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1 **ESPEN Guideline on home parenteral nutrition**

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22 Abstract

23 This guideline will inform physicians, nurses, dieticians, pharmacists, caregivers and other home
24 parenteral nutrition (HPN) providers, as well as healthcare administrators and policy makers,
25 about appropriate and safe HPN provision. This guideline will also inform patients requiring HPN.
26 The guideline is based on previous published guidelines and provides an update of current
27 evidence and expert opinion; it consists of 71 recommendations that address the indications for
28 HPN, central venous access device (CVAD) and infusion pump, infusion catheter and CVAD site
29 care, nutritional admixtures, program monitoring and management. Meta-analyses, systematic
30 reviews and single clinical trials based on clinical questions were searched according to the PICO
31 format. The evidence was evaluated and used to develop clinical recommendations implementing
32 Scottish Intercollegiate Guidelines Network methodology. The guideline was commissioned and
33 financially supported by ESPEN and members of the guideline group were selected by ESPEN.

34 Keywords

35 Caregiver, Central venous access device, Home parenteral nutrition, Intestinal failure,
36 Management, Monitoring, Multidisciplinary team, Parenteral nutrition admixture, Patient training

37 List of abbreviations

38 AIO, all-in-one parenteral nutrition admixture; CDC, Centers for Disease Control and Prevention;
39 CIF, chronic intestinal failure; CRBSI, catheter-related bloodstream infection; CVAD, central venous
40 access device; CVC, central venous catheter; EN, enteral nutrition; HPN, home parenteral
41 nutrition; IF, intestinal failure; NST, nutrition support team; PICC, peripherally inserted central
42 venous catheter; PN, parenteral nutrition; QoL, quality of life; RCT, randomized controlled trial

43

44 **Introduction**

45 Parenteral nutrition (PN) is a type of medical nutrition therapy provided through the intravenous
46 administration of nutrients such as amino acids, glucose, lipids, electrolytes, vitamins and trace
47 elements [1]. It is categorized as total (or exclusive) PN, where it meets the patient's nutritional
48 needs in entirety, and as supplemental (partial or complementary) PN, where nutrition is also
49 provided via the oral or enteral route [1]. PN can be administered either in, or outside, the
50 hospital setting; the latter defined as home parenteral nutrition (HPN) [1].

51 HPN is the primary life-saving therapy for patients with chronic intestinal failure (CIF) due to either
52 benign (absence of malignant disease) or malignant diseases [2-4]. HPN may also be provided as
53 palliative nutrition to patients in late phases of end-stage diseases [1]. As HPN is sometimes used
54 to prevent or treat malnutrition in patients with a functioning intestine, who decline medical
55 nutrition via the oral/enteral route, HPN and CIF cannot be considered synonymous [2]. Thus, on
56 the basis of underlying gastrointestinal function and disease, in tandem with patient
57 characteristics, four clinical scenarios for the use of HPN can be identified [2-4]: HPN as primary
58 life-saving therapy for a patient with CIF due to benign disease; HPN for CIF due to malignant
59 diseases, often transiently occurring during curative treatments; HPN included in a program of
60 palliative care for incurable malignant disease, to avoid death from malnutrition; HPN used to
61 prevent or treat malnutrition in patients with a functioning intestine, who decline other types of
62 medical nutrition ('no-CIF scenario'). The goal and characteristics of the HPN program, as well as
63 the specific needs of the patient, may differ among the four clinical scenarios (Table 1).

64 The first European Society for Clinical Nutrition and Metabolism (ESPEN) guideline on HPN was
65 published in 2009 [3]. It consisted of 26 recommendations, 10 were based on some evidence
66 (grade B recommendations) but 16 were mostly based on expert opinion ('grade C
67 recommendations') [3]. In 2016, ESPEN guidelines for CIF due to benign disease was published,

68 including 11 recommendations on HPN management, 17 on PN formulation and 22 on the
 69 prevention and treatment of central venous catheter (CVC)-related complications. [4]. The grade
 70 of evidence was very low for 31 recommendations, low for 14, moderate for 3 and high for 2,
 71 whereas the strength of the recommendations was weak for 18 and strong for 32 [4]. Most of the
 72 recommendations from both guidelines are still valid, particularly those covering nutritional
 73 requirements, metabolic complications and central venous access device (CVAD) management.
 74 Other guidelines and standards for HPN have also been provided by scientific societies and
 75 government bodies [5-15]; however, a systematic review revealed substantial differences among
 76 the recommendations published [10]. Furthermore, the management and provision of HPN differs
 77 among countries and among HPN centers within countries [16,17], although HPN provision by
 78 different programs should be homogeneous in order to ensure equity of patient access to an
 79 appropriate and safe HPN service.

80 Thus, an updated version of ESPEN guidelines on HPN care was commissioned in order to
 81 incorporate new evidence since the publication of the previous ESPEN guidelines, as well as to
 82 highlight recommendations on safe HPN administration and also to include the patient's
 83 perspective.

84 **Table 1. Aims of the HPN program, intravenous supplementation and patient care requirements,**
 85 **categorized according to the clinical scenarios based on the underlying clinical condition.**

HPN program and patient care requirement	Benign CIF scenario	Malignant scenarios	No CIF scenario
Aim (additional to avoiding death from malnutrition)	Social, employment & familial rehabilitation; improved quality of life; intestinal rehabilitation	<ul style="list-style-type: none"> • Treatment of CIF due to ongoing oncological therapy or to gastrointestinal obstruction • Palliative care 	Alternative to other potentially effective modalities of nutritional support (e.g. enteral) refused by the patient.
Expected duration	Temporary or permanent (life-long)	Mostly temporary: <ul style="list-style-type: none"> • Short <6 months 	Temporary or permanent

		• Long: >6 months	
Intravenous supplementation requirements	Supplemental or total; high fluid volume and electrolyte contents often required	CIF: mostly supplemental, but can be total; mostly normal volume (high volume may be required in GI obstruction) Palliative: mostly total; normal/low volume	Mostly supplemental with normal volume
Type of PN admixture more frequently required	“Tailored” or “customized” (compounded), requiring refrigeration	“Premade” or “premixed” (ready-to-use)	“Premade” or “premixed” (ready-to-use)
Patient mobility and dependency on caregiver	Mostly ambulatory and independent (depending on age and co-morbidity). Travelling for work and holidays often required	CIF: ambulatory or housebound, mostly dependent Palliative: housebound, from bed to chair, dependent	Ambulatory, or housebound (neurological disorders), sometimes dependent
Patient homecare nurse assistance requirement	Rare; depending on age and co-morbidity	Frequent	Sometimes

86 CIF, chronic intestinal failure; HPN, home parenteral nutrition; PN, parenteral nutrition

87

88 Aim

89 The aim of the present guideline is to provide recommendations for the appropriate and safe
 90 provision of HPN. This guideline does not include recommendations for the patient’s nutrient
 91 requirements in specific conditions, for which the reader can refer to previous ESPEN guidelines
 92 [3,4,15].

93

94 **Methods**

95 The present guideline was developed according to the standard operating procedure for ESPEN
96 guidelines [18]. It is an update of previous guidelines [3-15]. The guideline was developed by an
97 expert group from seven European countries, representing different professions including eight
98 physicians (LP, FB, FJ, SK, SL, AVG, GW, SCB), a pharmacist (SM), a nurse (KB) and two patient
99 representatives (ML, CW).

100 **Methodology of guideline development**

101 Based on the standard operating procedures for ESPEN guidelines and consensus papers, the first
102 step of the guideline development was the formulation of so-called PICO questions, which address
103 specific patient groups or problems, interventions, compares different therapies and are outcome-
104 related [18]. In total, 17 PICO questions were created and were split into six main chapters,
105 “indications for HPN”, “central venous access device (CVAD) and infusion pump”, “infusion line
106 and CVAD site care”, “nutritional admixtures”, “program monitoring” and “management”.

107 The PICO questions for the different topics were allocated to subgroups/experts who reviewed the
108 previous guidelines and standards [3-15] and performed a literature search to identify suitable
109 meta-analyses, systematic reviews and primary studies (for details see “search strategy” below). A
110 total of 71 recommendations were formulated to answer the PICO questions. The grading system
111 of the Scottish Intercollegiate Guidelines Network (SIGN) was used to grade the literature [19].
112 Allocation of studies to the different levels of evidence is shown in Table 2. The working group
113 added commentaries to the recommendations detailing the basis of the recommendations made.

114

115

116

117 **Table 2. Levels of evidence**

1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort or studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

118 According to the Scottish Intercollegiate Guidelines Network (SIGN) grading system. Source: SIGN 50: A guideline
 119 developer's handbook. Quick reference guide October 2014 [19]

120

121 Recommendations were graded according to the levels of evidence available (see Table 3). In
 122 some cases, a downgrading was necessary, for example, due to the lack of quality of primary
 123 studies included in a meta-analysis. The wording of the recommendations reflects the grades of
 124 recommendations; level A is indicated by "shall", level B by "should" and level 0 by "can/may". A
 125 good practice point (GPP) is based on experts' opinions due to the lack of studies; in this situation,
 126 the choice of wording was not restricted.

127 **Table 3. Grades of recommendation [18]**

A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population; or A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+
0	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2++ or 2+
GPP	Good practice points/expert consensus: Recommended best practice based on the clinical experience of the guideline development group

128

129 Between February 21th and March 25th 2019, online voting on the recommendations was
 130 undertaken using the “guideline-services.com” platform. All ESPEN members were invited to agree
 131 or disagree with, and to comment upon, each of the original 72 recommendations and 7
 132 statements generated by the guideline committee. A first draft of the guidelines was also made
 133 available to participants at the same time. 61 recommendations and 5 statements reached an
 134 agreement of >90 %, 10 recommendations reached an agreement of >75 – 90 % and 2 statements
 135 reached an of agreement ≤75 %. Those recommendations/statements with an agreement >90 %
 136 (i.e. those with a strong consensus) were directly passed, while all others were revised according
 137 to the comments made and then voted on again during a consensus conference which took place
 138 in Frankfurt on April 29th 2019. Apart from one, all recommendations received an agreement of
 139 >90 %. Two former statements were transformed into recommendations, both with >90%
 140 agreement. Three of the original recommendations were deleted. Thus, the final guidelines
 141 comprise of 71 recommendations and 5 statements (Table 4). To support the recommendations,
 142 the ESPEN guideline office created evidence tables of relevant meta-analyses, systematic reviews
 143 and (R)CTs, all of which are available online as supplemental material to these guidelines.

144 **Table 4. Classification of the strength of consensus and results of the online and consensus**
 145 **conference voting.**

		Online Voting	Consensus Conference
Strong consensus	Agreement of >90% of participants	61 R + 5 S	10 R
Consensus	Agreement of >75 - 90 % of participants	10 R	1 R
Majority agreement	Agreement of >50 - 75 % of participants	2 S*	-
No consensus	Agreement of <50 % of participants	-	-
Deleted		-	3 R**

146 R = Recommendation; S = Statement

147 * These two statements were converted into recommendations

148 ** Two recommendations were deleted during the revision after the online voting, one recommendation was deleted
 149 during the consensus conference

150

151 Search strategy

152 The literature search was performed separately for each PICO question in March 2018. Pubmed,

153 Embase and Cochrane databases were searched using the filters “human”, “adult” and “English”.

154 Table 5 shows the search terms used for the PICO questions. The results were pre-screened based

155 on the abstracts of articles. In addition to the above databases, websites from nutritional (nursing)

156 societies in English speaking or bilingual countries including the English language were searched

157 for practice guidelines.

