multi-act

Deliverable D1.4

Consolidated mapping of existing patient engagement initiatives and analysis of gaps and barriers to patient engagement in current health R&I processes

PROJECT DESCRIPTION:	A Collective Research Impact Framework and multi-variate models to foster the true engagement of actors and stakeholders in Health Research and Innovation
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Short description of the Deliverable (as in the amended DoA):
The preliminary landscape analysis is validated through interviews of key stakeholders and an in-depth literature review which integrate D1.3 findings and help building a consolidated map and prioritization of gaps and barriers to be tackled.

REVISION HISTORY			
REVISION	**DATE**	**COMMENTS**	**AUTHOR (NAME AND ORGANISATION)**
V0.1	21/03/2019	First draft	FISM: Deborah Bertorello
V0.2	16/04/2019	Second draft	FISM: Deborah Bertorello, Giampaolo Brichetto, Gabriele Dati, Elisa Ferrara, Paola Zaratin; ARSEP: Emmanuelle Plassart; DIA: Natalia Matuszak, Marcin Kautsch; EY: Federica Bertolani, Corrado Paternò Castello.
V0.3	19/04/2019	Integration of preliminary comments by WP1 partners, Patient Engagement Group (PEG)	FISM: Deborah Bertorello, Valentina Tageo, Paola Zaratin; ARSEP: Emmanuelle Plassart; EY: Federica Bertolani, Corrado Paternò Castello; EBC: Giovanni Esposito, Patient Engagement Group: Timothy Coetzee - National MS Society, MSIF Research Staff Network, Federica Balzani - European MS Platform, Paola Kruger - EUPATI, Paola Mosconi - Mario Negri Institute, Danish Board of Technology Foundation, Engage2020 L. Kluver.

V0.4	30/04/2019	Integration of comments by Patient Forum (PF), External Advisory Board (EAB), reviewers	External Advisory Board; Patient Forum; Reviewers: Eija Vinnari (TUNI), Mateusz Lichoń (DiA).
V0.5	31/05/2019	Consolidation and revision	Deborah Bertorello, Luca Carra, Sergio Cima, Paola Zaratin (FISM)
V0.6	04/06/2019	Final editing	Valentina Tageo (FISM)
V0.7	21/11/2019	New version resubmitted including modifications in the Appendix 4 which address the request in the letter received from the EC on the 4th of November 2019 (Ref. Ares(2019)6817984).	Deborah Bertorello, Paola Zaratin, Valentina Tageo (FISM)

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STATEMENT OF ORIGINALITY:

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1. EXECUTIVE SUMMARY

One of the objectives of the project is to provide guidance for all R&I stakeholders about who and how to engage patients in Research & Innovation (R&I)[1], when and what information is required, to enable 'science with/of patients input' within the MULTI-ACT Collective Research Impact Framework (CRIF). What began as an extension of patient advocacy has evolved into an emerging scientific discipline to be developed *with* patients as key stakeholder and by using patients' data into the decision-making processes of evaluating the impact of R&I (science *of* patient input). The first actions undertaken in WP1 have been the set-up of a dedicated group of experts in Patient Engagement Group with whom identifying R&I processes where patient engagement can be instrumental to reach impact and defining a methodology for the collection and mapping of existing PE procedures in R&I. This document intends to present the background, scope, objectives and actions that have been put in place to perform a landscape analysis of existing patient engagement (PE) experiences in each step of the R&I path with the aim to identify areas of unmet needs and come up with a prioritization of intervention. The landscape analysis focused on Multiple Sclerosis (MS) and brain disorders and has been developed with different methodological steps: Literature review, Web research, Interviews, Surveys and Connection with other relevant RRI initiatives. The collection of existing patient engagement procedures, experiences and best practices in R&I will be instrumental to develop the MULTI-ACT patient engagement guidelines.

The literature review found that the majority of studies focus on discussing guidelines and recommendations engaging patients in healthcare and/or clinical research process rather than engaging patients in the governance of wider R&I programs. However, much of the data on the actual involvement of patients in health care research analysed by the review will be used as a basis for developing innovative solutions to engage patients also in the governance of R&I. Future research should aim to conduct well designed studies to assess the impact of patient engagement and to develop new tools for PE in brain research and innovation.

The web-search on mapping portals and European repositories found that they mainly focus on clinical trials and drug development, in which patients are not engaged from the very beginning of the research but consulted for feedbacks. The research projects in the health sector appear to have a rather limited repertoire of methods used for engaging patients. The methods are not discussed in terms of their (potential) impact. In conclusion, it was not possible to determine return on engagement of the methods based on the literature.

However, interviews with the Patient Forum show that patient engagement is an increasingly emerging practice and needs for standardization of procedures and metrics to determine its effectiveness. In order to break boundaries between R&I and patients it is important to interact with policy makers, journals editors and media for transparency, privacy and security rules and conditions. The general goal of patient engagement requires also a cultural change in Research Funding and Performing Organisations.

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[1] WP1 "Enabling the science with/of patient input"

The landscape analysis also examined the most relevant networks of MS societies (MSIF and EMPS), to assess the level of patient involvement in the R&I process, which varies considerably between organisations, requiring standardisation and harmonisation across countries.

Finally, the consortium is starting to connect with other relevant Responsible Research and Innovation (RRI) projects in order to co-design the MULTI-ACT guidelines for patient engagement, which is one of the outcomes of the project and will be integrated into the Collective Research Impact Framework.

The present version has been modified following the first periodic review and the subsequent reception of the letter from the EC Ref. Ares(2019)6817984 asking for "providing further information on the 'Interview of Patient Forum', specifically description of the group interview set up and process". To this aim, the Appendix 4 describing the group interview has been modified and improved.

2. ABBREVIATIONS

Acronyms	
CRIF	Collective Research Impact Framework
EAB	External Advisory Board
EC	European Commission
EU	European Union
GA	Grant Agreement
MS	Multiple Sclerosis
NDD	Neurodegenerative diseases
PE	Patient Engagement
PEG	Patient Engagement Group (see D1.2 for PEG rationale and composition)
PF	Patient Forum
PaMS	People affected by MS (family, caregivers)
PwMS	People with Multiple Sclerosis
PwaMS	People With & Affected by MS
MS Society	National organization advocating for MS (e.g. Italian MS Society Foundation FISM)
PROs	Patient Reported Outcomes
PROMs	Patient Reported Outcome Measures
R&I	Research and Innovation
RRI	Responsible Research & Innovation
ROI	Return on Investment
ROE	Return on Engagement (in WP1 it refers to the value of Patient Engagement[2])
RFOs	Research Funding Organisations (organisations that fund research)
RPOs	Research Performing Organisations (organisations that perform research)
RFPOs	Research Funding & Performing Organisations
WP	Work Package

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[2] https://imi-paradigm.eu/determining-the-value-of-patient-engagement/

Entities Acronyms	
EARLS	European Alliance Restless Legs Syndrome
ECF	European Charcot Foundation
ECHAlliance	European Connected Health Alliance
EFNA	European Federation of Neurological Associations
EMSP	European Multiple Sclerosis Platform
EPF	European Patient Forum
ERANET-NEURON	European Research Area Network of European Funding for Neuroscience Research
EUROATAXIA	Federation of European ataxia patient groups
EURORDIS	Rare Diseases Europe
GAMIAN	Global Alliance of Mental Illness Advocacy Networks
IAPO	International Alliance of Patients' Organisations
MSIF	Multiple Sclerosis International Federation
MSIF RSN	Multiple Sclerosis International Federation Research Staff Network
PCORI	Patient-Centered Outcomes Research Institute
PFMD	Patient Focused Medicines Development
PMSA	International Progressive Multiple Sclerosis Alliance
Initiatives/Projects	
Engage2020	Engaging society in Horizon 2020[3]
SYNaPsE	Synergizing Patient Engagement Initiatives[4]
iPRO	ECF-MSIF international Patient Reported Outcomes initiative
Work Packages	
WP1	Enabling the science with/of patient inputs - FISM
WP2	Development of the information sharing application (MULTI-ACT Toolbox 2.0) - INTRA
WP3	Integrated Accountability Model (IAM) model development & assessment to the case of research initiatives - UNITN
WP4	Implementation of the Multi-ACT model – EBC (amended title)
WP5	Health collaborative initiatives structures and policies - EY
WP6	Collective Research Politics: governance and guidelines - DiA
WP7	Transferability and test of the methodology beyond MS - EBC
WP8	Dissemination and exploitation - EBC
WP9	Project Coordination, Management and Quality Assurance - FISM
WP1 Deliverables	
D1.1	Scoping methodology of existing procedures and initiatives for patient engagement across R&I (M6, FISM)
D1.2	Patient engagement focus group (PEG) establishment (M3, FISM)

D1.3	Preliminary landscape analysis of patient engagement initiatives and gaps identification (M9, FISM)
D1.4	Consolidated mapping of existing patient engagement initiatives and analysis of gaps and barriers to patient engagement in current health R&I processes (M12, FISM)
D1.5	Preliminary version of the MULTI-ACT Patient Engagement in Health R&I guidelines (M14, FISM)
D1.6	Final version of the MULTI-ACT Patient Engagement in Health R&I guidelines (M20, FISM)
D1.7	White paper for innovative routes for patient engagement (M27, EBC)
D1.8	Report on the integration of Patient reported outcomes and perspective into the CRIF (M20, FISM-UNITN)
Partners Acronyms	
FISM	Fondazione Italiana Sclerosi Multipla FISM Onlus
UNITN	Università Degli Studi Di Trento
EY	Ernst & Young Financial Business Advisors
UBU	Universidad De Burgos
TAU	Tampereen Yliopisto
EBC	European Brain Council
INTRA	Intrasoft International
EHMA	European Health Management Association
ARSEP	Fondation Pour L'aide A La Recherche Sur La Sclérose En Plaques
DiA	Dane-I-Analizy.Pl Sp Zoo
UCP	Universidade Catolica Portuguesa

3. INTRODUCTION

Responsible Research Innovation (RRI) is changing our concept of science. It states that excellence, validity and relevance also depend on the involvement of people and society in research as key decision makers. Early in 2014 the European Commission appointed an expert group to monitor the evolution and benefits of Responsible Research and Innovation (MoRRI[5,6]) in the dimensions of governance, ethics, public engagement, open access and science literacy and scientific education, to identify and/or propose indicators and gaps. The MoRRI project had the aim of establishing a monitoring system that measures how, where, and to what extent RRI has become integrated within European Research practices[7]. The monitoring of the evolution and benefits of RRI has highlighted among others an unmet need in the area of public engagement.

In line with RRI approach, there is an increasing need for patient engagement (PE) in the healthcare sector to make the R&I process more effective and responsive to patients' expectations and needs. The aim of this document is to carry out a landscape analysis of the literature and other resources concerning PE in health research and innovation.

3.1 The science with/of patient input

For the most of history, patients have been considered as the passive recipients of medical care with little or no role in health research. Even as research subjects, patients were not required to give informed consent prior to adoption of the Nuremburg Code in 1947. In 1984 the HIV/AIDS movement in United States catapulted patient needs to the forefront of research and created the force for change that dramatically altered regulatory approval processes at the U.S. Food and Drug Administration (FDA), funding formulas and emphasis at the U.S. National Institutes of Health (NIH), and the path forward for disease advocacy organisations.

What began as an extension of patient's advocacy needs now to overcome this "system" inertia and evolve into a scientific discipline aimed at understanding and incorporating patient needs and perspectives into the processes of governing and sustaining health research, developing, regulating, and delivering new therapies as well as improving care: the science of patient input. Many efforts have been launched to advance the science of patient input. Significantly, FasterCures[8] tracked more than 70 initiatives that are defining and shaping this developing field[9].

However, research agenda for science of patient input still deserves attention and resources being considered the most relevant priority in enabling the patients' community[10] to participate in research

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[5] https://morri.netlify.com/

[6] https://ec.europa.eu/programmes/horizon2020/en/news/monitoring-evolution-and-benefits-responsible-research-and-innovation-morri

[7] https://publications.europa.eu/en/publication-detail/-/publication/fdd7dd10-c071-11e8-9893-01aa75ed71a1/language-en/format-PDF/source-87584048

[8] https://www.fastercures.org/programs/patients-count/science-of-patient-input-resources/

[9] Anderson M, McCleary KK, On the path to a science of patient input. Sci. Transl. Med. 8, 336ps11 (2016).

[10] "Patients community" in MULTI-ACT include: **Patients**, (a) people with the disease (PwMS); (b) people affected by the disease: family members, caregivers (PaMS). **Patients Organisations:** the organisations that are involved with the population of interest.

processes and decision making as a key stakeholder. Through a multistakeholder consensus-building approach, the actors involved in such processes establish a research agenda to prioritize gaps in the knowledge base about the science of and with patient input that could be best addressed through coordinated research activities, and commit to reassess and update it periodically. Thus, within MULTI-ACT project we refer to the following:

- **Science *with* patient input** occurs when patients meaningfully and actively collaborate in the governance, priority setting, and conducting of research, as well as in summarizing, distributing, sharing, and applying the results.
- **Science *of* patient input** occurs when data of people with a disease are used (active and passive contribution) to evaluate impact of R&I.

In the context of MULTI-ACT, the **Science *with* patient input** aims to **maximize** the impact of R&I toward a transformational mission[11] by engaging patients in R&I, while the **Science *of* patient input** aims to **evaluate** the impact of R&I toward outcomes that matter most to patients. The Science *with* patient input will be executed in the MULTI-ACT Governance model[12] by applying innovative patient engagement guidelines[13]. The Science *of* patient input will be instrumental to generate, evaluate and identify the impact of a certain mission. It contributes to assess the Patient Reported Dimension of research impact and is reflected by indicators included in the CRIF Master Scorecard, a tool that measures impact of health research programmes and projects along five comprehensive dimensions[14].

3.2 The seven steps of patient engagement in R&I path

In order to develop science with patient input we need to identify the sequence of activities in the R&I continuum where patients can and need to be engaged in order to maximize the impact of R&I. Patient

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[11] Mission as transformational or transformative means 'changing forms'. Transformational health research is a term that became increasingly common within the science and health policy community in the 2000s for research that shifts or breaks existing scientific paradigms.

[12] Developed in WP5 "Health collaborative initiatives structures and policies").

[13] Developed in D1.5, D1.6.

[14] The Master Scorecard is one of the two core pillars of the Collective Research Impact Framework developed by MULTI-ACT, along with the governance model. It provides a selection of (qualitative and quantitative) indicators of research impact enable the translation of MULTI-ACT mission and agenda into action, integrating a set of top indicators on efficacy, efficiency, excellence, social impact and patient reported impact, co-selected within a multi-stakeholder perspective.. Each multi-stakeholder research initiatives will develop its own multidimensional scorecard depending on the relevance and measurability of the specific metrics in relation to its mission and agenda. In particular, the Patient Reported Outcomes (PROs), representing emerging patient reported dimension indicators, will be included in the CRIF Master Scorecard. Italian MS Society Foundation in 2013 promoted and funded the initiative: "A new functional PROfile to MOnitor the PROgression of disability in Multiple Sclerosis" (PROMOPRO-MS). PROMOPRO-MS has developed PROMs related to domain of symptoms, abilities and quality of life that most matter to MS patients (manual ability, bladder functions, mobility, cognitive, psycho-social fatigue, anxiety and depression, quality of life) that will be included in the CRIF master scorecard and further consolidated in T1.5 "Integration of Patient Reported outcomes and perspective into the CRIF".

engagement group (PEG), together with Patient Forum (PF)[15], and External Advisory Board (EAB)[16], has identified 7 steps in the R&I path in which patients can contribute in different forms[17].

Figure 1. Patient Engagement R&I Path: Programs vs Projects
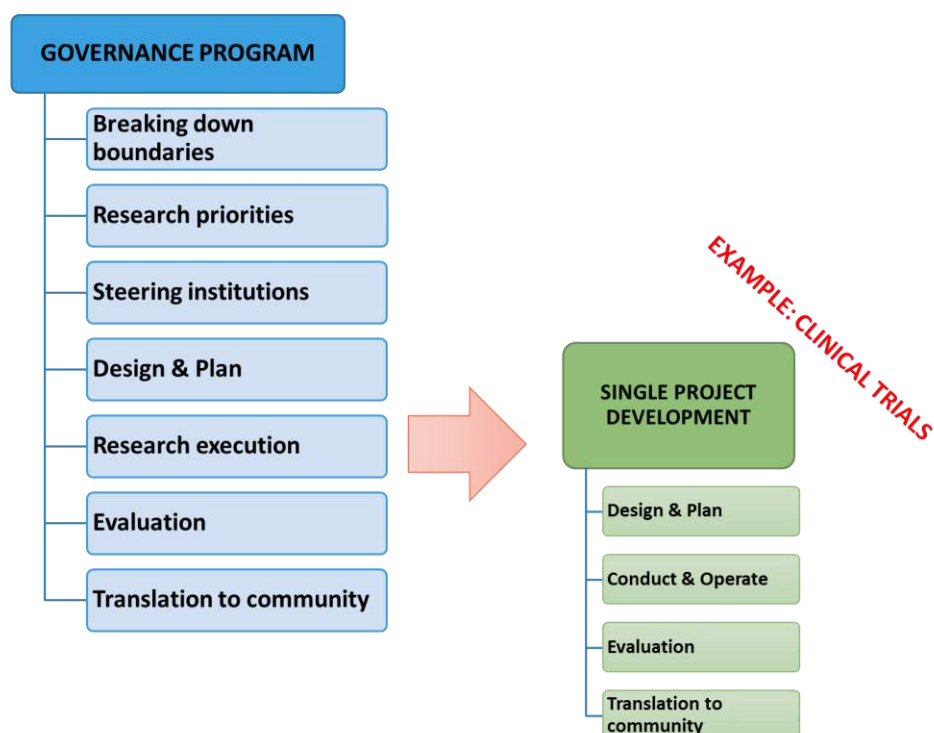
The steps identified so far in the R&I path are:

1. BREAKING DOWN BOUNDARIES: this area includes the conditions that should be set in Research Funding and Performing Organisations (RFPOs) in order to facilitate patient engagement as standard practice. Boundary refers to a physical or conceptual divide between Patient Engagement and organisations[18].

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[15] Patients Forum (PF) includes representatives from the European MS Platform, the International MS Federation, the European Patient Forum EPF, the European Patient Academy EUPATI, the FasterCures, the European Federation of Neurological Associations EFNA, the Accelerated Cure Project for MS and its iConquerMS initiatives, the European Alliance Restless legs syndrome, the EuroAtaxia, the Global Alliance of Mental Health Illness Advocacy Networks GAMIAN.

[16] External Advisory Board (EAB) includes representatives from the International Economic Policy and Sustainability Management, Polytechnic University of Milan, the European Federation of Pharmaceutical Industries and Associations EFPIA, The Italian Ministry of Health, The Neurology Sapienza University, the European Charcot Foundation, the European Connected Health Alliance ECHAlliance, the European Research Area Network ERANET NEURON and Rare Disease Europe EURORDIS and the Chair of the MULTI-ACT Patient Forum (the European Patient Forum EPF).

[17] It is possible that after the analysis we realize that patient engagement is specifically important to maximize the impact of R&I only in some of the identified steps or in certain steps more than others.

[18] Understanding boundary conditions would help in breaking down barriers between the RFPOs and the patient community. MULTI-ACT aims to facilitate a more open and collaborative research eco-system and infrastructure by creating a more horizontal management structure that encourages patient engagement and empowers the patient community. Breaking down boundaries means also mitigating the risk of tokenism and underrepresentation in patient engagement towards more genuine engagement (Hahn et al., 2017). Moreover, breaking down boundaries includes the assessment of the value of patients input in R&I (e.g., evaluate PE models and share lessons learned).

2. RESEARCH PRIORITIES: all actions necessary to prioritize the Research Agenda and formulate its objectives. Involving patients in setting priorities implicitly implies the direct allocation of funding. Patients may be engaged to co-design research agendas, exercises of prioritization[19].

3. STEERING INSTITUTIONS: all actions performed to establish steering and advisory committees and boards. An advisory committee and board is usually made up of high level stakeholders and/or experts who provide guidance on key issues such as company policy and objectives, rules and role, budgetary control, marketing strategy, resource allocation, and decisions involving large expenditures[20]. Patients may be invited to be member of research & governance committees and boards (Pushparajah et al., 2018)[21].

4. DESIGN & PLAN: the design of all the activities that lead to the realization of a concept or idea and which helps to achieve the objectives set, i.e. the formulation and assignment of tasks, rules, roles and execution times in order to achieve the objectives set. Patients may be invited to co-design specific programs (e.g. design of project objectives, endpoints, work plan and related budget).

5. RESEARCH EXECUTION: all activities to implement a research program or a specific project in order to achieve the objectives set. Patients may be engaged in the development and monitoring of specific programs (e.g. release of call for proposals, selection of projects to be funded; monitoring of funded projects) or projects (e.g. Information and Communication Technology ICT device development).

6. EVALUATION: all activities to determine the value of a research program or project, establishing their outputs and results, the degree of achievement of its objectives (process evaluation) and its impact. Patients may be involved in the evaluation of the results of research programs (e.g. publications, Impact Factors, application of new parameters) or projects (e.g. evaluation of an ICT device by the user).

7. TRANSLATION TO COMMUNITY: activities to promote and facilitate the adoption of the results of research programs or projects, including all aspects of engagement in communication of results and advocacy. At project level, translation to the community includes information for regulatory authorities (e.g. medical development, ICT tools, HTA, etc.).
Patients may be engaged in promoting change in society resulting from the results of research programs (e.g. development of guidelines and advocacy activities, implementation of specific care models) or projects (e.g. communication activities and advocacy to exploit the ICT device).

The sustainability of the program and alignment of incentives, including the definition of the budget/funding needed to allow patient engagement is another barrier to break: on one side it is essential to ensure effective funding to facilitate PE (e.g. application of specific methods) and on another side, to further investigated the aspects related to remuneration of patients.

[19] E.g. James Lind Alliance. Moreover, several MS Societies have co-create the research agendas priorities together with patients (e.g. Italian MS AGENDA 2020; Bill of rights - https://www.aism.it/intro_aism_fism_eng; https://agenda.aism.it/2018/).

[20] http://www.businessdictionary.com/definition/steering-committee.html

[21] Pushparajah DS. Making Patient Engagement a Reality. Patient. 2018 Feb;11(1):1-8. doi: 10.1007/s40271-017-0264-6.

Figure 2. Concept for the Patient Engagement Health R&I Path.

3.4 The levels of engagement

In addition to the seven steps of patient engagement in R&I, this study aims to define the different possible levels of engagement. Patients can contribute to scientific research simply by getting informed, or with increasing degrees of participation. For this reason, we built on the degrees of commitment proposed by Patient Focus Medicine Development (PFMD)[22], and propose the levels present below.

Inform: patients are informed about research priorities, activities, outcomes and impact.

Consult: patients are asked to provide feedback to decision-makers on their analysis and/or decisions. Patients participate by being asked for advice and opinion, by expressing their views and having discussions. It does not usually include any participation in decision-making.

Involve: patients partnering and contribute in research design and development as co-researchers. Patients are engaged in research project activities with an active role by providing their perspective and data on a specific topic (e.g. gathering patients' perspective on the functional domains that matter most to them, co-creation of PROMs[23] for clinical trials development). However, the project is designed and initiated by the professionals and patients are not engaged in the co-design of the project.

Co-design: patients are engaged from the very beginning of the steps of the PE R&I Path (i.e. governance and agenda setting, execution, evaluation and exploitation of research) with a decision making role. They are engaged throughout the research continuum and their voice is equal to the other stakeholders.

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[22] PFMD - Collaborative Patient Engagement: Mapping the Global Landscape: http://www.thesynergist.org/wp-content/uploads/2016/07/Mapping-the-global-landscape-of-patient-engagement.pdf

[23] Today PROMs are designed by clinicians and administered to patients, the needed shift is that patients are engaged also in the definition of the PROMs that they matter most.

4. LANDSCAPE ANALYSIS SCOPE AND OBJECTIVES

The scope of the first work package of MULTI-ACT is to provide guidance for all R&I actors about who and how to engage, when and what information is required, to enable patient engagement. This deliverable[24] is the second release of a landscape analysis of patient engagement experiences across R&I in Europe and beyond. This mapping exercise serves the ultimate goal of disseminating innovative practices, methodologies, tools and strategies for patient engagement in R&I to all stakeholders in the health sector, including research funding and execution (RFPO) organisations and multi-stakeholder initiatives. The landscape analysis is the first key output of Work Package 1 (see figures 3).

Figure 3. WP1 Objectives and activities
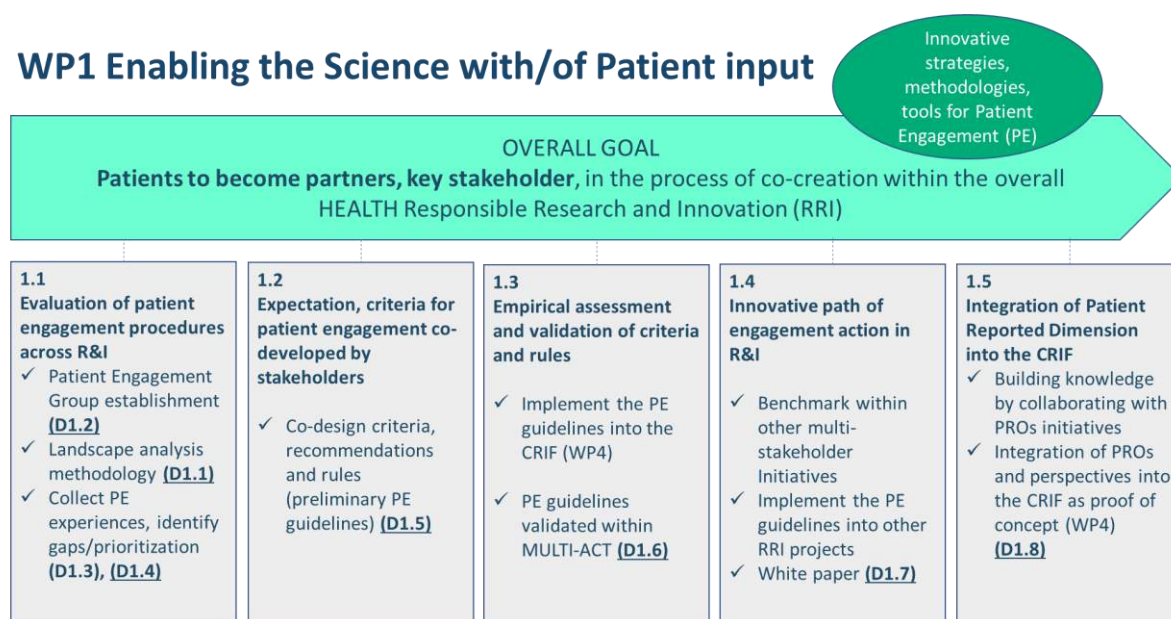
The landscape analysis relies on a consensual methodology[25]. The mapping exercise[26] aims to capture a **baseline assessment** to benchmark the evolution of patient engagement (PE):

- to provide an overview of the **current PE initiatives** in order to **identify gaps and prioritize interventions**;

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[24] D1.4 "Consolidated mapping of existing patient engagement initiatives and analysis of gaps and barriers to patient engagement in current health R&I processes" is the fourth deliverable of WP1 "Enabling the science with and of patient input", under the ''Task 1.1 Evaluation of patient engagement procedures across R&I".

[25] The methodology is detailed in D1.1 "Scoping methodology of existing procedures and initiatives for patient engagement across R&I".

[26] As defined in D1.1, the mapping exercise has been divided into two releases: a preliminary overview based on a desk research performed by the Consortium and focused on MS as case study (ST1 Literature review and ST2 Web research) in D1.3 and an established mapping actualized by engaging relevant stakeholders in the discussion to validate the research of the Consortium (ST3 Interviews, ST4 Survey, ST5 Connection) in D1.4.

- to **benchmark with the identified PE initiatives** considering the R&I steps or path identified by patient engagement group*;

- to **provide existing positive experiences** as material to develop innovative PE guidelines;

- to provide **useful documents** to be included in the MULTI-ACT digital toolkit as PE enabling material.

The landscape analysis included the following activities:

- **step 1: Literature review** focus on MS/BRAIN as MULTI-ACT case study and extended to brain disorders;
- **step 2: Web-search**
  - Scouting platform mapping PE experiences
  - Benchmarking with the public engagement domain
  - Other mapping portals;
- **step 3: Interviews** with Patient Forum (PF) members and their networks[27];
- **step 4: Surveys:**
  - of MSIF Research Staff Network to gather MS Societies PE experiences & practices and people with MS (PwMS) priorities for the Health R&I critical path
  - of EMSP to gather PE experiences & practices in the European Panorama (EU Organisations, Policy Makers, Regulatory Agencies)
  - of other MS actors (MS 21st Century);
- **step 5: Connection:** verifying synergies with relevant patient engagement initiatives[28].

In particular, **general questions** underlying the landscape analysis are:

1. Are MS/brain patients engaged in Health R&I?
2. In which steps of the Health R&I path have they been engaged so far?
3. How have they been engaged?
4. Within the identified PE experiences/methods, is there evidence of the "return on engagement" (RoE[29])? How can successful and unsuccessful measures be identified?
5. Have the PE experiences produced any output (e.g. guidelines, tools, etc.) useful for MULTI-ACT (e.g. inclusion in Digital Toolkit)?

Moreover, insights and broader consensus from other stakeholders on the impact of PE experiences and practices will be consolidated by engaging the External Advisory Board. Results of the Landscape analysis serve as material for the development of the PE guidelines[30] that are a preliminary guide to

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[27] 1st PF Virtual Meeting of Patient Forum (25th March 2019). See the Appendix 4.

[28] See Appendix 5.

[29] Return on engagement (RoE) is the benefit and impact resulting to performing patient engagement in R&I. Evaluating whether engagement adds value for different stakeholder groups can be an effective tool to further support patient engagement and requires the development metrics to measure the RoE. It is the "value of Patient Engagement": https://imi-paradigm.eu/determining-the-value-of-patient-engagement/

[30] To be released in D1.5.

engage the community of MS patients in R&I. The consolidated guidelines[31] will serve to engage **brain patients** in R&I when applying the CRIF[32] (Figure 4).

Figure 4. Steps of the landscape analysis (two releases: preliminary and consolidated).

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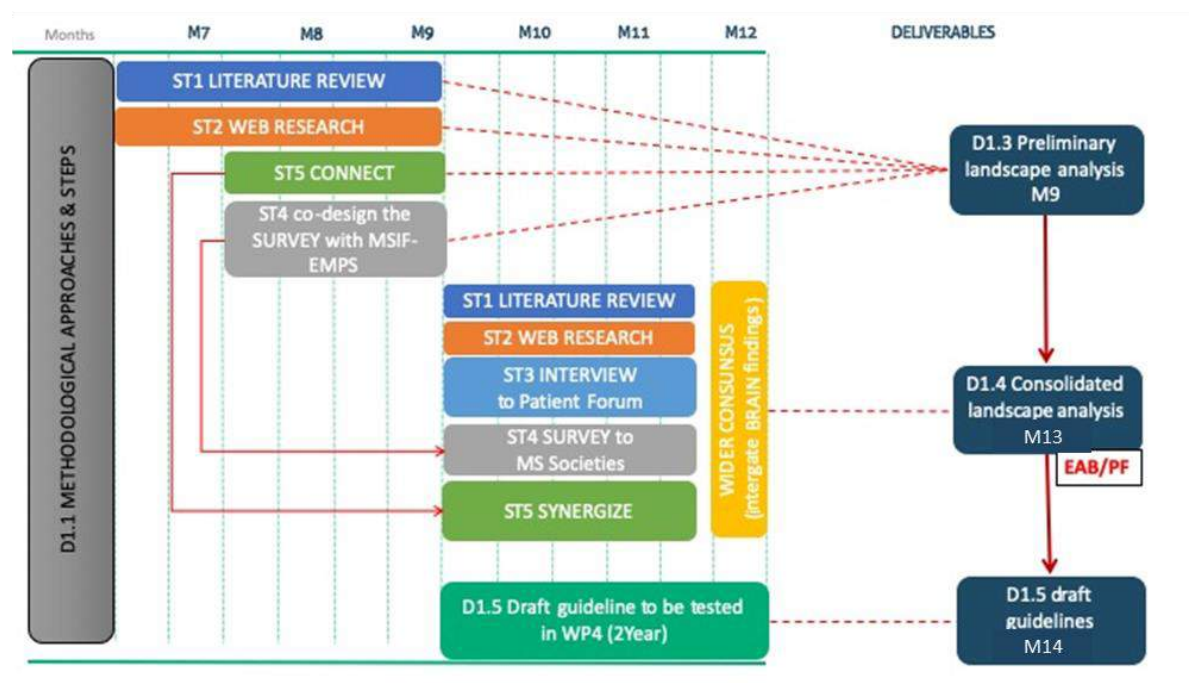
[31] To be released in D1.6. Figure 4 shows the amended timeline of WP1.

