Stronger Together

London North West Healthcare NHS
NHS Trust

Parenteral nutrition & End stage malignancy

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St Mark's Hospital

IF study day, Dec 2017

The Lennard-Jones Intestinal Failure Unit

St MARK'S HOSPITAL

Overview

- Prevalence
- UK opinion survey
- ESPEN guidelines
- Survival length
- QOL
- Type of feed
- Cancer cachexia
- Patient selection
- Summary

Prevalence

Study	Country	Period/point prevalence	Prevalence of malignancy as indication for HPN	Source of data
Vafa et al, 2010	Belgium	1987-2007	48%	Single academic centre
Soo and Gramlich, 2008	Canada	Jan-Dec 2006	48%	North Alberta HPN database
Cazzaglio et al, 1997	Italy	1983-1990	43%	Italian HPN registry
Smith et al, 2016	UK	*Point prevalence 31/12/2015*	15%	BANS database
Baxter et al, 2003	Scotland	Aug 2000 – Aug 2001	10%	Managed Clinical Network

UK Opinion Survey (2014)

- PN to improve QOL, regardless of life prolonging – 89%
- PN to improve performance status, regardless of life prolonging – 75%
- PN only if life prolonging – 17%

- Only in presence of IF – 87%
- But had used it as supplementary – 35%

Naghibi et al, Abstract, BAPEN 2014

ESPEN 2009 Guidelines

ESPEN Guidelines on Parenteral Nutrition: Non-surgical oncology

F. Bozzetti [a], J. Arends [b], K. Lundholm [c], A. Micklewright [d], G. Zurcher [e], M. Muscaritoli [f]

- PN - Incurable cancer with intestinal failure:
  - Expecting survival length due to tumour progression >2-3 months
  - Expecting PN to stabilise or improve performance status/QOL
  - Patient desires PN
- Grade C

Clinical Nutrition 28 (2009) 445–454

ESPEN 2016 Guidelines

Patients with a comparably good prognosis and an expected overall survival of at least several months [453,455] as well as patients with low tumor activity and no inflammatory reaction (CRP < 10 mg/dl) [454] should receive adequate nutritional counselling and support including oral, enteral or, if required, parenteral nutrition, or combinations. Performance status should not influence decision making for or against nutritional support in these patients. Patients, who, despite oncologic therapy, have rapidly progressive disease, activated systemic inflammation, and/or an ECOG performance status of ≥3, are less likely to benefit from nutritional support. However, patients should be assessed on an individual basis and, if appropriate, a trial of oral nutritional support should be offered with the aim of providing primarily symptomatic benefit.

