance their projects, and some publicly funded projects to build patient involvement capabilities (with outputs that you had to already know about in order to have the information needed to search and find them). Materials used different terminology (a debate that we still have within the patient involvement ecosystem today) and almost all focused on slightly different aspects of patient involvement. Very few companies had created positions specifically for patient engagement and advocacy. At the start of this initiative, almost all of the pharmaceutical members had only just begun their "patient-centricity" activities or functions, and many were struggling to get leadership endorsement, or cross-company recognition… a problem that some companies still struggle with today.

Much of the early patient engagement work focused on activities in the United States and Europe. Elsewhere in the global south and east, the concept of patient involvement was not yet established in a notable way, and a bigger focus in some Asian countries was on universal health coverage, patient advocacy for access, reimbursement of certain treatments, and patients engaging and taking more of an initiative in their own healthcare (e.g., when and how to seek for medical advice rather than engaging with pharmaceuticals in drug development). Of course, there were some exceptions to this in 2016 and 2017, but these were very hard to find.

Despite the different angles, disparate approaches, and potential geographical bias in patient involvement methodology development, one message was clear for those who were active in this space: patients do have valuable information, lived experience and preferences that can improve knowledge about the condition and make drug research and development (R&D) exponentially better in addressing the most pressing needs of patients who eventually will need to use them.

Since these early days I've continued in the field, working in various roles relating to patient involvement and engagement, directly driving projects, delivering patient involvement activities, undertaking patient research, and continuing to manage large consortia of interested parties to advance patient involvement and healthcare. However, apart from a relatively short time within a pharmaceutical company, my viewpoint is primarily that of a change agent, a convener of viewpoints, or a consultant supporting organizations to involve patients. I have been lucky enough to have worked closely with many different stakeholders, to have gained invaluable insights to their backgrounds and struggles and am privileged to continue to help shape the field. It's from this perspective that I reflect throughout the rest of this essay.

What have we achieved since 2016?

Patient involvement has seen its ups and downs in the past nine years, but there have been huge strides forward across the globe. It's not possible to describe them all here, but some great wins and highlights are worth mentioning.

- One of the biggest wins in my opinion is the conversion from just a few voices to a (more or less) global agreement that the patients' voice and experiences are valuable in informing health research and medical product development and decision-making, even though how that information should be gathered or used by decision-makers is still debated.
- Advancements in regulatory authority, ethics committee, and health technology assessment (HTA) practice are now driving a mass cultural shift towards

needing systematic patient involvement across research and development. These include regulatory guidance on gathering and using patient experiences in drug development and decision-making, requirements to include patient involvement in health research grant applications, and the inclusion of patient involvement language in good clinical practices and other harmonized guidance.

- We have also seen a broad increase in the number of people with the capabilities to deliver patient involvement activities to the highest standard. These include a rise in the number of patient engagement and advocacy functions within the pharmaceutical and medical technology industry as well as an increase in the capabilities of consultancies and other agencies that support patient involvement activities. The patient community has also increased its capacity and capabilities to work with these different stakeholders and regulators, and patient groups are becoming more organized to equip their own members to do the same individually.
- The shift towards involving patients earlier in drug development (rather than only in launch preparation/commercialization) is increasing the impact and benefit from patient involvement. This means that the design and focus of medicine development is changing not only to meet the clinical, regulatory and scientific requirements, but also to ensure that the medicine or medical device delivers benefits that make a meaningful difference for patients from their perspective AND do this in a way that works for them. Standing patient councils that partner with R&D teams through a medicine's development are also becoming more common.

What about the challenges?

These have all been great advancements, but (and yes, there is a "but" unfortunately), there have also been some struggles along the way that continue to shape the overall progress made.

One of the pitfalls in implementing systematic patient involvement emerges from the daily realities of company structure. For large companies it is natural for silos to occur. Functions are expected to hit their departmental targets and, to make these fair for individuals, they're usually focused on that function's expertise, then translated into personal objectives in a mostly individual way, as free as possible from reliance on cross-functional collaboration and co-creation (so that they are clear, achievable and measurable). Throughout key strategic activities such as due diligence when in-licensing a product, or organizational restructuring, many companies have so far observed the need for patient-centricity, but not always recognized consistent and systematic patient partnership as an essential strategic leverage that can derisk investments and future change. Frequently, restructures result in scrapping previous advancement a company made in increasing its patient involvement capabilities and leadership position, and "reinventing the wheel" as another person is brought in and another new approach is tried. Rather than building on and improving, new hires frequently have an almost free reign to implement what they understand as "integrating the patient voice in drug development" — which can be drastically different to the known good practices, in some cases removing almost all interaction with patients and replacing it with social listening and database scraping rather than gathering direct understanding. Activities such as restructuring are essential for ongoing efficiency and serve a bigger purpose; however, if delivered whilst recognizing the need for patient involvement as a key strategic advantage alongside other core requirements, then transformative change is within reach. One that builds on the integration of direct patient partnership with qualitative and quantitative data collection, supporting many functions to unite, strengthening strategies after the change, and directly tackling key recognized challenges such as lack of adherence to treatment, the cost of clinical trials, and being able to address precisely what is needed by both doctors and patients in the real world.

When delivering patient involvement activities, challenges occur through differences in understanding of what patient involvement is, what it is for, and how to engage in a way that is compliant with codes and guidance. For small companies, this may result from a lack of capability build as they race to develop. For large companies this is more often experienced as large amounts of real and perceived "red tape." Instead of engagement being strategic, integrated, planned and slick, it's often an activity done "later in the day" and begun without compliance and legal teams being included in the design of the patient involvement activity because they're perceptually linked with slowing or stopping progress. In addition, where there are teams that lead patient involvement efforts, they're generally a very small group of people in a very big company. They sit alongside other departments helping a myriad of functions. This hub of expertise is wonderful, but introduces a very practical challenge. As they support many functions, they generally aren't within the "core" team for all of them. Activities in their remit then become perceived as an important but non-core activity. This increases the likelihood of these teams having to shout louder to be integrated and given equal priority, patient involvement either being "added on" later in the process or missed entirely because it wasn't planned in, or timelines being shortened and patient involvement is considered something that can be trimmed. In addition, as regulatory expectations increase around patient involvement being a standard activity, these teams may find themselves struggling with scale-up at the same time as having to defend the budget for patient involvement, move their field forward within the company, deliver high priority activities, and educate and train the whole organization.

The aftermath of all this can be an impact on trust and reputation for those in existing collaborations and partnerships. In some cases, patient groups are left hanging for months without knowledge of what has happened and whether projects or partnerships are to be continued. Funding can sometimes dry up as priorities change and, combined with staff turnover, there is no way to smooth the transition from partnership into radio silence. As this is the patient community the pharmaceutical company is developing drugs for, it can have longer-term impact on the hard-earned trust and willingness to work together in the future, slowing in the longer term the progress made towards strategic integration of all stakeholders in product development. After witnessing this happen frequently in the past nine years, I'm left wondering, what will it take to break out of this cycle? Change is needed, because at the moment this cycling is limiting the scale-up of patient involvement within companies, and the development of trusting, compliant partnerships to ensure that new medicines optimally integrate clinical aspects and meaningful difference in patients' daily lives. Without addressing these fundamental challenges of collaboration, equal prioritization, using a strategic approach, and then ongoing connectivity and partnership, companies are likely to struggle with the next step being asked of them — gathering diverse and representative input. Going all the way back to the origins, medicines do not work if people will not take them. Currently the patient representation within clinical development lacks the diversity of population needed to transition smoothly into real-world use. This is noted by the authorities and requirements for improving diversity are becoming more prevalent. However, diversity and representation in research starts with engaging patients, understanding and then meeting the needs of a more diverse and representative patient population, and this requires patient involvement. There are reasons some groups don't, or can't, engage currently in patient involvement activities — addressing the previous challenges, and finding a way to make involvement simpler, better, more accessible, and more widely known is going to be essential for this expected progress to be made within clinical research and medicines development.

As in any product development process, when human-centered design is applied, the speed for that product to get to market is accelerated and its chances to succeed grow manifold.

This leaves us in the current situation that, despite efforts from all stakeholder groups, patient involvement still seems often a sporadic, activity-at-a-time kind of thing for most — nowhere near the systematic practice it should be. As in any product development process, when human-centered design is applied, the speed for that product to get to market is accelerated and its chances to succeed grow manifold. It's time for medical products to also follow this route and reap the benefits, especially as there is effectively no product without patients using the therapies in the real world, in practice, and changing their health, quality of life and even life expectancy.

What should be done, then?

The great news is that the field is consistently moving forward and improving, even though currently from observation, this progress appears to be more of an ongoing cycling pattern than a strategic and honed straight line. Luckily, it's something we can fix with collaboration and the strategic imperative to do so.

- Make that systematic shift to requiring patient involvement across the company. Make patient involvement the underpinning theme that cuts across all R&D phases so that NOT having it would raise red flags across the company immediately. Ensure that it's an essential requirement at every decision-making point and every "go/no-go" evaluation from business development, investment opportunities and early research all the way through development phases, regulatory submissions, commercial activities, market access and beyond. Start documenting all the differences in behavior change, in outcomes, timelines, investment and cost of R&D, and impact to the business and patient community. Publish the journey of how you got there, the results, and the impact. This way you support this shift and lead the charge in truly making systematic patient involvement happen and improving health outcomes.
- Make patient involvement a mandatory training for all and create annual objectives for all staff to be part of patient involvement activities regularly — recognizing that timely cross-collaboration and sharing is a key and essential for maximizing the benefit. Praise this co-creation and sharing as part of the process that can be measured. This way internal capacity and capabilities grow exponentially and it does not fall on any one or two small teams to fight their corner and ensure that patient insights are integrated to inform decision-making.
- Alongside these changes, broaden the models and inputs used to measure return on equity (ROE) and return on investment (ROI) including elements such as the impact of increased trust and reputation that helps you partner with patients, increase in focus and data supporting target product profiles, clear line of sight from these target profiles defining defensible, integrated and relevant research questions, leading to the developed drugs that both clinicians and patients value, need and use. By doing this, it will become increasingly possible to compare results with those from the time before patient involvement. Publishing the impact will boost further both reputational gains and advance the field to make it even easier to engage with the broad representation of voices needed to create a future where people have life-changing medicines no matter what their background, ethnicity, location or belief system is.

Change is coming whether people like it or not. Strategically embracing this has the potential to be transformative across many areas — health outcomes, medicine/medical device development timelines, uptake and access, and reputation. We need to work together to address the known challenges, and reach for this future, because without it, everyone, including you and I, will suffer the consequences of not involving patients in drug development, by not having the right medication or treatment when we need it.

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With nearly a decade of experience in patient engagement and involvement, Chi Pakarinen has been at the forefront of initiating and leading global multi-stakeholder programs that aim to drive and accelerate the uptake of patient involvement in drug development. Chi's expertise spans strategic planning and practical implementation, with a proven ability to foster collaboration among diverse stakeholders within the healthcare ecosystem. Taking a solutions-oriented and inclusive approach, Chi has consistently delivered impactful results in advancing patient-centric initiatives.

Chi began her journey in this field with PFMD, contributing significantly to the initiative's growth from its early days into the widely recognized name it is today. After PFMD, she worked with a pharmaceutical organization gaining valuable experience and perspective before joining MediPaCe in 2022. MediPaCe is a values-driven patient involvement and research consultancy continuing to champion innovative strategies to elevate patient involvement on a global scale. Chi also works with Project-COMFORT, a multi-stakeholder, public-private partnership that aims to make patient-centric blood microsampling an accepted alternative to venous blood-draw across Europe.

What drives Chi is the belief in making meaningful change happen to achieve better health outcomes for the future, and she is deeply committed to doing her part in this transformative journey. She feels proud working in patient involvement field and hopes that her parents will be able to benefit from the results — a more inclusive healthcare and treatments that fits their needs when the time comes.

Disclaimer: The views, opinions and statements made in this presentation are solely those of Chi Pakarinen and may not reflect the views of MediPaCe or its affiliates.

CHAPTER 12

The state of patient-centricity in drug development is strong and getting stronger! But we all have work yet to do...

ASHLEY F. SLAGLE

I wish to thank Matt Reaney for coming up with this interesting book idea and for inviting me to participate as a contributor. I am passionate about patient-centered drug development, and healthcare decision-making more broadly, and it has been a pleasure to reflect back over the past 25 years of my involvement in drug development to think about the evolution of patient-centricity! I also want to thank the reader for taking time to read — the text below was a fun (to me) sort of stream-of-consciousness approach to sharing my perspectives. It is strange to write something so personal rather than a scientific research paper. Enjoy. Or don't. But I enjoyed writing this.

I had the privilege to work at the United States Food and Drug Administration (U.S. FDA) in the early years of patient-focused drug development (PFDD) and patient experience data (PED) — helping to shape the development and encourage the implementation of important legislation, which in my view has moved drug development squarely into the era of true PFDD. Now outside of the FDA, much of my work continues to focus on PED intended for use in regulatory decision-making. Therefore, my contributions to this book are largely from the U.S. regulatory perspective but are informed from working with pharmaceutical companies pre-FDA and post-FDA.

In general, I am pleased with the success of the patients, the FDA, pharmaceutical companies, healthcare providers, and other stakeholders who have encouraged and embraced meaningful PFDD. We have more work

The author, 25 years ago, excitedly beginning her pharmaceutical research pursuits, but not yet aware of how fulfilling a career in patient focused drug development and patient experience data would ultimately be.

to do, and we cannot stop striving for improvements in PFDD, but for now, I hope we can take some time to reflect on just how far we've come in a fairly short timeframe. In the course of maybe 15 years, I have seen the change from patient perspectives not being widely included in drug development to today when the majority of industry sponsors are to some extent incorporating patient experience data into their drug development plans.

In the mid-2000s, I remember speaking with a key opinion leader (KOL) who was a clinical expert in a particular disease area. Two of us were speaking with this KOL to gain some early insights on patient experience with a particular condition and its treatments to be better prepared for upcoming patient interviews. I started the discussion asking the KOL what he could tell me about the patient experience with the condition. He had little to say other than discussing some biomarkers he uses to decide if patients are "doing well." Then, I asked him to help me understand the patient experience with a certain class of drugs widely used in the condition (anecdotal evidence at the time suggested there were some tolerability concerns). His response was, "I don't

really care what the patients think. The drugs work. That's it." I was flabbergasted. Here I was, a new patient-reported outcome (PRO) researcher, excited to learn all I could about the patient experience and the possibility of participating in the development of new drugs that "worked" but also did not have the same tolerability issues. After my colleague helped me out by stepping in to try to facilitate some awkward follow-up discussion, we found a question that seemed to help the KOL be (albeit begrudgingly) more concerned about patient experience. I asked, "Do you ever hear patients raise concerns about these tolerability issues and that these issues have led them to discontinue or be less adherent to the prescribed treatment regimen?" Suddenly, the KOL cared about tolerability and the patient experience! Because tolerability experiences did indeed impact adherence, and when this happened, patient outcomes (as he assessed them) were poorer. The KOL then helped us better understand the patient experience of tolerability so that we could hopefully play a part in developing more tolerable drugs. His ultimate goal was to have these newer drugs developed so that patients would "listen to him and be adherent to his orders!" We achieved our goal — that is, we had some early insights to inform our very important discussions with patients (where we learned how the tolerability issues were truly impacting them).

I learned a valuable insight from that interaction. That is, when people fail to appreciate the importance of the patient experience, which occurred regularly back then, it is important to find the link for them as to why they *should* care about patient experience. For this KOL, he needed to see the link between patient experience and being compliant with his prescriptions. For drug company decision-makers, they often need to understand how incorporating patient experience will improve drug approval and reimbursement decisions or uptake once on the market. For FDA reviewers, it is often related to ensuring that outcome measures in clinical trials, upon which they base their approval and labeling decisions, are reflecting how patients feel or function in daily life, and that changes in outcomes observed in clinical trials are indeed meaningful at the patient level.

There are thousands of arguments for why patient experience should be incorporated into drug development, but to me it sort of boils down to: we are *all* patients at some point; we should all want patient voices, our voices, to be heard and incorporated into health decision-making. I know that in drug development with tight timelines, limited resources, and big egos, sometimes there are challenges still in listening to patients. But I am happy to report that over time, the kinds of experiences I had with that KOL and others rarely occur. Maybe I've learned how to interact with people better to encourage PFDD, but I like to think that as a society we are constantly growing and increasingly embracing patient experiences and PFDD.

The FDA, in my view, has played a huge role in encouraging PFDD. When I arrived at the FDA in 2012, we were tasked with implementing the Prescription Drug User Fee Act (PDUFA) 5th Reauthorization. This was the first piece of legislation (that I recall) that highlighted PFDD. It provided more funding and a commitment to add more FDA staff to review PRO-based endpoints. It also began the now well-known "PFDD meetings" and the resulting Voice of the Patient reports that would come from those meetings. I was thrilled to be able to help plan and participate in PFDD meetings, beginning with the very first one for chronic fatigue syndrome. FDA staff were incredibly focused and worked hard to make those meetings successful. We viewed success as being able to truly understand what patients experienced with their condition and treatments, what is important to them for treatments, how they weighed benefits and risks, and anything else they viewed as important for us to know. I participated in or attended almost all of the first 20 FDA-led PFDD meetings. In my view, the meetings were a success and the evidence from those meetings was used internally to better understand the patient experience when reviewing and providing advice for drug development programs. FDA then encouraged

external groups to hold PFDD meetings, and these have been conducted across a wide range of health conditions, generating important early information on patient experience.

At first I thought that Congress, lobbied by patient groups, unilaterally drafted legislation and then the FDA was "forced" to implement that legislation. But I quickly learned that we at the FDA had a voice in shaping FDA-related legislation. For the subsequent legislation that helped to further encourage PFDD, Congress did not unilaterally force FDA to undertake PFDD activities. Rather, FDA proposed PFDD-related activities that we thought would help us better encourage and implement PFDD. The development of additional legislation while I was still at the FDA, specifically the 21st Century Cures Act and PDUFA VI, was a collaboration among FDA staff, pharmaceutical companies, patient groups and others. We all contributed components of the legislation that from our collective experiences would help facilitate better PFDD. This collaborative effort by various stakeholders, overseen by Congress and codified into law, has undoubtedly improved (and continues to improve) PFDD, and in a relatively short timeframe.

PROs have traditionally been the most widely used type of patient experience data in regulatory decision-making. I would therefore be remiss if I didn't mention the FDA PRO Guidance.[1] I know that there are mixed views on this guidance from internal FDA staff as well as external stakeholders. But here I offer my own personal view. Prior to the PRO Guidance, the use of PROs in drug development was the Wild West. Industry was pulling questionnaires off the shelf because the literature described them as "validated" and the name of the measure suggested it assessed something that might be important to measure. Or clinicians and researchers were drafting questions for PRO questionnaires without any patient involvement. I've heard old stories about a group of clinicians drafting a PRO measure on a napkin over beers! These various measures were included as the basis of trial endpoints and in some cases made it into FDA product labeling without consideration of whether the measure was truly fit for the purpose of evaluating treatment benefit (that meant something to patients) in clinical trials!

The Study Endpoints and Labeling Development Staff (SEALD) in FDA's Center for Drug Evaluation and Research (CDER), was instrumental in reigning in questionable PRO labeling claims that were likely an overstatement of benefit and potentially false or misleading, by diligently working on the PRO Guidance to put rigor around the research and evidence required to support the use of PRO measures for regulatory purposes (i.e., approval and labeling). The SEALD group was tasked with reviewing PRO evidence using the principles in the guidance to help review divisions make approval and labeling decisions. It is sometimes a thankless job to put rigor into something that previously was not rigorous, and there were complaints from industry that it was now "too hard" to get PROs in labeling. Many blamed the guidance. But to me, the PRO Guidance did three things:

1. It ensured that PRO labeling claims would be based on things that are important to patients.
2. It safeguarded against claims being potentially false or misleading or overstating benefits.
3. It highlighted the FDA's interest in patient-reported data from clinical trials.

Reining in the Wild West was not easy, and there were many frustrations as drug companies tried and sometimes (often?) failed to achieve PRO labeling. SEALD was a small group and did not have the staff to provide as much advice as early as could have been useful to pharmaceutical companies. Companies also cut corners (or didn't fully understand what was necessary vs. "nice to have") on PROs, hoping to still achieve labeling. It was a trying time. But, with more outreach by those of us in SEALD (later renamed to Clinical Outcome Assessment (COA) staff, and now Division of Clinical Outcome Assessment (DCOA)) and growing the staff to be able to

better provide more collaborative advice throughout the drug development timeline, it seems that PRO evidence and labeling is not as hard to achieve as it once was. Though I do not want to gloss over the challenges DCOA has with staffing and difficulty meeting timelines due to this. This is just a reflection of the success DCOA has had — the submissions to them continually outnumber the staff they have available to provide advice. This speaks to the increasing importance and use of patient experience data. And, if anyone in Congress happens to be reading my book chapter, please, please, please consider increasing funding further at the FDA to hire more COA and PED experts!

Back to the PRO Guidance… to me, it was the start of something big. It was a focus on the need for rigorous methods to more objectively measure patients' subjective experiences. To document a PRO measure as fit for purpose, one critical required step was — wait for it — actually talking to patients! To the newer researchers reading this, you may find it hard to believe that patient input was not always gathered when developing PRO measures. But now, this is common practice, thanks to the FDA PRO Guidance. Of course, we've seen additional guidances from the FDA in more recent years, particularly the PFDD Guidance Series,[2] which expands the discussion of evidence to all COAs (not just PROs) and highlights more methods of generating important PED beyond just PROs used as endpoints in trials.

Over the last 15 or so years, we've seen a real evolution in the development and use of PRO data. It finally feels (to me) that we are in a pretty good place with PRO measures intended to support approval or labeling claims. There are still some misses, but all in all, this field seems fairly mature and is working reasonably well between the FDA and industry, and I hope patients feel they can obtain meaningful outcome information through FDA labeling, publications and plain language summaries that are increasingly provided by industry. This is not to say we cannot continue to improve, though.

While PRO endpoints are becoming more comfortably used, we are still in the earlier stages of figuring out how best to use and generate evidence for other types of PED for regulatory purposes. For example, patient preference studies, including patients more directly in benefit-risk decision-making, engaging patient experts on drug development teams or even regulatory review teams are all areas where there are not yet well established, agreed-upon methods and processes. Exciting times lie ahead as we try to better implement and use these methods and more! And I see a willingness on the part of the FDA and industry sponsors to collaborate with patients to figure all of this out.

Exciting times lie ahead as we try to implement and use better methods of generating patient experience data!

Reflecting back again on my career in the early 2000s, I remember talking to people about making drug development more "patient-centric." One site investigator told me, "We ARE patient-centric, we have patients as subjects in our trials." Ugh. Well, after 25 years in this industry, I can say that I no longer hear this kind of comment. At least we've moved to a point where if someone is thinking this, they know better than to say it out loud! Seriously, though, over time, I've seen a real evolution in thinking. Of course, we still need and value the willingness of people to participate in clinical trials. There would be no drug development if it were not for this willingness. But I am also seeing other interesting ways of involving patients in drug development.

For PRO measure evidence generation, we engage in qualitative research with patients (e.g., interviews or focus groups conducted with rigorous methods). This research can be used to achieve other objectives as well, including understanding qualitatively what is meaningful change on endpoints from a patient's perspective, how patients value benefits in the context of possible risks, and so on.

I am seeing much more collaboration with patients in the form of patient expert consultants to pharmaceutical companies. For example, patients are reviewing and providing advice on trial protocols. There have been several times when I have seen patient input fundamentally change a study design, which likely saved companies from failing to recruit or retain patients in a trial. And, unfortunately, I've seen trials fail to recruit due to design issues that probably could have been caught in advance had patients reviewed the protocol.

One unfortunate trend I'm seeing is that some in industry want to collect PED for optics or "credit" from the FDA. Patient engagement activities are conducted, and studies are run with patients just to be able to tell the FDA, "Look how patient-centered we were!" Literally, I've heard that as a stated objective. This is exactly NOT what the FDA is asking for. Of course, the FDA is encouraging PFDD. But the FDA has been very specific (see the PFDD Guidance Series[2]) that they view PED as another type of data that should be collected rigorously to **answer defined research questions** that can inform their decision-making. Embedding patient experience data into internal decision-making and to assist in FDA decision-making should be the overarching goal. Collecting PED for PED's sake wastes industry resources and patient time and does not win any favors with the FDA.

What I think may be the next evolution of patient involvement with pharmaceutical companies is for patient experts to participate in research teams. This is not yet common, but I had the pleasure of being involved in one program where the research team, whose objective it was to develop a novel PRO measure, included measurement scientists, a regulatory expert, clinical experts, and *patient experts*. This collaboration was the first of its kind for me, and I truly valued the experience. I expect (hope) these types of collaborations will continue and become more frequent into the future. If you are interested in reading more about this collaboration, enjoy the open access article.[3]

The biggest challenge I'm seeing currently with PED is that there is a disconnect sometimes between what PED sponsors choose to provide to the FDA and how FDA uses PED. As I noted above, the FDA does not want to review PED for PED's sake. The PED should be rigorous and be able to be relied upon for FDA decision-making. It is also helpful to tell the FDA how the PED relates to a decision they need to make.

- Is the sponsor asking the FDA to allow a shorter trial than originally recommended based on patient input? Discuss that patient input with the FDA when discussing study design.
- Is the sponsor using data from a natural history study to justify the frequency of assessments in a trial? Discuss that natural history study data when discussing the protocol and assessment frequency.
- Is the sponsor submitting evidence that a COA is fit for purpose as the primary efficacy endpoint in a pivotal trial? Provide that evidence in a COA dossier.

Unfortunately, what I have seen too often is that sponsors will develop one huge "patient experience data dossier" which is a document that includes everything possibly related to patient experience. When packaged like this — and not linked to decisions the FDA needs to make — these huge dossiers risk going unread. When they are not read, important information will be missed! But it is asking too much for busy FDA reviewers to read 1,000 pages to find the 10 pages of information relevant to a decision they must make. When sponsors sense that the FDA did not read the PED dossier in full, they become frustrated and think that no PED is worth generating. This is unfortunate and has sadly led some sponsors to discontinue many of their PED activities. My hope is that sponsors will do a better job of integrating PED into drug development decisions, rather than siloing it off as a checkbox exercise, and do a good job communicating this information to the FDA (and any other stakeholder). I also hope that the FDA continues to publicly share how it views PED fitting in and how it has used PED in decision-

making, and provides suggestions on how to better communicate PED to the FDA so that important PED is not overlooked and can inform decision-making.

