The impact of home parenteral nutrition on the burden of disease including morbidity, mortality and rate of hospitalisations

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1 **Abstract**

2 Introduction: Home parenteral nutrition (HPN) provides fluid and nutrition essential for the survival of
3 patients with type 3 intestinal failure (IF). However, it is associated with complications and re-
4 admissions to hospital. This study aims to investigate the effect of HPN burden on mortality, morbidity
5 and hospital re-admission rates in patients with IF.

6 Method: This is a retrospective cohort study. All patients newly dependent on HPN discharged over a
7 4-year period between 2011- 2015 were included. Patients' characteristics, nutritional status and
8 diagnosis were recorded, along with frequency and duration of HPN administration. Outcomes
9 collected included hospital re-admissions, morbidity, catheter related blood stream infections
10 (CRBSIs) and mortality. Regression analyses were performed to estimate the rate of different
11 outcomes adjusted for prognostic factors.

12 Results: There were 210 patients included in the analysis, 561 separate HPN prescriptions equating
13 to 110,537 catheter days. A total of 196 re-admissions to hospital were recorded for a total of 5594
14 days, 69 (33%) of these re-admissions were unplanned (2484 days in hospital). Principle reasons for
15 unplanned re-admissions included: CRBSIs (n=31, 45%); other sepsis (n=10, 14.5%) and abdominal
16 symptoms (n=9, 13%). CRBSIs were recorded in 22 (10%) patients, equating to a rate of 0.199 per
17 1000 catheter days. Days per week on HPN increased the relative rate (RR) of time in hospital due to
18 any reason or for unplanned re-admissions, RR 1.50 (95% CI: 1.26, 1.78 p<0.001) and RR 1.39 (95%
19 CI: 1.10, 1.75 p=0.006) respectively. However, there was no association between days per week on
20 HPN and CRBSI occurrence.

21 Conclusion: Unplanned re-admissions for patients with IF accounted for a third of all hospitalisations
22 in those on HPN and the majority were due to CRBSI. The number of HPN dependent days per week
23 was related to all-cause unplanned re-admissions, although not to CRBSI rate.

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29 Introduction

30 Intestinal failure (IF) is defined as the reduction of gut function below the minimum necessary for the
31 absorption of macronutrients, fluid or electrolyte that requires intravenous supplementation to
32 maintain health.¹ There are three types of IF: types 1 and 2 describe acute conditions, while type 3 IF
33 is a chronic condition, occurring in metabolically stable patients, requiring intravenous
34 supplementation or home parenteral nutrition (HPN) over months or years.² It may be reversible or
35 irreversible.¹ Administration of HPN can be over one to seven days per week via a central venous
36 catheter (CVC). Home parenteral nutrition is a life-sustaining treatment for patients with type 3 IF and
37 survival for these patients is primarily determined by the patient's underlying condition.^{3,4} The principal
38 underlying conditions leading to IF include Crohn's disease, mesenteric ischaemia, and surgical
39 complications.⁵ In some instances, and where appropriate, patients with underlying cancer may
40 require HPN in palliation.⁶

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42 Delivery of HPN does not come without risk and these include catheter thrombosis, catheter related
43 blood stream infections (CRBSIs), IF associated liver disease (IFALD) and metabolic bone disease. In
44 adult patients with benign chronic IF, death has been attributed to IFALD in 4%, CRBSI in 8% and
45 catheter-related thrombosis in 2%.⁷ The complications associated with HPN can also lead to
46 significant morbidity, including the need for recurrent hospital admission for associated therapy
47 combined with long-term clinic attendance for monitoring purposes.⁸ The effect of HPN dependence
48 on patients' lives is substantial and has generated an increasing interest in evaluating quality of life
49 (QoL) in this patient group.⁹ Issues important to patients that impact on QoL include the restrictive
50 nature of overnight HPN leading to limited mobility, fatigue, social isolation, sleep interference and
51 psychological problems associated with the highly regulated lifestyle required for intravenous
52 feeding.^{10,11} Furthermore, the majority of those on HPN rarely return to gainful or satisfying
53 employment adding to the sense of social isolation and lack of purpose.^{12,13} Moreover, patients also
54 state that the fear associated with complications impacts negatively on their QoL.¹⁴ Notably, removing
55 some restrictions on lifestyle through maximising parenteral nutrition free days has been highlighted
56 as a way of improving QoL in patients on HPN.¹⁵

57

58 The frequency of HPN needed per week has also been reported to impact on CRBSI rate in some
59 studies,^{16,17} but not all published series.^{18,19} However, there are limited data detailing the health care
60 utilisation, re-admission rates and reasons for re-admission in the HPN population, nor data on the
61 impact of HPN burden (as reflected by the number of HPN-dependent days per week). The aim of this
62 study was therefore to determine the impact of HPN burden on clinical outcomes including hospital re-
63 admission rates, HPN-related complications and mortality.

