Wide variation in organisation and clinical practice of paediatric intestinal failure teams: an international survey

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ABSTRACT

Background & aims

We aimed to assess the current organisation and clinical practice of teams treating children with intestinal failure (IF) across Europe and compare the results with the current guideline.

Methods

A two-part online survey was sent to all the major European specialist IF services. The first part concerned general information about the team and patients monitored. The second part concerned important care topics such as vascular access and monitoring of complications. No patient identifiers were collected.

Results

Seventy-three respondents completed the first part, representing 61 teams in 20 countries. The median number of children on parenteral nutrition (PN) at home per team was 15 (range 1–125). Teams consisted of the following members: paediatric gastroenterologist (present in 100% of the teams), dietitian (95%), specialist nurse (92%), paediatric surgeon (89%), pharmacist (82%), psychologist (66%), social worker (62%), speech therapist (48%), physiotherapist (38%), general paediatrician (33%). The second part was completed by 67/73 respondents (59/61 teams). Vascular access care was comparable with the guideline. Somatostatin analogues were prescribed by 14% of the IF teams and probiotics by 44% of the teams. Prophylactic anticoagulation was used by 46% of the teams. In 81% of the teams a multicomponent lipid emulsion containing fish oil was routinely used. Bone densitometry was regularly performed in 75% of teams, but never performed in 19%.

Conclusions

In conclusion, there is a wide diversity of composition of IF teams and their number of patients treated. Overall, there is good compliance to the current guideline. Clinical practice that varied most was the standard use of medication such as probiotics and somatostatin analogues, and standard monitoring of long-term complications. Experience regarding specific treatment options should be shared. Moreover, international agreement on standards of care with focus on implementation of the guideline is needed to optimise care and improve outcomes of children with IF.

INTRODUCTION

Children with intestinal failure (IF) depend on parenteral nutrition (PN). When IF is irreversible for several months, PN can be given at home as home PN (HPN). Despite the complexity of the treatment, there is a scarcity of available evidence-based guidelines for the treatment of these patients. The guideline that is currently mostly used in Europe is provided by the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN).[1] This is a guideline on paediatric PN, including chapters on HPN and complications of PN. Due to the lack of good quality trials in children with IF, many of the recommendations provided by this guideline are based on limited evidence and largely driven by expert opinion. Additionally, this guideline was based on literature published before 2004 and clinical practice may have changed since then.

One of the recommendations of this guideline is that the management of children with HPN should be undertaken by multidisciplinary teams, including physicians, pharmacists, nurses, dietitians, social workers and psychologists.[1] There are, however, no data available about the organisation of existing paediatric IF teams and current clinical practices are unknown. The purpose of our study was therefore to provide an overview of the organisation and current practice of specialised paediatric IF teams across Europe and compare these results to the ESPGHAN/ESPEN guideline.[1] With this knowledge, future harmonisation and optimisation of clinical guidelines could be achieved. Our hypothesis was that the current guideline has not been universally implemented, leading to a wide variation in clinical practice. We expected that differences are the most striking in areas with the weakest evidence. To assess the differences and similarities, we performed a survey among European paediatric IF teams.

MATERIAL AND METHODS

We conducted a two-part online survey between September 2016 and January 2017. The online survey consisted of 40 questions regarding local protocols and strategies and was provided in English. The questionnaire is available as supplement (Supplementary data 1). Testing of clarity and relevance of the survey was performed by four independent clinicians in four centres (Erasmus Medical Center-Sophia Children's Hospital, Rotterdam, the Netherlands; Academic Medical Center-Emma Children's Hospital, Amsterdam, the Netherlands; University Hospital of Gent, Belgium; and Great Ormond Street Hospital, London, United Kingdom).

In the first part of the survey, respondents were asked to fill in some general information about their IF team and the number of patients monitored by their team. Respondents who completed the first part of the survey were invited for the second part. This part concerned specific topics important in the care of children with IF on HPN. Several reminders via e-mail were sent after the first invitation. If more than one questionnaire was returned from a single IF team, the mean of the received answers was used.

Since there is no overall list available of centres providing HPN in Europe, an invitation to the survey was electronically sent to members of the ESPGHAN Network for IF and Transplantation, to members of the British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) and to members of the special interest group Paediatrics of ESPEN (not necessarily known to have an IF team). In addition, respondents were asked to forward the survey to other IF teams in their country or members or colleagues involved in the management of children with IF. Therefore, it is not known exactly how many IF teams were invited to complete the survey.

The local Institutional Review Board of the Erasmus MC in Rotterdam waived the need for informed consent (MEC-2016-503) since no patient identifiers were collected. The trial was registered in the Dutch Trial Register at number 6062 (http://www.trialregister.nl).

Statistical analysis was performed using IBM SPSS statistics 21 for Windows (IBM, Armonk, New York). Categorical variables were summarised as frequencies and percentages, and continuous variables as mean ± SD when normally distributed or as median and interquartile range (IQR) or range when not normally distributed. Data obtained from the survey were compared to the current ESPGHAN/ESPEN guideline.[1] Differences between teams with ≤ 10 patients on HPN and teams with >10 patients on HPN were analysed using the Chi-square test. Statistical significance was defined as a p-value <0.05.

RESULTS

Part one: general information of IF teams

Seventy-four respondents completed the first part of the survey. One was a duplicate reply and therefore deleted. None of the other questionnaires were removed because of missing data. Seventy-three questionnaires were analysed, representing 61 teams in 20 countries, as shown in **Figure 1**.

Figure 1. Sixty-one teams (in yellow) from 20 countries (in blue) participated in the survey. Israel is not shown on map.

