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Improving healthcare decisions

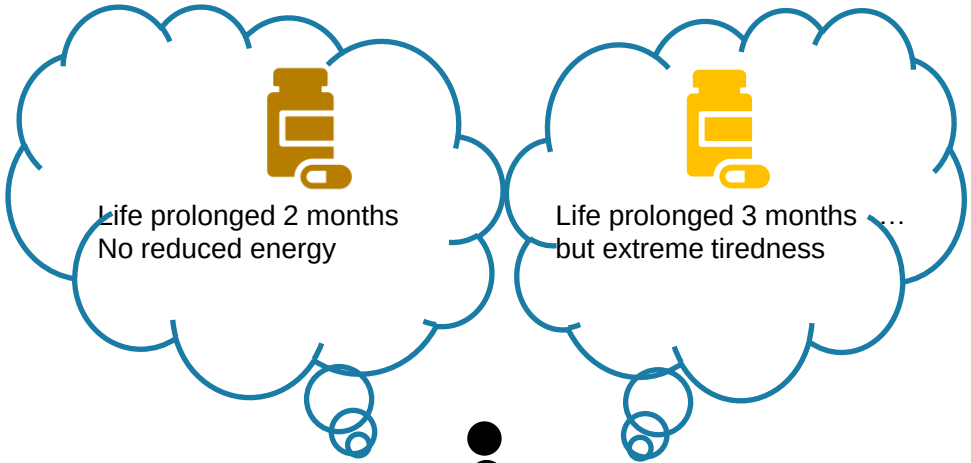
How to Assess and Implement Patient Preferences in Decision-Making Along the Medical Product Life Cycle?

Forum Session

9 November, ISPOR Europe 2022 Conference

Patient preference studies

Patients

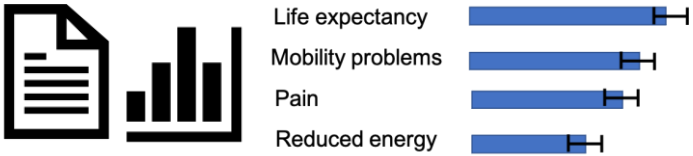


What matters to patients?

Patient's preferences

?

Developers, regulators, payers, ...



Qualitative and quantitative data

Aim of today's Forum

Share insights on how results from patient preference studies can inform decision-making along the drug life cycle

- Regulatory perspective
- Research perspective
- Patient perspective
- Panel Discussion

Meet the speakers

Francesco Pignatti

Head of Oncology, Haematology and Diagnostics

European Medicines Agency (the Netherlands)

Rosanne Janssens

Postdoctoral Researcher

KU Leuven (Belgium)

Ananda Plate

Executive Director

Patvocates (Germany)

Liese Barbier

Postdoctoral Researcher

KU Leuven (Belgium)

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Francesco Pignatti

Patient Preferences in Regulatory Decisions and Communications

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Patient Preferences in Regulatory Decisions and Communications

ISPOR Europe 2022 Forum on Patient Preferences

Presented by Francesco Pignatti
Head of Oncology, Haematology and Diagnostic Products
The views presented are personal and not those of EMA and its scientific committees.

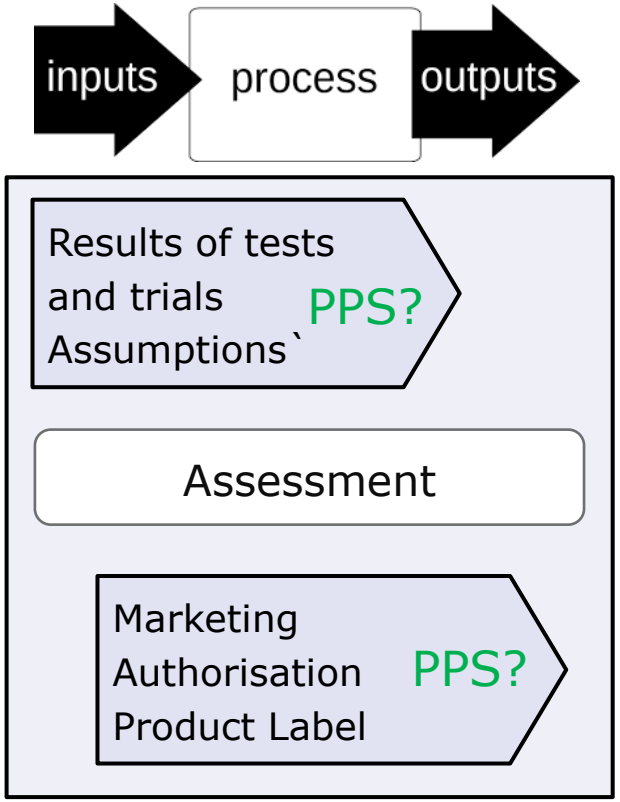
When looking at products or services I am interested in “user reviews”

1. **Strongly disagree**
2. **Disagree**
3. **Neutral**
4. **Agree**
5. **Strongly Agree**

Basic principles for regulatory decisions

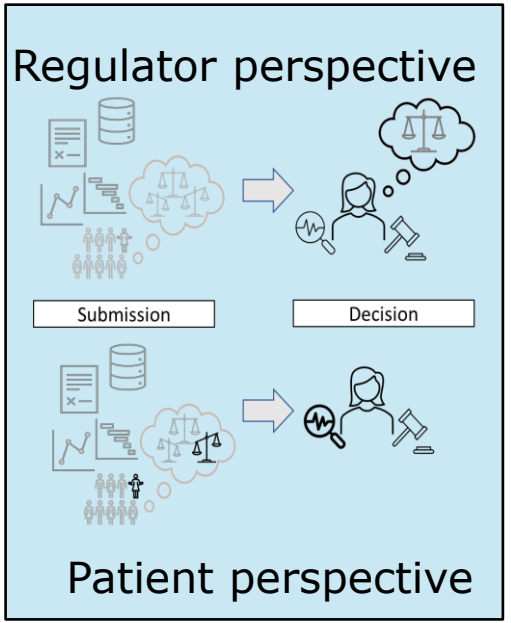
- Companies submit the results of studies to fulfil requirements
- Regulators **assess** if the requirements are fulfilled and **communicate** to inform clinical decisions
- Legal requirements
  - Drug ≻ Placebo
  - Value judgments about pharmacologic effects; no other considerations (e.g., economic)
  - Subjective value judgments (generally, no agreed clinical or other measure of "value")

What role for patient preference studies (PPS)?