To ensure that new drugs are developed in line with patient priorities, preferences and needs, I think we need to expand on the good science and methods that we have already established for PRO data: expanding methods to allow us to better rely on patient preference studies, patient benefit-risk weighing, patient treatment goals… FDA is already focused (thanks to PDUFA VII) on developing methods for these additional PED types. So, in part, I think we need to be patient. We also need to be proactive — take calculated risks (when we can) to try new methods. Invest in rigorous, objective-driven science. Make patient-centricity always top of mind. We need to be strategic, thoughtful and kind. We have come a long way in patient-centricity in drug development, but we have more to do. And remember, as we and our loved ones are all patients at some point, we should all be striving for patient-centricity together!

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Dr. Ashley F. Slagle is the Principal and Founder of Aspen Consulting, LLC where she provides strategic regulatory and scientific advice to drug developers on matters related to patient focused drug development (PFDD), with a particular focus on patient-centered endpoints and clinical outcome assessments (COAs) to support medical product development and approval. Ashley's experience includes 25 years of pharmaceutical outcomes research, policy analysis and COA development, implementation and analysis to evaluate treatment benefit for regulatory purposes. She participates in scientific advisory boards and advises sponsors across a broad range of therapeutic areas to ensure the patient's voice is meaningfully incorporated into drug development to inform stakeholder decision-making.

She previously served on the COA Staff at the FDA. There she provided oversight on reviews and recommendations related to the development and use of COAs and worked closely with CDER review divisions to make drug approval and labeling decisions. Ashley participated in FDA policy and guidance development and legislative activities related to PFDD, COAs and endpoints. She received her MS and PhD in Pharmaceutical Health Services Research from the University of Maryland, Baltimore.

Why is Ashley passionate about patient focused drug development? Because it matters. What is the point of developing drugs if not to make patients meaningfully feel and function better? And how do we know what is important to patients feeling and functioning better if we do not incorporate their voices into the drug development process? And she also really enjoys the strategy of it. How do we fit the puzzle pieces together to incorporate patient experiences into drug development, and do it in a way that provides evidence the FDA needs to make decisions and provides pharmaceutical companies with evidence to de-risk trials and bring good, valuable drugs to the market? And finally, she enjoys PFDD because there are some really great people working in this field. She feels privileged to spend her days working with smart people who are doing their best to incorporate patient experiences into drug development.

CHAPTER 13

Why patient-centricity is not fit for purpose: Mutual investment, the new people-centric model for research and advocacy

AMELIA HURSEY

Introduction

Putting "the patient at the center of research" is the current position being taken by industry, health care researchers and advocacy experts. However, if you have a conversation with many in the field, exactly what this means in a practical sense is often unclear, misunderstood and inconsistent. Just doing a quick search through websites, publications and classification documents about this initiative, much of the terminology used in the activity of "patient-centricity" is littered with confusion. What does each stakeholder mean by patient engagement or involvement? When is it only consultation? When does it become meaningful collaboration or co-production? How do we even evaluate that it made a difference?

If you haven't noticed, all of these terms are very unlikely to be used by the patients themselves, especially with the imparted meaning intended. It's like a lexicon game of piggy in the middle where the bigger kids (industry and researchers) are throwing the beanbag to each other over the head of the younger, more naive child (patients and patient organizations) and saying to the parents that they are making the game about their younger sibling. I think we all remember these moments, and I'm pretty sure that the game ended when the younger child got fed up with not being able to catch the beanbag. Yes, this is a triad model; however, it is more of an isosceles triangle rather than an equilateral one (the holy grail).

So why have we continued to pursue this vexatious model in the world of research and think that we are doing the right thing? The comms and optics look great, but the reality of the activity lacks satisfaction and cultural change for all parties involved. So, I would like to suggest we move into a new era of mutual investment, putting the outcomes of high quality research at the center and dissolving the "us and them" attitude.

History of patient-centricity and patient and public involvement

If you look back through history, most of the time the person experiencing an affliction led the way with their medical care. They described their symptoms to a trusted person within their community. The trusted person then suggested some solutions which the individual tried and decided if they worked or not, informing the trusted person of the outcome (if they lived). The trusted person would then gather insights that would hopefully make the next time they treated another member of their community more successful. However, at the heart of this interaction was trust.

In our modern-day societal version of this, community trust has been lost.

This was the motivator for the first patient involvement activities to spring up as a grassroots movement in the 1970s. People in the UK with disabilities lost trust in the research that was happening and impacting their lives, and so proposed a model that equalized their relationship with researchers, making them empowered

patients instead of research subjects. All other involvement models since have requested the same recognition. This is not the same as putting the patient on a central pedestal. Doing that still utilizes the "us" and "them" aspect rather than recognizing the collective position. Without all stakeholders represented in a way that feels equitable, no progress will be made. We don't want the youngest child to walk away from the game.

The stakeholders and their values

To bring my concept of mutual investment to life, I am going to venture away from the usual titles to help underpin the different values that each trusted stakeholder group in our community can bring to the table. There are going to be some mavericks that fit within all three groups and can wear whichever hat fits best, multiplying the value output. Also, the values I have listed are not exhaustive; I have only identified the most apparent and visible values, from which we may achieve adoption of them by all stakeholders.

- **Lived experience experts**
  Primarily these are people who are diagnosed with a specific medical condition, their partners and family members. Also included in this group are friends, advocates and patient organizations who work with individuals within the identified health community.

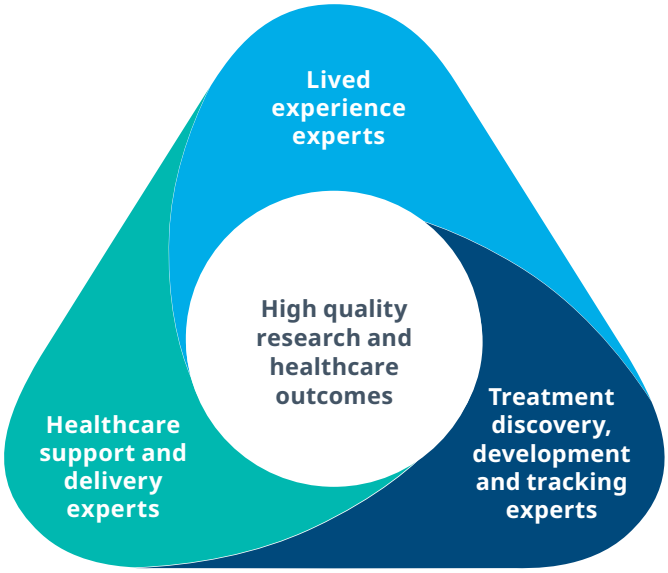
  The value this group brings to the table is not only of individual daily lived experience of the condition but also the collection of those individual voices into a mass of intelligence and insight, helping to provide a global perspective.

- **Healthcare support and delivery experts**
  These are professionals working in medical healthcare systems across the globe and individuals working in paid care delivery systems. These individuals have collective knowledge of what they have observed in the professional setting they work in, as well as their professional training and accreditation.

  The value this group embodies is clinical expertise, understanding the challenges within healthcare system delivery and innovation, and global networks of shared knowledge with professional peers.

- **Treatment discovery, development and tracking experts**
  Within this group are pharmaceutical industry personnel, health tech developers and academic researchers. The main focus for the collective output from this group is new treatments or therapeutics, technologies or discoveries that will improve health outcomes.

  The value output from this group is understanding the global market, scientific, technological, research methodology, licensing and governance expertise, and money.



How to achieve the mutual investment — values being recognized by consensus

Lived experience experts can rarely bring enough financial strength to the table to see a treatment all the way from inception to licensing and use in healthcare systems. Neither can healthcare support and delivery experts, but they can help with understanding how a

product may actually work in a real-world health system. Treatment discovery, development and tracking experts rarely have real world experience linked to the work they are doing. So, in simple terms, each stakeholder has a value that the others don't. Without each stakeholder, the potential for new research discoveries and outcomes is extremely limited and unlikely.

In the research world there are many individuals, communities and groups who are underrepresented, or not represented at all. This is not just in those who take part in and lend their voice and expertise to research, but also in those conducting and delivering research. Part of this is due to the lack of "seeing themselves" in this world. If these individuals can see their values or value systems being included into research in an understandable and accessible way, they then may be more able to see themselves as a valued stakeholder in research, increasing the trusted community and making it representative of the whole world, not just the Caucasian west.

To create a trusted community linked to research, each stakeholder group's values need to be recognized and evaluated in relation to each other. This doesn't mean that their inputs must be equal — that will never be achievable. Whatever each of the stakeholders can put into the research process must be seen as of equitable value, making each stakeholder feel like their input is of equal importance. All stakeholders need to agree on the currency and exchange rate of values.

As an example, time is something we all hold in a value state. Whatever time one of the stakeholders can put into a project, it holds its value. For a patient organization, due to the number of its personnel, the time they can put into a project may be limited to five hours a week, whereas a tech company that is driving forward a new product may have many staff members and can give 30 hours a week. This doesn't make the five hours any less valued than the 30 hours. Both stakeholders have recognized that due to their circumstances, their input is equitable as the focus of their activities is still the same — a new product that will be available to improve the well-being of people with the condition they are both invested in and will get returns from. This then creates a trust community that others can see and understand. It removes the small naive child from the piggy in the middle and recognizes them as an equitable partner in the game.

How to implement the idea into cultural change

The first step is to establish a "values system" that is relevant to your organization or project and make sure it can be adopted by all stakeholders, i.e., comparable inputs such as time, expertise, finances, etc. This will avoid tokenism and putting one person at the center, bringing a shared language to the activities that everyone can buy in to. The terms selected in the value system also need to be words that everyone can understand, including people in the street, so they can see themselves represented in this work.

When you've used that value system once, you can see how easy it is to map it to the rest of your organizational activities and therefore start to change the culture. This cultural change needs to be supported and incorporated by all stakeholders, who should also support each other in the adoption of these new behaviors into their individual communities. It is only when the demand reaches a critical mass of voices which is repeated multiple times that cultural change (especially on an organizational level) is invested in and enacted. This is not a quick process, but an ongoing, time-intensive commitment that should be systematically reviewed and reflected upon to maintain its effectiveness and to make sure it's achieving its desired impact, removing the risk of it becoming tokenistic.

On top of this, the things you will learn from each research project that follow those values will start to produce mappable universal truths that can easily be measured and shared. Beyond the metric of a treatment item being brought to market, the learnings of where value inputs have been made by the different stakeholders can then be evaluated to justify more investment in those activities in the future. When outcomes are transparent and recognition of value is

an explicit activity, then trust communities can be created and sustained. I recognize I have not considered the governance and legal hurdles that will need to be overcome to achieve this; however, this is not my area of expertise, so I will allow those better informed to step forward with that solution.

In conclusion, if we aim for a mutual investment state, the future of research as a truly inclusive system with equitable meaningful representation of all stakeholders can be achieved.

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Amelia joined the Parkinson's Europe team in January 2022 as Research Manager, progressing to Strategic Director from January 2025. She has developed Parkinson's Europe's Research Strategy, embedded a volunteer Research Steering Group into the organisation and helped to increase the presence of Parkinson's Europe in the clinical research world. She is also focused on bringing new initiatives to the table, such as the Parkinson's Europe's Engagement Network, which better connects the Parkinson's community across Europe. Parkinson's Europe is now a partner member of EUPATI, of the nonprofit coalition to support advancements of Disease Modifying Treatments for Parkinson's, Dementia with Lewy Bodies and Biologically related disorders, and the Critical Path for Parkinson's. She co-developed Parkinson's Europe's new 2025-2028 strategy and will be leading its delivery.

Amelia has been working in the field of Neurodegenerative research since 2009, is a Patient Organisations board member with EUPATI and a member of EAN's Guidance Production Group. She previously worked for the UK NIHR's DeNDRoN delivering clinical trials and then at Parkinson's UK from July 2015 as Research Participation Lead. She was responsible for initiatives to increase research participation for people affected by Parkinson's, health care professionals and researchers, and created the innovative Parkinson's UK Take Part Hub and co-produced the Staying Connected toolkit in collaboration with the HRA UK.

As soon as she started working in clinical research in the NHS, Amelia became aware of the absence of the patient voice in research design and inception. The complexity of what clinicians were trying to share with patients about the medications they were going to have to take for the rest of their lives could have been so much simpler if the end user (patient) had really been consulted during the research phase of the therapeutic development. This was 15 years ago.

Although improvements have been made to engage with end users in the research process and there are some fantastic examples of it out there, as a research community we are not consistently doing so. This is why Amelia is still passionately pushing towards a more equitable inclusive model of collaboration between the patient community, researcher and the health and pharmaceutical industry, aiming to improve the future for all of us, as one day we will all be patients.

Disclaimer: The views, opinions and statements made in this presentation are solely those of Amelia Hursey and may not reflect the views of Parkinson's Europe or its affiliates.

CHAPTER 14

United in purpose and founded in trust: Transforming clinical research through grassroots initiatives

SARAH McKEOWN-CANNON, VICKY DiBIASO, ANGELA RADCLIFFE

Reflections: A vision born in a creative throwdown

It all began during a "creative throwdown" at a New York City ad agency. Frustrated by the traditional, transactional approach to clinical trial recruitment, the Heartbeat team dared to imagine something completely different — something rooted in trust and genuine collaboration with underrepresented communities. The idea was brought to leaders at Sanofi, who immediately saw its transformative potential. Together, they laid the foundation for *Reflections,* a grassroots initiative designed to reshape how clinical research engages communities. From the beginning, they understood one crucial truth: meaningful change requires intentional listening, partnering and involving the community every step of the way — not relying on assumptions or outdated practices.

Grounding the vision in community voices

As *Reflections* evolved, the vision expanded into a cross-industry, community-led, disease-agnostic collective. A months-long listening tour followed to deeply understand community perceptions and barriers to clinical trial participation and to pressure test a novel concept that would connect art with engagement. Guided by the Collective's co-chairs, they brought together patient advocates, clinical trial sites, industry sponsors, healthcare providers and community leaders to collaborate, identify and address systemic barriers to research participation. Without a precedent to model from, *Reflections* partnered with the PALADIN Consortium, leveraging its framework to support logistical complexities of a pre-competitive, community-based, collaborative approach to addressing complex clinical trials diversity and inclusion issues.

During the listening tour in Atlanta, *Reflections* asked community members about their lived healthcare experiences, perceptions of, and perceived challenges to participating in clinical trials. One of the most revealing and powerful questions was: *What would be meaningful to you?* The responses were clear. Complex challenges ranged from mistrust stemming from past injustices, physical and geographical barriers to care, and mixed opinions within family and social networks. Despite these challenges, the community emphasized the importance of being represented in clinical research to ensure outcomes that reflected diverse experiences.

Atlanta, with its rich tradition of storytelling and art as tools for dialogue, wanted something reflective and expressive. A public art installation, crafted by local artists, telling their stories. Rejecting generic health fairs and presentations, the community wanted something that celebrated their resilience and identity. In response, *Reflections* commissioned three Atlanta-based artists, to create works inspired by the community's unique experiences. These pieces weren't just art — they were mirrors, showing people that their voices and experiences mattered.

Reflections art installation to showcase people's lived experiences with research

Building *Reflections:* More than an event

The art installation was the centerpiece, but *Reflections* was never just about a single moment. With 10 organizations involved from inception, the Collective built a sustainable ecosystem of ongoing education, advocacy partnerships and a user-friendly website. As local stakeholders gained trust and industry partners saw the value, the initiative nearly doubled in size to more than 18 organizations. The initiative ultimately went beyond highlighting disparities — it aimed to dismantle systemic barriers and tackle complex challenges like policy reform, site-level support, education, and creating sustainable momentum for long-term impact.

At its launch, *Reflections* conducted a survey that revealed tangible progress in fostering inclusive clinical research. Key findings included:

- A 20% increase in the willingness to participate after visiting the installation
- 50% of attendees actively exploring clinical trial options through the newly launched trial finder tool
- 18 individuals consented to a single clinical trial during the launch with others signing up for future studies

A lesson learned in Atlanta

The installation stood as a powerful testament to the strength and diversity of the community, sparking meaningful conversations about clinical research. But there was something that the Heartbeat team couldn't ignore: the quiet streets surrounding the event. The nearby stadium, even on an away game night, loomed large. It became clear that if it had been a home game, the community's attention would have been elsewhere. This realization inspired a shift: instead of asking communities to come to us, why not meet them where they already are? Tailgates, farmers' markets and parades — these weren't just community events. They were the heartbeats of community life.

The lesson from Atlanta inspired something new: the Heartbeat Activate Community Program.

The birth of the Heartbeat Activate Community Program

The Heartbeat model: Meeting communities where they are

The plan was bold but simple: step into the heart of community life. Instead of expecting people to enter the world of clinical research, Heartbeat would step into their worlds.

Event strategy for 2025

Heartbeat Clinical Research is establishing a consistent presence in 10–12 cities, chosen based on real-world data to align with sponsor pipelines and community health priorities. In each location, Heartbeat will participate in two events per month — block parties, library events, festivals and more — creating natural, authentic connections.

Long-term commitment

This isn't about a single trial or a one-time partnership. It's about embedding in the community, fostering trust, and building coalitions that can partner with clinical research for years to come.

Community coalitions

Each city will act as a hub for local partnerships — advocacy groups, healthcare providers, researchers, patients and business leaders. These coalitions will work together to identify barriers and develop solutions tailored to their unique community.

Bringing value without strings

At every event, Heartbeat is focused on delivering immediate, tangible value — no strings attached. Ideas include:

- **Hyper-local health dashboards:** Sharing community-specific health data with actionable insights.
- **Pop-up specialty clinics:** Free screenings, mental health support, and pediatric care.
- **Tech tryouts:** Opportunities to test wearable health trackers or learn about AI-driven tools.
- **Caregiver support stations:** Resources and respite care for family caregivers.
- **Community storytelling booths:** Spaces for sharing health stories that amplify local voices.
- **Life-skills workshops:** Covering topics like financial literacy for health costs, cooking for health, and mental health first aid.
- **Community-driven research co-creation:** Flipping the script by inviting people to shape research priorities and protocols.
- **Career development in health:** Training opportunities for clinical research coordinators and STEM workshops for students.
- **Sustainability and wellness initiatives:** Hosting "walk-and-talk" health events, distributing garden starter kits, and more.
- **Community champions fund:** Offering micro-grants to grassroots leaders tackling health barriers.

The goal isn't recruitment — it's trust. By showing up, contributing meaningfully, and letting the community guide what's next.

The cost of doing the right thing

Here's the reality: doing this the right way costs less in the long run. Study sponsors spend millions on recruitment campaigns that often fall short. By investing in sustained community engagement, they can reduce reactive spending and build a pipeline of informed, engaged participants. This model bridges the trust gap that has long plagued clinical research — resulting in better studies, stronger outcomes and healthier communities.

A call to action

This program is more than an initiative — it's a movement. It's an invitation to rethink old assumptions and embrace a new way of building trust and collaboration. The Heartbeat Activate Community program isn't just about attending events or handing out resources; it's about laying the foundation for a new era in clinical research — one built on transparency, collaboration and a genuine commitment to doing what's right. But to make this a reality, we need you.

We're inviting all stakeholders — patients, sponsors, healthcare providers and community leaders — to bring your ideas, your passion and your creativity.

- To patients and communities: Share what matters most to you. What makes research relevant and inclusive.
- To sponsors and industry leaders: Join us in creating a sustainable model for diversity, equity and inclusion. Build authentic sustained relationships with patients and communities who understand and value research.
- To R&D and commercial teams: Create a unified approach that benefits everyone — patients, sponsors and the healthcare ecosystem at large — by amplifying these efforts and aligning on shared goals. Create pathways to connect with the same audiences in a manner that feels authentic and supportive, not exploitative.

It isn't enough to simply do the right thing or improve recruitment metrics above study — it's about achieving better outcomes for studies and for communities, it's about building a pipeline of trust — one that will yield dividends for years to come in both research and health outcomes. This is the clearest evidence that doing good and doing well are not mutually exclusive. Ethical, patient-centered engagement is more than a moral imperative — it's a strategic advantage.

Let's build a future where clinical research is a trusted partner in improving health for everyone. Together, we can create a system that doesn't just serve one study or one city — but generations of patients and communities worldwide.

What about *Reflections?*

Reflections is still going strong in Atlanta, continuing its mission to break down barriers and build connections. It's a reminder of what can be achieved when industry, advocacy and the community partner together. *Reflections* continues to welcome new members to join the Collective.

The future of clinical research is collaborative, transparent and inclusive. And it starts here — with all of us, united in purpose.

Let's get to work.

About the authors

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Sarah McKeown-Cannon is the Senior Vice President and Head of Clinical Research at Heartbeat, where she leads transformative initiatives that redefine clinical trial engagement. With a deep passion for human-centered design and a steadfast commitment to health equity, Sarah empowers clients, partners and teams to challenge conventions and create lasting impact in clinical research. At Heartbeat Clinical Research, Sarah spearheads efforts to revolutionize patient activation by shifting the focus from simple recruitment to meaningful engagement. Her team transforms eligible participants into active advocates for their health, accelerating clinical development timelines and driving global diversity in trials. Her dedication to health equity is evident in her work amplifying the voices of underrepresented populations and designing inclusive trials that reflect the patients they serve. This commitment is further exemplified in her role as Co-Chair of the *Reflections* Collective. Recognized as an MM&M 40 Under 40 honoree, Sarah reimagines clinical trial design by prioritizing the human experience — always treating patients as people first. She seamlessly bridges global healthcare intelligence with patient-centered insights, delivering tailored strategies that achieve measurable, meaningful outcomes. Through her visionary leadership, Sarah remains dedicated to advancing healthcare for all, inspiring her clients, collaborators and teams to push boundaries and create enduring change in clinical research.

Growing up in the UK, Sarah began university with the goal of becoming a doctor, but her path shifted when she fell in love with research. Working on several clinical trials allowed her to contribute to advancements in medicine, but it was her own healthcare journey that shaped her perspective on patient-centricity. Even with a medical research degree,

navigating the healthcare system felt overwhelmingly complex and often disheartening. If she struggled despite her background, she could only imagine how daunting it must be for others without the same knowledge. This realization became the foundation of her purpose: to create meaningful change in the patient experience. Having experienced both the UK and U.S. healthcare systems, Sarah has come to believe that transforming outcomes and experiences requires a fundamental shift — from viewing patients as participants to seeing them as whole people. When she reflects on her own healthcare journey, she doesn't define herself solely by her medical history, and neither should the healthcare system define the people it serves this way. Patients are individuals with unique lived experiences, motivations and challenges. By embracing this understanding, we can foster an approach to healthcare that truly prioritizes the person behind the patient, driving meaningful improvements in both care and outcomes.

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Vicky DiBiaso is the Head of Patient Informed Development & Health Value Translation within Sanofi Research & Development. She is a nurse with a Master of Public Health and has over 25 years of clinical research experience. She was one of the earliest industry pioneers to establish clinical trial site and patient advisory networks, revolutionizing R&D models by embedding patient and healthcare provider perspectives into research and development programs. This work earned her recognition as one of the Top 20 Industry Innovators. Vicky founded and chaired the PALADIN Consortium, fostering collaboration between advocacy and industry leaders to transform the pace of medicines development, and currently co-chairs *Reflections*, a collective focused on enhancing clinical trial diversity at the community level. A passionate advocate for Parkinson's disease, Vicky has championed clinical research education, completed five marathons, and summited Mount Kilimanjaro on behalf of the Michael J. Fox Foundation and the Parkinson's disease community.

The commitment to integrating patient communities into clinical research is deeply rooted in understanding the profound impact their advisory support has on shaping overall research and development decision-making. By integrating patient communities, clinical research more accurately focuses on the most critical unmet needs and priorities that improve health-related quality of life. Collaborating with those who have lived experiences ensures that the development of new therapies reflects what matters most to patients and their carers, supports acceleration, and increases the probability that those who can benefit from a clinical trial, or the approved treatment, have access.

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Angela Radcliffe is a best-selling author, speaker and advocate for teaching health, data and AI literacy. Drawing on 20+ years of experience centered around healthcare innovation, Angela combines deep AI healthcare expertise with authentic storytelling to engage diverse audiences and empower children and adults to succeed in a data-centric world.

Driven by the preventable loss of her 21-year-old brother to an undiagnosed heart condition, Angela champions health literacy while navigating the complexities of raising three children across different technological generations, including a neurodivergent learner. This unique intersection of personal tragedy and parenting challenges and her journey from poverty to escaping domestic violence fuels her mission to advance health, data and AI literacy for the next generation.

As the author of *Quantum Kids Guardians of AI,* a narrative-based activity book for children and teens, Angela teaches AI fundamentals such as neural networks, large language models, data ethics and prompt engineering, all woven into stories about school life, social media and robotics. The book makes complex AI concepts accessible and enjoyable, encouraging young minds to think about technology's role in addressing challenges like bullying, climate change, and health inequity and empowering them to make better health and other critical life decisions and take more control of how their personal data gets used by third parties to reduce exploitation or becoming a victim of fraud.

As a senior executive in health tech, patient engagement & education, and overseeing clinical operations programs, including Managing Director of Heartbeat's Clinical Research practice, a division of Publicis Health, and Head of Digital Performance Improvement and Innovation for Research and Early Development IT for Bristol Myers Squibb, Angela translates complex concepts into actionable insights, helping families and organizations thrive.

Her unique background and her stellar communications and interpersonal skills make Angela a sought-after speaker for podcasts and with life sciences, patient education, mental health, data privacy, teacher and parent organizations.

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CHAPTER 15

Voices of experience: Enhancing clinical trials through patient and site engagement

DEIRDRE BeVARD

Patient-centricity in drug development is a multifaceted approach that integrates the perspectives of various stakeholders, including regulatory and health authorities, the biotech industry, healthcare professionals, **and patients.**

The controlled nature of clinical trials inherently poses challenges to achieving true patient-centricity. While efforts are made to incorporate patient perspectives, the primary focus of these trials remains on ensuring scientific validity and regulatory compliance — as it should. The biopharmaceutical industry has changed its mindset over the last few decades from developing drugs "on behalf" of patients to taking a more patient-informed approach to ensure patient needs are met and trials are designed in a way that makes participation manageable.

Note I did not say easy.

I have worked on clinical trials for over 35 years and have seen the industry earnestly evolve in the effort to balance scientific rigor with genuine patient engagement, ensuring that patient voices are not only heard but also meaningfully integrated into the drug development process. Make no mistake, however, that clinical trials must remain science-focused… and in my experience, patients agree. There must be, first and foremost, a strong scientific foundation to bring an asset through this very rigorous process. That is the price of entry into this space. But there also must be discipline — operationally focused discipline — not to overburden the trial with so much scientific interest and testing that it becomes nearly impossible for providers to conduct it in a healthcare setting, and for patients and their caregivers to navigate the burden of participation.