In 9 centres, more than one member of the IF team completed the first part of the questionnaire with a maximum of 3 completed questionnaires in one centre. The questionnaire was filled in by different members of the IF teams, distributed as follows: 58 paediatric

gastroenterologists, 4 dietitians/nutritionists, 3 paediatric surgeons, 3 paediatricians, 3 nurses/nurse practitioners, 1 paediatric hepatologist and 1 paediatric metabolic diseases specialist. Ninety percent of the teams were linked to university hospitals and 9 of the teams (15%) were combined with an adult IF team. All IF team characteristics are shown in **Table 1**. Regarding the composition of the IF team, 46% of the teams consisted of a physician, pharmacist, nurse, dietitian, social worker and psychologist. Other IF teams members mentioned besides the ones shown in Table 1, were transplant surgeon, occupational therapist, endoscopist, home team nurses, interventional radiologist, microbiologist and a nutrition physiologist.

Part two: specific topics important in the care of children with IF

In total, 67 respondents (92%) also completed the second part of the survey, representing 59 of the 61 IF teams (97%) completing the first part.

Vascular access

According to the survey, most IF teams (97%) used tunneled central venous catheters (CVC) (for example Broviac® or Hickmann®) as their first choice. A port-a-cath was (also) standardly used by 10% of the teams, followed by a peripherally inserted central catheter (PICC) in 7% of the teams.

Catheter lock solutions were used by 90% of the teams; in 42% of the teams taurolock™ (combination of taurolidine and citrate) was standardly used, and in 22% and 15% of the teams heparin lock and taurosept® (containing taurolidine) were used respectively (multiple answers per team possible).

Forty-six percent of the teams used anticoagulation as primary prophylaxis in the prevention of catheter-related thrombosis or occlusion. LMWH was the standard in 14% of the teams, whereas heparin lock and vitamin K antagonists were standardly used in 12% and 2% (multiple answers per team possible). LMWH was sometimes used in 19%, followed by heparin lock and vitamin K antagonists in 17% and 14% of the teams (multiple answers per team possible). Reasons for not giving anticoagulation were no evidence (17%), not necessary/no thrombosis seen (7%) and potential side effects (3%). Other reasons mentioned not to give anticoagulation were to decrease the number of manipulations of the CVC and to avoid incompatibility. Additionally, in 19% of the teams anticoagulation was given only when there was a coagulation disorder/hypercoagulable state, for example if there were genetic hyper-coagulation factors present, or other risk factors (previous thrombosis, infection episodes), or when acute thrombosis was suspected or diagnosed.

Table 1. Characteristics of the IF teams (number of teams = 61)

Characteristic			
Experience of IF team	**% of teams**		
<1 year	2		
1 – 5 years	5		
6 – 10 years	15		
11 – 20 years	49		
>20 years	30		
Types of specialists represented in IF teams	**% of teams**	**Number: median (min-max)**	**Hours per week working for IF team per health care professional (median, (IQR)**
Paediatric gastroenterologist	100	2 (1-6)	5 (2-10)
Dietitian	95	1 (0-4)	5 (2-11)
Specialist nurse	92	1 (0-8)	10 (3-20)
Paediatric surgeon	89	2 (0-5)	1 (1–2)
Pharmacist	82	1 (0-3)	5 (2-15)
Psychologist	66	1 (0-2)	2 (1-5)
Social worker	62	1 (0-2)	2 (1-5)
Speech therapist	48	0 (0-2)	2 (1-5)
Physiotherapist	38	0 (0-3)	3 (1-8)
General paediatrician	33	0 (0-5)	5 (2-14)
Number of children on HPN per team	**Median (IQR, min-max)**		
Total	15 (7-21, 1-125)		
Infants (1 month – 1 year)	1 (1-3, 0-25)		
Children (1 – 5 years)	5 (2-9, 0-45)		
Children (5 – 10 years)	3 (2-5, 0-34)		
Children (10 – 15 years)	2 (1-5, 0-30)		
Adolescents (>15 years)	1 (0-2, 0-15)		
Underlying diseases of children on HPN per team	Median (IQR, min-max)		
Short bowel syndrome (SBS)	8 (4-12, 0-88)		
Motility disorder	3 (2-7, 0-29)		
Enteropathy	2 (0-5, 0-23)		
Monitoring of children weaned off HPN	93% of teams		
Number of children weaned off PN monitored by the IF team	Median (IQR, min-max) 11 (6-20, 1-114)		

Abbreviations: HPN, home parenteral nutrition; IF, intestinal failure; IQR, interquartile range; SBS, short bowel syndrome.

Parenteral nutrition

HPN was provided pharmacy-customised and age-weight specific in 78% of the IF teams, as commercial mixed bags in 25% of teams and as commercial mixed bags customised by the pharmacy in 31% of teams (multiple answers per team possible). The type of lipid emulsions used are shown in **Table 2** and an overview of the lipid targets used for infants and older children by the IF teams are shown in **Figure 2**.