Patient preferences are informative for decision (regardless of perspective)

- Patient preferences:
  - As **evidence** to drive regulatory decision (*Is the balance of benefits and harms positive for some patients in the right decision context?*);
  - To **inform** the regulator's preferences (regulators lack experience) for regulatory decision;
  - To inform about **heterogeneity** (subgroups);
  - Allow applicant companies to **support claims** with data

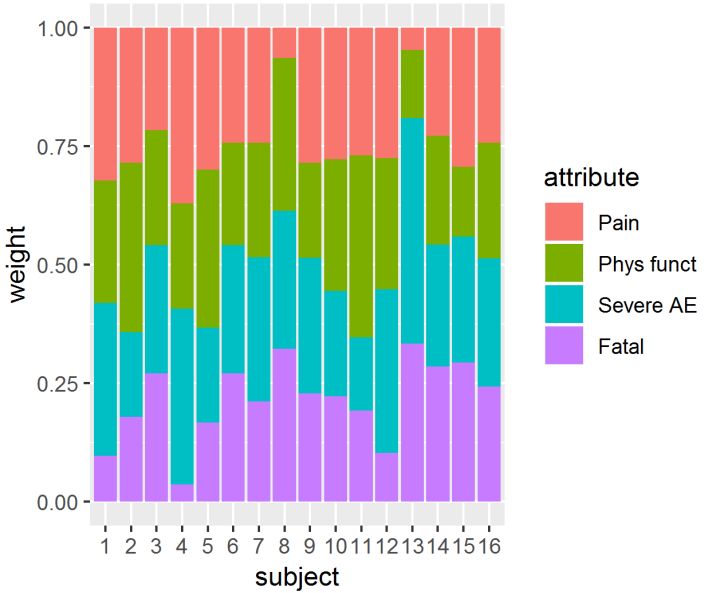


Pignatti, Wilking *et al*. (2021) *The value of anticancer drugs: A regulatory view*. Nat. Rev. Clin. Oncol

Exploring usefulness of preference elicitation at advisory meetings

Experience so far:

- Helps clearly describe the weight experts give to each effect
- Intuitive display of the trade-offs
- Allows exploring thresholds, sensitivity to assumptions, scenario analysis



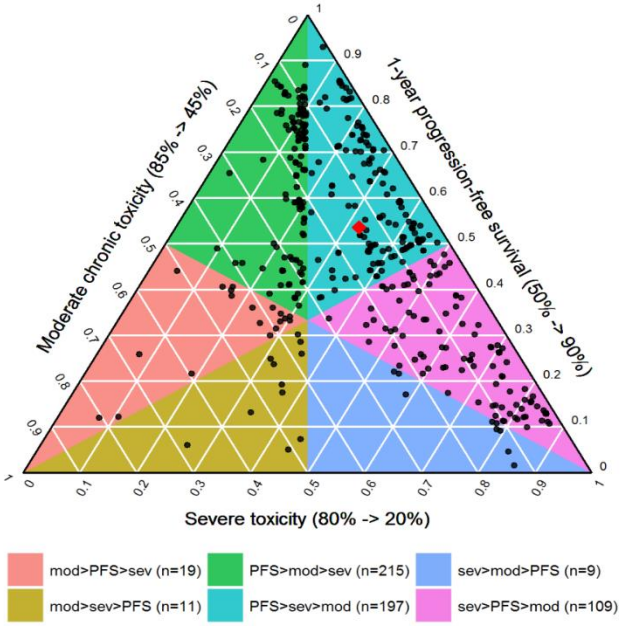
Can patient preferences in the label be informative for users (regardless of the decision model)?

- Patient preferences **in the label** similar to "star rating", to:
  - Help users decide especially **when harms are high**
  - Highlight situations of **heterogenous preferences** to doctors where more attention needed
  - Allows to **consider both expert and user** reviews
  - Build **trust** including negative reviews

Example: Trade-offs communicated explicitly

Myeloma UK survey

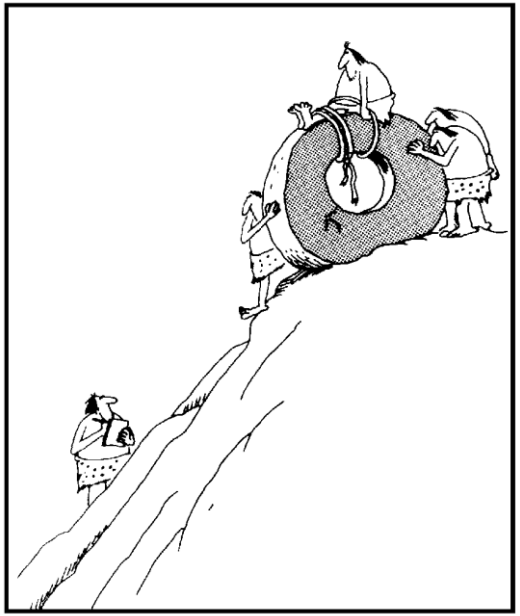
- Ixazomib example (approximation)
  preferred over placebo by 76%
  participants
- Severe toxicity ranked higher among
  younger, **working**, and looking after
  dependent family members and who had
  more frequently experienced severe toxicity



D. Postmus *et al*. (2017)

Summary/Challenges

- Patient preference studies facilitate and modernise decision-making and communications
  - Regulatory decisions: Replace assumptions with evidence
  - Product label: Inform about other patients' preferences ("user review") and heterogeneity
- Challenge: Lack of familiarity and guidance



Early experiments in transportation

There should be a standard section in the Product Label about “patient preferences”

1. Strongly disagree
2. Disagree
3. Neutral
4. Agree
5. Strongly Agree

Thank you for listening

Further information

Francesco.pignatti@ema.Europa.eu
Official address Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands
Telephone +31 650089433
Send us a question Go to www.ema.europa.eu/contact

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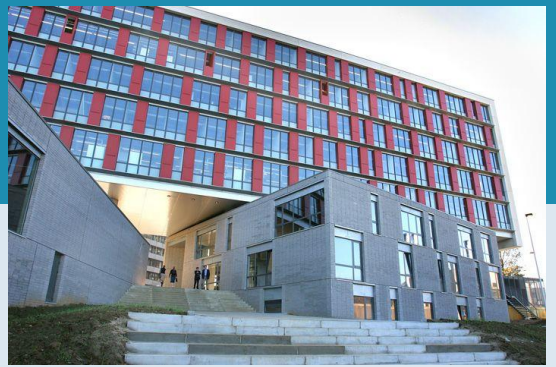
Rosanne Janssens

Qualitative and quantitative research methods in patient preference studies

KU LEUVEN

Qualitative and quantitative research methods in patient preference studies

Case studies in Multiple Myeloma, Inflammatory Bowel Disease and Duchenne



Dr. Rosanne Janssens

ISPOR Europe 2022 Vienna (virtual session)

November 9th 2022

- What are key challenges according to you for the design and conduct of patient preference studies?

Please scan the QR code and share your thoughts

What are research questions that can be meaningfully addressed in patient preference studies?

What are (hypothetical) **treatment outcomes** that are most important to patients?

What are symptoms and side effects that patients want to see addressed in drug development?

What are the **dimensions that affect the trade-offs** that patients are (un-)willing to make?

What are side-effects that patients (do not) find acceptable?

What are **uncertainties** that patients (are not) willing to take?

How do different **symptoms and side-effects** impact patients' quality of life?

What is the **relative importance (weight) of relevant treatment attributes** according to patients?

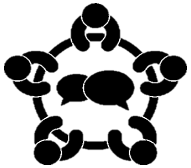
How do patients **trade off between (hypothetical) treatment effects**?

What are **patient characteristics that (significantly) affect patients' preferences** (preference heterogeneity)?

