

A SYSTEMATIC LITERATURE REVIEW OF HEALTH ECONOMIC EVALUATIONS OF TREATMENTS FOR RARE DISEASES



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Introduction

Rare diseases are those that affect a small number of people (no more than 5 in 10,000 people)¹. Specific issues are raised in relation to their rarity, for instance, there is often limited knowledge of natural history and epidemiology or a lack of long term outcome data, which can lead to difficulties when undertaking health economic assessments of new medical treatments². Given this, a systematic literature review (SLR) was conducted to critically appraise the methodological approaches frequently taken when developing health economic evaluations of treatments for rare diseases, and to assess the potential impact of data scarcity.

Methods

An SLR was conducted following the Cochrane Handbook for Systematic Reviews of Interventions³ in March 2016, to identify health economic evaluations of treatments for rare diseases. The study question was defined according to the population, intervention, comparator, outcome and study framework. The search protocol was implemented in MEDLINE, Embase and the Cochrane Library. The main inclusion criteria consisted of health economic evaluations for treatments of rare disease with orphan drug designation appraised by the National Institute for Health and Care Excellence (NICE) since 2010 (including highly specialised technology appraisals), detailed description of the modelling approach, and the reporting of costs and health benefit. Data on type of model, perspective, model development, drivers, data gaps and main assumptions were extracted. A validated quality assessment tool⁴ and level of adherence to NICE reference case⁵ were used to ascertain study quality.

Results

A total of 584 studies were identified. Twelve studies met the inclusion criteria and were included in the narrative synthesis. Relapsed ovarian cancer was the most common disease evaluated (42%), followed by chronic lymphocytic leukaemia (17%), metastatic pancreatic cancer (17%), chronic myeloid leukaemia (17%) and multiple myeloma (8%).

