

The impact of intestinal transplantation on quality of life

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Abstract

Introduction

Intestinal failure (IF) and intestinal transplant (ITx) are associated with poor quality of life (QoL). Disease-specific assessment of QoL for IF and ITx is challenging, owing to the different problems encountered. We have sought to compare QoL pre-ITx with post-ITx and have compared generic QoL with a stable IF population.

Methods

Two prospectively maintained databases of patients referred for and undergoing ITx and a chronic (Type 2 & 3) IF cohort were interrogated. QoL instruments used were generic (EQ-5D-5L and SF-36) and disease-specific (HPN-QOL and ITx-QOL). Analysis used Student's t-test and one-way ANOVA with Bonferroni correction for multiple comparisons. Data were collected pre- and post-ITx at 3, 6, 12-months and yearly thereafter.

Results

All QoL instruments improved following ITx to levels comparable with a cohort of stable IF patients not requiring ITx. Both the visual analogue score component (EQ-5D-5L) and the effect of underlying illness on QoL (HPN-QOL/ITx-QOL) were higher following ITx than either pre-ITx or when compared with the IF cohort. Effects on general health, ability to eat and drink, to holiday and travel were improved as early as 3 months post-ITx. Other components did not before 6-12 months following ITx, but were maintained to at least 24 months. Patient personal financial pressures are greater following ITx, even in a publically funded healthcare system.

Conclusion

ITx has beneficial effects on QoL compared to those assessed for or awaiting ITx. QoL following ITx is similar to patients with IF not requiring ITx. A QoL instrument that covers the journey of patients

51 from IF through ITx would assist longitudinal analysis of the value and timing of ITx at an individual
52 level.

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55 **Keywords**

56 Intestinal failure; intestinal transplant; quality of life; home parenteral nutrition; immunosuppression;
57 composite tissue allograft

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59 **Abbreviations**

60 ANOVA = Analysis of variance

61 BRC = Biomedical Research Centre

62 CRBSI = Catheter-related blood stream infection

63 HPN = Home parenteral nutrition

64 ICU = Intensive Care Unit

65 IF = Intestinal failure

66 IFALD = Intestinal failure-associated liver disease

67 ITx = Intestinal transplant

68 NIHR = National Institute for Health Research

69 PN = Parenteral nutrition

70 PNIQ = Parenteral Nutrition Impact Questionnaire

71 PROM = Patient reported outcome measure

72 QALY = Quality adjusted life year

73 QoL = Quality of life

74 SD = Standard deviation

75 UK = United Kingdom

76 VAS = Visual analogue scale

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Introduction

Intestinal transplantation (ITx) has emerged as a viable therapy for selected patients with intestinal failure. In the United Kingdom, transplantation assessment is indicated for patients who have i) developed life-threatening complications of parenteral nutrition (PN) (including central venous catheter related infection or thrombosis, and intestinal-failure associated liver disease (IFALD)), ii) who need abdominal evisceration for conditions such as desmoid disease, or iii) where transplantation of another organ is necessary but patient survival would be adversely affected without simultaneous ITx. Occasionally, ITx may be indicated in patients for reason of very poor quality of life (QoL) on PN in the presence of irreversible intestinal failure, in situations in which ITx is felt likely to improve this. It is therefore logical not only to measure QoL for patients on PN, but also to determine whether this is improved by ITx.

Many studies over the last forty years have attempted to measure QoL in patients with intestinal failure. In 2007 a systematic review¹ of 26 studies of patients on home PN (HPN) demonstrated variation in QoL, but also showed that patients on HPN experience a lower QoL than the healthy population, or those on other nutritional therapy and those with end stage renal failure. A subsequent study reported that patient-reported QoL on PN was “good” to “wonderful”². Negative effects of PN have been demonstrated on employment, sexual activity, psychological health and freedom to go on holiday^{1,3,4}. More recently, the Parenteral Nutrition Impact Questionnaire (PNIQ), brought together through patient related outcome measures (PROMs)⁵, has demonstrated similar QoL between patients with IF, cancer, or IBD and better QoL for patients with dysmotility on PN compared to patients on PN due to other conditions⁶. It is important to recognise that QoL does not simply reflect the impact of PN, but also the aetiology of intestinal failure⁷.

