

Clinical practice guideline

AuSPEN clinical practice guideline for home parenteral nutrition patients in Australia and New Zealand

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Abstract

Objective: Evidence based guidelines for home parenteral nutrition (HPN) were commissioned by the Australasian Society of Parenteral and Enteral Nutrition (AuSPEN) and developed by a multidisciplinary group. The guidelines make recommendations in four domains: patient selection, patient training, formulation and monitoring regimens, and preventing and managing complications.

Methods: The Appraisal of Guidelines Research and Evaluation guideline process was used to focus questions and identify evidence by systematic literature reviews of meta-analyses and randomized control trials in the Cochrane Library, Medline, Embase, and Cinahl to mid-2007. Where no randomized control trial evidence was found, the search was broadened to observational studies and expert opinion from related national and international guidelines as assessed by a validated appraisal process.

Results: Selection of patients must assess individual risk/benefit and medical ethics. Patient training should be undertaken within a structured framework. Access devices should be selected for lowest risk of complications, including occlusion, sepsis, and breakage and be managed by early diagnosis and treatment. HPN should be formulated according to individual patient requirements by professionals with relevant skills and training. Pumps and ancillary products should conform to quality standards. Other intravenous medications may be prescribed provided these are reviewed for compatibility and effects on metabolic status.

Conclusion: Overall there is a lack of randomized control trials to provide high-quality evidence-based guidance but graded recommendations can be made. Multidisciplinary teams in centers with HPN management expertise are required for optimal care. This guideline should improve outcomes and quality of life for HPN patients in Australia and New Zealand. © 2008 Elsevier Inc. All rights reserved.

Keywords: Intravenous nutrition; Central venous catheter; Homecare

The Australasian Society of Parenteral and Enteral Nutrition provided travel assistance to Guideline Development Group (GDG) members to attend one GDG meeting. No member of the GDG received financial support from any commercial provider of home parenteral nutrition other than expenses for educational lectures. Industry representatives from Baxter Healthcare Pty Ltd., a provider company, gave travel assistance to some members of the GDG and provided a meeting room for the initial meeting but thereafter were not part of the GDG. All authors comprised the GDG.

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Objective

The objective is to provide evidence-based clinical practice guidelines for feeding adults intravenously at home or in the community when they have intestinal failure (IF) and are unable to meet oral nutritional and fluid requirements. This is commonly known as home parenteral nutrition (HPN). These guidelines have been written to support all health care professionals involved with the care of patients referred for HPN.

Aims

1. The guidelines will be factually up-to-date and reflect current, evidence-based best-practice HPN.
2. The guidelines will aid nutritional support (NS) personnel in their use of evidence-based recommendations to improve clinical and professional practices for HPN in Australia and New Zealand.
3. The guidelines will serve as a tool to help policy makers, health care organizations, and NS professionals to allocate sufficient resources to deliver safe and appropriate HPN in Australia and New Zealand.

Introduction

Intestinal failure occurs when there is reduced intestinal absorption so that intravenous nutrients and/or water and electrolyte supplements are needed to maintain health and/or growth. Undernutrition and/or dehydration occur if no treatment is given or if compensatory adaptive mechanisms are inadequate. Patients are usually trialed on diet modification, oral nutritional supplements, and enteral feeding before a clinical diagnosis of IF is made. IF can be short (<1 y) or long term. Periods of HPN may be appropriate for patients with short-term IF. Long-term IF is due to irreversible pathology and patients should be considered for entry into an HPN program and/or small bowel transplantation [1].

Home parenteral nutrition does not preclude oral intake and, if tolerated, this may also reduce the requirement for daily HPN.

Some common diagnoses and underlying conditions in patients with long-term IF are listed in Table 1.

It was estimated in 1992 that there were 40 000 individuals in the United States supported by HPN for IF and that the economic and quality-of-life burden for these patients is high. However, the North American Registry that provided these data was abandoned in 1993 [2]. The United Kingdom prevalence for HPN in 2006 was reported to be 12 per million [3].

In 2006 about 5–7 per million people were receiving HPN in Australia and New Zealand [4]. Patients maintained on HPN are few in number but consume significant resource

Table 1
Some common diagnoses and underlying conditions in patients with long-term intestinal failure

Diagnosis	Underlying condition
Short bowel syndrome	Volvulus
	Mesenteric vascular disease
	Mesenteric tumors
Radiation enteritis	Crohn's disease
Chronic intestinal obstruction	Neoplastic disease
	Diffuse intra-abdominal adhesions or certain malignancies
Intestinal pseudo-obstruction	Enteric neuropathies or myopathies
	Secondary amyloidosis
Chronic intestinal fistulae	Crohn's disease
	Adhesive disease
	Malignancy

in funding and personnel. Costs in New Zealand were estimated to be \$A76 500 per patient per annum in 2006 [5], but are significantly less than long-term institutional care. Overall survival and rehabilitation are highest in pediatric patients 0–18 y of age and lowest in those >65 y old [6]. Patients with inflammatory bowel disease have a >90% 5-y survival rate [7] and quality of life is fair to good in >80% of cases [8,9].

The Australasian Society of Parenteral and Enteral Nutrition (AuSPEN) recognizes that some patients in Australia and New Zealand are potentially disadvantaged by living distant from centers that have developed expertise in the care of patients on HPN. These guidelines are also intended to provide standards of care formed from evidence-based practice. They are also intended to provide support and recommendations to clinicians caring for patients on HPN infrequently or in remote situations and in established centers of expertise.

The HPN guideline was supported and endorsed by AuSPEN and was developed in accordance with the Appraisal of Guidelines Research and Evaluation (AGREE) guideline development process [10].

The health benefits of applying the guideline may include improved patient selection, quality of life, and minimization of complications.

Methods

A multidisciplinary working party of Australia and New Zealand health professionals with extensive experience in the provision of HPN was convened in 2005. This working party consisted of doctors, dietitians, pharmacists, scientists, and nurses and was later formalized into the AuSPEN HPN Guideline Development Group (GDG).

