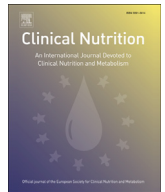




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Meta-analyses

A systematic review with meta-analysis of survival, quality of life and cost-effectiveness of home parenteral nutrition in patients with inoperable malignant bowel obstruction[☆]

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SUMMARY

Background and aims: Inoperable bowel obstruction is the most common and judicious indication for long term parenteral nutrition in patients with palliative malignancy. Considerable uncertainty exists about the survival length, quality of life (QOL) and associated health economics of home parenteral nutrition (HPN) for this patient group.

Methods: A systematic review was carried out for survival length and QOL of adult patients treated with HPN due to malignancy causing inoperable bowel obstruction in the palliative phase. Whenever possible, individual patient data were extracted to allow meta-analyses. Health economic evaluation was undertaken to calculate cost and incremental cost effectiveness ratio (ICER).

Results: Twelve studies involving 437 patients, met the inclusion criteria. Meta-analyses of extracted survival length data, representing the largest published cohort of HPN patients with palliative malignancy and inoperable bowel obstruction ($n = 244$ patients), revealed a mean survival of 116 days, median 83 days, with 45% and 24% still alive at 3 and 6 months, and only 2% survival at one year. Limited evidence suggests QOL deteriorated before death in a highly symptomatic group. The ICER is £176,587 per quality adjusted life year.

Conclusions: This is the first health economic evaluation and systematic review of survival and QOL for patients with inoperable bowel obstruction receiving HPN during the palliative phase of malignancy. Meta-analyses reveal a short survival and health economic analysis demonstrates high associated costs. This information can be used by clinicians to inform and guide selection of patients in this cohort for HPN treatment.

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Q2 1. Introduction

Bowel obstruction (BO) is a recognised complication of advanced malignancy and contributes to malnutrition with adverse effects on survival length and quality of life. At first presentation of BO secondary to malignancy surgical resolution can be achieved in the majority of cases [1], but recurrent BO can render repeat surgery unsuccessful, hence termed inoperable bowel obstruction (IBO). If not already so, the focus of treatment for the patient becomes palliation at this stage. Survival of palliative patients with

malignant IBO is likely to be limited (<2 weeks to 2 months) without parenteral support [2] depending on grade of obstruction and pre-morbid state.

In several countries there has been a trend towards increasing use of home parenteral nutrition (HPN) in palliative malignancy, with and without BO [3–6], but considerable uncertainty exists about indications. Advocates argue that HPN extends survival and facilitates palliative chemoradiotherapy; but others argue that the treatment is expensive, with a high burden to patients and family members during limited remaining life span.

Uncertainty regarding the prevalence of palliative malignancy patients receiving HPN, with or without IBO, is due to mixed reporting of different patient groups. There are three distinct malignancy patient groups receiving PN for different reasons: short-term support during radical therapy; HPN for ‘cured’ malignancy with subsequent intestinal failure caused by therapies; and short or

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long-term PN during the palliative phase. Table 1, summarises the prevalence rates of PN use in malignancy patients, though this data is difficult to evaluate, partly because not all studies distinguish between the three patient groups mentioned above, and partly because the prevalence rates are expressed in different ways (variable period prevalence or point prevalence).

Despite these limitations, it is clear that the practice of HPN for palliative malignancy is widespread. The lowest reported rates appear to be in the UK [6, 7] and highest in Italy and USA, with strong increasing trends worldwide [1,3,5–9].

National and international guidelines [10–12] for clinical practice have been useful but these have not been informed by a systematic evidence-based approach. In addition, none of the previous reviews of palliative HPN have extracted individual patient data to establish a more powerful database, allowing meta-analysis and providing additional insights into survival length. A further difficulty is that recent reviews [10,13] which have generally supported the use of HPN in palliative malignancy, have been unduly influenced by two favourable palliative HPN clinical trials [14,15], which have subsequently been retracted because they were not conducted in the manner described.

Economic considerations could also influence decisions about the use of HPN in this patient group, and although information is available regarding the health economics of HPN for benign disease [16,17] data are lacking for palliative malignancy.

