EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Patient preferences in regulatory decisions: Opportunities and challenges

RSNN Workshop 2022

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The views presented are personal and not those of EMA and its scientific committees.

Basic principles of regulatory decisions

- Companies submit the results of studies to fulfil legal requirements.
- Regulators assess if the legal requirements are fulfilled, and communicate characteristics to inform clinical decisions.
- Legal requirements: Quality, safety, efficacy, and *benefit-risk balance*:
  - Gains > Losses; Drug ≻ Placebo
    - Requires value judgments
  - No other considerations (e.g., economic)

Why patient preferences studies in regulatory decisions?

1. Whose perspective: Patients, regulator, others
2. Preferences: Explicit trade-offs v implicit value judgments
3. Studies: large surveys, small focus groups, assumptions
4. Challenges and opportunities

From Quality, Safety, Efficacy to Benefit Risk Balance

65/65/EEC

Harmful or,

Therapeutic efficacy is lacking

75/318/EEC

Harmfulness and therapeutic efficacy can only be examined in relation to each other;

Therapeutic **advantages must outweigh potential risks**

2004/27/EC

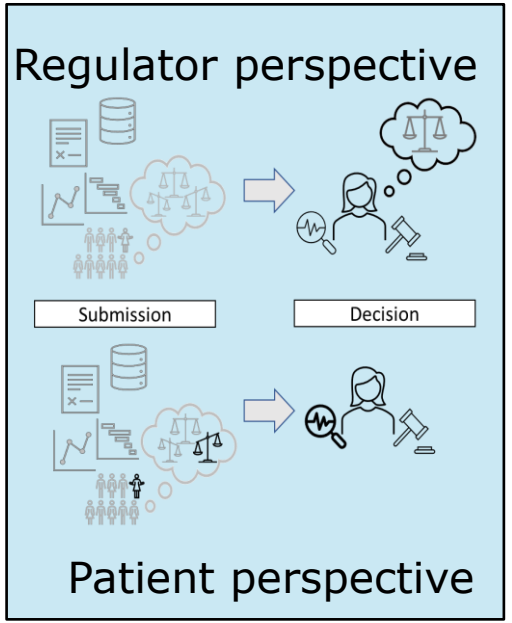
The **risk-benefit balance** is not considered to be favourable

Therapeutic efficacy is insufficiently substantiated

Patient preferences are informative (regardless of perspective for decision)

There is nothing in the measure of a clinical outcome that measures its importance ("value").

- Regulator perspective for decision
  - Patient preferences may inform the regulator's preferences
  - Regulators may lack experience except for the most obvious situations
- Patient perspective for decision
  - Patient preferences as key evidence to drive regulatory decision



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

Plausibility of patient perspective

- Lots of different decision models locally (e.g., shared decision; paternalistic; etc.)
- Regulatory question:
  - Are there patients in the right decision context who think the balance of benefits and arms is positive?
- Safeguards
  - Clinical decisions in the right local context (informed patients with doctor if needed; risk management measures)

S. Harris *The New Yorker*

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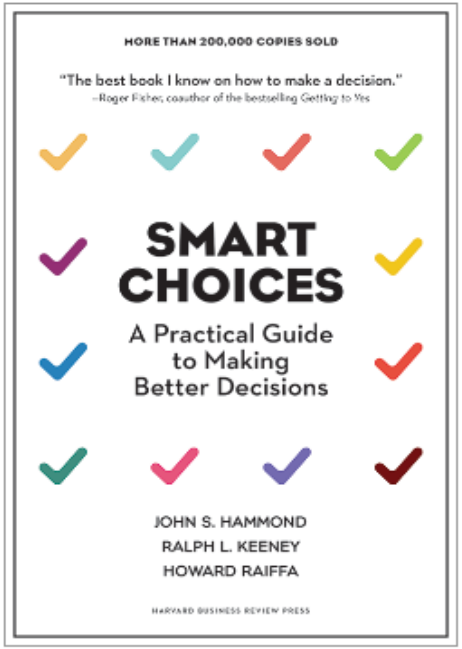
Communicating value judgments (transparency and accountability for reasonableness)

The Committee for Medicinal Products for Human Use (CHMP) Members have, during the review process, agreed that **the application contains sufficient clinical data to support clinical safety and efficacy** allowing a positive recommendation for granting marketing authorisation.

