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ESPEN endorsed recommendation

ESPEN endorsed recommendations. Definition and classification of intestinal failure in adults

Loris Pironi [a, *], Jann Arends [b], Janet Baxter [c], Federico Bozzetti [d], Rosa Burgos Peláez [e], Cristina Cuerda [f], Alastair Forbes [g], Simon Gabe [h], Lyn Gillanders [i], Mette Holst [j], Palle Bekker Jeppesen [k], Francisca Joly [l], Darlene Kelly [m], Stanislaw Klek [n], Øivind Irtun [o], SW Olde Damink [p], Marina Panisic [q], Henrik Højgaard Rasmussen [j], Michael Staun [k], Kinga Szczepanek [n], André Van Gossum [r], Geert Wanten [s], Stéphane Michel Schneider [t], Jon Shaffer [u], the Home Artificial Nutrition & Chronic Intestinal Failure and the Acute Intestinal Failure Special Interest Groups of ESPEN

[a] Center for Chronic Intestinal Failure, St. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy
[b] Tumor Biology Center, Albert-Ludwigs-University, Freiburg, Germany
[c] Tayside Nutrition Managed Clinical Network, Dundee, UK
[d] Faculty of Medicine, University of Milan, Milan, Italy
[e] Nutritional Support Unit, University Hospital Vall d'Hebron, Barcelona, Spain
[f] Nutrition Unit, Hospital General Universitario Gregorio Marañón, Madrid, Spain
[g] University of East Anglia, Norwich Research Park, Norwich, UK
[h] The Lennard-Jones Intestinal Failure Unit, St Mark's Hospital and Academic Institute, Harrow, UK
[i] National Intestinal Failure Service, Auckland City Hospital (AuSPEN), Auckland, New Zealand
[j] Centre for Nutrition and Bowel Disease, Department of Gastroenterology, Aalborg University Hospital, Aalborg, Denmark
[k] Rigshospitalet, Department of Gastroenterology, Copenhagen, Denmark
[l] Centre for Intestinal Failure, Department of Gastroenterology and Nutritional Support, Hôpital Beaujon, Clichy, France
[m] Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, Rochester, Minnesota and Oley Foundation for Home Parenteral and Enteral Nutrition, Albany, NY, USA
[n] General and Oncology Surgery Unit, Stanley Dudrick's Memorial Hospital, Skawina, Poland
[o] Dept. of Gastroenterologic Surgery, University Hospital North-Norway, Tromso, Norway
[p] Department of Surgery, Maastricht University Medical Centre, Maastricht, The Netherlands
[q] Department for Perioperative Nutrition, Clinic for General Surgery, Military Medica Academy, Belgrade, Serbia
[r] Medico-Surgical Department of Gastroenterology, Hôpital Erasme, Free University of Brussels, Belgium
[s] Intestinal Failure Unit, Department of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands
[t] Gastroenterology and Clinical Nutrition, CHU of Nice, University of Nice Sophia Antipolis, Nice, France
[u] Intestinal failure Unit, Salford Royal Hospital, Salford, UK

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SUMMARY

Background & aims: Intestinal failure (IF) is not included in the list of PubMed Mesh terms, as failure is the term describing a state of non functioning of other organs, and as such is not well recognized. No scientific society has yet devised a formal definition and classification of IF. The European Society for Clinical Nutrition and Metabolism guideline committee endorsed its "home artificial nutrition and chronic IF" and "acute IF" special interest groups to write recommendations on these issues.
Methods: After a Medline Search, in December 2013, for "intestinal failure" and "review"[Publication Type], the project was developed using the Delphi round methodology. The final consensus was reached on March 2014, after 5 Delphi rounds and two live meetings.
Results: The recommendations comprise the definition of IF, a functional and a pathophysiological classification for both acute and chronic IF and a clinical classification of chronic IF. IF was defined as "the reduction of gut function below the minimum necessary for the absorption of macronutrients and/or

* Corresponding author. Center for Chronic Intestinal Failure, Department of Gastroenterology, St. Orsola-Malpighi Hospital, University of Bologna, Via Massarenti, 9, 40138 Bologna, Italy. Tel./fax: +39 051 6363073.
E-mail address: loris.pironi@unibo.it (L. Pironi).

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water and electrolytes, such that intravenous supplementation is required to maintain health and/or growth".

Conclusions: This formal definition and classification of IF, will facilitate communication and cooperation among professionals in clinical practice, organization and management, and research.

