

Burden of Congenital Hyperinsulinism in the United Kingdom: A Cost of Illness Study

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PSY59

Objectives

- To estimate the annual cost of illness (COI) of all people with congenital hyperinsulinism (CHI) in the UK from a service provider perspective (National Health Service, NHS) based on the current treatment pathway, and to explore the distribution of these costs within the patient population.

Background

- CHI is a rare disease characterised by excessive and unregulated insulin secretion from the β -cells of the pancreas, which causes persistent hypoglycaemia (low blood glucose).¹
- Approximately 95 infants are born with CHI in the UK each year.^{2,3}
- These infants present with severe symptoms such as shakiness and seizures within the first days of life.^{1,4} If left uncontrolled, hypoglycaemia can result in permanent brain damage.^{1,5}
- Current treatment approaches depend on the severity of the disease—patients on the more severe end of the spectrum may need to have almost all of their pancreas removed (near-total pancreatectomy) and as a result are at high risk of developing type 1 diabetes mellitus (T1DM).⁴ The current treatment pathway for the management of CHI is presented in Figure 1.

Methods

- The model used a prevalence-based approach to calculate the direct costs to the NHS of all patients diagnosed with CHI in the UK. Patients were divided into four treatment groups (Figure 1) and costs were stratified by age to better reflect resource use at different stages of treatment.
- The treatment pathway was developed following a pragmatic literature review conducted in MEDLINE via the PubMed platform on 4 September 2015 (supplemented with grey literature searches).
- The pathway was validated and refined in collaboration with clinical experts at Great Ormond Street Hospital (GOSH).²
- Model inputs were informed by the pragmatic literature review in conjunction with the NHS Reference Costs (2014–15), British National Formulary (BNF, 2015) and Office of National Statistics (ONS) National Life Tables (Mid-2014).^{6–8} All inputs were verified by clinical experts at the two centres of excellence in CHI (GOSH and the Northern CHI Service [NORCHI]).^{2,3} Key model inputs are presented in Table 1.
- Patient numbers were estimated by age for each treatment group, and multiplied by individual "per patient" costs to give the total COI.
- A deterministic sensitivity analysis (DSA) was run at 10% to determine major cost drivers.

Results

Patients in their first year of life incur the highest annual per patient costs

- Figure 2 shows the annual cost of a single patient in each treatment group, stratified by age.

- For all treatment groups, costs were highest in Year 1 and then declined. Only CHI patients with diffuse disease who are surgically managed incurred costs beyond Year 5 due to the long-term management of T1DM.

The total COI to the NHS was £4,561,827.58 per year

- The average cost of CHI to the NHS per patient per year was £1,388.26.
- The distribution of costs was skewed among CHI patients, with just 95 patients in their first year of life (2.9% of all CHI patients) contributing to 42.1% of the total costs (Figure 3).

CHI patients with diffuse disease treated surgically had the greatest contribution to total costs

- CHI patients with diffuse disease who are surgically managed (Group 4) were the most costly to the NHS, as compared to other treatment groups (Figure 4).
- This was due in part to patients aged 10 years and older who contributed to 66.1% of the annual costs incurred by this treatment group (Group 4); the majority of these costs were associated with the treatment of T1DM.

Lack of response to first-line therapy was the greatest driver of the COI

- The DSA identified the proportion of patients responsive to first-line drug therapy to be the major driver of first year and total annual costs.
- The number of newly diagnosed CHI patients was also a strong driver of first year costs (Figure 5A), while the proportion of patients receiving treatment for T1DM contributed greatly to total annual costs (Figure 5B).