There are few studies assessing quality of life in adult patients following ITx. Such as there are vary in their comparator group (e.g. healthy population, pre-ITx, or those established on HPN), which has been the subject of a systematic review⁸. This review highlighted a positive effect of transplantation

on psychological wellbeing, leisure/recreation and sleep; perhaps not surprisingly, QoL following ITx remains lower than that of the healthy population⁹. The literature is biased towards the few centres which have published their QoL data, with one in the USA¹⁰⁻¹⁵, one in Italy^{9,16,17}, and one in the UK^{18,19}. Published UK experience to date has demonstrated similar QoL post-ITx compared to PN and reported that both groups exhibit a better QoL than those with complicated intestinal failure (patients in whom transplantation is indicated, but not deemed feasible)¹⁸. Subsequent analysis reported trends to improved QoL following ITx in 50%, decline in 25% and no change in 25%, compared to pre-ITx¹⁹. The questionnaires used to assess QoL vary between studies, none of which have been fully validated for the ITx population. An ITx-specific questionnaire, referred to as ITx-QOL, was developed in 2012¹⁷ as an adaptation of the validated HPN-QOL²⁰ questionnaire.

In this study we aimed to measure QoL using the disease-specific HPN-QOL for patients with IF or ITx-QOL following ITx, alongside two validated generic QoL instruments, SF-36 and EQ-5D-5L. Patients were assessed before and after ITx at fixed time-points and compared with a cohort of patients on PN not requiring transplantation or assessment.

Methods

Comparative, retrospective analysis of two prospectively maintained adult databases at Oxford University Hospitals NHS Foundation Trust between October 2007 and April 2018 for the ITx cohort and August 2014 – December 2015 for the IF cohort. The database of all patients undergoing assessment for intestinal transplantation includes patients for whom, after assessment (and, if appropriate, discussion at the UK National Adult Small Intestinal Transplant forum), transplantation was not deemed appropriate or necessary. The database of patients with chronic IF (Type 2 or Type 3 on HPN²¹) includes patients who did not warrant transplantation or assessment. QoL data were collected on all patients with IF on HPN and those undergoing transplantation assessment. QoL data were then collected after transplantation at defined intervals, but retrospective recall of quality of life prior to ITx were excluded. Data collection occurred pre-ITx assessment, at 3, 6, 12-months and then yearly. Data for the IF cohort were collected at an outpatient clinic appointment and again typically after 1 year. Assessment of QoL forms part of routine clinical care in our unit and therefore this study did not require ethical approval.

Paper questionnaires were manually inputted into the electronic database. Analysis was carried out on Excel (Microsoft®, USA) spreadsheets and Prism v7 (GraphPad, USA). Comparisons were made between pre-ITx vs. any time point post-ITx; pre-ITx vs. IF cohort; post-ITx (all time points) vs IF cohort.

Statistical hypothesis used two-tailed, unpaired Student's T test, or one-way ANOVA with Bonferroni correction for multiple comparisons. Unless otherwise specified, all data are displayed as mean ± standard deviation.

QoL assessment

The instruments used were the generic EQ-5D-5L^{22,23}, SF-36⁴, and disease-specific HPN-QOL²⁰ and ITx-QOL¹⁷ which have previously been subject to varying degrees of validation. Rigorous validation

includes not only tests of reliability (internal consistency, test-retest reliability, inter-rater reliability) but also of validity (see references for examples²⁴⁻²⁶).