Abbreviations

AIF	acute intestinal failure
CIF	chronic intestinal failure
CIPO	chronic idiopathic pseudo-obstruction
EC	enterocutaneous
ESPEN	European Society for Clinical Nutrition and Metabolism
IF	intestinal failure
ITx	intestinal transplantation
HAN&CIF	home artificial nutrition and chronic intestinal failure
HPN	home parenteral nutrition
SBS	short bowel syndrome

1. Introduction

Intestinal failure (IF) was first defined in 1981 by Fleming and Remington as "a reduction in the functioning gut mass below the minimal amount necessary for adequate digestion and absorption of food" [1]. IF may be due to acquired or congenital, gastrointestinal or systemic, benign or malignant diseases, which may affect all age categories [2,3]. It may have an abrupt onset, or may be the slow, progressive evolution of a chronic illness, and may be a self-limiting short-term or a long-lasting condition (chronic intestinal failure, CIF). Treatment of CIF relies on intestinal rehabilitation programs that aim to restore bowel function through nutrition, pharmacological and/or surgical therapy [4]. Patients with irreversible CIF are destined to need life-long home parenteral nutrition (HPN) or to undergo intestinal transplantation (ITx) [5].

The definition of IF by Fleming and Remington has been revised by other experts [2–6], but no scientific society has yet devised a formal definition and classification of IF. Indeed, IF is not included in the list of PubMed Mesh terms, as failure is the term describing a state of non functioning of organs. A PubMed search on March 15th 2014, using "intestinal failure" as general term, nonetheless generated a total of 981 items, and showed that the number of publications has rapidly grown in the past decades, indicating an increased awareness of this condition (Table 1).

The European Society for Clinical Nutrition and Metabolism (ESPEN) has two "special interest groups" devoted to IF, "the home artificial nutrition and chronic intestinal failure group (HAN&CIF)" established in 1992 and the "acute intestinal failure group (AIF)" established in 2010 [7]. The Guideline Committee of ESPEN committed the two groups to develop the ESPEN guidelines on IF [8] and endorsed them to support the Guidelines with recommendations on the definition and classification of IF.

2. Material and methods

The project of writing "recommendations on definition and classification of IF in adults" was agreed on March 14th 2013, with a member of the ESPEN Guideline committee to assist the development of the guidelines on IF, and was formally approved by the AIF and the HAN&CIF special interest groups at their meetings held at the ESPEN Congress in Leipzig, September 2013. All the members of the two groups were invited to be part of the expert panel.

The work was carried out between December 2013 and February 2014, using Delphi round methodology [9]. The results of the Delphi rounds were also discussed during the face-to-face winter meetings of the two groups.

Each Delphi round consisted of a proposal, to which each expert replied as "agree", "agree, with suggested minor changes", or "disagree, with suggested major changes". The first proposal was based on a MedLine Search, performed on 10/12/2013, for "intestinal failure" AND "review"[Publication Type], which resulted in a total of 298 articles. Only publications in English specifically dedicated to the definition and classification of IF were selected. Any pertinent publications retrieved from the references of the selected papers were also considered. In order to avoid duplicates, only those articles with an "original" definition and classification were chosen. These initially selected papers, used as starting point for the first round are reported in Table 2. The subsequent proposals were based on the collected comments as well as on any further publications found non systematically but suggested by the experts. All the proposals were prepared and circulated by LP. The final consensus was reached on March 1st 2014, after 5 Delphi rounds (on 16/12/14, 27/12/14, 19/01/14, 25/02/14 and 01/03/14) and two live meetings (AIF 11/01/14, HAN&CIF 22/02/14). For the purpose of the paper, the following terms were used: "oral feeding", to indicate the ingestion of food, "oral supplementation"

Table 1
PubMed search on March 15th, 2014.

	1946–1959	1960–1969	1970–1979	1980–1989	1990–1999	2000–2009	2010–2014 March	Total
Intestinal failure [general term]	0	0	0	20	118	450	399	981
Kidney failure [MeSH Term]	393	4226	13012	18086	24268	39768	21790	120939
Heart failure [MeSH Term]	2184	5141	7372	9420	13218	30803	16811	84385
Liver failure [MeSH Term]	153	833	1572	1594	3719	6627	3382	17788
Respiratory failure [MeSH Term]	4	3942	9154	7892	10633	13216	5805	50433

Table 2
Main original definitions and classifications of Intestinal Failure reported in the literature prior to March 15th 2014, in order of publication date. Bold characters indicate the original contribution of each paper.

