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RE	Restricted to a group specified by the consortium (including the Commission Services)	
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Key word list

Intestinal failure
Short bowel syndrome
Cost of care
Health economics
Productivity
Hospital care
Community and in-home care

Definitions and acronyms

Acronyms	Definitions
IF	Intestinal failure
SBS	Short bowel syndrome
CVAD	Central venous access device
UCL	University College London
PN	Parenteral nutrition
EN	Enteral nutrition

1. Introduction

1.1 General context

Intestinal failure (IF) is a life-limiting and resource-demanding disease. Patients receive intensive in-hospital and outpatient care requiring long-term input of multiple medical and surgical, allied health, and nursing specialties. Unless the patient achieves enteral autonomy, there is no cure for IF, with intestinal transplantation providing an expensive life-prolonging but non-curative therapy. Long-term nutritional support, enteral or parenteral, is extremely costly, but does not tell the whole story of the current cost of IF care.

INTENS is a multi-national consortium with the primary aim of developing new therapy for IF utilizing tissue engineering strategies. Despite the clear benefits to patients and the community of a curative treatment for IF, the research and development cost of such a therapy are clearly substantial, as exemplified by the significance of the INTENS grant.

In this context, there is a need for detailed study of the economics of IF to (a) provide a comprehensive description the current cost of care across multiple health systems, and (b) provide a baseline to which the cost of future therapies can be compared.

1.2 Deliverable objectives

A study for publication in a peer-reviewed journal will be undertaken, as previously published work does not sufficiently address the issue.

Study Aims

1. Estimate total cost of care for intestinal failure (IF), combining:
 - a. In-hospital care
 - b. Home- and community-based care
 - c. Lost productivity
2. Estimation of these costs to the patient/family *and* to the health care system/insurers (3rd parties)

The cost of intestinal transplantation will not be assessed, as its cost is described in the literature and its availability limited.^{1,2}

2. Methodological approach

Literature Review

A review of existing evidence describing the current cost of current treatment of intestinal failure was undertaken. The literature search included the following search terms:

- Paediatric
- Child
- Infant
- Intestinal failure
- Short bowel syndrome
- Parenteral nutrition
- Enteral nutrition
- Nutritional support

Study Methodology

Possible Experimental Designs

1. *Single centre from each participating country (retrospective cohort)*
 - a. **Favoured approach – current focus of data collection**
 - b. Advantages
 - i. Contained data collection to within a single health service for each collaborator
 - ii. Centralised provision of IF services in countries involved in INTENS consortium makes the proposed centres representative of IF treatment costs in each country
 - iii. Published literature contains only two publications involving multiple centres
 - c. Disadvantages
 - i. Data restricted to care provided through the single centre, therefore some out-of-hospital costs provided by community services may be underestimated
 - ii. Cost estimates based on data from IF specialist centres only
2. *Multi-centre multi-country (retrospective cohort) and/or registry data*
 - a. From multiple centres in each country or from registries (where available)
 - b. Advantages
 - i. More comprehensive assessment of costs in each country
 - ii. Possible increase in generalisability of cost estimates
 - iii. Published literature contains only two publications involving multiple centres
 - c. Disadvantages
 - i. Registry data are derived from large inpatient insurance databases, which is problematic for studying IF as there is

- no unifying diagnostic code,³ or extrapolated from databases of home PN, of which IF patients are presumed to make up a substantive majority, and are usually focussed on adult patients.⁴⁻⁶
- d. Attempt to model costs of care with established health economic modelling methodologies based on real-world cost inputs from interviews with expert clinicians
 - e. Advantages
 - i. No ethical approval required, as no access to patients or health records required
 - ii. Tuneable to best, worst, and average scenarios
 - iii. Rapidly completed
 - f. Disadvantages
 - i. Thought experiment only
 - ii. Modelling of PN costs using similar methodology has been described in the literature before⁷
 - iii. Entirely based on assumptions and opinion of expert clinicians, therefore estimates will lack precision

Option 1 is currently in progress with the potential to add other collaborating centres within a given country if data collection and analysis for original centre proves feasible and appropriate to extend to other centres.

Data Collection

Patient Population

Inclusion Criteria

- Ages: birth to 16 years
- Diagnosis of intestinal failure
- Majority of IF care at collaborating centre
- Minimum period of care for IF: 1 year

Exclusion Criteria

- Temporary nutritional support only

Exit from study

- Death
- Discontinuation of supplementary enteral or parenteral nutrition
- Five years since IF diagnosis

Subgroup Analyses

- Supplementary enteral nutrition alone
- Parenteral nutrition

Data Points – Background

Data point	Source	Comments
Patient demographics	Hospital record	Distance from hospital could be used to estimate transport costs
Aetiology of IF	Hospital record	Anatomical SBS vs functional, congenital vs acquired
Date of diagnosis	Hospital record	
Mortality	Hospital record	
Achievement of enteral autonomy	Hospital record	

Data Points – In-Hospital Costs

Data points	Options	Comments
Hospital room charges	Hospital administration List of tariffs	
Procedures	Hospital administration Government or 3 rd party insurers	
Diagnostic testing	Hospital administration Government or 3 rd party insurers	
Medications	Hospital pharmacy	
Implanted devices	Hospital administration	Particularly CVAD and enteral feeding buttons/tubes
Parenteral nutrition	Hospital pharmacy	
Enteral nutrition	Hospital pharmacy	
IV fluid therapy	Hospital pharmacy	
Nutritional supplements	Hospital pharmacy	Enteral and parenteral
Readmissions	Hospital record	Number of episodes per year, duration per episode
Labour cost	Staff survey Hospital record List of tariffs	Usually expressed as time per staff member per patient for given tasks (eg: consultation with surgeon, compounding of PN by pharmacist), multiplied by hourly rate of staff member.

