Patient Preference Studies in HTA for Ultra Rare Diseases: A Cross-country Analysis of EU-4, UK and Canada

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BACKGROUND

- Patient preference studies (PPS) are being recognized as valuable tool by Health Technology Assessment (HTA) bodies to evaluate patient-valued attributes and associated trade-offs particularly among rare diseases where clinical evidence is limited
- PPS use informs utility derivation when direct measures are infeasible, highlight patient priorities, and demonstrating the value of patient-centered evidence in rare disease technology assessments
- However, integration of PPS in technology appraisals particularly in ultra rare conditions remains unclear across the globe.

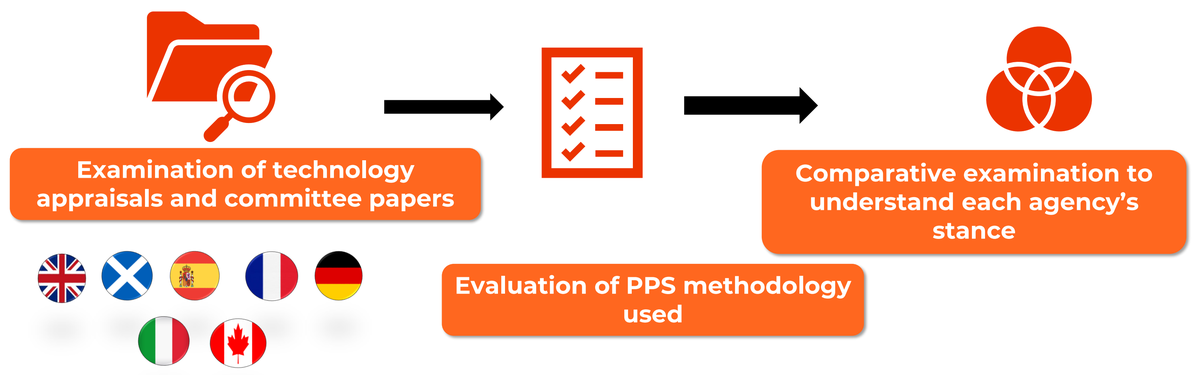
OBJECTIVE

- To explore the adoption of PPS in HTAs in ultra rare diseases across EU-4, UK and Canada.
- Summarize dominant methodologies and highlight how PPS influences recommendations

METHODS

- Technology appraisals for ultra rare diseases published in the last 5 years (2020 to present) in NICE (UK) were reviewed, followed by evaluations of the submissions for the same indications in SMC (Scotland), HAS (France), IQWiG/G-BA (Germany), AIFA (Italy), AEMPS (Spain) and CDA (Canada)
- Additionally, committee papers were reviewed to understand each agency's stance on the use of PPS in the evaluation of technologies for rare diseases (Figure 1)

Figure 1: Methodological approach for determining PPS integration across countries