Arends et al, 2016 Clin Nut

ESPEN 2016 Guidelines

- Prognosis of at least a few months

  Or

- Low tumour activity & CRP<10

Performance status

- Rapidly progressive disease

  Or

- Systemic inflammation

  Or

- ECOG (WHO) PS >3

Less likely to benefit from PN

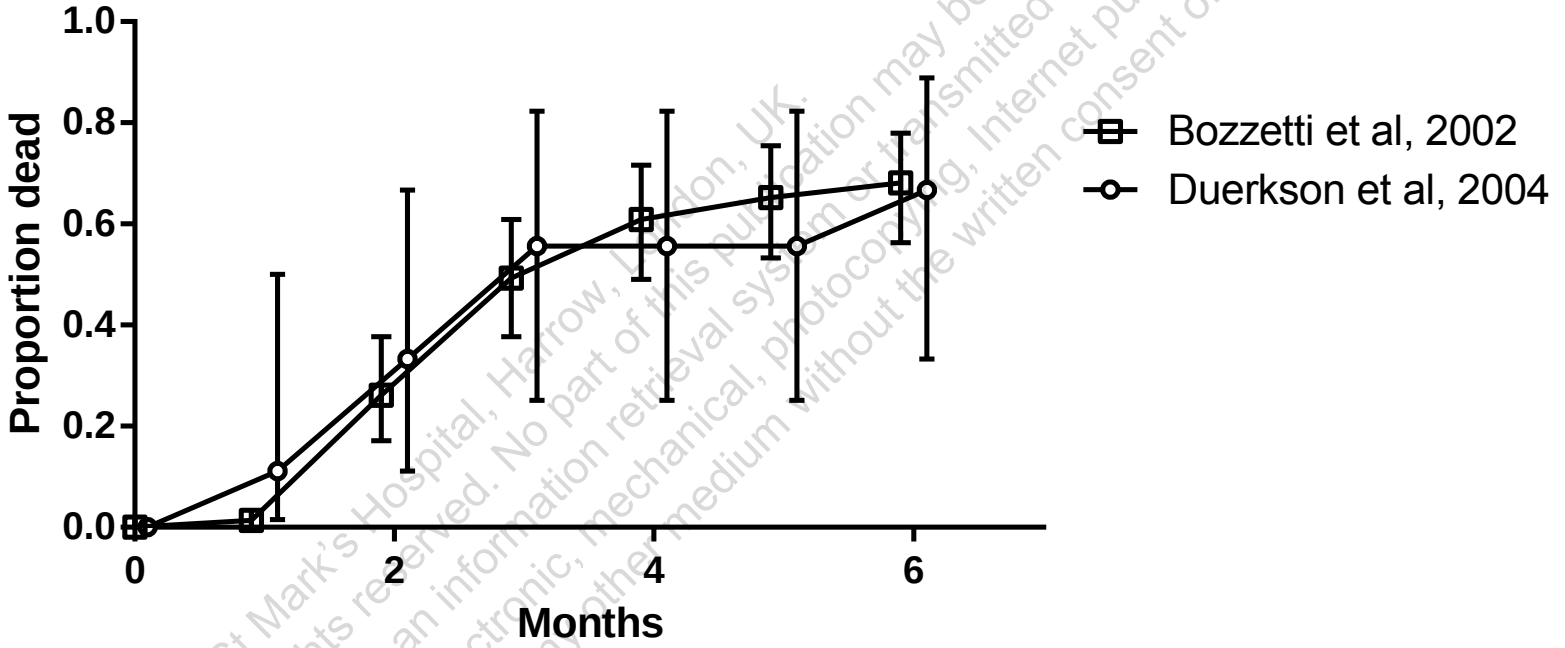
Arends et al, 2016 Clin Nut

Survival

Survival

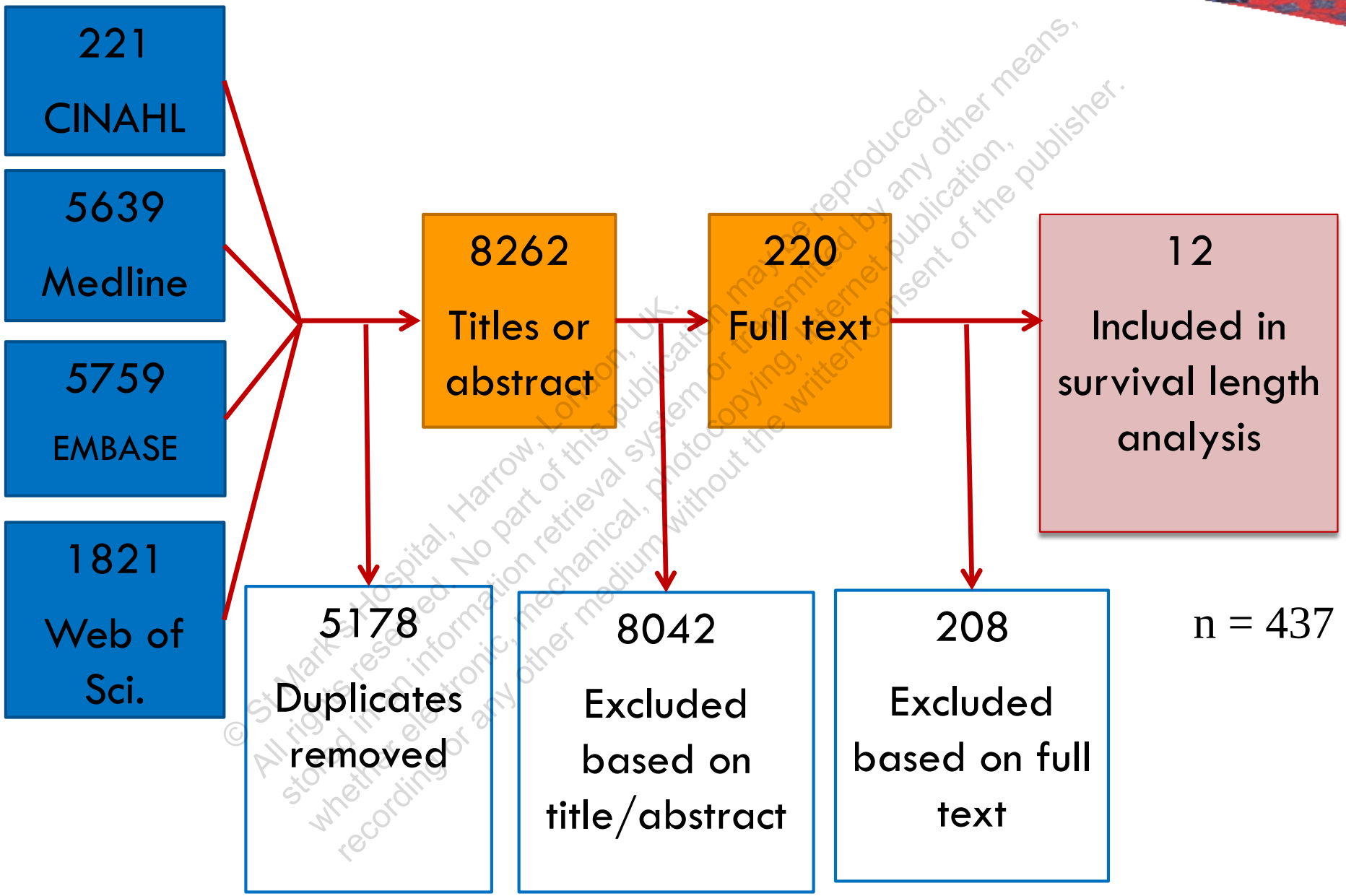
Article	Definition of the beginning of measuring survival length	N=	Mean days	Median days	Range of days
August 1991	Date of discharge with HPN to death	17	72	53	5-208
Pasanasi 2001	Not defined	76	98	74	6-301
Bozzetti 2002	Date PN started in hospital to death	69	156	91	30-426
Duerksen 2004	Date PN started in hospital to death	9	166	84	27-433
Brard 2006	Diagnosis of intestinal obstruction	28	90	74	16-485
Soo 2008	Not defined	33	164	89	8-1004
Chermesh 2011	Not defined	28	130	140	20-783

