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**Regionally acquired intestinal failure data suggest an underestimate in national service requirements.**

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## ABSTRACT

**Objectives, setting and patients:** With complete case referral for prolonged parenteral nutrition (PN) beyond term equivalent, serving a stable population of 1.25 million people, we describe the long term outcome and survival of patients referred to an intestinal failure (IF) nutrition support team over the first eight years of existence at a regional paediatric centre, and extrapolate to potential numbers of national home parenteral nutrition (HPN) cases and intestinal transplantation data.

**Design and outcome measures:** Retrospective analysis detailing patient demographics, interventions, use of home parenteral nutrition (HPN), occurrence of intestinal failure associated liver disease (IFALD), and outcomes of enteral adaptation, survival, and referral for and receipt of organ transplantation.

**Results:** 23 patients were referred over eight years, 20 being PN dependent within the neonatal period. Diagnoses included short bowel syndrome (SBS) (18), neuromuscular abnormalities (4) and congenital enterocyte disorder (1). 12,696 days of PN were delivered with 314 confirmed episodes of sepsis at a median of twelve episodes per patient. 144 central venous catheters (CVC) were required at a median of four per patient. IFALD occurred in seventeen (73%) patients, with ten (44%) referred for transplant assessment. Thirteen (56%) children received HPN. Overall mortality was 44%. A significant predictor for survival in the SBS group was residual bowel >40cm (82% vs. 28%, p=0.049).

**Conclusions:** Survival for IF at 56% was lower than reported from non UK supra-regional centres, and nationally collected data, possibly reflecting pre-selected referral populations. Data from regional centres with complete ascertainment may be important both when counselling parents and when planning regional and national HPN and IF specialist services.

## **Abbreviations**

IF- intestinal failure, PN- parenteral nutrition, IFALD- intestinal failure associated liver disease, SBS –short bowel syndrome, NEC- necrotising enterocolitis, CIPOS- congenital intestinal pseudo-obstruction syndrome, RHSC- Royal Hospital for Sick Children Edinburgh, CSBLT- combined small bowel liver transplant, HPN- home parenteral nutrition, ICV- ileocaecal valve, CVC- central venous catheter, ILT- isolated liver transplant, NST- nutrition support team NST.

## **OBJECTIVES**

Intestinal failure (IF) is defined as the reduction of functional gastrointestinal mass below that needed for digestion and absorption of fluid and nutrients for maintenance in adults and growth in children (1-3), and can be separated into three main groups by pathogenesis (4;5). 1. Short bowel syndrome (SBS) (6). 2. Neuromuscular disorders of the gastrointestinal tract including; Long segment aganglionosis (Hirschsprung's Disease) and congenital intestinal pseudo-obstruction syndromes (CIPOS)(7). 3. Congenital enterocyte disorders (8;9). Parenteral nutrition (PN) has dramatically improved the previously dismal prognosis for this patient population (1;5;10). However, significant complications of management, such as central line sepsis, intestinal failure associated liver disease (IFALD) and growth failure, have contributed to long-term morbidity and mortality in IF (1;5;11). Combined small bowel and liver transplantation (CSBLT) now offers alternative treatment for patients surviving with irreversible IF (5;12). Currently care for IF in the UK is performed in regional paediatric gastroenterology and nutrition services with multidisciplinary nutrition support teams (NST). (13) There is a single intestinal transplantation unit located at Birmingham Children's Hospital. Outwith the U.K., national centres of excellence for management of long-term IF and HPN exist (14). Outcomes for patients with longstanding IF appear to be improving from data both collected from national centres of excellence (outwith the U.K.) and from intestinal transplantation services (14;15). However there is a paucity of incidence and outcome data for such patients from regional centres. This study aimed to describe the incidence, prevalence and long-term outcome of IF referred to a regional nutrition support team (NST), when all cases from a geographical region are obtained, and to extrapolate these data for potential use of national HPN and intestinal transplant services.