It's toward this balance that I believe the industry is evolving and making strong efforts to do better by patients. But we still have a long way to go. I would miss an important element, however, if I did not include the need to support clinical sites in their efforts — after all, they are the ones conducting the trials. The real value is in being ***both*** site-centric and patient-centric. Designing our clinical trials to be more pragmatic, less complex, and in-tune with the delivery of care to the extent possible while maintaining scientific integrity is critical to developing a therapeutic option that can then become part of patient-centric healthcare.

Sites report a number of factors that make conducting clinical trials more and more challenging, and not just in the efforts to find, enroll and retain participants. For example, we are all talking about DCTs (decentralized clinical trials) and the use of technology in these models. The concept is good — allow the patient to participate from places in or closer to home rather than at a brick-and-mortar site. However, over half (55%) of sites find the setup and training on sponsor-provided technology to be extremely burdensome.[1] The need to manage multiple systems and logins further complicates their workflows. This reinforces the notion that to be patient-centric we must also be site-centric.

An additional factor is protocol complexity. The increase in the number of assessments or questionnaires,

etc., may be the result of the right scientific intent or interest, but it comes with a major concern about complexity, cited by 38% of sites.[2] This includes managing intricate protocols, regulatory requirements and data collection processes.

There were numerous ways to approach this topic and I chose to approach this essay as an opinion piece. Recognizing that focusing only on my industry-centric view would fly in the face of being "patient-centric," I have included the perspectives of two patients who have inspired me and countless others.

Meet **Karen Peterson.** Karen is a stage IV cancer survivor thanks to a clinical trial. She is African-American with the experience of how hard the medical system can be. She had to fight her way into the trial that saved her life and now advocates for cancer patients of color, helping them navigate their cancer experience. Karen has established Karen's Club, whose mission is to empower patients of color with the knowledge and trust to pursue clinical trials that can save or extend their lives.

Meet **Barry Nelson**. Barry is an experienced speaker at conferences, drawing from his personal journey as a cancer survivor and clinical trial participant to engage audiences. His speaking roles are varied and all with the goal of educating audiences about the lived experience of a patient for whom standard treatment did not work and then went on to participate in clinical trials.

I asked Karen and Barry to provide their perspective — the patient perspective from their own experiences and those of the many patients Karen's Club supports and Barry has learned about through his advocacy.

Deirdre: How important is the patient perspective to drug development and how has it changed over time?

Karen: The patient perspective is very important, as all roads in drug development begin and end with the patient. It's the "in-between" process that evaporates the patient experience and the contribution to the process that can get lost. Think about it, one of the great debates is efficacy vs. quality of life. On one hand as patients, we are grateful and appreciative of new innovative drugs that enter the market and extend life, but on the other hand, at what cost? And I'm not just talking about how much money do we have to spend (because that can make the options unobtainable) but I'm talking about the quality of life. That overriding question of "Do I have to sacrifice a good quality or even decent quality of life, just to trade it in for a life riddled with side effects that can be so overwhelming that my quality of life suffers tremendously?" The aspect of my perspective that has changed is how difficult it is to include the patient feedback and experience into clinical trial development. That's where the business side kicks in, and unless somewhere in the pipeline a leader for the pharma that is developing the drug truly believes in "building in those important educational and social support factors" into the individual site experience, then nothing is really changing.

Barry: When I was diagnosed, I was like the first of my generation… and wasn't aware of, you know, clinical trials to a degree. I was aware of a lot of treatments and surgeries that I saw my mother and her sisters go through, and you know the ups and downs that they experienced. But for me, clinical trials were really something new. Now,

when I was initially diagnosed, I was going to one institution and… these people basically told me I had less than six months to live, OK? […] But I did get a second opinion. And so when things weren't working out for me, then I talked to my primary care. I said I can't go back there anymore; I need to see a lung cancer specialist. Back then he says one of the things that will be helpful for you is that they have clinical trials. So again, I was being introduced to something. So it was a lot that I was going to have to learn along with balancing this new diagnosis and all the other stuff you have going.

But I had a wonderful team. You know, the first thing when I went back, when I went to Dana Farber for that first appointment, you know, after I had switched institutions, the doctor said, listen, we have plenty of tools in the toolbox, and we're going to use all of them to fight as hard as you fight.

So it was an opportunity. A research team was assigned to me and they brought be up to speed and showed me where to find information. You know, what trials were, stage 1 trial, stage 2 trial, stage 3 trials, etc. It was a process to grasp all of this because in a way I kind of was like out there by myself, because there was another family crisis going on at the time, and I really hadn't shared with my family what that diagnosis was.

What Karen and Barry both highlight in just that question is the need to understand both what matters to the patient in the treatment and its impact on their lives and the need to bring clinical trial awareness to the patient and their support network in a way that allows them to make educated choices. The patient and the provider perspective bring key insights and inputs to the way our industry designs and delivers clinical trials. In Karen's case, she had to relentlessly pursue the option that finally saved her. In Barry's case, a trial was presented; however, it was also in the context of needing to educate him about his disease.

For all of the work that has been done and is continuing to evolve by our industry, we will not have the valuable impact we strive for if two big hurdles are not overcome. **Awareness and access**. To be truly patient-centric, we need to come together across the industry — and beyond — to significantly improve both of these areas. To consider participating in a clinical trial, one has first got to be aware that it is an option. Even more fundamental, one has to know what clinical trials are and how they work. This is especially true for patients with rare and life-threatening illnesses, many of whom either have no treatment options (often the case in rare disease) or have exhausted effective options (often the case in life-threatening disease).

Deirdre: How has the pharmaceutical industry involved patients during drug development and how should they change it in future drug development?

Karen: Some big pharma companies have been very intentional in regard to providing opportunities for patients to become more involved in certain aspects of drug development. So, if we look at instances where patients are sitting on steering committees, participating in the FDA's [U.S. Food and Drug Administration] Patient Focused Drug Development Guidance Series, or having direct contact with drug developers via targeted outreach and engagement, the level of "reaching across the table and working together" has increased. My career has changed significantly because opportunities to provide real value to clinical researchers in their quest to "close the gap" have increased by 100%. My partnership with the Mt. Sinai Tisch Cancer Institute's Phase I Program was

a perfect example of using the patient experience (as myself the patient navigator) to provide support to research-naive patients, who may be on the fence about joining a clinical trial. Not only was I successful as one of the few grassroots patient-led navigation services, but I also provide "real world feedback" case studies to the clinical research staff about the unique perception barriers that plagued participating in studies. Oftentimes as a patient-led navigation service, the clinical research staff was surprised and shocked at the level of transparency I divulged to them about what the patients they were recruiting really thought vs. what the patients told the clinical staff during the "recruiting, onboarding" stage. Being able to translate this information to the research staff provided a level of valuable insight that they in turn were able to address in their 1:1 oncology consults for the Phase I program, ultimately improving the communication and transparency aspect of the patient experience at their clinic.

Barry: I'm going to start with the team. The team was very good. I mean from a clinical perspective. They shared information with me, about the pharmaceutical company that was working on the drug, their background, their relationship with that company. Even at one point I got to meet the scientists in the institution where I was that was working with that team. You asked me what do I feel they could improve? It's how are things communicated. A number of times I've been invited to speak to organizations, drug developers about my experience in the clinical trial... I've been given the opportunity to use my voice not just for me, but for so many other patients out there who don't have a seat at the table. I do see some progress being made, but kind of go back to they only hear my voice, but to hear other patient's voices that are waiting in the wings. Because maybe there isn't a trial available to them. Maybe they have a rare disease or some other situation that the morbidities or whatever else they're dealing with excludes them from participating in the trial. I think there's so much more opportunity to continue to develop and extend it to more people.

There is much that our industry can do, but we cannot do it alone. We must consider that there is higher trust and greater power in patients hearing from patients like them who have a shared or similar experience. Karen provides that perspective in her coaching of patients navigating their care options and in providing the healthcare institutions and pharma industry with the lived experience of patients like her. Barry shares his story both on stage and in informal interactions with other cancer patients. He can authentically provide a view that being in a clinical trial can be done through a trusting relationship with researchers. The key for him was that the staff at the healthcare institution took the time to explain the protocol and the role the ethics committee plays.

They both highlight the need for our industry to work with patients and providers to be able to put the clinical trial into context in a patient-centric way, meaning in relatable and understandable terms that allow them to make an informed choice. This is even more essential when we have underserved populations or communities who are well aware of the history of when patients were not treated with the respect they deserve. We have many examples of how patient advocacy and involvement can have significant impact on drug development.
For example:

- In the 1980s, patient advocacy groups were activated and played a crucial role in accelerating the development of HIV/AIDS treatments. Their efforts led to the creation of the FDA's compassionate use mechanisms as well. There are current examples

as well of how patients can galvanize and motivate communities to invest more in research.

- Thanks to Michael J. Fox and his advocacy, the Michael J. Fox Foundation for Parkinson's Disease has significantly increased funding for Parkinson's research, leading to advancements in treatments and a greater focus on finding a cure.
- The Cystic Fibrosis Foundation funds research and development for cystic fibrosis treatments. Their investment in Vertex Pharmaceuticals led to the development of breakthrough drugs like Kalydeco and Trikafta, which have dramatically improved the quality of life for patients.

These examples, Karen and Barry's perspectives, and my own experiences underscore the importance of trust, holistic support and continued advocacy to ensure that patient voices are at the forefront of medical innovation. The key takeaways from my discussions with Karen and Barry can be summarized as follows:

Challenges to patient engagement

The expectations, vantage points and interests of the industry, healthcare systems and patients are not the same, but managing the differences can allow us to address these challenges. Karen faced significant challenges early in her advocacy career, including being the only patient voice in a room full of doctors and executives. She noted that patients often feel intimidated and overwhelmed in clinical settings, which can deter them from participating in trials. Her role as one who has experienced it first-hand allows her to serve as a "translator" between patients and researchers, helping patients navigate their options and understand the clinical trial process. This involvement addresses patient concerns, providing support, and ensuring that patients are well-informed before meeting with clinical teams.

Barry shared a positive experience from his cancer treatment trial where he felt like part of a team working towards a larger goal. This was contrasted sharply with a sterile and impersonal experience he had in a COVID-19 vaccine trial. He emphasized the importance of making patients feel valued and involved, which can significantly enhance their experience and willingness to participate in trials. We should be focused on what we can do within the confines of a controlled study to humanize the experience for participants.

Building trust and communication

Establishing trust through transparent communication and addressing patient concerns early on is crucial. Karen's role in helping patients navigate their options is a testament to this strategy. She emphasizes the need for better communication between patients and researchers to ensure that patients feel valued and understood.

Barry highlighted the importance of building trust within the community. He shared an example of a friend who was skeptical about clinical trials, viewing them as treating patients like "lab rats." Through his own experience, Barry learned about the rigorous protocols and oversight in place to ensure patient safety, which he communicated to others to help dispel myths and build trust.

There are still many people, especially people of color, who have a lack of trust in the industry and a skepticism of clinical trials. This low trust stems from factors such as historical exploitation, lack of representation of their community, and healthcare access disparities. Peer communities can play a crucial role in establishing and building trust. When information comes from trusted peers and culturally relevant leaders, it is often seen as more credible and relatable. Hearing about positive experiences like those, both Karen and Barry can help dispel misperceptions and help to encourage others to consider participation.

Advocacy and representation

Barry has become an advocate for patient involvement in clinical trials. He participates in patient advisory councils and speaks at conferences to share his experiences and insights. He believes in the importance of including diverse patient voices in the drug development process to ensure that treatments are effective and accessible for all.

Karen's advocacy efforts have led to better trial designs and support services. Her involvement has also benefited institutions like New York University (NYU), which have seen positive outcomes from investing in patient-centric practices. She highlights the long-term value of such investments, noting that her positive experience has paid dividends for NYU in terms of reputation and patient trust.

CHALLENGE	DESCRIPTION	EASE OF OVERCOMING
Site burden	The logistical and operational demands on clinical trial sites.	Difficult
Communication	Ensuring clear, transparent and effective communication with patients.	Easy
Designing trials focused on patient preferences	Creating trials that align with patients' operational preferences and needs.	Difficult
Cultural sensitivity	Addressing diverse cultural needs and preferences of patients.	Moderate
Cost management	Balancing the costs associated with patient-centric initiatives.	Difficult

Future directions

Karen plans to expand her advocacy efforts, aiming to engage with more pharmaceutical companies and ensure that patient voices are heard in the development of new treatments. She advocates for the inclusion of patient perspectives in all stages of drug development to create more effective and patient-friendly treatments.

Barry suggests that pharmaceutical companies should conduct public service announcements and involve patient voices to educate the public about the drug development process. He advocates for more holistic and personal approaches to patient engagement, emphasizing the need for collaboration between pharmaceutical companies, healthcare institutions and communities.

One thing that is clear from my experience: the view of these wonderful patient advocates and many others I have spoken with is that the role of the biopharmaceutical industry to ensure we are applying sound and innovative science to the development of new medicines. No one wants that to be compromised, not even in the name of patient-centricity. By virtue of clinical trials needing to test if a drug is safe and effective, trial designs must be scientifically designed to prove out a hypothesis vs. be designed around the needs of any *one* patient. Once that is established, then it is incumbent upon those of us lucky enough to work on these therapies to target the profile of a drug based on patient needs and to operationally design and "humanize" the trial experience.

Once again, we must do this along with designing trials to be conducted with the most minimal disruption possible to the care process. This is not easy, but it's up to us to make sure it isn't any harder than it has to be to test the drug. This point is very personal for me as I write this while sitting with my dear mother who has end-stage dementia. It's a humbling, heartbreaking

experience that drives home the point that the clinical care is between the patient and the care provider, not the patient and the pharmaceutical company. It's those dedicated, compassionate professionals who make the difference. Her experience, her spirit and her dignity are very much in the hands of her care team, and they often go out of their way to overcome the challenges of the medical system.

Our role is to make the medicines that improve the human condition. In the context of clinical trials our role is to design our requirements in a way that allows patients to have as many choices in their decisions as it possible within the integrity of that trial, and to allow the care team to optimize the trial experience. By involving patients in the drug development process, the industry can create more effective and patient-friendly treatments. The experiences shared in the interviews underscore the importance of trust, holistic support and continued advocacy to ensure that patient voices are at the forefront of medical innovation. As the industry continues to evolve, it is essential to build on these insights and foster a more inclusive and patient-centered approach to healthcare.

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About the author

DEIRDRE BeVARD, BSc
Senior Vice President, R&D Strategic Operations, CSL

Deirdre BeVard brings over three decades of expertise in drug development and is known for authentic and transformative leadership. As the Senior Vice President of R&D Strategic Operations at CSL, she oversees a global team focused on R&D strategic and portfolio management, clinical operations delivery, integrated business operations, digital strategies and patient-centered drug development. Deirdre's leadership philosophy emphasizes collaboration, integrity and innovation, creating inclusive environments where teams thrive and deliver impactful results. Her leadership style reflects her mindset to take her work seriously, but maintain a lighthearted approach about herself and have fun along the way.

Her diverse experience spans key roles at Elligo Health Research, Nektar Therapeutics, and Endo Pharmaceuticals, as well as a CRO and a start-up software company. This broad perspective gives her a diverse viewpoint and fuels her passion for bridging clinical research and healthcare through partnering with patients, communities and providers to accelerate medical advancements and enhance health equity.

Deirdre more or less tripped over this industry and once she fell in, she was joyfully stuck. She is committed to making an impact and doesn't believe there is a more motivating "why" in that pursuit than to improve the lives of patients. She has seen friends and loved ones benefit from clinical trials and has experienced the heartbreak of not having that option for sometimes avoidable reasons. For that reason, she has focused a significant part of her career on finding ways to ease the burden of participation by giving both sites and patients a voice in the development of medicines.

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CHAPTER 16

The missing voice: Why patient perspectives must drive MS drug development

SARA LOUD, HOLLIE SCHMIDT

This chapter represents a collaborative exploration of patient-centered drug development in multiple sclerosis (MS), where the voices of those living with the disease are elevated from passive subjects to active partners in research and innovation. By weaving together organizational insights from Accelerated Cure Project and *direct perspectives from people with MS (in the callout boxes),* we illuminate the critical importance of lived experience in shaping meaningful, responsive pharmaceutical research and treatment strategies.

> *"Always, always, always involve patients in the development of anything."*

Accelerated Cure Project (ACP) is a patient-founded nonprofit with a mission of accelerating research to improve the health, healthcare and quality of life of people with multiple sclerosis (PwMS). Our activities include the development of a biosample and data repository to support basic science discovery in MS; the creation of a people-powered research network, iConquerMS, which involves PwMS in MS research as partners as well as participants; and initiatives focused on engaging members of historically marginalized populations in MS research.

Our approach to engagement of PwMS as we execute on our mission has evolved since our founding in 2001. While we have always viewed and conducted ourselves as a patient-centered organization, our engagements with PwMS in the earliest days were through our founder, volunteers, and the enrollment of PwMS and family members as participants in our biosample repository. In 2013, in recognition of the value of including lived experience in the design and execution of our initiatives, we began inviting PwMS to contribute to the shaping of our programs through advisory boards. With the conception and launch of iConquerMS that same year, we have expanded our engagement of PwMS and caregivers to full research partnership. iConquerMS members have opportunities to participate in all phases of research including the submission and prioritization of the research questions to be answered, contributing to the design of studies and study success measures, and driving the methods and execution of the dissemination of research evidence. PwMS are also equal partners in our inclusive research initiatives: the MS Minority Research Engagement Partnership Network, a multistakeholder alliance launched in 2016, and the RIDE (Research Inclusion Diversity and Equity) Council, a group of 28 PwMS representing historically underrepresented populations that provide guidance to ACP and other researchers.

ACP not only engages with PwMS and their family members to integrate their insights and lived experience into the organization's initiatives and research, but also works to connect PwMS with members of the research community, both commercial and academic. We bring together PwMS, family members and caregivers in conversation with research teams throughout the world to channel the value of their perspectives into research and development activities. We consider these perspectives as vital to pharmaceutical drug development and decision-making. Given the amount

of money and effort invested in the development of a single medicinal product, it seems irresponsible to not take full advantage of the perspectives of the end-user of that product.

"How is it possible to design a pharmaceutical trial without the input of probable users of what's being tested? It's hard for me to believe that pharmaceutical companies and/or research methodologists don't know this, and I hope they continue to engage us and listen to us in the process of their research design and testing."

Our work with pharmaceutical partners has evolved in recent years as more companies have initiated the inclusion of the patient perspective into their drug development activities. We are pleased that the value of patient input is now more widely recognized, but unfortunately the process of seeking it out and incorporating it in meaningful ways is still conducted at a minimal level. Our organization has helped to facilitate individual interactions, such as one-time interviews and focus groups, and on a few occasions extended interactions, including standing patient advisory councils. All of these have delivered direct benefits — such as more intuitive and relevant data collection tools, clearer study materials, and more culturally sensitive outreach methods — and have also provided opportunities for mutual enlightenment and understanding. However, these engagements fall short of representing a full partnership in the design or development of any particular therapeutic or an individual clinical trial.

For instance, we advocate for the inclusion of the patient and caregiver perspectives as early as possible in the research process and at every subsequent step of the way. However, our constituents are usually not brought into a drug development program until Phase III, when many aspects of the program have already been firmly defined. Additionally, the potential impact of patient input is usually constrained through patients being asked to provide feedback on ideas generated by others, as opposed to being invited to co-create plans and solutions.

"Don't wait until a drug is almost ready for market to involve patients. Engage with us early in the development process to understand our needs, concerns, and how we define success in treatment. And don't stop there — keep the dialogue open even after the product is launched."

Insights from healthcare providers (HCPs) have traditionally been highly valued in drug development decisions, and HCPs are often viewed as being able to competently represent patient concerns as well as professional perspectives. We feel this view is incorrect, except for those instances where an HCP is also diagnosed with the condition in question. There is no substitute for the actual lived experience of being diagnosed with and managing a specific disease. People living with MS, for example, have unique insights not accessible to most HCPs into the disabling nature of MS-related fatigue, the experience of administering multiple injections per week, and the energy expenditure required to navigate a sprawling clinical research facility using crutches. The demographic and socioeconomic

characteristics of the HCP community may also not match those of the patient community, making it difficult for HCPs to adequately represent the cultural considerations or economic constraints of the patient population when providing input.

"To ensure that new drugs are developed in line with patient priorities, preferences and needs, there has to be more focus on involving patients in every stage of the drug development process. Pharmaceutical companies and researchers need to listen to the communities they serve, especially those that are often overlooked."

We understand that the pharmaceutical industry must overcome many challenges to achieving true "patient-centricity" in drug development. For instance, there is enormous time pressure to bring innovative new products to market as quickly as possible. However, we believe that even with the rush to get a new product tested and into market, time can be found for forming partnerships and obtaining meaningful input from those who will eventually use the product. Indeed, it seems short-sighted not to do so, considering that this input could result in fewer trial delays, faster recruitment and greater retention, as well as greater end-user satisfaction and adherence should the product make it to market. We encourage the pharmaceutical industry to leverage learnings from other industries on incorporating "voice of the customer" into their research and development (R&D) activities, and successfully navigating the trade-offs between the value of end-user guidance and the cost of its acquisition.

"We hope that our perspective provides insight regarding living with a chronic illness and what is important to us regarding treatment, access to care, and improving our quality of life. We would like that insight to be requested and considered in every aspect of drug and research development."

Looking toward the future, pharmaceutical companies will need to change their culture and processes to incorporate the patient voice from the very beginning of a development program. Ideally, any new product would have patient advisors who are engaged throughout the product's development cycle. Other voices would be brought in through interviews, meetings and/or surveys to add breadth and depth when needed. This requires buy-in from the top and incorporation into group and employee goals and evaluations. The development of established models that can be easily and efficiently implemented will be instrumental in achieving industry-wide change. Sophisticated, research-savvy patient advocacy groups can help to facilitate the acquisition of end-user input and also provide higher-level guidance similar to HCPs/key opinion leaders. Consortia such as PALADIN (https://paladinconsortium.org) can be helpful in generating and promoting patient advocacy group-industry partnership models with supporting documentation to facilitate their implementation.

"Use us as we know — intimately — what this disease causes and how it affects us and those around us. We are able, willing and happy to share our thoughts and ideas with you."

Incorporating input from a diverse range of voices is also critical to identify hidden flaws in clinical trial design that could impact recruitment and retention, as well as issues with the product itself or its administration that may be relevant to certain segments of the patient population. Partnering with demographically diverse communities is also helpful in devising recruitment strategies that enable the trial to meet or exceed its inclusivity and equity goals.

"I think our contributions to the [program] were impactful because we brought a unique perspective shaped by our personal experiences, education and cultural backgrounds. We worked to ensure that underrepresented voices were considered in discussions, especially when it came to topics like health equity and accessibility."

To summarize, we recognize the progress that has been made in recent years toward incorporating patient perspectives in drug development, and also recognize that opportunities for new breakthroughs and deeper partnerships still lie ahead. These include opportunities to seek patient input throughout the entirety of a drug development program, engage patients as co-creators in addition to consultants, and intentionally include voices that have been excluded or disregarded in the past. We have no doubt that expanding the influence of the patient voice in these ways will have immense payoffs for all involved. We look forward to being part of this important transformation.

"Ultimately, the more pharmaceutical companies prioritize patient perspectives, the better their treatments will be — and the more trust they'll earn. This isn't just about business; it's about improving lives, and that starts with listening."

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Sara Loud is the CEO of Accelerated Cure Project, Inc. (ACP), a nonprofit organization dedicated to accelerating multiple sclerosis (MS) research for faster diagnosis, improved treatments, and a cure for MS. Under Sara's leadership, ACP works in collaboration with people living with MS, caregivers, healthcare providers, researchers, industry partners and other MS stakeholders to develop and deploy centralized research resources to enable scientific discovery. ACP's resources include the ACP Repository; iConquerMS, a people-powered research network; the MS Minority Research Engagement Partnership Network; and the Research Inclusion Diversity and Equity (RIDE) Council, each designed to facilitate inclusive and people-centered MS research.

Sara's professional journey began as an electrical engineer, focusing on people and project management in high tech startups. Eager to apply her expertise to more impactful work, she transitioned to the nonprofit world in 2005, joining ACP as Repository Director to build the ACP Repository, a centralized collection of biosamples and data supporting MS researchers worldwide. Sara assumed the role of Chief Operating Officer of ACP in 2015 and that of CEO in 2019. Sara holds BS and MS degrees in electrical engineering from Northeastern University and received her MBA from Babson College.

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Hollie has an MS in Management, as well as a BS and MS in Materials Science and Engineering, all from the Massachusetts Institute of Technology. She serves on the Institutional Review Board of Beth Israel Deaconess Medical Center, is a board member for the International FOP Association, and is Secretary for the Multiple Sclerosis Coalition.

Before joining Accelerated Cure Project, Hollie's endeavors included co-founding two software companies where she gained an appreciation of the imperative to center new product designs on the needs and preferences of the end user. She brings an entrepreneurial spirit and a love of discovery, collaboration and inclusivity to solving problems and achieving breakthroughs in partnership with the MS community.

CHAPTER 17

The road to co-creation: Patients and pharma shaping the future of clinical research

JAYNE SPINK

What if the way we involve patients in clinical trials today isn't the pinnacle of patient-centricity, but merely the opening chapter of its story? Decades ago, the seeds of change sparking a shift in practice and attitudes were planted, and they have grown steadily, nurtured by evolving perspectives and technological breakthroughs. Now, as we move further into the 21st century, could it be that we stand on the brink of a transformation so profound that it will redefine the very architecture of clinical research? A revolution not just in process, but in mindset — one so powerful that its full impact remains beyond our current capacity to foresee? Or will we pause, mistaking progress for completion, resting on our laurels?

Changing any system is rarely a linear process. It is gradual, sometimes messy, and, when it comes to rethinking how medicines are developed, deeply human. True transformation requires more than process updates; it depends on a fundamental shift in perspective. It demands that we see patients not as passive participants but as partners, active collaborators in the research journey. At the heart of this shift lies a growing recognition within the pharmaceutical and regulatory industries that patient experience and values must guide every phase of clinical research, from design to delivery.

This change is no longer aspirational; it is unfolding in real and measurable ways. Evolving attitudes, technological advancements, and a broader societal embrace of patient empowerment are driving a profound reimagining of clinical research. Patients' voices are no longer just acknowledged; they are becoming integral to shaping the development of medicines that truly address their needs. From working with patients to co-designing trials to incorporating patient-reported outcomes (PROs), these efforts reflect a deepening commitment to making clinical research more inclusive, relevant and impactful for the very people it is meant to serve.

The early days: A one-way street

Let me take you back to the 20th century, a time when clinical trials prioritized scientific data over the human experiences behind the numbers. Trials were meticulously designed by pharmaceutical companies and researchers, with little consideration for what patients found meaningful or relevant to their daily lives. In those days, patients were seen as passive subjects, participants without any say in the study's design or direction.