[32] To be validated in WP4 and endorsed by PF.

5. THE LITERATURE REVIEW

The literature review aims to identify current initiatives and methods **to engage patients in the R&I path** in order to maximize the impact of research and to provide material for the development of the MULTI-ACT guidelines[33] and White paper[34].

The literature review builds on the preliminary actions connected to the collection and analysis of relevant sources related to the topic as specified by the Consortium. While previous literature analysis has largely focussed on MS, the second and final release has analysed relevant publications related to brain domain, in particular, patient Engagement in brain R&I experiences and methods to be included and categorized into the database[35].

Following a method specified in the Appendix 1.1, the review has selected 49 research papers. The inclusion criteria were applied to studies published in English from 2016 to 2019 that concern patient engagement in R&I, with particular attention to studies that report patients with brain diseases. Since only 14 studies that focus on patients with brain diseases were found, we have also included studies that report patient engagement in other areas of health. The articles were analysed trying to answer the 5 questions posed by the consortium: 1) Are MS/brain patients engaged in Health R&I? 2) In which steps of the Health R&I path have they been engaged so far? 3) How have they been engaged? 4) Within the identified PE experiences/methods, is there evidence of the "return on engagement" (RoE)? How can successful and unsuccessful measures be identified? 5) Have the PE experiences produced any output (e.g. guidelines, tools, etc.) useful for MULTI-ACT (e.g. inclusion in Digital Toolkit)?

5.1 The science with/of patient input

This section illustrates the outcomes of the literature review conducted along the above mentioned five research questions and discusses its findings.

5.1.1 Are MS/brain patients engaged in Health R&I?

Not many studies deal with MS/brain patients engagement in R&I. Köpke et al (2019) showed the importance of including MS-patients in the formulation of guideline questions by using mixed-methods (international online survey in eight countries after pilot-testing debriefing on patient, and organising focus group meetings among MS patients and their caregivers). The involvement was resource- and time-intensive, but rewarding because it was the key for the formulation of the 10 guidelines questions and for the identification of patient-important outcomes.

Rae-grant et al. (2018) discussed in their practice guideline recommendations that patients should be involved more in the research and innovation for disease-modifying therapies for adults with multiple sclerosis (MS). The MS in the 21st Century Steering Group has been set up to foster patient engagement through a series of open-forum joint workshops (Rieckmann et al. 2018).

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[33] D1.5, D1.6.

[34] D1.7.

[35] The review has been performed in two releases: First release in D1.3 (January 2019) focused on Multiple Sclerosis. Second/final release in D1.4 (April 2019) extended to Brain disorders reviewed by EAB/PF. The first release has produced the n.14 papers indicated in D1.3. In D1.4. The analysis of the literature gathered in the first release has been used as a basis for the literature review conducted at the second release.

5.1.2 In which steps of the Health R&I path have they been engaged so far?

The majority of studies focus on discussing guidelines and recommendations engaging patients in Healthcare and/or clinical research process and projects rather than engaging patients in the governance of wider R&I programs. Out of 49 studies selected, around 60% focus on engaging patients in clinical & research projects (single project level), around 30% focus on engaging patients in healthcare, 10% discuss other aspects related to patient engagement[36].

The overall impression is that there is not much evidence on engaging patients in the governance of R&I programs with respect to the 7-steps R&I path. The main steps covered in the selected studies focused on 1. Breaking down boundaries (20% of the included studies), 2. Research priorities (5 %), 3. Steering institutions (5%), 4. Design and planning the research and innovation program (around 40%), 5. Research Execution (10%), 6. Evaluation (5%), 7. Translation to the community (10%).

With respect to the Level of Engagement, out of 49 studies: most studies consider patients to be involved and consulted in all different steps of the medicine development process (e.g. EUPATI). Insights from the initiative medicine life-cycle focus will be used as baseline to develop innovative solutions for engaging patient in the governance of the wider R&I. The governance criteria developed by MULTI-ACT will foresee a Patient Engagement Coordination Team dedicated to meet the above requirement[37]. A categorization of the literature revived with respect to the 7-steps R&I path is presented in figure n.5 and in Appendix 1.2.

Figure 5. Literature revived categorized with respect to the 7-steps R&I path.

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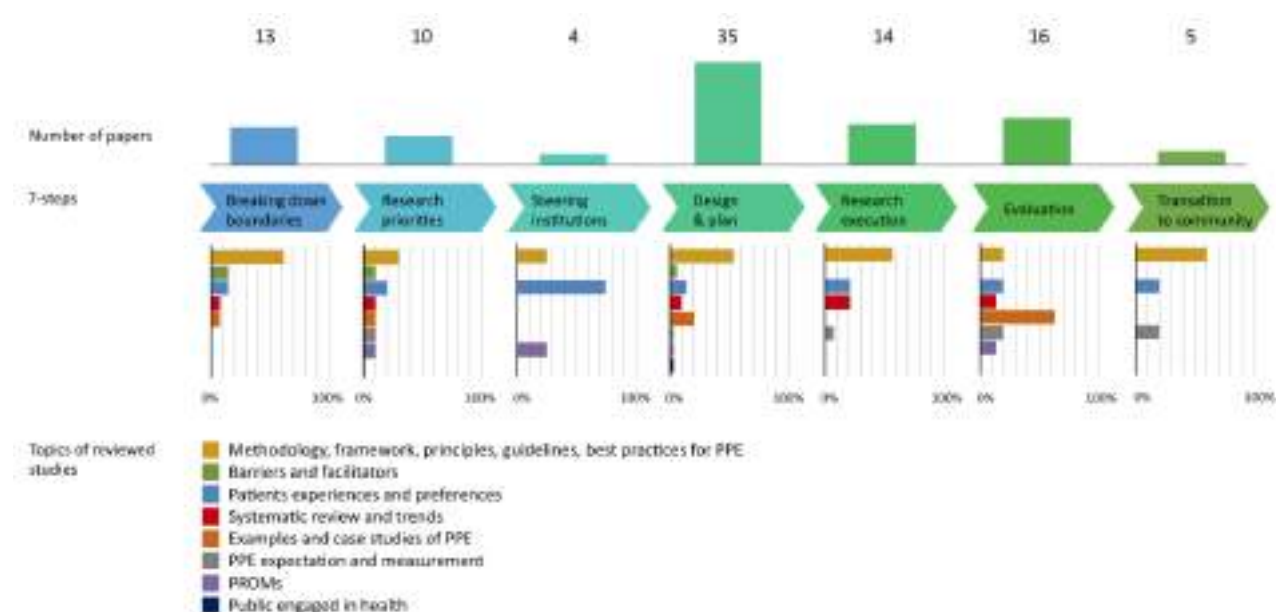
[36] The criteria for including the studies on patient engagement in the systematic review were studies published in English between January 2016 and March 2019. After reading the full articles, it was established if the main focus of the study was on engaging patient in clinical and research projects, in the medicine development process, in healthcare, or other aspects related to patient engagement.

[37] This aspect will be fully exploited in the guidelines develop in D1.5, D1.6

5.1.3 How have they been engaged?

Engaging patients, caregivers, and other health care stakeholders in every step of the research process has been discussed widely in the literature as unmet need to enable effective patient engagement. Engaging in research is believed to be an instrumental way to improve clinical decision making and outcomes (Sheridan et al., 2017). Many researchers, patients, and stakeholders, however, **lack clarity about when and how to engage** patients in the clinical research process. Most studies discussed their own experiences of patient engagement and suggest potential different framework for future research on how to involve patients in clinical research. The need for an harmonization of results obtained so far and toward consolidated guideline for patient engagement is emerged in line with the EU RRI requirements.

Rae-grant et al. (2018) discussed in their practice guideline recommendations that patients should be more involved in the research and innovation for disease-modifying therapies for adults with multiple sclerosis (MS). The MS in the 21st Century Steering Group has been set up to foster patient engagement through a series of open-forum joint workshops. In order to increase patient engagement in research and innovation, they conducted two workshops with a diverse pool of important stakeholders in MS care, including neurologists, an MS nurse, a health economic specialist, a patient group representative, a neuro-rehabilitation specialist and a neuropsychologist (Rieckmann et al., 2018). These workshops have shown that seven overall principles should support research and treatment of MS: personalized care, patient engagement, commitment to research, regulatory body education and reimbursement issues, new endpoints in clinical trials, more therapy options, and MS centres of excellence [38].

In addition, Köpke et al. (2019) showed the importance of including MS patients in the formulation of guideline questions using mixed-methods. The involvement was resource- and time- intensive, but very rewarding because it was the key for the formulation of 10 guidelines questions and for the identification of patient-relevant outcomes. Patient engagement in MS can be divided into some steps: 1) setting and facilitating engagement education and confidence-building; 2) increasing the importance placed on quality of life and patient concerns through patient-reported outcomes; 3) providing credible sources of accurate information; 4) encouraging treatment adherence through engagement; 5) empowering through the provision of sense of responsibility (Rieckmann et al., 2018).

Morby et al. (2019) consulted people living with dementia and care partners to design an accessible Delphi survey to facilitate participation in core outcomes set for development [39]. In addition, Murtagh et al. (2017) showed in their ECOUTER-methodology for stakeholder engagement in translational

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[38] These include: personalized care, patient engagement, commitment to research, regulatory body education and reimbursement issues, new endpoints in clinical trials, more therapy options, and MS centres of excellence.

[41] Strategies include the provision of adequate training to help them explore the capabilities of a patient portal in monitoring health; receiving support of caregivers at healthcare facilities to use their influence to interact and help older adults to navigate through a patient portal; and receiving caregivers´ and physicians´ support to develop frequent correspondence with older adults through the patient portal.

research that characteristics such as flexibility, adaptability and openness are important elements for successful stakeholder engagement[40].

Jennings et al. (2018) conducted a critical literature review on patient and public involvement (PPI) in research to develop a methodology for PPI researchers in collaboratively analysing qualitative mental health research data with academic researchers. After piloting and refining the methodology, a best practice framework for collaborative data analysis (CDA) of qualitative mental health research was created on the basis of the evidence gathered on successful involvement. The authors have shown that four collaborative data analysis approaches can be identified, namely: (1) consultation, (2) development, (3) application and (4) development and application of a coding framework. The collaborative data analysis is co-produced, realistic regarding time and resources, and demands of the process are manageable for patient and public involved researchers. In addition, group expectations and dynamics are effectively managed. This study shows the importance of developing a typology of approaches to collaboratively analysis of qualitative data in mental health research, identified from available evidence the characteristics of successful involvement (see Figure 6 Phases of collaborative data analysis (CDA).

Figure 6 Phases of collaborative data analysis (CDA) (Source Jennings et al., 2018).
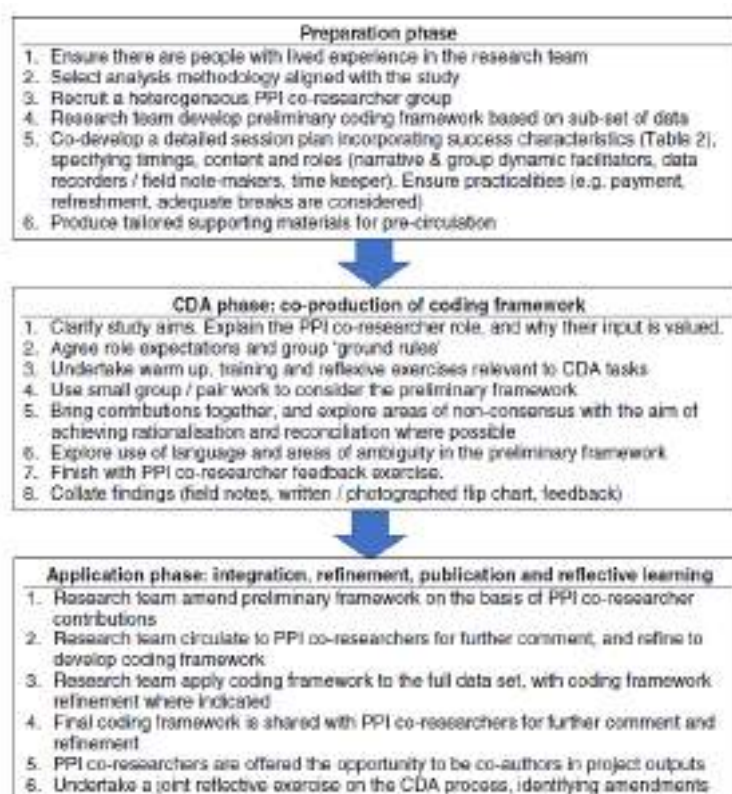
Adams et al. (2017) developed the "Steps Model", which is a practical tool for engaging communities to improve health-related outcomes and uses different steps to show that all parties must remain sensitive to one another's needs. Armstrong et al. (2017) propose a ten-step framework to increase patient engagement in guideline development in clinical practice. At the developer level, patients can assist in topic nomination (step 1), setting priorities (step 2), and selecting guideline development group (step 3). Within the specific guideline projects, patients' options may be better incorporated by framing the question (step 4), creating an analytic framework and research plan (step 5), conducting the systematic review and conclusion (step 6), developing recommendations (step 7), dissemination and implementation (step 8). At the end of the process, patients can re-involved at the developer level helping determine when guidelines need to be updated (step 9) and to assess the developer's approach to patient engagement (step 10). The "Steps Model" is in line with the 7-steps R&I path identified by the PEG.

Furthermore, Blackwell et al. (2017) have shown that experience-based co-design is a useful approach for encouraging collaborative working between vulnerable patients, family and staff in complex healthcare environments, as it is the case with patients with brain diseases.

Grant et al. (2018) analysed the practical considerations for using online methods to engage patients in the development for guidelines and found that online methods can facilitate greater openness and honesty by patients.

Ghisoni et al. (2017) held a one-day workshop named 'Getting involved in research: priority setting" to establish ideas and suggestions for research priorities from people who have experience of mental health services and found it was an efficient way to involve patients to a larger extent.

Nguyen, Palisano and Graham (2018) argue that it is important to engage youth and families in research in all the steps that need to be conducted. In addition, patients should be involved (1) in all aspects related to designing the proposals, including the development of meaningful questions, (2) in the co-production of the process to be used during and throughout the project, (3) as investigators and members of the leadership team, (4) in the analysis and interpretation of findings, (5) in the dissemination of findings and results through reports, articles, presentation, and potentially as co-authors. Nguyes et al. approach is in line with the 7-steps R&I path (project level).

When working with people with disabilities, it is important to provide clarity about roles, power and authority to ensure that all member's contributions are equally valued while expectations are managed adequately. In addition, an environment of co-learning, trust, respect, reciprocity and shared decision making should be created.

Baines and de Bere (2017) have assessed the active involvement of patients and the public through an extensive systematic review and identified nine principles covering areas such as health and social care services, research, education and regulation across medicine, dentistry and nursing. They found that (1) working in equal partnership and (2) sharing information achieved the highest consensus rate by experts that reviewed the literature. This was followed by (3) communication and information provision, (4) listening, assessing and responding, (5) supporting and preparation, (6) acknowledgement, reward and value for everyone involved (i.e. in line with the MULTI-ACT RoE). Lastly, it involves the (7) accommodation of individual and collective needs, (8) evaluation and (9) a tailored working-together approach as important principles that should be taken into account.

Rashid et al. (2016) discussed that improving the recruitment of guideline group chairs, widening evidence reviews to include patient preference studies, adapting guidance presentation to highlight patient preferences points and providing clearer instructions on how patient organisation can submit their intelligence in research and innovations are emerging proposals that may help overcome barriers experienced by patients to further enhance patient and public involvement in their processes. One example is the study protocol by Samalin et al. (2018) that examines the efficacy of shared decision-making on treatment adherence of patients with bipolar disorder. To engage the community in research, Sand et al. (2017) propose a "dyad" model, whereby a patient and a primary care provider collaborate to learn about and engage in primary care, primary care research, grant review, proposal development and advocacy. In addition, a series of educational trainings were held during the study in conjunction with national primary care conferences, international webinars and local symposia. Smith et al. (2017) found that developing patient education material using a participatory design methodology is most productive and in line with a person-centred care philosophy, with a strong focus on partnership and equality.

Colorafi (2015) showed that there are numerous initiatives underway to use health information technology to support patient engagement. However, Simblett et al. (2018) conducted a systematic review and showed that there are different barriers and enablers to engage patients with remote measurement technologies to manage their health. The review reveals that health status, perceived utility and value, motivation, convenience and accessibility, and usability are among the most commonly mentioned factors that encourage the usage of remote measurement technologies. The use of health information technologies and other factors such as health literacy can be a significant obstacle to effectively involving older adults, while young people consider themselves immune to poor health and are therefore less likely to use personal health data technologies (Akubuiro et al. 2018). Arauwou (2017) showed that modifying older adult's perceptions to use a patient portal for engagement in their healthcare is important[41].

Gabel et al. (2019) show that glioma patients should be involved in developing health related quality of life outcomes to improve the metrics for future use in larger clinical research and clinical trial settings. Robillard and Feng (2017) in turn claim that patient engagement and research ethics collide and that bridging the gap between researchers and patients calls for reforms of current standards in dementia research.

Burke et al. (2018) found that active medical conditions in the hospital that made decision-making difficult, prior experiences with hospital readmission, relative level of caregiver support, and pressure to make a decision quickly were important contextual themes in a qualitative study evaluating patient decision-making regarding post-acute care, suggesting that similar barriers may be found also with respect to decision making in R&I.

Paul and Holt (2017) showed that health participants valued the perspective of PPI in research to mental health and learning disabilities, but indications of frustration with tokenistic approaches to the

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[41] Strategies include the provision of adequate training to help them explore the capabilities of a patient portal in monitoring health; receiving support of caregivers at healthcare facilities to use their influence to interact and help older adults to navigate through a patient portal; and receiving caregivers´ and physicians´ support to develop frequent correspondence with older adults through the patient portal.

additional work to include the involvement of patient was also found. In addition, the authors identified cultural and attitudinal barriers to integrate PPI across the full research process.

Graffigna et al. (2017) show that the "therapy" for promoting effective patient engagement is first to fertilize a patient engagement ecosystem, as is shown in Figure 7. The patient engagement eco-system. It reveals that a holistic and complex approach is needed to solve underlying causes to engage patient and public in research and health care. In addition, patient engagement measurement should be a routine[42]. Also, clinicians and researchers must be engaged, actively share and discuss scientific literature, seminars, workshops, conferences. In that regard, continuing and distance education are fundamental tools with which to make patient engagement a shared goal of clinicians and researchers, rather than being a prescription to comply with. Lastly, in line with MULTI-ACT approach, partnering with the caregivers and family will be an important step towards ensuring the most effective patient engagement for increasing patients´ engagement in research.

Figure 7. The patient engagement eco-system. (Source: Graffigna et al., 2017).
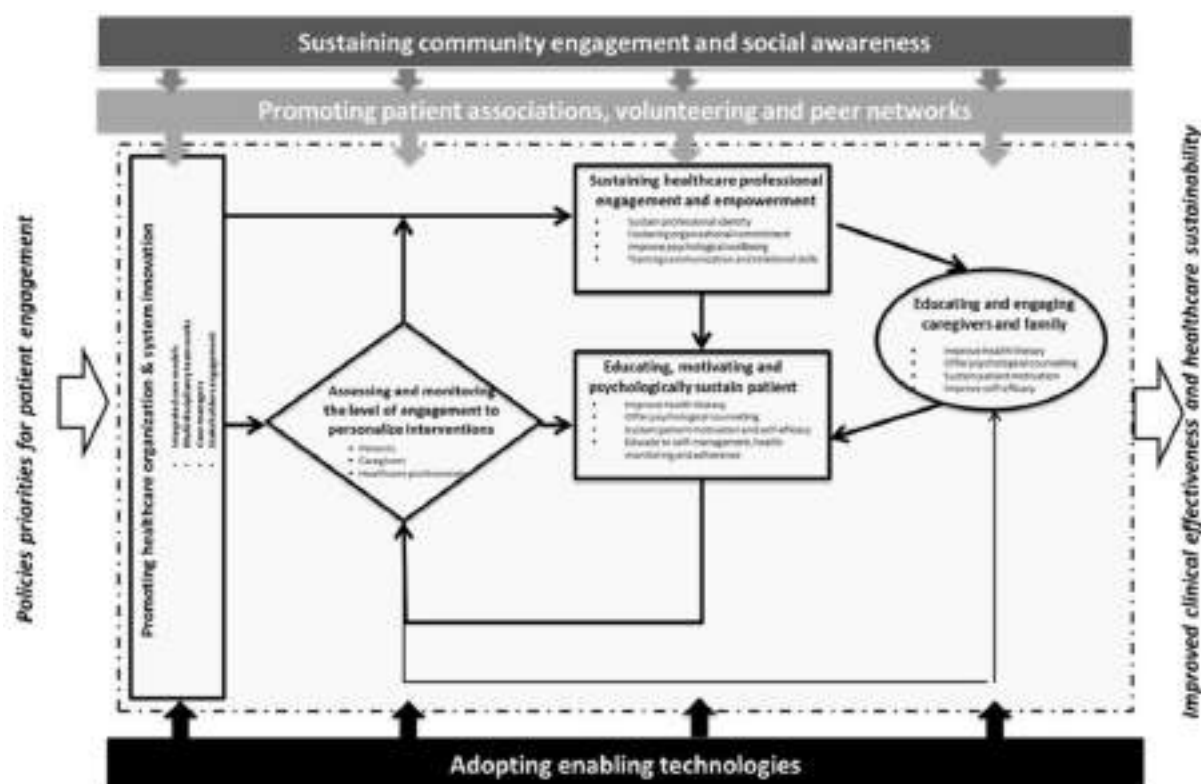
The literature reveals some important insights as concerns specific age groups. For example, Colorafi (2015) showed that older adults need to have a positive relationship with the provider, and the distribution of a meaningful summary at the end of the visit in order to have clear take-away messages. Menichetti et al. (2016) examined the design, development and optimization of a theoretically-driven intervention program (PHEinAction) to increase patient engagement in older chronic populations, and

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[42] Validated measures of patient engagement can fulfil several purposes, as they may constitute a powerful communication and advocacy tool to give a voice to patients and their families. Eventually, it is the only way to ensure personalization of intervention and the incorporation of patients and family caregivers' perspectives in the design of research and innovations.

showed that it is important to consider emotional, psychological, and behavioral processes. In addition, Persson, Hagquist and Michelson (2017) showed that involving children and adolescents in mental health treatment in outpatient and community mental health clinics in Sweden is evaluated as positive and negative. Young people's recommendations for improving practice in mental health care was categorized as improving the (1) accessibility, (2) being heard and seen, and (3) the usefulness of sessions.

Akubuiro (2018) advocates for policy directives that establishes technological requirements to motivate millennials to participate. Another example is the study by Heffernan et al. (2017) who show that a youth-adult partnership model in youth mental health systems research, the McCain Y-AP initiative, can be used to engage youth in decisions that affect them in a way that draws on their unique skills and expertise. Flexible engagement, multifaceted mentorship, reciprocal learning and authentic decision making have led to successful partnerships providing multiple opportunities for growth for all those involved.

Van der Weijden et al. (2018) conducted a 12-month development and consensus study to develop patient-directed knowledge tools related to clinical practice guidelines. They showed that an 8-step guidance was needed to reach consensus. The authors describe minimal criteria for (1) the team composition, (2) setting the scope, (3) identifying needs, (4) the content and format, (5) testing the draft, (6) finalizing and approval, (7) dissemination and application, and lastly, (8) ownership and revision. Archambault et al. (2018) recommends that in order to increase patient engagement in patient-oriented emergency medicine research they need to have an overarching positive recommendation[43].

As for translational research in biomedical research, Boenink et al. (2018) suggest that patients should be enabled to (1) put forward their experiential knowledge, (2) develop a rich view of what an envisioned innovation might look like and to (3) connect their experiential knowledge with the envisioned innovation. The authors have therefore developed a method called "Voice of patients", which is successful in mobilizing patients' experiential knowledge, stimulating their imaginaries of the innovation under the discussion and to some extent, also in connecting these two. It is argued, however, that since scientists and patients frequently presuppose that patients first need is to be educated before any meaningful communication about research is possible, patients become "pseudo-professionals", which goes against the major reason to involve patients in research: **to harvest and use their experiential knowledge. Meaningful patient involvement therefore requires that the difference between scientific and clinical expertise, patients' experiential knowledge is acknowledged and made productive, instead of erased** (Van de Bovenkamp et al. 2009). **Empowering the experiential knowledge of patients is the basis of the MULTI-ACT patient engagement strategy.**

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[43] In addition, the authors propose seven policy-level recommendations for the association of emergency physicians to support the creation of a national patient council with the aim to develop, adopt and adapt training material, guidelines, and tools for patient engagement, and to support increased patient engagement in emergency medicine research. Lastly, they provide nine pragmatic recommendations about engaging patients in the preparatory, execution, and translational phases of emergency medicine research.

5.1.4 Within the identified PE experiences/methods, is there evidence of the "return on engagement" (RoE)? How can successful and unsuccessful measures be identified?

The literature reviewed reported not many evidence on the impact or return on investment of patient engagement in R&I. As put forward by Jennings et al. (2018), **future research should develop a standardized measure of collaborative research impact and (cost-)effectiveness** and **conduct PPI in research to evaluate the impact**, in line with MULTI-ACT scope.

For patient with rheumatology, Hamilton et al. (2017) have developed a framework for advancing the reporting of patient engagement, based on 30 publications related to patient engagement in this line of research. Three main categories were developed: (1) **Who** (Who engages in the research), (2) **How** (How these patients/caregivers engage in research, and (3) **When** (When during a research project these patients/caregivers engage in research). These categories should be reported in order to have a better idea about the effectiveness and impact of patient engagement in research. MULTI-ACT innovative guidelines builds on these categories and adapt them to the 7 steps in research and innovation process.

In a systematic review conducted by Evans et al. (2018) on the extent, quality and impact of patient and public involvement in antimicrobial drug development research, they only found one relevant protocol paper between 1996 and 2016. Despite strong policy guidance encouraging PPI at international and national levels, and anecdotal accounts of patient engagement taking place, **evidence for the extent, quality and impact of PPI continues to be very scarce**. MULTI-ACT aims to provide guidelines and tools to fulfil this gap.

Most studies have described the importance of patient engagement and how this can be achieved, and what could be the outcomes, but **the impact or return on investment has only seldom been studied** (Jennings et al., 2018). For example, meaningful patient engagement in the development of medicines during the life cycle of a product requires active participation of all stakeholders and a clear understanding of respective expectations (Boudes et al., 2018). Despite its importance, the authors show that no stakeholder has a clear view on how to engage with patients in a meaningful way. The authors raise attention to the fact that there are educational gaps and advocate for a guidance for patient engagement. Effective collaboration requires consensus on roles, responsibilities and expectations to synergize efforts to ensure significant patient engagement in research and innovation and medicines life cycle.

As Pushparajah (2018) explains, while all stakeholders agree on the fact that patient perspectives should be taken into account in the research and innovation of therapies, interventions and medicines, the **lack of standardized best practices and metrics** has made challenging to achieve consistency and to measure success in patient engagement. UCB (Union Chimique Belge) has therefore developed an internal model for patient group engagement, incorporating four key principles that are essential elements for effective collaborations based on shared ambition, transparency, accountability, and respect.

None of the selected studies discuss clear impact or metrics, they rather suggest impact aspects for future research and provide subjective observations on the outcomes of PE. In the studies reviewed, the most mentioned aspect considered - when evaluating the impact and return on investment of patient engagement in research and innovation - is recognizing patients' contributions and empowering them in well-informed healthcare decisions and respecting the rights of citizens in healthcare policy. Furthermore, the goal that most of the guidelines, recommendations and

discussions include is the development of more patient-centred, trustworthy and effective guidelines that lead to improved implementation and quality of care.

For example, Kristensen et al. (2018) showed that patient-reported outcome measures were included in the treatment of patients diagnosed with depression and schizophrenia using an iterative co-creation process between patients and healthcare professionals. Zhang et al. (2017) followed the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to integrate patient values and preferences in healthcare decision-making of practice guideline development. The GRADE "Evidence-to-Decision framework" that was developed provides an empirical strategy to find and incorporate values and preferences in guidelines by performing systematic reviews and eliciting information from guidelines panel members and patient representatives. However, there is a need for more well-conducted research in order to be able to use evidence-based advice.

Adams et al. (2017) have shown in their Steps-methodology that there are metrics to assess impact of patient engagement in every step. In the first step (No engagement; 0-1 year), the metrics are initial contact/meetings, core partners identified, and community needs/goals identified. In the second step (Preliminary Engagement; 1-2 years), the metrics are partnership planned, and initial pilot work under way. In the third step (Initial Partnership; 2-4 years), the metrics are tangible products of collaboration (funding, data, training) realized, and community advisory board facilitating work. In the fourth step (Extended Partnership; >4 years), the metrics are extended academic services to students, increased capacity of community/employment in research, and increased connections to other investigators and potential projects. Finally, in step five (Full Partnership > 5 years), the metrics are broad recognition of academic-community partnership, broader impact on community health, publications, tenure, multiple shared grants, student training, and increased community funding.

Kreindler and Struthers (2016) developed a score-sheet for tangible effects of patient participation (STEPP) to assess the organizational impact of patient involvement. The items assess the magnitude of each recommendation or issue brought forward by patients, the extent of the organization's response, and the apparent degree of patient influence on this response. The composite scores appeared to credibly reflect the degree of organisational impact and were associated with salient features of the involvement initiatives. Furthermore, participants described the STEPP as easy to use and useful for monitoring and accountability purposes.

Ree et al. (2019) conducted a systematic review to assess to what extent patient involvement is measured in patient centeredness scales for health professionals and found that **there is a lack of patient centeredness scales focusing on direct and proactive involvement of patients in quality improvements**. They argue that it would be useful to develop such instruments to further study the role of patient involvement in quality improvements in healthcare. They could also be used as important tools in quality improvement interventions.

Devonport et al. (2018) showed that it is very important to assess the way you involve patients and public in the development of health research. According to their study results, practitioners and researchers should first of all ensure clarity as concerns the patients' and public involvement and resolve differences in aims and priorities through clear communication. Secondly, they should support relevant disclosure whilst managing risk and safety. At the same time, they should balance alongside the ethical principles of respecting patients' autonomy and confidentiality. Thirdly, from the earliest planning phase onwards they should pay attention to relational dynamics, particularly perceived

power and to the methods used to communicate as a means to minimize tacit mixed messages. Fourthly, they should create opportunities to share and establish difference as a valued component of the research process. Finally, practitioners and researchers should acknowledge constraints and limitations so these can be addressed in due time.

Patients can also be involved to develop recruitment strategies. In that regard, patients provide valuable insights when involved to optimize and target recruitment, for example to gain better insights into patient opinions for clinical trial information materials, to develop more user-friendly clinical trial websites, to define best time to recruit patients for patient-reported outcome measures, to develop clinical trial decision aids, and to develop the study brand to increase recruitment and retention (see also Jennings et al. (2018) for an overview). Subsequently, patient and public engagement in developing methods or entire study designs can increase the probability for relevant research, population-specific sensitivity, validity and ethics of the method and the research designs. Additionally, it can also serve to ensure relevant education and information that can help reduce health disparities, to develop guidelines how to conduct research and to identify patient-important outcomes (Köpke et al., 2019). None of the above studies actually assessed the impact patient engagement has had, conducted (cost-) effectiveness analyses, or tested whether it is a valuable return on investment.

5.1.5 Have the identified PE experiences produced any output (e.g. guidelines, tools, etc.) useful for MULTI-ACT (e.g. inclusion in Digital Toolkit)?

The systematic review identified a few examples of tools, such as guidelines, recommendations and digital devices, that were developed in collaboration with patients and that could be considered for further development in the framework of the MULTI-ACT project.

One of them is the **PCORI Engagement Rubric**, developed by the Patient-centred Outcomes Research Institute (PCORI). The Rubric provides a framework for operationalising the integration of patient engagement and other stakeholders in research steps that may be conducted to the 7-steps R&I path. Importantly, it includes principles of engagement, definitions of stakeholder types, key considerations for planning, conducting and disseminating engaged research, potential engagement activities, and examples of promising practices from PCORI-funded projects. For example, there was a study conducted for stroke survivors, whereby the participants identified the number of days living at home and not in an institution or the hospital as an important outcome to measure. Wilson et al. (2018) showed that it is very important to include patients in the selection and development of outcome assessments for medical product development, and therefore developed a framework for future studies.