Figure 1. Type of economic model

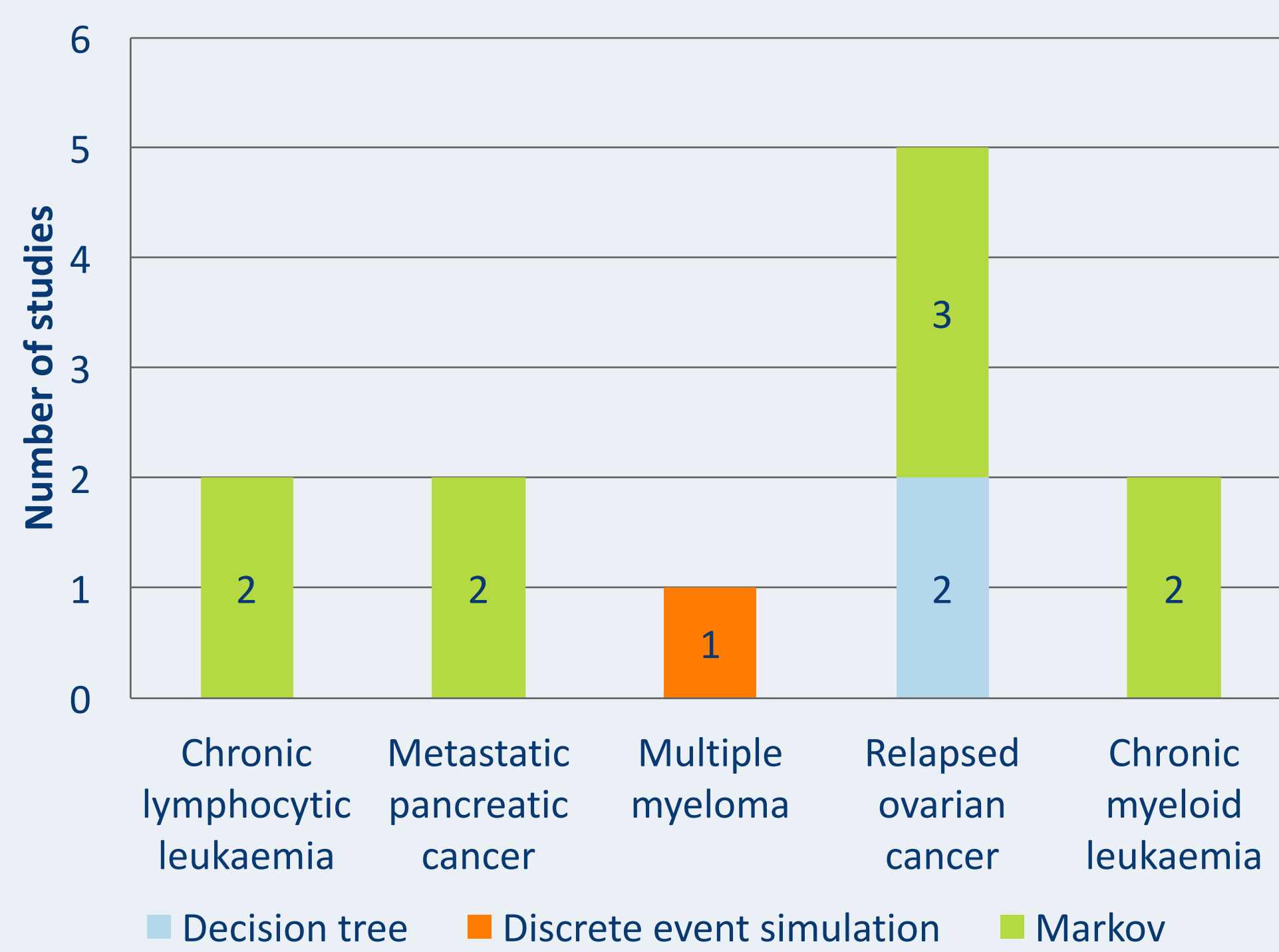


Figure 2. Highest