## **METHODS**

### **SETTING AND PATIENTS**

Following the appointment of a consultant in paediatric gastroenterology and nutrition in August 1997, the Royal Hospital for Sick Children, Edinburgh (RHSC) developed a multidisciplinary IF NST. This consisted of a consultant paediatric gastroenterologist, consultant paediatric surgeons, specialist paediatric nutrition nurse, paediatric dieticians, specialist paediatric pharmacist, ward nursing staff, and specialist social worker. RHSC serves as the single tertiary paediatric unit to the region of SE Scotland with a stable population of around 1.25 million and provides all PN to post-term infants and children. Referral to the team is made from within RHSC (Medical or Surgical teams), from four other district general paediatric units, two level three NICU and two level two neonatal nurseries within the region. The aims of the team were to optimise the long term outcome of patients identified as having IF by maximising enteral nutrition, facilitating the use of parenteral nutrition at home (HPN) and acting as a point of referral to UK national transplantation services when required.

In-patients are managed in a combined medical and surgical ward and are reviewed by the multidisciplinary ward-round on a daily basis with alterations to therapies and PN being made to optimise bowel adaptation. PN prescription is done in conjunction with a senior specialist paediatric pharmacist. Central lines are placed and removed by paediatric surgeons dedicated to the NST. Training and supervision of line-care by ward staff, junior doctors and parents is coordinated by a dedicated nutrition nurse

specialist. PN is always cycled to an optimal level dependent upon age, prematurity and clinical status. Enteral feeding is modified by the NST specialist paediatric dietician. As a rule, when available, mother's milk is the first feed. When not tolerated a semi elemental feed is normally trialled followed, if necessary, by completely elemental diet. Feeds high in MCT are given when patient is significantly cholestatic. Modular feeds are reserved for patients with specific indications, such as suggestion of very low threshold of carbohydrate tolerance. Bilirubin, liver enzymes and synthetic function are assessed weekly with micronutrient nutritional screening on a monthly basis. When IFALD is identified management involves a protocol of investigation for other causes of cholestatic liver disease, a review of enteral and parenteral nutrition and commencement of ursodeoxycholic acid. A standard sepsis protocol of broad spectrum antibiotics for fever above 38.5<sup>0</sup>C or recurrent fever above 38.0<sup>0</sup>C exists. Individual patient sepsis protocols are established in conjunction with a specialist consultant microbiologist and are available on the front of patient's case notes. The specialist nutrition nurse trains parents to handle PN and the dedicated social worker identifies and rectifies non-medical hindrances to discharge. HPN patients are discussed in a multidisciplinary meeting weekly, with emphasis being placed on optimising enteral nutrition, sepsis prevention and management and quality of life issues. Patients are seen in a dedicated IF clinic after discharge. We work within the Scottish HPN managed clinical network ([www.shpnmcn.scot.nhs.uk](http://www.shpnmcn.scot.nhs.uk)) which aims to facilitate excellence and standardisation of care for all HPN patients across Scotland.

## **DESIGN AND OUTCOME MEASURES**

Data were obtained retrospectively from the medical records of patients from the IF NST database, logged prospectively from August 1997 to June 2005. These data were analysed by database Excel for Windows (Microsoft Office XP). Entry criteria were patients referred to the regional paediatric NST with a primary gastrointestinal disorder, and whom must have received > 28days PN by completion of study. Demographic data obtained for patients at point of referral to the team were date of birth, age at referral, birth weight, gestational age at birth, diagnoses, weight at referral and number of days of PN at referral. Patients were grouped according to cause of IF - SBS, neuromuscular disease or enterocyte disorder.