The GDG held three formal meetings and communicated regularly by e-mail and telephone. A consensus approach was used to develop the guideline. A separate pediatric working party will develop additional guidelines for infants and children.

Development of clinical questions

The GDG prepared a list of clinical questions related to the initiation, administration, and monitoring of HPN. The questions were developed to investigate the benefits, risks, cost, resource utilization, and feasibility of this mode of NS in the Australian and New Zealand settings.

Types of study interventions

The GDG agreed on the definition of terms and the inclusion and exclusion criteria for HPN. These were included in the search strategies and considered throughout the process of systematic reviewing.

Types of study population

The search strategies were restricted to adult patient/population groups because the GDG wished to determine the likely benefit or risks of home NS to these groups.

Types of outcomes

The GDG requested that all clinical and biochemical outcomes, including biochemical markers where appropriate, should be recorded.

Search strategy

Seven existing guidelines identified from our literature search that contained material relating to PN were appraised using a validated instrument (AGREE) for evaluation of clinical practice guidelines.

- The National Institute for Health & Clinical Excellence (NICE) Nutrition Support in Adults [11]
- The American Society of Parenteral and Enteral Nutrition (ASPEN) Nutrition Support in Clinical Practice: review of published data and recommendations for future research directions [12]
- ASPEN Guidelines for Use of Parenteral and Enteral Nutrition in Adult and Pediatric Patients [2]
- The Canadian Clinical Practice Guidelines (CCPG) for Nutrition Support in Mechanically Ventilated Critically Ill Adult Patients [13]
- Scottish Home Parenteral Nutrition Managed Clinical Network Protocols (SHPNMCN) [14]
- Centers for Disease Control and Prevention (CDC) Guidelines for the Prevention of Intravascular Catheter-Related Infections [15]
- Epic2: National Evidence-Based Guidelines for Preventing Health Care–Associated Infections in National Health Service Hospitals in England [16]

The UK NICE guidelines are recently published, patient-centered, and systematically developed for NS in hospitals

and the community, based on trial evidence whenever possible. The NICE offers best-practice advice on the care of adults who have IF and require short- and long-term PN support. Good coordination between the hospital and the home or community is emphasized when transferring patients between settings. Key clinical and organizational priorities for implementation of HPN are well covered in these guidelines.

The NICE guideline development process followed the principles outlined in the AGREE tool and comprehensively reviewed more than 380 publications in the English language [11]. No specific reviews were performed for HPN but those publications and recommendations relating to long-term PN have been assessed and incorporated into this guideline.

The original ASPEN document [12] was not intended to establish practice guidelines for NS, but rather to review the published literature and to make recommendations for future research directions. The more recently updated ASPEN guidelines reflect a more evidence-based approach to NS and include sections with recommendations for HPN [2]. The CCPG [13] were developed for NS in mechanically ventilated, critically ill adults. These publications provided useful references but did not meet the criteria set for this guideline on HPN.

The SHPNMCN [14] protocols provided useful references and practical advice that have been used where appropriate and when evidence was lacking.

The CDC [15] guideline was developed for practitioners who insert central venous catheters (CVCs) and for persons responsible for surveillance and control of infections in hospitals and home health care settings. These guidelines are intended to provide evidence-based recommendations for preventing catheter-related infections and have been systematically developed with graded evidence. The CDC guidelines have also been incorporated into the guideline without duplicating the CDC review process according to the GDG study selection criteria. In addition the epic2 guideline [16] (which was based on the CDC evidence for preventing infections associated with the use of central venous access devices) was reviewed for new or additional evidence. These two guidelines remain consistent with each other.

There was no systematic attempt to search for all the “gray literature” (conferences, abstracts, theses, and unpublished literature). However, we searched for guidelines and reports from relevant websites. Bibliographies of identified reports and guidelines were also checked to identify relevant literature.

The NICE literature search

The NICE literature review was conducted to identify relevant evidence from the published literature. Search strategies were developed for PN, nutritional screening, monitoring, and patient issues.

Search filters to identify systematic reviews and randomized controlled trials (RCTs) were applied to the search strategies. No language restrictions were applied to the search; however, foreign-language papers were not requested or reviewed.

Types of studies

The NICE study design was restricted to RCTs, systematic reviews, and meta-analyses of RCTs, because of the potential bias associated with observational study designs.

The following databases were included in the NICE literature search:

- The Cochrane Library up to 2005 (issue 1)
- Medline (Dialog Datastar) 1966–2005 (week)
- Embase (Dialog Datastar) 1980–2005 (week)
- Cinahl (Dialog Datastar) 1982–2005
- Allied & Complementary Medicine (Dialog Datastar) 1985–2005
- British Nursing Index (Dialog Datastar) 1994–2005

Each database was searched by the NICE from its start date up to March 3, 2005 and was not duplicated by the GDG. The references for HPN were reviewed for validity and levels of evidence.

Papers identified after this date and up to June 2007 by the GDG were searched by the same method and the same validity criteria.

The GDG literature search

The following relevant interventions were extracted by the GDG from the systematic review by the NICE for NS in adults [11]:

- Enteral nutrition versus PN
- Venous access for PN through a tunneled catheter versus a non-tunneled catheter
- Complications from PN
- Tailored PN preparations versus standard PN preparations
- Energy, protein, fluid, electrolytes, minerals, and micronutrient requirements.

Note: Immune-enhancing substances were not reviewed by the NICE and were not considered to be part of the GDG HPN remit at this time.

GDG guideline study selection criteria for HPN

For each meta-analysis/review paper included in our review process, the GDG assessed the intervention, number of trials, population selection criteria, search strategy, independent validity assessment, method of pooling results, assessment of homogeneity, and other outcomes.

Where no meta-analyses, RCTs, or reviews were identified and no evidence was found using existing guideline

references by hand searching the reference lists of retrieved review papers, the GDG search strategy was broadened to include observational studies related to HPN.