This is the approach that prevailed through much of the 20th century. The focus was on clinical endpoints like tumor shrinkage or survival rates, often at the expense of patient-centered outcomes such as quality of life. As noted by the Cochrane Collaboration, trials were primarily structured to meet regulatory requirements, emphasizing data collection for scientific validity while overlooking the lived experiences of patients.[1] PROs, when considered at all, were an afterthought, as the process of developing new medicines seemed rarely to take a holistic view of how patients managed their conditions day to day.

By the 1990s, the desirability of listening to the preferences of patients had started to gain recognition. The Medical Outcomes Study, which led to the creation of the SF-36 health survey, was instrumental in helping to develop a conceptual framework for PROs and embed them into clinical research.[2] However, tailoring treatments to individual needs or including patients in decision-making remained a foreign concept. Doctors and pharmaceutical companies maintained near-total control over medicine development and trial assessments, focusing largely on traditional clinical endpoints. As the Institute of Medicine observed, clinical trials largely disregarded patient perspectives, favoring objective scientific data.[3]

This disconnect often led to a misalignment between trial goals and the real-world challenges patients faced. Cancer trials, for instance, frequently applied a "one-size-fits-all" approach, failing to account for the significant variations in how patients experienced illness or responded to treatment. It wasn't until patient advocacy movements began to grow towards the very end of the 20th century that the necessity of a more inclusive, patient-focused approach became evident. As highlighted by the Patient-Centered Outcomes Research Institute (PCORI), this period marked the beginning of a broader shift towards incorporating patient perspectives in clinical research. Today, we understand that addressing both medical outcomes and the lived experience of illness leads to better, more personalized care.

As the century reached its end, the traditional structure of clinical trials was facing increasing scrutiny, and things were beginning to change. Yet, progress toward patient-centricity remained slow and fraught with challenges. I vividly recall sitting in meetings where trial designs felt immutable, as though etched in stone. The concept of revising protocols to reflect patient needs was almost unthinkable. Yes, tools like PROs existed but were often incorporated as an afterthought; just another box to tick rather than a meaningful effort to capture the lived experience of illness. The focus remained narrowly confined to clinical measures, with little regard for how patients were coping in their daily lives. PROs were often relegated to secondary importance, excluded from the core of trial design. Patients and advocates were rarely viewed as collaborators with valuable insights to contribute. This rigid framework not only limited the impact of clinical trials but also alienated the very people they were meant to help. The gulf between clinical goals and patient realities was becoming increasingly apparent, underscoring the need for a more human-centered system.

Amid what could be described as a period of stagnation, a quiet but powerful movement began to take root. Patients and advocacy groups started pushing boundaries, demanding recognition not merely as subjects but as active participants in shaping the future of research. They were individuals with families, careers, hopes and fears — determined to have their voices heard. This growing call for inclusion was more than a protest; it was the beginning of a transformation that would reshape the way we think about clinical trials. Subtle but determined, this movement planted the seeds of the patient-centered focus that is now bearing fruit today.

The turning point: Listening

As the World Health Organization noted in 2007, incorporating patient perspectives was becoming recognized as essential to enhancing the quality and relevance of health interventions.[4] The recognition of patient input in clinical research emerged from patient advocacy movements, particularly in areas like cancer and HIV/AIDS, which exposed the limitations of traditional, top-down approaches. Without the persistent efforts of patient advocacy groups, it's unlikely that regulators would have moved as quickly toward recognizing the importance of patient perspectives in drug development. Failures in clinical trials that neglected real-world patient experiences, combined with evidence showing the value of PROs and an ethical imperative to respect patient autonomy, prompted

regulators like the Food and Drug Administration (FDA) in the U.S. and the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK to prioritize patient-centricity as a pathway to more effective, trusted and market-relevant therapies.[5,6]

The digital revolution: A game-change

The 2010s digital explosion brought a seismic shift in patient engagement. Platforms like PatientsLikeMe and the rise of social media gave patients a powerful voice, allowing them to initiate conversations about their health and treatments, as widely documented.[7] This shift to interactive, educational and community-driven engagement marked a key milestone in patient-centric clinical research.

Initiatives like The Infopool by Prostate Cancer Research (PCR) exemplify this transformation.[8] By enabling patients to share experiences and access vital information about diagnoses and treatments, The Infopool fostered connection and learning. This empowered patients to make informed decisions, including about clinical trial participation.

Digital technologies revolutionized clinical trials by supporting decentralized trials and telemedicine. These advances have equipped the pharmaceutical industry to meet patients geographically, emotionally and practically, making them central figures in the research process. For example, wearable devices have reduced patient burdens, increased accessibility and provided real-time, nuanced data.[9]

Evolution of the concept of patient-centricity in pharmaceutical clinical trials

	FOCUS	PATIENT INVOLVEMENT	TRIAL DESIGN
Early 2000s: Traditional model	Predominantly on clinical endpoints & drug efficacy.	Minimal; clinical trials often lacked consideration for patient quality of life or preferences.	Standardized protocols with limited flexibility for patient needs.
Mid 2000s–Early 2010s: Growing awareness	Increasing recognition of the importance of patient quality of life & experience.	Introduction of patient-reported outcomes (PROs) and more attention to side effects and overall well-being.	Slight shift towards incorporating patient feedback into trial designs and considering patient preferences in protocol development.
Mid 2010s to late 2010s: Enhanced model	More holistic view including not just clinical outcomes but also patient preferences and experiences.	Increased patient advocacy & involvement in trial design, often through advisory boards.	More adaptive and flexible trial designs, with emphasis on patient-centered outcomes, supportive care and real-world evidence.
2020–present	Integration of patient perspectives into all aspect of trials (design, execution & reporting).	Use of digital tools & technologies to enhance patient engagement & data collection. Personalized treatment approaches based on individual patient profiles & preferences.	Implementation of decentralized trials and adaptive designs that cater to patient convenience and better reflect real-world scenarios.

The stubborn challenges

Of course, progress doesn't equate to perfection. Despite the strides made in patient involvement, significant challenges persist. A critical remaining challenge is the lack of diversity in clinical trials. The FDA's 2021 report highlights that underrepresentation of minority groups, women and low-income populations limits understanding of drug efficacy across diverse demographics.[10] These disparities aren't just statistical gaps — they directly affect the safety and effectiveness of medications for underrepresented groups. Without diversity, medical research risks skewing toward narrow insights, neglecting the varied populations relying on these treatments.

Another pressing issue is the exclusion of patients with cognitive differences, such as those with neurodegenerative diseases, cognitive impairments, autism spectrum disorder (ASD), or learning disabilities.[11] This necessity of inclusive research is underscored by the World Health Organization (WHO) World Report on Disability, which seeks to encourage the inclusion of individuals with cognitive disabilities in clinical research and highlight the barriers they face in accessing healthcare.[12]

Trials often rely on rigid protocols, complex questionnaires, and assessments that unintentionally exclude those with cognitive challenges. For instance, individuals with autism may face overwhelming barriers like sensory overload or logistical difficulties traveling to clinical sites. Caregiver support adds further financial and logistical strain, compounding these obstacles. Without systemic change, research risks excluding those who could benefit most, perpetuating a healthcare system that overlooks their needs.

Inclusive trial designs are essential — not just for equity but to ensure treatments address the full spectrum of patient needs. Listening to the lived experiences of underrepresented patients is vital to creating equitable and effective healthcare solutions.

The vital role of the third sector

The perspectives of patients and caregivers can help define research priorities and improve the overall quality of research, particularly when the role of the patient is that of an active and involved research partner.[13] By drawing on a deep understanding of a condition and its impact, and leveraging their networks and communities, charities have played a transformative role in ensuring that patient voices are integral to clinical development. Their expertise in lived patient experiences and their ability to foster meaningful involvement have been vital.

Charities are supporting patient-centric research in a variety of ways, many of which are explored in a 2023 report from the TAR (Translating and Accelerating Research) Network, a collaborative of around 30 UK medical research charities.[14] Many medical research charities now actively collaborate with industry to facilitate the integration of patient input into trials. The TAR report highlights the capabilities of third sector organizations in influencing commercial development in a manner that directly targets unmet need.

This importance of patient involvement is underscored by initiatives like the EURORDIS (Rare Diseases Europe) Charter for Clinical Trials in Rare Disease, which emphasizes transparent and effective collaboration between sponsors and patient organizations. By ensuring that patient perspectives are integral to the design and execution of clinical trials, the Charter highlights a growing recognition of the need for patient-centered approaches in research.[15]

Through their efforts, charities have not only improved trials but have reshaped the concept of patient engagement, emphasizing inclusivity and meaningful involvement at every stage.

The future: True partnership

Looking ahead, the next frontier in patient-centricity is the cementing of the principle of co-creation. Imagine involvement of patients from day one as being the norm rather than the exception — not just being consulted but actively shaping research questions and trial design.

We also need to rethink how we define success. Inclusion of PROs is a start, but they're just one piece of the puzzle. Integration with real-world evidence and feedback from patients could give us a much richer understanding of how treatments impact lives. Ultimately, we need a system that isn't just patient-centric, but truly patient-driven.

Some study sponsors continue to treat patient involvement as a superficial exercise, or conflate engagement and involvement, falling short of the goal of fostering genuine collaboration. As a result, patient involvement can become a box-ticking activity with limited real impact. Additionally, defining success and monitoring levels of involvement and its impact can vary significantly across trials, making it challenging to identify and replicate successful models.[16]

Prostate Cancer Research (PCR) is an example of a charity that has recognized the power of combining PROs with real world evidence, and in response launched the *Prostate Progress* initiative in 2024.[17] By linking clinical data with PROs, *Prostate Progress* provides a holistic view of treatment impact, capturing both medical and personal patient experiences. Additionally, the initiative provides a platform to facilitate and support patient involvement, engagement and targeted study recruitment. Such projects demonstrate the capabilities of charities and the ways in which they are harnessing their potential to create initiatives that pave the way for treatments that are not only effective but also aligned with patients' real-world needs and experiences.

Reflections

After two decades in advocacy and research roles, I've learned more from patients than any textbook or conference could offer. Patients and advocates have driven every significant change in clinical trials and drug development, showing remarkable resilience and hope.

I've also witnessed the transformation in attitudes toward patient involvement in clinical research. Though there's still progress to be made, the impact is clear. However, it's important to acknowledge the pressures faced by both patients and advocates. Many patients, even knowing a trial might not benefit them, participate for the sake of future patients, often bearing emotional burdens. It's also important to recognize that advocates often operate with limited resources and face competing pressures. Robust support structures are essential to ensure they can sustain their vital work and avoid burnout.

As clinical trials evolve, patient input will surely remain central. If the industry continues to listen and value this input, future breakthroughs will continue to be clinically effective and aligned with the real-world needs of those living with illness. Through deeper collaborations, patients are placed at the heart of research — and the best is yet to come.

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Dr. Jayne Spink holds a PhD from Cambridge University and began her post-doctoral career as a molecular and cellular research scientist. She currently serves as Director of Translational Research at Prostate Cancer Research (PCR), where she is dedicated to driving patient-centric innovations towards clinical application. Throughout her career, Jayne has held pivotal roles in both the public and third sectors. She was previously a Principal Scientist with the Department of Health, an Associate Director at the National Institute for Health and Care Excellence (NICE) and has spent over two decades working within advocacy and research-focused organizations. Her previous leadership positions include Director of Policy and Research at the Multiple Sclerosis Society, CEO of Genetic Alliance UK, Chair of Rare Disease UK, and CEO of the Tuberous Sclerosis Association. Jayne has also contributed as a non-executive board member for various national and international committees, including EURORDIS.

Jayne's personal and professional experiences have profoundly shaped her commitment to patient-focused medicines development. Over decades of working closely with patient communities in advocacy and research, she has seen the importance of putting patients at the center of treatment development. As a parent of a son diagnosed with a rare disease when just a few weeks old, and as a carer towards the end of their lives for her mother with Alzheimer's, and her stepfather with colon cancer, she has gained firsthand insight into the emotional and practical challenges faced by patients and their families. These experiences have reinforced her belief that healthcare solutions must not only be scientifically innovative but also deeply attuned to the needs, voices and lived experiences of those who matter most — the patients themselves.

Disclaimer: The views, opinions and statements made in this presentation are solely those of Jayne Spink and may not reflect the views of Prostate Cancer Research (PCR) or its affiliates.

CHAPTER 18

Patient advocacy group and pharmaceutical industry collaboration to drive patient-centric practices and accelerate the development of new medicines

PATRICIA B. DAVIDSON

The rise of patient advocacy groups and their focus on patient-centricity

Before the 1960s, the healthcare system was predominantly paternalistic, with patients having minimal involvement in decision-making regarding their own care. But in the 1970s and '80s, there was a shift toward greater patient involvement with the rise of patient rights, empowerment, increased access to information and informed consent. Patient advocacy groups (PAGs) emerged to provide patient support and services, as well as a collective voice for patient needs. Over time "patient involvement" evolved into "partnering with patients" and "patient-centricity," with PAGs leading efforts to understand preferences, needs, values, satisfaction, feedback and cultural considerations. These groups have become more involved in research, such as gathering patient insights, identifying outcomes that matter to patients, and collecting quality of life data, which in turn has led to partnership opportunities with pharmaceutical companies.

There are now more than 3,300 PAGs currently operating in the United States, and more than a third were created in the last decade.[1] These groups vary in size, expertise and focus. Some larger, more experienced PAGs have developed patient registries, online communities and conduct research activities.

While some advocacy groups may invest in clinical research activity, for many their primary mission is not to conduct clinical trials. Biopharmaceutical companies, on the other hand, are focused on expediting and improving the clinical trial process and in bringing new therapies to market.

Untapped potential to leverage patient advocacy group collaboration

The past decade has seen a proliferation in the number of investigational therapies and the number of companies sponsoring active clinical trials. At the same time, an unprecedented number of collaborations between PAGs and biopharmaceutical companies have formed. Companies report partnering with patient advocacy groups largely to support recruitment and retention on 36% of clinical trials in 2023, up from 19% in 2019.[2] Beyond clinical trials, partnership engagements involve providing input into clinical development plans, ensuring outcomes relevant to patient communities are reflected in drug development activity, and supporting access to clinical trials for historically underserved communities.

Pharmaceutical companies need to harness patient insights and perspectives to improve care, inform research and drive innovation. However, engaging patients

effectively can be overwhelming for pharmaceutical companies and patients alike. PAGs can serve as effective intermediaries, bridging the gap between individual patients and the broader healthcare system to bring structure, organization, focus and a patient-centered approach to otherwise fragmented efforts.

PAGs are often considered the trusted partner in a patient's health journey, making them an untapped resource for pharmaceutical companies that may not be seen as trusted sources by patients. In 2023, 12% of patients reported first learning about clinical trials through a PAG, up from 5% in 2019.[2] This growing recognition highlights the critical role PAGs play in connecting patients to clinical research opportunities and to the broader healthcare system. As trusted partners, PAGs empower patients to make informed decisions, advocate for their needs and navigate healthcare complexities. Moreover, PAGs understand how to convey patient needs and insights into terms that align and resonate with industry stakeholders. By serving as intermediaries, PAGs ensure patient voices are integrated into the clinical research process in actionable and industry relevant language, underscoring the need for pharmaceutical companies to collaborate with them.

There are a number of benefits for PAGs in partnering with pharmaceutical companies beyond ensuring trials incorporate patient insights, including access to novel therapies, technologies and treatments, as well as clinical and scientific expertise. Education about and awareness of opportunities to participate in clinical research drive informed decision-making and provide access to treatment options, which is especially important for those with limited options. Harnessing patient insights through efficient and effective PAG/industry collaboration can ultimately lead to more patient-centered care, improved health outcomes and accelerated medicines development that meet patient needs.

A need for more efficient and effective PAG/ industry collaboration

In recent years, through forums like U.S. Food and Drug Administration (FDA) Patient-Focused Drug Development meetings and social media, patient communities and their families are calling upon their advocacy organizations, healthcare providers, drug developers and the clinical research enterprise to communicate and collaborate more effectively in order to accelerate the development of new therapies, with the ultimate goal of increasing access to life-saving treatments.

While well-intentioned, collaborations between patient advocacy groups and industry have (with few exceptions) been limited in their effectiveness in making clinical research faster and more efficient. A very high percentage — more than 65% — of PAG/industry partnerships in 2023 receive low marks for efficiency and effectiveness. This is largely due to wide variation and inconsistency in collaboration expectations, processes and practices.[2] A major opportunity exists to standardize and structure these research and development (R&D) driven collaborations to optimize their impact and reduce the risk of repeating past mistakes. Specific optimization opportunities include:[3]

- Improving understanding of respective operating objectives, processes, restrictions, needs, priorities and timelines
- Establishing standards for contractual arrangements and fair market value assessment
- Increasing transparency around effective organizational and governance structures, training, operational support, monitoring and evaluation/assessment
- Improving understanding of funding requests and delivery cycles

- Promoting earlier communication to anticipate short- and long-term mutual interests and promote effective planning of resources and timelines
- Developing mechanisms to routinely and continuously apply lessons learned and measure value and impact to improve future collaborations

Co-developing the PALADIN Consortium

The good news is that all of the underlying conditions and opportunities to optimize collaborative efficiency and effectiveness are addressable. Biopharmaceutical companies and patient advocacy groups have devoted significant attention, effort and financial investment to establishing partnerships. However, there has been limited attention and investment devoted to determining and communicating *how* industry and PAGs can best collaborate and to establishing an accessible repository of resources, standardized practices and lessons learned.

Recognizing this opportunity, in the spring of 2023, more than 20 charter companies launched the PALADIN (Patient Advocacy Leaders And Drug Development Industry Network) Consortium with project management support from the Tufts Center for the Study of Drug Development (CSDD), part of Tufts University School

Real-world challenges PALADIN Consortium members faced:

" We are frequently approached to help with recruitment campaigns but do not know what already exists. We really do not want to recreate tools and it is hard to know what works."

— Advocacy member

" We have experienced times when PAGs were inundated with unanticipated industry requests and did not have the resources to take on new projects."

— Industry member

" Some industry partners are asking us how to initiate a collaboration and where they should start."

— Advocacy member

" Expectations were not clear or stated from the start of the collaboration. This meant that the PAG had one idea of what they were bringing to the relationship while we (the sponsor) had a somewhat different idea."

— Industry member

of Medicine. PALADIN is a pre-competitive, disease-agnostic consortium whose mission is to optimize advocacy group-industry collaboration to ultimately accelerate the pace of medicines development by collectively developing:

- Common foundations that improve industry and advocacy R&D-focused collaborations
- Guidance and trainings for advocacy and industry representatives on how to implement patient- and caregiver-informed R&D approaches
- Measures to improve diversity in clinical trials through best-practice sharing across the industry
- Awareness programming aimed at educating and connecting patients to clinical trials, and
- Knowledge-sharing across therapeutic areas to reduce silos and maximize learnings.

Although there are impactful programs and collaborations ongoing between PAGs and industry, the industry is still experiencing lengthy development timelines, increasing complexity, and challenges to consistently achieve representative diversity in all clinical trials.

The PALADIN Consortium is unique in that it is co-designed by patient advocacy groups and biopharmaceutical companies with a shared passion and commitment to reshape and transform *the very processes that guide collaboration,* ensuring alignment of efforts and the adoption of best practices. The Consortium fosters a culture of continuous improvement in how we collaborate to reduce operational inefficiencies, do more with the resources we have, and begin to understand what it will take to reverse the timeline and complexity trends seen in drug development. We aim to elevate collaboration to a dynamic driver of greater innovation and stronger outcomes.

PALADIN's primary workstreams

PALADIN has formed four primary workstreams and identified pillars for collaborative success:

1. Consensus-driven standards to reducing variability in ways of working across companies and advocacy groups, including lessons learned.
2. A curated repository of resources that makes it easy for teams to quickly identify, based on a topic, frameworks and templates fit-for-purpose based on the project being initiated.
3. Skills and training resources to reduce the uncertainties about initiating projects as well as frameworks to support sustainable multistakeholder community engagement for diversity and inclusion in clinical trials.
4. A framework to assess collaboration success to set expectations for PAG/industry collaboration success and investment.

PALADIN workstreams meet monthly to develop their respective work products. Each workstream is composed of, and co-chaired by, representatives from PAGs and industry to ensure that insights, recommendations and resources are relevant and useful. The Consortium's governance includes one member of each participating PAG and biopharmaceutical company. All Consortium workstream activity and deliverables are consensus-driven.

During our launch year, the PALADIN Consortium produced a Playbook and Repository of Resources to provide foundations for effective PAG/industry collaboration. Although there is interest in forming partnerships, it is not always clear how to get started. The Playbook and Repository offer insights, guidance, templates and best-in-class resources for understanding how to develop collaborations that are productive and mutually beneficial.

Suggestions for effective collaboration among patient advocacy groups and biopharmaceutical companies (industry)

Value of patient advocacy group/industry collaboration throughout development

RESEARCH

PRE-DISCOVERY

- Learn about patients' lived experience, diagnostic journey & burden of disease
- Identify patient/care partner barriers & unmet needs
- Understand access and experience with current treatments
- Define research questions and outcomes relevant and important to patient
- Define meaningful outcomes to the patient and health care community
- Evaluate possibility of conducting a clinical trial in geographical region(s)

Pharma Contacts: Medical Affairs & Clinical Operations Study Lead

Patient Advocacy Group Contact: Leadership

STUDY CO-DESIGN

- Create research objectives based on prioritized unmet needs
- Determine meaningful endpoints and patient-reported outcomes (PROs)
- Design patient-friendly informed consent
- Define acceptable benefit-risk tradeoffs
- Identify and co-design recruitment, retention, and patient engagement strategies
- Incorporate what was learned in pre-discovery around pressing challenges (i.e., quality of life and access issues)
- Strategize efforts to disseminate study findings – focused both in scientific and community avenues

Pharma Contacts: Medical Affairs & Clinical Operations Study Lead

Patient Advocacy Group Contact: Leadership

DEVELOPMENT

PRE-CLINICAL

- Provide spotlight on barriers to recruitment and participation
- Organize clinical research education and awareness-building campaigns
- Plan for drug administration and care delivery

Pharma Contacts: Medical Affairs & Clinical Operations Study Lead

Patient Advocacy Group Contact: Leadership

CLINICAL

- For each study phase, reference co-developed research strategy from Study Co-Design step when writing study concept and outline.
- Ensure study designs incorporate the meaningful endpoints that were discussed in earlier planning stages
- Walk through proposed study procedures and drug administration with patients and health care providers to determine feasibility and level of comfort
- Co-create patient-friendly educational materials
- Work with trusted channels to raise awareness about clinical trials and support diverse patient participation
- Select/recruit trial sites
- Ask for patient perspective and overall satisfaction with clinical trial experience

Pharma Contacts: Medical Affairs & Clinical Operations Study Lead

Patient Advocacy Group Contact: Leadership

REGULATORY

- Pharma to ensure patient input has been included in race & ethnicity diversity plans and in overall development program
- Co-develop drug label language
- Collaborate on FDA Patient Listening Sessions
- Patient preference studies

Pharma Contacts: Medical Affairs

Patient Advocacy Group Contact: Leadership

COMMERCIALIZATION

APPROVAL

- Co-design patient education
- Continue to break down barriers and misconceptions about research through multistakeholder awareness-building campaigns
- Translate scientific research into publications, manuscripts and co-develop plain language versions

Pharma Contacts: Medical Affairs & Public Affairs/ Patient Advocacy

Patient Advocacy Group Contact: Leadership

POST-APPROVAL

- Co-create and disseminate study results/plain language summaries
- Collect real world evidence and identify unmet needs
- Create access strategies
- Continue to address unmet needs and challenges
- Collaborate on a long-term discovery and development strategy to improve treatment options and access

Pharma Contacts: Medical Affairs, Public Affairs/Patient Advocacy, Commercial Marketing

Patient Advocacy Group Contact: Leadership

We are now gathering metrics on our impact and use cases on our work. We are identifying systematic and tangible ways of involving PAGs early in the drug development process, such as in the target product profile, to ensure the patient voice is integrated. The key to PALADIN's success is establishing the highest level of engagement, collaboration and consensus among member organizations and creating best-in-class resources (i.e., standard practices, guidelines and skills training) that are assessed for continuous improvement. The Consortium's resources are being recognized, applied and adopted by the broader community of patient advocacy and drug development organizations. PALADIN is publishing updates and articles on its progress and provides easy access to finished work products at https://paladinconsortium.org.

Concluding thoughts

There is a broad movement to meaningfully include patients throughout the healthcare ecosystem along with a multitude of patient engagement initiatives by communities, coalitions, collaborations, and consortia on the local, state, national and global levels. With the patient voice becoming more pivotal to advance patient care, and disruptive innovation reshaping how treatment is delivered, it will be essential for pharmaceutical companies and patient advocacy groups to work collectively to leverage technology and real time data sharing, manage risks and opportunities ushered in by artificial intelligence and explore new modalities to transform patient care.

The clinical research landscape is rapidly evolving and with it "patient-centricity" is sure to evolve. New approaches to communication and coordination of efforts, curation and adoption of best practices, and the courage to openly and transparently share lessons learned and what does not work, will be essential to maximizing the impact of PAG/industry collaboration. We are just getting started on addressing these challenges, which are complex. To truly transform the pace of medicines development, we must understand how to work differently to reverse the trends in lagging timelines and complexity seen in drug development so that we may address unmet patient needs. PAG involvement throughout the medicines development lifecycle and beyond affirms the trust patients put in PAGs, and ensures structured, consistent, systematic patient engagement that ultimately drives advances that patients expect and need.

To learn more about the PALADIN Consortium and PAG and biopharmaceutical company participation or provide feedback on PALADIN assets, please visit https://paladinconsortium.org.

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Trish Davidson has over 20 years' experience developing and directing patient and professional educational programs, research symposia and consortia involving diverse stakeholder communities in clinical care and clinical research. She collaborates with Tufts CSDD Executive Director Ken Getz on a variety of initiatives involving building and sustaining relationships with professionals in government, advocacy, academia and industry. Trish holds a Master of Public Administration (MPA) from the University of South Carolina.

Accelerating medicines development is both a deeply personal and professional commitment. Witnessing the devastating effects of lupus in her family early on in life — and later, the profound loss her mother to a rare cancer — has instilled in her an unwavering determination to do everything she can to create opportunities that improve health outcomes. Her experiences are part of countless stories and voices of others, and this drives her to make a meaningful difference. She is honored to collaborate with extraordinary individuals who devote their expertise and passion to improving health around the world.

CHAPTER 19

Cautious optimism: My experience in pushing the patient-first narrative throughout biopharma

INGOLF GRIEBSCH

The below is a transcript of a conversation between Matt Reaney and Ingolf Griebsch. The conversation had only one goal: Find out how Ingolf, a veteran of 25 years in the biopharmaceutical industry, feels about "patient-centricity."

