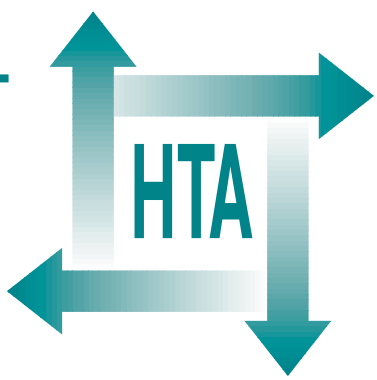
Health Technology Assessment 1997; Vol. 1: No. 1

Review

Home parenteral nutrition: a systematic review

D M Richards
J J Deeks
T A Sheldon
J L Shaffer

Health Technology Assessment
NHS R&D HTA Programme



Standing Group on Health Technology

Chair: Professor Sir Miles Irving,
Professor of Surgery, University of Manchester, Hope Hospital, Salford †

Dr Sheila Adam, Department of Health

Professor Martin Buxton, Professor of Economics, Brunel University †

Professor Angela Coulter, Director, Kings Fund Centre for Health Services Development †

Professor Anthony Culyer, Deputy Vice-Chancellor, University of York †

Dr Peter Doyle, Executive Director, Zeneca Ltd, ACOST Committee on Medical Research & Health

Professor John Farndon, Professor of Surgery, University of Bristol †

Professor Charles Florey, Department of Epidemiology & Public Health, Ninewells Hospital & Medical School, University of Dundee †

Professor John Gabbay, Director, Wessex Institute for Health Research & Development †

Dr Tony Hope, The Medical School, University of Oxford †

Professor Howard Glennester, Professor of Social Science & Administration, London School of Economics and Political Science

Professor Sir John Grimley Evans, Department of Geriatric Medicine, Radcliffe Infirmary, Oxford †

Mr John H James, Chief Executive, Kensington, Chelsea & Westminster Health Authority

Professor Richard Lilford, Regional Director, R&D, West Midlands †

Professor Michael Maisey, Professor of Radiological Sciences, UMDS, London

Dr Jeremy Metters, Deputy Chief Medical Officer, Department of Health †

Mrs Gloria Oates, Chief Executive, Oldham NHS Trust

Professor Michael Rawlins, Wolfson Unit of Clinical Pharmacology, University of Newcastle-upon-Tyne

Professor Martin Roland, Professor of General Practice, University of Manchester

Mr Hugh Ross, Chief Executive, The United Bristol Healthcare NHS Trust †

Professor Ian Russell, Department of Health, Sciences & Clinical Evaluation, University of York

Professor Trevor Sheldon, Director, NHS Centre for Reviews & Dissemination, University of York †

Professor Mike Smith, Director, The Research School of Medicine, University of Leeds †

Dr Charles Swan, Consultant Gastroenterologist, North Staffordshire Royal Infirmary

Professor Tom Walley, Department of Pharmacological Therapeutics, University of Liverpool †

Dr Julie Woodin, Chief Excutive, Nottingham Health Authority †

† Current members

HTA Commissioning Board

Chair: Professor Charles Florey, Department of Epidemiology & Public Health,
Ninewells Hospital & Medical School, University of Dundee †

Professor Ian Russell, Department of Health, Sciences & Clinical Evaluation, University of York *

Mr Peter Bower, Independent Management Consultant, Newcastle-upon-Tyne †

Ms Christine Clarke, Director of Pharmacy, Hope Hospital, Salford †

Professor David Cohen, Professor of Health Economics, University of Glamorgan

Mr Barrie Dowdeswell, Chief Executive, Royal Victoria Infirmary, Newcastle-upon-Tyne

Dr Mike Gill, Brent and Harrow Health Authority †

Dr Jenny Hewison, Senior Lecturer, Department of Psychology, University of Leeds †

Dr Michael Horlington, Head of Corporate Licensing, Smith & Nephew Group Research Centre

Professor Sir Miles Irving (Programme Director), Professor of Surgery, University of Manchester, Hope Hospital, Salford †

Professor Martin Knapp, Director, Personal Social Services Research Unit, London School of Economics and Political Science

Professor Theresa Marteau, Director, Psychology & Genetics Research Group, UMDS, London

Professor Sally McIntyre, MRC Medical Sociology Unit, Glasgow

Professor Jon Nicholl, Director, Medical Care Research Unit, University of Sheffield †

Dr Tim Peters, Department of Social Medicine, University of Bristol †

Professor David Sackett, Centre for Evidence Based Medicine, Oxford

Dr David Spiegelhalter, MRC Biostatistics Unit, Institute of Public Health, Cambridge

Dr Ala Szczepura, Director, Centre for Health Services Studies, University of Warwick †

Professor Graham Watt, Department of General Practice, Woodside Health Centre, Glasgow †

Professor David Williams, Department of Clinical Engineering, University of Liverpool

Dr Mark Williams, Public Health Physician, Bristol

* Previous Chair
† Current members

National Coordinating Centre for Health Technology Assessment, Advisory Group

Chair: Professor John Gabbay, Wessex Institute for Health Research & Development

Professor Mike Drummond, Centre for Health Economics, University of York

Professor Charles Florey, Department of Epidemiology & Public Health, University of Dundee

Professor Sir Miles Irving, Department of Surgery, Hope Hospital, Salford

Ms Lynn Kerridge, Wessex Institute for Health Research & Development

Dr Ruairidh Milne, Wessex Institute for Health Research & Development

Ms Kay Pattison, Research & Development Directorate, NHS Executive

Professor James Raftery, Health Economics Unit, University of Birmingham

Dr Paul Roderick, Wessex Institute for Health Research & Development

Professor Ian Russell, Department of Health, Sciences & Clinical Evaluation, University of York

Dr Ken Stein, Wessex Institute for Health Research & Development

Professor Andrew Stevens, Department of Public Health & Epidemiology, University of Birmingham

How to obtain copies of this and other HTA Programme reports.
An electronic version of this publication, in Adobe Acrobat format, is available for downloading free of charge for personal use from the HTA website (http://www.hta.ac.uk). A fully searchable CD-ROM is also available (see below).

Printed copies of HTA monographs cost £20 each (post and packing free in the UK) to both public **and** private sector purchasers from our Despatch Agents.

Non-UK purchasers will have to pay a small fee for post and packing. For European countries the cost is £2 per monograph and for the rest of the world £3 per monograph.

You can order HTA monographs from our Despatch Agents:

– fax (with **credit card** or **official purchase order**)
– post (with **credit card** or **official purchase order** or **cheque**)
– phone during office hours (**credit card** only).

Additionally the HTA website allows you **either** to pay securely by credit card **or** to print out your order and then post or fax it.

Contact details are as follows:

HTA Despatch
c/o Direct Mail Works Ltd
4 Oakwood Business Centre
Downley, HAVANT PO9 2NP, UK

Email: orders@hta.ac.uk
Tel: 02392 492 000
Fax: 02392 478 555
Fax from outside the UK: +44 2392 478 555

NHS libraries can subscribe free of charge. Public libraries can subscribe at a very reduced cost of £100 for each volume (normally comprising 30–40 titles). The commercial subscription rate is £300 per volume. Please see our website for details. Subscriptions can only be purchased for the current or forthcoming volume.

Payment methods

Paying by cheque
If you pay by cheque, the cheque must be in **pounds sterling**, made payable to *Direct Mail Works Ltd* and drawn on a bank with a UK address.

Paying by credit card
The following cards are accepted by phone, fax, post or via the website ordering pages: Delta, Eurocard, Mastercard, Solo, Switch and Visa. We advise against sending credit card details in a plain email.

Paying by official purchase order
You can post or fax these, but they must be from public bodies (i.e. NHS or universities) within the UK. We cannot at present accept purchase orders from commercial companies or from outside the UK.

How do I get a copy of *HTA on CD*?

Please use the form on the HTA website (www.hta.ac.uk/htacd.htm). Or contact Direct Mail Works (see contact details above) by email, post, fax or phone. *HTA on CD* is currently free of charge worldwide.

The website also provides information about the HTA Programme and lists the membership of the various committees.

Home parenteral nutrition: a systematic review

Mr D M Richards [1]
Mr J J Deeks [2]
Professor T A Sheldon [3]
Dr J L Shaffer [1]

[1] The University of Manchester Intestinal Failure Unit, Hope Hospital, Salford

[2] Centre for Statistics in Medicine, Nuffield Department of Medicine, University of Oxford

[3] The NHS Centre for Reviews and Dissemination, University of York

Final manuscript received July 1996

This report should be referenced as follows:

Richards DM, Deeks JJ, Sheldon TA, Shaffer JL. Home parenteral nutrition: a systematic review. *Health Technol Assess* 1997;**1** (1).

NHS R&D HTA Programme

The overall aim of the NHS R&D Health Technology Assessment (HTA) programme is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and work in the NHS. Research is undertaken in those areas where the evidence will lead to the greatest benefits to patients, either through improved patient outcomes or the most efficient use of NHS resources.

The Standing Group on Health Technology advises on national priorities for health technology assessment. Six advisory panels assist the Standing Group in identifying and prioritising projects. These priorities are then considered by the HTA Commissioning Board supported by the National Coordinating Centre for HTA (NCCHTA).

This report is one of a series covering acute care, diagnostics and imaging, methodology, pharmaceuticals, population screening, and primary and community care. It was identified as a priority by the Pharmaceuticals Panel (see inside back cover).

The views expressed in this publication are those of the authors and not necessarily those of the Standing Group, the Commissioning Board, the Panel members or the Department of Health.

Series Editors: Andrew Stevens, Ruairidh Milne and Ken Stein
Assistant Editor: Jane Robertson

The editors have tried to ensure the accuracy of this report but cannot accept responsibility for any errors or omissions. They would like to thank the referees for their constructive comments on the draft document.

ISSN 1366-5278

Published by Core Research, Alton, on behalf of the NCCHTA.
Printed on acid-free paper in the UK by The Basingstoke Press, Basingstoke.

Copies of this report can be obtained from:

The National Coordinating Centre for Health Technology Assessment,
Mailpoint 728, Boldrewood,
University of Southampton,
Southampton, SO16 7PX, UK.
Fax: +44 (0) 1703 595 639 Email: hta@soton.ac.uk
http://www.soton.ac.uk/~hta

Contents

List of abbreviations

ASPEN	American Society for Parenteral and Enteral Nutrition
BAPEN	British Association for Parenteral and Enteral Nutrition
CI	confidence interval
ESPEN	European Society for Parenteral and Enteral Nutrition
HPN	home parenteral nutrition
MVD	mesenteric vascular disease
MVO	mesenteric vessel occlusion
QALY	quality-adjusted life year
QoL	quality-of-life
SCI	Science Citation Index
TPN	total parenteral nutrition

Summary

Objectives
The objective of this Review was to locate, appraise and summarise evidence from scientific studies on home parenteral nutrition (HPN) in order to answer specific research questions on the effectiveness of this technology.

The following questions were asked. What patients have received HPN? What has been the experience of patients on HPN programmes? How have HPN programmes been organised, and what techniques and equipment have been used, and to what effect? What comparative information is available on effectiveness? What evidence exists for the cost-effectiveness of HPN? What questions about the provision of HPN could be answered with additional research, and what studies would be most suitable?

Data sources
A comprehensive list of studies was provided by an extensive search of electronic databases (including MEDLINE, Embase, Science Citation Index, Uncover, Cinahl, Caredata, Food Science and Technology Abstracts, NTIS, Pascal, Psychlit, and Economic Literature Index), relevant journals (including *Journal of Parenteral and Enteral Nutrition, Clinical Nutrition, American Journal of Clinical Nutrition, Nutrition, Clinical Gastroenterology, Nutrition Reviews, Annals of Nutrition and Metabolism, Nutrition and Cancer, Nutrition and Health,* and *Journal of Paediatric Nutrition and Metabolism*), and scanning of reference lists, as well as other search strategies outlined in the protocol.

Study selection
Studies relevant to the questions were selected. The inclusion criteria were fairly broad because of the quality of the studies located.

Data extraction
Data extraction forms were used to collect data from studies included in the review. The data was checked by a second researcher to reduce error.

Data synthesis
Quantitative analysis was difficult owing to the type of studies located. The data is discussed in a qualitative manner. Where complication rates have been given, we have attempted to combine the results in a quantitative manner.

Results
The age and sex of patients on HPN varies according to the underlying disease but, on the whole, patients are young (see *Tables 4a* and *4b*). There are trends showing an increased use of the technology at the extremes of the age range. There are marked differences between countries on the underlying diseases for which HPN is indicated. For example, many more patients with an underlying malignancy are treated in Italy and the USA than in the UK (40–67% versus 8%). Morbidity rates for the majority of patients are acceptable (see *Table 8*), the complications tend to be related to the central venous catheter. It is fairly clear that a minority of patients are susceptible to recurrent problems and that many patients have very few complications. The mortality rate for HPN patients (see *Table 10*) was good for those patients with benign underlying disease (for example, 5% of Crohn's HPN patients die per year), and there are very few reports of patients dying from complications of the technology. The survival of those with malignant disease and AIDS is poor, almost all having died from the underlying disease at one year; despite this, most programme growth worldwide is due to an increase in the numbers of patients with these diagnoses (see *Table 5*). Quality of life is reasonable for patients with benign disease (see *Table 9*); no studies were found that examined the quality of life of HPN patients with malignant disease. Economic analysis shows that the cost of HPN treatment is cheaper than the alternative of in-patient care (see *Table 18*). There is a paucity of comparative studies examining different aspects of the technology, and this accounted for the majority of gaps in the evidence.

Conclusions
The use of HPN for benign intestinal failure is supported by evidence from the scientific studies located. There are, however, large gaps in the evidence, particularly relating to the use of HPN in malignant disease and AIDS. A programme of research is suggested at the end of this review.

Chapter 1

Background information

Home parenteral nutrition (HPN) is a complex technology involving the intravenous infusion of liquid nutrition directly into a central vein. The patient, or carer, is taught to manage the complicated sterile routine, enabling transfer of care to the home. It is an expensive and time-consuming routine which may be required for many years or, in some cases, life. It intrudes into the patient's life and any alteration from the daily routine requires planning. This is likely to have an effect on the quality of life experienced by both the patient and his or her family.

The technology is used to treat intestinal failure, defined as an inadequate intestinal function for absorption of fluid electrolyte and nutrient requirements. Intestinal failure can be caused by destruction of the available absorptive surface (for example, Crohn's disease), chronic intestinal obstruction (malignant disease and motility disorders), or by extensive removal of the absorptive surface (following mesenteric artery occlusion or extensive small bowel resection). There is a range of severity of intestinal failure from complete to partial. Complete failure suggests that the patient will require all fluids, nutrients and trace elements to be given parenterally, suggesting that the patient would die quickly of a combination of dehydration and malnutrition without treatment. Partial failure usually means that some parenteral support is required (possibly only fluids) but that intensive enteral support might suffice. Adaptation of the intestinal mucosa may allow 'weaning' of parenteral support, and is one reason why patients can stop HPN treatment. Recovery from the underlying disease is the other main reason for stopping parenteral support. The liquid nutrition is infused (usually overnight) through a sterile, pemanently in-dwelling, central venous access device. The complex techniques of infusing the nutrition safely are mastered by the patient or a carer, usually before the patient is discharged from hospital.

Patient referral patterns for HPN treatment are inconsistent, some regions in the UK having very few HPN patients. However, there are several large centres in the UK where HPN is considered as an essential, life-saving treatment. The prevalence of HPN patients in the northwest of England and Scotland is approximately 18–20 per million. This figure is comparable to that from Denmark, a country with a very similar disease profile to the UK. (The UK national average is 2.6 per million, reflecting the fact that higher rates are seen close to major referral centres.)

The NHS Research and Development Programme's Standing Group on Health Technology Assessment prioritised HPN as a technology requiring further assessment because of cost, effect on quality of life, variable referral patterns and uncertainty regarding effectiveness. The aim, therefore, of this systematic review was to assess the extent and quality of evidence on HPN and to identify that which should inform practice.

Chapter 2

Research questions addressed

The aim of this review is to locate, acquire and synthesise studies concerning the use, effectiveness and cost-effectiveness of home parenteral nutrition. The review falls into five main sections, illustrated by the research questions below; for each of these the literature on both adults and children is reviewed. The first four sections are included in chapter 4 – Results; the fifth is covered in chapter 6 – Conclusions.

Searching the HPN literature suggests that there are very few comparative studies available. Most of the literature consists of case series. The research questions were formulated bearing this is mind, so as to make the best use of what information is available.

Section 1. *Which patients have received HPN?*
It is important to identify the types of patients who have received HPN treatment. We aimed to describe the age, sex and diagnostic profiles of patients and to outline trends that may be taking place.

Section 2. *What has been the experience of patients on HPN programmes?*
We aimed to describe the type and incidence of complications, survival, duration of HPN treatment, quality of life and why HPN treatment was discontinued, so that an accurate profile of 'life on HPN' could be constructed. We also aimed to identify any moderating factors.

Section 3. *(a) How have HPN programmes been organised, and what techniques and equipment have been used, and to what effect? (b) What comparative information is available on effectiveness?*
We aimed to find out what methods of organisation of HPN programmes existed and whether any organisational model was superior. We also wanted to identify what comparative evidence exists on different aspects of the technology.

Section 4. *What evidence exists for the cost-effectiveness of HPN?*
The aim of this section was to compare the cost-effectiveness of HPN with any alternative treatments that might be available. In addition, an examination of the costs involved with an HPN programme was undertaken.

Section 5. *What questions about the provision of HPN could be answered with additional research, and what studies would be most suitable?*
Our aim was to highlight gaps in the research knowledge and also to identify key research questions which need to be answered.

Chapter 3

Review methods

A protocol was developed for the systematic review of HPN following the NHS Centre for Reviews and Dissemination Guidelines (Deeks *et al,* 1996).

Section 1 Which patients have received HPN?

A longitudinal inception study would provide actual patient numbers being treated on HPN by subgroup, whilst a cross-sectional sample would only provide a snapshot of the types of patients being treated with HPN. The results will differ according to the length of time spent on HPN. The results of the two types of studies will be interpreted separately. Retrospective data collection is prone to be less complete than prospective data collection.

Complete assessment or random sampling are the best ways of maintaining representativeness. Both rely on the correct identification of a sampling frame. When these are not available, it may be possible to validate sample coverage by taking a sample using a second source and noting the degree of similarity in sample members. Non-response and missing data in a survey reduces its validity.

Inclusion criteria

(a) Surveys of HPN use.
(b) Information from databases of HPN users.
(c) Data from cohorts of HPN patients.

Points for assessing validity

(a) Are the patient numbers based on new patients in a given period, or from a cross-sectional sample?
(b) Was the data collected prospectively or retrospectively?
(c) What proportion of patients were sampled and how was the sample chosen?
(d) From what group was the sample selected and how representative is it?
(e) Was the sample coverage validated and if so was it found to be acceptable?
(f) For what proportion of selected patients was no information available?
(g) How complete was the data that was acquired?

Section 2 What has been the patient experience of HPN?

Studies which have been included in Section 1 may also be of interest here. Ascertainment of outcomes should be free from bias. Where excessive patient investigations are carried out, a higher number of events may be detected than in case series with less active investigation. The instruments used to measure subjective issues like quality of life need to be validated. A potential problem is this area is the choice of denominators for the calculation of rates, whether they are patient numbers, patient years, or the way in which data has been analysed. When reporting rates it is important to make the distinction between per 1000 per year, which implies a group of patients are all followed up for the same length of time, and per 1000 patient years.

Inclusion criteria

(a) Studies reporting the experience of inception cohorts of HPN users.
(b) Studies giving information on length of treatment, mortality, complications, or quality of life.

Points for assessing validity

(a) Is data collected prospectively or retrospectively?
(b) What cohort was recruited?
(c) How much of the cohort was successfully recruited?
(d) How complete was the follow-up?
(e) What procedure was used to detect complications?
(f) What quality-of-life instrument was used and how was it validated?

Section 3a Organisation

Inclusion criteria

Surveys assessing issues in the delivery of HPN since 1980.

Points for assessing validity
Any study which has assessed how HPN programmes have been organised.

Section 3b Comparative data

The validity of comparisons between, for example, different procedures, will greatly depend on the study design. In addition, different aspects of validity will be important to different designs of study. The studies will be grouped according to their design in the analysis.

Studies to be included
Any comparative study.

Points for assessing validity
(a) What was the study design? Descriptive or comparative?
(b) Is data collection prospective or retrospective?
(c) Was a comparison made?
(d) How were allocations to treatment made?
(e) Was follow-up complete?
(f) Were the groups comparable with respect to age and diagnosis?
(g) What outcomes were measured?
(h) Was the length of follow-up more than 3 months in all cases?
(i) How were outcomes assessed?

Section 4 Cost-effectiveness of HPN

Inclusion criteria (economic analyses)
Any economic evaluation of an HPN programme.

Validity
(a) What methodological technique has been applied?
(b) What was the comparison made with?
(c) What perspective was adopted?
(d) Were all costs considered?
(e) Were costs measured appropriately?
(f) Were all outcomes considered?
(g) Were they measured appropriately?
(h) How was quality of life assessed?
(i) Was a marginal analysis performed?
(j) Was the robustness of the result tested in a sensitivity analysis?

Section 5 What gaps are there in the evidence?

Which questions remain unanswered?
What gaps in knowledge exist?
What clinical issues need to be addressed?
What methodological issues need to be addressed?

Literature search strategy and study retrieval

The aim of the literature search was to provide a comprehensive list of primary studies. It included all types of study design and included all possible aspects of HPN technology.

