D1.1 Survey analysis report on stakeholder-specific preferences, needs and expectations

777450 - PARADIGM

Patients Active in Research and Dialogues for an Improved Generation of Medicines

[WP1 – Defining stakeholders' preferences, needs and expectations]

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[1] R: Document, report (excluding the periodic and final reports)
[2] PU = Public, fully open, e.g. web;

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Document History

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V1.3	15/02/2019	Final version for submission

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Definitions

Definition of 'patient engagement'

We define patient engagement (PE) as the effective and active collaboration of patients, patient advocates, patient representatives and/or carers in the processes and decisions within the medicines lifecycle, along with all other relevant stakeholders when appropriate. (PARADIGM, 2018)

Stakeholder categories in the survey

Patients, patient representative, patient advocate	This stakeholder group also includes carers and family of patients. Also referred to (together with patient organisations) as *patient community* in some occasions throughout the report.
Patient organisation	"Patients' organisations are defined as not-for profit organisations which are [patient-]focused, and whereby patients and/or carers (the latter when patients are unable to represent themselves) represent a majority of members in governing bodies" (EMA, 2018a)
Research and academia	Researchers are the people who do the research. They may do research for a living, and be based in a university, hospital or other institution, and/or they may be a service user or carer. (INVOLVE, 2019)
Healthcare professional (HCP)	"This category of stakeholders is broad and heterogeneous by definition as it encompasses general practitioners, nurses, clinical investigators/academics, pharmacologists, etc. However --- the category of healthcare professionals that our consortium should prioritise is the **clinical academics**." (PARADIGM, 2018)
Pharmaceutical/ biotechnology/ medical technology industry	Representatives from pharmaceutical and biomedical industry that are relevant to the three key decision-making points (i.e. scientists and managers)
Policymaker or regulator	A regulatory body that is responsible for "...the scientific evaluation and safety monitoring of medicines..." (EMA, 2017b).
Health technology assessment (HTA) body	A body that undertakes or commissions health technology assessment to form recommendations or advice for healthcare funders and decision-makers on the use of health technologies
Research funder	Institutions that mainly fund health research
Payer	Insurer or other organisation paying for healthcare

Vulnerable / underrepresented groups	The terms 'vulnerable' and 'underrepresented' stakeholder groups will be used interchangeably throughout the report to refer to the selected stakeholder groups that PARADIGM will make an effort to engage with throughout its work. These groups include children and young people, unaffiliated patients, people with dementia and HTA community.

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Three main decision-making points/ phases of the medicines lifecycle

With 'decision-making points' discussed in this report, we mean the key points (in time) in the development of medicinal products. To clarify, this term helps us refer to the specific stages of the medicines development and is not meant to imply that these stages include only decision-making. "PARADIGM will focus on three decision-making points, during which integration of the patient perspective is critical (if not essential) for the medicine lifecycle." (PARADIGM 2018).

Research priority setting	I.e. providing opinion, providing evidence and/or being part of a group that decides what is important to research
Design of clinical trials	I.e. designing protocols, discussing patient burden, discussing patient-related outcomes
Early dialogues with regulators and Health Technology Assessment bodies	I.e. early (multistakeholder) discussions between industry, HTA agencies and regulators (and in some contexts with payers) to discuss developmental plans for a medicinal product and to ensure they meet the requirements. ** Early dialogue is not a decision-making time for any party. In practice it more closely resembles consultation with the chance for feedback and input (two-way communication).*

Partners of the PARADIGM Consortium are referred to herein according to the following codes:

- **EPF**. EUROPEAN PATIENTS FORUM (Luxembourg) – **Project Coordinator**
- **EURORDIS**. EUROPEAN ORGANISATION FOR RARE DISEASES ASSOCIATION (France)
- **EATG**. EUROPEAN AIDS TREATMENT GROUP (Germany)
- **AE**. ALZHEIMER EUROPE (Luxembourg)
- **AIFA**. AGENZIA ITALIANA DEL FARMACO (Italy)
- **HTAi**. HEALTH TECHNOLOGY ASSESSMENT INTERNATIONAL (Canada)
- **IACS**. INSTITUTO ARAGONES DE CIENCIAS DE LA SALUD (Spain)
- **FSJD**. FUNDACIO SANT JOAN DE DEU (Spain)
- **VU-ATHENA**. STICHTING VU (The Netherlands)
- **UOXF-CASMI**. THE CHANCELLOR, MASTERS AND SCHOLARS OF THE UNIVERSITY OF OXFORD (United Kingdom)
- **EFGCP**. EUROPEAN FORUM FOR GOOD CLINICAL PRACTICE (Belgium)
- **SYNERGIST**. THE SYNERGIST (Belgium)
- **SYNAPSE**. SYNAPSE RESEARCH MANAGEMENT PARTNERS SL (Spain)
- **EFPIA**. EUROPEAN FEDERATION OF PHARMACEUTICAL INDUSTRIES AND ASSOCIATIONS (Belgium) - **Project Leader**
- **MSD Corp.** MERCK SHARP & DOHME CORP (United States)
- **UCB**. UCB BIOPHARMA SPRL (Belgium)
- **ABPI**. THE ASSOCIATION OF THE BRITISH PHARMACEUTICAL INDUSTRY (United Kingdom)
- **AMGEN**. AMGEN LIMITED (United Kingdom)
- **BAYER**. BAYER AKTIENGESELLSCHAFT (Germany)
- **GSK**. GLAXOSMITHKLINE RESEARCH AND DEVELOPMENT (United Kingdom)
- **GRT**. GRUENENTHAL GMBH (Germany)
- **JANSSEN**. JANSSEN PHARMACEUTICA NV (Belgium)
- **LILLY**. Eli Lilly and Company Limited (United Kingdom)
- **LUNDBECK**. H. LUNDBECK AS (Denmark)
- **MERCK**. MERCK KOMMANDITGESELLSCHAFT AUF AKTIEN (Germany)

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- **NOVO NORDISK**. NOVO NORDISK A/S (Denmark)
- **PFIZER**. PFIZER LIMITED (United Kingdom)
- **ROCHE**. F. HOFFMANN-LA ROCHE AG (Switzerland)
- **SERVIER**. INSTITUT DE RECHERCHES INTERNATIONALES SERVIER (France)
- **VFA**. VERBAND FORSCHENDER ARZNEIMITTELHERSTELLER EV (Germany)
- **SARD**. SANOFI-AVENTIS RECHERCHE & DEVELOPPEMENT (France)
- **NOVARTIS**. NOVARTIS PHARMA AG (Switzerland)
- **COVANCE**. COVANCE LABORATORIES LTD (United Kingdom)
- **ALEXION**. ALEXION SERVICES EUROPE (Belgium)

- **Consortium.** The PARADIGM Consortium, comprising the above-mentioned legal entities
- **Consortium Agreement**. Agreement concluded amongst PARADIGM participants for the implementation of the Grant Agreement. Such an agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

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1 Executive summary

Patients Active in Research and Dialogues for an Improved Generation of Medicines (PARADIGM) is an EU project funded by the Innovative Medicines Initiative (IMI) and the European Federation of Pharmaceutical Industries and Associations (EFPIA). Its mission is to participate in the co-creation of sustainable, systematic, meaningful and ethical patient engagement (PE) within the medicines R&D process.

To understand the needs, expectations and preferences from the perspective of different stakeholders, Work Package 1 (WP1) co-created with other WPs an online survey. The survey received 372 English language responses and 169 responses from 13 other European languages during the June and July in 2018. In addition to the survey, between June and October 2018, four different face-to-face consultations were carried out to involve the following vulnerable/ underrepresented and specific stakeholder groups[3]: people with dementia, children and young persons and people with rare diseases, as well as Health Technology Assessment (HTA) bodies.

Overall the key findings that this report suggests are:

I. That current perception of PE is low, yet ideal expectations are high and consistent across all stakeholder groups.
II. The greatest experience of PE is dominated by industry, patient, and research and academia communities. The least experience of PE is with regulators, policymakers, Health Technology Assessment (HTA) bodies, research funders and payers.
III. The greatest challenge identified by a majority of stakeholders is that 'Patient input is not part of [the] decision-making process' and when patient input is sought it is currently mainly at the level of informing and consulting. The patient community differed - reporting the top challenges as 'Communications were not clear and open' and a 'Lack of shared vision/goals'.
IV. This latter point from finding III is mirrored in that the greatest desired outcomes for PE across the 3 decision-making points being that, patient preferences, needs and experience are both integrated into the decision-making process and properly reflected in the outcomes of the PE activity.
V. Most stakeholders feel confident and ready to engage with a PE activity, but need continued and improved support to do so through internal processes, knowledge, human resources, managing competing interests, and setting priorities in [a] PE strategy.
VI. The patient community particularly needs extra support through expert knowledge of the particular stakeholder and decision-making process in question, and one-to-one mentorship of individual patients.
VII. The patient community needs better financial resources to undertake PE, as well as better compensation for their engagement activities.
VIII. Industry sector has high levels of dedicated PE functions within their organisations with lower levels for regulators, policymakers, Health Technology Assessment (HTA) bodies, research funders and payers. Despite stakeholders having dedicated PE functions, they appear to be proportionally underused.

[3] The terms 'vulnerable groups', 'underrepresented groups' will be used interchangeably throughout the report to mean the stakeholder groups that PARADIGM will make an effort to engage with throughout the work. These groups are children and young persons, unaffiliated patients, and people with dementia. In addition, other specific stakeholder groups include the HTA bodies.

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IX. Across all stakeholder groups, Standard Operating Procedures (SOP) to undertake PE and methods to record outcomes and impact exist or were available, however they can be sparse and are often underused - the greatest resource needs for more effective PE was identified as being 'A way to measure impact' and 'Better methods and materials of how to do it more effectively'.

X. There appear to be some differences between preferences from English language survey respondents to non-English language survey respondents. For non-English responses a higher proportion of the patient community did not receive any financial compensation, the industry respondents dedicated less time of their PE function activities outside of clinical trial design, and a higher proportion of industry, HCP and regulators, policymakers, HTA bodies, research funders and payers community lacked SOPs, or any methods or metrics with which to measure PE.

Additionally specific stakeholder groups (including vulnerable and underrepresented groups) reported that:

XI. Vulnerable populations specifically identified that the voice of the individual person living with the condition must be used over that of the carer or parent where possible.

XII. Myths and misconceptions must be addressed so that all parties can realise and utilize effectively the value that these populations can bring

XIII. Extra considerations of structure, material, timing, training, and location of any PE activity must be considered and accounted for to permit meaningful engagement

XIV. HTA agencies confirmed that PE adds value to early dialogues. Barriers that still need to be addressed include; difficulties finding patients with the appropriate profile and capacity to take part, the lack of resources across HTA agencies to administer PE processes and the lack of adaptable tools that create a consistent framework for PE during these early dialogues.

The combination of a wide-reaching survey, covering all major stakeholders' needs, preferences and expectations, combined with dedicated focus group consultations to reach specific stakeholders, vulnerable populations and HTA bodies adds substantial credence to what is preferred and expected by all involved in order to enhance and sustain meaningful PE in medicines development. The work presented here has underpinned a robust Delphi methodology which will further refine the consensus of all stakeholders' preferences for PE at three key points in the medicine life cycle that are poorly understood and reported. Only then can new resources be co-created to further support and sustain meaningful PE.

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2 Background and introduction

PARADIGM, stands for Patients Active in Research and Dialogues for an Improved Generation of Medicines, is an EU project funded by the Innovative Medicines Initiative and the European Federation of Pharmaceutical Industries and Associations (EFPIA). Its mission is to participate in the co-creation of sustainable, systematic, meaningful and ethical PE within the medicines R&D process. Building on previous initiatives, while focusing on closing gaps, it develops practical tools on the Who, What, When and How of PE. PARADIGM focuses on three key decision-making points in the lifecycle of a medicine, i.e. research priority setting, design of clinical trials and early dialogue with regulators and Health Technology Assessment (HTA) bodies.

A unique feature of PARADIGM is the inclusion of the voice of young people living with a medical condition, people with dementia and unaffiliated patients.

The overall objective of PARADIGM is to develop a framework that allows structured, meaningful, sustainable and ethical PE in the three key decision-making points with a set of recommendations for improved capacity, and tools to better support the implementation and sustainability of PE.

In order to achieve this, the work within PARADIGM is divided into seven work packages (WP), each building on each other and focusing on an important aspect in the framework. The two deliverables expected from WP1 are (1) a report (this document) on the main findings of the online survey and consultations carried out - and (2) a set of minimum criteria for PE (developed using a modified Delphi methodology[4]) which will inform the other WP's work on stakeholders' expectations when engaging patients in the above-mentioned three decision-making points.

3 Scope and objectives

The objective of this deliverable is to understand the expectations, needs and preferences for meaningful PE from key players in each stakeholder group at the local and international level that will, in turn, inform the work of other WPs. As a first step, to achieve this, an online survey with general and specific sections for different stakeholders and four consultations (i.e. with people living dementia, young patients, people with rare disease and HTA bodies) were conducted. The findings of WP1 will inform the further development work of WPs 2 to 6 in identifying gaps in PE practices, designing a framework to measure outcomes and impact, develop recommendations for capacity and capability needed for PE, new tools to facilitate PE and sustainability models.

This report shall be regarded as deliverable D1.1 per the current IMI PARADIGM agreement.

4 Online survey

4.1 Online survey methodology

The survey was constructed in two phases along with the other work packages. Questions and questionnaires based on previous literature[5] were collected together with the consortium partners to

[4] The Delphi is a consensus technique used to identify and prioritise the common expectations and preferences over a specific issue. For more information, please see Annex 1

[5] Literature and past surveys reviewed: "CTTI Survey" (Patrick-Lake B., 2018), "EUPATI Survey" (2015), "PFMD Survey" (Boudes M. et al. 2018), Levitan B. et al. July 2017.

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inform the creation of general questions and structure for the survey. Each WP defined preliminary questions important to them. A total of over 70 questions were submitted by the different WPs. The questions were reviewed during a face-to-face workshop, which took place during the first Open PE Forum of PARADIGM in April 2018[6]. The questions were consolidated and reduced to fit a survey structure that could generate quality data without overburdening the respondents. After construction, the survey was piloted using respondents from each respective stakeholder group to ensure the questions applied to their sector and were relevant for the overall questionnaire topic. Piloting took place over 2 weeks at the end of May and feedback was given to the survey-building-team for further refinement and modification of the survey questions.

The survey was uploaded to SurveyGizmo and respondents were asked to complete the questionnaire online. The consortium partners used a snowball technique to cascade the survey within their network and invited stakeholders to participate. The PARADIGM communications team shared the survey on social media channels (Twitter and LinkedIn) and via direct emails.

The survey comprised 15 general questions that all stakeholder groups could answer. Within this general section, 2 questions were in matrix style allowing more than one choice per row (these questions were optional due to the difficulty and the burdensome nature of the questions), 6 questions were in gliding scale and 4 questions were multiple choice, allowing for more than one option to be chosen. The stakeholder groups such as the patient community, industry, regulators, policymakers, HTA bodies, research funders, payers and healthcare professionals also had a separate section to which they were directed after the general section was completed. These sections included specific questions of interest for each of the different stakeholder groups and comprised different styles from matrices to multiple choice questions, which led to some results having a bigger overall number of responses compared to the total number of respondents.

The English survey[7] was live online from 1st June to 31st July 2018. Versions of the survey in twenty-three other EU languages were uploaded into the survey system by June 18th. All versions of the survey were closed out on July 31st 2018.

Technical considerations: Temporary technical issues with the functionality of the online survey caused a delay for respondents to complete the survey. Some drop down functions were inoperable for a period of approximately 2 weeks in the beginning. Also, some respondents reported that they could not understand questions due to a coding misalignment that caused the questions to be cut off and mixed with other questions. The misalignment was corrected as soon as it was noticed by the central team.

Translation considerations: The translations of the survey were found to be partially inaccurate for certain languages and were corrected during the period the survey was live. It is uncertain how the translation quality has affected the respondents' interpretation of the questions. As a result, the responses (<30) from five languages were excluded from the dataset (Bulgarian, Portuguese, Polish, Maltese and Lithuanian) and removed from the analysis. The remaining 17 languages were analysed. Due to the uncertainty and effect on the external validity of the survey, the English language responses and the 17 other languages were analysed separately. Six languages had no responses from the survey and 13 languages were analysed as one separate dataset.

[6] The first PE Open forum was organised by PARADIGM, EUPATI and PFMD to kick-off PARADIGM project on April 10th 2018 in Brussels. The event was for the PARADIGM consortium partners and members of the PARADIGM International Liaison Group (PILG). Report available at: https://imi-paradigm.eu/1st-paradigm-forum/
[7] See the final survey questions in Appendix 2

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All completed survey responses were converted and analysed using a statistical software package (IBM SPSS Statistics for Macintosh, Version 25.0, Amrock, NY: IBM Corp.) and Microsoft Excel (for Macintosh, Version 16.20). Descriptive statistical analysis was performed (primarily by Suzanne Ii/ CASMI). Responses to the open-ended questions from the non-English versions of the survey were back-translated into English[8], analysed for themes and quoted when responses differed from the survey responses for the respective questions. Findings are represented as total responses, or percentage of respondents to a given question or theme.

4.2 Results from English version of the survey

The following sections were answered by all stakeholder respondents.

4.2.1 Demographic background of the study population

The total respondents who completed the survey in English were 372 (Table 1). The stakeholder groups were separated into eight groups. The largest respondent (stakeholder) group was the patient community, followed by industry which together accounted for two thirds of the respondents. Research, academia and HCP followed. HTA, regulator and policymaker and research funder were the groups with the lowest representation. This imbalance between the responder groups should be taken into account while drawing conclusions especially for the groups with the lowest representations.

Table 1 Stakeholder respondents

Survey open	June 1st - July 31st, 2018	
English language responses	372	
Stakeholders		
Patient community [Patients (including carers)/ Patient advocates, Patient organisations]	133 (45/ 88)	35.8%
Industry	130	34.9%
Research and Academia	38	10.2%
Healthcare Professionals (HCP)	25	6.7
Health Technology Assessment bodies (HTA)	12	3.2%
Regulator or Policymaker	10	2.7%
Research Funder	3	0.8%
Other	21	5.6%

Country of origin

Respondents completed the survey from 48 countries. The majority of responses originated from the UK and US [28.2% (n=105) and 16.9% (n=63), respectively]. The group 'Other' comprises 42 countries, both within and outside the European Union.