level of efficacy and safety data used

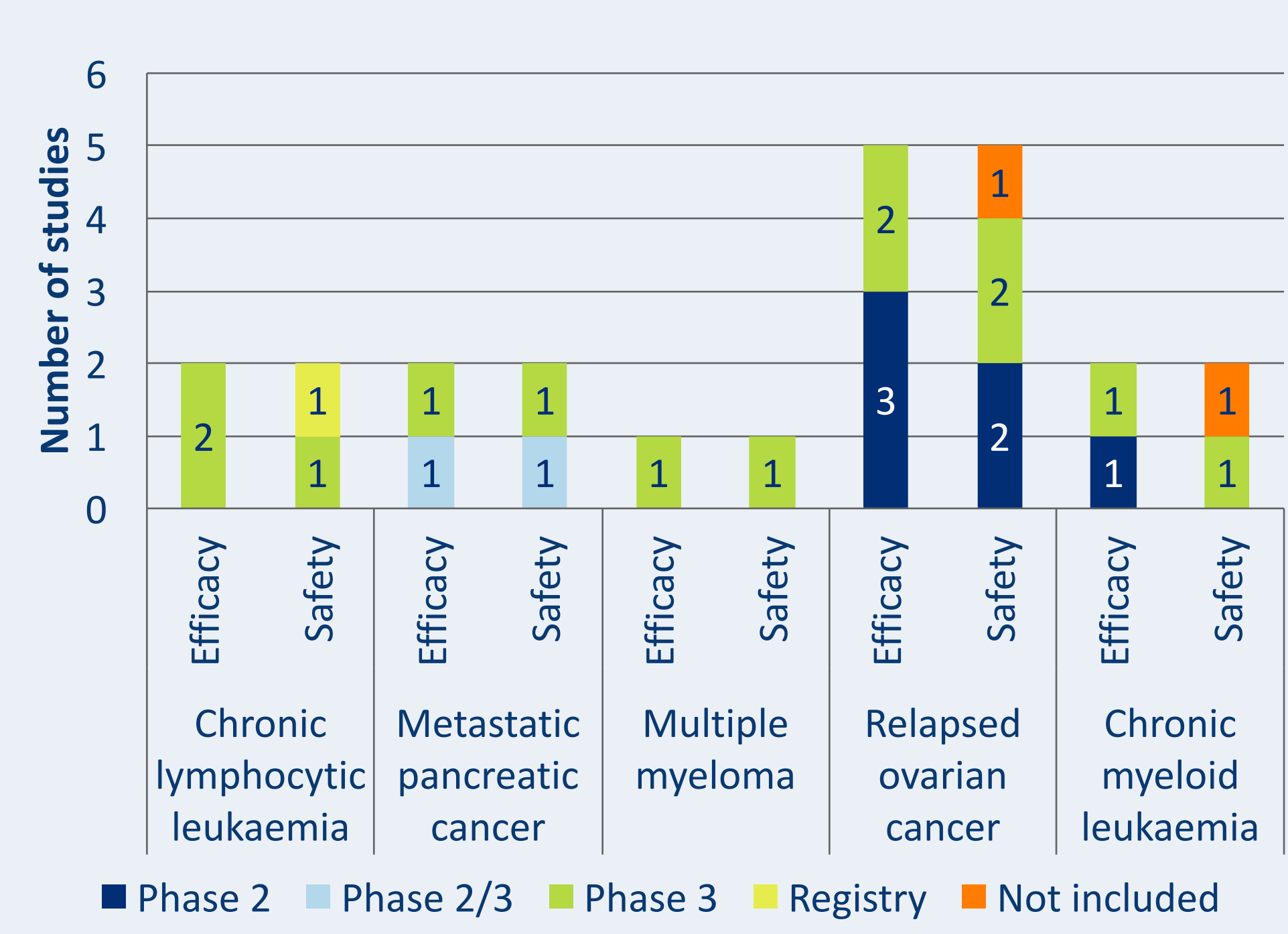


Figure 3. Limitations