Before starting the search, advice was sought from an information scientist at the NHS Centre for Reviews and Dissemination, York, and from a senior medical librarian based at Hope Hospital, Salford.

The following possible sources of data were identified.

- Electronic databases
- Hand-searching of relevant journals
- Personal literature collections
- Conference proceedings
- Writing to all major centres in Europe and the USA
- Science Citation Index
- Scanning reference lists of studies located

Electronic databases
It is well documented in the literature that many studies can be missed if searches are limited to only one database. We searched 11 separate databases from 1968 onwards, that is, from the origins of HPN (see Appendix 2 Review protocol).

Hand searching
Ten journals were hand searched for the period, January 1980–July 1995 (or for whatever period within this frame they were available).

Conference proceedings
Proceedings of the annual conferences of the following bodies were obtained.

- ASPEN (American Society for Parenteral and Enteral Nutrition) – 1993, 1994, 1995
- ESPEN (European Society for Parenteral and Enteral Nutrition) – 1993, 1994, 1995
- BAPEN (British Association for Parenteral and Enteral Nutrition) – 1994

Personal literature collections
We examined the studies collected by Professor Sir Miles Irving who was one of the founders of HPN in the UK.

Letters to experts
We contacted major European and American centres requesting published and unpublished studies, and any details of on-going work.

Visits to major meetings
Two members of the project team attended the ESPEN meeting in Rome (September 1995) and the BAPEN meeting (December 1995).

Selection of eligible studies, checking validity and data extraction
One researcher checked articles for eligibility for each of the research questions, graded their validity, and extracted the necessary data.
A second researcher validated these decisions by processing a 10% random sample of included and excluded studies.

Study synthesis
Because of the lack of comparability of data, quantitative synthesis is not appropriate. The results are therefore, discussed in a qualitative manner except in the case of the complications where a weighted average is calculated. The qualitative analysis takes into account the magnitude of the results and the size and validity of the studies, together with any moderating factors.

Peer review
Once completed the manuscript was submitted for peer review to the following experts.

- Professor Bernard Messing, Paris
- Dr Karin Ladefoged, Copenhagen
- Professsor Anne Ferguson/Dr Subrata Ghosh, Edinburgh
- Dr Andre Van Gossum, Brussels
- Professor John Lennard-Jones, London
- Mr Kenneth Fearon, Edinburgh

Chapter 4
Results

Located studies

A total of 256 studies were located using the methods described. The number of additional articles located by each method is shown.

Electronic databases

The numbers of additional articles found by searching relevant electronic databases are shown in *Table 1*.

TABLE 1 *Number of additional studies located in each database compared to those in MEDLINE*

Database	No of studies found
MEDLINE (*Index Medicus* on-line)	59
EMBASE (*Excerpta Medica* on-line)	13
UNCOVER	10
CINAHL	0
CAREDATA	0
Food Science and Technology Abstracts	0
NTIS	0
PASCAL	0
PSYCHLIT	2
Economic Literature Index	0

Hand searching of relevant journals

The numbers of additional references found by searching appropriate journals are shown in *Table 2*.

Conference proceedings

We found 58 abstracts that were relevant to the review. Attempts to locate completed studies from the authors were successful in eight cases. Abstracts for which no full report was available were not included in the review.

Personal literature collections

A search of personal literature collections yielded 15 additional papers.

TABLE 2 *Number of studies located by hand searching relevant journals*

Journal	No of studies found
American Journal of Clinical Nutrition	2
Annals of Nutrition and Metabolism	1
Clinical Nutrition	15
Clinical Gastroenterology	4
Journal of Paediatric Gastroenterology and Nutrition	4
Journal of Parenteral and Enteral Nutrition	28
Nutrition	7
Nutrition and Cancer	2
Nutrition and Health	0
Nutrition Reviews	0

Letters to experts

Replies were received from seven of the 24 centres contacted. The replies included details of a total of 25 papers, of which eight had not been previously identified. We did not receive any data relating to work in progress.

Visits to major meetings

The amount of relevant on-going work was disappointing. Experts from centres were contacted and asked to supply further data if they had not already done so. No additional studies were located.

Scanning of reference lists

Scanning the reference lists of these studies located a further 56 articles. A further scan of the studies located by this method identified an additional 19 studies and a third scan found three more papers.

Science Citation Index

A search of the Science Citation Index for the following names was carried out; Scribner, Jeejeebhoy, Shils, Wilmore, Rhoads, Vars, Ladefoged, Irving, Messing and Howard. We did not locate any new studies.

Issues of study validity

Inclusions and exclusions

A total of 256 studies were located and retrieved, not including abstracts, letters, editorials, case reports and review papers.

There was one disagreement between reviewers in the excluded sample, which resulted in the inclusion of that study. No further discrepancies were found. In all, 191 studies did not satisfy the inclusion criteria. The main reason for their exclusion is given in the reference section. Many of the studies retrieved were only relevant to hospital TPN and included peri-operative feeding, chemotherapy and short-term feeding. Some hospital-based studies were relevant to HPN, for example, studies looking at care of central lines, but most were not relevant. Another common reason for exclusion was the age of the study. HPN use in the UK was rare prior to 1980 but was used in the USA during the 1970s. During early HPN use, complication rates were relatively high and were probably related to the type of catheters that were available, the quality of the intravenous solutions available, and the protocols that were followed. Elimination of early studies was important, to prevent learning curve bias skewing the results of more recent HPN use. The studies from the 1970s tended to be case series and included only small numbers of patients. No well-designed studies with large numbers of patients were excluded as a result of the age exclusion criteria being applied.

The majority of studies found were case series and the centres producing case series tended to report experience as their HPN population grew. This led to much data duplication; many studies included the same patients as in previous reports plus the new cases. For these studies only, the latest and most comprehensive report was included.

Some studies were relevant to HPN patients but were not specifically related to the questions we had set. These studies tended to relate to the biochemical details of total parenteral nutrition (TPN) and their consequences.

Review papers were excluded when they contained no original empirical data, but they were useful sources of citations. The unreliable nature of data contained in abstracts meant that they were not used for data extraction; letters were excluded for the same reason.

Out of 256 studies, 65 fulfilled the inclusion criteria and were used to provide evidence to answer the research questions. These studies, which are listed in the references, were subjected to data extraction, and the results of this are outlined below.

Design of studies included in the review

The types of study design identified in the studies included in the review are shown below. Only one randomised trial was identified. The economic appraisals of HPN were limited to a cost–utility analysis from Canada (Detsky, 1986) and a cost-utility analysis from the UK (Richards, 1996). In addition, there were several simple cost analyses. There were 54 case series. Only six studies had any form of comparative data.

Section 1 (Which patients have received HPN?)	
Case series	15
Section 2 (Patient experience?)	
Case series	49
Quality-of-life questionnaires	7
Section 3a (Organisation)	
Case series	1
Section 3b (Comparative data)	
Randomised controlled trial	1
Prospective controlled	1
Comparative studies	4
Section 4 (Economic analysis)	
Cost–utility analysis	2
Simple cost analysis	5

The total number is greater than 64 because some studies were relevant to more than one section.

Results for Section 1 Which patients have received HPN?

Fifteen studies were relevant to this section. Seven were from the USA and eight were from Europe (see *Table 3*). All the studies were longitudinal case series and only one was prospective. Patients were often included more than once in the results of a study, as several sources of data were used which overlapped. The sample sizes ranged from nine to more than 9000. It was often impossible to say what proportion of the total HPN population had been sampled by these studies, and there were no studies that randomly sampled a HPN population. Few studies reported how many patients were lost to follow-up.

It can be seen from *Tables 4a* and *4b* that there is a trend towards the use of HPN in older age groups and the very young. The increasing age of HPN

TABLE 3 *Summary of studies selected for Section 1: Which patients have received HPN?*

Study (Country)	Date	Study design	Patients included in more than one study	Sample size	Proportion of HPN population sampled (%)	Sampling frame	Random sampling	% lost to follow-up
Bisset, 1992 (UK)	1987–92	Case series; longitudinal; retrospective	possible	10		none	no	0
DePotter, 1992 (France)	1981–90	Case series; longitudinal; retrospective	possible	156	?	none	no	? 0
Goutebel, 1987 (France)	1979–85	Case series; longitudinal; retrospective	yes	85	?	none	no	? 0
Griffith, 1984 (UK)	1978–83	Case series; longitudinal; retrospective	possible	9	100	none	no	? 0
Howard, 1993 (USA)	1985–90	Case series; longitudinal; retrospective	yes	2275	10 (E)	patient registry	no	?
Howard, 1991 (USA)	1984–87	Case series; longitudinal; retrospective	yes	1594	7.8 (E)	none	no	7
Howard, 1986 (USA)	1983–85	Case series; longitudinal; retrospective	yes	2556	?	five separate sources	no	?
Howard, 1995 (USA)	1985–92	Case series; longitudinal; retrospective	yes	9288	5	two separate sources	no	?
Messing, 1989 (Europe)	1974–85	Case series; longitudinal; retrospective	yes	194	?	27 centres	no	?
Messing,1995 (France/Belgium)	1980–89	Case series; longitudinal; retrospective	yes	217	?	nine centres	no	0
O'Hanrahan, 1992 (UK)	1977–91	Case series; longitudinal; retrospective	yes	400	?	none	no	?
Ralston, 1984 (USA)	1977–82	Case series; longitudinal; retrospective	possible	14	?	one centre/ < 2 months of age	no	35
Schmitt-Sommerfeld, 1990 (USA)	1980–85	Case series; longitudinal; retrospective	possible	35	?	none	no	? 0
Van Gossum, 1995 (Europe)	1993–94	Case series; longitudinal; prospective	yes	496	80 (E)	95 centres	no	?
Vargas, 1987 (USA)	1976–86	Case series; longitudinal; retrospective	possible	102	?	none	no	? 0

?, Not known or not given; E, estimated.

TABLE 4a *Section 1. Results – Age and sex of adult patients commenced on HPN*

Study	Mean age (range)	% in an age group	Mean age by diagnostic group	Male:Female	Trends
Goutebel, 1987	Median 50 (18–79)				
Griffith, 1984	32.8 (22–45)			5:4	
Howard, 1991			Crohn's 36 MVD 57 AIDS 29	More than 80% of those with radiation enteritis were women	
Howard, 1993			Crohn's 35 Radiation enteritis 57 Cancer 43	3:5 1:2 9:10	
Howard, 1995			Crohn's 36 MVD 49 Cancer 44 AIDS 33		
Messing, 1989	44			1.08	
Messing, 1995	46.5	age < 40 40–60 60+ % 40 37 23			
O'Hanrahan, 1992		age 0–30 31–50 50+ % 31 54.5 14.5 % 44 38.5 17.5			Slight increases at the extremes for the second 200 patients
Van Gossum, 1995		age 16–40 41–60 61+ % 36 41 23			

TABLE 4b *Section 1. Results – Age and sex of paediatric HPN patients*

Study	0–24 months n (%)	2–10 years	11–18 years	Male:Female	Trends
DePotter, 1992	51	25	24	90:66	
Schmitt-Sommerfeld, 1990	17 (1–12 months)	20 (1–12 years)	63 (12–23 years)		
Vargas, 1987	59 (0–36 months)	12	29		

patients is almost certainly explained by its increasing use in malignant disease. The use of HPN in Crohn's disease is associated with younger patients and it is used more commonly in females, reflecting the prevalence of Crohn's disease in the UK. The use of HPN in radiation enteritis is naturally associated with older female patients. As the incidence of atherosclerosis increases with age, it is apparent that patients with mesenteric vascular disease (MVD) who require HPN are in the older age range.

In paediatric practice the main use of HPN is in the 0–24-month age group, with an excess of males. The diagnostic subgroups in paediatric practice are varied, but Crohn's disease remains common in older children. The small numbers of patients in the studies meant that no firm conclusions could be made regarding the use of HPN in children, particularly in the UK.

In the UK and **some** European countries, the largest diagnostic group comprises patients with Crohn's disease; the use of HPN for patients with a cancer diagnosis is exceptional (see *Tables 5* and *6*). Anecdotal evidence suggests that many UK cancer patients receive enteral rather than parenteral nutritional support. In the USA and Italy,

TABLE 5 *Patients recruited to adult HPN programmes by country and diagnostic group*

Country (Study)	Sample size	Crohn's disease (%)	MVD (%)	Malignancy (%)	Radiation enteritis (%)	Motility disorder (%)	AIDS (%)	Others (%)	Trends
USA (Howard, 1986)	465 153 224 1351 268 89	NR 20 OF 40 CR 20 CI 26 CII 12 CIII 9	10 9 7 0 0 1	44 3 25 28 41 48		5 7 14 2 3 4		21 41 34 44 44 36	Increased use in cancer patients. In 1978, 17% on HPN had cancer. This increased to 44% in 1983
USA (Howard, 1991)	1594	1984 25 1985 19 1986 14 1987 12	14 14 7 8	16 26 30 39	11 6 4 4	13 9 8 8	1 2 3 2		Increased use in cancer versus benign diagnostic groups
USA (Howard, 1993)	1672	1985 17 1987 11 1989 7		35 43 46	5 4 2				90% of programme growth accounted for by new patients with malignant disease
USA (Howard, 1995)	9288	11	6	41	3	5	6	22	Use of HPN doubled between 1989 and 1992
France/ Belgium (Messing, 1995)	217	25	27	20	22		11		
France (Van Gossum, 1995)	133	15.7	16.5	21	17.2		6	23	
Italy (Pironi, 1993)	135	2	9.7	67	5.2		0.7	14	
Scandinavia (Van Gossum, 1995)	55	18	6	56	0		0	18.5	
Germany (Van Gossum, 1995)	38	10.5	2.6	81	0		0	5	
Belgium (Van Gossum, 1995)	25	4	8	45	12.5		25	4	
UK (Van Gossum, 1995)	56	44.5	10.5	8.9	3.5		3.5	28	Increased use in cancer and AIDS
UK (O'Hanrahan, 1992)	400	45.5	12	5	5.5		5	24 (96 patients)	5-fold programme growth from 1980 to 1990

NR, National Registry; OF; Oley Foundation; CR, Commercial Registry; CI, CII and CIII are three commercial suppliers.

TABLE 6 *Patients recruited to paediatric HPN programmes by diagnosis*

Study	Country	Crohn's disease (%)	Chronic pseudo obstruction (%)	Intractable diarrhoea (%)	Immune deficiency (%)	Short bowel syndrome† (%)	Malignancy (%)	Others (%)	Trends
DePotter, 1992	France	15	19	5	8	41		12	
Schmitt-Sommerfeld, 1990	USA	57	0.3			23		17	
Vargas, 1987	USA	22	10	15			10	44	

†, *Not elsewhere classified.*

the main diagnostic group comprises patients with malignant disease, although there are still many HPN patients with Crohn's disease. Italy has the highest percentage of HPN patients with a cancer diagnosis. Anecdotal evidence suggests this is related to the uncommon use of enteral nutritional support for these patients (there is a low consumption of enteral nutrition products in Italy compared with the rates of consumption in other similar European countries).

The trends indicated by the studies show that there is an increasing use of HPN in cancer patients and that this increase is responsible for the majority of programme growth (90% in the USA) in those countries where the use of HPN for malignant disease is high. In the UK, the number of HPN patients with malignant disease is small but has increased from 5% in 1992 to 8.9% in 1994. The wasting associated with AIDS is also becoming an increasingly common reason for HPN therapy and, in a recent paper from the USA (Howard, 1995), 6% of more than 9000 patients had this diagnosis. In the UK, AIDS was the reason for HPN being used in two of 53 patients registered during 1993.

Results for Section 2 Patient experience on HPN

A total of 56 studies were relevant to Section 2 and these are summarised in *Table 7*. Of these, 37 studies were from the USA and the rest were from Europe. In 41 studies only adults were included, seven looked at a mixture of adults and children, and seven looked at children only; one study did not give ages. The sample sizes were similar to those for Section 1. Retrospective case series predominated, the only other study design being a quality-of-life assessment. As with Section 1 studies, it was unusual to see the numbers lost to follow-up being reported. Complications were reported in 43 studies; 12 studies examined the quality of life of HPN patients; ten studies reported survival; 26 studies recorded the duration of HPN, and 28 studies reported the reasons for discontinuing HPN.

One of the main complications of HPN is sepsis (see *Table 8* and *Figure 1*)and the most common focus for sepsis is the central venous catheter. Catheter sepsis is to some extent related to how well patients are trained in HPN techniques and, in turn, patient training is related to the skill and experience of the nutrition nurse. The larger series show a narrow band of episodes per catheter year (0.38–0.50). Smaller series seem to have fewer episodes of catheter sepsis; however, the confidence intervals are much wider. A weighted average of the rate of catheter sepsis was 0.34 (95% CI, 0.32, 0.37) episodes per catheter year. The number of patients experiencing an episode of sepsis per catheter year indicates that this complication occurs several times in a minority of patients, and that many patients remain sepsis free. Two studies have a much higher rate of catheter sepsis; these rates are probably explained by one patient group being immunosuppressed and another group including an excess of paediatric patients.

The weighted average rate for catheter occlusion was 0.071 (95% CI, 0.059, 0.083) episodes per catheter year (see *Figure 2*). Catheter occlusion might be caused by faulty catheter care or by an inappropriate infusion regimen. Central lines which can not be cleared by thrombolysis require removal and replacement.

The overall rate for central vein thrombosis was 0.027 (95% CI, 0.02, 0.034) episodes per catheter year (see *Figure 3*). Thrombosis is associated with difficulties with venous access in the future, and may also be related to an inappropriate infusion regimen or faulty catheter placement.

TABLE 7 *Summary of studies relevant to Section 2: the experience of patients on HPN*

Study: Country (Time frame)	Sample size (A/P)	Inception cohort	% of HPN pop inc.	Study design	% lost to follow-up	Compli-cations reported	Quality of life measured	Survival measured (months)	Duration of HPN use measured (months)	Reported reason for stopping HPN
August, 1991: USA (1980–89)	17 (A)	yes	26	Case series; retrospective	0	no	no	yes	yes	yes
Beers, 1990: USA (1975–88)	107 (A)	yes	100	Case series; retrospective	0	yes	no	no	yes	no
Bisset, 1992: UK (1987–92)	10 (P)	yes	100	Case series; retrospective	0	yes	no	no	no	yes
Bowyer, 1985: USA (1975–82)	9 (A)	yes	15	Case series; retrospective	?	yes	no	no	yes	no
Buchman, 1993: USA (?)	41 (A)	yes	?	Case series; retrospective	?	yes	no	no	no	no
Buchman, 1993: USA (15 years)	33 (A)	yes	?	Case series; retrospective	0	yes	no	no	no	no
Buchman, 1994(b): USA (1973–91)	527 (A/P)	yes	?	Case series; retrospective	?	yes	no	no	yes	no
Buchman, 1994(a): USA (1973–91)	527 (A/P)	yes	?	Case series; retrospective	2% of inf.	yes	no	no	yes	no
Burnes, 1992: USA (1986–89)	63 (A)	yes	?	Case series; retrospective	?	yes	no	no	no	yes
Byrne, 1979: USA (?)	106 (A/P)	yes	?	Case series; retrospective	?	yes	no	no	no	yes
Carlson, 1996: UK (1992)	73 (A)	no	93	Q-o-L interviews; retrospective	0	no	p	no	no	no
DePotter, 1992: France (1981–90)	156 (P)	yes	?	Case series; retrospective	?	yes	no	no	yes	yes
Detsky, 1986: Canada (1970–82)	37 (A)	yes	51	Q-o-L interviews; prospective	49	no	p	no	no	no
Dollery, 1994: UK (1983–93)	34 (P)	yes	?	Case series; retrospective	?	yes	no	yes	no	no
Duclaux, 1993: France (?)	44 (P)	yes	?	Case series; retrospective	0	no	p	no	no	no
Dudrick, 1984: USA (1974–83)	133 (A/P)	yes	?	Case series; retrospective	?	yes	no	no	yes	no
Foldes, 1990: USA (19 months)	10 (A)	yes	?	Case series; retrospective	100	yes	no	no	no	no
Galandiuk, 1990: USA (1976–87)	39 (A)	yes	21	Case series; retrospective	?	yes	p	no	yes	yes
Gouttebel, 1987: France (1979–85)	85 (A)	yes	?	Case series; retrospective	?	yes	no	no	yes	yes

continued

?, Not stated or not known; Q-o-L, quality of life; A, adult; P, paediatric; p, patient centred assessment of Q-o-L; f, functional assessment; E, estimated.