Last but not least, the European Patients Academy on Therapeutic Innovation (EUPATI) has developed guidelines on patient involvement in research and development (Spindler et al., 2018). EUPATI has set up structures to develop and disseminate accessible, well-structured, comprehensive, scientifically reliable, and user-friendly educational material for patients on the process of medicines research and development. They argue that once armed with a deeper and better understanding of patients, patient experts, and patient advocates, it will be easier to work more effectively with the relevant authorities, healthcare professionals and industry. This in turn will positively affect medicine development processes, benefitting patients and society. The qualitative secondary analysis conducted by Hamilton et al. (2018) using in-depth interviews with patient research partners revealed that patients experience the collaboration and work with researchers generally as positive. Eight themes emerged to be

important for patients: (1) procedural requirements, (2) convenience, (3) contribution, (4) support, (5) team interaction, (6) research environment, (7) feel valued, and (8) benefits. Linking these themes together formed a conceptual framework, called PEIR, that can help explain the phenomenon of meaningful patient engagement research.

5.2 Literature review: discussion

The "why" and the "what" of patient engagement

The current advances in medicine, technology and healthcare services, with their promises of longevity and improved quality of life (see for example Espay et al., 2016; Hollis et al., 2015; Pii et al., 2019; Silva et al., 2015), acknowledge the importance of patient engagement. More specifically, advances in digital technology has the potential to transform healthcare by connecting patients, services and health data in new and efficient ways that could lead to more tailored and personalized health interventions. As a consequence, these interventions will be more (cost-) effective than traditional forms of health interventions (Hazo et al., 2019; Hollis et al., 2015). For example, digital and mobile applications can offer patients greater access to information and services and enhance clinical management and early intervention through access and usage of real-time patient data. MULTI-ACT aims to maximize and provide evidence of the value of patient engagement also for R&I. In addition, recent studies have shown that key characteristics of big data and how medical and health informatics, translational bioinformatics, sensor informatics, and imaging informatics can expand our knowledge to test for new hypotheses about brain diseases management, from diagnosis to prevention to personalized treatment (Andreu-Perez et al., 2015). However, substantial gaps still exist in the evidence base underlying the adoption and usage of these new technologies. More specifically, Zafra-Tanaka et al. (2019) recently showed that clinical practice guidelines should follow adequate methodologies using an evidence-bases approach to provide reliable and valid recommendations, but most evaluated clinical practice guidelines did not take into account the patient's viewpoints and did not clearly formulate the process used to reach the recommendations.

In order to make effective use of new health-related technological developments, it is essential to involve and engage all stakeholders continuously in developing and testing potential solutions and clinical guidelines and working in a multidisciplinary way with all stakeholders to ensure that people with brain diseases are included in shared decision-making and disease management (Armstrong et al., 2017; Ruco et al., 2016).

Moreover, patient engagement has been labelled as the 'blockbuster drug of the century' (Rieckmann et al., 2015), in particular for upcoming and rapidly developing methodologies like health information technology (Colorafi, 2015) and personal health records (Hawthorne et al., 2017). Rationales for patient engagement in developing clinical guidelines include recognizing patients with important contributions and empowering them in well-informed healthcare decisions and respecting the rights of citizens in healthcare policy. Current goals and recommendations for brain research are to follow more patient-centred, trustworthy and effective guidelines in future research that lead to improved implementation and quality of care (GIN Public Working Group, 2015). Abma et al. (2010) highlights the importance of patient engagement in the treatment of brain diseases in order to optimize health outcomes for patients, society, and healthcare systems.

Patient engagement can be described as actions that patients must conduct to obtain the greatest benefit from the healthcare services available to them (Holmes Rovner et al., 2010). Scholars worldwide agree on the urgency of engaging patients in their care in order to achieve a more sustainable management of the healthcare system (Fisher et al., 2016; O'hara et al., 2016), also in mental health research (Hazo et al., 2019; Ghisoni et al., 2017). To make it more targeted and effectively, Graffigna et al. (2017) have promoted and disseminated an Italian Consensus Conference on Patient Engagement (ICCPE), in order to set the basis for drafting recommendations for the provision of effective patient engagement interventions and research. Reliance on the patient's knowledge, skills and motivation to access the acquired benefits through the advances in medicine, technology and healthcare services are increasingly necessary in order to make use of the promises of longevity and improved quality of life and improve the outcomes of the health interventions. This contributes to a wide "system" inertia - one that is really difficult to be overcome and puts the research field at risk for any forms of innovation, although studies have come up with a framework for advancing the reporting of patient engagement in research projects (Hamilton et al., 2017). In general, the level of patient engagement is largely influenced by institutional ideologies, professional attitudes and the readiness of patients to accept new and engaging roles (Marlett et al., 2015).

In-depth analysis of literature findings

The systematic literature review has selected 49 studies (published in English between 2016 and 2019) on patient engagement in health research and development, 14 of which are dedicated to patients with MS or other brain diseases. The reviewers then provided preliminary answers the 5 research questions posed by the Consortium on the basis of the literature examined. Answering the research questions serve as basis to develop the MULTI-ACT Patient Engagement guidelines[44].

Regarding the first question (**"Are MS/brain patients engaged in Health R&I?"**)**,** not many studies show such involvement so far. However, the few conducted experiences have been resource- and time- intensive, but rewarding in the production of new models of care and treatment. It should also be noted that these **experiences of involvement mainly concern adherence to medical treatments, participation in clinical trials etc., but very rarely the governance of research and innovation according to the dictates of RRI**.

The answer to the second question ("**In which steps of the R&I path have they been engaged so far?**") obtained more results, showing that the main steps covered in the selected studies are**: 1. Breaking down boundaries (20% of the included studies), 2. Research priorities (5%), 3. Steering institutions (5%), 4. Design and planning the research and innovation program (around 40%), 5. Research Execution (10%), 6. Evaluation (5%), 7. Translation to the community (10%).**These data suggest a prevalence of studies on facilitation methods to overcome the barriers that have always divided the world of health professionals from the world of patients, their families and others involved in the disease. However, there is also a predominance of studies dedicated to participatory research design and planning at project level. This phenomenon appears to be growing and suggests that researchers also perceive the added value of collaborating with patients in this crucial area.

As regards to the third question ("**How have they been engaged?**"), as Domecq et al. (2014) have shown, there is a lack of research dedicated to identifying the best methods to achieve patient

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[44] D1.5 Preliminary version of the MULTI-ACT Patient Engagement in Health R&I guidelines; D1.6 Final version of the MULTI-ACT Patient Engagement in Health R&I guidelines

engagement, although it is highly needed. Most of the studies included in this systematic review focus on the **early stages of research (agenda setting and protocol development) and less commonly during its execution and translation to the community**.

Nevertheless, the knowledge available in the field of health care is expanding rapidly. Maintaining and exploiting this knowledge is a challenge, particularly when patient involvement is needed to improve the level of health interventions. Wilson et al. (2018) identify threefold needs: **firstly, there is a need for clear and evidence-based methods for guidance on how to engage patients and public at all stages of research and innovation initiatives. Secondly, there is a need for the development of minimum quality criteria for the development, content, and governance of patient engagement. Thirdly, clear methodologies to assess the impact and (cost-) effectiveness of patient engagement in research and innovation is needed.** Patients should be involved at all stages of R&I, but also in the development of research focus, the development of research design, recruitment, data generation, data processing, and research dissemination (Nguyen et al., 2018). In addition, **clear and constructive communication and professional management of all stakeholders is very important**. This includes communication of the principles of engagement, definitions of stakeholder types, key points for planning, conducting and disseminating research, potential engagement activities and examples of promising practices. Adams et al. (2017) argue that it is very important to build trust over time, develop and communicate about mutually beneficial outcomes, and construct clear metrics for assessing impact. As the Step guidelines have shown, patient engagement is a long process, and it is influenced by institutional ideologies, professional attitudes and patient readiness to accept new and engaging roles (Marlett et al., 2015). In the end, most of the studies noted that the involvement was intense in terms of resources and time, but found it rewarding because it was the key to the formulation of the final guidelines (Köpke et al., 2019).

As regards the fourth question ("**Within the identified PE experiences/methods, is there evidence of return on engagement (RoE)? How can successful and unsuccessful measures be identified? ")**, **there is no evidence, or there is only very limited evidence of return on engagement.** Future research should develop a standardised measure of the impact of collaborative research and effectiveness (in terms of costs) and conduct patient and public engagement in the research to assess its impact. For patients with rheumatology, for example, attempts are being made to develop a framework to advance patient engagement reporting (Jennings et al., 2018; Hamilton et al. (2017). However, some authors have tried to develop methodologies to measure RoE. For example, Zhang et al. (2017) followed the GRADE approach to integrate patient values and preferences into health decision-making and the development of practical guidelines. Adams et al. (2017) have demonstrated in their Step-methodology approach that there are metrics to assess the impact of patient engagement at each stage. Kreindler and Struthers (2016) developed a Patient Participation Tangible Effects Assessment Sheet (STEPP) to assess the organisational impact of patient engagement, as reported in the previous chapter on results. It was also noted that all stakeholders believe that patient perspectives should be taken into account in research and innovation of therapies, interventions and drugs, and the lack of good practices and standardized metrics has made it difficult to achieve consistency and measure success in patient involvement (Pushparajah, 2018).

Also, the last question asked by the consortium ("Have the identified patient engagement experiences produced any outputs useful for MULTI-ACT and the Digital Toolkit?), although the most of recommendations and guidelines are medicine lifecycle focused, the experiences of PCORI Engagement Rubric, the EUPATI guidelines dedicated to PE and other initiatives show promising

developments in the field of standardization of patient engagement and the development of tools (including digital) dedicated to making this practice more effective and measurable and will serve as benchmark for developing the MULTI-ACT guidelines focused on empowering the experiential knowledge of patients, as co-researcher and key a stakeholder.

In this context, MULTI-ACT Master Scorecard is then a promising step forward in this direction since it will include the patients reported dimension with the aim to also measure impact on the functional domains that matter most patients

6. WEB RESEARCH

The second phase of landscape analysis intends to identify additional projects, methods and initiatives related to patient involvement in MS and brain domain to complement the literature review. To this end, it was decided to consult the following European and international repositories and web portals:

- SYNaPsE
- European Repositories: CORDIS EU research results[45], DG SANTE EU Health Programme[46], EIT Health[47], European Innovation Partnership on Active and Healthy Ageing[48], Health INTERREG[49], IMI Innovative Medicine Initiative[50]
- International initiatives beyond Europe: the Patient-Centered Outcomes Research Institute (PCORI)[51]
- ENGAGE2020 Action Catalogue

6.1 Results

Through these platforms we retrieve and describe some interesting projects and activities of patient engagement. The Methods and details of this research can be read in the Appendix 2.
Here we can mention the most relevant examples found in **SYNaPsE** than can integrate the results of Literature review:

One initiative that engage patients at an "inform" level is the "**From Anecdotal to Actionable: The Case for Patient Perspective Data**" implemented by FasterCures. Indeed, with patient input in high demand, momentum is building to find more systematic ways of capturing and integrating this transformative resource into decision-making. So, borrowing methods from the fields of health economics, marketing, and engineering, a new science of patient input has emerged, embracing data as a means for measuring patient-centered outcomes and quantifying patient preferences. Following this approach, the initiative's goal was to build a model for advancing the collection and application of Patient Perspective Data, along with initial ideas for how such data might inform drug development and regulatory processes. In this case, patients are engaged more as informers together with other key actors, in order to identify and eliminate the obstacles for faster cures.

An example of a "consult" approach at program level is provided by the initiative "**PFMD - Patient Focused Medicines Development**". Established in 2015, it is an independent multinational coalition, managed in collaboration with The Synergist. Its goal is 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. PFMD

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[45] https://cordis.europa.eu/

[46] http://ec.europa.eu/chafea/health/programme/index_en.htm

[47] https://www.eithealth.eu/

[48] https://ec.europa.eu/eip/ageing/home_en

[49] https://www.interregeurope.eu/

[50] http://www.imi.europa.eu

[51] www.pcori.org/

works on multiple projects simultaneously, which all aim at driving public and patient involvement and engagement forward.

For the "involve" approach, an interesting example to consider is the initiative "**Kids Barcelona**". It focuses mainly on clinical trials, but the goal is to include Patient advocacy in the field of paediatric drug development. Indeed, KIDS Barcelona is a YPAG (Young Persons' Advisory Group) that works as a scientific council of teenagers to improve the clinical trials performed by Sant Joan de Déu Children's Hospital in Barcelona (Spain). The group comprises 16 teenagers: half of them are patients of the hospital and several have experience as participants in clinical trials. The members have been trained in the field of biomedicine, research, clinical trials and innovation, and the objective of the group is to include the voice of patients, their needs, and to ensure that the projects are patient-centred. Always in relation to this approach, but more at programme level, it is worth mentioning the initiative "**Co-creation of the Patient Engagement "Meta-Framework"**". The aim of the project is to co-produce tools for meaningful patient, a public engagement and involvement across the research and medicines lifecycle continuum, for all stakeholders[52].

For the "Co-design" approach, there are several approaches from the analysis that could be examined, both at program or project level. At project level for example, in August 2011, the Canadian government launched the **Strategy for Patient Oriented Research (SPOR)** through the Canadian Institutes for Health Research (CIHR). The strategy focuses on ensuring that: research is relevant to patients, that patients are engaged in the research process, and that research findings are quickly integrated into patient care[53].

At program level, an initiative that followed a "co-design" approach is the "**ADAPT SMART**" project launched in September 2015. It is an enabling platform that supports activities related to Medicines Adaptive Pathways to Patients (MAPPs) within the Innovative Medicines Initiative (IMI). MAPPs seek to foster access to beneficial treatments for the right patient groups at the earliest appropriate time in the product life span in a sustainable fashion. The 30-month project funded through IMI aims to facilitate and accelerate the availability of MAPPs to all healthcare stakeholders. ADAPT SMART

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[52] The approach encompasses the following steps: (a) A landscape analysis that aimed at checking what kind of PE activities are being done and where stakeholders are in the PE landscape, followed by an analysis of existing PE frameworks to see where are the gaps and what will be needed to address them in order to drive and support a more systematic and meaningful patient engagement throughout the medicines development continuum by all relevant stakeholders; (b) A survey to find out what relevant stakeholders' expectations were in PE and of each other. This became the Stakeholders' Expectations Matrix; (c) Involvement of PE experts in 3 working groups (for pre-clinical, clinical phases, and post-approval) to identify the gaps, the fragmentation and to prioritise the needed actions to be taken in order to create a PE meta-framework that would be truly operational and useful for all stakeholders wanting to do patient engagement. (d) Organization of several workshops to co-create, test and validate a practical PE guidance (PE Quality Guidance) and also put it through public consultation to validate the need for, the content of and the usefulness of the content of this work.

[53] Canada's SPOR goals will be achieved through a number of methods, one of which has been the development of provincial centers called SPOR Support for People and Patient-Oriented Research and Trials (SUPPORT) Units. Alberta was the first province in Canada to launch a provincial SPOR SUPPORT Unit in November 2013, and seven province-wide platforms have been established, including the Patient Engagement Platform. The goal of the Patient Engagement Platform is to support the engagement of patients and researchers in one or more phases of the spectrum of health research, through initiatives related to research consultation (including governance), mobilization and matching, assessment/orientation/education, facilitation/mentorship, guidance with patient compensation, and evaluation of patient engagement activities.

supported projects under the second Innovative Medicines Initiative (IMI2) investigating MAPPs tools and methodologies[54].

PARADIGM Patient Active in Research and Dialogues for an Improved Generation of Medicines is a public-private partnership and is co-led by the European Patients' Forum and EFPIA, represented both in the MULTI-ACT EAB. PARADIGM's mission is to provide a unique framework that enables structured, effective, meaningful, ethical, innovative, and sustainable patient engagement (PE) and demonstrates the 'return on the engagement' for all players in the medicine development process.

PCORI published a **thematic analysis** of published literature from PCORI-funded research awards on the contributions of engagement "**Patient Engagement In Research: Early Findings From The Patient-Centered Outcomes Research Institute**" (Forsythe et al., 2019). Charged with ensuring that research produces useful evidence to inform health decisions, the PCORI requires investigators to engage patients and other health care stakeholders, such as clinicians and payers, in the research process. Many PCORI studies result in articles published in peer-reviewed journals that detail research findings and engagement's role in research. To inform practices for engaging patients and others as research partners, n.126 articles have been analysed in the thematic analysis that described engagement approaches and contributions to research. Many articles reported that **engagement provided valuable contributions to research feasibility, acceptability, rigor, and relevance, while a few noted trade-offs of engagement, such as using unvalidated measures to assess high-priority outcomes or alternative randomization schemes to align with partners' desires to maximize the number of people receiving a clinical intervention (**McElfish et al., 2017; Gesell et al., 2017)**.** The findings suggest that engagement can support more relevant research through better alignment with patients' and clinicians' real-world needs and concerns.

Moreover, as resulted also from the literature review, the **"PCORI Engagement Rubric"** provides a framework for operationalising the integration of patient engagement and other stakeholders in all phases or research. The Engagement Rubric relies on the six PCORI Engagement Principles:

- **Reciprocal Relationships:** This principle is demonstrated when the roles and decision-making authority of all research partners, including the patient and other stakeholder partners, are defined collaboratively and clearly stated.
- **Co-Learning:** This principle is demonstrated when the goal is not to turn patients or other stakeholder partners into researchers, but to help them understand the research process; likewise, the research team will learn about patient-centeredness and patient/other stakeholder engagement, and will incorporate patient and other stakeholder partners into the research process.
- **Partnerships:** This principle is demonstrated when time and contributions of patient and other stakeholder partners are valued and demonstrated in fair financial compensation, as well as in reasonable and thoughtful requests for time commitment by patient and other stakeholder partners. When projects include priority populations, the research team is committed to diversity across all project activities and demonstrates cultural competency, including disability accommodations, when appropriate.

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[54] ADAPT-SMART aligned a number of major stakeholders eager to progress towards MAPPs implementation. The ADAPT-SMART Coordination and Support Action (CSA), will act as a neutral collaborative framework to establish the platform that will engage with all relevant stakeholders, including patients, industry, regulators, Health Technology Assessment bodies (HTAs), payers (national and European Networks), clinicians, governments/policy makers.

- **Transparency, Honesty, and Trust:** These principles are demonstrated when major decisions are made inclusively and information is shared readily with all research partners. Patients, other stakeholders, and researchers are committed to open and honest communication with one another.

Finally, **Engage2020 Action Catalogue**[55] is a tool that presents 57 stakeholder engagement methods gathered and analysed by the Engage2020 project[56]. Engage2020 explored current stakeholder engagement concepts and practices, with a focus on civic society and research projects[57]. Based on the criteria set for each area of the R&I path[58], 13 methods were selected: Citizen summit, Citizens Hearing, Consensus Conference, Crowd Wise, Deep Democracy – The Lewis Method, Distributed Dialogue, E-conference (tool), Focus Groups (tool), Future Workshop, Hackathon, Perspective Workshop, Science Theatre, World Café. Only four methods appeared related to our issue[59].

Consensus Conference

In the medical field, consensus conferences gathered practitioners and experts to build a consensus on either health knowledge (e.g. diagnostic criteria) or practices (e.g. best practices, treatment protocols). The format of these consensus conferences differs from event to event and cannot always be equated with the Consensus Conference engagement method, which has wider application. This literature review found only a few papers describing engagement of patients using the consensus conference method in the course of research with the view of formulating guidelines or core outcomes.

Focus Group is undoubtedly the most widespread technique of engagement. It is rooted in qualitative studies, where it is a standard way of gathering patients' input and learning about their views and experiences. Its scope of application has widened in recent years, with the method being used for decision-making and guidelines formulation (Doria et al. 2018), not without some criticism regarding insufficient separation of these two functions.

Delphi Method, along with modified Delphi Method, emerged as the second most popular patient engagement technique after Focus Group. Initially designed for panels of experts to arrive at decisions without influencing one another, it is increasingly used for including patients, either forming their own panel, or together with experts and other stakeholders (e.g. community, healthcare professionals) (Hall et al. 2018). Delphi can be applied online and it often is. Delphi Method appears to be a popular tool for prioritisation of core-outcomes in patient-centred guidelines (Humphrey-Murto and de Wit 2019), often in multi-stakeholder initiatives. Consequently, Delphi is of special interest for MULTI-ACT.

World Café was not a popular method of engaging patients in the healthcare context, although some examples emerged. This may be in part due to the open-ended feature of the method. It is suitable for generating and sharing ideas, but does not guarantee a structured result, and does not support structured decision-making.

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[55] http://actioncatalogue.eu/search

[56] http://engage2020.eu/news/

[57] This task has been assigned to DiA.

[58] Listed in the Appendix n.2 Sheet n.1.

[59] For details, please see Appendix 2, Sheet n. 2.

Other two methods of stakeholders engagement can be relevant also for patient engagement:

Citizens Hearing Some examples shows how citizen hearing has been used to investigate the preferences of patients with respect to specific issues such as for example the use of health data[60] and the status of health rights[61]. This method showed enhanced understanding and awareness of the barriers to achieving positive solutions to help overcome them; and seek commitment on a joint plan for monitoring and acting on the topics.

Community Advisory Board (suggested by the PF) is one of the methods used in Leukaemia communities[62] and also by the HIV movement. In the Community Advisory method patient advocates leaders all around the world to to improve outcomes of patients, covering patient information, research priorities, access to treatment and capacity building in the patients' community.

Other initiatives and practices have been retrieved from repositories like **CORDIS EU, DG SANTE EU Health Programme, EIT Health, European Innovation Partnership on Active and Healthy Ageing, Health INTERREG, IMI Innovative Medicine Initiative**. Most of them are mainly confined to gathering patients' views and incorporate them into the project. Where the grade of engagement is very high, it often focuses on a co-creation process linked with research[63]. MULTI-ACT aims to build on the medicine development domain and to extend the focus on the wider Health 7-steps R&I that precede the clinical process and focus on the governance of R&I beyond the drug development process.

The US "**Patient-Centered Outcomes Research Institute (PCORI)**"[64] showed interesting activities related topatient engagement, such as the "**PCORI Research Awards CER".** Its portfolio demonstrates a variety of approaches and ways that engagement has had an impact on research projects and healthcare decision making[65].

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[60]https://understandingpatientdata.org.uk/sites/default/files/2019-03/Public%20attitudes%20study%20summary.pd;

https://www.connectedhealthcities.org/chc-hub/public-engagement/citizens-juries-chc/citizens-juries/

[61] https://www.alliance-scotland.org.uk/blog/events/citizens-hearing-on-the-right-to-health/

[62] https://www.cmladvocates.net/cml-cab

[63] For a comprenhensive list, see Appendix 2.3

[64] PCORI has been authorized and funded in the 2010 in United States with the Patient Protection and Affordable Care Act, funds comparative clinical effectiveness research for the purpose of generating evidence that helps patients and their health care providers to better understand their diagnostic and treatment options and make more informed clinical decisions. A representative from PCORI, has been contacted following the International Progressive MS Alliance Industry Forum Meeting (January 22, 2019 Washington, D.C.) in order to indicate initiatives under the PCORI funded-projects relevant for the WP1 landscape analysis. https://www.pcori.org/

[65] Details in Appendix 2.3.

7. ENGAGING THE MS SOCIETIES

In order to gather global feedback on best practices of Patients engagement in R&I, the PEG member has agreed to leverage on the connection with MSIF and EMPS, the most relevant network of MS Societies. MSIF and EMPS are also represented in the PEG group and linked to FISM and ARSEP. Engaging with these two entities means to reach a global coverage of MS organisations.

7.1 Concept for engagement

The MSIF and EMSP have been engaged with different roles (figure 8).

Figure 8. Concept for differentiation of role between MSIF and EMSP.

In particular, this means two different surveys:

- Survey to MSIF Research Staff Network will serve to gather MS Societies PE experiences & practices and patients with MS (PwMS) priorities for the Health R&I critical path.
- Survey to EMSP will serve to grasp PE experiences and practices in the European Panorama (EU Organisations, Policy Makers, Regulatory Agencies)

7.2 Results

7.1.2 MSIF Research Staff Network

MSIF RSN members were further surveyed to assess the landscape of patient engagement in the R&I process. Responses were received from the Australian, German, UK and US MS Societies. These described patient engagement activities were coded for their patient engagement level and alignment to the 7 steps of the R & I process. As illustrated in figures 9-13, the MSIF RSN organisations provided a range of opportunities for patient engagement in the R&I process. It is also evident that the level of patient engagement varies considerably across the MSIF RSN organisations.

Figure 9. Australian MS Society Patient Engagement Initiative Map.
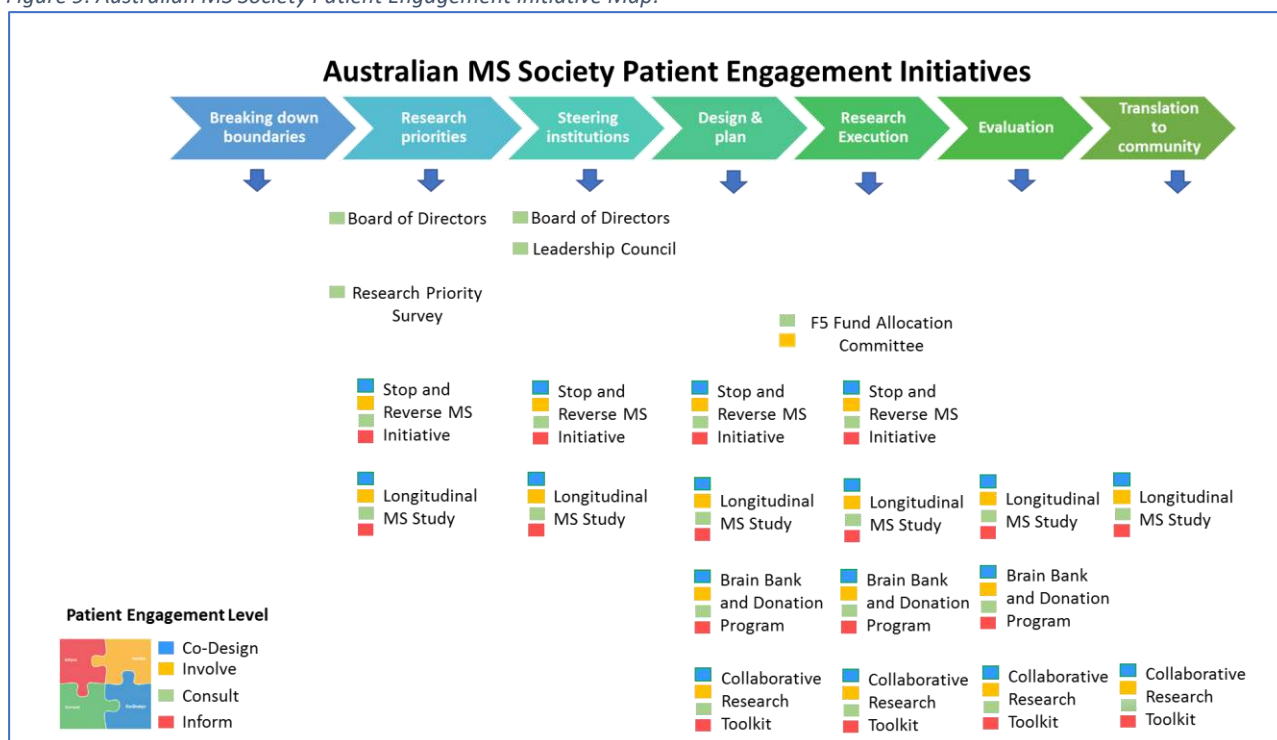
Figure 10. German MS Society Patient Engagement Initiative Map.
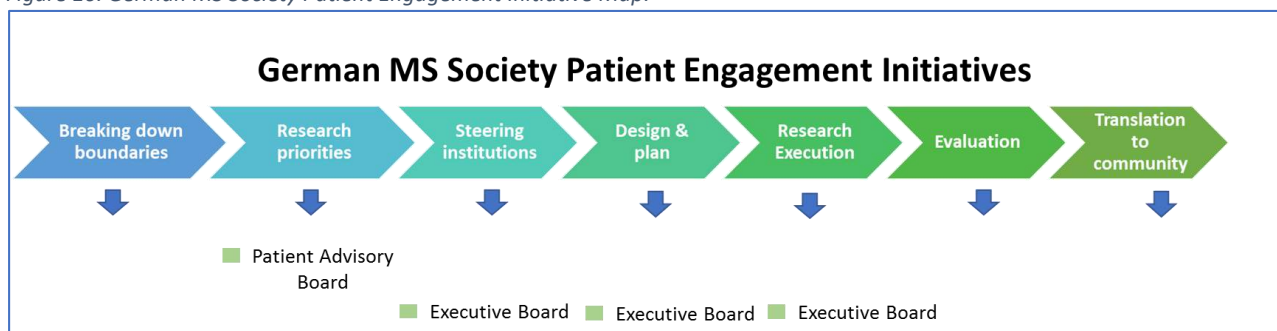
Figure 11. Italian MS Society Patient Engagement Initiative Map.

![multi-act logo]
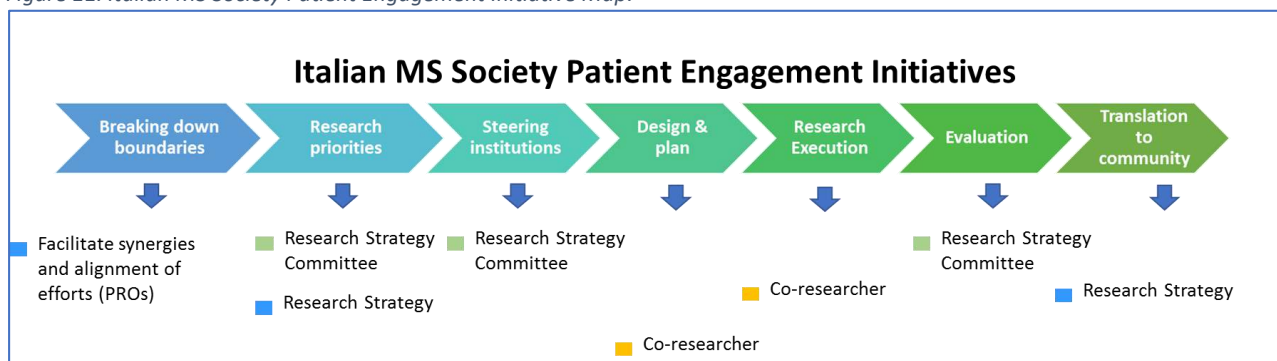
Figure 12. UK MS Society Patient Engagement Initiative Map.
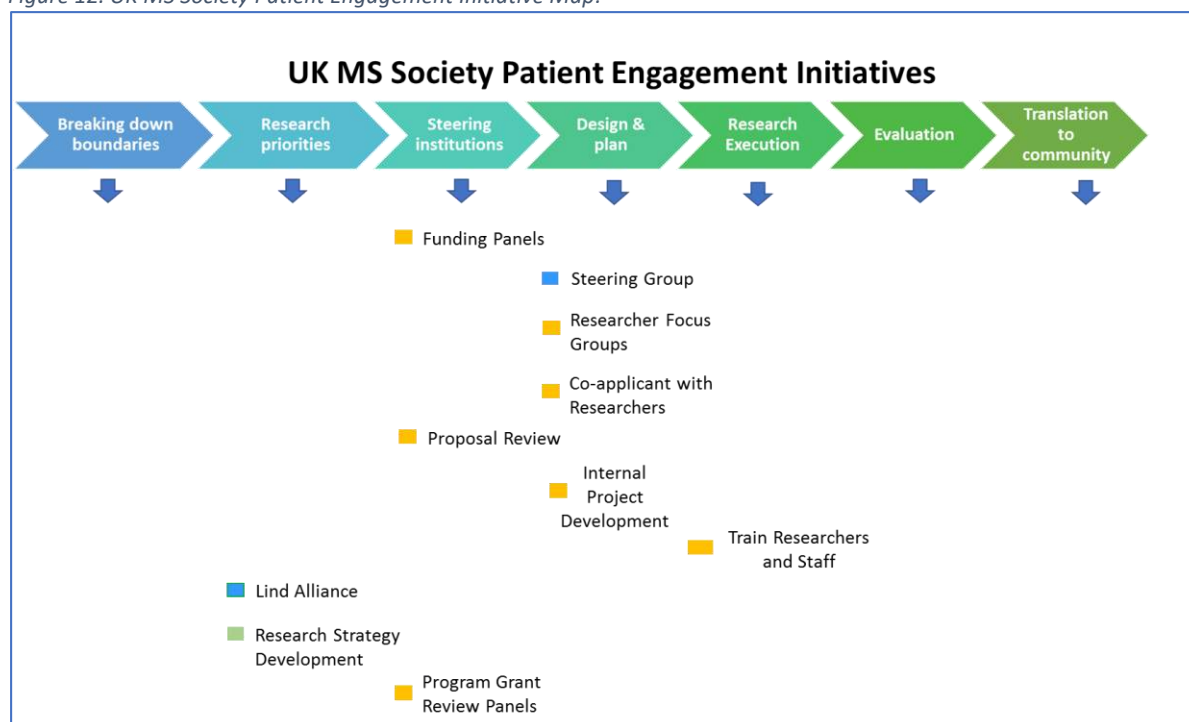
Figure 13. US National MS Society Patient Engagement Initiative Map.
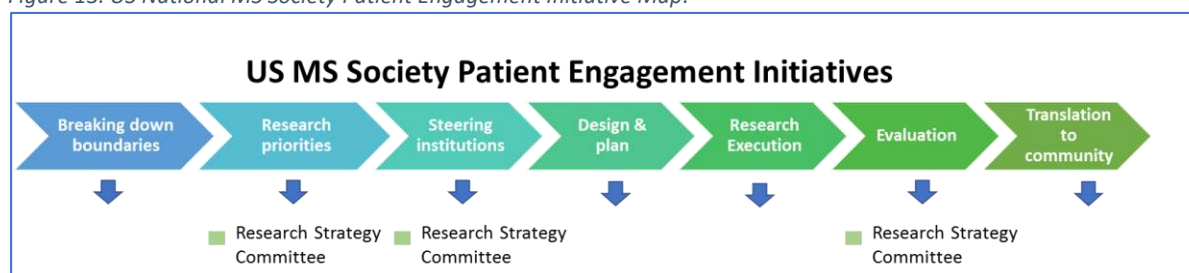
7.2.2 European MS Platform EMSP

As a pan-European umbrella organization, EMSP represents the MS Organisations and at the same time represents individual people, by including them in the governance. EMSP representatives were surveyed to consolidate the landscape analysis by providing their vision for what it means to capture patients' voice and by integrating their knowledge about patient engagement in the R&I process done by European organisations, regulatory agencies and policy makers[66]. To capture the voice of more than 700,000 people EMSP strategy is based on consultation (surveys and studies) and strong evidence-based information. With respect to the 7-steps R&I path, the following gaps, priorities and needs for engaging people with and affected by MS (PwaMS) in the European Health Research & Innovation (R&I) have been identified:

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[66] A tailored survey protocol has been developed and is available in Appendix n.5b. For EMSP, representing the voice of people affected by MS aims at improving their quality of life by addressing their needs and challenges and influence changes in the policy decision making processes that have an impact on their quality of life. To do so, the organisations and their members should be representative, inclusive and democratic.