[8] Appendix 3

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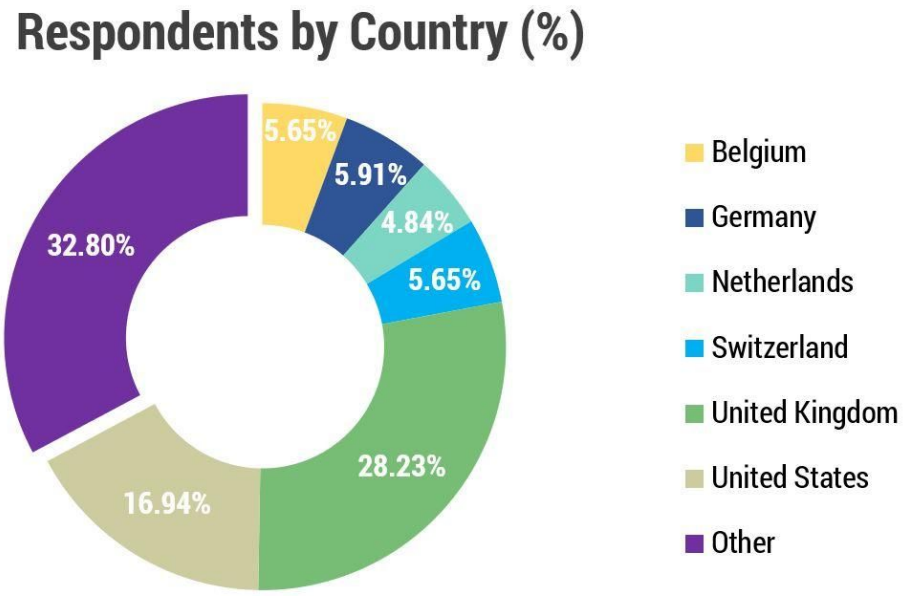

Figure 1 Stakeholder respondents by country

4.2.2 Previous engagement opportunities with other stakeholders

Respondents were asked about their previous involvement with other stakeholders at the three decision-making points (i.e. *informing* - giving one's opinion and perspective but no channel for feedback-, *consulting* - giving one's opinion and perspective and the ability to provide feedback-, and *decision-making*- ability to give opinion, provide feedback and make the final decision). This optional question was in a matrix format that allowed multiple choices.

The highest reported PE experiences for an individual stakeholder group was the industry group (n=1458) and the lowest was for the research funder group (n=55).

Patients (including Carers)	428
Patient Advocates and Patient Organisations	1129
Research and Academia	527
Healthcare Professional	375
Biotechnology/Pharmaceutical/Medical Technology	1458
Regulator or Policymaker	110
Health Technology Assessment (HTA) bodies	140
Research Funder	55
Other	284

Table 2 Overall previous PE experience by stakeholder group

Respondents had the lowest total number of engagement experiences with the industry sector (n=411) and patients (including carers), patient advocates and patient organisations (n=422). The two listed sectors will be reported further below.

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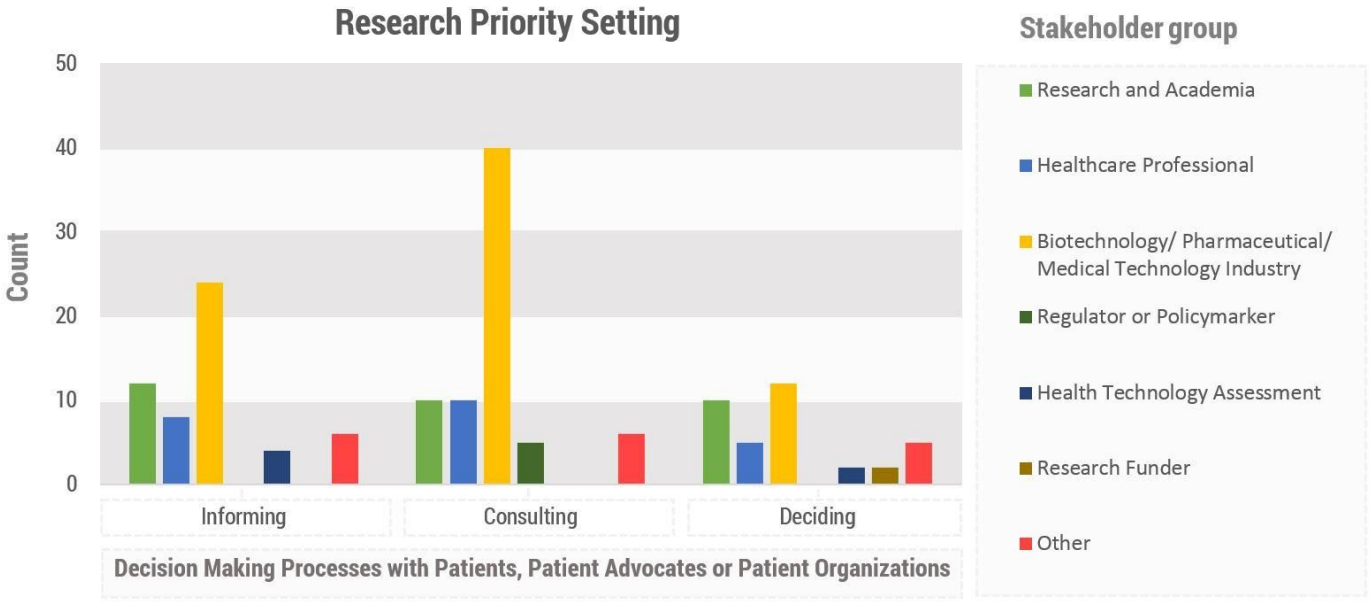
4.2.2.1 Previous engagement opportunities with patients, patient advocates and patient organisations

Respondents were asked about their previous involvement with other stakeholders at the three decision-making points. This optional question was in a matrix format that allowed multiple choices.

Research priority setting

Overall, the industry stakeholder group reported the highest level of engagement with patients, patient advocates and patient organisations for the three types of involvement (consulting n=39, informing n=23 and deciding n=12)



Some of the stakeholders, such as regulators/ policymakers and research funders are largely missing from any type of previous engagement with patients, patient advocates or patient organisations.

Figure 2 Decision making processes with patients, patient advocates or patient organisations at the Research Priority Setting (Total Respondents) (by type of decision making)

Design of clinical trials

Similarly, at the clinical trials design stage, engagement with patients, patient advocates and patient organisations drops to <13 for all of the stakeholder groups except industry (consulting n=61).

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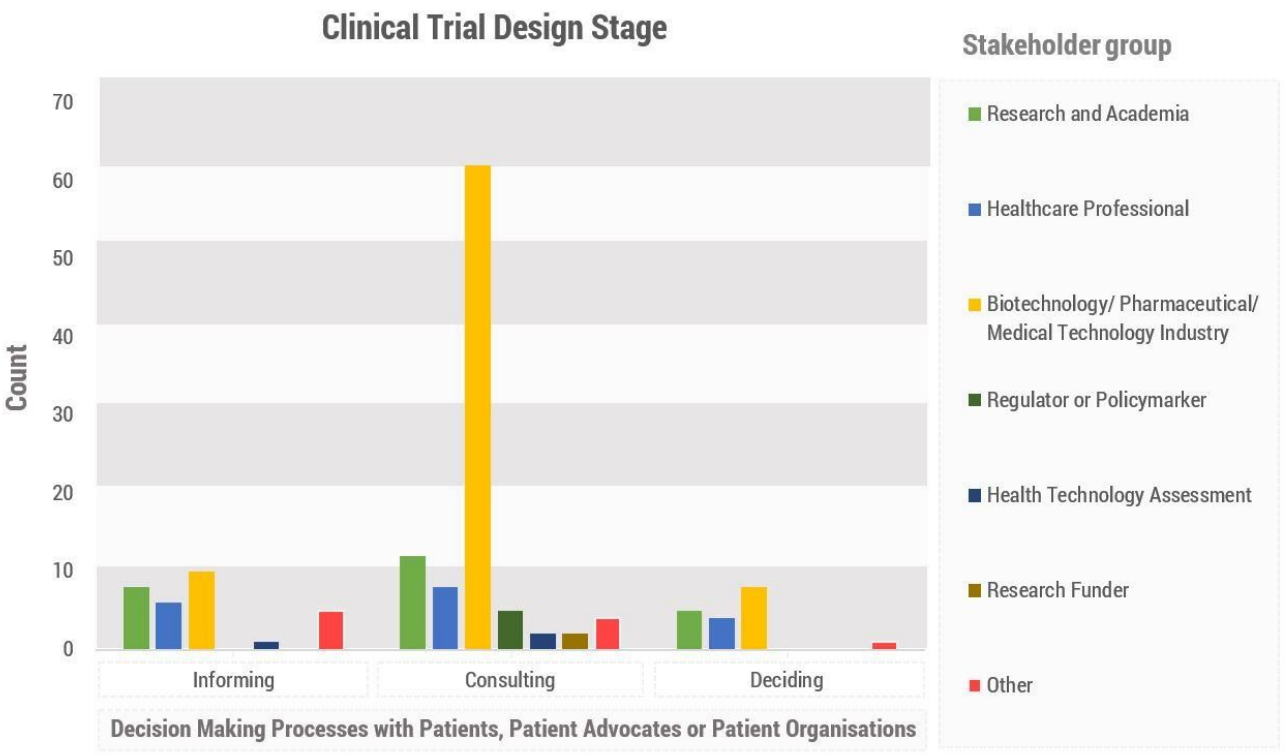

Figure 3 Decision-making processes with patients, patient advocates or patient organisations at the Clinical Trials Design Stage (Total Respondents) (by type of decision-making)

Early dialogues with regulators and HTA bodies

At the stage of early dialogues with regulators and/or HTA bodies, the industry and research & academia groups reported the highest number of engagement activities with patients, patient advocates and patient organisations at the informing level (n=22 and n=12, respectively) and the consulting level (n=43 and n=9, respectively). Healthcare professionals have the second highest number of counts at the consulting level (n=10). The other stakeholder groups reported very few engagements at any of the decision-making levels (all < 6).

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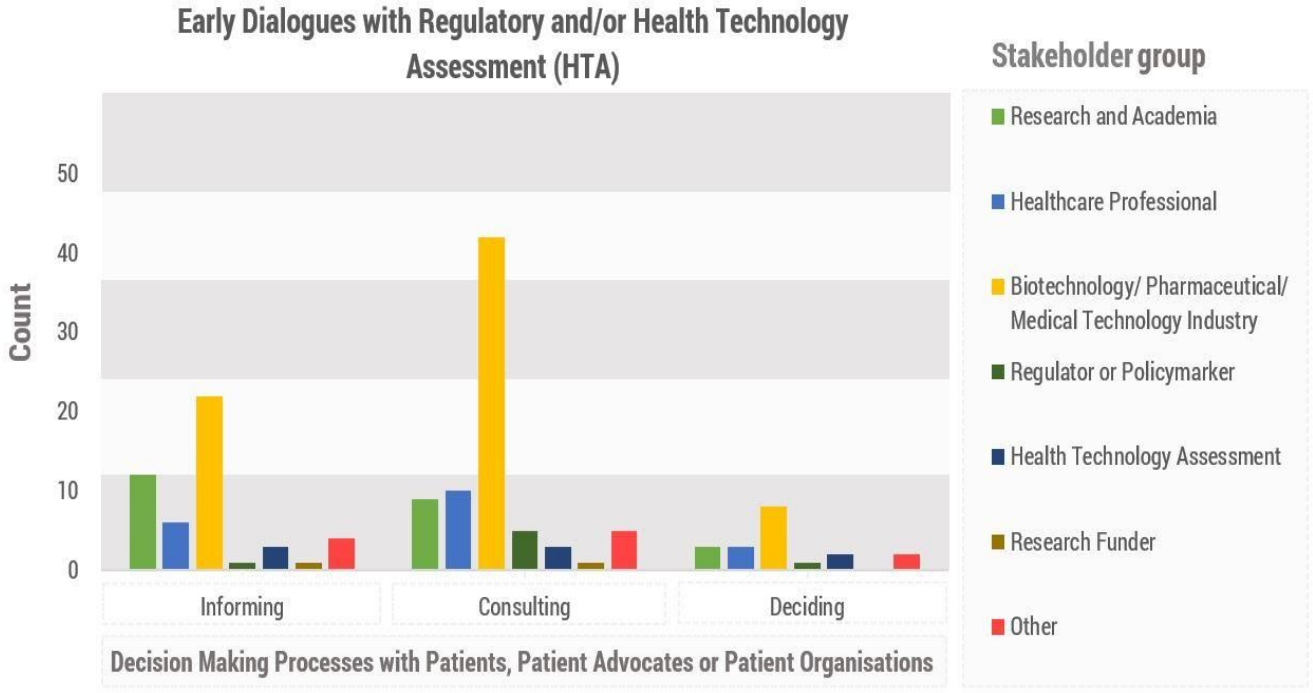

Figure 4 Decision-making processes with patients, patient advocates or patient organisations at the early dialogues with regulators and/or Health Technology Assessment (HTA) (Total Respondents) (by type of decision-making)

4.2.2.2 Previous engagement opportunities with biotechnology/ pharmaceutical/ medical technology industry

Respondents were asked about their previous involvement with other stakeholders at the three decision-making points. This optional question was in a matrix format and multiple choices were allowed.

Research priority setting

Patient advocates and patient organisations reported the largest number of previous engagement with the industry stakeholders (informing, n=26 and consulting, n=25). Patients (including carers) also reported 11 counts of engagement experience with industry at the consulting level and healthcare professionals with 11 counts of engagement experience at the informing level. All of the other stakeholders reported below 10 counts at any of the other decision-making levels and no stakeholder group reported over 5 counts at the deciding level.

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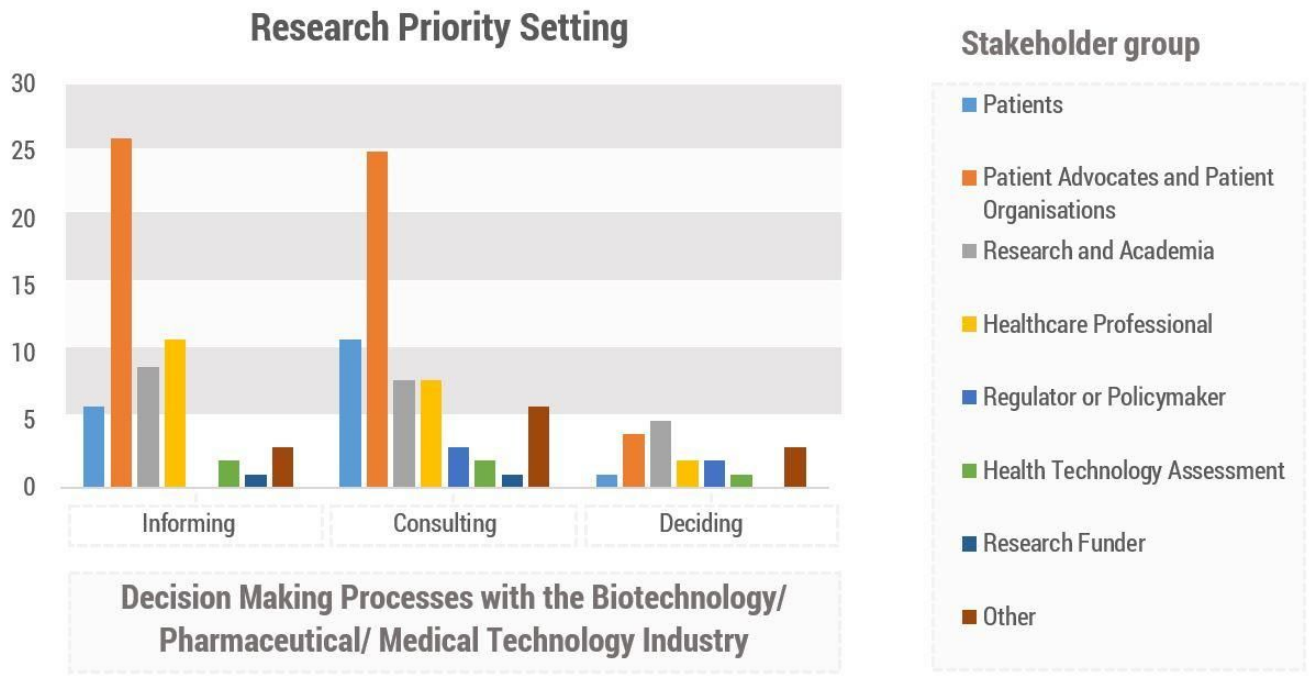

Figure 5 Decision-making processes with the Biotechnology/Pharmaceutical/Medical Technology Industry sector at the Research Priority Setting (Total Respondents) (by type of decision-making)

Design of clinical trials

At the clinical trials design stage, the engagement experience with the industry stakeholders was higher than at the research priority setting. Patient advocates and patient organisations had the highest counts of all stakeholders at the informing and consulting levels of decision-making (n=25 and n=28, respectively). Individual patients (including carers) also engaged at the consulting level (n=10) while healthcare professionals engaged at the informing level (n=9).

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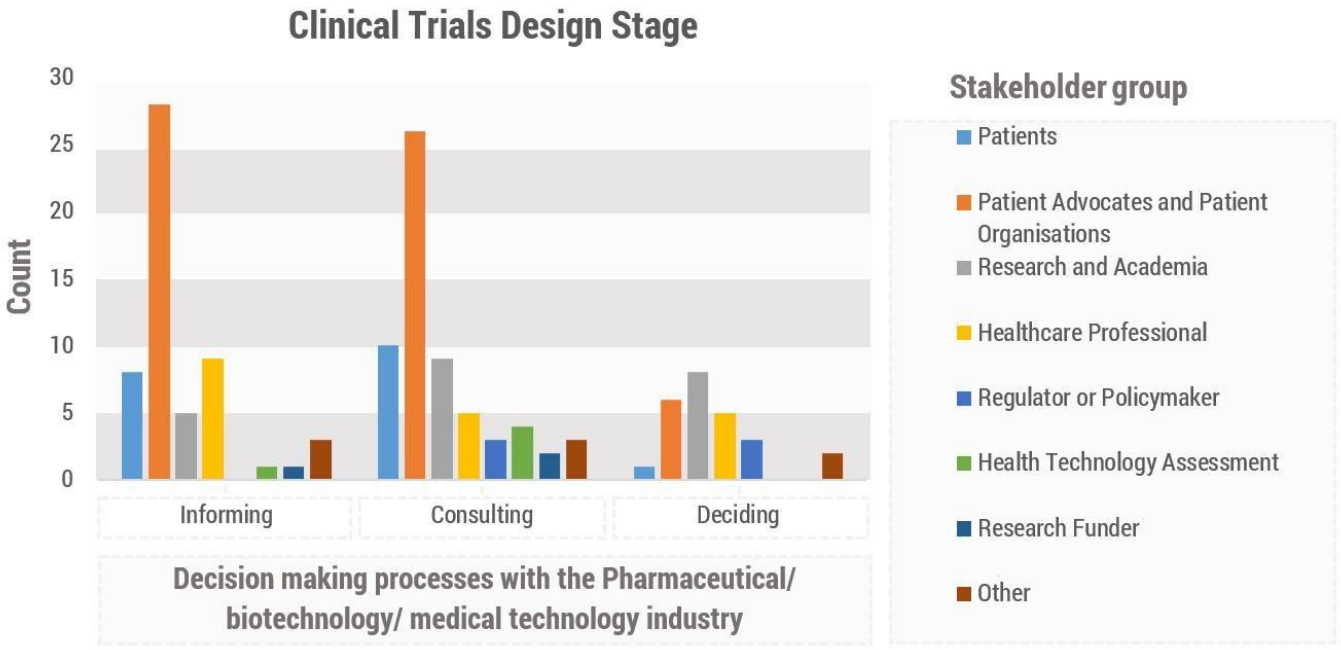

Figure 6 Decision-making processes with the Biotechnology/Pharmaceutical/Medical Technology Industry sector at the Clinical Trials Design Stage (Total Respondents) (by type of decision-making)

Early dialogues with regulators and HTA bodies

At the early dialogues stage with regulatory and/or HTA bodies, the majority of engagement experience was at the consulting level, particularly for patients advocates and patient organisations (n=14) and for industry and patients (n=9 and n=9, respectively).