TABLE 7 contd *Summary of studies relevant to Section 2: the experience of patients on HPN*

Study: Country (Time frame)	Sample size (A/P)	Inception cohort	% of HPN pop inc.	Study design	% lost to follow-up	Compli-cations reported	Quality of life measured	Survival measured (months)	Duration of HPN use measured (months)	Reported reason for stopping HPN
Grabowski, 1989: USA (?)	4 (A)	yes	?	Case series; retrospective	0	no	no	yes	yes	yes
Griffith, 1984: UK (1978–83)	9 (A)	yes	100	Case series; retrospective	0	yes	no	no	yes	yes
Herfindal, 1992: USA (1980–87)	56 (A/P)	yes	90	Case series; retrospective	10	yes	no	no	yes	no
Herfindal, 1989: USA (?)	347 (A)	no	30	Q-o-L interviews; prospective	?	no	p	no	no	no
Howard, 1993: USA (1985–90)	2275 (A)	mix	10 (E)	Case series; retrospective	?	yes	no	yes	no	yes
Howard, 1991: USA (1984–87)	2916 (A)	mix	7.9 (E)	Case series; retrospective	7	yes	no	yes	no	yes
Howard, 1986: USA (1983–85)	2550 (A)	mix	?	Case series; retrospective	?	yes	no	yes	yes	yes
Howard *et al,* 1995: USA (1985–92)	9288 (A)	mix	5 (E)	Case series; retrospective	?	yes	no	yes	no	yes
Hurley, 1990: USA (?)	23 (A)	yes	?	Case series; retrospective	?	yes	no	no	no	no
Johnston, 1994: UK (1980–93)	34 (A)	yes	?	Case series; retrospective	0	yes	no	no	no	no
Johnston, 1993: Scotland (1980–92)	30 (A/P)	yes	100	Case series; retrospective	0	yes	no	no	yes	yes
King, 1993: USA (1981–90)	61 (A)	yes	?	Case series; retrospective	?	yes	p	yes	yes	yes
Ladefoged, 1981: Denmark (1978–79)	13 (A)	yes	?	Q-o-L interviews; prospective	0	no	p	no	no	no
Manji, 1989: USA (1989)	5 (A)	yes	45	Case series; retrospective	0	yes	no	no	yes	no
Mercier, 1995: Canada (1992–95)	16 (?)	yes	?	Case series; retrospective	?	no	no	no	no	yes
Messing, 1995: France/Belgium (1980–89)	217 (A)	yes	?	Case series; retrospective	0	no	no	yes	yes	yes
Messing, 1989: Europe (1974–85)	194 (A)	yes	?	Case series; retrospective	?	yes	f	no	yes	yes
Miller 1979: USA (1970–78)	10 (A)	yes	?	Case series; retrospective	0	no	no	no	yes	yes

continued

?, Not stated or not known; Q-o-L, quality of life; A, adult; P, paediatric; p, patient centred assessment of Q-o-L; f, functional assessment; E, estimated.

TABLE 7 contd *Summary of studies relevant to Section 2: the experience of patients on HPN*

Study: Country (Time frame)	Sample size (A/P)	Inception cohort	% of HPN pop inc.	Study design	% lost to follow-up	Compli-cations reported	Quality of life measured	Survival measured (months)	Duration of HPN use measured (months)	Reported reason for stopping HPN
Mukau, 1992: USA (1988–90)	50 (A)	yes	?	Case series; retrospective	?	yes	no	no	no	no
Nightingale, 1995: UK (1984–92)	17 (A)	no	100	Case series; retrospective	0	yes	no	no	no	no
O'Hanrahan, 1992: UK (1977–91)	400 (A/P)	yes	?	Case series; retrospective	?	yes	f	no	yes	yes
Perl, 1981: USA (1 year)	10 (A)	no	45.5	Case series; prospective	0	yes	no	no	no	no
Pironi, 1993: Italy (1986–93)	18 (A)	yes	?	Case series; retrospective	0	yes	f	no	yes	yes
Ralston, 1984: USA (1977–82)	9 (P)	yes	?	Case series; retrospective	33	yes	no	no	no	yes
Richards, 1995: UK (1995)	51 (A)	no	80	Q-o-L interviews; prospective	0	no	p	no	no	no
Robb, 1983: USA (?)	42 (A)	yes	86	Q-o-L interviews; prospective	?	yes	yes	no	yes	no
Roslyn, 1983: USA (1976–80)	128 (A)	yes	100	Case series; retrospective	?	yes	no	no	no	no
Schmidt-Sommerfeld, 1990: USA (1980–85)	35 (P)	yes	?	Case series retrospective	?	yes	no	no	yes	yes
Shike, 1980: USA (?)	16 (A)	yes	?	Case series; prospective	0	yes	no	no	no	no
Shike, 1986: USA (?)	12 (A)	yes	57	Case series; prospective	0	yes	no	no	no	no
Singer, 1991: USA (1987–88)	22 (A)	yes	?	Case series; retrospective	9	yes	no	no	yes	yes
Smith, 1993: USA (?)	116 (A)	no	?	Q-o-L interviews; prospective	?	no	p	no	no	no
Staun USA (?)	15 (A)	yes	?	Case series; prospective	?	yes	no	no	no	no
Steiger, 1983: USA (1976–81)	39 (A)	yes	78	Case series; retrospective	?	yes	no	no	yes	yes
Van Gossum, 1995: Europe (1993–94)	211 (A)	yes	80 (E)	Case series; prospective	?	no	no	yes	no	yes
Vargas, 1987: USA (1976–86)	102 (P)	yes	?	Case series; retrospective	?	yes	no	no	yes	yes
Weiss, 1982: USA (1978–80)	9 (A)	yes	?	Case series; retrospective	0	yes	no	no	yes	yes

?, Not stated or not known; Q-o-L, quality of life; A, adult; P, paediatric; p, patient centred assessment of Q-o-L; f, functional assessment; E, estimated.

TABLE 8 *Complications of HPN (episodes per catheter year, unless indicated)*

Study	Catheter sepsis (95% CI)	Catheter sepsis (patients per catheter year) (95% CI)	Catheter occlusion (95% CI)	Central vein thrombosis (95% CI)	Liver/ biliary problems (95% CI)	Metabolic bone disease (95% CI)	Other
Beers, 1990	–		–	0.04 (0.02, 0.07)	–	–	–
Bisset, 1992	–		–	–	–	–	Sepsis 0.73
Bowyer, 1985	–		–	–	15% (7%, 27%) liver problems. 3% (0.4%,12%) deaths	–	–
Buchman, 1994(a)	–		0.07 (0.06, 0.09)	0.02 (0.01, 0.03)	–	–	–
Buchman, 1994(b)	0.23 (0.2, 0.27) not possible to calculate rates for children	0.23 (0.2, 0.26)	–	–	–	–	–
Buchman, 1993							Low plasma-free choline levels are prevalent, associated with elevated serum aminotransferases
Buchman, 1993							Fall in renal function of 3.5 ± 6.3% per year
Burnes, 1992	0.27 (0.2, 0.35)		–	–	–	–	–
DePotter, 1992	0.40 (0.33, 0.49)	0.23	0.04 (0.02, 0.07)	–	0.03 (0.01, 0.05)	–	–
Dollery, 1994	–		–	16 episodes of major thrombosis in 12 of 34 patients	–	–	–
Dudrick, 1984	0.39 (0.26, 0.54)	0.15 (0.08, 0.26)	–	–	–	–	–
Foldes, 1990	–		–	–	–	90% (56%, 99%)	–
Galandiuk, 1990	0.27 (0.19, 0.38)		–	–	–	–	–
Gouttebel, 1987	0.70 (0.49, 0.97)	0.42 (0.26, 0.4)	–	–	–	–	–

continued

TABLE 8 contd *Complications of HPN (episodes per catheter year, unless indicated)*

Study	Catheter sepsis (95% CI)	Catheter sepsis (patients per catheter year) (95% CI)	Catheter occlusion (95% CI)	Central vein thrombosis (95% CI)	Liver/ biliary problems (95% CI)	Metabolic bone disease (95% CI)	Other
Herfindal, 1992	0.46 (0.3, 0.7)	0.14 (0.06, 0.28)	0.22 (0.12, 0.39)	–	0.42 (0.27, 0.63)	0.05 (0.01, 0.15)	Metabolic complications 0.61
Howard, 1993			–	–	–	–	Total complication rate is higher for those under 18 years
Howard, 1986	0.37 (0.33, 0.42)		–	–	–	0.013 (0.005, 0.025)	–
Hurley, 1990	0.30 (0.17, 0.49)		0.20 (0.06, 0.47)	–	–	–	Total complications Cancer 2.22 (1.4, 3.4) Benign 0.89 (0.64, 1.2) $p < 0.01$
Johnston, 1993	0.16 (0.05, 0.47)		–	0.28 (0.15, 0.47)	–	–	–
King, 1993	0.54 (0.22, 1.11)	?	–	–	–	–	–
Manji, 1989	–		–	–	Symptomatic gallstones in 100%	–	–
Messing, 1989	0.38 (0.30, 0.48)	?	0.18	0.07	–	–	–
Mukau, 1992	0.2 (0.1, 0.35)	?	–	0.07 (0.02, 0.17)	–	–	–
Nightingale, 1995	24 fungal infections. Total no of lines not given		–	–	–	–	Four developed eye infections. Two had recurrent infection
O'Hanrahan, 1992	0.47 (0.38, 0.58)	?	0.44 (0.36, 0.55)	0.06 (0.03, 0.11)	–	–	Metabolic complications 0.12 (0.08, 0.18)
Perl, 1981	–		–	–	–	–	Depression 80% (44, 98)
Pironi, 1993	0.12 (0.03, 0.3)		0.03 (0, 0.16)	0.09 (0.02, 0.26)	0.15 (0.05, 0.34)	–	–
Robb, 1983	0.42 (0.25, 0.68)		0.1 (0.03, 0.24)	–	–	–	–
Roslyn, 1983	–		–	–	Symptomatic gallstones in 23% (15%, 32%)	–	–

continued

?, Data in the study not sufficient for calculation of rates; A, AIDS; C, cancer; H, HPN.

TABLE 8 contd *Complications of HPN (episodes per catheter year, unless indicated)*

Study	Catheter sepsis (95% CI)	Catheter sepsis (patients per catheter year) (95% CI)	Catheter occlusion (95% CI)	Central vein thrombosis (95% CI)	Liver/ biliary problems (95% CI)	Metabolic bone disease (95% CI)	Other
Schmidt-Sommerfeld, 1990	0.71 (0.5, 0.97)		0.29 (0.17, 0.47)	0.07 (0.02, 0.19)	–	–	–
Shike, 1986	–		–	–	–	67% (35%, 90%)	–
Shike, 1980	–		–	–	–	75% (48%, 93%)	–
Singer, 1991	A 0.43 (0.05, 1.55) C 0.2 (0.07, 1.43) H 0.1 (0.04, 0.22)		A 0.21 (0.05, 1.2) C 0.03 (0, 0.18) H 0.06 (0.02, 0.16)	–	–	–	Metabolic disturbance A 0.43 (0.05, 1.55) C 0.49 (0.28, 0.81) H 0.17 (0.08, 0.3)
Staun	–		–	–	–	4% decrease in bone mineral content per year	–
Steiger, 1983	–		–	–	–	–	% of hospitalised days Crohn's 24% MVD 58% Radiation enteritis 13%
Vargas, 1987	0.37 (0.29, 0.46)	0.20 (0.15, 0.28)	–	–	Any 0.06 (0.03, 0.1) Severe 0.024 (0.008, 0.057)	–	–
Weiss, 1982	0.2 (0.01, 1.11)		0.2 (0.01, 1.11)	–	–	–	–

?, Data in the study not sufficient for calculation of rates; A, AIDS; C, cancer; H, HPN.

The incidence of liver abnormalities was difficult to assess from the evidence located. Severe problems were rare (0.025 episodes/catheter year: Vargas, 1987) but minor abnormalities are probably very common. To some extent the incidence of liver abnormalities will vary according to how thoroughly the patient is investigated.

Metabolic bone disease can cause severe, debilitating illness but incidence rates are difficult to determine. Metabolic bone disease in mild forms is probably very common if it is looked for carefully.

Metabolic complications such as fluid and electrolyte imbalance are also probably very common. Often these complications are sorted out on an outpatient basis and, therefore, mild derangements are probably not recorded. The studies we located rarely gave details of more severe abnormalities. When metabolic problems were reported they were fairly common (range, 0.12–0.61 episodes/catheter year).

There were many other rare complications of HPN, which were usually reported as interesting cases. These were wide-ranging and often related to catheter sepsis, such as subacute bacterial endocarditis, septic thromboembolism, or candida endopthalmitis. Depression has been commonly reported, and is one of a range of psychiatric illnesses that have been noted in HPN patients. The severity of the underlying condition and the dependence on a machine are amongst the commonest underlying causes of depression.

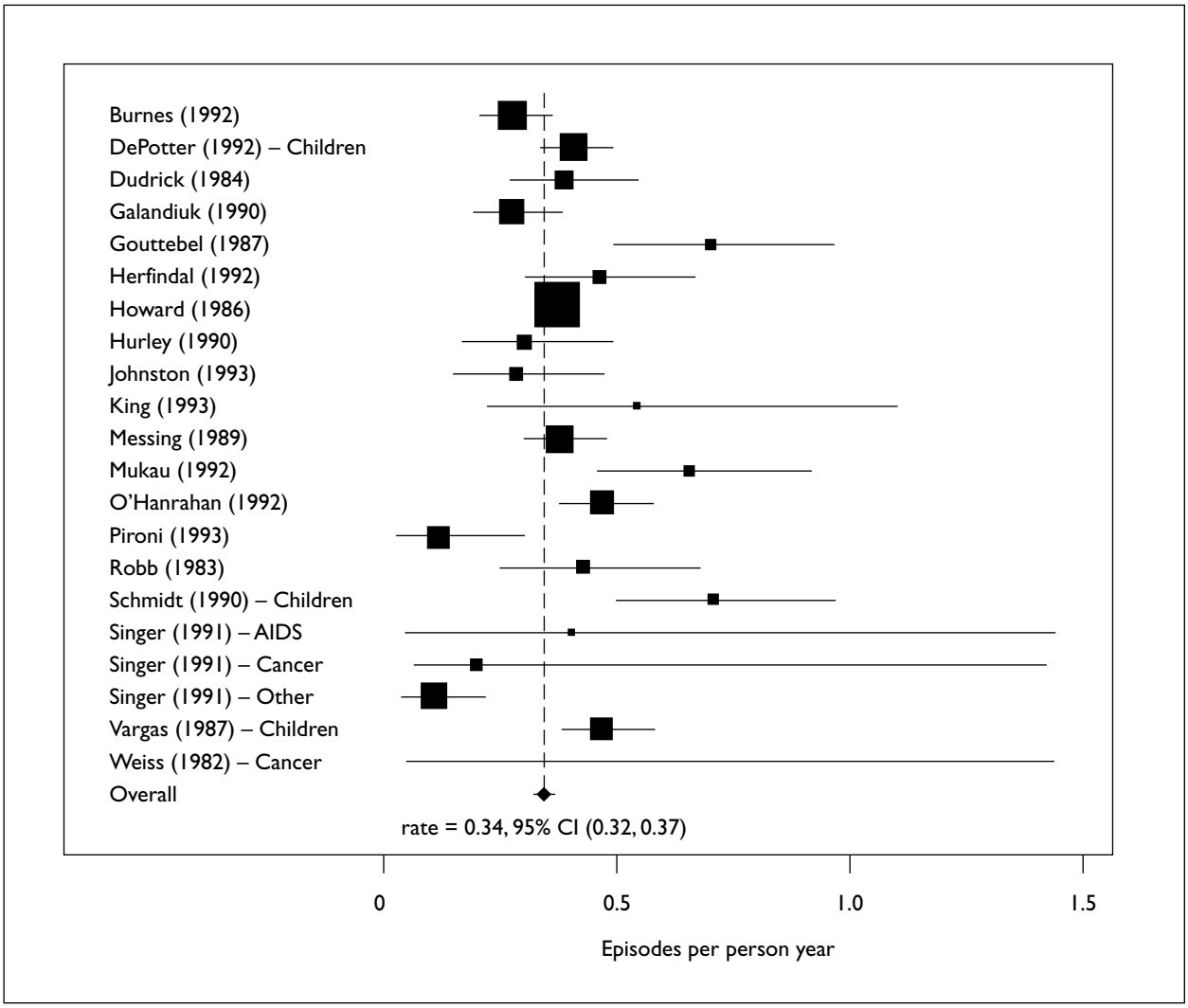


FIGURE 1 *Incidence of catheter sepsis*

Renal function is thought to deteriorate by approximately 5% per year. There is usually a multifac-torial pathophysiology behind the deterioration, hence the need to avoid dehydration and nephrotoxic drugs and to monitor renal function on a regular basis.

Only one study (Hurley, 1990) described the differences in total complication rates between a group of patients with malignant disease and a benign group. There were an excess of complications in the malignant group (2.2 versus 0.9 events/catheter year).

Quality of life (see *Table 9*) was measured using validated instruments in five studies. Index scores on a 0–1 scale (0 = death, 1 = best possible) varied from 0.51 to 0.73. Detsky (1995) recently admitted that the score he produced in 1986 (0.73) was probably not correct because the methods he used to measure quality of life overestimated the true value, which was somewhat less. The best quality of life was seen with young patients, longer duration of treatment, high self-esteem, a good relationship with a partner, wealth and employment. The worst quality of life was experienced by patients who were older, addicted to narcotics, poor, single, unemployed, had a short duration of treatment and few family coping skills.

Functional assessments have been used to assess outcomes in several series and they are estimated by the physician. The best functional outcomes are seen in younger patients with Crohn's disease. The worst functional outcomes are seen in older patients with an underlying malignancy, pseudo-obstruction or Crohn's disease. Only one study (Galandiuk, 1990) has examined quality of life before and after HPN was started. This study, which was carried out only on patients with Crohn's disease, showed that quality of life improved on HPN.

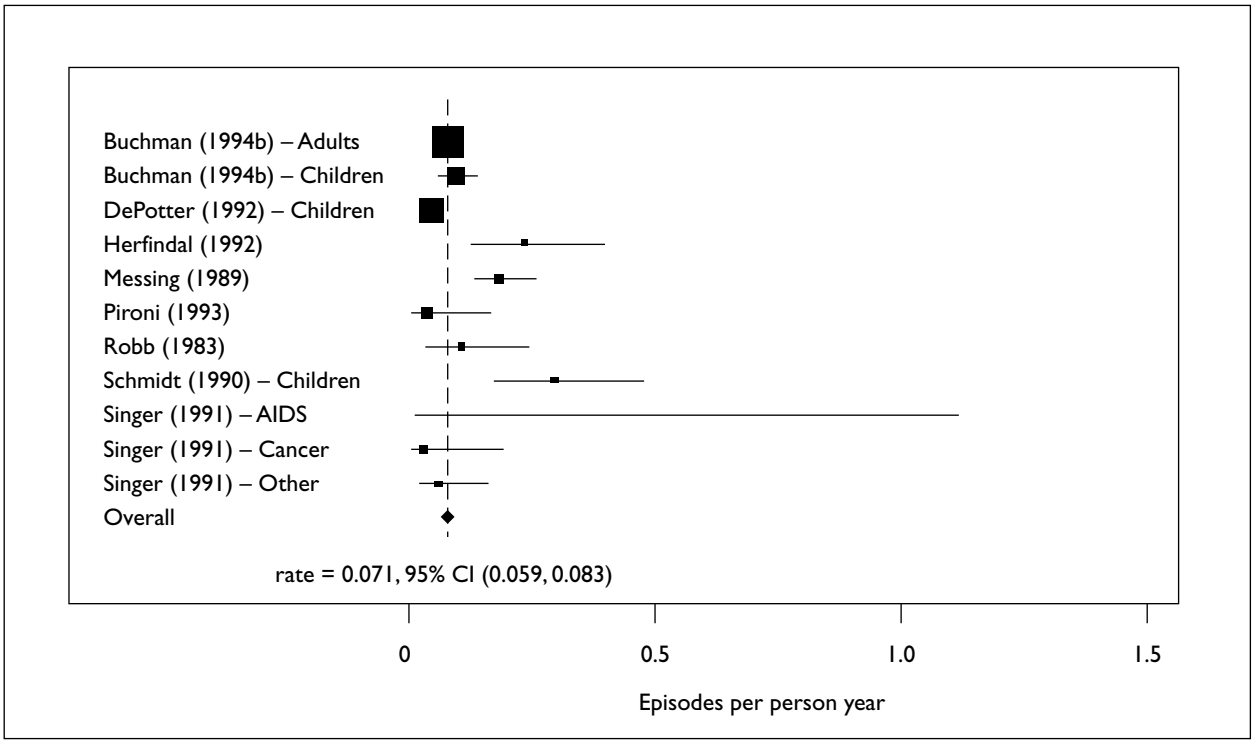


FIGURE 2 *Incidence of catheter occlusions*

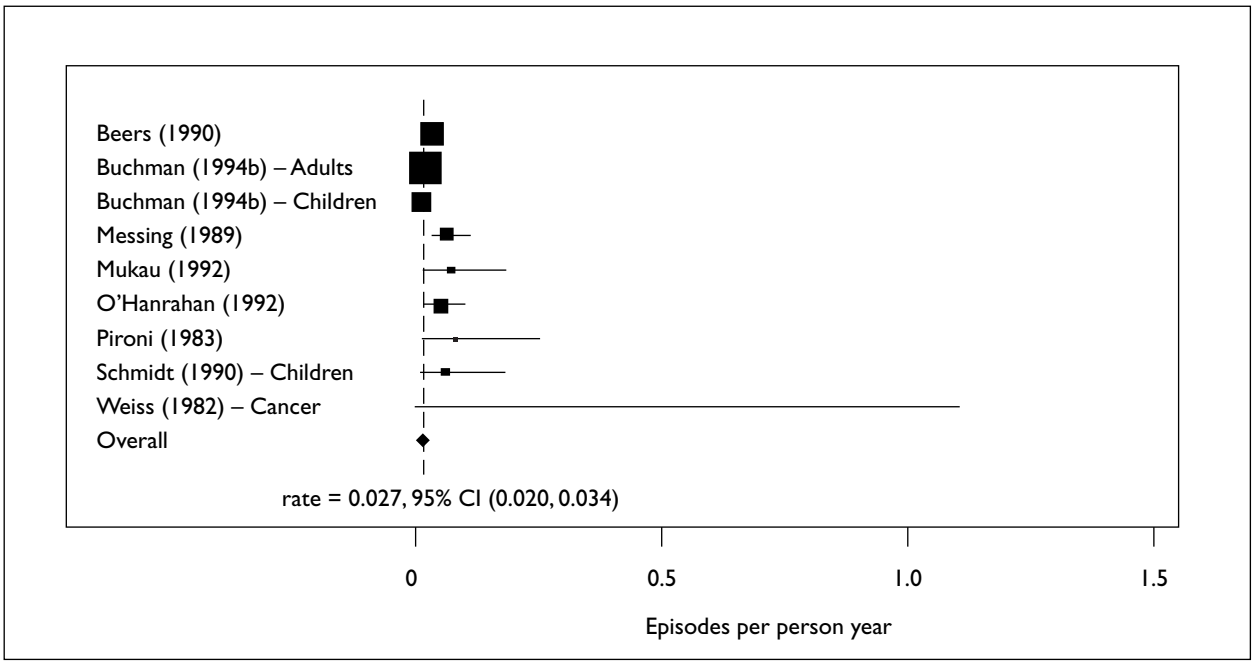


FIGURE 3 *Incidence of central vein thrombosis*

Survival on HPN *(Table 10)* is best for patients with benign disease. Of the subgroups, Crohn's disease seems to have the best survival rate, with several series reporting a better than 90% 1-year survival. The reported 1-year survival for HPN patients with malignant disease varies from 15% to 30%. Carcinoma of the ovary seems to have a particularly poor outcome, with one study measuring the mean survival as only 30 days.