What are data collection methods available to address these?

Qualitative research methods

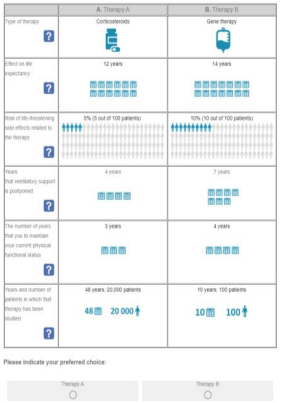
(*e.g.,* focus group discussions, individual interviews – descriptive and thematic analysis)



- **In-depth information** on attributes that matter most and **why**
- Sensitive and appropriate attribute selection → increase **internal validity** of survey prior to survey
- Aid **interpretation** of findings subsequent to preference survey

Quantitative research methods

(*e.g,* discrete choice experiment, swing weighting, threshold technique – descriptive and statistical analysis)



- **Quantify relative importance of attributes**
- Investigate **preference heterogeneity**
- Allow **inclusiveness & broader patient outreach**
- Allow **specific questioning techniques** to investigate trade-offs
- Application of **statistical methods** to identify which **attributes** statistically impact choices

Schoefs et al., 2022 *Janssens et al., 2021*

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Qualitative data collection methodologies useful in patient preference studies

PubMed

Embase®

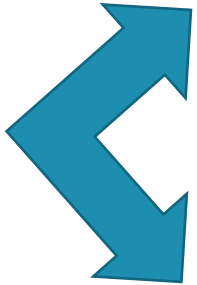
Scoping and systematic **literature reviews** of prior patient preference studies, clinical trial database and regulatory document analysis

EU Clinical Trials Register

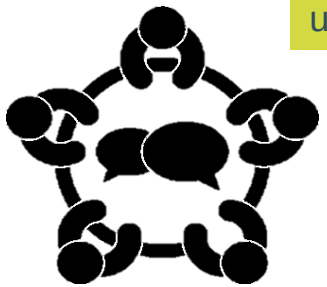
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/726358/2021
EMEA/H/C/004214

Xeljanz (tofacitinib)
An overview of Xeljanz and why it is authorised in the EU



AND/OR



Focus group discussions
using nominal group technique

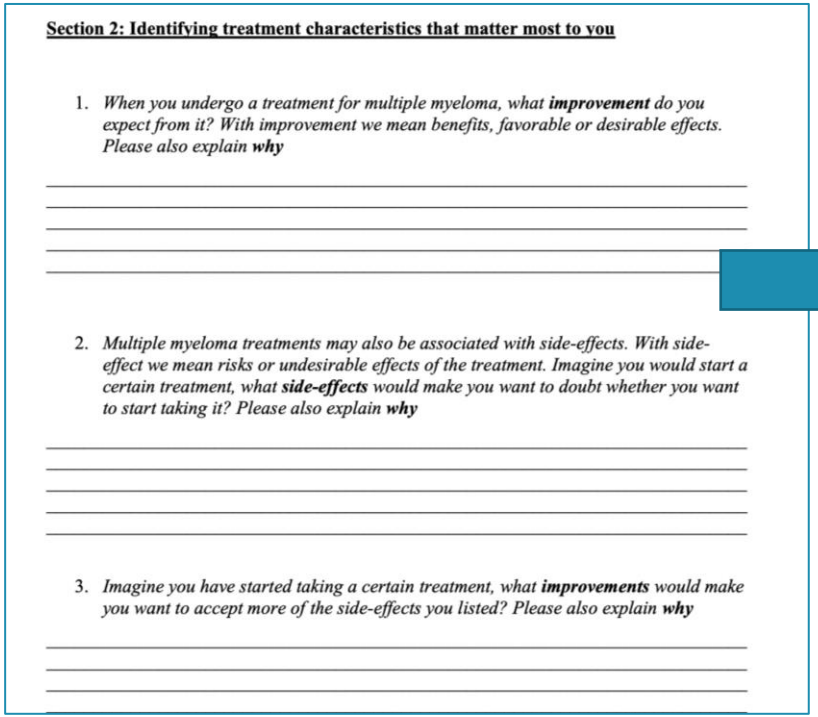
Characteristic	Explanation	Grading
Arrhythmia	- The heartbeat is irregular, too fast, or too slow. - This can occur in up to 6% of myeloma patients[2].	
Bleeding	- Abnormal bleeding, for example when brushing your teeth, (spontaneous) bruising, or the presence of blood in urine or feces. - This can occur in up to 62% of myeloma patients.	
Bone or back pain	- This can occur in up to 23% of myeloma patients.	
Cancer	- New cancer, e.g. cancer of the bladder, the blood cells, intestines. - This can occur in up to 10% of myeloma patients.	
Chest pain	- This can occur in up to 11% of myeloma patients.	
Fever	- A temperature above 38 degrees. - This can occur in up to 40% of myeloma patients.	
Nausea	- Feeling of sickness or discomfort in the stomach that may come with an urge to vomit. - This can occur in up to 65% of myeloma patients.	
Headache	- This can occur in up to 30% of myeloma patients.	
Rash	- Reddish discoloration of the skin. - This can occur in up to 42% of myeloma patients.	
High or low blood pressure	- A high blood pressure is blood pressure reading higher than 140 millimeters of mercury (mm Hg) for the top number (this is the upper pressure) and/or 90 mm Hg for the low number (this is the under pressure). - A low blood pressure is blood	

Individual interviews

→ **Patients' involvement** to understand most suited method in given disease/patient context
→ **Clinicians' involvement** to ensure accuracy of descriptions towards patients

Schoefs et al., 2022 *Janssens et al., 2021*

Nominal group technique to trigger discussion on most important attributes



Section 2: Identifying treatment characteristics that matter most to you

1. *When you undergo a treatment for multiple myeloma, what **improvement** do you expect from it? With improvement we mean benefits, favorable or desirable effects. Please also explain **why***

2. *Multiple myeloma treatments may also be associated with side-effects. With side-effect we mean risks or undesirable effects of the treatment. Imagine you would start a certain treatment, what **side-effects** would make you want to doubt whether you want to start taking it? Please also explain **why***

3. *Imagine you have started taking a certain treatment, what **improvements** would make you want to accept more of the side-effects you listed? Please also explain **why***

Characteristic	Explanation	Grading
Arrhythmia	- The heartbeat is irregular, too fast, or too slow. - This can occur in up to 6% of myeloma patients[2].	
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Janssens et al., 2021 Members in Medicine, 2

Qualitative research findings in IBD and MM

- Ensured inclusion of **patient-relevant attributes**; inclusive of all aspects important to patient decision-making
- Ensured attribute descriptions were **understandable and clear**
- **Heterogeneous patient population** in terms of disease and treatment experience
- Involvement of **patients' and patients' organizations** to help interpretation of findings

"For me fatigue is something I could not accept as a side-effect."

Inflammatory Bowel Disease

Decreased libido

Fatigue

Frequency of having to go to the toilet

Risk of undergoing surgery

...

