

Introduction

- In France, since 2013, pharmaceutical and medical device companies have been required to submit an economic analysis to HAS for presumed innovative products according to submission criteria updated in 2022 (1)
- The CEESP evaluates the efficiency dossier and publishes EOs (2)
- This study aimed to synthesise outcomes of these evaluations in oncology, including solid-tumour oncology and onco-haematology (therapeutic areas that are widely represented in published EOs), and tracking these outcomes over time

Results

- Overall, during the entire period analysed, 106 EOs in oncology (solid-tumour and onco-haematology) were collected, representing 53% of all the EOs published by HAS (n=199) before the end of December 2022. This list of EOs consisted of 86 (81%) solid-tumour oncology and 20 (19%) onco-haematology treatments
- Almost half of the submissions (n=52) sought an extension of indication, 41% (n=43) applied for a first registration, 8% (n=9) requested a reassessment, 2% (n=1) sought an indication change, and 2% (n=1) requested an indication extension and reassessment
- Of these oncology EOs, 55% were granted early access (n=58)
- Moreover, 55% (n=58) were assessing a monotherapy drug, 40% (n=42) assessed a combination drug, 5% (n=4) targeted multiple indications with either a monotherapy or a combination drug, and 1 EO assessed a radiotherapy drug

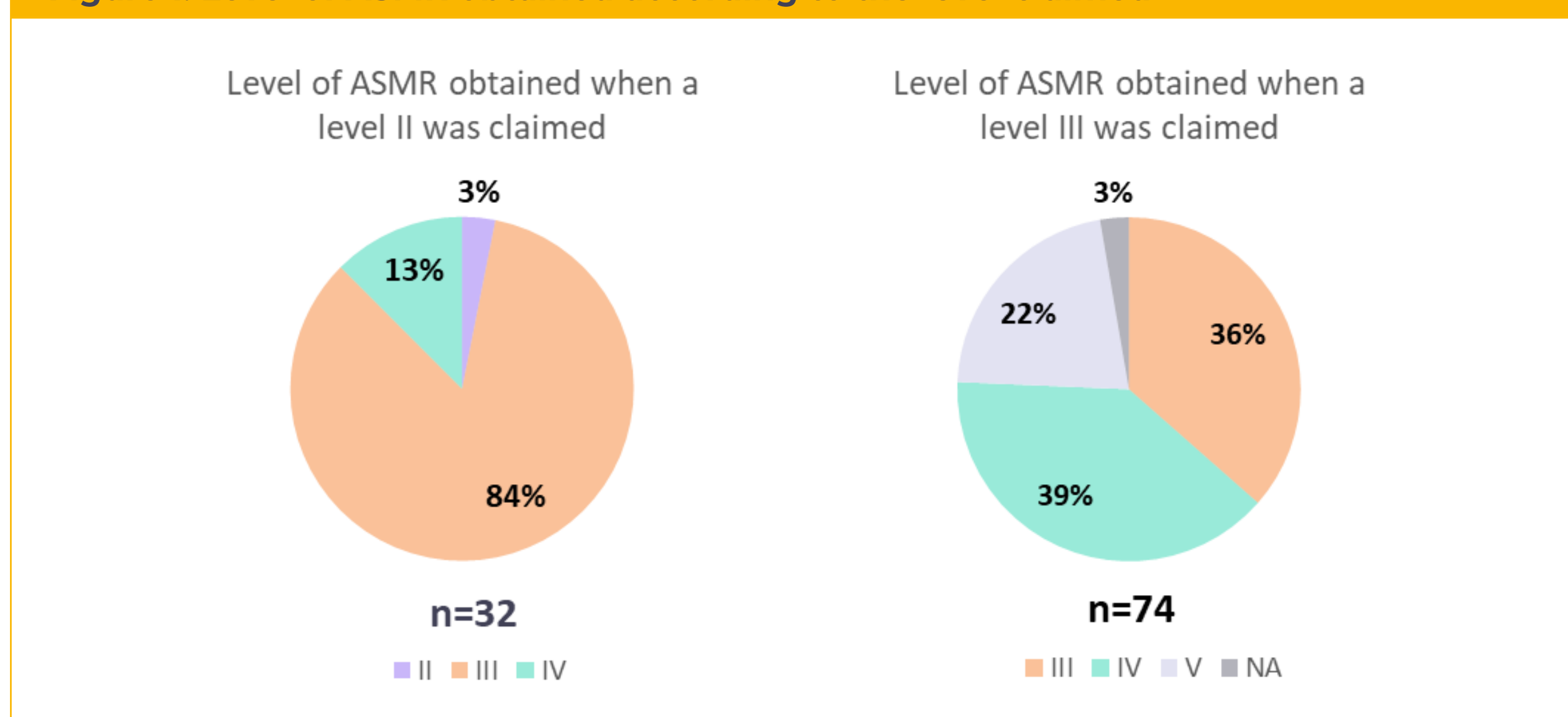
Clinical benefit (SMR)

