

Considerations and learnings from Use-cases

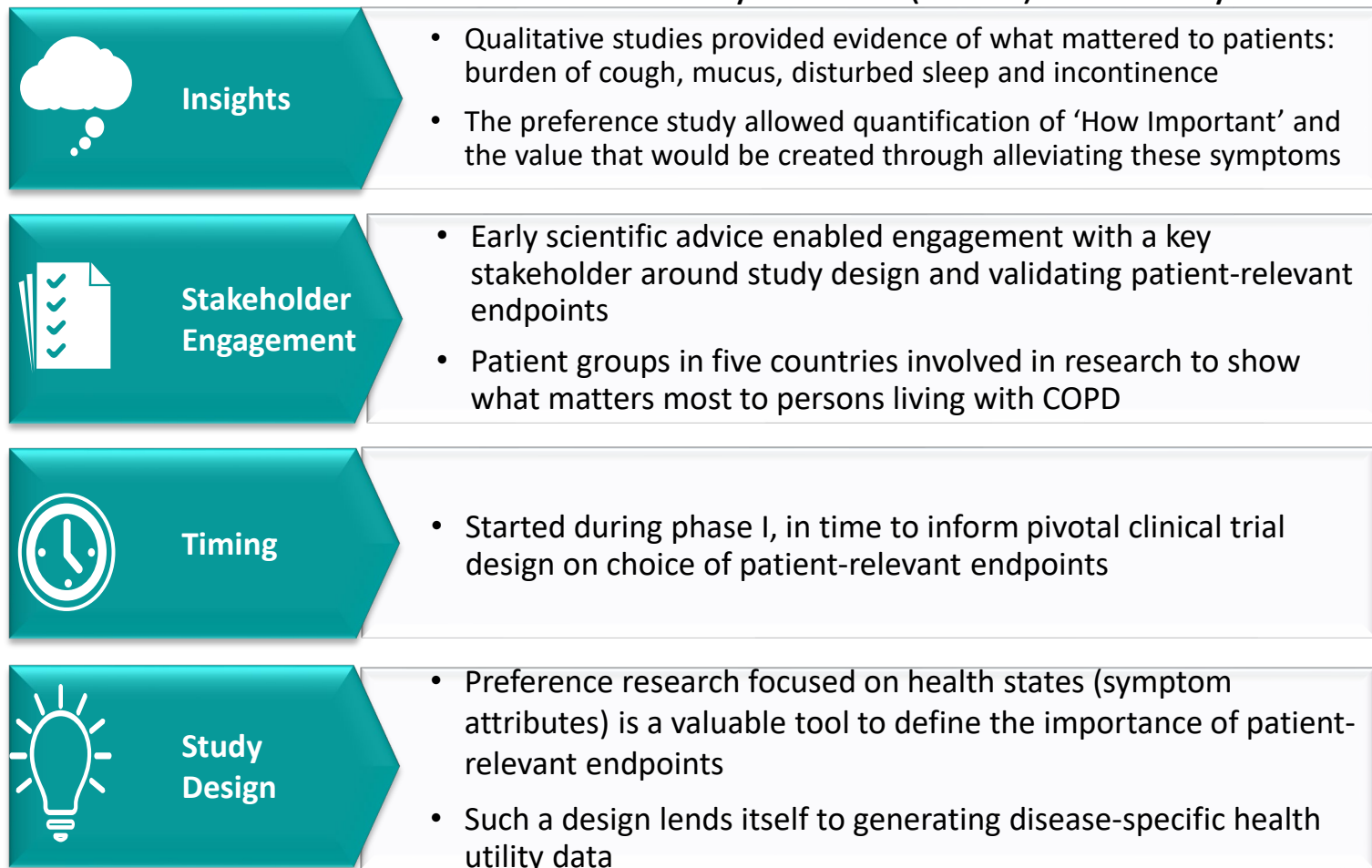
EMA Multi-stakeholder workshop

Patient experience data in medicines development and regulatory
decision-making

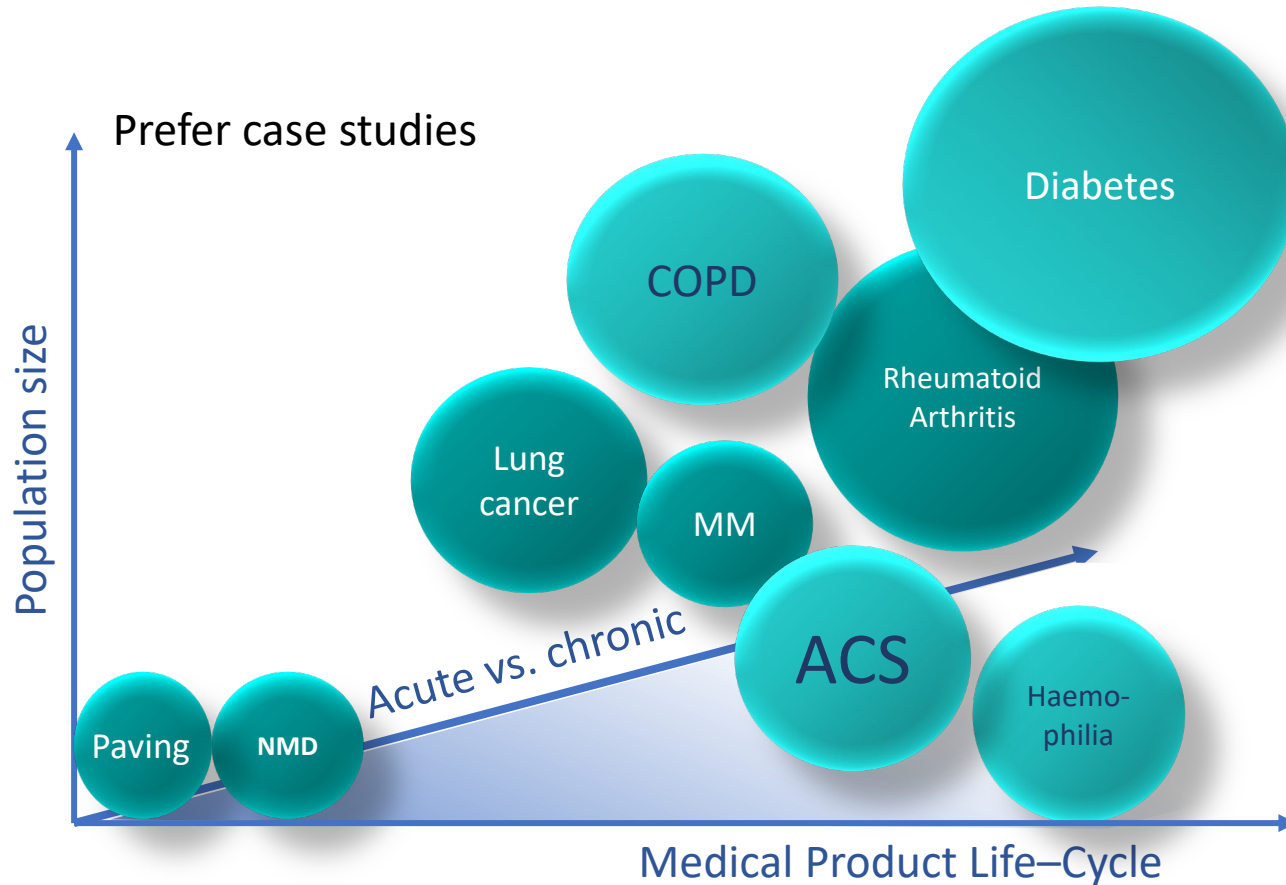
What are important use cases? An example

- Patient preferences are useful to inform preference-sensitive decisions during multiple phases of the medical product life cycle
- Patient preference data is intended to inform decision-making as supplementary information to clinical evidence
- Use cases where patient preference studies are especially useful:
 - Selection of patient-relevant outcomes
 - Patient's perspective might elicit endpoints which remarkably matter to patients in addition to traditional clinical endpoints
 - Patients' acceptability of trade-offs between the various treatment characteristics
 - Benefit / risk decisions