Survival

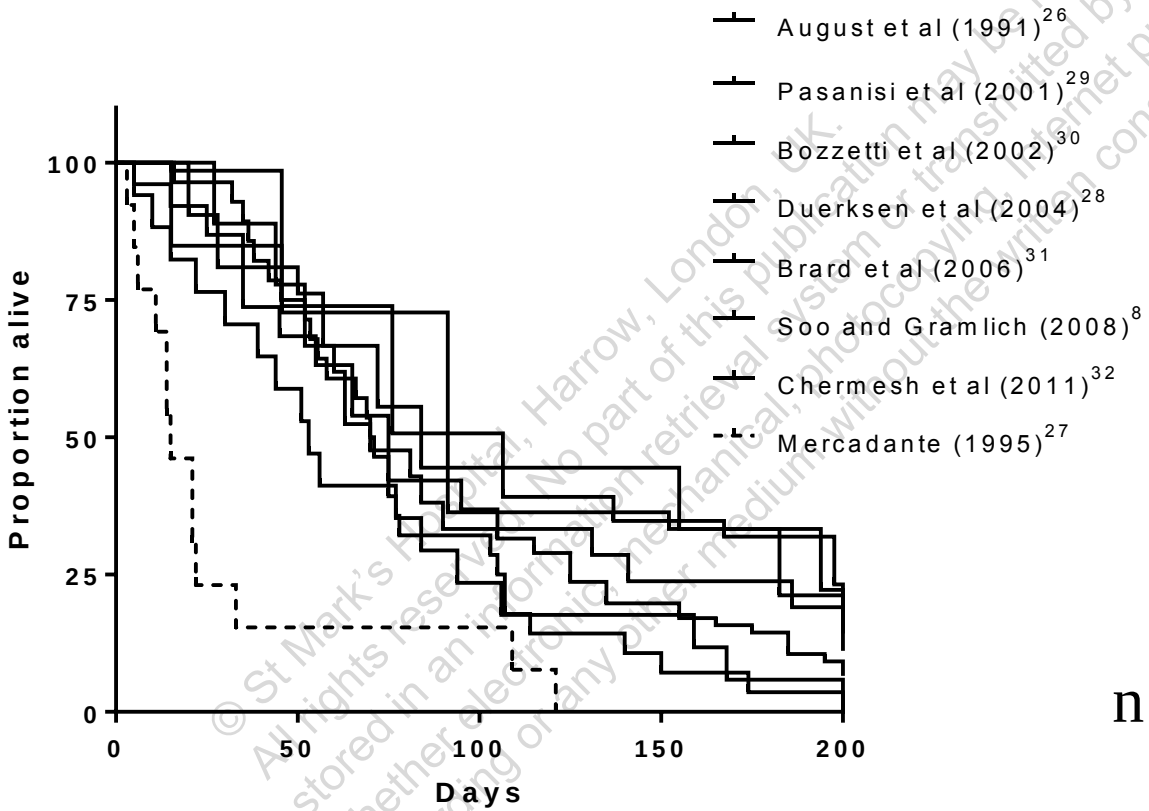


Systematic review

- What is the length of survival for patients with palliative malignancy causing inoperable bowel obstruction treated with HPN?

