



Background

- Hirschsprung disease is a congenital defect where the end of the neonate's bowel lacks nerve cells. This leads to bowel obstruction as the stool is not be able to move through the bowel as expected.
- The prevalence of Hirschsprung disease is 1:5,000 in newborns, The overall male: female ratio is 3:1 to 4:1, nevertheless, when the entire colon is involved the gender ratio is 1:1.
- Constipation and intestinal obstruction are the main symptoms.
- Hirschsprung is a life-threatening disease and surgery is the only available treatment currently. surgery results in lifelong complications, especially in severely affected patients, where little of the bowel remains. Cell therapy, in conjunction with surgery, seems promising in treating patients with Hirschsprung disease.
- A regenerative therapy is being developed by Researchers at Sheffield university and the Institute of Child Health (ICH) in London. The work is presently pre-clinical. Once stem cells can be identified and isolated, it is believed that they can be used to replace the missing cells in the regions of the intestine.

Objective

- This research intends to investigate the potential cost-effectiveness and maximum acceptable price (MAP) of cell therapy adjacent to surgery for the treatment of short segment Hirschsprung disease in pediatric patients.
- This research is the first cost-effectiveness model for Hirschsprung disease.

Methods

- A cost-effectiveness analysis was used to assess the expected cost (£) and quality adjusted life years (QALY) associated with adding cell therapy to surgery for short segment Hirschsprung patients.
- A time horizon of 100 years and an NHS perspective was used. The model used a cycle length of one year. A discount rate of 3.5% was used.
- The model structure was developed through semi-structured interviews of paediatric surgeons and gastroenterologists and an examination of treatment guidelines (Figure 1).
- The model has six health states describing chronic health (i.e. normal bowel function, constipation or incontinence) and events with associated short-term costs and health impact (i.e. surgery and further surgery), plus death.
- In order to capture the time-dependent nature of the disease, separate transition matrices were used for 0-5 years, 6-10 years, 11-15 years and >15 years¹.
- The model was populated through targeted literature searches and expert opinion (Table 1). Death has zero utility and was assumed to incur zero cost.
- The analysis based on scenarios describing different level of efficacy defined by the percentage of patients returning to normal bowel function (i.e. a cure). Scenarios examined proportions of patient being cured of 100%, 75%, 50%, and 25%.
- MAP was identified by estimating incremental net monetary benefit (INMB) of treatment at zero price.
- The analysis estimated MAP for cost-effectiveness thresholds of £20,000, £30,000 and £100,000).

Results

- When cell-therapy has a price of zero, the 100% curative scenario produced 23.03 QALYs and a cost of £8,243 per patient (Table 2).
- INMB for the 100% curative scenario was £34,343 at a threshold of £20,000 (highest INMB) , which implies a MAP of that value. MAPs at 75%, 50% and 25% effectiveness were £33,365,£31,733, and £26,602, respectively.