The aim of this systematic review is to establish an evidence base, of clinically relevant outcomes (survival time, QOL and cost-effectiveness) in the palliative malignant IBO patient group to help inform and guide clinical practice for HPN therapy.

2. Methods

2.1. Eligibility criteria

This systematic review was performed according to the Cochrane Handbook for systematic reviews [21], and the PRISMA

Table 2
Inclusion and exclusion criteria for identifying relevant studies via search strategy.

Inclusion criteria	Exclusion criteria
≥18 years old	<80% inoperable bowel obstruction as the indication for HPN in malignant patient group
Confirmed diagnosis of malignancy in the palliative phase of disease with inoperable bowel obstruction treated with PN	Bowel obstruction caused by pseudomyxoma peritonei and desmoid tumours
Intention at time of commencing PN was to discharge to a home environment, regardless of eventual outcome	Lack of survival or QOL data Data from letters or abstracts, case reports or case series ≤ 3
± Palliative chemoradiotherapy	
English language	
≥ Year 1970	

(Preferred reporting items for systematic reviews and meta-analyses) statement. [22]

In order to identify relevant trials, a broad search strategy was implemented using pre-determined inclusion and exclusion criteria (Table 2). Included participants were adults, ≥18 years old, with a confirmed diagnosis of active malignancy during the palliative phase of disease (no further curative treatment available).

Studies were excluded if they did not provide data in which at least 80% of patients had a diagnosis of malignant IBO. A distinction was not made between patients where the mechanical cause of IBO was directly due to the malignant tumour, its metastasis or a benign process (e.g. adhesions) in the context of palliative malignancy.

HPN was defined as initiation of PN with intention to discharge to a home environment, even if home discharge with PN was not ultimately achieved.

IBO caused by malignancies such as pseudomyxoma peritonei and desmoid tumours were excluded because these tumours behave very differently (more favourable long-term outcome) than other types of malignancies causing gastrointestinal obstruction. Duplicate studies of the same patients were excluded.

Table 1
Prevalence of malignant conditions as indication for home parenteral nutrition.

Study	Country	Terminology of cancer indication	Total HPN patients	Number of HPN patients with cancer as indication	Proportion of HPN with cancer as indication	Period or point prevalence (years)	Data source
Vafa et al., 2010 [18]	Belgium	Advanced cancer	125	60	48%	Period prevalence (1987–2007)	Single academic centre database
Soo and Gramlich, 2008 [8]	Canada	Advanced cancer	158	38	48%	Period prevalence (Jan–Dec 2006)	North Alberta Home Total Parenteral Nutrition program database
Cazzaglio et al., 1997 [4]	Italy	Terminal malignancy	125	75 ('Majority considered terminal')	60%	Period prevalence (1983–1990)	Italian Home Parenteral Nutrition registry
Wanden Berghe et al., 2011 [5]	Spain	Palliative cancer	148	29	20%	Period prevalence (Dec 2009–Dec 2010)	Nutricion Artificial Domiciliaria y Ambulatoria (NADYA) database
Gillanders et al., 2011 [9]	Australia and New Zealand	Cancer	124	19	15%	Period prevalence (July 2010–July 2011)	Australian Society of Parenteral and Enteral Nutrition (AuSPEN) database
Jirka et al., 2011 [19]	Czech Republic	Cancer	138	51	37%	Period prevalence (2010)	National Home Parenteral Nutrition registry (Poster abstract)
Takagi et al., 1995 [20]	Japan	Malignant	231	93	40%	Period prevalence up to 1990 (start not reported)	National survey
Baxter et al., 2003 [7]	Scotland	Malignancy	72	7	10%	Period prevalence (Aug 2001–Aug 2001)	Managed Clinical Network Database
Smith et al., 2011 [6]	UK	Cancer	523	42	8%	Point prevalence 31/12/2010 (Percentage of new registrations during 2010–14%)	British Artificial Nutrition Survey (BANS) database
Howard et al., 1995 [3]	USA	Neoplasm	4520	2122	49%	Period prevalence (1985–1992)	North American Home Parenteral Nutrition database

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