The language of the recommendations is linked to the strength of the evidence for PN allocated by the NICE and adapted where appropriate to the Australasian HPN experiences. The guidelines were developed to apply to the average patient with IF in a general situation. We recognize that these recommendations may not apply in all situations and individual patient or site characteristics will need to be considered.

Absence of literature

The recommendations in the NICE and ASPEN guidelines have been systematically and rigorously developed. However, for a number of the clinical questions there was an absence of RCT evidence because the clinical questions did not lend themselves to controlled trials and systematic reviewing or there were too few trials identified to make substantive recommendations. Invariably, we needed to use additional approaches such as surveys or informal/formal consensus development to assist with some areas of the guideline. These include:

- Nutritional screening
- Indications
- Ethical and legal issues
- Prescription of nutrients
- Monitoring
- Nutritional assessment
- NS teams
- Patients' and carers' views

The process indicated that a number of clinical questions were not addressed by the published literature or the guidelines currently available. Frequently guidelines have been based on expert opinion alone. In addition, many of the HPN questions for Australia and New Zealand are about processes, people, and treatment outcomes.

Taking this into consideration, it was decided that the most valuable documents that could be developed in relation to the provision of HPN would be a consensus guideline using levels of evidence where available. Where no evidence existed, some references have been included outside the agreed literature search criteria to provide sign posts for interested clinicians. This is one way of providing clinicians a justification of intervention because HPN cannot be always primarily based on prospective randomized trials. The National Health and Medical Research Council evidence grading system is used [17].

- Level 1: Evidence is obtained from a systematic review of all relevant RCTs.
- Level II: Evidence is obtained from at least one properly designed RCT.

- Level III-1: Evidence is obtained from well-designed pseudo-RCTs (alternate allocation or some other method).
- Level III-2: Evidence is obtained from comparative studies with concurrent controls and allocation not randomized (cohort studies), case–control studies, or interrupted time series with a control group.
- Level III-3: Evidence is obtained from comparative studies with historical controls, two or more single-arm studies, or interrupted time series without a parallel control group.
- Level IV: Evidence is obtained from case series, post-test or pre-test and post-test.

However, as was identified by the European Paediatric Parenteral Nutrition Guideline [18], there are problems using such a clinical system in matters such as parenteral admixture stability and medication coadministration where laboratory investigations or basic scientific principles are more appropriate. For example, calcium and phosphate in the right proportions will always precipitate, or a free-running infusion set will always carry a risk of heart failure and death. It is therefore necessary to reflect appropriately the levels of supporting evidence when it is other than RCTs. The following system has been adopted:

- Level I-S: Evidence from multiple well-conducted laboratory studies or from widely accepted laws of chemistry or physics.
- Level II-S: Evidence from only one or two studies, well designed, and undertaken in respected institutions or multiple studies but with questionable reliability.
- Level III-S: Evidence from only one study and a questionable method and/or source and/or a conflict of interest.
- Level IV-S: Evidence extrapolated from basic principles, but not formally tested in context (Table 2).

Guideline development process

The draft guidelines were written and compiled by a small group of volunteers and then circulated to all members of the GDG for several revisions before approval. The guidelines were developed by GDG consensus and did not represent any individual view.

Most aspects and recommendations of a draft version of the guideline were piloted in a non-structured manner by members of the GDG during the development process and feedback was elicited. The draft guideline was used by centers of expertise in New Zealand and Australia and by isolated practitioners in both countries. The perspectives of patients on HPN on the draft guidelines were also ascertained from a small selected group of Australian and New Zealand patients on HPN. Revisions were made after commentary from all these groups before submitting the guidelines for structured external review.

Table 2
Language recommendations

Conditions	Language of recommendation
If there were no reservations about endorsing an intervention	“Strongly recommended”
If evidence was supportive but there were minor uncertainties about the safety, feasibility, or costs of the intervention	“Recommended”
If the supportive evidence was weak and/or there were major uncertainties about the safety, feasibility, or costs of an intervention	“Should be considered”
If there was inadequate or conflicting evidence	No recommendation, i.e., “insufficient data,” but “by consensus the GDG recommends” when it is necessary to provide a response to the clinical question.

GDG, Australasian Society of Parenteral and Enteral Nutrition Home Parenteral Nutrition Guideline Development Group

The guideline was peer-reviewed in Australia and New Zealand and by internationally recognized HPN practitioners.

External reviewers were asked to critique the process, provide feedback on whether there were additional studies pertinent to HPN, and state whether the guideline was logical, clear, and practical. The GDG considered all feedback and further revised the guidelines accordingly. The final guideline was approved by all the members of the GDG and then by the AuSPEN Council.

The guideline should be reviewed and updated by a GDG convened by AuSPEN every 2 y with a complete review after 5 y.

Clinical and practical questions for HPN

Ten clinical questions were identified for inclusion in the AuSPEN HPN guideline. Each question is answered by reviews of the evidence and summaries of the GDG discussion, and a final recommendation is made (summarized in Appendix).

1. What are the criteria for selection for an HPN program?
2. How should patients be trained for HPN?
3. Who should provide care for patients on HPN?
4. How should CVCs for HPN be selected and placed?
5. How should HPN prescriptions be formulated and provided?
6. How should infusion pumps and ancillary products be selected and provided?
7. How should CVC-related complications be managed?

8. Can patients on HPN be safely prescribed other intravenous medications?
9. How should HPN be monitored?
10. How is HPN funded in Australia and New Zealand?

1. What are the criteria for selection for an HPN program?

1.1. There are no trials that provide evidence of efficacy of HPN versus no HPN in documented IF. Long-term PN in this setting is a life-preserving therapy. The GDG was thus unable to make a graded recommendation. The GDG by consensus developed principles with reference to the SHPNMCN [14] and with regard to medical ethics.

