Objectives: The rising disease burden and high price of new oncology medicines, combined with uncertainty in clinical and economic evidence, have brought substantial challenges to payers and health technology assessment (HTA) in making decisions on coverage. This review intended to comprehensively summarize the significant predictors and their relative importance in HTA decisions for cancer drugs. ***Methods:*** A systematic literature search was performed in MEDLINE and EMBASE databases from inception to July 2020. The studies were eligible for inclusion if they conducted quantitative analysis of HTA related decisions for cancer drugs. The factors with p-values below the confidence level of 0.05 were considered as the statistically significant predictors for HTA decisions and odd ratios were calculated for categorical factors. ***Results:*** A total of 9 studies including 1146 decisions from 6 committees in 6 different countries were eligible to be included for review. Among the included studies. the number of HTA decisions ranged from 17 to 393 (median=75) and most studies (n=6) had no specific restrictions on the types of cancers. From the univariable analysis, improvement on effectiveness and cost-effectiveness were found as the significant predictors for the committees in Australia, Belgium, Korea and Canada. From the multivariable analysis, cost-effectiveness was found as the strongest positive predictor for the recommendations for the committees in England, Korea and Canada. Few of factors related to characteristics of disease and technology were found significantly associated with decisions among the studied committees. ***Conclusions:*** Despite the different drug reimbursement systems and the socioeconomic situations, cost-effectiveness and/or improvement on clinical outcomes seem to be the most important predictors for recommendations of cancer drugs in the majority of committees. ***Keywords:*** Factors, health technology assessment, decision makers, cancer drugs

HTA45
CARE FOR RARE: MARKET ACCESS EVIDENTIARY REQUIREMENTS FOR RARE CANCERS

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Objectives: With tightening healthcare budgets, drugs for rare oncology indications are being increasingly scrutinized for their impact on overall healthcare cost putting greater focus on the evidence to substantiate clinical benefit. Launch of multiple, high-cost, combination regimens targeting early-stage disease increasingly impact payer budget and their willingness to pay. As such, the evidence benchmark for these therapies continue to rise. To characterize that trend, the objectives of this study were to:

- Identify evidence criteria driving payer decisions,
- Characterize differences in HTAs decisions across global markets,
- Outline differences in evidence requirements across lines of therapy and for combination therapies compared with monotherapies.

Methods: A review of HTAs and reimbursement decisions (n=110) published from 2016-2021 was conducted for Australia, Belgium, Canada, France, Germany, the UK and the US, spanning a variety of rare oncology diseases, including chronic lymphocytic leukemia (CLL), renal cell carcinoma (RCC), acute lymphoblastic leukemia (ALL), multiple myeloma (MM), among others. Reviews were characterized for clinical and economic evidence requirements, and impacts on recommendations. ***Results:*** Despite similar evidence packages, decisions varied across agencies, including: recommended, recommended with restrictions, or rejected. Increasing segmentation of the patient population and launch of innovative agents have significantly modified payer evidence requirements. Key criteria evaluated by HTA agencies included: 1) clinical effectiveness, 2) sufficiency/strength of evidence, 3) endpoint selection, 4) comparator, 5) safety, and 6) cost-effectiveness. While payers are currently employing clinical trial data, use of supplementary patient-centric and real-world data is growing to mitigate any uncertainty with trial data, with payer scrutiny and expectations of incremental improvement becoming stricter. ***Conclusions:*** This study demonstrates the variability in pivotal decision criteria and drivers across HTA agencies for high-priced oncology products. Optimal global market access for oncology drugs for rare diseases hinges on monitoring evolving evidentiary requirements and planning to collect evidence early in the developmental cycle.

