

Handling Uncertainty in Health-Economic Assessments: Experience From COVID-19 in France

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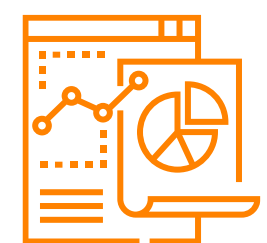
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OBJECTIVES

- > This study aims to **describe how health economic analyses were assessed in France** to appraise COVID-19 treatments **in a context of parametric and structural uncertainty**.
- > **Identify key areas of improvement for future health-economic evaluations** to be submitted at the French HTA body in the COVID-19 context.



RESULTS

- > **Four economic opinions** published by HAS on COVID-19 treatments were analyzed **concerning 3 treatments** (including prophylaxis) to prevent severe forms of COVID-19.

Table 1 – Economic opinions on COVID-19 treatments

Product	Indication	Date of CEESP opinion
EVUSHELD (tixagevimab/cilgavimab)	Treatment of adults and adolescents (aged 12 years and older weighing at least 40 kg) with COVID-19, who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19.	March 14 th 2023
EVUSHELD (tixagevimab/cilgavimab)	Pre-exposure prophylaxis of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg	August 30 th 2022
XEVUDY (sotrovimab)	Treatment of COVID-19 in adults and adolescents (from 12 years of age and weighing at least 40 kilograms) who do not require supplemental oxygen and who are at increased risk of the disease becoming severe.	July 19 th 2022
PAXLOVID (nirmatrelvir/ritonavir)	Treatment of COVID-19 in adults who do not require supplemental oxygen and who are at increased risk for progressing to severe COVID-19.	April 16 th 2022

- > **Economic modeling** relied on 1 Markov model (using DICE simulation), and three decision tree + Markov models, **all modeling ambulatory and hospital care for COVID-19, then long-COVID and death**.

- > **No one modeled inter-individual transmissions** nor reinfections.

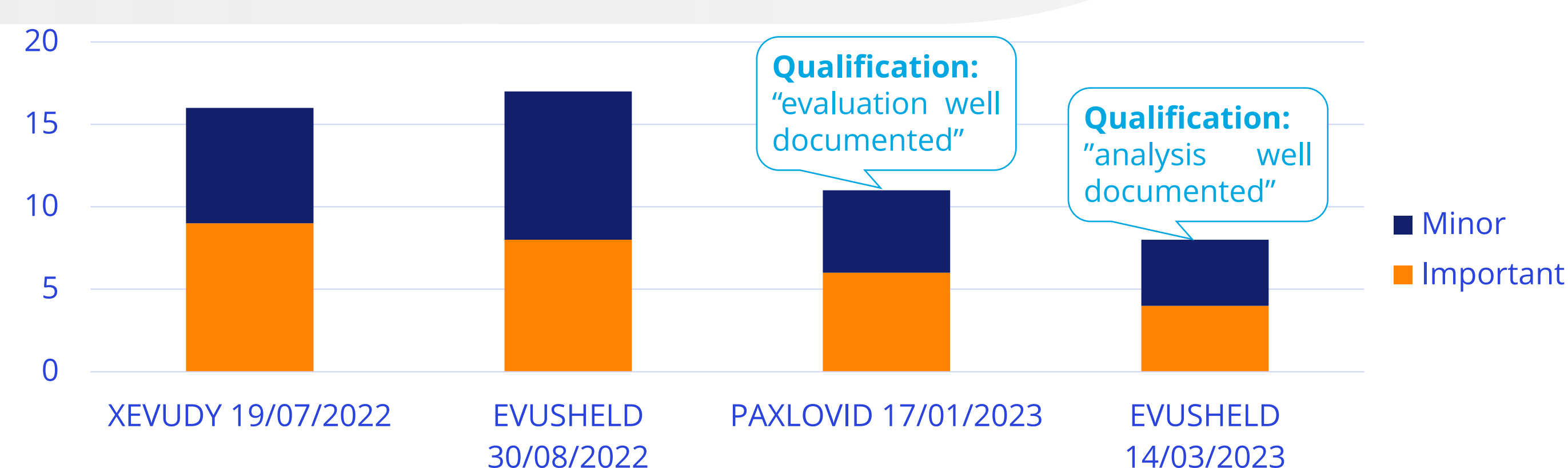


Figure 1 - Number of total methodological reservations by grade in each opinion

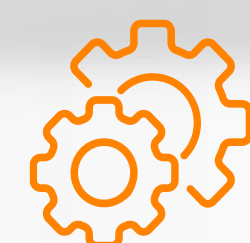
- > **Main reservations** from CEESP concerned:

- o **Simulated population**: 1 important reservation for **transposability of trial population** to current practice et epidemic situation for all opinions;
- o **Modeling**: 1 important reservation due to the **lack of modeling of reinfections** for 3 opinions;
- o **Transition probabilities and extrapolations**: a global **lack of details and discussion and heterogeneity of data sources** lead respectively to 2 important reservations (XEVUDY), 2 important and 1 minor reservation (EVUSHELD-2022), 1 important reservation (PAXLOVID) and 1 minor reservation (EVUSHELD-2023);
- o **Utility estimations**: **heterogeneity of data sources and limited sensitivity analyses + plausibility of some values and assumptions**, lead respectively to 2 important reservations (XEVUDY), 1 important and 1 minor reservation (EVUSHELD-2022), 1 important reservation (PAXLOVID) and 1 minor reservation (EVUSHELD-2023);



CONCLUSION

- > While modelling was used by Ministry of Health in the early COVID-19 pandemic to guide public health measure in France², **authorities now show stronger risk-aversion towards economic models' uncertainty**. HAS' clinical committee was able to conclude on COVID-19 treatments' efficacy, and other HTA agencies such as NICE³ concludes on efficiency whereas HAS' economic committee did not. However **real-world data on COVID-19 are available to tackle parametric and contextual uncertainty**.



METHODOLOGY

- > Descriptive Review of economic opinions from the HAS (French HTA body) medico-economic commission (CEESP), published from January 2020 to June 1st 2023 on COVID-19 treatments. A focus on uncertainty management is made, considering epidemiological context and ability of modelling to quantify and explore uncertainty to guide decision making.

- > **Other inconsistencies** could be noted in reservations across opinions:

- o Cycle length was criticized and conducted to important and minor reservation for XEVUDY and PAXLOVID;
- o Test of confidence interval was missing in sensitivity analyses and led to important reservation in XEVUDY vs minor in PAXLOVID;
- o Some reservations are duplicated for the same methodological item (test of infection rate in budget impact analysis for EVUSHELD-2022 leading to 2 reservations), unlike specified in CEESP's doctrine¹.