1.2. There is no international consensus for the indications of HPN in malignancy [19]. The GDG reviewed the available evidence and agreed on principles only without statements about specific malignancies or expected length of survival.

1.3. Freedom from hunger and malnutrition is a basic human right and alleviation is a fundamental prerequisite for human (and national) development [20]. However, when considering HPN for the treatment of any condition, quality-of-life expectations should be assessed. Patients and their carer/families need to choose appropriate therapies for themselves, with adequate explanation being provided to them regarding treatment options and associated risks and benefits (Table 3) [21].

- All patients who are considered for entry into an HPN program should have documented IF that, despite maximal medical therapy, would lead to deteriorating nutrition and/or fluid status.
- In cases of short bowel syndrome, patients should first have undergone a trial of enteral nutrition.
- Patients with documented IF should be assessed by a clinician and/or multi-professional group with an expertise with IF.
- The patient and/or carer(s) must be physically and emotionally able to undertake HPN training.
- The ability of the patient to co-operate with therapy should be taken into account when assessing for HPN. An assessment should be made of the appropriateness of the domestic situation.

Patients who have intestinal failure because of cancer may be suitable for HPN but the following additional points should be considered carefully:

- Likelihood of response to oncologic treatment
- An awareness of the diagnosis and likely prognosis

- Quality of life
- End-of-life issues, withdrawal of treatment

1.4. Provision should be made to review cases and ongoing need for HPN at regular intervals (see question 9—How should HPN be monitored?).

2. How should patients be trained for HPN?

2.1. There are no published trials that compare outcomes of training patients in HPN management by different methods. The GDG thus was unable to make a graded recommendation. A qualitative research in education processes suggests that successful learning characteristics can be developed into a framework for teaching delivery of home infusions [22].

2.2. By consensus the GDG recommends that the patient be trained in the management of HPN as an inpatient in preparation for the home environment. The patient will need to be stable on the HPN regimen before being discharged. The training process may take from several days to weeks depending on the patients' ability to learn the techniques to ensure safe practice in the home. In some few instances, care in a residential care facility may be an option. The patient will also need to be stable on the HPN regimen before being discharged.

2.3. *Key criteria for patient HPN competency training.* Training institutions will determine competency to self-manage HPN before discharge. A checklist of criteria for patients/carer(s) and trainers to sign-off as a written record of demonstrated competence may be helpful.

The patient/carer(s) will be able to:

- Demonstrate understanding of principles of asepsis and its importance
- Demonstrate safe delivery of HPN according to institutional protocol guidelines
- Recognize specific problems and symptoms and respond appropriately. These commonly include mechanical problems with the line and febrile episodes
- Have a connected telephone for medical support, emergency services, and logistics planning and delivery
- Live independently or have adequate care and support
- Have a home environment that provides a clean space for sterile additions, HPN setup, and connection
- A dedicated refrigerator may be needed for HPN solution storage

3. Who should provide care for patients on HPN?

3.1. There are no published trials that compare outcomes of patients cared for by different types of professional groups and/or institutions. The GDG thus was unable to make a graded recommendation.

3.2. Several retrospective studies have shown improved benefits of HPN therapy when patients are referred early to

Table 3
Four-principle approach to medical ethics [21]

Benevolence	Providing benefit
Non-maleficence	Deliberate avoidance of harm
Autonomy	Principle of self-determination
Justice	Equitable provision of resources to all

expert centers, where multidisciplinary teams exist [23–25]. The NICE guidelines [11] and SHPNMCN [14] protocols emphasize that patients receiving HPN should be supported by a co-ordinated multidisciplinary team with experience in delivery of HPN.

3.3. The GDG recommends by consensus that there is a named lead clinical consultant for an HPN service that ensures co-ordination and appropriate management of a patient within a multidisciplinary team.

Training can involve (but is not limited to) the following health professionals:

- Consultant medical staff
- Specialist nurses with expertise in management of long-term CVC and HPN management protocols
- Dietitians
- Pharmacists
- Allied health (psychologists, social workers, physiotherapists, occupational therapists)
- Nurses/pharmacists/dietitians or other expert staff employed by HPN product and service supply companies
- General practitioners
- District or community nurses

3.4. The patient and carer should receive an individualized care plan that includes overall aims and monitoring plan.

Patients and their families/carers should know all people who have significant roles in their care (with a written record of their names, positions, and contact details).

The patient may be provided with an open admission letter and/or written pathway for emergency/ambulance services. The patient may also be provided with a summary document of his/her condition.

3.5. *Patient support groups.* Organizations such as Patients on Intravenous and Nasogastric Nutrition Therapy (United Kingdom) and the Oley Foundation (United States) provide assistance, encouragement, moral support, and social interactions for some patients in other countries [26,27].

4. How should CVCs for HPN be selected and placed?

4.1. The CDC guidelines for the prevention of intravascular catheter-related infections [15] are designed to reduce the infectious complications associated with intravascular catheter use. The CDC notes that recommendations should be considered in the context of the institution's experience with catheter-related infections, experience with other adverse catheter-related infections (e.g., thrombosis, hemorrhage, and pneumothorax), and availability of personnel skilled in the placement of intravascular devices. Recommendations are provided for 1) intravascular catheter uses in general; 2) specific devices; and 3) CVC use for PN. Recommendations regarding the frequency of replacing catheters, dressings, administration sets, and fluids also are provided.

The CDC and others recommend that practitioners select the catheter, insertion technique, and insertion site with the lowest risk for complications (infectious and non-infectious) for the anticipated type and duration of intravenous therapy [28–30] (level II).

The GDG by consensus recommends use of this guideline.

4.2. There is limited RCT evidence regarding long-term catheter usage in patients on HPN. However, there is evidence regarding long-term catheter usage in oncologic patients [31]. This has been extrapolated to provide evidence for HPN catheter selection.

The ideal for HPN is a single-lumen catheter specifically placed for the purpose, in consultation with the patient and/or carers, to ensure that the exit site is accessible for self-management and so that it may be concealed under clothing (level III-2).