Matt: Why do you think patient-centricity is important in intervention development?

Ingolf: For me, patient-centricity is the logical consequence of abandoning a medical practice of paternalism where the doctor decides what is best for the patient and where patients' views and wishes are not necessarily considered. There is now, I believe, recognition that without considering the perspective of patients, doctors may miss some vital information in making important treatment decisions. The perception of what is best for a patient may be different from the perspectives of an HCP *[healthcare professional]* and a patient.

Patients are the most knowledgeable experts for their own condition and their experience with treatments and its effect on functioning levels, symptoms and quality of life — particularly for non-acute treatments where patients will develop of a lot of experiences with their medical treatments. And if we recognize that patients know their condition better than others, including doctors, they have a vital role to play in guiding researchers in the biopharmaceutical industry to prioritize new treatments, to educate them about their condition, symptoms and expectations towards the efficacy of new treatments as well as endpoints that are meaningful and relevant to them. Furthermore, they can teach us how to set up trials in an optimal way to reduce hurdles for them to participate and to better understand the opportunity and burden of them being part of a clinical trial.

The ultimate aim of patient-centricity in intervention development together with other efforts — for example, including PROs *[patient-reported outcomes]* in clinical practice to measure treatment experience and outcomes — is to improve patient care and outcomes. It's not just about getting an intervention approved, but about developing a treatment that can improve patients' lives. Information derived from patients during the development process of drugs and other interventions can enhance shared decision-making between patients and their treating physician and improve treatment outcomes by involving patients in that process.

Matt: Are you surprised how long it has taken us to get to this point and why has it taken so long?

Ingolf: I think a mixture of everything, really. When we had our second SISAQOL *[Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life Endpoints; an international consortium of experts that develops recommendations for analyzing PRO data in cancer randomized trials]* meeting back in 2017, I was surprised to see that there wasn't enough agreement which basic terms to use, whether it was health-related quality of life or PROs, and about the definitions of these. While there was enough guidance out there on how to develop PROs, translate and culturally adapt them, and report data, published studies took a rather heterogenous approach to reporting and analyzing PRO data. The research hypotheses of the PRO analyses, the rationale for selecting statistical approaches, and transparency in the application of these approaches was missing. And this contributed to the uncertainty on the part of regulators and other stakeholders on how to interpret the data.

And of course, operational complexities. As an industry, we have needed to make Phase II studies leaner, less complex and costly, and as a result, PROs were often omitted. This meant that we ended up with a lack of data to inform Phase III PRO strategies. There was also a concern that patients might be overburdened with the number of questions posed to them.

Further, PRO are subjective data, which many in the medical profession think is somehow less valid than objective data. But the two can and should complement each other. For example, the reporting of AEs *[adverse events]* in oncology using the CTCAE *[Common Terminology Criteria for Adverse Events used in all oncology clinical trials to capture information on adverse events as reported by the investigator]* may be sometimes different than what patients self-report using the PRO-CTCAE system, where patients report directly and HCPs are not involved. This is confusing for some clinical colleagues, as is it when there appears to be a non-logical relationship between PRO and non-PRO data. For another example, patients report high scores for diarrhea and then say their overall QoL *[quality of life]* remained the same. Of course, this is possible (if diarrhea is not having an adverse effect on a patient's life), but it is hard for clinical people used to considering adverse event data as problematic to comprehend.

In addition, we also heard from patient advocacy organizations that we really need to make sure that patients do understand why, for example, PROs are collected in a trial and to get re-assurance that everything they report will not affect the care they are getting in that particular trial. We then started to develop leaflets to make sure that patients understand that the information provided by them will benefit future patients and will not affect them.

And most importantly, the difficulty of getting label claims: a fact that is often used by senior management in biopharma not to include PROs in clinical trials, since it was then difficult for them to understand the purpose of this exercise.

If there is stable and continuous demand not just for PROs but for patient-relevant information from regulators and payers or HTAs *[health technology agencies]* alike, then companies would see the point of collecting this information on a routine basis. And I think we are currently moving in that direction, which is encouraging.

Matt: But if regulators and payers stopped caring, would pharma?

Ingolf: Wow, this is a thought-provoking and difficult question to answer. I think companies engaged in PFDD *[patient-focused drug development]* already see the advantages of more closely interacting with patients. It may shorten their development timelines, contribute to more meaningful development of medicines that can address patients' unmet needs, and may also improve trial recruitment. It is difficult to see that these developments could be easily ignored. And there are also the HTA agencies which sometimes do not accept surrogate or intermediate image-based endpoints like PFS *[progression-free survival].* In these cases it is so

important to collect PRO, since these data are sometimes the only means of showing patient-relevant benefits, in terms of how some HTAs may define and interpret patient relevance.

I see also a lot of people working in our industry that are deeply driven by the purpose to develop medicines that may change patients' lives. And then not involving patients in this process does not make sense to me. But I may be wrong and this applies not to everyone. Who knows?

Matt: What are you doing to change things?

Ingolf: Education, education and education, particularly focusing on cases where such data made a difference.

Matt: What is the return on investment from a sponsor perspective?

Ingolf: Shorter development timelines, a more meaningful and more tolerable product for patients and hence more successful product, faster regulatory approval, and better and broader patient access.

Matt: What advice would you give to the CEO of a biotech group who approached you at first-in-human dosing asking about patient-centricity in drug development?

Ingolf: Definitely include PFDD considerations from the beginning and consider recent papers that look into dose-finding studies and PROs, and recommendations and learnings from the U.S. Food and Drug Administration (FDA) Optimus Initiative, which aims to identify optimal doses of novel oncology drugs and biologics which are both efficacious, safe and tolerable. The earlier you start with these activities, the higher the chances of getting the data accepted and achieving a label claim and achieving a level of acceptance in any HTA evaluation and reimbursement decision.

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Dr. Ingolf Griebsch has 26+ years' experience in designing and conducting cost-effectiveness analyses using trial-based and decision-analytical modelling approaches, patient-reported outcome studies and analyses, and various other outcome research projects to describe the burden of disease and real-world effectiveness. Ingolf was the co-initiator, founding member and industry lead (until January 2023) of Setting International Standards in Analysing Patient-Reported Outcomes and Quality of Life Endpoints Data (SISAQOL) and the SISAQOL-IMI Consortium, which involves an international, multi-stakeholder group of experts whose goal is to develop recommendations for the analysis of PRO and QOL data in cancer clinical trials.

Ingolf advocates patient focused drug development for its potential to ultimately improve patient care and outcomes. He is convinced that each single patient with their unique views and perspectives should be in the center of their own care. Patient-reported outcomes and patient-focused drug development considerations in general can hugely contribute to incorporate these perspectives in the development process of medicines.

Disclaimer: The views, opinions and statements made in this presentation are solely those of Ingolf Griebsch and may not reflect the views of Ferring Pharmaceuticals or its affiliates.

CHAPTER 20

It's the economy, stupid: Drug developers will invest in patient-centricity when the R&D economics are clear

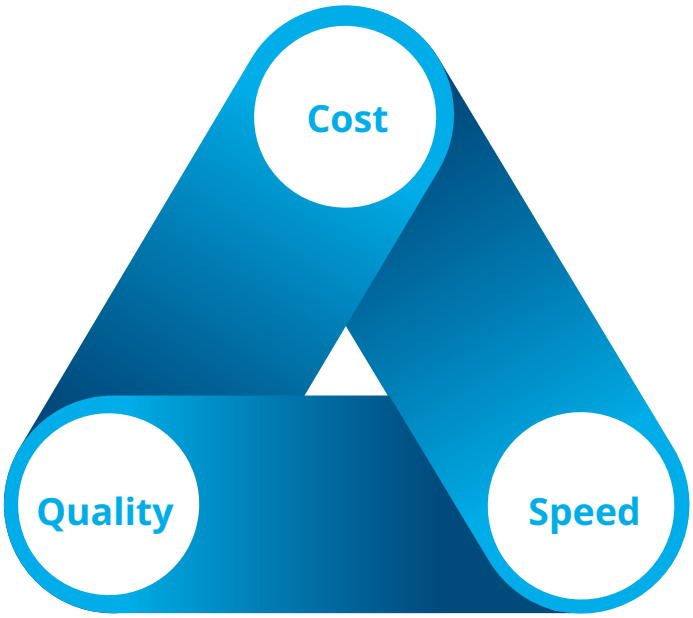
PAUL SJ MILLER

> *How important do you believe the patient perspective is in pharmaceutical drug development and decision-making in 2024; and how has your perspective on this changed over time?*

The short answer is, whilst intuitively relevant, drug-developers do not really know (or cannot yet evaluate) how important the patient perspective is in getting their products on the market.

As patients are the end-users of medicines developed in a very long, costly and risky research and development (R&D) process, it has always been somewhat intuitive for drug developers to at least consider the patient perspective in both their product design and development of their evidence packages for external review by regulatory, reimbursement and clinical decision-makers. Just how important this patient perspective can be to any given drug development program is likely to be subject to R&D project management decision-making and basic economics.

Drug developers are clearly presented with very many project options and many competing interests in which to invest their scarce R&D resources, all with the goal of optimizing project success. At a fundamental project management level, investment by a drug developer in any project to enhance patient perspectives, as any other project, must be assessed according to the basic "project triangle":



Some assessment of a project's overall cost impact is of course required: generation of patient-focused information will likely require additional resources but may also displace other costs; absence or insufficient use of patient-focused information could also potentially incur costs elsewhere and/or downstream. Some

assessment of a project's impact on speed is required: will the generation of patient-focused information extend or reduce product development time? Some assessment of a project's impact on quality is also required: to what extent is a drug product (and its evidence package) enhanced by patient-focused projects? Is this enhanced quality valued by regulatory, reimbursement and clinical decision-makers?

Classic project management theory states that ordinarily all three attributes cannot be improved by one project strategy at the same time, and so trade-offs must be made. For drug developers this may typically mean that many patient-centric projects evidently cost more and take longer (to varying degrees with different strategies under their control to some extent) but they offer the potential for a better-quality product (including evidence package). In a commercial R&D setting, this then becomes an investment decision that can be guided by economic evaluation: in short, is the value of the product quality improvement greater than the costs (time and money) of delivering the project? Is there a return on investment (ROI)?

Over recent years, the key stakeholders/customer groups for drug developers' products have indeed signaled that they attach some value to the inclusion of patient-centric approaches to drug development.

Regulatory agencies (Medicines and Healthcare products Regulatory Agency (MHRA), European Medicines Agency (EMA), Food and Drug Administration (FDA)) have published patient-focused drug development guidance documents to address how drug developers can collect and submit patient experience data and other relevant information from patients and caregivers for medical product development and regulatory decision-making.

Health technology assessment (HTA) bodies have explicitly designed the patient perspective into their methods and processes of evaluation. For example, the National Institute for Health and Care Excellence (NICE) invites written submissions from all patient and carer organizations involved in the evaluation to provide perspectives on:

- The experience of having the condition (before or after diagnosis) or caring for someone with the condition
- The experience of receiving care for the condition in the healthcare system
- The experience of having specific treatments or tests for the condition
- Treatment outcomes that are important to patients or carers (which may differ from the outcomes measured in the relevant clinical studies and the aspects of health included in generic measures of health-related quality of life)
- The acceptability of different treatments and modes of treatment
- Their preferences for different treatments and modes of treatment
- Their expectations about the risks and benefits of the technology

Drug developers' HTA submission dossiers can be assessed against these and many other criteria.

Currently (in 2025), however, drug-developers are largely unclear what difference inclusion of various patient-centric drug development strategies can make to regulatory, reimbursement or clinical decision-making outcomes. R&D decisions are of course frequently made under conditions of information uncertainty, but basic R&D economics will require some plausible assessment of the impact a patient-centric project can have on key business metrics, such as the probability of approval (regulatory and reimbursement), label wording, price, market access (volume), prescribing behaviors (uptake), and ultimately on the product's sales forecast. Where patient-centric projects are lower-level (low resource/cost/time), there

may be a greater propensity for drug-developers to invest at risk or based on unquantified analyses, but as the scale of projects and their investment increases, assessment of ROI cannot be ignored.

My own experience of HTA decision-making with NICE is that the patient perspective is indeed positively received as it is by design a deliberate component of the process. The extent to which this can influence the HTA outcome very much depends on what the drivers of the incremental cost-effectiveness ratio (ICER) are. For example, for many advanced oncology treatments, a company may indeed be criticized if patient-reported quality of life measures are not included to characterize the net effects on the patient experience. However, it is often very clear that this actually makes little quantitative difference to the ICER calculations, since increases in overall survival (OS) dominate the value assessment as captured by the quality-adjusted life-year (QALY).

How has the pharmaceutical industry involved patients during drug development, how has this changed in your career, and how should it change in future drug development?

Some 20 years ago, I had experience of a pharmaceutical industry global development project team where a patient was invited to attend to give an account of their experiences with the disease and their own treatments. This was an extremely informative and positive experience for the development team, who were immediately keen to action many of the patient insights gathered. However, as a research exercise, this was clearly an n of 1 survey. Drug developers can of course choose to make internal development decisions however they wish, but to impact external decision-makers who will ultimately license, fund and prescribe the drug, more systematic methodologies will inevitably be required.

The increasing volume of patient-centric drug development projects, pilots and publications would suggest that drug developers are increasingly conscious of their potential importance. To what extent methodologies for patient-centric projects have actually transitioned from largely anecdotal evidence to more systematic methods is less clear.

Published literature in this area can be grouped into three broad themes. First, there are examples of patient input to product design (medicines, medical devices and digital support tools). Second, there is a body of literature focused on the role of patient input to enhance the process of clinical research activities. Third, there is literature on the role of patient input to enhance the design of evidence packages in support of products.

It is argued that patient input to pharmaceutical chemistry, manufacturing and control (CMC) is also valuable, since the patient's treatment experience can be shaped through the product's presentation, modality, route of administration, and quality attributes.[1] Product formulation is a key interface directly with the patient, and so adherence and compliance can be influenced by patient-centric research to ensure that medicines can be used by all patient groups (including young, older, multimorbid, etc.) as intended.[2-4] Patient-centered packaging design can also impact the patient experience but is largely underused.[5] Other relevant pharmaceutical design aspects involve the selection of the route of administration, the tablet size and shape, the ease of opening the package, the ability to read the user instructions, or the ability to follow the recommended storage conditions.[6]

Several publications report on efforts to improve the efficiency of clinical research activities by leveraging patient experience data. Patient input is used to develop strategies that may improve clinical trial

feasibility, motivation, engagement and satisfaction for participants, enhance recruitment, and involve fewer dropouts and protocol amendments.[7-10] Patient insights have been explored through various methods such as patient advisory boards,[11] patient appointments to drug developer clinical development teams,[12] and harvesting social media health networks.[13] There are also several attempts to develop qualitative and quantitative tools to assess the impact on pharmaceutical organizations of patient-centric input to drug development.[14-19]

Whilst explicitly understanding patient experiences can of course be used to make products and the clinical research process more acceptable to patients, which can have great value, robust evidence that clinical outcome assessment (COA) is meaningful to patients is likely the key area for patient-centric research to add value in the future. There are some published examples of development of patient-relevant COAs in digital health technologies,[20] neuroscience,[21] sickle cell disease,[22] rare diseases,[23-24] real-world evidence,[25] pediatrics[26] and oncology.[27] COAs are a pivotal element in characterizing a product's treatment effects and value proposition; if external decision-makers in regulatory, reimbursement and clinical contexts value evidence of patient relevance to validate COAs, then this can create an incentive for drug developers to do so. Greater clarity on how exactly external decision-makers intend to use patient-relevant COAs in their processes can potentially increase these incentives for drug developers.

Future European harmonization efforts such as the Joint Clinical Assessment (JCA) process could perhaps provide an opportunity for different payer archetypes to influence one another more. For example, the well-rehearsed focus on the patient relevance of endpoints in the German HTA system could make the patient perspective more prominent within a joint assessment than countries whose decision-making is more traditionally dominated by budget-impact or cost-effectiveness would otherwise have.

What opportunities have there been, and are there now, for patients to share their stories to inform pharmaceutical drug development and decision-making?

Advances in formal regulatory guidance on systematic methodologies for patient-focused drug development offer significant opportunities for these data to become an integral and valued component of regulatory and potentially reimbursement (and clinical) decision-making. For example, the four guidance papers published by the U.S. regulator, the Food and Drug Administration (FDA), give clear instruction to drug developers about what the regulator expects from patient-centric information within their submissions. The FDA has essentially provided a manual on collecting comprehensive and representative input; methods to identify what is important to patients; selecting, developing or modifying fit-for-purpose COAs; and incorporating COAs into endpoints for regulatory decision-making. This guidance and similar from other agencies can ideally provide drug developers with the clarity needed for the "how" and "what" of patient-centric research.

EUnetHTA (European Network for Health Technology Assessment), incepted in 2004, is clearly an important organization in European (EU) HTA, including championing the role of patient perspectives. It is made up of 82 national, regional and not-for-profit agencies from 29 EU member states and the UK. The main goal of EUnetHTA is to provide a platform for HTA agencies across Europe to exchange HTA information and develop HTA methodologies in order to ultimately facilitate the harmonization of HTA approaches across member states. Whilst it could be argued that EUnetHTA methodological

guidance on health-related quality of life (HRQoL) has been much narrower than the patient-centric research perspective suggests, EUnetHTA actions have resulted in the adoption of the EU HTA regulation, which sets out the regulatory basis for JCA across EU member states.

What have been, and are, the challenges to "patient-centricity" in the pharmaceutical drug development and decision-making around drug development?

The key challenges to date have been that, whilst there are several published examples of good practice regarding patient-centric drug development, this is not yet a consistent, standardized or default element of the process. Drug development organizations have tremendous resources and competencies to do almost anything that is required to deliver patient-centric evidence, but they must be persuaded that this is an effective way to use these resources. To some extent there will be a challenge by entrenched patterns of internal decision-making and influence within drug development organizations, where scientific, technical, regulatory, clinical, payer and commercial voices have varying influence at different development stages. The patient-centricity research agenda will benefit from having champions within these organizations, but it is likely that these need to come from diverse departments within the traditional organizational structures.

The European Federation of Pharmaceutical Industries and Associations (EFPIA)[28] has described the fundamental challenge being that there is currently no clear understanding of how/when patient evidence collected during drug development will be considered by regulators to be sufficiently fit-for-purpose for benefit-risk decision-making and/or inclusion in the regulatory documents and product information. There may now be more clarity on research methods, but what impact this has or can have on decision-making is still far from clear. To encourage and optimize implementation of a more evidence-driven patient-centric approach, greater transparency is required, which will enable drug developers to better develop internal business cases for investment in these projects.

What do you think should (or must) happen in the future to ensure that new drugs are developed in line with patient priorities, preferences and needs?

Incentives and information will be the key to changing behaviors within the pharmaceutical industry. Regulatory, reimbursement and clinical decision-makers have gone some way to signaling that they place value on patient-centric information. Clearer information about how much value this has is needed to create the real incentive to drug developers to respond to this. External decision-makers could, for example, simply mandate minimum patient-centric data requirements under certain scenarios and circumstances, with greater clarity as to when failure to meet these requirements leads to a project's rejection.

To consistently invest in patient-centric evidence generation projects during the drug development process, drug developers require better understanding of the potential (even if uncertain) impact that investment in this evidence generation can have on their key metrics of success. In early development, this may be characterized simply (perhaps qualitatively) as a component of a target product profile (TPP) and a product value proposition. In later stages, some quantification of impact becomes necessary; for

example, how is this evidence estimated to impact price, market access and sales? What are the impacts/costs of not having this evidence?

Without clear business metrics to guide internal investment decision-making, there is a risk that patient-centricity remains in the "nice to have" category for drug developers, rather than becoming an integral part of driving product value that is recognized and rewarded by external decision-makers.

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Dr. Paul Miller has over 20 years' experience as a professional health economist in the pharmaceutical industry, NHS and academia. He has held numerous roles over that time, including being a member of the independent NICE Appraisal Committee in the UK that makes recommendations to the NHS for the reimbursement of new medicines with international impact. He has also held Global Payer, Market Access, Pricing & Reimbursement roles for major brands within respiratory, inflammation, cardiovascular and oncology for leading pharma companies. He continues to be Honorary Research Fellow at University of Nottingham and is a lead author for Cochrane reviews.

Acknowledging that medicines development is a very long, complex, costly, risky but ultimately valuable activity, Paul thinks that finding better ways for the pharma industry to routinely incorporate patient-centric approaches to R&D is a huge opportunity to deliver better medicines (and evidence) most valued by patients.

CHAPTER 21

Patient-centricity: Reflections from a former academic, consultant, regulator and now patient representative

BELLINDA KING-KALLIMANIS

Have you ever stared at the columns and rows of numerical responses in a patient-reported outcome (PRO) dataset that we use to understand how a clinical trial participant feels and functions and wondered what those people were thinking when they selected their response? I have. During my time in the Oncology Center of Excellence (OCE) at the U.S. Food and Drug Administration (FDA), I would look at these rows of participants, especially those rows with participants who had experienced deep and remarkable responses to what were then groundbreaking targeted and immune treatments that were reshaping the cancer treatment landscape. These were outliers — a small group of individuals who lasted far longer than most. Because most advanced cancer trials for targeted/immune treatments end when the participant's disease progresses, PRO strategies generally will have participants completing PRO measures "until treatment ends." The rows I was staring at were those few participants with 35 cycles — or about three years or so of treatment. That small group, at each cycle, had sat down and completed yet another PRO assessment. Seeing these sparse rows made me feel happy because, for this small group, the treatment was working… but also a little sad.

Sad because, at the end of the day, these data collected at 35 cycles out from baseline were not really being used to determine benefit and risk of new treatments. While their responses were likely buried in a table somewhere in the clinical study report, there was not much that could be gleaned from this handful of participants who kept filling in those PROs. This situation is a classic case of data waste! People with a serious stage IV cancer diagnosis were taking their precious time to report how they were feeling and functioning, and we were not putting those data to good use.

Inefficiencies associated with data collection and ultimately data utilization start with the study protocol. While at FDA, I reviewed many clinical trial protocols and the schedule of assessments for PRO data capture. It was no anomaly to see that PRO data collection was slated to continue, once per cycle, until disease progression or "until treatment ends." There was often a weak connection between the research question that was being posed and the schedule of PRO data collection. I believe this is a result of PRO strategies that attempt to please all the various stakeholders involved in drug development and their heterogenous needs which ultimately ends up falling short because in the end regulatory stakeholders are prioritized.[1] I deeply appreciate the importance of drugs that are safe and effective. But payers, whose focus is aligned with value alongside high-quality treatments to patients, need robust comparative data for their evaluations. Unfortunately, there is often insufficient follow-up data to meet that need, especially post-disease progression in oncology.[2] We also must admit that only so much can be achieved in a single study.

Much like everything in medicine, collecting PRO data is as much art as it is science. There is no single recipe that will lead to a thoughtful PRO strategy from data collection, through data analysis to dissemination of the findings to the appropriate stakeholders. Though to help sponsors, the FDA recently put out four dedicated guidance documents that lay out the considerations that industry trial sponsors should account for as they build out a PRO strategy for their clinical trial.[3] In addition to the general guidance documents, there are also specific therapeutic guidance documents to help navigate some of the nuances associated with different diseases.[4-5] And still… there is no single exact recipe for a clinical trial that will turn out the perfect patient experience label claim and please all stakeholders, and there never will be.

Much like everything in medicine, collecting PRO data is as much art as it is science.

These guidance documents provide useful direction and advice but cannot offer suggestions for every challenge encountered. This is in part because primary data collection is hard. I do not think we adequately acknowledge the complexities and unpredictable challenges that arise. Over the course of my career that has encompassed academia, industry, regulatory and currently advocacy, I have stepped in and out of the role of collecting primary data. I am currently deep in primary data collection. The reality I am constantly reminded of is that the best laid-out plan in a protocol will be, to varying degrees, challenged in implementation by factors that are difficult to foresee when writing a protocol. This returns us to the issue that only so much can be achieved within a single trial protocol because of data collection schedules. Stakeholder priorities aside, there is also the issue, often less discussed, that the ideal time to measure physical function might vary from the ideal time to measure nausea and vomiting based on treatment and disease trajectory. In oncology trials where tumor growth and survival are the primary outcomes, ideal timing for capturing PRO concepts is often relegated to alignment with the convenient clinic visits. A clinic visit may be the optimal time to have the participant complete the PRO measure but not the optimal time to measure nausea and vomiting, nor physical function.

While the FDA's OCE has provided an "example PRO assessment frequency for first 12 months of advanced cancer trial,"[3] again, there are nuances to the schedule that are based on the treatment(s) under study, which cancer is being studied (e.g., indolent vs. aggressive) and other study specific considerations. What we all need at this junction is probably not more guidance, but increased collaboration with the community for whom the treatment is being developed. In the following paragraphs I will outline some thoughts on good practices for patient-centered engagement, but first, what exactly does the term *patient-centricity* mean?

When a group of patients and caregivers alongside researchers co-created a definition of patient-centricity within drug development the definition, they arrived at was, "Putting the patient first in an open and sustained engagement of the patient to respectfully and compassionately achieve the best experience and outcome for that person and their family."[6] This is a lofty definition, one that I worry creates unrealistic expectations of what a clinical trial could offer and is fundamentally misaligned with the goal of clinical trials. What I mean by this is that a clinical trial is designed to answer research question(s), which by the nature of experimentation will expose those who sign up to some degree of risk in order to, primarily, help future people living with the disease. Because of the shift in priorities of a clinical trial which centers treatment around a research question from that of clinical care where the patient's needs come first, I am not sure that we can ever achieve "the best experience and outcome for that person and their family" when talking about drug development. This is not to say that all hope is lost; we just need to be thoughtful in how we put the patient first

and not overpromise what can be realistically achieved in the clinical trial setting.

Keeping these tensions in mind, how have things changed and what are some low-hanging fruits to help us achieve greater patient-centricity in clinical trials? Backing up, when I was in high school in Australia in 1993, a law was created in the United States that required the inclusion of females in National Institute of Health sponsored clinical trials.[7] Using this important legislation as a benchmark, in the past 31 years a lot has changed that has led drug development to be more patient-centric. Importantly, we have to remember that 31 years is only a handful of drug development cycles because of the years it takes from inception to product licensing, if successful. Fast-forwarding to the 21st century when I started my career, the first FDA draft Guidance to Industry on PRO Measures[8] was published while I was working at my first job after receiving my Master of Science degree. I was working as a statistician in the Florida Mental Health Institute at the University of South Florida in the department of Aging and Mental Health. This guidance, for many reasons, was far away from the work I was doing analyzing data from behavioral health interventions for substance misuse in older adults. My focus then was solely on the numbers in my data files, which was fitting because the primary driver of my decision to pursue the Master of Science was a desire to concentrate on data analysis and limit the need for extensive interaction with others (when I tell patients and caregivers this story now, they actually think I am joking with them!). My career starting point, during this consequential time for the inclusion of the patient voice in drug development, was a far, far reach from the idea of patient-centricity. Never would I have predicted back then that I would be involved in trying to better understand the patient voice in drug development, running focus groups to learn about patient experiences and hugging participants after we wrapped up. But here I am, and I do not want to go back to just looking at numbers!

