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18. The Role of Patients in Market Access

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18.1 Patients are Active Partners

'Meeting the needs of patients' is increasingly important in developed healthcare systems. In this context, active patient involvement should ensure that patient perspectives are considered throughout the research, development, and stakeholder decision-making process. Today, patients rightly expect an active role in managing their disease. Throughout the '90s, some patients started to prepare for the doctor-visit with own research about their symptoms and potential remedies, and even challenged the doctor's recommendations, which before had mostly been accepted without question.

Active patients formed networks and alliances and requested shared decision-making on an individual level. By forming alliances and patient organizations, they also started to demand a voice in decisions about health policies and research. Famous examples are the HIV-community in San Francisco during the '80s, campaigning for the right to participate in decisions that directly affected their lives, or the French Muscular Dystrophy Association, which meanwhile even funds its own research and the development of new therapies [1,2].

Doctors began acknowledging the importance of discussing with their patients the therapeutic options related to their health. Indeed, it became clear that patients often had different views or expressed different needs from those things considered important by healthcare professionals or researchers, justifying a more direct role of patients in developing measures and criteria important in healthcare decisions [3].

Even Patient Reported Outcomes, or PROs, which are supposed to reflect the patient benefits, are sometimes not necessarily considered as *important* or *relevant* by the patients for which the products are intended [4-6]. Many healthcare decision makers now ask for Patient *Relevant* Outcomes and patient experiences when they consider access to new technologies or their reimbursement [7]. A recently released book on 'Patient Involvement in Health Technology Assessment' lays a foundation for more standardized approaches and best practices for including the patient perspective in the evaluation of new therapies [8].

For the practice of medicine, this development has also shaped the newest revision of the "Geneva Physician's Pledge", the modern successor to the Hippocratic Oath for phy-

sicians around the world which was approved by the World Medical Association in November 2017 [9]. The new pledge reflects the changing relationship between physicians and their patients. For the first time, the new pledge makes specific reference to respecting the *autonomy* and *dignity* of the patient and to aim for *health* and *well-being* of the patient[1].

18.2 "Nothing About me Without me"

Who decides which criteria or endpoints are relevant to patients? Is it the doctor, with the academic training and the experience of seeing and talking to thousands of patients? Is it the decision-maker charged with ensuring fair and equal access to treatments for all patients? Is it the patient who must live with the disease in her or his specific environment? Or the care person, who sometimes knows best, what is important to the patients they care for and to their life? What about society in general and citizen's (tax payers) view on how the healthcare budget should be spent? While there is no right answer, it has become clear that a multi-stakeholder involvement is needed and that patients and their carers should be heard for the key questions leading to essential decisions on their health or ability to live with a certain quality of life. Indeed, as patient advocates often say: "Nothing about me without me" [10].

18.3 Is Industry Prepared for the Change?

Developers of new health technologies need to be well prepared in order to answer questions about how their new therapeutic intervention provides incremental benefit to those patients for whom they are intended; and also, increasingly, how and to what extent were patients involved in the design of the studies to evaluate the new intervention and its benefits. Before a decision is made on marketing authorization, access or reimbursement, patients will be asked to describe the value from their perspective (see examples of patient considerations in Figure 1) [11-13].

Thus, to ensure that a new technology meets the needs of patients, companies start to more actively involve patients throughout the entire development process and life cycle of the product [14]. This is a new and daunting task for many manufacturers because until now, product development was product or approval centric; direct contact to patients was not systematic nor frequently done. Patient organizations were sponsored and viewed as advocates at the time of decision-making meetings, rather than considered

[1] «As a member of the medical profession: i solemnly pledge to dedicate my life to the service of humanity; the health and well-being of my patient will be my first consideration; I will respect the autonomy and dignity of my patient […]» [9]

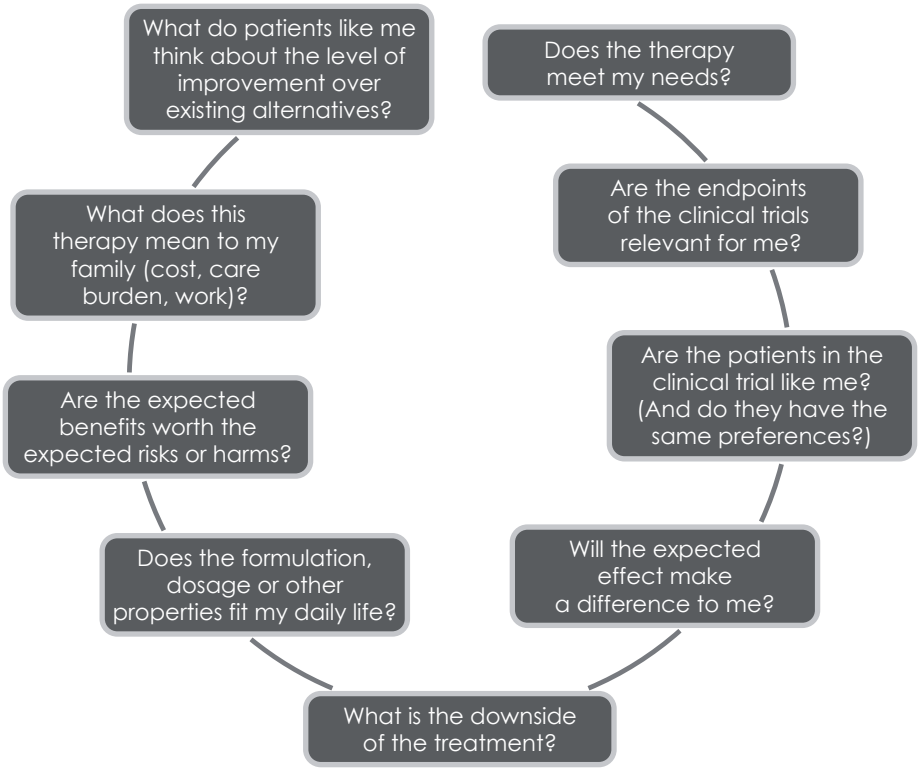

Figure 1. Key questions concerning the differential value of new therapies from the patient perspective

partners with joint interests and inputs to the innovation process [15]. Even for those companies that recognized early on that patients can contribute significantly to a successful development, there was still uncertainty around the 'How', 'What', and 'When' of their involvement [15,16].