Multiple Myeloma

Additional

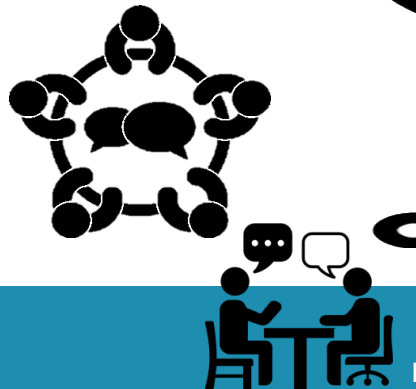
Risk of life-threatening side effects

Mobility problems

...

"Lengthened life span is of course most important, I think that the most desirable effect of myeloma treatment would be longer life."

"If something were found that would improve the whole tingling sensation that has become chronic."



EFCCA European Federation of Crohn's & Ulcerative Colitis Associations

MPE Myeloma Patients Europe

IBD: Inflammatory Bowel Diseases; MM: Multiple Myeloma

Schoefs et al., 2022 Janssens et al., 2021

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Towards the PPS survey: final list of attributes & levels developed using patient language in qualitative phase

Inflammatory Bowel Disease

Risk of undergoing SURGERY
This is the risk that you need to undergo surgery because: medical therapy cannot adequately control your intestinal inflammation (…).

FREQUENCY of having to go to the toilet
This is the frequency that you have to go to the toilet.

URGENCY and PAIN of having to go to the toilet
This is the urgency that you have to go to the toilet and the pain that you experience with it.

Severity of daily ABDOMINAL PAIN and CRAMPS
This is the severity of abdominal pain and cramps you may experience daily.

Severity of FATIGUE
This is the severity of an overwhelming sense of tiredness, lack of energy, or feeling of exhaustion that is not relieved after rest of sleep.

Frequency of SLEEPING PROBLEMS
This is the frequency you may experience sleeping problems such as difficulty falling asleep, difficulty staying asleep (…).

Multiple Myeloma

	**Additional LIFE EXPECTANCY in YEARS** This is the expected number of years you are alive starting from the beginning of the treatment.
	**Risk of LIFE-THREATENING SIDE EFFECTS** This is the risk that you may experience life-threatening side effects such as developing another cancer (…).
	**Expected TREATMENT RESPONSE** This is the expected result of your laboratory and imaging tests that indicates whether the treatment was able to reduce the signs of cancer (…).
	**Duration and severity of nerve or bone problems affecting MOVEMENT** This is the duration and severity of the following which may cause mobility problems: bone damage and fractures (…).
	**Duration and severity of THINKING PROBLEMS** This is the duration and severity of the following thinking problems that you may experience: difficulties to think clearly and concentrate (…).
	**Duration and severity of INCREASED SUSCEPTIBILITY to INFECTIONS** This is the duration and severity that you are more susceptible to infections such as lung infections (…).
	**Duration and severity of REDUCED ENERGY** This is the duration and severity of the following problems that may cause reduced energy: tiredness (…).
	**Duration and severity of PAIN** This is the duration and severity of the following pains that you may experience: bone pain (for example in the back, chest, feet or hips) (…).

Schoefs et al., 2022 Janssens et al., 2021

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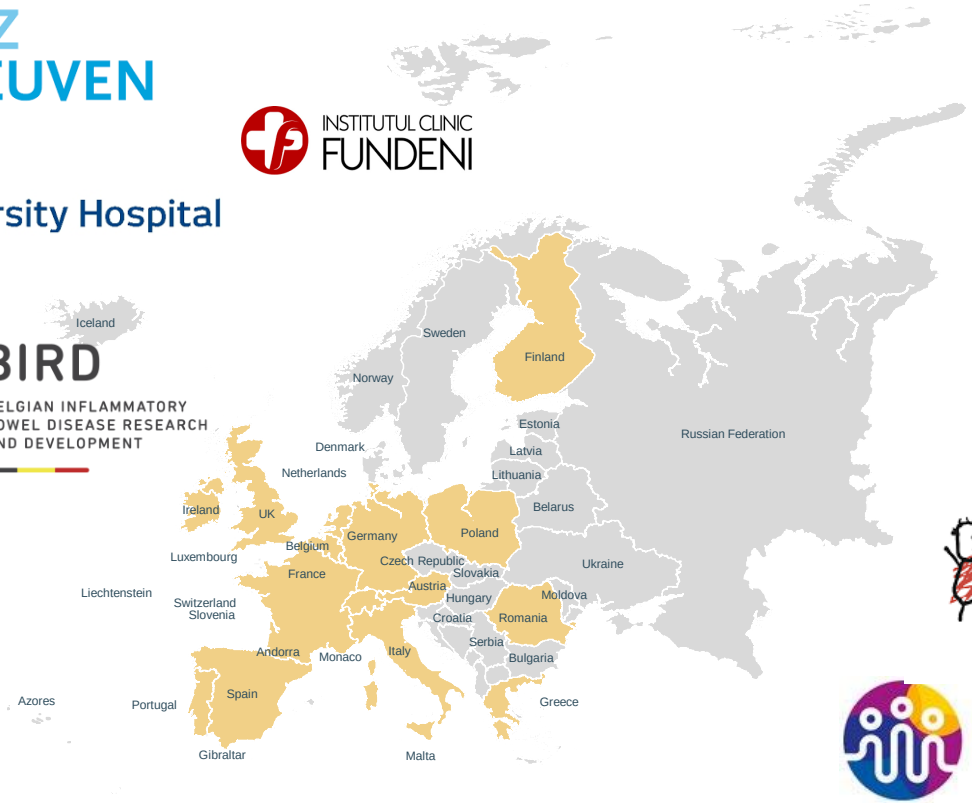
Piloting, translation, and dissemination of the survey

UZ LEUVEN

Oslo University Hospital

INSTITUTUL CLINIC FUNDENI

BIRD
BELGIAN INFLAMMATORY BOWEL DISEASE RESEARCH AND DEVELOPMENT



- European scope
- Recruitment: patient organizations + clinicians
- Involvement of patients, patients' organisations and
- clinicians for accurate translation, piloting and broad dessimination