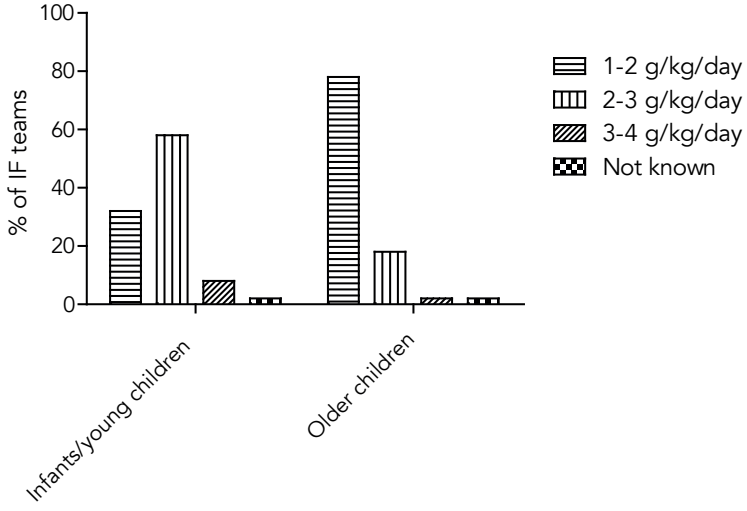
Concerning the maximum amount of parenteral carbohydrates used, 92% of teams reported 16-20 g/kg/d. The protein target as described by the ESPGHAN/ESPEN guideline was followed by 97% of the teams. One team used 2.5-3 g/kg in infants <2 year,

Table 2. Parenteral lipid emulsions used for HPN

Lipid emulsions	Number of IF teams n (%)		
	Standard	**Sometimes**	**Never**
100% soybean based (for example Intralipid®)	4 (7)	12 (20)	43 (73)
Soybean/MCT/olive/fish oil (for example SMOFlipid®)	48 (81)	10 (17)	1 (2)
100% Fish-oil (for example Omegaven®)	3 (5)	33 (56)	23 (39)
Olive/soybean (for example Clinoleic®)	15 (25)	16 (27)	28 (48)
Soybean/MCT (for example Lipoplus®)	4 (7)	4 (7)	51 (86)

Abbreviations: HPN, home parenteral nutrition; IF, intestinal failure; MCT, medium chain triglycerides.

Figure 2. Parenteral lipid targets in infants and older children in g/kg/day



Legend: Boxes represent the number of IF teams.
Abbreviation: IF, intestinal failure.

2-2.5 g/kg for children 2-10 years and 2 g/kg/d for children >10 years, and 1 team used the ratio between calories and nitrogen. In children on full PN, lipids were given 7 nights/week by 46% of the teams, in 5-6 nights by 34% of the teams, in less than 5 nights by 17% of the teams.

In 90% of the teams, HPN was administered by the parents. In other teams, it was administered by home care companies (9%) or hospital nurses in 1 team. In almost all teams, parents were trained by hospital nurses, sometimes continued at home by the companies that provide HPN or by home care companies. The duration of the training varied between 10 hours and 3 months, most of them between 1 and 4 weeks. The HPN was funded by government and/or hospital in 48% of the teams, by health insurance in 39% of the teams, or a combination (2%). In one team, the HPN was paid by the parents.

Enteral/oral nutrition

When oral or enteral nutrition (EN) was started in neonates/infants, breast milk was recommended by 88 % of the teams (**Table 3**). In older children, solid oral feeding was mostly used.

EN was given as a combination of intermittent and continuous feeding (for example 20 h tube feeding with 2 bolus/bottle feeds during the day) by 44% of the IF teams. Some of the teams mentioned that they start with bolus feeds and try continuous feeds overnight combined with bolus feeding during the day when reaching the limit of increasing the EN, whereas other teams mentioned that they start with continuous feeding and later start oral bolus feeding.

In 70% of the IF teams, a speech therapist was involved in the introduction of oral feeding.

Table 3. Use of different types of nutrition in neonates/infants and older children

Number of IF teams n (%)	Standard	Sometimes	Never	Unknown
Neonates/infants				
Breast milk	52 (88)	6 (10)	1 (2)	-
Polymeric formula	9 (15)	42 (71)	7 (12)	1 (2)
Oligomeric formula	13 (22)	44 (75)	2 (3)	-
Monomeric formula	7 (12)	45 (76)	4 (7)	3 (5)
Older children				
Polymeric formula	30 (51)	27 (46)	2 (3)	
Oligomeric formula	15 (25)	39 (66)	4 (7)	1 (2)
Monomeric formula	5 (9)	43 (73)	10 (17)	1 (2)
Solid oral feeding	33 (56)	22 (37)	3 (5)	1 (2)

Abbreviation: IF, intestinal failure.

Nutritional status/bone health/micronutrients

For standard monitoring of growth and nutritional status, weight (100%), height (98%), blood parameters (92%) and head circumference (81%) were used most frequently. Two of the teams mentioned that also bio-electrical impedance analysis was used, and 2 of the teams also monitor body composition and perform indirect calorimetry. **Supplementary Table 1** shows the frequency of micronutrient monitoring. 25-OH vitamin D was measured by all teams (54% every 3 months), whereas vitamin B1, B2, B6 and active vitamin B12 were measured by 45-60% of the teams. In addition, manganese, aluminium and chromium were measured in 32-56% of the teams.

Bone health was monitored with blood parameters in all teams (in 95% every 6 months), whereas DEXA scans were performed regularly in 75% of teams (yearly in 32%) (**Supplementary Table 2**).

Psychomotor development

According to 64% of the IF teams, most of the children go to regular schools. In 31% of the teams, most of the children go to regular schools but with extra assistance. Only in 5% of the IF teams, most of the children go to special needs schools due to medical or intellectual reasons.

In 49% of the IF teams, neuropsychological and psychomotor development is standardly assessed.

Surgery

Serial transverse enteroplasty (STEP) procedures can be performed by 71% of the teams (with a maximum of 15 procedures per centre/year) and Bianchi procedures by 42% of the teams (with a maximum of 25 procedures per centre/year). In 20% of the IF teams, intestinal transplantation was performed with a maximum of 8 intestinal transplants in an individual centre per year.

Medication

Medication such as antibiotics as treatment for small intestinal bacterial overgrowth, antidiarrheal/antimotility agents and probiotics were regularly prescribed in 90%, 73% and 44% of the IF teams respectively (**Table 4**).

