Principles of Successful Patient Involvement in Cancer Research

September 2021

Preamble

This document is a compilation of input provided by cancer patients and researchers for cancer patients and researchers. It is intended to provide a first point of information with views and perspectives for all regional, national or international stakeholders in cancer research and patient advocacy across Europe who wish to strengthen active patient involvement in their respective fields of activity. In this paper, the term "involvement in research" is used with reference to interpretations by the UK National Institutes of Health Research (NIHR)[1].

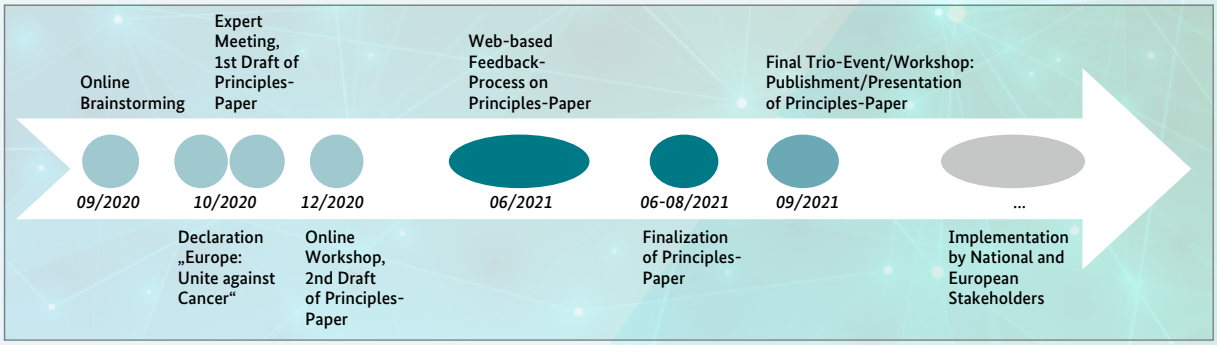

Figure 1: Principles of Successful Patient Involvement in Cancer Research: Timeline of Trio-Initiative

From September to December 2020, over 130 contributors from 16 countries across Europe[2] came together in a bottom-up process[3] to collect and discuss basic principles for successful patient involvement. They represented patient organizations, cancer research, participatory research, medical and healthcare professions, industry, research management, funding organizations and the policy-making level. When collecting these principles, the contributors drew on their respective opinions and areas of knowledge, expertise and occupations as well as on findings from other ongoing efforts to enhance patient involvement they were either part of or aware of. The final results of this process are presented in this document. This collection of principles is not an academic paper. It is not meant to be exhaustive or reflect all existing knowledge of how to conduct meaningful involvement in cancer research. Rather, the contributors intend it to serve as an initial point of reference and a resource for further information and future steps of implementation, possibly also in other areas of health research. For more in-depth reference, we refer readers to the ample relevant literature available in Europe and abroad. It is beyond the scope of this paper to provide a comprehensive overview of the knowledge already in existence. In the interest of neutrality, we refrain from naming specific organizations. The appendix to this paper provides a collection of resources that were pointed out as helpful by the contributors to this process.

1 The term "involvement in research" is understood as "research being carried out 'with' or 'by' members of the public rather than 'to', 'about' or 'for' them." "Successful" or "meaningful" involvement is intended to indicate involvement with real benefit for all parties or "an active partnership between patients, carers, members of the public (or other stakeholders) with researchers that influences and shapes research". The paper takes into account the existing range of possible levels of involvement, from which individual strategies for involvement may be derived (cf. chapters 2.2. and 2.3.). cf. also: https://www.nihr.ac.uk/documents/briefing-notes-for-researchers-public-involvement-in-nhs-health-and-social-care-research/27371; https://www.nihr.ac.uk/patients-carers-and-the-public/i-want-to-help-with-research

2 Belgium, Cyprus, Denmark, France, Germany, Greece, Ireland, Italy, Netherlands, Norway, Portugal, Slovenia, Spain, Sweden, Switzerland, UK

3 After signing the Berlin-Declaration "Europe: Unite against Cancer", the Trio Presidency of the European Council of Germany, Portugal and Slovenia launched a bottom-up initiative for enhanced patient involvement in cancer research. First steps were taken by the contributors at an initial online brainstorming event involving young scientists and patients in September 2020. This event was succeeded by two online workshops in October and December 2020. Minutes of each event were taken by the DLR Project Management Agency on behalf of the German Federal Ministry of Education and Research, and used for for-mulating a succession of draft principles papers reflecting the input of the contributors to the bottom-up process. Drafts were produced based on the input of several rounds of feedback from the group of contributors. A last round of online-based public feedback open to the general public was conducted from June 7 to 27. Its input was used to produce the final version of the principles paper at hand.

The following chapters, 1) A Shared Vision, 2) Strategy, Level and Timing of Involvement, 3) Communication, Understanding and Relationships, 4) Resources, Knowledge and Skills, 5) Methods and Approaches, and 6) Ethical and Legal Aspects, present the collated principles in detail, as derived from discussions in the workshop series during the bottom-up process.

