Assessing treatment efficiency indicated in rare diseases: learnings from the CEESP (HAS) economic opinions

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CONTEXT

Rare diseases pose major challenges for health economic evaluations, driven by scarce data, limited treatment options, and significant uncertainty surrounding long-term patient management. In France, there are no specific guidelines on how to account for the "rare" character of these diseases in the CEESP evaluations. Current methodological recommendations available might not be adapted when considering these disease areas, which can lead to unadapted methodologies and results criteria, therefore such analyses are a necessity, to account for current economic issues.

OBJECTIVES

To review CEESP economic opinions and determine whether rare disease evaluations present specific methodological characteristics, and how these influence results and reservations.

METHODS

A database composed of **all economic opinions (N = 108) published by the CEESP between 2020 and 2025** was developed, based on the year of updates of the methodological guide.

Data was analysed regarding **methodological choices, inputs, results (ICER, costs and health outcomes) and reservations. This poster focuses on methodological differences on quality-of-life data, comparators and ITCs, and their impact on the ICER.**

RESULTS

During the review, 108 evaluations were screened, and 95 economic opinions were included in the analysis.

<u>First observation : comparators and ITC</u>

In the context of rare diseases, one of the major difficulties encountered when preparing a CEESP dossier **is scarcity of available data**. This lack of data is particularly evident **in the comparisons made in the efficiency model**. While the proportion of clinical trials versus a SOC arm does not differ between rare and non-rare diseases a smaller proportion of indirect treatment comparisons were made in rare diseases (Fig.1 and Table 1.)

Table 1. ITC in rare diseases and non-rare disease evaluations.

	Rare diseases (N - %)	Non-rare diseases (N - %)
Clinical trials with SOC comparator (%)	37 %	37 %
ITC conducted	8 (21 %)	18 (32 %)
No ITC conducted	30 (79 %)	39(68 %)
Total	38 (100 %)	57 (100 %)

These differences can be explained by several elements :

- Lack of available treatments for rare diseases;
- Feasibility assessment conditions unmet : heterogeneity between studies (design, population, etc.) or absence of common comparator treatment arm.

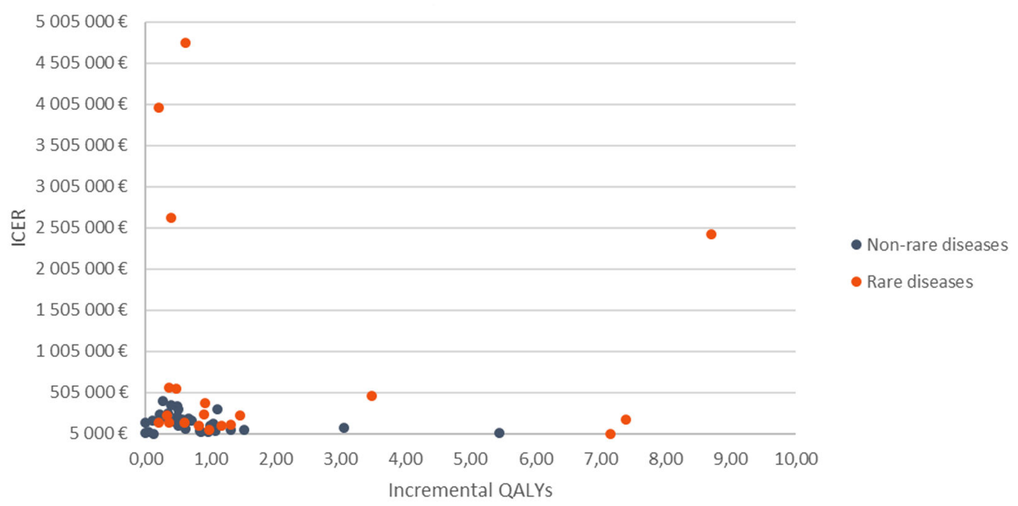
<u>Second observation : CEESP results</u>

This lack of data **has a direct impact on the model results and reservations from the CEESP.**

Regarding the results, no conclusion can be made on the level of ICER. However, this analysis highlighted that incremental costs tend to be higher when evaluating rare diseases, which can be directly associated with data gaps in comparators.

In terms of QALYs, incremental results seem similar between the two categories. Some CEESP opinions reported considerably high results in terms of ICER, which seem to be associated with low incremental QALYS. One evaluation reported a high ICER and high incremental QALYs (evaluation of Oxlumo, 2021), which was also associated with high incremental costs.

Figure 1. ICER levels based on incremental QALYs.



→ In rare diseases, 16 % of the CEESP opinions reported an ICER higher than 500 000€/QALY, which was never the case in non-are diseases. On the contrary, non-rare diseases CEESP opinions reported more ICER lower than 50 000€/QALY (19 % versus 5 % in rare diseases).

→ It seems important to underline that these skyrocketing values of incremental QALYS (resp. ICER) in rare diseases, can be associated with different factors, including disease area, availability of comparators, or even study population.

DISCUSSION

Given the wide range of pathologies and treatment types analyzed, establishing a reference ICER threshold or clear methodological guidance for rare diseases in French HTA evaluations remains challenging. Focusing the analysis on specific therapeutic areas, such as oncology, could provide more consistent insights. Overall, the results suggest no major differences between MR and MNR evaluations. However, it remains uncertain whether the assumptions used truly reflect the characteristics of each pathology or are primarily shaped by compliance with methodological guidelines.

CONCLUSION

Economic evaluations can encounter difficulties when dealing with rare diseases, due to data gaps in terms of comparators and lack of quality of ITCs, quality of life data or to higher incremental costs, although no significant difference in terms of methodology can be highlighted. Understanding the specific characteristics of rare diseases in the context of CEESP assessments could contribute to better price negotiations. Innovative modelling methods as well as numerous sensitivity analyses might be useful tools to challenge uncertainty and increase result robustness.

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<u>REFERENCES</u>

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