- Between 2014 and 2022, 95% (n=101) of the EOs identified focused on drugs with an *important* SMR rating, of which 11% (n=11) had also been judged *insufficient* for part of their indication. Drugs granted a *moderate* or an *insufficient* SMR each accounted for only 2% of oncology EOs (n=2 for both categories), and 1% (n=1) of EOs related to drugs with a *poor* SMR

Clinical added value (ASMR)

- A comparison of the ASMRs claimed and obtained was carried out for each of the 106 oncology EOs
- 74% (n=78) of the ASMRs obtained were different from the ASMRs claimed; only 26% (n=28) were equivalent
- The dissimilarity between the ASMRs claimed and obtained was further investigated. The exploration revealed that:
 - An ASMR II was claimed in 30% of cases (n=32), among which:
 - 84% (n=27) obtained an ASMR III
 - 13% (n=4) obtained an ASMR IV
 - only 1 EO obtained the ASMR II for which the dossier was submitted
 - An ASMR III was claimed in 70% of requests (n=74):
 - 39% (n=29) were granted an ASMR IV
 - 36% (n=27) obtained the ASMR III for which the dossier was submitted
 - 22% (n=16) obtained an ASMR V
- Figure 1 presents the main levels of ASMRs claimed and obtained. In this figure, NA represents the EOs for which no ASMR was provided by the HAS because the treatment had an *insufficient* SMR

Figure 1. Level of ASMR obtained according to the level claimed



Incremental Cost-Effectiveness Ratio

- In the entire database, ICERs published for solid-tumour oncology and onco-haematology EOs varied from €7,392/QALY to €1,437,359/QALY. The mean ICER validated in oncology by the CEESP was €188,000/QALY (median €142,000/QALY)
- A comparison of mean ICERs in oncology in the whole database shows that the mean ICER of onco-haematology EOs (€312,076/QALY) was higher than the mean ICER in solid-tumour oncology (€172,664/QALY). The same comparison assessing median ICERs showed the same rough estimates (€337,362/QALY vs. €139,436/QALY, respectively)
- Figure 2 shows the distribution, in a boxplot representing 50% of the values (between quartiles 1 and 3), of validated ICERs in each cluster. It shows the evolution of the minimum, median, mean, and maximum ICERs between 2014-2018 and 2019-2022