A sound and transparent process of involving patients through the product life cycle is therefore essential. At each step of this involvement it should be clearly defined, 1) what the objective of the involvement is, 2) which target audience will be best able to give the required information, 3) which are best (most informative, robust, reliable and fit-for-purpose) methods to elicit the information, 4) what the consequences of the new information would be (how it will inform decisions to be made), and 5) how it will be communicated or disseminated to which target audience, including those in the patient community who contributed. There is no best practice established yet, but there are models emerging, which see patient insights and preferences as important pillars in the development of the evidence-based value proposition of new products [14,16,17].

18.4 Industry Should be Interested: Improved Commercial Attractiveness Through Patient-centric Product Development

Next to meeting expectations of decision makers, solid commercial reasons support the investment in patient (stakeholder) involvement and engagement, as summarized in Figure 2. Aspects such as the optimization of the design of clinical trials and the design of the product itself, increased relevance of the results to patients and decision makers and, potentially, a decrease in the drop-out rate due to better compatibility with patient needs, have been described by other authors [18,19]. If patient representatives or organizations are convinced that the product confers meaningful additional patient benefit, they will support the development and request access to the products.

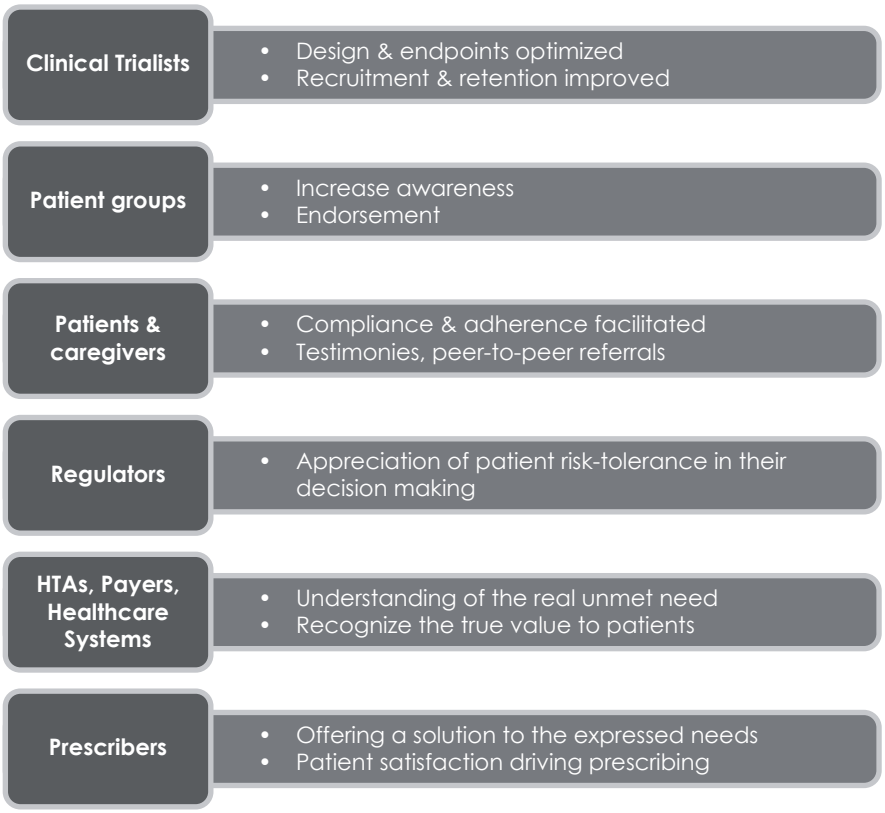

Figure 2. Positive effects of stakeholder involvement throughout the entire product life cycle

Patients may disseminate early information about the technology or upcoming clinical trials or they may explain the evidence from patients' perspective. Regulatory or reimbursement related authorities may better recognize the unmet need and the value of the technology to patients if this information has been elicited from and with patients throughout the development of the product (Figure 2). Prescribers will see that the new technology addresses otherwise unmet patient needs, which will increase the willingness to prescribe it and thus, the uptake of the product.

Levitan et al. estimated the financial value of patient engagement for an oncology program by calculating the expected net present value (ENPV) based on the key business drivers cost, time, revenue, and risk [20]. For a pre-phase-2-program they found a cumulative increase in ENPV of $35 million and for a pre–phase-3 program $75 million and claimed that patient engagement can lead to ENVP increases by more than 500-fold the investment.

18.5 What do Patients Expect from the Engagement Activities?

The values of patients for engaging in quality of life research during product development was recently examined through a world café[2] approach. The participants expressed a strong need for "building genuine, collaborative and deliberative relationships - underpinned by honesty, respect, co-learning and equity". Their motivation was to improve the quality and relevance of the research through their engagement [21]. Patient organizations complained that they saw no reason for being involved only at a late stage of clinical development after study completion. They preferred to see an honest engagement strategy of a company, which allowed them to make an impact on the quality of the data and hence, on the relevance of the product and the underlying evidence. A survey conducted in 2014 among patient organizations identified 6 key expectation categories for engaging in clinical research: 1) relevance to real patients, 2) safety in studies, 3) comprehensible information to study participants, 4) making a contribution to useful therapies 5) making effective therapies accessible, and 6) being part of the team, not just a study object [22]. Therefore, effective patient engagement strategies should build on continuous collaboration and productive relationships between the partners involved. Once more companies engage earlier and throughout development with patients, we can expect a much better alignment of all stakeholders concerning product benefits evaluated and patient unmet needs.