PREFER Chronic Obstructive Pulmonary Disease (COPD) case study



Building experience in Patient Preference Studies



COPD: Chronic Obstructive Pulmonary Disease
ACS: Acute Coronary Syndrome
MM: Multiple Myeloma
NMD: NeuroMuscular Disorders

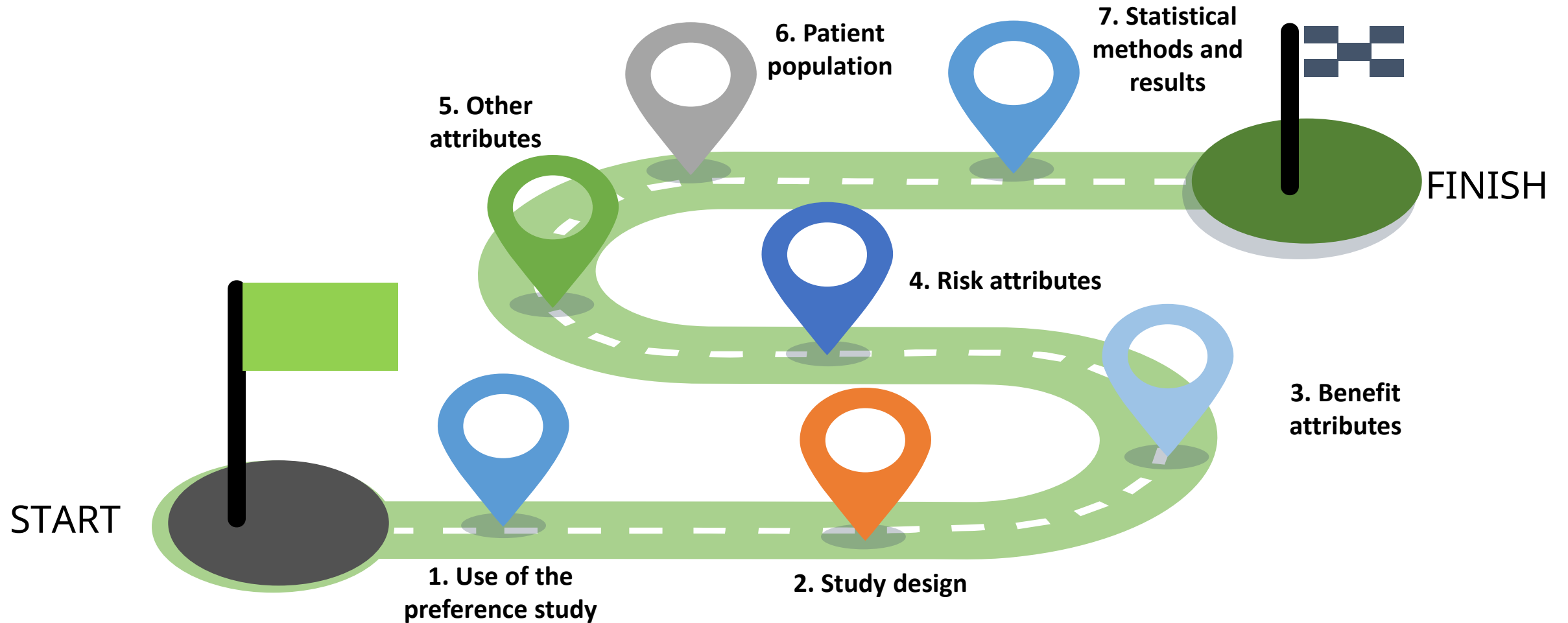
- Patient preferences are useful for informing preference-sensitive decisions during multiple phases of the **medical product life cycle**
- Experience in Preference studies is growing exponentially and now covers a broad spectrum of
 - different organ systems & various diseases from **orphan to common** conditions
 - **acute to chronic** conditions, **severe to milder** diseases
 - different **populations**: paediatrics, elderly
 - quantifying the preferences based on ethnicity, cultural differences, geographies