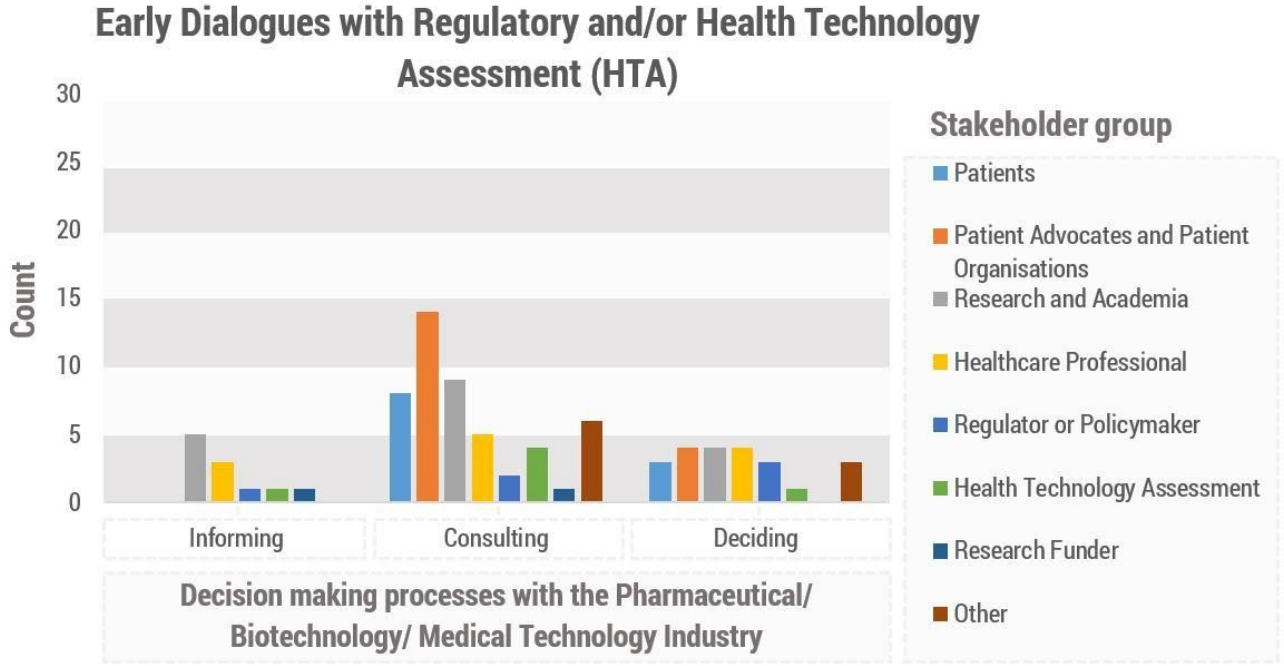

Figure 7 Decision-making processes with the Biotechnology/ Pharmaceutical/ Medical Technology Industry sector at the Early Dialogues with regulators and/or Health Technology Assessment (HTA) stage (Total Respondents) (by type of decision-making)

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4.2.3 Challenges with other stakeholders in PE

Respondents were asked about the challenges they had experienced with other stakeholders in their previous PE collaborations. Thirteen challenges were given with the option of adding 'Other' and specifying a challenge outside of those listed. Respondents were able to choose multiple stakeholders per challenge (including with the stakeholder group that they identified with), which is reflected in a high number of counts in each challenge.

Of the 13 challenges, across all stakeholders, the top five by order of importance were (Fig 8):

- *Patient input was not part of decision-making* (n=769),
- *Lack of shared visions/goals with other stakeholders* (n=660),
- *Communications were not clear and open* (n=659),
- *Lack of openness to have patient output* (n=649)
- *Delays in activities due to bureaucratic processes* (e.g. contracts, IP, etc) (n=596).

The top overall challenge 'Patient input was not part of decision-making' was also top for research and academia, HTA, research funders, payers and joint top with pharma/ biotech (along with 'Delays in activities due to bureaucratic processes').

For the patient stakeholder group (patients, patient advocates and or patient organisations), the two top challenges were different from the majority of other stakeholders and were, 'Communications were not clear and open' and 'Lack of shared vision/goals' (n=69 and n=77 respectively). The top overall challenge, 'Patient input was not part of decision- making', was broken down into further detail to understand which stakeholder groups experienced the challenge with other stakeholder groups (Fig 9).

All stakeholder groups reported to have experienced the challenge ('Patient input was not part of decision-making') with patients, patient advocates or patient organisations (patient stakeholder group). Other stakeholder groups, except for the patient group, reported they experienced the said challenge with the industry group. The patient group in particular, experienced this challenge with policymakers or regulators group (n=16) where the other stakeholders did not (n<3 for all of the other stakeholder groups).

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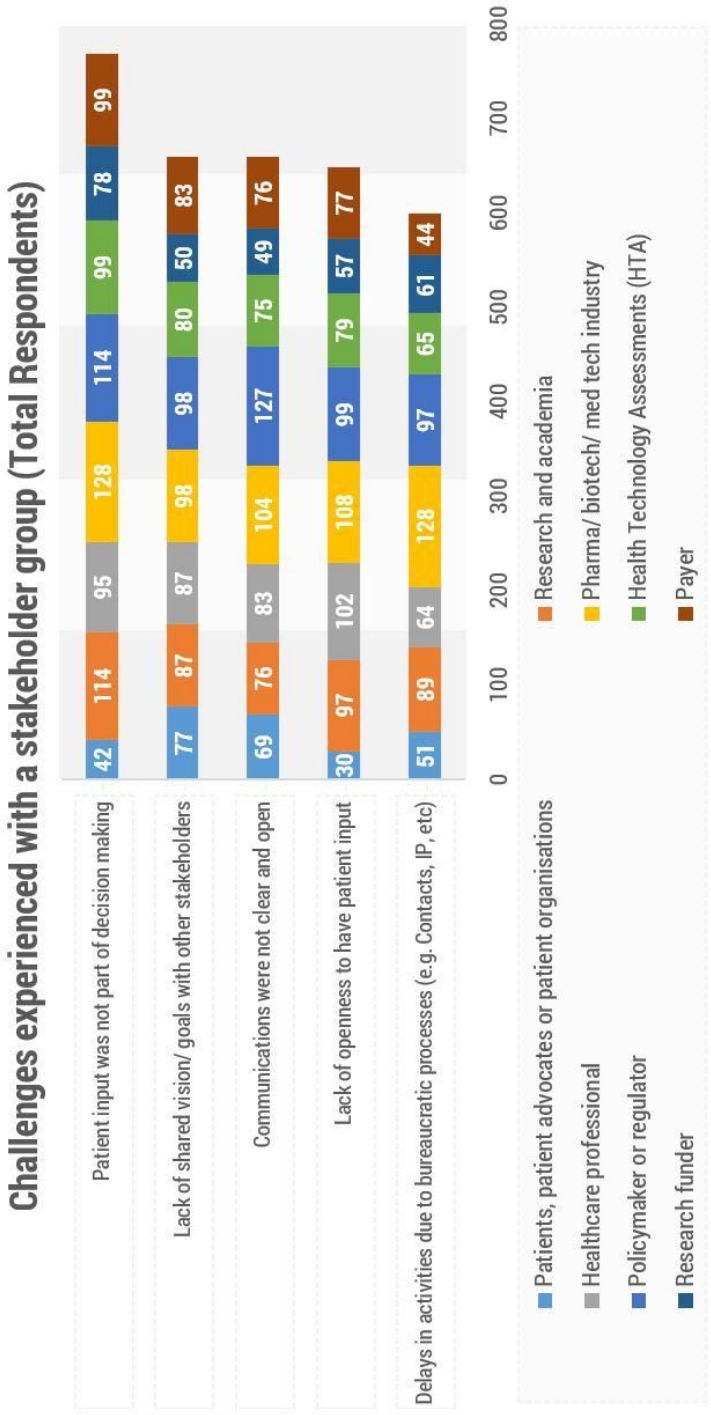
Figure 8 Top five challenges experienced with a respondent indicated stakeholder group



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4.2.4 Resources needed for more effective PE

Respondents were asked what was necessary to conduct more effective PE (Fig 10). Eight choices were given with the option of adding 'Other' and specifying a resource outside of those listed and respondents were asked to choose all that applied. Out of the nine options given, 'A way to measure the impact' was chosen the most (n=272). The option with the second highest rate was to have 'Methods, materials and information on how to do more effective patient engagement' (n=177). In the 'Other' category, the resources that were listed included: a clear framework and guidelines on how to engage with patients and funding/ financial support from other stakeholders, particularly in providing funding/ reimbursement/ tokens of gratitude for patients.

When broken down by stakeholder group, four stakeholder groups reported higher rates among the nine options that differed from the option, 'A way to measure the impact'. Research and academia group respondents reported that they require more 'Training on how to implement PE processes in your organisation' (n=22), HTA respondents need more 'Methods, materials and information on how to do more effective patient engagement' (n=8), and the patient community, in addition to measuring impact (n=29), also require 'Methods to identify and evaluate where your contribution would be most valuable' (n=29). Research funder respondents had two additional areas in addition to measuring impact that they require: 'Methods, materials, and information on best patient engagement practices' (n=3) and 'Methods to identify and evaluate where your contribution would be most valuable' (n=3).

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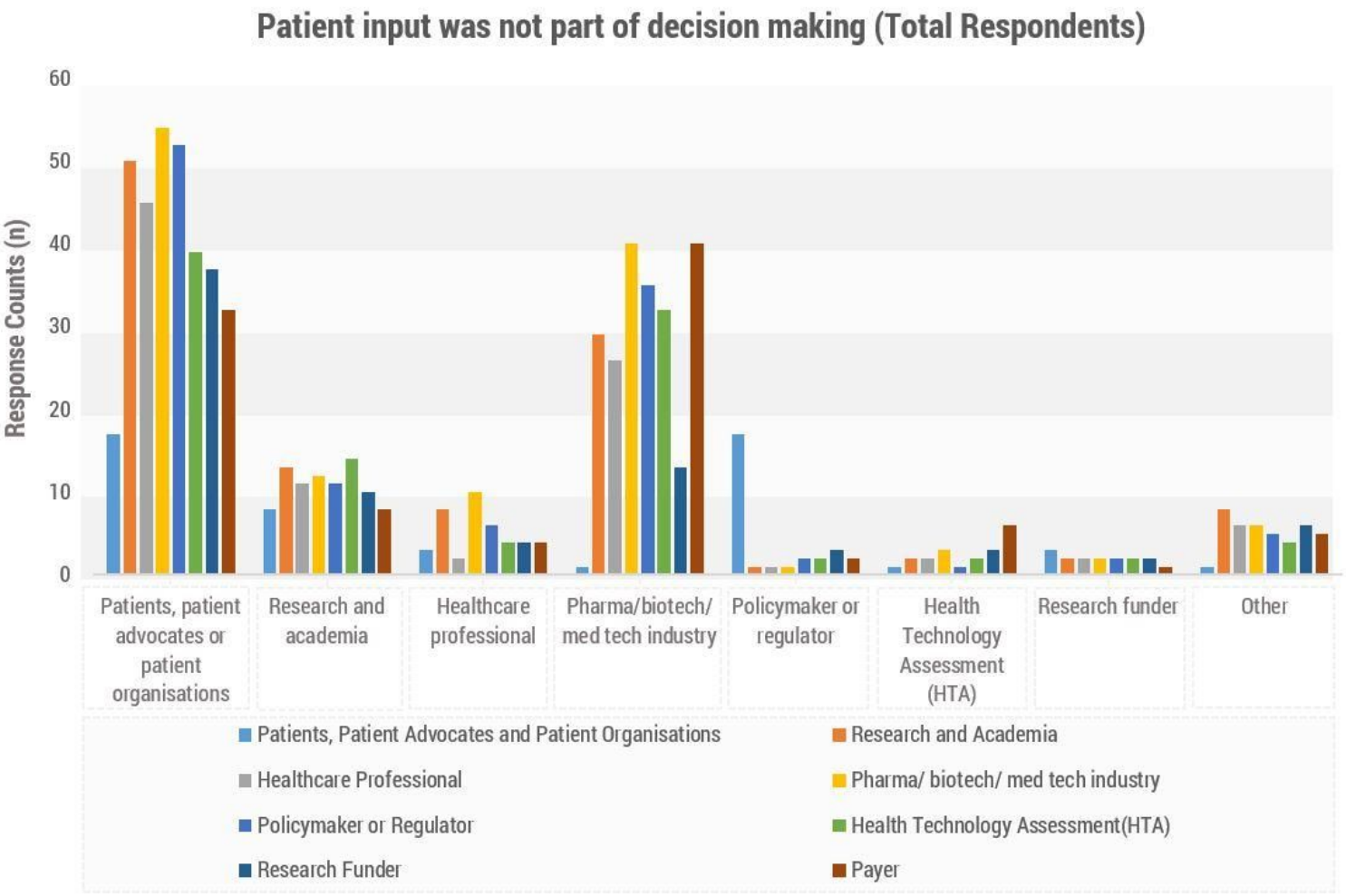

Figure 9 Challenge 'Patient input was not part of decision-making' broken down by stakeholder groups

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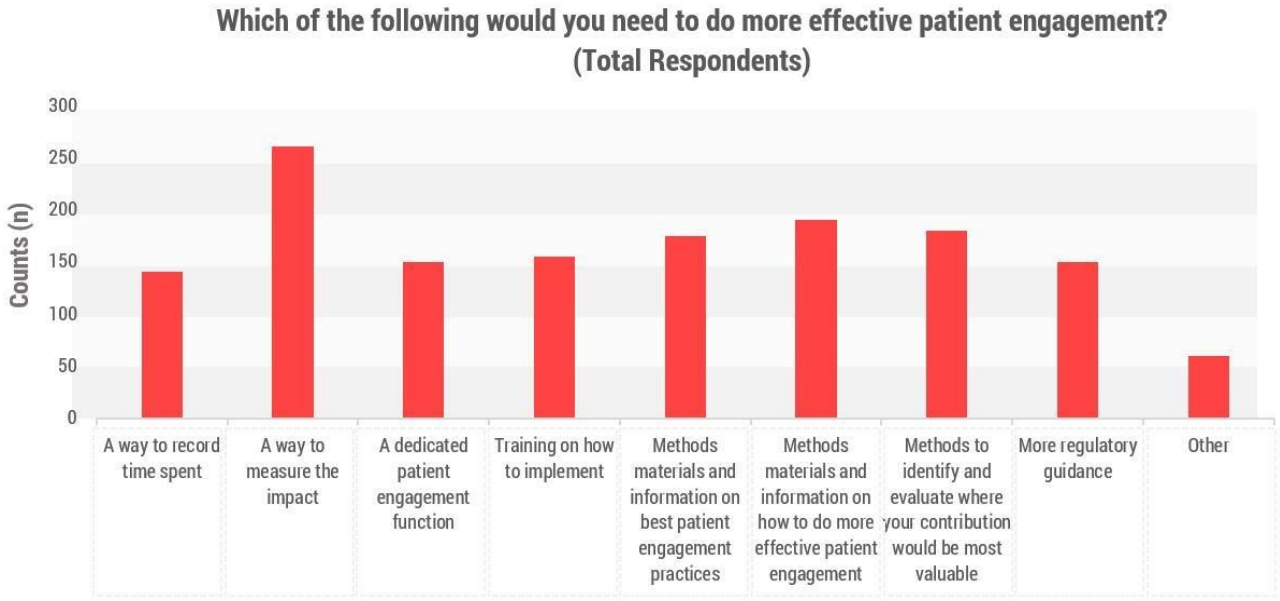

Figure 10 More effective patient engagement methods

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4.2.5 Current impression and the ideal expectations of the PE landscape

Respondents were asked to express their impression of the current PE compared to the ideal situation for PE in different stages of medicines development by moving the grid scale accordingly (scale from 0 (none) to 100 (ideal). The current impression/ perception of the PE landscape at all of the settings in the medicines research and development process were low (Blue line, Fig 11). On a 0-100 scale, the means for total scale points for each setting were below 35. The highest average respondent count was the clinical trials setting at 33.8±22.6 points on the scale. The lowest average respondent count was for the pricing and reimbursement decision process at 20.5±20.9 points on the scale. Each individual stakeholder group had similar views for the current impression and ideal expectation of PE at each of the settings.

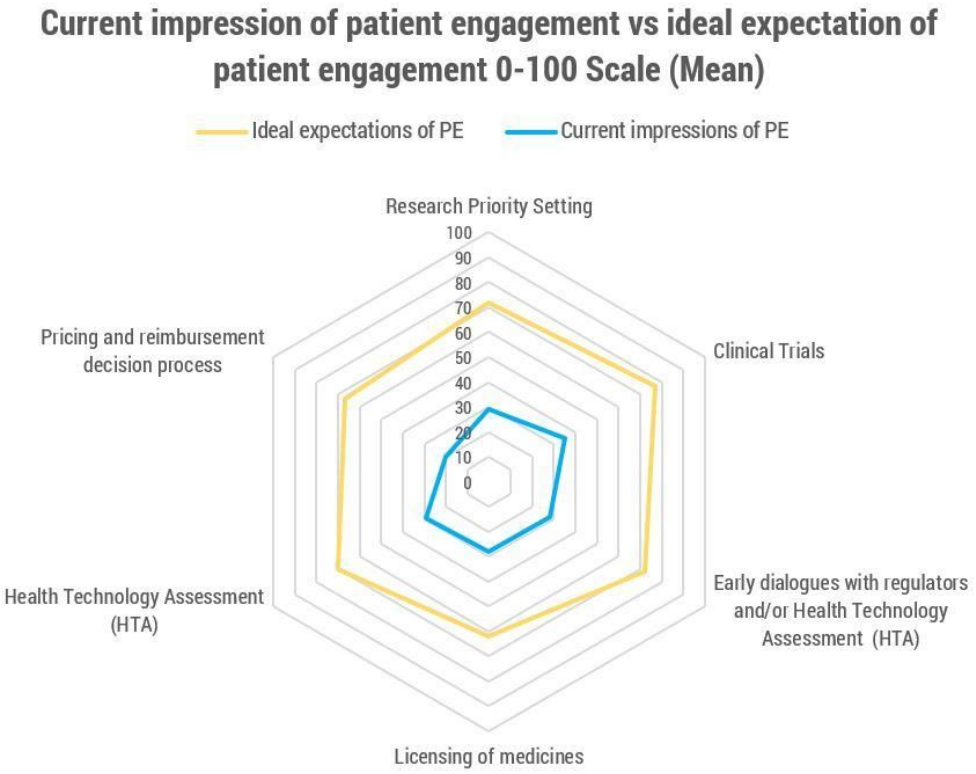

Figure 11 Current impression of PE and the ideal expectation of PE (0-100 Scale) (Mean)

For the ideal expectation of PE, the average total respondents scale points ranged from 65.2 to 77.0 (Yellow line Fig 11). The highest average respondent count was for clinical trials at 77.0±25.5 points on the scale and the lowest average was the pricing and reimbursement decision-making point, at 65.2±30.4 points on the scale.

4.2.6 Desired outcomes of PE

Respondents were asked to indicate up to three most desired outcomes of PE in the three decision-making points: research priority setting, clinical trial design, and medicines licensing and health technology assessment (HTA).