Figure 2: Word cloud of 45 phrases collected by participants in session 1 “Vision” of the online workshop in December (in response to the question: “Which catch words would you choose to describe your personal vision or ambition regarding active patient involvement in cancer research?”)

1. A Shared Vision

1.1. A principal aim of cancer research is to improve the lives of those affected by the disease. Thus, their voices must be heard. Without them, the picture remains incomplete. Involving patients, carers or patient advocates makes cancer research – and ultimately also treatment choices or clinical practice – more meaningful, relevant and valuable by focusing it on the actual needs and demands of the target group. Patients are "experts by their personal experience". They know what it means to live with a certain condition. They will bring diverse and new points of view, questions and solutions to the table for further discussion and may thus improve research quality. Patient involvement is also a means for addressing societal expectations about the transparency and accountability of research that is often publicly funded. Involvement will strengthen public support for research programmes and projects, increase acceptance of research results and enhance their transfer into prevention, clinical practice and health care. It can also support the more equitable allocation and accessibility of research results. For cancer patients and their carers, involvement has an immense empowering effect and adds to their autonomy. On the policy level, patient involvement supports the promotion of open science and data sharing and thus contributes to making the best possible use of collected data.

1.2. Involving patients and other stakeholders to the mutual benefit of all parties is no easy task. There is still a notable level of inequality in European countries with regard to acknowledging the benefits of patient and public involvement and providing the necessary support and resources for its implementation. Involvement requires a genuine interest, aspiration, openness, flexibility, altruism, pragmatism, holistic thinking and the willingness to continue to learn, reflect and improve. It also requires a rethinking of existing hierarchies and mechanisms in traditional health-related science and thus changes in the mind sets of scientists, patients and other stakeholders from health care, funding bodies and politics. In view of the current philosophy and reward system in research, this might even require a shift in research culture as a whole. This shift will help change the current paradigm of involvement from patient-centred maternalism to productive partnership, from giving input to co-designing, from expressing needs to participating in priority setting and thus from mere dissemination to actual implementation.

1.3. Several minimal requirements must be met in order to enable successful involvement. Above all, patients must not be viewed as mere research objects. They should be systematically involved as active partners or co-researchers at eye-level, and they should hold an appropriate share of decision-making power in the research process. Moreover, all stakeholders should be willing to start small and be patient to let things grow. It requires time and effort to find individuals to involve in research and build effective partnerships based on mutual trust. Ideally, partnerships should extend beyond individual research projects and form the basis for sustained collaboration. Sufficient time, funding and flexibility are required to enable fruitful involvement. In this regard, it is crucial to support not only participatory research itself, but also meta-research for providing an overview, benchmarking ongoing efforts, developing methods and assessing the multiple impacts of involvement. Provided that such principles are applied, involvement of patients, carers and other stakeholders in cancer research will fulfil its full potential for all over time.

2. Strategy, Level and Timing of Involvement

2.1. When planning cancer research projects with the aim of involving patients or the public, it is important to **consider all aspects of successful patient involvement very early in the process**, and together with all groups to be involved. Ideally, this will happen even before the actual start of the project, i.e. in the ideation or initiation phase. Only well founded and clearly defined, specific goals and strategies will make involvement meaningful and actionable in relation to the relevant research area, project or question.

2.2. Depending on the specific research question to be addressed, the goals and resulting **involvement strategies may differ widely**. In some cases, a pragmatic, outcome-oriented or more "top-down" approach may suffice while in others a democratic, rights-based or more "bottom-up" approach may be the better choice.

2.3. In any case, it should be decided and made clear from the beginning who leads a project, which level of involvement is appropriate[4], or **how decision-making power will be shared** between partners. For certain projects, it may be sufficient to solely consult the persons or organizations involved. However, tokenism, mere afterthought or tick-box exercises must be avoided. In other cases, higher levels of involvement are justified, manifesting as genuine collaboration, co-creation or even putting "patients in the driver's seat", i.e. giving patients control over the research process. Patient-led or patient-driven research activities[5] should be strengthened and supported wherever possible. In general, higher levels of patient involvement require increasing opportunity to impact on and co-shape research in order to create added value (cf. footnote 4).

2.4. In the planning or ideation phase, a participatory **stakeholder analysis** will provide answers as to who needs to be part of the project and what their respective interests, costs and benefits are. It will also help to decide whom or which organization not to involve, for instance due to vested interests or bias. In general, all stakeholders in cancer prevention, treatment and care have valuable input to contribute. Patients and their carers or advocates, members of the public, different scientific disciplines as well as health professionals or representatives of healthcare systems, research funding, policy and industry: they all have their own characteristic viewpoints or forms of knowledge and the full potential of involvement can only be realized when **all groups, which are relevant for addressing a certain research question**, are included. However, the choice of whom to involve will always depend on the particular research area, project or research question. It is important to always ask yourself "What are we looking for?" or "Who do we need to understand the problem at hand?" and then to match the right persons or entities to the right project.