SBS patients had additional data recorded for primary diagnosis. Initial surgical records were reviewed and residual small bowel length recorded. Where only length of bowel resected was recorded, an estimated residual bowel length was calculated using a standardised formula against gestation (16). Other surgical details recorded were; primary anastomoses, defunctioning stomas, and whether the ileo-caecal (ICV) valve had been removed. Patients with neuromuscular disease had primary diagnosis and subsequent surgical procedures noted. Longitudinal data were then obtained to evaluate patient management and outcomes in the following categories:

**1. PN and enteral adaptation;** Recorded items were the total number of days of PN, total number of semi-permanent tunnelled central venous catheters (CVC) required and other complications of PN (line occlusion, thrombosis, growth failure, pubertal delay, IFALD), proportion of patients who received HPN, and the number of confirmed episodes of bacterial/fungal sepsis (defined as clinical signs of sepsis in combination with a significant growth of appropriate organism from CVC culture, peripheral line culture or peripheral venous culture, with resolution of symptoms with

appropriate antibiotic therapy). Further cultures of the same organism were not considered to be a separate septic episode until patient had remained afebrile for five days off antibiotic treatment. We defined enteral adaptation as <10% weight loss after cessation of PN followed by sustained weight gain. Time to adaptation was recorded in months and enteral feed regimen at time of adaptation was also recorded.

**2. IFALD, transplantation and outcome;** Patients were defined as having IFALD (direct bilirubin >50 $\mu$ mol/l) (17) or severely cholestatic (direct bilirubin >100 $\mu$ mol/l) either at referral or during their course of treatment. Criteria for referral to the intestinal transplantation unit were conjugated Bilirubin > 150 $\mu$ mol/l outwith septic episodes, or progressive fibrotic liver disease on biopsy, lack of vascular access, poor long-term prognosis or very impaired quality of life for parents/carers or patient. We noted whether patients required referral for assessment for CBSLT or ILT and if they received this assessment, we also noted whether patients were then listed for transplantation, and if so, whether they received transplantation. All transplantation and transplant assessment was performed at the UK supra-regional Intestinal Transplant Assessment Centre at Birmingham Children's Hospital, Birmingham, UK. Outcome data recorded included patient survival, death, age at death, cause of death and death whilst awaiting organ transplantation.

**3. Extrapolation of regional results to national situation;** To determine how our data would translate into national statistics, we calculated our service population to be 2.1% of the UK (1.25/60million x 100%). We then extrapolated what annual registration of HPN patient, annual referral to the intestinal transplantation unit, CSBLT and ILT would be based on these figures ((n x 100/2.1)/ 8 years). We compared our figures with current published UK data on paediatric HPN registration (18) and referral to the intestinal transplantation unit (15).

Normally distributed continuous data are described as mean (Standard Deviation), non-normally distributed continuous data are described as median (range), and categorical data described as number (%). All statistical analyses were performed using Minitab version 14 (Microsoft office XP) and a p value of  $\leq 0.05$  was considered significant. Ethical approval is not required for this type of study, confirmed by correspondence with our Local Research Ethics Committee.

## **RESULTS**

Twenty-three patients were referred to the team (18 SBS, 4 neuromuscular disorders, 1 epithelial disorder). Patients referred had a median gestation of 35wk (range 25-38 wk), birthweight of 2.44kg (range 0.65-3.55kg), and were referred at a median age of two months (7 days-81 months) having received 35 days PN (0-370 days) respectively. (Patient histories are available as a supplemental file). Some variability existed in time to referral as a small proportion of patients were already established on PN before the creation of the NST. Patient demographics are summarised in table 1. Out of the SBS cohort, seven (39%) had residual bowel length less than 40cm, with eight (44%) having had their ICV removed.