Comparison of smaller and larger centres and comparison with current guideline

We compared teams with ≤ 10 patients on HPN (41% of the teams) to teams with >10 patients on HPN (58%). Smaller centres were more often combined with adult teams (28% versus 6%, p = 0.015). Additionally, they significantly less often had a dietitian in the team (88% versus 100%, p = 0.033). There were no significant differences for

the other team members and no significant difference regarding the number of centres fulfilling the recommendation of the ESPGHAN/ESPEN guideline[1] for a multidisciplinary team between smaller and larger centres.

Table 4. Medication standardly used by IF teams (>1 answer possible per IF team)

Medication standardly used	Number of IF teams (%)
Antibiotics as treatment for small intestinal bacterial overgrowth (e.g. metronidazole)	53 (90)
Proton pomp inhibitor (e.g. omeprazole)	53 (90)
Antidiarrheal/antimotility agents (e.g. loperamide)	43 (73)
Bile acid sequestrant (e.g. cholestyramine)	38 (64)
Histamine receptor antagonist (e.g. ranitidine)	32 (54)
Probiotics	26 (44)
Prokinetic agents (e.g. erythromycin)	22 (37)
Somatostatin analogue (e.g. octreotide)	8 (14)
A2-adrenergic receptor agonist (e.g. clonidine)	2 (3)
Growth factors (e.g. Glucagon-like peptide-2 analogue teduglutide)	2 (3)

Abbreviation: IF, intestinal failure.

Prophylactic anticoagulation was used significantly more frequently in the teams with more patients (59% versus 28%, p = 0.019), as well as DEXA scans to monitor nutritional status (41% versus 16%, p = 0.038). Bianchi procedure was performed in 20% of the smaller centres compared to 59% of the larger centres (p = 0.003), whereas intestinal transplantation was performed in 8% of the smaller centres compared to 29% of the larger centres (p = 0.043). Regarding medication, proton pump inhibitors were more often used standardly in large centres (97% versus 80%, p = 0.032). For other standardly used medication there were no significant differences. Similarities and differences between the guideline and current practice according to our survey are shown in **Table 5**.

Table 5. Overview of recommendations by ESPGHAN/ESPEN and clinical practice based on the present survey

Element	ESPGHAN/ESPEN (2005) [1] - PN in infants, children and adolescents	Survey - practices of IF teams
Composition of IF team	Multidisciplinary team including physician(s), pharmacist(s), nurse(s), dietitian(s), social worker(s) and psychologist(s). (No GOR)	46% of the teams consisted of a physician, pharmacist, nurse, dietitian, social worker and psychologist.
PN - amino acids	Preterm infants: 1.5-4 g/kg/d (GOR A-B) Neonates: 1.5-3 g/kg/d (GOR D) 2 m – 3 y: 1.0-2.5 g/kg/d (GOR D-C) 3 – 18 y: 1.0-2.0 g/kg/d (GOR B-D)	Almost all teams follow guideline
PN - carbohydrates	Preterm infants: start with 4-8 mg/kg/min (GOR C), maximum 12 g/kg/d after birth (LOE 2-3) Term neonates/children - 2 y: maximum 18 g/kg/d (GOR C) Cyclical PN: maximal infusion rate 1.2 g/kg/hour (GOR C)	Varying glucose targets, mostly 16-18 g/kg/d, maximum of 20 g/kg/d
PN - lipids	Infants: maximum of 3-4 g/kg/d (GOR B) Older children: maximum of 2-3 g/kg/d (GOR D)	Lower lipid targets: 58% 2-3 g/kg/d for infants, 73% 1-2 g/kg/d for older children
PN - lipid emulsions	No evidence supporting the advantage of any of the lipid emulsions. (GOR D)	Most teams routinely used soybean/medium chain triglycerides/olive/fish oil.
PN - composition	Standard PN mixtures usually not suitable for long-term PN in infants and young children. (GOR D) PN solutions providing macro- and micronutrients should be adjusted to individual patient needs. (GOR D)	HPN was provided pharmacy-customised, age-weight specific in 78% of the teams.
Cycling PN	May be used from 3 to 6 months of age (GOR C)	Cycling of PN was mostly based on stable glucose levels, but also on having an older age, weight, enteral intake and a combination of these factors.
Training of parents	By a structured teaching and training programme, conducted by a nurse from the HPN centre's nutrition support team. (GOR D)	Parents were mostly trained by hospital nurses, with a training duration between 1 and 4 weeks.
Vascular access	PICC's and tunneled CVC's should be used in neonates and children receiving long-term PN. (GOR C)	Almost all teams used tunneled CVC's as their first choice. PICC's was standard practice in 7% of teams.
Occlusion of CVC	Urokinase or alteplase for suspected blood deposits and ethyl alcohol and hydrochloric acid for suspected lipid or drug deposits. (GOR D)	97% had a standard procedure, consisting of: urokinase (66%), heparin lock (19%) and alteplase (17%). Other medication used: sodium hydroxide, streptokinase, 70% ethanol and hydrochloric acid.
Prevention of catheter-related occlusion/ thrombosis	Vitamin K antagonists or LMWH may be given prophylactically to patients on long-term PN at risk of or with previous thrombo-embolism. (GOR B)	46% of the teams used anticoagulation: LMWH (standard in 14%, sometimes in 19% of the teams), heparin lock (standard in 12%, sometimes in 17% of the teams), vitamin K antagonists (standard in 2% and sometimes in 14% of the teams) (multiple answers per team possible). Main reason not to give anticoagulation: no evidence.