A multilumen catheter may be preferred when a patient requires other concurrent parenteral therapy [32]. Dedicating particular lumens to specific functions, e.g., HPN, chemotherapy, etc., reduces the potential for error [33] (level III-2).

Patients may be referred and accepted for HPN with an existing catheter. The GDG recommends by consensus that, even if such catheters are not ideal for the individual in terms of catheter choice, site of insertion, or catheter tip position, if the line is clean and functional, suitable for self-care, and acceptable to the patient, its use may be preferable to placement of a new catheter.

4.3. Current CVC types, materials, and connectors and alternative access choices in Australia and New Zealand are:

- Tunneled catheters (e.g., Hickman/Broviac with or without Groshong valve silicone catheters; Bard Access Systems, Salt Lake City, UT, USA): These offer acceptable rates of sepsis and thrombosis and ease of use. The visible length may be repaired if damaged (level III-2).
- Fully implanted catheters: (e.g., Port-a-cath): These CVCs are accessed through the skin by a needle and are favored by some patients for functional and cosmetic reasons, e.g., bathing and swimming, and could be considered for patients with a coexistent stoma. These are often also better suited for intermittent rather than daily use (level IV).
- Peripherally inserted CVCs: These are acceptable for short-term HPN (can provide access for up to 12–18 mo) [34]. Because the exit position effectively disables one hand, self-care may be difficult (level III-2).
- Arteriovenous fistulae: This type of access can be useful when central venous access becomes impossible.

4.4. *CVC material.* Standard silicone catheters are robust and soft and can last for 10–15 y [33,35,36]. There is

insufficient evidence to currently recommend alternative CVC materials (Teflon, antibiotic impregnated lines).

4.5. *CVC line connectors.* All connections should be Luer-locked to prevent accidental disconnection and air embolus. All external tunneled catheters should have a clamp and be locked under positive pressure. Patients should be informed of the alternatives and participate in the choice of catheter as appropriate.

4.6. *CVC placement and care.* To minimize complications or side effects, the smallest single-lumen catheter should be inserted into the largest possible vein. Almost always the vein selected will be the subclavian or internal jugular. When the internal jugular is used, an exit site on the neck is uncomfortable for the patient and difficult for self-care; the line must be tunneled to a more suitable position [33] (level IV).

The tip of the CVC should be positioned in the lower portion of the superior vena cava. Alternative access through the inferior vena cava is possible when there is obstruction of the superior vena cava.

4.7. *CVC insertion and exit site.* Surgical or radiologically guided percutaneous insertion using an aseptic technique should be used to insert a CVC. For skin preparation 2% aqueous chlorhexidine is the antiseptic of choice [15]. All catheter insertions solely for HPN should be undertaken by practitioners who are skilled in the technique and understand the needs of HPN therapy. Procedures should be minimally invasive. Image intensification is essential to confirm tip position [32] (level III-2).

Exit site dressings. Dressings for the CVC exit site are recommended for about the first 10 d. Highly permeable transparent dressings or dry gauze are acceptable. The former should be changed weekly in the absence of a specific indication (blood, pus) and the latter daily. With a dry healed exit site, dressings are not necessary except for peripherally inserted CVC lines [15] (level II).

5. How should HPN prescriptions be formulated and provided?

5.1. It is essential to estimate nutritional requirements before instigating HPN. Because inadequate or excessive macronutrient or micronutrient provision can be harmful, recommendations on appropriate levels would ideally be based on large studies comparing the effects of different levels of feeding at home on clinical outcomes, e.g., complications and mortality.

However, few such studies have been published and there is insufficient evidence for the GDG to make a graded recommendation on formulation. In the absence of such studies the GDG recommends by consensus that patients prescribed PN should have their nutritional requirements determined by health care professionals with the relevant skills and training in the prescription of NS before selection of a particular PN product.

5.2. *Formulation.* The prescription for HPN should be individualized to the patient's requirements. Many stable patients on HPN are satisfactorily maintained on prescriptions that provide 30–35 mL of fluid, 0.8–1.4 g of protein (0.13–0.24 g of nitrogen), and 20–35 kcal of total energy (including that from protein) per kilogram per day [11], with about one-third of the energy as lipid [37]. In exceptional circumstances larger proportions of lipid may be appropriate when persistent hyperglycemia is a problem [38]. The HPN formulation must also include adequate electrolytes and micronutrients in amounts that are optimally tailored to the clinical and intestinal status of the patient [2,39,40]. Additional fluids and electrolytes may be required in the HPN prescription if there are significant gastrointestinal losses (level III-2).

5.3. Parenteral nutrition can be administered as a continuous infusion (24 h) or cyclically (intermittently over shorter periods, e.g., 10–18 h). For patients on long-term PN, cyclical administration allows patients periods of free movement and potential metabolic benefits. However, controversy persists as to the optimal method of PN administration and the NICE guideline group conducted a review to compare PN given cyclically with PN given continuously [11].

The NICE group identified six RCTs but three were in patients who received peripheral PN only and described the incidence of infusion phlebitis. The other three studies included patients receiving central venous PN but were hospitalized short term. The NICE group concluded that, although continuous PN resulted in more efficient utilization of nutrients, none of these studies applied to patients on HPN and these patients should have cyclical administration to help maintain free movement and quality of life. Cycling HPN may also have metabolic advantages in minimizing longer-term liver complications [41] (level IV).

The prescription must be reviewed periodically and will always need to reflect individual patient requirements [11,42]. Where a non-standard formulation is required, a specific stability statement should be obtained from the admixture supplier [43] (level I-S).

5.4. *Preparation.* The HPN admixture must be sterile and non-pyrogenic. It is usually supplied in a single “all-in-one” bag or multichamber bag for mixing before use (level IV).