reported by authors by category

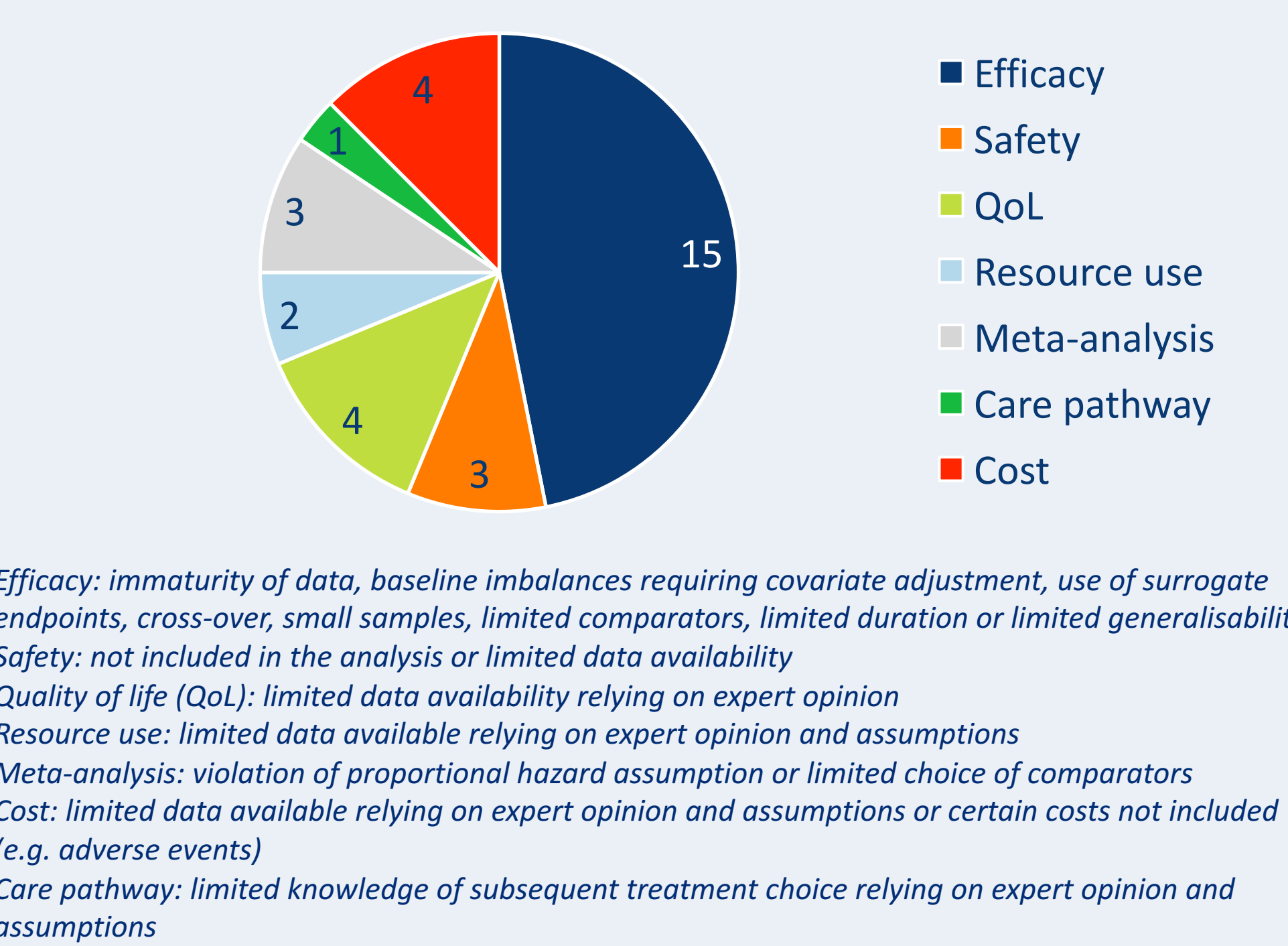


Figure 4. Sensitivity analysis