Table 5. Overview of recommendations by ESPGHAN/ESPEN and clinical practice based on the present survey (continued)

Element	ESPGHAN/ESPEN (2005) [1] - PN in infants, children and adolescents	Survey - practices of IF teams
Removal of CVC	CVC should be maintained until the child is on full EN. (No GOR)	CVC was removed a median of 12 weeks (range 1-26 weeks) after reaching full EN.
Nutritional assessment	Regular monitoring of growth and body composition. (GOR D) Regular measurements of height, weight, and head circumference (<3 years). (LOE 4)	Measurement of weight (100% of teams), height (98%), blood parameters (92%), head circumference (81%), BMI (70%), upper arm/calf circumference (48%), skinfold thickness (34%) and dual energy X-ray absorptiometry (31%).
Monitoring bone health	Regular assessment of bone mineralisation. (GOR D) Bone densitometry: 6 m-1 y interval. (No GOR)	Bone densitometry was used yearly by 32% of teams, never used by 19% of the teams.
Monitoring micronutrients	Periodically monitoring of trace elements. (GOR D) Zinc: 1-3 month interval, vitamin A, E and D: 6 months-1 y interval. (No GOR)	Zinc was measured every 3 months by 41% of the teams. Vitamin A, E and D were monitored with varying frequency ranging from 3 monthly – yearly.
Type of EN	In newborn infants with SBS: breast milk to optimise adaptation. (No GOR) Children with a primary gastrointestinal disease usually require a specific formula when weaning. (GOR D)	Breast milk was recommended in neonates in 88% of the teams. In older children, solid oral feeding was recommended by 56% of the teams.
Mode of EN	EN can be introduced as liquid EN continuously infused over 4 to 24 h. (GOR D) Liquid EN can be given as bolus or sip feeds (orally or artificially). (GOR D) Whenever possible small volumes of oral feeds should be maintained. (GOR D) Bolus feeds or continuous feeding both possible, decision by an expert gastroenterology team. (No GOR)	EN was given as a combination of intermittent and continuous feeding by 44% of the teams, and as oral bolus feeding by 37% of teams. 14% of teams gave EN as continuous feed.

Legend: GOR and LOE according to the Scottish Intercollegiate Guideline Network (SIGN) are defined in **Supplementary Table 3**.
Abbreviations: BMI, body mass index; CVC, central venous catheters; EN, enteral nutrition; GOR, grade of recommendations; HPN, home parenteral nutrition; IF, intestinal failure; LMWH, low molecular weight heparin; LOE, levels of evidence; NA, not applicable; PICC's, peripherally inserted central catheters; PN, parenteral nutrition.

DISCUSSION

The results of our European survey show that there is a large diversity in the composition of paediatric IF teams and the number of patients they are treating. When compared to the current ESPGHAN/ESPEN guideline[1] clinical practice that differed most were lipid targets, the type of catheter lock solution, prophylactic anticoagulation, and monitoring of bone health. In addition, the use of specific medication and the monitoring of psychomotor development were not mentioned in the guideline, but varied widely between the teams.

Regarding the composition of paediatric IF teams, our survey shows that only 46% of teams followed the recommendation of the ESPGHAN/ESPEN guideline[1] and consisted of a physician, pharmacist, nurse, dietician, social worker and psychologist. Previously, it has been shown that treating these children in multidisciplinary teams reduces complications and improves outcome[2-4] and that the risk of death is increased by the absence of a specialist team.[5] When comparing smaller (≤ 10 patients on HPN) versus larger teams (>10 patients), the only member less often present in smaller teams was the dietitian. Next to the composition of IF teams, the number of patients cared for by individual IF teams also varied widely. This variation has been reported previously in the United Kingdom[6,7] and might be due to geographic and organisational reasons, for example the resources available to provide HPN for newly presenting patients.

In general, many similarities between the clinical practice of the teams and the ESPGHAN/ESPEN guideline[1] were found. Beforehand, we hypothesised that the most prominent differences would occur in the areas with the weakest evidence. Our results show, however, that also many similarities were found in these specific areas. The most striking difference between the different teams was the medication routinely used. For example somatostatin analogues were routinely used by 14% of the teams and probiotics by almost half the teams. In addition, half the teams used anticoagulation in the prevention of catheter-related thrombosis or occlusion. Lack of studies about the use of these specific medications most likely explain the variation in clinical practice. Although, limited evidence is available for probiotics[8-11], somatostatin analogues[12-14], A2-adrenergic receptor agonists[15-17] and growth factors[18-22], no directions for clinical use can be given so far and larger intervention studies are definitely needed.

In contrast, prophylactic catheter lock solutions were used by almost all teams. The type of catheter lock solution, however, differed widely, which was also previously reported in a survey among Belgium centres.[23] This might also be explained by financial reasons, since not all catheter lock solutions are reimbursed in every country. In the current guideline nothing is stated about catheter lock solutions, since most research regarding lock solutions has been published after the publication of the current guideline.[24-28]

Since long term PN administration is associated with complications such as low bone mineral density[29,30] and micronutrient deficiencies[31,32], the guideline recommends regular monitoring of bone health and micronutrient status.[1] In contrast to the guideline, bone densitometry was never performed by 19% of the teams, whereas micronutrients such as aluminium and vitamin B12 were not monitored by all the teams.

Another variation in practice when compared to the ESPGHAN/ESPEN guideline[1] was the use of lower parenteral lipid targets. Although not particularly assessed in this survey, this may reflect the increased awareness of possible development of intestinal failure associated liver disease. Most teams routinely used a multicomponent lipid emulsion (SMOF®), in accordance with the ESPGHAN Committee on Nutrition Position Paper that has been published since the guideline.[33]

Ultimately, it is desirable for all children to have a good quality of life and to grow up as normal as possible. According to the survey, in most teams children went to regular schools, sometimes with extra assistance. It is, however, notable that in only half of the teams neuropsychological and psychomotor development was standardly assessed. A recent study showed that children with IF might be at risk of developmental delay[34], emphasizing the importance of neurodevelopmental follow-up.