Patients with AIDS have a particularly poor outcome, with only 7–12% surviving 1 year. This statement on survival obviously reflects the natural history of the underlying disease and is not meant to reflect the effectiveness of HPN therapy. It does serve to illustrate that as patients with malignant disease and AIDS usually only survive for short periods, patient selection for HPN is very important.

TABLE 9 *Quality of life on HPN*

Study	Whose values?	Instrument used	Profile or index	Index scores	Best Q-o-L or outcome	Worst Q-o-L or outcome	Comments
Carlson, 1995	Patient	Non-validated questionnaire	Index	0.64 (0–1 scale**)	–	–	Q-o-L independent of variables tested. Younger patients keen on intestinal transplantation.
Detsky, 1986	Patient	Category scaling, time trade-off + one other	Index	0.73 (0–1 scale**)	Scores improve with time and peak at 4–5 years	Lowest scores seen in the first year of HPN	Scores were measured for 37 and estimated for 36. No subgroup analysis was performed.
Duclaux, 1993	Doctor	Non-validated simple questionnaire	Profile				Q-o-L much improved at home. Development and psychological well-being much improved.
Galandiuk, 1990	Patient plus doctor	Q-o-L score, social activity score, psycho-logical score	Index	Pre-HPN, 7.1 On HPN, 5.3#	–	–	Index scores were better on HPN; pre-HPN Q-o-L was significantly worse ($p < 0.01$). All patients in this study had Crohn's disease.
Herfindal, 1989	Patient	Multiple-validated instruments	Profile		Long duration (> 6 months)	Duration < 6 months	HPN patients had lower (worse) scores than renal transplant recipients and normal US population.
King, 1993	Doctor	Q-o-L assessed by retrospective case note review	Profile		–	–	All patients with gynaecological malignancy. Improvements noted in pain, vomiting, fatigue, morale and social inter-actions ($p < 0.05$) com-pared with pre-HPN status.
Ladefoged, 1981	Patient	Non-validated questionnaire	Profile	–	Acceptable in 2/3 of cases	–	Q-o-L parameters were independent of all variables. BUT, not enough data to test.
Messing, 1989	Doctor	Functional assessment	–	–	Age < 65 years, benign	Age > 65 years, malignancy, pseudo-obstruction	Simple 4-stage rehabilitation profile. Stage decided by physician, not the patient.
O'Hanrahan, 1992	Doctor	Functional assessment	Profile	–	Crohn's disease	All other diagnostic groups	Data overlap with Messing (1989). Same 4-point scale used.
Pironi, 1993	Doctor	Functional assessment	Profile	–	–	–	Same 4-point scale as Messing and O'Hanrahan. Two-thirds in the upper two groups.

continued

*# Scale 3 to 9, 9 = severe disablement and 3 = best possible Q-o-L. ** Scale 0 to 1, 0 = death, 1 = best possible Q-o-L.*

TABLE 9 contd *Quality of life on HPN*

Study	Whose values?	Instrument used	Profile or index	Index scores	Best Q-o-L or outcome	Worst Q-o-L or outcome	Comments
Richards, 1995	Patient	SF 36 and EuroQoL	Both	0.51	Age < 45 years	Age > 55 years, narcotic addiction	No significant difference between disease subgroups, stomas, recent hospitalisation, and duration of HPN.
Smith, 1993	Patient	Multiple-validated instruments	Profile	–	Stable relationship	Long duration of HPN, poor income	Loss of friends, loss of employment and depression were noted in two-thirds of families.

[#] Scale 3 to 9, 9 = severe disablement and 3 = best possible Q-o-L. [**] Scale 0 to 1, 0 = death, 1 = best possible Q-o-L.

TABLE 10 *Survival on HPN*

Study	Benign underlying disease	Malignant underlying disease (including AIDS)
August, 1991	–	Average months survived. Cancer ovary 1.3; Cancer colon 3; Cancer appendix 6
Grabowski, 1989	Scleroderma. 3 (of 4) died at 12, 14, 17 months.	–
Howard, 1991	1-year mortality rates: Crohn's disease 5%; MVO 20% (4% thereafter); Pseudo-obstruction 20%	1-year mortality rates: Cancer 75%; AIDS 93%
Howard, 1993	1-year survival: Crohn's disease 95%; Radiation enteritis 76%	1-year survival: Cancer 30%
Howard, 1986	50% survival at 36 months 15% survival at year 8	50% survival at 6 months 15% at 1 year. All dead by 23 months
Howard, 1995	1-year survival > 90% (age 0–55) 1-year survival ~ 65% (age > 55)	
King, 1993	–	Gynaecological malignancy Median survival 2 months (range 0–26)
Messing, 1995	1-year survival 91% 2-year survival 70% 3-year survival 62%	–
Van Gossum, 1995	6-month mortality rates: Crohn's disease 0%; MVD 8%; Miscellaneous 13%; Radiation enteritis 7%	6-month mortality rates: Cancer 71%; AIDS 88%

The duration of HPN use (*Table 11* and *Figure 4*) reflects the survival and the disease activity. In Crohn's disease there are two peaks; the first is from 0 to 6 months, and reflects the use of HPN for fistulas, perioperative nutrition support and exacerbation of the disease. Longer duration of use (more than 2 years) reflects the use of HPN for established short bowel syndrome. More than 50% of Crohn's patients are on HPN for more than 2 years. The duration of use in malignant disease is

TABLE 11 *Duration of HPN use*

Study	Duration of HPN use (by diagnostic subgroup where possible)		Length of follow-up
Beers, 1990	3.54 years	(all benign)	6 years
Bowyer, 1985	8–95 months	(all benign)	7 years
DePotter, 1992	615 days (range 30–3532 days)	(all benign)	9 years
Galandiuk, 1990	1083 days (range 33–3258)	(all Crohn's) 51% on HPN for > 2 years	11 years
Grabowski, 1989	12–86 months	(all scleroderma)	?
Griffith, 1984	Average 9.6 months	(all benign)	5 years
Messing, 1995	Median 19 months (range 1–137)	(all benign)	9 years
Pironi, 1993	22 ± 22 months	(all benign)	7 years
Robb, 1983	42.7 months (range 6–114)	(all benign)	?
Schmidt-Sommerfeld, 1990	577 days (range 58–2633)	(all benign)	5 years
Steiger, 1983	Crohn's disease MVD Radiation enteritis	842 days (mean) 884 days 494 days	5 years
Miller, 1979	15.7 months (range 1–52)	(all radiation enteritis)	8 years
Gouttebel, 1987	Benign group Malignant group	357 days (30–4155) 93 days (30–421)	6 years
August, 1991	53 days (range 5–208)	(malignant)	9 years
King, 1993	75 days (range 2–414; median 28)	(malignant)	9 years
Singer, 1991	2.5 months (range 0.7–10.8)	(all AIDS)	1 year
Weiss, 1982	6.2 months (range 0.5–19)	(malignant)	2 years

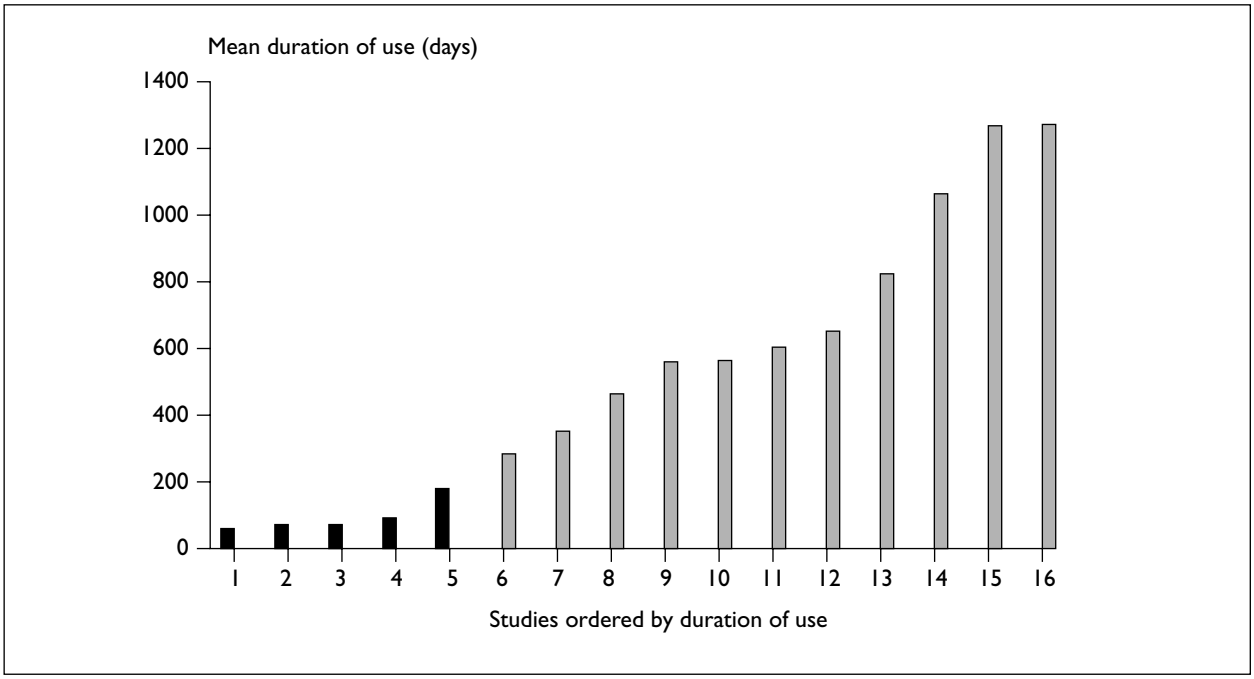


FIGURE 4 *Mean duration of HPN use (■, malignant; □, benign)*

generally very short, with only a minority of patients continuing on HPN for more than 1 year. More accurate analysis of this data is impossible because the reported duration of HPN use is affected by the length of the study follow-up. For example, a short period of observation would show more patients continuing treatment and survivors than a long study.

It is difficult to generate accurate figures from the available evidence concerning the reasons for discontinuing HPN (*Table 12*). This is because there are wide variations in the follow-up times; we have, therefore, only included studies which compare different disease subgroups. However, it is clear that the main reason for discontinuing HPN for patients with malignant disease is death (range, 60–100%). The patients with benign disease tend to either recover (range, 40–70%) or continue on HPN for long periods (range, 25–50%); only a minority are discontinued because of death (range, 2–30%).

TABLE 12 *Reasons for discontinuing HPN*

The length of follow-up in each study varied considerably (see *Table 7*), and it was not, therefore, possible to compare individual studies. The studies below reported reasons for discontinuing HPN for subgroups as indicated; studies which did not report subgroup outcomes were not included.

Study	Diagnosis	Still on HPN (%)	Recovered (%)	Dead (%)	Lost (%)
Byrne, 1979	Benign	45	39	16	0
	Cancer	0	0	100	0
Gouttebel, 1987	Crohn's disease	?	?	28	?
	Cancer	9	0	91	0
Howard, 1993	Crohn's disease	25	70	< 5	?
	MVD	50	25	25	
	Cancer	10	25	65	
Howard, 1991	Crohn's disease	47	38	5	7
	MVD	?	16	20	
	Pseudo-obstruction	48	21	20	
	Cancer	25	?	75	
	AIDS	?	?	93	
Howard, 1986	Crohn's disease	?	?	28	?
	Cancer	?	?	100	?
Howard, 1995	Crohn's disease	25	70	2	
	MVD	48	27	19	
	Cancer	8	26	63	
	AIDS	6	13	73	
Messing, 1989	Crohn's disease	35	57	8	?
	MVD	32	40	28	
	Pseudo-obstruction	20	40	40	
	Cancer	26	13	60	
	Radiation enteritis	26	26	47	
Steiger, 1983	Crohn's disease	?	?	26	?
	MVD			43	
	Radiation enteritis			38	
Van Gossum, 1995	Crohn's disease	75	25	0	?
	MVD	65	27	7	
	Cancer	14	15	71	
	AIDS	0	12	88	
	Radiation enteritis	81	12	6	
Vargas, 1987	Benign	21	50	30	0
	Cancer	0	0	100	

TABLE 13 *Summary of studies selected for Section 3 How have HPN programmes been organised? What comparative evidence is available on effectiveness?*

Studies – Section 3a	Time frame	Study design	Groups compared	Sample size	Comparable groups	Length of follow-up	% lost to follow-up	Outcomes assessed?
Van Gossum, 1995	1993–94	Case series; retrospective	Different countries	211	N/A	6–12 months	?	Organisation, survival, catheter type
Studies – Section 3b	**Time frame**	**Study design/ Grade of evidence**	**Groups compared**	**Sample size**	**Comparable groups**	**Length of follow-up**	**% lost to follow-up**	**Outcomes assessed?**
Howard, 1989	1983–88	Case series retrospective Grade C	Reservoir vs external catheter	58	No	1 month–4 years	?	Catheter complications
Hyltander, 1991	10 weeks	Randomised controlled trial; prospective Grade R	HPN vs no HPN during chemo-therapy	33	Yes	10 weeks	0	Nutritional status
Jarrard, 1980	1978	Prospective controlled, non-randomised; Grade C	Daily vs alternate day dressings	38	No	11–31 days	?	Catheter colonisation
Johnston, 1994	1980–93	Case series; retrospective Grade H	Effect of unit experience on complica-tion rate	34	N/A	1.7 years	0	Complication rates
Pithie, 1988	6 years (1980s)	Case series; retrospective Grade C	Catheter tip position	69	N/A	NS	0	Superior vena cava thrombosis
Rannem, 1990	1976–88	Case series; retrospective Grade H	Before and after use of disinfectants	58	N/A	2 months–11.5 years	?	Catheter sepsis

N/A, not applicable; ?, not known or not stated; Grade R, evidence from randomised comparison; Grade C, evidence from concurrent non-randomised comparison; Grade H, evidence from historical non-randomised comparison.

Results for Section 3a and b Organisation and comparative data

Organisation

Only one study has reported data on the organisation of HPN programmes in different countries (Van Gossum, 1996) (see *Table 13*). The study was a multicentre collection of all new patients commenced on HPN in Europe, between 1993 and 1994, and examined organisation, outcomes in terms of survival, and types of catheters used. Since the experience of the major European centres was pooled, the variation between countries was not reported. The tables are, therefore, a general profile of European HPN activity.

The organisation of HPN programmes is poorly documented in the literature. In Europe, the prescribing hospital and commercial supply companies supply most HPN (see *Table 14*). Most patients in Europe are trained in hospital (for an average of 14.2 days) and according to protocols in 63% (see *Table 15*). Surprisingly, only 43% were self-caring after training (Van Gossum, 1996).

TABLE 14 *Delivery of solutions, disposables and pumps*

Supplier	TPN solutions	Disposables	Pumps
Prescribing hospital	57%	58%	53%
Local hospital	1.4%	1.6%	1.2%
Local pharmacy	2.4%	7%	4%
Delivery company	37%	31%	18%
Others	1.2%	1.4%	10%

TABLE 15 *Training*

Trained in hospital	83%
Trained outside hospital	15%
Training protocol used	63%
Training manual supplied	63%
Self-caring after training	43%
Cared for by relatives	29%
Community nurse carer	26%
Average training time	14.2 days

Central venous catheters

The commonest central venous access system used in Europe is an external catheter, such as a Broviac or Hickman line,used in 74% of cases. Implanted reservoir type catheters, which have no external components when not in use, (such as the Porta-cath) were used less frequently (26% of cases). The external catheters have a section which lies permanently outside the skin to which the infusion is attached.

Comparative data

Six studies were included in Section 3b on comparative data (see *Table 13*). One was a randomised, controlled trial (Hyltander, 1991), one was a prospective non-randomised trial (Jarrard, 1980), three were case series (Howard, 1989; Johnston, 1994; Pithie, 1988) and one used historical cohorts (Rannem, 1990). The sample sizes were small (33–69) and were not well matched in some studies. The length of follow-up was often short and may be considered insufficient for technologies such as HPN, which are often used for years. Comparative data on aspects of HPN technology was available in only six (7.5%) of the 79 studies which satisfied the inclusion criteria. The randomised, controlled trial of patients with testicular tumours having chemotherapy showed that HPN did not affect the nitrogen balance but did maintain weight owing to fat accumulation. The short duration of the study did not allow important outcomes such as survival to be measured. The other comparative studies suggested that patients would benefit if iodine tincture or chlorhexidine disinfectants and alternate day dressings were used. One study showed that catheter tip position in the right atrium was associated with fewer complications than if the tip was in the superior vena cava; however, this was a small retrospective study and guidelines on ideal catheter tip position cannot be confidently made from such a study. The results of these studies are summarised in *Table 16*.

TABLE 16 *Comparative studies examining aspects of the process of HPN therapy*

Study	Time frame	Study design	Groups compared	Sample size	Outcomes assessed?	Findings
Howard, 1989	1983–88	Comparison of experience; non-randomised	Reservoir vs external catheter	58	Catheter complications	The implanted reservoir was associated with significantly fewer ($p < 0.05$) complications than the external catheter.
Hyltander, 1991	10 weeks	Randomised controlled trial	TPN vs no TPN in chemotherapy	33	Nutritional status	Body weight was preserved but this was simply fat accumulation. Nitrogen balance was not maintained. Exercise tolerance was not improved by HPN.
Jarrard, 1980	1978	Prospective controlled	Daily vs alternate day dressings	38	Catheter colonisation	Daily dressing changes reduced catheter colonisation but this was not significant. Daily dressing was expensive and time-consuming.

continued

TABLE 16 contd *Comparative studies examining aspects of the process of HPN therapy*

Study	Time frame	Study design	Groups compared	Sample size	Outcomes assessed?	Findings
Johnston, 1994	1980–93	Case review plus before and after	Current patients compared with historical controls	34	Complication rates	Increasing experience was associated with a reduction in the complication rate ($p < 0.0001$). Loss of an experienced nutrition nurse did not change the complication rate.
Pithie, 1988	6 years (1980s)	Case review	Catheter tip position	69	Superior vena cava thrombosis	Positioning of the catheter tip in the right atrium reduced the incidence of superior vena cava thrombosis compared with catheters placed in the superior vena cava ($p < 0.01$) using glucose as the energy source.
Rannem, 1990	1976–88	Case series; non-randomised	Catheter sepsis using various disinfectants	58	Catheter sepsis	Incidence of catheter sepsis was significantly higher ($p < 0.05$) when povidone iodine was used as a disinfectant rather than iodine tincture or chlorhexidine.

Results for Section 4 Economic analysis

There were seven studies that examined economic aspects of HPN therapy, and these are summarised in *Table 17*. Two studies were from the UK, four from the USA and one from Canada. All examined the costs of HPN from the health service perspective and ignored patient costs. Two studies examined costs and benefits as part of a formal cost–utility analysis and these studies included marginal quality-of-life and sensitivity analyses. The evidence from these studies for the cost-effectiveness of HPN is presented in *Table 18*.

Two cost–utility analyses were located. The marginal cost per quality-adjusted life year (QALY) varied from Canadian $14,600 (Detsky,

TABLE 17 *Section 4. What evidence exists on the cost-effectiveness of HPN? Summary of studies*

Study: Country (Period)	Case mix	Perspective	Methodology	Costs	Benefits measured	Q-o-L assessment	Marginal analysis	Sensitivity analysis
Detsky, 1986: Canada (1970–82)	Benign	Hospital	Cost–utility analysis	Hospital	Patient	yes	yes	yes
Richards, 1996: UK (1995)	Benign	Hospital	Cost–utility analysis	Hospital	Patient	yes	yes	yes
Bisset, 1992: UK (1992)	Benign	Hospital	Cost analysis	Some	None	no	no	no
Wesley, 1983: USA (1983)	Benign	Hospital	Cost analysis	Some	None	no	no	no
Wateska, 1980: USA (1980)	Benign	Hospital	Cost analysis	Hospital	None	no	no	no
Dzierba, 1984: USA (1982–83)	Benign	Hospital	Cost analysis	Hospital	None	no	no	no
Baptista, 1984: USA (1984)	Benign	Hospital	Cost analysis	Hospital	None	no	no	no

TABLE 18 *Section 4 Results. Economic evaluations of HPN. Evidence of cost-effectiveness of HPN*

Study	Country (Year)	Perspective	Methodology	Findings (costs are given as reported and are not adjusted to 1995 values)	Sensitivity analysis	% difference between hospital TPN and HPN
Baptista, 1984	USA (1984)	Health service	Cost analysis	Regular assessment of all aspects of patient care can result in significant fiscal savings.	–	–
Bisset, 1992	UK (1992)	Health service	Cost analysis	HPN solutions, pump and consumables cost £23,000–30,000 per year.	–	–
Dzierba, 1984	USA (1982–83)	Health service	Cost analysis	Hospital TPN more expensive than HPN. $32,850 per year for HPN. Approx $57,000 for hospital TPN.	–	72
Wateska, 1980	USA (1980)	Health service	Cost analysis	First year cost of HPN $21,465, thereafter $19,700 per year. Hospital TPN costs $73,720.	–	73
Wesley, 1983	USA (1983)	Health service	Cost analysis	$33,000–36,000 per year for HPN; $182,000 for hospital TPN.	–	81
Richards, 1996	UK (1995)	Health service	Cost–utility analysis	First year cost of HPN is £44,288. The marginal cost per QALY was £69,000. One year of hospital TPN costs £93,000.	Sensitive to the age of the patient.	65
Detsky, 1986	Canada (1970–82)	Health service	Cost–utility analysis	Marginal cost per QALY $14,600. Increase of 3.3 years of quality-adjusted survival compared with the alternative of intermittent hospital nutritional support. Cost–utility compares favourably with other health care programmes when used for benign diseases.	Sensitive to the assumptions made regarding the costs of alternative treatments.	