GOVERNANCE PROGRAMS

Areas of the PE R&I path	Priorities and needs to be addressed
Breaking down boundaries	Acknowledgement of patient's expertise by the Scientific and Research Community Inclusion of patients in the pre-research phase Better understanding of patients' needs and challenges for better focused outcomes
Research priorities	Progressive MS, Paediatric MS
Steer institutions	Inclusion of patients/carers fully trained and equipped to meaningfully contribute
Evaluation	Indicators to be developed with patients
Translation to community	Improved communications by easy to understand material Outcomes fitting real needs of patients will be better endorsed by patients and the Community

PROJECT DEVELOPMENT

Areas of the PE R&I path	Priorities and needs to be addressed
Design & plan	Consultation with the MS community at large at the conception stage in a meaningful way
Translation to community	Lay language translation for wider community (patients and their entourage)

Considering the R&I European Health R&I panorama, the barriers for engagement of patients in R&I and related mitigation identified by EMSP are:
- Meaningful participation requires trained, informed and equipped people. There is a lack of training and literature or tools available to involve people with or affected by MS
- Representation: inclusion and diversity is not ensured as the pool of patients is limited, there is often a low number of "professional experts" rather than a wider pool of "expert" patients.
- Language and education level can represent obstacles to achieve better involvement of patients within the R&D processes.

As European organisations are limited in outreach, in recent years they have developed tools, resources and training to ensure the involvement of a wider pool of patients. However, the work would be improved by stronger implementation at national level. European organisations should encourage their national members to disseminate training, share information and reach more people. This work will also require public investment to educate patients and their related communities.

8. CONCLUSIONS

The thinking underling Responsible Research Innovation wants to challenge our notion of good science as such. It argues that excellence, validity and relevance are connected by engaging patients and society in the research continuum as key stakeholder with decision making role. The monitoring of the evolution and benefits of Responsible Research and Innovation has highlighted among others an unmet need in the area of patients' engagement.

The **literature review** shows that PE initiatives are mainly treatments and disease management driven. Out of the 49 studies selected, around 60% focus on engaging patient in clinical trials & research projects (single project level), around 30% focus on engaging patient in healthcare, 10% discuss other aspects related to patient engagement. With respect to the Level of Engagement, most studies consider patients to be involved and consulted at all stages of the medicine lifecycle process (e.g. EUPATI).

Current promising experience of patients involvement in clinical and health care research will be used as a basis for developing innovative solutions to engage patients also in the governance of R&I. Limited evidence of RoE and the impact of patient engagement in research has been found. Future research should aim to conduct well-designed studies to assess the cost-effectiveness of patient involvement in MS and brain research and innovation.

The **web-search** on mapping portals, tools and repositories[67] (found that they mainly focus on clinical trials and drug development, in which patients are not engaged from the very beginning of the research with decision making role but consulted for feedbacks.

By analysing the Engage2020 Action Catalogue, that includes method for public engagement, **the Consortium identified twelve methods suitable for patient engagement**: Deliberative Online Forum, Delphi Method, e-conference, Science Theatre, World Café, Focus Group, Distributed Dialogue, Deep Democracy - The Lewis Method, Crowd Wise, Consensus Conference, Citizen Summit, Citizens Hearing.

All the above analysis indicate that the research projects in the health sector appear to have a rather limited repertoire of methods used for engaging patients. The methods are not discussed in terms of their (potential) impact. In conclusion, it was not possible to determine return on engagement of the methods based on the literature.

A search on repositories of the European Commission (i.e. CORDIS EU research results, DG SANTE EU Health Program, EIT Health, European Innovation Partnership on Active and Healthy Ageing, Health INTERREG) shows few results for projects where patients are involved in the governance structure and agend, as stakeholders. Patient engagement is mainly confined to consult patients' and incorporate them into the project. Where the grade of engagement is very high and focuses on a co-creation approach it is strictly linked with research impact on society.

With regard to the IMI Innovative Medicine Initiative. Synergies with relevant IMI-funded projects will be activated via MULTI-ACT Patient Forum to benchmark the evolution on patient engagement.

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[67] SYNaPsE platform, Engage2020 ActionCatalogue, CORDIS EU research results, DG SANTE EU Health Programme, EIT Health, European Innovation Partnership on Active and Healthy Ageing, Health INTERREG, IMI Innovative Medicine Initiative, Patient-Centred Outcomes Research Institute PCORI.

A thematic analysis of published literature from the US Patient-Centred Outcomes Research Institute (PCORI) awards of patient engagement in research reported that engagement provided valuable contributions to research feasibility, acceptability, rigor, and relevance, while a few noted trade-offs of engagement, such as using unvalidated measures to assess high-priority outcomes or alternative randomization schemes to align with partners' desires to maximize the number of people receiving a clinical intervention (McElfish et al., 2017; Gesell et al., 2017

The most relevant network of MS Societies (MSIF and EMPS), have been surveyed to assess the level of patient engagement in their R&I process. Responses received from the Australian, German, Italian, UK and US MS Societies described patient engagement activities coded for their patient engagement level and alignment to the 7 steps of the R&I process. The level of patient engagement is perceived as varying considerably across the organisations, demanding for standardization and harmonization across countries.

MSIF underlined the importance to share best practices on the engagement of People with MS in R&I among MS societies in order to exchange lessons learnt and facilitate cross-country dissemination. in In order to address the needs of patients in MS research agendas, MSIF perceived the need to improve the co-designing with patients in order to address the needs of patients. MULTI-ACT WP1 aims to serve to meet this scope need by producing innovative guidelines and tools for patient engagement as well as for the assessment of the impact this that engagement actions produce.

Focusing on the European Health R&I panorama, EMSP, as voice of people with and affected by MS in Europe, considers training and information important, but also the criteria of representation, based on reaching a big number of patients. Language and education level can represent obstacles to achieve better involvement of patients within the R&I processes. MULTI-ACT WP1 wish to provide guidance and tools to help MS organisations to facilitate patient engagement and educate patients to be the key stakeholders in the 7-steps R&I path as well as in the process of engagement its-self.

As also showed by interviews with the Patient Forum (Appendix 4), patient engagement is going to become a consolidated standard practice. A prerequisite for effective co-creation is the commitment of stakeholders to the funding of the research mission. Education and training are being included in R&I projects to tackle such need. In order to break boundaries between R&I and patients it is important to interact with policy makers and also journal editors and media for transparency, privacy and security rules and conditions. The general goal of patient engagement requires also a cultural change in Research Funding and Performing Organisations, e.g. showing a Return on Investment for the time, budget and other resources needed to engage patients (Return on Engagement). The value of the patient's contribution to the research process should be understood and measured. In addition, "tokenism" and underrepresentation in patient involvement should be mitigated in the direction of a more genuine commitment (Hahn et al., 2017).

MULTI-ACT started connecting and synergizing with other relevant Responsible Research and Innovation (RRI) projects, such as the NewHoRRIzon (Appendix 5). Synergy will help to co-design guidelines for patient engagement in a co-creation approach that is actually at the heart of the MULTI-ACT project.

The data included in this report confirmed that patients' engagement in line with RRI's vision still deserves attention and innovative guidelines. Empowering the experiential knowledge of patients, as co-researcher and a key stakeholder, is indeed at the root of the MULTI-ACT patient engagement

strategy and related guidelines. MULTI-ACT governance model[68] has already focused on the strategy to enable this approach (see figure 14). In particular, MULTI-ACT Governance Criterion 2 (Participatory Governance) foresee two main actions to enable truly effective PE:

1)   Appoint an "Engagement coordination team", that will be in charge of coordinating the involvement of stakeholders, including patients and caregivers, in all the operations;

2)   Create a "Patient Advisory Board", a specific group of patients and caregivers within the "Stakeholders Advisory Board", to be involved and engaged throughout the entire development of the initiative, providing advices, insights and perspectives on the activities of the initiative[69].

The adoption of MULTI-ACT governance criteria will pave the way to create the institutional and organizational conditions needed to foster co-accountability of multi-stakeholder research initiatives and enable participatory decision making processes.

Figure 14. The value of patient engagement

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APPENDIX 1 – Literature review

1.1 - Literature review methodology

Envisaged as a roadmap, the literature review followed a pre-established protocol detailing the objectives and planned methodological and analytical approach of the review process. The advantage of following a review protocol rests with a transparent documentation of the methodology followed and the anticipation of potential problems due to the careful planning of steps prior to initiating the actual review. In the following sub-sections we detail each of these steps that have been followed to gather and review the literature.

1.1.1 Process and stages

In total, the review process followed seven, interrelated steps as depicted in the figure A1 below:

Figure A1. Stages in the review process.

Stage in literature review process	Steps to be taken by the research team
STAGE 1 Set review's objectives and research questions	Confirm the objectives for the literature review and formulate the research questions guiding the review.
STAGE 2 Identify sources to be searched Identify and pilot search terms	Identify electronic databases with facilities to search academic and/or grey literature. Identify specialist websites to hand-search. Define combinations of search terms. Pilot and refine search terms.
STAGE 3 Conduct initial search and create initial database of references	Enter search terms systematically into the databases. Create Endnote database of all 'hits'.
STAGE 4 Remove duplicates, apply inclusion/exclusion criteria by reading title and abstract	Remove duplicated hits. Apply the inclusion/exclusion criteria by reading title and abstract.
STAGE 5 Read full text of included sources, complete data extraction template	Extract information relevant to research questions from each source using a data extraction template. Exclude sources that upon reading do not meet inclusion criteria.
STAGE 6 Hand-search and follow-up references and citations	Supplement the systematic search by hand-search of bibliographies of key sources.
STAGE 7 Quality assessment and synthesis	A narrative review approach: develop a summary of the available evidence pertinent to the review's research questions while taking into consideration the quality of included studies, as appropriate

In stage 1, the research questions and the purpose of the literature review were defined, confirmed and refined (see Section 3.3: *Are MS/brain patients engaged in Health R&I? In which step of the Health R&I path have they been engaged so far? How have they been engaged? Within the identified PE experiences/methods, is there evidence of the "return on the engagement" (return on PE, RoE): evidence demonstrating the impact of patient engagement on multistakeholder research agenda (return on meaningful engagement)? How can successful and unsuccessful measures be identified? Have the identified PE experiences produced some outputs (e.g. guidelines, tools, etc.) useful for MULTI-ACT (e.g. inclusion in Digital Toolkit)?).* In stage 2, sources to be searched were identified. In this context, a combination of academic and grey literature was considered. Also in stage 2, a series of

search terms were developed, along with a set of inclusion criteria. The search terms included key words and phrases that were used in databases to identify relevant sources and documents and defined to capture possible variation in terminology in the research area in question.

In stage 3, we performed the actual search. For the current systematic review, the following bibliographic databases were searched: PubMed, Cochrane Library, PsychInfo and EMBASE. The search strategy that was used was conducted with three different levels. At the first level, the following search words were used: "*patient engagement, patient participation, patient involvement, patient support, patient co-creation, patient empowerment, patient consultation, patient decision making*". At level 2, the following search words were used: "*research, research and development, research and innovation*". At level 3, the following search words were used: "*guideline, protocol, practice guideline, recommendations, practices, and best practices*".

Two independent reviewers screened the search results looking for studies that were considered eligible according to the information provided in the abstracts. Disagreements between reviewers were resolved by consensus. The bibliographic search was conducted in March 2019 and was restricted to peer-reviewed papers or dissertations written in English between 2016 and 2019. Additional papers were identified by manually searching the reference lists of the retrieved articles and previous systematic reviews (stage 6).

In stage 4 results were screened by title and by abstract against the inclusion and exclusion criteria. Items which did not meet the inclusion criteria were discarded. In stage 5 full texts of the included sources were retrieved and reviewed. In the last stage, a quality assessment and narrative synthesis was conducted.

1.1.2 Selection

Two reviewers independently identified potentially eligible records through title and abstract screening and for selecting studies for final inclusion through full text screening in accordance with the steps outlined above. The inclusion criteria were studies that reported on patient engagement or participation in research and innovation or responsible research. Furthermore, we were specially looking for studies reporting patient with brain diseases. For the search strings used, few studies (n.14 papers have been identified in D1.3 and have been included in this comprehensive analysis) were published only for patients with brain diseases or related to brain research specific, therefore we included also studies reporting patient engagement in health in general. Exclusion criteria included papers not handling patient engagement and R&I and non- English papers.

In total, 49 articles met the inclusion criteria and were included in the narrative synthesis (see figure A2).

Figure A2. PRISMA Flow diagram of selection of papers.
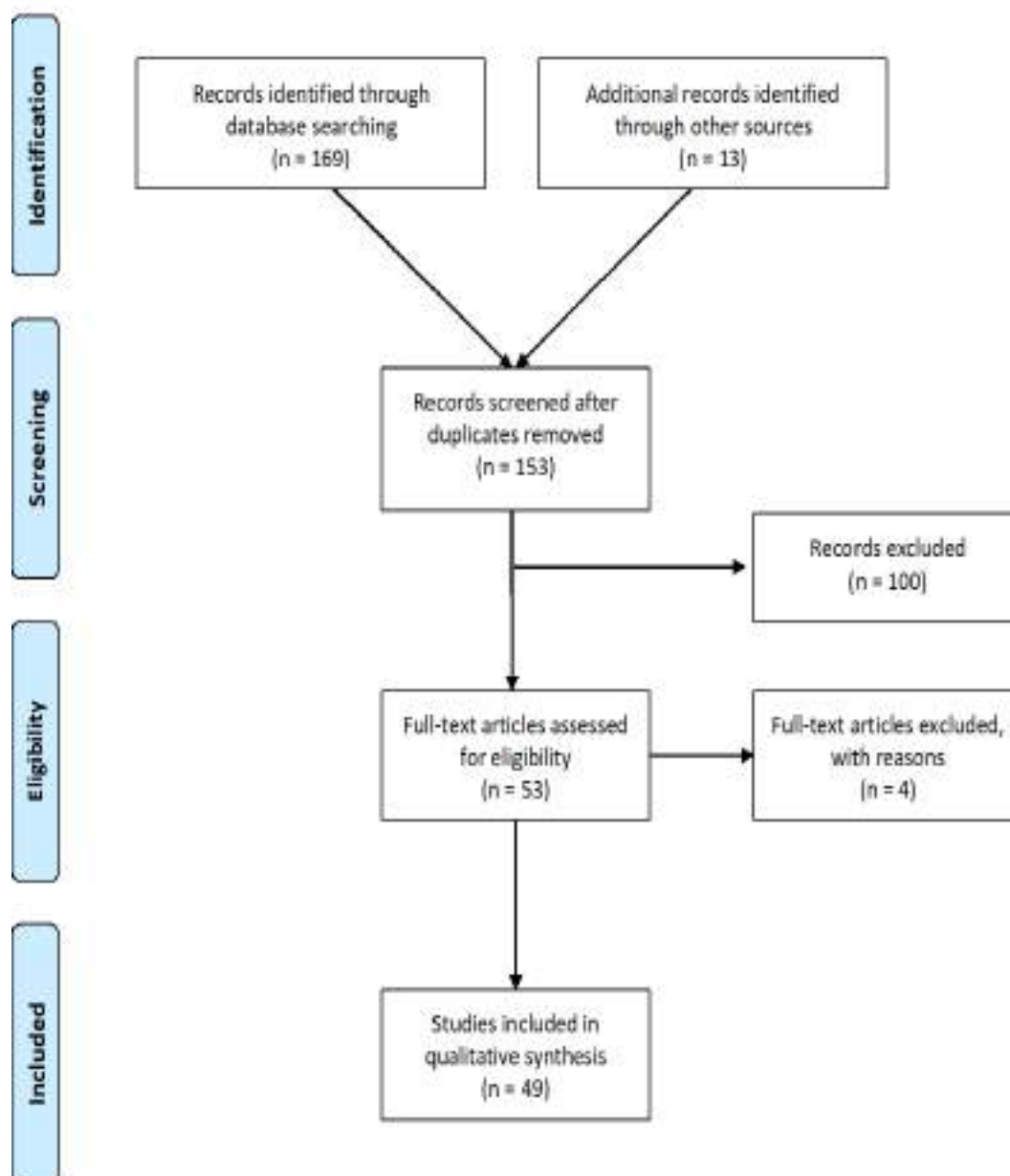
1.1.3 Synthesis

Summary data for all relevant literature under review were closely linked with the initial aims and research questions guiding this literature review. In the remainder we report the narrative synthesis of the literature reviewed.

1.2 Final list of literature reviewed

Table 1. Final list of literature reviewed.

Author	Year	Title	Abstract / Summary	Focus
Adams et al.	2017	*The Steps Model: A Practical Tool for Engaging Communities to Improve Health Outcomes*	The Steps Model emphasizes three key ingredients for community-engaged research: trust building over time, mutually beneficial outcomes, and clear metrics for assessing impact.1,2 Metrics assess project planning, resource allocation, research impact, and sustainability. Movement up the steps indicates a deepening of academic–community engagement, trust, and impact over time. The partnership must be organic. All parties must remain sensitive to one another's needs and maintain a willingness to go down steps along the way to rebuild the partnership as necessary. The Steps Model of partnership can enhance research and the translation of findings into applications that can truly improve community health over time.	Key ingredients for community-engaged research
Akubuiro	2018	*A Quantitative Study of the Factors Affecting Health Care Technology Use in the Millennial Generation*	Health information technology such as personal health records (PHRs) has advanced the health care industry in order to provide patients an opportunity to increase their involvement in health delivery. To achieve increases in quality and reductions in cost, leaders at the U.S. Department of Health and Human Services are establishing payment incentives for increasing the use of electronic health records for physicians, and PHRs for patients, as part of a national health care information network. Electronic health record (EHR) use, noticeably, continues to increase among physicians, though, personal health record use is only 3% and 7% in the general U.S. population and estimated to be half of this among Millennials. The number of Millennial generation in U.S. exceeds 75.4 million of Baby Boomers. If the Millennials, estimated at 83.1 million in the United States are unwilling proactively engage	Electronic health record (EHR) use by millennials

			in monitoring health changes before they become a problem, believing they are immune to poor health, the potential impacts include increase in overall health costs in the United States. Increasing the use of health information technology products, such as PHR is likely to offset a portion of Millennials health care expenses by increasing information access, optimizing communications, and decreasing health care waste. The framework of the diffusion of innovation (DOI) theory was referenced to determine if gender, health status, privacy, and innovativeness predict the impact of engaging with PHRs in U.S. Millennials (born 1982-1998). Data was collected from 122 Millennials using a SurveyMonkey Audience. Data was analyzed using nonparametric correlation to explain rate of adoption of personal health record (PHR) in Millennials. The variance ratio compares the independent variables. The findings confirmed the correlation of the variables and the hypothesis for each of the research questions rejected. Increase the awareness associated with benefits of PHR, and a policy directives that establishes technological requirements are recommendations.	
Archamb ault et al.	2018	*Recommendations for patient engagement in patient-oriented emergency medicine research*	To make pragmatic recommendations on best practices for the engagement of patients in emergency medicine (EM) research. We created a panel of expert Canadian EM researchers, physicians, and a patient partner to develop our recommendations. We used mixed methods consisting of 1) a literature review; 2) a survey of Canadian EM researchers; 3) qualitative interviews with key informants; and 4) feedback during the 2017 Canadian Association of Emergency Physicians (CAEP) Academic Symposium. We synthesized our literature review into categories including identification and engagement, patients' roles, perceived benefits, harms, and barriers to patient engagement; 40/75 (53% response rate) invited researchers completed our	Best practices for the engagement of patients in emergency medicine (EM) research

			survey. Among respondents, 58% had engaged patients in research, and 83% intended to engage patients in future research. However, 95% stated that they need further guidance to engage patients. Our qualitative interviews revealed barriers to patient engagement, including the need for training and patient partner recruitment. Our panel recommends 1) an overarching positive recommendation to support patient engagement in EM research; 2) seven policy-level recommendations for CAEP to support the creation of a national patient council, to develop, adopt and adapt training material, guidelines, and tools for patient engagement, and to support increased patient engagement in EM research; and 3) nine pragmatic recommendations about engaging patients in the preparatory, execution, and translational phases of EM research. Patient engagement can improve EM research by helping researchers select meaningful outcomes, increase social acceptability of studies, and design knowledge translation strategies that target patients' needs.	
Arauwou	2017	*Older Adults' Perceptions of the UTAUT2 Factors Related to Intention to use a Patient Portal for Engagement in their Healthcare*	The evolution of patient engagement in patient-centered care has led to the development of online personal health record (PHR) systems, which are accessed through use of a patient portal. Researchers have found that older adults are among those yet to adopt its use. The UTAUT2 factors are used to help understand an individual's intention to use technology and help explain older adults' perception of information technology and their intention to use a patient portal for engagement in their healthcare. The problem addressed by this study is older adults' non-use of patient portals for engagement in their healthcare. The purpose of this qualitative study was to explore older adults' perceptions of the UTAUT2 factors related to intention to use a patient portal for engagement in their healthcare. Face-to-face interviews were conducted with a final sample of 15 older	Patient engagement in patient-centered care

			adults from 2 senior centers and 2 residential service agencies. The themes included (a) Monitoring Health, (b) Refresh memory (c) Research (d) Interaction at health facility (e) Associated to Healthcare (f) Knowledge, and (g) Saving time and money and (h) No transportation needed. Recommendations for practice include (a) the provision of adequate training to help older adults explore the capabilities of a patient portal in monitoring health will help support and aid in the management of their health; (b) caregivers at health care facilities to use their influence to interact and help older adults navigate a patient portal; (c) caregivers including physicians to develop frequent correspondence with older adults through the patient portal.	
Armstrong	2017	*Framework for enhancing clinical practice guidelines through continuous patient engagement*	Patient engagement in clinical practice guideline (CPG) development is recommended by multiple institutions and instruments measuring guideline quality. Approaches to engaging patients, however, vary between oversight organisations, quality tools and guideline developers. We propose a ten-step framework outlining steps and options for patient engagement in guideline development with the goal of highlighting steps for patient engagement and methods by which this can be achieved. This framework provides a model for continuous patient engagement in CPGs by outlining ten steps of guideline development occurring at the levels of the developer/committee and the individual guideline project. At the developer level, patients can assist in topic nomination (step 1), topic prioritization (step 2) and guideline development group selection (step 3). Within specific guideline projects, patients' opinions may be incorporated when framing the question (step 4), creating an analytic framework and research plan (step 5), conducting the systematic review and conclusion formation (step 6), development of recommendations (step 7) and	Clinical practice guidelines through continuous patient engagement

			dissemination and implementation (step 8). At the end of process, patients can again be engaged at the developer level by helping determine when guidelines need updating (step 9) and evaluating the developer's approach to patient engagement (step 10). Patient engagement at each CPG development step has different purposes, mechanisms, advantages and disadvantages, and implications for resource utilization. This framework can serve as a resource for guideline developers desiring to increase patient engagement and reference for researchers investigating engagement methodology at different steps of the CPG lifecycle.	
Baines & Regan de Bere	2018	*Optimizing patient and public involvement (PPI): Identifying its "essential" and "desirable" principles using a systematic review and modified Delphi methodology*	There is international interest in the active involvement of patients and the public. However, consensus on how best to optimize its application is currently unavailable. To identify and assess the underlying principles of patient and public involvement (PPI) in health and social care services, research, education and regulation across medicine, dentistry and nursing. A four-phase methodology: (i) an extensive systematic review of published and grey literature; (ii) inductive thematic analysis of review findings; (iii) development of best practice principles; and (iv) consensus testing of identified principles using a modified Delphi methodology. Twelve systematic reviews and 88 grey literature publications were reviewed leading to the unique identification of 13 principles later assessed by 18 PPI experts. Essential consensus (>75% agreement) was obtained for nine principles re-viewed. Working in equal partnership and sharing information achieved the highest consensus rates: 16/17 essential 94.1%; 1/17 desirable 5.8%. The four remaining principles that failed to reach essential consensus were categorized as desirable by expert respondents. No principles were considered irrelevant. No alternatives were suggested. Expert respondents	Patient and public involvement (PPI)

			suggest essential principles must be achieved to optimize PPI best practice. To advance PPI practice, desirable principles should also be aspired to wherever possible. This study's innovative approach advances existing knowledge by providing previously unavailable consensus about PPI best practice. Research findings hold important theoretical and practical implications for educators, regulators, re- searchers and practitioners looking to effectively work together.	
Blackwell et al.	2017	*Using Experience-based Co-design with older patients, their families and staff to improve palliative care experiences in the Emergency Department: A reflective critique on the process and outcomes*	Increasing use of emergency departments among older patients with palliative needs has led to the development of several service-level interventions intended to improve care quality. There is little evidence of patient and family involvement in developmental processes, and little is known about the experiences of and preferences for – palliative care delivery in this setting. Participatory action research seeking to enable collaborative working between patients and staff should enhance the impact of local quality improvement work but has not been widely implemented in such a complex setting. Objectives: To critique the feasibility of this methodology as a quality improvement intervention in complex healthcare settings, laying a foundation for future work. An Emergency Department in a large teaching hospital in the United Kingdom. Experience-based Co-design incorporating: 150h of nonparticipant observation; semi- structured interviews with 15 staff members about their experiences of palliative care delivery; 5 focus groups with 64 staff members to explore challenges in delivering palliative care; 10 filmed semi- structured interviews with palliative care patients or their family members; a co-design event involving staff, patients and family members. The study successfully identified quality improvement priorities leading to changes in Emergency Department-	Patient engagement in patient-centered care

| | | | palliative care processes. Further outputs were the creation of a patient-family- staff experience training DVD to encourage reflective discussion and the identification and application of generic design principles for improving palliative care in the Emergency Department. There were benefits and challenges associated with using Experience-based Co-design in this setting. Benefits included the flexibility of the approach, the high levels of engagement and responsiveness of patients, families and staff, and the impact of using filmed narrative interviews to enhance the 'voice' of seldom heard patients and families. Challenges included high levels of staff turnover during the 19 month project, significant time constraints in the Emergency Department and the ability of older patients and their families to fully participate in the co-design process. Experience-based Co-design is a useful approach for encouraging collaborative working between vulnerable patients, family and staff in complex healthcare environments. The flexibility of the approach allows the specific needs of participants to be accounted for, enabling fuller engagement with those who typically may not be invited to contribute to quality improvement work. Recommendations for future studies in this and similar settings include testing the 'accelerated' form of the approach and experimenting with alternative ways of increasing involvement of patients/families in the co-design phase. | |
| **Boenink et al.** | 2018 | *Giving Voice to Patients: Developing a Discussion Method to Involve Patients in Translational Research* | Biomedical research policy in recent years has often tried to make such research more 'translation- al', aiming to facilitate the transfer of insights from research and development (R&D) to health care for the benefit of future users. Involving patients in deliberations about and design of biomedical research may increase the quality of R&D and of resulting innovations and thus contribute to translation. However, patient involvement in biomedical | Patient engagement in Translational Research |

			research is not an easy feat. This paper discusses the development of a method for involving patients in (translational) biomedical research aiming to address its main challenges. After reviewing the potential challenges of patient involvement, we formulate three requirements for any method to meaningfully involve patients in (translational) biomedical research. It should enable patients (1) to put forward their experiential knowledge, (2) to develop a rich view of what an envisioned innovation might look like and do, and (3) to connect their experiential knowledge with the envisioned innovation. We then describe how we developed the card-based discussion method 'Voice of patients', and discuss to what extent the method, when used in four focus groups, satisfied these requirements. We conclude that the method is quite successful in mobilising patients' experiential knowledge, in stimulating their imaginaries of the innovation under discussion and to some extent also in connecting these two. More work is needed to translate patients' considerations into recommendations relevant to researchers' activities. It also seems wise to broaden the audience for patients' considerations to other actors working on a specific innovation.	
Boudes et al.	2018	*What do stakeholders expect from patient engagement: Are these expectations being met?*	Meaningful patient engagement (PE) in medicines development and during the life cycle of a product requires all stakeholders have a clear understanding of respective expectations. A qualitative survey was undertaken to understand stakeholder expectations. The survey explored 4 themes from the perspective of each stakeholder group: meaning, views, expectations and priorities for PE. Participants were grouped into 7 categories: policymakers/regulators; health-care professionals (HCPs); re-search funders; payers/purchasers/HTA; patients/patient representatives; pharmaceutical/life sciences industry;	Stakeholder expectations on patient engagement

			and academic researchers. Fifty-nine interviews were conducted across a range of geographies, PE experience and job seniority/role. There was consensus across stakeholders on meaning of PE; importance of promoting PE to a higher level than currently; need for a more structured process and guidance. There was little consensus on stakeholder expectations and roles. Policymakers/regulators were expected by others to drive PE, create a framework and facilitate PE, provide guidelines of good practice and connect stakeholders, but this expectation was not shared by the policymakers/ regulators group. HCPs were seen as the link between patients and other stakeholders, but HCPs did not necessarily share this view. Despite broad stakeholder categories, clear themes emerged: there is no "leader"; no stakeholder has a clear view on how to meaningfully engage with patients; there are educational gaps; and a structure and guidance for PE is urgently required. Given the diversity of stakeholders, there needs to be multi-stakeholder collaborative leadership. Effective collaboration requires consensus on roles, responsibilities and expectations to synergize efforts to deliver meaningful PE in medicines life cycle.	
Burke et al.	2018	*Evaluating the Quality of Patient Decision-Making Regarding Post-Acute Care*	Despite a national focus on post-acute care brought about by recent payment reforms, relatively little is known about how hospitalized older adults and their caregivers decide whether to go to a skilled nursing facility (SNF) after hospitalization. We sought to understand to what extent hospitalized older adults and their caregivers are empowered to make a high-quality decision about utilizing an SNF for post-acute care and what contextual or process elements led to satisfaction with the outcome of their decision once in SNF. Qualitative inquiry using the Ottawa Decision Support Framework (ODSF), a conceptual framework that describes key components of high-quality	Quality of patient decision making

			decision- making. Thirty-two previously community- dwelling older adults (≥ 65 years old) and 22 caregivers interviewed at three different hospitals and three skilled nursing facilities. We used key components of the ODSF to identify elements of context and process that affected decision-making and to what extent the outcome was characteristic of a high-quality decision: informed, values based, and not associated with regret or blame. The most important contextual themes were the presence of active medical conditions in the hospital that made decision-making difficult, prior experiences with hospital readmission or SNF, relative level of caregiver support, and pressure to make a decision quickly for which participants felt unprepared. Patients de- scribed playing a passive role in the decision-making pro- cess and largely relying on recommendations from the medical team. Patients commonly expressed resignation and a perceived lack of choice or autonomy, leading to dissatisfaction with the outcome.	
Carlini	2016	*Transcranial magnetic stimulation and antidepressant medication for the treatment of major depression: A cost-effectiveness comparison to assist patient-physician decision making*	Shared decision making between a physician and a patient with a major depressive disorder can have positive implications for the patient's overall health. The complexity of technological innovations, emphasis on patient-centered care, and an evolution from paternalistic to shared and informed decision making warrants attempts to provide the physician-patient dyad with the best available cost and efficacy evidence to render an informed decision. In psychiatric practice, a key decision point occurs after one less than adequate response to an initial trial of antidepressant treatment. The purpose of this research was to perform a cost-effectiveness analysis (CEA) of FDA-approved transcranial magnetic stimulation (TMS) and antidepressant medication with the end goal of developing a decision aid for the psychiatrist and the patient. Both treatments have been empirically tested	Patient-physician decision making