[2] World Café workshop: A method allowing each individual in a larger group of participants to actively contribute to the discussion or the development of a theme [Juanita Brown, David Isaacs: The World Café. Shaping Our Futures Through Conversations That Matter, McGraw-Hill Professional]

18.6 Who is the Patient?

The term "patient involvement" does not specify which patient is involved and how patient participants are selected. Different types of input can come from patients, carers, patient advocates and patient organizations in different collaborative processes or context. In many situations, the term 'patient' implicitly also includes caregivers (for examples the parents caring for children or the family member caring for elderly patients). In addition to the patients, citizens as representatives of the public may be involved, which is often the case in the context of health technology assessment and reimbursement decisions. It should be noted, that their perspective may differ substantially from that of patients [23]. It is important to understand, which type of involvement is required at each step of product development and which person or organization can best fulfil that requirement. For example, the stage in the patient journey should be considered as well as the purpose of the patients' or organizations' advocacy efforts, which audience they target, and which level of expertise they should have (see Figure 3).

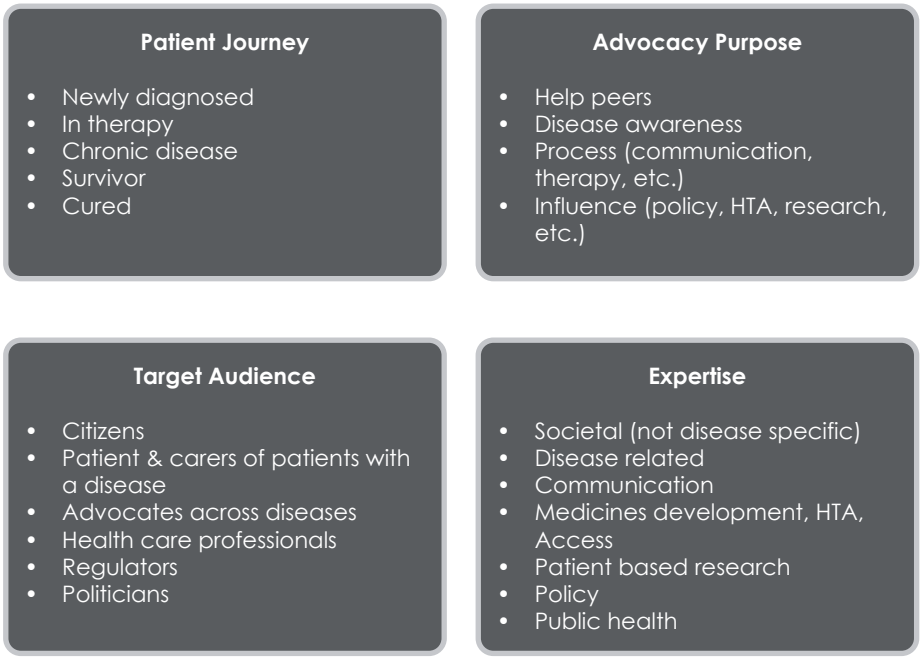

Figure 3. The universe of patient advocates or patient organizations

18.7 Guidance on Involvement in Industry Research, Regulatory Processes, or HTA

Triggered by the Innovative Medicines Initiative (collectively supported by the EU Commission and the European Pharmaceutical Industry), the European Patients' Academy on Therapeutic Innovation Project (EUPATI) was formed as a consortium of patient organizations, academic institutions and pharmaceutical companies under the leadership of the European Patient Forum (EPF) to increase Patient and Public Involvement (PPI) and public awareness of medicines R&D across Europe [15]. EUPATI developed courses to increase the capacity of patient experts for active involvement in medicines R&D, a toolkit for patient advocates to facilitate dissemination of information on medicines R&D to the patients they represent, and an online library of medicines R&D information for the public. Finally, they developed and released after broad consultation a multi-layer guidance on the best approach to interaction of patients with pharmaceutical industry-led medicines R&D, regulatory authorities, ethics committees and HTA agencies [24]. The guidance is targeted to patients and to the respective party involving the patient representatives.

In the USA, the Patient-Centered Outcomes Research Institute (PCORI, http://www.pcori.org) pushes for processes to ensure that researchers work with patients in the design and conduct of a clinical trial. The vision of the institution is that "Patients and the public have information they can use to make decisions that reflect their desired health outcomes". The institute supports involvement of patients and other stakeholder in research through developing guidance, establishing case examples, and building awareness.

Other guidance documents have been developed by various organizations and mostly focused on specific aspects of patient involvement such as legal or ethical issues described by EFPIA [25] or the 'European Medicines Agency (EMA) Framework of Interaction' between the EMA and patients, consumers and their organizations, which outlines the basis for involving patients and consumers in Agency activities [26].

Several groups have produced guidance for various stakeholders such as clinical and outcomes researchers [27], those who develop guidelines [28], or those who evaluate technologies or therapies through formal health technology assessment processes [7]. Relating to health technology assessment, an international multi-stakeholder workgroup (HTAi Patient and Citizen Involvement Special Interest Group) collaborates and advocates since several years to strengthen the exchange of experience and the continuous methodological development in this area [8,29].

Moreover, organizations have started to set up own organization-specific principles and recommendations for engagement. Over time, it can be expected that these diverse but overlapping guidance initiatives will complement each other, converge, and become accepted and adopted more universally. Specifically as a collaborative approach, the Innovative Medicines Initiative 'PREFER' (2016-2021) aims to assess when and how patient preferences on benefits and risks should be incorporated into decisions on medicinal products and to develop methodological guidance for patient involvement in the development, approval, and post-approval of new therapies (see Table in Appendix) [30,31].