Patient	Diagnosis	Gestation (weeks)	Birth weight (kg)	Age referral (Months)	No of Days PN	Cholestatic
Patient 1	SBS ( NEC)	28	0.65	1	36	no
Patient 2	SBS (gastroschisis)	36	2.75	3	75	yes
Patient 3	SBS ( NEC)	31	1.38	1	35	yes
Patient 4	SBS (NEC)	38	2.3	13	370	yes
Patient 5	SBS (NEC)	32	1.73	21	210	no
Patient 6	Long segment Hirschsprungs	39	2.78	16	0	no
Patient 7	SBS (NEC)	30	1500	4	14	no
Patient 8	Congenital enterocyte disorder	40	3.98	<1	0	no
Patient 9	Long segment Hirschsprungs	38	3.91	3	0	no
Patient 10	SBS (NEC)	33	2.1	2	45	yes
Patient 11	SBS (SMA thrombosis)	37	3.0	6	0	no
Patient 12	CIPOS	39	3.21	81	0	no
Patient 13	SBS (NEC)	25	0.86	3	90	yes
Patient 14	SBS (ileal atresia)	35	2.68	<1	21	no
Patient 15	SBS ( gastroschisis)	36	2.44	<1	3	no
Patient 16	SBS (NEC)	25	0.85	3	55	yes
Patient 17	SBS (NEC)	29	1.7	2	46	yes
Patient 18	CIPOS	36	4.1	2	50	yes
Patient 19	SBS (ileo-jejunal atresia)	36	3.55	2	21	no
Patient 20	SBS (NEC)	30	1.68	4	45	no
Patient 21	SBS ( ileal atresia)	35	2.8	<1	0	No
Patient 22	SBS (meconium ileus)	39	2.8	<1	12	no
Patient 23	SBS (NEC)	29	1.18	1	43	yes

**Table 1: Demographic data of 23 IF patients referred over eight years**

Cholestasis was defined as serum bilirubin >30 umol/L. Patients were referred before commencing PN (i.e. were commenced on PN by the NST).

**1. PN, Sepsis, HPN and adaptation** 12,696 patient days of PN were delivered at a median of 310 days per patient (range 58-2730 days). Thirteen (56%) patients received HPN. There were no significant differences in demographic details between these patients and those in whom adaptation occurred prior to discharge from hospital. There were 314 confirmed episodes of bacterial sepsis (median of twelve episodes per patient (2-52)) at a mean of one septic episode per 40.4 patient days. Bacterial and fungal growths identified in blood culture are summarised in table 2.

	<i>Positive Cultures</i>	<i>%</i>
<i>Coagulase Negative Staphylococcus</i>	145	43
<i>Enterococcus Faecalis</i>	43	12
<i>Klebsiella</i>	36	11
<i>Enterobacter Cloaccae</i>	35	11
<i>E. Coli</i>	18	5
<i>Candida</i>	15	4
<i>Staphylococcus Aureus</i>	12	3
<i>Streptococcus</i>	11	3
<i>Pseudomonas</i>	10	3
Other	11	3

**Table 2: 314 Positive cultures from Central Lines from 23 IF patients receiving PN**

A total of 144 CVC were placed (median four per patient (range 1-24)). 13/23 patients received HPN. Patients who achieved HPN had a significantly lower infection rate in comparison to those who received all PN in the hospital (1 infection per 45.1 PNdays vs. 1 per 30.2 PNdays  $p=0.023$ , 95%CI -27.6,-2.3). CVC lasted a mean of 80.6 patient days, and only five CVC (3%) were removed because of total line occlusion. We identified three major thrombotic complications (one right internal jugular thrombosis, one bilateral iliac and one vena cava right atrial). No patients were referred for transplant assessment because of loss of vascular access. Only ten (44%) patients achieved full enteral adaptation, two of these being post CSBLT and one post ILT. Adaptation was achieved at a median of 31 months (range 9-47 months).

**2. IFALD, organ transplant and outcome** Nine (39%) patients had IFALD at referral with six (27%) having severe cholestasis. Of the SBS cohort, eight (44%) cases had already developed IFALD at time of referral with six (33%) being severely cholestatic. Seventeen (73%) patients developed cholestasis during the study. Early age of referral to the NST (<3/12) and frequent episodes of infection (<30 days) positively correlated with subsequent IFALD development (table 3).