158 Table 5. Search strategy

PICO question	Search terms used in combination with “home parenteral nutrition”, “human” and “adult”
1. What are the indications for HPN? 2. What are the criteria for an effective HPN program? 3. What are the criteria for a safe HPN program?	"guidelines" "registries" "indications" "malignant" OR "cancer", " program" "organization and administration OR management" "multidisciplinary" AND "team"
4. Which venous access device should be chosen 5. Which infusion control devices should be used for HPN?	"central venous catheter" OR "central venous access device" "peripherally AND inserted AND central AND catheters" "infusion pumps"
6. Which should be the appropriate infusion line management?	"central venous catheter related infection" "catheter-associated infection OR contamination OR sepsis OR complications OR occlusion" "catheter dressing OR ointment OR lock" "catheter hub" "skin antisepsis" "aseptic technique" "catheter exit site" "hand decontamination"

	<p>"swimming OR bathing OR showering"</p> <p>"sutureless device"</p> <p>"catheter securement"</p> <p>"administration set OR intravenous tubing"</p> <p>"gloves"</p> <p>"needleless connector OR device"</p> <p>"antiseptic barrier cap"</p> <p>"port needle"</p> <p>"pre-filled syringes"</p> <p>"taurolidine"</p>
<p>7. Which nutritional admixture bag should be chosen</p> <p>8. What are the critical steps during the preparation of PN admixtures?</p> <p>9. How should PN admixture be delivered?</p> <p>10. What should be the HPN admixture time and rate of infusion?</p>	<p>"admixture"</p> <p>"premade OR premixed OR multichambered OR ready to use OR "all in one"</p> <p>"compounded OR customized"</p> <p>"stability"</p> <p>"delivery"</p> <p>"infusion"</p> <p>"rate"</p> <p>"blood glucose"</p> <p>"glycaemia"</p>
<p>11. How should patients on HPN be monitored?</p>	<p>"monitoring"</p> <p>"follow-up"</p> <p>"tolerance"</p> <p>"complications"</p> <p>"quality of care"</p>
<p>12. Which are the local and personnel preconditions for home parenteral nutrition?</p> <p>13. Which are the requirements for the hospital centers that care for HPN patients?</p> <p>14. Which are the requirements for the nutritional support team?</p> <p>15. How should emergencies be managed?</p> <p>16. How should travelling with HPN be organized?</p> <p>17. Which criteria should be used to monitor the safety of HPN program provision?</p>	<p>"intestinal failure"</p> <p>"central venous catheter complications"</p> <p>"program"</p> <p>"organization and administration OR management"</p> <p>"multidisciplinary AND team"</p> <p>"emergency"</p> <p>"admission"</p> <p>"central venous catheters complications"</p> <p>"travel OR travelling"</p> <p>"quality of health care"</p> <p>"quality of care"</p>

160 **1. Indications for HPN**

161 *1. What are the indications for HPN?*

162 **Recommendation 1**

163 **HPN should be administered to those patients unable to meet their nutritional requirements via**
164 **the oral and/or enteral route and who can be safely managed outside of the hospital.**

165 **Grade of Recommendation: GPP – Strong consensus (95.8% agreement)**

166 **Commentary**

167 Several guidelines and standards on HPN have been published [3-15]. PN is a life-saving therapy to
168 those unable to meet their nutritional requirements by oral/enteral intake . Clearly, no
169 randomized controlled trial (RCT) can be conducted to compare HPN with placebo to confirm the
170 life-saving efficacy of HPN therapy in this condition [3]. Furthermore, no absolute
171 contraindications exist to the use of PN. However, the presence of organ failures and metabolic
172 diseases, such as heart failure, renal failure, type 1 diabetes, may be associated with reduced
173 tolerance to PN and may require careful and specific adaptations of the HPN program to meet the
174 patient's specific clinical needs.

175 Six guidelines and one expert opinion-based standard on HPN in this setting were compared in a
176 systematic review [10]. Although the guidelines generally covered the same topics, substantial
177 differences were observed among the recommendations. Most did not provide information on
178 intravenous medication, metabolic bone disease and indications in patients with malignant
179 disease. Moreover, grading discrepancies among various guidelines were found, as identical
180 recommendations were often labeled with different grades. Thus, the present guideline updates
181 the recommendations from previous guidelines and standards relating to the appropriateness and
182 safety of HPN. Nutritional requirements in specific clinical conditions, as well as the diagnosis and

183 treatment of CVAD and metabolic complications are not addressed in the present guideline.
184 Recommendations in previous ESPEN guidelines about the latter topics are still valid [3,4].

185

186 *2. What are the criteria for effective HPN program ?*

187 **Recommendation 2**

188 **HPN should be prescribed as the primary and life-saving therapy for patients with transient-**
189 **reversible or permanent-irreversible CIF due to non-malignant disease**

190 **Grade of Recommendation B – Strong consensus (94.7% agreement)**

191 **Commentary**

192 CIF has been defined as a chronic “reduction of gut function below the minimum necessary for the
193 absorption of macronutrients and/or water and electrolytes, such that intravenous
194 supplementation is required to maintain health and/or growth”, in metabolically stable patients
195 [2]. CIF can be due to either benign or malignant disease and may be reversible or irreversible [2].

196 The underlying diseases and the mechanisms of CIF due to benign disease in adults have been
197 described in a recent international ESPEN survey [21]. Crohn’s disease, mesenteric ischemia,
198 surgical complications, chronic intestinal pseudo-obstruction and radiation enteritis were the main
199 underlying diseases, accounting for around 75% of cases. Short bowel syndrome was the main
200 mechanism (around two-thirds of cases), while the remaining 33% of cases were due to intestinal
201 dysmotility, enterocutaneous fistulas, intestinal mechanical obstruction and extensive mucosal
202 diseases [21].

203 HPN is the primary and life-saving therapy for CIF [4]. The outcome of patients on HPN for CIF due
204 to benign disease has been reported in many single and multicenter retrospective studies [22-28]
205 and by an ESPEN prospective five year follow up [29-31]. These studies demonstrated that:

206 weaning from HPN after one to two years of starting may occur in 20% to 50% of patients; the five
207 year survival probability on HPN ranges from 70 to 80% depending on the underlying disease; CIF
208 may be associated with life-threatening complications of either the underlying disease or HPN, the
209 latter accounting for around 14% of total deaths (such as CVAD-related complications and
210 intestinal failure associated liver disease); the outcome of patients in terms of reversibility,
211 treatment-related morbidity and mortality, and survival probability is strongly dependent on care
212 and support from an expert multidisciplinary nutrition support team (NST).

213 In Europe, the prevalence of HPN for CIF due to benign disease has been estimated to range from
214 five to 20 cases per million population [22], with the exception of Denmark, where 80 cases per
215 million have been recently reported [26].

216 **Recommendation 3**

217 **HPN can be considered for patients with CIF due to malignant disease**

218 **Grade of Recommendation 0 – Strong consensus (95.8% agreement)**

219 **Recommendation 4**

220 **HPN should be prescribed to prevent an earlier death from malnutrition in advanced cancer**
221 **patients with CIF, if their life expectancy related to the cancer is expected to be longer than one**
222 **to three months, even in those not undergoing active oncological treatment.**

223 **Grade of Recommendation B - Consensus (90% agreement)**

224 **Commentary**

225 A mean survival of around 48 days has been reported in patients with malignant obstruction
226 receiving palliative care without artificial nutritional support [32]. International guidelines [15,33-
227 35] generally advocate the use of PN in patients with malignancy who have failed oral and enteral
228 nutrition (EN) and who have an expected survival longer than one to three months, which is the

229 longest predictable survival in an individual unable to maintain adequate oral nutrition without
230 artificial nutritional support.

231 A meta-analysis by Naghibi et al. [36] reported that 45% of incurable cancer patients receiving
232 HPN for malignant intestinal obstruction can survive more than three months. The median and
233 mean survival length was found to be 83 days and 116 days, respectively (55% mortality at three
234 months and 76% mortality at six months, respectively) [36]. These data are in keeping with those
235 of a large prospective multinational case series of 414 patients on HPN, 67% of whom had
236 intestinal obstruction, (median survival 91 days, 50% mortality three months and 77% mortality at
237 six months) [37].

238 The clinical challenge is to accurately identify those patients who are likely to survive long enough
239 to benefit from HPN treatment. Recently, a nomogram has been developed from variables
240 recognized as independent prognostic factors (Glasgow prognostic score, presence and site of
241 metastases and Karnofsky performance status), aimed at estimating the 3-, 6-months and overall
242 survival of incurable aphagic cachectic cancer patients considered for HPN [38].

243 It is noteworthy that the authors of a recent Cochrane review [39] concluded that they were very
244 uncertain whether total HPN improves length of life in people with malignant bowel obstruction,
245 largely as a result of the lack of published evidence. However, the authors reached these
246 conclusions after applying strict Cochrane methodology (allocation concealment, comparability of
247 treatment groups, blinding of participant and personnel) when reviewing the literature; this
248 approach may be appropriate for evaluating medication efficacy, but may be less applicable to
249 assessing the role of essential nutrition [40].

250 Six prospective studies [41-46] on HPN-dependent patients for ≥ 1 month showed a benefit on
251 health related quality of life (QoL) measured by validated tools (EORTC QLQ-C30 or FACT-G, or TIQ).
252 There are three RCT evaluating the impact of HPN in patients outcome [47-49], with the largest

253 [48,49] reporting an improvement in energy balance and, as-treated analysis, prolonged survival,
254 increased body fat and a greater maximum exercise capacity. The most recent RCT [50] comparing
255 the effects of 6-month HPN to 'best nutritional care' in cachectic gastrointestinal cancer patients
256 reported that HPN maintained or increased fat-free mass and improved QoL. It is noteworthy that
257 a group of experts has identified QoL as one of the most important outcome indicators of HPN in
258 cancer patients [51].

259 Specific contraindications for HPN support in cancer patients include [33]:

- 260 a) patients who are not adequately informed about the aims of HPN, of its limited benefits and
261 potential complications
- 262 b) patients who are not informed of their predicted prognosis, or of the possibility of
263 changing/withdrawing the treatment when it becomes futile
- 264 c) patients who are not sufficiently metabolically stable to be discharged home on PN

265 **Recommendation 5**

266 **HPN can be considered for patients without intestinal failure who are not able or do not want to**
267 **meet their nutritional requirements via the oral/enteral route. The patient should be clearly**
268 **informed about HPN benefits and risks.**

269 **Grade of Recommendation GPP – Consensus (89.5% agreement)**

270 **Commentary**

271 HPN surveys and registries report a percentage of cases who were not categorized as having either
272 benign or malignant intestinal failure (Table 6) [52-57]. These may include patients needing
273 artificial nutritional support who refused - or were not able to cope with - otherwise effective and
274 clinically-recommended EN [58]. Such patients may have cancer and an indwelling CVAD for
275 chemotherapy; alternatively, they may have dysphagia and elect not to have EN [59-61]. Since it is

276 difficult to deny nutritional support in clinical practice, HPN can sometimes be prescribed in these
 277 settings. Patients without CIF who are not able or do not want to meet their nutritional
 278 requirements via the oral/enteral route should be fully informed about the risks of PN therapy,
 279 which will likely be higher (including life-threatening risks related to HPN) than EN in this setting
 280 [3,4,58].