64

65 **Methods**

66 The study design was a retrospective cohort longitudinal investigation. Data on patients were
67 prospectively recorded and summarised by the clinical team. All patients referred for HPN to a
68 national U.K. IF Unit at Salford Royal Foundation Trust were included in the study. All patients were
69 over 16 years old and discharged between 01 January 2011 and 31 March 2015; all had type 3 IF.
70 Patient demographics, nutritional status, underlying disease, central venous catheter type and
71 management were recorded from an electronic patient record system. Clinical outcomes recorded
72 included: number of CRBSI; rate of hospital re-admissions (all-cause and unplanned); number of days
73 re-admitted to hospital and mortality rates. Diagnosis of a CRBSI was based on quantitative and
74 qualitative assessment of central and peripheral pour plates as previously described.^{20,21} The reason
75 for admission was also documented. Data on HPN prescriptions included duration on each
76 prescription, volume, energy content, and number of infusions per week.

77

78 **Statistical analysis**

79 Regression analysis was performed to evaluate the effect of clinical outcomes and differences in
80 factors including the number of HPN infusions per week; full details on covariates are presented in
81 Table 1. Analyses were performed using SAS (Version 9.4) using proc glimmix on the following
82 outcomes: rate of CRBSI; odds of death; time in hospital (separate models performed for all and
83 unplanned admissions) and rate of hospital re-admissions (separate models performed for all and
84 unplanned re-admissions).

85

Dichotomous outcomes (mortality) were analysed using logistic regression, whereas count data (rate of CRBSI and rate and duration of admissions) were analysed using negative binomial regression. To better estimate the uncertainty in the data, a negative binomial model was chosen over a Poisson regression model. A negative binomial model allows for over-dispersion in the data and avoids the assumption in a Poisson model that the mean and variance are equal.²² As the nature of the study was to generate hypotheses, hypothesis testing was not performed, and confidence intervals and p-values should be treated as descriptive. The dataset captured each new prescription for a patient over the period of data collection for HPN. The record captured where a change in HPN was observed in any of: number of days HPN per week, type of HPN (customised admixture glucose alone, customised admixture lipids alone or fluid-electrolytes alone), volume or energy. An individual patient could therefore contribute multiple records to the analyses; to account for the within-patient correlation, a random effect was fitted to patient identification in the data set. As the duration of each record varied, an offset to capture the duration of each record was used.

99

100 **Ethics**

Ethical approval was gained for this study from an Ethics Committee (Ref No 2015/096GRU) and NHS Trust was obtained prior to starting the study in accordance with governance arrangements.

103

104 **Results**

105 ***Patient Characteristics***

There were 211 patients newly referred to our service discharged on HPN in to the community identified for the inclusion in the study, however one patient's HPN records could not be recovered, therefore, 210 patients were included in the analyses. Patients' characteristics and underlying diagnoses are displayed in table 2.

110

111 ***Clinical Outcomes***

Clinical events and frequency HPN per week are shown in table 3. During the study period, there were a total of 44 deaths; 23 occurred in patients with a known malignancy (causal to the need for HPN) and 21 in patients with underlying benign disease (Table 4).

There were 22 CRBSIs that occurred during the study period, equating to 0.199 CRBSI episodes per 1000 catheter days. A total of 5594 hospital days were recorded for re-admissions during the 4-year study period. Unplanned hospital re-admissions accounted for 69 out of 196 (35.2%) of re-admissions, of which the majority 34 (49.3%) were related to CVC complications (Table 5). There were 28 out of 69 (40.6%) re-admissions that occurred due to underlying IF disease and 7 out of 69 (10.1%) of re-admissions occurred due to other causes un-related to IF. All data, including the reasons for unplanned re-admissions to hospital, are shown in Table .

Associations with HPN days per week

Full regression analyses results are presented in Table 6. An increase of one day HPN treatment per week was shown to increase the re-admission (all-cause) days in hospital (RR=1.50, $p<0.001$). In addition, an increase in one day HPN treatment per week was also seen to significantly increase the unplanned time patients spent in hospital (RR=1.39, $p=0.006$). CRBSI rate (or death) were not associated with HPN requirement per week.