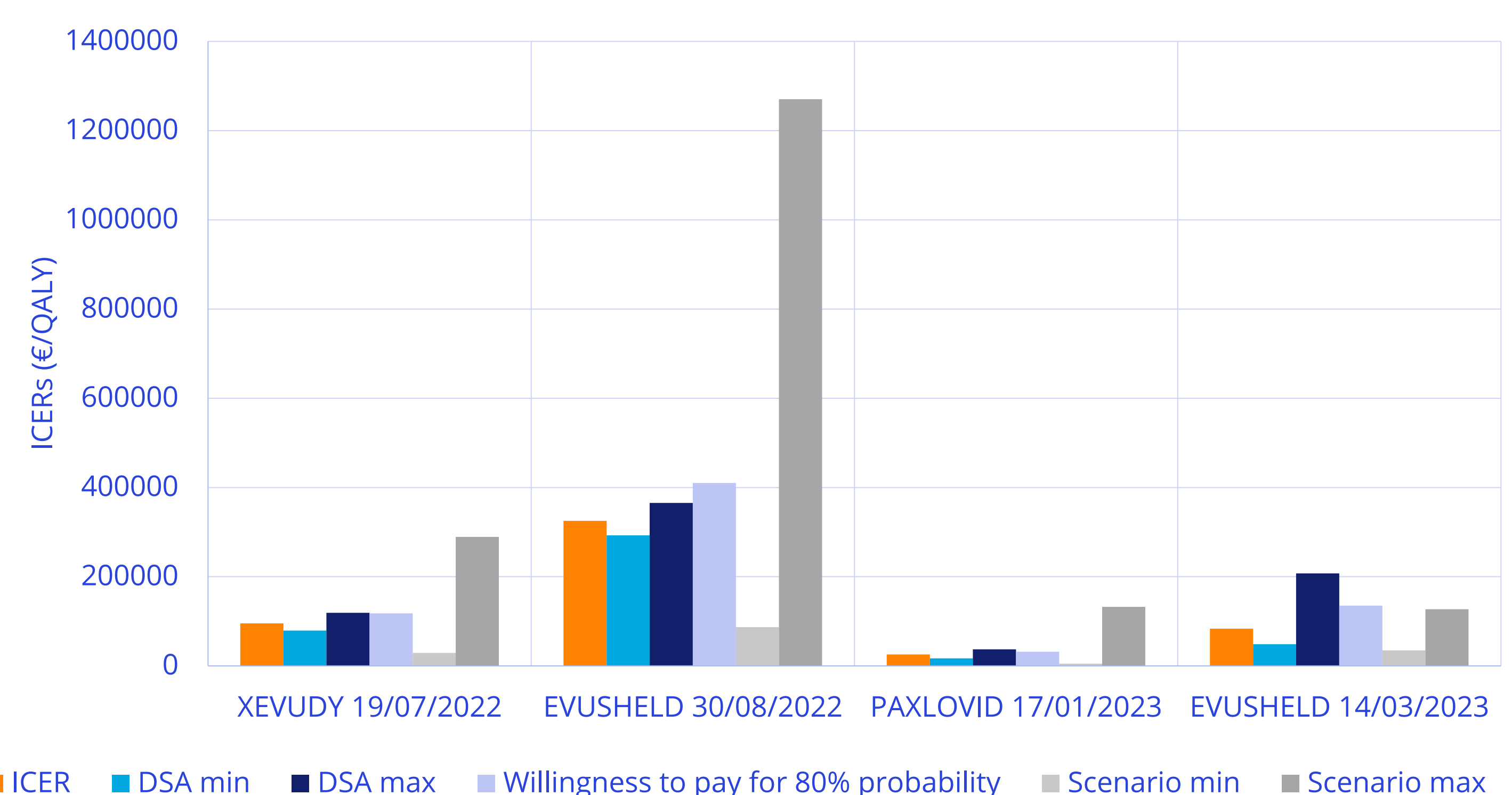


Figure 2 – Uncertainty exploration by COVID-19 treatments

- > Uncertainty was explored through sensitivity analyses in opinions and was quite variable depending on the products (figure 2), PAXLOVID showing the lowest and most contained ICERs [5 218 - 132 301]. Whereas EVUSHELD in prophylaxis (30/08/2022) showed high variability. (Figure 2)
- > However, **HAS' economic committee wasn't able to conclude on efficiency** of the products **due to global major uncertainty**. Global major uncertainty objected were based on the following:
 - o **Systemic uncertainty due to epidemiological context**: number and severity of epidemic waves, clinical data temporality and transposability, evolution of level of care through time and loss of efficacy of treatments.
 - o **Modelling and methodological uncertainty** due to assumptions made, considering lack of data and knowledge in the COVID-19 context.
- > However, **the committee did not invalidate the methodology for any of the manufacturers' analyses**, neither for cost-utility analyses (N=4) nor budget impact analyses (N=4), and **for 2 opinions, analyses were qualified as "well documented"**.



REFERENCES

- https://www.has-sante.fr/upload/docs/application/pdf/2021-09/doctrine_de_la_ceesp_version_anglaise_2021-09-29_11-14-2_803.pdf
- <https://modelisation-covid19.pasteur.fr/>
- <https://www.nice.org.uk/guidance/ta878>
- <https://www.santepubliquefrance.fr/dossiers/coronavirus-covid-19/coronavirus-chiffres-cles-et-evolution-de-la-covid-19-en-france-et-dans-le-monde>