281 **Table 6. Indications for HPN in adult patients in different countries according to data from**
 282 **national registries and surveys.**

National report, year (ref #)	Total Patients (n.)	Benign GI disease (%)	Cancer on treatment (%)	Cancer-palliative (%)	Others (%)
SPAIN (SENPE Registry), 2016 [52]	256	44	10	25	Not specified, 21
US (ASPEN Registry), 2011-2014 [53]	1064	89	3	0.5	Malnutrition, 4.5 Neurological swallowing disorder, 0.1 Not specified, 2.9
UK (BANS report) 2015 [54]	1144	81.5	18.5		Indications for HPN in the total cohort: <ul style="list-style-type: none"> - Short bowel, 47 - Fistula, 8 - Malabsorption, 20 - GI obstruction, 10 - DR-Malnutrition, 6% - Swallowing Disorder. or Anorexia, 1 - Others, 8
ITALY (SINPE survey), 2012 [55,56]	46.1 (/10 ⁶ inhabitants)	20	61		Neurological disease, 12% Not specified, 7
CANADA (CNS Registry), 2011-2014 [57]	187	66	34		

283 GI, gastrointestinal; DR, disease-related

284

285

286

287

288 3. *What are the criteria for a safe HPN program?*

289 **Statement 1**

290 **For a safe HPN program, the patient and/or the patient's legal representative have to give fully**
291 **informed consent to the treatment proposed.**

292 **Strong consensus (95.7% agreement)**

293 **Statement 2**

294 **For a safe HPN program, the patient has to be sufficiently metabolically stable outside the acute**
295 **hospital setting.**

296 **Strong consensus (91.3% agreement)**

297 **Statement 3**

298 **For a safe HPN program, the patient's home environment has to be adequate to safely deliver**
299 **the therapy proposed.**

300 **Strong consensus (95.7% agreement)**

301 **Statement 4**

302 **For a safe HPN program, the patient and/or the caregiver has to be able to understand and**
303 **perform the required procedures for the safe administration of therapy.**

304 **Strong consensus (95.7% agreement)**

305

306 **Recommendation 6**

307 **The patient and/or the caregiver should be trained by a NST to safely infuse the PN with**
308 **appropriate monitoring and prompt recognition of any complications.**

309 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

310 **Recommendation 7**

311 **The prescribed nutritional admixture and ancillaries required for safe and effective therapy**
312 **should be delivered by an experienced/certified health care provider.**

313 **Grade of Recommendation GPP – Strong consensus (95.7% agreement)**

314 **Recommendation 8**

315 **The NST should provide appropriate monitoring and treatment for routine and/or emergency**
316 **care, with appropriate contact details provided to the patient 24 hours per day, seven days per**
317 **week.**

318 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

319 **Commentary**

320 HPN is a complex, life-saving therapy that may result in serious harm if not properly prescribed,
321 prepared and administered. The aims of an HPN program include provision of evidence-based
322 therapy, prevention of HPN-related complications such as catheter-related bloodstream infection
323 (CRBSI) and metabolic complications, as well as ensuring QoL is maximized [3,4]. The HPN program
324 shall provide an individualized, safe, effective and appropriate nutrition support plan at discharge
325 from hospital which should then be supervised and evaluated on a regular basis in the community
326 [62,63].

327 Previous guidelines and standards recommend that prescription, implementation and monitoring
328 of an individualized HPN program shall be managed by a NST in centers with HPN management
329 expertise [3,10,51,64-74]. Patients managed by such a dedicated patient-centered NST have better
330 outcomes and possible lower overall costs of care [22,64].

331 The overall care plan includes a variety of pre-discharge and post-hospital care assessments that
 332 require coordination between several health-professionals and care providers within and outside
 333 the hospital (Table 7). In addition, besides involvement of the key-members of a NST (physician,
 334 dietician, nurse, pharmacist), specific patients will require input from physiotherapy, psychology
 335 and occupational therapy colleagues [3,67-70]. Communication with the caregivers at home
 336 (especially the home care nurse) and in the hospital seems to be a key-factor for patients [62,70].
 337 An experienced and certified health care provider is also required for the appropriate delivery of
 338 nutritional admixture and ancillaries to patient's home. The 'adequate' metabolic and clinical
 339 stability of a patient can be assessed by vital parameters, energy, protein, fluid and electrolyte
 340 balances and glycemic control; here, the where term adequate means no immediate risk of acute
 341 imbalance after hospital discharge.

342 If the patient can achieve a stable HPN regimen and his/her overall clinical condition is acceptable,
 343 an education program for patients and/or caregivers should be initiated to teach correct and
 344 proper HPN care.

345 The home care environment should be assessed before the education program starts.

346 **Table 7. Items to be included in the assessment at patient discharged on HPN [63,74]**

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- 347
- 348 • Medical, physical, psychological and emotional suitability/stability of the patient
 - 349 • Stability of the PN regimen (dosage and admixture)
 - 350 • Level of home care and support required
 - 351 • Lifestyle/activities of daily living
 - 352 • Rehabilitative potential
 - 353 • Potential for QoL improvement
 - 354 • Potential for learning self-management of HPN (patient/caregivers)
 - 355 • Knowledge and experience of the home nursing team (if no self-management)
 - 356 • Basic home safety, facilities and general cleanliness instruction
 - 357 • Need for extra equipment (e. g. backpack, infusion pump, hospital bed, extra drip stand)
 - 358 • Home care provider of nutritional admixture, equipment and ancillaries
 - 359 • Reimbursement for bags, services and supplies
 - 360 • Around the clock (on-call) availability of an experienced home care provider
 - 361 • Post-discharge monitoring necessities/possibilities (including scheduled laboratory tests)
 - 362 • Medication prescription with administration details
-

364

365 **2. CVAD and infusion pump**

366 *4. Which CVAD should be chosen?*

367 **Recommendation 9**

368 **The choice of CVAD and the location of the exit site shall be made by an experienced HPN NST,**
369 **as well as by the patient.**

370 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

371 **Recommendation 10**

372 **The exit site of the CVAD should be easily visualized and accessible for self-caring patients.**

373 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

374 **Recommendation 11**

375 **Tunneled CVAD or totally implanted CVADs shall be used for long-term HPN.**

376 **Grade of Recommendation GPP – Strong consensus (90.9% agreement)**

377 **Recommendation 12**

378 **Access to the upper vena cava should be the first choice for CVAD placement, via the internal**
379 **jugular vein or subclavian vein.**

380 **Grade of Recommendation B – Strong consensus (100% agreement)**

381 **Recommendation 13**

382 **Right-sided access should be preferred to the left-sided approach to reduce the risk of**
383 **thrombosis.**

384 **Grade of Recommendation B – Strong consensus (95.2% agreement)**

385 **Recommendation 14**

386 **The tip of the CVAD should be placed at the level of the right atrial-superior vena cava junction.**

387 **Grade of Recommendation B – Strong consensus (100% agreement)**

388 **Commentary**

389 The literature search did not add any new information relating to this question when compared to
390 the previous ESPEN guideline for CIF in adults [4]. The process of choosing a CVAD for HPN must
391 involve the patient and the NST, including the specific professional (e.g. anaesthetist, radiologist or
392 surgeon) responsible for placing the CVAD [76,77]. The patient should be involved in choosing the
393 location of the cutaneous exit site which should, of course, also facilitate optimal self-care [78].
394 Proximity to wounds, prior exit sites, tracheotomies, stomas or fistulae should be avoided.
395 Tunneled CVAD (such as Hickman, Broviac or Groshong) or totally implantable devices (port) are
396 usually chosen for long-term HPN (>6 months). [3]. A single lumen CVAD is preferred, as infections
397 have been reported to occur more frequently with multiple lumen CVAD [73,79,80].
398 The risk of venous thrombosis is reduced with right vs. left-sided CVAD insertion [81] and,
399 regardless of the type of catheter used and the insertion side, when the CVAD tip is located at the
400 superior vena cava-right atrium junction [81-83].

401

402 **Recommendation 15**

403 **Peripherally inserted central venous catheters (PICCs) can be used if the duration of HPN is**
404 **estimated to be less than six months.**

405 **Grade of Recommendation 0 – Strong consensus (100% agreement)**

406 **Commentary**

407 ESPEN and ASPEN guidelines [4,84] for CIF do not recommend PICCs for long-term HPN. However
408 many series have reported successful use of PICCS for up to four years [53,85-93].

409 The concern of long term PICC use relates to the putative risk of catheter-related vein thrombosis
410 and CRBSI compared to tunneled CVADs. A study comparing PICCs with other CVADs in long-term
411 HPN found no difference in the CRBSI rate, a higher frequency of catheter removal because of
412 venous-thrombosis and a shorter time between catheter insertion and the first complication in the
413 PICC cohort [90]. A meta-analysis of comparative studies showed a lower rate of CRBSI in HPN
414 patients using PICCs; however, no difference between PICC and tunneled CVADs was observed
415 when the single-arm studies were analyzed [94].

416 In summary:

- 417 a) better description of the reasons for placement and outcomes of long-term PICC use in routine
418 clinical practice is required
- 419 b) PICCs seem to be associated with a lower risk of CRBSI and a possible higher risk of catheter-
420 related venous thrombosis;
- 421 c) the time to the occurrence of the first catheter-related complication seems to be shorter with
422 PICCs.

423

424

425 5. Which infusion control devices should be used for HPN?

426 **Recommendation 16**

427 **HPN should be administered using an infusion pump for safety and efficacy reasons.**

428 **Grade of Recommendation GPP – Strong consensus (91.3% agreement)**

429 **Recommendation 17**

430 **In exceptional circumstances a flow regulator can be temporarily used for HPN; administration**
431 **sets with only a roller clamp should not be used.**

432 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

433 **Commentary**

434 The introduction of infusion pumps has been one of the major technologic advances for the safe
435 administration of PN [95]. An infusion pump is a medical device that delivers fluids, such as
436 nutrients and medications, into a patient's body in controlled amounts [96]. The use of an
437 electronic (ambulatory) infusion pump with compatible delivery sets is considered as good
438 practice [6,97,98]. Because of the (large) fluid volume, the hypertonicity of the PN admixture and
439 the amount of glucose and potassium delivered, rapid administration or 'free flow' can potentially
440 cause serious harm [98].

441 It is therefore strongly recommended to use this device whenever possible to manage and
442 monitor the delivery of HPN [3,4,6,13,51,99]. The characteristics of a safe and effective infusion
443 pump for HPN are described in Table 8.

444

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447 **Table 8. Necessary features for an HPN infusion pump [4,6,96,98]**

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- Easy to clean (splash-proof)
 - Operating silently
 - User friendly interface (display/keyboard)
 - Portability: it should maximize patient’s mobility (e.g. possibility to carry it in a backpack together with the PN-bag)
 - Availability of a variety of pump-compatible sets with different line lengths
 - Rechargeable battery pack(s) with several hours operating time
 - Safety features:
 - audible and visual alarms
 - self-test at power-up
 - upstream and downstream occlusion alarms
 - anti-free flow control
 - Easy to use instructions
 - Safe operation
 - Alarm silencing, modification, disabling
 - Programmable mode options that include ramp-up/ramp-down and continuous infusion modes
 - Option to “lock out” those infusion modes not required and control the panel lock to prevent accidental or child tampering
 - Wireless interface (optional):
 - Infusion parameters remotely controlled
 - Pre-warnings or warnings on mobile phones
 - Service and maintenance contract provided, with regular testing of proper functioning

472

473 **Recommendation 18**

474 **A portable pump can improve the patient’s QoL when compared to stationary pumps.**

475 **Grade of Recommendation 0 – Strong consensus (95.7% agreement)**

476 **Commentary**

477 Two studies on the use of portable infusion pumps found that the ambulatory pump enabled HPN

478 patients to gain independence [100,101]. Benefits included maintaining desired flow, low noise,

479 long battery life as well as increased probability of social and working rehabilitation and of good

480 QoL. If an ambulatory pump is not available (or appropriate because of the patient's condition), a

481 standard volumetric pump with an intravenous stand is an alternative [4].

482

483

484 **3. Infusion line and catheter site care**

485 *6. Which should be the appropriate infusion line management?*

486 **Recommendation 19**

487 **Either a sterile gauze or sterile, transparent, semipermeable dressing should be used to cover**
488 **the CVAD exit site.**

489 **Grade of Recommendation B – Strong consensus (90.9% agreement)**

490 **Recommendation 20**

491 **When transparent dressings are used on tunneled or implanted CVAD exit sites, they can be**
492 **replaced no more than once per week (unless the dressing is soiled or loose).**

493 **Grade of Recommendation 0 – Strong consensus (95.5% agreement)**

494 **Recommendation 21**

495 **A tunneled and cuffed CVAD with a well healed exit site might not require dressing to prevent**
496 **dislodgement.**

497 **Grade of Recommendation GPP confirmed – Strong consensus (100% agreement)**

498 **Commentary**

499 The purpose of a dressing is to secure the CVAD, as well as providing barrier protection from
500 microbial colonization and infection. Different kinds of dressings can be used for protecting the
501 CVAD site, including (semi-permeable) transparent polyurethane dressings and gauze and tape.
502 Transparent dressings permit continuous visual inspection of the CVAD site and require less
503 frequent changes unless the dressing becomes damp, loose, or visibly soiled. If there is visible pus
504 exuding from the exit or the site is bleeding, it is better to use a gauze dressing (may be replaced
505 every two days or sooner) until the problem is resolved [73].