The top three desired outcomes for the research priority setting were: 'When patients' needs are leading in the research agenda (n=218), 'When it results in new insights and new perspectives for policymakers and regulators and research funders' (n=214) and 'When researchers get better insight in the patients' journey' (n=188).

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The top three desired outcomes for clinical trials were: 'When it results in more patient-relevant outcomes for clinical trials' (n=267), 'When patients can share their experiences and increase knowledge of the clinicians' (n=108) and 'When it leads to higher patient satisfaction during the trial' (n=106).

The top three desired outcomes for Health Technology Assessment (HTA) were: 'When the voice of the patient is reflected in the decision' (n=265), 'When patients' needs are better met' (n=245) and 'When it results in improving transparency and openness in decisions' (n=181).

4.2.7 Stakeholder-specific sections

At the beginning of the survey, participants were asked to identify themselves with a stakeholder group or affiliation (e.g. patients, patient advocates and patient organisations, biotechnology/ medical technology/pharmaceutical industry, healthcare professional, policymaker/ regulator). After completing the general set of questions, each participant was automatically taken to a set of questions which was linked to the group or affiliation they had identified themselves with. The number of questions per stakeholder group varied. The following sections report on these stakeholder-specific questions (that were only visible to those specific stakeholders).

4.2.7.1 From the perspective of the patients, patient advocates and patient organisations - stakeholder groups

Demographics

The total number of patient respondents was 45 and patient advocates and patient organisation respondents was 88. The majority of the participants from the patient community were between 36 and 65 years old (70%) (Table 3), female (n=82, 61.7%) and had a higher education degree (including vocational) (n=105, 78.9%).

Age	Counts	Percentage (%) of total respondents
18-25 years old	1	0.8
26-35 years old	13	9.8
36-45 years old	31	23.3
46-55 years old	30	22.6
56-65 years old	32	24.1
65+ years old	25	18.8
Prefer not to answer	1	0.8

Table 3 Patient age (by age group). Total respondents 133

Previous experience of PE activities

The patient community was asked about their background experience and on what basis they provide their input when they engage in PE activities with other stakeholders. Nine options were given with a possibility to choose all that applied. The patient community largely based their input on personal experience (n=113), survey of patients (n=74) and/or focus groups (n=70). In previous PE

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activities, patient respondents were asked whether they received compensation. The highest number of responses was for receiving reimbursement for transport/accommodation/food (n=83). Forty-one respondents stated they do not receive compensation for PE activities.

When asked whether they felt confident in participating in PE activities, the majority of respondents stated 'Yes' (n=113), while 13 respondents said they were 'Not sure'. The respondents were also confident to participate in the three decision-making points of the medicines lifecycle (Fig12). Individual patients in particular, were most confident to participate at the clinical trials stage (n=29) while patient advocates and patient organisations were most confident at the research priority setting (n=64).

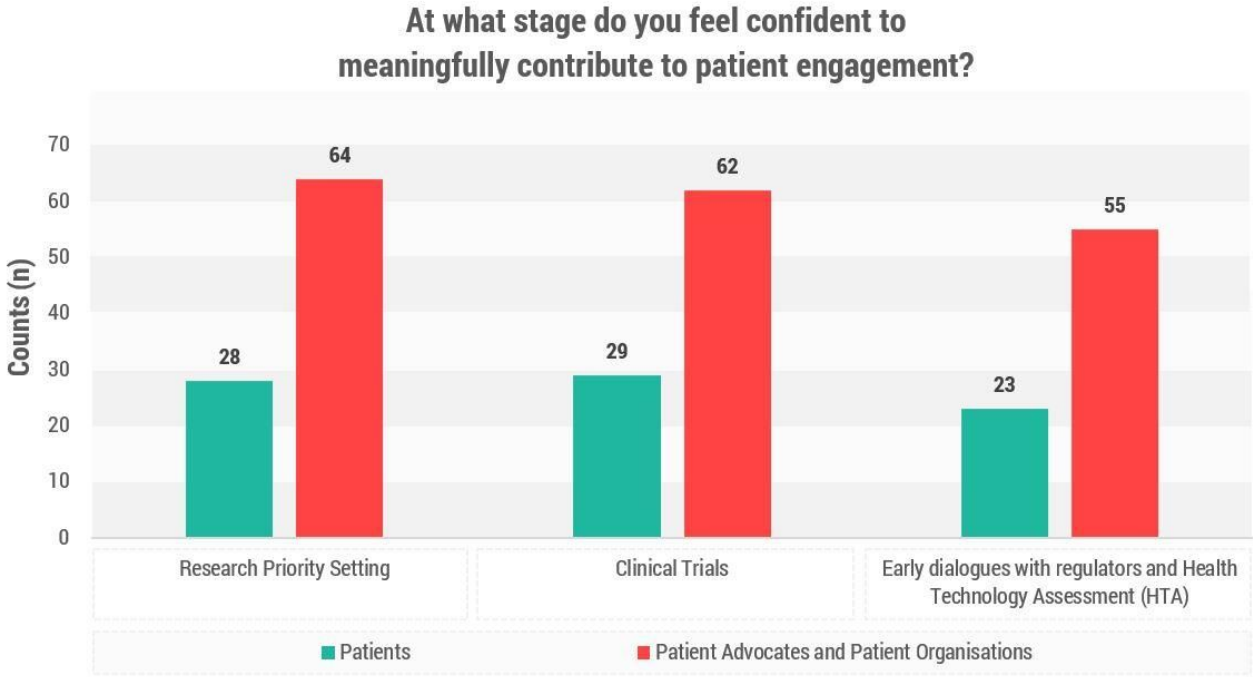

Figure 12 Patients' confidence to contribute to PE at three decision-making points

Methods to increase participation in PE activities for patients, patient advocates and patient organisations

Respondents were asked how PE activities should be financed. Of the 4 options given (+ 'Other'), the patient community stated that they would prefer 'One-to-one support given directly to individual patients' [N=77, Patients (n=30), patient advocates and patient organisations (n=47)]. When asked what type of support or mentorship they would like when they participate in PE activities, patient respondents stated they would like a 'Person/group with in-depth knowledge about the area of the planned engagement' (n=28), while patient advocates or patient organisation respondents would like 'Other stakeholders who are responsible for the activity I (we) want to engage in' to provide support (n=61).

Additional question for patient organisations

In addition, participants from patient organisations were asked to rate the preparedness of their organisation in the following areas: 'internal processes', 'knowledge' (information and expertise), 'human resources', 'financial resources', 'managing competing interests', and 'setting priorities in your PE strategy'. For a majority of the listed areas, respondents stated their organisation is

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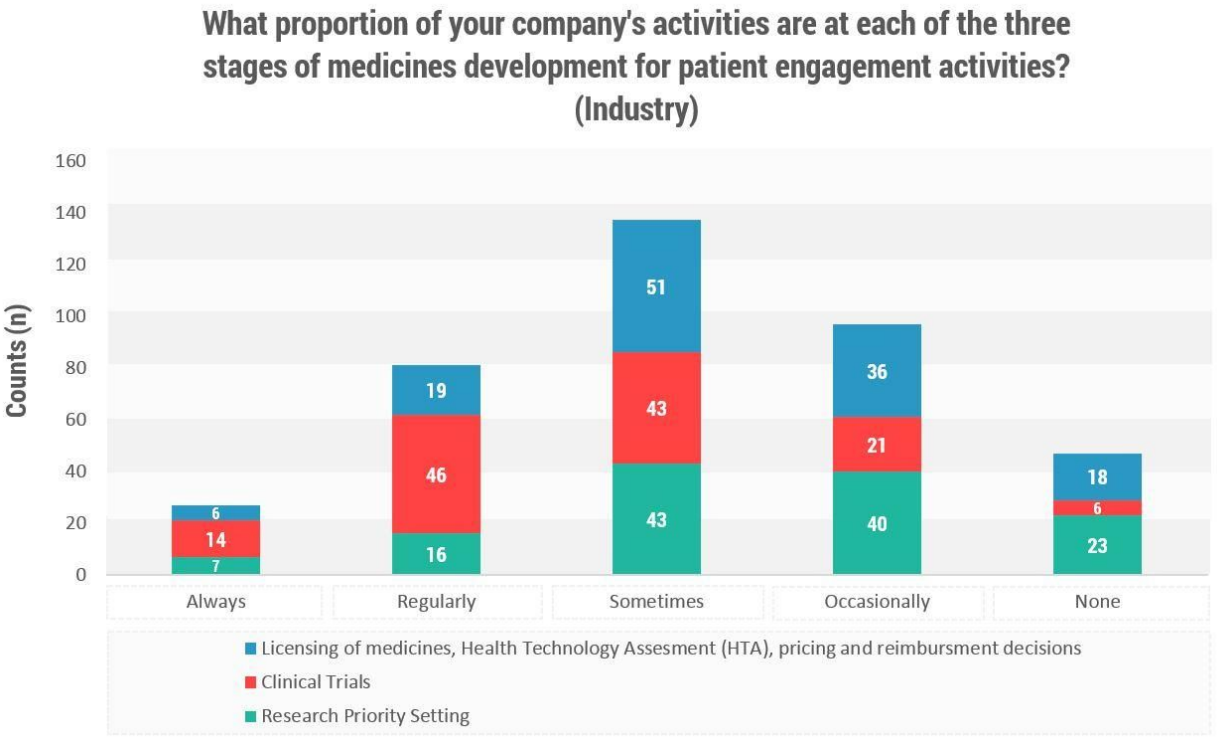
'prepared' to actively participate in PE, but they still 'require support' to do so [knowledge (n=56), internal processes (n=48), setting priorities in your patient engagement strategy (n=43), managing competing interests (n=40) and human resources (n=39)]. Additionally these respondents stated that for financial resources they '*did not have the appropriate preparation and required more support*' (n=42).

4.2.7.2 From the perspective of biotechnology/ medical technology/ pharmaceutical industry stakeholder groups

PE capacity and capability



When asked if their organisation has a dedicated PE function, industry respondents stated that a majority have a dedicated PE function in their organisation (n=99). Industry respondents indicated that the largest proportion of the company's activities are 'regularly engaged' in clinical trial design (n=46) and only 'sometimes engaged' at the research priority setting (n=43) and at the licencing, HTA and pricing and reimbursement decisions stages (n=51) respectively (Fig 13).

Figure 13 PE activities at the three stages of medicines development

Industry respondents stated that a majority do not have 'Metrics or methods to determine impact of patient involvement' in neither the short-term nor the long-term (n=103). However, they also stated that their organisations are 'Making a good effort' to move their PE activities from intentions to outcomes (n=97) and PE was 'very important' to their organisation (n=45). When asked about Standard Operating Procedures (SOP) and if they are in place in the organisation, industry respondents stated they have an SOP or other guidance on interactions with patients/ patient organisations in PE and it is used in practice (n=67).

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4.2.7.3 From the perspective of the regulators, policymakers, HTA bodies, research funders and payers- stakeholder groups

PE capacity and capability

The total number of respondents in the regulators, policymakers, HTA bodies, research funders and payers groups is 25. Twelve respondents from these groups reported that they have a dedicated PE function within their organisation, while 10 respondents said they do not.

Involvement of patients in the work of regulators, policymakers, HTA bodies, research funders and payers

Respondents were asked how patients are involved in their work (i.e. not involved, informing, consulting, deciding) and they were able to select all involvement levels that applied at each decision-making point. The majority of respondents reported 'no involvement' with patients or their representatives in their work at the three decision-making points: research priority setting (n=11), designing clinical trials (n=13) and early discussions with regulators and/or HTA bodies (n=8) (Fig 14).

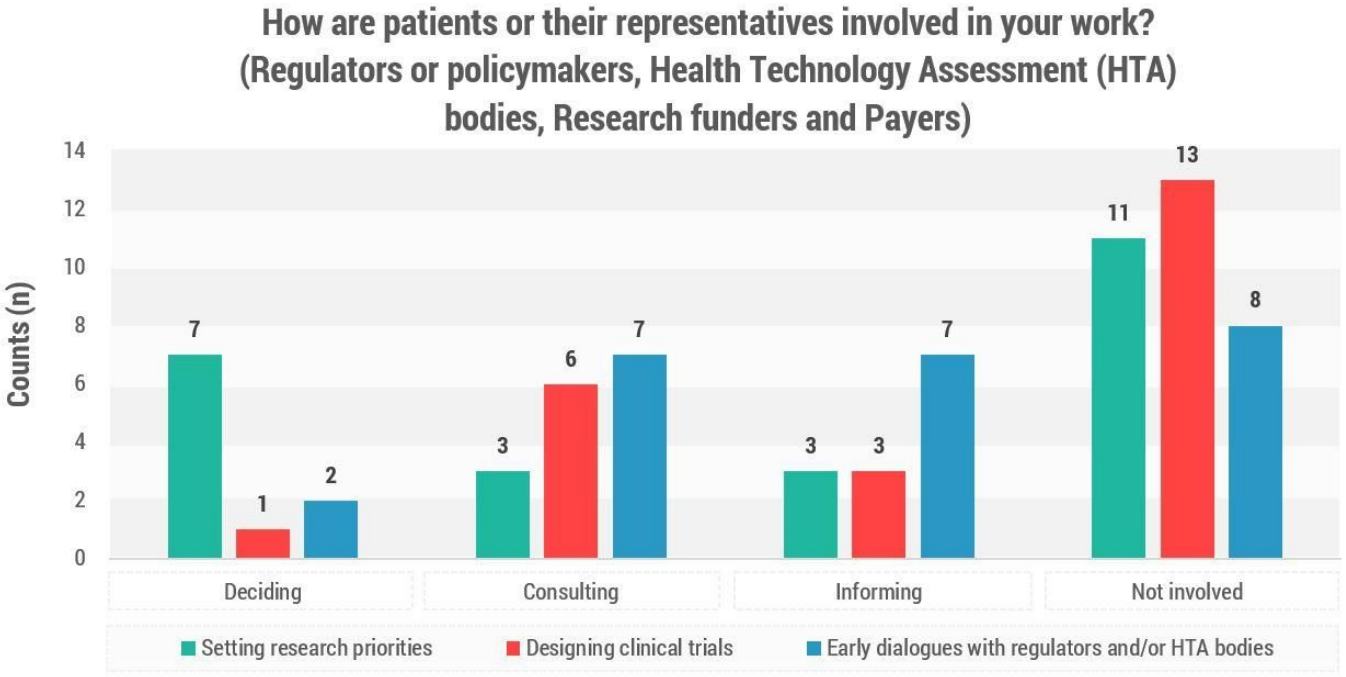

Figure 14 Patients' involvement and decision making in PE activities

In addition, a majority of respondents indicated they do not have a method to determine the impact of PE (n=11), while 8 respondents stated that they do have a method to determine the impact of PE. The majority of respondents from the regulators, policymakers, HTA, research funders and payer groups stated that they provide feedback to patients they have engaged with in their PE activities (n=15).

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4.2.7.4 From the perspective of HCP - stakeholder group

Patients' involvement in PE activities

HCP respondents reported that approximately a third of patients are "consulted" for setting research priorities (n=7) and for the design of clinical trials (n=9). Another third reported that patients are not involved in setting research priorities and the design of clinical trials. Ten respondents stated they do not have involvement with patients in the early dialogues with regulators and/or HTA bodies (Fig 15).

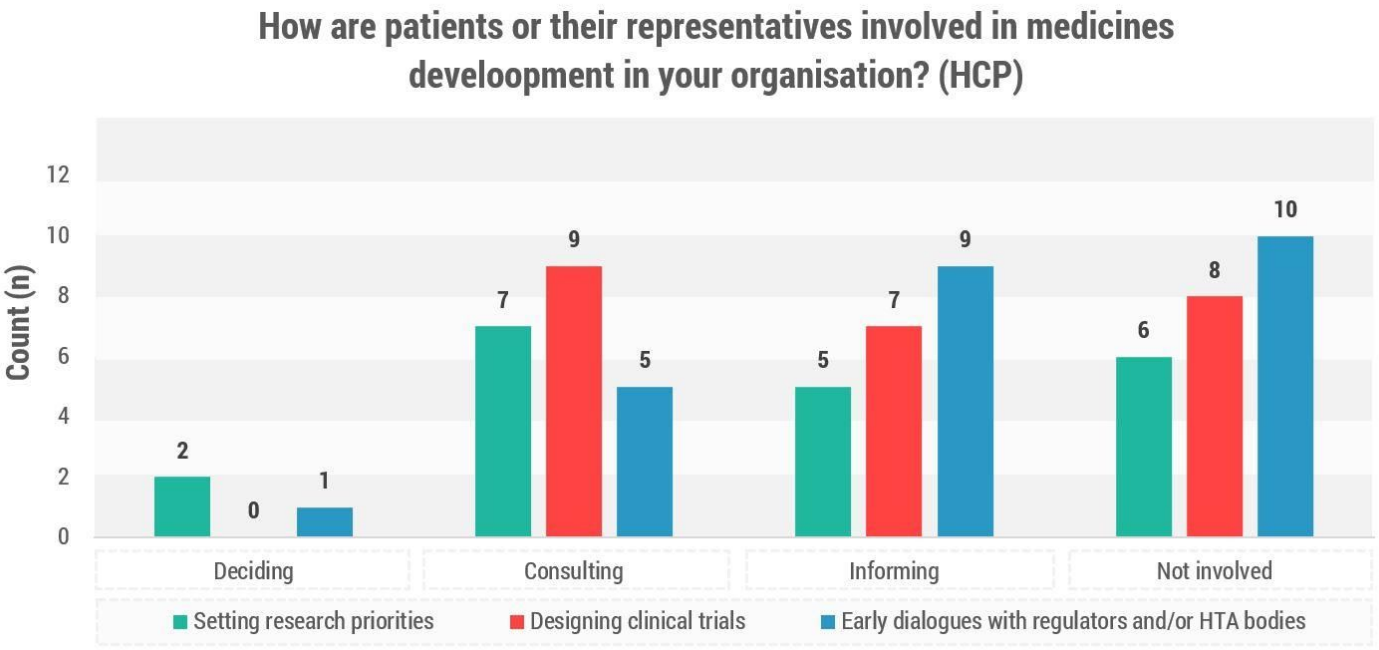

Figure 15 Patients' involvement and decision making in PE activities

Capacity and capability to engage in PE activities

Healthcare professionals were asked if their organisation was prepared to actively participate in PE in medicines development. Respondents indicated that for every item listed (internal processes, knowledge, human resources, financial resources, managing competing interests and setting priorities in your patient engagement strategy) they are 'prepared but still require support' (n=15, 13, 10, 9, 11, 13, respectively) (Fig 16).

Cop

Figure 16 Preparedness to participate in PE activities

A majority of HCP respondents indicated they do not have a SOP or other guidance on interactions with patient/ patient organisations in PE and it needs to be established (n=11). Moreover, healthcare professionals stated that they do HCP respondents indicated that they 'do not have methods to determine the impact of PE' (n=20).

4.3 Results from non-English versions of the survey

There were fewer non-English versions of responses, than for English versions, and for some stakeholder groups and some questions response rates were <10. The following data is therefore presented in tables or as text for ease of reading.

4.3.1 Demographic background of the study population

The total respondents who completed the survey were 169. The stakeholder groups were separated into nine groups. The largest respondent group was the patient community (n=67, 39.6%), followed by industry (n=48, 28.4%) (Table 4).