WORLD DUCHENNE ORGANIZATION
UPPMD

MPE Myeloma Patients Europe

EFCCA
European Federation of Crohn's & Ulcerative Colitis Associations

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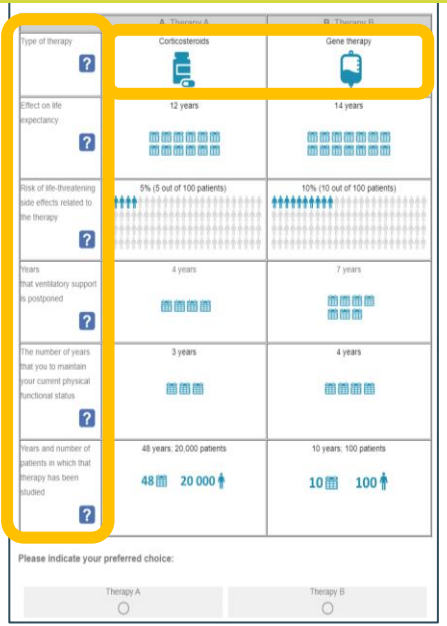
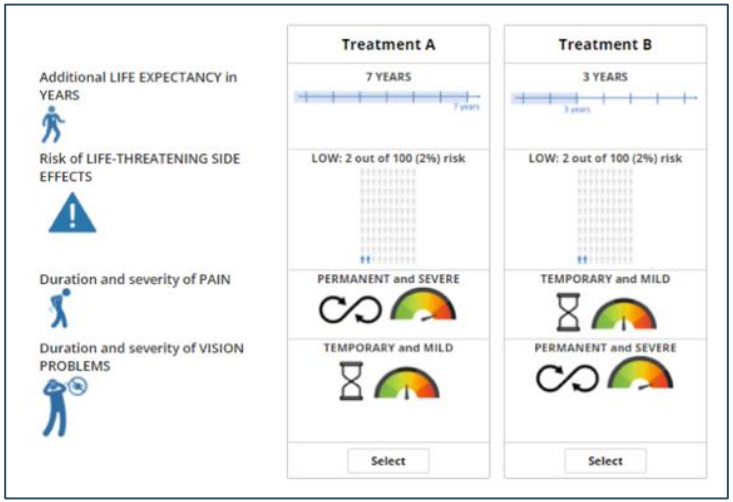
Quantitative data collection methodologies useful in patient preference studies

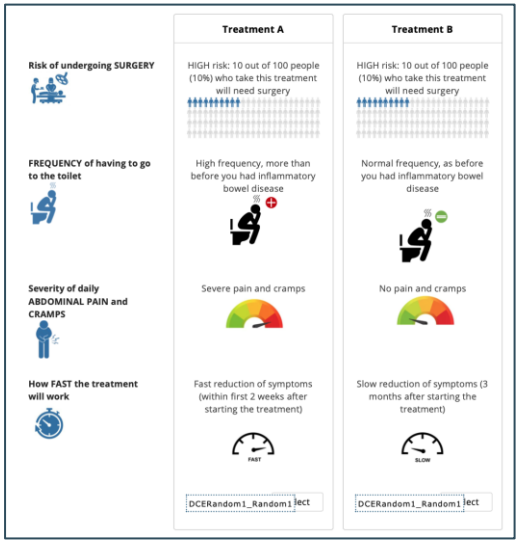
Duchenne Muscular Dystrophy



Multiple Myeloma



Inflammatory Bowel Disease



ATTRIBUTES AND LEVELS

Probabilistic Treshold Technique

Discrete Choice Experiment

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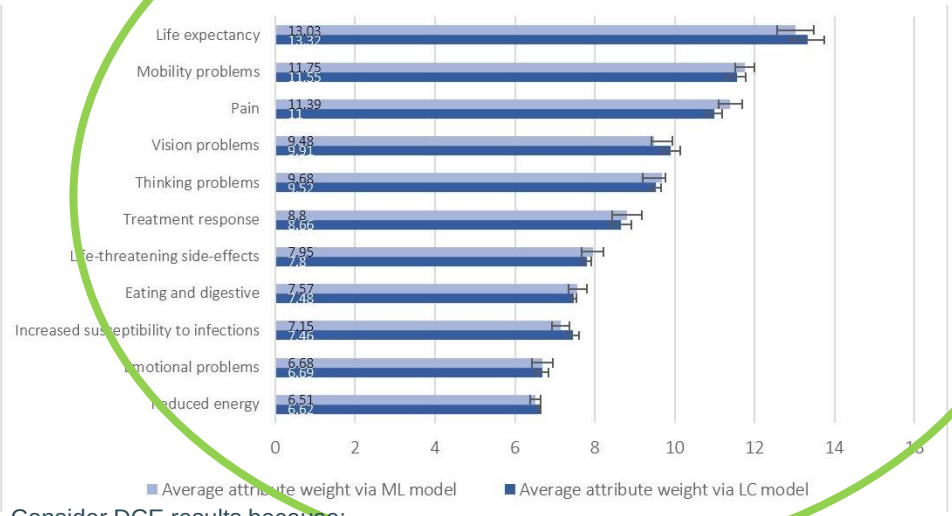
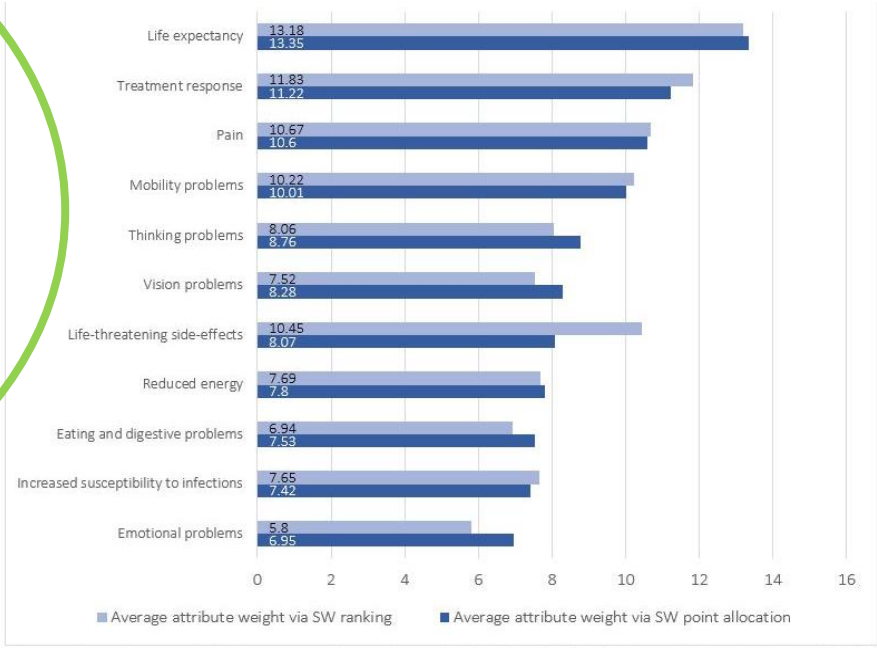
Quantitative research findings in MM: relative average attribute weights

Discrete Choice Experiment (n=475)



Swing Weighting
(n=371 point allocation; n=322 ranking)



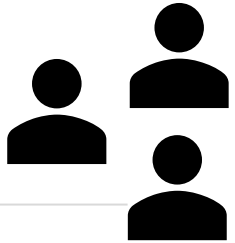
Consider DCE results because:

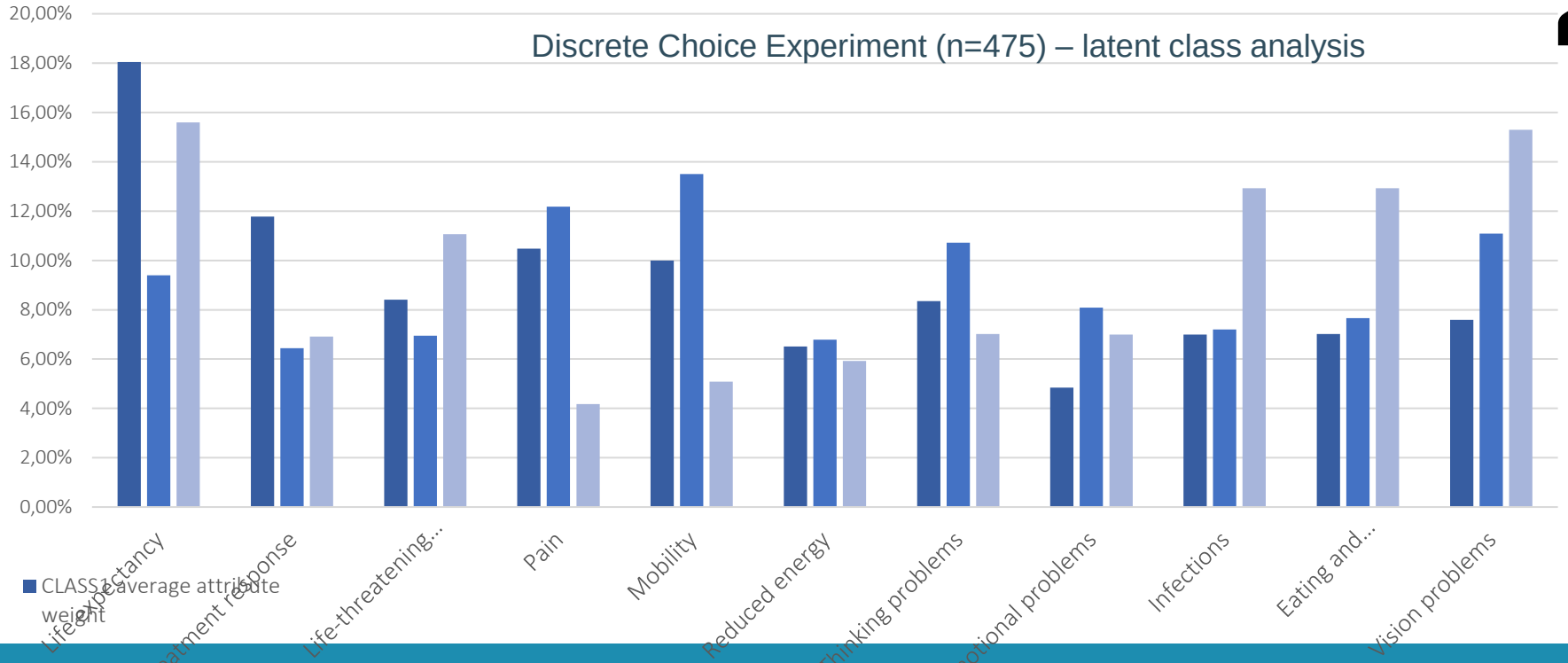
- No statistical model and uncertainty information for SW weights
- Patients' feedback; 32% preferred DCE vs 15 SW allocation; 10% SW ranking

MM: Multiple Myeloma

Janssens et al., 2022 (manuscript accepted)

Quantitative research findings in MM: preference heterogeneity





MM: Multiple Myeloma

Janssens et al., 2022 (manuscript accepted)

Janssens et al., manuscript submtted, 202

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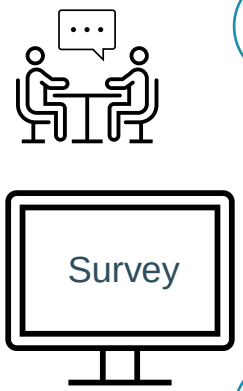
Key methodological learnings for **qualitative and quantitative research** methods in PPS



- Obtain input from **patients and patient organizations** to **co-develop the questions,** the attributes, levels, and explanations
- **Extensively pilot the questions** to assess whether patients understand the questions
- Collect and provide a detailed description of **participants' background characteristics**
- Transparently document and describe the study design and methodological choices to enable reviewers to contextualise the study results and evaluate their usefulness for decision-making
- Combine different recruitment strategies to increase transferability of the findings - being as inclusive as possible to include all patient types
- Organize review rounds by the study team (ideally **inclusive of patients' and/or patient organizations**) and undergo **external peer-review** by experts in the field in academic journals

PPS: patient preference study

Janssens et al., Frontiers in Medicine, 2021 *Janssens et al., 2022 (manuscript accepted)*

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Key methodological learnings for **qualitative and quantitative research** methods in PPS

- Ensure the qualitative study design needs meets the needs of the participant population
- Obtain ethical approval and contractual agreements with hospitals in all countries where needed
- Meaningfully involve patient and clinical partners via explaining them the PPS and ensuring flexibility in terms of timelines
- Investigate and describe whether and how the **attribute weights are statistically influenced by patient background variables** (e.g., via latent class analyses in discrete choice experiments)
- Ensure findings become **publicly available and provided back to patients**

PPS: patient preference study

Janssens et al., Frontiers in Medicine, 2021 *Janssens et al., 2022 (manuscript accepted)*

Which decisions along the medical product life cycle can be informed by patient preference studies?

Drug discovery & early development → **Clinical development** → **Regulatory decision-making and marketing authorization** → **HTA and reimbursement decision-making** → **Post-marketing phase**

- Resource allocation
- Identification of **patient unmet needs**

- Scientific advice on **patient-relevant endpoints**
- Joint EMA/EUnetHTA scientific consultations

- Evaluation of **unmet n**
- Assessment of **perfo endpoints**
- **F**
- U

- Evaluation of **unmet needs**
- Assessment of **clinical trial endpoints & outcomes**
- Understand **trade-offs patients are willing to make between benefits & risks**
- Understand **patient-relevant effect sizes**
- Identification of key (un-)favorable effects and **uncertainties**

patient- ers

- P **approval**
- Payer decision about **continued reimbursement**

- **New product developments** based on unmet needs

prefer.
PATIENT PREFERENCES

CHMP Qualification Opinion identifies “endpoint selection” and “identify and value trade-offs for benefits and risks” as applications of preference studies

> Based on PREFER qualitative studies with patients, patient organisations, industry, regulators, HTA bodies and payers, and clinicians; involving 6 literature reviews, 143 individual interviews, and 8 focus group discussions

References: Janssens *et al.*, 2019; van Overbeeke *et al.*, 2019; Whichello *et al.*, 2019

HTA= health technology assessment

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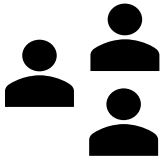
Remaining research questions related to the assessment and implementation of PPS in decision-making



- How can PPS be **efficiently conducted** to meaningfully inform stakeholders?
  - Need for **different PPS**' to satifsfy information needs of different stakeholders?
  - Implications in terms of time, effort for patients, patient organisations? – survey fatigue?
  - Designing/using **product independent PPS vs more compound focused approach**?
  - Designated stakeholder for financing, designing, conducting and coordinating PPS including data governance?

- Dealing with **preference heterogeneity**
  - MM study found heterogeneity between subgroups of patients
  - Relevant for decisions on unmet needs, marketing authorization, HTA and reimbursement?