506 A recent systematic review included eight studies with patients in adult bone marrow
507 transplantation (n=101), hemodialysis (n=138), gastroenterological (n=72), adult ICU (n=21),
508 pediatric and adult oncology units (n=98) and general wards (n=76) and reported that there was
509 no clear difference between gauze and tape and polyurethane dressings on the incidence of CRBSI.
510 All included studies had a high risk of performance bias and were of low quality evidence [102]. A
511 previous systematic review came to the same conclusion but the quality of the included studies
512 was also low with small sample sizes and underpowered studies comparing different types of
513 dressings [103]. Finally, in an older systematic review, the use of transparent dressings on CVAD
514 was significantly associated with an elevated relative risk of catheter tip infection (RR = 1.78; 95%
515 CI, 1.38 to 2.30) compared with gauze dressings [104].

516 The frequency of dressing change also remains a question of some debate. In a multicenter study,
517 399 bone marrow transplant patients with a tunneled CVAD (n = 230) were randomly allocated to
518 receive CVAD polyurethane dressing changes at different time intervals (Group 1: every two or five
519 days, Group 2: every five or ten days). There was no difference in the rate of local infection but
520 more skin toxicity was reported in the group with shorter interval dressing changes [105].
521 Nevertheless, a recent systematic review concluded that there is currently inconclusive evidence
522 as to whether longer intervals between CVAD dressing changes are associated with more or less
523 CVAD-related infections [106].

524 After the healing period (+/- 3 weeks), it remains unclear if a dressing is necessary [73]. The recent
525 ESPGHAN/ESPEN/ESPR/CSPEN guideline for pediatric parenteral nutrition access states that a
526 tunneled CVAD with a well-healed exit site does not require dressing to prevent dislodgement
527 (GPP); however, in children it is useful to have CVADs looped and covered [107].

528 A dressing could also potentially act as a reservoir for pathogens. One study tested this hypothesis
529 by removing the CVAD exit site (gauze) dressing. Seventy-eight individuals with cancer and newly

530 inserted CVADs, stratified for gender (37 men and 41 women) and transplant status, were
531 recruited and randomly assigned to receive either a gauze dressing or no dressing, once their
532 CVAD insertion site had healed (three weeks). There was no significant difference in CRBSI
533 episodes ($p = 0.28$) or rehospitalization rates ($p = 0.41$) between the dressing and no-dressing
534 group, but individuals in the dressing group developed CRBSI sooner ($p = 0.02$) than did individuals
535 in the no-dressing group [108].

536

537 **Recommendation 22**

538 **Tubing to administer HPN should be replaced within 24 hours of initiating the infusion.**

539 **Grade of Recommendation B – Strong consensus (100% agreement)**

540 **Commentary**

541 PN is considered as a medium where several factors may influence microbial growth leading to
542 CRBSI risk [109]. In a prospective, randomized study, an intention-to-treat analysis demonstrated a
543 higher level of intravenous tubing (administration set) colonization in tubes changed every 4- to 7-
544 days vs. those only changed every 3-days; however, the two groups had a comparable rate of
545 colonization when patients receiving PN ($n = 84$) were excluded from this study [110]. Another
546 randomized trial specifically involving PN infusion, found that changing tubing every 4 days vs.
547 every 2 days did not impact on hub contamination and CRBSI rates [111]. A Cochrane systematic
548 review found: a) no evidence to demonstrate that CRBSI rate was affected by frequent changes of
549 non-lipid containing tubing; b) some evidence suggesting that mortality increased within the
550 neonatal population with infrequent giving set replacement. However, much of the evidence
551 evaluated in this Cochrane review was derived from studies of low to moderate quality [112,113].

552 Currently there is no evidence that it is safe to extend the period of administration sets that
553 contain lipids beyond an interval of 24 hours and this is generally accepted as best practice
554 [112,113]. Furthermore, the Center for Disease Control and Prevention (CDC) consider PN as an
555 independent risk factor for CRBSI and recommend infusion set replacement after 24 hours [73].
556 Given that HPN patients are very often on cyclic PN, infusion sets normally will be replaced every
557 24 hours.

558

559 **Recommendation 23**

560 **Strict aseptic technique for the care of home CVAD shall be maintained.**

561 **Grade of Recommendation A – Strong consensus (100% agreement)**

562 **Commentary**

563 A recent systematic review revealed that there is not enough evidence to confirm whether
564 patients receiving PN are more at risk of developing CRBSI than those who did not receive PN
565 therapy [114]. Nevertheless, CRBSI is a common complication in patients receiving HPN. In a study
566 of 172 adult HPN patients, 94 CRBSIs were diagnosed on 238 CVADs. Previous catheterizations and
567 the presence of an enterocutaneous stoma were significantly related with a higher infection risk
568 [115]. In another study with HPN patients, 465 CRBSIs developed in 187 patients (18%) during the
569 three years study period [116].

570 Cotogni et al [117] reported that the incidence of CRBSIs is low (0.35/1000 catheter-days),
571 particularly for PICCs (0/1000; $P < .01$ vs Hohn and tunneled catheters) and for ports (0.19/1000; P
572 $< .01$ vs Hohn and $P < .05$ vs tunneled catheters)

573 A systematic review in adult patients receiving HPN showed an overall CRBSI ranged between 0.38
574 and 4.58 episodes/1000 catheter days (median 1.31). Gram-positive bacteria of human skin flora
575 caused more than half of infections [118].

576

577 **Recommendation 24**

578 **Hand antisepsis and aseptic non-touch technique should be used when changing the dressing on**
579 **CVADs.**

580 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

581 **Commentary**

582 Hand antisepsis is the most important measure to prevent contamination. Using gloves does not
583 obviate the need for hand antisepsis. Gloves can be used when contact with blood, body fluids,
584 secretions and excretions can be anticipated. The CDC leaves the choice of using gloves to local or
585 federal regulations, rules, or standards [73]. There is only indirect evidence demonstrating the use
586 of non-sterile gloves is not inferior to sterile ones even in more invasive procedures such as minor
587 skin excisions and outpatient cutaneous surgical procedures, [119,120].

588

589 **Recommendation 25**

590 **A 0.5 - 2% alcoholic chlorhexidine solution shall be used during dressing changes and skin**
591 **antisepsis; if there is a contraindication to chlorhexidine, tincture of iodine, an iodophor, or 70%**
592 **alcohol shall be used as an alternative.**

593 **Grade of Recommendation A – Strong consensus (95.2% agreement)**

594 **Commentary**

595 There is a body of evidence that demonstrates that the incidence of CRBSI is significantly reduced
596 in patients with CVAD who receive chlorhexidine gluconate versus povidone-iodine for insertion-
597 site skin disinfection [73,121-125]. This is also the reason why chlorhexidine is mentioned in most
598 checklists for CVAD insertion [126]

599

600 **Recommendation 26**

601 **Hand decontamination, either by washing hands with soap and water but preferably with**
602 **alcohol-based hand rubs, should be performed immediately before and after accessing or**
603 **dressing a CVAD.**

604 **Grade of Recommendation B – Strong consensus (95.2% agreement)**

605 **Commentary**

606 Hand decontamination is a key factor in the prevention of health-care related infections which
607 includes CVAD-related infections [73]. Several products are available: alcohol-based
608 decontamination, non-alcohol-based decontamination, antimicrobial/antiseptic hand-washes or
609 agents or liquid soap and water. Before using a hand-rub solution, hands should be free from dirt
610 and organic material. The solution must come into contact with all surfaces of the hand. The hands
611 must be rubbed together vigorously, paying particular attention to the tips of the fingers, the
612 thumbs and the areas between the fingers, until the solution has evaporated and the hands are
613 dry. This should be done immediately before and after direct patient care or contact and after
614 removal of any gloves [127].

615 Results from a systematic review supported the use of alcohol-based hand rubbing: it removed
616 microorganisms effectively, required less time and irritated hands less often than did handwashing
617 with soap or other antiseptic agents and water [128]. Furthermore, the availability of bedside

618 alcohol-based solutions increased compliance with hand hygiene among health care workers [128].

619 Other randomized trials also favored the use of alcohol-based solutions [129,130].

620

621 **Recommendation 27**

622 **A needle-free connector should be used to access intravenous tubing.**

623 **Grade of Recommendation B – Strong consensus (100% agreement)**

624 **Recommendation 28**

625 **Needle-free systems with a split septum valve may be preferred over some mechanical valves**
626 **due to increased risk of infection with mechanical valves.**

627 **Grade of Recommendation 0 – Strong consensus (100% agreement)**

628 **Commentary**

629 Needleless connectors are an easy access point for infusion connection. They were introduced and
630 mandated to prevent needlestick injuries, reducing the risk of transmission of blood-borne
631 infections to healthcare personnel [73]. In several studies, the use of needleless connectors
632 appears to be effective. Compared to the use of standard caps or 3-way stopcocks, they can
633 reduce internal microbial contamination and so the incidence of CRBSI, but they have to be
634 properly disinfected [131-133].

635 The majority of needleless connectors fall into one of two categories; namely those with no
636 moving internal parts (e.g. an external split septum) and connectors which moving internal
637 components. Based on available data, split septum connectors should be preferentially used
638 instead of mechanical valves [73,134]. The issue becomes more complicated when the risk of (tip)
639 occlusion due to negative displacement or blood reflux is also taken into account, depending on

640 the type of connector used [135]. Needleless connectors have to be changed no more frequently
641 than every 72 hours or according to manufacturers' recommendations [73].

642

643 **Recommendation 29**

644 **Contamination risk shall be minimized by scrubbing the hub connectors (needleless connectors)**
645 **with an appropriate antiseptic (alcoholic chlorhexidine preparation or alcohol 70%) and access it**
646 **only with sterile devices.**

647 **Grade of Recommendation A – Strong consensus (100% agreement)**

648 **Recommendation 30**

649 **For passive disinfection of hub connectors (needleless devices) antiseptic barrier caps should be**
650 **used.**

651 **Grade of Recommendation B – Strong consensus (90.9% agreement)**

652 **Commentary**

653 Needleless connectors are used on virtually all CVAD, providing an easy access point for infusion
654 connection. Infection guidelines strongly recommend proper disinfection of access ports [136]. A
655 systematic review revealed that the greatest risk for contamination of the CVAD after insertion
656 was the needleless connector, with 33-45% contaminated, and compliance with disinfection was
657 as low as 10%, but the optimal technique or disinfection time were not identified [137]. Another
658 systematic review recommended scrubbing with chlorhexidine-alcohol for 15 seconds [138].
659 However, if the membranous septum of a needleless luer-activated connector is heavily
660 contaminated, conventional disinfection with 70% alcohol does not reliably prevent entry of
661 microorganisms [139]. Since compliance with a time-consuming manual disinfection process is low,
662 the use of an antiseptic barrier cap (placed on a luer needleless connector), which cleans the

663 connection surface by continuous passive disinfection, was associated with a decrease in CRBSI
664 [139,140].

665

666 **Recommendation 31**

667 **If HPN is delivered via an intravenous port, needles to access ports should be replaced at least**
668 **once per week.**

669 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

670 **Commentary**

671 An implanted intravenous port is a small device with direct access to a central vein, used to draw
672 blood and give treatments, including intravenous fluids, drugs, blood transfusions and PN. The
673 port is placed just underneath the skin, usually in the chest. A catheter is attached to a
674 subcutaneous pocket (made of titanium) with the tip ending at the right atrial-superior vena cava
675 junction. To gain access, a needle is inserted through the skin and the rubbery self-healing
676 membrane of the port. The CDC guideline considers the timeframe to replace needles as an
677 ‘unresolved’ issue [73]. There is also a possible higher risk of colonization of administration sets
678 with PN. On the other hand, one retrospective study demonstrated that weekly changing of exit-
679 site needles and transparent dressings on intravenous ports seems to be safe and cost-effective
680 but, in this study, patients on PN had a significantly greater risk of developing an infection from
681 Candida Species [141]. In a study with patients on continuous chemotherapy, needles were in
682 place for an average of 28 days without adverse effect [142]. Because there is no clear evidence,
683 we suggest replacing port needles at least once-a-week with the use of PN. This also gives the
684 opportunity for some patients to safely take a bath or shower when the needle has been removed
685 and replaced afterwards.