			and found to be efficacious, safe, and non-invasive. Peer-reviewed, randomized controlled studies were used to define effectiveness, conceptualized as treatment efficacy. The components of cost, such as treatment cost and the cost of a patient's time, were determined using established treatment guidelines, as well as Current Procedural Terminology, Red Book, Healthcare Blue Book and advertised pharmaceutical retailer pricing, Centers for Medicare and Medicaid Services Local Coverage Determinations, the U.S. Department of Labor Bureau of Labor Statistics, and the National Center for Health Statistics.	
Colorafi	2015	*Patient-Centered Health Information Technology: Engagement With the Plan of Care Among Older Adults With Multi-Morbidities*	A core principle in multiple national quality improvement strategies is the engagement of chronically ill patients in the creation and execution of their treatment plans. Numerous initiatives are underway to use health information technology (HIT) to support patient engagement however the use of HIT and other factors such as health literacy may be significant barriers to engagement for older adults. This qualitative descriptive study sought to explore the ways that older adults with multi-morbidities engaged with their plan of care. Forty participants were recruited through multiple case sampling from two ambulatory cardiology practices. Participants were English-speaking, without a dementia-related diagnosis, and between the ages of 65 and 86. The older adults in this study performed many behaviors to engage in the plan of care, including acting in ways to support health, managing health-related information, attending routine visits with their doctors, and participating in treatment planning. A subset of patients engaged in active decision-making because of the point they were at in their chronic disease. At that cross roads, they expressed uncertainly over which road to travel. Two factors influenced the engagement of older adults: a relationship with the provider that met	Patient-Centered Health Information Technology

			the patient's needs, and the distribution of a Meaningful Use clinical summary at the conclusion of the provider visit. Participants described the ways in which the clinical summary helped and hindered their understanding of the care plan. Insights gained as a result of this study include an understanding of the discrepancies between what the healthcare system expects of patients and their actual behavior when it comes to the creation of a care plan and the ways in which they take care of their health. Further research should examine the ability of various factors to enhance patient engagement. For example, it may be useful to focus on ways to improve the clinical summary to enhance engagement with the care plan and meet standards for a health literate document. Recommendations for the improvement of the clinical summary are provided. Finally, this study explored potential reasons for the infrequent use of online health information by older adults including the trusting relationship they enjoyed with their cardiologist.	
Devonpo rt et al.	2018	*It's not just 'What' you do, it's also the 'Way 'that you do it: Patient and Public Involvement in the Development of Health Research*	This article presents a reflective account of Patient and Public Involvement (PPI) in the development of obesity and binge eating research. We established Patient Advisory Groups (PAGs) at two English regional National Health Service (NHS) weight management services. PPI was evaluated as follows: (i) PAG members completed a Post Participation Evaluation Questionnaire, (ii) PAG meetings captured group discussion on PPI involvement, (iii) practitioner and researchers produced written reflections on PPI and (iv) sources one to three were consolidated during reflections that took place via e-mail and telephone correspondence between researchers and practitioners, culminating in a summary SKYPE meeting between one practitioner and one researcher involved in the PAGs. Results in the form of reflections suggest guidelines on undertaking PPI were helpful with regard 'what to do', but less	Patient and Public Involvement in the Development of Health Research

			helpful on 'how'. For example, suggestions for the management of interpersonal factors such as eliciting self-disclosure and managing power differentials are insufficiently addressed in existing guidelines. The present case study illustrated how interpersonal considerations can help or hinder the optimal use of PPI. Recommendations for practitioners and researchers planning PPI are offered.	
Gabel et al.	2019	*Health Related Quality of Life in Adult Low and High-Grade Glioma Patients Using the National Institutes of Health Patient Reported Outcomes Measurement Information System (PROMIS) and Neuro-QOL Assessments.*	Health related quality of life (HRQOL) measures have become increasingly important in the management of glioma patients in both research and clinical practice settings. Functional impairment is common in low-grade and high-grade glioma patients as the disease has both oncological and neurological manifestations. Natural disease history as well as medical or surgical treatment can negatively influence HRQOL. There are no universal standards for HRQOL assessment in glioma patients. In this study, we examine patient perspectives on functional outcome domains and report the prevalence of impairments rates using the National Institutes of Health (NIH) Patient Reported Outcomes Measurement Information System (PROMIS) and Neuro-QOL item banks as measures of HRQOL. Retrospective analysis of a prospectively collected dataset involving 79 glioma patients reveals that quality of life concerns are the most important consideration behind making decisions about treatment in 80.7% of patients. The prevalence of functional impairment by PROMIS and NEURO-QOL assessment is high, ranging from 28.6% in the physical function domain to 43.9% in the cognitive function domain. Pain and anxiety related to physical decline is higher in LGG patients compared to HGG patients. Aphasia severity also impacts HRQOL. The results of this study suggest that the PROMIS and NEURO-QOL assessments may be important HRQOL	HRQOL assessment standards in glioma patients

			metrics for future use in larger clinical research and clinical trial settings.	
Ghisoni et al.	2016	*Priority setting in research: user led mental health research*	Involving people in health research is increasingly recognised as being important to make sure that research is focused more on the needs of people who use health services. At present, ideas about what should be researched most often comes from researchers and/or health professionals like doctors and nurses rather than people with a lived experience of mental illness. In this study, we will talk with this group of people from across Wales to explore what they think research into their health services should focus on. The findings from this work will help to influence the work of the National Centre for Mental Health Research Partnership Group; as well as` researchers and health professionals and others who concentrate on mental health research. The Research group is a partnership between people with a lived experience of mental ill health and professionals with an interest in mental ill health. The group plan to take forward the ideas that came from this research and some of the ideas have already been used to increase funding in the area of mental health research.	Patient engagement in health research
Graffigna et al.	2017	*Fertilizing a patient engagement ecosystem to innovate healthcare: Toward the first Italian consensus conference on patient engagement*	Currently we observe a gap between theory and practices of patient engagement. If both scholars and health practitioners do agree on the urgency to realize patient engagement, no shared guidelines exist so far to orient clinical practice. Despite a supportive policy context, progress to achieve greater patient engagement is patchy and slow and often concentrated at the level of policy regulation without dialoguing with practitioners from the clinical field as well as patients and families. Though individual clinicians, care teams and health organisations may be interested and deeply committed to engage patients and family members in the medical course, they may lack clarity about how to achieve this goal. This contributes to a	Patient engagement ecosystem to innovate healthcare

			wide "system" inertia—really difficult to be overcome— and put at risk any form of innovation in this filed. As a result, patient engagement risk today to be a buzz words, rather than a real guidance for practice. To make the field clearer, we promoted an Italian Consensus Conference on Patient Engagement (ICCPE) in order to set the ground for drafting recommendations for the provision of effective patient engagement interventions. The ICCPE will conclude in June 2017. This document reports on the preliminary phases of this process. In the paper, we advise the importance of "fertilizing a patient engagement ecosystem": an oversimplifying approach to patient engagement promotion appears the result of a common illusion. Patient "disengagement" is a symptom that needs a more holistic and complex approach to solve its underlined causes. Preliminary principles to promote a patient engagement ecosystem are provided in the paper.	
Grant et al.	2018	*Practical Considerations for Using Online Methods to Engage Patients in Guideline Development*	Clinical practice guidelines (CPGs) have been widely used in healthcare policy, practice, and for suggesting future research. As patients increasingly become involved in CPG development to produce patient-centered recommendations, more research is needed on methods to engage patients, particularly methods allowing for scalable engagement of large, diverse, and geographically distributed groups of patients. In this article, we discuss practical considerations for using online methods to engage patients in CPG development. To inform this discussion, we conducted a rapid, systematic review of literature on patient involvement in CPG development and used qualitative evidence synthesis techniques to make inferences about potential advantages and challenges of using online methods to engage patients in this context. We identified 79 articles containing information about involving patients in CPG development. Potential advantages	Patient engagement in Guideline Development

			include the ability of online methods to facilitate greater openness and honesty by patients, as well as to reflect the diversity of patient views, which in turn further improve the utility of CPGs. Potential challenges of using online methods may include the extra skill, time, and certain types of resources that may be needed for patient engagement, as well as the difficulty engaging specific patient populations. However, these challenges are mitigated by growing calls for patient engagement as normative for CPG development in addition to patients' increasing familiarity with online technologies. These practical considerations should be examined empirically as guideline development groups further explore the appropriateness of using online methods to engage patients across different stages of CPG development.	
Hamilton et al.	2018	*An empirically based conceptual framework for fostering meaningful patient engagement in research*	Patient engagement in research (PEIR) is promoted to improve the relevance and quality of health research, but has little conceptualization derived from empirical data. To address this issue, we sought to develop an empirically based conceptual framework for meaningful PEIR founded on a patient perspective. We conducted a qualitative secondary analysis of in-depth interviews with 18 patient research partners from a research centre-affiliated patient advisory board. Data analysis involved three phases: identifying the themes, developing a framework and confirming the framework. We coded and organized the data, and abstracted, illustrated, described and explored the emergent themes using thematic analysis. Directed content analysis was conducted to derive concepts from 18 publications related to PEIR to supplement, confirm or refute, and extend the emergent conceptual framework. The framework was reviewed by four patient research partners on our research team. Participants' experiences of working with researchers were generally positive. Eight themes emerged:	Patient engagement in research

			procedural requirements, convenience, contributions, support, team interaction, research environment, feel valued and benefits. These themes were interconnected and formed a conceptual framework to explain the phenomenon of meaningful PEIR from a patient perspective. This framework, the PEIR Framework, was endorsed by the patient research partners on our team. The PEIR Framework provides guidance on aspects of PEIR to address for meaningful PEIR. It could be particularly useful when patient-researcher partnerships are led by researchers with little experience of engaging patients in research.	
Hamilton et al.	2017	*Framework for advancing the reporting of patient engagement in rheumatology research projects*	The term "patient engagement in research" refers to patients and their surrogates undertaking roles in the research process beyond those of study participants. This paper proposes a new framework for describing patient engagement in research, based on analysis of 30 publications related to patient engagement. Recent Findings Over the past 15 years, patients' perspectives have been instrumental in broadening the scope of rheumatology research and outcome measurement, such as evaluating fatigue in rheumatoid arthritis. Recent reviews, however, highlight low-quality reporting of patient engagement in research. Until we have more detailed information about patient engagement in rheumatology research, our understanding of how patients' perspectives are being integrated into research projects remains limited. When authors follow our guidance on the important components for describing patients' roles and function as "research partners," researchers and other knowledge users will better understand how patients' perspectives were integrated in their research projects.	Patient engagement in rheumatology research projects
Heffernan et al.	2017	*Implementation of a youth-adult partnership model in youth mental health*	By integrating Youth–Adult Partnerships (Y-APs) in organizational decision making and programming in health-care settings, youth can be engaged in	Patient engagement in youth mental

		systems research: Challenges and successes	decisions that affect them in a way that draws on their unique skills and expertise. Despite challenges, Y-APs can have many benefits for youth and adults alike, as well as for the programmes and initiatives that they undertake together. This article describes the development, implementation and success of a Y-AP initiative at the McCain Centre at the Centre for Addiction and Mental Health, a large urban hospital. The McCain Y-AP has integrated youth into a wide range of mental health and substance use-related initiatives, including research projects, conferences and educational presentations. The model of youth engagement is flexible to include varying degrees of involvement, allowing youth to contribute in ways that fit their availability, interest and skills. Youth satisfaction has been strong and both the youth and adult partners have learned from the experience.	health systems research
Hoffman et al.	2018	*Current trends in patient and public involvement in cancer research: A systematic review*	Patient and public involvement (PPI) in health research is on the rise worldwide. Within cancer research, PPI ensures that the rapid development of medical and technological opportunities for diagnostics, treatment and care corresponds with the needs and priorities of people affected by cancer. An overview of the experiences, outcomes and quality of recent PPI in cancer research would provide valuable information for future research. To describe the current state of PPI in cancer research focusing on the research stages, applied methods, stated purposes and outcomes, and challenges and recommendations. A search was conducted on PubMed, CINAHL and PsycINFO for literature published from December 2006 to April 2017. Original research studies describing the involvement of cancer patients, stakeholders and carers as active partners at any stage of the research process were included. Twenty-seven studies were included, the majority reporting PPI at the early stages of research, that is, during the definition	Patient and public involvement in cancer research

			and prioritization of research topics and the development of recruitment strategies. Few studies reported PPI at later stages and across the research process. Challenges and recommendations were only briefly described, and critical reflection on the PPI process was lacking. PPI needs to be integrated more broadly in the cancer research process. The quality of reporting PPI should be strengthened through greater critical reflections including both positive and negative experiences of the PPI process. This will contribute to the further development of PPI and its potential in cancer research.	
Jennings et al.	2018	*Best practice framework for Patient and Public Involvement (PPI) in collaborative data analysis of qualitative mental health research: methodology development and refinement*	Patient and Public Involvement (PPI) in mental health research is increasing, especially in early (prefunding) stages. PPI is less consistent in later stages, including in analysing qualitative data. The aims of this study were to develop a methodology for involving PPI co-researchers in collaboratively analysing qualitative mental health research data with academic researchers, to pilot and refine this methodology, and to create a best practice framework for collaborative data analysis (CDA) of qualitative mental health research. In the context of the RECOLLECT Study of Recovery Colleges, a critical literature review of collaborative data analysis studies was conducted, to identify approaches and recommendations for successful CDA. A CDA methodology was developed and then piloted in RECOLLECT, followed by refinement and development of a best practice framework. From 10 included publications, four CDA approaches were identified: (1) consultation, (2) development, (3) application and (4) development and application of coding framework. Four characteristics of successful CDA were found: CDA process is co-produced; CDA process is realistic regarding time and resources; demands of the CDA process are manageable for PPI co-researchers; and group expectations and dynamics are	Patient and Public Involvement in qualitative mental health research

			effectively managed. A four-meeting CDA process was piloted to co-produce a coding framework based on qualitative data collected in RECOLLECT and to create a mental health service user-defined change model relevant to Recovery Colleges. Formal and informal feedback demonstrated active involvement. The CDA process involved an extra 80 person-days of time (40 from PPI co-researchers, 40 from academic researchers). The process was refined into a best practice framework comprising Preparation, CDA and Application phases.	
Köpke et al.	2019	*Patient and caregiver involvement in the formulation of guideline questions: findings from the European Academy of Neurology guideline on palliative care of people with severe multiple sclerosis*	Patient and public involvement in clinical practice guideline development is recommended to increase guideline trustworthiness and relevance. The aim was to engage multiple sclerosis (MS) patients and caregivers in the definition of the key questions to be answered in the European Academy of Neurology guideline on palliative care of people with severe MS. A mixed methods approach was used: an international online survey launched by the national MS societies of eight countries, after pilot testing/ debriefing on 20 MS patients and 18 caregivers, focus group meetings of Italian and German MS patients and caregivers. Of 1199 participants, 951 (79%) completed the whole online survey and 934 from seven countries were analysed: 751 (80%) were MS patients (74% women, mean age 46.1) and 183 (20%) were caregivers (36% spouses/ partners, 72% women, mean age 47.4). Participants agreed/strongly agreed on inclusion of the nine pre-specified topics (from 89% for 'advance care planning' to 98% for 'multidisciplinary rehabilitation'), and <5% replied 'I prefer not to answer' to any topic. There were 569 free comments: 182 (32%) on the pre-specified topics, 227 (40%) on additional topics (16 guideline-pertinent) and 160 (28%) on outcomes. Five focus group meetings (three of MS patients, two of caregivers, and overall 35 participants)	Patient and caregiver engagement in guideline development

			corroborated the survey findings. In addition, they allowed an explanation of the guideline production process and the exploration of patient-important outcomes and of taxing issues. Multiple sclerosis patient and caregiver involvement was resource and time intensive, but rewarding. It was the key for the formulation of the 10 guideline questions and for the identification of patient-important outcomes.	
Kreindler & Struthers	2016	*Assessing the organizational impact of patient involvement: a first STEPP*	Patient involvement in the design and improvement of health services is increasingly recognized as an essential part of patient-centred care. Yet little research, and no measurement tool, has addressed the organizational impacts of such involvement. The paper aims to discuss these issues. The authors developed and piloted the scoresheet for tangible effects of patient participation (STEPP) to measure the instrumental use of patient input. Its items assess the magnitude of each recommendation or issue brought forward by patients, the extent of the organization's response, and the apparent degree of patient influence on this response. In collaboration with teams (staff) from five involvement initiatives, the authors collected interview and documentary data and scored the STEPP, first independently then jointly. Feedback meetings and a "challenges log" supported ongoing improvement. Although researchers' and teams' initial scores often diverged, the authors quickly reached consensus as new information was shared. Composite scores appeared to credibly reflect the degree of organizational impact, and were associated with salient features of the involvement initiatives. Teams described the STEPP as easy to use and useful for monitoring and accountability purposes. The tool seemed most suitable for initiatives in which patients generated novel, concrete recommendations; less so for broad	Organizational impact of patient involvement

			public consultations of which instrumental use was not a primary goal.	
Kristensen et al.	2018	*Conceptualizing patient-reported outcome measures for use within two Danish psychiatric clinical registries: description of an iterative co-creation process between patients and healthcare professionals*	Denmark has national clinical indicator programs for adult patients diagnosed with depression and schizophrenia, respectively. Within each program, the responsible steering group (SG) decided to add some indicators based upon patient-reported outcome measures (PROMs). An interdisciplinary SG of healthcare professionals and a Patient Peer Board (PPB) representing both patient groups co-created the output in an iterative process. The work included literature search, PPB workshops, SG meetings, ratings of PROM topics and items, and a pilot. The PPB discussed the following: item relevance, mode of data collection, graphical format of the online PROMs, and display of results. Finally, requirements for PROM patient information were identified. Based upon input from the PPB, the SG selected the items and specified the measurement concept. The PPB prioritized 20 of 53 suitable items and suggested alternative wording and answer categories. A pilot was performed and 19 items covering well-being, lack of well-being, impairment of functioning, and overall health were selected for clinical testing. The patients recommended concrete, unambiguous, easily understandable information and procedures for data collection and display of results.	Patient engagement in psychiatric clinical registries
Menichetti, J. & Graffinga, G.	2016	*"PHEinAction":Development and Modeling of an Intervention to Improve Patient Engagement among Older Adults*	The increasing prevalence of chronic conditions among older adults constitutes a major public health problem. Thus, changes in lifestyles are required to prevent secondary conditions and sustain good care practices. While patient engagement received great attention in the last years as key strategy to solve this issue, to date no interventions exist to sustain the engagement of older chronic patients toward their health management. This study describes the design, development, and optimization of PHEinAction, a theoretically-driven intervention	Patient engagement in health management

			program to increase patient engagement in older chronic populations and consequently to foster healthy changes that can help reduce risks of health problems. The development process followed the UK Medical Research Council's (MRC) guidelines and involved selecting the theoretical base for the intervention, identifying the relevant evidence-based literature, and conducting exploratory research to qualitatively evaluate program's feasibility, acceptability, and comprehension. The result was a user-endorsed intervention designed to improve older patients' engagement in health management based on the theoretical framework of the Patient Health Engagement (PHE) model. The intervention program, which emerged from this process, consisted of 2 monthly face-to-face 1-h sessions delivered by a trained facilitator and one brief telephonic consultation, and aimed to facilitate a range of changes for patient engagement (e.g., motivation to change, health information seeking and use, emotional adjustment, health behaviors planning). PHE in Action is the first example of a theoretically-based patient engagement intervention designed for older chronic targets. The intervention program is based on psychological theory and evidence; it facilitates emotional, psychological, and behavioral processes to support patient engagement and lifestyle change and maintenance. It provides estimates of the extent to which it could help high-risk groups engage in effective health management and informs future trials	
Morbey et al.	2019	*Involving people living with dementia in research: an accessible modified Delphi survey for core outcome set development*	Recent recommendations promote the inclusion of people living with dementia beyond the role of 'participant' to involvement in all areas of the research process. This reflects shifts in dementia studies from 'research on' to 'research with' people living with the condition. In this paper, we describe the design process and features of a modified Delphi survey devised through consultation	Patient engagement in dementia in research

| | | | with people living with dementia. This article focusses on consultation with people living with dementia and care partners to design an accessible Delphi survey to facilitate participation in core outcome set development. We used the COINED model of co-research developed through the ESRC/NIHR Neighbourhoods and Dementia Study to structure consultation on three features of modified Delphi design. Consultation was achieved through 1:1 and group sessions with a total of 28 individuals (18 people living with dementia and seven care partners). A flexible, responsive and adaptive approach to ongoing consultation with people living with dementia and care partners through 1:1 face-to-face sessions facilitated: (1) the development of a 3-point non-categorical importance scale; (2) the translation of 54 outcome areas into 'accessible statements' for a two-round Delphi survey administered to five stakeholder groups (people living with dementia, care partners, health and social care professionals, policymakers and researchers); and (3) the delivery of a Delphi survey. These features of core outcome set development facilitated the involvement of people living with dementia in study design and as research participants in the data collection phase. Involvement of people living with dementia as a key stakeholder group is not reflected in studies using Delphi survey methods for core outcome set development. Time, resources, researcher expertise and support, underpinned through targeted funding facilitate meaningful and productive inclusive approaches, now an expectation of dementia research. | |
| **Murtagh et al.** | 2017 | *The ECOUTER methodology for stakeholder engagement in translational research* | Because no single person or group holds knowledge about all aspects of research, mechanisms are needed to support knowledge exchange and engagement. Expertise in the research setting necessarily includes scientific and methodological expertise, but also expertise gained through the experience | Stakeholder engagement in translational research |

			of participating in research and/or being a recipient of research outcomes (as a patient or member of the public). Engagement is, by its nature, reciprocal and relational: the process of engaging research participants, patients, citizens and others (the many 'publics' of engagement) brings them closer to the research but also brings the research closer to them. When translating research into practice, engaging the public and other stakeholders is explicitly intended to make the outcomes of translation relevant to its constituency of users. In practice, engagement faces numerous challenges and is often time-consuming, expensive and 'thorny' work. We explore the epistemic and ontological considerations and implications of four common critiques of engagement methodologies that contest: representativeness, communication and articulation, impacts and outcome, and democracy. The ECOUTER (Employing COnceptUal schema for policy and Translation Engagement in Research) methodology addresses problems of representation and epistemic foundationalism using a methodology that asks, "How could it be otherwise?" ECOUTER affords the possibility of engagement where spatial and temporal constraints are present, relying on saturation as a method of 'keeping open' the possible considerations that might emerge and including reflexive use of qualitative analytic methods. This paper describes the ECOUTER process, focusing on one worked example and detailing lessons learned from four other pilots. ECOUTER uses mind-mapping techniques to 'open up' engagement, iteratively and organically. ECOUTER aims to balance the breadth, accessibility and user-determination of the scope of engagement. An ECOUTER exercise comprises four stages: (1) engagement and knowledge exchange; (2) analysis of mindmap contributions; (3) development of a conceptual schema (i.e. a map of concepts and their relationship); and (4) feedback,	

			refinement and development of recommendations. ECOUTER refuses fixed truths but also refuses a fixed nature. Its promise lies in its flexibility, adaptability and openness. ECOUTER will be formed and re-formed by the needs and creativity of those who use it.	
Nguyen, Palisano & Graham	2018	*Perspectives and Experiences with Engaging Youth and Families in Research*	Engaging youth with disabilities and families in research is critical in facilitating knowledge utilization to impact processes and outcomes of services and interventions. Organisations such as INVOLVE in the United Kingdom, the Canadian Institutes of Health Research and the Patient-Centered Outcomes Research Institute in the United States advocate for engaging stakeholders in all aspects of the research process. Despite these efforts, there is a need for research to identify best practices and approaches for stakeholder engagement in research as current descriptions around processes are lacking. In this perspective paper, we share our insights and experiences with engaging youth with disabilities and families as members of the research team. We offer considerations and strategies for stakeholder engagement, as well as identify relevant frameworks to facilitate stakeholder engagement in research. We encourage researchers to share and document their experiences with stakeholder engagement in research to provide guidance for others with shared interests. We hope this paper will initiate conversations among researchers about best practices to maximize the full potential of stakeholders' time and input.	(Youth and Family) Patient engagement in Research
Paul & Holt	2016	*Involving the public in mental health and learning disability research: Can we, should we, do we?*	Patient and public involvement (PPI) is integral to UK health research guidance, however implementation is inconsistent. There is little research into the attitudes of NHS health researchers towards PPI. Using a qualitative methodology, semi-structured interviews were conducted with a purposive sample of eight researchers. A framework approach was	Public engagement in mental health and learning disability research

			used in the analysis to generate themes and core concepts. Participants valued the perspective PPI could bring to research, but frustration with tokenistic approaches to involvement work was also evident. Some cultural and attitudinal barriers to integrating PPI across the whole research process were identified.	
Persson Hagquist & Michelson	2017	*Young voices in mental health care: Exploring children's and adolescents' service experiences and preferences*	The development of 'youth-friendly' services has become a priority across a wide range of healthcare contexts. However, relatively few studies have specifically examined users' experiences of, and preferences for, child and adolescent mental health care. The current study investigated young service users' views of outpatient and community mental health clinics in Sweden, based on two data sources. First, focus group interviews were conducted with seven children and adolescents (aged 10–18 years) to explore both positive and negative experiences of mental health care. Second, written suggestions about specific service improvements were obtained from 106 children and adolescents. Qualitative content analysis revealed three overarching themes: 'Accessibility', 'Being heard and seen' and 'Usefulness of sessions'. Young people's recommendations for improving practice included more convenient appointment times, offered in welcoming settings; opportunities to communicate more openly with clinical staff, enabling sensitive discussion of mental health and wider personal issues; and more structured treatments that offer greater credibility and relevance to young people's mental health and developmental needs. Young people also discussed being compelled by parents and school professionals to engage in treatment. Attending to young people's preferences must be a priority in order to overcome ambivalence about session attendance, and enhance treatment participation and outcomes.	Young patient engagement

Phil et al.	2017	*Extent, quality and impact of patient and public involvement in antimicrobial drug development research: A systematic review*	Patient and public involvement (PPI) is increasingly recognized as bringing a range of benefits to clinical and health services research. Recent systematic reviews have identified and synthesized many benefits (eg higher recruitment rates) and some costs (eg extra time need). Much of the literature focuses on PPI in long-term conditions rather than more acute health care in which the majority of microbiological research is undertaken. The aim was to identify the extent, quality and impact of PPI in antimicrobial drug development research. Objectives were to identify any relevant reporting of PPI in antimicrobial research; appraise the quality of reporting on PPI using recognized PPI reporting and critical appraisal tools; and extract and synthesize data on the impact of PPI. A systematic review was undertaken with a search strategy based on four word groups (PPI, patients, antimicrobial drug development and outcomes). Eight online databases were searched. English language publication, publication between 1996 and 2016 and studies describing PPI in antimicrobial drug development research. No studies were found through online searching that met the search strategy and inclusion criteria. One relevant protocol paper with a brief mention of PPI was identified through expert recommendation. Commentary papers recommending PPI were identified through website searching and expert opinion. Despite strong policy guidance encouraging PPI at the international and national levels, and anecdotal accounts of PPI taking place, evidence for the extent, quality and impact of PPI in antimicrobia	A systematic review on patient and public involvement in antimicrobial drug development research
Pushpara jah	2018	*Making patient engagement a reality*	Patients are increasingly recognised as the true customers of healthcare. By providing insights and perspectives, patients can help the wider healthcare community better understand their needs and ultimately enhance the value of healthcare solutions being developed.	Patient and public engagement in antimicrobial drug development research

| | | | In the development of new medicines, for example, meaningful patient engagement can enable the pharmaceutical industry, healthcare providers and other stakeholders to achieve more meaningful health outcomes. While both the pharmaceutical industry and regulators have achieved some progress in incorporating patient perspectives into their activities, the lack of standardised best practices and metrics has made it challenging to achieve consistency and measure success in patient engagement. Practical guidance for patient engagement can facilitate better interactions between patients or patient groups and other collaborators, e.g. industry, regulators and other healthcare stakeholders. Accordingly, UCB has developed an internal model for Patient Group Engagement incorporating four key principles, based on shared ambition, transparency, accountability and respect, essential for effective collaborations. | |
| **Rae-Grant et al.** | 2018 | *Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis* | A multidisciplinary panel developed DMT recommendations, integrating findings from a systematic review; followed an Institute of Medicine–compliant process to ensure transparency and patient engagement; and developed modified Delphi consensus–based recommendations concerning starting, switching, and stopping DMTs pertinent to people with relapsing remitting MS, secondary progressive MS, primary progressive MS, and clinically isolated syndromes of demyelination. Recommendations were supported by structured rationales, integrating evidence from one or more sources: systematic review, related evidence (evidence not from the systematic review), principles of care, and inference from evidence. Thirty recommendations were developed: 17 on starting DMTs, including recommendations on who should start them; 10 on switching DMTs if breakthrough disease develops; and 3 on | Practice guideline recommendations MS |

			stopping DMTs. Recommendations encompassed patient engagement strategies and individualization of treatment, including adherence monitoring and disease comorbidity assessment. The panel also discussed DMT risks, including counselling about progressive multifocal leukoencephalopathy risk in people with MS using natalizumab, fingolimod, rituximab, ocrelizumab, and dimethyl fumarate; and made suggestions for future research to evaluate relative merits of early treatment with higher potency DMTs vs standard stepped-care protocols, DMT comparative effectiveness, optimal switching strategies, long-term effects of DMT use, definitions of highly active MS, and effects of treatment on patient-specified priority outcomes. This guideline reflects the complexity of decision making for starting, switching, or stopping MS DMTs. The field of MS treatment is rapidly changing; the Academy of Neurology development process includes planning for future updates.	
Rashid et al.	2017	*Patient and public involvement in the development of healthcare guidance: an overview of current methods and future challenges*	Clinical guidelines and health technology assessments are valuable instruments to improve the quality of healthcare delivery and aim to integrate the best available evidence with real-world, expert context. The role of patient and public involvement in their development has grown in recent decades, and this article considers the international literature exploring aspects of this participation, including the integration of experiential and scientific knowledge, recruitment strategies, models of involvement, stages of involvement, and methods of evaluation. These developments have been underpinned by the parallel rise of public involvement and evidence-based medicine as important concepts in health policy. Improving the recruitment of guideline group chairs, widening evidence reviews to include patient preference studies, adapting guidance presentation to highlight patient preference points and	Patient engagement in development of healthcare guidance

			providing clearer instructions on how patient organisations can submit their intelligence are emerging proposals that may further enhance patient and public involvement in their processes.	
Ree et al.	2019	*How patient involvement is measured in patient centeredness scales for health professionals? A systematic review of their measurement properties and content*	Patient centeredness is an important component of patient care and healthcare quality. Several scales exist to measure patient centeredness, and previous literature provides a critical appraisal of their measurement properties. However, limited knowledge exists regarding the content of the various scales in terms of what type of patient centeredness they represent and how they can be used for quality improvement. The aim of this study was to explore the measurement properties of patient centeredness scales and their content with a special focus on patient involvement, and assess whether and how they can be used for quality improvement. A systematic review of patient centeredness scales was conducted in Medline, CINAHL, Embase, and SCOPUS in April and May 2017. Inclusion criteria were limited to articles written in English published from 2005 to 2017. Eligible studies were critically appraised in terms of internal consistency and reliability, as well as their content, structural, and cross-cultural validity. Type of studies included were scale-development articles and validation studies of relevant scales, with healthcare personnel as respondents. We used directed content analysis to categorize the scales and items according to Tritter's conceptual framework for patient and public involvement. Eleven scales reported in 22 articles were included. Most scales represented individual, indirect, and reactive patient involvement. Most scales included items that did not reflect patient centeredness directly, but rather organizational preconditions for patient centered practices. None of the scales included items explicitly reflecting the use of patient experiences of quality improvement. There is a lack of patient	Measurement of patient engagement

