Standardising Patient Engagement in Drug Development: The Emerging, yet Already Noteworthy Case of Patient Focused Medicines Development (PFMD) and its Materials

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Abstract

Initiatives to increase patient engagement in drug development have recently been accompanied by growing calls for standardisation due to considerable uncertainties about how to best perform patient engagement and use it in drug marketing applications. We focus on materials developed by the Patient Focused Medicines Development (PFMD), a multi-stakeholder group founded in 2015, and investigate what these materials seek to standardize on patient engagement in drug development and what visions of patient engagement are being constructed by them. We take a material-semiotic approach, whereby the materials analysed are seen as influential actors, which can work upon and transform issues of concern. The findings indicate that these materials seek to standardise a new beginning for the drug development trajectory, which they (re)locate to the patients' needs and preferences, and long-term relationships between researchers and patients developed through specific methods. A new type of patient is thus envisioned, while researchers and patient organisations are ascribed more complex roles.

Keywords: Patient Engagement, Standardisation, Drug Development

Introduction

Since the 1990s, patient and public involvement (PPI) initiatives in healthcare have proliferated (Doekhie et al, 2018; Caron-Flinterman et al, 2007; Tritter and McCallum, 2006). These initiatives have been fuelled, on the one hand, by democratic arguments advocating for citizens' right to engage in matters directly concerning them and, on the other, by technocratic rationales, which conceive of (some sections of) the public as a valuable source of knowledge and insights (Martin, 2008; Epstein, 2007, 1996). Behind both these two rationales are manifold challenges and critiques, articulated in many areas of healthcare since the late 1960s. Specifically with regards to pharma-

ceutical and medical research, many scholars have condemned the focus on the 'standard' bodies of white, middle-class men, and research approaches whereby the bodies of women have been rendered into "inconvenient research vessels"(Criado Perez, 2019: 202). Such scholars have thus challenged the deep-seated ideal of "one-size-fits-all medicine" (Epstein, 2007). Another line of scholarship has focused on power inequalities that permeate drug development and revealed, for instance, how pharmaceutical companies would often enrol impoverished, so-called 'ready-to-consent' populations in clinical trials for drugs intended mainly for affluent Western consumers (Fisher, 2015; Petryna, 2009). Furthermore, a prolific and impactful scholarly discussion has concerned the fairer and less exploitative distribution of costs and benefits of medical research and drug development among all those involved (Simpson et al, 2015; Sunder Rajan, 2017).

Yet, for a long time drug development has remained a field where (some kinds of) patients could only become engaged as clinical trial participants (Zvonareva et al, 2022; Perfetto et al., 2015). This state of affairs started to change significantly around 2010, when regulators and governmental bodies, such as the Food & Drug Administration (FDA) in the U.S. and the European Medicines Agency (EMA) in the European Union, initiated a series of measures meant to substantially increase patient engagement in this area (Getz, 2019). For instance, in 2012, the FDA formally introduced the concept of 'patient-focused drug development' (PFDD) and started organising public consultations with patients from 30 disease areas to allow the agency to make more informed decisions in their evaluation of the risks and benefits of new therapeutic approaches (Chalasani et al., 2018; FDA a, n.d). Importantly these developments have been taking place in the context of the growing use of social media and other digital platforms among patients and patient organizations interested to acquire or share insights about their treatment needs and experiences (Egher, 2019).

As regulatory agencies and pharmaceutical companies have noted considerable variation and lack of clarity in how different stakeholders understand patient engagement in drug development, its implementation, assessment, and the role it should play in the evaluation of marketing applications, growing calls have been made for its standardisation (Hoekman and Boon, 2019; Vat et al, 2020). Pharmaceutical companies have been among the main proponents of standardisation, which they frame as a way to ensure the uniformity, comparability, and quality of patient engagement projects. These calls have already been accompanied by substantial undertakings, such as the establishment of new organisations and the development of new tools to standardise patient engagement in this area (Vat et al., 2021; Schuitmaker-Warnaar et al., 2021). The Patient Engagement Management Suite developed by the Patient Focused Medicines Development (PFMD) (PFMD, n.d.) and the Patient Engagement Toolbox that the Patients Active in Research and Dialogues for an Improved Generation of Medicines (PARADIGM) (PARADIGM a, n.d., PARADIGM b, n.d.) put forward are relevant examples.

Yet, rather than being neutral solutions, standards constitute powerful tools through which particular visions are imposed, certain types of knowledge are legitimated, and roles and responsibilities are (re)distributed in ways that enhance the authority of some actors rather than others (Timmermans and Berg, 2003). We aim to make a contribution by considering these aspects and by focusing on the case study of PFMD, a large multi-stakeholder group in the field of patient engagement in drug development (PFMD, n.d.). As PFMD is widely known and influential in this field despite lacking the formal authority to impose standards, in this paper we answer the following questions: What do the PFMD-produced materials aim to standardize in regard to patient engagement in drug development? What visions of patient engagement in drug development are constructed by these materials?

A note on how we use the term 'patient engagement' here is in order. Whereas initially practitioners in the field advocated for the term 'patient involvement' (see Hoos et al, 2015), which they believed better highlighted the active role of patients, in recent years 'patient engagement' has been predominantly used. In this article, we align our terminology to the one encountered among the practitioners and in the artefacts we studied and therefore use 'patient engagement' as an

emic term. There has not been much conceptual work to define patient engagement specifically in drug development, yet one definition put forward to date proposes to understand patient engagement as "the effective and active collaboration of patients, patient advocates, patient representatives and/or carers in the processes and decisions within the medicines lifecycle, along with all other relevant stakeholders when appropriate." (PARADIGM, in Vat et al, 2020:7)

As the standardisation efforts of the PFMD-produced materials are ongoing, we cannot analyse their full trajectory from inception to final acceptance or failure. Instead, we draw on the existing literature on standardisation to understand how these materials, consisting of documents and data collected from online public events, attempt to mould a diverse set of practices in patient engagement in drug development. Overlooking the question of these materials' actual impact upon practices, we focus instead on how a particular take on standardisation is architectured and structured through them. Thus, we take a material-semiotic approach, whereby we understand the materials and events PFMD has developed and organised as important actors, that work upon, shape, and even transform patient engagement. We build upon Asdal's (2015) and Asdal and Hobaek's (2016) perspective on the role of documents, to argue that these materials actively seek to shape the future in a way that bears the imprint of PFMD's own position, while being agents in their own right.

