

Comparison of Enteral Nutritional Therapy to Induce and Maintain Remission in Paediatric Patients with Mild-to-Moderate Crohn’s Disease: A Cost-Effectiveness Analysis in the UK

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INTRODUCTION

- Crohn's disease (CD) is a **multifactorial, inflammatory disease** characterised by inflammation of the lining of the digestive tract and periods of remission and relapses. CD can cause disabling life-altering symptoms (e.g., severe abdominal pain, frequent diarrhoea, rectal bleeding, fever, nutritional deficiencies, and weight loss), significant complications, and reduced quality of life¹
- While CD can occur at any age, paediatric-onset CD is often more severe than adult-onset CD and can lead to **impaired growth, delayed puberty, and undernutrition**²
- Multidisciplinary, tailored management includes nutritional therapy, corticosteroids, immunosuppressants, anti-tumour necrosis factor (TNF), and surgery³
- The European Crohn's and Colitis Organisation (ECCO) and European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) guidelines recommend **exclusive enteral nutrition** (EEN) as the **first-line treatment to induce remission** in children and adolescents with acute active CD and **partial enteral nutrition** (PEN) (at least 50% of daily energy requirements), as maintenance therapy **to prolong remission**³
- Modulen® IBD is a clinically proven, nutritionally complete, specialised formula, suitable for oral and tube feeding and designed for the dietary management of CD in paediatric, adolescent, and adult patients. It may be used for EEN for several weeks or given as PEN⁴