			centeredness scales focusing on direct and proactive involvement of patients in quality improvement. It would be useful to develop such instruments to further study the role of patient involvement in quality improvement in healthcare. Furthermore, they could be used as important tools in quality improvement interventions.	
Rieckma nn et al.	2018	*Unmet needs, burden of treatment, and patient engagement in multiple sclerosis: A combined perspective from the MS in the 21st Century Steering Group*	Patient engagement is vital in multiple sclerosis (MS) in order to optimise outcomes for patients, society and healthcare systems. It is essential to involve all stakeholders in potential solutions, working in a multidisciplinary way to ensure that people with MS (PwMS) are included in shared decision-making and disease management. To start this process, a collaborative, open environment between PwMS and healthcare professionals (HCPs) is required so that similarities and disparities in the perception of key areas in patient care and unmet needs can be identified. With this patient-centred approach in mind, in 2016 the MS in the 21st Century Steering Group formed a unique collaboration to include PwMS in the Steering Group to provide a platform for the patient voice.	Patient engagement in multiple sclerosis
Robillard & Feng	2017	*When patient engagement and research ethics collide: lessons from a dementia forum*	The importance of patient engagement in research has been gaining recognition since the turn of the 21st century. However, little is known about the perspectives of people with dementia on the process of discovery. To fill this gap and to inform priorities in patient engagement in the context of dementia research, the Clinic for Alzheimer Disease and Related Disorders at the University of British Columbia hosted an interactive session for members of the patient community and of the general public to share their views on various ethical aspects of the research process. Results from the session indicate that several current research ethics policies and norms in dementia research are not in line with participants' preferences. Here we discuss the importance of	Patient engagement and research ethic

			bridging the gap between researchers and patients and call for reforms in current standards of dementia research.	
Ruco & Nichol	2016	*Patient engagement in research and innovation: A new framework*	Patient engagement is a hot topic across Ontario's health system. This imperative is based on evidence that patient engagement contributes to improved patient experience and outcomes and is evident through recent local and system-level changes, including the release of the Patients First: Action Plan for Health Care Report [3]. Patient engagement in research is a growing area of interest with evidence showing that it ensures appropriate topics and outcomes are chosen for study, increases study enrolment rates, and aids researchers to secure funding [4]. Interestingly, the literature shows that patient engagement in research was most feasible and most commonly done at the beginning of the research process, during the agenda setting and protocol development stage [4]. Locally, a multilevel Patient Engagement in Research framework has been developed to guide and capture the range and scope of patient engagement in practice-based research and innovation (PBRI) at Sunnybrook Health Sciences Centre, a leading multisite academic hospital in Toronto. Sunnybrook defines PBRI as "the systematic approach to creating new understandings of practice with the purpose of integrating this knowledge into innovative approaches to care" and focuses on engaging health professionals at the point of care in research and innovation to advance practice and improve patient care. This paper presents an overview of current local and global patient engagement in research frameworks and describes in detail how our Sunnybrook framework has guided patient engagement in PBRI at the researcher, organization, and system levels.	Research Framework of patient engagement in research and innovation
Samalin et al.	2018	*Efficacy of shared decision-making on treatment adherence*	Shared decision-making (SDM) is a model of interaction between doctors and patients in which both actors	Shared decision-making on treatment

| | | *of patients with bipolar disorder: a cluster randomized trial* | contribute to the medical decision-making process. SDM has raised great interest in mental healthcare over the last decade, as it is considered a fundamental part of patient-centered care. However, there is no research evaluating the efficacy of SDM compared to usual care (CAU), as it relates to quality of care and more specifically treatment adherence, in bipolar disorder (BD). This is a 12-month multi-centre, cluster-randomized controlled trial comparing the efficacy of SDM to CAU. Adult BD patients (n = 300) will be eligible after stabilization for at least 4 weeks following an acute mood episode. The intervention will consist of applying the standardized SDM process as developed by the Ottawa Hospital Research Institute in order to choose the maintenance treatment of BD. A multidisciplinary team developed a decision aid "choose my long-term treatment with my doctor" for BD patients to clarify possible therapeutic options. Primary outcome will assess the patient's level of adherence (based on hetero-evaluation) of ongoing treatment at 12 months. Secondary outcomes will assess the difference between the 2 groups of patients in terms of adherence to maintenance drug therapy based on other measures (self-assessment scale and plasma levels of mood stabilizers). Additionally, other dimensions will be assessed: decisional conflict, satisfaction with care and involvement in decision making, beliefs about treatment, therapeutic relationship, knowledge about information for medical decision and clinical outcomes (depression, mania, functioning and quality of life). The primary endpoint will be analysed without adjustment by comparison of adherence scores between the two groups using Student t-tests or Mann–Whitney tests according to the variable distribution. A set of secondary analyses will be adjusted for covariates of clinical interest using generalized linear mixed regression models. | adherence of patients with bipolar disorder |

| Sand et al. | 2017 | *The North American Primary Care Research Group's Patient and Clinician Engagement Program (PaCE): Demystifying patient engagement through a dyad model.* | Community engagement in research is essential for translating the best evidence into community and clinical practice to improve the health and well-being of the population. North American Primary Care Research Group's Patient and Clinician Engagement Program (PaCE) program aims to develop a robust community of patients and primary care providers with knowledge and understanding of the unique features of patient-centred outcomes research related to primary care in order to advocate for and engage in research. PaCE employs a 'dyad' model in which a patient and a primary care provider collaborate to learn about and engage in primary care, primary care research, grant review, proposal development and advocacy. A series of educational trainings held in conjunction with national primary care conferences, international webinars and local symposia make up the foundation of the PaCE curriculum. To date, 186 participants have completed the full-day, interactive PaCE training, and more than 250 people have participated in PaCE webinars and/or symposia. A 6-month follow-up sent to PaCE participants evaluates engagement activities following training. | Patient and Clinician Engagement Program |
| Sheridan et al. | 2017 | *The PCORI engagement rubric: promising practices for partnering in research* | Engaging patients, caregivers, and other health care stakeholders as partners in planning, conducting, and disseminating research is a promising way to improve clinical decision making and outcomes. Many researchers, patients, and other stakeholders, however, lack clarity about when and how to engage as partners within the clinical research process. To address the need for guidance on creating meaningful stakeholder partnerships in patient-centered clinical comparative effectiveness research, the Patient-Centered Outcomes Research Institute (PCORI) developed the PCORI Engagement Rubric (Rubric). PCORI developed the Rubric drawing from a synthesis of the literature, a qualitative | Patient Engagement in Research |

			study with patients, a targeted review of engagement plans from PCORI-funded project applications, and a moderated discussion and review with PCORI's Advisory Panel on Patient Engagement. PCORI designed the Rubric to illustrate opportunities for engagement to researchers interested in applying for PCORI funding and to patients and other stakeholders interested in greater involvement in research. By encouraging PCORI applicants, awardees, and others to apply the rubric, PCORI hopes to shift the research paradigm from one of conducting research on patients as subjects to a pursuit carried out in collaboration with patients and other stakeholders to better reflect the values, preferences, and outcomes that matter to the patient community.	
Simblett et al.	2018	*Barriers to and Facilitators of Engagement With Remote Measurement Technology for Managing Health: Systematic Review and Content Analysis of Findings*	Remote measurement technology refers to the use of mobile health technology to track and measure change in health status in real time as part of a person's everyday life. With accurate measurement, remote measurement technology offers the opportunity to augment health care by providing personalized, precise, and preemptive interventions that support insight into patterns of health-related behavior and self-management. However, for successful implementation, users need to be engaged in its use. We conducted a systematic review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines involving original studies dating back to the last systematic review published in 2014. We included studies if they met the following entry criteria: population (people using remote measurement technology approaches to aid management of health), intervention (remote measurement technology system), comparison group (no comparison group specified), outcomes (qualitative or quantitative evaluation of the barriers to and facilitators of engagement with this system), and study design (randomized controlled trials, feasibility studies, and	Patient Engagement With Remote Measurement Technology for Managing Health

			observational studies). We searched 5 databases (MEDLINE, IEEE Xplore, EMBASE, Web of Science, and the Cochrane Library) for articles published from January 2014 to May 2017. Articles were independently screened by 2 researchers. We extracted study characteristics and conducted a content analysis to define emerging themes to synthesize findings. Formal quality assessments were performed to address risk of bias. A total of 33 studies met inclusion criteria, employing quantitative, qualitative, or mixed-methods designs. Studies were conducted in 10 countries, included male and female participants, with ages ranging from 8 to 95 years, and included both active and passive remote monitoring systems for a diverse range of physical and mental health conditions. However, they were relatively short and had small sample sizes, and reporting of usage statistics was inconsistent. Acceptability of remote measurement technology according to the average percentage of time used (64%-86.5%) and dropout rates (0%-44%) was variable. The barriers and facilitators from the content analysis related to health status, perceived utility and value, motivation, convenience and accessibility, and usability. The results of this review highlight gaps in the design of studies trialing remote measurement technology, including the use of quantitative assessment of usage and acceptability. Several processes that could facilitate engagement with this technology have been identified and may drive the development of more person-focused remote measurement technology. However, these factors need further testing through carefully designed experimental studies.	
Smith, Wallengren & Öhlén	2017	*Participatory design in education materials in a health care context*	Written patient education material, for example, discharge-information is commonly used in hospital settings. Despite following guidelines on how to best present text and using patients as consultants, improvements can still be	Participatory design in education materials in a health care

			made from a patient's perspective. Here, we describe the process of developing patient education material using a participatory design methodology, with patients, clinicians, researchers and designers working as co-designers following a structured process map. The method emphasises coping with conflicting interests and using this as a source of development. The philosophies behind action research and person-centred care were combined in a practical setting, enhancing both perspectives and generating actionable knowledge to be further used in patient involvement projects. The results reveal that predominant areas of tensions focused on power, organization, content and clinical usability. This study is one of the first to involve patients as co-designers of education materials in the health care context, and not only as consultants. Working as co-designers was found to be productive and in line with person-centred care philosophy, with focus on partnership and equality. The results of this study can therefore benefit both patients and other relevant stakeholders in the healthcare system in developing written patient education materials.	
Spindler, P. & Lima, B.	2018	*Editorial: The European Patients Academy on Therapeutic Innovation (EUPATI) Guidelines on Patient Involvement in Research and Development*	The European Patients' Academy on Therapeutic Innovation (EUPATI) was established as part of the partnership between the European Union and the European pharmaceutical industry, the so-called Innovative Medicines Initiative (IMI). EUPATI has set up structures to develop and disseminate accessible, well-structured, comprehensive, scientifically reliable, and user-friendly educational material for patients on the processes of medicines research and development (R&D). Like EUPATI, we believe that once armed with a deeper understanding patients, patient experts and patient advocates will be even more empowered to work effectively with the relevant authorities, healthcare professionals and industry to influence the medicines development process for	Patient Engagement with remote measurement technology

			the benefit of patients and society. Patient organisations, academia, not-for-profit organisations, and pharmaceutical companies are represented in the EUPATI partnership. Together, through reviews and a process of public consultation, sets of policies and standards for patient's involvement in medicines research and development have been published. Thus, through the collaboration between multiple stakeholder and interest groups, conflict of interest in presentations and views is managed and controlled through transparent procedures. We therefore envisage that the guidelines will be used in relevant stakeholder communities and that they will contribute to the development of internal operating procedures in organisations and companies.	
van der Weijden et al.	2018	*Developing quality criteria for patient-directed knowledge tools related to clinical practice guidelines. A development and consensus study*	Patient-directed knowledge tools such as patient versions of guidelines and patient decision aids are increasingly developed to facilitate shared decision making. In this paper, we report how consensus was reached within the Netherlands on quality criteria for development, content and governance of these tools. A 12-month development and consensus study. The consortium worked on four work packages: (a) reviewing existing criteria; (b) drafting the quality criteria; (c) safe-guarding the acceptability and feasibility of the draft criteria by participatory research in on-going tool development projects; and (d) gaining formal support from national stakeholders on the quality criteria. We reached consensus on a 8-step guidance; describing minimal quality criteria for (a) the team composition; (b) setting the scope; (c) identifying needs; (d) the content and format; (e) testing the draft; (f) finalizing and approval; (g) dissemination and application, and (h) ownership and revision. The participants of the on-going tool development projects were positive about the quality criteria in general, but divided as to the degree of detail. Whereas some	Patient engagement in clinical practice guidelines

			expressed a clear desire for procedural standards, others felt that it would be sufficient to provide only general directions. Despite the different views as to the degree of detail, consensus was reached in three stakeholder meetings. We successfully collaborated with all stakeholders and achieved formal support from national stakeholders on a set of minimum criteria for the development process, content and governance of patient-directed knowledge tools.	
Wilson et al.	2018	*Beyond study participants: a framework for engaging patients in the selection or development of clinical outcome assessments for evaluating the benefits of treatment in medical product development*	Patients are participating more actively in health care decision-making with regard to their health, as well as in the broader realm of assessing the value of medical products and influencing decisions about their registration and reimbursement. There is an increasing trend to include patients' perspectives throughout the stages of medical product development by broadening the traditional study participant role to that of an active partner throughout the process. Including patients in the selection and development of clinical outcome assessments (COAs) to evaluate the benefit of treatment is particularly important. Still, despite widespread enthusiasm, there is substantial uncertainty regarding how and when to engage patients in this process. This manuscript proposes a methodological framework for engaging patients at varying levels in the selection and development of COAs for medical product development. Framework The framework builds on the Food and Drug Administration's roadmap for patient-focused COA. Methods for engaging patients across each stage in this roadmap are summarized by levels of engagement. Opportunities and examples of patient engagement (PE) in the selection and/or development of COAs are summarized, together with best practices and practical considerations.	Patient engagment in the selection or development of clinical outcome assessments

| Zafra-Tanaka, J. H. et al. | 2019 | *Characteristics and quality of clinical practice guidelines for depression in adults: a scoping review* | Clinical Practice Guidelines (CPGs) should follow an adequate methodology using an evidence-based approach in order to provide reliable recommendations. However, little is known regarding the quality of CPGs for Depression, which precludes its adequate use by stakeholders and mental health professionals. Thus, the aim of this study was to conduct a scoping review to describe the characteristics and quality of CPGs for Depression in adults. We searched CPGs for Depression in adults in eighteen databases. We included those that were published in English or Spanish between January 2014 and May 2018 and were based on systematic reviews of the evidence. Two independent authors extracted the characteristics, type and number of recommendations, and quality (using the Appraisal of Guidelines for Research and Evaluation-II [AGREE-II]) of each included CPG. We included eleven CPGs, of which 9/11 did not include the participation of patients in the development of the CPG, 4/11 CPGs had a score ≥ 70% in the overall evaluation of AGREE-II, and 3/11 CPGs had a score ≥ 70% in its third domain (rigor of development). In addition, only 5/11 CPGs shared their search strategy, while only 4/11 listed the selected studies they used to reach recommendations, and 7/11 CPGs did not clearly state which methodology they used to translate evidence into a recommendation. Most of evaluated CPGs did not take into account the patient's viewpoints, achieved a low score in the rigor of development domain, and did not clearly state the process used to reach the recommendations. Stakeholders, CPCGs developers, and CPGs users should take this into account when choosing CPGs, and interpreting and putting into practice their issued recommendations. | Patient engagement in clinical practice guidelines for depression |
| Zhang et al. | 2017 | *Using patient values and preferences to* | There are diverse opinions and confusion about defining and including | Patient engagement in |

		inform the importance of health outcomes in practice guideline development following the GRADE approach	patient values and preferences (i.e. the importance people place on the health outcomes) in the guideline development processes. This article aims to provide an overview of a process for systematically incorporating values and preferences in guideline development. In 2013 and 2014, we followed the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to adopt, adapt and develop 226 recommendations in 22 guidelines for the Ministry of Health of the Kingdom of Saudi Arabia. To collect context-specific values and preferences for each recommendation, we performed systematic reviews, asked clinical experts to provide feedback according to their clinical experience, and consulted patient representatives. We found several types of studies addressing the importance of outcomes, including those reporting utilities, non-utility measures of health states based on structured questionnaires or scales, and qualitative studies. Guideline panels used the relative importance of outcomes based on values and preferences to weigh the balance of desirable and undesirable consequences of alternative intervention options. However, we found few studies addressing local values and preferences.	practice guideline development

APPENDIX 2 – Web research

2.1 SYNaPsE

SYNaPsE - Patient Engagement Mapping Tool[70] is a platform that promotes and synergise patient engagement. In order to do that, they have been developed 4 tools: a search engine to explore the global patient engagement initiatives scene, an experts network to showcase experience and connect with like-minded people, an organisation repository to discover what other organisations are doing in the patient engagement field, and a resource library that could be already interesting in the library search.

2.1.1 Action plan and method

The search on SYNaPsE has been assigned to EY, who has completed the following tasks:

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[70] https://involvement-mapping.patientfocusedmedicine.org/

First release in D1.3:

1. Analyze the initiatives resulting from searching SYNaPsE using the keyword "Multiple Sclerosis"
2. Select the initiatives resulting from this search that engaged PwMS or that has the potential to engage them
3. Categorize the selected initiatives (first selection)

Second release in D1.4:

4. Analyze and select the initiatives resulting from searching SYNaPsE with a set of qualitative selection criteria already available in the platform, beyond the mere research of those initiatives that might relate to MS. The purpose is to analyze how patient engagement is carried out also in relation to other brain diseases
5. Select those initiatives that might have the potential to engage PwMS
6. Include results of applying specific selection criteria and filters to the database in D1.4 Consolidated Landscape analysis. Selection criteria in the second selection of initiatives using the SYNaPsE filters includes:
   o PARTNERSHIP TYPE, optioning in relation to Inform, Consult, Involve and Co-design
   o PRIMARY FOCUS, optioning in relation to Research, Organization / System development, Access, Policy and Gap Analysis (excluding Education and Care Delivery)

Figure A3. SYNaPsE filters: PARTNERSHIP TYPE and PRIMARY FOCUS.

The *MULTI-ACT_WP1_Landscape_analysis_D1.4_Appendix 2_SYNAPSE_v0.2* contains list and categorization of PE experiences resulting by searching SYNaPsE with Multiple Sclerosis keyword and SYNaPsE filters.

1. Sheet 2.a List of PE experiences resulting by searching SYNaPsE with Multiple Sclerosis keyword
2. Sheet 2.b List of PE experiences resulting by searching SYNaPsE with qualitative options

2.1.2 Results

The web platform has been consulted either for PE experience related to MS and for other brain diseases[71]. 21 initiatives have been selected, only one directly related to MS[72].

The initiatives that have been identified on the SYNaPsE Platform involve patients at different levels: 2 initiatives have an "inform" approach[73]; 4 initiatives have a "consult" approach[74] ; 9 initiatives have

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[71] The excel file collecting the selected PE initiatives is available in Appendix 2 and in Appendix 3.

[72] "Multiple Sclerosis Outcome Assessments Consortium".

[73] Patient Centered Drug Development: Engage and CISCRP; "From Anecdotal to Actionable: The Case for Patient Perspective Data"

[74] Multiple Sclerosis Outcome Assessments Consortium, Patient Partner Project; MDIC Framework for Incorporating Information on Patient Preferences Regarding Benefit and Risk into Regulatory Assessments of New Medical Technology, PFMD - Patient Focused Medicines Development

an "involve" approach[75]; 4 initiative seem to implement a "co-design" approach with the patients' community[76].

2.2 ENGAGE2020 – Action Catalogue

Engage2020 Action Catalogue[77] is a tool that presents 57 stakeholder engagement methods gathered and analysed by the Engage2020 project[78]. Engage2020 explored current stakeholder engagement concepts and practices, with a focus on civic society and research projects[79]. The engagement methods selected through the analysis of the Action Catalogue are supposed to be used as lessons learnt from projects that used facilitation and stakeholder engagement methods. Only methods that could be used in the PE R&I path had been analysed[80].

2.2.1 Selection of methods

In order to perform a preliminary selection of the methods, DiA and FISM searched the Action Catalogue selecting specific criteria for each area of the R&I Path (section 2), as suggested by Lars Klüver, Coordinator of Engage2020 project and member of the PEG.

The file titled *MULTI-ACT_WP1_Landscape_analysis_D1.4_Appendix_3_Engage2020_v0.2* contains preliminary criteria and selected methods. t is composed by four sheets which are included hereafter and also attached in excel format for the sake of readability.

- Criteria for searching the ActionCatalogue
- Preliminary test of criteria and findings
- List and categorization of public engagement methods as lessons learnt in (including background D1.3)

2.2.2 Action plan and method

In order to understand the Action Catalogue prioritization tool, Engage2020 publications[81] were consulted. Differences in terminology regarding the level of engagement and project stages were noted and taken into account. Lars Klüver who coordinates the Engage2020 project (PEG member),

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[75] Patient Groups & Clinical Trials (PGCT) Project, Share4Rare; First systematic literature review, planned and conducted with patient experts, on patient involvement in preparing clinical trial peer-reviewed publications or results summaries, Kids Barcelona, Product Development Patient Insights, R&D Patient Engagement Strategy and Key Priorities, Co-creation of the Patient Engagement "Meta-Framework", IMI PARADIGM, 1st European Patient Groups Advisory Board meeting for Leber's Hereditary Optic Neuropathy (LHON)

[76] Patient membership in EMA management board and scientific committees; IMI PARADIGM, Recommendations for Patient Research Partners Involvement, SPOR - Strategy for Patient-Oriented Research.

[77] http://actioncatalogue.eu/search

[78] http://engage2020.eu/news/

[79] This task has been assigned to DiA.

[80] For the Action plan and methods see Appendix 3.

[81] http://engage2020.eu/media/D3-2-Public-Engagement-Methods-and-Tools-3.pdf

was also consulted regarding the prioritization and selection methodology. The default importance was set as 50 on the scale of 0-100. Engagement is highly sensitive to context in terms of what is possible and what works best; therefore, suitability of the methods selected with the help of the tool for the MULTI-ACT context was additionally assessed based on their long description

The action of choosing a method relies on the purpose mentioned in Section 3 and on the following questions.

2.2.3 Questions

- Considering the scope of the Landscape Analysis (Section 3), are some public engagement experiences relevant for the development of the PE guideline D1.5?
- Does the ActionCatalogue contain methods that can be useful for enabling PE in the phases of the 7-steps R&I path?
- Were the selected methods applied to patient community as specific stakeholder target of the engagement?

The main actions put in place to extract suitable methods from Engage2020 initiative have been:

- Choosing specific criteria for each area of the 7-steps R&I Path (see Appendix 3, sheet n.1)
- Searching the catalogue with the criteria consolidated by the PEG member Lars Klüver (a search for each area). Relative importance of the chosen criteria was left at the default level. The criteria not described in the Appendix 3 were not set. The default importance of each criterion (50%) was left unchanged.
- Select the initiatives ranked above 3.0 for each area and include them in the database (see Appendix 3, sheet n. 2).
- Removing the methods that, despite filtering, are not suitable for MULTI-ACT. Action Catalogue does not include a criterion related to patients, who are quite a unique group to engage.
- Select methods relevant for MULTI-ACT scope and compile the qualitative description for the selected methods, focusing on potential applicability for specific steps of the R&I Critical Path. (see Appendix 3, sheet n. 3).

2.2.4 Literature review of methods

Literature review was performed in a twofold process which included identification of relevant papers based on the keywords and preliminary shortlisting them based on the analysis of the content. With that in mind the methodology consists of:

A. Criteria for searching relevant papers
B. Criteria for shortlisting relevant papers

Please find below the criteria used for performing the literature review.

2.2.5 Criteria for searching relevant papers

1. **Topic:** *Patient engagement techniques in health research.*

2. ***Timeframe:*** *to start looking from 2018 (include earlier years if there are no results or they are not satisfactory)*
3. ***Language:*** *English*
4. ***Clouds of keywords:***
   a) ***Name of engagement technique (only one per each search) with variants:*** *Deliberative Online Forum (Deliberative Forum, Deliberation Forum, Deliberative Fora…), Delphi Method (Delphi), e-conference (e-conferencing, web conference), Science Theatre (Science Theater), World Café (World Cafe), Focus Group (Focus Groups), Distributed Dialogue, Deep Democracy - The Lewis Method (Deep Democracy), Crowd Wise, Consensus Conference, Citizen Summit (Citizens Summit), Citizens Hearing (Citizen Hearing).*
   b) *AND **Patient** (OR patients)*
   c) *AND **Engagement** (OR Involvement)*
   d) *AND **Research** (OR R&I, Research & Innovation, RR&I)*
5. ***Sources:***
   a) <u>*Free sources:*</u> *Pubmed; Google Scholar, Wiley Online Library, Mendeley*
   b) <u>*Subscription sources:*</u> *Cochrane Library; ISI web of science; Scopus*
1. ***Paper type:*** *review, original article, letters, comments, congress abstract, etc.*

2.2.6 Preliminary analysis and exclusion criteria

Qualitative selection of papers was based on reading the abstracts. Sometimes, more in-depth analysis was required to determine whether the method in question was actually used (e.g. "consensus conferences" in the medical field serve to establish a common understanding or guidelines, but they do not necessarily use the "consensus conference" method).

Exclusion criteria:

- the engagement technique was not used to engage patients (but e.g. only experts)
- it was not possible to determine whom the technique was used to engage
- it was not possible to establish whether method described in an article matched the one in the Action Catalogue (e.g. "deliberative methods" could not be unequivocally interpreted as Deliberative Online Forum).
- patients' engagement was not related to research or trials, e.g. they were engaged in local health policy.

2.2.7 Collection of papers

Consensus Conference

1. Bunn F, Goodman C, Jones PR, et al. Managing diabetes in people with dementia: a realist review. Health Technol Assess (Rockv). 2017;21(75):1-140. doi:10.3310/hta21750
2. Bunn F, Goodman C, Reece Jones P, et al. What works for whom in the management of diabetes in people living with dementia: a realist review. BMC Med. 2017;15(1):141. doi:10.1186/s12916-017-0909-2
3. Klaprat N, MacIntosh A, McGavock JM. Gaps in Knowledge and the Need for Patient-Partners in Research Related to Physical Activity and Type 1 Diabetes: A Narrative Review. Front Endocrinol (Lausanne). 2019;10. doi:10.3389/fendo.2019.00042

4. Peltzer-Jones J, Nordstrom K, Currier G, Berlin J, Singh C, Schneider S. A Research Agenda for Assessment and Management of Psychosis in Emergency Department Patients. West J Emerg Med. 2019;20(2):403-408. doi:10.5811/westjem.2019.1.39263

5. Sadiqi S, Lehr AM, Post MW, et al. Development of the AOSpine Patient Reported Outcome Spine Trauma (AOSpine PROST): a universal disease-specific outcome instrument for individuals with traumatic spinal column injury. Eur Spine J. 2017;26(5):1550-1557. doi:10.1007/s00586-017-5032-8

Focus Groups

1. Armstrong MJ, Mullins CD, Gronseth GS, Gagliardi AR. Recommendations for patient engagement in guideline development panels: A qualitative focus group study of guideline-naïve patients. Ito E, ed. PLoS One. 2017;12(3):e0174329. doi:10.1371/journal.pone.0174329

2. Brighton LJ, Pask S, Benalia H, et al. Taking patient and public involvement online: qualitative evaluation of an online forum for palliative care and rehabilitation research. Res Involv Engagem. 2018;4(1):14. doi:10.1186/s40900-018-0097-z

3. Doria N, Condran B, Boulos L, Curtis Maillet DG, Dowling L, Levy A. Sharpening the focus: differentiating between focus groups for patient engagement vs. qualitative research. Res Involv Engagem. 2018;4(1):19. doi:10.1186/s40900-018-0102-6

4. Faulkner M, Alikhaani J, Brown L, et al. Exploring Meaningful Patient Engagement in ADAPTABLE (Aspirin Dosing. Med Care. 2018;56:S11-S15. doi:10.1097/MLR.0000000000000949

5. Haynes SC, Rudov L, Nauman E, Hendryx L, Angove RSM, Carton T. Engaging Stakeholders to Develop a Patient-centered Research Agenda. Med Care. 2018;56:S27-S32. doi:10.1097/MLR.0000000000000785

6. Köpke S, Giordano A, Veronese S, et al. Patient and caregiver involvement in the formulation of guideline questions: findings from the European Academy of Neurology guideline on palliative care of people with severe multiple sclerosis. Eur J Neurol. 2019;26(1):41-50. doi:10.1111/ene.13760

7. Lacerda EM, McDermott C, Kingdon CC, Butterworth J, Cliff JM, Nacul L. Hope, disappointment and perseverance: Reflections of people with Myalgic encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) and Multiple Sclerosis participating in biomedical research. A qualitative focus group study. Heal Expect. January 2019. doi:10.1111/hex.12857

8. Lee DS, Armstrong R, Mohamed S. Patient engagement in a trial testing a new strategy of care for acute heart failure. Can Med Assoc J. 2018;190(Suppl):S34-S36. doi:10.1503/cmaj.180462

9. Matthews AK, Rak K, Anderson E, et al. Evaluation of 3 approaches for increasing patient engagement in clinical research: Feedback from a community engagement advisory board. J Clin Transl Sci. 2018;2(1):14-19. doi:10.1017/cts.2018.12

10. Pickett J, Murray M. Editorial: Patient and public involvement in dementia research: Setting new standards. Dementia. 2018;17(8):939-943. doi:10.1177/1471301218789290

11. Poureslami I, Pakhale S, Lavoie KL, et al. Patients as research partners in chronic obstructive pulmonary disease and asthma research: Priorities, challenges and recommendations from asthma and COPD patients. Can J Respir Crit Care, Sleep Med. 2018;2(3):138-146. doi:10.1080/24745332.2018.1443294

12. Rising KL, LaNoue M, Gentsch AT, et al. The power of the group: comparison of interviews and group concept mapping for identifying patient-important outcomes of care. BMC Med Res Methodol. 2019;19(1):7. doi:10.1186/s12874-018-0656-x

13. Rutten LJF, Morris M, Schrader L, et al. Approaching patient engagement in research: what do patients with cardiovascular disease think? Patient Prefer Adherence. July 2015:1061. doi:10.2147/PPA.S84980

14. Simacek KF, Nelson T, Miller-Baldi M, Bolge SC. Patient engagement in type 2 diabetes mellitus research: what patients want. Patient Prefer Adherence. 2018;Volume 12:595-606. doi:10.2147/PPA.S159707

15. Stuhlfauth S, Knutsen IR, Foss C. Coming from two different worlds-A qualitative, exploratory study of the collaboration between patient representatives and researchers. Heal Expect. February 2019. doi:10.1111/hex.12875

Delphi Method

1. Baines RL, Regan de Bere S. Optimizing patient and public involvement (PPI): Identifying its "essential" and "desirable" principles using a systematic review and modified Delphi methodology. Heal Expect. 2018;21(1):327-335. doi:10.1111/hex.12618

2. Biggane AM, Brading L, Ravaud P, Young B, Williamson PR. Survey indicated that core outcome set development is increasingly including patients, being conducted internationally and using Delphi surveys. Trials. 2018;19(1):113. doi:10.1186/s13063-018-2493-y

3. Callis Duffin K, Merola JF, Christensen R, et al. Identifying a Core Domain Set to Assess Psoriasis in Clinical Trials. JAMA Dermatology. 2018;154(10):1137. doi:10.1001/jamadermatol.2018.1165

4. Collins M, Long R, Page A, Popay J, Lobban F. Using the Public Involvement Impact Assessment Framework to assess the impact of public involvement in a mental health research context: A reflective case study. Heal Expect. 2018;21(6):950-963. doi:10.1111/hex.12688

5. Dinglas VD, Faraone LN, Needham DM. Understanding patient-important outcomes after critical illness. Curr Opin Crit Care. 2018;24(5):401-409. doi:10.1097/MCC.0000000000000533

6. Dos Santos F, Drymiotou S, Antequera Martin A, et al. Development of a core outcome set for trials on induction of labour: an international multistakeholder Delphi study. BJOG An Int J Obstet Gynaecol. 2018;125(13):1673-1680. doi:10.1111/1471-0528.15397

7. Fish R, Sanders C, Adams R, et al. A core outcome set for clinical trials of chemoradiotherapy interventions for anal cancer (CORMAC): a patient and health-care professional consensus. Lancet Gastroenterol Hepatol. 2018;3(12):865-873. doi:10.1016/S2468-1253(18)30264-4

8. Hamilton CB, Hoens AM, McQuitty S, et al. Development and pre-testing of the Patient Engagement In Research Scale (PEIRS) to assess the quality of engagement from a patient perspective. Pomey M-P, ed. PLoS One. 2018;13(11):e0206588. doi:10.1371/journal.pone.0206588

9. Hepworth LR, Rowe FJ. Using Delphi methodology in the development of a new patient-reported outcome measure for stroke survivors with visual impairment. Brain Behav. 2018;8(2):e00898. doi:10.1002/brb3.898

10. Johnson MO, Neilands TB, Koester KA, et al. Detecting Disengagement from HIV Care Before It's Too Late. JAIDS J Acquir Immune Defic Syndr. February 2019:1. doi:10.1097/QAI.0000000000002000

11. Lacerda EM, McDermott C, Kingdon CC, Butterworth J, Cliff JM, Nacul L. Hope, disappointment and perseverance: Reflections of people with Myalgic encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) and Multiple Sclerosis participating in biomedical research. A qualitative focus group study. Heal Expect. January 2019. doi:10.1111/hex.12857

12. Laidsaar-Powell R, Butow P, Boyle F, Juraskova I. Facilitating collaborative and effective family involvement in the cancer setting: Guidelines for clinicians (TRIO Guidelines-1). Patient Educ Couns. 2018;101(6):970-982. doi:10.1016/j.pec.2018.01.019

13. Leyenaar JK, Rizzo PA, Khodyakov D, Leslie LK, Lindenauer PK, Mangione-Smith R. Importance and Feasibility of Transitional Care for Children With Medical Complexity: Results of a Multistakeholder Delphi Process. Acad Pediatr. 2018;18(1):94-101. doi:10.1016/j.acap.2017.07.005

14. Leyenaar JK, Shevenell M, Rizzo PA, Hill VL, Lindenauer PK. Multi-Stakeholder Informed Guidelines for Direct Admission of Children to Hospital. J Pediatr. 2018;198:273-278.e7. doi:10.1016/j.jpeds.2018.03.007

15. Llewellyn A, McCabe CS, Hibberd Y, et al. Are you better? A multi-centre study of patient-defined recovery from Complex Regional Pain Syndrome. Eur J Pain. 2018;22(3):551-564. doi:10.1002/ejp.1138

16. Morbey H, Harding AJE, Swarbrick C, et al. Involving people living with dementia in research: an accessible modified Delphi survey for core outcome set development. Trials. 2019;20(1):12. doi:10.1186/s13063-018-3069-6

17. Ní Shé É, Morton S, Lambert V, et al. Clarifying the mechanisms and resources that enable the reciprocal involvement of seldom heard groups in health and social care research: A collaborative rapid realist review process. Heal Expect. February 2019:hex.12865. doi:10.1111/hex.12865

18. Odgers HL, Tong A, Lopez-Vargas P, et al. Research priority setting in childhood chronic disease: a systematic review. Arch Dis Child. 2018;103(10):942-951. doi:10.1136/archdischild-2017-314631

19. Poulin P, Shergill Y, Romanow H, et al. Researching what matters to improve chronic pain care in Canada: A priority-setting partnership process to support patient-oriented research. Can J Pain. 2018;2(1):191-204. doi:10.1080/24740527.2018.1433959

20. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis. Neurology. 2018;90(17):777-788. doi:10.1212/WNL.0000000000005347

21. Smith AB, Chisolm S, Deal A, et al. Patient-centered prioritization of bladder cancer research. Cancer. 2018;124(15):3136-3144. doi:10.1002/cncr.31530

22. Toledo-Chávarri A, Alvarez-Perez Y, Triñanes Y, et al. Toward a Strategy to Involve Patients in Health Technology Assessment in Spain. Int J Technol Assess Health Care. March 2019:1-7. doi:10.1017/S0266462319000096

World Café

1. Kim KK, Helfand M. Engagement in PCORnet Research Networks. Med Care. 2018;56:S1-S3. doi:10.1097/MLR.0000000000000958

2. Kimminau KS, Jernigan C, LeMaster J, et al. Patient vs. Community Engagement. Med Care. 2018;56:S53-S57. doi:10.1097/MLR.0000000000000772

3. MacFarlane A, Galvin R, O'Sullivan M, et al. Participatory methods for research prioritization in primary care: an analysis of the World Café approach in Ireland and the USA. Fam Pract. September 2016:cmw104. doi:10.1093/fampra/cmw104

4. Snow ME, Tweedie K, Pederson A. Heard and valued: the development of a model to meaningfully engage marginalized populations in health services planning. BMC Health Serv Res. 2018;18(1):181. doi:10.1186/s12913-018-2969-1

5. Zhu H, Thomassen S. User-driven innovation and technology-use in public health and social care: A systematic review of existing evidence. J Innov Manag. 2018;6(2):38-169. http://hdl.handle.net/10216/113222.