Theoretical approaches to standardisation

Standards are often assumed to be neutral or even democratising tools, and tend to appear as particularly desirable solutions in situations where variation and diversity of practices are seen as problematic. For example, in healthcare, standardisation has historically been at the heart of professionalization efforts, as standards have been used to support the medical professionals' claim to exclusive expertise in this domain (Abbott, 1988; Timmermans and Berg, 2003). By centralising and uniformising the education medical professionals received and the skills and tools they used, these professionals could be better distinguished from amateurs and charlatans, and their overall prestige and authority could be increased. This means, however, that far from being neutral tools, standards designate mechanisms of control and accountability and ascribe roles and responsibilities (Busch, 2011). Similarly, the democratising potential of standards and their ability to contribute to levelling the playing field have also been challenged. Thus, Science and Technology Studies (STS) scholars have highlighted that standards reflect the opportunities and limitations inherent in the contexts in which they emerge (Bowker, 2008; Lampland and Star, 2009), and that standardisation proceeds through important negotiations (Epstein, 2021).

Who takes part in the development of standards and in what ways depends on the types of knowledge that are considered most valuable in relation to the practices under discussion, on the level of authority and prestige one enjoys, and on the specific goals that standards are meant to achieve. For instance, the success of the Pap smear as a standard cancer prevention tool hinged on a gendered division of labour, one that maintained the status of the (male) pathologists. As most cytotechnicians who performed the analysis of the histological slides were low-paid women, the overall costs could remain low, thereby fulfilling one of the requirements for a public health intervention (Casper and Clarke, 1998). Standards can thus come to function as means through which those with sufficient power and authority manage to impose their own views and ideals upon others. As such, standards can be powerful tools through which certain types of knowledge are legitimated at the disadvantage of others and through which additional rights and privileges may accrue in the hands of those who are already influential.

Standards also play important roles in jurisdictional struggles, as they can be used by new stakeholders to penetrate a given field of practice and to establish themselves as influential to the detriment of 'traditional' holders of authority. For instance, in the 19th century, physicians could extend their jurisdiction over child delivery and replace midwives through the influence they exercised over the development of standards and regulations that restricted certain medical

interventions and the use of particular tools, such as the forceps, to their professional group (Mol and van Lieshout, 1989). In this sense, Timmermans and Berg (2003: 19) noted that "[s]tandards … may become the unfair advantage that the powerful outsiders (...) impose on powerless insiders." These aspects are particularly relevant when studying the standardisation of patient engagement, given the considerable differences in power and authority that have marked relations between patients, researchers and pharmaceutical companies.

Equally relevant to our study is the fact that standards not only reflect knowledge and power relations at a given time, but also actively shape them. Building upon insights put forward by Voß (2016: 129) on instruments of governance and their performativity, we could say that standards "programme the doing of a particular ….reality". Thus, standards are not merely tools through which certain processes can be rendered more efficient, comparable and of similar quality, but they have a productive character. They produce new entities and help bring new realities into being. Furthermore, standards act in conjunction with human actors in what Timmermans and Berg (2003) referred to as processes of 'mutual transformation'. This means that standards can change the practices in which they are embedded and the positions that the involved humans and nonhumans occupy, but they can also be changed through the processes of adaptation and alignment that are required for them to be embedded in the practices they are meant to govern (Timmermans and Berg, 2003; Lampland and Star, 2009; Timmermans, 2015). We can think here of various approaches through which physicians and nurses adapt and circumvent standards to achieve their goals, be that the continuation of disability benefits for some patients, or the selection of a mental health diagnosis that would not be overly stigmatising, while maintaining access to treatment (Bowker and Star, 2000).

It is important to mention that standards have a voluntary character: they emerge as a result of various alliances, and acquire, retain, or lose traction depending on the strength of these alliances. For standards to function, they need to be persuasive and present important advantages to the actors meant to follow them. Such advantages may range from instrumental benefits, such as heightened efficiency and productivity, to social gains, such as a greater reputation and public standing. These aspects are relevant to understanding how the PFMD-produced materials envision future practices, so that they motivate important actors to support patient engagement in drug development.

Standardising patient engagement in drug development: An overview of the field

Efforts to standardise patient engagement in drug development are not necessarily surprising, given that standardization has now penetrated most medical settings and considering the growing interest to assess the impact of patient engagement in drug development (Vat et al, 2021). As already indicated, in both the U.S. and Europe, growing efforts have been made in this sense over the last decade (Hoekman and Boon, 2019). In this section, we briefly delineate the most important initiatives in the field to locate our case - the standardisation efforts of PFMD-produced materials - among them.

Important early initiatives to standardise patient engagement in drug development were launched by regulatory bodies. After the PFDD initiative was inaugurated in 2012, on December 13, 2016, the 21st Century Cures Act was signed into law in the U.S. The Act is meant to "help accelerate medical product development and bring new innovations and advances to patients who need them faster and more efficiently" (FDA b, n.d.). One of its provisions requires the FDA to introduce methodological guidances to support PFDD, and this is highly important, given that guidelines are the main tools through which practitioners and policy makers seek to reduce variability and to increase efficiency in healthcare (Borgstrom and Dekker, 2022). By July 2022, the FDA had issued two guidances: "Patient-Focused Drug Development: Collecting Comprehensive and Representative Input" (June 2020) and "Patient-Focused Drug Development: Methods to Identify What Is Important to Patients" (February 2022) (FDA a, n.d.). As their titles suggest, these

guidances contain authoritative statements about the types of patient insights that can be relevant for drug development, and they prescribe the course of action pharmaceutical companies and drug researchers should undertake to collect such insights. Both documents bear the subtitle "Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders". This indicates the expectation that these recommendations are accepted and taken up by the main actors in this field, which is central to the adoption of new standards. Considering how roles and responsibilities are distributed in the development and marketing approval of new medicines, this subtitle also implies that these documents contain actionable information meant to guide the regulatory assessment of patient insights. Supporting this point is the fact that two additional guidances are under construction at the time of writing: one focusing on selecting, developing, or modifying fit-for-purpose clinical outcome assessments and one on incorporating clinical outcome assessments into endpoints for regulatory decision-making (FDA a, n.d.). Even though the EMA has not yet engaged in explicit standardisation efforts, in 2016, it set up a 'cluster' on patient engagement together with the FDA. The cluster aims "to share experiences and best practices on the way the two agencies involve patients in development, evaluation and post-authorization activities related to medicines." (EMA, n.d.) The guidances discussed above are likely to feature prominently in these exchanges, and as such, they might also inform the standardisation of the use of patient insights in drug development in Europe.