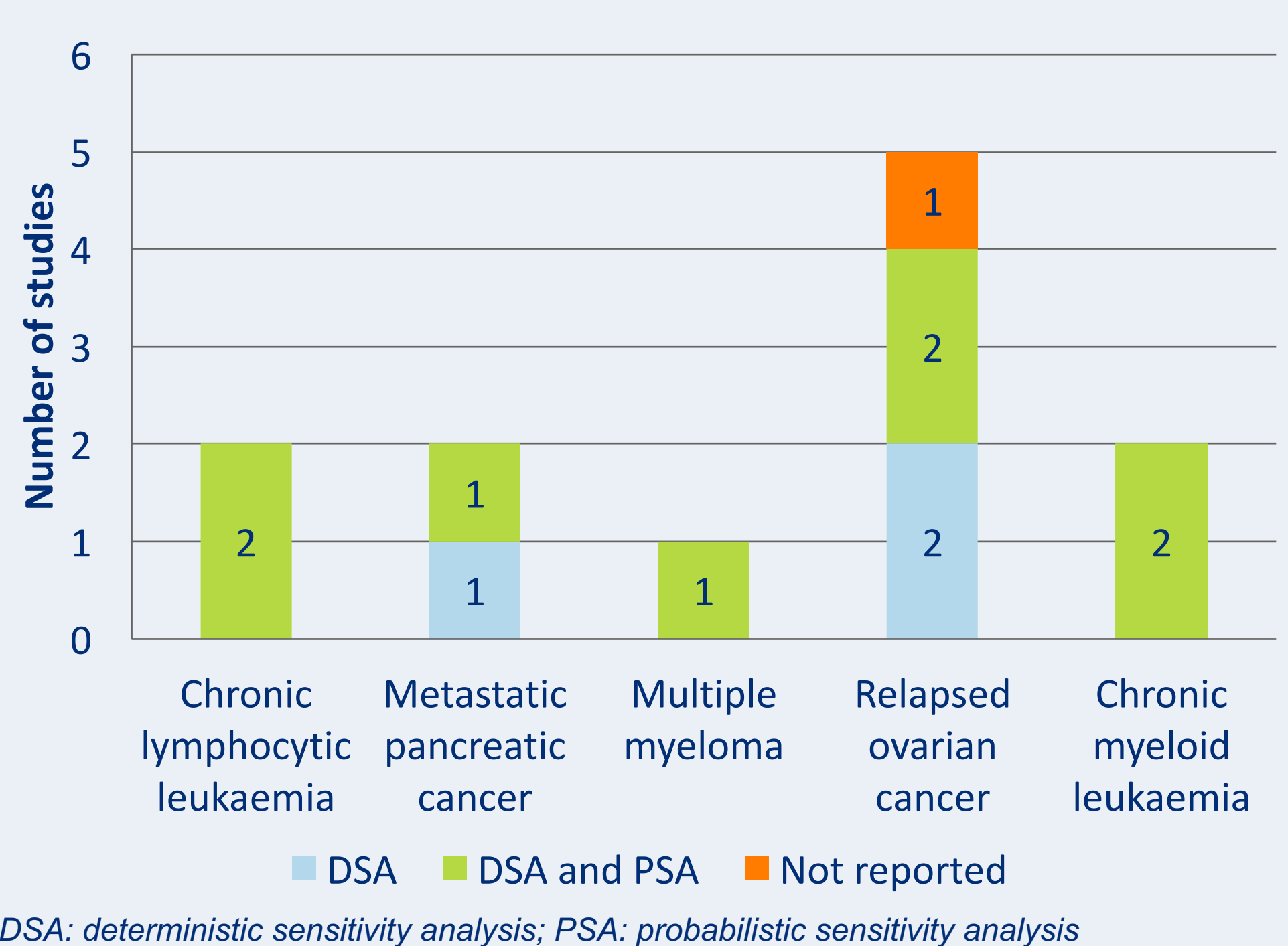
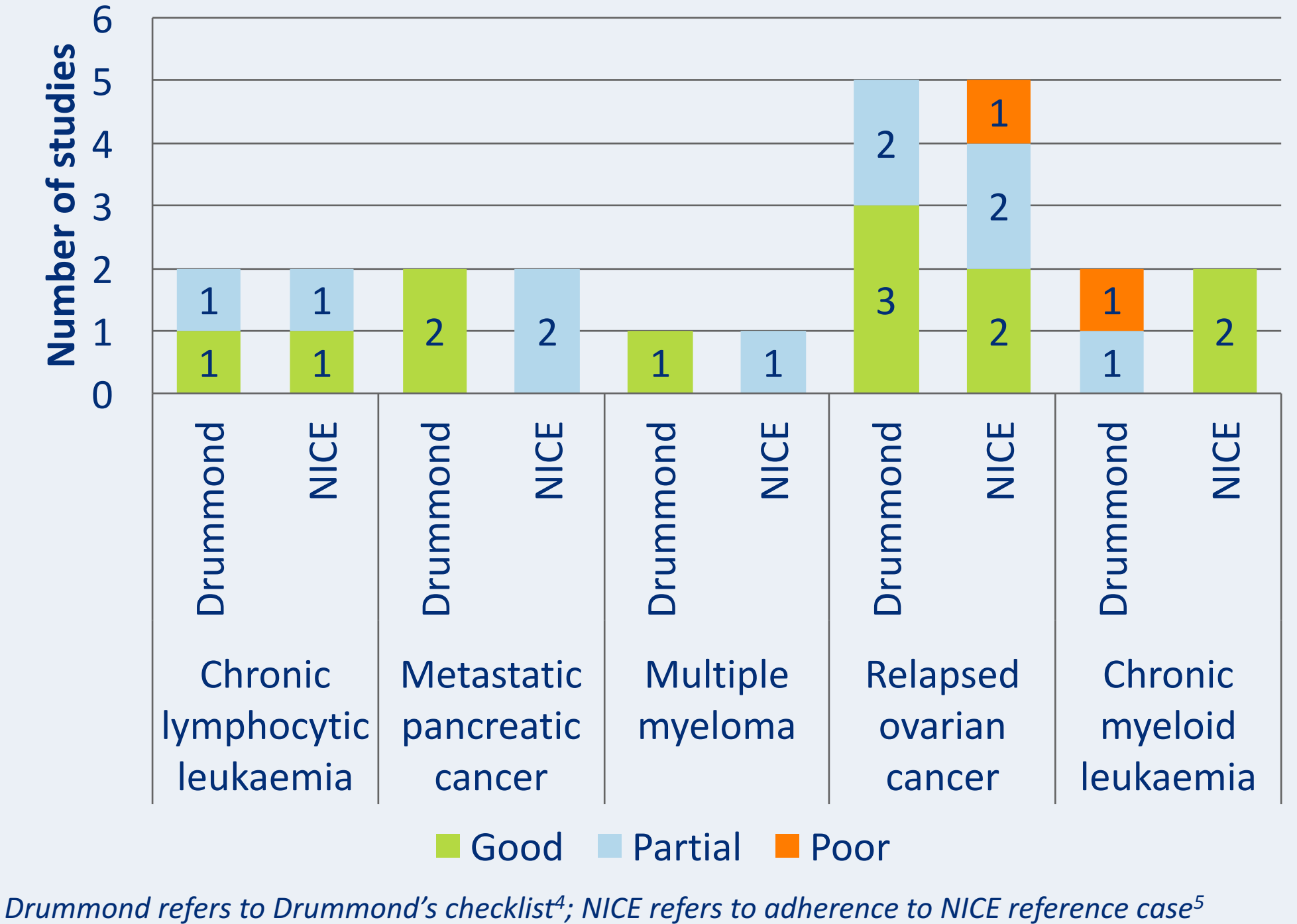