Table 4 Stakeholder Groups (non-English respondents)

Responses to non- English surveys	169	
Stakeholders		
Patient community [Patients (including carers), Patient Advocates, Patient organisations]	67 (31/36)	39.6%
Industry	48	28.4%
Research and Academia	18	10.7%
Healthcare Professionals (HCP)	7	6.7
Health Technology Assessment (HTA)	8	4.7%
Regulator or Policymaker	11	6.5%
Research funder	1	0.6%
Payer	1	0.6%
Other	8	4.7%

Languages and country of origin

Of the 18 European language versions of the survey available (after excluding 5 languages), respondents completed the survey in 13 European languages: Croatian, Czech, Danish, Dutch, Finnish, French, German, Greek, Hungarian, Italian, Slovenian, Spanish and Swedish from 20 countries worldwide. The highest number of responses were in Italian (n=65, 40.2%), Spanish (n=24, 14.2%) and Dutch (n=23, 13.6%). The majority of respondents were located in Italy (n=67, 39.6%) and the Netherlands (n=21, 12.4%).

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4.3.2 Previous engagement opportunities with other stakeholders

Respondents were asked about their previous involvement with other stakeholders at the three decision-making points (i.e. *informing* -giving one's opinion and perspective but no channel for feedback-, *consulting* -giving one's opinion and perspective and the ability to provide feedback-, and *decision-making*- ability to give opinion, provide feedback and make the final decision). This optional question was in a matrix format and allowed multiple choices.

4.3.2.1 Previous engagement opportunities with patients, patient advocates and patient organisations

For the three decision-making points, stakeholders had the lowest number of previous engagements with patients, patient advocates and patient organisations compared across all of the stakeholder groups. The total counts of engagement at the research priority setting was 52; industry had the highest number of previous engagements with the patient community at the informing level (n=12).

At the clinical trial design stage, total engagement drops to a total count of 48, and the industry group had an increase in number of HTA bodies, industry respondents reported more engagement activities with patients, patient advocates and patient organisations at the informing level (n=14) and the deciding level (n=3). At the consulting level, policymakers or regulators, as well as HTA respondents each respectively had 4 counts of engagement.

4.3.2.2 Previous engagement opportunities with research and academia

Respondents reported the highest total counts of engagement with research and academia. At the research priority setting, the total counts of engagement was 92, and the three highest counts among individual stakeholder groups was patient advocates and patient organisations (n=27), Patients (n=20) and industry (n=25). At the informing level, patients and industry had the highest counts of engagement (n=12 and n=11, respectively). At the consulting level and deciding level, patient advocates and patient organisations had the highest counts of engagement (n=12 and n=7, respectively).

At the clinical trial design stage, the total counts of engagement decreased to 89. Industry respondents had the highest counts of engagement at all three decision-making levels (informing, n=13, consulting, n=10 and deciding, n=5).

At the early dialogues with regulators and/or HTA bodies stage, patient respondents and patient advocates or patient organisation respondents had the highest counts of engagement at the informing level (n=13 for both). Industry respondents had the highest counts at the consulting level (n=12) and the lowest total counts of engagement were at the deciding level overall (n=3).

4.3.3 Challenges with other stakeholders in PE

Respondents were asked about the challenges they had experienced with other stakeholders in their previous PE collaborations. Thirteen challenges were given with the option of adding 'Other' and specifying a challenge outside of those listed. Respondents were able to choose multiple stakeholders per challenge (including the stakeholder group they identified with), which is reflected in a high number of counts in each challenge.

The top 5 challenges reported by the respondents by order of importance were:

- *Patient input was not part of decision-making (n=417)*

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- *Lack of shared vision/goals with other stakeholders (n=351)*
- *Communications were not clear and open (n=334)*
- *Lack of openness to patient input (n=317)*
- *Delays in activities due to bureaucratic processes (e.g. contracts, IP, etc) (n=260)*

All of the stakeholder groups experienced the challenge 'Patient input was not part of decision-making' with patients, patient advocates or patient organisations. Each stakeholder group had the highest counts of the said challenge with patients, patient advocates or patient organisations. Furthermore, policymaker or regulator respondents had the highest counts of the said challenge (n=35) of any other respondent group.

4.3.4 Resources needed for more effective PE

Respondents were asked what was necessary to conduct more effective PE. Eight choices were given with the option of adding 'Other' and specifying a resource outside of those listed and respondents were asked to choose all that applied.

Respondents from languages other than English indicated that they require more 'Methods, materials and information on how to do more effective patient engagement' (n=107). The second and third required resource was 'A way to measure the impact of patient engagement activities you are involved in' and 'Methods, materials and information on best patient engagement practices related to your stakeholder group' (n=95 for both). Some of the comments from the 'Other' category include 'real patient involvement in decision-making processes', 'active engagement of patients in the definition of outcomes and in decisions on approval and payment for medications' and 'clear goals and support for patient involvement'.

When broken down by stakeholder group, patients reported that they also required more 'Training on how to implement patient engagement processes in your organisation' (n=18). Patient advocates and patient organisations required more 'Methods to identify and evaluate where your contribution would be most valuable' (n=29). Industry respondents reported they needed 'A way to measure the impact of patient engagement activities you are involved in' and 'Methods, materials and information on best PE practices related to your stakeholder group' (n=28 for both). HTA respondents also required a 'A way to measure the impact of patient engagement activities (n=7), while respondents from the 'Other' group indicated they need 'a dedicated patient engagement function in your organisation' (n=5).

4.3.5 Current impression and the ideal expectations of the PE landscape

Respondents were asked to express their impression of the current PE compared to the ideal situation for PE in different stages of medicines development by moving the grid scale accordingly (scale from 0 (none) to 100 (ideal). The current impression of the PE landscape in all of the listed settings was low (Overall Means <25). The highest average respondent count was the clinical trials setting at 24.7±19.7 points on the scale and the lowest was the pricing and reimbursement decision process at 13±15.6 points on the scale.

For the ideal expectation of PE, the highest average respondent count was for clinical trials at 72.1±26.9 on the scale and the lowest average was the pricing and reimbursement decision process at 59±32.5 points on the scale.

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4.3.6 Desired outcomes of PE

Respondents were asked to indicate up to three most desired outcomes of PE at the three decision-making points: research priority setting, clinical trial design, and medicines licensing and Health Technology Assessment.

The top three desired outcomes for the research priority setting were: 'When it results in new insights and new perspectives for policymakers and regulators' (n=95), 'When patients are leading in the research agenda' (n=94) and 'When researchers get better insight in the patients' journey' (n=75).

The top three desired outcomes for clinical trials were: 'When it results in more patient-relevant outcomes for clinical trials' (n=92), 'When patients can share their experiences and increase knowledge of the clinicians' (n=82), and 'When information is better communicated to patients' (n=77).

The top three desired outcomes in the early dialogues with regulators and HTA were: 'When patients' needs are better met' (n=102), 'When it results in improving transparency and openness in decisions' (n=99) and 'When the voice of the patient is reflected in the decision' (n=95).

4.3.7 Stakeholder-specific sections (non-English responses)

4.3.7.1 From the perspective of the patients, patient advocates and patient organisations- stakeholder groups

Demographics

Of the respondents who completed the survey in languages other than English, the largest patient group was from 46 to 55 years old.

Table 5 Patient Age (by age group)

Age	Counts	Percentage (%)
26-35 years old	6	9.0
36-45 years old	10	14.9
46-55 years old	24	35.8
56-65 years old	14	20.9
65+ years old	10	14.9
Prefer not to answer	3	4.5

Patient respondents were largely female (n=46, 68.7%) while males made up 29.9% (n=20) of the respondent group (the rest respondents chose not to specify their gender). A large majority of the respondent group had a higher education degree (including vocational) (n=50, 74.6%) (Table 5).

Previous experience of PE activities

The patient community was asked about their background experience and on what basis they provide their input when they engage in PE activities with other stakeholders. Nine options were

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given with a possibility to choose all, if applicable.

For previous PE activities, the patient community stated that they base their input on 'personal experience' (n=56), 'survey of patients' (n=45) and individual interviews (n=38). When asked if they received compensation in their previous PE activities, 33 respondents said they do not receive compensation. Thirty-one respondents received compensation in the form of travel/ accommodation/ food.

The majority of patient respondents stated that they are confident to contribute meaningfully to PE (n=55). When asked at which stage of the medicines lifecycle they were most confident, patients were most confident at the research priority setting (n=15). Patient advocates or patient organisations were most confident at the clinical trials stage (n=24).

Methods to increase participation in PE activities for patients, patient advocates and patient organisations

When asked how PE activities should be financed, a majority of patient respondents stated that 'One-to-one support be given directly to individual patients' (n=44). When respondents were asked what would help increase their confidence to participate in PE activities, 18 patient respondents chose 'my organisation'. Patient advocates or patient organisation respondents stated they would like 'People with experience in patient engagement' to help them increase their confidence (n=25).

Participants from patient organisations were asked about the preparedness of their organisation to actively participate in PE. For all of the following areas, patient organisations stated they are prepared but still in need of support in: 'internal processes' (n=16), 'knowledge' (information and expertise) (n=24), and 'human resources' (n=19). Respondents also said they are 'not prepared and need support' for the following areas: 'financial resources' (n=20), 'managing competing areas' (n=14) and 'setting priorities in your patient engagement strategy' (n=15).

4.3.8 From the perspective of biotechnology/ medical technology/ pharmaceutical industry- stakeholder groups

PE capacity and capability

When asked if their organisation has a dedicated PE function, the majority of industry respondents stated 'yes' (n=29). However, industry respondents indicated that at the research priority setting and the licensing of medicines, HTA, pricing and reimbursement decision-making, the proportion of their company's activities were 'None' (n=16 and n=18, respectively). At the clinical trials stage, the company occasionally dedicated a proportion of their company's activities to PE (n=15).

Industry respondents stated they do not have methods/ metrics to determine the impact of PE in the short and long-term (n=40). They stated that PE in medicines development in their organisation is 'very important' (n=13) and their organisation was 'Making a good effort' to move PE from intentions to outcomes (n=29). When asked if industry respondents' organisations have a Standard Operating Procedure (SOP) in their organisation, nineteen respondents said 'No and it should be established'.

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4.3.9 From the perspectives of the regulators, policymakers, HTA bodies, research funders and payers- stakeholder groups

Patients' involvement in PE activities

Out of 21 respondents, 12 reported that a patient engagement function is in place at their organisation. However, patients or their representatives are largely 'not involved' in the work of the policymaker or regulator and HTA respondents at the research priority setting and clinical trial design stage (n=3, n=5 and n=2 and n=5, respectively). At the early dialogues with regulators and/or HTA bodies stage, HTA respondents and policymaker or regulator respondents 'consult' with patients and their representatives (n=8 and n=5).

The majority of respondents stated they do not have a 'Method to determine [the] impact of PE' (n=19). Respondents also provide feedback to their patients who have engaged in their processes (n=13).

4.3.10 From perspective of the HCP - stakeholder group

Patients' involvement in PE activities

HCP respondents are involved with patients or their representatives at the research priority setting at an 'informing' and 'deciding' level (n=3 for both). For clinical trials and early discussions with regulators and/or HTA bodies, patients or their representatives are 'not involved' in the process (n=3 for both.)

PE capacity and capability

Healthcare professionals indicated that their organisation is 'Prepared but still needs support' for the following areas: 'knowledge' (information and expertise) (n=5), 'human resources' (n=4) and 'financial resources' (n=3). For 'internal processes' and 'managing competing interests', respondents stated they are not prepared and need support (n=3 for both). For 'setting priorities in your patient engagement strategy', respondents equally indicated that they are not prepared and do not need support (n=2), not prepared and need support (n=2) and prepared but still need support (n=2).

HCP respondents indicated that PE is 'very important' in their organisation (n=3) and they provide feedback to patients who have been involved in their processes (n=4), however they indicated that they do not have an SOP or guidance on interactions with patients/ patient organisations in medicines development and it should be established (n=5).

5 Consultation with vulnerable/ underrepresented and specific stakeholder groups

Consultations were held with the following groups: people with dementia and their carers, children and young people, people with rare diseases, and HTA bodies (see methods).

Section 5 is divided into two main subsections due to the different nature of the consultations for the vulnerable populations and the HTA community. Subsection 5.1 focuses on these specific

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stakeholder groups starting with the methodology used in the consultations, followed by key findings in each group.

Vulnerable patients such as people living with dementia (and their carers), and children and young people, share many of the needs, expectations and aspirations expressed by other patient groups. However, there are additional and specific considerations which need to be taken into account when engaging these populations during medicines development. Additionally, in this study the chosen method of data collection (i.e. an online survey) was not considered ideal for some of these groups, thus a different and complementary approach was taken to gather these patients' views and needs. This involved face-to-face consultations. This work was led by Alzheimer Europe (AE) (in the case of people with dementia and their carers) and Sant Joan de Déu Research Foundation (FSJD) (in the case of children and young people).

In the case of people with rare diseases, EURORDIS took the opportunity of its Summer School for patients to gather some input face-to-face in addition to the contribution received via the online survey.

In addition, it was recognised that many HTA bodies across Europe have diverse remits with often limited capacity or capability for PE activities, are often underrepresented in exiting PE initiatives, and a detailed understanding of their opinions on how to improve PE is missing. Thus to better understand the barriers and enablers to their participation in PE activities around early dialogues, additional focus group consultations were organised by Health Technology Assessment International (HTAi) and reported in subsection 5.2 below (starting with methodology and followed by key findings).

5.1 Consultation with specific stakeholder groups

5.1.1 Methodology

5.1.1.1 Approach for people living with dementia

The consultation on dementia involved members of AE's European Working Group of People with Dementia (EWGPWD)[9] and their carers. The consultation[10] was carried out on June 27th-28th 2018 in Brussels and aimed to gain a better understanding of the expectations, motivations, needs and expected outcomes of people with dementia and their carers when taking part in PE activities in the process of developing medicines.

The consultation was facilitated by two experienced AE staff members who knew well the members of the group, a PhD student linked to AE, and three colleagues from PARADIGM representing different stakeholders (i.e. academia, HTA and a pharmaceutical company) and with experience in the three decision-making points.

A guide for the facilitators was developed by AE in collaboration with WP1 leaders and co-facilitators. It included (i) a set of overarching questions about the different topics of interest to PARADIGM, that allowed a free-flowing discussion, and (ii) several prompt questions to be used as needed. In addition, vignettes related to the three decision-making points of interest to PARADIGM (i.e. research agenda setting, design of clinical trials, and early dialogues with regulators and HTA bodies) were developed. Members of the EWGPWD received all relevant information about

[9] The EWGPWD was set up in 2012 and is comprised entirely of people with different forms and stages of dementia who are nominated by their national Alzheimer associations for terms of two years. The EWGPWD has been involved in several consultations with European projects (e.g. IMI, FP7, Horizon2020 projects etc.).
[10] For more information on the consultation with people with dementia, please see the detailed report from attachments.

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PARADIGM and the consultation two weeks in advance of the meeting. The consultation itself was conducted in two half-day meetings.

In total, 11 people with dementia and 10 carers from 10 countries[11] participated in the consultation.

The first part of the consultation addressed their understanding of PE in general, PE in the context of medicines development, and what they thought were the main barriers and facilitators for engaging patients in this way in their country. During the second day, participants were split in three smaller groups and each group worked on one of the three decision-making points. Facilitators adapted the questions in the guide to the needs and dynamics of the group. A positive and respectful environment which could encourage people to share their perspectives and views was promoted.

With permission from people with dementia and their carers, all the discussions of the consultation were audio-recorded. In addition, during the meeting summaries of the discussions were recorded in a flipchart. A thematic approach to analysis was used to consolidate all the inputs provided during the discussions and highlight common themes relevant to people with dementia. In order to achieve a Patient and Public Involvement (PPI)-informed perspective on the data, two members of the EWGPWD and one carer were also invited to review the way the input was presented and their feedback was included in the resulting report.

5.1.1.2 Approach for the consultation with children and young people

The consultation with the members of the Kids Barcelona group- the Young Persons' Advisory Group (YPAG) of the Sant Joan de Déu Research Foundation- was held on September 14th 2018[12] by two experienced facilitators. There were 14 participants aged 15 to 18 years old. The level of prior experience of participants of PE in medicines development was varied, and the topics under discussion potentially complex. To ensure comprehensive participation by all attendees, content was translated into Spanish and the session was divided in two parts that included illustrative case studies as follows;

1. An introduction to the purpose of the PARADIGM project was given to offer the appropriate background about the different decision-making points and PE activities in medicines development (i.e. research priority setting, clinical trial design and early dialogue with regulators and HTA bodies), the clinical trials unit coordinator provided a theoretical explanation about the two decision-making points in which PARADIGM focuses and the scope of the activities of Kids Barcelona. Additionally a video was shown to the participants at the end to summarise the most relevant information.
2. Two case studies were analysed and discussed with the group. One focused on the topic of research priority setting and the second focused on clinical trial design. This second part of the session was conducted by Begonya Nafria, coordinator of the Kids Barcelona YPAG.

A thematic analysis of results was undertaken, and compared with those from people with dementia. Many common themes were highlighted and described in the results section below.

[11] Belgium, Bosnia & Herzegovina, Czech Republic, Finland, Germany, Ireland, Portugal, Slovenia, Switzerland, Scotland and Wales

[12] For more information on the consultation with children and young people, please see the detailed report from attachments.

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5.1.1.3 Approach for the consultation with rare disease patient advocates

During the Expert Patient and Researcher EURORDIS Summer School (ExPRESS)[13] face-to-face training held on June 11-15th 2018 an internal consultation was organised by EURORDIS to explore with its members the different dimensions of the sustainability of PE in medicines research and development. EURORDIS co-leads the work package on sustainability in PARADIGM and it was felt important to hold this consultation in order to help elicit the position of EURORDIS and to be able to more accurately represent the views of its membership. While this activity was not initially foreseen in the description of actions and although it does not follow the same methodology (for the reasons explained above), the outcome of this consultation is adding to the knowledge generated within the PARADIGM Consortium and is thus included into this deliverable.

During the session, a total of 9 patient representatives were involved. The session was preceded by a quiz in the morning in which all ExPRESS students had the opportunity to participate. The quiz consisted of 8 simple questions to test how students felt about their previous engagement experience, their priorities to improve it, and how the future PE framework in Europe should be organised in terms of governance and funding models.

Dynamics of the internal consultation

The session was facilitated by two experienced moderators (EURORDIS and EPF staff members). In advance, participants were provided with background literature on the sustainability of PE and making assets arising from public-private partnerships sustainable (Boudes et al. 2017, Aartsen et al. 2018). The session was audio-recorded with the consent of all participants.

Following a brief introduction on the objectives of PARADIGM, participants were first asked their opinion on what makes PE sustainable. They wrote down their views and shared them with the group. Participant views were consolidated then prioritised. In the second part of the exercise, the three pillars of PE sustainability were discussed broadly, namely; i) processes, ii) resources and iii) culture, and which specific elements within those three pillars were considered to be the most important in order to support and sustain PE in medicines R&D in the long term.