RESULTS

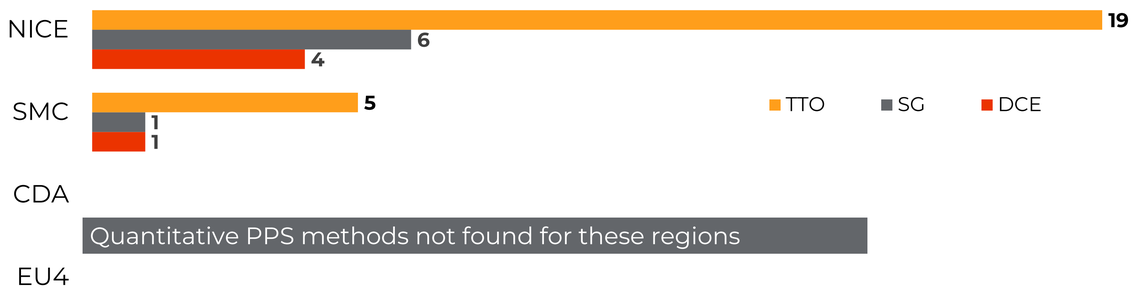
- NICE and SMC demonstrated explicit use of quantitative patient preference methods such as discrete choice experiment (DCE), time-trade-off (TTO) and standard gamble (SG) in technology appraisals for ultra rare conditions (Table 1).
- Among these, TTO and SG were commonly studied patient preference methodologies in NICE and SMC for utility derivation and informing quality of life (QoL) assessments when direct QoL data were not feasible to collect (Figure 2).
- For instance, in technology appraisal for generalized and partial lipodystrophy in NICE, DCE was used to estimate utility values associated with different health states, providing supplementary quantitative evidence on patient preferences for health outcomes (Table 1).
- Technology appraisals in SMC also demonstrated robust qualitative engagement process, through the Patient and Clinician Engagement (PACE) program, that allows for capturing structured qualitative patient preferences, influencing recommendations for rare conditions including spinal muscular atrophy and PNH.
- Additionally, the Canadian agency (CDA) was also observed to integrate qualitative patient group input in every reimbursement review, with emphasis on treatment administration preferences and burden, as seen in cases like hATTR amyloidosis and PNH, contributing to positive conditional reimbursement decisions.
- No explicit evidence of PPS use was identified in technology appraisals conducted in Germany, France, Italy, or Spain, however review of committee papers[8,9] suggested varying degrees of patient engagement opportunities in these regions.
- Countries such as the UK, Scotland, and Canada, demonstrated higher integration scores (3–5), supported by established frameworks (e.g., SMC's PACE program, CADTH's Patient Input process) (Table 2).
- EU4 agencies exhibited limited or ad-hoc inclusion practices, although growing interest in incorporating patient preferences was observed within their scientific advice processes.[8,9]

Table 1: Different PPS methods used and their influence on HTA decisions across countries

Agency	PPS terminology	Disease example	Influence on Decision
NICE (UK)[1]	DCE, TTO, SG (quantitative)	Lipodystrophy, AADC deficiency, PNH	Informed utility derivation and unmet need discussions
SMC (Scotland)[2]	DCE, SG, TTO PACE (qualitative)	SMA, PNH	Influenced acceptance through patient/clinician perspectives
CDA (Canada)[3]	Patient group input (qualitative)	hATTR amyloidosis, PNH	Considered in reimbursement recommendations with conditions
EU-4[4-7]	No PPS use identified	–	No formal PPS evidence

AADC: Aromatic L-amino acid decarboxylase; DCE: Discrete choice experiment; hATTR: Hereditary transthyretin; HTA: Health technology assessment; PACE: Patient and clinician engagement; PNH: Paroxysmal nocturnal hemoglobinuria; PPS: Patient-preference studies; SMA: Spinal muscular atrophy; SG: Standard gamble; TTO: Time trade off

Figure 2: Quantitative PPS methods utilized for ultra rare diseases across HTA agencies[1]



DCE: Discrete choice experiment; SG: Standard Gamble; TTO: Time trade off

Table 2: Level of integration of PPS in HTA decision making across various countries[8,9]

HTA agency (Country)	Formal decision	Methodological rigor	Integration in HTA	Impact on decision
NICE (UK)	5	5	5	5
SMC (Scotland)	4	4	4	4
CDA (Canada)	3	3	3	3
HAS (France)	3	3	3	2
IQWiG/G-BA (Germany)	3	1	2	2
AIFA (Italy)	1	2	2	2
AEMPS (Spain)	1	2	2	2

Low 1 2 3 4 5 High — Level of integration

HTA: Health technology assessment; PPS: Patient-preference studies

Conclusion

- Quantitative PPS methods such as TTO, SG, and DCE were reported in NICE and SMC appraisals for orphan and ultra-rare indications, while CDA primarily incorporated qualitative patient input through structured submissions.
- Across these appraisals, PPS evidence mainly informed utility estimation and contextual committee judgments, rather than serving as standalone decision-making evidence.
- No explicit use of quantitative PPS was identified in Germany, France, Italy, or Spain, where patient engagement opportunities remain limited within current HTA processes.
- These findings underscore a methodological gap and a future opportunity for HTA frameworks to formally integrate PPS beyond utility derivation, fostering more patient-centered and transparent value assessments.

References

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