Considerations for optimizing PPS

- Study sponsors should seek scientific advice prior to starting a study for use of patient preference information in regulatory decision-making
- Especially pertinent when the patient preference data is to
 - be used in dossiers to inform regulatory/HTA decisions
 - assist in the interpretation of clinical study data
- Scientific advice discussion allows a patient preference study to be designed such that its results are useful to the decision-maker
- Benefits of scientific advice for patient preference studies can be maximized by:
 - Considering all available **guidance**
 - Initiating scientific advice procedures **as early as possible**
 - For **quantitative studies**, it is imperative to obtain advice **before finalizing study design and conduct**
 - Allowing sufficient time to include the relevant **patient preference elicitation experts**
 - Involving **patients as research partners**
 - **High quality** briefing book



The Prefer checklist



How use cases can contribute to better regulatory decision making

Patients' experience



What matters to patients?



How much does it matter to patients?



What trade-offs do patients find acceptable?



What about patient preference heterogeneity?

Regulatory impact

- Increases certainty in the development and presentation of PPI
- Transparency on what type of patient evidence data is considered acceptable to support regulatory decision-making
- Increased confidence of regulators in assessing and using patient evidence data in regulatory decisions
- Patient evidence obtained during drug development and submitted to support the Marketing Authorisation Application is adequately and transparently reflected in the European Public Assessment Report (EPAR) and/or in the SmPC (Summary of Product Characteristics)*
- Lays a foundation to inform eventual guidelines

[final-efpia-position-on-transparency-of-patient-evidence-in-regulatory-decision-making-and-product-information.pdf](#)



Conclusions and outlook

- IMI Preferred case studies demonstrated the value of patients' involvement by encouraging the inclusion of patient evidence, such as patient preferences in drug development and decision-making
- It provided drug developers with a better understanding of how patient evidence can be used in development e.g., for end point selection and to regulators, HTAs and payors for their decision making (trade-offs acceptability, benefit-risk decisions)
- Fostered a transparent dialogue between all stakeholders e.g., Regulators, Health Technology Assessment (HTA) bodies, developers and patients on the utilization of patient evidence, which needs to be sustained
- Development of guidance would further establish patient evidence → alignment on approaches and expectations relating to patient experience data to avoid duplication of efforts and disharmonized expectations
- Enhancing transparency on how patient evidence has been considered in the different use cases will benefit the entire society

Back-up

More information

PREFER Recommendations

- See the Zenodo PREFER community

PREFER templates

- See the Zenodo PREFER community

Webinars

- See the YouTube IMI-PREFER channel

Publications

- See [Start - PREFER \(imi-prefer.eu\)](http://imi-prefer.eu)

Qualification

- See EMA website

Case studies

- See [HPSTR](#)

Case Study #1

Introduction/ Background

Bayer had a dialogue with FDA on a patient preference study for an investigational product to obtain data regarding the patients' choice of treatment and to evaluate the relative importance of each product characteristic (attribute) that drives treatment choice, intended to be included in the product label:

- Bayer requested feedback on the appropriateness of the study approach
- Bayer requested feedback on whether the proposed study design concept would be eligible for presentation in the clinical studies section of the product label.
- Bayer asked which considerations for methodology FDA would have to support the inclusion of the study results in the product label.

Tasks and Actions by Sponsor and HA

Sponsor:

- Conducted literature reviews to identify relevant attributes for questions, then discussed these attributes with specialists to develop the so-called discrete choice experiment (DCE) survey (in line with FDA guidance).
- Provided the proposed study design concept together with the results of the literature review and interviews with external clinical experts to the HA for review in a comprehensive briefing book.

HA

- FDA evaluated the adequacy of the study design concept and provided recommendations for inclusion in the label both in written as well as in a formal meeting

Outcome/ Impact (of Agency Interaction)

- **Feedback from Agency:** Amongst others, FDA indicated that US regulations state “The labelling must contain a summary of the essential scientific information needed for the safe and effective use of the drug.” As such, any data that do not pertain to the safe and effective use of a medical product would not be included in product labelling.