5.1.2 Key findings from consultations with specific stakeholder groups

5.1.2.1 Key findings from the consultation with people with dementia and their carers

The vignettes used at the consultation looked at the perspectives of people with dementia and their carers at each of the three PARADIGM decision-making points separately. However, the majority of the issues and concerns raised were quite similar across the three points. Thus, in the presentations of the findings, differentiation between the three points is only made when necessary, otherwise the suggestions and concerns are applicable to the three points. Three main topics emerged from the analysis of the input provided by the members of the EWGPWD and their carers:

1. Who should be engaged?
2. How to enable meaningful engagement in the case of dementia and barriers that may prevent that?
3. The expected outcomes from participating in a PE activity

1. Who should be engaged in PE

[13] For more information on the consultation with rare disease patients, please see the detailed report from attachments.

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- There was strong agreement that the voice of the person with dementia is critical and should, in all cases, be prioritised over the voice of others such as patient representatives or carers. The people with dementia are the "experts by experience" and their input is unique as the people living with the condition can bring knowledge and experience that other experts, such as clinicians or researchers, may not always have. The organisers of patient activities in the development of medicines should be clear and transparent about who was engaged in the activity (e.g. the person with the condition, the carer, or a patient representative).
- The diversity of the patients involved in any PE activity was important (e.g. age group, country, type and stage of dementia etc.).
- Raising awareness of the relevance of PE in research and the opportunities that exist to do this, were perceived as an important step to connect with and be inclusive of a diverse community of patients. This was considered an important task where Alzheimer societies and related organisations could play a significant role in facilitating this.

2. How to enable meaningful engagement in the case of dementia and barriers that may prevent that

- An issue of concern was that of the existing stereotypes, misconceptions, and stigma surrounding dementia. Members and carers explained that once a person is diagnosed, there is often an assumption about what a person can and can no longer do, combined with a tendency to focus on images which are more representative of advanced dementia. Thus, an important enabler to their engagement in PE activities is by better **addressing the existing myths and misconceptions about dementia.**
- The meaningful engagement of people with dementia is dependent upon measures taken to ensure the accessibility needs of those people are met. The group emphasised the importance of reasonable accommodation or adjustments being acknowledged and accounted for during a PE activity as this would help **provide an equal opportunity for a person with dementia to participate**. Discussions on this topic focused on two key aspects:
    - The structure and format of the PE activity should take into consideration the needs of the person with dementia and adjustments should be made as appropriate.
    - The contents of the PE activity should be adjusted and suited to the needs of the person. Some of the issues highlighted included: the accessibility of the materials received, the use of plain language and avoiding the use of jargon, acronyms and highly technical terms. Efforts should also be made to ensure that the questions asked and the way in which the questions are presented, are appropriate for patients.
- Many people with dementia may need to be supported to be able to take part in a PE activity. The type of support required can include travel-related support and preparation for and during the PE activity - the person providing such support may also be different for each individual person. These considerations should be discussed with the person(s) with dementia early on during the planning and organisation of any PE activity so that they can be accounted for where possible. **Travel and accommodation costs incurred should be covered for both the person with dementia and his/her carer.** In addition, the organiser of the PE activity should designate a **"named person or a single point of contact"** with whom the person with dementia could speak to freely if any problem arose, and who could provide information and support to the person with dementia and carer throughout the process.

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- **Accessible and understandable information about the PE activity was perceived as a key enabler for the participation of any patient, with or without dementia.** The person should have enough information and understanding of the PE activity, so that he/she can make an informed decision about whether he/she wants to take part or not. All information ('written' and verbal) provided should be clear, in an accessible format and in a language that is plain, respectful to the person and free of jargon. The use of a clear layout, enhanced text contrast, short sentences and bullet points whenever possible, can also greatly improve the accessibility of the documents. This information should be provided to the person in advance of the meeting/ activity so that the person has enough time to get prepared, and during the meeting/ activity enough time should be allowed for the person to read and process any new information.
- **People with dementia and carers involved in PE should be offered induction sessions or training.** This was considered to be particularly important due to the nature and complexity of topics discussed during PE activities and it was particularly important in the case of PE in the design of clinical trials. Similarly, professionals and researchers organising or involved in a PE activity should also have some basic understanding of dementia (beyond medical aspects) and skills to support a person(s) enabling them to contribute in a meaningful way.
- There is a need to **build a good relationship with a person with dementia and carer throughout the process of engagement.** Key principles that should guide this relationship included: autonomy, respect and equality. In particular, respect could be demonstrated by listening, valuing and taking into account what a person with dementia has to say and, by them receiving feedback about how their contribution had been used and the progress of the activity for which they had provided input. This type of relationship was described as, "...a relationship where all different parties involved (e.g. professionals and patients) should work as equals".
- Some of the most **relevant barriers for PE** in the process of developing medicines included: i) **late diagnosis of dementia** in many countries (e.g. at moderate or severe stages), ii) **the natural progression of the disease** (it may be more challenging to engage people in the more advanced stages of dementia), iii) stigma of dementia and prevailing stereotypes, iv) **lack of awareness among patients and carers regarding the possibilities to take part in PE activities**, v) a lack of awareness and reluctance from the organiser of a PE activity (organisation/ researcher) about **how and why to involve people with dementia**, and vi) reluctance from 'gatekeepers' to facilitate such participation. For example, carers or patient organisations may act as a gatekeeper and decide on behalf of the person, which may result in the person with dementia not even being asked if she/he wants to take part.

3. The expected outcomes from participating in a PE activity

Some of the most relevant outcomes for the person included:

- **Feeling valued, empowered, or gaining purpose or hope**. These were considered to be particularly relevant in the context of dementia as after diagnosis many people feel disempowered or hopeless.
- **Conveying the lived experience of the person with dementia** to the different stakeholders involved in the development of medicines.
- **Changing attitudes of different stakeholders** involved in the development of medicines, their perception of patients and the way patients are involved.

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- **Gaining knowledge about the disease and new treatments** or creating new personal connections with expert professionals and researchers.
- **Helping to develop better medicines for future generations** (such as family members who may develop dementia and the broader population). Participants felt that most of the medicines currently being developed and tested are for people in the very early stages of dementia, or even prevention. In many cases, they felt any new medicine would as likely as not be suitable to them.
- In the case of the design of clinical trials, another important outcome was for the participants in the clinical trial to have **a better experience during the trial.**

5.1.2.2 Key findings from the consultation with young people

The children and young people focus group methodology was aligned with the activity done in the consultation with people with dementia. The key findings were addressed in the same areas of analysis and regarding these two phases of drug development: research priority setting and clinical trials design.

The following key themes emerged from the consultation:

1. Who should be engaged in PE:

- **Include the voice of the person living with the condition.** The only way to include the voice of young persons in medicines development is by allowing and including their contributions as patient experts whenever feasible and possible. Young people and children considered that if they are trained, qualified and supported they can be involved in the same way as are adult patients. The direct involvement of young people brings the value of their personal experience with the disease and the value of the age group that cannot be substituted by consultation with their parents.
- **Diversity of age, sex, country and other features were also considered relevant.** The greater the diversity, the better it was considered for the consultation. The involvement of a small number of children and young people will be less significant than the contribution of groups of young advocates from different countries. The proposal by the young people was to perform patient involvement activities simulating the scenario in which paediatric clinical trials are developed: i.e. in a multi-country approach.
- **Myths and misconceptions.** It is important to involve young persons and not only their parents or carers as the experience of the disease is very personal. It is important to redress misconceptions about young people, such as, they are unable, or unwilling to contribute properly to PE. Young people offer the greatest experience of their condition (compared to their parents). Other relevant misconceptions regarding the involvement of young people, in which the Young Persons' Advisory Groups (YPAG) are generating strong evidence, are: the early engagement in a research priority setting is feasible; the experience and/ or support young patients can provide in the design of clinical trials protocols, participation in regulatory activities is feasible if a suitable framework is established. Clinical trial outcomes must be communicated to paediatric patients in the same way as is the case for lay adult patients, etc.

2. How to enable meaningful engagement in the case of young people:

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- **Accessibility and reasonable accommodation/adjustment.** Considerations should be discussed and acted upon to allow the involvement of young persons in PE activities. These might include organising meetings outside of school times or conducting them in their native language.
- **Information and training.** Training or specific preparation needs to be mandatory in order to ensure that young people can contribute with the right background. (i.e. the training and information to qualify young people's participation needs to be focused in two main areas of knowledge: medicines development and patient involvement). Children and young people constitute a vulnerable group of patients that need the right environment and preparation to be engaged. Ethical concerns need to be addressed and in this sense the support of a facilitator from a YPAG or from a patient organisation was well appreciated.
- **Personal support**. Educational material and information (written and verbal) should be adapted to young persons' needs (i.e. age and education level with appropriate language). Additionally, a facilitator from a YPAG should be available to provide the right personal support to a young person in both the preparation and during the PE activity. Format and content need to be user- friendly for minors and consider the specific features of paediatric clinical trials. Content developed to train adult patients was not considered appropriate for training children and young people.
- **Guiding principles**. Promoting autonomy, respect and equality. This helps to build a positive and long lasting relationship between young people and other stakeholders. Ethical principles and the children's rights need to be considered in the design of involvement activities for children and young people.
- **Regarding financial support.** All costs should be reimbursed (i.e. travel and accommodation) for the young person's time to participate. A lack of compensation can lead to a negative bias to participate, because this can be considered an activity in which an economical benefit can be obtained for young people. The main reward for the young people involved in PE activities is to know that they are helping their peers with such diseases and the future impact with future patients when a drug receives market authorisation. Another benefit was increased knowledge of the history of a disease, even if a drug is ultimately not approved.

3. The following barriers to participation of young persons in PE activities were identified:

- **HTA bodies have limited or no experience with the involvement of young persons in PE.** Likewise young people have no knowledge of HTA processes or how their input could be meaningful. In general, there is limited experience of involving young people in PE across Europe. Stakeholders need a change in mindset to actively consider that young people are able to contribute directly and meaningfully.

5.1.2.3 Key findings from consultation with rare disease patient representatives

1. What makes PE sustainable?

The views of the participants on what makes PE sustainable spanned from efficient training to an open, trusted and coherent financial process, in order to create value for all the players involved.

- **Training**. Participants stated that training programmes such as the EURORDIS Summer School enable participants to learn about medicines research and development including:

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clinical trial methodology, ethics in clinical research, European regulatory framework from orphan designation to marketing authorisation and health technology assessment. In addition, participants learn how to engage in medicines development at different levels and with different stakeholders: starting a Community Advisory Board (CAB), engaging with the European Medicines Agency (EMA scientific committees, scientific advice, public hearings, benefit-risk assessment) or engaging with HTA bodies (EUnetHTA). However, such training should not be restricted just to patients but be extended to all the key stakeholders involved in PE activities. This allows for balanced and equal relationships to be developed and maintained among all stakeholders. Additionally, it was highlighted that researchers and healthcare professionals should be educated so that they can realise the full value of PE and the contribution that people with rare diseases can make.

- **Financial compensation** for volunteers as well as for processes adapted to facilitate patient involvement were also important aspects for the long-term sustainability and continuity of engagement.
- **Motivation** was highlighted as a key driver for patients to be engaged in medicines R&D, but a process of regular feedback should be implemented in order to show that their contributions are valued and implemented.

2. Which sustainability dimensions should be prioritised?

In the second part of the discussion, the three pillars of sustainability were introduced, namely processes, resources and culture. Within those pillars, the specific elements of governance (process), trust (culture) and, revenue stream and financial viability (resources) were identified as the most important elements with which to support and ensure the sustainability of PE in medicines R&D in the long term.

- **Governance structure**. Participants proposed a solution comprised of an entity that is in charge of organising all PE at the European level. It could take the form of a European public-private consortium with an umbrella patient organisation in the driving seat. Different options were proposed but most included a European body (e.g. European Medicines Agency), the pharmaceutical industry body (e.g. the European Federation of Pharmaceutical Industries and Associations) and a variety of patient organisations. A rotating governance scheme was suggested with the aim of not favouring one patient organisation or disease versus another. In this model, patient representatives should be trained with high-quality standards and be able to represent and work in the interests of the patient community as a whole. Professionalisation of the processes was also suggested.
- **Building trust**. Writing a charter will help to build trust and mitigate distrust, as well as leading by example through concrete and robust work and processes. Patients becoming too professional can also create distrust among the patient community because of the fears that non trained patients' needs and views are not taken into account. Other elements identified as trust-building were: open communication, mutually agreed goals, mutual benefit, having allies outside the rare disease space and having checkpoints.
- **Revenue stream and financial viability.** A potential business model in PE should be not-for-profit. There should be an income structure to ensure that the activities can be performed. Income generation through a fee-for-service or subscription model was discussed with mixed reactions from participants who feared that such models would trigger competition between patient representatives. A fee-for-service was preferred over

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subscription or flat fee, because this latter could favour large pharmaceutical companies. Corporate social responsibility models in which part of the companies' profit could be given to this new entity organising PE was also suggested, although the legal enforcement of such practice is important for sustainability.

5.2 Consultation with HTA agencies

PARADIGM / HTAi workshop on patient involvement in Early Dialogues[14]

HTAi and PARADIGM convened a workshop on October 19th 2018 with HTA agencies to discuss PE in the early dialogues stage. Early dialogues (also called Scientific Advice) are multi-stakeholder discussions about confidential plans for key research studies planned to demonstrate the value of a health technology. These discussions may be led by HTA or Regulatory agencies, or run in partnership between these agencies. At the workshop, the rationale for involving patients was articulated, along with some of the common objections to involving patients. Attendees described the current processes of PE, the challenges with implementing these processes and the desired tools and resources that could make PE in Early dialogues more consistent, predictable and with baseline standards.

5.2.1 Methodology

Eleven representatives from HTA agencies were invited to attend a full-day session. Various methods were used to gain insights from the attending HTA representatives and to drive discussions on critical needs to further advance patient and patient representative involvement in Early dialogues. These methods included:

- Presentations by three HTA agencies (National Institute for Clinical Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), European Network of Health Technology Assessment (EUnetHTA)) on their approach and rationale for PE in Early dialogues
- Individual work to capture a variety of perspectives on the rationale for involving patients in Early dialogues;
- Breakout group working sessions to define and explain the methodologies currently in use and the resources that are needed to advance this field;
- Whole-room discussions to identify key barriers;
- Prioritisation exercises to identify the most critical resources to develop.

5.2.2 Key findings from the consultation with HTA agencies

1: The rationale for patients to be involved in early dialogue was defined as:

- Improvement in the quality of the dialogue and the advice given to pharmaceutical companies.
- Early dialogues are the right point in time for the patient input to have most impact because it will affect future clinical programmes and investments.
- Increase in the transparency of HTA processes and it represents good governance practices.
- Patients need to have a voice in these early dialogues as patients are the end users of

[14] For more information on the consultation with HTA agencies please see the detailed report from attachments.

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existing and new therapies, thus are the stakeholders most affected.

2: Common objections heard against PE in early dialogues:

- Some perceive that patients may not be able to make objective inputs into early dialogues.
- The details under discussion during the early dialogues may be too complex for patients to engage with.
- Continuing concerns exist over conflicts of interest between patient organisations and the pharmaceutical industry.

3: Common challenges with implementing PE processes in the early dialogues stage:

- Difficulty in finding a patient with the right therapeutic or knowledge profile for a particular early dialogue with the capacity to participate due to the effects of the illness.
- Involvement of patients takes a lot of internal resources within HTA Agencies - time and financial resources available to dedicate to PE may be very limited.
- Lack of clarity on exactly 'how' to involve patients at this stage. For example methods, guidance, and tools are largely missing.

4: Areas identified where additional tools, resources and guidance are needed:

1. **Patient recruitment processes** – including developing criteria and guidance to help HTA agencies find, select and enroll patients into the early dialogue processes.
2. **Patient interview guidance** – including interview guides, standard questionnaires and guidance on adapting them to particular early dialogue topics.
3. **Minimum standards framework** – including a framework of methods with guidance on their use, guidance for meeting chairs and patients and adaptation to meeting formats to accommodate specific patient needs.
4. **Rationale for PE in the early dialogues stage** – including metrics that show the impact of PE, case studies demonstrating how this can be achieved, definitions of early dialogues, and better articulated rationale for PE.

In addition to prioritising the tools and resources required to improve PE in Early dialogues, the group identified existing tools to consider or adapt[15]. Overall the group expressed the need to:

1. Create consistency and predictability across patient engagement in early dialogue processes
2. Have a menu of methodologies and approaches that could be applied
3. Set a minimum standard of patient involvement in early dialogues

6 Discussion

6.1 Discussion of online survey results

To address the need to enhance effective, meaningful and sustainable PE in medicines development this study set out to build upon existing knowledge and surveys of patient involvement and PE in medicines development. This existing body of work broadly explored current beliefs and expectations of PE practices of one or more stakeholder groups such as academia, industry

[15] See 4.4 of Attachment 4 in the HTA report

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(Parsons, S., et al. 2016, Smith, S K., et al. 2015, Forsythe, L., 2015, Bellows, M., et al. 2015), or patients and/ or public (Parsons, S., et al. 2015, Boudes, M., 2018). Previous work often focused broadly across the whole PE continuum, across patient populations, and is not specific to a decision-making point (i.e. clinical trial design). Here we have added value in several ways. Firstly, the detailed preferences, needs and expectations for meaningful PE from all major stakeholder groups (patients (inc carers), the industry sector, HTA and payers, regulators, research, funders and policy makers and, HCP) and specific populations involved (people with dementia and young people), involved in medicines development have been explored. Secondly, we have sought to identify those expectations at 3 key decision-making points where good PE practices are currently lacking or poorly reported compared to further downstream decision-making points (i.e. benefit risk and post market access, except clinical trials (Levitan, B., et al. 2017, Smith, S K., et al. 2015)). Thirdly, we have collated data from a larger data pool, broader geographical coverage, and non-English speaking languages (across 22 different countries and 13 languages other than English) compared to existing similar reports (see above). Thus, our results here should permit the incorporation of this greater range of views to ultimately benefit a greater number and diversity of stakeholder and patient groups.

The survey respondents were predominantly from the patient stakeholder group and industry stakeholder group, followed by the research and academic group. This may reflect the relative ease at accessing these stakeholder groups. The demographics of respondents was largely female and had a higher education degree. This may reflect the general demographic of more females being involved in or leading PE activities within an organisation and the general level of education and specialist knowledge needed of other stakeholders remits, knowledge and processes.

Overall the key findings that this survey suggests are:

I. That current perception of PE is low, yet ideal expectations are high and consistent across all stakeholder groups.
II. The greatest experience of PE is dominated by industry, patient, and research and academia communities. The least experience of PE is with regulators, policymakers, HTA bodies, research funders and payers.
III. The greatest challenge identified by a majority of stakeholders is that ‘Patient input is not part of [the] decision-making process’ and when patient input is sought it is currently mainly at the level of informing and consulting. The patient community differed - reporting the top challenges as ‘Communications were not clear and open’ and a ‘Lack of shared vision/goals’.
IV. This latter point from finding III is mirrored in that the greatest desired outcomes for PE across the 3 decision-making points is that patient preferences, needs and experience are both integrated into the decision-making process and properly reflected in the outcomes of the PE activity.
V. Most stakeholders feel confident and ready to engage with a PE activity, but need continued and improved support to do so through internal processes, knowledge, human resources, managing competing interests, and setting priorities in [a] PE strategy.
VI. The patient community particularly needs extra support through expert knowledge of the particular stakeholder and decision-making process in question, and one-to-one mentorship of individual patients.
VII. The patient community needs better financial resources to undertake PE, as well as better compensation for their engagement activities.