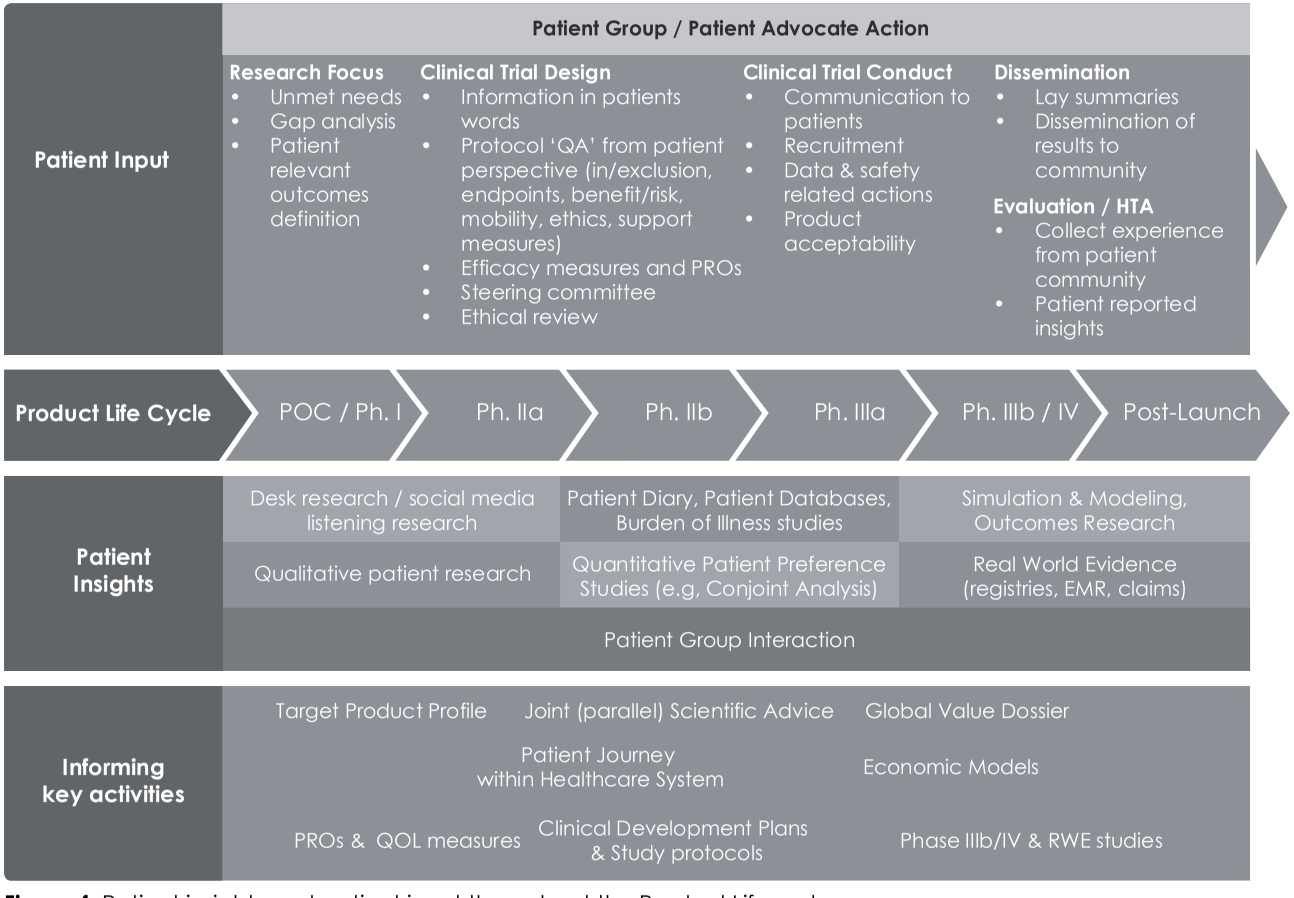

Figure 4. Patient insights and patient input throughout the Product Lifecycle

EMR = Electronic Medical Record; HTA = Health Technology Assessment; Ph. = Phase; POC = Proof of Concept; PRO = Patient Reported Outcomes; QA = Quality Assurance; QoL = (Health Related) Quality of Life

18.8 Activities for Gaining Patient Insights and for Patient Involvement

Gaining patient insights through patient involvement and by collecting information on the *patient perspective* is an ongoing process throughout the entire product lifecycle which starts already in early development phases (phase 1 or pre-clinical). A structured process as outlined in the 'Insights' part of Figure 4 may start with qualitative research on patient behaviors, patient interactions with their environment, and their current choices.

This may be useful for better understanding the disease or condition and its impact on patients, identifying outcomes most important to patients, and understanding benefit-risk trade-offs for treatments. Patient insights can inform the clinical trial protocols or the formulation of specific research questions to quantify certain aspects in the subsequent development steps. After launch, this information can also drive the collection of real life outcomes data on aspects which are beyond the clinical trial context.

The process should be accompanied by patient advisors (patient organizations) with a good knowledge of both the patient perspective and the framework of clinical trial design and medicines development. Their input on various aspects of the clinical studies and their collaboration in the communication to patients as exemplified in the 'Input' part of Figure 4 can help in ensuring that the product-related evidence is important to patients and can facilitate a better uptake and utilization of the product.

Importance of Gaining Patient Insights in Early Development

Better understanding of what the patient values and what their needs are, can inform clinical trial planning including development of educational material about the clinical trials, potential venues for recruitment, convenience to participants, and which terminology is familiar to the patients. There are several observational approaches existing to gather this information. Real life observation of patients or analysis of discussions on social media sites or in bespoke Online Bulletin Boards can reveal valuable information about patient needs or patient values [32,33].

Social media listening is gaining in popularity because it is comparably quick and easy to conduct and can yield a lot of valuable patient and disease information [34,35]. This approach is nice in that it listens to the discussions that are already happening online, in the *words* and through the discourse that patients/caregivers *routinely* use, without in any way influencing those conversations. Hence, without burdening the patients/patient groups with additional surveys, a lot of insights can be gathered on the needs and concerns of patients, to inform drug development and access strategies, as shown in Figure 5.