In order to support the inclusion of the patient preference study results in the label, FDA asked to evaluate patient preferences in relation to the actual data on the efficacy and safety of the investigational product.
- **Risks/ Challenges:** at this stage, remaining uncertainty about the best timing during development and whether the results of a patient preference study conducted outside of the clinical trial context would lead to the inclusion of these data in the label, especially without further consulting FDA.
- **(Potential) Solutions:** a more continuous dialogue between Applicant and Regulatory Agency with a dynamic exchange process would help to decrease the uncertainties. Where patient representatives are available for a particular disease, their views would be important in this dialogue.

Results/Impact on Development

- Due to uncertainty about whether the results of a patient preference study would qualify for inclusion in the product label and about its utility in regulatory decision-making, Bayer decided to postpone the decision to conduct the study to a later stage of the development of the product.

Key Takeaways

- Inclusion of patient preference studies in labelling is not the rule but should be discussed in-depth with the Regulatory Agency to understand when it may be possible.
- Alignment between the Applicant and Regulatory Agency on the utility of a patient preference study is critical. Globally accepted regulatory guidance would support the implementation of patient preference research.

Case Study #2

Introduction/ Background

This case study demonstrates the value of integrating the patient and caregiver voice into the decision-making process in all phases of medical product development. The early and systematic partnerships between the spinal muscular atrophy (SMA) community and Roche helped shape the company's clinical development programme in SMA and was central to ensuring faster and broader patient access and improving outcomes. Furthermore, through work with patients and COA measurement experts, a new scale was developed, validated and used in the regulatory submission to solve for the challenge that there were no well defined endpoints in SMA.

SMA is a genetic disease affecting the central nervous system, peripheral nervous system, and voluntary muscle movement (skeletal muscle).

Actions by Sponsor to develop a new Clinical Outcome Assessment

The sponsor partnered with the SMA community throughout development. In this section we would like to share specifically the development of a novel Clinical Outcome Assessment as an outcome of these partnerships.

The sponsor conducted patient and caregiver interviews to better understand the disease burden in Type 2 and non-ambulant Type 3 SMA patients. Through in-depth qualitative concept elicitation and cognitive interviews, we identified maintaining/improving independence related to the level of assistance needed for activities of daily living as a key outcome relevant to patients with Types 2 and non-ambulant Type 3 SMA. Since existing patient- and observer-reported outcome measures used in this population do not capture this concept of interest, we developed the SMA Independence Scale - Upper Limb Module (SMAIS-ULM) for the SMA community with COA measurement experts. Psychometric evaluation of the longitudinal and cross-sectional measurement properties was conducted using quantitative survey data and clinical trial data from a phase 3, double-blind, randomized, placebo-controlled trial evaluating risdiplam in Type 2 and non-ambulant Type 3 SMA. As FDA emphasized in its recent draft PFDD 3 Guidance, sharing of COAs between sponsors and researchers will help to promote efficiency and maximize the returns on the efforts made by patients in developing these tools. Therefore, following updates to the scale and further cross-sectional validation, we have made the SMAIS-ULM available to the public via the ePROVIDE platform. As such it can be used in clinical practice and future trials to monitor patients/assess benefit, and is already being used globally, including in large registries.

Outcome/ Impact on Health Authority review process and decision

Patient Advocacy Groups advanced the sponsor's understanding regarding the existing unmet need, and what treatment effects were most relevant. In addition, they were also key in the HA review process. Members of the SMA Foundation were invited to regulatory meetings to provide the HA with insights from people living with SMA directly. In addition, patient views, published data from PAG-led surveys (e.g., Voice of the Patient report, EUPESMA) alongside the patient-reported outcome data (SMAIS) from clinical trials, were included in regulatory applications to capture the unmet need and real-life value of SMA treatments. This supported HAs in their review, as evidenced in the mention of the SMAIS score showing evidence of the benefit of the medicines in the EPAR (Risdiplam Public Assessment report, EMA/216061/2021).