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VIII. Industry sector has high levels of dedicated PE functions within their organisations with lower levels for regulators, policymakers, HTA bodies, research funders and payers. Despite stakeholders having dedicated PE functions, they appear to be proportionally underused.

IX. Across all stakeholder groups, SOPs to undertake PE and methods to record outcomes and impact exist or were available, however they can be sparse and are often underused - the greatest resource needs for more effective PE was identified as being 'A way to measure impact' and 'Better methods and materials of how to do it more effectively'.

X. There appear to be some differences between preferences from English language survey respondents to non-English language survey respondents. For non-English responses a higher proportion of the patient community did not receive any financial compensation, the industry respondents dedicated less time of their PE function activities outside of clinical trial design, and a higher proportion of industry, HCP and regulators, policymakers, HTA bodies, research funders and payers community lacked SOPs, or any methods or metrics with which to measure PE. Discussion of findings from consultations with the specific stakeholder groups.

6.2 From the consultation with people with dementia

The importance of engaging people with dementia in research and service development has been recognised in several European countries. However, the landscape across Europe remains diverse. In some countries, there is a general lack of interest in dementia and dementia research, and thus very little or nothing has been done in PE in this area. PE in the area of medicines development can be of interest to people with dementia and their carers, yet it is not a standard practice. Some Alzheimer organisations have developed good collaborations with pharmaceutical companies. However, they are often focused on raising awareness of existing clinical research in their country and/ or to help with recruitment of research participants for a trial. In countries such as the UK and Ireland, some progress has been made in recent years and, although that is still not to an ideal standard, there has been an improvement on the way patients are engaged by different stakeholders.

Several barriers were identified for involving people with dementia in the process of developing medicines, such as prevailing misconceptions about dementia, the stigma surrounding the condition and diagnosis often happening at late stages of the disease. However, the consultation confirmed the importance of and need to engage people with dementia themselves in the process of developing medicines. They can bring an "expert voice" to the process of developing medicines. They should have the same opportunities to participate in a PE activity as any other patient with any other condition. People with dementia can meaningfully contribute if the appropriate support is provided. Reasonable accommodation should cover and be applied to not only the contents but also the format and structure of the meeting/ PE activity.

Communication is very important and should always be open and transparent. Sufficient and accessible information, and when necessary, training should be provided for them. During a PE activity, enough consideration should be given to ways of making their engagement possible and meaningful. Their input should be valued and appropriate feedback about how it has been used should always be provided. Important principles guiding PE should include promoting and respecting autonomy, respecting people's needs and contributions and working in equal partnerships.

People with dementia often perceive PE in terms of hope for a better future. It can also empower

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them and help them feel valued and respected. They expect their involvement will contribute towards changing attitudes of healthcare professionals, ensuring that the lived experience of the patient is taken into account and ultimately, to improving the experiences of clinical trial participants and developing better medicines and a better world for people with dementia in generations to come.

6.3 From the consultation with children and young people

The involvement of children and young people in drug development is still a limited practice in the research community. The publication “Principles on the involvement of young patients/consumers within EMA activities” (EMA, 2017c) has established the first framework at the European level to promote the involvement of minors in medicines development from the regulatory perspective. Further consensus with other stakeholders, guidances and opportunities to increase the evidence of the return on investment and engagement will help to develop PE activities on a regular basis and with the ethical approach that requires the involvement of minors in research. The consultation of the KIDS Barcelona YPAG within the PARADIGM project allowed us to obtain relevant outcomes as follows:

- Patient involvement with young people is feasible but training and support is required. This needs to be designed and addressed considering the right content and format for minors (different age groups) and inclusion of the specificity of paediatric clinical research.
- It is better to involve children and young people whenever feasible, instead of their parents. The value of PE in this case can’t be equated with the value of parents’ participation - considering the fact that they are not living with the disease, the impact of age biais is crucial.
- The outcome of involvement is a reward that is not always offered in return to the patients. The main compensation for them is to know that they are helping to improve science and to help other patients.
- There is preference to be involved in a group and in an individual way also at international level as this allows for a broader feedback. Ethical concerns and support from a facilitator were considered valuable and necessary in order to achieve a meaningful impact with their participation.

6.4 From the consultation with rare disease patients

This consultation confirmed some factors already known to positively influence engagement in the rare disease patient community. Due to the scarcity of specialist knowledge, rare disease patients and patient organisations have always been deeply engaged in activities related with research and development from funding basic and clinical research to more specialized areas such as clinical trial design and shaping research agendas to cover their unmet needs. Rare disease patient organisations have been pioneers in progressing from an "auxiliary model" to a "partnership model" of engagement, in which patients are specialist partners in their own right (Rabeharisoa V. 2003). This was corroborated during the consultation as a key factor for long-term sustainability of PE in medicines R&D. In order to help build an equal relationship, participants highlighted the following elements: demonstrating the value of PE for all stakeholders; the need for specific training of all stakeholders in areas such as clinical research (with considerations for small populations) and orphan product regulatory/ HTA environment and access to rare disease therapies; and to improve communication among all stakeholders involved across the medicines R&D spectrum. To enhance patient motivation (one of the key drivers for sustainable PE), their contributions should be

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acknowledged and measures taken to fully incorporate their input into the outputs and outcomes of a given PE activity. In addition, considering the serious burden of care that rare disease patients face, processes should be adapted as much as possible to facilitate patient involvement (e.g. meeting time and format). Sustainable PE was also considered related to financial aspects such as the economic compensation of patient representatives, better funding to patient organisations to support their functioning and funds to be allocated to PE within the medicines R&D budget.

With regard to the sustainability model needed to systematize meaningful PE, there was no consensus on the type of legal structure that could support this, but a public-private consortium including patients (in the form of an umbrella patient organisation) and a rotating governance would be a fair system to ensure stakeholder and disease representation. Not surprisingly, building trust among partners through robust processes and transparency were two main features associated with the sustainability of this new PE framework, according to patients' experience in their own areas of work. However, the professionalisation of patients might reduce trust among the patient community and this could negatively impact sustainability. There was less clarity on the financial model of this new potential entity with emphasis made on the non-profit nature of PE and the need to avoid competition between patient organisations.

6.5 From the consultation with HTA agencies

Many HTA agencies have experience of PE in HTA, but few in early dialogues. All attending HTA agencies confirmed that PE adds value to early dialogues and brings a perspective to the dialogues that is unique and valuable. However, there remain barriers to sustained and systematic PE at this time-point, including difficulties finding patients with the appropriate profile and capacity to take part, the lack of resources across HTA agencies to administer PE processes and the lack of adaptable tools that create a consistent framework for PE during these early dialogues.

Many expressed that PE in early dialogues is still at an early stage, with only a few agencies having established processes. There is a process of piloting approaches across many agencies, facilitated by the work of EUnetHTA, and this is providing an opportunity to test approaches and understand the resources needed to create sustained PE at this time-point. These pilots are already starting to reveal the advantages and disadvantages of several methodologies. Participants prioritised tools that would help them overcome some of the barriers to PE in Early dialogue, and identified existing tools that could be used or adapted

The work of PARADIGM is seen as timely by this group, who agreed to work together with consortium member HTAi to further define and develop the tools and resources needed.

6.6 Study strengths and limitations

Survey

There are limitations to this survey and the interpretation of its results. It was an online survey, completed only by those who are familiar with the technology and have internet access. Despite a piloting phase it is impossible to identify how respondents (English or non-English) interpreted the questions in the wider context. The survey was designed by a consensus approach and could be biased to the prior knowledge of those involved in its design (i.e. confirming what we know vs. what we do not know). Through snowball techniques, consortium members reached out to their respective stakeholder groups to include them in the survey. Despite this, responses were dominated by patient and industry communities, thus the interpretation of conclusions for other

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stakeholders (particularly regulators, policy and HTA bodies where total response rates were often low, <10) should only be considered alongside other evidence (i.e. specific focus groups and Delphi outputs). Similarly, responses for English and non-English languages were dominated by the UK, US and central EU countries (i.e. Italy and Netherlands). Hence caution is needed with interpreting findings from other countries and languages (where response rates were often low, <5).

The two aforementioned additional technical and translational issues with the survey resulted in a small number of languages and respondents being excluded entirely from the analysis, resulting in reduced total response numbers and the strength and impact of some of the conclusions. Finally, there are also barriers and enablers to PE that could not be fully understood from this survey due to the practicality of the relatively short survey and short data collection timeline. More in-depth work supporting these conclusions should be drawn from the focus groups and the Delphi methodology that will prioritise key themes applicable to all stakeholders across the three decision-making points. Conclusions should be taken from all three of these data sources together.

Consultation with the specific stakeholder groups and HTA

An important strength of the work conducted in PARADIGM is that it incorporates groups of patients and other stakeholders which, for different reasons, are often not included or underrepresented in this type of work. A qualitative approach was used to collect their experiences and views, which has provided a richer and more detailed understanding of their needs, priorities and expectations. Despite efforts to identify differences for the three decision-making points, the needs and expectations which were expressed by the participants were very similar for the three points. Various reasons, including the fact that the participants did not have experience in all the three points may have influenced this. On the other hand, this may support the idea that there are a number of “key basic issues” and principles which are important and may be shared across the three decision-making points. Another important issue to bear in mind is that this was conceived as a consultation in the context of PE and not as qualitative piece of research and thus the input provided by participants should be interpreted in this context.

There are a vast number of HTA agencies across the EU with varying remits and structures. While a variety of member states was represented in the consultation, a generalisation across other HTA agencies is not appropriate at this time.

7 Conclusions and next steps

Overall, these combined results suggest that **all stakeholders felt that in the process of developing medicines PE is crucial and there is a strong desire for more engagement, involving more stakeholders, and in a more effective way.** The greatest challenge from all stakeholders’ perspectives is that patient input does not (as yet) form part of the decision-making process. That being that patient input is not, or cannot (through lack of suitable mechanisms) be effectively utilised and integrated into a decision making process and that the patient input largely remains as a point of reference. This situation can be partly addressed at several levels by; establishing and embedding recognised PE practices in patient dialogues in stakeholder communities where current experience, opportunities and practices are limited (such as in early dialogues), and to moving current patient input from the level of informing or consulting (where it predominates today) to a decision-making level (where outcomes and impact of the patient input can be better demonstrated), when it is appropriate and feasible to do so. Interestingly the patient

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community differed from the majority of others with its top challenges being, 'Communications were not clear and open' and 'Lack of shared vision/goals'. This emphasises the importance that the patient community gives to the relationship with the other stakeholders and in particular, to making for, and ensuring, clear and transparent communication. This finding strongly resonates with the input provided by the vulnerable groups, who also placed great value on all the communication aspects throughout the PE process. It also suggests that there remains a mismatch in the perceived purpose and goals of engaging with patients and the net value that they can bring. Such a disparity still needs to be addressed.

This issue is mirrored somewhat in the reported greatest desired outcome from enhanced PE is that 'patient preferences, needs and experiences must both be integrated into the decision-making process and properly reflected in the outcomes of the PE activity'. This desired outcome is further strengthened by the need to properly acknowledge and account for the voice of the person living with the condition, not just a carer or representative. Integrating the 'lived experience' into dialogues and any decision-making process greatly enhances the quality of that process and subsequent outcomes to all stakeholders involved.

With the reported desire to improve the quality, effectiveness and sustainability of PE, most stakeholders felt confident and ready to engage in a PE activity. However, almost all reported the need for some level of continued support to do so through mechanisms of; 'internal processes', 'knowledge', 'human resources', 'managing competing interests', and 'setting priorities in your PE strategy'.

For most stakeholders what is currently missing is manifested on two levels. One level is *what to do* - for example, new guidances and systematic processes for HTA bodies. The other level is, *how to do it* - for example better methodologies, tools and templates, better use of existing SOPs, better materials to support the implementation of guiding principles and the sustainability of systematic processes. Both are needed by industry, regulators, payers, academia, policymakers, research funders and HCP. The industry respondents indicated that although dedicated PE function and SOPs largely already exist within their organisation, both were reported to be proportionately underused. This suggests that current SOPs may not be fit for purpose and that there is a general lack of consensus of what effective PE looks like. In addition, the greatest resource needs identified across all stakeholders was a way to measure the impact of a given PE activity. Demonstrating the net value (of PE) within and among the various stakeholder groups is an integral mechanism to facilitate a long term and sustained shift in mindset and approach to enhanced PE, but it is also very complex. The existing material that can support measuring the net value or impact of a given PE activity to a stakeholder or process is sparse and fragmented[16]. Linking context, process, mechanisms, outputs, outcomes and impact requires a validated framework that can be modified for a given decision-making point and for the different outputs and outcomes for each stakeholder group. The PARADIGM consortium is developing such a framework.

Better knowledge of, and practical experience with, other stakeholder groups was a common theme identified here that could help sustain PE. This could be addressed through training individual stakeholder groups on PE practices, the specific knowledge of medicines development, and the decision-making point of interest (for example through the EUPATI platform[17] and EURORDIS Summer School[18], but also training all stakeholder groups about each of the other key stakeholder

[16] PARADIGM Work package 3: Systematic review - Pending publication
[17] EUPATI Platform (https://www.eupati.eu/)
[18] EURORDIS Summer School (https://openacademy.eurordis.org/summerschool/)

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groups - for example understanding how decision-making occurs. This improves transparency, trust, builds sustainable relationships, provides common learning, and can redress common myths and misconceptions about a particular stakeholder group, and as identified here, also about how to incorporate the unique experiences of vulnerable populations (i.e people with dementia and young people).

The patient community identified specifically that they need additional support to sustain PE activities with other stakeholder groups such as a direct contact person within the organisation undertaking a PE activity, and within their own organisation, a one-to-one mentor for individual patients. In the case of vulnerable patient groups, the provision of support and a deep understanding of the impact of their medical condition in their lives and of their needs and capabilities is of utmost importance, as addressing them, could enable their participation in PE activities.

Compared to the status quo today, improved financial support for the patient community as a whole and the individual patient for their time, travel and accommodation is needed and will only improve the level, quality, and broader inclusiveness of patients in dialogues with stakeholders. This could come from new funding models directed to patient organisations, more dedicated resources for PE activities within current stakeholder budgets (i.e. R&D budget for industry, grant budgets for academia, funders and policymakers), combined with a more professional structure in relation to the implementation of PE at European level. Similar models may not work for HTA agencies or regulators who have different resource constraints. Regulators[19] continue to expand their framework for interactions with patients, the HTA agencies are piloting several alternative models and leveraging knowledge exchange through platforms such as EUnetHTA[20] and the academic and research funders increasingly support and require dedicated PE/PPI resources in their calls[21].

The inherent capacity, capability and culture of each stakeholder group to impact upon PE must be acknowledged as being quite different - despite a general consensus regarding the desire from all to improve beyond the current status quo. Capacity, capability and culture present both enablers and barriers to a greater or lesser extent depending on the stakeholder group. We have identified here in a large survey and complementary focus group consultations just what some of those key enablers and barriers are to achieve better dialogues with patients, from the perspective of different stakeholders. We have identified some of the key processes, mechanisms and tools which can be improved, co-created and implemented to drive and attain a meaningful and sustainable improvement in PE compared with the situation today.

These learnings have been translated into the next phase of the PARADIGM consortium - a Delphi methodology (see Appendix 1) that will systematically consolidate and prioritise the needs and preferences of all stakeholders for effective and meaningful PE. Those outputs will inform other PARADIGM work packages as to what tools, methods and metrics need to be developed and how they could or should cover most of the specific needs of the various stakeholders.

[19] For example, European Medicines Agency, Stakeholders and Communications Division, (October 2014-b).
[20] For example, European network for Health Technology Assessment, (April 2018).
[21] For example, National Institute for Health Research, Research Design Service, (2014).

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9 Attachments

Report from consultation with **people living with dementia** by Alzheimer Europe	http://imi-paradigm.eu/Paradigm-documents/Report-on-consultation-with-EWGPWD-2018_10-FINAL.pdf
Report from consultation with **children and young people** by FSJD	https://imi-paradigm.eu/Paradigm-documents/Report-for-consultation-with-young-persons-FSJD-final.pdf
Report from consultation with **rare disease patients** by EURORDIS	http://imi-paradigm.eu/Paradigm-documents/Report-PARADIGM-ESS2018-internal-consultation_FINAL.pdf
Report from consultation with **HTA community** by HTAi	http://imi-paradigm.eu/Paradigm-documents/Report-on-PARADIGM-HTA-Early-Dialogues-Workshop-FINAL.pdf

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Annex 1 – Delphi methodology

The Delphi method includes

Delphi Questionnaire Development
Three separate questionnaires, one for each the decision-making points of medicines development, are developed and used to support the 2 rounds in each Delphi. The initial questionnaires are based on the information obtained from different sources: results from the online survey in task 1.1, consultations for vulnerable groups organised within WP1, PFMD Quality criteria, and the review of literature obtained from institutions and practices related to PE in each of the decision-making points of medicines development.

A first version of the questionnaire is developed by the Delphi team (IACS) and reviewed, subsequently, by the Consortium in a specific Workshop and in an iterative process through email. The final version of the questionnaire is the one used in the first online round.

Delphi Rounds

First Online Round

Stakeholders are asked to assess the relevance of each item through a Likert scale (1= not relevant at all- to 9 = highly relevant). Only those items for which agreement converged around 'relevant' by the experts remain in the second round. The stakeholders are also given the option of adding missing items.

Second Online Round

Stakeholders are asked to prioritize each of the items rated as relevant in the first round using a Likert scale (1 = low-priority to 9 = high priority). Those items over which no agreement was reached in the first round, are presented again in the second for experts to re-rank their view on each item according to the proposed relevance scale (from 1 = not relevant at all to 9 = highly relevant).

Face–to-Face Meeting

Once the second round is finished, a face-to-face meeting will be held in Brussels. This meeting is devoted to reviewing and refining the results of the two online rounds. The main objective is to identify potential inconsistencies and solve eventual redundancies within the selected items to organise them into criteria with sub-categories.

Through a voting process, the group allocates relative weights to each item. The result is a final set of weighted criteria to assess PE practices at the corresponding decision-making point.

From the 3 Delphi panels we obtain 3 separate sets of criteria, one specific for PE practices in a research priority setting, another in a research priority setting, and the third in early dialogues

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Annex 2 – Online survey questions

Needs and Expectations for Patient Engagement in the Medicines Research and Development Lifecycle

Aim of the Survey

The aim of this survey is to understand the needs and expectations of people who are involved in medicines development and patient engagement, particularly during the following phases of the medicines lifecycle:

- research priority setting (i.e. providing opinion, providing evidence and/or being part of a group that decides what is important to research);
- design of clinical trials (i.e. designing protocols, discussing patient burden, discussing patient-related outcomes); and,
- early discussions with regulators and Health Technology Assessment bodies (e.g. early discussions between industry, HTA agencies and regulators (and in some contexts with payers) to discuss developmental plans for a medicinal product and to ensure they meet the requirements).

It is part of a research project called PARADIGM: Patients Active in Research and Dialogues for an Improved Generation of Medicines. You can see more information about PARADIGM at http://imi-paradigm.eu. The data provided through this survey will be stored securely and processed by the PARADIGM team as part of the project; it will be deleted once the project is completed.

Our Definition of Patient Engagement

We define patient engagement as the effective and active collaboration of patients, patient advocates, patient representatives and/or carers in the processes and decisions within the medicines lifecycle, along with all other relevant stakeholders when appropriate.