2.5. Even within one individual stakeholder group, there are differences, which must be considered carefully. With regard to the group of patients, we must acknowledge the conceptual differences between individual patients and their carers, patient advocates, patient organization representatives and patient experts as well as their varying impact and expertise[6]. Even though including a variety of perspectives can be very beneficial, the question of **representative insight** should be reflected critically. For instance, patient needs and preferences on a general level may be better reflected by representatives of patient organizations while in other cases involvement of individual or untrained patients may be the right choice.

4 For descriptions of different levels of involvement cf. e.g. Arnstein, Sherry "A ladder of citizen participation" (cf. appendix for link).

5 Cf. e.g. Patient Led Research Hub in the UK.

6 "Individual patients" means individuals with personal experience of living with a condition, who can share their subjective experience.
The term "carers" describes persons who support individual patients.
"Patient advocates" refers to persons who have the insight and experience in supporting a larger population of patients living with a specific condition. They may or may not be affiliated with an organization.
"Patient organization representatives" means persons who are mandated to represent and express the collective views of a patient organization on a specific issue or disease area.
"Patient experts" are people who, in addition to disease-specific expertise, have the technical knowledge in R&D and/or regulatory affairs.
The term "citizens" refers to users or potential users of health services, defined not in terms of their use of services but by their status in the community.

2.6. It is also important to be aware of the **heterogeneity** of individuals with regard to age, gender, ethnic and/or cultural background and perspective, education and incentives or disincentives to become involved and to make sure to reflect this heterogeneity in any group to be involved. In this context, it is important to note that heterogeneity is also a factor with regard to patient organizations. It is generally beneficial to establish connections with as many patient organizations as possible in a given field.

2.7. When defining the goals and strategy of involvement, the **appropriate timing** must be decided. In general, systematic and continuous involvement processes with clear concepts and milestones have better chances of generating added value than the ad-hoc involvement of stakeholders only at particular, short time points during a project. Accompanying a project throughout its lifetime, including during periods of development and challenges, is more likely to create meaningful involvement and relations. However, the appropriate timing will always depend on the nature of and prerequisites for an individual project.

2.8. Patients or the public can be involved **across the whole research** cycle, from strategic priority setting, programme or call design or the review of grant applications to the planning and implementation of individual research projects, dissemination of their results and evaluation. Involving patients and other stakeholders **from an early stage** of the development of calls and projects is particularly beneficial as this places the focus on their specific viewpoints and demands right from the start. Patients and other stakeholders should definitely be involved already in prioritizing and selecting research questions and discussing scientific approaches. Patient-related impacts or outcomes of a project become strongest when patients are involved from the very beginning and before decisions are made. Ideally, the goals and strategies of the involvement process itself should also be jointly defined by all intended project partners in a participatory manner. The important role of clinical cancer registries for performing well-planned evidence-based research should also be noted in this process.

2.9. With regard to **different types of research**, involvement can be fruitful across the entire research continuum ranging from academic to industry-led research and from basic research to clinical trials to healthcare evaluation. It also plays a vital role in prevention research. Here, healthy individuals representing the general public or certain societal groups must be involved, rather than patients.

2.10. Even when developing and implementing research infrastructures such as **biobanks or data repositories**, patient involvement can prove to be very beneficial. New ways of engaging patients and the public should be explored to ensure the best possible use of the data or material that is being collected. Moreover, participatory processes can be used to discuss and define innovative ways for patients to donate data or for shaping the rules and regulations for data protection and data sharing in order to reduce scepticism and promote the use and value of existing data.

2.11. Several health research organizations across Europe have already set up **permanent patient panels or advisory boards** whose members provide counsel on priority setting, the conception of in-house programmes or individual project design. They have thus made patient orientation and patient involvement an integral part of their research activities. Such structural steps provide another valuable option in addition to involvement in individual projects. They will help to make involvement more systematic and synergistic, less ad-hoc and thus more valuable. They will support the ongoing process of making patients actual team partners, rather than mere objects of study, both in cancer research and beyond. Funding organizations and policy-makers across Europe can support this process by further increasing the demand for participatory research in their respective field of activity or by promoting the formation of community or patient advisory boards that are independent of individual research organizations.

2.12. Involvement processes should be designed and organized based on the principle of **equity, also with regard to participation in clinical studies. Accessibility to and participation in international or multicentric clinical studies should be offered to all countries in an equal manner**. This refers in particular to smaller countries that, in the past, might have experienced inequity in this domain.