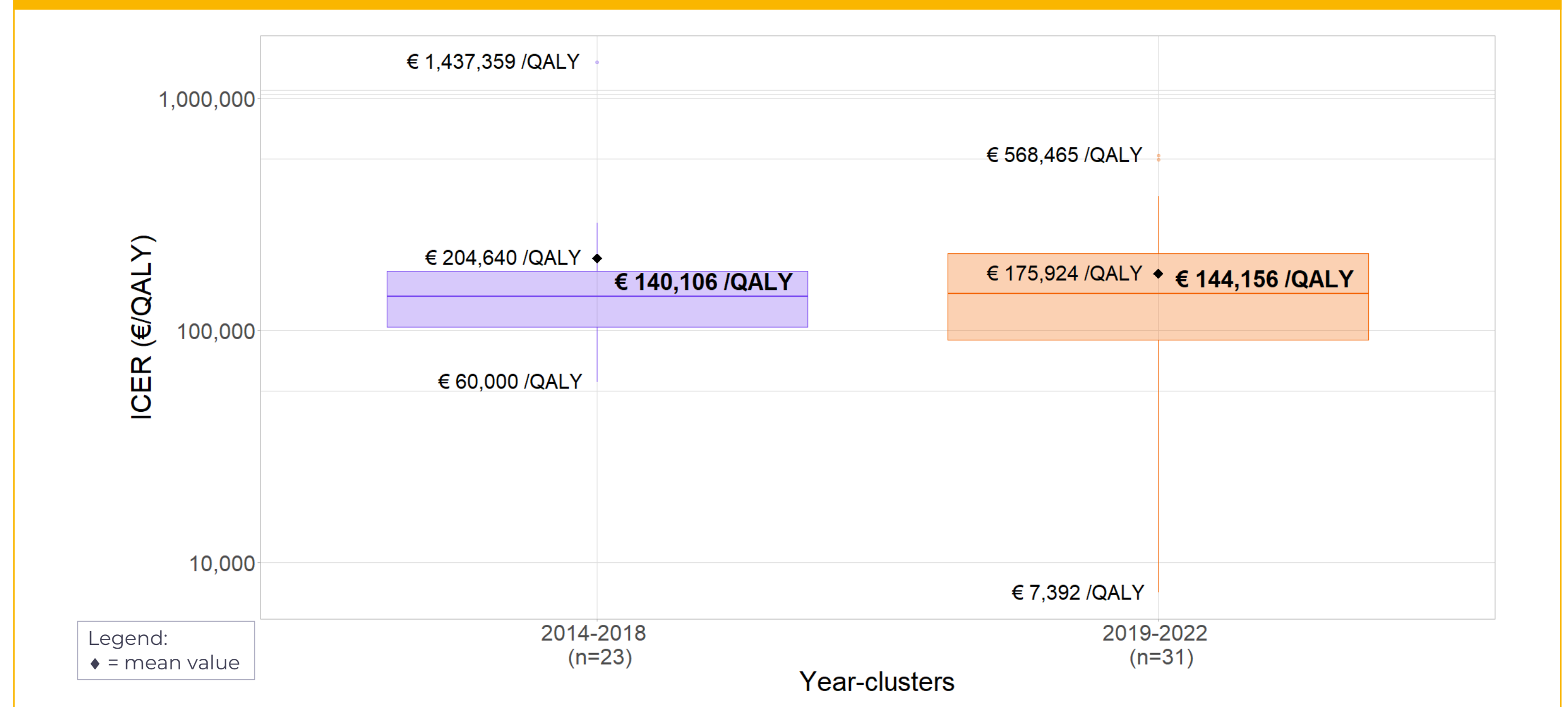
Conclusion

- The mean ICER validated by the CEESP during its almost 10-year history of medico-economic evaluations is **€188,000/QALY (median €142,000/QALY)**. Since 2018, mean validated ICERs decreased by ~15%, whereas the median ICER remained steady over time. Moreover, early access was granted for nearly half of the drugs evaluated. Among treatments for which ASMR III was claimed, nearly a third obtained it (36%); among treatments for which ASMR II was claimed, only 1 reached it (3%). The **major reservations** most frequently raised concerned **clinical data, comparison methods, and comparators**
- This analysis shows that, in France, mean published, validated ICERs tended to decrease in CEESP evaluations in oncology. This could be explained either by the therapeutic environment changes** (more and more evaluations concern cancer at early stage with long time-horizons), or **the appearance of drugs on efficiency frontiers** (leading to lower incremental cost differences)

Methods

- The HAS website was screened and all the EOs in oncology released by the CEESP before the end of December 2022 were extracted and aggregated within an internal Putnam database
- For each EO, information including type of submission, therapeutic area, SMR, ASMR, ICER, MRs, and CEESP conclusion was extracted
- Different year-clusters were used to analyse the evolution of EO outcomes
- ICERs validated by CEESP were analysed (excluding dominating and dominated cases in order to capture only numeric data). If multiple ICERs were presented in the CEESP EO conclusion, the lowest ICER was considered
- The MRs within each extracted EO were reviewed by 2 assessors and categorised as 1 of 19 dimensions. The classification was done blindly, and when a discrepancy arose, a third reviewer selected the most appropriate dimension

Figure 2. Evolution of ICERs between 2014-2018 and 2019-2022 for both solid-tumour oncology and onco-haematology EOs