Online bulletin boards (OBB) are an asynchronous, online tool for qualitative market research, similar to a chat room, that allows invited participants to answer pre-defined questions in a comprehensive manner. The discussion typically runs over 4-5 days,

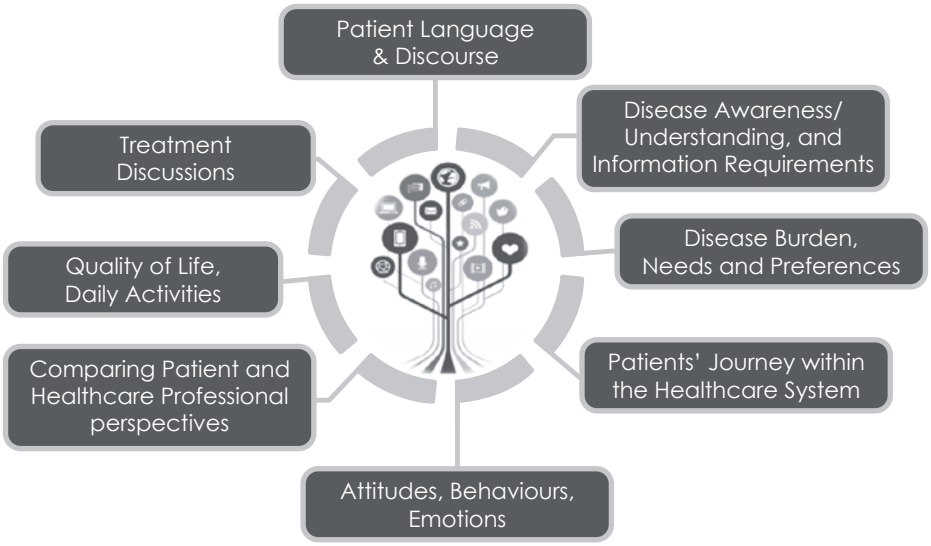

Figure 5. Developing patient insights from social media listening studies to inform early drug development and access strategies

is moderated, structured and allows open answered (free text) answers as well as responses to the posts of the other participants. Typically, 10-12 patients with a specific disease are invited to participate, with the conversation over the course of the study following an outline like that shown in Figure 6. Participants chose nicknames, *providing* anonymity, hence the OBB lends itself very well to uncovering patient insights which might not be revealed in focus groups or telephone interviews, particularly on more sensitive, embarrassing, or emotional issues, that people often have difficulty to talk about openly. The technique *can be used to conduct patient or caregiver research* in highly prevalent conditions as well as extremely rare diseases [36]. Since the online conversation extends over several days, *it also provides the opportunity to go deeper on interesting points that arise, ask for clarification, or explore commonality and differences among participants*.

Patient Preference Studies: building on the insights from qualitative research, patient preference studies can be important as a form of patient-based evidence for highlighting the needs in a quantitative form [37-39]. A task force of the International Society of Pharmacoeconomics and Outcomes Research (ISPOR) has started to define best practices for some of the quantitative methods such as conjoint analysis and discrete choice experiments [40,41] and this is also the subject of the IMI PREFER project [31]. Such studies can be used to show the relative importance to the patient of different treatment attributes for a product in clinical development, i.e. to reveal the value of different product profiles, which is important for informing HTA discussions. Whilst most preference research to date has focused on drugs in late stage development, to show the benefits conferred by the new drug compared to existing ones, increasingly patient preference

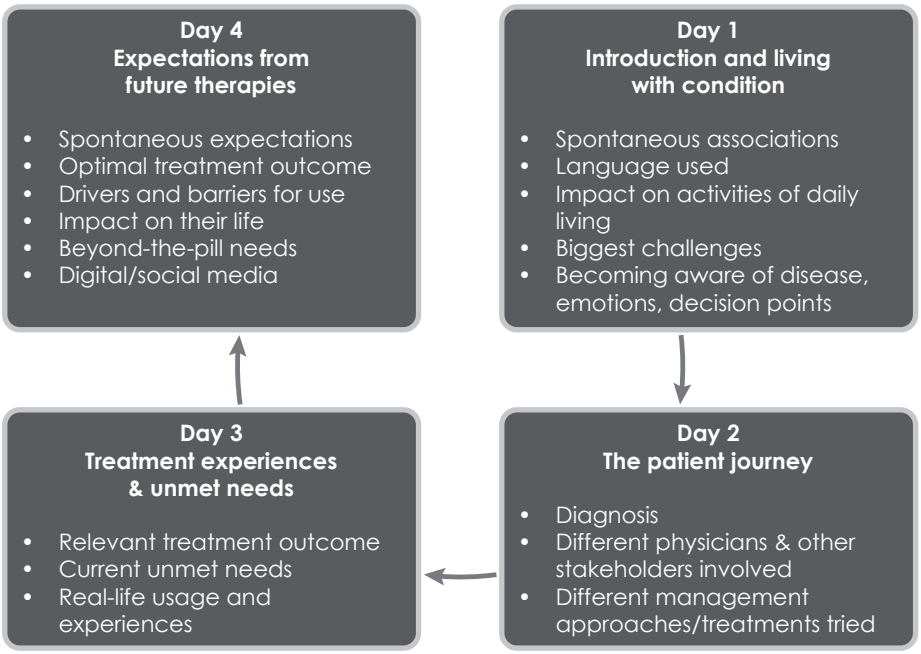

Figure 6. Online bulletin board (OBB) example of typical daily discussion and project flow over 4 days

studies are being conducted much earlier, to highlight the important value drivers from a patient perspective and thereby inform the design of PROs, pivotal clinical trials, and observational studies (Figure 7). The insights and evidence generated through these early development patient preference studies, provide a good foundation for early dialogue/scientific advice discussions with HTA and regulatory agencies, to align on the importance of patient endpoints and evidence to capture in further development phases. From the regulatory perspective, there is high interest in understanding the benefit/risk profile of new drugs, and whether there are subgroups of patients with different preferences concerning the benefit/risk trade-off [42].