- **Unmet need discussion:** "relative" needs of MM/IBD/Duchenne patients compared to other patients (disease areas)
  - Potential for generating **inequities** between disease areas?
  - Decisions made **within a certain disease/indication** can "easily" be informed by a disease specific PP study
  - **Across indication/disease decision making** may require "generic" attributes/comparable PP study results

PPS: patient preference study; MM: Multiple Myeloma
IBD: Inflammatory Bowel Disease

Janssens et al., 2019; van Overbeeke et al, 2019, Janssens et al., 2019, van Overbeeke et al., 2020

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Thank you

Questions? Feel free to reach out to rosanne.janssens@kuleuven.be

Ananda Plate

The patient perspective on Patient Preference Studies

The patient perspective on Patient Preference Studies

How to Assess and Implement Patient Preferences in Decision-Making Along the Medical Product Life Cycle?

ISPOR 2022

Ananda Plate

Executive Director, Patvocates Research
Board Member, Myeloma Patients Europe
Former Chair, WECAN

It’s a matter of perspective…

- **Patients live with the disease and are the end users of medicines.** Preference research helps us better understand what patients value in their lives and what they want from treatment.
- Patients have **different experiences**, perspectives and wants.
- It cannot be assumed all patients want the same thing.

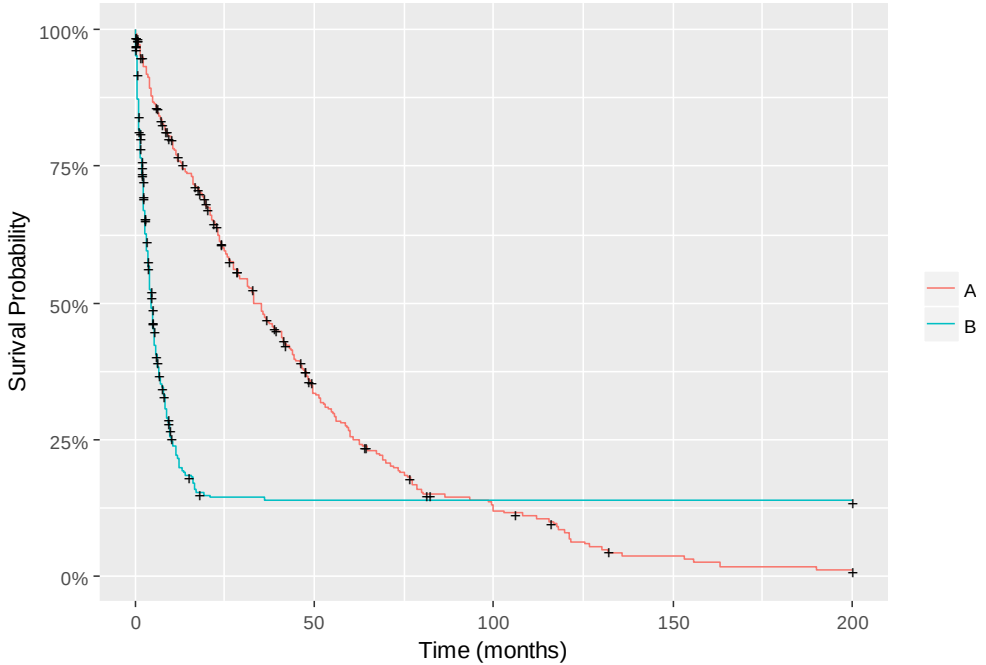
Adapted from Zack Pemberton-Whiteley

Preferences vary a lot depending on who expresses them

In the following example:

- Drug A:
  - 50% of patients will be alive in 3 years
  - all patients will be dead in 8 years
- Drug B:
  - 85% of patients will be dead in 2 years
  - 15% patients with long-term survival

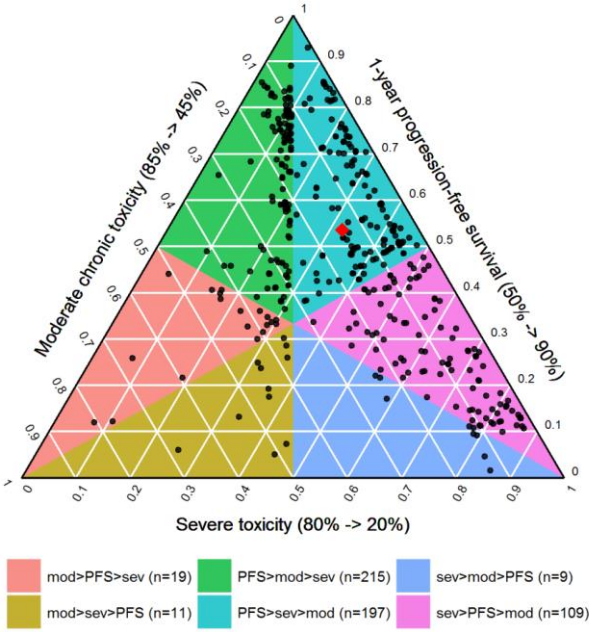
- From a regulatory perspective, drug A might be better because more patients respond longer
- However, some patients may prefer treatment B because of the rare chance of surviving



Adapted from Francesco Pignatti

Preferences even vary within one single disease

- For example, Myeloma UK used multi-criteria decision-making analysis to elicit the preferences of **560 patients** with myeloma regarding the possible benefits and risks of treatments.
- There is considerable heterogeneity: clear subgroups within single diseases with very different preferences and risk attitudes.
- Participants who gave a higher weight to severe or life-threatening toxicity were more **frequently younger,** working, and looking after **dependent family members** and had **more frequently experienced severe or life-threatening side effects.**