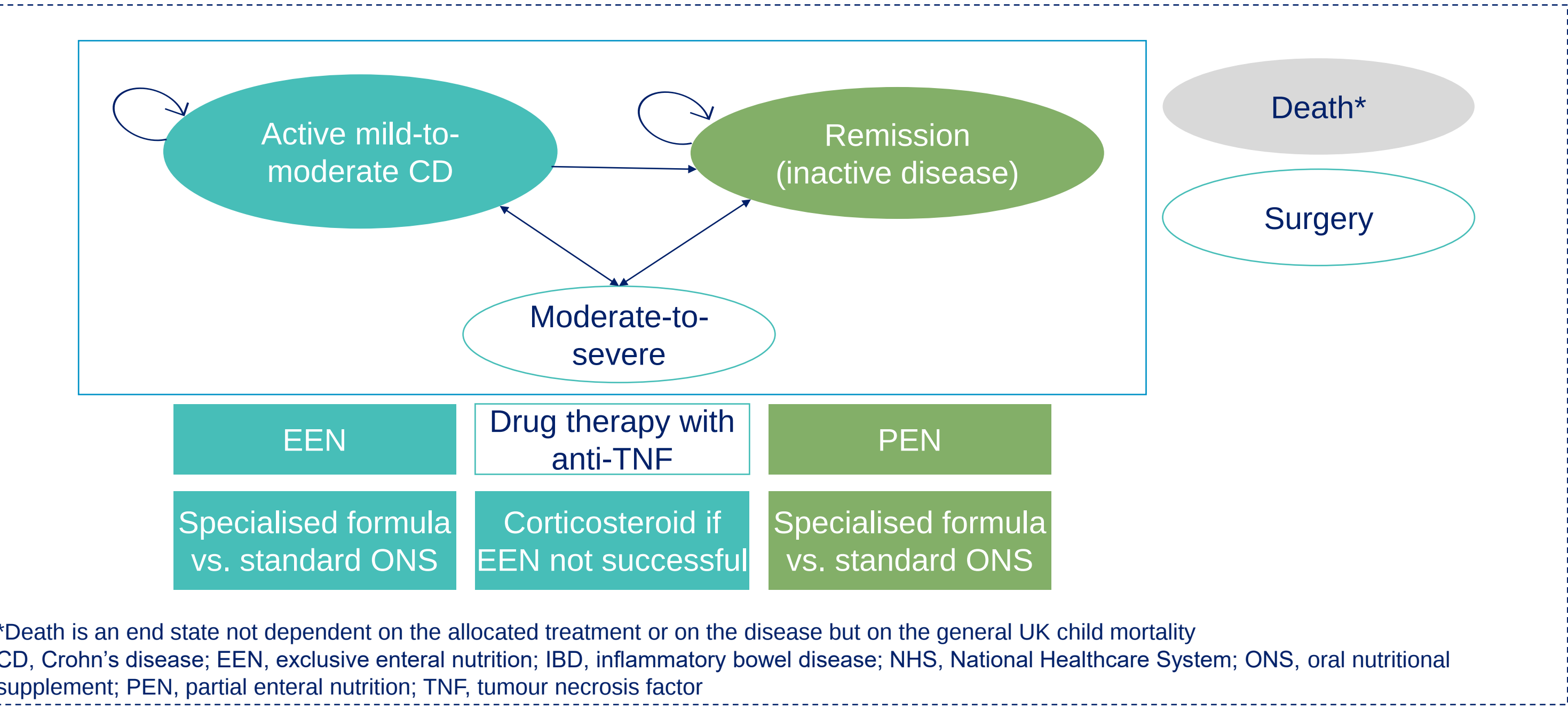
OBJECTIVES

- The aim of this cost-effectiveness analysis (CEA) was to investigate **the cost-effectiveness (CE) of a specialised formula compared to standard oral nutritional supplements** (ONS) for the dietary management of mild-to-moderate CD in paediatric patients, from the perspective of the UK National Healthcare System (NHS) and over a one-year time horizon

METHODS

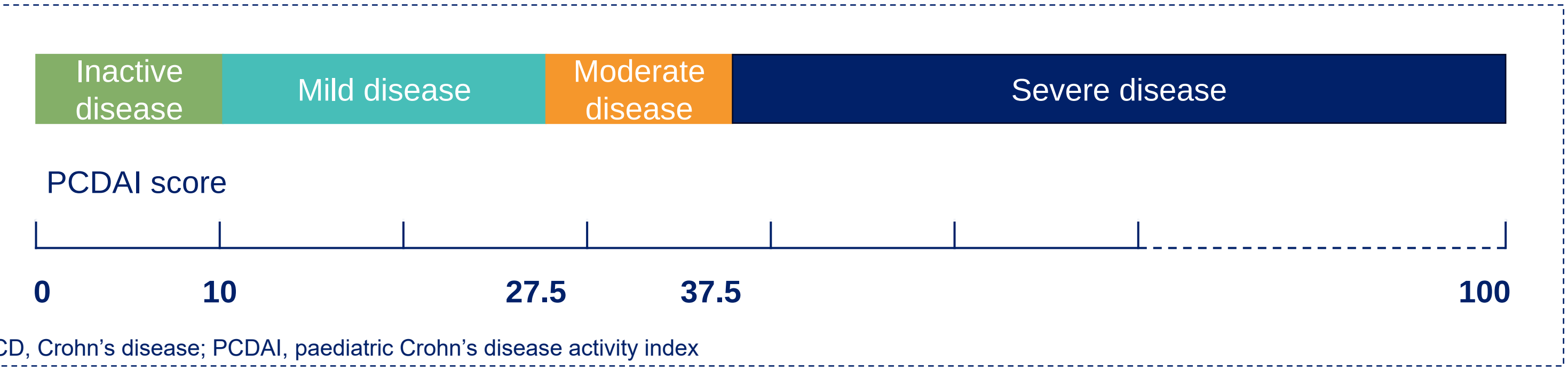
- We developed a **Markov model** to compare the specialised formula versus standard ONS from the UK NHS perspective over a one-year time horizon and an 8-week cycle, based on a typical treatment monitoring for EEN according to ECCO/ESPGHAN consensus guidelines.³ The structure of the model is shown in **Figure 1**

Figure 1 – Markov model structure



- The model considered **five health states**: remission, mild-to-moderate, moderate-to-severe, surgery and death. Health states were **defined according to the paediatric CD activity index** (PCDAI) (**Figure 2**). Patients entered the model in the mild-to-moderate state receiving EEN (either with the specialised formula or standard ONS) and could remain or progress to each of the health states. If they remained or relapsed to the mild-to-moderate health state more than two times, they received corticosteroids; if they moved into full remission, they switched to PEN. Transitions to a moderate-to-severe state led to treatment with anti-TNF, while surgery was an exit state; finally, the model assumed that CD did not affect mortality, with the “death” state only reflecting general UK child mortality by age

Figure 2 – CD classification



- The target **population** consisted of paediatric patients with mean age of 13 years with mild-to-moderate CD. The baseline characteristics were informed by the clinical study used to populate the model
- The **efficacy** of the specialised formula and standard ONS were measured through the **clinical remission rate** which was sourced from the literature (**Table 1**)

Table 1 – Clinical remission rates

Intervention	Clinical remission rate	Source
Specialised formula in EEN	83%	Moriczi M et al. 2020 ⁵
Standard ONS in EEN	63%	Dawson R et al. 2022 ⁶
Specialised formula in PEN	60%	Lionetti et al. 2005 ⁷
Standard ONS in PEN	60%	Assumption

EEN, exclusive enteral nutrition; ONS, oral nutritional supplement; PEN, partial enteral nutrition