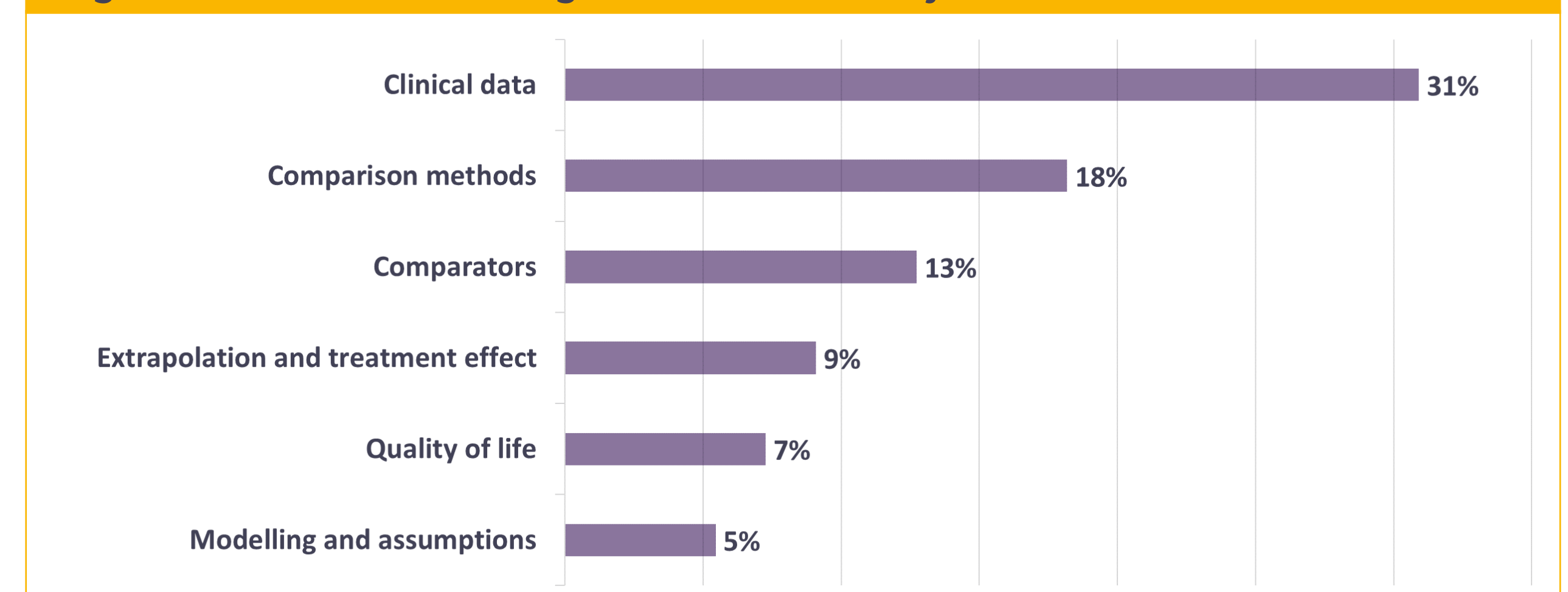


- On one hand, the mean ICER in oncology decreased from €204,640/QALY in 2014-2018 to €175,924/QALY in 2019-2022 (a 14% decrease)
- On the other hand, median ICER was steady: €140,106/QALY in 2014-2018 and €144,156/QALY in 2019-2022

Cost-effectiveness analysis MRs

- The CEESP issued 792 MRs, of which 446 (56%) were qualified as *minor*, 291 (37%) as *important*, and 55 (7%) as *major*
- Special interest was given to *major* MRs due to their impact on the CEESP conclusion
- Figure 3 shows the dimensions each accounting for >5% of *major* MRs: These 6 dimensions represent 83% of MR classifications. The 3 most important dimensions are clinical data (31%), comparison methods (18%), and comparators (13%)

Figure 3. Dimensions covering more than 5% of major MRs



- Other dimensions include modelling and assumptions, results presentation, population and subpopulation, and validation, which each account for between 2% and 4% of the *major* MRs
- We observed no *major* MR caused by economic analysis and result criteria choice, treatment duration, time horizon, perspective, costs, or tolerance during the whole period analysed
- Across all oncology EOs, 38% (n=38) reported at least one *major* MR. Half (n=10) of onco-haematology EOs contained a *major* MR, whereas only 35% (n=30) of solid-tumour EOs reported *major* MRs

CEESP conclusions on economic evaluation

- Overall, 45% (n=48) of oncology EOs were considered invalid, and 22% were deemed valid under conditions (n=18) or under a reduced scope (n=5)
- Between 2014 and 2018, the EO invalidation rate was 43% (n=19), and it remained steady (47%, n=29) between 2019 and 2022

References

- Décision n°2022.0212/DC/SED/SEM du 23 juin 2022 du collège de la Haute Autorité de santé relative à l'impact significatif sur les dépenses de l'assurance maladie déclenchant l'évaluation médico-économique des produits de santé revendiquant une ASMR ou une ASA de niveaux I, II ou III. Paris: HAS; 2022
- Haute Autorité de Santé. Avis économiques rendus par la Commission d'évaluation économique et de santé publique [CEESP] [Economic opinions issued by the CEESP]. Available at: https://www.has-sante.fr/jcms/p_3149875/fr/avis-economiques-rendus-par-la-commission-d-evaluation-economique-et-de-sante-publique-ceesp

Abbreviations: ASMR, amélioration du service médical rendu; CEESP, Commission D'Évaluation Économique et de Santé Publique; EO, economic opinion; HAS, Haute Autorité de Santé; ICER, incremental cost-effectiveness ratio; MR, methodological reservation; NA, not applicable; QALY, quality-adjusted life year; SMR, service médical rendu

Contact

Marine Sivignon
marine.sivignon@putassoc.com

Find out more at putassoc.com