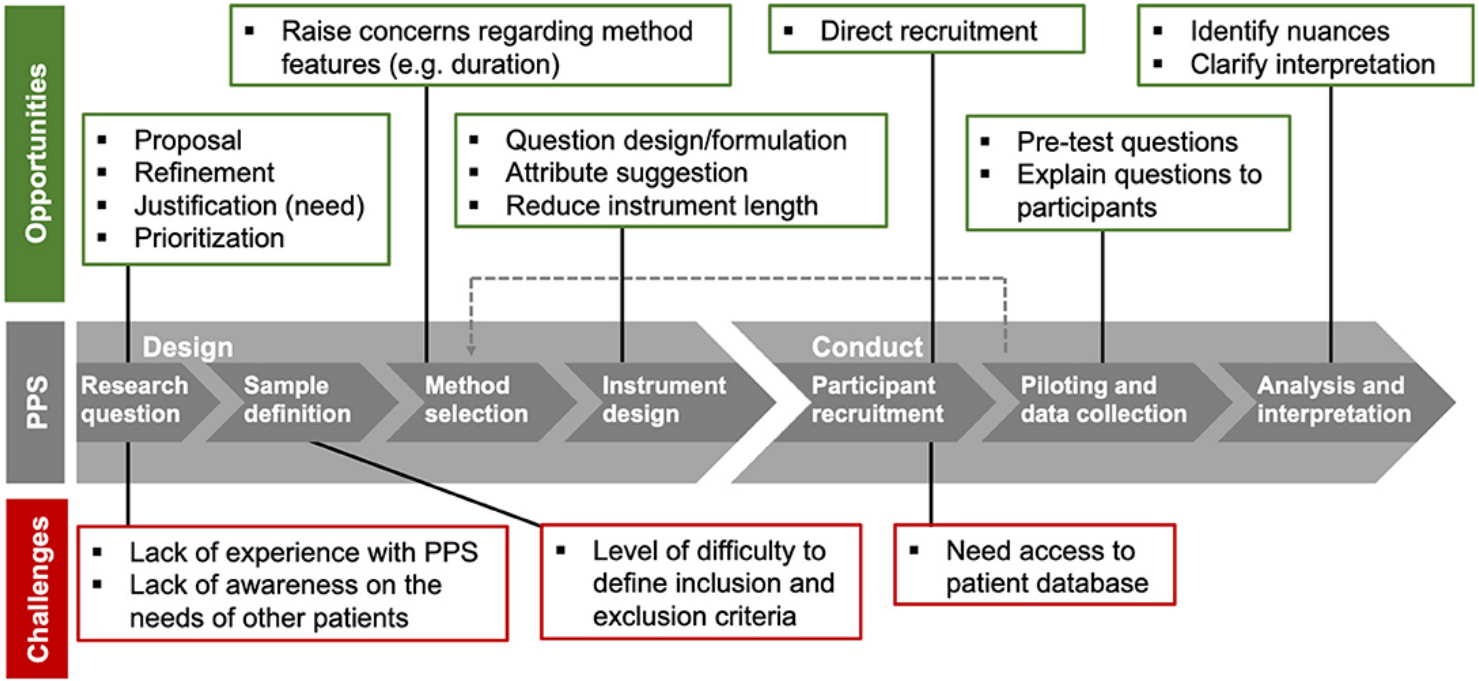


Survey with 560 myeloma patients from the Myeloma UK, replicating the pilot of MPE, MPNE and EMA.
D. Postmus *et al*. (2017) *The Oncologist*

Adapted from Kate Morgan

Patient organisations' contribution to running PPS is essential to accurately capture and interpret the data

Overview of **opportunities** and **challenges** for patient involvement in patient preference studies (PPS).



van Overbeeke E, Vanbinst I, Jimenez-Moreno AC, Huys I. Patient Centricity in Patient Preference Studies: The Patient Perspective. Front Med (Lausanne). 2020 Mar 20;7:93.

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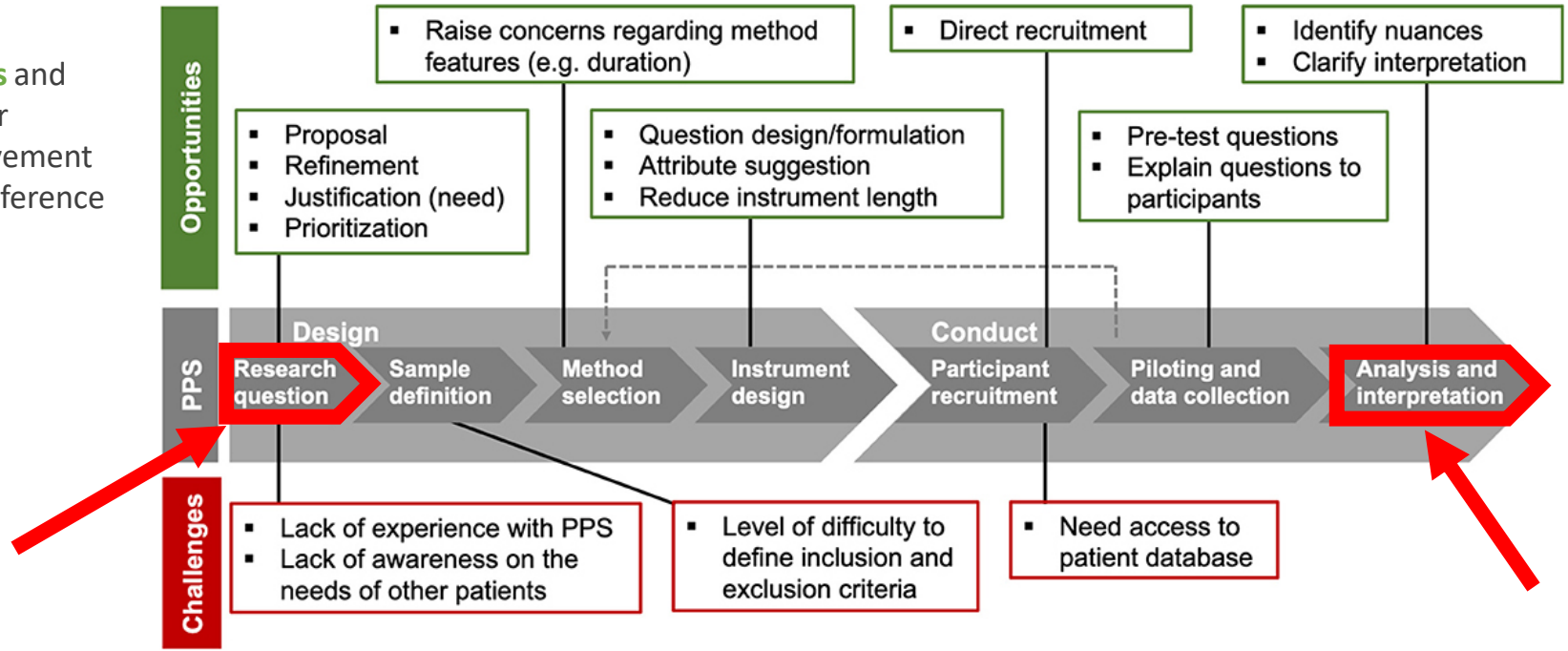

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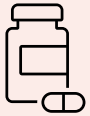
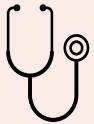
Patient preference data can impact a wide range of decisions

Patvocates

Stage	Idea for use
 **Clinical development**	• Appropriate selection of endpoints in clinical trials (e.g. PFS vs OS vs QoL). • Is a treatment acceptable to patients? (e.g. CAR-T).
 **Regulation**	• Benefit risk assessments by EMA. • Frames and provides context for decision-making (in a more robust way). • Answer specific questions from committees (such as value patients place on administration, survival gains or QoL). • Is the treatment acceptable to patients?
 **Reimbursement**	
 **Clinical practice**	• Doctors ensure they discuss relevant questions with patients in their decision-making. • Inform and interpret clinical guidelines (e.g. EHA – ESMO myeloma guidelines).

Listening to patients at each stage of drug development is extremely important!

Adapted from Kate Morgan

Conclusions

- Not all patients have the same preferences
- Patient preferences can impact a wide range of decisions:
  Informing regulators and payers, but also researchers and clinical decision-making
- Patient involvement in PPS is essential:
  Highest impact in design and analysis stage of PPS
- Patient preferences are not product specific, therefore PPS shouldn't be either
- PPS should aim to understand the heterogeneity of patient needs – NOT their preferences regarding product characteristics

This is why patient organisations should be involved in the development and analysis of PPS from the very beginning!

Patvocates

Thank you!

ananda@patvocates.net

Panel Discussion

Thank you for your attention and participation!

For questions, please feel free to reach out to our Speakers and Moderator liese.barbier@kuleuven.be