Industry players also joined these standardisation efforts early on. In the same year that the FDA launched the PFDD Initiative (2012), TransCelerate Biopharma Inc. was founded, a non-profit organisation aiming to promote collaboration among all pharmaceutical companies. TransCelerate has focused its standardisation activities on a more granular level than the FDA, creating tools meant to guide and, thus, render general and uniform engagement practices at specific stages of the pre-market life of medicines (TransCelerate a, n.d.). Thus far, TransCelerate has developed a Patient Protocol Engagement Toolkit (P-PET) "to guide the engagement of patients early in protocol development" (TransCelerate Biopharma Toolkits Core Team et al., 2020: 1489) and the Study Participant Feedback Questionnaire (SPFQ) to assess the experiences of patients participating in clinical studies (TransCelerate b, n.d.). TransCelerate seems to aspire to standardise these practices at an international level, as the templates of the SPFQ have been made available in over 15 languages. Furthermore, other materials developed for this initiative can be accessed in at least one other language, such as Japanese, Mandarin, or Chinese.

New multi-stakeholder initiatives to standardise patient engagement in drug development have also emerged. One of the most established is the European Patients' Academy on Therapeutic Innovation (EUPATI), a public-private group founded in 2012. It was jointly funded by the European Commission and the European Federation of Pharmaceutical Industries and Associations. EUPATI has made substantial efforts to centralise and uniformise the education it frames as necessary for patients to fruitfully participate in the research and development of new medicines (EUPATI, n.d.). Thus, EUPATI's Patient Expert Training Programme includes an extensive list of domains and competencies expected of patients who have undergone the training. The graduates of the program are granted the title of patient experts, which serves as proof of their 'professionalism' and helps distinguish them from patients whose insights about drug development may not be as broad, thorough, and systematic. The activities of PARADIGM are also worth noting here, as this organisation has been funded by the Innovative Medicines Initiative (IMI) between 2018-2020 to develop a toolbox meant to help standardise patient engagement in drug development. Thus, the tools, methods, and metrics developed by PARADIGM are intended to reduce "inconsistency and fragmentation" and "to support mainstreaming the integration of patient perspectives and experiences" (PARADIGM b, n.d.) by aligning them with the frameworks and approaches developed by EUPATI and PFMD. Furthermore, the PARADIGM Patient Engagement Monitoring and Evaluation Framework provides standardised information to guide how the costs and benefits of patient engagement activities in drug development are calculated for all stakeholders involved.

As this overview indicates, regulators, the industry, and other relevant stakeholders have made important efforts to standardise (various aspects of) patient engagement in drug development. Established in 2015, PFMD, the initiative whose materials we explore here, is relatively a newcomer in this arena. However, it provides a suitable vantage point for understanding the formation and dissemination of standards and visions of patient engagement in drug development. PFMD's suitability is due to its being a stable and long-term collaboration rather than a time-bound project such as PARADIGM. It is also informed by its exclusive focus on patient engagement and its aspiration to provide exhaustive guidance for every stage of drug development. The latter distinguishes it from organisations such as TransCelerate, where patient engagement is only one of the core topics in their portfolio and where standardisation efforts have focused on a limited and very specific set of instances. Lastly, PFMD's global aspirations are another important aspect of its scholarly appeal, which sets it apart from the nation- or region-bound relevance typically pursued by regulators. In the following section, we provide more information about this organisation and the methodological decisions underpinning our analysis and the findings presented here.

Methodology

PFMD currently includes 40 members, ranging from important patient organisations, such as the European Organisation for Rare Diseases (EURORDIS) and the National Kidney Foundation in the U.S., to international pharmaceutical companies, such as Pfizer, Lilly, and Janssen, and national advisory organisations, such as the National Health Council in the U.S. or the Health Research Authority in the U.K. This diversity is also at the heart of PFMD's mode of governance, as its board comprises representatives of patient organisations and of the pharmaceutical industry, with efforts underway to include members of regulatory bodies and of Health Technology Assessment (HTA) agencies in the future. Its funding stems mostly from membership fees and the industry training it provides. Even though PFMD's main partners to date are based in Europe and North America, the group has global aspirations, which it is actively pursuing, as a few recent inroads in Asia suggest. On its website, PFMD positions itself as "The patient engagement platform" (PFMD, n.d.), and openly alludes to its standardisation ambitions. Thus, it states that its mission is "to bring together initiatives and best practices that integrate the voice of the patient thereby speeding up **the creation and implementation of an effective, globally standardised framework** – that involves patients as partners – as well as the necessary tools, services and support to allow the adoption of the framework by various stakeholders" (PFMD, n.d., emphasis ours).

Sampling and Data Collection

To understand how the PFMD-produced materials seeks to standardise patient engagement in drug development, we relied on the following data: three How-To Guides (HTGs) that PFMD developed in the period 2019-2022 and which were available when this study was initiated[2]; the Patient Engagement Training (PET), which is the only training PFMD has thus far developed and which is mainly intended for the pharmaceutical industry (followed online by one of the authors); and the content of three Patient Engagement Open Forum (PEOF) sessions (2020-2021) observed by one of the authors. These materials were selected as they are part of PFMD's core output and are deemed central actors. This is because they are intended for varied audiences and are the products of different types of collaborations: between different stakeholders with a specific mandate and common goal in the case of the HTGs; between pharmaceutical companies as commissioners and clients and PFMD as the developer and provider of PET; and between different organisations seeking to further public dialogue and cohesion about patient engagement in drug development through PEOF. We considered this aspect important, because the materials developed through such collaborations can be understood as statements of common understanding in a very complex and charged field. Furthermore, such close involvement of important stakeholders increases the chances that the standards these materials prescribe will be widely adopted. The analysis

of these different types of materials allowed us to understand whether the framing of patient engagement they put forward was aligned and circulated throughout and across all of PFMD's collaborations or whether important differences could thereby be identified in relation to different stakeholders.