Admixtures should be prepared to well-validated formulations [43] under good pharmaceutical manufacturing practice conditions [44]. Basic principles for compounding all-in-one admixtures have been established [45] and several stability assessment techniques are now available [46]. The ASPEN guidelines for safe practices for PN have been extensively revised [47], leading to improved compliance in the United States, but there are still significant variations in PN ordering and labeling [48].

The HPN compounding is usually undertaken by a specialist HPN supply company or a hospital-based aseptic compounding unit. Care should be taken when using standard PN bags or multichamber bags that have not had

tailored additions of electrolytes or micronutrients made under pharmaceutical conditions [11].

Currently no large randomized trials have compared the use of standardized PN formulations with individualized PN with respect to safety outcomes. Most studies have been non-randomized or historically controlled and none have involved patients on HPN. Two prospective trials with adults and pediatric hospitalized patients demonstrated potential cost advantages [49,50]. A statement on PN standardization has been published by ASPEN [51].

The GDG is unable to provide a graded recommendation about standardized versus tailored PN.

5.5. Delivery. Delivery of HPN admixtures to patients should be in stout containers with known temperature/time characteristics to ensure admixture storage requirements are not exceeded in transit. Attention should be paid to patients living in particularly hot or cold regions [43]. The ambient temperature of the HPN solution must be kept at 4–28°C and air excluded from the all-in-one admixture [52]. National and international travels are possible with prior planning and consultation with clinicians and the supply companies (level I-S).

The patient should be consulted to establish stock-holding and delivery schedules. These should as far as possible not require regular intervention by the patient (routine pattern deliveries). It should be possible for the patient to easily obtain additional items to allow for items contaminated during opening and other similar problems [53,54].

Questions or concerns from the patient or carer(s) regarding treatment should be directed to the NS team or clinicians currently caring for the patient.

Questions or concerns the patient or carer(s) may have regarding the delivery times, service, or condition of any of the items (admixtures or consumable accessories used) that are delivered to the home should be directed to the supplier (the hospital pharmacy or a product supply company).

6. How should infusion pumps and ancillary products be selected and provided?

6.1. There is no RCT evidence comparing different pumps and ancillary product usage by patients on HPN. The GDG was unable to make a graded recommendation. The GDG used a consensus approach and consultation with professional staff employed by a homecare product supply company [55] that provides HPN in New Zealand and Australia.

6.2. Electronic pumps with appropriate delivery sets should be used to manage and monitor the delivery of the HPN. An ambulatory pump is ideal to maximize the patient's ability to remain independent and mobile [56]. If an ambulatory pump is not available (or appropriate because of the patient's condition), a standard volumetric pump with an intravenous stand is an alternative. The range of other sterile consumable products or accessories required for use by the patient at home will vary, dependent on the pump in use and individual patient requirements.

The pump should have the following features:

- Intuitive and easy to operate
- Easy to clean
- Service and maintenance contract provided
- Battery backup
- Variable audible alarm control
- 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
- Is equipped with standard safety features that include [57]
 - Air-in-line alarm
 - Upstream and downstream occlusion alarms
 - Free-flow protection device
 - Variable pressure delivery options
- A variety of pump-compatible sets should be available with different line lengths
- In-line filtration can be an option [58,59]
- Compliant with ECRI Institute safety recommendations [60]

Patients must be provided with comprehensive instruction on pump use and must demonstrate their competence. A 24-h × 7-d troubleshooting backup service by telephone from the hospital biomedical engineering department or supply company should be expected (level III-S).

7. How should CVC-related complications be managed?

7.1. There are no randomized trials that compare different management strategies for CVC-related complications.

The major CVC problems encountered by patients established on HPN are occlusion, catheter-related sepsis, and catheter breakage. There are a number of studies including well-validated laboratory studies that enable graded recommendations to be made regarding some clinical situations.

7.2. If sepsis is suspected, early diagnosis and management are important. Cultures through the line and two peripheral blood cultures should be undertaken as soon as there is concern [15,61]. Doppler ultrasound, transesophageal echocardiography, linograms, central venography, computerized tomography, and magnetic resonance imaging have been used to successfully define the extent of thrombosis and monitor response to therapy [62].

7.3. *Occlusion.* Prevention is better than cure. Occlusion, partial or complete, can be related to the presence of an expanding fibrin sheath, blood clot in or around the catheter, drug precipitates, lipid sludge, catheter kinking, or the catheter tip impinging on the wall of the vein [33,63].

Correct catheter placement, thorough patient or carer training, meticulous asepsis, and proper flushing may help to avoid occlusions and limit the problem.

Catheter occlusion should be promptly resolved or it may

lead to the more serious complications of sepsis and thrombosis [33] (level IV).

7.4. Central venous thrombosis. Symptoms include distended veins, ipsilateral limb swelling, chest pain, interscapular pain, and superior vena cava syndrome. Management will depend on the time of presentation, presence or absence of sepsis, anticipated difficulty with cannulating the patient to provide a new catheter, and the perceived risks of thrombolysis.

Management strategies include thrombolysis, anticoagulation, and radiologic stenting, but the GDG was unable to make a graded recommendation because there are insufficient data. By consensus the GDG suggests, if within 3–4 d of onset, “low-dose” thrombolysis to limit hemorrhagic complications be employed.

Thrombolysis with urokinase, streptokinase, and tissue plasminogen activator using boluses or infusions over a wide range of doses has been used successfully to unblock catheters [62].

The GDG found insufficient data to make evidence-based recommendations on preferred thrombolysis agents.

By consensus the GDG recommendation was that thrombolysis with tissue plasminogen activator is the currently preferred thrombolytic agent. If imaging and clinical response confirm successful resolution, the catheter can remain in place and anticoagulation therapy considered.

A hematology consult is recommended. Long-term warfarin is recommended in some patients who can absorb warfarin and maintain a therapeutic international normalized ratio.

Radiologic “stripping” of CVCs to remove the fibrin sheath can be performed in some centers.

In some radiologic centers stenting of the partially occluded superior vena cava can be performed, re-establishing patency to enable reinsertion of a CVC at a later date.