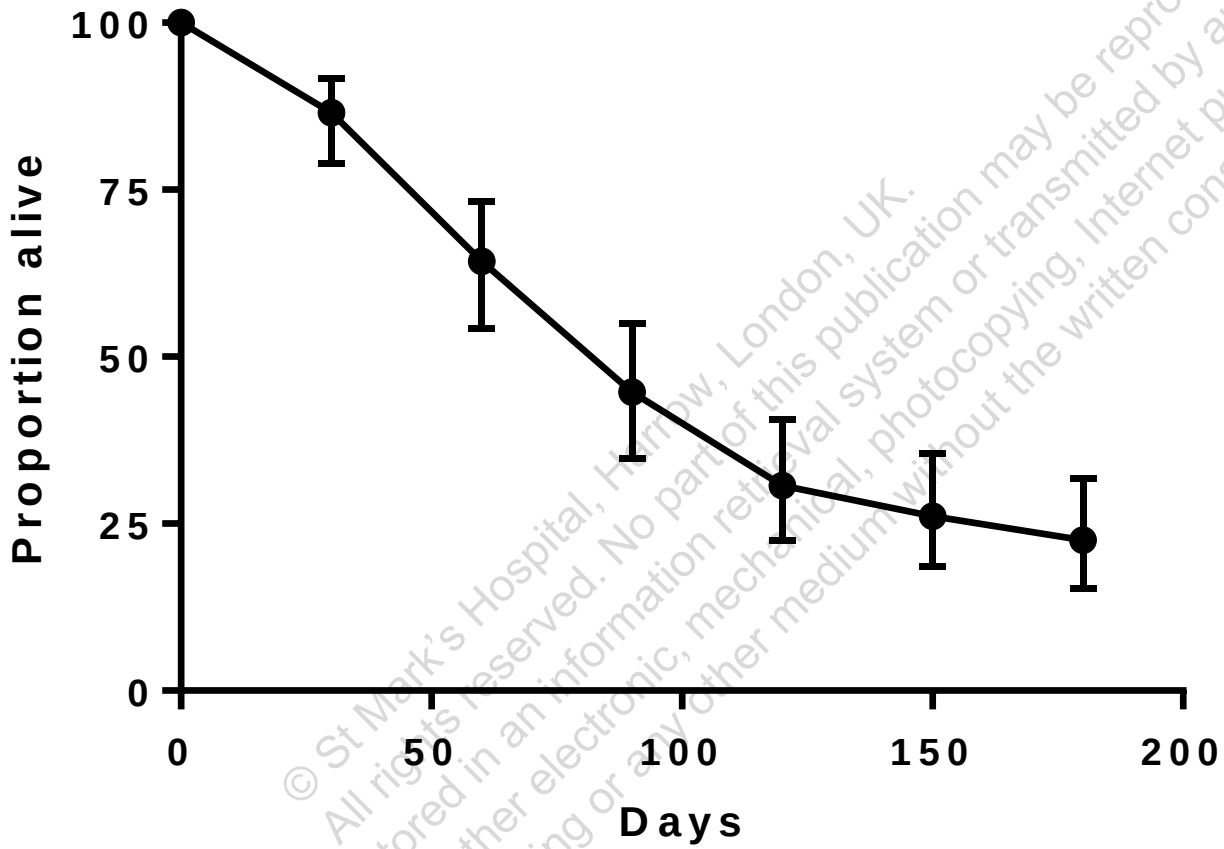


Patient survival



n = 265

Meta-analysis – Length of survival



Mean survival **3.8** mths

Median survival **2.7** mths

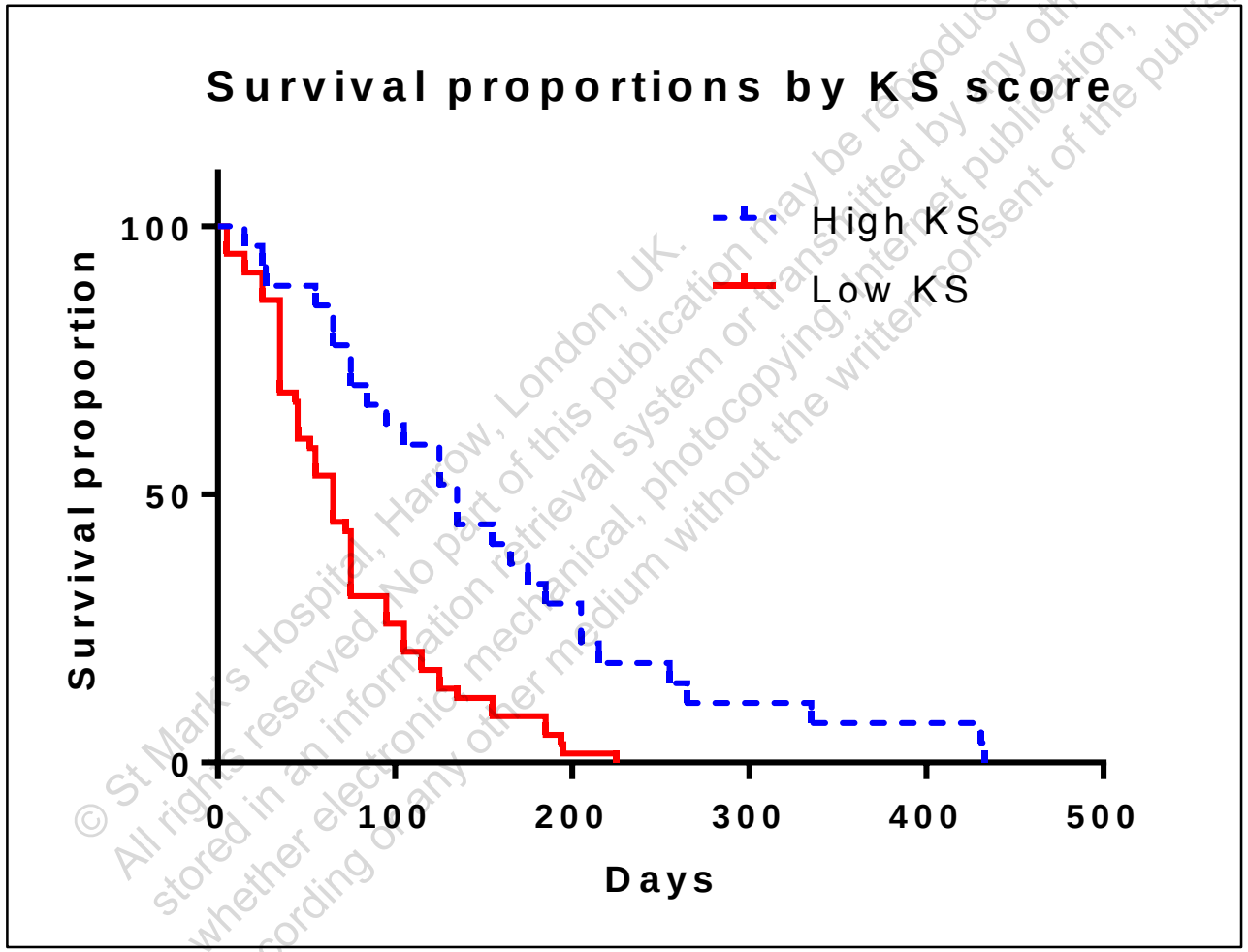
55% mortality at 3 mths

76% mortality at 6 mths

n = 244

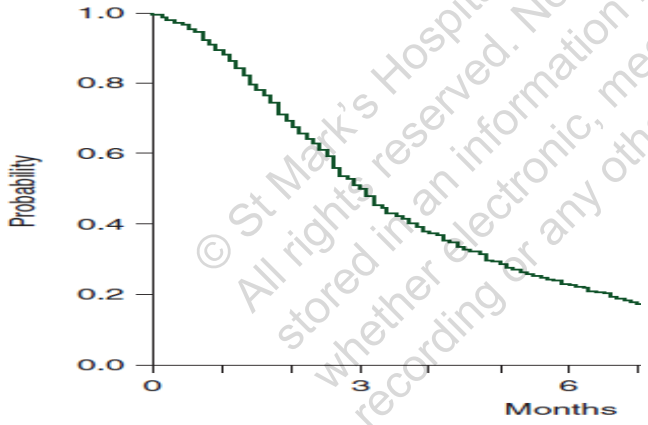
M. Naghibi et al. / Clinical Nutrition (2014) 1–13

Performance Status



Bozzetti et al 2014

- International, multi-centre case series
  - N=414, all palliative cancer
  - 67% inoperable bowel obstruction
  - Median survival **3.0** mths
  - 50% mortality at 3 mths
  - 77% mortality at 6 mths



- *Median survival **2.7** mths*
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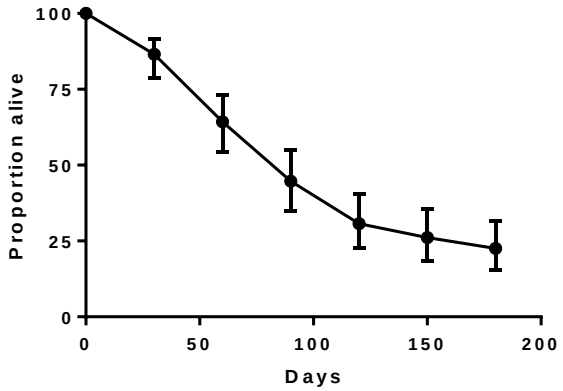