A good example of the use of patient preference studies is Myeloma UK, who have been working with the EMA to explore patient preference for different benefit and risk outcomes in myeloma treatment [43]. A further investigation has since been conducted to understand what myeloma patients want from treatments, to inform further R&D activities in myeloma, inform discussions with stakeholders, and to provide a basis for patient-physician conversations around therapy choices [44]. Myeloma UK are also collaborating with NICE on an exploratory project to enable the development of the quantitative methodology to incorporate patient preferences into HTA.

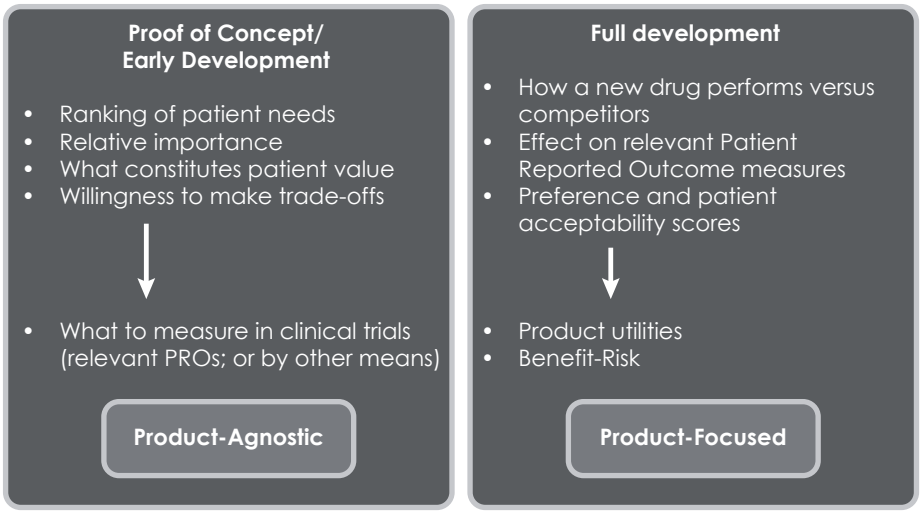

Figure 7. The need for different approaches to address Patient Preferences across the product life cycle. The methodologies may differ depending on the stage of product development and the questions to be answered.

Incorporating Patient Preferences into Health Economic Evaluations. Economic analyses can be conducted from different perspectives such as that of payers, hospitals, the public or the patient. The types of costs and outcomes included in the analysis will be specific to the specific stakeholders' interests (perspective). Currently, not many health economic studies are conducted from the patient perspective. However, both health outcomes and cost will impact the patients' decision on using the therapy and should therefore be more routinely studied [45]. Whilst health economic evaluations have traditionally focused on generic PRO instruments like EQ5D as the basis of the evaluation (e.g., of Quality-Adjusted Life Years), patients often criticize that these generic instruments do not fully capture the aspects that are important to them, and factors beyond Quality of Life are not taken account of in the economic evaluations [6,46]. For example, willingness to pay may be another component of patient preference research, to inform in future the economic evaluations [47].

Addressing patient insights in a stepwise process

Not all options for gaining patient insight may be required for all products and therefore, a patient insight strategy should be developed for each product. Such a strategy is outlined below in Figure 8 and it exemplifies how each step in this process may inform the design of the next step and lead to a more robust clinical trial design and HTA strategy.

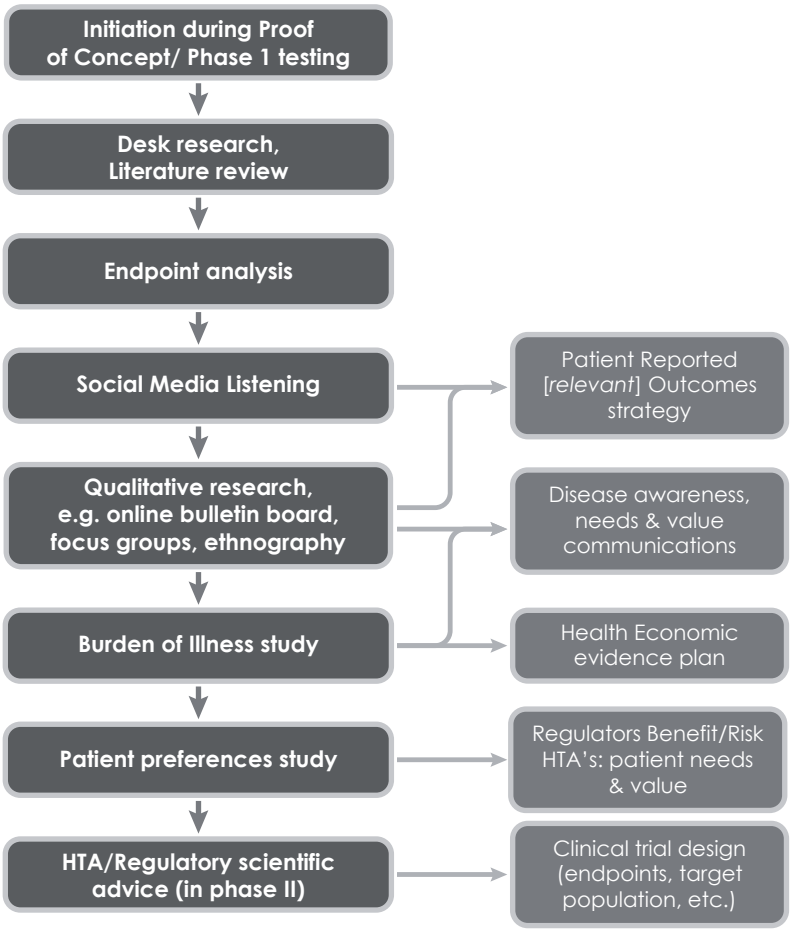

Figure 8. A structured process for patient insight gathering in early drug development

Examples of Patient Input

Patients as Research Partners (PRP): The patient is an equal partner and in direct dialogue with the researcher throughout the design, conduct and evaluation of the research including managerial and oversight roles [48,49].