1986) to UK £69,000 (Richards, 1996). Reflation of the 1986 Canadian value equates to approximately £12,000 per QALY. The most recent estimate of costs to the NHS were £45,000 for the first year and £36,000 for subsequent years.

The studies showed that HPN was 65–80% cheaper than the alternative hospital treatment. The cost–utility analyses suggested that the cost–utility of treating younger patients was more favourable than older patients.

Chapter 5
Discussion

Home parenteral nutrition and intestinal failure

Home parenteral nutrition has been used for the treatment of varying degrees of intestinal failure on both a short and long term basis. Intestinal failure is defined as an inability of the gastrointestinal system to absorb sufficient fluid, electrolyte and/or nutrients for metabolic requirements. Intestinal failure is one aspect of the short bowel syndrome. The clinical features of this syndrome are intractable diarrhoea, weight loss, dehydration, steatorrhoea, malnutrition, and vitamin and mineral deficiency. If the fluids, electrolytes and nutrients are not replaced then there is a progression from dehydration and malnutrition to death. The speed at which this condition progresses is dependent on the degree of intestinal failure. The degree of intestinal failure depends in turn on the length and function of the intestinal remnant. There are other factors which will affect how good the function will be; these include: the pre-existing disease; the amount of residual disease; the adaptive capacity of the bowel; the site of resection, and the presence or abscence of the ileo-caecal valve.

There are many disease processes which can result in intestinal failure. Congenital problems are uncommon and usually result from intestinal atresia or malrotation of the gut around a congenital band. Another common subgroup in paediatric practice are patients with intractable diarrhoea. Conditions which interrupt the vascular supply of the intestine are common and include mesenteric thromboses or emboli, various coagulopathies, intestinal malrotation or volvulus, and intestinal strangulation. Crohn's disease can result in a short bowel syndrome as a result of extensive disease activity or through multiple intestinal resections. Internal or external enteric fistulation can also result in temporary or permanent intestinal failure. Malignant disease can result in intestinal failure as a result of disease extent or as a result of treatment (for example, extensive removal of bowel or irradiation of parts of the abdominal cavity).

The treatment of intestinal failure is complex. The treatment options include parenteral nutrition, enteral nutrition and small bowel transplantation.

Small bowel transplantation is not widely available at the present time in the UK. Most of the world's experience with this procedure is in the USA. Successful transplantation has been hampered by problems with immunosuppression and infection by viral agents. In the UK, patients who have tolerated HPN very well have been advised to continue with HPN treatment until the morbidity and mortality associated with small bowel transplantation improves. While awaiting a suitable donor organ, the patient will require parenteral nutrition.

Enteral nutrition is suitable for patients with lesser degrees of intestinal failure. It has certain advantages over parenteral nutrition in that it is physiologically more acceptable, villus height is maintained, bacterial translocation is reduced, it is simple to administer, and it is much cheaper than parenteral nutrition. However, there are disadvantages in that it can not be used as the sole means of nutritional support in patients with severe short bowel syndrome. This is because there is simply insufficient absorption due to inadequate function or length of bowel. The large volume of enteral fluid required in the severe cases would exacerbate the enteric fluid loss, and lead to dehydration, malnutrition and electrolyte loss. There is scanty evidence describing the use of enteral feeding for short bowel syndrome and, in particular, we are not aware of any studies comparing the use of enteral with parenteral nutrition. It is difficult to predict which patients with intestinal failure will manage with enteral nutrition alone. Absolute bowel length is not a good predictive factor and patients often have to be monitored over a period of weeks and months to ensure that the nutritional support is adequate.

For severe cases of intestinal failure the mainstay of treatment is parenteral nutrition. As the intestine adapts over a period of up to 2 years, it may be possible to wean the patient from parenteral nutrition to enteral nutrition and, possibly, to a normal diet. Until weaning is completed, the patient is dependent on the parenteral administration of fluid and nutrient requirements. A proportion of patients will never have sufficient bowel left to allow adaptation to take place, and will require parenteral nutrition in order to survive and consideration for a small bowel transplant. Any patient

requiring parenteral nutrition for a significant length of time is a candidate for home therapy. When compared to the alternative of in-patient care, HPN is thought to be more acceptable for the patient and cheaper, and it releases beds for the treatment of others.

The need for the review

Expansion of the technology into areas where its effectiveness has been questioned, the need for data on use of HPN in the UK, the effect on the quality of life of patients, variable referral patterns, and the cost of treatment, led to the prioritisation of HPN as a technology in need of assessment.

The research questions were designed to outline the important aspects of current practice. The review also attempted to identify areas of current practice that were backed by good evidence of effectiveness and those areas that were not.

Finding the research

The literature search revealed that evidence was restricted to data from case series, there being very few comparative trials. Although the MEDLINE database was the most productive to search, almost 80% of the HPN research literature would have been missed by a search limited to MEDLINE. Other databases fell a long way behind. Hand searching of the main European journal (*Clinical Nutrition*) and the main American journal (*Journal of Parenteral and Enteral Nutrition*) was fruitful but searching the less well-known journals was not. It would appear that most centres publish their HPN work in these two journals.

Locating abstracts from meetings was useful, as it indicated the type and scope of studies which are on-going. The response to the letters we sent to 24 major centres in Europe and America was disappointing (seven replies containing eight new studies). The poor response was possibly due to the timing of the letters, which were sent out in mid-summer when many people may have been on vacation. We did not receive any details of unpublished or on-going research.

Repeated scanning of reference lists was the most successful method of locating additional studies. The Science Citation Index (SCI) was also a useful method of locating studies; however, we had already collected a large number of studies before trying out the SCI, and no additional studies were found.

The standards of the literature

Of the 256 studies identified, only 65 satisfied the inclusion criteria. The reasons for exclusion were mainly due to the study being hospital based or pre-1980. Only one randomised, controlled trial was identified. Many studies contained data on patients that may have been included more than once. This was due to sampling patients from different sources and including patients who had been entered on to a national database or registry. This is a key issue when pooling data from several sources and may be a source of bias in reporting.

Trends of use

The quality of the studies satisfying the inclusion criteria for describing use was generally poor. The main problems being non-random samples of the HPN population, retrospective case series and the possibility of patients being included more than once in a study because of data pooling. There was a general increase in the number of patients with malignant disease being entered into HPN programmes. This accounted for 90% of programme growth in the USA and an increase from 5% to 8.9% in the UK recently. In the UK, the trend is opposite to this, with many patients with malignant disease being supported with enteral nutrition. The use of HPN for the treatment of wasting associated with AIDS is also becoming more common, despite the lack of evidence of effectiveness in this disease.

The use of HPN in paediatric practice is uncommon in this country, and this was reflected in the small number of studies located. The larger series originate from the USA and France but the small number of patients in these studies prevent firm conclusions being drawn regarding HPN use in paediatrics.

Quality of care

Many of the problems with the quality of the studies also applies to those describing patient experience of HPN. Sepsis arising from the central venous catheter was the most common serious complication associated with HPN treatment. The infections were limited to a minority of patients who had recurrent episodes of sepsis. Thus, the incidence of patients with sepsis per catheter year is low. The incidence of infections varied from 0.11 to 0.71 episodes per catheter year (see *Figure 1*). It can be assumed that centres in different countries will have, at least, some differences in training techniques and catheter care protocols and, given the range in incidence of

sepsis, these differences may be important. It has been suggested that the type of catheter used affects sepsis rates and that there is a lower incidence of infection if reservoir catheters are used. We did not locate any convincing evidence to support this view. There is evidence from the study by Singer (1991) which shows that episodes of catheter sepsis are more common in the patients with AIDS and cancer than in patients on HPN with benign diseases (see *Table 8*).

Episodes of central line sepsis, occlusion and central vein thrombosis often require catheter removal. This raises problems with venous access for patients on long-term treatment and can be associated with significant morbidity and mortality. The evidence collected does not allow firm guidelines to be developed in order to minimise these complications. There is a need to know which catheters should be placed where and which nutrient solutions are associated with fewest complications. There is anecdotal evidence which suggests that more reservoir catheters are being used for long-term HPN. The evidence to support this change is based on one study (Howard, 1989), which showed that fewer infections occurred when reservoir catheters were used. However, the study design was weak and based on a comparison of non-randomised groups.

The relationship between complication rates and study size is unclear. Experienced centres that have dealt with large cohorts of patients seem to have similar results to smaller units. There does seem to be a learning curve for new centres and early years can be marred by unacceptable complication rates (Johnston, 1994). It is important for new centres to build on the experience of established centres, in order to avoid the problems of the learning curve.

The quality of life experienced by patients with benign disease is reasonable, considering that this treatment is life-saving and the alternative for many patients would be death. There is no evidence describing the quality of life experienced by those patients with malignant disease or AIDS. There is a clear need for this type of information for this patient group, where the emphasis should be on adding quality as well as quantity of life.

The survival figures reflect the underlying disease and it can be seen that the survival figures for patients with benign disease are good. The survival statistics for patients with malignant disease and AIDS are poor, and this is further evidence of the need to assess these subgroups more thoroughly than in the past, with particular emphasis on the best way of providing nutrition (parenteral or enteral). We do not know how survival has been affected by giving HPN to patients with terminal malignancy or AIDS, and this requires further investigation.

Organisation and evidence of effectiveness

The organisation of HPN patients has not been examined by comparative study. The remarkable similarity in complication rates shown in larger studies suggests that experience is more important than organisation. There is a need to demonstrate more clearly the role of small units and to assess whether larger units are more effective. The question of where patients should be trained is largely an economic one but patients may benefit from the reassurance of hospital surroundings during early training (according to anecdotal evidence) and this should be taken into consideration.

There were few comparative data on aspects of HPN and the studies were of poor design (such as lack of compatability) and small sample size. These factors prevent any firm conclusions being made regarding most of the aspects that were examined (such as which catheter to use, or the ideal site for the catheter tip).

Economic appraisal

All the evidence found examining the economic aspects of HPN treatment demonstrated that it is cheaper than in-patient treatment. The cost per QALY measured in two studies was reasonable for benign disease, particularly in young patients, and especially considering the life-saving nature of the treatment. There is a complete lack of economic appraisal of HPN for malignant disease and AIDS.

Chapter 6
Conclusions

What gaps in the evidence exist? (Section 5 of the review method)

The quality and range of evidence of effectiveness was disappointing. The technology of HPN has been present for almost 30 years and yet there is still very little good quality evidence to support many aspects of it.

Section 1

The type of patient who has received HPN has been fairly well documented. There is evidence that, in the UK, there is an increase in the number of those with terminal malignant disease and wasting due to AIDS being treated with HPN. It is hoped that accurate data concerning those patients entered into HPN programmes will continue to be collected as part of a national register, administered by the British Association for Parenteral and Enteral Nutrition Council. Trends in the UK could then be monitored more efficiently.

Section 2

The complications, survival, duration of treatment, and reasons for discontinuing treatment are fairly well documented. The quality of life of patients on HPN has been poorly assessed in the past particularly those with malignant disease and AIDS. A clear survival advantage has been demonstrated for those with a benign underlying disease. However, there is less evidence to indicate whether the complication rates differ for the disease subgroups.

Section 3

Organisational models for HPN programmes have been poorly assessed and there are no comparative data that we could locate looking at this aspect of the technology; for example, who should deliver the training and where should patients be trained? Comparative data on many aspects of the technology are completely absent, and those which do exist are marred by non-randomised, poorly-designed, retrospective investigations performed on small samples.

Section 4

There is some up-to-date evidence looking at the cost of HPN to the health service. Patient and community costs have not been measured. Only two studies have used a formal methodology for economic appraisal (cost–utility analysis) and these were performed in 1986 (Canada) and 1995 (UK). Comparisons with other technologies have not been made. There are no economic appraisals of HPN used for malignant disease.

Which questions need to be addressed?

- What is the cost per QALY of HPN for subgroups of patients to determine, for example, if it is cost-effective to use HPN in AIDS and cancer patients and other subgroups where the underlying condition is terminal; that is, is HPN of use in palliative care? As part of such a study it is necessary to calculate the typical quality-of-life profile (measured by repeated assessments using a set of validated health status instruments) of patients before, during and after HPN treatments, and to identify moderating factors such as underlying disease. Also, what is the expected survival for patients with terminal malignant disease and AIDS on HPN, and can 'long survivors' be identified?

- What are the most cost-effective organisational models for HPN programmes and does any one model contribute to an improved outcome (for example, small versus large units)?

- What is the best method for training patients for HPN, and should the training be done at home or in hospital?

- Are reservoir catheters associated with less septic episodes than traditional external catheters? Who should then insert central venous catheters, surgeons or interventional radiologists, and what is the ideal position of the catheter tip?

- How cost-effective is HPN compared with other expensive but life-saving technologies?

What methodological issues need to be addressed in future research?

As mentioned previously, study design has been the downfall of many investigations into the

effectiveness of HPN. Larger, multicentre, studies should be performed. They should be prospective with a clearly defined aim. Comparative studies should have a control group and be randomised. Quality-of-life assessments and economic analyses should follow validated methodologies.

- It is important to have complete up-to-date registries measuring patient characteristics and experience. Collaboration and adequate funding is essential.

- Episodes of catheter sepsis, occlusion, central vein thrombosis and metabolic imbalance should be documented as part of centre audit. Standards of care should be compared and maintained.

- Patients should be monitored for the development of liver and bone disease, and these should be recorded as part of the 'total patient experience'.

- All changes in the delivery and management of HPN should be properly evaluated. Comparisons of alternative modes of delivery should preferably be assessed by randomised, controlled trial.

References

Studies satisfying the criteria for inclusion in the review

August DA, Thorn D, Fisher RL, Welchek CM, 1991. HPN for patients with inoperable malignant bowel obstruction. *J Parent Ent Nutr*;**15**:323–7.

Baptista RJ, Lahey MA, Bistrian BR, *et al,* 1984. Periodic reassessment for improved, cost effective care in HPN; a case report. *J Parent Ent Nutr*;**8**:708–10.

Beers TR, Burnes J, Fleming CR, 1990. Superior vena caval obstruction in patients with gut failure receiving home parenteral nutrition. *J Parent Ent Nutr*;**14**:474–9.

Bisset WM, Stapleford P, Long S, Chamberlain A, Sokel B, Milla PJ, 1992. HPN in chronic intestinal failure. *Arch Dis Childhood*;**67**:109–14.

Bowyer BA, Fleming CR, Ludwig J, Petz J, McGill DB, 1985. Does long term home parenteral nutrition in adult patients cause chronic liver disease? *J Parent Ent Nutr*;**9**:11–17.

Buchman AL, *et al,* 1993. Serious renal impairment is associated with long term HPN. *J Parent Ent Nutr*;**17**:438–44.

Buchman AL, Moukarzel A, Goodson B, *et al,* 1994a. Catheter related infections associated with HPN and predictive factors for the need for catheter removal. *J Parent Ent Nutr*;**18**:297–302.

Buchman AL, Moukarzel A, Ament ME, *et al,* 1994b. Catheter thrombosis and SVC/ IVC syndrome are rare complications of long term TPN. *Clin Nutr*;**13**:356–60.

Burnes JU, O'Keefe SJD, Fleming R, Devine RM, Berkner S, Herrick L, 1992. Home parenteral nutrition – a 3 year analysis of clinical and laboratory monitoring. *J Parent Ent Nutr*;**16**:327–32.

Byrne WJ, Ament ME, Burke M, Fonkalsrud E, 1979. Home parenteral nutrition. *Surgery Gyn Obstet*;**149**:593–9.

Carlson GL, Maguire G, Williams N, Bradley A, Shaffer JL, Irving MH, 1996. Quality of life on home parenteral nutrition and attitudes towards intestinal transplantation. A single centre study of 37 patients. *Clin Nutr;* in press.

DePotter S, Goulet O, Lamor M, 1992. 263 patient years of HPN in children. *Transplant Proc*;**24**:1056–7.

Detsky AS, McLaughlin JR, Abrams HB,1986. A cost utility analysis of the HPN program at Toronto general hospital: 1970–1982. *J Parent Ent Nutr*;**10**:49–57.

Detsky AS, McLaughlin JR, Abrams HB, 1986. Quality of life of patients on long term total parenteral nutrition at home. *J Gen Internal Med*;**1**:26–33.

Dollery CM, Sullivan ID, Bauraind O, Bull C, Milla PJ, 1994. Thrombosis and embolism in long term central venous access for parenteral nutrition. *Lancet*;**344**:1043–5.

Duclaux IL, DePotter S, Pharaon I, Olives JP, Hermier M, 1993. Qualité de vie des enfants en nutrition parentérale à domicile et de leurs parents. *Pediatrie;*(7/8):555–60.

Dudrick SJ, O'Donnel JJ, Englert DM, *et al,* 1984. 100 patient years of ambulatory home total parenteral nutrition. *Ann Surgery*;**199**:770–81.

Dzierba SH, Mirtallo JM, Grauer DW, Schneider PJ, Latolais CJ, Fabri PJ, 1984. Fiscal and clinical evaluation of HPN. *Am J Hosp Pharmacy*;**41**:285–91.

Foldes J, Rimon B, Muggia-Sullam M, 1990. Progressive bone loss during long term home total parenteral nutrition. *J Parent Ent Nutr*;**14**:139–42.

Galandiuk S, O'Neill M, McDonald P, Fazio VW, Steiger E, 1990. A century of HPN for Crohn's disease. *Am J Surgery*;**159**:540–5.

Gouttebel MC, Saint-Aubert B, Jonquet O, Astre C, Joyeux H, 1987. Ambulatory home total parenteral nutrition. *J Parent Ent Nutr*;**11**:475–9.

Grabowski G, Grant JP, 1989. Nutritional support in patients with systemic scleroderma. *J Parent Ent Nutr*;**13**:147–51.

Griffith CDM, Quayle AR, Clark RG, Gurnell P, 1984. Home parenteral nutrition in Sheffield 1978–1983. *J Roy Coll Surgeons Edin*;**29**:335–8.

Herfindal ET, Bernstein LR, Wong AF, Hogue VW, Darbinian JA, 1992. Complications of HPN. *Clin Pharm*;**11**:543–8.

Herfindal ET, Bernstein LR, Kudzia K, Wong A, 1989. Survey of home nutritional support patients. *J Parent Ent Nutr*;**13**:255–61.

Howard L, 1993. Home parenteral and enteral nutrition in cancer patients. *Cancer Suppl*;**72**:3531–41.

Howard L, Heaphey LL, Fleming R, Lininger L, Steiger E, 1991. Four years of North American Registry HPN outcome data and their implications for patient management. *J Parent Ent Nutr*;**15**:384–93.

Howard L, Claunch C, McDowell R, Timchalk M, 1989. Five years experience in patients receiving home nutrition support with the implanted reservoir: a comparison with the external catheter. *J Parent Ent Nutr*;**13**:478–83.

Howard L, Heaphey LL, Timchalk M, 1986. A review of the current national status of HPN and HEN from the provider and consumer perspective. *J Parent Ent Nutr*;**10**:416–24.

Howard L, Ament M, Fleming CR, Shike M, Steiger E, 1995. Current use and clinical outcome of home parenteral and enteral nutrition therapies in the United States. *Gastroenterology*;**109**:355–65.

Hurley RS, Campbell SM, Mirtallo JM, Wade VR, Murphy C, 1990. Outcomes of cancer and non cancer patients on HPN. *Nutr Clin Pract*;**5**:59–62.

Hyltander A, Drott C, Unsgaard B, *et al,* 1991. The effect on body composition and exercise performance of HPN when given as an adjunct to chemotherapy of testicular carcinoma. *Eur J Clin Invest*;**21**:413–20.

Jarrard MM, Olson CM, Freeman JB, 1980. Daily dressing change effects on skin flora beneath subclavian catheter dressings during total parenteral nutrition. *J Parent Ent Nutr*;**4**:391–2.

Johnston DA, Pennington CR, 1993. HPN in Tayside 1980–1992. *Scot Med J*;**38**:110–11.

Johnston DA, Richards J, Pennington CR, 1994. Auditing the effect of experience and change on HPN related complications. *Clin Nutr*;**13**:341–4.

King LA, Carson LF, Konstantinides N, *et al,* 1993. Outcome assessment of HPN in patients with gynecologic malignancies: what have we learned in a decade of experience? *Gyn Oncol*;**51**:377–82.