Marketing Authorisation for Taxotere (docetaxel, 1995)

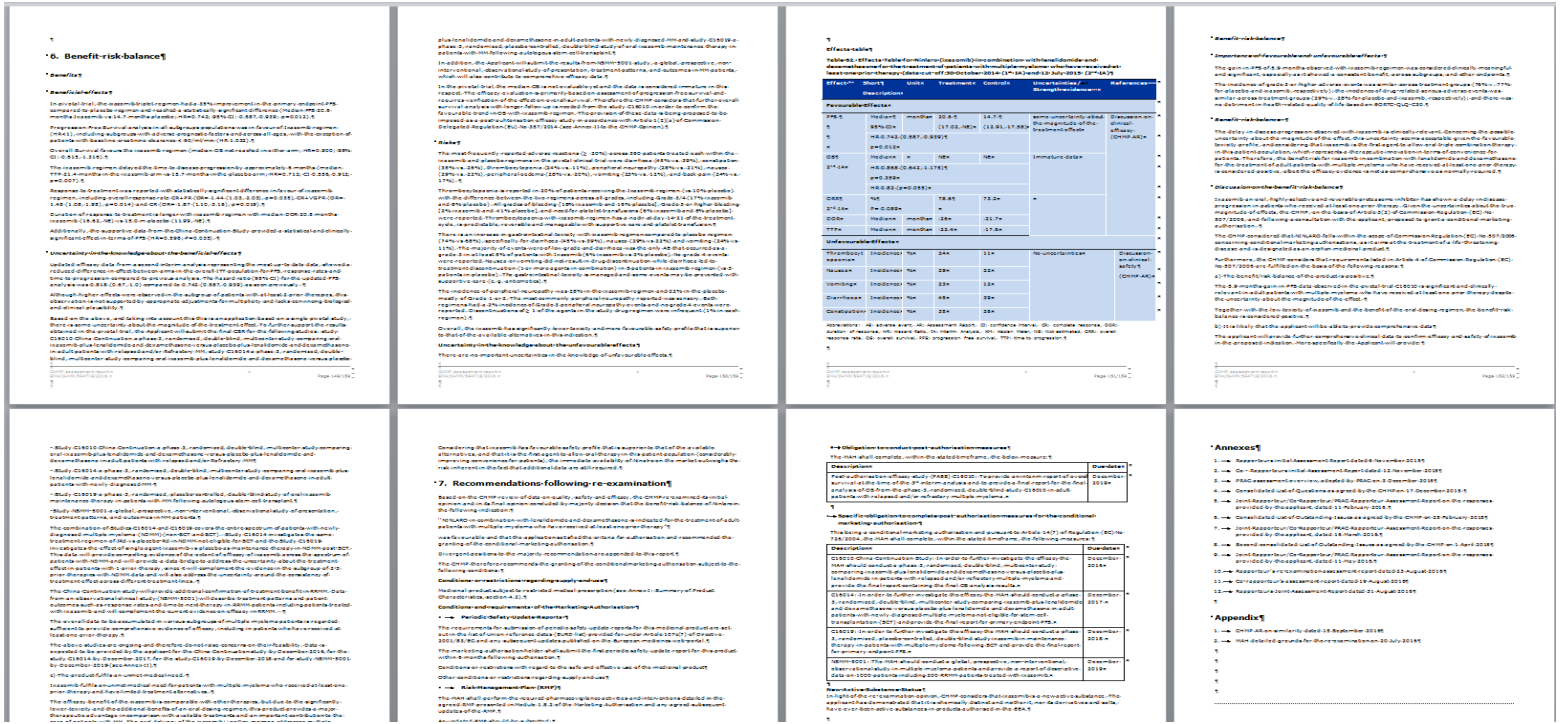
EMA Benefit-Risk framework

- **Pr**oblem: Is Benefit-Risk balance positive?
- **O**bjective: Goal of therapy? Attributes
- **A**lternatives
  - Approve; reject; (reframe, e.g., restrict indication)
- **C**onsequences of alternatives
  - Estimated based on data
- **T**rade-offs
  - Based on value judgments
- **U**ncertainties (and how to cope with them)
- **R**isk-attitude and **L**inked decisions