Figure 5. Quality assessment⁴ results and adherence to NICE reference case⁵



Drummond refers to Drummond's checklist⁴; NICE refers to adherence to NICE reference case⁵

Markov models using parametric survival methods were the most frequent model type (Figure 1). Even though the majority of the efficacy and safety data used in the economic analyses were obtained from phase 3 clinical trials (Figure 2), the data often presented limitations. These included: small sample sizes and study duration, leading to uncertain estimates and a lack of generalisability; baseline characteristic imbalances or allowing for cross-over requiring covariate adjustment; and data gaps requiring expert opinion or assumptions, among others (Figure 3). Most of the studies underwent extensive scenario testing in the form of deterministic and probabilistic sensitivity analyses to ascertain the robustness of the results (Figure 4). The infrequent inclusion of productivity costs or insufficient reporting of model parameters were the main reasons for lower scores in the quality assessment⁴, although the studies were of good quality overall (Figure 5). Overall partial adherence to NICE reference case⁵ was predominantly due to input differences between countries (e.g. 3% discount rate instead of the 3.5% recommended by NICE). UK studies showed higher adherence to NICE reference case⁵ (e.g. both studies in chronic myeloid leukaemia).

Conclusion

Our analysis showed that, even though rigorous economic evaluations were identified, challenges intrinsic to rare diseases were frequent. The economic evaluations addressed these challenges through sophisticated statistical methods (e.g. covariate adjustment or extensive sensitivity analyses), in order to produce robust estimates that enable payers to adopt treatments that represent value for money in a rapid, equitable and sustainable manner.

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