Ladefoged K, 1981. Quality of life in patients on permanent HPN. *J Parent Ent Nutr*;**5**:132–7.

Manji N, Bistrian BR, Mascioli EA, Benotti PA, Blackburn GL, 1989. Gallstone disease in patients with severe short bowel syndrome dependent on parenteral nutrition. *J Parent Ent Nutr*;**13**:461–4.

Mercier C, Hill D, 1995. La nutrition parenterale totale a domicile. *L'Inferm Queb*; Jan/Feb:34.

Messing B, Landais P, Goldfarb B, Irving MH, 1989. Home parenteral nutrition in adults: a multicentre survey in Europe. *Clin Nutr*;**8**:3–9.

Messing B, Lemann M, Landais P, *et al,* 1995. Prognosis of patients with nonmalignant chronic intestinal failure receiving long term HPN. *Gastroenterology*;**108**:1005–10.

Miller DM, Ivey M, Young J, 1979. Home total parenteral nutrition in the treatment of severe radiation enteritis. *Ann Internal Med*;**91**:858–60.

Mukau L, Talamini MA, Sitzmann JV, Burns C, McGuire ME, 1992. Long term central venous access vs other home therapies: complications in patients with acquired immunodeficiency syndrome. *J Parent Ent Nutr*;**16**:455–9.

Nightingale JMD, Simpson AJ, Towler HMA, Lennard-Jones JE, 1995. Fungal feeding line infections; beware the eyes and the teeth. *J Roy Soc Med*;**88**:258–63.

O'Hanrahan T, Irving MH, 1992. The role of HPN in the management of intestinal failure – report of 400 cases. *Clin Nutr*;**11**:331–6.

Perl M, Peterson LG, Dudrick SJ, Benson DM, 1981. Psychiatric effects of long term home hyperalimentation. *Psychosomatics*;**22**:1047–63.

Pironi L, Miglioli M, Ruggeri E, *et al,* 1993. Home parenteral nutrition for the management of chronic intestinal failure; a 34 patient year experience. *Ital J Gastroenterol*;**25**:411–18.

Pithie A, Soutar JS, Pennington CR, 1988. Catheter tip position in central vein thrombosis. *J Parent Ent Nutr*;**12**:613–14.

Ralston CW, O'Connor MJ, Ament M, Berquist W, Parmelee AH, 1984. Somatic growth and developmental functioning in children receiving prolonged home total parenteral nutrition. *J Paed*;**105**:842–6.

Rannem T, Ladefoged K, Hengoj J, Hylander-Moller E, Bruun B, Jarnum S, 1990. Catheter related sepsis in long term parenteral nutrition with broviac catheter. An evaluation of different disinfectants. *Clin Nutr*;**9**:131–6.

Richards DM, Irving MH, 1996. A cost-utility analysis of HPN. *Br J Surgery*;**83**:1226–9.

Richards DM, Irving MH, 1996. Using the SF36 and EuroQol to measure the quality of life on HPN. Unpublished.

Robb RA, Brakebill JI, Ivey MF, Christensen DB, Young JH, Scribner BH, 1983. Subjective assessment of patient outcomes on HPN. *Am J Hosp Pharmacy*;**40**:1646–50.

Roslyn JJ, Pitt HA, Mann L, Ament ME, DenBensten L, 1983. Gallbladder disease in patients on long term parenteral nutrition. *Gastroenterology*;**84**:148–54.

Schmidt-Sommerfeld E, Snyder G, Rossi TM, Lebenthal E, 1990. Catheter related complications in 35 children and adolescents with gastrointestinal disease on HPN. *J Parent Ent Nutr*;**14**:148–51.

Shike M, Shils ME, Heller A, *et al,* 1986. Bone disease in prolonged parenteral nutrition: osteopenia without mineralisation defect. *Am J Clin Nutr*;**44**:89–98.

Shike M, Harrison JE, Sturtridge WC, *et al,* 1980. Metabolic bone disease in patients receiving long term total parenteral nutrition. *Ann Internal Med*;**92**:343–50.

Singer P, Rothkopf MM, Kvetan V, Kirvela O, Gaare J, Askanazi J, 1991. Risks and benefits of HPN in the acquired immunodeficiency syndrome. *J Parent Ent Nutr*;**15**:75–9.

Smith CE, 1993. Quality of life in long term total parenteral nutrition patients and their family caregivers. *J Parent Ent Nutr*;**17**:501–6.

Staun M, Tjellesen L, Thale M, Rannem T, Schaadt O, Jarnum S, 1994. Bone mineral content in patients on home parenteral nutrition. *Clin Nutr*;**13**:351–5.

Steiger E, Srp F, 1983. Morbidity and mortality related to HPN in patients with gut failure. *Am J Surgery*;**145**:102–5.

Van Gossum A, *et al,* 1996. Current practice in home parenteral nutrition in adults: results of a large survey in Europe. *Clin Nutr*;**15**:53–9.

Vargas JH, Ament ME, Berquist WE, 1987. Long term HPN in paediatrics; ten years of experience in 102 patients. *J Paed Gastroenterology Nutr*;**6**:24–32.

Wateska LP, Sattler LL, Steiger E, 1980. Cost of a HPN program. *JAMA*;**244**:2303–4.

Weiss SM, Worthington PH, Prioleau M, Rosato FE, 1982. Home total parenteral nutrition in cancer patients. *Cancer*;**50**:1210–13.

Wesley JR, 1983. Home parenteral nutrition; indications principles and cost effectiveness. *Compr Therapy*;**9**:29–36.

Other references

Deeks JJ, Glanville J, Sheldon TA, 1996. Undertaking systematic reviews of research on effectiveness. CRD guidelines for those carrying out or commissioning reviews. University of York, NHS Centre for Reviews and Dissemination; CRD report 4.

Dudrick SJ, Wilmore DW, Vars HM, Rhoads JE, 1968. Can intravenous feeding as the sole means of nutrition support growth in the child and restore weight loss in the adult? An affirmative answer. *Ann Surgery*;**169**:974–84.

Scott NA, Leinhardt DJ, O'Hanrahan T, Finnegan S, Shaffer JL, 1991. Spectrum of intestinal failure in a specialised unit. *Lancet*;**337**:471–473.

Scribner BH, Cole JJ, Christopher TG, Vizzo JE, Atkins RC, Blagg CR, 1970. Long term total parenteral nutrition. The concept of an artificial gut. *JAMA*;**212**:457–63.

Wilmore DW, Dudrick SJ, 1968. Growth and development of an infant receiving all nutrients exclusively by vein. *JAMA*;**203**:860–4.

Studies not included in the systematic review of HPN and the reasons why

Study	Reason for exclusion
Ament ME, Vargas J, Berquist WE, 1986. HPN in the infant. *Clin Perinatology*;**13**:213–27.	Duplicate data.
Aron JM, 1991. Toward rational nutritional support of the HIV infected patient. *J Parent Ent Nutr*;**15**:121–2.	Review. No empirical data.
Askari A, *et al,* 1980. Zinc, copper and parenteral nutrition in cancer. A review. *J Parent Ent Nutr*;**4**:561–71.	Review. No empirical data.
ASPEN, 1995. Home nutrition; quality and cost effectiveness. ASPEN Pharmacists' Workshop;311–23.	No empirical data.
Belcastro S, *et al,* 1990. Thrombosis of the superior vena cava due to a central catheter for total parenteral nutrition. *J Parent Ent Nutr*;**14**:31–3.	Hospital based.
Booth IW, 1992. Parenteral nutrition; an update. *Eur J Clin Nutr*;**46**:S15–20.	No HPN outcomes.
Bordos DC, Cameron JL, 1975. Successful long term intravenous hyperalimentation in the hospital and at home. *Arch Surgery*;**110**:439–41.	Historical. Pre-1980.
Braga M, *et al,* 1994. Parenteral and enteral feeding in hospitals in Italy. A national survey. *Clin Nutr*;**13**:153–9.	Hospital based.
Braxton C, Lowry SF, 1995. Parenteral nutrition and liver dysfunction-new insight. *J Parent Ent Nutr*;**19**:3–4.	No empirical data.
Brothers TE, *et al,* 1988. Experience with subcutaneous infusion ports in three hundred patients. *Surgery Gyn Obstet*;**166**:295–301.	No HPN outcomes.
Broviac JW, Cole JJ, Scribner BH, 1973. A silicone rubber right atrial catheter for prolonged parenteral alimentation. *Surgery Gyn Obstet*;**136**:602–6.	Historical. Pre-1980.
Broviac JW, *et al,* 1974. Prolonged parenteral nutrition in the home. *Surgery Gyn Obstet*;**139**:24–8.	Historical. Pre-1980.
Buchman AL, *et al,* 1994. Selenium renal homeostasis is impared in patients receiving long term TPN. *J Parent Ent Nutr*;**18**:231–3.	No relevant outcomes for this review.
Buchman AL, *et al,* 1995. Excessive urinary oxalate excretion occurs in long term TPN patients both with and without HPN. *J Am Coll Nutr*;**14**:24–8.	No relevant outcomes for this review.
Buchman AL, *et al,* 1994. Choline pharmacokinetics during intermittent intravenous choline infusion in human subjects. *Clin Pharmacol Ther*;**55**:277–83.	No relevant outcomes for this review.

continued

continued

Study	Reason for exclusion
Buchman AL, *et al,* 1992. Lecithin increases plasma free choline and decreases hepatic steatosis in long term TPN patients. *Gastroenterology*;**102**:1363–70.	Not relevant to sections of the review.
Buchman AL, Ament ME, 1991. Comparative hypersensitivity in intravenous lipid emulsions. *J Parent Ent Nutr*;**15**:345–6.	Case report.
Burt ME, *et al,* 1983. A controlled randomised trial evaluating the effects of enteral and parenteral nutrition on protein metabolism in cancer bearing man. *J Surg Res*;**34**:303–14.	Not HPN. Outcomes not relevant to the review.
Byrne WJ, *et al,* 1977. HTPN; an alternative approach to the management of children with severe chronic small bowel disease. *J Paed Surgery*;**12**:359–65.	Historical. Pre-1980.
Campbell IT, 1993. Nutrition and immunocompetence. *Br J Intensive Care*;Feb:75–6.	No empirical data.
Cannon RA, *et al,* 1980. HPN in infants. *J Paed*;**96**:1098–1104.	Duplicate data.
Carlson GL, Irving MH, 1992. Home parenteral nutrition in the UK. *Intake*;**5**:2–4	No new data.
Chaet MS, *et al,* 1994. Intensive nutritional support and remedial surgical intervention for extreme short bowel syndrome. *J Paed Gastroenterol Nutr*;**19**:295–8.	No HPN outcomes.
Chamsi-Pasha H, *et al,* 1989. Cardiac complications of TPN: the role of two dimensional echocardiography in diagnosis. *Ann Roy Coll Surgeons*;**71**:120–3.	No empirical data.
Clark-Christoff N, *et al,* 1992. Use of triple lumen subclavian catheters for administration of TPN. *J Parent Ent Nutr*;**16**:403–7.	Not HPN.
Clarke PJ, *et al,* 1991. Liver function tests in patients receiving parenteral nutrition. *J Parent Ent Nutr*;**15**:54–9.	Short term and hospital based.
Copeland EM, 1990. Total parenteral nutrition in the cancer patient. The present as viewed from the past. *Nutrition*;**6**:2S–3S.	Hospital based.
Currie IC, *et al,* 1995. Experience of an implantable central venous access system in a district general hospital. *J Roy Coll Surg Edin*;**40**:31–4.	Not HPN.
Dahlstrom KA, *et al,* 1985. Nutritional status in children receiving HPN. *J Paed*;**107**:219–24.	Duplicate data.
Dalton MJ, *et al,* 1984. Consultative total parenteral nutrition teams; the effect on incidence of TPN related complications. *J Parent Ent Nutr*;**8**:146–52.	Hospital based.
Daly JM, *et al,* 1990. Nutritional support in the cancer patient. *J Parent Ent Nutr*;**14**:244S–7S.	No empirical data.
De Cicco M, *et al,* 1993. Parenteral nutrition in cancer patients receiving chemotherapy; effects on toxicity and nutritional status. *J Parent Ent Nutr*;**17**:513–8.	Hospital based.
Detsky AS, *et al,* 1984. Cost effectiveness of preoperative parenteral nutrition in patients undergoing major gastrointestinal surgery. *J Parent Ent Nutr*;**8**:632–7.	Hospital based.
Detsky AL, 1995. Evaluating a mature technology; long term HPN. *Gastroenterology*;**108**:129–31.	No empirical data.
Dorney SFA, *et al,* 1985. Improved survival in very short small bowel of infancy with use of long term parenteral nutrition. *J Paed*;**107**:521–5.	Duplicate data.
Dudrick SJ, *et al,* 1979. New concepts of ambulatory home hyperalimentation. *J Parent Ent Nutr*;**3**:72–6.	Historical. Pre-1980.
Dudrick SJ, *et al,* 1968. Can intravenous feeding as the sole means of nutrition support growth in the child and restore weight loss in an adult? An affirmative answer. *Ann Surgery*;**169**:974–84.	Historical. Pre-1980.
Eisenberg JM, 1993. Does perioperative total parenteral nutrition reduce medical care costs? *J Parent Ent Nutr*;**17**:201–9.	Hospital based.

Study	Reason for exclusion
Eyer S, *et al,* 1990. Catheter related sepsis; prospective randomised study of three methods of long term catheter maintainance. *Crit Care Med*;**18**:1073–9.	Short-term hospital TPN.
Faubion WC, 1986. Total parenteral nutrition catheter sepsis; impact of the team approach. *J Parent Ent Nutr*;**10**:642–5.	Hospital based.
Ferrel BR, *et al,* 1992. Home care; maintaining quality of life for patient and family. *Oncology*;**6**:136–40.	Not HPN.
Fleming CR. Hepatobiliary complications in adults receiving nutrition support. *Dig Dis Sci* 1994;**12**:191–8.	No empirical data.
Fleming CR, *et al,* 1980. HPN for management of the severely malnourished adult patient. *Gastroenterology*;**79**:11–18.	Historical. Pre-1980.
Freund HR, Rimon B, 1993. Outcome of HPN. *J Parent Ent Nutr*;**17**:196.	Letter.
Fry ST, 1990. Ethical issues in TPN. *Nutrition*;**6**:329–32.	No empirical data. Hospital based.
Gatti JE, *et al,* 1981. Endocarditis complicating home hyperalimentation. *Arch Surgery*;**116**:933–5.	No empirical data.
Goel V, 1990. Economics of total parenteral nutrition. *Nutrition*;**6**:332–5.	Review paper.
Grant JP, 1990. Proper use and recognised role of TPN in the cancer patient. *Nutrition*;**4**:6S–8S.	No empirical data.
Grey P, *et al,* 1994. Which nutritional measurements assess proein energy nutritional status in patients receiving HPN? *Clin Nutr*;**13**:29–34.	No empirical data relevant to the review.
Grundfest S, Steiger E, 1980. Home parenteral nutrition. *JAMA*;**244**:1701–3.	No empirical data.
Grundfest S, *et al,* 1979. The current status of home total parenteral nutrition. *Artificial Organs*;**3**:156–60.	Historical. Pre-1980.
Gulledge AD, 1985. Common psychiatric concerns in HPN. *Cleveland Clinic Q*;**52**:329–32.	No empirical data.
Gullege AD, *et al,* 1980. HPN for the short bowel syndrome, psychological issues. *Gen Hosp Psych*;**2**:271–81.	Not an inception cohort.
Gutcher GR, Chesney RW, 1978. Iatrogenic rickets as a complication of a TPN programme. *Clin Pediatr*;**8**:17:817–9.	Case report.
Haire WD, *et al,* 1994. Urokinase versus recombinant tissue plasminogen activator in thrombosed central venous catheters. *Thromb Haemostasis*;**72**:543–7.	Not HPN.
Haire W, Leiberman RP, 1992. Thrombosed central venous catheters; restoring function with six hour urokinase infusion after failure of bolus urokinase. *J Parent Ent Nutr*;**16**:129–32.	Not relevant.
Heizer WD, Orringer EP, 1977. Parenteral nutrition at home for 4 years via arteriovenous fistulae. Supplemental intravenous feedings for a patient with severe short bowel syndrome. *Gastroenterology*;**72**:527–32.	Historical. Pre-1980.
Helfrick FW, *et al.* Intravenous feeding of a complete diet in a child. *J Paed* 1944;**25**:400–403.	Historical interest only.
Hickey MS, Weaver KE. Nutritional management of patients with ARC or AIDS. *Gastroenterol Clin N Am*;**17**:545–60.	No empirical data.
Hopefl AW, 1998. What is the role of parenteral nutrition in AIDS? *Clin Pharmacy*;**7**:512–3.	No empirical data.
Howard L, 1992. Home parenteral nutrition in patients with a cancer diagnosis. *J Parent Ent Nutr*;**16**:93S–9S.	Duplicate data.

continued

continued

Study	Reason for exclusion
Howard L, 1989. Home nutritional support; the patient point of view. *Nutr Clin Pract*;**4**:49–50.	No empirical data.
Howard L, Malone M, 1994. What factors determine the appropriateness of home parenteral and enteral nutrition in the cancer patient? *Home Care Consultant*;**1**:18–27.	Data included elsewhere.
Howard L, *et al,* 1987. Home nutritional therapy from the consumer perspective. *Clin Nutr*;**6**:40–6.	Data included elsewhere.
Howard L, *et al.* Home parenteral nutrition in adults.In: Rombeau J, Caldwell M, eds. Parenteral nutrition. 2nd ed. Philadelphia, WB Saunders; 814–39.	No new empirical data.
Hughes BA, *et al,* 1980. Patient compliance with a HPN program. *J Parent Ent Nutr*;**4**:12—14.	No usable data.
Hurley DL, 1990. Long term parenteral nutrition and metabolic bone disease. *Endocrin Metab Clin N Am*;**19**:113–31.	No empirical data.
Imperial J, *et al,* 1983. Limitation of central vein thrombosis in total parenteral nutrition by continuous infusion of low dose heparin. *J Am Coll Nutr*;**2**:63–73.	HPN patients excluded. Follow-up less than 3 months.
Irving MH, 1986. Ethical problems associated with the treatment of intestinal failure. *Aust NZ J Surgery*;**56**:425–7.	No empirical data.
Irving MH. Intestinal failure and its treatment by home parenteral nutrition. *Adv Clin Nutr*;	No empirical data.
Irving MH, 1982. The UK HPN Register. *Gut*;**23**:A438.	Data included elsewhere.
Irving MH, *et al,* 1985. Three years experience with an intestinal failure unit. *Ann Roy Coll Surgeons Eng*;**67**:2–5.	Hospital based. No new data.
Ivey M, *et al,* 1975. Long term parenteral nutrition in the home. *Am J Hosp Pharm*;**32**:1032–6.	Historical. Pre-1980.
Jeejeebhoy KN, *et al,* 1976. Total parenteral nutrition at home; studies in patients surviving 4 months to 5 years. *Gastroenterology*;**71**:943–53.	Historical. Pre-1980.
Jeejeebhoy KN, 1983. Therapy of the short gut syndrome. *Lancet*;**i**:1427–30.	No empirical data.
Jeejeebhoy KN, *et al,* 1973. Total parenteral nutrition at home for 23 months without complication and with good rehabilitation. *Gastroenterology*;**65**:811–20.	Historical. Pre-1980.
Johnston JE, 1981. HPN – The costs of patient and family participation. *Social Work Health Care*;**7**:49–66.	No empirical data.
Kemp L, *et al,* 1994. The effect of catheter type and site on infection rates in TPN patients. *J Parent Ent Nutr*;**18**:71–4.	Not HPN.
Keohane PP, 1983. Effect of catheter tunnelling and a nutrition nurse on catheter sepsis during parenteral nutrition. A controlled trial. *Lancet*;**ii**:1388–90.	Hospital based.
Klein GL, 1995. Aluminium in parenteral solutions revisited – again. *Am J Clin Nutr*;**61**:449–56.	No relevant data.
Kohlhardt SR, *et al,* 1994. Peripheral versus central intravenous nutrition; comparison of two delivery systems. *Br J Surgery*;**81**:66–70.	Hospital based.
Koo WWK. Parenteral nutrition related bone disease. *J Parent Ent Nutr*;**16**:386–94.	No empirical data.
Kushner RF, *et al,* 1986. Endoscopic radiographic and clinical response to prolonged bowel rest and HPN in crohns disease. *J Parent Ent Nutr*;**10**:568–73.	Outcomes not relevant to the review.
Ladefoged K, 1982. Intestinal and renal loss of infused minerals in patients with the short bowel syndrome. *Am J Clin Nutr*;**36**:59–67.	Not relevant to the review.
Ladefoged K, Jarnum S, 1978. Long term parenteral nutrition. *BMJ*;**2**:262–6.	Data presented in other papers.