686

687 **Recommendation 32**688 **The CVAD or CVAD site should not be submerged unprotected in water.**689 **Grade of Recommendation B – Strong consensus (95.2% agreement)**690 **Commentary**

691 A study in children suggested that swimming did not increase the risk of tunneled CVAD-related
692 infections [143]. No firm recommendation could be made in a review of 45 articles and 16
693 pediatric HPN programs regarding swimming and CVADs but the authors also reported a fatal
694 event immediately after swimming [144]. Using a closed-hub system and waterproof catheter hub
695 connections significantly reduced the incidence of CRBSIs (particularly infections caused by gram-
696 negative pathogens) in another group of pediatric patients [145].

697 The CDC guidelines (recommendation B) allow showering if precautions can be taken to reduce
698 the likelihood of introducing organisms into the catheter (e.g. if the catheter and connecting
699 device are protected with an impermeable cover during the shower) [73]. The
700 ESPGHAN/ESPEN/ESPR/CSPEN guideline for pediatric PN access allows swimming (GPP) when a
701 water-resistant dressing is used to cover the whole catheter and, after swimming, the exit site
702 should be cleaned and disinfected [107].

703

704 **Recommendation 33**705 **Sodium chloride 0.9% instead of heparin should be used to lock long-term CVAD.**706 **Grade of Recommendation B – Strong consensus (95.5% agreement)**707 **Commentary**

708 Historically, heparin was the most commonly used catheter lock solution. However, a
709 retrospective study [146], a randomized prospective study [147] and two systematic reviews
710 [148,149] demonstrated that normal saline flushing is not inferior to heparin flushing regarding
711 CVAD occlusion, reflux dysfunction and flow dysfunction. ASPEN guidelines state that “no
712 recommendations can be made as to which flush solution should be used to maintain patency for
713 HPN CVAD due to the lack of studies” [84].

714 For the primary prevention of CVAD-related venous thrombosis, ESPEN guidelines for CIF
715 recommend insertion of the catheter using ultrasound guidance and placement of the tip at the
716 superior vena cava-right atrium junction, suggest flushing CVAD with saline and do not
717 recommend routine thromboprophylaxis with drugs (heparin, warfarin) [4]. ESPEN guidelines for
718 CIF do not recommend heparin for the prevention of CRBSIs [4], because it promotes intraluminal
719 biofilm formation and therefore potentially increases the risk of CRBSIs [150,151]. German
720 guidelines give a GPP grade for their recommendation of using saline and a grade B for their
721 recommendation of not using heparin [11]. A grade B recommendation for the use of saline
722 instead of heparin to flush and lock the CVAD is appropriate, given that this approach does not
723 increase the risk of CVAD occlusion and has a lower risk of biofilm formation in the CVAD lumen.

724 **Recommendation 34**

725 **As an additional strategy to prevent CRBSIs, taurolidine locking should be used because of its**
726 **favorable safety and cost profile.**

727 **Grade of Recommendation B – Strong consensus (100% agreement)**

728 **Commentary**

729 For the primary prevention of CRBSI, ESPEN guidelines for CIF [4]:

730 a) recommend education of staff and patients/caregivers; implementation of an adequate policy
731 of hand washing and disinfection by patients and staff; handwashing and disinfection by patients
732 and caregivers before touching CVAD as well as after CVAD care; disinfection of the hub connector
733 every time it is accessed; use of tunneled single-lumen catheters whenever possible; use of
734 chlorhexidine 2% for antiseptic of hands, CVAD exit site, stopcocks, catheter hubs and other
735 sampling ports and regular change of IV administration sets.

736 b) suggest performing site care, including catheter hub cleaning on at least a weekly basis;
737 changing CVAD dressings at least once weekly; avoiding CVAD care immediately after changing or
738 emptying ostomy appliances and disinfecting hands after ostomy care.

739 c) do not recommend the use of in-line filters; routine replacement of CVADs; antibiotic
740 prophylaxis and heparin lock.

741 ESPEN guidelines for CIF were published in 2016. Since then, no additional relevant literature was
742 found concerning the above recommendations, but two high quality double blinded RCTs
743 [152,153] and one extensive retrospective analysis [154] have been published on antimicrobial
744 CVAD locking with various taurolidine formulations, that have considerably changed the available
745 body of evidence and the strength of recommendation about the use of taurolidine for the
746 prevention of CRBSI. All studies were performed in the setting of HPN support for adult benign CIF.
747 Tribler et al. investigated CVAD locking with taurolidine 1.4%-citrate-heparin in comparison to
748 control (low-dose heparin 100 IE/mL) in a single center study in 41 high-risk Danish HPN patients
749 who had been stratified according to their prior CRBSI incidence [151]. In 20 patients who received
750 the taurolidine-containing formulation, no CRBSIs occurred in contrast to CRBSIs in 7 out of 21
751 controls (incidence 1.0/1000 CVC days; $p < 0.05$). Costs in the taurolidine arm were lower because
752 of fewer admission days related to CRBSI treatment.

753 Since locking with heparin solutions has been suspected of promoting CRBSI, Wouters et al.
754 compared a pure taurolidine 2% lock to another control (saline 0.9%) in a multicenter trial [153].
755 Patients were stratified in a new catheter group and a pre-existing catheter group. Overall 102
756 patients were analyzed. In the new catheter group, CRBSIs/1000 catheter days were significantly
757 lower (0.29 vs 1.49) in the taurolidine arm while in patients who entered the trial with a pre-
758 existing catheter CRBSI rates were also lower in the taurolidine arm (0.39 vs 1.32; $p > 0.05$ due to
759 under-powering). Mean costs per patient were significantly lower for taurolidine. Drug-related
760 adverse events were rare and generally mild.

761 Wouters et al also retrospectively analyzed long-term complications and adverse events in adult
762 HPN patients from a national referral center who all used taurolidine locks between 2006 and
763 2017 [154]. In total, 270 HPN patients used taurolidine during 338.521 catheter days. CRBSIs,
764 catheter related venous thrombosis and occlusions occurred at rates of 0.60, 0.28, and 0.12 events
765 per 1000 catheter days, respectively. In 24 (9%) patients, mild to moderate adverse events
766 resulted in discontinuation of taurolidine. A subsequent switch to 0.9% saline resulted in an
767 increased CRBSI rate (adjusted rate ratio 4.01, $P = 0.02$). Several risk factors were identified for
768 CRBSIs (including lower age and increased infusion frequency), thrombosis (site of vein insertion),
769 and occlusions (type of access device).

770

771 **Recommendation 35**

772 **If a PICC is used for HPN, a sutureless device should be used to reduce the risk of infection.**

773 **Grade of Recommendation B – Strong consensus (100% agreement)**

774 **Recommendation 36**

775 **For the securement of medium- to long-term PICCs (> 1 month) a subcutaneously anchored**
776 **stabilization device can be used to prevent migration and save time during dressing change.**

777 **Grade of Recommendation 0 – Strong consensus (100% agreement)**

778 **Commentary**

779 A prospective study with 254 HPN patients revealed that use of sutureless devices for CVAD
780 securement decreased the risk of CRBSI and dislocation ($p < 0.001$) [117]. A multiple treatment
781 meta-analysis found that sutureless securement devices were as likely to be the most effective at
782 reducing the incidence of CRBSI but the quality evidence was low [102]. For the securement of
783 medium- to long-term PICCs, a subcutaneously anchored stabilization device can be used; it seems
784 safe and cost-effective [155]. In the UK, the National Institute for Health and Care Excellence
785 (NICE) recommends the adoption of this device (SecurAcath) for securing PICCs within the National
786 Health Service in England [156]. Another study demonstrated that the use of SecurAcath saved
787 time during dressing change compared with an alternative securement device (Statlock) but
788 training on correct placement and removal was critical to minimize pain [157]. Besides sparing
789 time during dressing change, it also can prevent migration of the PICC [158].

790

791 **Recommendation 37**

792 **In multilumen catheters, a dedicated lumen should be used for PN infusion.**

793 **Grade of Recommendation GPP – Strong consensus (95.5% agreement)**

794 **Commentary**

795 A previous ESPEN guideline recommended use of a single-lumen CVAD or of a dedicated lumen on
796 a multilumen CVAD for PN administration [9]. The CDC guidelines gave no recommendation
797 regarding the use of a dedicated lumen for PN [73]. Recently, Australian authors reviewed the
798 available literature for comparative rates of CRBSIs in patients who received their PN in any health
799 setting through a dedicated lumen compared with those who had PN administered through
800 multilumen CVADs from 2286 records that were identified through database searching; they found
801 only two studies that fit inclusion criteria in a qualitative synthesis [159]. These studies included
802 650 patients with 1349 CVADs showing an equal distribution of CRBSIs between groups [159]. This
803 lack of evidence for the use of a dedicated lumen to reduce infections most likely resulted from
804 the poor way study results were reported with a high risk of bias, indicating the need for well-
805 powered high-quality research in this field. Therefore, the panel of the present guideline strongly
806 agreed to confirm the recommendation made by the earlier ESPEN guidelines [9]

807

808 **Recommendation 38**

809 **Routine drawing of blood samples from CVAD should be avoided if possible due to an increased**
810 **risk of complications.**

811 **Grade of Recommendation B – Strong consensus (95.2% agreement)**

812 **Commentary**

813 When risk factors for CRBSI occurrence were retrospectively studied in 125 adults who received
814 HPN by reviewing medical records from a national home care pharmacy in patients who used HPN
815 at least twice weekly for > 2 years between 2006 and 2011, it was found in adults (331 CVADs,
816 CRBSI rate 0.35/1000 catheter days) using univariate analysis that the use of subcutaneous
817 infusion ports instead of tunneled catheters ($p = 0.001$), multiple lumen catheters ($p = 0.001$),

818 increased frequency of lipid emulsion infusion ($p = 0.001$), obtaining blood from the CVC ($p <$
819 0.001), and infusion of non-PN medications via the CVC ($p < 0.001$), were significant risk factors for
820 CRBSI occurrence [160].

821 Although high quality studies in the field of (H)PN are lacking, indirect evidence from a
822 retrospective multivariate analysis of 452 totally implantable vascular devices in French cystic
823 fibrosis patients that were used for administration of antibiotics, showed that removal, either due
824 to obstruction (21%), infection (9%), septicemia (7%) or vascular thrombosis (5%), could be linked,
825 apart from the CVC material (polyurethane vs silicone), to their routine use for blood sampling
826 (versus never) [161].

827

828 **4. Nutritional admixtures**

829 *7. Which nutritional PN admixture bag should be chosen?*

830 **Statement 5**

831 **The HPN-admixture shall meet the patient's requirement.**

832 **Strong consensus (95.7% agreement)**

833 **Recommendation 39**

834 **Either commercially available ready-to-use admixtures or customized and tailored to the**
835 **individual patient's requirements admixtures can be used for HPN.**

836 **Grade of Recommendation GPP – Strong consensus (95.7% agreement)**

837 **Recommendation 40**

838 **Customized and tailored HPN admixtures can be prepared either by individual compounding or**
839 **by ready-to-use prepared and adapted commercial multi-chamber bags, according to the**

840 **manufacturer instructions and using aseptic admixture technique preferably in a laminar flow**
841 **cabinet.**

842 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

843 **Commentary**

844 The PN admixture provided for HPN should meet the individual patient's requirements [3,4]. PN
845 admixtures can be compounded in single bags, dual chamber bags or three in one/all-in-one (AIO)
846 bags (these contain separate compartments for lipid emulsion/glucose/amino acids to be opened
847 and mixed before infusion). Vitamins and trace elements can be added prior to infusion in the
848 home setting, if appropriate compatibility and stability [3,4]. Dual and three chamber bags have
849 advantages for HPN patients as they have a longer shelf life. Some AIO bags do not require
850 refrigeration, which provides advantages for HPN patients while travelling. Stability is also
851 markedly prolonged by refrigeration that requires a dedicated refrigerator for HPN storage [4].

852 The clinical advantages or disadvantages of individually compounded ("tailored" or "customized")
853 PN admixture in comparison with commercially available ready-to-use ("premade" or "premixed")
854 PN admixture adapted to the patient's requirements has been addressed by previous guidelines,
855 but published data did not support definitive recommendations. ESPEN guidelines do not address
856 whether commercial ready to use bags (with or without additions) have any advantages over
857 customized bags in the home setting [3,4]. ASPEN clinical guidelines state that commercial ready
858 to use bags are considered as an available option for patients alongside customized PN
859 formulations to best meet patients' needs [162] However, this was based on literature comparing
860 different types of bags in the hospital inpatient setting and not at home. The guideline also states
861 that an evaluation of clinical outcomes, safety and cost should be considered before making the
862 final determination. However, they highlight that most of the controlled clinical trials do not
863 directly compare the use of commercial ready-to-use bags with customized PN systems for patient

864 outcomes, efficacy or safety and focus instead on evaluations following conversion from one
865 delivery approach to another system [162]. German guidelines advocate the use of "all-in-one
866 nutrient mixtures" and advise that multi-bottle systems should not be used because of increased
867 risks and more difficult handling [11,163].