Our study had some limitations. No response rate could be calculated, since it is unclear which European centres have a paediatric IF team. Therefore it is unknown how many teams did not participate. We have sent an invitation to the survey to a minimum of 45 paediatric IF teams and also received some responses from other teams not directly invited by us. Since all teams involved in the ESPGHAN Network for IF and Transplantation have completed the survey and additionally also smaller teams, we believe that a rather complete overview of paediatric IF care in Europe is provided.

Another limitation is that the guideline from 2005 is not very recent and that clinical practice may have changed since then. Currently, the ESPGHAN/ESPEN is working on a new PN guideline in children, including one chapter on HPN. However, from personal communication with the authors we know that the recommendations in this guideline will only slightly be different and the new guideline will therefore not lead to different conclusions. Next to this, this study describes the compliance with the current guideline, but does not describe actual outcome measures as a quality index. For example, no information is provided regarding the actual nutritional status of the children on HPN, neither on their quality of life, or the number of children able to wean off PN. It was beyond the scope of this survey to relate individual practices to patient outcomes. For example it could be that certain practices might increase the risk of complications. Other practices such as the method of feeding might have an effect on how quickly a child can be weaned off PN. Finally, the heterogeneity of the population of children with IF

may have caused difficulties with completing some questions. The treatment is highly individualised: some questions required an unambiguous answer and only the most applicable answers were provided.

In conclusion, our study is the first to assess organisation and clinical practices of paediatric IF teams in relation to the current guideline. We conclude that wide diversity exists in the organisation of paediatric IF teams and in the clinical practice of these teams in terms of medication and monitoring of long-term complications. To improve the quality of care and optimise outcome for children with IF, there should be agreement on organisation of IF teams and standards of care. In line with the guideline it should be clear which members should at least be part of the multidisciplinary team. Next to this and because of the complex care needed, it is recommended that teams have enough experience to provide HPN care for children. The need for sufficient experience is an important argument for establishing regional referral centres in areas with multiple teams treating few patients. Regarding topics such as the use of specific medication, experience should be shared. This survey provides valuable information that can be used to develop both practical protocols and recommendations with focus on implementation of the guideline, and to develop new international research collaborations between centres.

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SUPPLEMENTARY DATA

Supplementary data 1: Survey

Part 1. General information

In this first part of the survey, we would like to ask you some general information about your IF team.

What is your email-address?

We need your email-address to make sure that part 1 and part 2 of the survey can be linked. Results of the survey will be analysed anonymously.

1. What is your country of work?
2. What is the name of your institution?
3. What type of hospital do you work in?
   - o General hospital
   - o University hospital
   - o Children's hospital (non-university)
   - o University/teaching-children's hospital
   - o Other: ……
4. What is your profession?
   - o Paediatric gastroenterologist
   - o Paediatric surgeon
   - o Paediatrician
   - o Dietician/nutritionist
   - o Nurse/nurse practitioner
   - o Other: ……
5. How long has your IF team been managing children on home parenteral nutrition (HPN)?
   - o <1 year
   - o 1 – 5 years
   - o 6 – 10 years
   - o 11 – 20 years
   - o >20 years
6. How many years of experience do you have in working in an IF team?
   - o <1
   - o 1 – 5
   - o 6 – 10
   - o 11 – 20
   - o >20

7. Is the paediatric IF team combined with an adult IF team?
   - o Yes
   - o No

8. Where does your IF team consist of? Please fill in the numbers of members and the total numbers of hours per week that they work for the IF team (for example if 2 paediatric surgeons work 5 hours per week for the IF team, fill in 2 and 10 respectively).

Please fill in zero if not applicable.

Profession	Number	Hours per week
Paediatric gastroenterologist		
Paediatric surgeon		
General paediatrician		
Dietician/nutritionist		
Nurse/nurse practitioner		
Pharmacist		
Psychologist		
Social worker		
Speech therapist		
Physical therapist		
Other, please specify in comments		

Patients

9. What is the current number of children (<18 years) on HPN attending your IF team?
10. Please specify the distribution of underlying causes of IF of the children on HPN attending your team.

	Number of children
• Short bowel syndrome:	.....
• Motility disorder:	.....
• Enteropathy:	.....

11. Please specify the age categories of children on HPN attending your team.

	Number of children
• Neonates (0 – 1 month):	.....
• Infants (1 month – 1 year):	.....
• Children (1 – 5 year):	.....
• Children (5 – 10 year):	.....
• Children (10 – 15 years):	.....
• Adolescents (>15 years):	.....

12. Does your IF team also continue monitoring children weaned off HPN?
    - o Yes
    - o No

- *If yes, please go to question 14*
- *If no, please go to question 15*

13. What is the current number of children (<18 years) weaned off PN attending your team?
14. Do you have anything to add to this survey?

Part 2

What is your email-address?

To make sure part 1 and part 2 of the survey are linked to the same person, we ask you to fill in your email-address. Results of the survey will be analysed anonymously.

Vascular access

1. What kind of central venous line do you use for the administration of HPN?

	Standard	Sometimes	Never
Central venous catheter – tunneled (for example Broviac® or Hickmann®)			
Central venous catheter – untunneled			
Peripheral inserted central catheter (PICC)			
Port-a-cath			
Other, please specify in comments			

2. Do you use catheter lock solution(s) other than normal saline?
    - o Yes
    - o No

If yes:

What kind of catheter lock solution(s) is/are used?

	Standard	Sometimes	Never
Taurosept® (taurolidine)			
Taurolock™ (taurolidine and citrate)			
Ethanol			
Heparin			
Other, please specify in comments			

If no:

Please explain why catheter lock solution(s) are not used by your IF team.