Study	Reason for exclusion
Langer B, *et al,* 1973. Prolonged survival after complete small bowel resection using intravenous alimentation at home. *J Surg Res*;**15**:226–33.	Historical. Pre-1980.
Leaseburge LA, *et al,* 1992. Liver test alterations with total parenteral nutrition and nutritional status. *J Parent Ent Nutr*;**16**:348–52.	Hospital based.
Lees CD, *et al* 1981. Home parenteral nutrition. *Surg Clinics N Am*;**61**:621–33.	Historical. Pre-1980.
Leibowitz AB, Iberti TJ, 1992. Home TPN and AIDS patients. *J Parent Ent Nutr*;**16**:496.	No empirical data (letter).
Leinhardt DJ, *et al,* 1992. Endocarditis complicating parenteral nutrition; the value of repeated echocardiography. *J Parent Ent Nutr*;**16**:168–70.	No empirical data.
Lennard Jones JE, Wood S, 1985. The organisation of intravenous feeding at home. *Health Trends*;**17**:73–5.	Data presented elsewhere.
Lennard Jones J, 1990. Indications and need for long term parenteral nutrition; implications for intestinal transplantation. *Transplant Proc*;**22**:2427–9.	No empirical data.
Levenson SM, *et al,* 1984. Early history of parenteral nutrition. *Federation Proc*;**43**:1391–1406.	Historical. Pre-1980.
Levien DH, *et al,* 1985. The use of cyclic home hyperalimentation for malabsorbtion in patients with scleroderma involving the small intestines. *J Parent Ent Nutr*;**9**:623–5.	Case report.
Linares J, *et al,* 1985. Pathogenesis of catheter sepsis; a prospective study with quantitative and semi quantitative cultures of catheter hub and segments. *J Clin Microbiol*;**21**:357–60.	Hospital based.
Lipman TO, 1993. The cost of TPN is the price right? *J Parent Ent Nutr*;**17**:199–200.	Hospital based.
Lipman TO, 1990. Efficacy and safety of TPN. *Nutrition*;**6**:319–29.	Review – no new empirical data.
Lokich JJ, *et al,* 1985. Complications and management of implanted venous access catheters. *J Clin Oncol*;**3**:710–17.	Chemotherapy, not HPN.
MacFarlane K, *et al,* 1991. A usage evaluation of total parenteral nutrition in paediatric patients. *J Parent Ent Nutr*;**15**:85–8.	Hospital based.
Macfie J, Nordenstrom J, 1992. Full circle in parenteral nutrition. *Clin Nutr*;**11**:237–9.	Historical. Pre-1980.
MacRitchie KJ, 1978. Life without eating or drinking. *Can Psych Assoc J*;**23**:373–9.	No empirical data.
Madan M, *et al,* 1994. Right atrial electrocardiography; a technique for the placement of central venous catheters for chemotherapy or intravenous nutrition. *Br J Surgery*;**81**:1604–5.	Not relevant to the review.
Mahmood T, Rubin AD, 1992. Home based intravenous therapy for oncology patients. *N Jersey Med*;**89**:43–6.	No empirical data.
Mailloux RJ, *et al,* 1993. Pulmonary embolism as a complication of long term total parenteral nutrition. *J Parent Ent Nutr*;**17**:578–82.	No empirical data.
Maki DG, *et al,* 1988 An attachable silver impregnated cuff for prevention of infection with central venous catheters. A prospective randomised multicentre trial. *Am J Med*;**85**:307–14.	Short-term hospital TPN.
Makismak M, *et al,* 1982. Comparison of the pediatric broviac silastic catheter with a standard no 3 french silastic catheter for central venous alimentation. *J Paed Gastroenterol Nutr*;**1**:227–32.	Overlapping data. Old data (pre-1980).
Malone M, Howard L. Long term hyperalimentation. *Curr Opin Gastroenterology* 1994;**10**:227–34.	Data included elsewhere.
Matuchansky C, *et al,* 1981. Cyclic (nocturnal) TPN in hospitalised adult patients with severe digestive diseases. Report of a prospective study. *Gastroenterology*;**81**:433–7.	Hospital based.

continued

continued

Study	Reason for exclusion
Matuchansky C, *et al,* 1992. Cyclical parenteral nutrition. *Lancet*;**340**:588–92.	No new data.
May J, *et al,* 1993. Peripheral and central parenteral nutrition; a cost comparison analysis. *Health Trends*;**25**:130–2.	Hospital based.
McGill DB, 1974. Long term parenteral nutrition. Letter. *Gastroenterology*;**67**:195–6.	Historical. Pre-1980.
Messing B, *et al,* 1983. Does total parenteral nutrition induce gallbladder sludge formation and lithiasis. *Gastroenterology*;**84**:1012–19.	Hospital based.
Miglioli M, Pironi L, 1995. Chronic intestinal pseudo obstruction. *Clin Nutr*;**14**:S21–3.	Review, no new data.
Mhugal M, Irving MH, 1986. HPN in the UK and Ireland. *Lancet*;**i**:383–7.	Data included elsewhere.
Milewski PJ, Irving MH, 1980. Parenteral nutrition in Crohn's disease. *Dis Colon Rectum*;Sept:395–400.	Only 3 HPN, included elsewhere.
Miller SJ, *et al,* 1990. Antibiotic therapy of catheter infections in patients receiving HPN. *J Parent Ent Nutr*;**14**:143–7.	Not an inception cohort.
Moley JF, *et al,* 1986. HPN for patients with advanced intraperitoneal cancers and gastrointestinal dysfunction. *J Surg Oncol*;**33**:186–9.	Only 3 patients. No empirical data.
Monturo CA, *et al,* 1990. Efficacy of thrombolytic therapy for occusion of long term catheters. *J Parent Ent Nutr*;**14**:312–4.	Not relevant to the review.
Moukarzel AA, *et al,* 1992. Excessive chromium intake in children receiving TPN. *Lancet*;**339**:385–8.	Not relevant to this review.
Moukarzel AA, *et al,* 1992. Iodine supplementation in children receiving long term TPN. *J Paed*;**121**:252–4.	Not relevant to this review.
Moukarzel AA, *et al,* 1992. Carnitine status of children receiving long term TPN: A longitudinal prospective study. *J Paed*;**120**:759–62.	Not relevant to this review.
Moukarzel AA, *et al,* 1994. 230 patient years experience with home long term parenteral nutrition in childhood. Natural history and life of central venous catheters. *J Paed Surgery*;**29**:1323–7.	Overlapping data.
Mughal M, Irving MH, 1986. HPN in the UK and Ireland. *Lancet*;**i**:383–7.	Data included elsewhere.
Multiple Authors, 1980. HPN in England and Wales; Report on a symposium held at Hope Hospital, Salford, on July 3 1980. *BMJ*;**281**:1407–9.	Data included elsewhere.
Nordenstrom J, 1967. Pioneers in parenteral nutrition. *Postgrad Med J*;**43**:307–16.	Historical. Pre-1980.
Nordenstrom J, Thorne A, 1994. Benefits and complications of parenteral nutrition support. *Eur J Clin Nutr*;**48**:531–7.	Hospital based review, no new data.
Nussbaum MS, 1992. Total parenteral nutrition and tumour metastases (letter). *J Parent Ent Nutr*;**16**:86–7.	No empirical data (letter).
O'Brien DD, *et al,* 1986. Recommendations of nutrition support teams promote cost containment. *J Parent Ent Nutr*;**10**:300–302.	Hospital based.
O'Keefe SJD, *et al,* 1994. Recurrent sepsis in HPN patients; an analysis of risk factors. *J Parent Ent Nutr*;**18**:256–63.	Not an inception cohort.
Parrish RH, *et al,* 1982. Behavioral management concepts with application for HPN patients. *Drug Intell Clin Pharm*;**16**:581–6.	No empirical data.
Passaro M, *et al,* 1994. Long term silastic catheters and chest pain. *J Parent Ent Nutr*;**18**:240–2.	Not an inception cohort. Case report.
Payne-James JJ, *et al,* 1992. Artificial nutritional support in hospitals in the UK – 1991; second national survey. *Clin Nutr*;**11**:187–92.	Hospital based.
Pennington CR, 1992. HPN; an appraisal. *Scot Med J*;**37**:69–70.	No new data.

Study	Reason for exclusion
Perl M, 1980. Psychological aspects of long term HPN. *J Parent Ent Nutr*;**4**:554–60.	Duplicate data.
Perl M, 1987. HPN and the family. *Psych Clinics North Am*;**10**:121–7.	No empirical data.
Perl M, *et al,* 1980. Psychological aspects of long term home hyperalimentation. *J Parent Ent Nutr*;**4**:554–60.	Duplicate publication.
Pironi L, *et al,* 1994. Morphologic and cytoproliferative patterns of duodenal mucosa in two patients after long term TPN. *J Parent Ent Nutr*;**18**:351–4.	Case reports only.
Pironi L, *et al,* 1994. Rottura intravenosa spontanea ed embolizzazione di un catetere tipo broviac: caso clinico. *Riv Ital Nutriz Parent Enter*;**12**:24–6.	Case report.
Pironi L, Tognoni G, 1995. Cost benefit and cost effectiveness analysis of home artificial nutrition: reappraisal of available data. *Clin Nutr*;**14**:S87–S91.	Review, no new data.
Pithie AD, Pennington CR, 1987. The incidence, aetiology and management of central vein thrombosis during parenteral nutrition. *Clin Nutr*;**6**:151–3.	Data elsewhere.
Pitt HA, *et al,* 1983. Increased risk of cholelithiasis with prolonged total parenteral nutrition. *Am J Surgery*;**145**:106–12.	Duplicate data.
Pollack PF, *et al,* 1981. 100 patient years experience with the broviac silastic catheter for central venous nutrition. 1981. *J Parent Ent Nutr*;**5**:32–6.	Historical. Pre-1980.
Powel-Tuck, *et al,* 1978. Team approach to long term intravenous feeding in patients with gastrointestinal disorders. *Lancet*;**ii**:825–8.	Hospital based. Dated.
Price BS, Levine EL, 1979. Permanent total parenteral nutrition: psychological and social responses of the early stages. *J Parent Ent Nutr*;**3**:48–52.	No empirical data.
Puntis JWL, 1993. Update on intravenous feeding in children. *Br J Intensive Care*;August:299–305.	No HPN outcomes.
Quigley E, *et al,* 1993. Hepatobiliary complications of total parenteral nutrition. *Gastroenterology*;**104**:286–301.	No empirical data.
Rault RMJ, Scribner BH, 1977. Treatment of Crohn's disease with HPN. *Gastroenterology*;**72**:1249–52.	Historical. Pre-1980.
Raviglione MC, *et al,* 1989. Infections associated with Hickman catheters in patients with AIDS. *Am J Med*;**86**:780–6.	Results for HPN patients not separated.
Rhoads JE, *et al,* 1981. The development of intravenous hyperalimentation. *Surg Clinics North Am*;**61**:429–35.	Historical. Pre-1980.
Robinovitch AE, 1981. HTPN; a psycho social viewpoint. *J Parent Ent Nutr*;**5**:522–5.	No empirical data.
Rombeau JL, Rolandelli RH, *et al,* 1987. Enteral and parenteral nutrition in patients with enteric fistulas and short bowel syndrome. *Surg Clinics North Am*;**67**:551–71.	No empirical data.
Rothkopf M, 1990. Fuel utilisation in neoplastic disease; implications for nutritional support in cancer patients. *Nutrition*;**66**:14S–16S.	No empirical data.
Ryan J, *et al,* 1974. Catheter complications in TPN. A prospective study of 200 consecutive patients. *N Engl J Med*;**290**:757–61.	Hospital based.
Sax HC, Souba WW, 1993. Enteral and parenteral feeding. *Med Clinics North Am*;**77**:863–80.	Hospital based.
Schneider PJ, Mirtallo JM, 1981. Home parenteral nutrition programs. *J Parent Ent Nutr*;**5**:157–60.	No relevant data.
Schropp K, *et al,* 1988. Catheter related sepsis; a review of experience with Broviac and Hickman catheters. *Nutrition*;**4**:195–200.	Data included in other papers.
Scott NA, *et al,* 1991. Spectrum of intestinal failure in a specialised unit. *Lancet*;**337**:471–3.	Hospital based.

continued

continued

Study	Reason for exclusion
Scribner BH, Cole JJ, 1979. Evolution of the technique of home parenteral nutrition. *J Parent Ent Nutr*;**3**:58–61.	Historical. Pre-1980.
Scribner BH, *et al,* 1970. Long term total parenteral nutrition. The concept of an artificial gut. *JAMA*;**212**:457–63.	Historical. Pre-1980.
Shanbhogue LKR, Molenaar JC, 1994. Short bowel syndrome; Metabolic and surgical management. *Br J Surgery*;**81**:486–99.	Review – no new empirical data.
Shapiro RS, 1990. Ethical and legal issues in the use of TPN. *Nutrition*;**6**:397–401.	No empirical data.
Sharp JW, Roncagli T, 1992. HPN in advanced malignancies. *J Parent Ent Nutr*;**16**:190–1.	No empirical data.
Sharp JW, Roncagli T, 1993. HPN in advanced cancer. *Cancer Pract*;**1**:119–24.	No empirical data.
Shenkin A, *et al,* 1986. Essential trace element provision to patients receiving home intravenous nutrition in the UK. *Clin Nutr*;**5**:91–7.	Data not relevant to the review.
Shike M, *et al,* 1981. A possible role of vitamin D in the genesis of parenteral nutrition induced metabolic bone disease. *Ann Internal Med*;**95**:560–8.	Not an inception cohort. Old data. Bulk of the paper not relevant.
Shils ME, 1975. A program for total parenteral nutrition at home. *Am J Clin Nutr*;**28**:1429–35.	Historical. Pre-1980.
Shils ME, 1984. Historical aspects of minerals and vitamins in parenteral nutrition. *Federation Proc*;**43**:1412–16.	Historical. Pre-1980.
Silk D, 1995. Malnutrition in hospital. *Hosp Update*; February:55–61.	No new data.
Singer P, *et al,* 1992. Clinical and immunological effects of lipid based parenteral nutrition in AIDS. *J Parent Ent Nutr*;**16**:165–7.	? repetitive data. Also ? relevance.
Steinbrook R, Lo B, 1988. Artificial feeding – solid ground not a slippery slope. *N Engl J Med*;**318**:286–90.	No empirical data.
Stephens L, *et al,* 1995. Are clinical signs accurate indicators of the cause of central venous catheter occlusion. *J Parent Ent Nutr*;**19**:75–9.	Hospital based.
Stokes MA, Irving MH, 1988. How do patients with Crohn's disease fare on HPN? *Dis Colon Rectum*; June:454–8.	Data presented elsewhere.
Stokes MA, 1988. HPN; a review of 100 patient years of treatment in 76 consecutive cases. *Br J Surgery*;**75**:481–3.	Data included in other papers.
Stokes MA, Irving MH, 1989. Mortality in patients on HPN. *J Parent Ent Nutr*;**13**:172–5.	Data included elsewhere.
Storch K, 1992. Home parenteral nutrition. *N Jersey Med*;**89**:36–40.	No empirical data.
Stuart R, *et al,* 1990. Perioperative nutrition in cancer patients. *Nutrition*;**6**:4S–7S.	Hospital based.
Treasadern JC, *et al,* 1984. Maintainance of pregnancy in a HPN patient. *J Parent Ent Nutr*;**8**:199–202.	Not relevant.
Twomey PL, Patching SC, 1985. Cost effectiveness of nutritional support. *J Parent Ent Nutr*;**9**:3–10.	Perioperative TPN.
Vars HM, 1980. Early research in parenteral nutrition. *J Parent Ent Nutr*;**4**:467–8.	Historical interest only.
Veleisis RA, *et al,* 1980. Prospective controlled trial of parenteral nutrition associated cholestatic jaundice: effect of protein intake. *J Paed*;**96**:893–7.	Hospital based.
Watters DAK, *et al,* 1984. Changes in liver function tests associated with parenteral nutrition. *J Roy Coll Surgeons Edin*;**29**:339–44.	Hospital based.
Wilcock H, *et al,* 1991. Artificial nutrition support for patients in the Cambridge health district. *Health Trends*;**23**:93–100.	No outcomes for the 3 HPN patients included in this study.

Study	Reason for exclusion
Wilkinson AW, 1963. Historical background of intravenous feeding. *Nutr Dieta*;**5**:295–7.	Historical. Pre-1980.
Williams N, *et al,* 1994. Incidence and management of catheter related sepsis in patients on HPN. *Br J Surgery*;**81**:392–4.	Not an inception cohort.
Williams N, *et al,* 1993. The incidence and management of catheter occlusion in patients on HPN. *Clin Nutr*;**12**:344–9.	Not an inception cohort.
Wilmore D, Dudrick SJ, 1968. Growth and development of an infant receiving all nutrients exclusively by vein. *JAMA*;**203**:140–4.	Historical interest only.
Winters RW, *et al,* 1984. History of parenteral nutrition in paediatrics with emphasis on amino acids. *Federation Proc*;**43**:1407–11.	Historical. Pre-1980.
Wood RJ, 1985. Calciuretic effect of cyclic versus continuous TPN. *Am J Clin Nutr*;**41**:614–9.	Small number of patients. No controls, no randomisation. Short period of TPN.
Woolman SL, *et al,* 1979. Zinc in TPN; requirements and metabolic effects. *Gastroenterology*;**76**:458–67.	Not relevant to the review.

Appendix 1

The history of HPN

Home parenteral nutrition is a life-saving technology which was developed in the USA during the late 1960s (Scribner,1970; Dudrick, 1968; Wilmore, 1968). It became possible due to the production of safe, stable solutions of protein, fat and glucose. Dudrick and colleagues (1967) showed that puppies fed by intravenous nutrition, developed and grew normally. Wilmore and Dudrick (1968) described their initial efforts to provide intraven-ous nutrition for a neonate with intestinal atresia. A solution containing the required nitrogen, calories and trace elements, was infused into the superior vena cava for a period of 44 days. Normal growth and development was seen to occur. This would appear to be the first well-documented case of a human patient not only gaining weight, but passing into a significant and continuing anabolic state on the basis of parenteral nutrition alone. Using this technique, Dudrick and colleagues (1969) reported the progress of 30 adult patients; they noted good wound healing, weight gain, increased strength and fistula closure in some patients.

Scribner (1970) described the concept of an artificial gut which could provide prolonged nutritional support for a patient incapable of enteric feeding. In Scribner's system, an arterio-venous shunt was used for venous access and nutrients were delivered by gravity or pump. The external arterio-venous shunt was created using a silicone rubber tube with a side arm for the infusion of nutrients. Scribner postulated that once the system was up and running it should be possible to discharge the patient home and with appropriate training he or she should be self caring. This is the first mention of HPN in the literature. The likely costs involved in maintaining a patient on prolonged nutrition at that time were $5 per day or $1800 per year, with an initial outlay of approximately $1000 for pumps, etc. Scribner and Cole (1979) subsequently criticised their study (1970) as being rather premature. The system which they described worked well in the uraemic patients whom they used as controls; however, when it was tried in malnourished patients the standard arterio-venous shunts clotted in almost 100% of cases. The adverse effects of poor quality veins and normal clotting parameters on graft function had not been anticipated. When they realised that the shunts were not going to be suitable they were forced into trying a new technique which involved inserting a Tenckhoff catheter via the subclavian route into the right atrium. This catheter initially worked very well and adequate nutrition was restored. Unfortunately, the mechanical trauma suffered by the superior vena cava resulted in thrombosis, obstruction and failure of the catheter. The stiff Tenckhoff catheters were replaced by a newly-developed flexible, soft, silicone rubber tube. This basic change in the design meant that vascular trauma was minimised, resulting in successful long-term venous access.

Broviac (1973) reported experience with a silicone rubber right atrial catheter. The thin intravascular portion was positioned in the right atrium for maximal dilutional effect and the thicker extravascular portion is brought out via a long tunnel on the anterior chest wall. A Dacron® cuff was positioned beneath the skin and, after about 3 weeks, the ingrowth of collagen fibres led to a firm anchor being created. The catheter was flexible, inert and anti-thrombogenic, allowing it to move with each heartbeat, ensuring that the tip did not irritate one particular portion of endocardium. Broviac reported local and generalised infection as the main complication and a mean catheter life of 144 days per patient. This compared favourably with the previously reported average catheter lifespan of 24 days (Wilmore, 1969).

The gravity system of infusion was found to be unreliable when used overnight and required constant vigilance. A powered portable device, contained in a specially desiged vest, was developed which eliminated this problem. Some of the patients criticised the 'wearable' infusion device which delivered the fluids during the day. It was seen as cumbersome and unnecessary and was soon abandoned, being replaced by portable stands and, later, by cyclical night-time infusion.

Jeejeebhoy (1973) reported the experience of a patient who had received HPN for 23 months without complications and with good rehabilitation. The lipid infusions were given separately, as they could not pass through the filters. The lipid infusion provided half of the required calories and was regarded as an absolute requirement if

essential fatty acid deficiency was to be avoided. Jeejeebhoy also suggested that the use of fat prevented the development of a fatty liver.

As experience grew with the technique of home parenteral nutrition further favourable reports appeared (Ivey, 1975; Bordos, 1975; Shils, 1975; Heizer, 1977). An estimate of costs in 1975 revealed that the initial basic costs were about $700 but the costs of the infusions had increased to $7200–$12,000 per year depending on requirements and on the type of amino acid infusion used. Scribner treated 40 patients in this manner; five patients died but four deaths were as a result of the underlying disease. The average length of treatment was 11 months. The commonest complications were sepsis, thrombo-embolism, metabolic imbalance and fat infiltration of the liver. The choice of patients in Scribner's series was of interest as the diagnostic subgroups were very similar to current practice in the UK. The main indication for HPN being benign disease (Crohn's and MVD). Current practice in the USA has changed significantly and now includes large numbers of patients with malignant disease.

Cases of intestinal failure which were previously beyond the help of medical technology became 'treatable' (Bordos, 1975). Shils (1975) reported his experience with 11 patients maintained at home on intravenous nutrition. He used a standard portable pump system which was equipped with infusion rate monitors. This allowed safe administration overnight, thereby allowing patient freedom during the day and improving the patient's quality of life. Shils noted that most patients were able to learn the necessary techniques within a few weeks if they received daily training sessions. The more controversial aspect of this paper deals with the selection of patients suffering from terminal malignancy; even though this paper was published 20 years ago, controversy still exists. The author justifies his decision to use HPN for these patients with the statement that they are often able to spend a rewarding last few months (or even years, in some cases) at home.