<b>Comparator</b>	<b>IFALD development (%)</b>	<b>Significance</b>
NEC vs. Non NEC	7/11 (64%) vs. 9/12 (75%)	$p=0.667$
Age <3/12 vs. $\geq$ 3/12 at referral	11/11 (100%) vs. 5/12 (42%)	$p=0.005$
Infection rate <30 days vs. $\geq$ 30 days	9/9 (100%) vs. 8/15 (53%)	$p=0.022$
Preterm vs. Non preterm	13/15 (86%) vs. 5/8 (62.5%)	$p=0.297$

**Table 3: IFALD development according to patient characteristics**

Twelve (52%) patients developed cholestasis reaching levels which indicated need for referral to the intestinal transplantation unit in Birmingham for assessment (total bilirubin consistently  $>150\mu\text{mol/l}$  out-with septic episodes). Ten were assessed; one family declined assessment and another patient died whilst awaiting assessment. Five (22%) patients have received transplants (four CSBLT, one ILT) and two patients died whilst awaiting transplantation. Three remained on the transplant list at the close of audit. In total ten (44%) patients died. Causes of death included end stage liver disease (4), sepsis (2), gastrointestinal haemorrhage, post-transplant multi-organ

failure, renal failure and CMV encephalopathy post-transplant. Median age of death was 12 months (range 7-107). Significant predictors for survival in the SBS group were residual bowel length >40cm (82% vs. 28%, p=0.049), >3 months age at referral to NST (81% vs. 33%, p=0.036) and proceeding to HPN (77% vs. 30%, p=0.04) (table 4).

Comparator	Survival (%)	Significance
NEC vs. Non NEC	8/11 (73%) vs. 4/12 (34%)	p=1.000
Age <3/12 vs. ≥3/12 at referral	4/12 (33%) vs. 9/11 (81%)	p=0.036
Preterm vs. Non Preterm	9/15 (60%) vs. 4/8 (50%)	p=0.685
HPN vs. Non HPN	10/13 (77%) vs. 3/10 (30%)	p=0.040
Cholestatic vs. Non Cholestatic at referral	8/14 (57%) vs. 5/9 (55%)	p=1.000
Residual bowel length ≥40cm vs. <40cm	9/11 (82%) vs. 2/7 28%	p=0.049
ICV intact vs. ICV removal	6/10 (60%) vs. 5/8 62.5%	p=1.000
Infection rate <30 days vs. ≥30days	2/9 (22%) vs. 10/15 (66%)	p=0.089

**Table 4: Outcome statistics according to patient characteristics**

**3. Extrapolation of regional results to national situation;** We calculated that our total eight year caseload of 23 patients, thirteen HPN patients and twelve patients with indications for referral to transplantation services extrapolate to 1095, 619 and 571 respectively nationally over eight years. Ten (77%) of our HPN patients had SBS in comparison to the national average of 40%(18). 11/12 (92%) of our patients indicated for referral to transplantation services and 9/10 (90%) of patients referred had SBS, compared to 89/159 (55%) in the intestinal transplantation unit (15). Our extrapolated annual national registration of HPN patients of 77.4 compares with 14.8 (89/6years) from the BANS report 2000-2005 (18) and our annual rate of referral to the intestinal transplantation unit of 71.4 compares to 17.3 (104/6 years) actual referrals to the intestinal transplantation unit (15) (figure 1).

## DISCUSSION

IF in the paediatric population now appears to have a better prognosis in comparison to adults (14;19), with a greater proportion of patients achieving complete enteral adaptation over time. PN and HPN are the mainstay of medical therapy whilst awaiting this adaptation process. Most reviewers relate increased survival to improved safety of delivery of PN, development of NST and earlier identification of patients with irreversible disease or complications such as IFALD that require referral to transplant services.

On initial reflection our data relating to sepsis rate (1 per 40.4 patient days), severe IFALD (52%), and survival rate (56%) over eight years represent disappointing outcomes in comparison to other published work (14;15). However, this may be partially attributable to variations in reporting in terms of definition of IF, and our local case mix. This may then have secondary effects on complications of IF treatment such as sepsis and development of IFALD. IF has been defined in paediatric

surveys as any patient requiring PN for greater than 28 days. Other case series have included patients without primary intestinal disorders (including oncology and intensive care patients requiring PN support during prolonged courses of inpatient illness), or patients whom have not required PN beyond term (20). HPN is not an issue for these patients, and they are not candidates for CBSLT. Data gathered from national centres outwith the U.K. may reflect a pre-selected group that have demonstrated stability on PN for a period of time, and thus produces a referral bias which can lead to improved long-term outcomes (1;15). Other regions may also have patients with IF being managed beyond term by service that would not fulfil the criteria for NST. Our institution serves a region of 1.25 million population; it has a unique service organisation. As the only centre performing neonatal surgery for the region, with a single NICU providing PN after term, and a single NST, we are confident that we have complete early ascertainment of patients with primary intestinal disorders who have a potential requirement for PN beyond term (as well as all of the older infants, children and teenagers requiring PN). These neonatal patients are those who are likely to require tertiary NST services, as they are the patients who have potential to receive HPN and/or require referral to transplant services.