The HTGs are documents developed and made publicly available by PFMD and are presumably widely circulated among its network. The initiative to develop these materials belonged to this group itself, which used the initial PEOF sessions to identify the main topics on which the HTGs should focus . Subsequently, working groups consisting of different types of volunteering stakeholders were created for each HTG, with the task of developing an initial HTG draft. This document subsequently underwent several alterations, as a result of internal consultations, of public feedback received on a draft version made available online for a period of several months, and of reactions acquired during PEOF sessions. Therefore, each official HGT emerges as a result of multi-stakeholder collaboration. PFMD PET has been developed specifically for members of the pharmaceutical industry. It consists of two levels and involves presentations, brief interviews, examples of patient engagement activities, and two survey-based tests. If they score sufficiently (70% or higher), training participants can receive a Patient Engagement Certification upon completion. PFMD claims that over 30,000 researchers have completed the PET so far. The PEOF was initiated in 2019 and currently consists of a series of multi-stakeholder public meetings that PFMD organizes four times per year, together with EUPATI and the European Patients' Forum. Even though the PEOF sessions have a public character, we decided to anonymise the participants discussed in this article by replacing their names with pseudonyms and mentioning only the stakeholder group they belong to.

Data analysis

The data were analysed using thematic analysis. Inspired by the work of Latour (1987) and Asdal (2015), we took a material-semiotic approach, attending to these materials not merely as particular descriptions of a given reality but as actors that actively shape this reality, "working upon, modifying, and transforming" it (Asdal, 2015: 74). This approach allowed us to analyse the materials we collected as agents working to set particular changes into motion in the field of patient engagement in drug development. The early stage when we studied these materials did not allow us to engage in document ethnography (Asdal and Reinertsen, 2021) and observe the constellations that they come to be part of and the effects they have. Nevertheless, this approach enabled us to look at what these materials *do*, to study them as aspirational *tools of governing* (Asdal and Reinertsen, 2021: 42), which seek to (re) shape roles and responsibilities regarding patient engagement in drug development. Asdal and Reinertsen (2021) emphasise that a document (or a material as we term the PFMD outputs) entails action and its analysis can discern what it does. This is an important difference compared to other useful analytical approaches, such as discourse analysis. This material-semiotic approach allowed us to focus on what the collected materials do and enable through the rhetorical strategies they contain, the concepts they mobilise, and the alliances they establish with other documents and actors (Asdal and Reinertsen, 2021). It also allowed us to be mindful of the types of engagement these different materials allow for and of those they constrain. Most importantly, this material-semiotic approach served as a powerful reminder that our analysis is positioned within the specific context of these materials' emergence and that the trajectory we trace here is only the beginning.

Findings

Analytic codes and categories were constructed iteratively through multiple engagements with the data collected and with the relevant literature. The main themes that we identified focused on the object(s) of standardization at the heart of these materials, on the transformations that the stakeholders that were framed as relevant were expected to undergo, and on the properties of the materials. This allowed us to better understand how the content, form, and positionality of these materials framed the object(s) of standardization and the transformations identified. For

an overview of the main coding scheme, please see Appendix 1.

The analysis indicates that despite the uncertainty and diversity currently characterising patient engagement activities, the PFMD materials we studied target a specific aspect in their efforts to standardize patient engagement in drug development. They also convey a clear vision of the ways in which patient engagement should be implemented in drug development. These materials thus position themselves as authoritative maps, orienting their users regarding the actions to take and their appropriate sequence, to ensure that patients are engaged substantially in drug development. As may be expected given the specific genre to which they belong, the HTGs and the training are action-oriented and function as tools for the realisation of a specific vision of patient engagement in drug development. They frame certain approaches as necessary and desirable while closing off others. We argue that in so doing, these materials seek to shape the currently vague contours of patient engagement and to configure coordinates for its future development. In what follows, we show that the PFMD-produced materials seek to standardise patient engagement in drug development by relocating the beginning of the drug development trajectory and advising that patients and researchers develop long-term relationships through the use of specific tools and methods. These materials put forward a new type of patient, who will fulfil the roles of representative and research consultant, while drug developers are to act as hospitable hosts to patients, and patient organisations are to function as mediators and education providers in ways that we discuss in more detail below.

A different starting point for drug development

The PFMD-produced materials seek to ensure that the engagement of patients in drug development becomes standard practice by relocating the starting point of the drug development trajectory from the evaluations and considerations of researchers, where it has been traditionally situated, to the patients' needs and preferences. They do so by switching the focus from the degree to which currently available treatments effectively act upon biological processes or meet the expectations of medical professionals, to the experiences and levels of satisfaction of patients. Thus, before setting out to study or develop any new molecule, drug developers are advised to consult with patients, as most of the PFMD-produced materials showcase the following question as the main consideration for drug developers to bear in mind: "Are we addressing an unmet need with this research?" (HTG_CTP, 2021: 21) Similarly, patient engagement is described as contributing to "the identification or prioritisation of unmet patient needs" (HTG_EP, 2021: 5), "potential gaps in clinical care" (HTG_EP, 2021: 21), and "outcomes [that] are important to patients"(HTG_EP, 2021: 24).

This approach was also mobilised at the PEOF sessions observed, where a researcher sought, for instance, to transform the understanding of health by arguing that it could no longer be defined from the (clinical) disease perspective but that it had to be informed by the patients' perspective (P8, PEOF, June 24, 2021). Similarly, the PFMD patient engagement trainees are informed that patient engagement is highly necessary because**:**

> We are beginning to recognize that whereas in the past surrogates spoke on behalf of patients, and they were well intended, their understanding about the outcomes that are most important to patients was often wrong. It's critical that we focus on how people feel, function and survive. But if you're going to understand how people weigh those three issues, you have to engage them. And you'll be seeing a complete paradigm shift in how we conduct research, develop new medicines, and bring those medicines into delivery systems, and provide them to people in a meaningful way that addresses their clinical outcomes, but also the social and behavioural determinants of health and the issues that just simply are important to them and their families. The concept of patient engagement is not new; we've engaged patients and their families at the point of care for many, many years. What is new is engaging patients and sub-populations of patients to understand what outcomes are important to them and how they weigh those outcomes. (T1, PET, Level 1)

As this quote indicates, to relocate the starting point of the drug development trajectory to patients' needs and preferences, the training

materials expand the meaning of effectiveness beyond biomedical evaluations to include social and personal considerations. Thus, the process of drug development itself becomes an issue belonging to patients, whereby their participation is legitimated and made into an obvious solution rather than a problematic or controversial move. This indicates that one aspect of the standardisation of patient engagement in drug development that the PFMD-produced materials seek to operate is the uniform relocation of the beginning of the drug development trajectory to patients' needs and preferences.