Data Points – Outpatient, Community & Home Costs

Data points	Options	Comments
In-home consultations	Hospital record	Eg: nursing, allied health, or medical specialist visits
Hospital outpatient visits	Hospital record	Surgical, medical, allied health, nursing appointments

Primary care consultations	Parent survey	Parent survey to estimate out-of-network IF care costs
Emergency department attendances	Hospital record Parent survey	Parent survey to estimate out-of-network IF care costs
Diagnostic testing	Hospital administration Government or 3 rd party insurers	
Medications	Hospital pharmacy	Prescriptions, over-the-counter
Implanted devices	Hospital administration	Particularly CVAD and enteral feeding devices
Parenteral nutrition	Hospital pharmacy	
Enteral nutrition	Hospital pharmacy	
IV fluid therapy	Hospital pharmacy	
Nutritional supplements	Hospital pharmacy	Enteral and parenteral
Labour cost	Staff survey Hospital record List of tariffs	Usually expressed as time per staff member per patient for given tasks (eg: consultation with surgeon, compounding of PN by pharmacist), multiplied by hourly rate of staff member.
Pump hire	Hospital administration List of tariffs	
Consumables	Hospital administration List of tariffs	Including stoma appliances, tubing, dressings, etc. Data likely to be highly variable in quality.
Transport cost	Demographics Parent survey	Eg: car mileage, cost of public transport, parking
Accommodation costs	Parent survey Hospital administration	

Lost Productivity

Data points	Options	Comments
Days off work	Parent survey	
Loss of employment	Parent survey	Loss of employment or inability to return from parental leave following diagnosis of IF in child
Change in need for government pension/welfare	Parent survey	Practical, if simplistic, estimate of change in financial circumstance associated with IF diagnosis

3. Summary of activities and research findings

Summary of activities

Detailed planning meetings have occurred between members of the INTENS consortium and local grant administrators to define and develop the study design, including agreeing to undertake such a detailed work as that described above.

Researchers at UCL Great Ormond Street Institute of Child Health have undertaken a series of consultations with expert health economists to ensure the robustness of the economic analyses, utilizing best in practice economic modelling techniques and analytics. These collaborations will continue through the data collection and analysis phases of the work.

Recruitment of data collection staff is currently underway at multiple centres.

Summary of literature review

Scope of current evidence base

- The most robust assessment of comprehensive care of paediatric IF was undertaken by Teitelbaum's group covering patients from 1992 to 2005 treated through the CS Mott Children's Hospital in Michigan, USA⁸
- Majority of cost estimates were published in the 1990s⁹⁻¹²
- Majority of studies focus on adult or mixed populations
- Cost estimates vary widely in the literature depending on methodology and context of study, in particular:
 - Era of study
 - Scope of estimate – in particular, most studies estimate the cost of provision of PN only, rather than comprehensively assessing IF care
 - Health care system payer model
- Minimal study of family fiscal costs or lost parental productivity^{13,14}

Major drivers of cost in IF care

- Requirement for PN
 - Study of ambulatory IF care in Canada demonstrated significantly higher annual cost per patient for those on home PN (CAD\$320,369), compared to patients on home EN (CAD\$8969)¹⁴
 - PN requirement is associated with many other high cost interventions in IF care, including hospital admissions and treatment for infectious complications^{10,14,15}
 - Cost of PN has been estimated in Europe at:
 - For neonates – €55 per bag of PN per day
 - For infants – €84 per bag of PN per day
 - For children – €118 per bag of PN per day⁷
- Hospital accommodation costs

- Mean annual hospital charges can be as high as US\$420,000⁸
- Home care costs
 - Providing PN in the community is less costly than hospital-based PN^{1,8,16}
 - However, Spencer et al observed home care costs to rise each year of the first 5 years of IF care, which was explained by persistently high cost of PN and the need for additional therapies, particularly enteral nutrition and antimicrobial therapy⁸
- Infectious complications
 - Up to US\$10,000 per episode requiring hospital admission, more if CVAD requires replacement¹⁰
 - Antimicrobial therapy makes substantial contribution to home care cost⁸

Patient factors in cost of IF care

- Length of residual intestine
 - Strong positive correlation between small intestine length <10% of predicted for gestational age and higher cost of care⁸
- Time to weaning of PN
 - According to Spencer et al, cost of care highest in the first year following diagnosis (>US\$500,000), but rapidly reaches a plateau of around US\$250,000-300,000 in subsequent years⁸
- Eventual IF-related mortality⁸

Importantly, there are no currently available studies that simultaneously address:

- Paediatric IF specifically (i.e. not simply supportive nutrition alone, nor a mixed adult and paediatric cohort)
- Hospital and community-based care
- Parenteral and enteral nutritional support
- Comparison of costs across multiple centres across separate continents

4. Conclusions and future steps

Published evidence to this point does not adequately describe the economic burden of the current standard of care for paediatric intestinal failure. Published work either does not specifically address the IF population, especially in children, or it is specific to a particular service. However, it is known that the costs of hospital accommodation, surgery and other procedures, consumables, and staff time are high for treatments used in intestinal failure care.

The study currently underway seeks to provide a definitive answer to the cost of the current standard of intestinal failure care in hospitals involved in the INTENS consortium, which exist across diverse health care systems. The study's methodology will allow other centres to estimate their own local costs easily,

thereby providing a reference to which intestinal failure centres can compare themselves.

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