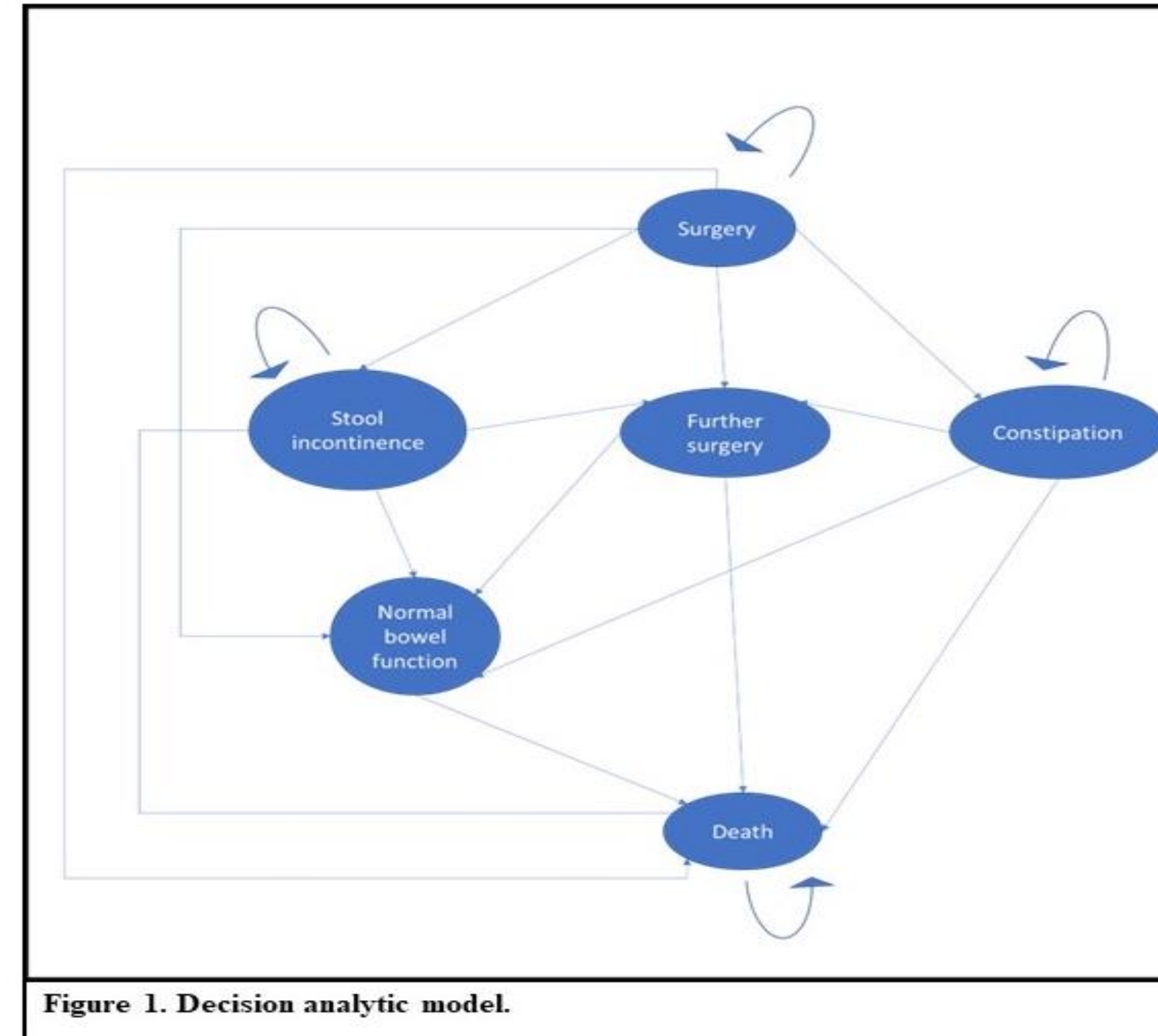


Table 1. Utility and cost values					
Parameter	Utility	Cost			
		Age (0-1)	Age (1-5)	Age (5-10)	Age (10-15)
Redo surgery ²	0.280	£7,605			
Further surgery ²	0.280	£7,890			
Stool incontinence ³	0.775	£4,408	£4,204	£3,795	£3,590
Constipation ⁴	0.813	£868	£663.63	£255	£50
Normal bowel function ⁵	0.890	£818	£613.33	£204	£0

Table 2. Scenario analysis and incremental net monetary benefit results					
	standard of care	Cell therapy being 100% curative	Cell therapy being 75% curative	Cell therapy being 50% curative	Cell therapy being 25% curative
Total costs (undiscounted)	£44,861	£8,970	£9,390	£10,138	£13,558
Total QALYs (undiscounted)	66.78	69.49	69.45	69.40	69.14
Total discounted costs	£21,929	£8,243	£8,624	£9,277	£11,331
Total discounted QALYs	21.99	23.03	23.00	22.95	22.79
Incremental Cost vs standard of care		-£13,687	-£13,305	-£12,652	-£10,598
Incremental QALYs vs standard of care		1.033	1.003	0.954	0.800
INMB 20 "Maximum price at £20,000"		£34,343	£33,365	£31,733	£26,602
INMB 30 "Maximum price at £30,000"		£44,672	£43,395	£41,274	£34,604
INMB 100 "Maximum price at £100,000"		£116,970	£113,604	£108,057	£90,617

Conclusions

- The modelling illustrates that cell-therapy has the potential to be cost-effective at a price of over £25,000 even if only 25% effective.
- In addition to producing effectiveness data, the modelling highlighted that important quality of life and natural history data were lacking and the need for research into these issues if a credible value proposition for cell therapy is to be developed.

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