3. Communication, Understanding and Relationships

3.1. When embarking on research involving patients (or other stakeholders), all those involved in the project should treat each other as equal partners and with mutual respect. The involvement process should be bidirectional and balanced, and all stakeholder contributions should be accepted and respected. All viewpoints are important and relevant in order to obtain comprehensive results. Patients should be duly recognized for their input. If patients or their representatives in fact collaborate with researchers on project design, data analysis and drafting of the results, they can be offered co-authorship as a clear signal of sharing of power. Sharing responsibilities and distributing roles such as chairing meetings, leading discussions and summarizing results evenly among all those involved is also a sign of equality. **Governance structures and decision-making processes** should be designed with this in mind and should also make full use of the rooms for manoeuvre or flexibility for sharing power in a given project.

3.2. Carefully deciding where to participate or whom to involve, overcoming existing or perceived hierarchies and **building relationships based on mutual trust** and empowerment of all those involved are fundamental prerequisites for successful involvement. Forming relationships of this kind and an atmosphere of ease and confidence to enable fruitful collaboration requires understanding, effort, dedication and, above all, time. When attempting to involve vulnerable groups with particularly special backgrounds and needs, it may take years to develop functional relationships. In order to overcome initial reservations, it may be beneficial for patients to only interact with other patients in the first instance. This may be less intimidating and patients are able to embark on working on a project with more perceived empathy and commonalities. The initial investment of time and effort into building relationships is very worthwhile because usually, once they have been established, such contacts last beyond individual research projects and form the basis for sustained collaboration. In any case, dedicating time and effort to building long-lasting relationships between all those involved on the basis of openness and trust will create an environment that is conducive to active patient involvement and hence to more meaningful and relevant cancer research.

3.3. When building relationships, it is important to **understand and prioritize the motives, incentives and mutual expectations** of all parties and every individual involved[7] and to assess the potential return on investment for the different groups. Expectations must be managed with regard to the nature and probability of project results, the time and effort to be invested and the potential impact of the actual involvement process itself. It has to be made clear that research can always fail and hopes may not be fulfilled. From the very beginning of a project, all partners should carefully define what constitutes the "success" of patient involvement in a research activity for each stakeholder group. Depending on the choice of approach to involvement, this could be impact and/or process measures. It is also vital to be aware of and avoid negative impacts of patient involvement such as the instrumentalization of patients or using collaboration to stifle critical voices.

7 Cf. "stakeholder analysis" (2.4.).

3.4. Thoughtfulness, openness, transparency, a team spirit and real teamwork create an important basis for building trust on all sides. Opportunities for **regular personal encounters** and adequate physical space for collaboration or group work should be provided to allow personal relations to grow. Wherever possible, formats for meetings and exchange should be employed that enable patients to become involved even if they experience health-related limitations. In general, information must be provided on a regular basis and presented in a form that is understandable and accessible for all. This form will differ widely depending on the groups of persons to be involved as well as their specific backgrounds, requirements and needs. Wherever possible, scientists should make sure that they provide lay summaries, glossaries or descriptions of the scientific background, aims and methodology of their project in order to make them accessible to the respective audience. **Dialogue and listening** are key to communication. All those involved should be given the opportunity to lead discussions and summarize results from their perspective as this strengthens their empowerment and their role in the project.

3.5. For any given project, **clear lines of communication and full transparency** concerning goals, prerequisites, governance structures, codes of conduct, rules, decision-making processes and pathways of information should be ensured. As a rule, the timing, milestones and critical decision points of a project as well as patient roles, expected contributions and time requirements should be known to all those involved. Furthermore, there should always be **timely feedback** about the proceedings, decisions taken, progress and results of the research project. "One-off communication" where partners are not kept up to date with what is being done with the outcomes after an involvement phase must be avoided. Moreover, means and methods of communication must be adapted to the diversity, needs and capabilities of the particular groups that are to be involved. Specific guidelines for communication and feedback should be supplied to all participants.

3.6. Since patients and their representatives aim to inform and empower their communities, it is also important to **discuss and agree what information on a given project and its results they can or should communicate**. Trainings on public relations work and media use will further empower all stakeholders and foster the flow of valuable, quality-assured information to all interested parties.

4. Resources, Knowledge and Skills

4.1. In order to realize meaningful involvement in research with real benefits and added value for all sides, sufficient resources must be allocated. It all starts with the **mind sets and dedication** of not only researchers, patients and other stakeholders, but also those designing and implementing funding schemes as well as their opportunities and framework conditions. Research that involves patients is different. It requires more time and effort than conventional research. Nevertheless, it needs to be valued for its benefits and accepted as "real" research work.

4.2. The organic nature of research involving patients or the public requires **sufficient time, funding and, above all, flexibility** on all sides to enable the development of sound relationships and increase the probability of success. The **staunch support of funding organizations** plays a crucial role in this context. It is important not only to include both demands and specific financial resources for active patient involvement in funding programmes or calls where ever appropriate and necessary, but also to design programmes and calls to be conducive to involvement. For instance, in participatory research, resources may often have to be re-allocated due to necessary adaptions or changes that become apparent only after some time. Funding structures and the underlying legal frameworks as well as funding criteria must allow for the required flexibility. They should also provide incentives and innovative ways of bringing patients and researchers together. Sufficient resources should be provided for adequate communication and relationship building over the whole project lifetime, for workspaces for all parties involved and for learning or training opportunities for all partners. It is crucial to allocate enough time and personnel or capacity on the side of the researchers for these tasks. Moreover, there should be fair, market-value compensation for the time or income lost by the patients involved.