Author, date (ref)	Definition and classification of intestinal failure
Fleming CR and Remington M. 1981 [1]	**A reduction in the functioning gut mass below the minimum amount necessary for adequate digestion and absorption of food**
Irving M. 1995 [10]	The **spectrum of intestinal failure** covers a wide range of diseases but essentially they can be placed in **four major categories:** short bowel syndrome, motility disorders of the bowel (chronic pseudoobstruction), small bowel parenchymal disease, intestinal fistula
Irving M. 2000 [11]	Intestinal failure can be **complete or partial**, the former typically following total small bowel enterectomy, whilst the latter is seen following partial resection. The condition can be **acute and temporary**, as seen with recoverable motility disorders such as ileus and obstruction, or chronic and permanent. Although a wide spectrum of conditions can be associated with IF, four **major underlying causes** can be identified. These are: (i) the short bowel syndrome; (ii) total parenchymal bowel disease (e.g. Crohn's disease); (iii) motility disorders, such as visceral myopathy and chronic intestinal obstruction; and (iv) small bowel fistulation causing premature loss of enteric content. **The principal resulting nutritional disorders are starvation and dehydration**, but loss of body mass is frequently made worse by catabolism from associated sepsis. **Treatment** is complicated, but has at its core the provision of **nutritional support, principally through the intravenous route**. **Resolution of IF can occur spontaneously** by the process of intestinal adaptation.
Jeppesen PB and Mortensen PB. 2000 [12]	**Intestinal failure** may be defined by the **minimum energy and wet weight absorption required to avoid home parenteral nutrition** Patients with **intestinal insufficiency** who maintained intestinal autonomy and did not depend on parenteral supplements Involuntary ingestion below the minimal amount necessary to maintain nutrient and fluid balance, frequently termed **oral failure**, is seen in patients with pseudoobstruction and dysmotility syndromes.
Nightingale J. 2001 [13]	Intestinal failure occurs 'when there is **reduced intestinal absorption so that macronutrient and/or water and electrolyte supplements** are needed to maintain health and/or growth'.
Shaffer J. 2002 [14]	**A novel classification of intestinal failure** was recently devised to reflect this: **Type I** intestinal failure is classified as self-limiting intestinal failure as occurs following abdominal surgery; **Type II** is intestinal failure in severely ill patients with major resections of the bowel and septic, metabolic and nutritional complications requiring multidisciplinary intervention with metabolic and nutritional support to permit recovery; **Type III** is chronic intestinal failure requiring long-term nutritional support.
Buchman AL et al., 2003 [15]	It has been suggested that intestinal failure is better defined in terms of fecal energy loss rather than residual bowel length. However, fecal energy loss is a function of both energy intake and energy absorption. **Patients who are unable to increase their oral intake sufficiently or are unable to absorb sufficient energy despite significantly increased intake,** are defined as patients with intestinal failure and require parenteral nutrition support.
Ding LA and Li jS. 2004 [16]	**Staging** of intestinal failure: Acute intestinal failure, Chronic intestinal failure **Grading** of intestinal failure: severe, moderate, mild
Goulet O et al., 2004 [17]	Intestinal failure can be defined as the reduction of functional gut mass below the minimum needed for **digestion** and absorption of nutrient and fluids required for maintenance in adults or growth in children. It has been suggested that IF is better defined in terms of fecal energy loss rather than residual bowel length in patients with short bowel syndrome. Another approach is **to define the degree of IF according to the amount of PN required** for maintenance in adults and growth in children
Kocoshis SA, 2004 [18]	Although intestinal failure can be defined by excessive fecal energy loss, a more widely accepted definition is "**the inability of the gastrointestinal tract to sustain life autonomously**".
Jeejeebhoy KN. 2005 [19]	Gastrointestinal function is inadequate to maintain the nutrition and hydration of the individual without supplements given **orally** or intravenously
O'Keefe SJD. 2006 [3]	Intestinal failure '**results from obstruction, dysmotility, surgical resection, congenital defect or disease–associated loss of absorption and is characterized by the inability** to maintain protein-energy, fluid, electrolyte **or micronutrient balance**'
Lal S. (2006) [20]	Causes of intestinal failure are varied, with self-limiting or '**Type 1**' intestinal failure occurring relatively commonly following abdominal surgery, necessitating short-term fluid or nutritional support. The rarer, '**Type 2**' intestinal failure, is associated with septic, metabolic and complex nutritional complications, usually following surgical resection in patients with Crohn's or mesenteric vascular disease. In broad terms, intestinal failure **can result** from **intestinal resection, inflammation or fistulization, from mechanical or functional intestinal obstruction, or indirectly from the effects of sepsis on the gastrointestinal tract**
Messing B and Joly F [21]	The recognized definition of **chronic intestinal failure** is a nonfunctioning small bowel either removed after severe disease leading to very short bowel syndrome, or present but **impossible to use by enteral support** even accessed through jejunostomy (eg, chronic intestinal pseudo-obstruction or extensive villous atrophy diseases).
Nightingale J and Woodward JM (2006) [22]	IF may be defined and quantified by balance study techniques; however, only few centres have the facilities for these difficult metabolic studies, and therefore **nutrient/fluid requirements determine whether IF** is termed **severe, moderate, or mild. Severe is when parenteral, moderate when enteral, and mild when oral nutritional fluid supplements are needed**.
Beath S et al., 2008 [23]	Intestinal failure is defined as the **inability of the alimentary tract** to digest and absorb sufficient nutrients to maintain normal fluid balance, growth and health.
Gillanders L. et al., 2008 [24]	Intestinal failure occurs when there is reduced intestinal absorption **so that intravenous** nutrients and/or water and electrolyte supplements are needed to maintain health and/or growth. IF can be **short (<1 y) or long term**.
NHS National Commissioning Group for Highly Specialised Services. 2008 [6]	Intestinal Failure comprises a group of disorders with many different **causes**, all of which are characterised by an inability to maintain adequate nutrition via the intestines. **It results from obstruction, abnormal motility, major surgical resection, congenital defect or disease–associated**