To ensure that the alignment between patients' needs and technical considerations is retained throughout the remainder of the drug development process, these materials further attempt to standardise the development and maintenance of long-term relationships between researchers and patients. This is a future-oriented endeavour; although such relationships are currently largely absent, and the regulatory and organisational environment required to support them does not yet exist, these materials frame them as necessary for the acquisition of patients' insights. To enact these relationships, the PFMD materials reconceive patients from mere participants in clinical trials into "[p]atients [who] are part of the research team"(HTG_EP, 2021: 26) or "patient partners" (HTG_CTP, 2021: 9; HTG_EP, 2021: 5). These materials also transform the type of interactions between patients and researchers, which in this area have hitherto been largely absent or indirect at best, into "sponsor-patient partnership in research"(HTG_CTP, 2021: 9), and rapports of "co-creation", "co-development", and "co-design".

These interactions are accompanied by the creation of new obligations and responsibilities, such as the need to ensure that "long term partnerships with patients are created and nurtured" (HTG_EP, 2021: 8) and that "[t]his Patient-Researcher collaboration should be dynamic and continuous, not a one-off event"(HTG_EP, 2021: 19). In many countries, such exchanges have been and remain illegal due to power differences between patients and pharmaceutical companies, which have prompted many to consider such encounters too risky and problematic. The novelty of these exchanges is enacted in the PFMD-produced materials through the provision of detailed advice regarding how relations between these stakeholder groups should be set up, developed, and maintained. Nevertheless, such exchanges are also framed as a sine qua non condition for ensuring not only that the patients' needs and preferences become the starting point of the drug development trajectory but that they also substantially shape the remainder of this process. To be firmly embedded in drug development, these exchanges require modifications in regulation, legislation, financing, and reimbursement. Thus, in seeking to standardise long-term relationships between researchers and patients, these materials orient future actions across numerous domains where novel approaches are required to ensure their successful implementation.

The PFMD-produced materials also configure the development and maintenance of such relationships as requiring standardised methods and tools. Thus, they mobilise the Patient Engagement Quality Guidance (PEQG), which is itself the result of PFMD-initiated co-production activities, as the right instrument for this goal: "The PEQG should be used as a reference in setting up partnerships, planning, and preparing for involving patients as partners in your research. The seven Quality Criteria can help consider others' expectations and manage them." (HTG_EP, 2021: 8). Another HTG frames it in a similar fashion: "[t]he Patient Engagement Quality Guidance (PEQG) is proposed as a reference in planning and preparing for involving patients in the process of designing a clinical trial protocol"(HTG_CTP, 2021: 3). Furthermore, to shape patient engagement in drug development, the materials we analysed need to be taken up in future practice and for this, they need to demonstrate their merits. Such demonstrations are performed rhetorically by highlighting their ease of use and highly practical character, as the following quote illustrates:

> Our objective was to develop a practical how-to guide that describes the process of publication related PLS [Plain Language Summaries] creation and dissemination through a straightforward 7-step approach that ensures early patient engagement. While navigating this stepwise process, the user will be guided towards tailored

> tools and examples, as well as a methodology to assess the importance of involving patients at each key milestone. The guidance can be used from planning through to the delivery of a PLS to encourage co-creation with the intended target audience. (HTG_PLS, 2021: 6)

To increase the likelihood that the standards they put forward are taken up in practice, the PFMD-produced materials mobilize visions of patient engagement in drug development whereby the roles and responsibilities of those whom they frame as the main issue holders are re-configured. These re-configurations do not seem to diminish the standing and authority of any one stakeholder but rather to provide each of them with important benefits. In the next sub-sections, we show that these materials operate a series of transformations in regard to how patients, researchers, and patient organisations are understood, so that the relations between them appear balanced and fruitful.

Patients as knowledgeable drug development partners

In their attempts to standardise patient engagement in drug development in ways that are appealing to the main stakeholders, the PFMD-produced materials put forward a new type of patient, who is ascribed new roles and responsibilities based on the many skills they are envisioned to possess. At the most basic level, these patients are called upon to act as representatives, as they are expected to be capable not only of describing their own experiences with illness and treatment in ways that are understandable to researchers but to also relay collective states, needs, and preferences. In this role, they are ascribed responsibility for developing and maintaining long-term relations with researchers. To achieve this, they are advised to display reflexivity and communication skills, to be understanding, and to show that they are able to accept that the development of new drugs takes time and does not always lead to the desired results. Not all patients are envisioned as being equally able to function as representatives, however, and their level of familiarity with the drug development process is used in the PFMD-produced materials to operate important distinctions between them. This is illustrated by the enumeration under "the type of patient partner profile needed (i.e., 'naïve' patient, patient advocate, patient expert, carer or family member, patient community)" (HTG_CTP, 2021: 8) and by the following quote:

> Involving patient partners with varying degrees of exposure to/involvement in clinical trial protocol development is important for gaining a diversity of perspectives that will help improve the clinical trial design. Also, involving patient partners who have never taken part in a clinical trial before can be insightful. (HTG_CTP, 2021: 20)

To fulfil such responsibilities, patients are required to reflect upon their experiences and those of others and to choose the ones they find most urgent. Thus, these materials pave the way toward a future hierarchy of patients' needs and preferences.

This new type of patient is further ascribed the role of research consultants, entrusted with the responsibility of guiding research. For instance, patients are expected "to direct the preclinical research focus" (HTG_EP, 2021: 23) and to assist researchers in their prioritisation endeavours: "[t]he goal of patient engagement is to work together to determine what is a 'must-have' compared to 'nice to have' within the scientific capabilities of the research" (HTG_EP, 2021: 14). Similarly, one of the advantages of early engagement with patients highlighted at a PEOF session was the fact that "you don't do studies that don't make any sense" (P11, PEOF, June 23, 2021).