J Hammond *et al*. (1999) Smart Choices: A Practical Guide to Making Better Decisions

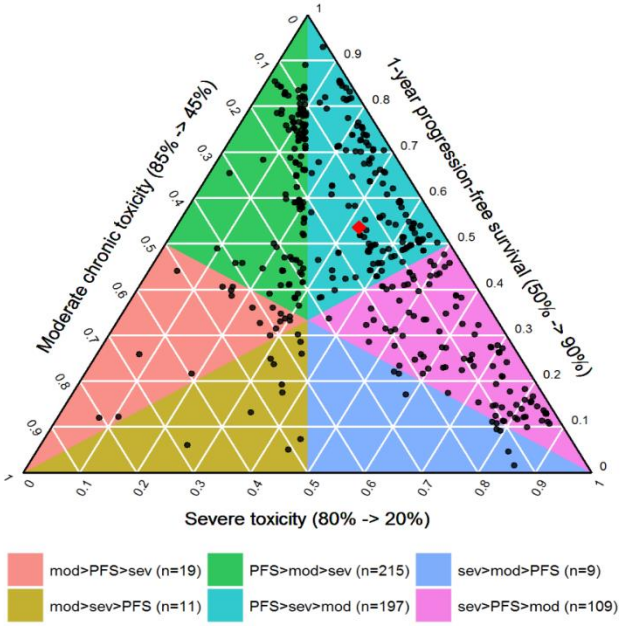
Example: Benefit-risk assessment ixazomib (2016)



Example: Trade-offs communicated explicitly

Example: Myeloma UK survey

- Severe toxicity ranked higher among younger, working, and looking after dependent family members and who had more frequently experienced severe toxicity
- Ixazomib example (approximation): The proportion of patients ranking the ixazomib-containing regimen above the placebo-containing regimen was 76%



D. Postmus *et al*. (2017)

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Do we really need more data?

The average cost of bringing drugs to market is 1-2 billion USD

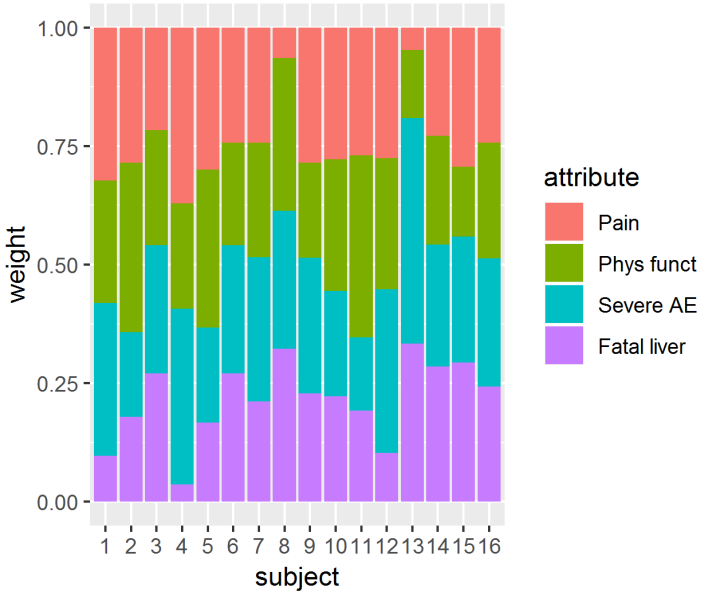
Need proportionate study designs and data quality standards

- Look at array of suitable methods
  - Stated preference studies; focus groups; structured frameworks

Tangled up in red: clinical trials in Europe are complicated by bureaucracy, scientists claim. *Nature* (2009)