(*continued on next page*)

Table 2 (*continued*)

Author, date (ref)	Definition and classification of intestinal failure
	loss of absorption. It is characterised not only by the inability to maintain protein-energy, but also often in difficulties in maintaining water, electrolyte or micronutrient balance, particularly when there has been a major loss of length of the small bowel. **If it persists for more than a few days it demands treatment with the intravenous delivery of nutrients and water–parenteral nutrition**. **Type I** – this type of Intestinal Failure is short-term, self limiting and often peri-operative in nature. Type I Intestinal Failure is common and these patients are managed successfully in a multitude of healthcare settings, especially surgical wards, including all units which perform major, particularly abdominal surgery. Some patients on high dependency units (HDU) and intensive care units (ICU) will also fall into this category Care location: Wards, (HDU, ITU) **Type II** – Type II IF occurs in metabolically unstable patients in hospital and requires prolonged parenteral nutrition over periods of weeks or months. It is often associated with sepsis, and may be associated with renal impairment. These patients often need the facilities of an Intensive Care or High Dependency Unit for some or much of their stay in hospital. This type of IF is rarer and needs to be managed by a multi-professional specialist intestinal failure team. Effective management of Type II IF can reduce the likelihood of the development of Type III Intestinal Failure. Care location: HDU, ITU (Wards) **Type III** – Type III is a chronic condition requiring long term parenteral feeding. The patient is characteristically metabolically stable but cannot maintain his or her nutrition adequately by absorbing food or nutrients via the intestinal tract. These are, in the main, the group of patients for which Home Parenteral Nutrition (HPN) is indicated. Care location: Wards to home
Fishbein TM. 2009 [25]	Intestinal failure refers to a**ctual or impending loss of nutritional autonomy due to gut dysfunction.** The condition **is initially managed by parenteral delivery of nutrition**.
Staun M et al., 2009 [26]	Intestinal failure is defined as a condition with reduced intestinal absorption to the extent that macronutrient and/or water and electrolyte supplements are needed to maintain health and/or growth. Intestinal failure is **severe when parenteral nutrition and or additional parenteral electrolytes and water are required**. The condition may be **transient** if gut function can be restored, but HPN is indicated for patients with **chronic** intestinal failure.
Rudolph A and Squires R. 2010 [27]	Intestinal failure, defined as an inability of a child to achieve adequate weight and growth without intravenous nutritional support, **has two principal components: the intestine is too short as a consequence of surgical resection and the intestine is dysfunctional despite adequate length.**
Gardiner KR. 2011 [28]	The term intestinal failure was introduced by Fleming and Remington(1) and defined as a 'reduction in functioning gut mass below the minimum necessary for adequate digestion and absorption of nutrients'. Initially, this definition was used interchangeably with the need for parenteral nutrition. Since that time the definition has been broadened and is now recognised to occur when 'gastrointestinal function is inadequate to maintain the nutrition and hydration of the individual **without supplements given orally or intravenously**. IF has been sub-classified into three types on the basis of duration and irreversibility.
Krawinkel MB. 2012 [29]	The term "**chronic intestinal failure**" (CIF) refers to the **body's inability** to meet its energy and nutritional needs through the gastrointestinal tract
Murray JS and Mahoney JM. 2012 [30]	IF is defined as the **inability of the gastrointestinal system** to properly function for the adequate digestion and absorption of necessary nutrients and fluids for growth and development Other experts describe this illness as a state in which **gastrointestinal function** is not adequate to support sufficient growth and physiological balance in children
Pironi L. et al., 2012 [5]	Intestinal failure results from reduction in the functioning gut mass characterized by the inability to maintain protein-energy, fluid, electrolyte **and/or micronutrient** balance.
Squires RH et al., 2012 [31]	Intestinal failure in infants and children is a **devastating condition** that can be broadly defined as the inability of the gastrointestinal tract to **sustain life** without supplemental parenteral nutrition