Annals of Oncology 25: 487–493, 2014

QOL
Pironi et al (1997)

- n = 29 – Ovarian Ca with GI obstruction HPN,
- Median survival 56 days (range 14-343)
- QOL assessment by Nutrition Team
  - 19/29 – well accepted
  - 7/29 – displayed annoyance
  - 3/29 – scarcely tolerated

- “HPN can be applied without causing additional burden or distress”

J R Soc Med 1997;90:597–603

Bozzetti et al (2002)

- n = 69, various palliative Ca HPN
  - 58/69 (84%) GI obstruction
  - Survival median 91 days (range 30-426)
  - QOL assessed monthly Rotterdam Symptom Check List

Thirty patients were aware of their cancer diagnosis, though only six were fully aware of their prognosis. However, all patients and their relatives were familiar with management, possible benefits and adverse effects of HPN, and gave their informed consent to be given the treatment.

Clinical Nutrition (2002) **21 (4)**: 281–288

Bozzetti et al (2002)

- Results
  - 1st month of HPN
    - 40% improved
    - 50% decline
  - Remained stable until 2 months prior to death

- Conclusion:
  - Therefore on average those expected to survive > 3 month have enough time to benefit

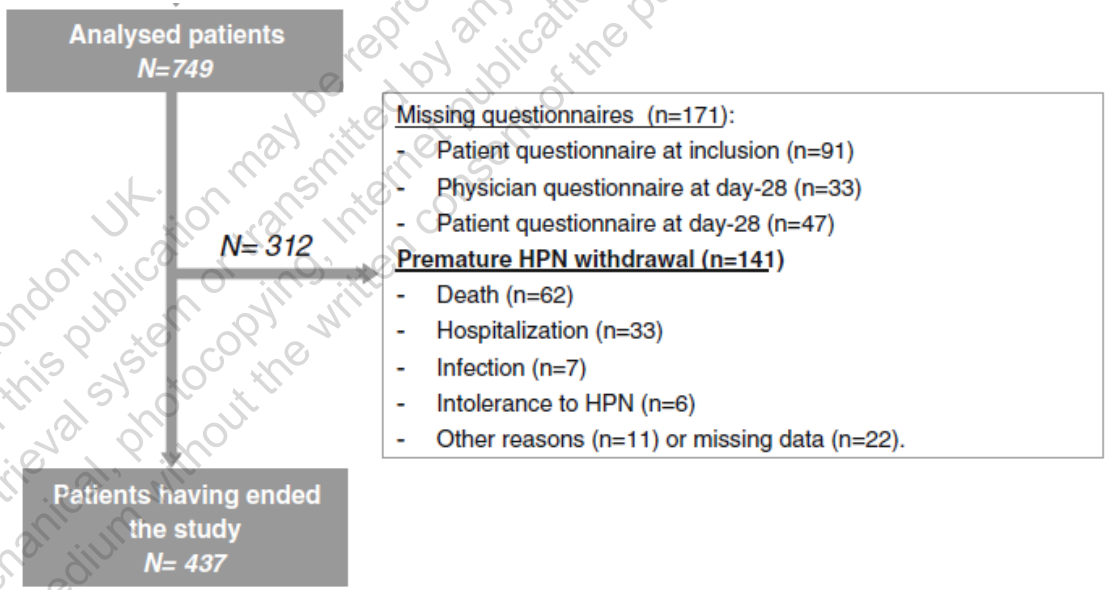
Clinical Nutrition (2002) **21 (4)**: 281–288

Culin et al (2014)

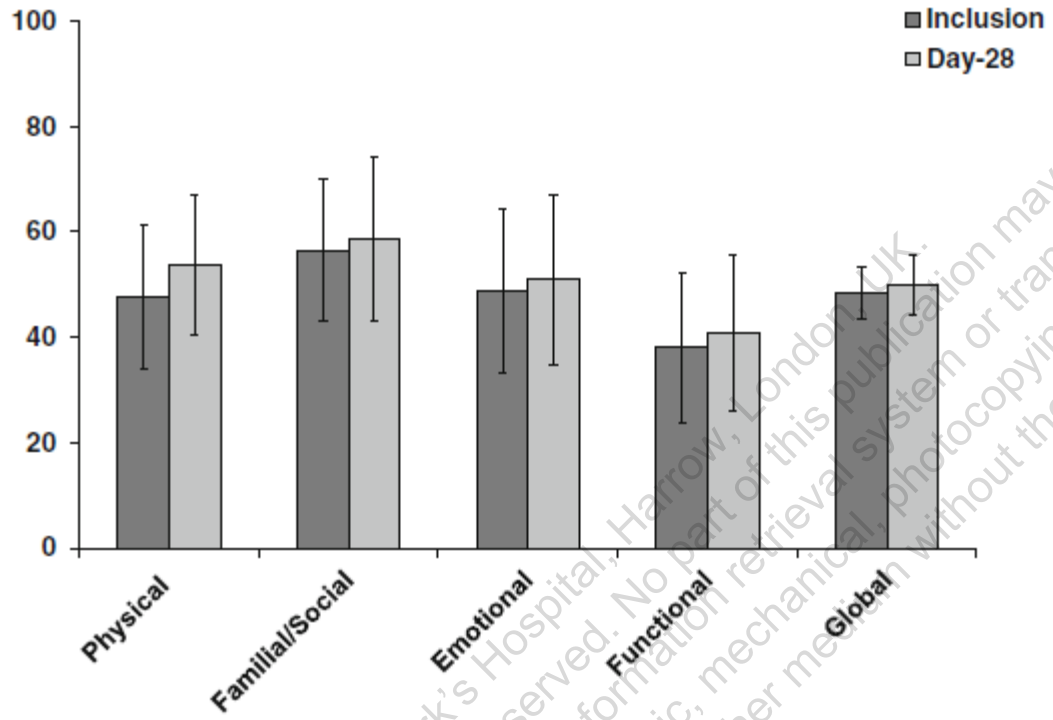
- Prospective observational study
- 176 centres
- QOL questionnaire (FACT-G)
  - Patient, family and physician
  - Day 0 and 28 of HPN
- Excluded
  - Haematological cancers
  - Survival less than 1 month