In their role as consultants, patients are further ascribed the responsibility to contribute to the development of methodological tools, as the following quote indicates:

> Co-creating questions provides the research team with direct patient insights on the condition experience. Because patients know best how they prefer to be asked about their condition, they should be consulted regarding such questions. Involving patient organisations and patients (usually in a steering group) in shaping these questions, can make them feel that their opinions matter and are respected, promoting effective engagement. (HTG_EP, 2021: 19)

Another responsibility that patients are expected to fulfil in their role as research consultants in drug development is the evaluation of the appropriate-

ness of tools and approaches for specific projects. Thus, researchers are advised on "working with patients to evaluate and identify the optimal approaches to address research objectives (both in the laboratory and clinical research)" (HTG_EP, 2021: 9) as well as to "generate patient-focused insights which can ultimately facilitate the development of outcome measures for future clinical studies" (HTG_EP, 2021: 23). Patient contributions are thus envisioned as helping to bridge the gap between the measures and outcomes currently used in drug development and what actually matters to patients, which are framed by these materials as being rather different.

As could already be noted in some of the quotes provided above, these materials ascribe patients the roles of representatives and especially consultants largely indirectly, by calling upon researchers to give them the opportunity to fulfil the responsibilities these roles entail. This tactic may be meant to placate drug developers concerned about the consequences that the standardisation efforts of these materials may have on their authority and standing. Thus, the partnership these materials configure is one in which the researchers' authority is not diminished by acknowledging patients as epistemic agents.

To summarise, the PFMD-produced materials articulate a new type of patient, expected to be able to function as representatives and/or research consultants in drug development, depending on the skills, types and level of knowledge with which they are endowed. Although patients are ascribed a much more prominent role by this configuration, care is taken not to obfuscate the researchers, whose collaboration is needed for the standards encoded in these materials to be implemented in daily practices. However, this does not mean that the researchers involved in drug development are not expected to significantly change their ways. On the contrary, they are called upon to diversify their skills and methods, as we shall see below.

Researchers as knowledge-developers through proficiency in diversity

The PFMD-developed materials sketch a different role for the researchers involved in drug development, who are urged to act as hospitable hosts to patients for the sake of developing better medications. Thus, these materials encourage researchers to become better and more empathetic communicators and to take an open and inclusive stance toward patients. For instance, they emphasise how important it is that "the patient voice is heard and understood in all research projects involving Patients" (HTG_EP, 2021: 23) and argue that "minimizing the burden on the patient community is crucial, as well as ensuring that their input is respected and acted upon" (HTG_CTP, 2021: 16). Whereas the technical knowledge with which researchers are endowed is depicted as obvious and readily available, the PFMD-produced materials frame the degree to which they appreciate patient engagement as variable. As such, those interested in pursuing patient engagement are advised to "[i]dentify if sponsor research teams need to be trained on the value of the patient engagement and how to engage patients" (HTG_CTP, 2021: 16). Being willing to engage with patients in the development of new drugs is thus framed as a new capability that researchers need to develop to ensure the success of such interactions. Furthermore, researchers are expected to become proficient in "the new science of patient output", as the acquisition of patient insights is framed as requiring a new systematic approach:

> I don't see any expert who is adequately trained to adequately engage with patient organisations, with patient experts… There are not the right expectations even before we start the engagement. No stakeholder is fully ready and equipped now to engage with patients. (P1, PEOF, July 2020)

To function as hospitable hosts for patients in drug development, researchers are called upon to broaden the variety of methods and tools they use. They are urged to acquaint themselves with research and data collection approaches specific to the social sciences, to learn how to conduct interviews and organize focus groups. Furthermore, they are expected to develop the necessary skills to engage via social media, through play, or storytelling with different categories of patients. Researchers are advised to make their instruments more accessible or understandable to patients and to use new and more appealing tools for patient engagement. For instance, paediatric

researchers are encouraged to consider the use of cuddly white or red cells, Lego-based depictions of certain disease aspects, or vividly coloured instruments to acquire richer insights into the illness experiences of their young patients and their unresolved treatment needs.

As the PFMD-produced materials transform the methods and tools that researchers are expected to work with, the types of relevant and actionable data are also diversified. Thus, researchers are envisioned as being able to make sense of structured and unstructured quantitative and qualitative data in their work, as the latter are substantially shaped by patient engagement. Illustrative in this sense is a remark by a PEOF participant working on a new integrative approach, who stated that "standardised, meaningful, interpretable data, leading to action outcome sets, that integrate the perspective of different actors, need to be developed as a first priority" (P8, PEOF, June 22, 2021). Such data, however, may not only have a more subjective character but may also be unstable, dynamic, hard to measure and compare. From this point of view, acting as welcoming hosts to patients seems to require a substantial expansion of what is currently understood as scientific evidence in drug development. Although the PFMD-produced materials remain silent about this aspect, it would constitute a reorientation both at the level of practice and ideology that not all researchers and the other stakeholders involved may be prepared for and that may require different legal provisions.

By stating the importance of clear knowledge of the patients' needs and preferences, the materials analysed also ascribe researchers their share of responsibility in developing and maintaining long-term relationships with patients:

> The patient community needs to know how their input made a difference and how they influenced the decision-making, reporting, and dissemination process. Patient partners should also know when their input could not be considered and the reasons should be explained to them. Sponsors should be prepared to proactively provide feedback to patient partners. (HTG_CTP, 2021: 12)

Even though these long-term relationships are one of the main aspects that the PFMD-produced materials seek to standardise, the uniformity they seek to achieve does not seem to extend to the format of the encounters between researchers and patients. Although various formats are suggested —ranging from Patient Research Exchange Meetings, which seem to take the shape of roundtable talks, to the organisation of focus groups, or direct consultations— no specific one is prescribed. Instead, this aspect is left at the discretion of the organisers of patient engagement activities, which testifies to the researchers' role as hosts, given that most of the time these organisers are understood to be pharmaceutical companies.

To achieve this new envisioned role, the PFMD-produced materials seek to enrol the pharmaceutical companies to which the researchers belong as allies, as resources need to be made available and organisational changes are required. These materials therefore enthuse about the benefits of patient engagement: "[e]ngaging patients "as early as possible" is recommended to improve research outcomes, de-risk early science, and avoid systematic errors, reputational losses, and further disinvestments…" (HTG_EP, 2021: 5). Thus, they re-frame the role of pharmaceutical companies by addressing them not only as commercial but also as societal actors, interested in furthering the common good: "[t]his [patient engagement] permits drug development to focus on what is important to Patients and caregivers, ultimately improving their daily quality of life and their long-term contribution to society" (HTG_EP, 2021: 5).