Discussion

This study provides a unique contemporary narrative of the impact of HPN on individuals in a national referral centre. As alternative therapies such as intestinal transplantation, small bowel lengthening and growth factors evolve to reduce the burden of HPN, it is vital to understand the current clinical outcomes of patients with type 3 IF initiated and then remaining on HPN. There were a total of 196 re-admissions to hospital over the 4-year data collection period and from these unplanned admissions accounted for 33% of all cause admissions and 2484 inpatient days. The most frequently occurring reason for unplanned re-admission was catheter related issues with the most frequent issue being CRBSI.

In agreement with the findings from the present study the most frequently reported HPN complication requiring hospitalisation was CRBSI in a large European cohort in the first year after discharge²³.

Other reasons for readmission included underlying disease in 27% of days admitted to hospital, HPN complications in 48% and other medical reasons in 25%.²³ However when shorter periods of time are evaluated at 30-days post discharge re-admission rates showed that from 224 patients on HPN

31.6% (n = 71) had unplanned re-admissions within 30-days of hospital discharge and the majority of these were due to HPN (n = 15, 21%) with only a small number due to CRBSI.²⁴

Incidence of re-admissions has been reported as an outcome for evaluating interventions as it is considered a major component of service delivery for patients on HPN. In 93 patients discharged from hospital there were 103 reported re-admissions over a 15 month period and all due to CRBSI, other reasons for re-admissions were not reported here²⁵ In the evaluation of intestinal transplants re-admissions are considered in the HPN costs and were cited as €13,276 for treatment introduction, €77,652 for annual maintenance including all HPN products, nursing support, outpatient visits, home care, and hospital admission for the treatment of HPN-related complications,²⁶ these costs are based on pricing index for 2012 in the Netherlands.²⁷ For seven days hospital admission for HPN related complications the cost attributed were €4258 using these guidelines. In healthcare systems internationally there is an obvious benefit regarding the utilisation of resources to minimise HPN related complications.

In addition to the economic impact of re-admissions to hospital, a contemporary report of the clinical burden of HPN is important for patients. Type 3 IF has a considerable effect on patient's lives associated with repeated hospitalisation and complications from HPN.²⁸ It is established that it is not just the hospital re-admission that impacts adversely on patients' QoL, the actual fear of re-admission and complications can equally harm an individuals' QoL.^{14,15}

The present study found a CRBSI rate of 0.199 episodes per 1000 catheter days in new patients placed on HPN. This is a very low CRBSI rate when compared to the published literature. While a systematic review detailed a varied CRBSI rate reported from different centres of between 0.38 and 4.58 episodes per 1000 catheter days,²⁹ a more recent series from the USA. reported a CRBSI rate as high as 11.5 per 1000 catheter days.³⁰ It is clear that the reported CRBSI rate will vary according to the method of CRBSI diagnosis; indeed, relying on a clinical diagnosis rather than the more objective use of paired quantitative and qualitative blood cultures, as recommended by European Guidelines,⁸ can lead to over-diagnosis and unnecessary therapies.³¹

The diagnosis of CRBSI reported in the present study was based on paired quantitative blood cultures in all patients, as previously reported.²¹ Moreover, the patient cohort studied and duration of follow-up may influence the CRBSI rate reported; for example, we previously reported a CRBSI rate of 0.38 per 1000 catheter days in a very large cohort of patients needing HPN at our centre; the latter study included patients new to, and those already established on HPN, followed up for a longer time period between 1993 and 2011. More recently, we reported a CRBSI rate of 0.31 per 1000 catheter days in all patients (new patients to our service initiated on HPN and those already established on HPN) managed at our centre between 2012 and 2016;³² again, the latter rate is likely higher than that reported in this paper, since the present study only included patients new to HPN and not those already established on HPN. Indeed, the duration of previous HPN has been shown to be associated with an increased risk of one or more CRBSIs.²¹ Nonetheless, the low CRBSI rates recorded also underscore the importance of an experienced and multidisciplinary IF team in managing patients in hospital and in the community.⁵

We suggest that the low levels of CRBSI reported is low because of a robust approach to the HPN catheter care program involving meticulous training by nurses of patients and family members to administer the PN. If self-administration is not possible, then home care nurses administer the PN according to the same meticulous catheter care protocol. By focussing on key catheter care principles (e.g. including hand washing, preparation of the aseptic pack, exit site dressings etc.) these low CRBSI rates are achieved without the use of antimicrobial locks.