After having connected with many patients and caregivers in the cancer community over the years, there is one vital truth I hear time and time again that we often lose sight of, which is that many people want to help push research forward and support scientists to make research more accessible. After all, regardless of how patient-centricity is defined, there is no patient-centricity without patient engagement. We can lean more into the desire from the community to help, but relationship-building takes time and resources, requires consistency in showing up and following through on different tasks. However, the time investment in relationship-building could have longer-term time gains because of valuable input from patients and caregivers. Though the pathway to patient-centricity via meaningful engagement is not as simple as relationship-building and asking people to review some documents to gather feedback. Working with patients from all different backgrounds requires creativity. For example, not everyone has access to Microsoft Word or a compatible version of the program. To overcome this barrier, one option might be to mail a hardcopy to the patient, and they can either return in a postage-paid envelope or photograph their handwritten comments and send via email. Or another option might be to email a PDF attachment and have the patient fill the comment boxes in Adobe Reader to provide feedback. Beyond technological considerations that are required when working with the community, it is critically important to consider how feedback, insights and past experiences will be elicited, incorporated and implemented. The process of incorporating the community's thoughts is essential for sustained engagement, but it is important to acknowledge with patient or caregiver advisors that not all aspects of the clinical trial can be changed for a variety of reasons, which I won't delve into here. However, to be respectful of people's precious time and the effort they are making, transparency is one important key. Clearly outlining which aspects of the clinical trial can be improved and the research questions that could be reframed will go a long way in setting a foundation for sustained engagement.

As has been suggested for some time now, many good practices from the community-based participatory research framework can be used.[9] Implementing all elements from the framework is not feasible for clinical trials, but engagement with the disease community, patients and caregivers does not need to be all or nothing. Being sincere about where the engagement falls on the continuum will be helpful to build trust and also set realistic expectations. Finally, though perhaps most importantly, we need an ethical and sustainable payment model to compensate patient and caregiver advisors for time and effort. Such a model should also be able to accommodate people receiving disability payments or who have Medicaid. These and similar programs outside of the U.S. impose strict requirements on income, which can be a barrier to fair compensation for engagement. Addressing this issue requires us, working in patient-focused drug development, to have more conversations about how to navigate these situations.

CALLOUT FOR INDUSTRY SPONSORS WHO WANT TO HAVE MORE ENGAGEMENT

There are great models for patient engagement.[10] Start with advocacy groups in the disease area. However, do not stop there; work with your advocacy relations teams to help you navigate relationships with the community and take time to follow-up. One of the most common things I hear from patients is "show up and keep showing up" — it is appreciated and the community notices.

CALLOUT FOR PATIENTS AND CAREGIVERS WHO WANT TO ENGAGE

"Patients/people are more than the sum of their parts. Behind every data point is a person whose life and family are profoundly impacted beyond statistics and survival. Our perspective is the missing piece that makes the difference between research that's incremental and research that changes lives. Your voice is essential."[11]

All of this might sound challenging, given the time constraints that are placed on drug development programs. I appreciate that community engagement takes time. However, I have sat in enough meetings where patients have shared with the research team information that has improved some component of the study. For example, it may be the research question that after patient feedback better reflects the experiences that matter most to the community. A few years ago, I was working on a project where the goal was to look at pain as an outcome in breast cancer clinical trials investigating CDK4/6 inhibitors. The research team had been focused on change in patient-reported pain scores. The patient we were working with agreed that this was important, but emphasized that patients want to know, on average, how long it takes for pain to become moderate to severe and how long it takes to receive pain relief treatment — only then were they interested in how long pain lasted. This reprioritization of questions made the results more meaningful and useful to people living with stage IV breast cancer who were about to initiate CDK4/6 inhibitor treatment.

It is also not enough to have a thoughtful and patient-centric research question. Just the other day a patient advocate lamented to me, as we were discussing a new survey project, that people are tired of filling in surveys. There are possibly a few reasons why people might be feeling this way, some of which cannot be addressed via well-designed, patient-centric PRO strategies. However, when there is collaboration with the community, I still believe the value can be explained and shown so that resistance will fade. Regarding the value shown, we as a research community do very little to give digestible results back to study participants. This, to be quite frank, is shameful. Since working in patient advocacy, I have had several opportunities to share research results with the community. What I have found is that people love seeing how what they have shared is transformed into something tangible, such as an online data dashboard or an infographic that can be used to help others with the same illness navigate their care. After all, a primary reason people take part in research is to help others.[12]

In regard to explaining the value of participating in research, too often trial participants do not understand the link between the PRO items and learning about the benefits and risks of the treatment being studied. Participants are often just handed a tablet and asked to fill in the survey. There is nothing patient-centered about this process. This sometimes leads participants to worry that their responses may impact their ability to remain on trial[13] or feel frustrated by the repetition of questions seemingly unrelated to their treatment experience side effect items. Providing a clear description at the start of the survey as to why their responses are important, who is monitoring, and why some items may seem irrelevant is likely to be more effective at encouraging thoughtful and complete answers than trying to identify an ideal number of items that will not frustrate participants. These are all low-hanging fruits and they highlight the importance of including patient perspectives in drug development.

In regard to explaining the value of participating in research, too often trial participants do not understand the link between the PRO items and learning about the benefits and risks of the treatment being studied.

Some fruits, though, are harder to reach. For example, can we make PRO measures more engaging and relevant for participants? Weinfurt[14] describes it well: a PRO measure is a standardized and practical tool that serves as a good model for much richer one-on-one conversations that are too difficult to have with every trial participant. Our measures are indeed a convenient tool. The 0s, 1s, 2s, etc., can be summarized in tables and figures for all trial participants that are quite easily done today. But while it is efficient, is it sufficient to make an impact?

I ask because I have a confession: I am a psychometrician by training, and I would struggle with how to choose between some of these numbers we use to represent the response options. For example, the response options *severe* or *very severe* for a symptom. Clearly, one is more than the other, but if you asked me on two different days, all else being equal, I might select *severe* one day and *very severe* the next. Henri Poincaré, the mathematician said over a century ago that "it may happen that small differences in the initial conditions produce very great ones in the final phenomena." Could small variations like selecting *severe* over *very severe* have the potential to cause significant differences in the trial conclusions? I do not have the answer to this question, but it is certainly worth considering.

This question is further amplified when considering some conversations I've had with patients over the years. Some years back I was debriefing a PRO measure with a patient. I asked him to explain to me what the seven-day recall period meant to him. He understood perfectly that he was being asked to think back over the past week. But when I specifically asked about his interpretation of one the response options, *rarely*, he then told me that would mean the side effect occurred about once in a blue moon. Blue moons take place approximately every two to three years, certainly not in the past seven days! I was observing a disconnect, complete comprehension of the recall period, but the response option of *rarely* was not contextualized within that period. I conducted this interview nearly a decade ago, and yet this piece of the interview has always stuck with me, because it left me wondering to myself, are we really measuring what we think we are, and can we do better? More recently, in a focus group one patient told the group that too often the response options do not reflect her experience, and when there are too many difficult items, she would stop filling in the survey. There was much nodding in agreement as this patient was describing her experience.

These conversations, in my mind, lead to the question, what do the average scores created from a PRO measure tell us about the impact of a treatment? Which brings me to the last conversation I will include in this section, with a clinician who also shared this sentiment. She told me for these results to be useful for her clinical practice, they need to help her to sharpen her clinician lens, and too often they were not adding anything over a thorough conversation with her patients.

I am sharing these stories to highlight a need to consider reimagining how to create PRO measures to foster patient-centricity in clinical trials. This, in my opinion, matters not only to avoid burdening participants with surveys that do not quite fit, but also because recruitment for clinical trials remains a significant challenge. While I do not believe patient-centricity alone will solve this challenge, I do believe it would help. This is in part because patients do talk to one another about the clinical trials they are on. If they feel they are seen as more than "patient id ABC123" and recognize that the trial, from its design through to the questions asked, genuinely seeks to understand their experiences, they will talk about how great the trial is. This in turn will generate interest and possibly encourage others to seek more information about the trial from their doctor. This is another reason why I believe patient-centricity remains relevant to pharmaceutical drug development.

I appreciate that the suggestion to reimagine how a PRO measure might look is not an appealing idea, but quality of life is an intertwined complex construct that, if you ask me, cannot be confined to main effects in regression models. I do believe though that the regular and consistent inclusion of patient-reported side effects, however we measure this, is an effective means to capture how trial participants experienced this specific aspect of treatment. The idea that these data are "subjective" is one of the long-lasting remnants of patriarchy in medicine. Clinician reports of AEs are also "subjective" and filtered through their experiences or biases they hold, and their reporting impacts all the participants they recruit, not one observation. Which means that could have a larger impact on reporting of certain side effects, especially those that cannot directly be observed like fatigue and nausea. Also, for anyone who has cracked open an adverse events datafile, they know there are a lot of missing dates with regards to resolution of all the different side effects. While duration and timing of the different side effects are not listed on the drug label, it is useful information to patients and their families, and these patient-reported data can help fill this gap using the patients' voice.

In conclusion, I would never want to see the general ideas behind patient-centricity disappear from pharmaceutical drug development. Over the past four decades substantial progress has been made. However, tensions arise because the patients of today are less focused on how far we have come and more concerned with how things can improve now. By collaborating with patients and caregivers for whom we are developing treatments, we can enhance trial delivery, refine how and what data are captured, and ensure those data are effectively used to treat patients of tomorrow in the clinic. However, I would like to end with a call for reflection: would you, dear reader, invite your family members to participate in a clinical trial you are involved with if they needed the treatment? And by family, I mean your parents and siblings, but also your grandparents and even those cousins you rarely talk to. If, for any reason, your answer is no, take a moment to ask yourself why not, and consider what changes could be made to make your answer yes.

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Dr. Bellinda King-Kallimanis is the Senior Director of Patient-Focused Research at LUNGevity Foundation, where she works to amplify patient and caregiver voices in decision-making processes across diverse stakeholders. She spearheaded the development of LUNGevity's pilot Citizen Scientist program, empowering patients and caregivers to actively contribute to research and advocacy. Before joining LUNGevity, Bellinda served on the Patient-Focused Drug Development team at the U.S. Food and Drug Administration's Oncology Center of Excellence. During her tenure, she played a pivotal role in creating and launching the pilot of Project Patient Voice, an innovative resource that provides patients, caregivers and healthcare providers access to patient-reported symptom data from cancer clinical trials.

Bellinda brings a wealth of experience from industry and academia, with over 70 peer-reviewed publications to her name. She holds a Bachelor of Social Science and a Master of Science in applied statistics from Swinburne University of Technology in Melbourne, Australia, and earned her PhD in psychometrics from the Academic Medical Center in Amsterdam, Netherlands.

In her early 20s, within a short period of time, both of her grandfathers died, and she was with both during their passing. That is where the similarities stop: one had a very patient- and family-centered experience and death, the other a very medicalized experience with little regard for his wishes. It was these experiences that led her down the path to explore how people experience care, treatment and share their needs. Clinical trials offer the first glimpse at how people experience new treatment options, and Bellinda feels that it is a privilege to be involved. She loves helping to pull in the experiences from patients and their support networks to keep moving towards care that puts people first.

Disclaimer: The views, opinions and statements made in this presentation are solely those of Bellinda King-Kallimanis and may not reflect the views of LUNGevity Foundation or its affiliates.

CHAPTER 22

Peering beyond the slogans and assumptions: Are companies sincere about the patient voice in drug development?

MARK GIBSON

Defining our company with one phrase is always a challenge. We work across the entire lifecycle of drug and device development, in areas as diverse as real-world evidence, submissions and pharmacovigilance, fields that have little to do with each other. So, what ties all these together? What is the invisible glue that binds these different sectors? The answer is simple: they all include points of patient engagement.

That's what defines us: the patient voice. Our work involves testing documentation and technologies designed for patients. Whether this is qualitative interviews, cognitive debriefing, human-factor analysis, comprehension or health literacy testing, these are simply different methods of eliciting the patient voice.

My dedication to capturing the patient voice predates my entry into the commercial sector, going back to my first qualitative interview in the mid-1990s. This commitment is deeply personal. Those who have worked with me know that I am *"all in."* At our core, we believe in the power of the patient voice not because it's a trend or a regulatory checkbox, but because it genuinely transforms how we understand patients. The patient's voice should be heard, valued and integrated into all aspects of therapeutic development.

I've witnessed various incarnations of the "patient voice" agenda come and go: patient empowerment, engagement, perspectives, centricity, insights, and so on. Turn the noun *"patient"* into an adjective or a prefix and add another noun that sounds *"enabling"* and there you have the next buzzword. Each time the concept resurfaces, it feels like another turn of the wheel, without many truly new ideas. Recommendations to do with the patient voice published in journals today have already appeared in articles and conferences decades ago, only under other names, in other contexts, in other disciplines. And because most people work in silos, we rarely have exposure to trends in related disciplines, even where there is significant overlap.

Yet, barely a decade ago, patient voice research was a tough sell. It was undervalued and dismissed by sponsors as an optional pursuit — a "nice to do" activity. Fast-forward to today, the patient voice agenda has gained widespread credibility and, more crucially, is enforced: now it is a "must do" activity (for now). In recent conferences, nearly every company with a booth loudly proclaims two things: "We use AI" and some slogan or other about elevating the "patient voice." These have become the new bandwagons, the new mantras. I feel that the messaging about the patient voice often rings hollow. I frequently question the true commitment of many of these companies or even their understanding of where the term comes from.

I am a skeptic but only so because I have peered behind the slogans. We have partnered with dozens of companies that display a wide range of attitudes regarding the patient voice, from dedication to tokenism. I feel these companies could be measured along a 10-point *"Patient Voice Scale of Sincerity,"* ranging from phony to committed. The true nature of their commitment often reveals itself in subtle and simple ways, to be explored later.

For many organizations, embracing the patient voice is a commercial opportunity in the sense that it is trendy. This is strengthened because it is driven by new regulations and guidance, such as the U.S. Food and Drug Administration's (FDA's) Patient Focused Drug Development (PFDD).[1] Without this framework in place, would they bother? Almost all of the projects I've been involved with happened precisely because a Competent Authority told them to do it.

Why is the patient so important?

By involving patients early and throughout the research and development process, patient input — or engagement — helps reduce late-stage failures, enhance recruitment and retention, and improve overall drug quality. This could make drug approvals faster. That is the theory.

Therefore, the pharmaceutical industry and regulatory frameworks correctly assume that patients possess valuable insights and preferences that can inform drug development and improve health outcomes. In addition, the pharmaceutical industry recognizes that aligning treatments with patient needs and preferences boosts acceptance and adherence, driving demand and market success.

This is a significant cultural shift, where patients' experiences and narratives are valued as essential contributions to the development of new therapies. So, patients become important stakeholders in drug development, alongside providers, payers, policymakers, shareholders, etc. All good so far — again, in theory.

What is this shift based on?

The notion of the patient voice is anchored on philosophies around patient-centered care. This assumes that there has been a wholesale move away from care in the traditional, biomedical sense to one where the patient is at the center of care provision. This approach redefines patients as active partners, emphasizing three core values: addressing individual needs and experiences, encouraging patient participation in care, and fostering strong patient-doctor partnerships through empathy, effective communication and emotional intelligence.[2]

Patient-centered care seeks to understand each patient's unique perspective and context, ensuring that treatment decisions align with their values through shared decision-making. This means that doctors need to treat patients holistically, considering factors like illness history, emotional distress, culture and socioeconomic status. Drug development is wedded to the assumption that patient-centered care is a widespread reality: you cannot have personalized medicine without it.

The patient voice rests on the myth of widespread patient empowerment

If the patient voice rests on assumptions around patient-centered care, then the latter is based on a whole range of assumptions around the "empowered patient" in wider healthcare provision. This is the idea, circulating for decades in policymaking, that patients are increasingly viewed as consumers with the right to choose their medical care.[3] This is similar to decisions consumers take about their own education or lifestyle, such as what food to eat, what information to consume or what vehicle to drive.

In chronic disease management, partnership and self-management are essential. Self-management empowers individuals to handle symptoms, treatments and lifestyle changes, forming the foundation of the expert patient model. This approach focuses on improving treatment adherence and enabling patients to use their skills and resources to control their health. By fostering active

participation and collaboration, healthcare providers support better health outcomes and create a more cooperative and effective healthcare environment.[4]

This is a nice idea and, in many cases, this is precisely how some patients approach healthcare: in partnership with their doctor, discussing decisions, bringing their lived experiences to the fore and expecting to be taken seriously by their doctors. In countries like the UK or U.S., these patients are usually white, have higher incomes, higher education, a socially prestigious profession, middle class and above, living in urban centers or suburbia. They also draw upon a whole range of characteristics in their own backgrounds, such as the confidence to feel comfortable enough to take an assertive role in their health. This is the type of patient who becomes a patient advocate, engages actively in patient communities, real or virtual, and takes part in patient voice research projects. This does not reflect the diversity of experience of the majority of people in our societies, where there is a real and growing empowerment gap.[5]

Who is not empowered?

Vulnerable populations, including marginalized communities, individuals with low socioeconomic status, racial and ethnic minorities, and those with limited healthcare access often lack the information, resources and support required for empowerment. People with cognitive impairments, such as cognitive disabilities, mental health conditions and neurodegenerative diseases, may also struggle to articulate their experiences or participate in decision-making, resulting in their underrepresentation in research despite their valuable insights. Older adults face challenges like mobility issues, sensory impairments and cognitive decline, which hinder their active participation and ability to provide informed consent.

Then there is low health literacy, which further exacerbates empowerment gaps, affecting around one in three adults in the U.S. Factors contributing to this include lower educational levels, language barriers, cognitive or mental health issues, and cultural beliefs that influence understanding and engagement with health information. The impacts of low health literacy are significant, leading to misunderstandings, medication errors, poor healthcare access, delayed treatments, higher hospitalization rates, and increased healthcare costs. Additionally, complex written materials and insufficient time for explanations in healthcare interactions make it difficult for individuals to understand and act on health information. Ultimately, this worsens health outcomes and self-care practices. If health literacy is a prerequisite for empowerment, and empowerment is an assumption not only in patient-centered care but also in the patient voice agenda, then this means that one-third of Americans are excluded. Patient empowerment then becomes a cruel illusion, a convenient fiction.

Yet, if you repeat enough times that patient empowerment is real, you will start believing it. Then others will follow. Then it gains currency and is eventually enshrined in policy. Decades later, it becomes a pervasive assumption in drug development. But it does not have to be so hollow: the challenge in the design of patient voice research, to keep it real and grounded, should be to acknowledge that patient-centered care and patient empowerment are only concepts and do not reflect the realities of the majority of patients worldwide. For patient voice research to be meaningful, it needs to access those who are not empowered, the 99%.

The knowledge gap

There is a knowledge gap between medical professionals and patients: expert knowledge (the voice of medicine) versus lay knowledge (the voice of the lifeworld). Whether the medical profession widens or closes the knowledge gap is a choice: they can choose to accommodate to the patient (and empower them) or to alienate them by the lexical and stylistic choices they

make. This extends to the pharmaceutical industry and how it tends to communicate with its patients. It is the norm for patients to receive materials that are consistently difficult to access, process and act upon. There is little to no appetite for change.

Consider the following information points:

- Clinical study **informed consent forms**, often in excess of 20 pages, that are written in a mixture of medicalese and legalese — the worst of both worlds. Consider the format in which they are given to patients: is it paper-based or electronic? If the latter, are patients reading it or they skipping through the pages, treating it like terms and conditions (T&Cs) on a social media website?
- **Clinical outcome assessments** (COAs) that have been developed without any awareness of best practices in information design and questionnaire design. This is coupled with the possibility that cognitive debriefing is not perfect as a comprehension testing method. Another aspect is **conceptual equivalence across languages**. Are we not just forcing through Western concepts into non-Western contexts? How are these concepts really understood in the cultural contexts in question? Conceptual equivalence across languages also implies that the "look and feel" of the COA has to remain the same across languages: layout, "real estate" (how much space you can play with when adapting the questionnaire into another language), font, etc. Multiple times I see cognitive debriefing data from East Asian countries that plead for customization: Cordia for Thai or East Asian Gothic for the Korean Hangul script, or not to use "shared stem" questions in many languages. Very little attention is paid to how information is cognitively processed in other cultural settings, using scripts other than Latin: the assumption is that how people read in English is the same as how people read in Japanese or Arabic. Again, this is something that cognitive debriefing does not capture.
- **Package leaflets and medication guides**, still largely poorly written and understood. Despite several decades of regulations in many countries and mandatory user testing, e.g. in UK and Europe, the needle has hardly moved in terms of the quality of leaflet. The paper format itself, being snagged and chewed up in the slow machinery of regulation, is a sad vestige of information presentation from times past, Competent Authorities seemingly unable to grasp the affordances of what technology and artificial intelligence (AI) could do. The same could be said of the paper-and-staple risk awareness booklets that frequently accompany *risk management plans* due to pharmacovigilance obligations or *instructions for use* for medical devices. These could be opportunities for pharma and device companies to communicate with their prime consumers — the patients. All of them share a common fate: they end up in recycling, mostly unread.

These are only a few examples of where information provided by pharmaceutical and device companies serve to push patients away. This is the exact opposite of informing the patient voice. This is what I alluded to earlier about the true commitment of companies being revealed in simple and subtle ways: *how they communicate to their consumers.* Do you bring them closer to you or do you push them away? Words matter and it is a very simple choice. This directly impacts on empowerment.

Tokenism

The patient voice can become tokenistic when it is included in the drug development process without influencing decision-making or outcomes. Where enthusiasm for patient engagement exists, it is often a top-down initiative that meets resistance by the time it engages with middle management (for this, read VP and lower).[3] This is where new ideas clash with local organizational customs and practices, i.e. the *"this is not how we do things around here"* attitude.

Other factors that betray tokenism are as follows:

- When there is **limited engagement** where patients are consulted only at specific stages, such as at the end of the study or development, rather than throughout the development cycle. This is where patient engagement is an afterthought.
- When patients are only **superficially involved**, such as in the form of advisory boards where feedback is not seriously sought or is ignored. If feedback is included, then there is no action taken. This is patronizing.
- Where patients are **non-representative** of typical patient populations, such as only from the above-mentioned "empowered" demographic. This means that views from such patients presented through the prism of privilege are not representative, and the needs of a diverse patient population are not captured.
- When activities such as readability testing, concept elicitation, content validity, linguistic validation, and consent form development have input from patients — as participants in these activities — these are framed as patient voice initiatives. These are opportunities to understand more about the patients' lived experience, but this depends on how seriously the sponsor takes their input: Is this a piece of research or a box-checking exercise?

Patient involvement needs to be meaningful, ongoing and integrated into all phases of drug development. Authentic engagement comes from the extent to which pharma companies genuinely listen to and act on patient feedback.

Summary

This essay has taken a little glance behind the curtain of the patient voice, a small insight beyond the slogans. None of this is the stuff of advanced learning. What I have written here about the assumptions around patient-centered care and empowerment is sophomore bachelor's reading at most. Any 101-level textbook would tell you this. It is interesting to note how circular the conversation is. What I have written here about patient empowerment is only regurgitated from books and papers I read decades ago, some of which were published in the 1950s.

Why is it so circular? Why am I reading articles in 2025 such as *"Cervical screening knowledge gap 'costing lives,'"*[6] *"Clinicians have been urged to move away from the 'doctor knows best' view"*?[7] The latter article quotes the report, jointly written by the Universities of Cambridge and King's College London, that doctors are *"paternalistic"* to patients and should change *"to a more equal relationship where patients' lived experiences are taken on board."* This is the kind of recommendation found in reports published three decades ago. Even then, it felt tired.

There is a difference in how seriously companies take the patient voice agenda. I also wonder what commitment there would be if there were no longer any regulatory pressures in place. Here is a thought experiment: let's suppose that Trump 2.0 makes cuts to FDA that indirectly cause an unraveling of a raft of regulations and best practice guidance in relation to the patient voice, particularly in the area of diversity. Let's suppose this undoing has an impact on the ability of FDA to assess submissions, where capacity may disappear altogether. The result is that patient voice initiatives are no longer expected or properly regulated. No more real-world evidence (RWE) research required, no more cognitive debriefing, or comprehension testing, or risk evaluation and mitigation strategies (REMS) or anything to do with patient safety or health literacy. In this new reality, how many clinical research organizations (CROs) and pharma companies do you think would still insist on patient voice research in drug development? How many sponsors would do it voluntarily? How many patient voice slogans decorating their conference booths?

You would count them on one hand.

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Mark Gibson is the owner and (reluctant) CEO of Gibson Research Consultancy (GRC) Ltd. Based in Leeds, United Kingdom, GRC is a small company with a broad reach: it has staff across four continents, conducts patient voice-related projects in over 190 countries and partners with more than 22,000 professional research and health professionals around the world. Its business model is typically to "white label" for bigger partner companies, which means that it is possibly the most prolific purveyor of services like cognitive debriefing for COA or usability testing for eCOA that nobody has ever heard of.

Mark's interest in the patient voice spans three decades and has seen a number of manifestations of this. He became immersed in patient voice research (it was simply called "research" then) upon embarking on an academic career, and specialized early on in hard-to-reach and marginalized communities. The university career was unfortunately short-lived due to commercial activities, also in the area of the patient voice. Mark has never lost the passion and the commitment from those early days and hopes that this is reflected in the essay.

CHAPTER 23

Patient experience of what?

JEAN PATY

In sitting and reflecting to write this brief essay, I realized that I have been working in the area of understanding patient's experiences for over four decades now! I then asked myself to try to articulate what exactly have I been trying to understand. Further, I asked myself, what have I learned on this journey? Finally, I started to think about what comes next for me. I would like to share here some reflections, learnings, and what I hope to accomplish in the coming years…

What are we talking about when we say the patient experience?

Patient experience of what? Of when? Why does this matter?

As a starting place to answer myself regarding what is meant by "patient experience" and "patient experience data (PED)," I turned to descriptions/definitions from the 21st Century Cures Act in the United States and from the European Medicines Agency (EMA).

Section 3001 of 21st Century Cures Act[1]:

"(c) PATIENT EXPERIENCE DATA. — For purposes of this section, the term 'patient experience data' includes data that —

> "(1) are collected by any persons (including patients, family members and caregivers of patients, patient advocacy organizations, disease research foundations, researchers, and drug manufacturers); and
>
> "(2) are intended to provide information about patients' experiences with a disease or condition, including —
>
> > "(A) the impact of such disease or condition, or a related therapy, on patients' lives; and
> >
> > "(B) patient preferences with respect to treatment of such disease or condition.".