HTA46
KEY ISSUES IN HEALTH ECONOMIC ANALYSIS IN NICE HIGHLY SPECIALISED TECHNOLOGY APPRAISALS

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Objectives: To determine key themes and issues identified by Evidence Review Groups (ERG) and the NICE committee during the NICE Highly Specialised Technology (HST) Appraisal process. Also, to explore the relationship between issues that limit the ability of the NICE committee to approve a product, as well as looking at ways that companies mitigate uncertainty in their appraisals. ***Methods:*** All products that followed the NICE HST process (to December 2021) were identified and analysed. In addition, an analysis of committee papers and subsequent publications was carried out, along with a targeted literature review of associated publications. ***Results:*** Of the 16 products that have followed the NICE HST process, the most common major criticism (87.5% of products) from the Evidence Review Group was that resource utilisation estimates were inaccurate, or that the methodology used was not sufficiently robust. Other criticisms included utility modelling not being robust enough (68.75%), utility estimation by clinicians (56.25%), clinician estimates of efficacy (43.75%), model approaches not being sufficient for decision making (31.25%), and trial endpoint robustness (25%). This led to 93.75% of cases that resulted in a positive recommendation having managed access agreements and confidential discounts applied to them. Major criticisms of submissions tend to centre around the lack of a robust methodology for derivation of estimates (resource utilisation and utility values) from clinicians. ***Conclusions:*** Given that products that qualify for a NICE HST process tend to be in a rare disease area, there is typically a paucity of data. This usually leads to manufacturers turning to clinicians to seek estimates – it is crucial here to have a recognised, robust methodological process to elicit and validate estimates. Further review of NICE publications suggests that Modified Delphi and vignette studies may be most appropriate if carried out in a robust and meaningful way; validation across multiple stakeholders adds extra validity.

HTA47
RECOMMENDATIONS ON BEST PRACTICES FOR RWD STUDY DESIGN TO SUPPORT HTA DECISION PROCESS IN EUROPE

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Objectives: Health technology assessment (HTA) increasingly leverages real-world data (RWD) to support the evaluation of new technologies. This study assesses how RWD is used for decision-making by different HTA bodies. ***Methods:*** Technologies submitted to EMA/FDA between 2017-2021 using RWD to support regulatory approval, were identified from grey literature. Ten technologies, covering different disease areas and types of RWD were selected. The EU4+UK HTA reports of the selected technologies were reviewed and the acceptance of RWD was evaluated. To gain further insights, semi-structured interviews with six country-specific HTA experts (with prior experience in submission and assessment of new technologies) were performed. ***Results:*** According to the six HTA experts, RWD is commonly used to characterize disease epidemiology, treatment patterns (e.g., to inform added value assessments) and unmet need. Less commonly (rare diseases and, oncology), RWD may be considered to support efficacy with external control arms (ECAs). For ECA acceptance, demonstration of unfeasibility of direct comparison is necessary, additionally to appropriate study design and statistical analysis. ECA are more likely to be accepted in areas of high unmet need with limited alternatives (e.g., CAR-T cell therapies). Independently of the type of RWD, European HTA bodies consistently favor, representative, country and European RWD over US and rest of the world. The UK, Italy, France and recently Germany, can request RWD for technology re-evaluation. However, in the UK, expert interview, revealed that mature trial data weights more than RWD. Overall, RWD acceptance is context-dependent and heterogenous across countries, with the UK remaining more receptive to consider RWD, Italy relying on RWD to inform managed-entry-agreements, and France endorsing RWD to support technologies re-evaluations. ***Conclusions:*** In the context of HTA decision, RWD remains valuable to characterize the disease background, however, its use to support efficacy claims remains limited to cases where direct comparison is unfeasible and needs to be methodologically robust.

HTA48
MINIMUM FOLLOW-UP TIME REQUIRED FOR THE DETECTION OF THE IMPACT OF TREATMENTS ON NEUROPATHIC PAIN AND GASTROINTESTINAL COMPLAINTS IN FABRY DISEASE

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Objectives: Fabry disease (FD) is a metabolic disorder with clinical onset during childhood or adolescence. A high percentage of patients with FD suffer from neuropathic pain and gastrointestinal (GI) complaints. The positive effect of available treatments (enzyme replacement therapy with agalsidase alfa/beta (ERT) and migalastat) on these symptoms can improve patients' quality of life. We investigated the minimum time of follow-up in FD to detect the statistically significant impact on neuropathic pain and GI complaints after treatment with available therapies. ***Methods:*** A targeted literature review was conducted, and relevant clinical data were extracted. All publications of FD patients who received ERT or migalastat and measured treatment effect on neuropathic pain and GI disorders were included. ***Results:*** Thirty-five publications met the inclusion criteria of which 10 and 11 reported a statistically significant effect on neuropathic pain and GI complaints, respectively. Among publications which included at least 2 measurement timepoints, a significant reduction in pain symptoms associated with ERT was recorded as early as 6 months (2/10), 12 months (3/10), 24 months (4/10), or >36 months (1/10). No significant impact on pain was recorded for migalastat. The significant positive effect on GI symptoms generally started after 6 months for both ERT and migalastat (6/11 publications), but longer assessment timepoints have also been reported (12 months