We aimed to determine any association between the burden of HPN, as reflected by the number of days per week of PN, and clinical outcomes. While some,^{16,17} but not all^{18,19} studies found an association between HPN days per week and CRBSI rate, the present study did not. More frequent handling of the CVC through the week may place patients at higher risk of contracting an infection; however, there are a number of other factors that influence CRBSI rate, including the presence of a stoma, opiate use, individual caring for the catheter²¹. It is possible that no association was found with HPN days per week in this study because of the very low overall CRBSI rate recorded, such that the regression analysis was underpowered and unable to detect statistically significant differences. A further limitation of the regression analyses is that a large proportion of patients received HPN seven days a week, therefore meaningful categorisation of values less than seven days was difficult. As a

result, HPN days per week were analysed a continuous variable, which assumed that the difference in one day HPN per week would have the same effect for each additional day added. An additional limitation of this study is that the data were retrospective. A MDT collected the data prospectively in patients' records and the data were then transferred to a database. It is possible that data on the incidence of complications, hospital re-admissions and days in hospital were incomplete. The study demonstrated that the number of days of HPN was associated with an increased number of days patients spent re-admitted to hospital. The reason for this association is unclear, but may reflect those needing more days of HPN having more severe underlying disease, as recently found in a very large European multicentre study which demonstrated that fluid volume requirements were a key predictor of loss of intestinal function and disease severity.³³

In conclusion, the present study provides a detailed and contemporary evaluation of the clinical burden of HPN. These data are vital for payers, providers and, most importantly, patients. The study reports a very low CRBSI rate in a large cohort of patients placed on HPN managed at a national UK centre. The data also report a relatively low overall re-admission rate for patients dependent on HPN, a clearly important factor for pressurised health care economies as the overall incidence of HPN seems to be on the incline,^{34,35} but also a key factor in reducing morbidity and enhancing patients' quality of life.

Statement of Authorship

SB AM and SL designed the study and wrote the protocol, MH and NR undertook analysis and provided all statistical support, MT undertook preparation of data base and AT SL and AA provide clinical expertise. SB, SL and MH wrote the manuscript. All authors have inputted into the final manuscript and approved the final version.

Conflict of Interest Statement

SB and SL received unrestricted grant from NPS Pharma Limited.

SB and SL received unrestricted grant from Shire Pharmaceuticals.

229 MH and NR are full-time employees of BresMed Health Solutions. BresMed were paid consultants on
230 this work for the statistical analyses.

231

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235 Shire Pharmaceuticals for investigator-initiated research projects unconnected with the development
236 and writing of this particular research.

237

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331 Table 1: Covariates included in regression models

Covariate	Definition
Days of HPN per week	Included in models as a continuous variable (minimum 2, maximum 7)
Gender	Categorical variable: male or female
Diagnosis	Categorical variable: Crohn's, surgical complications or 'other'
Total time on HPN (1000 days)	Continuous variable, time on HPN was defined as the time since a patient started HPN
Age	Continuous variable, where age is age at time of HPN onset
CVC care ^a	Categorical variable: Nursed care or other (self or family care)
BMI ^a	Continuous variable, median BMI observed within time period of HPN record
Previous CRBSI	Categorical variable: yes or no
Patient	Included in the models as a random effect to capture within patient correlation for multiple HPN records per patient
HPN record length	Length of time on HPN for the given record. Included regression models as an offset.

332

333 BMI, body mass index; CRBSI, catheter related blood stream infection; HPN, home parenteral
334 nutrition

335 ^a Covariate only included in CRBSI regression model; ^b Covariate only included in the
336 deaths regression model.

337 Table 2: Patient baseline characteristics

Characteristic	Category	Frequency (%)
Age (N=210)		
	Mean (SD)	55.9 (14.8)
Gender (N=210)		
	Male	119 (56.7%)
	Female	91 (43.3%)
BMI (N=209*)		
	Underweight	26 (12.44%)
	Healthy	108 (51.67%)
	Overweight	50 (23.92%)
	Obese	25 (11.96%)
Region (N=210)		
England		198 (94.29%)
	North East	4 (1.90%)
	North West	165 (78.57%)
	Yorkshire and Humber	14 (6.67%)
	East Midlands	6 (2.86%)
	West Midlands	5 (2.38%)
	South West	3 (1.43%)