- Health state utilities** were sourced from a study that assessed discriminative validity by comparing utilities elicited using the child health utility-9-dimension (**CHU9D**) adult and youth tariffs, health utility index mark 2 (**HUI2**) and mark 3 (**HUI3**) across multiple disease activity scales in paediatric ulcerative colitis (UC) and CD⁸
- The costs were expressed in **£2023** and include **intervention costs**, obtained from the British National Formulary (BNF)⁹ and **healthcare resource costs**; annual resources involved in the provision of care in each CD health state had been provided by clinical experts while the cost had been retrieved from the NHS tariff database for the year¹⁰

METHODS (continued)

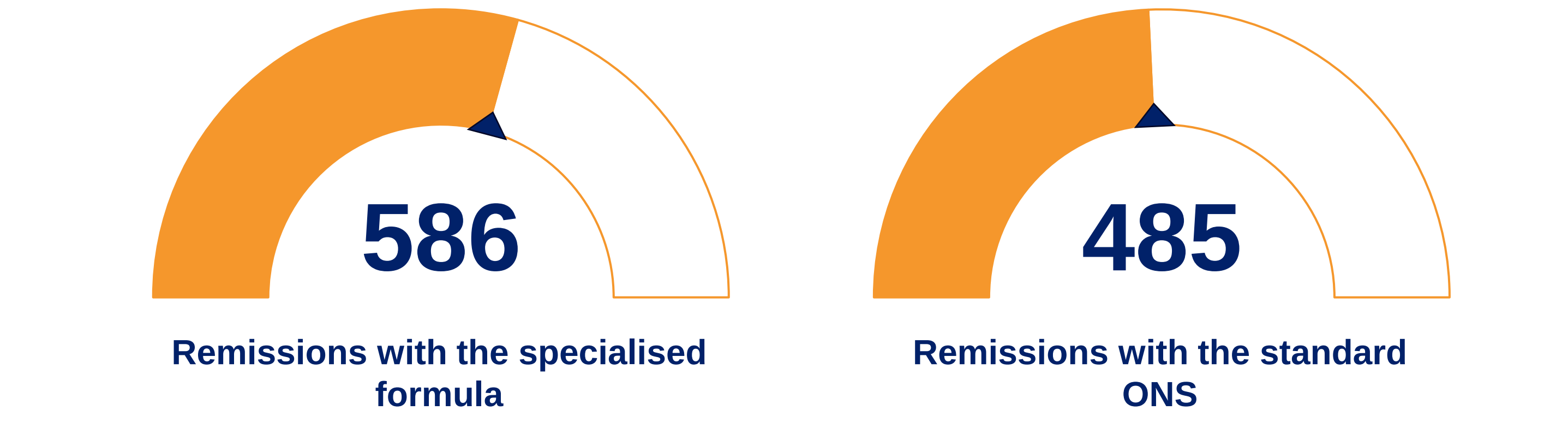
- Model design and validation of its structure were further developed with inputs from three clinical experts and two local payers responsible for the procurement of paediatric nutritional supplements
- The robustness of the findings was assessed by deterministic and probabilistic sensitivity analyses

RESULTS

- The base case results showed that the specialised formula **saves £746** with similar quality-adjusted life-years (QALYs) per patient over one year versus standard ONS. The incremental cost-effectiveness ratio (ICER) was negative, indicating that **the specialised formula dominated the standard ONS** (**Table 2**)
- The results also showed that in a hypothetical cohort of 1,000 patients, **586 inductions to remissions** could be achieved when using the specialised formula versus 485 when using the standard ONS