### **PN, HPN and adaptation**

We reported on over 12,000 patient days of PN with 56% of patients receiving HPN. Koglmeier et al (20) found that only 5% of IF patients required HPN over 2 years. This difference may in part be attributed to disease severity in our patients. Only 44% of our patients achieved enteral adaptation (not all of these patients required specialist NST input). Factors shown to predict time to enteral adaptation in SBS include length of remaining small bowel; a length of  $\geq 40$ cm has been shown to a significant factor for earlier adaptation (10). The loss of the ICV, intestinal inflammation and bacterial overgrowth also appear to negatively affect adaptation (21). The primary stimulus for the bowel adaptation process is enteral nutrition, with early post operative feeding predicting shortened period of dependency on PN (22). Other studies have reported marked success in weaning long-term PN patients when instituting an intestinal rehabilitation programme with Torres et al (23) achieving 31/37 HPN patients weaning successfully. This figure falls to 64% when dealing with neonatal onset diseases as described by Diamond et al (24). However the effects of prematurity on outcome are not described in either cohort.

### **Sepsis rates and IFALD**

We report a high incidence of bacterial sepsis with a median of twelve episodes of sepsis per patient at a rate of one per 40.4 catheter days. Clear guidance for the use of long term CVC for PN delivery now exist for paediatric patients; the use of dedicated single lumen subclavian catheters is recommended (25). A dramatic reduction in bacterial sepsis rates has been shown to be associated with both non-touch sterile access of catheters, and having a dedicated PN nurse formally training all ward staff, medical staff and parents on how to access CVC (25;26) Despite early institution of these measures our sepsis rate remains higher than other series, however the definition of septic episodes in the literature is often unclear (27-29) and there is a lack of a standardised method of reporting.

In our series 73% of 23 patients developed IFALD and 52% had indications for referral for transplant assessment. The relationship between IF, PN and cholestasis is not clear. Although individual constituents of PN have been shown to be hepatotoxic

(11;30;31), IFALD itself has a multifactorial aetiology. Patients who are able to take some of their nutrition enterally appear to have partial protection from IFALD in comparison to patients who receive all their calories intravenously (22;32). In addition normal functioning small bowel would appear to protect adult populations against cholestasis when receiving PN (33). Recurrent bacterial sepsis has been heavily implicated in the development of IFALD in neonates and children (11). Colomb et al (34) reported a much lower rate of 23% IFALD in HPN patients, although the proportion of patients who were term or older children was greater in this cohort. Koglemeier et al (20) reported that IFALD complicated 59% of paediatric cases of IF. Sondheimer et al (35) reported a similar incidence of IFALD (67%) in a series of 42 patients with SBS, and only 17% of these patients went on to develop liver failure. Our criteria for transplant assessment are mostly based on serum bilirubin rather than synthetic liver function, thus making direct comparison of results inappropriate. 52% of patients had indications for transplant assessment, 22% of our patients received organ transplantation and a further two patients died on the transplant waiting list. This exceeds the previously described figure of 15-20% requiring transplantation (1). This may partly be a reflection of the severity of disease in our cohort and also the relatively high incidence of bacterial sepsis predisposing to IFALD development. In our series, 48% of detected organisms on blood culture were found to be either gram negatives or fungal, both of which are strong predictors for IFALD development (35). We suggest that there is a greater burden of liver disease if all IF patients in a geographical area are ascertained, rather than the lesser burden suggested by either nationally gathered data (18) or data from a single or small number of centralised national referral centres(14;15).