Patient-Based Evidence: It has been suggested that in addition to clinical and health economic evidence, *patient-based evidence* should be considered in order to achieve high quality healthcare. The term "encompasses the diversity of information that patients provide in evaluating different aspects of care, including patient narratives, data on health-

related quality of life and patient experiences survey data" [50]. Several groups have started to work on Patient Experience Frameworks and to define the methodological specifications of such evidence [8,50].

Patient Centered Outcomes Measures (PCOMs): Like Patient-Based Evidence, the concept of PCOMs has emerged in the recent years to overcome the limitation of standardized 'generic' Patient Reported Outcomes instruments. PCOMs include a diverse group of methods which have in common that they are all reported directly by the patients or carers and that they directly quantify the impact of a disease and treatment on health outcomes that matter to patients [6].

Review of patient material: At many stages throughout the product lifecycle, patient advocates may become involved with reviewing activities to ensure the patient relevance and acceptability, and appropriate use of patient-friendly language.

Input on clinical trial protocol: Patient advocacy groups are invited in their specific disease area to look at draft clinical trial protocols. The advocacy groups provide feedback about feasibility, recruitment, retention, outreach, or other important aspects from their viewpoint. The manufacturer will incorporate some of this before the protocol is finalized [3,49]. The input can happen through face to face discussions inside the team or as advisors, web based discussion, through advisory boards, or through other routes of communication [52,52]. An interesting new development is patient-led clinical trials (more specifically coordinated through patient support groups or organizations) which are increasingly gaining in popularity [53]. Whilst full development of a new drug, with all the regulatory and other hurdles to be overcome, is probably a daunting and unrealistic task for most patient organizations to consider, one could envisage an active role in partnering with clinical researchers to initiate and fund projects for the repurposing of already approved drugs in new indications (e.g. in rare cancers) [54].

Patient advocates or organizations as communication channel to patients: Patient advocates may form the bridge to the patient community by ensuring that documentation targeted to patients is understandable to patients or by translating and summarizing information related to clinical research or therapeutic information into patient-friendly language. If patient organizations are involved in the design of clinical studies and support the goals of the study, they may also encourage the patients who fit the inclusion criteria to enroll to the study e.g., through their healthcare provider.

Patient advocates or organizations as contributors to HTA: Healthcare systems are increasingly involving patients in the HTA or decision making processes with varying degree of formal processes [7]. Involvement can happen at any stage from horizon scanning through scoping to the actual assessment report and appraisal committee meeting. In order to learn from and improve the processes for patient involvement, any of the activities should be formally evaluated concerning their impact on decision making and the efficiency and acceptability of the process from both perspectives, the agency and the participating patients [55]. At the International Society for HTA, a multi-stakeholder work group (the Patient and Citizen's Involvement Group; http://www.htai.org/interest-groups/patient-and-citizen-involvement.html) is collaborating in order to improve the methodological, contextual and procedural ground for patient involvement in HTA. This work recently

resulted in the publication of a first comprehensive guidance book, including the current status of patient involvement in HTA in numerous countries across the globe [8].

Development of treatment guidelines: It is suggested that patients should be involved in the development of treatment guidelines [56]. A systemativ review by Selva et al. of guidance documents for developing clinical guidelines from 56 institutions revealed that 71.4% of them recommended to include patients in one or several steps of creating the guidance (recommendation, reviewing the final version, formulating clinical questions, scoping, disseminating, implementing) [28]. However, it was not very well defined how this input should be generated. In future, clearer definitions can be expected for patient involvement as relating to the recruitment of the appropriate patients, the routes how patient based evidence or patient insights can be contributed, the acceptance of patient preference studies as appropriate evidence, adapting guidance presentation to highlight patient preference points and guidance on how a guideline can be best used for patient centric and shared decision making [57]. Patient involvement may gain a critical impact on the future adoption of new technologies by guidelines.

Two different groups, ICHOM (International Consortium for Health Outcomes Measurement; http://www.ichom.org) and COMET (Core Outcome Measures in Effectiveness Trials; http://www.comet-initiative.org/ppi/poppie) are engaged in the development of standard sets of outcomes measures for clinical trials and research in key diseases; both organizations actively engage patients to ensure the outcomes that matter to patients are captured and that these measures are adopted internationally. Already certain HTA agencies are referring to these standard outcome sets in their assessments of new drug submissions.

18.9 Up for Discussion

In this chapter, we have laid out the principles and opportunities for patient involvement in order to achieve market access. Whereas patient-focused drug development may once have been considered a 'nice to have', it has since moved on to a point where patient involvement and partnership is now an essential and necessary component of the drug development process, in order to successfully meet the demands of regulatory and reimbursement authorities, and indeed deliver new products which meet the expressed needs of patients for which they are intended.

Activities for gathering patient insights or evidence, as described in the 'Insight' part of Figure 4, can and should now be an integral part of the R&D process of pharmaceutical or medical technology companies. Exactly when to do this, and in which format or with which methodology, is an evolving science with a lot of experimentation happening and efforts to integrate approaches in an efficient, timely and cost effective manner (examples in Figure 4, & Figure 8). Not all of these approaches lend themselves to all stages of development and therefore, it is important to consider at each step what the expected output is, which decisions are to be informed through the patient voice, and which method is best suited to attain it most effectively (see examples in Figure 7).