4.3. **Special emphasis should be placed on the planning phase of a project**. Phased approaches in funding structures, including funding for the pre-grant phase or upstream project development phase, have proven to be very beneficial. The generally non-funded pre-application phase, which is characteristic of non-participatory programmes and calls, does not allow for identifying, recruiting and getting to know partners, building relationships and obtaining preliminary data from initial encounters with the groups involved. Both patients and researchers simply do not have the means to do so. Ignoring this fact is bound to lead to tokenism, ad-hoc engagement rather than systematic and productive involvement and mere tick-box exercises.

4.4. In order to enable a fair assessment of the quality of the envisaged involvement strategy for any given project, meaningful **patient involvement should be made a proper and equitable selection criterion for all relevant funding programmes**. Moreover, patients, carers or their representatives should be involved in the respective review boards.

4.5. Besides time, financial means and flexibility, there is another fundamental resource that is a prerequisite for successful involvement: all parties must have sufficient knowledge and skills to conduct and participate in health research involving patients or the public. **Training** and capacity building for all relevant stakeholders **can happen both within individual projects and outside of projects** in dedicated programmes. Within projects, the management staff may aid in overseeing this process.

4.6. The ideal research project with active stakeholder involvement is designed as an iterative process that **includes training, education and learning on all sides** as part of the actual involvement process. In this light, it is important to acknowledge the **value of different forms of knowledge** and the complementarity of, for instance, scientific or technical and experiential knowledge. Ideally, both forms of knowledge should be combined. Patients or researchers, who come together in a participatory research project, should be familiar with not only their own field of knowledge, but also that of the other partners. Informed patient experts may have both the experiential knowledge of living with their conditions and at least partial technical knowledge of the prerequisites for good scientific practice in a clinical study. Researchers may be aware of the diversity of views, needs and opinions of the patients involved in their studies in addition to their scientific knowledge and skills. If knowledge of any kind or field is lacking at the onset of a project, participants must be trained in a suitable form. This will enable the change of perspectives that is necessary to enable mutual understanding and effective involvement.

4.7. **Patients, carers or their representatives typically benefit from education programmes providing medical expertise** (e.g. general health literacy, basic indication-specific knowledge, latest developments in the field), **methodological expertise** (e.g. overall research concepts and strategy, project governance and implementation, scientific methods, typical milestones or time-sensitive decision points, digital literacy as well as use of technology or devices) **and systems expertise** (e.g. knowledge about healthcare systems, regulatory processes or lab organization and hierarchies). Enhanced **communication or negotiation** skills are also very helpful. Training for patients should also include real-life examples of the kinds of projects they will be involved in in order to "make it real". This could be organized, for instance, in the form of symposia for patient audiences. In the context of patient-oriented training, it is also vital to consider the abilities and limitations of particular patient groups as well as language barriers or levels of existing knowledge. **On the part of the researchers,** training in patient organization landscapes, communication and social skills, use of lay language, methodology (e.g. qualitative and mixed research methods), power-sharing and governance has been shown to be very beneficial.

4.8. Even with regard to trained project members, it will be necessary to consistently monitor levels of understanding and exchange and provide **translations and explanations** wherever necessary. For instance, support may be provided if patient representatives do not have the technical expertise to translate their questions and needs into rigorous study designs.

4.9. The knowledge and management of motives and expectations makes it possible to derive and provide **incentives** or rewards for all of those involved in a participatory research process. These should go beyond altruism and mere financial compensation. For scientists, besides high-impact publications, career advancement, higher probabilities of funding or bringing new products to market, desirable incentives may be making a real difference by generating innovative insights and results with true benefit for patients, or establishing lasting relationships for future work. For patients, incentives may be supporting more meaningful research which is actually focused on their specific hopes and demands, or creating study designs which account for special needs and requirements of patients, and which include patient-oriented outcomes such as quality of life[8]. Patients may also want to gain a deeper insight and understanding of the relevant research and its mechanisms or even become (co-)authors of publications. They may also want to gain earlier access to drugs, novel diagnostic tools, innovative treatment options for their disease or simply enhance their quality of life. It is important to realize that patients or the organizations that represent them will only participate in involvement processes that they deem to be worth the effort. Today, they are being approached more and more often and are thus in a position to choose where to invest their time.

4.10. For planning and conducting participatory projects, it is not only knowledge about the inherent field of knowledge, interest, expertise and skills of each party that is required. All those involved should also be aware of the necessary time and effort to be invested by each partner as well as of the possible benefits and opportunities and they should have **skills with regard to the mechanisms and methodologies of active involvement in participatory research cooperation** as such. Even though approaches to involvement will vary from project to project, the basic principles and methodology will be applicable in the majority of cases. Knowledge of the "whys" and "hows" of involvement in research is not only important for those actively carrying out and taking part in projects.