3. Do you use anticoagulation in the prevention of catheter-related thrombosis/occlusion?
    - o Yes
    - o No

If yes:

What type of anticoagulation?

	Standard	Sometimes	Never
Low molecular weight heparin (for example nadroparin)			
Vitamin K antagonists (for example acenocoumarol)			
Heparin lock			
Other, please specify in comments			

If no:

Please explain why anticoagulation drugs are not used by your IF team.

4. Do you have a standard procedure in case of occlusion of the catheter?
   - o Yes
   - o No

If yes:

What do you use in case of occlusion of the catheter?

	Standard	Sometimes	Never
Heparin lock			
Urokinase			
Alteplase			
Other, please specify in comments			

Home parenteral nutrition

5. How is the HPN provided in your institution?
   - o Pharmacy-customized, age/weight specific
   - o Commercial mixed bags
   - o Commercial mixed bags customized by the pharmacy (for example a commercial mixed bag with specific mixture of vitamins and micronutrients by the pharmacy)
   - o Other: ……
6. Which lipid emulsion(s) is/are used for HPN?

	Standard	Sometimes	Never
Soybean lipid emulsions (for example Intralipid®)			
Soybean/medium chain triglycerides (medium-chain triglycerides)/olive/fish oil lipid emulsions (for example SMOFlipid®)			
Fish-oil lipid emulsions (for example Omegaven®)			
Olive/soybean lipid emulsions (for example Clinoleic®)			
Soybean/medium-chain triglycerides lipid emulsions (for example Lipoplus®)			
Other, please specify in comments			

7. Do you use the protein target as described by the ESPGHAN/ESPEN guideline (neonates 1.5-3 g/kg/d, 2 months-3 years 1-2.5 g/kg/d, 3-18 years 1-2 g/kg/d)?
   - o Yes
   - o No, please specify in comments what protein target is used by your IF team
   - o Unknown
8. A) What do you in general use as parenteral lipid target for infants and young children?
      - o 1-2 g/kg/day
      - o 2-3 g/kg/day
      - o 3-4 g/kg/day
      - o Unknown
      - o Other, please specify: ……
   B) What do you in general use as parenteral lipid target for older children?
      - o 1-2 g/kg/day
      - o 2-3 g/kg/day
      - o 3-4 g/kg/day
      - o Unknown
      - o Other, please specify: ……
9. In children on full PN, how many days/nights do you prescribe the lipids?
   - o All days
   - o 5-6 days
   - o Less than 5 days
   - o Other, please specify: ……
10. What is the maximum (parenteral) amount of carbohydrates used?
    - o 16 g/kg/day
    - o 18 g/kg/day
    - o 20 g/kg/day
    - o Unknown
    - o Other, please specify: ……
11. Which criteria do you use to decide whether cycling of the PN is possible (for example a certain age or weight of the patient)?
12. Who pays for the PN?
    - o Health insurance
    - o Hospital
    - o Unknown
    - o Other, please specify: ……
13. In general, who administers the HPN?
    - o Parents/caregivers
    - o Home care companies

- o Other, please specify: ……

If parents/caregivers:

Who trains the parents/caregivers to administer the HPN and take care of the central venous line? And how much time does this training take?

Enteral/oral nutrition

14. What type of feeding is recommended when nutrition is started in neonates/infants?

A) For neonates/infants:

	Standard	Sometimes	Never	Unknown
Human milk				
Polymeric (containing whole protein, complex carbohydrates and long-chain triglycerides)				
Oligomeric (containing protein hydrolysates, complex carbohydrates and medium-chain triglycerides)				
Monomeric (containing amino acids, complex carbohydrates and long-chain triglycerides)				

B) For older children:

	Standard	Sometimes	Never	Unknown
Polymeric (containing whole protein, complex carbohydrates and long-chain triglycerides)				
Oligomeric (containing protein hydrolysates, complex carbohydrates and medium-chain triglycerides)				
Monomeric (containing amino acids, complex carbohydrates and long-chain triglycerides)				
Solid oral feeding				

15. How is the enteral nutrition most often administered?
    - o Intermittent/bolus feeding (for example 6 feedings of 120 ml) – orally
    - o Intermittent/bolus feeding (for example 6 feedings of 120 ml) – by tube
    - o Continuous (for example continuous tube feeding of 30 ml per hour)
    - o Combination of intermittent and continuous feeding (for example 20 hours tube feeding of 30 ml per hour with 2 times a bottle of 60 ml)
16. When is on average the central venous line removed after reaching full enteral nutrition (i.e. after how many days/weeks/months)?
17. Is a speech therapist involved in the introduction of oral feeding?
    - o Yes
    - o No

Nutritional status/bone health

18. How is nutritional status monitored regularly?
    - o Weight
    - o Height
    - o Head circumference
    - o BMI
    - o Upper arm/calf circumference
    - o Skin fold thickness
    - o Dual Energy X-ray Absorptiometry
    - o Air displacement plethysmography
    - o Other, please specify: ……

19. On average, how often do you measure micronutrient levels?

Never – Every 3 months - Every 6 months – Yearly – Every 2 years – >2 years interval – Unknown

- o 25-OH vitamin D
- o Vitamin A
- o Vitamin E
- o Vitamin B1
- o Vitamin B2
- o Vitamin B6
- o Active vitamin B12
- o Total vitamin B12
- o Zinc
- o Aluminium
- o Copper
- o Chromium
- o Selenium
- o Manganese

20. How do you monitor bone health in children with IF? And how often?

Never – Every 6 months – Yearly – Every 2 years – >2 years interval – Unknown

- o Blood parameters (for example calcium, phosphate, vitamin D)
- o Dual energy X-ray absorptiometry
- o Digital X-ray radiogrammetry (X-ray of the hand with use of the BoneXpert software)

Surgery/medication

21. Which of the following procedures are performed in your centre?
    - o Serial transverse enteroplasty (STEP)
    - o Bianchi procedure

- o Intestinal transplantation
- o None of these procedures

22. What is the frequency of the procedures performed?
    Number of procedures/year
    - o Serial transverse enteroplasty (STEP)
    - o Bianchi procedure
    - o Intestinal transplantation

Please fill in zero if not applicable.