868 The literature search for this guideline provided eleven articles that were considered to have some
869 relevance to the question of comparison of commercial ready-to-use and customized PN
870 admixture in non-critically ill patients [164-174]. Only one of the eleven articles, a conference
871 abstract, compared different types of PN bags in the homecare setting, with all other articles
872 evaluating the use of PN in hospital inpatients [164]. The results suggested that customized PN
873 may be associated with a lower microbiological risk than commercial ready-to-use bags for
874 patients with CIF; however, differences were not-statistically significant and this paper has not
875 been published in full [164]. There were no studies found that compared commercial ready-to-use
876 and customized PN in relation to clinical outcome or cost in HPN patients. There are no data on
877 the use of different nutritional admixtures for people with CIF as result of benign vs. malignant
878 disease.

879 The results of the studies comparing commercial ready-to-use and customized PN in hospital
880 inpatients may have some relevance for further studies in HPN patients. A number of studies in
881 the hospital setting demonstrated that commercial ready-to-use PN is cheaper than customized
882 PN; this may be due to lower acquisition costs, reduced preparation time and avoidance of costs
883 associated with the development of CRBSI [165-169]. A retrospective study of in-hospital PN found
884 that adding supplements to multi-chamber PN bags on the hospital ward increased blood stream
885 infection risk [170], although this has not been confirmed in other studies [171]. Studies evaluating
886 ready-to-use and customized PN in hospital highlight that the commercial ready-to-use PN may
887 not suitable for all patients [166,172,173]. A recent systematic review comparing pharmacy

888 compounded PN bags and multi-bottle systems for in-patients noted that methodological factors
889 limited evidence quality and highlighted the need for more prospective studies [174].

890 Given the paucity of data in the HPN setting, further studies are clearly needed to investigate the
891 cost implications, safety and clinical outcomes of using commercial ready-to-use PN-admixtures
892 for patients with benign and malignant CIF.

893
894 *8. What are the critical steps during the preparation of PN admixtures?*

895 **Recommendation 41**

896 **Customized AIO admixture stability should be documented for the individual admixture based**
897 **on checks by appropriate lab methods.**

898 **Grade of Recommendation B – Strong consensus (100% agreement)**

899 **Recommendation 42**

900 **Customized AIO admixture stability shall not be extrapolated from the literature.**

901 **Grade of Recommendation GPP – Strong consensus (95.2% agreement)**

902 **Commentary**

903 AIO stability has to be documented for the individual admixture based on checks by appropriate
904 lab methods. Literature extrapolation for stability is not adequate due to the complexities of the
905 admixtures [11,175,176].

906 Electrolytes are prone to incompatibilities (precipitations, multi-valent cations and negative
907 charged lipid emulsifier leading to emulsion destabilization). Their correct admixing into the
908 appropriate macro-element component is crucial; in selected cases with a high calcium need,

909 organic instead of inorganic components might be preferable [176]. Easy to use and validated
910 methods may be used to check for stability like for the Oil/Water stability of AIO admixtures [177]

911

912 **Recommendation 43**

913 **AIO admixture shall be completed immediately before infusion by adding trace elements and**
914 **vitamins according to stability and compatibility data.**

915 **Grade of Recommendation GPP – Strong consensus (91.3% agreement)**

916 **Commentary**

917 AIO admixture shall be completed by adding trace elements and vitamins in aseptic conditions
918 according to stability and compatibility data. For structural/and or organizational reasons, the
919 addition may also be performed immediately before infusion through appropriately trained
920 persons.

921 In order to prevent incompatibilities, including degradation of essential elements, vitamins may be
922 preferably added by the end of the infusion cycle or as a bolus. Appropriate risk assessment for
923 the Good Manufacturing Practice modalities but also the extent of standardization have to be
924 addressed [11,178,179].

925

926 **Recommendation 44**

927 **Drug admixing into AIO admixture shall be avoided, unless specific pharmaceutical data are**
928 **available to document compatibilities and stability of the AIO.**

929 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

930 **Commentary**

931 AIO admixtures show a high potential of drug interactions leading to incompatibilities or stability
932 issues. They are normally not suited for drug admixing and, when necessary, the specific
933 pharmaceutical data have to be provided and documented as this final product represents an
934 individual drug product; the product performance and reliability after interaction with drugs is not
935 covered by the manufacturer [177,180].

936

937 **Recommendation 45**

938 **AIO admixtures shall be labelled for the individual patient indicating the composition (dose) of**
939 **the individual components according to standards, the date, the patient's name and indication**
940 **for handling such as storage, admixes to be made, infusion rate.**

941 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

942

943 **Commentary**

944 AIO admixtures have to be labelled for the individual patient. Labels shall indicate the patient's
945 name, the composition (dose) of the individual components according to standards, the date of
946 manufacturing and expiring, instructions for handling like storage, admixes to be made, infusion
947 rate, as well as avoidance of medication errors [178,180,181]. Specific pharmaceutical support
948 within the NST is required and efficacious [182].

949

950 *9. How should PN admixture be delivered?*

951 **Recommendation 46**

952 **For customized AIO admixtures, the cold chain should be guaranteed during transport and at the**
953 **patient's home.**

954 **Grade of Recommendation B – Strong consensus (100% agreement)**

955 **Commentary**

956 Clearly, pharmaceutical safeguards must be applied for PN delivery, storage and administration at
957 home throughout the patient's therapy. For customized AIO PN admixtures, the cold chain has to
958 be guaranteed [176].

959

960 *10. What should be the HPN admixture time and rate of infusion?*

961 **Recommendation 47**

962 **The hanging time for an HPN-admixture should be no longer than 24 hours.**

963 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

964 **Recommendation 48**

965 **At the end of cyclic PN administration, the infusion rate can be reduced to avoid rebound**
966 **hypoglycemia (e.g. half of the infusion rate over the last half an hour).**

967 **Grade of Recommendation GPP – Strong consensus (93.8% agreement)**

968 **Commentary**

969 The generally accepted maximum hanging time for a ready-to-use admixture are 24 hours. The
970 giving set has to be changed upon each new PN dosing [11,176,179,180].

971 At the end of a (cyclic) PN-infusion, the infusion rate has to be reduced to temper insulin need and
972 to avoid rebound hypoglycemia (e.g. half of the infusion rate over the last half an hour). Glucose
973 administration determines the maximum rate of PN infusion rate: (max. 5-7 mg glucose/kg/min;
974 corresponding to about a maximum of 200 g glucose over twelve hours in 70 kg adult [176,180] or
975 3-6 g glucose/kg per day [3].

976

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977 **5. Program monitoring**

978 *11. How should patients on HPN be monitored?*

979 **Recommendation 49**

980 **Patients receiving HPN shall be monitored at regular intervals, to review the indications, the**
981 **efficacy and the risks of the treatment.**

982 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

983 **Recommendation 50**

984 **The time between reviews should be adapted to the patient, care setting and duration of**
985 **nutrition support; intervals can increase as the patient is stabilized on nutrition support.**

986 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

987 **Recommendation 51**

988 **HPN monitoring should be carried out by the hospital NST in collaboration with experienced**
989 **home care specialists, home care agencies and/or general practitioners.**

990 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

991 **Recommendation 52**

992 **Patients and/or caregivers can be trained to monitor nutritional status, fluid balance and the**
993 **infusion catheter.**

994 **Grade of Recommendation O – Strong consensus (95.7% agreement)**

995 **Recommendation 53**

996 **Monitoring should comprise of nutritional efficacy, tolerance of PN, patient/caregiver**
997 **management of infusion catheter, QoL and quality of care (e.g. CRBSI rate, readmission rate etc.).**

998 **Grade of Recommendation GPP – Strong consensus (95.7% agreement)**

999 **Recommendation 54**

1000 **In clinically stable patients on long-term HPN, body weight, body composition and hydration**
1001 **status, energy and fluid balance and biochemistry (hemoglobin, ferritin, albumin, C-reactive**
1002 **protein, electrolytes, venous blood gas analysis, kidney function, liver function and glucose)**
1003 **should be measured at all the scheduled (e.g. every three to six months).**

1004 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

1005 **Recommendation 55**

1006 **In patients on long-term HPN, clinical signs and symptoms as well as biochemical indexes of**
1007 **vitamin and trace metal deficiency or toxicity should be evaluated at least once per year.**

1008 **Grade of Recommendation GPP – Strong consensus (95.7% agreement)**

1009 **Recommendation 56**

1010 **In patients on long-term HPN, bone metabolism and bone mineral density should be evaluated**
1011 **annually or in accordance with accepted standards (e.g. DXA at max. every 18 months).**

1012 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

1013 **Commentary**

1014 The purpose of monitoring is to “secure and improve QoL” of persons on HPN by assessing the
1015 nutritional efficacy of the HPN program, preventing and timely diagnosing and treating HPN-
1016 related complications and measuring QoL and quality of care [3,4]. Evidence-based guidelines for
1017 monitoring are not available due to the lack of published data [3-13]. Only one study has been
1018 published reporting monitoring practices for HPN across Europe [16]. The results showed that the
1019 majority of centers performed a 3-month monitoring interval for stable patients and emphasized

1020 that responsibility for monitoring should be assigned to a designated person on the hospital HPN
1021 specialist NST [16]. Prospective studies of the impact of different monitoring regimens on
1022 outcomes (including QoL) of HPN are warranted.

1023 Monitoring of HPN patients should be carried out by an experienced hospital NST and by home
1024 care specialists as well as by a home care agency with experience in HPN and should also involve
1025 the general practitioner. Healthcare professionals should review the indications, route, risks,
1026 benefits and goals of nutrition support at regular intervals. In long-term HPN, patients and
1027 caregivers should be trained in self-monitoring of their nutritional status, fluid balance and
1028 infusion catheter, as well as in recognizing early signs and symptoms of complications and
1029 responding to adverse changes in both their well-being and management of their nutritional
1030 delivery system.

1031 Parameters to be monitored, frequency and setting of monitoring are indicated in Table 9. The
1032 time between reviews depends on the patient, care setting, duration of nutrition support as well
1033 as the expected speed with which the impairment of a parameter is likely to occur. Monitoring
1034 should be more frequent during the early months of HPN, or if there is a change in the patient's
1035 clinical condition. Intervals may increase as the patient is stabilized on nutrition support. Fluid
1036 balance requires the most frequent monitoring, especially in the first period after discharge and in
1037 patients with short bowel syndrome with a high output stoma or with intestinal dysmotility with
1038 recurrent episodes of vomiting. Frequent acute dehydration episodes are responsible for kidney
1039 failure and re-hospitalization [183,184]. On the other hand, vitamin and trace metal deficiency
1040 may take more time to develop and to present clinical signs and symptoms, so that a six to twelve
1041 month interval of assessment is appropriate. However, monitoring of micronutrients is as
1042 important as monitoring other parameters, especially in patients on long-term HPN and in those
1043 who are undergoing intestinal rehabilitation and weaning from HPN. In the latter case, while

1044 intestinal rehabilitation is associated with maintenance of energy, protein, fluid and electrolyte
 1045 balance without PN support, this is not necessarily the case for micronutrient balance [4].
 1046 Decreasing or totally stopping PN infusion decreases micronutrient supplementation, thus creating
 1047 a risk for deficiency [4].

1048 After hospital discharge, it is critical that the HPN NST has contact with patients and caregivers on
 1049 a regular basis, initially every few days, then weekly and eventually monthly as the patient gains
 1050 confidence. The clinician who is in contact should be prepared to clarify confusing issues and also
 1051 to follow weight, urine output, diarrhea or stoma output, temperatures before and within an hour
 1052 of starting the HPN infusion, and general health.