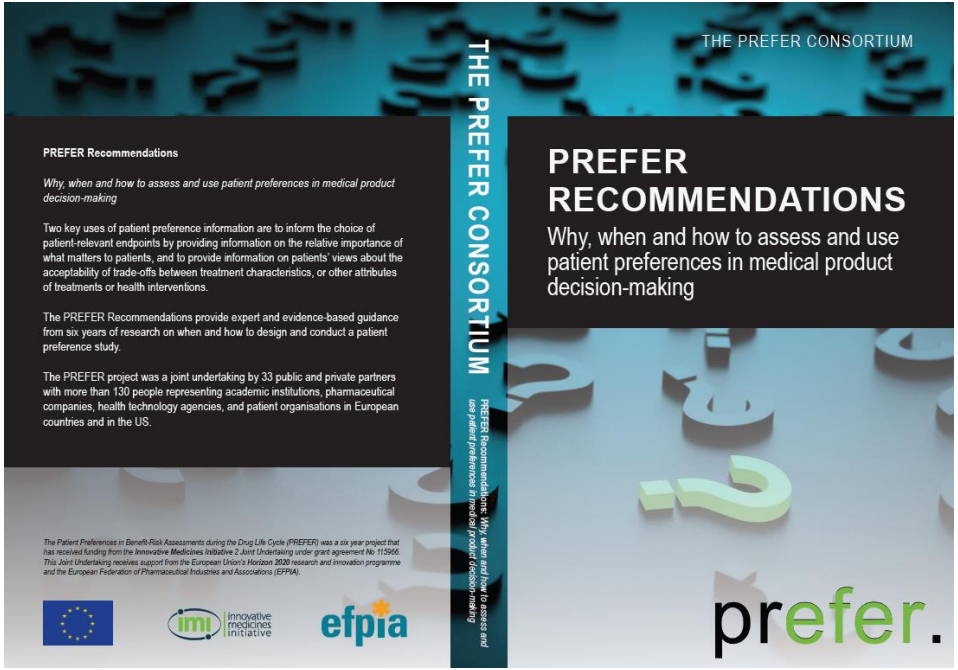
Example: Hypothetical preference elicitation at advisory meeting

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



PREFER Guidance

- PREFER framework
- Points to consider for method selection including five methods
- EMA Qualification
- Basis for upcoming ICH guidelines



Points to consider on **fit-for-purpose methods**

PREFER

- Describes a number of **established methods** and points to consider for methods selection in the context of health decision-making
- Identified **further research priorities**

Future work

- Disseminate and implement PREFER learnings
- Continue optimising methods and agree on balanced requirements and quality standards (harmonisation)

RANK	levels	Completed All BWS Qs (n=58)
1	Method selection guidance	
3	Changes in preferences over time	
3	Comparing methods	
3	Internal Validity / Data Quality	
5	Expressing uncertainty in patient preference studies	
6	Transferability across populations or related diseases	
7	Synthesis of Preferences Across Studies	
8	Mapping patient-reported outcomes to preference study attributes	
9	Individual preferences (shared decision making)	
10	Revealed preferences - external validity	

Some heterogeneity of ranking by stakeholder group.

prefer.

Source: Areas of Future Research in Patient Preferences, R. DiSantostefano (PREFER final meeting 2022)

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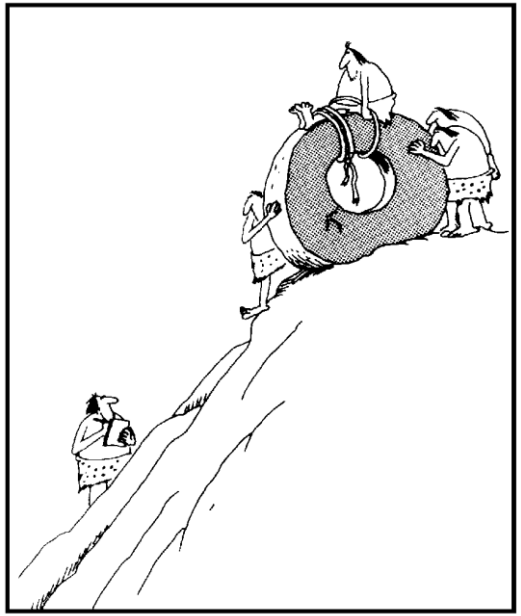
Challenges

- Lack of familiarity with type of evidence and studies; lack of guidance
- Industry: Anxiety about new methods
  - Why fix it if it's not broken (required)?
- The doctor/regulator:
  - We know best; the "squid technique" (hide behind a cloud of ink)



Early experiments in transportation

Opportunities

- Modernise decision-making and communications; develop harmonised guidance
- Augment development and decisions using evidence about behaviours
- Support robust and transparent claims/decisions

Thank you for listening

Further information

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