23. Which of the following medication do you use regularly for children on HPN?
    - o Histamine receptor antagonist (e.g. ranitidine)
    - o Proton pomp inhibitor (e.g. omeprazole)
    - o A2-adrenergic receptor agonist (e.g. clonidine)
    - o Somatostatin analogue (e.g. octreotide)
    - o Antidiarrheal/antimotility agents (e.g. loperamide)
    - o Bile acid sequestrant (e.g. cholestyramine)
    - o Prokinetic agents (e.g. erythromycin)
    - o Antibiotics as treatment for small intestinal bacterial overgrowth (e.g. metronidazole)
    - o Probiotics
    - o Growth factors (e.g. Glucagon-like peptide-2 analogue teduglutide)
    - o Other: ……..

Neuropsychological and psychomotor development/general questions

24. In general, how do the children on HPN treated by your team perform on an intellectual level when they go to elementary school?
    - o Most of them go to regular schools
    - o Most of them go to regular schools with extra assistance
    - o Most of them go to special needs schools (due to medical reasons)
    - o Most of them go to special needs schools (due to intellectual reasons)

Please enter your comment here

25. Is neuropsychological and psychomotor development standardly assessed in your IF team?
    - o Yes
    - o No

26. Do you have anything to add to this survey?

SUPPLEMENTARY DATA 2

Supplementary Table 1. Frequency of micronutrient monitoring among IF teams

Number of IF teams / N (%) Micronutrient	Every 3 months	Every 6 months	Yearly	Every 2 years	>2 years	Never	Unknown
25-OH vitamin D	32 (54)	21 (36)	6 (10)	NA	NA	NA	NA
Vitamin A	24 (41)	26 (44)	9 (15)	NA	NA	NA	NA
Vitamin E	26 (44)	23 (39)	9 (15)	NA	NA	1 (2)	NA
Vitamin B1	8 (14)	8 (14)	11 (19)	1 (2)	2 (3)	26 (44)	3 (5)
Vitamin B2	8 (14)	7 (12)	10 (17)	1 (2)	2 (3)	28 (48)	3 (5)
Vitamin B6	11 (19)	9 (15)	12 (20)	1 (2)	2 (3)	22 (37)	2 (3)
Active vitamin B12	7 (12)	10 (17)	8 (14)	NA	2 (4)	27 (46)	5 (9)
Total vitamin B12	26 (44)	17 (29)	13 (22)	NA	1 (2)	2 (3)	NA
Zinc	24 (41)	24 (41)	8 (14)	NA	NA	3 (5)	NA
Aluminium	4 (7)	8 (14)	8 (14)	NA	4 (7)	28 (48)	7 (12)
Copper	17 (29)	18 (31)	10 (17)	1 (2)	2 (3)	8 (14)	3 (5)
Chromium	4 (7)	3 (5)	8 (14)	1 (2)	3 (5)	32 (54)	8 (14)
Selenium	16 (27)	16 (27)	11 (19)	1 (2)	1 (2)	13 (22)	1 (2)
Manganese	10 (17)	8 (14)	11 (19)	1 (2)	3 (5)	25 (42)	1 (2)

Legend: Values expressed as N (%).
Abbreviation: NA, not applicable.

Supplementary Table 2. Frequency of bone health monitoring among IF teams

	Every 6 months	Yearly	Every 2 years	>2 years interval	Never	Unknown
Blood parameters	56 (95)	2 (3)	1 (2)	NA	NA	NA
Dual energy X-ray absorptiometry	1 (2)	19 (32)	10 (17)	14 (24)	11 (19)	4 (7)
Digital X-ray radiogrammetry (X-ray of the hand with use of BoneXpert software)	1 (2)	4 (7)	4 (7)	5 (9)	37 (63)	8 (14)

Legend: Values expressed as N (%).
Abbreviation: NA, not applicable.

Supplementary Table 3. Grading of levels of evidence (LOE) and grading of recommendations (GOR) according to the Scottish Intercollegiate Guideline Network (SIGN) 2000.

Level of evidence	Study design	Special conditions	Grading of recommendation
1++	High quality meta analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias.	If directly applicable to target population.	A
		Extrapolated evidence.	B
1+	Well conducted meta analyses, systematic reviews of RCTs, or CTs with a low risk of bias.	If directly applicable to target population and overall consistency of results.	A
		Extrapolated evidence.	B
1-	Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.		No supporting recommendation
2++	High quality systematic reviews of case-control or cohort studies. High quality case-control or cohort studies with a very low risk of confounding, bias, or chance, and a high probability that the relationship is causal.	If directly applicable to target population and demonstrating overall consistency of results.	B
		Extrapolated evidence.	C
2+	Well conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal.	If directly applicable to target population and demonstrating overall consistency of results.	C
		Extrapolated evidence.	D
2-3	Case control or cohort studies with a high risk of confounding, bias, or chance, and a significant risk that the relationship is not causal.		No supporting recommendation
3	Non-analytic studies, e.g. case reports.		D
4	Expert opinion.		

Abbreviation: RCT, randomized controlled trial.

PART III

DISCUSSION AND SUMMARY