Overall, the PFMD-produced materials seek to guide the actions, skills, and attitude of researchers toward a future where they act in accordance with these materials' specifications by being hospitable hosts to patients in drug development. The future that is thus being configured does not, however, bring new roles and responsibilities only to patients and researchers but also to patient organisations. As we shall see in the next section, the latter are ascribed a central position as mediators.

Patient organisations and their mediating role

The PFMD-produced materials envision the highly relevant relations between researchers and patients that they prescribe as requiring the medi-

ation of patient organisations. This is because individual patients and researchers are understood to be missing the type of knowledge that would allow them to successfully interact with each other directly. Patient organisations are ascribed the responsibility of addressing this knowledge gap and are made into the first points of access to patients for the researchers: "[p]atient organisations - where they exist - are the first and key point of contact to identify individuals and/or experts to engage to ensure the right match for the right activity" (HTG_CTP, 2021: 8). This position is reiterated by another guidance, that advises researchers to consider the following question: "Are there any patient organisations that could help you to reach a diversity of patients, or at least collect their voice?" (HTG_PLS, 2021: 27)

In their role as mediators, patient organisations are expected to be well informed about the broad range of illness experiences of their members: "Reach out to patient organisations to understand the comorbid conditions that might affect the target populations." (HTG_EP, 2021: 29) Furthermore, they are also ascribed the responsibility of selecting patient representatives. Thus, patient organisations are expected to be able to recommend 'the right type' of patients for specific patient engagement projects and to be able to correctly understand and apply norms and considerations regarding accessibility and diversity. For instance, those interested in developing patient engagement activities are warned that "[n]o one can speak for all patients with a particular disease. Patient organisations need to make reasonable efforts to reflect a diversity of opinions" (HTG_CTP, 2021: 16).

Patient organisations are also ascribed the role of trainers or education providers for patients, as the PFMD-produced materials bestow upon them the responsibility to prepare their members for patient engagement activities and to ensure that they have or can acquire the necessary competencies to fruitfully contribute to drug development. Thus, patient organisations are expected to train patients to reflect on their various illness experiences and to identify and appropriately articulate those with a collective character. The importance of these activities can be inferred from the fact that these materials urge the organisers of patient engagement initiatives to make sure that patient organisations have the necessary resources in this scope and suggest that they should otherwise be supported in their acquisition of needed resources. Beyond these considerations, however, these PFMD-produced materials do not engage with local differences and other types of inequality, which might make it difficult for some patient organisations to fulfil these responsibilities.

By ascribing patient organisations the role of mediators, the PFMD-produced materials seek to re-position them as authoritative stakeholders on par with the researchers. This is made obvious by the way in which these materials are structured. For instance, in one of the HTGs, the tasks to be undertaken in preparation for and during patient engagement activities are organized by focusing only on what researchers and patient organisations should do (HTG_EP, 2021). Furthermore, researchers are advised to engage in co-production with them, as the following excerpt illustrates: "Try to get the patient organisation to co-lead the outreach, co-organize the activity and co-facilitate" (HTG_EP, 2021: 47).

Whereas the PFMD-produced materials make patient organisations central actors in drug development, they also operate an important exclusion, as the type of patient they consider for engagement in drug development is the member of a patient organisation rather than any individual patient. Although, in principle, patient organisations may seek out unaffiliated patients out of their own initiative, these materials do not make any suggestions or recommendations in this regard. They, however, instate a distinction between the types of knowledge patients are endowed with depending on their membership in patient organisations and place different value on them. From this point of view, the new type of patient that these materials articulate appears to be one whose knowledge and skills can mainly be guaranteed or vouched for through such a membership. For instance, whereas the HTGs and the PET make the knowledge of patients active in patient organisations relevant and show appreciation for it, the knowledge of unaffiliated patients is largely excluded. Thus, even though there are several references to "patient groups and patients",

it is not obvious how the latter could participate in the drug development process, especially in the early stages, given that patient organisations are configured as first points of contact. That this distinction is performative and has already been taken up in practice became obvious at a PEOF session, in which some patients needed help to indicate the stakeholder category to which they belonged, as they were in doubt between 'patients' and 'patient organisation members'.

Discussion

The standardisation efforts this article has focused on can be understood as part of a broader tendency to "regulate and calibrate social life" through standards (Timmermans and Epstein, 2010: 70). Yet, even though the health domain in which these endeavours are undertaken has historically been characterised by the availability and strict enforcement of standards and regulations, the case we analysed is particularly interesting because it addresses a field up till now devoid of standards. It is important to reiterate, however, that PFMD is not the only initiative that focuses on standardising patient engagement in drug development. However, PFMD, perhaps, has the farthest-reaching ambition to achieve uniformity in patient engagement at every stage of drug development globally. As a non-regulatory initiative, it cannot exert direct influence, but it seeks to indirectly steer and mould practices by propagating its guidelines with the support of the pharmaceutical companies, patient organisations, and regulators with which it works.

PFMD's efforts are particularly relevant because the standards the materials they produce put forward are meant to ensure patient engagement in a field from which patients have thus far been largely excluded. Despite its complexity, these materials frame patient engagement as a feasible and manageable process, consisting of sets of action performed in a given order and at specific stages of the drug development process. Although standards are typically future-oriented, the PFMD-produced materials we analysed act across multiple temporal dimensions to achieve specific rhetorical effects. The depth and breadth of the transformations these materials envision certainly point toward and seek to shape the future. Yet, the use of the present tense situates the practices and approaches recommended in the here and now. This helps to minimize the gulf separating these envisioned practices from current reality. It also brings the future closer, thereby assuring the relevant stakeholders of the likelihood of achieving the vision these materials put forward.