1053 Healthcare professionals have identified incidence of CRBSI, incidence of rehospitalization and QoL
 1054 as the three major indicators of quality of care HPN patients with either a benign [71] or malignant
 1055 [51] underlying disease. Survival rate was also considered important when patients with benign
 1056 disease were considered [185].

1057

1058 **Table 9. Parameters, frequency (after baseline assessment) and setting of monitoring on**
 1059 **patients on HPN.**

Parameter	Frequency	Setting
General condition Body temperature	Daily if unstable, twice weekly to once a week if stable	Nurse at home Patient and/or caregivers
Body weight	Daily if unstable, twice weekly to once a week if stable	In the hospital (outpatient visit) Nurse at home Patient and/or caregivers
Body mass index	Monthly	In the hospital (outpatient visit) Nurse at home
Fluid balance - Urine output - Stoma output - Number or consistency of stools - Presence of edema	The frequency and type of parameters will depend on etiology of CIF, and stability of patients In case of high stool output (end jejunostomy), the monitoring after the first discharge should be daily, then twice weekly to once a week when stable	Nurse at home Patient and/or caregivers only in case of training program

Catheter cutaneous exit site	Daily	Nurse at home Patient and/or caregivers only in case of training program
Full count blood C-reactive protein Serum glucose Serum and urine electrolytes and minerals (Na, Cl, K, Mg, Ca and P) Serum Urea and Creatinine Serum bicarbonates Urine analysis	The frequency and type of parameters will depend on etiology of the underlying condition requiring HPN and the stability of patients Weekly or monthly, then every three to four months when stable	At home Verify at each visit
Serum albumin and prealbumin	Monthly, then every three to four months when stable	At home Verify at each visit
Serum liver function tests including INR	Monthly, then every three to four months when stable	At home Verify at each visit
Liver ultrasound	Yearly	In hospital
Serum Folate, vitamins B12, A and E	Every six to twelve months	Dosage at home or in the hospital
Serum ferritin iron,	Every three to six months	Dosage at home or in the hospital
Serum 25-OH Vitamin D	Every six to twelve months	Dosage at home or in the hospital
Serum zinc, copper, selenium	Every six to twelve months	Dosage in the hospital
Serum Manganese	Yearly	Dosage in the hospital
Bone densitometry (DEXA)	Every twelve to eighteen months	In the hospital

1060

1061 **6. Management (nutrition support team, training, emergency, travelling)**

1062 *12. Which are the local and personnel preconditions for HPN?*

1063 **Recommendation 57**

1064 **The suitability of the home care environment should be assessed and approved by the HPN**
1065 **nursing team before starting HPN, wherever possible.**

1066 **Grade of Recommendation GPP – Strong consensus (91.3% agreement)**

1067 **Recommendation 58**

1068 **A formal individualized HPN training program for the patient and/or caregiver and/or home care**
1069 **nurses shall be performed, including catheter care, pump use and preventing, recognizing and**
1070 **managing complications; training can be done in an in-patient setting or at the patient's home.**

1071 **Grade of Recommendation GPP – Strong consensus (91.3% agreement)**

1072 **Commentary**

1073 The management of PN in the home care setting differs from hospitalized patients because there
1074 is a shift in primary responsibility from health care professionals to patients and caregivers. The
1075 general goals in the education process are promoting independence with the infusion, (self-)
1076 monitoring of HPN, preventing complications and improving or maintaining QoL [3,4] (Table 10).
1077 The HPN center NST plays a key role in the individualized decision-making process and guides all
1078 the necessary measures or steps which have to be taken [3,10,51,64-74].

1079 Guidelines on core components for (catheter) infection control and prevention, considered as an
1080 important outcome indicator in HPN patients, give strong recommendations about the provision
1081 of education and training [72,73]. Besides preventing CRBSI and assessing QoL, the overall

1082 teaching program has many aspects to deal with and is very often driven by an experienced
 1083 (nutrition support) nurse who takes the lead and responsibility for this program [3,69].

1084

1085 **Table 10. Content of a teaching program for patients/caregivers discharged on HPN [3,10, 63,74]**

1086

-
- 1087 • Indication for HPN: short and/or long-term goals and HPN-regimen
 - 1088 • Issues around informed consent
 - 1089 • Role of the home care provider to provide parenteral formulations, equipment, supplies, and eventually
 1090 nursing care
 - 1091 • Determine learning abilities and readiness to self-management and self-monitoring
 - 1092 ○ If applicable: make a checklist for competencies achieved
 - 1093 • Reviewing evidence-based written policies and procedures complemented with oral instructions
 - 1094 • Home care environment
 - 1095 ○ General cleanliness (for example: Is there a clean area for aseptic/sterile procedures?)
 - 1096 ○ Presence of animals
 - 1097 ○ Basic home safety (telephone access, clean storage for supplies, dedicated refrigerator, toilet-bathroom,
 1098 sanitary water supply,...)
 - 1099 • Catheter care
 - 1100 ○ Principles of infection control and prevention (including aseptic techniques)
 - 1101 ○ Preventing, recognizing and managing catheter related complications
 - 1102 ○ Site care
 - 1103 • Storage, handling, inspection of admixtures (e.g. leaks, labels, precipitates, color), ancillaries and (medication)
 1104 supplies
 - 1105 • If applicable:
 - 1106 ○ Safe addition of vitamins, trace elements or other additives
 - 1107 ○ Safe administration of HPN
 - 1108 ○ Connecting and disconnecting IV tubing to the vascular access device
 - 1109 ○ Pre/post infusion flushing
 - 1110 ○ Periodically assessment of performance/compliance with aseptic techniques
 - 1111 • Pump use, programming, pump care and troubleshooting
 - 1112 • Preventing, recognizing and managing non-infectious related complications or problems
 - 1113 • Most common mistakes
 - 1114 • Available contact resources and post discharge support from the HPN center as well as the home care
 1115 provider
 - 1116 • Self HPN monitoring
 - 1117 • Concomitant drug therapy and administration mode (total regimen management)

1118

1119

1120 Training for HPN may be carried out in an in-patient setting or at patient's home and may take
 1121 several days to weeks depending on patient skills, duration of HPN and underlying condition.
 1122 [3,4,74]. A recent retrospective 5-year evaluation of CRBSI occurrence and CVC salvage outcomes
 1123 in adult patients requiring HPN managed at a national UK intestinal failure unit, demonstrated that

1124 by individual managing, patients can be educated at home which of course reduces hospital length
1125 of stay and may be preferable for some patients [75]. Multiple education interventions are
1126 possible including one-on-one counselling, teach-back method, written handouts, computer-
1127 assisted learning and interactive presentations. All these tools may not eliminate but reduce post
1128 discharge helpline contacts provided by telephone, videoconference or patient portals [63,68,74].
1129 Multiple education interventions are available including methods such as one-on-one counselling,
1130 written or printed materials, group meetings, demonstrations, videotapes, CDs/DVDs and internet
1131 education [3,4]. HPN is a complex therapy that requires coordination of many health care
1132 providers. The expertise of a NST is recommended to provide proper and patient-tailored
1133 education or therapy. Self-management and preventing complications are important goals to
1134 improve QoL and to avoid unnecessary costs to healthcare.

1135

1136 *13. Which are the requirements for the hospital centers that care for HPN patients?*

1137 **Recommendation 59**

1138 **Patients on HPN should be cared for by specialized, dedicated and a clearly identifiable hospital**
1139 **unit, normally termed “HPN center or IF center or intestinal rehabilitation center”.**

1140 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

1141 **Recommendation 60**

1142 **The HPN unit should have offices for outpatient visits and dedicated beds for patients who need**
1143 **hospitalization.**

1144 **Grade of Recommendation GPP – Strong consensus (91.3% agreement)**

1145 **Commentary**

1146 The human resources as well as structural facilities are key features to optimize the HPN care.

1147 Specific organization and structural facilities for HPN management have been described by a
1148 position statement of the British Intestinal Failure Alliance [12], that described five standards: Unit,
1149 Team, Practice, Relationship with other internal and external units/stakeholders and outcome.
1150 Key issues are the identification of the persons, structures and procedures responsible for the HPN
1151 care process [4,12,13], such as:

- 1152 • Professionals who coordinate and manage the different phases of HPN management
- 1153 • Place of initial care (center of intestinal failure, gastroenterology, surgery, other)
- 1154 • Place and methods of training programs (on hospital beds, in day hospital, at home)
- 1155 • Pathways of care in case of complications (example: emergency room, direct access to
1156 hospital beds, link with local hospitals of the patient residency)
- 1157 • Place and procedures for CVAD positioning and managing of complications

1158 Having access to dedicated hospital beds under the responsibility of the MDT is essential for initial
1159 care as well as for managing of complications. These beds may be within an independent structure
1160 of nutrition/intestinal failure or within a more general structure, such as department of
1161 gastroenterology, oncology, surgery or other. Hospitalization is required to monitor patients
1162 and/or evaluate intestinal function in order to better adapt treatments as well as to timely and
1163 appropriately treat complications according to the NST procedures.

1164 The HPN center needs to estimate the time that each professional has to dedicate to the single
1165 patient, in order to define the number of human resources required for managing their total
1166 number of HPN patients.

1167 In conclusion, for better care and visibility for patients, healthcare providers and public authorities,
1168 we recommend that departments dedicated to the care of these patients be recognized with
1169 dedicated beds and resources.

1170

1171 *14. What are the requirements of the NST?*1172 **Recommendation 61**

1173 **All HPN patients should be cared for by a NST with experience in HPN management,**
1174 **independent from the underlying disease leading to intestinal failure.**

1175 **Grade of Recommendation GPP – Strong consensus (100% agreement)**1176 **Recommendation 62**

1177 **The NST consists of experts in HPN provision. This can include a physician, specialist nurses**
1178 **(including in catheter, wound and stoma care), dietitians, pharmacists, social worker,**
1179 **psychologist, as well as an appropriate practitioner with expertise in CVC placement. Surgeons**
1180 **with expertise in intestinal failure should also be available for structured consultation.**

1181 **Grade of Recommendation GPP – Strong consensus (100% agreement)**1182 **Commentary**

1183 Because of its complex nature, current guidelines, including the recent ESPEN guideline on CIF,
1184 agree that only experienced NST should provide HPN treatment [3-14]. The relevance of expertise
1185 in this field has been shown previously in France where increased experience in HPN support had a
1186 positive impact on patient survival [186]. To assure optimal outcomes, the team should develop an
1187 individualized training and treatment plans based on standardized protocols. Notably, CRBSI rates,
1188 which are considered a proxy for the quality of HPN support, even in high-risk patients such as
1189 those with cancer, are the lowest in expert referral centers [64,65].

1190 The appropriate composition and size of a NST that provides HPN care to some extent depends on
1191 the number of patients under the team's care, which mostly also relates to the patient volume and

1192 scope of the hospital [187]. Key tasks of this team include establishing (contra)-indications for HPN
1193 support, development and implementation of individualized training and treatment programs,
1194 treatment of complications (vascular access related, metabolic derangements) and organization of
1195 home care [187].

1196 Also, because of the associated complications of HPN treatment, including venous access-related
1197 problems such as infections and occlusions, metabolic derangements, formulation and medication
1198 compatibility issues that pertain to various specialties, the team that provides HPN support should
1199 be multidisciplinary in nature and include physician specialists with a background in surgery and
1200 gastroenterology, specialized nurses, dieticians and pharmacists [66,67]. In light of the profound
1201 impact on personal and family life, psychologists and social workers should also form part of the
1202 team. This latter issue was highlighted in studies showing that many HPN patients experience the
1203 lack of attention for their psychosocial problems as a shortcoming [188,199].

1204 Concerning patients with active cancer, it is important to realize that selecting patients suitable for
1205 such a complex treatment as HPN support is challenging and discussion with the treating oncology
1206 specialist in this setting seems prudent before HPN initiation [15].

1207 Often forgotten, it is of key importance for patients that caregivers more close to the home, such
1208 as the general practitioner and homecare nurses, although not direct team members, should be
1209 kept informed of patients' clinical course after discharge from hospital [62,63,68,70]. It has been
1210 shown in adult HPN patients who were managed at a national UK referral center that under the
1211 well-organized care of such an experienced team in close collaboration with home nurses, even a
1212 delicate process such as patient education can take place at home, resulting in reduced hospital
1213 length of stay and improved psychosocial wellbeing of both patients and their family [75].