HPN technology diffused to Europe from the USA in the late 1970s and this systematic review examines the world experience from 1980 onwards.

Appendix 2

Review protocol

Introduction

The aim of this review is to locate, acquire and synthesise studies concerning the use, effectiveness and cost-effectiveness of home parenteral nutrition. The review will fall into five main sections:

Section 1. What patients have received HPN?
Section 2. What has been the experience of patients on HPN programmes?
Section 3. (a) How have HPN programmes been organised, and what techniques and equipment have been used, and to what effect?
(b) What comparative information is available on effectiveness?
Section 4. What evidence exists on the cost-effectiveness of HPN?
Section 5. What questions about the provision of HPN could be answered with additional research, and what design of study would be most suitable?

For each of the above sections we will consider both adults and children.

Searching the HPN literature suggests that there are very few comparative studies available. Most of the literature consists of case series. The questions above have been formulated bearing this is mind, so as to make best use of what information is available.

Section 1

Research question

What patients have been entered into HPN programmes with respect to numbers, age, sex, diagnoses, setting (country) and what trends exist?

Studies to be included

1. Surveys of HPN use.
2. Information from databases of HPN users.
3. Data from cohorts of HPN patients.

Points for assessing validity

1. Are the patient numbers based on new patients in a given period of time, or from a cross-sectional sample?
2. Was the data collected prospectively or retrospectively?
   [A longitudinal inception study will provide actual patient numbers being treated on HPN by sub-group, whilst a cross-sectional sample will only provide a snapshot of the sort of patients being treated with HPN. The results will differ according to the length of time spent on HPN. The results of the two types of studies will be interpreted separately. Retrospective data collection is prone to be less complete than prospective data collection.]
3. What proportion of people were sampled and how was the sample chosen?
4. What group was the sample selected from and how representative is the sample?
5. Was the sample coverage validated, and if so was it found to be acceptable?
   [Complete assessment or random sampling are the best ways of maintaining representativeness. Both rely on the correct identification of a sampling frame. When these are not available it may be possible to validate sample coverage by taking a sample using a second source and noting the degree of similarity in sample members.]
6. For what proportion of selected people was no information available?
7. How complete was the data that was acquired?
   [Non-response and missing data in a survey reduces validity.]

Data extraction (Section 1)

Study (Code Number)
Title
Journal
Author
Country Setting Unit size (new cases per year)

Eligibility

Does it include HPN patient numbers?
Is it a survey, database or cohort of HPN-treated patients?

Validity

Is it a cross-sectional or longitudinal study?
Is it retrospective or prospective?
What were the dates covered?
What was the source of data?
Who was eligible to be in the sample? (What was the sampling frame?)
What sampling fraction was used and was it random?
How was the sampling frame validated?

Patient numbers

Year	Crohn's	MVD	Pseud	Cancer	AIDS	Other	Mean age	Age range	M:F

Section 2

Research question

What has been the experience of patients on HPN programmes by diagnosis?
(i) What is the duration of HPN use?
(ii) What is the expected survival of HPN users?
(iii) What are the HPN discontinuation rates, and for what reasons?
(iv) What complications occur, and how often?
(v) What quality of life is experienced by patients receiving HPN?
Studies which have been used in Section 1 may also be of use in this section.

Inclusion criteria

1. Studies reporting the experience of inception cohorts of HPN users.
2. Studies giving information on length of treatment, mortality, complications, or quality of life.

Validity

1. Is data collected prospectively or retrospectively?
2. What cohort was recruited?
3. How much of the cohort was successfully recruited?
4. How complete was the follow-up?
5. What procedure was used to detect complications?
6. What quality-of-life instrument was used and how was it validated?

Ascertainment of outcomes should be free from bias. Where excessive patient investigations are carried out this may detect a higher number of events than in case series with less active investigation. The instruments used to measure subjective issues like quality of life need to be validated.

A potential problem in this area is the choice of denominators for the calculation of rates, whether they are patient numbers, patient years, and the way in which data has been analysed. When reporting rates, it is important to make the distinction between per 1000 per year, which implies a group of patients are all followed-up for the same length of time, and per 1000 patient years.

Data Extraction (Section 2)

Study (Code Number)
Title
Journal
Author
Country Setting Unit size (new cases per year)

Eligibility
Is a cohort of new HPN patients identified, recruited and followed?
What outcome information is contained?

Validity
Is data collected prospectively or retrospectively?
What proportion of the cohort was recruited?
How complete was the follow-up?
What procedure was used to detect complications?
What quality-of-life instrument was used and how was it validated?
What denominator is used to calculate the rates?

Type of study
Results
Period
Sample size
Age description at recruitment.
Male:Female

Complications

	Crohn's	MVD	Pseud	Cancer	AIDS	Other	

Quality of life

	Crohn's	MVD	Pseud	Cancer	AIDS	Other	

Survival

	Crohn's	MVD	Pseud	Cancer	AIDS	Other	
Year							
Year							
Year							

Duration of HPN use

	Crohn's	MVD	Pseud	Cancer	AIDS	Other	

Reasons for stopping HPN

	Crohn's	MVD	Pseud	Cancer	AIDS	Other	
Sample							
Still on							
Recover							
Dead							
Lost							

Section 3a

Research question

How have HPN programmes been organised, and what techniques and equipment have been used, and to what effect?

Studies to be included.

Surveys assessing issues in the delivery of HPN since 1980.

Issues

Only one study is known of which has assessed how HPN programmes have been organised.

Section 3b

Research question

Has HPN been compared with any alternative therapies? Have larger centres been compared with smaller centres? Have different techniques used in HPN been compared? What comparative information is available?

Studies to be included

1. Does the study look at: Alternatives?
   Techniques or equipment?
   The size of centres?
2. Does the study report the experience of patients on HPN?

Validity

1. What was the study design? Descriptive/Comparative?
2. Is data collection prospective or retrospective?
3. Was a comparison made?
4. How were allocations to treatment made?
5. Was follow-up complete?
6. Were the groups comparable with respect to age and diagnosis?
7. What outcomes were measured?
8. Was the length of follow-up more than 3 months in all cases?
9. How were outcomes assessed?

The validity of comparisons between different procedures, etc., will greatly depend on the study design. In addition, different aspects of validity will be important to different designs. The studies will be grouped according to design in the analysis.

Data Extraction (Section 3)

Study (Code Number)
Title
Journal
Author
Country Setting Unit size (new cases per year)

Eligibility

[This has been kept vague because of the lack of relevant studies.]

Does the study evaluate patient experience on HPN?
    What outcomes does it measure?
What technology does the paper assess?
    Organisation, management or delivery?
    Techniques or equipment?
    Patient education or nutrition?

Validity

What was the study design?
Is a comparison made, if so between what?
How were allocations to the different groups made?
What factors of comparability were checked at inception?
How complete was follow-up?
Was follow-up long enough for morbidity and mortality to occur?
What outcomes were assessed?
Was there potential for bias in outcome assessment (masked assessment, etc.)?

Patients included

Sample size
Description of age
Male:Female
Diagnoses

Interventions

How was the programme organised?
Nutrition team involvement (advisory, direct care, monitoring)
Home care company
Local pharmacy
Trained at home or in hospital

Outcomes

Outcomes measured and results

Catheters

Type	Sample	Sepsis	Thrombosis	Dislodge	Other	Lost
Reservoir						
Brov/Hick						

Results for comparisons

Observed difference and confidence interval
Statistical significance
Authors' conclusion

Section 4

Research question

What evidence exists on the cost-effectiveness of HPN? What alternatives to HPN have been considered?

Inclusion criteria

Any economic evaluation of an HPN programme
[Very few economic analyses are known.]

Validity

1. What methodological technique has been applied?
2. What was the comparison made with?
3. What perspective was adopted?
4. Were all costs considered?
5. Were costs measured appropriately?
6. Were all outcomes considered?
7. Were they measured appropriately?
8. How was quality of life assessed?
9. Was a marginal analysis performed?
10. Was the robustness of the result tested in a sensitivity analysis?

Data extraction (Section 4)

Study (Code Number)
Title
Journal
Author

Country	Setting	Unit size (new cases per year)

Eligibility

Does the study evaluate both costs and benefits of HPN programmes?

Validity

What methodological technique has been applied?
What was the comparison made with?
What perspective was adopted?
What costs were considered?
Were all important costs considered?
Were costs measured appropriately?
Were all outcomes considered?
Were they measured appropriately?
How was quality of life assessed?
Was a marginal analysis performed?
Were assumptions tested in a sensitivity analysis?

Results

What did the study find?

Section 5

Which questions remain unanswered?
What gaps in knowledge exist?
What clinical issues need to be addressed?
What methodological issues need to be addressed?

Literature search strategy and study retrieval

The aim of this search is to provide a comprehensive list of primary studies. The field of home parenteral nutrition is fairly well-defined and indexed. This means that it is relatively easy to search electronic databases. Preliminary work revealed that there were very few randomised, controlled trials pertaining to

some aspects of HPN technology. HPN is often life-saving which makes comparative investigation very difficult, especially given that there are few alternative treatment strategies. For this reason it was decided that we should attempt to collect all literature concerning the technology of HPN. The search would therefore include all types of study design and include all possible aspects of HPN technology.

The search will not be confined to studies published in English. There are only a small number of centres in Europe who regularly publish HPN data. These centres will be asked to supply any data published in a foreign language and these studies will be translated. It is unlikely that any significant foreign language study will be missed using this policy.

Before starting the search, advice will be sought from an information scientist based at the NHS Centre for Reviews and Dissemination, York, and from a senior medical librarian based at Hope Hospital, Salford.

The following possible sources of data were identified.
- Electronic databases
- Hand searching of relevant journals
- Personal literature collections
- Conference proceedings
- Writing to all major centres in Europe and the USA
- Science citation database
- Scanning reference lists of studies located

Electronic databases
The following key words will be used to search the databases.

Home care services/Economics, Hospital-based economics, Organisation, Statistical.
Home infusion therapy/Economics, Methods, Nursing.
Home parenteral nutrition, Home total parenteral nutrition, Home ambulatory nutrition/Therapy, Organisation, Economics, Complications.
Total parenteral nutrition/Home.
Total Parenteral/Nutrition, Home.
Nutritional support.
Nutrition disorders/Therapy.
Short bowel syndrome.
Intestinal failure.
Intestinal fistulas/Therapy.
Crohn's disease/Therapy.
Inflammatory bowel disease/Therapy.
Malignant bowel obstruction.
Intestinal obstruction/Therapy.
Mesenteric vessel occlusion/Thrombosis/Embolisation.
Mesenteric vascular disease/Thrombosis/Embolisation.
Mesenteric artery occlusion/Thrombosis/Embolisation.
Pseudo-obstruction.
Radiation enteritis.
Intestinal radiation damage.
Catheters indwelling.
Central venous access/Devices.
Catheters implantable.
Subcutaneous reservoirs.
Vascular access/Devices.
Quality of life/Home parenteral nutrition.
Economics/Home parenteral nutrition.

It is well-documented in the literature that many studies can be missed if searches are limited to only one database. We will search a number of databases as outlined below. The databases will be searched from 1968 onwards, i.e. from the origins of HPN.

1. MEDLINE (*Index Medicus* on-line)
2. EMBASE (*Excerpta Medica* on-line)
3. Science Citation Index
4. UNCOVER
5. CINAHL (US database, mainly nursing based)
6. CAREDATA
7. Food Science and Technology Abstracts
8. NTIS (US Research Reports)
9. PASCAL (French, scientific database which covers medicine)
10. PSYCHLIT
11. Economic Literature Index

Hand searching
The following journals will be hand searched for the following years; January 1980–July 1995 (if available during these years)

- *Journal of Parenteral and Enteral Nutrition*
- *Clinical Nutrition*
- *American Journal of Clinical Nutrition*
- *Nutrition*
- *Clinical Gastroenterology*
- *Nutrition Reviews*
- *Annals of Nutrition and Metabolism*
- *Nutrition and Cancer*
- *Nutrition and Health*
- *Journal of Paediatric Gastroenterology and Nutrition*

Conference proceedings
Proceedings will be obtained for the annual conferences of the following bodies.

- ASPEN (American Society for Parenteral and Enteral Nutrition) 1993, 1994, 1995
- ESPEN (European Society for Parenteral and Enteral Nutrition) 1993, 1994, 1995
- BAPEN (British Association for Parenteral and Enteral Nutrition) 1994

The published abstracts for these meetings will be examined and, if the abstracts are of specific relevance to the review, attempts will be made to obtain papers from the authors. The notoriously unreliable nature of data contained in abstracts means that we do not plan to use abstracts for data extraction.

Personal literature collections
We will examine the files of Professor Sir Miles Irving who was one of the founders of HPN in the UK. Over the past 20 years, he and his research staff have published widely on the technology of HPN, and this has led to the accumulation of many relevant papers.

Letters to experts
We will contact major European and American centres and explain the basis of the systematic review. The centres and experts were chosen because they publish regularly on aspects of home parenteral nutrition or they were members of the ESPEN Home Artificial Nutrition Study Group. The systematic review will be explained and the research questions we hope to answer will be included. We will request any relevant literature, published, unpublished and in progress. Permission will be sought if we need to include any unpublished work.

Visits to major meetings
Two members of the project team (DMR and JLS) will attend the ESPEN meeting in Rome (September 1995) and the BAPEN meeting (December 1995). Attempts will be made to meet with experts from Europe and the USA. The basis of the systematic review will be explained and comments invited. Those experts that we meet will be asked to supply any literature relating to HPN if they have not already done so.

Selection of eligible studies, checking validity and data extraction

One researcher (DR) will initially check articles for eligibility for each of the research questions, grade their validity, and extract the necessary data. A second researcher (JJD) will validate these decisions by processing a random sample of studies that are suitable and studies that the first researcher deemed to be unsuitable.

Where any researcher finds ambiguity or is unsure in any aspect of these selection procedures he will obtain independent advice from a third researcher.

Study synthesis

It is unlikely that it will be possible to combine the results of the research in a quantitative manner, it is anticipated that there are very few randomised, controlled trials and a lack of comparative studies, or any studies of similar design. Therefore, the results will be discussed in a qualitative manner. This will take into account the magnitude of the results, the size and validity of the studies together with any moderating factors.

Protocol modifications

Any further questions that arise from the review will be addressed. This protocol will be adjusted accordingly and the additional questions will be highlighted as *post-hoc* hypotheses generated by the review.

Acute Sector Panel

Chair: Professor John Farndon, University of Bristol †

Professor Senga Bond, University of Newcastle-upon-Tyne †

Professor Ian Cameron, SE Thames RHA

Ms Lynne Clemence, Mid-Kent Health Care Trust †

Professor Cam Donaldson, University of Aberdeen †

Professor Richard Ellis, St James's University Hospital, Leeds †

Dr David Field, Leicester Royal Infirmary NHS Trust †

Mr Ian Hammond, Hillingdon HA †

Professor Adrian Harris, Churchill Hospital, Oxford

Dr Chris McCall, General Practitioner, Dorset †

Professor Alan McGregor, St Thomas's Hospital, London

Mrs Wilma MacPherson, St Thomas's & Guy's Hospitals, London

Professor Jon Nicoll, University of Sheffield †

Professor John Norman, Southampton University

Professor Gordon Stirrat, St Michael's Hospital, Bristol

Professor Michael Sheppard, Queen Elizabeth Hospital, Birmingham †

Dr William Tarnow-Mordi, University of Dundee

Professor Kenneth Taylor, Hammersmith Hospital, London †

Diagnostics and Imaging Panel

Chair: Professor Mike Smith, University of Leeds †

Professor Michael Maisey, Guy's & St Thomas's Hospitals, London*

Professor Andrew Adam, UMDS, London †

Dr Pat Cooke, RDRD, Trent RHA

Ms Julia Davison, St Bartholomew's Hospital, London †

Professor MA Ferguson-Smith, University of Cambridge †

Dr Mansel Hacney, University of Manchester

Professor Sean Hilton, St George's Hospital Medical School, London

Mr John Hutton, MEDTAP Europe Inc., London †

Professor Donald Jeffries, St Bartholomew's Hospital, London †

Dr Andrew Moore, Editor, Bandolier †

Professor Chris Price, London Hospital Medical School †

Dr Ian Reynolds, Nottingham HA

Professor Colin Roberts, University of Wales College of Medicine †

Miss Annette Sergeant, Chase Farm Hospital, Enfield

Professor John Stuart, University of Birmingham

Dr Ala Szczepura, University of Warwick †

Mr Stephen Thornton, Cambridge & Huntingdon Health Commission

Dr Gillian Vivian, Royal Cornwall Hospitals Trust †

Dr Jo Walsworth-Bell, South Staffordshire Health Authority †

Dr Greg Warner, General Practitioner, Hampshire †

Methodology Panel

Chair: Professor Anthony Culyer, University of York †

Mr Doug Altman, Institute of Health Sciences, Oxford †

Professor Michael Baum, Royal Marsden Hospital

Professor Nick Black, London School of Hygiene & Tropical Medicine †

Professor Martin Buxton, Brunel University †

Dr Rory Collins, University of Oxford

Professor George Davey-Smith, University of Bristol

Professor Ray Fitzpatrick, University of Oxford †

Professor Stephen Frankel, University of Bristol

Dr Stephen Harrison, University of Leeds

Mr Philip Hewitson, Leeds FHSA

Professor Richard Lilford, Regional Director, R&D, West Midlands †

Mr Nick Mays, Kings Fund Institute, London †

Professor Ian Russell, University of York †

Professor David Sackett, Centre for Evidence Based Medicine, Oxford †

Dr Maurice Slevin, St Bartholomew's Hospital, London

Dr David Spiegelhalter, Institute of Public Health, Cambridge †

Professor Charles Warlow, Western General Hospital, Edinburgh †

Pharmaceutical Panel

Chair: Professor Tom Walley, University of Liverpool †

Professor Michael Rawlins, University of Newcastle-upon-Tyne*

Dr Colin Bradley, University of Birmingham

Professor Alasdair Breckenridge, RDRD, Northwest RHA

Ms Christine Clarke, Hope Hospital, Salford †

Mrs Julie Dent, Ealing, Hammersmith and Hounslow HA, London †

Mr Barrie Dowdeswell, Royal Victoria Infirmary, Newcastle-upon-Tyne

Dr Desmond Fitzgerald, Mere, Bucklow Hill, Cheshire †

Dr Alistair Gray, Wolfson College, Oxford †

Professor Keith Gull, University of Manchester

Dr Keith Jones, Medicines Control Agency

Professor Trevor Jones, ABPI, London †

Dr Andrew Mortimore, Southampton & SW Hants Health Authority †

Dr John Posnett, University of York

Dr Frances Rotblat, Medicines Control Agency †

Dr Ross Taylor, University of Aberdeen †

Dr Tim van Zwanenberg, Northern RHA

Dr Kent Woods, RDRD, Trent RO, Sheffield †

Population Screening Panel

Chair: Professor Sir John Grimley Evans, Radcliffe Infirmary, Oxford †

Dr Sheila Adam, Department of Health*

Dr Anne Dixon Brown, NHS Executive, Anglia & Oxford†

Professor Dian Donnai, St Mary's Hospital, Manchester †

Professor George Freeman, Charing Cross & Westminster Medical School, London

Dr Mike Gill, Brent & Harrow Health Authority †

Dr JA Muir Gray, RDRD, Anglia & Oxford RO †

Dr Ann Ludbrook, University of Aberdeen †

Professor Alexander Markham, St James's University Hospital, Leeds †

Professor Theresa Marteau, UMDS, London †

Professor Catherine Peckham, Institute of Child Health, London †

Dr Connie Smith, Parkside NHS Trust, London †

Dr Sarah Stewart-Brown, University of Oxford †

Professor Nick Wald, University of London †

Professor Ciaran Woodman, Centre for Cancer Epidemiology, Manchester †

Primary and Community Care Panel

Chair: Professor Angela Coulter, Kings Fund Centre for Health Services Development, London †

Professor Martin Roland, University of Manchester*

Dr Simon Allison, University of Nottingham

Mr Kevin Barton, Bromley Health Authority †

Professor John Bond, University of Newcastle-upon-Tyne †

Professor Shah Ebrahim, Royal Free Hospital, London

Professor Andrew Haines, RDRD, North Thames RHA

Dr Nicholas Hicks, Oxfordshire Health Authority †

Professor Richard Hobbs, University of Birmingham †

Professor Allen Hutchinson, University of Hull †

Mr Edward Jones, Rochdale FHSA

Professor Roger Jones, UMDS, London †

Mr Lionel Joyce, Chief Executive, Newcastle City Health NHS Trust †

Professor Martin Knapp, London School of Economics & Political Science †

Professor Karen Luker, University of Liverpool

Dr Fiona Moss, North Thames British Postgraduate Medical Federation†

Professor Dianne Newham, Kings College, London

Professor Gillian Parker, University of Leicester †

Dr Robert Peveler, University of Southampton †

Dr Mary Renfrew, University of Oxford

Dr John Tripp, Royal Devon & Exeter Healthcare NHS Trust †

* Previous Chair
† Current members

Health Technology Assessment 1997; Vol. 1: No. 1

Copies of this report can be obtained from:

The National Coordinating Centre for Health Technology Assessment,
Mailpoint 728, Boldrewood,
University of Southampton,
Southampton, SO16 7PX, UK.
Fax: +44 (0) 1703 595 639 Email: hta@soton.ac.uk
http://www.soton.ac.uk/~hta

ISSN 1366-5278