Based on our analysis, we have argued that these standardisation efforts rely on the substantial knowledge ascribed to patients, but require patients, researchers, and patient organisations to fulfil different roles. This highlights the political character of the PFMD-produced materials, as with these new roles they try to change the status quo and to redress power relations among the main stakeholders in drug development. What is novel and indicative of this group's commitment to collaborative approaches is the perspective on power and authority implied in these materials, as they do not approach these as a zero-sum game, but as a set of relations where all the stakeholders stand to profit, albeit in different ways. Thus, by positioning the different types of knowledge that patients, researchers, and patient organisations are ascribed as complementary, the materials we analysed seem to envision a new inclusive epistemic environment. From this point of view, the standardisation efforts in the PFMD-produced materials seem to contradict Callon's (2007) view that standardisation in techno-economic networks contributes to new forms of exclusion and to closing off relevant spaces to certain groups.

The openness and inclusivity of this knowledge space are challenged, however, by some of the other moves these materials make. Thus, the mechanism they lay out to engage patients in drug development resembles, to a large extent, the political party systems in democratic societies. Patients interested in contributing to drug development need to become members of patient organisations, whereupon their eligibility for specific patient engagement activities is determined by the latter. Yet, whereas in politics the party members placed on voting lists still need to be elected by the constituency they are meant to represent, in this case, it remains unclear how

the selection of patients is to be made, based on which criteria, and what checks and balances are or should be made available.

Despite this similarity to the mechanism through which political representatives are elected, the materials we analysed engage to a limited extent with the political dimension of patient engagement in drug development. This might largely stem from the fact that the PFMD-produced materials mainly conceive of patients as knowledge contributors and pay less attention to democratic arguments to justify their inclusion in drug development. As such, they touch tangentially upon the political aspects of this process through the responsibilities they place upon patient organisations to make available a heterogeneous group of patients for patient engagement activities. Yet, as we have seen above, no precise means are indicated to ensure this and the main focus on epistemic arguments may lead to an unequal distribution of the engagement opportunities. Such inequality may be further exacerbated by the discrepancies currently characterising the settings in which patient engagement in drug development is to be conducted and by the particularities of local contexts. Future studies on how patients are selected for engagement in drug development and on the various types of alignment required for implementation in different settings of the standards that the PFMD-produced materials seek to put forward will, therefore, be needed.

Whereas most of the literature on standards and standardisation has focused on the implications standardisation can have either upon newcomers or upon actors who are already influential in a given field, our analysis raises questions about the degree to which mediators might also profit from such processes. By placing considerable responsibilities upon patient organisations and highlighting the relevance of their knowledge, the PFMD-produced materials analysed make these organisations one of the central actors in regard to patient engagement in drug development. Although patient organisations might be overwhelmed by such responsibilities and fail to live up to such expectations, they might also manage to use their central position to exert considerable influence on the drug development process. The performative effects of this positioning and the ways in which these organisations understand to fulfil the responsibilities they are ascribed may help further democratise drug development by ensuring the substantial participation of broader and more diverse categories of patients. However, they may also, advertently or not, contribute to the development of new hierarchies and different types of inequality. The materials we studied therefore seem to be at the beginning of their career as potential standards, as are our epistemic adventures in this field.

Limitations and practical implications

Our study is confined to the initial stage in the trajectory of the PFMD-produced materials, when they have recently been published. Future studies will be needed to follow their trajectory, social life, and to take stock of their impact on this field. The focus on publicly available materials also means that our analysis cannot shed light onto the negotiations, conflicts, and compromises that must have taken place between their contributors. An ethnographic study tracing such materials from the very early stages of their development to their implementation across different settings would complement the insights put forward here. Furthermore, our focus in this paper has been limited to materials developed by PFMD, as we deemed its influential status and innovative approaches worthy of careful analysis. To acquire a better understanding of the broader landscape of patient engagement in drug development, it would be useful to compare these efforts with those undertaken by actors endowed with different levels of power and authority.

The findings of this study point to several practical implications relevant for practitioners and policy-makers. To ensure the uniform, substantial, and fruitful engagement of patients in drug development, materials such as the ones studied here need to be supported by adequate legislation and reforms. Only then will the collaborations between patients and other relevant stakeholders live up to the potential envisioned by the PFMD-produced materials. In particular, the recognition of the substantial role of patients in the development of new drugs should be translated into more daring changes

to guidelines, regulations, and consultancy agreements with commercial actors. Such changes would contribute to a fairer distribution of different types of benefits, including, but not limited to, financial ones. Furthermore, who the patients and patient organizations are that will be included in drug development matters. Practitioners should therefore be careful but also creative as they experiment with different approaches to include a broad diversity of patients and patient organizations in the development of new drugs.

Acknowledgements

This study was supported by the H2020European Research Council (no. 948073). This article reflects only the authors' views and the Agency and the Commission are not responsible for any use that may be made of the information it contains.

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Notes

1 PFMD has thus far developed a total of four guides.

2 The development of the PFMD guides -based on a step-by step approach, consisting of public consultations, followed by the development of a draft, then the making available of the draft for public comments, its subsequent improvement, and the publication of the final document- closely resembles that used by the FDA for its own guidances.

Appendix 1

Overview of the main coding scheme

Themes	Categories	Codes
Object of standardization	Processes	Different drug development processes
		Different patient engagement processes
	Tools	Questionnaires
		Guidelines/criteria used for evaluation
		Roadmaps/guide books
	Methods	Research methods
		Engagement Methods
Transformations for drug developers	Behaviors	New behaviors/attitudes
		Adjustments to current behaviors/attitudes
		Behaviors/attitudes to renounce
	Tools	New tools
		Adjustments to current tools
	Methods and skills	New research methods and skills
		Adjustments to current research methods and skills
		Renouncing/not using research methods and skills
	Responsibilities	New roles and duties
		Adjustments to current roles and duties
Transformations for patients	Behaviors	New behaviors and attitudes
		Adjustments to current attitudes and behaviors
		Renouncing current attitudes and behaviors
	Responsibilities	New roles and duties
		Adjustments to current roles and duties
	New characteristics	New knowledge and skills
		Adjustments to current types of knowledge and skills
		(No) Membership patient organization
Transformations for patient organizations	Responsibilities	New roles and responsibilities
		Adjustments to current roles and responsibilities
Properties of materials	Content	Topic
		Order of different components making up the topic
		Use of references/hyperlinks
		When/temporal dimension
	Modality	Text
		Image
		Table
	Inter-textuality/ Positionality	References to academic literature
		References to grey literature
		References to similar materials developed by other groups
	Type of engagement	Consumption only/mainly
		Pro-sumption/ Adjustable as needed