4.11. Those who design and implement funding for research projects with public or patient involvement, i.e. **policy-makers and funders, should also be trained** to be able to plan funding programmes and calls accordingly. The same is true for other relevant groups of stakeholders in health care and research such as insurers, practitioners or healthcare workers. Again, it is important to adapt any training programme to the special needs and requirements of the particular target audience.

4.12. Researchers and clinicians in particular should be exposed to patients and their communities early on in their careers. **Putting a face to patients or their representatives for young researchers**, for instance by inviting them to speak at summer schools or on similar occasions, helps pave the way for future involvement. Moreover, methods of communication, active patient involvement or co-research should become part of the curricula of medical schools or PhD programmes. Specific and systematic courses should be incorporated early in the educational systems in order to make involvement in collaborative activities part of the career development of young scientists in this field.

4.13. In order to define clear universal training standards for participatory research, **European curricula for educating patients as well as scientists** should be developed.

8 For example with regard to side effects of treatment such as fatigue, sleep problems or pain – all of which are still insufficiently assessed in many cases.

5. Methods and Approaches

5.1. Many approaches to active patient involvement have already been developed and put into practice. Thus, when embarking on participatory projects, it is important not to reinvent the wheel, but rather to **use existing, validated resources and reference points wherever possible.** However, depending on the particular research area, project or question that will be addressed or group of patients or stakeholders to be involved, **suitable** approaches will differ widely. **Existing resources are still far from covering all eventualities and situations, which may occur.** Moreover, existing approaches are not always easily identified. Literature searches or other forms of inquiries can be difficult because indexing and the vocabulary used is often not standardized or simply because titles of publications do not clearly refer to involvement in this specific project. Thus, **systematic overviews** of methods and methodologies in health research involving patients or the public **are still widely lacking.** The same is true for indicators and methods to evaluate the impact of patient involvement. Implementation research on the effectiveness of existing methods in various settings is as underdeveloped as the professional development of methods based on the results of this kind of research. Furthermore, needs and thoughts of patients, patient-related outcomes and other patient-centred aspects are currently mainly gathered in the form of individual studies or projects. Systematic overviews or registries of these research activities and, as a result, the most pressing research questions patients see in certain disease areas would provide a highly beneficial asset and point of reference for many researchers, beyond the scope of individual projects.

5.2. **Funding organizations,** which promote involvement in health-related research throughout Europe, can play a vital role in addressing the deficits described. They **are asked to provide the financial means for meta-research or "research on participatory research"**, which is aimed at providing a solid knowledge base for involvement in cancer research and beyond. Meta-research of this type would fill important gaps by monitoring and evaluating ongoing research at the national and European level and identifying not only best practices and success stories, but also failures and bottlenecks. Meta-research would also collect, compare and further develop methods for active involvement. Here, exploring methods used in other fields such as innovation theory, futures thinking, design thinking or action research may be helpful. It may also be beneficial to look into innovation processes in different industries outside of health R&D to see how they go about involving end users.

5.3. **Opportunities to conduct meta-research** can be offered within the framework of suitable calls for disease-oriented research allowing for the involvement of stakeholders via subprojects or individual accompanying projects ("Begleitprojekte" in German). Such opportunities can also be offered via independent, separate and specific calls or funding programmes dedicated exclusively to meta-research. Regardless of their origin, the results of publicly funded meta-research should be published in suitable peer-reviewed journals. Moreover, suitable platforms should be established and maintained to pool these results and make them accessible to all relevant stakeholders.

5.4. **At the level of individual, health-oriented research projects, which aim to involve stakeholders,** researchers should generally make sure to choose methods and instruments for gathering and disseminating information that are suitable for the particular project and groups to be involved (e. g. quantitative and/or qualitative methods).

5.5. Participatory projects can play a vital part **in adding to the growing stock of knowledge of theory based and/ or evidence-based involvement methods**. Wherever adequate, these projects should be designed to develop existing methods further or to develop novel methods while addressing their respective, primary research questions. Developing and/or promoting new means, tools or strategies of involvement and co-creation or innovative ideas for involvement-oriented institutions, labs, creativity platforms, funding or education will create added value far beyond the scope of the individual project. This effort should be supported by including elements of participatory (process) evaluation in programmes and projects wherever possible. Continuous monitoring and systematic reporting of participatory processes within a project will make the research team aware of the status of patient involvement in their project and provide data for evaluation.

5.6. Many funding programmes or calls still do not currently provide for sufficient resources or flexibility for successful participatory research. Until this is changed, considering other forms of funding such as **crowdsourcing or involving charities and advocacy groups** is beneficial especially with regard to efforts to obtain funding in the early phase of a project or for gathering preliminary data.