- EQ-5D-5L: Five questions about function and psychological wellbeing with an additional visual analogue scale (VAS). The five domains can be amalgamated into a single index value (utility score) adjusted based on valuation sets for the general population using online calculators freely available via EuroQol. This is a validated instrument²², a precursor of which (EQ-5D-3L) is used by the National Institute for Health and Care Excellence to calculate Quality-Adjusted Life Years (QALYs) in technology appraisal. A recent position statement²⁷ supports collection of 5L data but at present recommends the 3L to calculate utility values following a quality review of the valuation set^{28,29}.
- SF-36: 36 questions with varying depth of answers which are analysed by collating the answers into different groups to produce an overall result for different psychological, physical or social scenarios, according to the validated methodology. This is extensively used internationally and has been validated both initially³⁰⁻³² and then subsequently across a range of diseases³³.
- HPN-QOL: 46 questions about activities or scenarios and the effect that HPN has on an individual. This was used to assess QoL both in the IF cohort and also patients assessed for transplant (pre-ITx) regardless of whether they were subsequently transplanted. This was created and then validated specifically for HPN²⁰. We have not reported on results for 'Nutrition team' or 'Pump' as these are less applicable to patients following ITx.
- ITx-QOL: HPN-QOL questions were changed from "HPN" to "ITx" for questions 1, 2, 3, 4, 8, 17, 35, 36, 37 and 46 and from "catheter" to "ITx" in question 6, as previously described¹⁷. This was only used to assess QoL post-ITx. As an adaptation of the HPN-QOL, this questionnaire has never been formally validated.

177 The responses for HPN-QOL and ITx-QOL for patients undergoing transplantation were used as a
178 continuum given the similarity of questions and are displayed as such in the results. Analysis of SF-36
179 and HPN/ITx-QOL are predetermined: SF-36 combines different answers into domains of outcome
180 including physical functioning, emotional wellbeing, and pain; HPN/ITx-QOL have domains
181 including holidays and travel, sexual function and body image.

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Results

A total of 123 patients were referred to Oxford for consideration of ITx between June 2006 and April 2018. The flow of patients through assessment and transplantation is shown in Figure 1 together with details of the number of instruments used per patient in each group. Completion of QoL assessment was voluntary and not all patients wished to complete all three instruments. Of the transplanted cohort (n=43), 9 patients did not complete assessment of pre-ITx QoL, and 9 patients did not complete assessment of post-ITx QoL. These were, however, not the same nine patients in each group. No transplanted patient declined to complete both pre- and post-ITx QoL instruments. Between August 2014 and December 2015, 31/42 (74%) patients in our IF cohort were assessed for QoL using EQ-5D-5L and HPN-QOL. All patients completed both instruments. There were no data for SF-36 recorded for the Oxford IF cohort as this questionnaire was not in routine use for these patients during the period of study.

Disease-specific QoL

HPN-QOL and ITx-QOL

Pre-ITx cohort (20 responses): 16/43 (37%) patients completed pre-ITx QoL assessment, but 2 were excluded, because QoL was recorded following ITx in a retrospective assessment of pre-transplant QoL. This resulted in 14/43 (33%) ITx patients and an additional 6/42 (14%) patients who were assessed but not transplanted took the HPN-QOL, giving a total of 20/85 (24%) with HPN-QOL data.

Post-ITx cohort (30 responses): 18/43 (42%) had completed ITx-QOL on 30 occasions, mean 1.7 per patient at mean 18.2 (+/- 8.0) months post-ITx. There were nine (30%) responses at 3 months, five (17%) at 6 months, seven (23%) at 12 months, and nine (30%) at or beyond 24 months following ITx. 8/43 (19%) patients had both HPN-QOL and ITx-QOL data, with 10 ITx-QOL data recordings, mean 1.3 per patient.

IF cohort (53 responses): 31/42 (74%) patients undertook 53 recordings of HPN-QoL, mean 1.7 per patient. 15/30 (50%) undertook more than one recording of QoL separated by mean 5.6 (+/- 1.1) months.

Ratings for QoL from individual patients in the IF cohort did not vary over the period of measurement. QoL following ITx improved in 6 of 8 functional outcomes (Figure 2, Supplementary Table 1) with early improvement at 3 months shown for ability to holiday/travel and ability to eat/drink. Later improvements were shown for physical, emotional and sexual function, and employment, often not until 12 or 24 months following ITx. Within symptom outcomes (Figure 3, Supplementary Table 1) no effect of ITx was seen on body image, weight, immobility, sleep pattern or fatigue. This latter category was worse in patients undergoing ITx assessment (pre-ITx) than either those in the IF cohort or post-ITx cohort. Gastrointestinal symptoms, other pain, and stoma/bowel function were improved by ITx. This data also showed that the 'other pain' category post-ITx was better even than those patients in the IF cohort. Overall QoL and the effect of HPN or ITx on QoL (Figure 4) post-ITx was restored to similar levels as the IF cohort. The effect of underlying illness on QoL was improved following ITx compared to either other comparator group.