Culin et al (2014)

- Patients
  - 749 recruited
  - 437 completed
  - Mean 63 years
  - 65% metastatic
- Indications
  - 87% malnutrition
  - 5% intestinal failure



Culin et al (2014)



- 60% improved
- 15% no change
- 25% worse

Orevall et al (2005)

- n = 13 all palliative Ca HPN
  - Only 2/13 were for intestinal failure
  - Variable oral intake, therefore "supplemental" PN
  - Structured interview

- Results:
  - "Relief" and "security" that nutrition was being met
  - Negative impact on social interactions
  - Positive >> negative

Clinical Nutrition (2005) 24, 961–970

Cancer and type of feed

- Endogenous lipids well metabolised and oxidised
  - 60 - 80% of resting metabolic rate[1]
- Exogenous lipids cleared faster in cancer patients vs. healthy individuals[2]
  - LCT clearance (g/kg/day) 3.5 vs. 1.4
- Omega 3 fats
  - Increase cancer cell apoptosis
  - Reduce cancer cell proliferation
  - Reduce tumour microvascular density

1. Waterhouse et al, Cancer Res 1971
2. Lindmark et al, Ann Surg, 1986

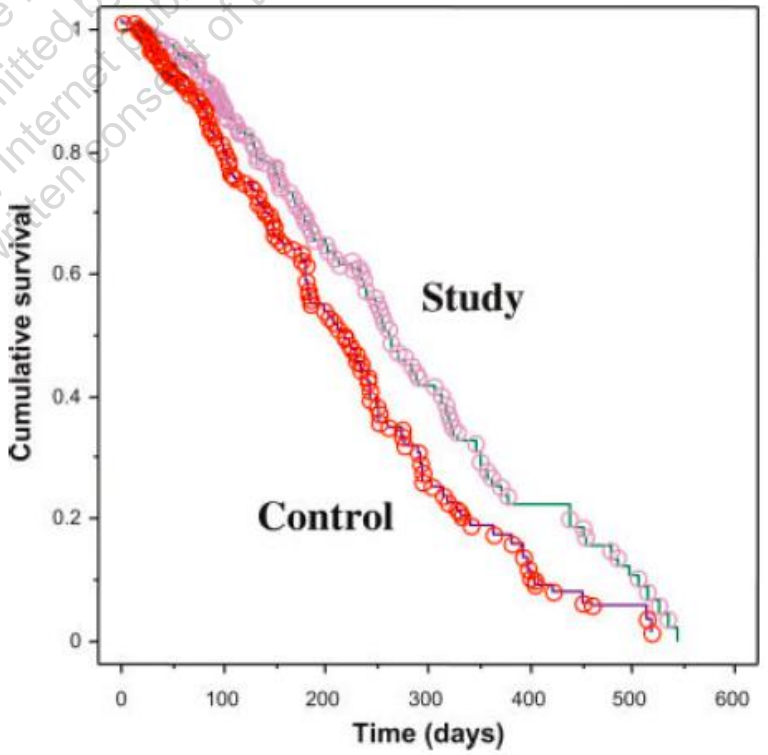
Cancer cachexia

- Definition
  - Ongoing weight loss <u>despite</u> supply of nutrients
  - A complex multifactorial syndrome
    - Inflammation
    - Insulin resistance
    - Loss of appetite

Fearon, NEJM, 2011

Multi-modal treatment

- RCT, n=309 - Not IF
  - All received
    - NSAIDs
    - EPO
    - Insulin
  - Randomised to supplemental PN or best oral
  - Improved survival on PN



Lundholm et al, Cancer 2004

Feeding the tumour?

- Irrelevant when IF present

Multi-modal treatment

- RCT, n=309 – Not IF
  - All received
    - NSAIDs
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    - Insulin
  - Randomised to supplemental PN or best oral
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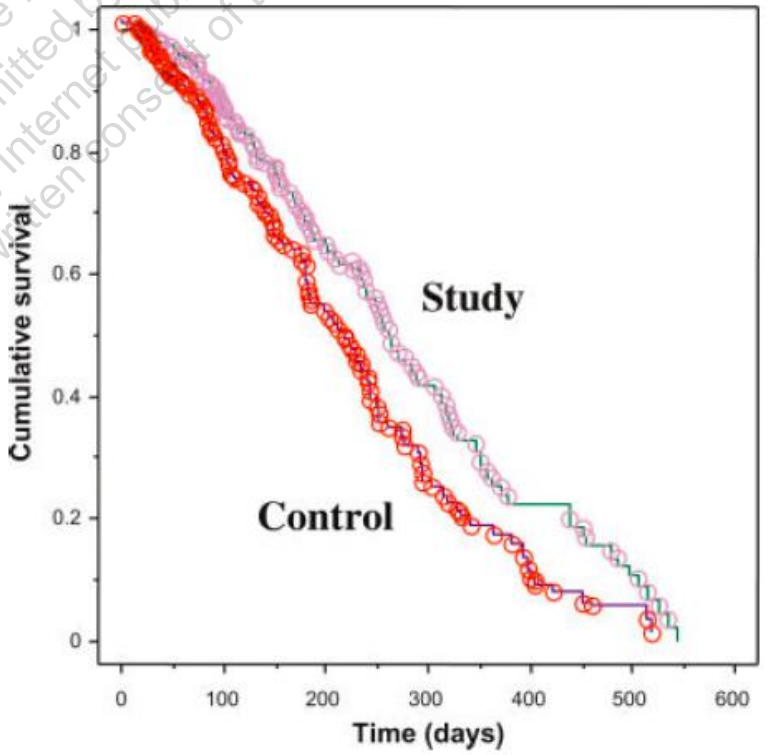