7.5. Catheter fracture and air embolism. Catheter fracture and the potential for air embolism can be a medical emergency. Patients on HPN must be educated on the technique of catheter clamping and immediately notify their health care team. CVC “repair kits” are available that enable preservation of the catheter.

7.6. Catheter migration. It is important that the external length of catheter protruding is documented and monitored. If the tip of the CVC migrates into the lumen of a smaller central vein, then there is an increased risk of major venous thrombosis [64].

CVC-related infection varies from mild fever with or without systemic symptoms to severe septic shock. The sudden onset of high swinging fevers (39°C to ≥40°C) accompanied by rigors is highly suggestive of CVC-related sepsis [61].

Patients must be made well aware of the significance of signs and symptoms and present promptly for treatment. An open admission letter for the patient could be of value, particularly if the patient must present to a facility other than the hospital managing the patient’s HPN (e.g., if the patient lives a long way from the HPN base provider).

7.7. Pathogenesis. The potential sources of infection are

the HPN admixture and administration system, the skin, and the CVC connections.

If the patient on HPN presents with sepsis, this should be presumed to be line infection (in the absence of another possible cause of sepsis). Blood cultures using CVC-aspirated blood (all lumens) should be taken along with peripheral blood cultures. Identification of the same species of bacteria from peripheral and central cultures is highly indicative of line sepsis [65] (level III-2).

If there are other possible sources of infection, particularly the abdomen, it is important to know with some certainty if the CVC is responsible. Unnecessary removal of the CVC should be avoided.

7.8. Management. HPN should be stopped while the cause is investigated (septic shock mandates CVC removal).

Blood cultures should be taken and institutional antibiotic protocols considered.

In some cases, CVCs can often be preserved by using decontamination techniques. Thrombolysis is an important component of decontamination because infection and thrombosis are often related [63,65].

Protocols generally include systemic treatment of the infection with broad-spectrum or appropriate intravenous antibiotics, antibiotic locks to eradicate infection within the catheter, and thrombolytic locks to break down fibrin buildup within the catheter. There is insufficient evidence to recommend ethanol locks [66] (level IV).

8. Can patients on HPN be safely prescribed other intravenous medications?

8.1. Medications are frequently prescribed for patients on HPN but unrecognized interactions between drugs and nutrients can lead to poor outcomes [2].

A drug–nutrient reaction may alter the kinetics and/or physiologic effect of a drug or nutrient, resulting in derangements in fluid–electrolyte balance, changes in vitamin status, and disturbances in acid–base balance [67]. Direct physical contact in the delivery system or the PN bag or during the compounding process may also affect the availability of the drug [68,69].

The United States Pharmacopoeia makes specific recommendations for coadministration of medications with PN that address compatibility and efficacy [70]. Nevertheless, drug–nutrient interactions can be so common that their clinical consequences are often not reported, thus limiting the data needed for evidence-based guidelines [2].

8.2. The GDG by consensus recommends that all medications of patients on HPN should be reviewed for potential effects on nutritional and metabolic status (level III-2).

Coadministration or an admixture of medications known to be incompatible with PN should be prevented. Any additive lacking compatibility and stability data in the proposed admixture should not be added to PN formulations (level II).

9. How should HPN be monitored?

9.1. The GDG found no prospective studies on the impact of different monitoring regimens on outcome including quality of life.

9.2. The NICE guideline states that it is essential that close support and monitoring by a hospital-based team experienced in looking after these complex patients is continued after discharge for as long as the patient requires HPN. However, they make no specific recommendations. The GDG considered a recent report on monitoring HPN in 42 centers in Europe [71] and the SHPNMCN [14] protocols. The European centers reported varying practices but only two-thirds had written guidelines. No cost-effective organizational model was proposed.

9.3. Quality of life describes health status from the patient's perspective and is an important component of ongoing monitoring. The GDG considers that there is a need for a standardized, validated HPN-specific instrument such as proposed by the SHPNMCN [9] to measure quality of life in this population, which should become part of the routine ongoing clinical monitoring.

9.4. By consensus and by reference to the NICE guideline and the SHPNMCN, the GDG recommends that the following framework may provide a basis for safe and appropriate monitoring (Table 4).

All patients on HPN must have a baseline nutritional assessment and individual regimens should be based on nutritional requirements.

Patients on HPN must be seen and assessed on a regular basis by the multidisciplinary NS team (optimally a nurse, dietitian, and doctor). The timing will depend on the status of the patient and may range from weekly to every 6 mo.

The HPN monitoring should include a written record of the assessment and outcomes, which becomes part of the patient's permanent medical record.

Adjustments to therapy should also form part of this record.

10. How is HPN funded in Australia and New Zealand?

10.1. Funding is required for short- and long-term care of patients on HPN. This is divided into two parts: one payment for the solutions used, and another payment for the consumables/accessories used as part of the therapy, i.e., infusion sets, dressings, and antiseptic solutions. Treatment costs vary per patient depending on the solutions and consumables/accessories used.

Funding differs between Australia and New Zealand.

10.2. *Australia.* Some private health funds provide an allowance for short-term PN therapy if it is directly related to the episode of care for which a patient has been hospi-

Table 4

Suggested framework for assessment and monitoring

Core monitoring	Weight (and height if young person) Oral intake Biochemistry including electrolytes, glucose, urea, creatinine, liver function tests (weekly until stable then every 3 mo) Hematology screen (weekly until stable and then every 3 mo) Longer-term patients should have a lipid screening Magnesium, zinc, copper, manganese, selenium, and iron status (baseline and 6 mo) Prescription/non-prescription medicines taken Extra renal losses (e.g., stoma losses) should be assessed for stability and adequate replacement planning Line status and adequacy of care Functional status
Additional monitoring	Glycemic monitoring if diabetic Bone health (DEXA) once per year for vulnerable groups including postmenopausal women Quality-of-life survey Body composition measurement, involving at least anthropometry (muscle mass and fat stores), to guide ongoing protein–energy prescribing Inflammatory markers if ongoing inflammatory disease Problem-solving checklists INR if anticoagulated

DEXA, dual-energy x-ray absorptiometry; INR, international normalized ratio

talized. If long-term care is required, the care of the patient usually becomes the responsibility of the local public hospital.