to indicate the ingestion of nutritional supplements, "enteral nutrition" to indicate enteral tube feeding and "parenteral nutrition" to indicate the intravenous infusion of nutritional admixtures or of water and electrolyte solutions.

The definitive recommendations consist in the "definition of IF", a "functional classification of IF", a "pathophysiological classification of IF" and a "clinical classification of chronic IF".

As there were no published data available to serve as a starting point for a "clinical classification", this was developed on the basis of the common experience of the panel experts. The applicability of the devised "clinical classification" was verified on two samples of randomly selected patients, currently on HPN for CIF due to either benign or active malignant disease. This consisted in a cross-sectional investigation of the energy content and volume of the parenteral nutrition admixture of 114 patients cared for at the Center for Benign Chronic Intestinal Failure of the S. Orsola-Malpighi University Hospital, Bologna (Italy) and of 50 patients with active cancer cared for at the Tumor Biology Center, Albert-Ludwigs-University, Freiburg (Germany).

3. Results

The definition and classification of IF are reported and discussed pathophysiological mechanisms of IF. The diseases that may determine an IF are listed in Table 5.

3.1. Definition of intestinal failure

Intestinal failure is defined as the reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes, such that intravenous supplementation is required to maintain health and/or growth.

The reduction of gut absorptive function that doesn't require intravenous supplementation to maintain health and/or growth, can be considered as "intestinal insufficiency" (or "intestinal deficiency" for those languages where "insufficiency" and "failure" have the same meaning).

The panel identified IF as a "state of non-functioning", where the gut function referred to was the "absorption of proteins, lipids, carbohydrates, water and electrolytes" [12,13,15,24,29,30], and the "threshold for loss of function" was the "need for intravenous supplementation" to maintain health and/or growth [6,12–14,21,24,31]. For this purpose, the original definition by Fleming and Remington was modified by deleting the term "mass", identifying "absorption" as the key gut function, replacing the term "food" with "macronutrients and/or water and electrolytes", and by

Table 3
ESPEN recommendations: definition and classification of intestinal failure.

Definition
Intestinal failure is defined as the reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes, such that intravenous supplementation is required to maintain health and/or growth.
The reduction of gut absorptive function that doesn't require intravenous supplementation to maintain health and/or growth, can be considered as "intestinal insufficiency" (or "intestinal deficiency" for those languages where "insufficiency" and "failure" have the same meaning).
Functional classification
On the basis of onset, metabolic and expected outcome criteria, intestinal failure is classified as:
- Type I – acute, short-term and usually self limiting condition
- Type II – prolonged acute condition, often in metabolically unstable patients, requiring complex multi-disciplinary care and intravenous supplementation over periods of weeks or months
- Type III – chronic condition, in metabolically stable patients, requiring intravenous supplementation over months or years. It may be reversible or irreversible.