One limitation is that the needs of the patients may change over time and most likely, also their preferences, e.g. due to changing market environment and availability of new treatments or management strategies. Therefore, the validity of this type of evidence may be short-lived and not be generalizable across healthcare systems and culturally different populations. Nevertheless, those companies will have a competitive advantage who refine their process to allow for sufficient patient insights and involvement and thereby, maximize the fit of their products to the needs of the users. Why would we develop products that are clinically and economically effective but not wanted or needed? Let's invest in a future where new innovative products also address the real needs of patients and provide the therapeutic outcomes they are looking for.

18.10 Appendix: Organizations vested in Patient Involvement

Organization	Focus	Description
ACRES Patient Engagement Initiative (PEI), (USA) http://www.acresglobal.net/about-us/initiatives/patient-engagement-initiative-pei	Clinical Research	ACRES, addresses the need to integrate patient centricity efforts across the research and healthcare environment while also considering the needs and priorities of the other stakeholders within the patient research and care eco-system.
BMJ Partnering with Patients (UK/global) https://involvement-mapping.patientfocusedmedicine.org/initiatives/partnering-with-patients	Research & development	Making medicines more relevant to those people who actually need it. Making sure that we have quality research and support doctors who are our main readers, to become better, more informed doctors. We aim to train doctors to become aware and applicable to patients' needs.
Center for Information and Study on Clinical Research Participation (CISCRP), (USA, global) https://www.ciscrp.org	Clinical research	Engage the public and patients as partners in the clinical research process. CISCRP provides a variety of resources, programs and services that are designed to assist clinical research stakeholders in understanding public and patient attitudes and experiences in research as well as improving volunteer participation experiences and satisfaction.
Center for Medical Technology Policy (CMTP) Real World Evidence, (USA) http://www.cmtpnet.org	Health policy, clinical development	(CMTP) is an independent non-profit organization dedicated to developing a health care system where patients, clinicians, healthcare policymakers, and payers have the evidence they need to make informed health decisions. CMTP focuses on providing methodological guidance, shaping health policy, and transforming clinical research. The work on methodological guidance is conducted under the umbrella of the Green Park Collaborative (GPC), a neutral forum to support dialogue and consensus among stakeholders on methodological standards for clinical research, focusing on real-world effectiveness and value.

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Organization	Focus	Description
Community and Patient Preference Research (CaPPRe), (Australia) http://www.cappre.com.au	Policy, patient preferences	An educated consumer voice will help signal to Government, clinicians, and industry the importance of consumer preferences Bringing the two worlds together will help strengthen the PBS for Australia.
Critical Path Institute (C-Path), (USA, UK) https://c-path.org	drug development and regulatory process for medical products	C-Path orchestrates the sharing of data, expertise and knowledge among industry, regulatory authorities, government, patient advocacy groups and academia in the pre-competitive space to generate the evidence needed to improve the drug development pathway.
European Medicines Agency http://www.ema.europa.eu/ema	Regulatory approval	The framework for interaction between EMA and patients and consumers and their organizations outlines the basis for involving patients and consumers in Agency activities.
European Patient Forum (EPF), (Europe) http://www.eu-patient.eu	Health policy, access	Our mission is to ensure that the patients' community drives policies and programs that affect patients' lives to bring changes empowering them to be equal citizens in the EU.
European Patients' Academy on Therapeutic Innovation Project (EUPATI), (Europe) https://www.eupati.eu	Lifecycle of medicines	pan-European project implemented as a public-private partnership by a collaborative multi-stakeholder consortium from the pharmaceutical industry, academia, not-for-profit, and patient organizations with focus on education and training to increase the capacity and capability of patients to understand and contribute to medicines research and development and also improve the availability of objective, reliable, patient-friendly information for the public.
Health Technology Assessment international (HTAi) Interest Group on Patient and Citizen Involvement in HTA (PCIG) http://www.htai.org/interest-groups/patient-and-citizen-involvement/pcig-home.html	Health Technology Assessment	The vision of the HTAi PCIG is "Patient and citizen perspectives improve HTA". Among others, the group has developed resources like 'Values' and various submission templates and hosts a mailing list on the subject [29].
Innovative Medicines Initiative 'PREFER' http://www.imi.europa.eu/content/prefer	Patient Preferences for benefits and risks	A multi-stakeholder collaboration (2016-2021) which aims to assess when and how patient preferences on benefits and risks should be incorporated into decisions on medicinal products. The goal of PREFER will be to provide a set of systematic methodologies and recommendations to assess, engage and include patient perspectives during the development, approval, and post-approval of new therapies.

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Organization	Focus	Description
International Children's Advisory Network (ICAN), (global) https://www.icanresearch.org	Children & families	A worldwide consortium of children's advisory groups working together to provide a voice for children and families in health, medicine, research, and innovation through synergy, communication and collaboration.
OMERACT Recommendations for Patient Research Partners Involvement, (Canada) https://www.omeract.org/patient_research_partners.php	Outcomes Measures in Rheumatology	Patient involvement strengthens outcomes research in rheumatology; the contribution of patient research partners to defining important outcome measures, such as minimum clinically important difference, recognizing domains of concern, such as sleep and fatigue, and ensuring feasibility of assessments, such as in the tolerability of MRI scanning times, has been manifest [15,26]
Patient Focused Medicines Development (PFMD), (Belgium/global) http://patientfocusedmedicine.org	Lifecycle of medicines, clinical research	An independent multinational and multi-stakeholder coalition, which aims to bring together initiatives and best practices that integrate the voice of the patient throughout the lifecycle of medicines development, thereby speeding up the creation and implementation of an effective, globally standardized framework.
PatientsLikeMe, (USA / global) http://www.patientslikeme.com	Real life health experience, clinical research, PRO development	PatientsLikeMe is committed to putting patients first. We do this by providing a better, more effective way for you to share your real-world health experiences in order to help yourself, other patients like you and organizations that focus on your conditions.

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