Citizens hearing (suggested by PF)

1. https://understandingpatientdata.org.uk/sites/default/files/2019-03/Public%20attitudes%20study%20summary.pdf

2. https://www.alliance-scotland.org.uk/blog/events/citizens-hearing-on-the-right-to-health/

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1. Doria, Nicole, Brian Condran, Leah Boulos, Donna G. Curtis Maillet, Laura Dowling, and Adrian Levy. 2018. "Sharpening the Focus: Differentiating between Focus Groups for Patient Engagement vs. Qualitative Research." *Research Involvement and Engagement* 4 (1): 19. https://doi.org/10.1186/s40900-018-0102-6.

2. Hall, Deborah Ann, Harriet Smith, Eithne Heffernan, and Kathryn Fackrell. 2018. "Recruiting and Retaining Participants in E-Delphi Surveys for Core Outcome Set Development: Evaluating the COMiT'ID Study." Edited by Bridget Young. *PLOS ONE* 13 (7): e0201378. https://doi.org/10.1371/journal.pone.0201378.

3. Humphrey-Murto, Susan, and Maarten de Wit. 2019. "The Delphi Method—more Research Please." *Journal of Clinical Epidemiology* 106 (February): 136–39. https://doi.org/10.1016/j.jclinepi.2018.10.011.

2.2.8 Results

Based on the criteria set for each area of the R&I path[82], 13 methods were selected: Citizen summit, Citizens Hearing, Consensus Conference, Crowd Wise, Deep Democracy – The Lewis Method, Distributed Dialogue, E-conference (tool), Focus Groups (tool), Future Workshop, Hackathon, Perspective Workshop, Science Theatre, World Café. Only three methods appeared related to our issue[83].

Moreover, the identified methods are most *offline* methods (engagement without using computers, smart phones, tablets, or other internet-connected device/digital systems). If we want to enable effective patient engagement, the individual patients' perspectives need to be captured overtime and also turned into a perspective that works at population level, avoiding the frequently left out and underrepresentation. Online methods (engagement through computers, smart phones, tablets, or other internet-connected device/digital systems) have the advantage to provide the possibility to outreach and involve a broader audience. However, they also have the risk to exclude groups that are not using or don't have access to online systems/platform. To enable effective patient engagement, we need both off and online methods.

Within this frame DIA run two tests for seeking in the Action Catalogue additional methods that are online-based. The analysis has been performed for all the stakeholders together and for each organizer separately with „context" set to online-only at 100% importance in order to eliminate non-online-based methods from the top of the list. Many methods returned by the tool that were above the 3% as indicated by the filtering tool on the Action Catalogue webpage. However, mainly offline methods made it to the top (e.g. Focus Group). Based on this result, DIA run a second test filtering the initiatives using an additional criterion of „**Is the method applicable in online setting?"** to select only the relevant ones.

Online methods retrieved by the tool are: E-conference, Delphi Method, Hackathon and Deliberative Online Forum. Hackathon and Only e-conference had appeared in the general method search in D1.3. Hackathon was excluded in a direct assessment of applicability to MULTI-ACT. The remaining methods were subsequently described in detail, and assessed for applicability in the steps of the R&I Path.

2.2.8 Literature review of methods to verify applicability of the identified methods

In order to identify the examples of implementation of the above selected methods of patient related environment, a literature review was conducted. It included a twofold process consisting of identifying relevant papers based on the keywords and then shortlisting them base on the analysis of the content (see Appendix 3).

No examples of use of the following methods for patients in health research were found: **Citizen summit, Crowd Wise, Deep Democracy – The Lewis Method, Distributed Dialogue, Science Theatre and E-conference (tool)**. No examples were found even for use of the methods in the healthcare sector in general.

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[82] Listed in the Appendix n.3 Sheet n.1.

[83] For details, please see Appendix 3, Sheet n. 2.

Consensus Conference

In the medical field, consensus conferences gathered practitioners and experts to build a consensus on either health knowledge (e.g. diagnostic criteria) or practices (e.g. best practices, treatment protocols). The format of these consensus conferences differs from event to event and cannot always be equated with the Consensus Conference engagement method, which has wider application. This literature review found only a few papers describing engagement of patients using the consensus conference method in the course of research with the view of formulating guidelines or core outcomes.

Focus Group is undoubtedly the most widespread technique of engagement. It is rooted in qualitative studies, where it is a standard way of gathering patients' input and learning about their views and experiences. Its scope of application has widened in recent years, with the method being used for decision-making and guidelines formulation (Doria et al. 2018), not without some criticism regarding insufficient separation of these two functions.

Delphi Method, along with modified Delphi Method, emerged as the second most popular patient engagement technique after Focus Group. Initially designed for panels of experts to arrive at decisions without influencing one another, it is increasingly used for including patients, either forming their own panel, or together with experts and other stakeholders (e.g. community, healthcare professionals) (Hall et al. 2018). Delphi can be applied online and it often is. Delphi Method appears to be a popular tool for prioritisation of core-outcomes in patient-centred guidelines (Humphrey-Murto and de Wit 2019), often in multi-stakeholder initiatives. Consequently, Delphi is of special interest for MULTI-ACT.

World Café

Research indicated that **World Café** was not a popular method of engaging patients in the healthcare context, although some examples emerged. This may be in part due to the open-ended feature of the method. It is suitable for generating and sharing ideas, but does not guarantee a structured result, and does not support structured decision-making.

Citizens Hearing

Some examples shows how citizen hearing has been used to investigate the preferences of patients with respect to specific issues such as for example the use of health data[84] and the status of health rights[85].

This method showed enhanced understanding and awareness of the barriers to achieving positive solutions to help overcome them; and seek commitment on a joint plan for monitoring and acting on the topics.

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[84]https://understandingpatientdata.org.uk/sites/default/files/2019-03/Public%20attitudes%20study%20summary.pd;

https://www.connectedhealthcities.org/chc-hub/public-engagement/citizens-juries-chc/citizens-juries/

[85] https://www.alliance-scotland.org.uk/blog/events/citizens-hearing-on-the-right-to-health/

2.2.9 Additional methods and thoughts by PF, PEG, EAB

This paragraph intends to capture main insights from survey and interviews of PEG, PF and EAB on the public engagement methods identified as relevant for patient engagement.

PF members suggest to consider the **Community Advisory Board** (CAB) method, one of the methods used in Leukaemia communities[86] and also by the HIV movement. The Community Advisory Board is a working group where patient advocates leaders from all world regions, work together to improve outcomes of patients covering patient information, research priorities, access to treatment and capacity building in the patients' community.

2.3 European repositories

2.3.1 CORDIS EU research results

In the active European projects (timeframe: since 2014), n° 193 are marked by European officers as taking an RRI approach with primarily focus on public engagement. Out of these, n. 80 are under the Societal Challenge: SC1 E-Health, Well-being and Ageing: n.7 PM, n.10 HCO, n.8 PHC, n.1 Health.

For the purpose of WP1 we selected a list of public engagement projects from the CORDIS European commission portal (https://cordis.europa.eu/) and assigning them relevance with respect to MULTI-ACT objectives.

The relevance has been established according to the grade of involvement of people, the health matters or frailty, and the specific topic of application in the project (ICT solutions, specific pathologies, etc.).

The **high relevance group** includes all the projects that involve people in research as patients or at least as possible fragile people (i.e. elderly). The grade of involvement is very high, often is a co-creation process that is reported in the methodology of the project and these projects are strictly linked with research or research impact on society.

The **medium relevance group** includes projects where patients or vulnerable people are engaged more at a "Inform" level, but not in research or in a therapy development.

The **Low relevance group** includes the projects that have a high impact on people for other topics (i.e. Food security), however they don't engage patients.

Name of the project and G.A. number in Cordis	Health context (Y/N)	Level of people involvement (L/M/H)	Level of relevance
Cimulact (665948) https://cordis.europa.eu/project/rcn/197909_en.html	Y	H	high

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[86] https://www.cmladvocates.net/cml-cab

Sparks : engagement in research and innovation (665825) https://cordis.europa.eu/project/rcn/198208_en.html	Y	H	High
Steps STrengthening Engagement in Public health research (217605) https://cordis.europa.eu/project/rcn/89073_en.html	Y	H	High
Health Matters: A Social Science and Ethnographic Study of Patient and Professional Involvement in the Governance of Converging Technologies in Medicine (229714) https://cordis.europa.eu/result/rcn/57212_en.html	Y	H	High
Improving science advice for health in Europe, EuSANH (229716) https://cordis.europa.eu/project/rcn/90985_en.html	Y	H	High
Personalized health monitoring (PHM)- Interdisciplinary research to analyse the relationship between ethics, law and psychosocial as well as medical sciences (230602) https://cordis.europa.eu/project/rcn/91074_en.html	Y	H	High
SIFORAGE Social Innovation on active and healthy ageing for sustainable economic growth (321482) https://cordis.europa.eu/project/rcn/108750_en.html	Y	H	High
PROSO (665947) https://cordis.europa.eu/project/rcn/199714_en.html	Y	H	High
eStandards eHealth Standards and Profiles in Action for Europe and Beyond (643889) https://cordis.europa.eu/project/rcn/196620_en.html	Y	H	High
EMPATITCS EMpowering PAtients for a BeTTer Information and improvement of the Communication SystemsMedium https://cordis.europa.eu/project/rcn/200191_en.html	Y	M	Medium
SENSE-Cog Ears, Eyes and Mind: The 'SENSE-Cog Project' to improve mental well-being for elderly Europeans with sensory impairment (668648) https://cordis.europa.eu/project/rcn/200473_en.html	Y	M	Medium
RESPONSIBLE-INDUSTRY (Responsible Research and Innovation in Business and Industry in the Domain of ICT for, Health, Demographic Change and Wellbeing) (609817) https://cordis.europa.eu/result/rcn/223043_en.html	Not only	M	Medium

PROGRESSIVE STANDARDS AROUND ICT FOR ACTIVE AND HEALTHY AGEING (727802) https://cordis.europa.eu/project/rcn/205817_en.html	Not only	M	Medium
WE4AHA Widening the support for large scale uptake of Digital Innovation for Active and Healthy Ageing https://cordis.europa.eu/project/rcn/211372 en.html	Y	M	Medium
DITOs Doing It Together science (709443) https://cordis.europa.eu/project/rcn/203160_en.html	N	H	Medium
Evaluating a Combination of Immune-based Therapies to Achieve a Functional Cure of HIV Infection (731626) https://cordis.europa.eu/project/rcn/207437_en.html	Y	M	Medium
EuroStemCell European Consortium for Communicating Stem Cell Research (652796) https://cordis.europa.eu/project/rcn/194815_en.html	Y	M	Medium
INSPIRES (Innovative Social and Employment Policies for Inclusive and Resilient Labour Markets in Europe) https://cordis.europa.eu/project/rcn/210055_en.html	N	L	Low
GCOFA Stepping stone approach towards the Genetics Clinic of the Future (643439) https://cordis.europa.eu/project/rcn/194066_en.html	Y	L	Low
My-AHA My Active and Healthy Aging (689592) https://cordis.europa.eu/project/rcn/200143 en.html	Y	L	Low
City4Age (689731) https://cordis.europa.eu/project/rcn/199899_ en.html	N	L	Low
OACTIVE Advanced personalised, multi-scale computer models preventing OsteoArthritis (777159) https://cordis.europa.eu/project/rcn/212457_en.html	Y	L	Low
BigO Big data against childhood Obesity (727688) https://cordis.europa.eu/project/rcn/206067_en.html	Y	L	Low
BIG PIC NIC (710780) https://cordis.europa.eu/project/rcn/203174_en.html	N	L	Low
SciSHOPS.EU(741657) https://cordis.europa.eu/project/rcn/210053_en.html	N	L	Low
ECO-COMPASS (710543) https://cordis.europa.eu/search/result_en?q=COMPASS	N	L	Low

2.3.2 EU Health Program, EIT Health, EIP -AHA, Health INTERREG

Moreover, a keyword search for Multiple Sclerosis and Brain in other repositories of the European Commission (i.e. DG SANTE EU Health Programme[87], EIT Health[88], European Innovation Partnership on Active and Healthy Ageing (EIP on AHA)[89], Health INTERREG[90]) has produced no results for projects where patients are involved in the governance structure. Patient engagement is mainly confined to gathering patients' views and incorporate them into the project ("Consult" level).

Two projects claim to be co-produced and co-designed with patients:

- A collaborative work carried out in the frame of the B3 Action Group on Integrated Care of the EIP on AHA titled "Positive patient experience with health and care services, co-production and supported self-management" with a specific focus on evidence on innovative integrated care solutions (https://ec.europa.eu/eip/ageing/commitments-tracker/b3/23-positive-patient-experience-health-and-care-services-co-production-and_en).
- An innovative practice stored in the EIP on AHA repository (https://ec.europa.eu/eip/ageing/repository/game-based-neurological-tele-rehabilitation_en): REHABILITY is the suite of serious games for patients with Multiple Sclerosis or Parkinson disease which allows patients to take part in rehabilitation therapy both within a specialist facility and from home with continuous remote medical support.

The EIT Health funded projects in the area of brain are essentially focused on the development of diagnostic tools.

2.3.3 IMI Innovative Medicines Initiative

The Innovative Medicines Initiative (IMI) is a public-private partnership aiming to speed up the development of better and safer medicines for patients. We explored also the IMI website with particular focus on the **IMI2 – 10th Call for proposals: Topic 7: Patient perspectives in medicines lifecycle**[91], as indicated in D1.1, that suggests a list of PE experiences in the Section "Potential synergies with existing consortia". The list includes relevant national, European (both research projects as well as research infrastructure initiatives), as well as non-European initiatives.

The list of existing consortia (IMI2, Call 10th - Topic 7) has been compared with the initiatives identified with the other steps of the landscape analysis, highlighting initiatives not covered by MULTI-ACT landscape analysis, such as:

Member of MULTI-ACT advisory bodies and/or initiatives identified in the landscape analysis steps:

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[87] http://ec.europa.eu/chafea/health/programme/index_en.htm

[88] https://www.eithealth.eu/

[89] https://ec.europa.eu/eip/ageing/home_en

[90] https://www.interregeurope.eu/

[91] https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/call-documents/imi2/IMI2_Call10_TopicsText.pdf

- Patient-Centred Outcomes Research Institute (PCORI) (www.pcori.org/) – Member of MULTI-ACT Patient Forum
- Patient Focused Medicines Development (PFMD) (http://patientfocusedmedicine.org/) – Member of MULTI-ACT Patient Forum
- Faster Cures (http://www.fastercures.org/) – Member of MULTI-ACT Patient Forum
- ADAPT SMART (www.adaptsmart.eu)
- Patient Active in Research and Dialogues for an Improved Generation of Medicines PARADIGM[92] (the project that won the Grant for the IMI2, Call 10th - Topic 7)

Initiatives not identified in the landscape analysis steps:

- DIA (http://www.diaglobal.org/en/get-involved/patients)
- ISPOR (http://www.ispor.org/sigs/patientcentered/pc_engagementinresearch.aspx)
- HTAi (http://www.htai.org/interest-groups/patient-and-citizen-involvement.html)
- International Consortium for Health Outcomes (ICHOM) (www.ichom.org/)
- National Health Council (NHC) (http://www.nationalhealthcouncil.org/meaningful-patient-engagement)
- Clinical Trials Transformation Initiative (CTTI) (http://www.ctti-clinicaltrials.org/home)
- TransCelerate (http://www.transceleratebiopharmainc.com/)
- DIA-Tufts initiative on Return on Engagement (https://www.ciscrp.org/)
- AURORA project (https://www.linkedin.com/groups/8548998/profile)
- PREFER (http://imi-prefer.eu)
- EMTRAIN (www.emtrain.eu)
- New project on patient engagement in Alzheimer Disease (AD) trials (see IMI2 Call 5 Topic 5, expected start date Q4 2016)
- Big Data for Better Outcomes projects (see IMI2 Call 7 topic 7, expected start date Q1 2017)
- UBiopred (http://www.europeanlung.org/en/projects-and-research/projects/u-biopred/home)
- https://ahrq-ehc-application.s3.amazonaws.com/media/pdf/stakeholders-engagement-others_research-2012-1.pdf

In line with the IMI program, the existing PE initiatives suggested by the programs are focused on the medicine development process. The most interesting IMI funded project is indeed the one addressing the mentioned IMI2, Call 10th - Topic, the Patient Active in Research and Dialogues for an Improved Generation of Medicines PARADIGM[93]. PARADIGM is a public-private partnership and is co-led by the European Patients' Forum and EFPIA, represented both in the MULTI-ACT EAB and its mission is to provide a unique framework that enables structured and effective patient engagement and demonstrates the 'return on the engagement' for all players in the medicine development process.

Synergies with relevant IMI-funded projects will be activated via MULTI-ACT Patient Forum to benchmark growth on Patient Engagement.

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[92] https://imi-paradigm.eu/

[93] https://imi-paradigm.eu/

2.4 International initiatives beyond Europe: the Patient-Centered Outcomes Research Institute PCORI

The Patient-Centered Outcomes Research Institute (PCORI)[94], authorized and funded in the 2010 in United States with the Patient Protection and Affordable Care Act, funds comparative clinical effectiveness research for the purpose of generating evidence that helps patients and their health care providers to better understand their diagnostic and treatment options and make more informed clinical decisions. PCORI helps people make informed healthcare decisions, and improves healthcare delivery and outcomes, by producing and promoting high-integrity, evidence-based information that comes from research guided by patients, caregivers, and the broader healthcare community.

A representative from PCORI, has been contacted following the International Progressive MS Alliance Industry Forum Meeting (January 22, 2019 Washington, D.C.) in order to indicate initiatives under the PCORI funded-projects relevant for the WP1 landscape analysis.

Building on the document prepared by PCORI for the PARADIGM initiative, 5 projects from "**PCORI Research Awards CER**" portfolio demonstrate a variety of approaches and ways that engagement has had an impact on research projects and healthcare decision making.

1. Comparing Ways to Improve Daily Functioning for Stroke Survivors After They Leave the Hospital. The COMPASS Study. (https://www.pcori.org/research-results/2015/comparing-ways-improve-daily-functioning-stroke-survivors-after-they-leave)

2. Does a Stress Management Program for African-American Parents Increase Asthma Symptom-Free Days for Their Children? The BEAMS Study (https://www.pcori.org/research-results/2013/does-stress-management-program-african-american-parents-increase-asthma)

3. Comparing Different Treatments for People Who Have Had a Stroke. Patient-Centered Research into Outcomes Stroke Patients Prefer and Effectiveness Research (PROSPER) Study (https://www.pcori.org/research-results/2013/comparing-different-treatments-people-who-have-had-stroke-prosper-study)

4. Helping Caregivers and Their Children with Early Appendicitis Make Treatment Decisions with an App (https://www.pcori.org/research-results/2013/helping-caregivers-and-their-children-early-appendicitis-make-treatment)

5. The MS Minority Research Engagement Partnership Network (https://www.pcori.org/research-results/2016/ms-minority-research-engagement-partnership-network)

The "**Eugene Washington PCORI Engagement Awards**" provide capacity building funding to prepare healthcare stakeholders to work together on patient-centered outcomes research.

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[94] https://www.pcori.org/

Two Engagement Award projects Bladder Cancer Patient Survey Network for Research Prioritization[95] and Patient Empowerment through Engagement Research Training in Bladder Cancer PCOR (PEER)[96] worked to build capacity amongst these partners, and prioritize research questions so that they successfully secured a PCORI Research Award, CISTO: Comparison of Intravesical Therapy and Surgery as Treatment Options for Bladder Cancer[97].

The Bladder Cancer Advocacy Network BCAN - Patient Survey Network illustrates how an Engagement Award allowed researchers, patients and an advocacy organization to come together to prioritize research questions, train their partners, and stream the importance of engaging and involving patients throughout the research process, leading to research funding success.

Figure A4. PCORI Engagement Awards: Bladder Cancer Advocacy Network - Patient Survey Network.
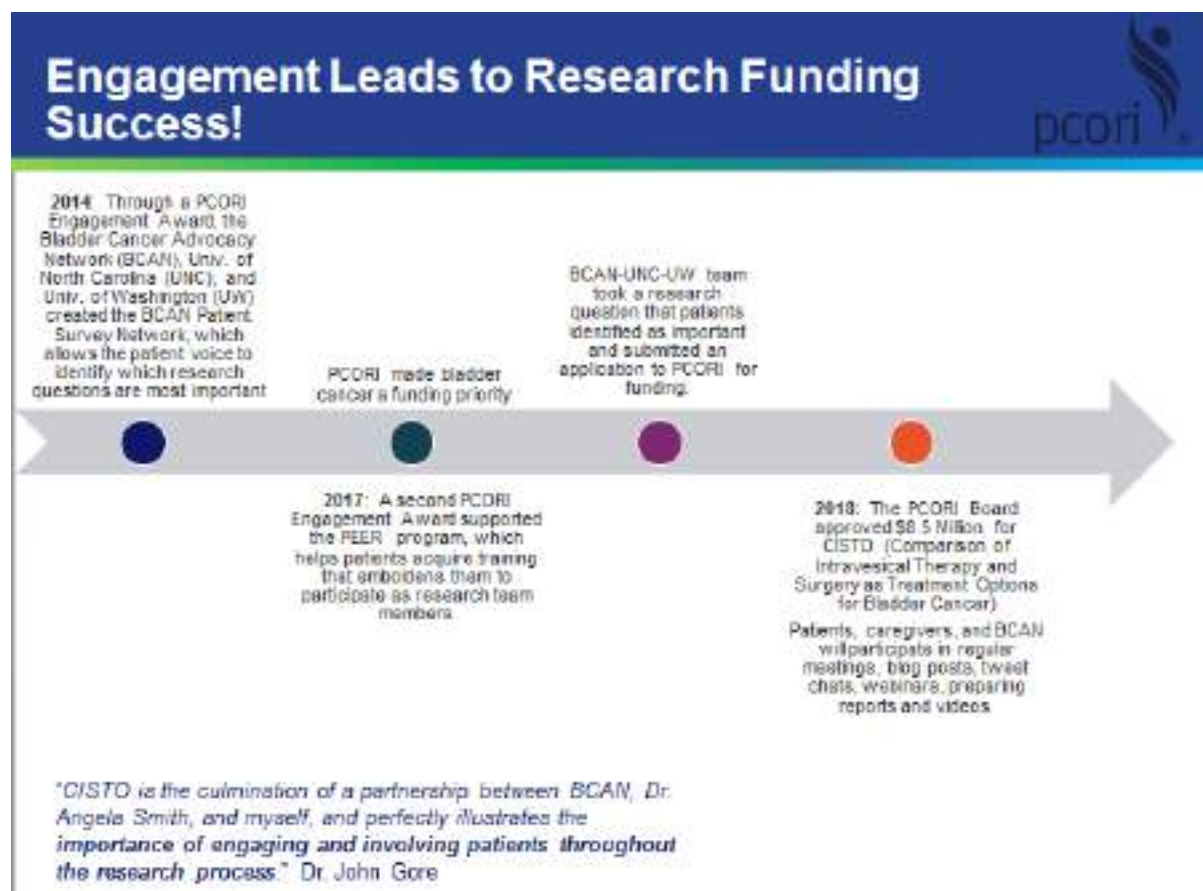
The PCORI Engagement Award "Family & Science: Bidirectional Translation of Knowledge and Need in Sex Chromosome Aneuploidy"[98], focused on building stakeholder community engagement to influence

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[95] https://www.pcori.org/research-results/2014/bladder-cancer-patient-survey-network-research-prioritization

[96] https://www.pcori.org/research-results/2017/patient-empowerment-through-engagement-research-training-bladder-cancer-pcor

[97] https://www.pcori.org/research-results/2018/cisto-comparison-intravesical-therapy-and-surgery-treatment-options-bladder

[98] https://www.pcori.org/research-results/2015/family-science-bidirectional-translation-knowledge-and-need-sex-chromosome

and redirect science toward outcomes that matter to them by listening to patients' needs, led to unexpected policy and systems change. The research team's response to patients' needs resulted in:

- Increasing Awareness about X & Y Variations
- Establishing the first Southeast Regional X & Y Support Group, Creation of a new regional multidisciplinary clinic "The eXtraordinarY Kids Clinic of Atlanta"
- Development of educational materials for physicians, schools, insurers and the justice system
- A documentary film project organized by Writer/Producer Dianne Steinkraus entitled, "Hidden In Plain Sight: Stories of Patients and Families affected by X & Y Chromosome Variations." (March 2017).

> " *The engagement process has indeed empowered patients and families to change not only research and patient-centered outcomes, but also to expand awareness and knowledge that may influence policy to their benefit.*
> **PCORI Awardee** Sharron Close, PhD;
> *Emory University Nell Hodgson Woodruff School of Nursing and AXYS*

PCORI published a **thematic analysis** of published literature from PCORI-funded research awards on the contributions of engagement "**Patient Engagement In Research: Early Findings From The Patient-Centered Outcomes Research Institute**"(Forsythe et al., 2019). Charged with ensuring that research produces useful evidence to inform health decisions, the PCORI requires investigators to engage patients and other health care stakeholders, such as clinicians and payers, in the research process. Many PCORI studies result in articles published in peer-reviewed journals that detail research findings and engagement's role in research. To inform practices for engaging patients and others as research partners, n.126 articles have been analysed in the thematic analysis that described engagement approaches and contributions to research. Many articles reported that **engagement provided valuable contributions to research feasibility, acceptability, rigor, and relevance, while a few noted trade-offs of engagement, such as using unvalidated measures to assess high-priority outcomes or alternative randomization schemes to align with partners' desires to maximize the number of people receiving a clinical intervention (**McElfish et al, 2017**;** Gesell et al. 2019)**.** The findings suggest that engagement can support more relevant research through better alignment with patients' and clinicians' real-world needs and concerns.

Moreover, as resulted also from the literature review, the **"PCORI Engagement Rubric"** provides a framework for operationalising the integration of patient engagement and other stakeholders in all phases or research. Importantly, it includes principles of engagement, definitions of stakeholder types, key considerations for planning, conducting and disseminating engaged research, potential engagement activities, and examples of promising practices from PCORI-funded projects. The Engagement Rubric illustrates how input from patient and stakeholder partners can be incorporated throughout the entire research process. The Engagement Rubric is intended to provide guidance to those planning or conducting research, merit reviewers, awardees, engagement/program officers (for creating milestones and monitoring projects), and interested patients, caregivers, patient/caregiver organisations and other stakeholders, regarding engagement in the conduct of research. The rubric provides a variety of options to incorporate engagement, where relevant, into the research process.

Applicants using the rubric can choose to include some, but not all, activities and are encouraged to include additional innovative approaches.

The Engagement Rubric relies on the six PCORI Engagement Principles:

- **Reciprocal Relationships:** This principle is demonstrated when the roles and decision-making authority of all research partners, including the patient and other stakeholder partners, are defined collaboratively and clearly stated.
- **Co-Learning:** This principle is demonstrated when the goal is not to turn patients or other stakeholder partners into researchers, but to help them understand the research process; likewise, the research team will learn about patient-centeredness and patient/other stakeholder engagement, and will incorporate patient and other stakeholder partners into the research process.
- **Partnerships:** This principle is demonstrated when time and contributions of patient and other stakeholder partners are valued and demonstrated in fair financial compensation, as well as in reasonable and thoughtful requests for time commitment by patient and other stakeholder partners. When projects include priority populations, the research team is committed to diversity across all project activities and demonstrates cultural competency, including disability accommodations, when appropriate.
- **Transparency, Honesty, and Trust:** These principles are demonstrated when major decisions are made inclusively and information is shared readily with all research partners. Patients, other stakeholders, and researchers are committed to open and honest communication with one another.

APPENDIX 3 – Survey of MS organisations

International Multiple Sclerosis Federation MSIF (www.msif.org)

MSIF is a unique global network of MS organisations with 48 members from around the world and links to many others. MSIF, established in 1967, links the activities of MS organisations in 95 countries worldwide, stimulating international cooperation. Their mission is to lead the global MS movement to improve the quality of life of people affected by MS and to support better understanding of the treatment of MS. They bring together the work of more than 100 MS organisations to deliver programs to help people affected by MS around the world. They strengthen those organisations in countries where there is little support for people with MS. Together they lead the fight against MS and work to improve the quality of life of people affected by MS in more than 90 countries. MSIF, as an umbrella organization of MS organisations, through cooperation with and among its Members, the International Research Staff Network (which includes staff from all the key MS organisations amongst the membership that have common research agendas and dedicated research infrastructures) and with their advisors from their International Medical and Scientific Board, stimulates, supports and partners international collaborations in areas of greatest need and promise for people with MS.

Figure A5. MSIF member organisations.

MSIF and MS members organisations focus their efforts on actions that will contribute to a world in which people with and affected by MS are able to benefit from. In order to foster collaboration among relevant stakeholders towards the common goal to "Better scientific understanding of MS and more ways to treat it - leading one day to prevention and a cure".

MSIF's strategy for 2017-2021 under its aim of Better Scientific Understanding Leading to New Ways to Treat, Prevent and Stop MS[99], identified the priority of "Ensuring people affected by MS are part of strategic research decision making processes across the Federation." (see figure A6).

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[99] http://www.msif.org/wp-content/uploads/2017/08/MSIF-Strategy-2017-2021-web.pdf

Figure A6. MSIF Strategic Agenda 2017-2021, Objective n.1, Action n.3.