Lundholm et al, Cancer 2004

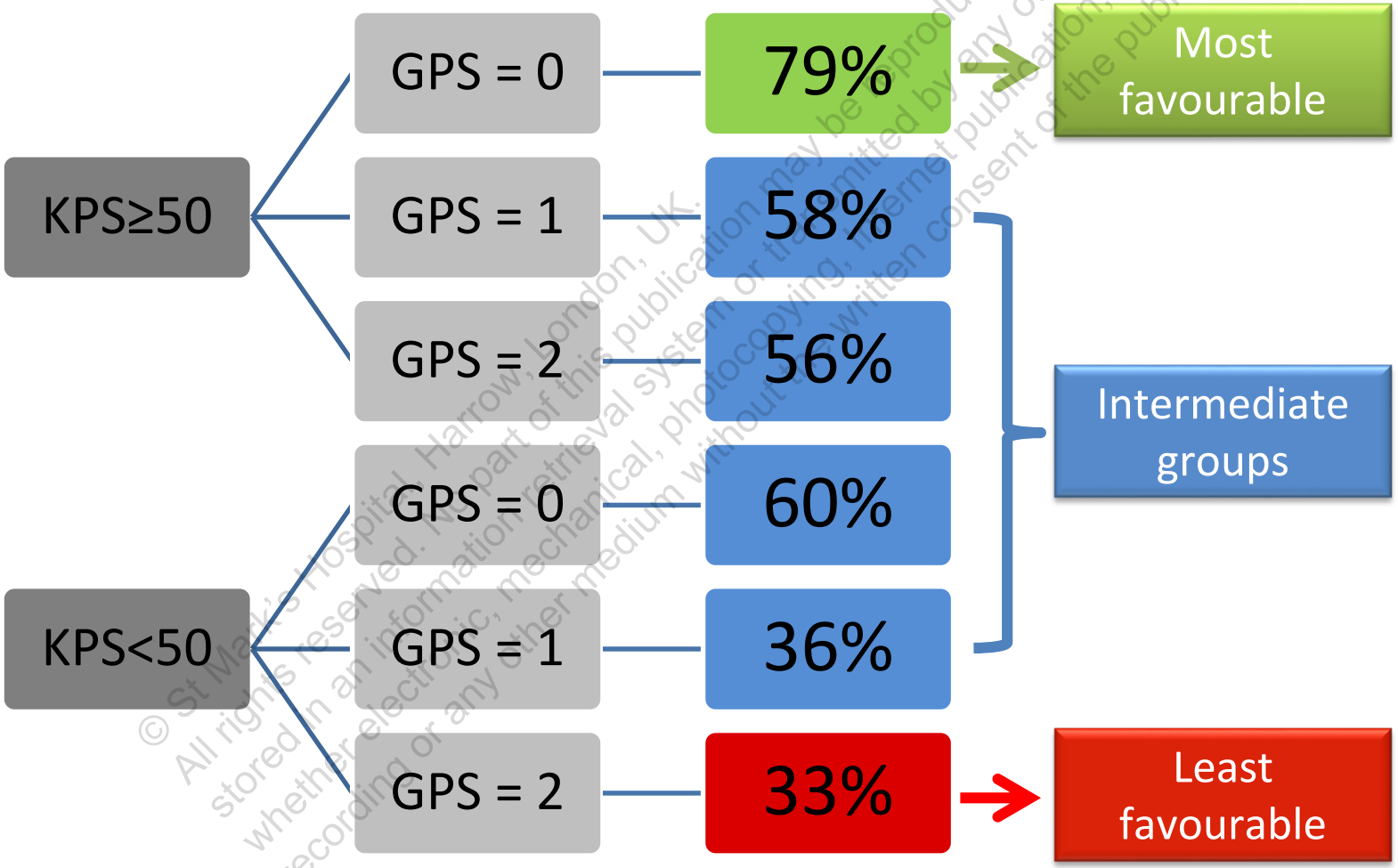
Patient selection

Prognostic score

- Bozzetti et al 2014 (n = 414) - 3 month survival:
  - KPS – Karnofsky performance status
    - Subjective functional level
    - 0-100
  - GPS – Glasgow predictive score
    - Objective based on serum Alb and CRP
    - 0, 1 or 2