(EMAIL ADDRESS TO CONTACT IF ANY PROBLEMS ENCOUNTERED WITH THE SURVEY) info-survey@imi-paradigm.eu

Notes to reader:

- *All questions were compulsory unless otherwise mentioned in red.*
- *The stakeholder-specific sections were visible only to those who identified as those specific stakeholders*

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Demographics

We would like to ask some questions about your background.

G1: Which group or affiliation best describes you?

- ☐Patient
- ☐Patient representative, Patient organisation or Carer
- ☐Research and academia
- ☐Healthcare professional
- ☐Pharmaceutical/biotechnology/medical technology industry
- ☐Policymaker or Regulator
- ☐Health technology assessment (HTA) body
- ☐Research funder
- ☐Payer (Insurer or other organisation paying for healthcare)
- ☐Other (please specify)

G2: Where are you located?

- *Drop down list with all countries*

Involvement with stakeholders in patient engagement activities

G3: In your patient engagement activities, how have you been involved with each of these stakeholders for each phase of medicines development? If you have been involved in more than one patient engagement activity, please answer on the basis of the most frequent type of engagement.

Deciding: patients or their representatives having shared decision making

Consulting: patients or their representatives providing an opinion or expertise, but without being part of decision making

Informing: patients or their representatives getting or receiving information, but not being able to contribute their opinion or expertise.

- *Optional question*

	In research priority setting	In designing clinical trials	In early discussions with Regulatory and/ or Health Technology Assessment (HTA)
Patients, patient representatives, patient organisations or carers	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing
Research and academia	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing
Healthcare professional	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing
Pharmaceutical/biotechnology/ medical technology industry	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing
Policymaker or Regulator	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing
Health technology assessment (HTA) bodies	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing
Research funder	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing	☐ Deciding ☐Consulting ☐Informing
Payer	☐ Deciding ☐Consulting	☐ Deciding ☐Consulting	☐ Deciding ☐Consulting

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	☐Informing	☐Informing	☐Informing

G4: Challenges to collaborations in PE activities

From the list of challenges below, with which stakeholders did you experience the following challenges?

- *Matrix - Challenges in rows and stakeholder groups in columns*
- *Choosing multiple stakeholder options per challenge possible*
- *Optional question*

Communications with other stakeholders were not clear or open				
Lack of shared vision/goals with other stakeholders				
Unclear about my role and responsibilities				
Lack of trust with other stakeholders				
Lack of receptiveness to patient input				
Patient input was not part of decision making				
Not enough financial resources to continue the activities				
Not enough time to continue the activities				
Not enough training to fully contribute to the activities				
Not enough support from other stakeholders				
Not enough support from my own organisation				
Delays in activities due to bureaucratic processes (e.g. contracts, intellectual property, etc.				
Lack of a clear legislative framework				
Other [free text]				

G5: Which of the following would you need in order to do more effective patient engagement, if any? Please select all that apply.

A way to record time spent or financial investment in patient engagement activities	☐
A way to measure the impact of patient engagement activities you are involved in or are conducting	☐
A dedicated patient engagement function in your organisation	☐
Training on how to implement patient engagement processes in your organisation	☐
Methods, material and information on best patient engagement practices related to your stakeholder group	☐
Methods, material and information on how to do more effective patient engagement	☐
Methods to identify and evaluate where your contribution would be most valuable	☐
More Regulatory/HTA guidance on how to do patient engagement	☐
Other (free-text):	☐

G6: What is your impression of how current patient engagement compares to ideal patient engagement at these different stages of medicines research? (0-100 distribution scale; 100 = ideal, 0 = none)

☐ Initial research priority setting
☐ Early discussions with Regulators and/ or Health Technology Assessment (HTA)
☐ Clinical trials
☐ Licensing of medicines
☐ Health Technology Assessment (HTA)
☐ Pricing and reimbursement decision process

G12 In your opinion, what are the **three most** desired outcomes of patient engagement in **research priority setting**?

- *Multiple choice*

[Field] When patients' needs are central in deciding the research agenda
[Field] When all parties come to agreement early in the process
[Field] When patients also have a say in what research gets funded
[Field] When it results in new insights and new perspectives for Policy makers, Regulators and research funders
[Field] When researchers get better insight in the patients' journey
[Field] When it results in mutual learning
[Field] When patients receive feedback about the impact of their engagement
[Field] Other [free text]

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G13 In your opinion, what are the **three most** desired outcomes of patient engagement in **clinical trials**?

- *Multiple choice*

[Field] When information is better communicated to patients
[Field] When patients can share their experiences and increase knowledge of the clinician
[Field] When it results in more patient-relevant outcomes for the clinical trial
[Field] When it improves recruitment
[Field] When it improves diversity in recruitment
[Field] When it leads to reduced drop-out rate
[Field] When it leads to better compliance
[Field] When it leads to fewer protocol amendments
[Field] When it leads to shorter timeline of trials
[Field] When it leads to an earlier stop of unsuccessful research
[Field] When it leads to higher patient satisfaction during the trial
[Field] When patients receive feedback about the impact of their engagement
[Field] Other [free text]

G14 In your opinion, what are the **three most** desired outcomes of patient engagement in **medicines licensing** and **Health Technology Assessment (HTA)**?

- *Multiple choice*

[Field] When the voice of the patient is reflected in the assessment
[Field] When patients' needs are better met
[Field] When it leads to reduced decision time
[Field] When it leads to better use in practice
[Field] When it results in improving transparency and openness in decisions
[Field] When patients receive feedback about the impact of their engagement
[Field] Other [free text]

The very last question of the survey for everyone (except those who answered none to all fields in G3):
We may wish to contact you for further participation in the project. Would you like to be contacted for future participation?
Yes [email]
No

Patient, Patient advocates and Patient organisation Questions

The following section is for patients, patient representatives, patient organisation or carer respondents only.

PO15 (1): How prepared is your organisation to actively participate in patient engagement in terms of:

- *Hidden for "Individual Patients"*

	1	2	3	4
	Not prepared and don't need support	Not prepared and need support	Prepared but need support still	Prepared and don't need support
Internal processes	☐	☐	☐	☐
Knowledge (information and expertise)	☐	☐	☐	☐
Human resources	☐	☐	☐	☐
Financial resources	☐	☐	☐	☐
Managing competing interests	☐	☐	☐	☐
Setting priorities in your patient engagement strategy	☐	☐	☐	☐

PO14 (2): What is the basis of the patient input that you provide?

- *Multiple choice*

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☐Personal experience
☐Individual interviews
☐Focus group
☐Public Consultations
☐Survey of patients
☐Results of other research
☐Through interaction with Regulators
☐Through interaction with HTAs
☐Community advisory boards or similar

PO15 (3): If you are involved in patient engagement activities either as a patient or as a member of a patient organisation, do you or patients you represent receive compensation/honoraria/ reimbursement for any of the following. Please select all that apply.

- *Multiple choice*
  - ☐ Time missed from work
  - ☐ Care (e.g. child care or caring for an ill or disabled person when you are participating in an activity)
  - ☐ Transport/ accommodation/ food
  - ☐ Equipment
  - ☐ Family support
  - ☐ Your expertise or experience as a patient
  - ☐ I/ patients do not receive compensation
  - ☐ Not applicable
  - ☐ Other (please explain) [free text]

PO16 (4): How should patient engagement activities be financed (e.g. receiving compensation for time missed from work, childcare, transport, etc.)?
Please select all that apply

- *Multiple choice*
  - ☐One to one support given directly to individual patients
  - ☐Funding support given to an umbrella entity that manages a global fund on behalf of all patients
  - ☐Initiatives funded at the national level
  - ☐ I don't think patient engagement should be compensated
  - ☐Other (please explain) [free text]

PO17 (5): Do you feel confident to meaningfully contribute to patient engagement?

☐Yes
☐No

a. If yes, at what stage of the medicines lifecycle? Please select all that apply.
   - *multiple choice for yes-option*

   ☐The research priority setting
   ☐Clinical trials
   ☐Early discussions with Regulators and/ or Health Technology Assessment (HTA)

b. If not, what would help you to increase your level of confidence? [Free-text]

PO18 (6): From whom would you like to receive support/mentorship when engaging in medicines development? Please select all that apply.

- *Multiple choice*
  - ☐My organisation
  - ☐The healthcare professionals treating me
  - ☐Other stakeholders who are responsible for the activity I (we) want to engage in
  - ☐People with experience in patient engagement
  - ☐Person/group with in-depth knowledge about the area of the planned engagement
  - ☐Other [Free-text]

PO19 (7): What is your age?

☐Primary school age (4-11 years old)
☐Secondary school age (11-18 years old)
☐18-25 years old
☐26-35 years old
☐36-45 years old

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☐46-55 years old
☐56-65 years old
☐65+ years old

PO20 (8): What is your gender?
☐Male
☐Female
☐Other/prefer not to answer

PO21 (9): What is your highest level of educational qualification?
☐Primary or secondary school
☐Higher education degree (including vocational)
☐Other

Pharmaceutical/Biotechnology and Medical Technology Industry Questions

The following section is for industry respondents only.

ID13 (1): Is there a dedicated patient engagement function in place at your organisation?
☐Yes
☐No
If yes, please enter your email address if we can contact you for more information [Email]

ID14 (2): Please rate the importance of patient engagement in medicines development for your organisation:

1	2	3	4	5
☐	☐	☐	☐	☐
Not at all important	Of little importance	Moderately important	Important	Very important

ID15 (3): How regular are patient engagement activities in your company at each of the three stages of medicines development?

	None	Occasionally	Sometimes	Regularly	Always
Initial research priority setting					
Clinical trials					
Licensing of medicines, Health Technology Assessment (HTA), pricing and reimbursement decisions					

ID16 (4): Do you have metrics/methods to determine impact of patient engagement in the short- and or long-term?
☐Yes
☐No
If yes, please enter your email address if we can contact you for more information [Email]

ID17 (5): How much is your organisation doing to move patient engagement from intentions to outcomes?
☐Not doing enough
☐Doing the bare minimum
☐Making a good effort
☐Doing everything it can

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ID18 (6): Have you established a Standard Operating Procedure or other guidance on interactions with patients/patient organisations in medicines development?

☐ Yes, and it is used in practice
☐ Yes, but it is not used in practice
☐ No, but it is not needed
☐ No, and it should be established.
If you answered yes, please enter your email address if we can contact you for more information [Email]

Regulators, Health Technology Assessment (HTA) Bodies, Research funders, Regulators, Policymakers and Payers

The following section is for Regulators, Research funders, Payers and HTA respondents only.

RH13 (1): Is there a patient engagement function in place at your organisation?

☐Yes
☐No
If yes, please enter your email address if we can contact you for more information [Email]

RH14 (2): How are patients or their representatives involved in your work? Please select all that apply.

- *Multiple choice*

Deciding: patients or their representatives having shared decision making
Consulting: patients or their representatives providing an opinion, but without being part of decision making;
Informing: patients or their representatives being actively provided information, but not being able to contribute to your work;
Not involved.

	Deciding	Consulting	Informing	Not involved
Setting research priorities	☐	☐	☐	☐
Designing clinical trials	☐	☐	☐	☐
Early discussions with Regulators and/ or HTA bodies	☐	☐	☐	☐

RH15 (3): Do you have methods to determine impact of patient engagement?

☐Yes
☐No
If yes, please enter your email address if we can contact you for more information [Email]

RH16 (4): Do you provide feedback to patients who have been engaged in your processes?

☐Yes
☐No

Healthcare professionals

- *The following section is for healthcare professional respondents only.*

HP13 (1): How prepared is your organisation to actively participate in patient engagement in medicines development in terms of:

	1	2	3	4
	Not prepared and don't need support	Not prepared and need support	Prepared but need support still	Prepared and don't need support
Internal processes	☐	☐	☐	☐
Knowledge (information and expertise)	☐	☐	☐	☐
Human resources	☐	☐	☐	☐
Financial resources	☐	☐	☐	☐
Managing competing interests	☐	☐	☐	☐

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Setting priorities in your patient engagement strategy	☐	☐	☐	☐

HP14 (2): Please rate the importance of patient engagement in medicines development for your organisation:

1	2	3	4	5
☐	☐	☐	☐	☐
Not at all important	Of little importance	Moderately important	Important	Very important

HP15 (3): How are patients or their representatives currently involved in medicines development in your organisation?

- *Multiple choice*

Deciding: patients or their representatives having shared decision making

Consulting: patients or their representatives providing an opinion, but without being part of decision making;

Informing: patients or their representatives being actively provided information, but not being able to contribute to your work.

	Deciding	Consulting	Informing	Not involved
Setting research priorities	☐	☐	☐	☐
Designing clinical trials	☐	☐	☐	☐
Early discussions with Regulators and/ or HTA bodies	☐	☐	☐	☐

H16 (4): Do you have methods to determine impact of patient engagement?

☐Yes
☐No
If yes, please enter your email address if we can contact you for more information [Email]

HP17 (5): Do you provide feedback to patients who have been engaged in your processes?

☐Yes
☐No

HP18 (6): Have you established a Standard Operating Procedure or other guidance on interactions with patients/patient organisations in medicines development?

☐ Yes, and it is used in practice
☐ Yes, but it is not used in practice
☐ No, but it is not needed
☐ No, and it should be established.
If you answered yes, please enter your email address if we can contact you for more information [Emai]

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Annex 3 – Free-text responses from languages other than English

SECTION: GENERAL QUESTIONS

G4. If you have experienced challenges, which stakeholders did you experience these challenges with?

1. (IT) Information about packaging materials, allergies
2. (IT) Definition of regulatory needs
3. (ES) A lack of technical training to actively involve patients

G5. Which of the following would you need in order to do more effective patient engagement, if any? Please select all that apply.

1. (NL) Clear goals and support for patient involvement
2. (ES) In small organisations a lack of staff who, either because of their health or because of their age, do not identify with these technologies
3. (DE) Face-to-face engagement in advising and decision-making processes
4. (NL) Financial means. All participants get paid for their time, except for the patients. These are unpaid volunteers who even have to pay their own travel and accommodation expenses. There should also be money made available to inform patient representatives about their disease.
5. (DE) General insight that patient engagement is important
6. (PT) Habit of regular consultation about methodology, outcomes, scales, etc.
7. (ES) Information to associations about how to participate
8. (IT) Greater transparency and information permeability
9. (ES) Greater patient involvement in all phases of the regulatory process
10. (NL) Method to measure what we've reached / impact
11. (IT) Real patient involvement in decision-making processes
12. (IT) Impact assessments
13. (DE) Active engagement of patients in the definition of outcomes and in decisions on approval and payment for medications
14. (FI) Open dialogue
15. (NL) Change of culture for all stakeholders
16. (HR) Additional regulatory guidelines
17. (ES) Educate the patient about their potential involvement in health policies
18. (NL) Education about equal decision making.
19. (IT) Already satisfied with the above choices
20. (IT) Greater patient preparation
21. (IT) Nothing
22. (FR) Compensate expert patients. Today, most are volunteers, already very busy between their work and their health. Make it a separate profession.
23. (IT) Different investigator protection
24. (BG) Taking part in the patient engagement procedure regarding clinical studies

G12. In your opinion, what are the three most desired outcomes of patient engagement in: Research Priority Setting?

1. (FR) When the patients are co-designers in research programs
2. (FI) When the researchers listen to the patient during the initial stage
3. (BG) After inclusion in the reimbursement list

G14. In your opinion, what are the three most desired outcomes of patient engagement in: Medicines Licensing and Health Technology Assessment (HTA)

1. (ES) Patients are not asked about the health technology assessment
2. (ES) When the value of the medicinal product changes in line with the results assessed by patients
3. (NL) Patients' needs are integrated in the decision and unnecessary drugs and technologies are not put on the market.
4. (ES) To improve the quality of the assessment with the knowledge provided by patients (e.g. feasibility of implementation, values and preferences in view of uncertainty).
5. (FI) When the patient's voice is heard during all stages of the process
6. (BG) Information is exchanged between the interested parties

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SECTION: PATIENTS, PATIENT ADVOCATES, PATIENT ORGANISATIONS

PO16. What is the basis of the patient input that you provide? (Select all that apply)

1. (ES) Information received at congresses and conferences
2. (IT) Reports from the national association of which I am vice-president
3. (ES) Constant interaction and two-way communication with the patient community
4. (IT) Data from the international literature
5. (FI) Experiences of close friends and family
6. (NL) Training, interaction with other patient experts
7. (BG) It is not carried through

PO17. If you are involved in patient engagement activities either as a patient or as a member of a patient organisation, do you or patients you represent receive compensation/ honoraria/ reimbursement for any of the following: (Select all that apply)

1. (NL) For some activities, there's a travel expense and food is served. For most activities, it has to be requested and often there is no budget available.
2. (FI) A fee as a member of the HUS (Hospital District of Helsinki and Uusimaa) customer panel
3. (ES) If you have to go to a congress we need to fund the costs of attending the congress or conference
4. (IT) Little consideration is given to the patient's opinion and resources are channelled towards other decision-makers, there is a lack of clear benefits for patients who participate in and contribute to research
5. (FI) Support for the organisation’s activities
6. (NL) Travel expenses and attention
7. (RU) We are not involved

PO18. How should patient engagement activities be financed (e.g. receiving compensation for time missed from work, childcare, transport, etc.)? (Select all that apply)

1. (IT) Financing of the body to which they belong (patient association of which they are a member)
2. (NL) I think the compensation of travel expenses, accommodation and consumptions and other things are important for patient participation
3. (NL) Patient organisations should be fully financed by the parties that benefit from them, such as the government and health insurance companies. If companies are involved in research, they should also finance patient participation. Independence can be achieved using an intermediary such as NPCF in the Netherlands.
4. (IT) REIMBURSEMENT FOR LOST WORKING HOURS
5. (ES) If the patient appears at a congress as a speaker, they should be compensated for their contribution, like other speakers
6. (NL) To the national patient organisation in question
7. (NL) Payment for participation should be paid to the patient organisation.
8. (FI) A daily allowance/remuneration for patients
9. (IT) On expenses documents
10. (BG) Financing of the patient organization activity

PO21. What would help you increase your level of confidence?

1. (IT) Training
2. (FR) Real involvement of patients
3. (IT) To treat patients as human beings and not guinea pigs
4. (DK) Better communication and information
5. (IT) Greater consideration by the pharma world, greater attention to my point of view, greater support for participation
6. (ES) More knowledge and training, collaboration with the doctors involved
7. (PL) Training on this subject
8. (FI) Financial support
9. (SL-SI) Training
10. (BG) Feedback

PO22. From whom would you like to receive support/mentorship when engaging in medicines development? (Select all that apply)

1. (IT) Product ingredient certificates
2. (ES) From expert medical staff

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3. (IT) Patients
4. (DE) Self-help umbrella associations
5. (NL) Education of investigators is required to talk on the same level with patients.
6. (DK) Researchers
7. (ES) Organisations that participate in similar activities for other diseases
8. (BG) Lawyers

PO25. What is your highest level of educational qualification?

1. (IT) Doctorate
2. (IT) Master's degree
3. (IT) Degree
4. (IT) Master's degree
5. (FR) PhD Health Economics
6. (IT) Degree
7. (SL-SI) Master's degree
8. (NL) University

SECTION: HCP

HP16. Do you have methods to determine impact of patient engagement?
If yes, could we contact someone within your organization for further information? Please provide email if possible. If not sure, please just skip

1. (NL) I'm not sure.

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