Characteristic	Category	Frequency (%)
Wales		10 (4.76%)
Scotland		1 (0.48%)
Ireland		1 (0.48%)
Offshore		1 (0.48%)
	Isle of Man	1 (0.48%)
Infusion care (N=210)		
	Self	80 (38.10%)
	Family member	10 (4.76%)
	Nursed	120 (57.14%)
IF diagnosis (N=210)		
	Active malignancy	20 (9.52%)
	Crohn's disease	36 (17.14%)
	Motility disorders	20 (9.52%)
	Radiation enteritis	5 (2.38%)
	Scleroderma	2 (0.95%)
	Surgical complications	89 (42.38%)
	Vascular	27 (12.86%)
	Other	11 (5.24%)
Key: BMI, body mass index; IF, intestinal failure; N, number of patients Notes: *patient 192 has no record of BMI		

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340 Table 3: Rate of clinical events by home parenteral nutrition administered per week
 341 expressed as per 1000 catheter days
 342

Days per week	no	HPN records	Time days	Days in hospital	Admissions all cause	Unplanned days in hospital	Unplanned admission all-cause	CRBSI	Deaths
2	11	11	2754	18 (6.536)	5 (1.816)	18 (6.536)	1 (0.363)	1 (0.363)	0 (0.000)
3	27	34	8532	67 (7.853)	11 (1.289)	26 (3.047)	2 (0.234)	1 (0.117)	2 (0.234)
3.5	3	3	85	0 (0.000)	0 (0.000)	0 (0.000)	0 (0.000)	0 (0.000)	1 (11.765)
4	39	65	1193 3	249 (20.867)	14 (1.173)	180 (15.084)	7 (0.587)	2 (0.168)	4 (0.335)
5	49	75	1403 9	584 (41.598)	20 (1.425)	194 (13.819)	4 (0.285)	0 (0.000)	2 (0.142)
6	34	54	9736	753 (77.342)	16 (1.643)	409 (42.009)	10 (1.027)	2 (0.205)	3 (0.308)
7	152	319	6345 8	3923 (61.820)	130 (2.049)	1657 (26.112)	45 (0.709)	16 (0.252)	32 (0.504)
All	210	561	1105 37	5594 (50.607)	196 (1.773)	2484 (22.472)	69 (0.624)	22 (0.199)	44 (0.398)

343 CRBSI- catheter-related blood stream infection, HPN- home parenteral nutrition
 344 All data expressed per 1000 catheter days
 345

346 Table 4: Cause of death classification

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Cause of death	HPN Related	Underlying IF disease	Non-IF-related	Frequency
Malignancy	0	16	4	23 (52.3%)
Pneumonia	0	0	11	11 (25.0%)
Cardiac	0	0	2	2 (4.5%)
Post-transplant	0	2	0	2 (4.5%)
Vasculitis	0	2	0	2 (4.5%)
GI Bleed	0	1	0	1 (2.3%)
Intracerebral haemorrhage	0	0	1	1 (2.3%)
Retroperitoneal haemorrhage	0	1	0	1 (2.3%)
Urinary sepsis	0	0	1	1 (2.3%)
Unknown	3			3 (6.8%)
Total deaths	0 (0.0%)	25 (56.8%)	19 (43.2%)	44 (100.0%)

348 GI- gastrointestinal, HPN- home parenteral nutrition, IF- intestinal failure

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351 Table 5: Classification of unplanned hospital admissions

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Unplanned admissions	HPN Related	Underlying IF disease	Non-IF-related	Frequency
CVC related issues	31	0	0	31 (44.9%)
Infection	19	0	0	19 (27.5%)
Malpositioning	4	0	0	4 (5.8%)
Exit site infection	3	0	0	3 (4.3%)
Fracture	3	0	0	3 (4.3%)
Occlusion	1	0	0	1 (1.4%)
Placement	1	0	0	1 (1.4%)
Venous thrombosis	3	0	0	3 (4.3%)
Abdominal pain (Obstruction/distension, weight loss, High stoma output)	0	9	0	9 (13.0%)
AKI	0	3	1	4 (5.8%)
Sepsis	0	5	5	10 (14.5%)
Abdominal sepsis	0	5	0	5 (7.2%)
Abdominal wall sepsis	0	0	1	1 (1.4%)
Cellulitis	0	0	1	1 (1.4%)
Perianal sepsis	0	1	0	1 (1.4%)
Pneumonia	0	0	2	2 (2.9%)