### **Outcome**

We report only 56% survival over 8 years which is lower than other recent studies. Diamond et al (24) reported 62.5% over three years in an SBS cohort, Colomb et al (34) reported 81% survival over 10 years in a paediatric HPN cohort, and Koglemeier et al (20) reported 94% survival over two years in a paediatric IF series. We would, however, again suggest that the differences in patient ascertainment and patient mix, namely high rates of early referral, prematurity and NEC (48% of our cohort had NEC as opposed to 24-30.8% in other paediatric IF populations (20;36)), may in part explain this low survival rate although numbers of patients are admittedly small. It is of note that of our population referred to the NST very early (<3 months of age), primarily because of early onset cholestasis, have a particularly poor prognosis (survival 33% compared to 88% if  $\geq 3$  months) and would have been omitted from other published cohorts of this condition (14). The 88% survival rate of those infants referred at or after 3 months of age is comparable to the survival data reported from large single centre HPN programmes, such as the 81% survival rate in 302 patients reported from Paris (34).

### **CONCLUSIONS**

The economic impact of HPN for paediatric patients is high (37). The cost effectiveness of CBSLT versus long term HPN is not clear (38), and is a somewhat artificial argument in light of donor organ shortage for the paediatric population. Local factors (high incidence of NEC) may contribute to our high use of HPN. The registration of paediatric HPN to the BANS registry is not compulsory and therefore this data is likely to be incomplete. However the great excess in our series of HPN usage and indications for CBSLT services, compared with nationally collected data

(15;18) strongly suggests that, nationally, patients may be lost due to early death, discontinuation of care, or non-referral, prior to reaching regional paediatric gastroenterology services, let alone transplantation services. Outcomes data are vital for service planning, but must reflect the full spectrum of the clinical arena; we suggest that with firmer establishment of managed clinical networks for paediatric nutrition support, that the patterns of care for IF patients in the UK will increasingly mirror the current practice in our region in terms of ascertainment and outcomes, with full referral of all cases of IF from early neonatal life. Such data may be of importance both when counselling parents and for future planning of regional IF and national transplant services. Our data also suggest there may be greater need for ILT and CBSLT assessment than currently recognised, and we suggest that the ongoing further national surveillance of IF may clarify the current position (BIFS study [http://bspghan.org.uk/working\\_groups/nutrition.shtml](http://bspghan.org.uk/working_groups/nutrition.shtml)).

The treatment of IF in the paediatric population remains a therapeutic challenge for the future. These patients have highly specialised needs, best served by tertiary care units where sufficient surgical, medical, dietetic and nursing expertise for their management can be developed yet delivered closer to home. Overall throughput is low in terms of numbers, even in large centres. This makes randomised controlled trials of therapies difficult to organise in terms of feasibility. In the absence of a robust evidence base, standardisation of care with clinical guidelines for PN usage (22) together with dissemination of skills through managed clinical networks are the best current ways to optimise care. Close working relationships between regional tertiary units and the central transplant centres is of particular importance. Patient populations in the regional centres may differ from the experience of intestinal transplantation units; sharing, and honest appraisal, of patient outcomes between regional and intestinal transplantation centres may also help the counselling of parents, regional and national service planning for both HPN and intestinal transplant services, and long-term outcomes for these patients within the U.K.

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**Conflicts of Interest:** None

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**What we already know on this subject:**

- **The prevalence of IF is rising and long-term survival of HPN patients from some national centres has risen to >90% in recent years**
- **IFALD contributes significantly to long term morbidity and mortality of these patients.**

**What this study adds:**

- **Outcomes from this regional data are poorer than previously described national data; this may reflect a fuller ascertainment and thus a greater burden of disease than currently recognised.**
- **Regionally obtained data suggest an underestimate in national resource requirements for HPN and CSBLT or ILT services.**





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## **Figure Legend**

**Figure 1:** Comparison of RHSC Edinburgh regional data and extrapolation to national situation in terms of HPN registration (18) and indication for referral to CBSLT services) (15) expressed as patients per year.