Some patients pay for their own therapy if they have the financial means or there is no other choice. With negotiation private health insurance may be prepared to cover the cost of HPN for short-term therapy. This has to be undertaken on an individual patient basis. To date no private health insurer in Australia has covered the long-term cost of HPN.

Before application for funding can occur, a patient's solutions and consumables must be costed and quoted by the company who will be supplying the products.

It is recommended that this quote be figured on a yearly basis.

10.3. *New Zealand.* Pharmac (Pharmaceutical Management Agency) currently funds all patients on HPN in New Zealand. A patient profile form must be completed and a prescription sent to the provider company.

Note: Pharmac (Pharmaceutical Management Agency) is a Crown entity that secures pharmaceutical treatments for eligible New Zealanders (pursuant to the New Zealand Public Health & Disability Act, 2000).

Appendix

Summary of topics and recommendations

1 *What are the criteria for patient selection for an HPN program?*

The GDG was unable to make a graded recommendation on published evidence.
By consensus we recommend that patients have documented intestinal failure, have failed enteral feeding, and be physically and emotionally able to cope with training and the therapy. Patients with cancer may be suitable for HPN but additional factors and QOL should be considered.

2 *How should patients be trained for HPN?*

The GDG was unable to make a graded recommendation on published evidence.
By consensus we recommend patients on HPN be trained as inpatients to achieve competency in key criteria, which include principles of asepsis, safe delivery of HPN, and use of pumps and devices. A stable home environment is also important.

3 *Who should provide care for patients on HPN?*

The GDG was unable to make a graded recommendation on published evidence.
By consensus we recommend a patient on HPN be cared for by a multidisciplinary team with experience in HPN including a named lead clinical consultant.
The patient on HPN should receive an individualized care plan that includes overall aims and a monitoring plan from the team.

4 *How should the CVC for HPN be selected and placed?*

The GDG strongly recommends that practitioners select the CVC, insertion technique, and insertion site with the lowest risk of complications for the patient on HPN (level II).
Single-lumen tunneled catheters made of silicone should be considered for long-term use. PICCs may be considered for shorter-term use (12–18 mo; level III-2).

5 *How should HPN prescriptions be formulated and provided?*

The GDG was unable to make a graded recommendation on published evidence.
By consensus we recommend PN requirements be determined by health care professionals with relevant skills and training.
The prescription for HPN should usually provide:
30–35 mL fluid · kg⁻¹ · d⁻¹
0.8–1.4 g protein (0.13–0.24 g nitrogen) · kg⁻¹ · d⁻¹
20–35 kcal · kg⁻¹ · d⁻¹ total energy (including that from protein) with about one-third of total energy being furnished by lipid.
The HPN formulation must also include adequate electrolytes and micronutrients in amounts that are optimally tailored to the clinical and intestinal status of the patient. The admixture should be compounded under sterile conditions in compliance with national GMP standards.
The infusion should ideally be cyclical so that patients can maintain QOL and minimize metabolic complications.

6 *How should infusion pumps and ancillary products be selected and provided?*

The GDG was unable to make a graded recommendation on published evidence.
By consensus we recommend that an ambulatory electronic pump with compatible delivery sets be used, to manage and monitor the delivery of HPN.

7 *How should CVC-related complications be managed?*

The major CVC problems encountered by patients on HPN are occlusion, catheter-related sepsis, and catheter breakage. Catheter fracture and the potential for air embolism can be a medical emergency.

By consensus the GDG recommends that patients are educated on the technique of catheter clamping if catheter fracture is suspected and to notify the health care team.

The GDG found insufficient data to make a graded recommendation on preferred methods of managing occlusions.

Catheter occlusion should be promptly resolved or it may lead to the more serious complications of sepsis and thrombosis.

By consensus the GDG recommend thrombolysis with tissue plasminogen activator as the preferred thrombolytic agent.

Patients on HPN presenting with sepsis should be presumed to have line sepsis and the HPN should be stopped.

Blood cultures using CVC-aspirated blood and peripheral cultures should be taken. Identification of the same species of bacteria from both cultures is highly indicative of line sepsis.

Systemic treatment of the infection with intravenous antibiotics, antibiotic locks to eradicate infection within the catheter, and/or thrombolytic locks to breakdown fibrin buildup within the catheter are recommended. Septic shock mandates catheter removal.

8 *Can patients on HPN take other intravenous medications safely?*

The GDG was unable to make a graded recommendation on published evidence.

Any intravenous medication may have a systemic effect on fluid–electrolyte status, vitamin levels, or acid–base balance.

By consensus the GDG recommends that all intravenous medications prescribed for patients on HPN should be reviewed for potential interactions. Co-administration in the PN admixture should be avoided.

9 *How should HPN be monitored?*

The GDG was unable to make a graded recommendation on published evidence.

By consensus the GDG recommends that all patients on HPN must have a complete baseline nutritional assessment and that individual regimens be based on nutritional requirements.

Patients on HPN must be seen and assessed on a regular basis by the multidisciplinary team (optimally a nurse, dietitian, pharmacist, and doctor). The timing will depend on the status of the patient and may range from weekly to every 6 mo.

10 *How is HPN funded in Australia and New Zealand?*

Funding is required before discharge but differs between Australia and New Zealand.

CVC, central venous catheter; GDG, Australasian Society of Parenteral and Enteral Nutrition Home Parenteral Nutrition Guideline Development Group; GMP, good pharmaceutical manufacturing practice; HPN, home parenteral nutrition; PICC, peripherally inserted central venous catheter; QOL, quality of life

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