5.7. There is no easy answer to the question of **where to find potential individuals or organizations to involve** in a project or how to make initial contact. This largely depends on the individual project, research area or question to be addressed. Several potentially helpful matchmaking tools, networks, platforms, registries, databases or contact points already exist at national, European and international levels[9]. However, these tools can only be as useful as the input that informs them. Thus, whenever a participatory project is conducted, careful attention should be given to **strengthening existing matchmaking tools or creating new information sources** by providing information on who was involved and how they were contacted. While establishing registries or matchmaking platforms to connect patients, carers and their representatives and researchers at the European level may be especially beneficial, national tools and access points will also remain important.

5.8. In general, **pooling and exchanging collected data, experiences, contacts or expertise on (virtual) platforms**[10], which are accessible beyond the scope of an individual project, and thus sharing stories of success and failure between researchers, patients and other stakeholders is key for enabling the exchange of knowledge, learning from previous projects or examples and preventing reinventions of the wheel. It will also make patient involvement activities more tangible.

5.9. Establishing and maintaining platforms, reference networks or databases for knowledge exchange creates effective points of access to information for all relevant stakeholders. Provided that they cater to the needs and requirements of many relevant groups, provided that a **sufficient level of accessibility**[11] can be achieved and provided that a large amount of knowledge generated from participatory research and the respective meta-research is fed into them, these platforms can provide guidance and useful frameworks for all parties that want to partake in participatory cancer research and beyond.

5.10. Once they have been established, platforms for matchmaking and knowledge exchange can also serve as a **basis for the formation of multi-stakeholder working groups on active patient involvement** or the development of innovative concepts ("labs") where different stakeholders can experiment with new ways of collaboration.

5.11. Although researchers and policy-makers in Europe are becoming more and more aware of the need for and benefits of participatory research, there are still **noticeable differences in implementation.** The reasons for these differences vary widely. Examples for underlying causes include differing scientific cultures, research capacities, size and composition of research landscapes or levels of patient or researcher organization. Funding organizations and the policy level can play a vital role in establishing platforms for networking and information sharing and in promoting their use. They can also promote the sharing of these resources and the accumulated knowledge on patient involvement between higher-income and lower-income countries or the accessibility of national funding programmes to foreign research groups. This would greatly help to **reduce inequalities between European countries** and streamline standards, indicators and methods for evaluating patient involvement across Europe.

9 Cf. appendix for a first point of reference.

10 Data pooling and data exchange must be in compliance with, for instance, the EU General Data Protection Regulation (GDPR).

11 Platforms should take account of language barriers, inequalities in education and health literacy, differences in research activity or differing degrees of knowledge and expertise when thinking about accessibility.

6. Legal and Ethical Aspects

6.1. For the conduction of projects involving patients or other stakeholders, it is important to **clearly specify, communicate and discuss underlying rules and legal issues** such as regulations regarding clinical trials with human subjects and data protection laws[12] that apply to a given project. For example, topics may include the general acceptability of regulations and procedures for all parties, confidentiality issues, pseudonymization, secondary use of clinical or routine data or commercial access to or use of genetic data.

6.2. Any **rights and obligations** included in contractual agreements **need to be specific, reasonable, proportionate and comprehensible** and should serve the interests of all parties involved. In general, project leaders should make sure that appropriate, jointly developed safeguards for all participants are installed. For instance, any liability risks for patients, their carers or their representatives need to be exposed and covered by insurance.

6.3. Especially **when generating rules, schemes and template texts for patient sample use, data sharing/ data protection or obtaining informed consent for projects, it is important to include patient voices** and to arrive at a mutually accepted agreement. It should be realized that while patients feel under-protected in many cases, the notion of "over-protection" and efforts to cater to patient needs that impair research efficiency can also exist among them. For all sides, it is crucial to realize that risk/benefit trade-offs are generally specific to the context of the respective research area and project. However, patient involvement with regard to the use of data and samples can also be fruitful beyond the scope of individual projects, i.e. with regard to developing new data protection policies for organizations or policy-makers. In general, established rules and mechanisms should be documented in management plans that are accessible to all organizations involved.

6.4. When it comes to **transnational projects**, it is of central importance to be aware of all applicable rules and regulations of individual partner countries as these may vary considerably (e.g. with regard to informed consent). There is also the often complex legal framework for sharing various kinds of data between countries and with non-EU countries in particular.

6.5. **Any relevant vested, financial or non-financial interests,** intellectual property rights, funding, sponsoring or affiliations of the parties involved **must be fully disclosed**. Appropriate mechanisms for disclosure and their control should be part of the governance structures of any academic or industrial research project. Moreover, it may be important for patients to manage conflicts of interests that may arise from receiving financial grants.