Enteral feeding issues (change of feed, failed DETF, feeding tube issues)	0	1	0	1 (1.4%)
Electrolyte imbalance	0	3	0	3 (4.3%)
Re-feeding	0	3	0	3 (4.3%)
HPN (start/alteration)	0	1	0	1 (1.4%)
Deranged LFTs	0	1	0	1 (1.4%)
Social	0		1	2 (2.9%)
Home Care (HPN) issue	0	1	0	
Vasculitis flare up	0	1	0	1 (1.4%)
Total unplanned admissions	34 (49.3%)	28 (40.6%)	7 (10.1%)	69 (100.0%)

353 AKI- acute kidney injury, CVC- central venous catheter, DETF- distal end tube feeding, HPN- home

354 parenteral nutrition; IF- intestinal failure, LFT- liver function tests,

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358 Table 6. Summary of regression analyses

Covariate	All-cause admissions RR* (95% CI) [p-value]	Unplanned admissions RR* (95% CI) [p-value]	Days in hospital (all-cause) RR* (95% CI) [p-value]	Days in hospital (unplanned) RR* (95% CI) [p-value]	CRBSI RR* (95% CI) [p-value]	Death OR* (95% CI) [p-value]
Total HPN days per week	1.12 (0.99 ,1.26) [0.0688]	1.19 (0.97 ,1.46) [0.0900]	1.50 (1.26 ,1.78) [<0.0001]	1.39 (1.10 ,1.75) [0.0060]	1.26 (0.88 ,1.79) [0.2046]	1.10 (0.82 ,1.47) [0.5150]
CVC care (nurse care vs self/family care)	Not included	Not included	Not included	Not included	1.32 (0.50 ,3.51) [0.5751]	Not included
Gender (male vs female)	1.18 (0.84 ,1.65) [0.3417]	1.17 (0.70 ,1.95) [0.5545]	1.40 (0.87 ,2.28) [0.1697]	1.84 (0.96 ,3.53) [0.0682]	1.62 (0.66 ,3.95) [0.2918]	2.23 (1.05 ,4.74) [0.0385]
Diagnosis (ref=other diagnosis)						
Crohn's disease	1.01 (0.64 ,1.57) [0.9792]	0.98 (0.50 ,1.90) [0.9481]	1.04 (0.55 ,1.96) [0.8986]	0.80 (0.34 ,1.88) [0.6128]	1.02 (0.33 ,3.21) [0.9664]	0.29 (0.08 ,1.02) [0.0537]
Surgical complications	1.03 (0.70 ,1.52) [0.8844]	0.91 (0.50 ,1.66) [0.7602]	1.05 (0.60 ,1.83) [0.8620]	0.42 (0.20 ,0.90) [0.0256]	1.05 (0.36 ,3.06) [0.9355]	0.61 (0.27 ,1.38) [0.2371]

Covariate	All-cause admissions RR* (95% CI) [p-value]	Unplanned admissions RR* (95% CI) [p-value]	Days in hospital (all-cause) RR* (95% CI) [p-value]	Days in hospital (unplanned) RR* (95% CI) [p-value]	CRBSI RR* (95% CI) [p-value]	Death OR* (95% CI) [p-value]
Previous CRBSI (yes vs no)	Not included	Not included	Not included	Not included	Not included	2.34 (0.65 ,8.47) [0.1951]
Time on HPN (1000 days)	0.71 (0.39 ,1.27) [0.2465]	0.89 (0.34 ,2.31) [0.8053]	0.38 (0.16 ,0.89) [0.0271]	1.35 (0.43 ,4.20) [0.6092]	2.59 (0.62 ,10.89) [0.2033]	0.14 (0.02 ,0.79) [0.0270]
BMI	Not included	Not included	Not included	Not included	1.00 (0.91 ,1.10) [0.9983]	Not included
Age of HPN onset (years)	0.98 (0.97 ,0.99) [0.0002]	0.98 (0.97 ,1.00) [0.0675]	0.98 (0.96 ,0.99) [0.0092]	1.00 (0.97 ,1.02) [0.6866]	0.98 (0.94 ,1.01) [0.1570]	1.04 (1.01 ,1.07) [0.0087]

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360 CI- confidence interval, CRBSI- catheter related blood stream infection, CVC- central venous

361 catheter, HPN- home parenteral nutrition, OR- odds ratio, RR- relative rate.

362 * relative to reference category (categorical variable) or one unit increase (continuous variable);

363 yellow highlighting indicates variable of interest.

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