Figure 1. Treatment pathway for the management of CHI

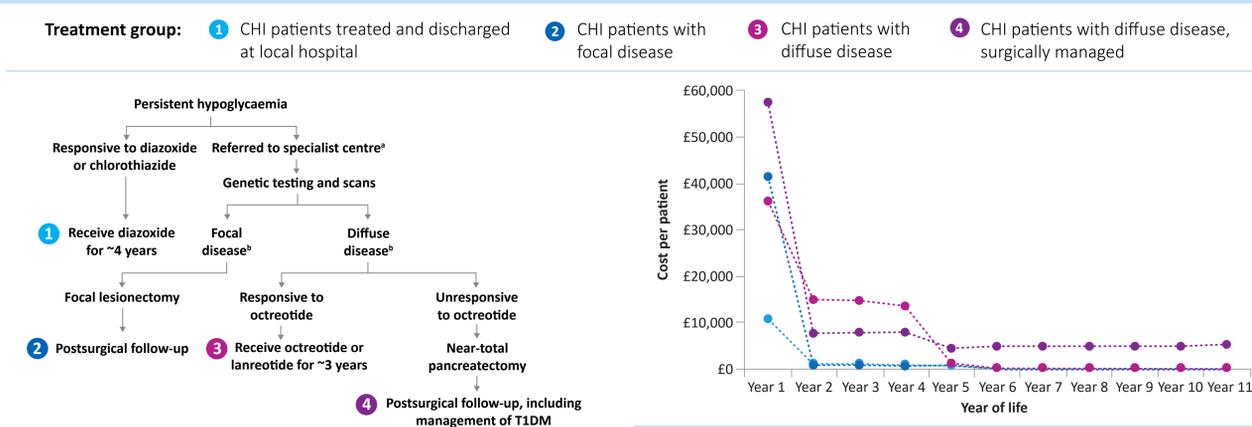


Figure 3. Estimated patient numbers and total costs of CHI patients (in Year 1 versus all years)

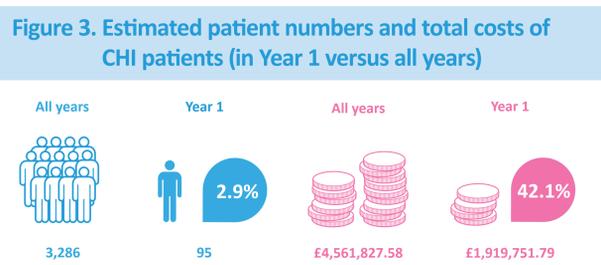


Figure 2. Annual per patient costs stratified by treatment group and age

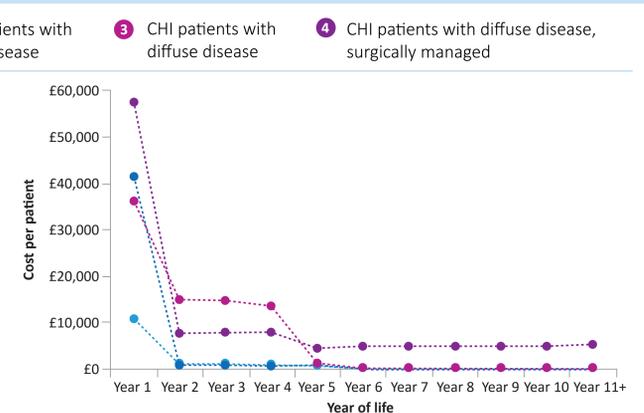


Figure 4. Total annual costs of all CHI patients by treatment group

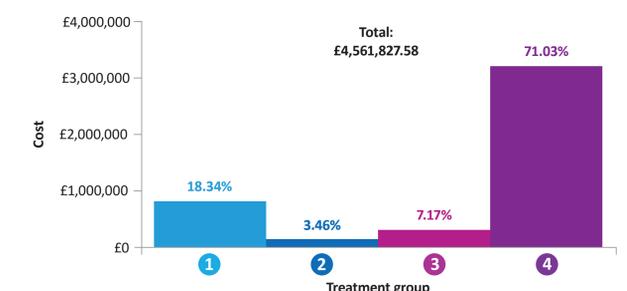


Figure 5. Tornado plots showing the ten greatest cost drivers as identified by the DSA