Table 2 – Base-case results

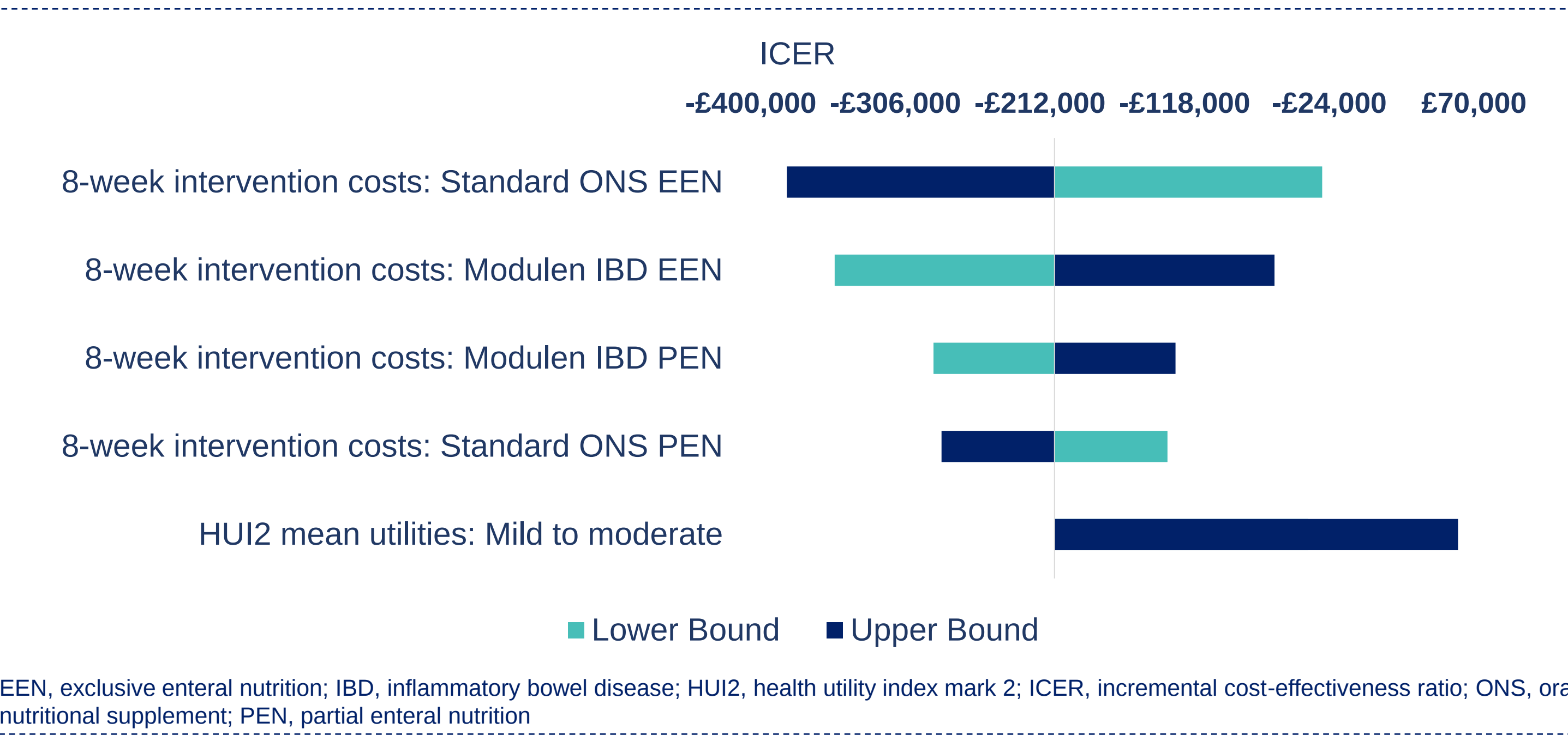
Effectiveness	QALYs/patient	Costs	Total costs (£)/patient
Specialised formula	0.87	Specialised formula	6,853.8
Standard ONS	0.86	Standard ONS	7,599.5
Difference	0.01	Difference	-745.7



QALY, quality-adjusted life-years; ONS, oral nutritional supplement

- A deterministic sensitivity analysis (DSA) showed that **key drivers** of CE were the **8-week intervention costs** (for standard ONS and specialised formula) and the **utility scores** (measured by the CHU9D youth instrument in the base case) in the mild-to-moderate health states (**Figure 3**)

Figure 3 – Tornado diagram



- Results of the probabilistic sensitivity analysis (PSA) showed **that at a willingness-to-pay threshold of £20,000 per QALY**, the specialised formula was **85% more likely to be cost-effective** compared to standard ONS (**Figure 4**)

Figure 4 – PSA results

DISCUSSION AND CONCLUSIONS

- To our knowledge, this is the **first CEA** comparing a specialised formula versus standard ONS. The present CEA shows that **the specialised formula is superior to standard ONS**, being less costly and more effective
- One of the main limitations of this model is the scarcity of clinical evidence for standard ONS which posed a challenge in sourcing input parameters for the analysis; nevertheless, our assumptions were validated by clinical experts
- Additionally, both deterministic and probabilistic sensitivity analyses validated the robustness of the results to variations of input data and assumptions

REFERENCES

- Petagna L et al. Biol. direct. 2020;15(1):1-0
- Moeeni V et al. ISRN Pediatr. 2011;2011:365712
- Van Rheenen PF et al. JCC 2021;15(2):171-94
- Modulen IBD, <https://www.nestlehealthscience.co.uk/>, accessed February 2023
- Moriczi M et al. Nutrients. 2020; 12(4)
- Dawson R et al. Inflamm. Bowel Dis. 2022; 28(12):1859-64
- Lionetti P et al. JPN 2005; 29:S173-8
- Bashir NS et al. Qual Life Res. 2023
- BNF UK, <https://www.bnf.org/>, accessed February 2023
- NHS 2022/23, www.england.nhs.uk, accessed February 2023

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