Pathophysiological classification
Intestinal failure can be classified into five major pathophysiological conditions, which may originate from various gastrointestinal or systemic diseases:
- short bowel
- intestinal fistula
- intestinal dysmotility
- mechanical obstruction
- extensive small bowel mucosal disease

Clinical classification of chronic intestinal failure
On the basis of the requirements for energy and the volume of the intravenous supplementation (IV), chronic intestinal failure is categorized into 16 subtypes

IV energy supplementation[b] (kcal/kg Body Weight)	Volume of the IV supplementation[a] (ml) ≤1000 [1]	1001–2000 [2]	2001–3000 [3]	>3000 [4]
0 (A)	A1	A2	A3	A4
1–10 (B)	B1	B2	B3	B4
11–20 (C)	C1	C2	C3	C4
> 20 (D)	D1	D2	D3	D4

[a] calculated as daily mean of the total volume infused per week = (volume per day of infusion x number of infusions per week)/7.
[b] calculated as daily mean of the total energy infused per week = (energy per day of infusion x number of infusions per week)/7.

health and growth". The panel was aware that balance study techniques, comparing nutrient requirement with nutrient absorption, would be the optimal way to identify and quantify IF in the individual patient [12]. However, considering that very few centres have the facilities for these difficult metabolic studies, the requirement of intravenous nutrient/fluid supplementation was used as a "surrogate diagnostic criterion". The exclusive need for intravenous supplementation was the most debated issue, because some previous definitions of IF included also oral supplementation and enteral nutrition [2,5,6,11,18,19,22,23,25,26,28]. Micronutrients were not mentioned in the definition in order to avoid any misunderstanding about impaired gut absorption resulting in micronutrient deficiency alone, as this would not be considered as IF [2,5,6].

The proposed definition indicates that for the diagnosis of IF two criteria must be simultaneously present: a "decreased absorption of macronutrients and/or water and electrolytes due to a loss of gut function" and the "need for intravenous supplementation". This facilitates an understanding of which conditions cannot be considered IF because only one criterion is present: patients with reduced food intake but normal gut function, like those with disease-related hypophagia, or with anorexia nervosa or any other psychiatric disorders; patients with altered gut function but conserved intestinal absorption, like neurological or especially children, with active Crohn's disease treated by enteral nutrition; patients treated by parenteral nutrition because of refusal of otherwise effective enteral nutrition; patients with a reduction of gut function impairing intestinal absorption but in whom health and growth can be maintained by oral supplementation, enteral nutrition, re-feeding enteroclysis (reinfusion of chyme to the distal limb of a high output small bowel fistula), or those who require only vitamins and trace element supplementation. For these last conditions, the panel proposes that the term "intestinal insufficiency or intestinal deficiency" could be considered [12]. The alternative between "insufficiency" and "deficiency" has been included to allow an appropriate translation in those languages where "insufficiency" and "failure" have the same meaning, such as in French, Italian and other Latin languages.

3.2. Functional classification

On the basis of onset, metabolic and expected outcome criteria, IF is classified as

- ***Type I*** *– acute, short-term and usually self limiting condition*
- ***Type II*** *– prolonged acute condition, often in metabolically unstable patients, requiring complex multi-disciplinary care and intravenous supplementation over periods of weeks or months*
- ***Type III*** *– chronic condition, in metabolically stable patients, requiring intravenous supplementation over months or years. It may be reversible or irreversible*

This classification, termed "functional", was also used in the UK project "A Strategic Framework for Intestinal Failure and Home Parenteral Nutrition Services for Adults in England" [6], and was first described in 2002 [14]. It aims to categorize the medical care, the professional expertise, the management, the treatment setting as well as the organization, logistic and administrative issues required for the treatment of IF.

Acute type I and type II IF have been extensively reviewed [20,28]. **Type I** IF is a common, short and often self limiting, condition, estimated to occur in about 15% patients in the perioperative setting after abdominal surgery or in association with critical illnesses such as head injury, pneumonia and acute pancreatitis. While intestinal function recovers, short-term parenteral fluid and nutrition support can be required. Post-operative ileus usually spontaneously resolves within a few days. This duration can be shortened by multimodal enhanced recovery techniques aiming to promote early mobilization and early introduction of oral nutrition [32]. Such patients are usually managed in surgical wards, although some patients in critical care environments also fit into this category.

Type II IF is an uncommon condition, most often seen in the setting of an intra-abdominal catastrophe (like peritonitis due to visceral injury) and is almost always associated with septic, metabolic and complex nutritional complications. Renal impairment may be present. It is originally an acute event, often occurring in a previously healthy subject (mesenteric ischaemia, volvulus or abdominal trauma) or complicating intestinal surgery (anastomotic leak; inadvertent and unrecognized intestinal injury) and necessitating massive enterectomy and/or resulting in one or more enterocutaneous fistulae, with or without a proximal stoma. Less frequently, it may be the complication of a type III chronic IF, representing a condition of "acute on chronic" IF. Type II IF requires prolonged parenteral nutrition over periods of weeks or months. These patients often initially need the facilities of an intensive care or high dependency unit and to be managed by a multi-professional

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