2022 EMA multi-stakeholder workshop[2]:

> "Patient Experience Data (PED) are data collected via a variety of patient engagement activities and methodologies to collect patients' experience of their health status, symptoms, disease course, treatment preferences, quality of life and impact of health care. For EU regulators, PED does not only involve quantitative sources of evidence (e.g., patient-reported outcomes or patient-reported experience measures) but also qualitative sources (i.e., any information obtained as part of patient engagement activities that reflect the wider perspective of patients' experience, for example, the outcome of focus groups, surveys or interviews)."

Based upon these definitions, and my own experience, I believe that patient experience and related PED are really anything about the patient's life with their disease or condition, the treatment(s) that they have had or seek, and how this all impacts their life in both small ways and perhaps in influencing major life decisions. Yes, this is large and vague — that is both the opportunity and challenge for those of us trying the capture PED and drive toward an understanding of the patient.

My personal journey

But, what is the essence of what we are getting at with "patient experience"? I have tried to step back and look at the opportunities I have had interacting with patients, clinicians, experts, regulators, and payers over the years. I want to share here my own journey with trying to understand the patient's experience — not as a trained healthcare worker, scientist, and measurement expert, but as a student of human health, and someone who has seen those of us in healthcare and life sciences just not really understand what people are experiencing.

What have I learned? I learned that I am not a good listener, neither to patients directly nor to their data — their real data reflecting what they are actually going through and experiencing when they are on treatment, before that treatment, and after that treatment. Please don't get me wrong. I am legitimately trying to listen and learn; at least, that is my intent. Yet, I know I am missing something when I try to explain to a patient, a caretaker, a clinician, or one of a number of other stakeholders who have a deep, vested interest in patients. They stare at me like they have no idea what I am saying. But… what am I missing?

I am now convinced that I am missing the richness and essence of the patient's story, the complete picture of their experience with their disease that could help me understand what a treatment may be doing or not doing for them. To understand that I need to go beyond our traditional look at the safety and efficacy of the treatment. While these are fundamental for regulators and others to make public health and reimbursement decisions, these two alone really do give a clear picture of what people are experiencing. There are additional metrics that we also count on, such as health utilization, treatment satisfaction, health-related quality of life, and others. However, I wonder, and I am wondering aloud here, if we try to put these pieces together, our traditional metrics of human health and treatment, in some sophisticated manner, like using an AI-based approach, if we will form a clear picture of the patient's story, and in turn, their experience? I actually believe we will not. I am taken back to my training as a psychologist a number of decades ago. The gestalt — that is, the whole that is more than the sum of the parts — of the patient story cannot be obtained from these data components that we normally capture. The patient story and the richness of understanding their experience is greater than the sum of the parts of our traditional human health and treatment metrics. And, if we are really going to evaluate and determine if our treatments are effective in improving the patient's experience, we need to have this gestalt, the full "patient story." We might then measure how this story evolves over time; we can work to understand the patient's own story about their disease. This story and its evolution are the true indicator of success for the patient, and for those of us seeking to care for and treat patients.

This now begs the question: Is it possible to get the full picture, to possibly understand an individual patient's full story, and maybe the combined story of multiple patients? I actually think so… and I want to explore this here. I am going to do my best to avoid technical terms and acronyms like ANOVA, ANCOVA, AI, ML, NLP, etc. Instead, I will do my best to describe what we might want to consider as we try to put together a patient's story and patients' stories, and consider what this might tell us as clinicians, researchers, regulators, payers and — most importantly — patients.

So, where do we start? In trying to listen and understand patients, I have come to believe that their full story will be best understood by combining qualitative data from the patient themselves, and from others with the same disease or condition, and quantitative data, expanding well beyond upon our traditional metrics. While difficult to combine, I do think that we can construct indices that reflect what a patient has actually said in their own words to us with measures of their movement, speech, biology and psychology (e.g., symptoms and feelings), etc. What might this look like? When we let patients speak about their disease or condition, in response to an open-ended question, and do not lead or influence their responses, it

is amazing how clear and articulate patients are in telling us what they are going through, how it has impacted their day-to-day and their life more broadly, and what they are looking for in a treatment for themselves. It can be surprising to those of us who are clinicians. For example, someone with terminal cancer saying they are not really looking for a cure, having resolved that the disease will eventually take their life. Instead, they talk about how they want to live the rest of their life; what is important for them to feel comfortable in their remaining time. I strongly believe we can then measure things that are relevant and important to them, and also determine what treatment(s) are best for their particular situation. In this case, that might be measuring if the patient is feeling less anxious and depressed and spending quality time with family and friends. For this same patient, the focus of treatments will be tied only to those areas, and may include depression and anxiety medicine, and pain reduction medicine. Further, for this person, no cancer treatments might be the best course because such treatment may negatively affect their primary goals for treatment, which are driven by how they want to live. We can then evaluate and determine if we have had an impact on their story via qualitative and quantitative assessments. Qualitative measures might include an interview with the patient where we capture, code and document key statements/metrics of how they are feeling and pain-related activities. Quantitative measures might include a depression, anxiety and pain questionnaire, movement from a watch-based device, and a general quality of life measure. The reflection of success will be combining these various sources of data into a simple index or two that gives us the gestalt — the patient story. I think such an index could be very robust, persuasive and meaningful to patients, their families, clinicians, and other stakeholders. If we show that these simple indices reflecting the patient story can be used to measure treatment efficacy and/or effectiveness, and to even compute things like health utilization measures, we will have succeeded in turning the patient story into something that can be used clinically, scientifically, and in the context of making public health decisions.

Does a patient story index exist today? I would argue it does not.

At first pass, one might think that what I am describing is "personalized medicine." A nice 2018 article from Goetz and Schork[3] summarized as follows: "Personalized medicine is rooted in the belief that since individuals possess nuanced and unique characteristics at the molecular, physiological, environmental exposure and behavioral levels, they may need to have interventions provided to them for diseases they possess that are tailored to these nuanced and unique characteristics."

In taking a quick look at more recent publications and reflections, personalized medicine is focused on tailoring treatment based upon a person's unique genetic profile and other characteristics, or what I will more generally call their biology. I strongly endorse that fully comprehending an individual's biology, or perhaps gaining an understanding across a number of similar individuals, can drive *how* we treat them to address the underlying disease or condition. I both applaud and admire the scientific, medical and analytic (e.g., AI) advances that are driving personalized medicine. However, I believe I am suggesting something different here. I believe that understanding the comprehensive patient experience, the patient's story, leads us to determine *what* to treat, and then personalized medicine will guide us on *how* to treat that person.

Bringing this back to my concept of the patient story index, such an index would not only guide treatment, but let us know if *what* we have understood and attempted to treat is of central importance in the evolving patient story. While on the surface, this may sound vague and intangible, I am convinced that we can use creative qualitative, quantitative and analytic methods to derive a fit-for-purpose patient story index. Further, we can refine this over time and perhaps this is the basis of "personalized patient story treatment." This type of treatment will be the result of a comprehensive capture, analysis and interpretation of patient experience data.

I want to be better

Yes, this is a play on the colloquialism "be better"! As I have reflected on the past four decades to write this brief essay, I am quite serious that moving into the next stage of my journey I want to be better. What does that mean? First, I need to truly listen better, to not speak, and then to try to use less biased (by my own thoughts) analytic techniques to understand what the patient has told me. I then need to convert that into metrics that a patient and those close to them can understand. Second, as a student of patient experience measurement and data, I need to develop newer, robust measures that support building a patient story from quantitative data on various aspects of the patient's life. Finally — and this will be the most satisfactory part — work hard to put all of this together into a simple "personalized patient story" index. I cannot wait! I will be better! ☺

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Dr. Jean Paty is an acknowledged leader in the effective strategies and practices of capturing patient experience data for use in the clinical development and commercial success of new medical products. He has not only published extensively in the areas of clinical outcome assessments (COA) and electronic COA (eCOA), but also on the regulatory guidance for development and implementation of ePRO. Jean has worked closely with the international industry and regulatory agencies on eCOA best practices. His work is well-referenced in a wide variety of peer-reviewed journals and in numerous conferences and events, where he has presented his findings on the scientific, clinical and regulatory implications of COA data collection in clinical trials.

Jean's passion for understanding the patient's experience with disease and treatment emerged in the context of working with regulators, biopharmaceutical companies, and most importantly, patients and their caregivers. He continues to pursue this passion professionally in his role as Chief Patient Experience Officer at IQVIA, looking for ways to encourage stakeholders who make decisions with and on behalf of patients to be strategic in incorporating patient experience is a central component of developing and commercializing treatments.

Jean has a B.S. in Psychology from the University of Toronto and an M.S. and Ph.D. in Psychology from the University of Pittsburgh.

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CHAPTER 24

A reality check on patient-centricity: The good, the bad and the ugly

ALEXANDRA LAUER

Patient-centricity, and the term patient-focused drug development (PFDD), have gained a lot of interest throughout the last years. With many big and mid-size pharmaceutical companies nowadays having their own versions of a patient-centered approach to drug development, scrutiny around the seriousness and ultimate impact of these programs prevails both inside the companies, as well as from the patient perspective.

My name is Alexandra Lauer, and I am working as an expert for psychometrics of clinical outcome assessments (COA) within the Biostatistics and Data Science department at Boehringer Ingelheim. The following essay provides my own personal view on the importance and hurdles around patient-centricity in the drug development process. It is meant to be a reality check, outlining the good, the bad, and the potentially ugly side in the context of both the regulatory submission and the reimbursement process.

Let us for now take a step back from the pharmaceutical industry. The sheer meaningfulness of the goal to put the patient, as the ultimate customer, at the heart of all endeavors seems glaringly obvious. After all, the consumer products industry invests heavily into finding out what their intended customers desire, at times even before these customers know this for themselves. If this wasn't the case, the aisle for breakfast cereals would probably only contain steel-cut oats, all wash detergents would have the same smell, and shampoo would serve the sole purpose of cleaning one's hair — tumbleweeds bouncing through almost empty supermarket aisles.

Finding out what matters to patients, and what would constitute a meaningful treatment effect, should be the first step in a patient-centered drug development process.

Jokes aside, medicines are not consumer products, and patients rely on the effectiveness of their medical intervention as a means of controlling their disease. Many patients are required to take their medication on a daily basis and will do so for their lifetime. Making sure these patients have an adequate quality of life is imperative. Understanding what "adequate" actually means in this context requires developers of medicinal products to work in close collaboration with patients, as well as clinicians and potential caretakers. It requires knowledge about the symptoms associated with the disease and the impacts on the daily life of patients.

Finding out what matters to patients, and what would constitute a meaningful treatment effect, should be the first step in a patient-centered drug development process. This task involves qualitative interviews with patients and the development of a disease conceptual model. Ideally, these activities start before the compound is moving into the clinic and inform the target product profile. Only when a drug developer knows what to measure can they move into the next stage and find out how to measure the formerly identified concept of interest. Under the perfect scenario, where the disease conceptual model had already been developed, the

drug developer can now take an informed decision around the choice of their measurement instruments for the outcome of interest. This decision process can be conducted in parallel to the first-in-human study. In all honesty, the sponsor might also find out that no such measure exists to date, a revelation that can cause anxiety with a lot of study teams. But remember, under this ideal scenario the drug developer started early and is still in the planning phase for their Phase II trial. Let us assume the formerly conducted qualitative research had led the drug developer to conclude that their concept of interest should ideally be measured via a patient-reported outcome (PRO), but no adequate PRO exists so far. In these situations, the use of item libraries, such as the ones by FACIT, PROMIS and EORTC, have gained a lot of traction. The drug developer would pull items from the selected item library that are aligned with the concepts identified in the disease conceptual model. Presumably, the resulting measure used in the hypothetical Phase II trial would not be ideal, in the sense that there is a high likelihood that too many items had been selected to measure the concept of interest and the level of redundancy is too high. Patients might also struggle to understand the questions or find they could not relate to their meaningfulness. Psychometric properties might be poor.

Again, because the drug developer started their endeavors early enough, they are in a position to conduct further analyses around their novel PRO. Cognitive debriefing exercises with patients can help to gain confidence around patients' adequate understanding of the questionnaire. On a more quantitative side, psychometric analyses of the collected Phase II data then allow for an identification of the potential to reduce the number of items and subsequently refine the instrument. Of course, this decision should then be backed up again by patients stating that the omission of the identified items is indeed sensible. At this stage, it's progress over perfection.

At the end of their Phase II trials, the drug developer now has a thorough understanding around the patients' perspective of their disease, health perception and quality of life, as well as the intended content, structure and preliminary reliability metrics of the outcome measure, i.e. the newly refined PRO, and their product's effect as measured by the respective PRO. Truth be told, the set of conducted analyses might not all support the hypothesis of a perfect fit-for-purpose measure at this point in time — or even ever. The sponsor could, for example, have found out that the fit statistics from the confirmatory factor analysis do not fully support the intended structure and scoring algorithm of the novel instrument. The numbers fairly failed to pan out in comparison to the pre-defined acceptance thresholds. This is when it is crucial not to solely rely on the numbers but look at the full picture from the qualitative and quantitative research. The factor analysis might tell the sponsor to reduce the number of items, while patient interviews specifically underscore the importance of the numerically redundant questions. A transparent reporting of findings is key here and, in my opinion, the drug developer should capitalize the voice of the patient over numerical pettiness — take it from a statistician.

In the design phase for their pivotal trials, they can, and should, now bring all of the collected qualitative and quantitative evidence to the regulators to provide a solid, scientific rationale for their strategy. On the "bad" side of things, this is often regarded as a far stretch, because of the novelty of the instrument and the vulnerability to criticism in the face of regulators. On the "good" side of things, however, the drug developer did their homework and can now lay out all the collected evidence to defend their strategy. Even more so, as the patient had been involved in every step of the way, they can do so with great confidence. The drug developer now has all necessary information to enter into their pivotal study phase. Data from the Phase III trials can then finally be utilized to perform further psychometric analyses around the PRO's measurement qualities in a larger patient sample. After read-out of the Phase III, the drug developer is now in a position to collate all collected evidence around the novel and refined PRO in a

clinical outcome assessment dossier as part of their New Drug Application. This allows for a holistic discussion of the compound's efficacy results in combination with measurement qualities of the underlying instrument. Leaving the latter out of the discussion is one-sided and never provides the full picture. It is like stating somebody earned an annual salary of 80,000, but leaving out the currency.

Of course, we skipped an important part of our trial design phase: the choice of the endpoint. More specifically, how are we measuring outcomes from our novel PRO, at which frequency, via which medium of administration, and finally… how do we analyze the data? Now of course, this is where every biostatistician rolls up their sleeves and happily gets to work. But a couple of upfront thoughts need to be entertained around the type of endpoint. Several options exist, and I will elaborate on the most prominent ones for PRO data:

- **Change from baseline to a landmark timepoint:** Change from baseline analyses require the presence of a continuous outcome. Biostatisticians appreciate these kinds of endpoints, as they are very efficient with regards to power. This means that the number of patients required to detect an effect, if it actually exists, is rather low in comparison to responder or time-to-event endpoints. Let us look into an example for such a continuous outcome: In the PRO world this could be total score from a questionnaire around physical functioning in patients, where patients are asked to rate their physical ability with regards to several activities of daily living. In the context of performance-based measures this could also be an assessment of the walking distance covered over a time of six minutes, i.e., the Six-Minute Walk Test. The choice of a change-from-baseline type of endpoint should be supported by an expectation around the direction of the treatment effect on a group-level. More specifically, the sponsor should have an anticipation for patients' average physical functioning on the investigational new drug to generally either improve or decline. As the focus is on the comparison of effects at the landmark timepoint only, a patient's state before or after this timepoint is also allowed to differ notably, both in direction and in magnitude of the effect. In the end, the estimated effect will provide a comparison of average changes in physical functioning from baseline between the treatment arm, receiving the new investigational drug, and the control. An additional benefit on an individual patient-level further needs to be shown. The choice of the landmark timepoint itself, and acceptance around changes prior to and after, also requires close alignment with patients' expectations of a meaningful change related to the concept of interest.
- **Time to event:** Time-to-event endpoints, as the name suggests, allow for an analysis of the time it takes for a particular event of interest to occur. An an example from the PRO world could be the time between randomization and the occurrence of full resolution of a particular symptom, say headache, in a trial for a new flu medicine. Our interest here lies in the detection of the first day when participants in the trial report that their headache is gone. The developer of the flu medication is well aware that sooner or later the headache will have resolved itself, but the anticipation around the treatment effect is for this to happen earlier under the new investigational drug. For the statistical modelling, the underlying assumption is for the effect to be of a monotone nature, meaning that even if the patient had another onset of headache after stating to be free of pain for the first time, one could still consider this a treatment benefit.
- **Response at a landmark timepoint:** Responder endpoints are similar to time-to-event endpoints in the sense that both of them are looking at the achievement of a certain responder criterion. Unlike in the time-to-event setting, however, we are not interested in the detection of temporal differences between the first achievement of response, but a simple assessment at the landmark timepoint of

interest. An example could come from the field of dermatology, where the sponsor is testing the effect of their topical treatment on skin itchiness two weeks after treatment initiation. The PRO could be a single question related to the severity of skin itch rated on a Likert scale. In a final analysis, the biostatistician would assign a binary response status to each patient, conditional on whether or not the respective person reported to be free of skin itch two weeks after treatment initiation, and compare the number of responders between treatment arms. In this scenario, the patient can fluctuate between response and non-response at all other timepoints with PRO assessments during the trial. The only interest lies in the status at two weeks after treatment initiation.

At this point, the attentive reader rightfully anticipates the choice of the endpoint to again be informed not solely by statistical considerations. Patients' expectations around the meaningfulness of the particular outcome need to align with the statistical design. The endpoint definition is therefore a multi-stakeholder exercise.

I have briefly touched upon the aspect of statistical power. Clinical studies usually involve a multitude of different endpoints. Some of them might be of clinical nature, like a change in a laboratory marker; others can be related to a PRO, or a performance measure. In a typical Phase II setting, the primary goal of the clinical trial is to establish the dose-response relationship characterizing the drug's efficacy, which is why treatment effects related to our PRO might only be of secondary interest. The respective study will therefore not be properly powered for the detection of these effects. Inference from the Phase II efficacy results alone can thus be quite challenging. More realistically, the early results should serve as an indicator for a potential benefit of the new drug related to our concept of interest in a future pivotal study.

Let us take a quick step back and imagine the drug developer had not invested in the disease conceptual model and all further patient-centered research, and had simply taken a generic off-the-shelf instrument, an approach that had been quite popular for decades now. The Phase II study would have probably contained an endpoint along the lines of "assess the effect of the compound on patients' health-related quality of life," without further knowledge around what quality of life here actually meant. Finally, when reading out the data from the Phase II trial, the drug developer could have likely found themselves in the situation where the compound's efficacy results around this distal concept of quality of life were ambiguous, or even negative. The reasons can now be manifold. Is the drug the problem, and the hypothesized effect does not exist? Is the measure the problem, and the drug actually did have an effect on some meaningful aspect of health to the patient, but the drug developer failed to detect it due to a poor design of their instrument? Is the concept of interest ill-defined? After all, health-related quality of life is a rather broad and distal concept, and there could have been a benefit in a more disease-specific domain, but very meaningful to patients with the particular disease. The drug developer just never cared to ask patients about their burden of disease, their notion of meaningfulness, and consequently failed to show their drug's benefit.

A lot has been said about the positive side of things, and I myself have to admit to being heavily biased towards this process of data-backed decision making. As a biostatistician, I prefer data over no data — one might call this an occupational bias on my end. So, for me a development of the measure based on a solid strategy in parallel to the drug's development lifecycle is definitely "The Good". But the development of novel measures should be taken with a pinch of salt, and it's time to introduce the antagonists in this patient-centered spaghetti western.

On the drug developer's side, the conduct of the qualitative and quantitative evidence to inform the content and structure of the instrument requires substantial investment, especially during the earlier phases of the development program. This is when there

is still a high level of uncertainty around the compound's efficacy, which is why a lot of sponsors prefer a leaner approach for the design of their early-phase studies and might tend towards the selection of existing generic measures. After all, the upfront investment might not lead to any long-term returns in case the compound fails. "The Bad" enters the scene, with a grim view of program budgets in relation to the expected return on investment.

On the regulator's side, heterogeneity around the acceptance related to the development process of new measurement instruments still exists. This can make it quite challenging for drug developers to generate evidence fulfilling expectations from multiple regulatory bodies with just a single instrument. Moreover, a transparent reporting, for example, based on the evidence collected at the end of the Phase II trials, might also turn the spotlight on shortcomings of the novel instrument. This could lead a regulator to believe the instrument was poorly designed and substantial changes should be undertaken, potentially catapulting the development back to square one, and jeopardizing all program timelines. However, to calm our nerves, the measure does not actually need to be perfect — in my point of view. It was progress over perfection, right? After all, the measure should be fit-for-purpose, which means that its measurement qualities should allow for the collection of data making it possible to test the hypothesis around the compound's treatment effect. If this is the case, and all former decisions are backed up by the voice of the patient, the sponsor can defend their informed decision around the instrument with confidence. The upfront strategized work saved the drug developer from the Mexican standoff with the regulator and a mutual agreement might be on the horizon.

Finally, on the payer's side, waters are unfortunately becoming a little muddier. The creation of new measurement instruments naturally leads to heterogeneity in the form of an increase in the sheer number of instruments across novel and historically conducted studies. The assessment of cost-effectiveness, as the basis of many reimbursement processes, however, requires an evaluation of the drug's relative effectiveness in the context of a national treatment landscape. The combination of efficacy results from multiple sources of evidence is only possible if the underlying clinical studies share certain design features, such as the utilized outcome measures. Failure to perform these tasks of evidence synthesis can notably decrease a drug developer's leverage in the reimbursement process. At last, "The Ugly" has revealed its grimace, threatening to push the sponsor's study team down the road of self-doubt in the face of their colleagues from market access. In reality, the natural way out of this dilemma is the addition of an established measure to allow for the synthesis of evidence across a multitude of studies, which comes at the price of potentially inferior measurement qualities and an increase of administrative burden on the patient's side.

Lastly, I would like to conclude with my own outlook around the future of patient-centered drug development. I have shared my two cents around a proper way to incorporate the patient into the drug development process, shedding a light on the Good, the Bad, and — yes — the Ugly side of increased patient-centricity. While I personally think that the juice is worth the squeeze, I also see the issues related to the increase in instrument heterogeneity in the reimbursement process. Nobody wins if the measurement landscape turns into the Wild West. A means to alleviate the divergence of measures could be the stronger collaboration with patient organizations, as well as academia across industry stakeholders. To people with a more protectionist attitude, this might seem like a radical thought, but I tend to disagree. Pharmaceutical companies are profit-oriented organizations, true. In our daily work we are seeking to improve the lives of patients, but still at the end of the day an aim for profitability on a company-level cannot be neglected. But even in this context, we should foster cross-industry collaborations because the true competitiveness is related to medicinal products, not measurement instruments.

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Dr. Alexandra Lauer is a biostatistician with a focus on psychometrics and clinical outcome assessments (COAs) at Boehringer Ingelheim. She is a mathematician by training with a strong interest in science at the intersection of qualitative and quantitative research. In her role at Boehringer Ingelheim she supports study teams with their COA strategies and psychometric analyses around measurement properties of COA instruments, as well as efficacy analyses from COA data in clinical studies with a focus on both the regulatory and the HTA context. Her mantra is to initiate the COA strategy early and develop the measure in parallel to the drug development lifecycle — only then can evidence gaps be properly identified and closed.

Prior to joining Boehringer Ingelheim, Alexandra had worked as a biostatistical analyst at Merck KGaA, Darmstadt, Germany, serving as a subject matter expert for COAs within the non-oncology biostatistics group.

Disclaimer: The views, opinions and statements made in this presentation are solely those of Alexandra Lauer and may not reflect the views of Boehringer Ingelheim or its affiliates.

CHAPTER 25

The luminous science of us: Healing beyond the algorithm

ANGELA RADCLIFFE

The holographic display cast a soft blue glow across Amara Nwosu's face as she studied the patient enrollment data scrolling through the air. Her reflection ghosted against the glass walls of the Pulse Center's war room, and for a moment, she saw herself as the frightened child she'd been in 2020, watching the world unravel on television.

She'd been nine then, cross-legged on the living room floor, hugging her knees as her mother stared at the endless stream of pandemic updates. Words like "vaccine study" and "flatten the curve" had hung in the air like smoke, incomprehensible yet suffocating.

"What's a research study?" she'd asked, her small voice cutting through the silence.

Her mother, Dr. Sarah Nwosu, had turned toward her slowly, kneeling until they were eye to eye. Her smile was thin but carried the weight of both worry and hope. "It's how doctors learn to make us better," she'd said softly. "People volunteer to help, so everyone can be safe."

That moment had planted a seed, though Amara wouldn't recognize it until years later. She watched her mother, an epidemiologist, work endless hours analyzing COVID-19 data. She saw their family friend, Mr. Taylor, volunteer for a vaccine trial and survive the virus. Most importantly, she witnessed how communities came together, sharing data and stories, fighting for a future when science would serve everyone equally.

The memory dissolved as Lumina's central AI core hummed to life around her. The sound usually brought comfort — a reminder of progress, of barriers broken. But today, it carried a different weight. Twenty years after that little girl watched the world change, Amara stood at the precipice of her own revolution.

"Display enrollment demographics," she commanded, her voice steady despite the flutter in her chest. The holographic interface expanded, projecting a three-dimensional map of participant data for the world's first AI-matched personalized cancer vaccine trial. Thousands of faces floated before her, each one a testament to how far they'd come.

A soft chime interrupted her review. The Lumina interface pulsed red: "Critical data gap detected. Algorithm recalibration needed for equity compliance."

Amara's hands clenched. She didn't need to read the details to know what it meant. Region 6B — her old neighborhood, an area historically overlooked by the healthcare system — was underrepresented. Again.

The irony wasn't lost on her. She'd spent the last decade building Lumina precisely to prevent this kind of oversight. The AI was supposed to be different — better than the biased systems of the past. She'd promised her mother that.

"Not today," she whispered, pressing the emergency team alert. "We didn't come this far to let AI become the problem it was meant to solve."

Dr. Elias Cheng arrived first, his weathered face creased with concern. He'd been her mentor since graduate school, the one who'd taught her that AI ethics weren't just guidelines — they were the difference between healing and harm. His gray-streaked hair caught the blue light as he studied the alert, his expression darkening.

"Region 6B," Amara said, though she knew he'd already spotted it. "The algorithm is under-matching participants from underserved communities."

Elias touched the holographic display, expanding the demographic data. "Tell me what you see, Amara."