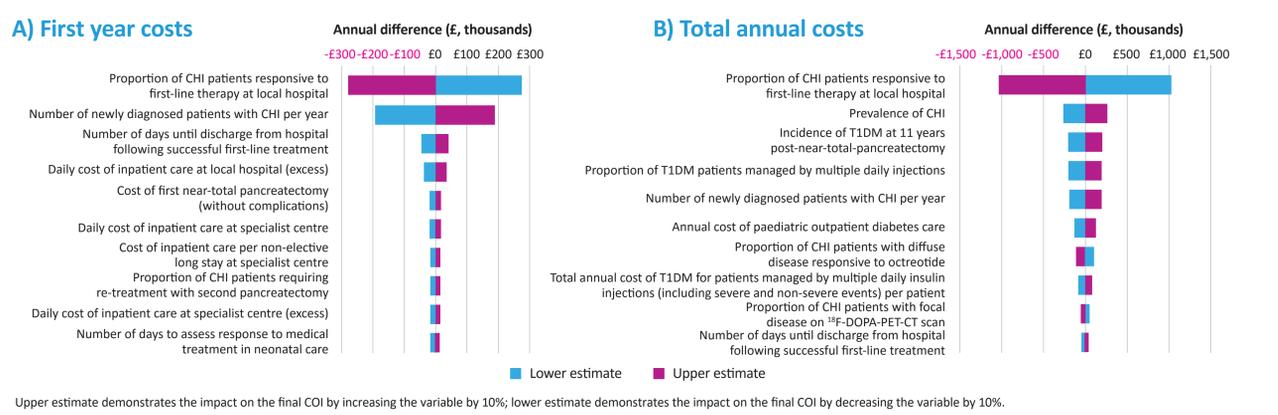


Table 1. Key inputs in the model

Input	Value	Reference
Population inputs		
Prevalence of CHI ^a	1/50,000	Orphanet (2015) ⁹
Number of newly diagnosed patients with CHI per year ^{a,b}	95	Expert opinion (GOSH and NORCHI, 2016) ^{2,3}
Cost inputs		
Daily cost of inpatient care at local hospital (excess) ^a	£435.86	NHS Reference Costs (2014–15) ⁶
Cost of first near-total pancreatectomy (without complications) ^a	£6,827.88	NHS Reference Costs (2014–15) ⁶
Daily cost of inpatient care at specialist centre ^a	£435.86	NHS Reference Costs (2014–15) ⁶
Cost of inpatient care per non-elective long stay at specialist centre ^a	£2,274.28	NHS Reference Costs (2014–15) ⁶
Daily cost of inpatient care at specialist centre (excess) ^a	£435.86	NHS Reference Costs (2014–15) ⁶
Annual cost of paediatric outpatient diabetes care ^a	£2,943	NHS National Tariff (2014–15) ¹⁰
Total annual cost of T1DM for patients managed by multiple daily insulin injections (including severe and non-severe events) per patient ^b	£2,111.70	Evans <i>et al.</i> 2015 ¹¹
Clinical inputs		
Proportion of CHI patients responsive to first-line therapy at local hospital ^{a,b}	75%	Expert opinion (NORCHI, 2016) ³
Proportion of CHI patients with focal disease on ¹⁸ F-DOPA-PET-CT scan ^a	34%	Expert opinion (NORCHI, 2016) ³
Proportion of CHI patients requiring re-treatment with second pancreatectomy ^a	60%	Expert opinion (GOSH, 2016) ²
Proportion of T1DM patients managed by multiple daily injections ^b	90%	Expert opinion (GOSH and NORCHI, 2016) ^{2,3}
Incidence of T1DM at 11 years post-near-total-pancreatectomy ^b	96%	Arya <i>et al.</i> 2014 ¹²
Proportion of CHI patients with diffuse disease responsive to octreotide ^b	30%	Expert opinion (NORCHI, 2016) ³
Number of days until discharge from hospital following successful first-line treatment ^{a,b}	14	Expert opinion (GOSH and NORCHI, 2016) ^{2,3}
Number of days to assess response to medical treatment in neonatal care ^a	10	Expert opinion (GOSH, 2016) ²

Key inputs shown include the ten greatest cost drivers of first year costs^a and the ten greatest cost drivers of total annual costs^b as identified by the DSA.

Conclusions

- Despite being a rare disease, the annual cost of CHI to the NHS was found to be substantial.
- The development and management of postsurgical T1DM as a major cost driver highlights the need for effective treatments which could potentially mitigate such consequences and costs.

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Author contributions

Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: SE, JE, AG, IB, KH, RST; Drafting of the publication, or revising it critically for important intellectual content: SE, JE, AG, IB, KH, RST; Final approval of the publication: SE, JE, AG, IB, KH, RST.

Acknowledgements

This study and poster were developed on a pro bono basis by Costello Medical Consulting on behalf of Findacure. This work is part of Findacure's rare disease drug repurposing social impact bond proof of concept study, which was funded by the Big Lottery Fund. The authors thank all those who contributed to this study including the teams at GOSH and the Northern CHI Service; colleagues at Costello Medical Consulting including Wrik Ghosh, William Marsh and Sachin De Stone; and all those at Findacure, in particular Flóra Raffai.