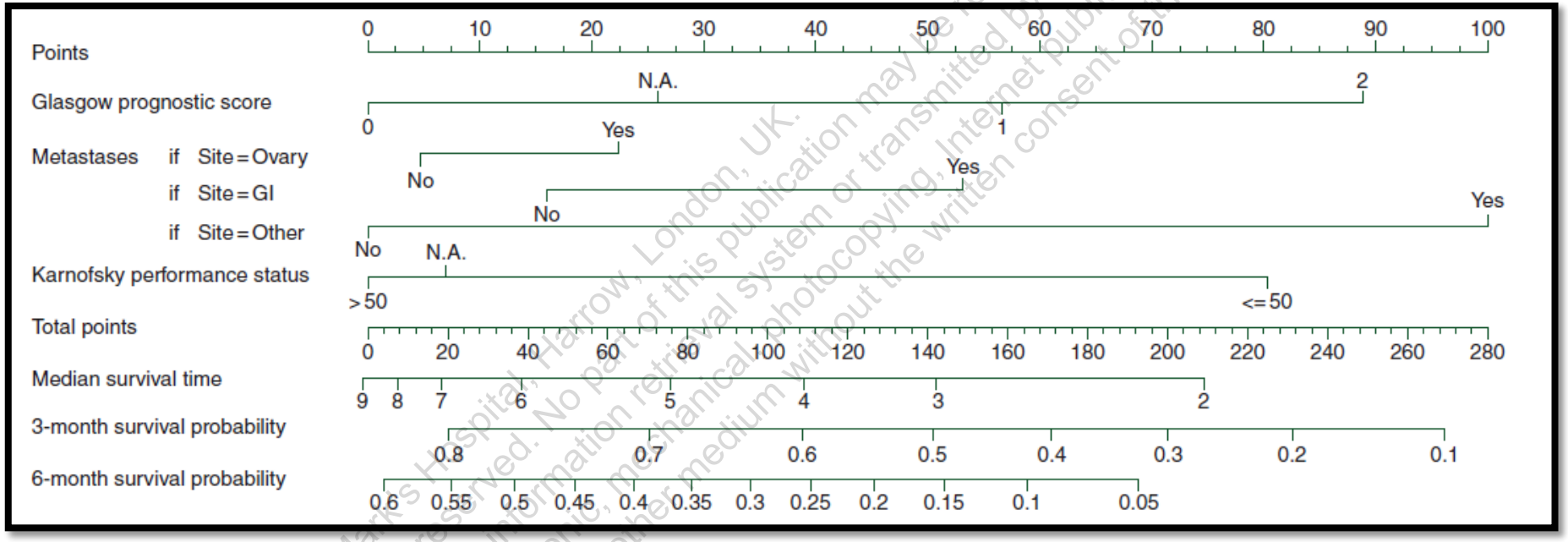
Annals of Oncology 25: 487–493, 2014

3 months survival prognosis



Annals of Oncology 25: 487–493, 2014

Prognosis Nomogram



Bozzetti et al, 2015 Ann Onc, 26(11)

St Mark's & Southampton – Nomogram validation

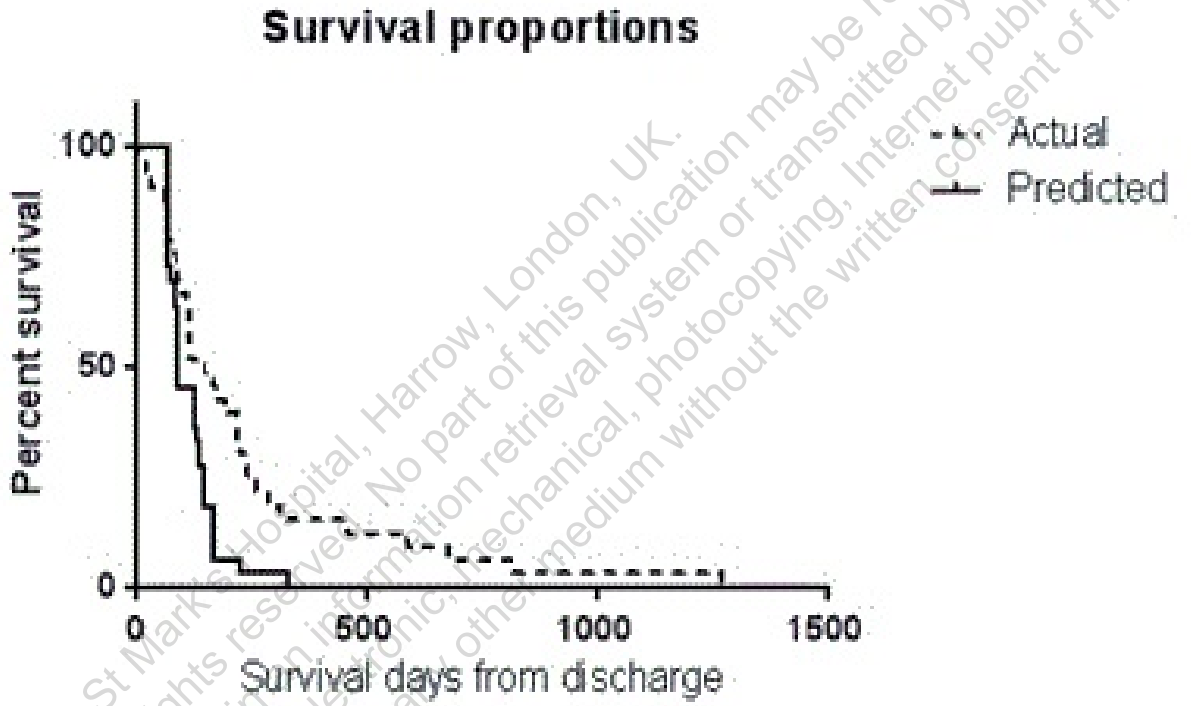
- Jan 2005 – Dec 2015
- St Mark's – 24 pts
- UHS – 20 pts
- Primary malignancy
  - Gastrointestinal – 26 (60%)
  - Ovarian – 9 (20%)
  - Other – 9 (20%)

StM/UHS - Nomogram validation

- Actual
  - Median survival – 2.8 mths
  - Mean survival – 5.1 mths

- Nomogram under/over estimation
  - 20% of patients - 25%-50% error
  - 40% of patients - >50% error

StM/UHS - Nomogram validation



n=44

Log rank (Mantel-Cox) test p=0.006

Summary

- Common and increasing HPN aetiology

- Survival – short, but variable
- QOL poorly understood – hint at improvement
- Multimodal treatment models

- Patient selection is key
  - MDT team
  - Prognostic scores – need validation