She frowned. "A failure. We're excluding the very people we promised to help."

"Look deeper." His voice carried the same patience he'd shown years ago, when she'd been a frustrated PhD student convinced AI could solve everything. "What's the pattern?"

Before she could answer, Kieran Mallory burst through the door. The youngest member of their team, he'd joined Lumina straight out of MIT, bringing with him a revolutionary approach to algorithmic fairness. His usual easy-going demeanor was replaced by intense focus as he pulled up the code interface.

"I wrote redundancies for this," he muttered, fingers flying across the haptic keyboard. "Triple-checked the equity protocols. The system should've —" He stopped, color draining from his face. "Oh no."

"What is it?" Amara moved closer, scanning the lines of code.

"The learning parameters." Kieran's voice was barely audible. "They're adapting to historical participation rates. The AI isn't just reflecting existing biases — it's amplifying them."

The revelation hit Amara like a physical blow. They'd been so focused on making the system learn from past research that they'd inadvertently taught it to perpetuate decades of exclusion.

The holographic display flickered as Maya Diaz joined remotely from Region 6B. As field director for the Community Data Mobilization Network, Maya had spent years building trust in communities that had every reason to be skeptical of research. Her avatar showed her in what looked like a church basement, surrounded by health monitoring equipment.

"I'm guessing you've seen the numbers," Maya said, her holographic form casting shadows on the real-world walls behind her. "But you haven't seen what I'm seeing. There are people here — right now — waiting to participate. They've been waiting for hours. The algorithm just keeps saying they don't match the criteria."

Amara watched an elderly woman pass through Maya's hologram, helped by what appeared to be her grandson. The woman's face carried both hope and resignation — an expression Amara had seen too often in her own grandmother's eyes.

"What are their stories?" Amara asked softly.

Maya's avatar smiled. "Come see for yourself."

The sun was setting by the time Amara's transport pod touched down in Region 6B. The neighborhood had changed since her childhood — solar panels glinted from every rooftop, and health nodes dotted the streets like high-tech phone booths. But the people were the same: resilient, proud and too often overlooked.

The church basement was packed. Health monitors lined the walls, their soft purple glow reminiscent of Lumina's core. But it was the faces that caught Amara's

attention — dozens of them, each carrying a story that the algorithm had deemed irrelevant.

Maya met her at the door, their first in-person interaction in months. “Mrs. Johnson over there?” She nodded toward the elderly woman Amara had seen in the hologram. “Three-time cancer survivor. Raised five kids by herself. Never been in a clinical trial because no one bothered to ask.”

Amara watched as Mrs. Johnson’s grandson helped her navigate the health node’s interface. The machine’s AI assistant spoke in clear, gentle tones, explaining each step of the process. But when it came to the matching algorithm, the same message appeared: “Current criteria not met.”

“The system thinks it’s protecting the study,” Kieran said from behind her. He’d insisted on coming, carrying enough computing equipment to run a small data center. “Historical data shows lower follow-up rates in this demographic, so it’s preemptively excluding them.”

“Since when is protection the same as exclusion?” The voice belonged to Mrs. Johnson herself, who had approached without them noticing. “My grandson here —” she squeezed the young man’s hand, “he’s studying computer science at the community college. Tells me all about AI and algorithms. Says they’re supposed to be smart.” She fixed Amara with a steady gaze. “Don’t seem very smart to me if they can’t see what’s right in front of them.”

The words hit Amara like a thunderbolt. They’d built Lumina to see patterns in data, but they’d forgotten to teach it to see people.

As Kieran set up his equipment, Amara’s mind drifted to another pivotal moment — the passage of the Human Data Ownership Act of 2031. She’d been in college then, watching as the world finally recognized what her high school mentor Richie had always known: that health data wasn’t just numbers in a database, but stories that belonged to real people.

The Act had declared that individuals owned their health data outright. It couldn’t be sold, traded, or accessed without explicit consent. But ownership meant more than just control — it meant the power to share, to contribute, to be part of something bigger.

Mrs. Johnson’s grandson Kevin helped Kieran connect to Lumina’s systems. As lines of code scrolled across their screens, Amara saw something she’d missed before: the algorithm wasn’t just learning from historical data, but from real-time interactions. Every rejection, every missed connection, was teaching it to perpetuate the very biases they’d tried to eliminate.

“We need to rewrite the learning parameters,” Kieran said, fingers flying across his keyboard. “Make it weight current intentions as heavily as historical patterns.”

Maya nodded. “And add community trust metrics to the matching criteria. Someone like Mrs. Johnson, with deep community ties? That’s worth more than any historical follow-up rate.”

As they worked through the night, Amara remembered another lesson from history — the Great Mental Health Reckoning of the 2030s. The pandemic’s trauma had lingered for years, creating waves of depression, anxiety and burnout that threatened to overwhelm the healthcare system.

But that crisis had taught them something crucial: healing wasn’t just about medicine. It was about community, about trust, about seeing people as more than just data points in a study. The most successful mental health interventions hadn’t come from algorithms alone, but from AI working in partnership with community leaders, faith groups and local organizations.

Now, watching Maya coordinate with church volunteers to set up additional health nodes, Amara saw the same principle in action. The algorithm might match participants to studies, but it was the human connections that would keep them engaged.

By sunrise, the changes were live. Lumina's core hummed with new understanding, its matching protocols rewritten to recognize the strength in community bonds. Mrs. Johnson was among the first to be matched under the new system, her grandson beaming as the health node displayed her acceptance into the trial.

But it wasn't just about the numbers. As Amara watched more community members step forward, she saw something her childhood-self had glimpsed during the pandemic: the power of people coming together, using technology not as a barrier but as a bridge.

Maya touched her arm, pointing to where Kevin was explaining the revised algorithm to a group of curious teenagers. "That's how change happens," she said softly. "One story, one connection at a time."

A month later, Amara stood in the Pulse Center again, but this time the holographic display told a different story. The study wasn't just filled — it was thriving, with participation rates in Region 6B among the highest in the program.

"The algorithm shows us what's possible," she told the global audience watching her presentation. "But it's people — connected, empowered and heard — who make it real."

In the front row, Mrs. Johnson sat with her grandson, both wearing the silver pins that marked them as study pioneers. Behind them, Maya and Kieran shared knowing looks. And somewhere, Amara knew, her mother was watching, seeing how that little girl's question about research studies had bloomed into something revolutionary.

As the presentation ended, a young girl approached the podium, her eyes wide with curiosity. "My mom says you're teaching computers to be fair," she said. "Is it hard?"

Amara knelt down, just as her mother had done so many years ago. "Sometimes," she admitted. "But you know what makes it easier? Remembering that behind every piece of data, there's a person with a story to tell. And when we listen to those stories — really listen — that's when technology becomes truly smart."

The girl nodded, understanding in her eyes. And in that moment, Amara saw the future: not just of AI or medicine, but of humanity itself — a future where technology and compassion walked hand in hand, lighting the way forward for generations to come.

Afterword: A future within reach

While Amara's story is fiction, and was created in collaboration with AI, the challenges and opportunities it presents are very real. As AI continues to reshape healthcare, we stand at a crucial crossroads. The technology we're building today will either reinforce existing inequities or help dismantle them — the choice is ours.

In 2024, global investment in AI well surpassed $100 billion, with healthcare use cases a significant contributor to that number. But numbers alone don't tell the whole story. The real measure of success isn't in dollars invested or algorithms deployed, but in lives touched and communities served.

The lessons of COVID-19 still echo: that health equity isn't just an ethical imperative but a scientific necessity, that data without context is incomplete, and that true progress requires both technological innovation and human connection.

The future envisioned in this story — where AI serves all communities equally, where data ownership empowers rather than excludes, where research is integrated seamlessly into care — is within our reach. But achieving it requires more than just better algorithms. It requires a fundamental shift in how we think about technology, health and human dignity.

What if we started now? What if every child grew up understanding not just how AI works, but how to ensure it works fairly? What if we built systems that learned from communities instead of just about them?

The next chapter of this story belongs to all of us. Let's write it together, with wisdom, compassion, and an unwavering commitment to a future where technology serves humanity — all of humanity — equally.

Together, we can make this vision not just a story, but our shared reality.

About the author

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Angela Radcliffe is a best-selling author, speaker and advocate for teaching health, data and AI literacy. Drawing on 20+ years of experience centered around healthcare innovation, Angela combines deep AI healthcare expertise with authentic storytelling to engage diverse audiences and empower children and adults to succeed in a data-centric world.

Driven by the preventable loss of her 21-year-old brother to an undiagnosed heart condition, Angela champions health literacy while navigating the complexities of raising three children across different technological generations, including a neurodivergent learner. This unique intersection of personal tragedy and parenting challenges and her journey from poverty to escaping domestic violence fuels her mission to advance health, data and AI literacy for the next generation.

As the author of *Quantum Kids Guardians of AI,* a narrative-based activity book for children and teens, Angela teaches AI fundamentals such as neural networks, large language models, data ethics and prompt engineering, all woven into stories about school life, social media and robotics. The book makes complex AI concepts accessible and enjoyable, encouraging young minds to think about technology's role in addressing challenges like bullying, climate change, and health inequity and empowering them to make better health and other critical life decisions and take more control of how their personal data gets used by third parties to reduce exploitation or becoming a victim of fraud.

As a senior executive in health tech, patient engagement & education, and overseeing clinical operations programs, including Managing Director of Heartbeat's Clinical Research practice, a division of Publicis Health, and Head of Digital Performance Improvement and Innovation for Research and Early Development IT for Bristol Myers Squibb, Angela translates complex concepts into actionable insights, helping families and organizations thrive.

Her unique background and her stellar communications and interpersonal skills make Angela a sought-after speaker for podcasts and with life sciences, patient education, mental health, data privacy, teacher and parent organizations.

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CHAPTER 26

Editorial

Moving from "patient-centricity" to "patient partnerships" to serve intervention development

MATT REANEY

It has been a real pleasure to collate all the chapters submitted for this collection. I have been impressed with the thoughtfulness and passion that people expressed in their writing; and the inventiveness in the delivery (there is a poem,[1] a fictional dystopian story,[2] a mock podcast[3]...!). My job was to read and reflect; to consider what stories people chose to tell, what thoughts they shared, and what hopes they expressed. Six clear themes struck me, which I will synthesize below.

1. We have come a long way in the past few decades

Numerous contributors reflected on a time before "patient-centricity" in drug development,[4-10] where biopharmaceutical companies and researchers rarely (at best) consulted patients on product development or study design and execution. During this time, it was commonplace for products to be developed based solely on medical innovation rather than priorities of patients. Studies to test these products were designed around convenience for researchers rather than study participants. How pretentious of us![1,4]

And this was just 10–20 years ago.

Over the past decade or two, however, evolving attitudes, technological advancements, and a broader societal embrace of patient empowerment have changed how we think about intervention development.[5,11]

There is now an acknowledgement by many in the field that for biopharmaceutical interventions to be successful — that is, to be approved for use, to be "chosen" by healthcare professionals and patients, and to improve health and well-being — they must be acceptable to patients as well as clinicians.[2,5-9,11-18]

Acceptability of an intervention by patients is increased if the intervention is developed to meet a need or offers something important to patients that other interventions do not. Other industries have long known this — consumer testing is common in development of new food and drink products, toys, technology and services. And we are now starting to see this happen in the biopharmaceutical industry — researchers listening to patients' experiences, priorities, preferences and needs before making important decisions about drug development.[4-5,17] There has also been a shift in the way that novel interventions are tested and evaluated. More clinical trials are being designed with input from patients to facilitate patient participation and to include outcomes that patients can report, and which patients believe are important and interpretable.[4-9]

This relatively recent focus on the patient in intervention development has been driven primarily by two groups: the regulatory bodies in the United States (U.S.) and Europe that make decisions on the value of data,[1,4-6,12,18-19] and the patients, charities and patient advocacy groups (PAGs), who wish to share their stories and have their voices heard.[2,6-7,9,11,15,20-21] Together they have propagated

an environment where patient-centered intervention development and clinical care is encouraged, at least in the U.S. and parts of Europe.

2. Applications of patient-centricity in intervention development are not consistent

In 2025 it is an expectation that the biopharmaceutical industry in the U.S. and Europe engages in patient-centered intervention development.[5-6,8,10,12,19] But what *is* patient-centered intervention development? Some contributors to this collection offered their own definitions, including:

- *Listening to patients implicitly and explicitly; to capture the patient's voice and incorporate it into intervention development and evaluation to better understand and enhance the patient experience*[1]
- *The concept and practice of involving the relevant patient community and members of the public in the research, design and development of drugs, treatment and care for a specific condition*[7]
- *Incorporating the patient's perspectives and preferences systematically into the design, assessment and production of an intervention*[12]
- *Developing interventions that are not only effective but also meaningful and accessible to the patients they aim to serve*[8]
- *Developing interventions that offer the best patient experience possible*[3]

These definitions, although quite general, clearly highlight the focus on the patient at the center of intervention development.[22] Exactly what patient-centered intervention development means in a practical sense, however, is often unclear, misunderstood and inconsistent. And truly putting the patient at the "center" is difficult. The nature of intervention development inherently poses challenges to achieving true patient-centricity, as the focus of clinical trials is on ensuring scientific validity and regulatory compliance.[9,20,23] As such, biopharmaceutical companies are taking inconsistent, sporadic and non-systematic approaches to involving patients in intervention development[7]; and the meaningful integration of patients into decision-making processes remains limited.[11,13,15] Rather, patients are engaged in short-term consultations — often to check a box rather than to meaningfully contribute.[5,14,23] This has further eroded trust in an industry that is increasingly claiming to be patient-centric.[15,19,22-24]

3. Patient-centricity is mostly manifesting through the collection of patient experience data (PED)

The primary mechanism by which patient-centered intervention development has taken hold is through the generation of patient experience data (PED) in clinical trials. That is, most global clinical trials now seek to elicit information from patients on how they feel or function;[4-9,11,13,16-17,20-21,23] to explore the extent to which their disease/condition and its treatment impacts their lives.[25] Although there are various forms of PED that can be derived in clinical trials (see Reaney et al.[26] for an overview), the most prominent PED comes from patient-reported outcome (PRO) measures.[4-5,7-9,12,16-17]

PRO measures are frequently used in clinical trials of new interventions to explore the effect of an intervention on symptoms, functioning and quality of life, and to assess patient-perceived tolerability of the intervention. PRO measures can inform pivotal trial endpoints that regulators and payers can use to understand whether the intervention confers (incremental) benefits, as perceived by patients. Well-defined, reliable and valid PRO measures, developed in partnership with patients, can be included in regulatory labeling for an intervention.[4-5,17] They can also facilitate clinical interactions and decision-making.

Although a lot of investment has been made in PROs, they can provide us with only one piece of the puzzle and actually to gather true PED, we need to listen — to use a combination of qualitative and quantitative

techniques to truly understand individuals' experiences and to measure what matters to them.[17,25] Even then, with a full understanding of the patient experience (if that is ever possible), can we claim to be patient-centric?[25] Patient-centricity in intervention development extends beyond the collection of PED.[11]

4. The biopharmaceutical industry needs to involve patients as true research partners

The term *patient-centricity* encourages biopharmaceutical companies to put the patient at the center of intervention development. But patients are not looking to be the all-knowing guiding light that can tell biopharmaceutical companies how to develop new interventions.[14,21] Rather, patients want to be considered as *partners* in biopharmaceutical intervention development along with other stakeholders: healthcare professionals, regulators and payers/health technology assessors (HTA).

Most patients want a meaningful voice at the table; to be involved in the co-development of interventions and their evaluations[11,15,23,24], to contribute and share their experiences and priorities.[11,15] But they also recognize that their priorities may not always be medically feasible or desirable in the context of clinical research, and that innovation can be defined differently among different stakeholders.[9] Bringing patients, biopharmaceutical companies, regulatory and health authorities, bioethicists, healthcare providers and payers together in a sustained environment is the optimal approach to intervention development.[5,14,20] This may not be "patient-centered" in its strictest form, but rather "equitable," where the patient voice speaks as loudly as (neither less nor more than) other key stakeholders in a collaborative approach to impactful intervention development.[16,22-23]

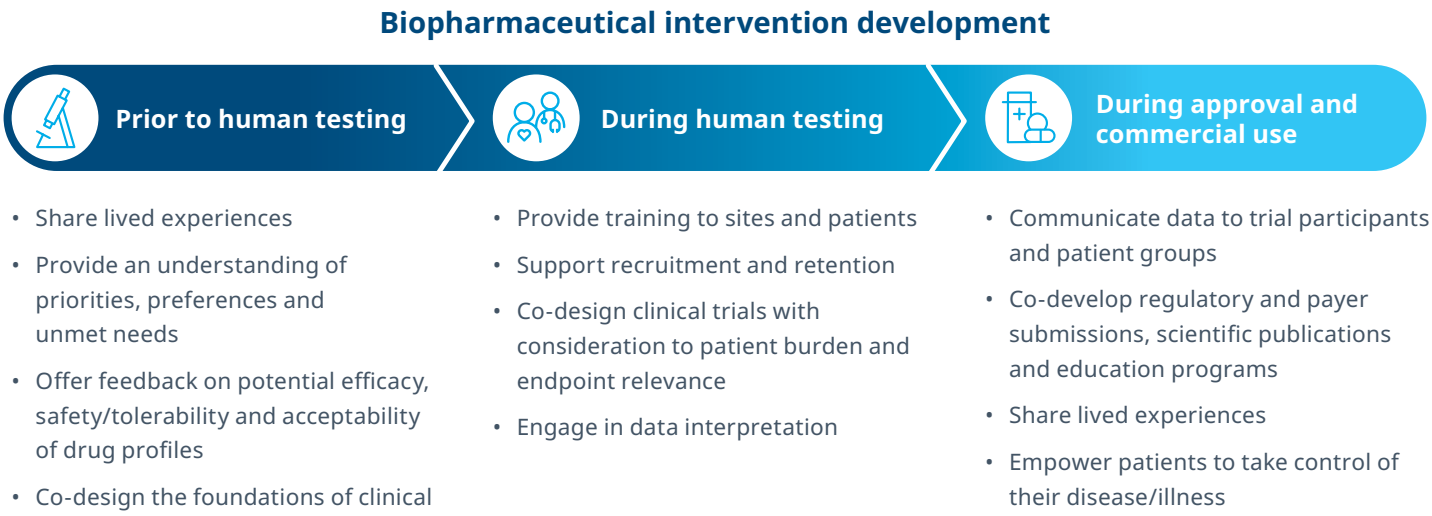
Patient partnerships should begin early in intervention development and continue throughout. Technology can be an enabler of patient partnerships, with artificial intelligence (AI), online forums and modern technology all increasing opportunities to broaden partnerships.[2,11]

First, biopharmaceutical companies should work with patients to understand their priorities, preferences and unmet needs.[4-6] If they are able to develop interventions that potentially align with these, they should get early insights on these interventions from patients (acceptability of efficacy, safety and tolerability profiles), and seek patient partnership to co-design the foundations for the clinical program to test the intervention in humans (populations to enroll, intervention comparators, etc.).[16,18,21,22]

If the intervention moves on to be tested in humans, patient partners can co-design trials to optimize the trial experience[2,9,16,20-21] (patients are often hesitant to participate in clinical trials due to concerns about time commitments, discomfort or disruptions to their daily lives[8]) and design endpoints that generate patient-relevant data[17,21] (when studies focus on outcomes that matter most to patients, participants are more likely to feel their involvement valued and meaningful[4,8]). Patient partners can also support clinical trial awareness and recruitment through peer-to-peer communication in relatable and understandable terms.[20-23] They can further co-design and co-deliver trial training for sites and patients, and aid in data interpretation.

Patient partnership in data dissemination is also key — including communicating to trial participants, patient communities, and the scientific and medical communities.[7,9] This is pertinent as more patients are participating in discussions about treatment options with their healthcare team,[3] and they need to have accurate and interpretable data to support it.[10] Patients can also help healthcare systems design protocols for continued collection of reliable and valid patient-reported data in routine care to provide a far more nuanced understanding of how treatments impact patients' lives beyond the clinic.[3,6,11]

Figure 1: Patient partnership opportunities during intervention development



This requires a fundamental shift in perspective in the biopharmaceutical industry.[8,10,11,15] Some contributors have offered thoughts on what needs to change to facilitate a patients-as-partners model to intervention development. These include:

- Biopharmaceutical companies must embed patient-centricity as a core value cross-functionally[4,8,10,14] and create annual objectives for all staff to be part of patient involvement activities regularly.[13]
- A standardized framework is needed to engage patients systematically in an ethical and transparent way across all stages of research,[4,6,8,12,14-15,21] ensuring that patients are supported to participate meaningfully and sustainably.[11]
- Education and trainings are required on both sides (industry and patients) to ensure a fruitful collaboration.[6-7,12,13,16]

5. Patients have heterogeneous experiences

When involving patients as partners in intervention development, it is important to consider which patients to include. One patient with specific experiences cannot represent a world of patients with a variety of experiences.[25] Multiple contributors highlighted the continued lack of diversity in biopharmaceutical intervention development and called on the biopharmaceutical industry to consider heterogenous patient perspectives as they are developing interventions.[1,3,8,10-11,15,22,24] This extends not only to race and ethnicity, but also socioeconomic status, geography, cognitive status and health literacy. Failing to account for the significant variations in how patients experience illness or respond to treatment means that we fail to develop interventions that are meeting the needs of a broad cross-section of society.[10,15,22] And we cannot reach a cross-section of society without investing in novel community approaches.[24]

In recognition that clinical trials have traditionally under-represented people of certain ethnic and racial groups, the U.S. regulator, the Food and Drug Administration (FDA), has been vocal in its desire to see more diverse samples recruited into clinical trials in the past few years. However, I write this editorial just days after the FDA's diversity guidance for clinical trials was removed from their website following orders from the current

administration to eliminate diversity, equity and inclusion practices in the U.S. government. It remains to be seen whether this has an impact on clinical trial recruitment.

Despite this, biopharmaceutical companies may continue to consider diverse patient experiences for reasons already stated. They can partner with PAGs, patient organizations and charities that can broaden the demographic reach of community research, bridge the gap between individual patients and the broader healthcare system, and bring structure and organization to partnerships between patients and the biopharmaceutical industry.[15,20]

6. The return on investment in patient partnerships needs to be established

Although U.S. and European regulators have been vocal in their suggestion that the pharmaceutical industry engage in patient-centric intervention development, it is still not a mandate, nor is the expectation globally harmonized.[8] In general, contributors to this book encourage the pharmaceutical industry to engage in patient-centric research "without a request,"[1] because it is the "responsible"[15] and "right"[7] thing to do, to build trust[23-24] and relationships.[22] After all, we will all be patients at some point[5] and we should all want patient voices to be heard and incorporated into health decision-making.

But there is also a recognition that there is as yet no clear and compelling reason for biopharmaceutical companies to engage patients as partners in a standardized and systematic way.[10,14,16,18,19-20] Resources in the biopharmaceutical industry are limited and their people are under time and budget pressures to bring innovative new products to market as quickly as possible.[5-6,15-17] It is thus important for biopharmaceutical companies to focus on what is likely to offer a return on investment (ROI).[7,12,20]

The process of truly involving patients as equal partners in intervention development is complex and time-consuming[11,15,16] and biopharmaceutical companies have constraints that make it difficult, including a lack of standardized processes, functional structures (silos), and methodological naivete.[7-8] The ROI for patient-centric drug development (is the value of the product quality improvement greater than the costs — time and money — of developing the product?) is not yet well established,[14,20] perhaps in part because of variance in definitions and applications.[15] Whilst PRO endpoints have been included in some regulatory drug labels and cited directly by payers/HTAs as a reason for authorizing access (which allows the biopharmaceutical sponsor to highlight the impact of treatment from the perspectives of patients), the hurdles for achieving this are high and there are many more failures than successes.[4-5,16,20] Without clear ROI metrics and an understanding of the value of patient-centricity to guide internal investment decision-making, there is a risk that patient-centricity remains non-systematic — a checkbox exercise for biopharmaceutical companies — rather than becoming an integral part of driving product value that is recognized and rewarded by external decision-makers. Indeed, if the regulators stopped asking for patient-centered intervention development, would the biopharmaceutical industry continue the trend towards increasing it?[10,16]

Call to action

When pitching this collection to the contributors, I expressed a personal hope: that this book can both encourage people by highlighting the progress made by the biopharmaceutical industry, and support researchers and stakeholders thinking how to make intervention development even more patient centric as we enter the second quarter of the 21st century. I think it has achieved that goal.

The contributors to this collection are clearly passionate about healthcare, protecting and improving people's

lives. All of them have been involved in patient-centric intervention development for many years — either as active participants or passive observers. They speak positively about how patient involvement in biopharmaceutical research has increased in recent years, but express disappointment in the non-systematized and non-sustained approach to patient-centric intervention development. It appears to be neither satiating patients nor fully realizing the potential benefits that the biopharmaceutical industry wishes to see around approvals, sales, and health and well-being.

Patient partnership (rather than patient-centricity) offers a potential alternative paradigm, which is inherently appealing and sensical — involving patients longitudinally throughout intervention development. This should enhance the ability of that intervention to offer the most benefit to patients. However, patient partnerships are not easy to implement in the regulated world of biopharmaceutical research and models will need to be defined, operationalized and implemented to drive the development of interventions. It is important to track the ROI of these models, extending from regulatory approval to payer/reimbursement decisions and market uptake.

I encourage you to engage in further discussion and action to create systematic partnerships between patients and the biopharmaceutical industry to enhance intervention development. This way, we can all look to a future where novel interventions are truly designed for all of us.

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Dr. Matthew Reaney has spent much of his life in and around the healthcare system. He is a son, spouse and parent of remarkably resilient people who live with chronic diseases that involve significant self-management, and he is passionate about helping them use their voices to inform healthcare decisions. It was with this in mind that he embarked on his first role in patient-centered care and patient-focused research more than 20 years ago. He has held positions in pharmaceutical companies, universities, charities, consultancies and hospitals since — sometimes simultaneously — advocating for the patient voice to be heard in intervention design and testing, and in clinical care decision-making.

In his role at IQVIA, Matt sets scientific direction for the Patient Centered Solutions team and oversees a variety of qualitative and quantitative research projects and patient-focused communication activities. Alongside this role, Matt maintains a variety of other positions including Expert in Residence at the University of Oxford, Scientific Advisory Council member at Breakthrough T1D, Co-chair of the Study Endpoints Committee at the DIA and Guest Lecturer at the Royal Holloway University of London. He is a Chartered and Practitioner Health Psychologist and a Chartered Scientist. He has a PhD and MSc in Health Psychology and a BSc in Psychology and has been awarded a Fellowship by the Royal Society of Medicine, a Fellowship by the Royal Society of Public Health, and an Associate Fellowship by the British Psychological Society.

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