1214 *15. How should emergencies be managed?*

1215 **Recommendation 63**

1216 **The NST for HPN/CIF shall have clear written pathways and protocols in place for the**
1217 **management of patients with complications relating to HPN.**

1218 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

1219 **Recommendation 64**

1220 **The NST for HPN/CIF shall provide patients and caregivers with written information relating to**
1221 **the recognition and subsequent management of HPN-related complications, including details**
1222 **(e.g. telephone number) of an appropriate NST member to contact in the case of an emergency,**
1223 **available 24 hours per day.**

1224 **Grade of Recommendation GPP – Strong consensus (91.3% agreement)**

1225 **Recommendation 65**

1226 **The NST for HPN/CIF shall disseminate clear protocols relating to the recognition, investigation**
1227 **and initial management of HPN-related complications to hospital emergency departments,**
1228 **where patients are likely to present; where appropriate and available, written protocols can also**
1229 **be carried by the patient or accessed electronically via a secure web-portal.**

1230 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

1231 **Recommendation 66**

1232 **When patients are admitted to hospital with HPN-related complications, their care shall be**
1233 **delivered by the NST for HPN/CIF; if patients are admitted to a hospital where such expertise**
1234 **does not exist, then clinical guidance should be provided by the NST for HPN/CIF, until the time**
1235 **when the patient can be transferred to the HPN/CIF center, as required.**

1236 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

1237 Recommendation 67

1238 **Written protocols for the management of HPN-related complications shall be developed and**
1239 **shared with the patient's local hospital, if it is likely that the patient will be admitted first to that**
1240 **hospital rather than to the HPN/CIF center in the event of an emergency; these should include**
1241 **contact details for the NST for HPN/CIF to advise on treatment and/or possible transfer to the**
1242 **HPN/CIF center. Where appropriate and available, written protocols can also be carried by the**
1243 **patient or accessed electronically via a secure web-portal.**

1244 **Grade of Recommendation GPP – Strong consensus (95.5% agreement)**

1245 Recommendation 68

1246 **Patients shall carry details relevant to their condition, and/or have access to a secure web-portal**
1247 **containing relevant clinical information, when travelling away from home, in order to aid clinical**
1248 **teams at other hospitals should emergency treatment be required.**

1249 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

1250 Recommendation 69

1251 **The NST for HPN/CIF shall ensure that patients, caregivers and general practitioners are aware**
1252 **of the roles and responsibilities of the health care professionals involved in aspects of the**
1253 **patient's condition that are unrelated to HPN, including any complications relating to the**
1254 **patient's underlying disease and other non-IF related conditions.**

1255 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

1256 Commentary

1257 **Minimal guidance and published literature exist to-date relating to pathways for the emergency**
1258 **management of patients with complications relating to CIF. Such complications should be**

1259 demarcated into those relating to HPN, those relating to the patient's underlying disease leading
1260 to CIF (including any underlying oncological condition) and those unrelated to CIF. The CIF team
1261 should ensure that patients and caregivers are aware of the roles and responsibilities of the health
1262 care professionals involved in each component of their condition.

1263 There are no published studies that have systematically evaluated best practice for the delivery of
1264 emergency care for patients with HPN-related complications, for patients with benign CIF,
1265 malignant CIF or no-CIF scenarios. Two studies have demonstrated patient-education programs
1266 aimed at minimizing hospital admissions for complications associated with CIF. A retrospective
1267 study evaluated the implementation of a protocol to treat dehydration at home for HPN patients
1268 by ordering additional intravenous fluids to be kept on hand and to focus patient education on the
1269 symptoms of dehydration; this led to a greater than two-fold increase in the number of episodes
1270 of dehydration identified and treated at home [184]. Implementation of a CVC self-management
1271 education program using a quasi-experimental, sequential cohort design study of patients with
1272 cancer led to a reduction in CVC-related complications and improved patients' abilities to resolve
1273 problems and adequately respond to CVC-related emergency situations by fostering greater self-
1274 care ability; however, this study was not limited to patients with CIF [190]. Two further studies
1275 demonstrated that diagnosis and management of CRBSI can be enhanced using quality
1276 improvement methodology. An emergency department quality improvement initiative reduced
1277 the mean time to antibiotic administration for febrile children with IF by 50%. Interventions
1278 included increasing provider knowledge of IF, streamlining order entry, providing individualized
1279 feedback, and standardizing the triage process. However, there was no difference noted in the
1280 total length of subsequent hospital and ICU stays [191]. Another quality improvement project in a
1281 tertiary cancer center involving staff education and blood culture source label introduction

1282 improved CRBSI diagnosis from 36% to 88% in patients with a CVC; however, this study was also
1283 not limited to patients with CIF [192].

1284 Established national and international guidelines clearly recommend that that CIF patients are
1285 cared for by a NST with skills and experience in both CIF and HPN management [4]. The British
1286 Intestinal Failure Alliance provide some guidelines on the emergency management of HPN-related
1287 complications [12]. The NST should be responsible for the management of patients with
1288 complications related to HPN, including CVC-related complications and intestinal failure-related
1289 liver disease. This should include the emergency management of any HPN-related issues 24 hours
1290 per day, seven days per week. Patients and carers must be provided with clear written information
1291 relating to the recognition and management of HPN-related complications, including contact
1292 details of the NST in case of any emergency. The NST should generate written protocols for the
1293 management of HPN-related complications and, importantly, should have systems in-place such
1294 that specialist advice from the NST is available at all times. Where patients cannot attend the CIF
1295 center with emergency issues (for example, if distance and/or clinical need mandates immediate
1296 care at a local hospital), the NST should ensure that shared cared-protocols have been
1297 disseminated to local hospitals in advance and that the patient also has relevant details of their
1298 condition available.

1299 Patients and caregivers should be aware that the NST may not be responsible for all aspects of
1300 their health, including the underlying disease leading to CIF. For example, patients with Crohn's
1301 disease may be under the care of a gastroenterologist at a local hospital for the monitoring and
1302 management of IBD-related issues. Similarly, for patients with malignancy, oncology and/or
1303 palliative care teams best manage emergencies relating to underlying disease. Thus, as soon as a
1304 patient is established on HPN, he/she and his/her general practitioner should be made aware of

1305 the relevant roles and responsibilities of the health care professionals involved in aspects of the
1306 patient's condition that are unrelated to HPN [3,11,14].

1307 Patients can suffer from non-IF related conditions and these can be a significant cause of
1308 morbidity and mortality (for example, cardiac disease, respiratory disease etc.). Care for these
1309 conditions, including any emergency needs, should continue as for patients without CIF [3,11,14].

1310 It is important that the NST is informed immediately of any changes in these conditions, including
1311 any alterations in medication for non-IF related problems, as well as any admissions to hospital.

1312

1313 *16. How should travelling with HPN be organized?*

1314 **Recommendation 70**

1315 **For a patient to travel safely, he/she shall receive a sufficient supply of PN and relevant**
1316 **ancillaries during the journey and at the destination and the NST responsible for the patient's**
1317 **care shall endeavor to establish contact with a skilled NST at the patient's destination, in case**
1318 **medical support is required.**

1319 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

1320 **Commentary**

1321 Patients on long-term HPN may need to learn how to adjust to lifestyle events such as bathing,
1322 showering, swimming, sports and travel [12]. Travelling with PN is an important factor for some
1323 patients' QoL [193,194] and independency [70,195]. However, none of the previous guidelines and
1324 position papers addressed this topic and a literature search did not provide any new information
1325 about this area in adults. So the recommendation and comments of the present guideline were
1326 based on statements of patients' representatives participating in the panel.

1327 Pre-travel planning is essential to ensure that the patients can meet their usual PN/IV fluid
1328 requirements as well as to be able to perform PN-related procedures safely. The
1329 patient/caregivers should discuss their travel plans with their healthcare professionals/NST to
1330 ensure that they/their child are fit to travel. The doctor should issue a letter/medical certificate for
1331 the patient/caregivers confirming that they are aware they are travelling, along with a brief
1332 overview of their condition and need for PN. Medical cover/travel insurance should be arranged
1333 prior to travelling to ensure that any medical treatment needed while travelling will be possible.
1334 The patient/caregivers should ask about the potential and suitability of multi-chamber bags for
1335 their trip instead of compounded PN if they would like to consider using them. The
1336 patient/caregivers should investigate different power supplies/plugs prior to travelling to ensure
1337 they can charge pumps and batteries. A spare infusion pump should be taken on all trips,
1338 alternatively check the possibility of a replacement pump at the destination. Using
1339 homecare/compounding services at the end destination should be investigated very early during
1340 the planning period where reimbursement is possible and is available via different healthcare
1341 systems. The patient/caregivers need to calculate the number of fluid bags (PN/IV fluids) and
1342 ancillaries/medical supplies that they will need for their trip allowing for extra supplies. It is the
1343 responsibility of the patient/caregivers to know the stability of the PN, how long compounded PN
1344 can be safely stored in the dedicated PN boxes supplied by homecare companies/hospitals, before
1345 it needs to be placed in a fridge. The patient/parents should plan for additional fluids for the
1346 duration of travel, where high temperatures may be experienced, to ensure hydration is
1347 maintained. All fluids and ancillaries/medical supplies must be appropriately packed to ensure safe
1348 storage and stability both in terms of preventing damage and maintaining cold-chain temperatures,
1349 where applicable. The type of accommodation should be carefully considered in advance,
1350 especially where a fridge is required for the storage of compounded PN at 2° – 8°C. In case of an

1351 emergency situation, a plan of action should be prepared beforehand and all important (doctor,
1352 family) contact numbers should be easily accessible. All modes of transport are possible for PN,
1353 travelling by plane will require more detailed planning. Attention to increased security checks
1354 must be respected. Prior to travel, if any special arrangements need to be made - such as
1355 additional space, extra baggage allowance, security approval – this must be arranged prior to
1356 departure. All PN/IV fluid boxes and ancillary/medical supplies baggage should be clearly labelled
1357 with a name, destination, date of travel and instructions not to open if cold-chain PN unless in the
1358 presence of the patient/caregivers. Usual healthcare professionals should consider establishing
1359 local medical support or a contact for the patient should medical support be required.

1360

1361 *17. Which criteria should be used to monitor the safety of HPN program provision?*

1362 **Recommendation 71**

1363 **Incidence of catheter-related infection, incidence of hospital readmission and QoL should be**
1364 **used as criteria to assess the quality of care of HPN program.**

1365 **Grade of Recommendation GPP – Strong consensus (100% agreement)**

1366 **Commentary**

1367 Three multicenter international studies have identified and ranked the interventions determined
1368 to be essential for good quality of care (also called ‘key interventions’) [51,71,185]. Two studies
1369 were based on the opinions of healthcare professionals with expertise on HPN and included either
1370 benign or malignant CIF [51,71]. The third study evaluated the desired outcomes of patients with
1371 CIF due to benign disease [70,185]. The two-round Delphi approach was used, which is a technique
1372 that transforms opinion into group consensus, and the resulting set of most highly ranked key
1373 interventions was then transformed into quality indicators [51,71,185].

1374 The top three outcome indicators identified by healthcare professionals were incidence of CRBSI,
1375 incidence of rehospitalizations and QoL for CIF due to either benign [71] or malignant [51] disease.
1376 The top three desired outcomes of patients with benign CIF were incidence of CRBSI, survival rate,
1377 and QoL on HPN [185].

1378 The key interventions identified should be measured annually in current practice, along with
1379 questionnaires on patients' satisfaction, to identify and address any areas for further
1380 improvement. [4].

1381 According to the Donabedian paradigm [196], the outcome indicators should not be measured
1382 alone. The Donabedian model provides a framework to assess the quality of care by working with
1383 quality indicators related to structure, process and outcome of health care: 'structure' refers to
1384 general administrative standards of the organization and people providing care; 'process' refers to
1385 the manner in which care is actually provided and administered; 'outcome' refers to a set of
1386 expected or desirable results for patients [196]. Therefore, the outcome indicators reported
1387 should be monitored along with the linked process as well as structure indicators which will help
1388 to drive quality improvement.

1389

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1942 Appendix A. Supplementary data