Results/Impact on Development program

The sponsor was able to design clinical trials that reflected the needs of the patient community (e.g., included broader age range, severely impacted patients [e.g., with scoliosis, contractures etc.]). Furthermore, the sponsor was able to include endpoints that capture what matters to patients (and provided in turn a better understanding on the medicine's profile).

In addition, better understanding of the disease also allowed for requesting and granting of special regulatory procedures for rare disease and areas of unmet need, such as for example Priority Medicine (PRIME) designation, Orphan drug designation, and Fast track granted in the US.

Key questions for the workshop

1. Even though the COA was reported in the EPAR, it remains unclear the extent to which HAs base their regulatory decisions on Patient Experience Data. We welcome more clarity and transparency on the impact of this data.
2. More clarity is also needed in terms of what PED constitutes (e.g., beyond PROs), sponsors welcome HAs to expand the scope of PED to also include insights collected from unstructured interactions (e.g., ad boards, consultations etc.)
3. It is essential that Health Technology Assessment Bodies also consider PEDs and that there is alignment between HTAs and Health Authorities on the use of patient-led insights for regulatory and access decision making.

Introduction/ Background

In addition to more traditional methods of understanding patient experiences (e.g., interviews, focus groups), there is a growing interest in leveraging social media data sources to generate patient-centered insights. This has been bolstered by the recent FDA PFDD Guidances which specifically discuss the role of social media in generation of Patient Experience Data (PED).

A recent development program in Parkinson's disease (PD) utilized social media data sources alongside a literature review, concept elicitation interviews and expert input to develop a conceptual model of the disease.

Tasks and Actions by Sponsor and HA

Individuals with PD experience a significant disease burden over time, including motor and non-motor symptoms which impact everyday life. In order to understand the most relevant symptoms and impacts at the early-stage of the disease (patients within 2 years of diagnosis, Hoehn & Yahr stage 1–2), the sponsor designed a multistage study which sought to create a conceptual model. A literature review of published qualitative research (25 articles), a quantitative social media listening analysis (review of 23,756 documents) and qualitative patient concept elicitation interviews (n = 35) were conducted, as well as the inclusion of therapeutic area expert input throughout the study. This study benefited from layering different methodological approaches to develop the conceptual model. The novel approach of including a social media listening analysis resulted in the development of a model that incorporates a uniquely patient-centered perspective and led to the identification of previously under-reported impacts in the literature, such as 'anxiety' and 'fear' which could then be further explored in the interviews. The conceptual model has since been used to help researchers to develop and select optimal patient-centered outcomes to measure treatment benefit in clinical trials of early-stage PD patients.

Outcome/ Impact (of Agency Interaction)

- **Feedback from Agency:**

We have no direct feedback from the EMA or FDA to share. The FDA PFDD Guidance 1 & 2 reference the potential value of social media data in patient-centered drug development.

- **Risks/ Challenges**

Social media is still considered as a complementary/exploratory source of PED. There are considerations regarding data privacy and confirmation of diagnosis and a lack of published data to reference with regards to its utility.

- **(Potential) Solutions:**

Data privacy and confirmation of diagnosis can both be managed with effective mitigation strategies e.g., prospective social media data generation can include physician diagnosis as per 'traditional methods'. In addition, the sheer volume of data generated may overcome the potential 'noise' of non-diagnosed patients and falsified online records. Moreover, recent studies have demonstrated that social media may elicit concepts that are not disclosed during traditional interviews (e.g., embarrassing symptoms), as well as capture the same concepts as other methods - see <https://pubmed.ncbi.nlm.nih.gov/29757313/>.

Results/Impact on Development

Social media data is an effective tool in understanding patient experiences and is an important complementary approach. It can enable rapid insights and more diverse samples than traditional methods.

Key Takeaways

Social media is an important source of PED and is often underutilized. It could be an important approach to increasing diversity and inclusion of patients and generally creating a more comprehensive understanding of a disease and unmet need. Recent guidance from FDA shows that they are increasingly receptive to social media PED but there remain outstanding barriers/risks that need to be managed, as well as a lack of guidance from other regulatory authorities. Despite these barriers, it is an important complementary tool and may also be a preferential approach in early insights efforts where speed is paramount.