European MS Platform EMSP www.emsp.org

EMSP brings together MS activists from across Europe, relying on a growing network of 40 member organisations from 35 European countries. EMSP is the MS organization that aims to influence health and other EU policies in collaboration with MSIF and MS Society members to integrate the global agenda perspectives. EMSP capacity was proven again in 2014, when EMSP received a European Commission grant to produce and promote a Pact for Employment supporting people with MS and other neurodegenerative diseases. At the same time, EMSP continues to strengthen ties with other patient organisations and federations – such as the European Patients' Forum (EPF), the European Federation for Neurological Associations (EFNA) and the European Brain Council (EBC). They are also in a position to leverage their direct access to the European regulator for pharmaceutical products, the European Medicines Agency (EMA).

3.1 Action plan and methodology

Tim Coetzee (National MS Society, PEG member) and Federica Balzani (EMSP, PEG member) have been asked to represent WP1 activities from MSIF RSN and EMSP respectively. Both in person (MSIF RSN, Washington on January 22nd 2019) and virtual (EMSP, February 2019) meetings have been held to introduce the MULTI-ACT project and the expectation for their engagement in the WP1 landscape analysis.

In particular, MSIF RSN and EMSP have been asked:
- to provide their feedback on the glossary, questions and database structure in order to co-design the survey
- to provide a short description of what it means to engage patients in research in the MS Societies they represent
- to answer to the survey/questionnaire (co-designed by MULTI-ACT and the MSIF RSN)
- to fill the database with PwMS engagement initiatives of the MS Society they represent

The *MULTI-ACT_WP1_Landscape_analysis_D1.4 Appendix 3* contains the surveys protocols and databases collecting experiences of PwMS engagement.

APPENDIX 4 – Patient Forum group interview

This appendix provides the context in which the group interview with stakeholders has been carried out, as well as the purposes and the characteristics of the interview.

4.1 Background and purposes of the group interview

Considering that the MULTI-ACT WP1 aims to consolidate the landscape analysis performed via literature review and web search and finally direct the work of WP1 towards the design of innovative Patient Engagement strategies and guidelines, the purposes of the group interview have been:

- To engage stakeholders in the "co-construction" of the MULTI-ACT Patient Engagement Strategy, with the characteristics stated above.

- To produce collective awareness and a common understanding of experiences of Patient Engagement in R&I for the identification of gaps and prioritization across disease areas.

- To achieve the objectives of **Task 1.1 Evaluation of patient engagement procedures across R&I** (collection of patient engagement experiences, identification of gaps and prioritization of actions) by corroborating and complementing the results of the literature review and web search with the knowledgeable inputs provided by key stakeholders.

- To collect their views and directions on the work to be done towards the completion of **Task 1.2 Expectation, criteria for patient engagement co-developed by stakeholders** (co-design criteria, recommendations and rules for patient engagement addressing gaps).

Specifically, to achieve those purposes, the group interview included guiding questions aimed at understating and build awareness on the following specific issues:

- The perspective of key stakeholders' representing different brain diseases in relation to the R&I phases and processes where Patient Engagement is instrumental to maximize the impact of research on outcomes that matter to patients, towards the conceptualization of an innovative path for Patient Engagement (i.e. the 7-steps R&I path) in Deliverables D1.5 (preliminary version) and later one D1.6 (final version).

- The existing experiences of patient engagement in brain diseases' areas toward the implementation of the landscape analysis include in this deliverable.

- The perception and relevance on measurements of Patient Engagement's effectiveness, based on evidence and existing experiences.

- The perception and relevance of evidence-based methods for Patient Engagement, based on existing experiences.

- Experiences and visions on the methods and tools for Patient Engagement as well as relevant initiatives collected in the literature review and web search and the degree of comprehensiveness and completeness of the analysis made so far.

The group interview allowed MULTI-ACT to integrate the landscape analysis with the voice of «authoritative» stakeholders towards the co-creation of the MULTI-ACT Patient Engagement Strategy and guidelines. The next task of Work Package 1 (Deliverable D1.5) will design the Preliminary Patient Engagement Guidelines building on the insights received from this Patient Forum group interview.
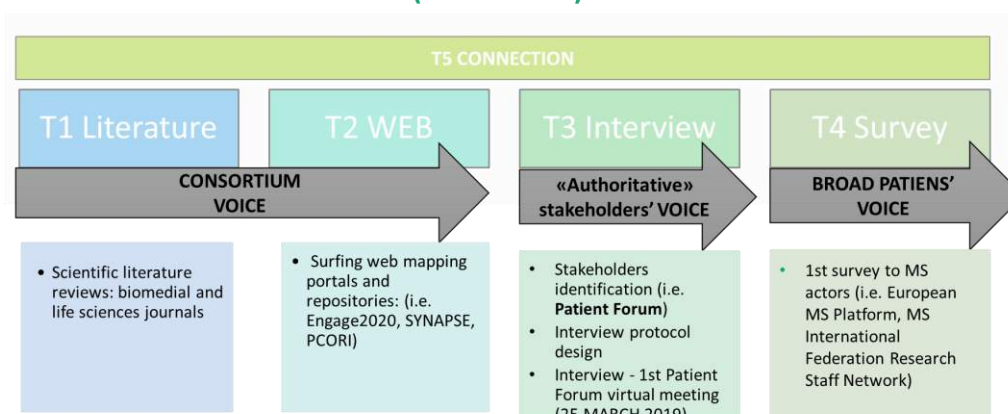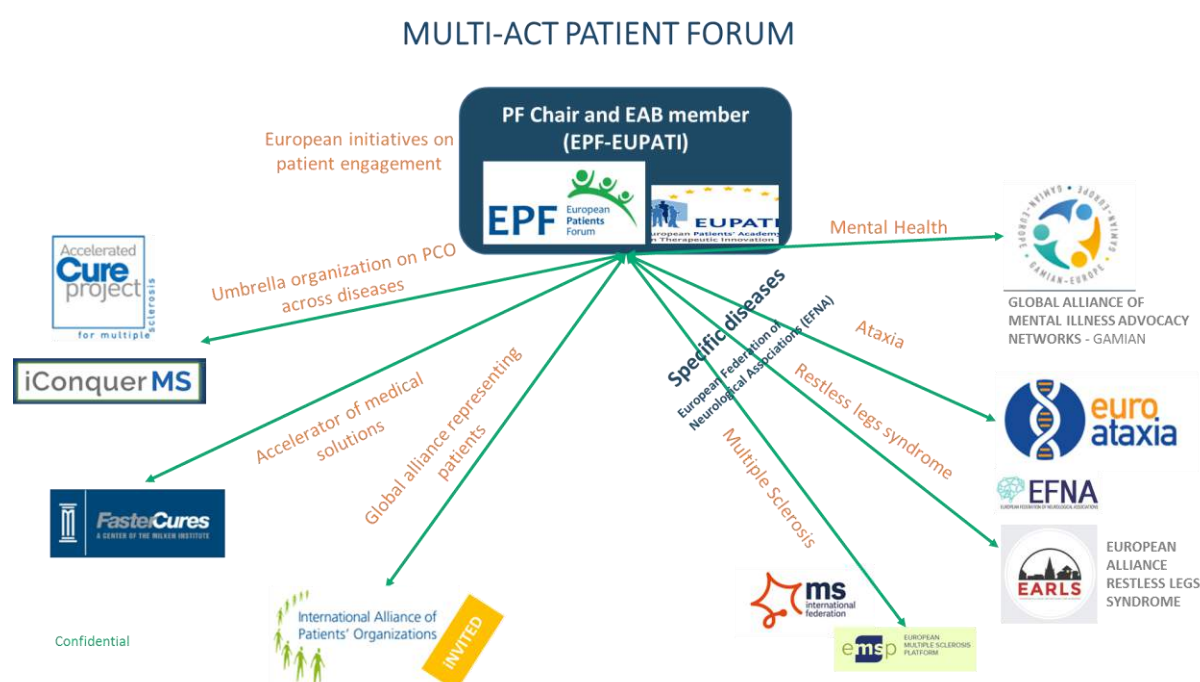
LANDSCAPE ANALYSIS (D1.3 – D1.4)

*Figure n.A7. Steps of the Landscape Analysis*

MULTI-ACT main activities and outcomes will be supervised and exploited by two MULTI-ACT advisory bodies: an **External Advisory Board (EAB)** and a **Patients Forum (PF)**[100].

Figure A8. MULTI-ACT Patient Forum.

MULTI-ACT PATIENT FORUM

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[100] Patients Forum (PF) includes representatives from the European Patient Forum EPF, the European Patient Academy EUPATI, the FasterCures, the European Federation of Neurological Associations EFNA, the Accelerated Cure for MS and iConquerMS initiatives, the European Alliance Restless legs syndrome, the EuroAtaxia, the Global Alliance of Mental Health Illness Advocacy Networks GAMIAN.

Figure A9. The involvement of patients and patients' representative in MULTI-ACT Governance: Patient Engagement Group (PEG), Patient Forum (PF) and External Advisory Board (EAB).
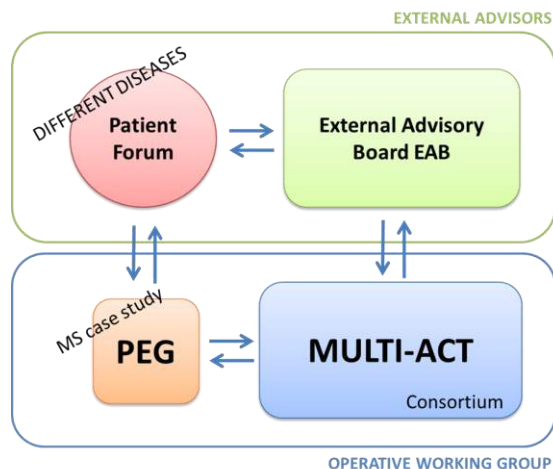
We used the interview protocol to engage with stakeholders who are included in the **Patient Forum** (PF) and we took advantage of the **First Patient Forum Virtual Meeting** that was held the 25th March 2019.

4.2 Inductive research and the semi-structured interview method

This section explains the characteristics of this research method and discusses the requirements for such group interview to produce reliable and relevant results.

The group interview to the PF of Deliverable D1.4 follows an inductive approach, where theory is developed starting from the raw data, thus running from the particular to generalization. Therefore, in inductive research, knowledge is not generated from some premises, but is produced directly from the examination of the data generated in the research. This approach is different from deductive methods, in which the researcher proceeds from a set of general premises to a more specific conclusion by testing some hypotheses on empirical data (Ketokivi & Mantere, 2010)[101].

We opt for an inductive approach as there is not a unique and best way to engage patients in health R&I, to define path, metrics, and stakeholders have different experiences as well as different opinions and interests with regard to this aspect. We decided to include in the landscape analysis both a group interview and a survey, because questionnaires usually depend heavily on research premises and hypotheses (Ketokivi & Mantere, 2010). Rather, an inductive research approach seems to add knowledge generated directly through the interaction between the researchers and the research field (Alvesson & Sköldberg, 2009)[102]. For that purpose, we used a semi-structured group interview (Crabtree & Miller, 1999)[103] as the inductive method to engage with stakeholders. We used an approach resembling the one that was used for the individual interviews to the EAB members in the activities of WP3 (see D3.3 Structure of the interviews to engage stakeholders). In particular, with the

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[101] Ketokivi, M., & Mantere, S. (2010). Two strategies for inductive reasoning in organizational research. *Academy of Management Review, 35*(2), 315-333.

[102] Alvesson, M., & Sköldberg, K. (2009). Reflexive Methodology: New Vistas for Qualitative Research (Second edition ed.). London: Sage Publications.

[103] Crabtree, B. F., & Miller, W. L. (1999). Doing qualitative research. Sage publications.

aim to guarantee reliable results a deep immersion into the focal phenomena is secured, implying interviews with knowledgeable actors and a profound knowledge of the issues by the interviewers. This knowledge is present in the MULTI-ACT consortium and its external consultative bodies and interviewing is a strategic research method to engage relevant stakeholders within and beyond the consortium.

Interviews should be designed following a protocol that ensures information reliability, authenticity and insightfulness. On the one hand, interviewees must be knowledgeable and willing to transparently convey their knowledge (Alvesson, 2003). On the other hand, the interviewers must be aware of several biases that might compromise information reliability and authenticity, in which impression management and retrospective rationalization are the first culprits (Eisenhardt & Graebner, 2007)[104]. It is therefore paramount to (i) select the interviewees and (ii) to design the interview protocol in such a way as to minimize these weaknesses.

Regarding the first issue, interviewees' selection, the members of the consortium decided, for the purposes of Deliverables D1.4, to interview stakeholders who participate in the **Patient Forum**. Due to their commitment, knowledge and centrality in the field of **brain diseases** and especially on **Patient Engagement** topic, they seemed to fit well the scope of inductive interviews. As mentioned above, we interviewed them in order to gather additional knowledge i) on experiences of Patient Engagement in R&I, ii) on perceived gaps and needs for prioritization, iii) on the most suitable methods for the engagement, and iv) measures that should be used to assess its effectiveness and impact.

Concerning the interview protocol design, we used **semi-structured group interview**. In general, an interview protocol lists the questions and issues that have been explored during the interview to guarantee that the same basic questions are addressed to each interviewee (also those who were absent were asked to answers to the questions by email). As also mentioned in D3.3, the protocol should be clear and theoretically driven, so that it guarantees four pillars: reproducibility, systematicity, credibility and transparency (Patton, 2002)[105].

FOUR PILLAR (Patton, 2002)	D1.4 Interview approach
Reproducibility: the protocol should be designed in order to be used multiple times and generate information on the topic of interest in the same conditions.	The protocol has a protocol that can be used multiple times, in fact it has been used during the Virtual Meeting and also later to gather feedback from the absents
Systematicity: the protocol should guarantee interviews are not targeting specific interviewees (picked to support or test pre-defined hypothesis).	The selected interviewees are not part of the MULTI-ACT consortium, they have an advisor role and are neutral in providing answers.

[104] Eisenhardt, K. M., & Graebner, M. E. (2007). Theory building from cases: Opportunities and challenges. *The Academy of Management Journal*, 50(1), 25-32.

[105] Patton, M. Q. (2002). Qualitative interviewing. Qualitative Research and Evaluation Methods, 3, 344-347.

Credibility: the protocol questions should be reasonable to generate new theory, being unbiased and based on theory.	The questions have been designed to generate a consensual view on the steps of the R&I process where patients should be engaged to maximize research impact, and to gather opinions on methods and measurements for effective Patient Engagement.
Transparency: the protocol should be formalized (i.e. written).	The protocol has been formalized in the presentation used during the Virtual Meeting and circulated among the PF members. The slide deck including the questions for the group interview is accessible here.

The protocol can be very structured and define closed-fixed questions, so that neither the interviewer nor the interviewee have the freedom to diverge from the protocol and the researcher's categories. Alternatively, the protocol can be flexible, and semi-structured, thus defining the themes and subject areas that the interviewers are free to explore, based on the general purposes of the research and the answers of the interviewee.

For our purposes, we relied on **semi-structured group interview** because we want to assess and gather feedback on specific topics with the interviewees having the freedom to articulate their own discourse. This would enable us to enrich our insights in developing the MULTI-ACT Patient Engagement Strategy. Core questions to be asked are highlighted to guarantee that all interviews cover the same topics.

To maximize the reliability and insightfulness of the collected information, we triangulated the interview by relying on multiple sources such as the literature review, the web search, the survey to MS Societies and the connection and exchange with other RRI projects and initiatives.

4.3 Communication, process and participants

The members of the Patient Forum have been invited to the Virtual Meeting by email early March and provided with a guidance document (describing their role, responsibilities and term of references), together with the full text of the Description of Action and two deliverables (D1.3 "Preliminary landscape analysis of patient engagement initiatives and gaps identification" and D5.3 "Compilation and analysis of selected experiences relevant for MULTI-ACT model").

All members received full presentations of the meeting afterwards as well as the draft deliverable that included the elaboration of group interview results. The members were given 2 weeks for reading materials ahead the meeting and 1 week to review the elaboration of the group interview included in the draft D1.4

During the meeting attendees have been introduced to the goal and strategy pursued by the MULTI-ACT project with a specific focus on patient engagement in the Responsible Research and Innovation (RRI) domain and how MULTI-ACT plans to contribute to its recognition and

consolidation. They have been engaged to consolidate landscape analysis with guiding questions on three specific topics: i) the 7-steps Patient Engagement R&I Path; ii) the Public and Patient Engagement methods and iii) the Co-design the MULTI-ACT PE Guidelines.

The attendees to the meeting have been:

1. Matthew May – representative for EUPATI-EPF (Chair)
2. Robert McBurney – representative for AcceleratedCure
3. Brenda Huneycutt – representative for FasterCures
4. Joke Jaarsma – representative for European Federation of Neurological Associations (EFNA) & European Alliance Restless Legs Syndrome (EARLS)

The members that couldn't attend the meeting *(5. Elisabeth Kasilingham* - representative for *EMSP, 6. H. Kärkkäinen* - representative for *GAMIAN, 7. Jette Bay* - representative for *MSIF, 8. C.W. van Doorne* - representative for *EFNA & Euro-ataxia)* were asked to answer to the guiding questions via email. This approach allowed us to collect and elaborate feedback from all members.

The elaboration consisted in capturing insights and suggestion from the replies of the Patient Forum's members, as consolidation of the landscape analysis and preliminary directions toward the MULTI-ACT Patient Engagement Guidelines.

Lastly, all PF's members have been asked to review the present deliverable, validating our elaboration of the interview.

4.5 Interview protocol – guiding questions

This section discloses the specific protocol for the group interview undertaken in WP1. The protocol considered three topics:

(1) The 7-steps Patient Engagement R&I Path

The PF has been asked for agreement and comments on the path MULTI-ACT is taking into consideration in order to assess the existing patient engagement practices, the gaps and the barriers. Specific questions have been:

- Do you agree with the 7 steps of the R&I Path, as the steps in R&I where patients need to be engaged in order to maximize the impact of research?
- Would you add some steps not yet considered?
- Would you prioritize some steps or are equally important?
- How can patient engagement in 7-steps R&I path be understood and measured?
- How can patient perspectives, priorities and values be examined and communicated?

(2) Public and Patient Engagement methods

The PF have been asked to provide their view on a comprehensive list of public engagement methods selected by the ENGAGE2020 Action Catalogue. In particular, whether they have additional methods to suggest or to comment about the appropriateness and feasibility of application to the patient community and their capacity to facilitate and enable truly engaged participation and whether there is evidence of the return on engagement of using specific methods.

Specific questions have been:

- Do you have any direct experience with one of the above methods?
- Is the method able to provide a perspective that works at population level rather than an individual perspective, so to avoid partial representativeness?
- Do you suggest other methods (e.g. on line methods)?
- Do you have evidence of the "return on engagement/benefit" of using a specific method?

3) Co-design the MULTI-ACT PE Guidelines (D1.5 first release)

In the process to develop innovative guidelines for PE in health R&I, preliminary content has been identified:

1. Exemplary processes where patients can be engaged (i.e. in the 7-steps

2. R&I Path)

3. Exemplary methods to be used for PE in the 7-steps R&I Path

4. Success stories, case studies of PE. Evidence of impact/Return of PE

5. Operational & ethics aspects (e.g. recruiting procedures, consent, etc.)

6. Criteria and Indicators to evaluate the impact/Return of PE

The PF has been asked to provide their view on the content for the preliminary version of the MULTI-ACT Patient Engagement guidelines with the specific guiding questions: Are the following proposed contents relevant? Would you add other content?

GROUP INTERVIEW PROTOCOL

Code	Core	Question	Purpose	Topic
WP1-1	**Core**	**Do you agree with the n. 7 steps of the R&I Path, identify by PEG members, as the steps in R&I where patients need to be engaged in order to maximize the impact of research?**	**Gather approval on the 7 steps R&I path as path where patients need to be engaged in order to maximize the impact of R&I**	WP1-TOPIC 1 – Consolidating the MULTI-ACT WP1 key concepts
WP1-1.1	Additional	Would you add some steps not yet considered?	Implement the 7 R&I steps with missing steps if any	WP1-TOPIC 1 – Consolidating the MULTI-ACT WP1 key concepts
WP1-1.2	Additional	Would you prioritize some steps or are equally important?	Prioritize the steps with respect to the state of art.	WP1-TOPIC 1 – Consolidating the MULTI-ACT WP1 key concepts
WP1-1.3	Additional	How can patient engagement in 7-steps R&I path be understood and measured?	Identify metrics to assess the effectiveness of patient engagement	WP1-TOPIC 1 – Consolidating the MULTI-ACT WP1 key concepts

WP1-1.4	Additional	How can patient perspectives, priorities and values be examined and communicated?	Identify approaches to enable science with patient input	WP1-TOPIC 1 – Consolidating the MULTI-ACT WP1 key concepts
WP1-2	**Core**	**Do you have any direct experience with one of the method selected from the Engage2020 ActionCatalogue?**	**Assess the experiences of stakeholders with respect to the identified methods (Action Catalogue – web-research)**	**WP1-TOPIC 2 – Consolidating the WP1 Landscape Analysis (D1.3 first release)**
WP1-2.1	Additional	Is the method able to provide a perspective that work at population level rather than an individual perspective, thus to avoid partial representativeness?	Assess the capacity of methods to ensure representativeness	WP1-TOPIC 2 – Consolidating the WP1 Landscape Analysis (D1.3 first release)
WP1-2.2	Additional	Do you suggest other methods (e.g. on line methods)?	Scope additional evidence-based methods	WP1-TOPIC 2 – Consolidating the WP1 Landscape Analysis (D1.3 first release)
WP1-2.3	Additional	Do you have evidence of the "return on engagement/benefit" of using a specific method?	Assess the benefit and (return on engagement) of applying the methods	WP1-TOPIC 2 – Consolidating the WP1 Landscape Analysis (D1.3 first release)
WP1-3	**Core**	**Are the following proposed contents relevant? Would you add other content?** **1. Exemplary processes where patients can be engaged (i.e. in the 7-steps R&I Path)** **2. Exemplary methods to be used for PE in the 7-steps R&I Path** **3. Success stories, case studies of PE. Evidence of impact/PE Return** **4. Operational & ethics aspects (e.g. recruiting procedures, consent, etc.)** **5. Criteria and Indicators to evaluate the impact/Return of PE**	**Define relevant content for the guidelines toward co-design**	**WP1-TOPIC 3 – Co-design the MULTI-ACT PE Guidelines (D1.5 first release)**

The group interview protocol includes also questions related to other WPs: WP5 Health collaborative initiatives structures and policies (EY) and WP3 Integrated Accountability Model (IAM) model development & assessment to the case of research initiatives (UNITN), and it is structured as follows:

1. **Introduction.** After the interviewer and the interviewee introduce themselves to each other, the interviewer started by providing information about i) MULTI-ACT vision and goal, ii) general overview and current status, iii) achievements (i.e. the CRIF model), iv) the purpose of the interview.

2. **Discussion topic 1: Consolidating governance criteria (WP5):** overview of WP5 activities and guiding questions for consolidating governance criteria.

3. **Discussion topic 2: engagement criteria for patients as a key stakeholder (WP1):** overview of WP1 activities and guiding questions for consolidating engagement criteria for patients as a key stakeholder.

4. **Discussion topic 3: Consolidating IMPACT metrics (CRIF):** overview of WP3 activities, focusing on the Patient Reported Dimension, and guiding questions for consolidating impact indicators.

This Appendix focuses on the guiding questions for WP1, Discussion topic 2: engagement criteria for patients as a key stakeholder (WP1), which entails the following sub-topics:

o   WP1-TOPIC 1 – Consolidating the MULTI-ACT WP1 key concepts

o   WP1-TOPIC 2 – Consolidating the WP1 Landscape Analysis (D1.3 first release)

o   WP1-TOPIC 3 – Co-design the MULTI-ACT PE Guidelines (D1.5 first release)

4.6 METHOD FOR ANALYSING INTERVIEW DATA

Different strategies may be followed to gain the most useful insights from interviews (Crabtree and Miller, 1999[106]; Miles and Huberman, 1994[107]). An overview of the strategy used for this group interview is presented below:

- Interviews were recorded to facilitate their analysis.

- Interviews were based on the formal protocol outlined in this document, allowing for transparency and comparability.

- Interviews were thematically coded to crystallize information and obtain the insights that are relevant for MULTI-ACT. Specifically, the WP1 sub-topics: Consolidating the MULTI-ACT WP1 key concepts, Consolidating the WP1 Landscape Analysis (D1.3 first release), Co-design the MULTI-ACT PE Guidelines (D1.5 first release).

- The coding and the thematic analysis of the group interview (analysis' step n.3) was driven by the outcomes of Deliverables D1.4, together with the literature reviews (analysis' step n.1), the web-search on specific mapping portals (analysis' step n.2), the survey with MS Societies

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[106] Crabtree, B. F., & Miller, W. L. (1999). Doing qualitative research. Sage publications.

[107] Miles, M. B., &Huberman, A. M. (1994). Qualitative data analysis: An expanded sourcebook. Sage Publications, London.

(analysis' step n.4) and the connections with relevant initiatives (analysis' step n.5). For example, the literature review for D1.4 will help us to align the analysis with the specific objectives of the deliverable, which focuses on identifying existing experience and benchmarking growth on Patient Engagement.

- MULTI-ACT priorities have been considered when analysing and coding the interviews to test the relevance of these priorities. Those priorities are included in the background Section 3 Introduction.

4.7 Insights and suggestions by PF

The group interview data (i.e. answer from PF's members to the questions) have been elaborated in main insights and suggestions per topic and the summary is presented below.

Topic 1

[*EUPATI-EPF*].
The importance of patients' engagement in the "funding" assignment process need to be highlighted in the definition of the R&I 7-steps identified by PEG.

[*Accelerated Cure Project for MS and its PCORI iConquerMS People-Powered Research Network*]. Research does not happen without funding. Thus, the engagement of funding stakeholders in a way that can create the ground for their receptivity towards the research mission is a pre-requisite for truly effective co-creation. Specific work packages related to education and training are being including in R&I projects to tackle such need.

[European Alliance Restless legs syndrome; European Federation of Neurological Associations (EFNA)]. The number of requests for patients to participate in studies and research projects is generally increasing while the number of trained patients who are able to successfully participate is limited, thus stressing the need for more training and educational programmes for patients.

[*Fastercures*]
In terms of other stakeholders to be involved in "breaking boundaries" step it is instrumental to closely interact with policy makers and also journal editors and media for transparency, privacy and security rules and conditions. The breaking down boundaries section could include actions related to funders, policy-makers, and journal editors (i.e., those who hold the levers for aligning incentives), or there could be an additional step of "reducing barriers and aligning incentives" that is broader than RFPOs but still impacts the way RFPOs function. Breaking down barriers could also include culture change at RFPOs (e.g., showing ROI for the time, budget and other resources needed to engage patients meaningfully throughout the research process) and capacity building/training for both sides of the engagement – patients and researchers/RFPO staff.
The Evaluation step should include both assessing the value of the research program/project and the value of patient input into the research process (e.g., evaluate PE models and share lessons learned). For medicine development domain, the Translation to Community should include information going to regulators.

Related to the content for the innovative MULTI-ACT PE guidelines, "methods to be used for PE" should include methods to determine who/when/about what to engage and not just the method to engage.

[*International MS Federation MSIF*]
1. Agreement on the 7 steps of the R&I path.
2. The frameworks and conditions (e.g. training of both patient representative and researcher) for patient participation at all levels in the research process must be included as a sub-criterion in the Governance WP5.
3. Direct experience, as a patient representative, in several research projects on steps 2 Research priorities, 3 Steering institutions, 4 Design & plan, 5 research execution and 6 Evaluation, primarily in the Danish MS Society.

[*EUROATAXIA; European Federation of Neurological Associations (EFNA)*]
Step 1: The concept of a collaborative Research Ecosystem within the context of patient empowerment is excellent. The sustainability issue indeed is key to this and needs to be urgently addressed.
Step 5: Important element is the mapping of patient (unmet) needs and priorities
Step 7: One of EFNA's key pillars of activity is engagement with stakeholders, which obviously means with society as a whole as well. Patient organisations can play a big role here. As the patient voice will be heard more clearly in the years ahead, our engagement in programs, guidelines production etc. will become more important.
Communicating to our constituencies is powerful and speaks for itself.

Topic 2

[*EUPATI-EPF*].
Community Advisory Board method to be added to reference patient engagement method. This approach is used in Leukaemia communities[108] and also by the HIV movement.

[*Fastercures*].
The participant to the interview does not have any direct experience in FasterCures with the engagement methods listed in terms of setting research agendas/conducting research, but they have convened groups of varying sizes (e.g., focus group or larger) to bring patients and/or other stakeholders together, and FDA has used what looks to be similar to the Summit method to solicit patient perspectives in its PFDD meeting series. See also FasterCures PFDD tracker (including FDA convened and external organization convened meetings).

Topic 3 and general considerations

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[108] https://www.cmladvocates.net/cml-cab

[*EUPATI-EPF*].

To identify mechanisms to ensure a wide representativeness of the Patient Forum (e.g. consultation of Patient Forum Organisations constituents), which does include different perspectives from different disease domain with the specific purpose to pave the way to scale MULTI-ACT results from MS to the whole brain disorder area.

The inclusion of compulsory fields related to patient engagement in the application forms for receiving funding from international programmes (such as EIT Health) is an example of the progressively increasing attention paid by funders to this. It is an ongoing, even if slow, process that should go towards becoming standard and generally accepted as a consolidated practice.

[*Accelerated Cure Project for MS and its PCORI iConquerMS People-Powered Research Network*]
We need to secure a faster path to facilitate the return of R&I on engagement of patients in terms of quality of care, because this is the ultimate interest of people having a health condition.

APPENDIX 5 - Connecting with PE initiatives

Based on results from the steps of the landscape analysis, we have decided to connect directly with the representatives of the PE initiatives most relevant to MULTI-ACT to verify synergies in a more efficacy approach. Toward the co-design of the MULTI-ACT innovative guidelines[109], some initiatives have already been approached directly by FISM in order to verify the interest in synergizing with MULTI-ACT and exploratory virtual meetings have been planned with:

1. IMI2 (https://www.imi.europa.eu/)
2. RRI NewHoRRIzon Health Social Lab (https://newhorrizon.eu/sl7/)
3. Patient Focused Medicines Development (PFMD) (http://patientfocusedmedicine.org/)

The following additional initiatives will be contacted in the next phase of WP1:

1. PARADIGM (IMI2 project) (https://imi-paradigm.eu/)
2. UK INVOLVE (https://www.invo.org.uk/)

5.1 Innovative Medicine Initiative IMI2

FISM had a preliminary contact with a representative from IMI2 who provides interesting material to be used for benchmarking growth on patient and stakeholder engagement.

In particular, we studied the IMI:

- works[110] and its objectives[111]
- relevant projects[112] to get in contact with
- success stories[113]
- progress analyses[114]
- Annual activity report 2017 (part on KPIs)[115]
- dissemination guidelines[116]
- stakeholders dedicated pages[117]

FISM is in contact with the responsible of the **patient engagement strategy** and **impact analysis specialist** in IMI2 in order to align effort in the next phases of WP1.

Moreover, The Chair of the MULTI-ACT Patient Forum, representing European Patient Forum and engaged in EUPATI and PARADIGM, is in charge to facilitate the connection and alignment with the

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[109] D1.5, D1.6,

[110] https://www.imi.europa.eu/about-imi/how-imi-works

[111] https://www.imi.europa.eu/about-imi/mission-objectives

[112] https://www.imi.europa.eu/projects-results/project-factsheets

[113] https://www.imi.europa.eu/projects-results/success-stories-projects

[114] https://www.imi.europa.eu/about-imi/reference-documents

[115] https://www.imi.europa.eu/sites/default/files/uploads/documents/reference-documents/IMI2-GB-DEC-2018_Annex1_AAR2017_signed_26JUNE2018.pdf

[116] https://www.imi.europa.eu/resources-projects/project-dissemination

[117] https://www.imi.europa.eu/get-involved

PARADIGM project in order to benchmark growth on Patient Engagement and to translate the knowledge already developed in the medicine development domain to the wider R&I process.

5.2 Patient Focused Medicines Development (PFMD)

FISM had a virtual meeting with PFMD with the aim to present MULTI-ACT and WP1 overview, strategy and vision and to gather PFMD's current activities in line with MULTI-ACT and discuss on potential synergies. The scope of collaboration with PFMD is to build on their effort on the medicine development domain and fill gaps with respect to the governance of wider R&I programs. The synergy will help in co-design the MULTI-ACT PE guidelines in a co-creation approach that is indeed at the root of MULTI-ACT.

5.3 NewHoRRIzon

MULTI-ACT aims to provide concrete tool to fulfil RRI criteria, including Public and Patient Engagement (See Section 1, MoRRI). Within this frame, WP1 guidelines for PE are under validation in a co-created approach with the collaboration of the NewHoRRIzon Health Social Lab (https://newhorrizon.eu/sl7/).