6.6. It is vital to **expose and discuss any ethical questions or dilemmas** touched upon by research projects or their respective foci at the very beginning of developing a research project. Ethical questions or dilemmas may arise from the involvement process itself. Examples include the legitimization of the individuals involved to represent their respective group, the "professional distance" of ill or suffering persons involved in the project, or questions regarding the involvement of vulnerable groups (e.g. cancer patients with low survival rates, children or incapacitated patients). Other ethical questions may arise from the study design. Examples include the exposition of participants to study-related risks, the anonymization of data versus the possibility to trace back information in case of rare or otherwise interesting findings, focusing on quality of life versus prolongation of life or reducing side effects versus greater medical benefits of treatments. Moreover, the necessity and process of obtaining the approval of ethics committees and the notion of confidentiality also have to be discussed with all those involved.

6.7. Finally, **participating in discussions about ethical and legal aspects of projects and their research foci requires training for all project partners**. Informed and unanimous decisions can only be made if all sides have sufficient expertise.

12 This includes the EU General Data Protection Regulation (GDPR).

7. Conclusion

7.1. Acting on the principles gathered in this paper may foster environments that are more conducive to active patient involvement in research on cancer and other areas of disease and may therefore produce more meaningful and relevant research. In order to unlock the full potential of patient or public involvement, it is fundamental that not only researchers, patients and the public, but also members of scientific and health systems, policy-makers and funding bodies join the effort. Only if all levels work together can they dedicate the necessary resources, time and effort.

7.2. The number of people and organizations that have understood the value of involvement in health-related research has grown continuously over the past years. Many scientific publishers have realized the benefits of involving patients and the public in research and have adapted their standards to include requirements for involvement. This can be viewed as a first step in changing scientific culture, scientific reward systems and mechanisms for career advancement towards increasing the focus on the actual needs and views of the users and recipients of research results.

7.3. In order to perpetuate the impetus generated by the initiative of the Trio Presidency of Germany, Portugal and Slovenia, it is now crucial for patients, researchers, science organizations, healthcare organizations, industry and decision-makers across Europe to act together. European, national and regional stakeholders of all levels and backgrounds are called upon to take up this initiative and take advantage of their own channels and means to actively support the translation of the accumulated knowledge into concrete steps.

Appendix

Links and Resources Mentioned in the Process (Alphabetical Order)

Arnstein, Sherry *"A ladder of citizen participation"*. Journal of the American Institute of Planners. 35 (4): 216–224 (1969). https://www.tandfonline.com/doi/abs/10.1080/01944366908977225; hdl: 11250/2444598

COCHRANE https://training.cochrane.org/international-ppi-network-learning-live-webinar-series

Count Me In https://joincountmein.org/

EATRIS Plus-Flagship in Personalised Medicine https://eatris.eu/projects/eatris-plus/

European Joint Programme (EJP) Rare Diseases https://www.ejprarediseases.org/wp-content/uploads/2021/03/SHORT-GUIDE-ON-PATIENT-PARTNERSHIPS-IN-RARE-DISEASE-RESEARCH-PROJECTS.pdf

European Patients' Academy on Therapeutic Innovation (EUPATI) https://eupati.eu/training/

European Reference Network (ERN) Genetic Tumour Risk (GENTURIS) https://www.genturis.eu/l=deu/Home.html

IMI Patients Active in Research and Dialogues for an Improved Generation of Medicines (PARADIGM) http://imi-paradigm.eu/petoolbox/monitoring-evaluation/

Irish Platform for Patient Organisations, Science and Industry (IPPOSI) https://www.ipposi.ie/

ISPOR — The Professional Society for Health Economics and Outcomes Research https://www.ispor.org/

James Lind-Alliance https://www.jla.nihr.ac.uk/

Krebsinformationsdienst of German Cancer Research Center https://www.krebsinformationsdienst.de/

Manual Thinking-Tools and spaces for co-creation https://manualthinking.com/

Open Responsible research and Innovation to further Outstanding kNowledge (ORION) https://www.orion-openscience.eu/index.php/publications/inspiring-stories/202011/introducing-co-creation-fundamental-life-sciences

Patient Engagement Synapse https://synapse.pfmd.org/

Patient Focused Medicine https://patientfocusedmedicine.org/

Patient Focused Medicines Development (PFMD) https://learning.pfmd.org/

Patient Innovation www.patient-innovation.com

RARE CANCER AGENDA 2030 https://www.rarecancerseurope.org/content/download/294217/5832976/1

Social_Construction_of_Technology (SCOT) Approach https://de.wikipedia.org/wiki/Social_Construction_of_Technology

UK National Institutes of Health Research (NIHR): Supporting patient and public involvement in research https://www.nihr.ac.uk/documents/briefing-notes-for-researchers-public-involvement-in-nhs-health-and-social-care-research/27371; https://www.nihr.ac.uk/patients-carers-and-the-public/i-want-to-help-with-research/

UPIM-Check – User-friendly Patient Information Material Checklist. An instrument to assess and optimise the quality of patient information material (PIM). http://archiv.imvr.de/en/key-figures/tools/eupim-check

Uveal Melanoma (UM) CURE https://www.umcure2020.org/en/