Financial issues

Greater financial issues were experienced by patients both pre-ITx (43.33 +/- 34.37) and post-ITx (44.44 +/- 30.74) compared to patients with IF (21.38 +/- 32.75). This persisted through all timepoints of follow up.

Generic QoL

1) EQ-5D-5L

Pre-ITx cohort (19 responses): 12/43 (28%) ITx patients and 7/42 (17%) ITx assessment patients undertook EQ-5D-5L; total data set was 19/85 (22%).

Post-ITx cohort (50 responses): 24/43 (56%) had completed the EQ-5D-5L with 50 recordings (mean 2.1 per patient) occurring at a mean 23.9 (+/- 6.55) months following ITx. There were four (8%) responses at 3 months, five (10%) at 6 months, twelve (24%) at 12 months, and twenty seven (54%) at or beyond 24 months following ITx. 8/43 (19%) have data for both pre- and post-ITx. It is not clear for 2 responses in this cohort at what timepoint following ITx the questionnaire was completed – this has been included in the overall cohort but not for specific timepoints.

IF cohort (49 responses): 31/42 (74%) HPN patients undertook 49 recordings of EQ-5D-5L, mean 1.6 per patient. 15/31 (48%) undertook more than one recording of QoL separated by mean 5 (+/- 1.34) months.

Ratings for QoL from individual patients in the IF cohort did not vary over the period of measurement. The VAS (Figure 5, Supplementary Table 2) demonstrated restoration of QoL following ITx to levels that even exceeds that of a stable IF cohort but that this does not occur for 6 months following ITx. However, the improvement was sustained to beyond 24 months. Improvements were seen in 4 of 5 individual domains, excluding anxiety/depression, but similar to VAS not for 6 months following ITx. Mobility was better following ITx than the IF cohort possibly related to fewer intravenous lines and infusions. The index values (utility scores) for this instrument followed a similar pattern to the VAS with a mean pre-ITx score 0.42 and post-ITx 0.75, comparable with the IF cohort 0.68.

2) SF-36

Pre-ITx cohort (25 responses): 14/43 (33%) and 11/42 (26%) transplant assessment patients undertook SF-36 at assessment for ITx. This resulted in a total pre-ITx cohort of 25/85 (29%) data sets.

Post-ITx cohort (41 responses): 23/43 (53%) undertook SF-36 41 times (mean 1.8 per patient) post-ITx at mean 21.9 (+/- 6.5) months. There were eight (20%) responses at 3 months, four (10%) at 6

months, nine (22%) at 12 months, and sixteen (39%) at or beyond 24 months following ITx. 11/43 (26%) had pre-ITx and post-ITx paired data and recorded post-ITx QoL data 25 times (mean 2.3 per patient) at mean 16.9 (+/- 7.2) months post-ITx. It is not clear for 3 responses in this cohort at what timepoint following ITx the questionnaire was completed – these have been included in the overall cohort but not for specific timepoints.

IF cohort: No data.

Summary scores for SF-36 both in physical and mental components (Figure 6, Supplementary Table 3) were improved following ITx meeting significance only from 12 months in the physical component. Individual domains (Figure 7) demonstrate a positive effect of ITx across 6 of 8 areas. Frequently the benefits were not seen for 6-12 months following ITx but general health improves as early as 3 months post-operatively. No effect was demonstrated for emotional well-being.

Discussion

The World Health Organization defines QoL as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. Clinical studies have historically focussed on hard scientific endpoints, but increasing attention is being given to PROMs as useful measures to assess outcomes of treatments. It is, after all, a goal of any therapy to improve the quality of life of patients. Measuring QoL is therefore important to inform changes to practice and to assess the value of therapeutic interventions³⁴.

In this study we have defined the effect on QoL of ITx using different instruments, both generic (EQ-5D-5L and SF-36), and disease specific (HPN/ITx-QOL). Across all instruments used, patients being assessed for ITx have a lower QoL than those established on HPN, but without complications necessitating assessment. ITx restores overall QoL to that of the patients established on HPN. Interestingly, two domains suggest QoL following ITx is even better than those established on HPN (VAS component of EQ-5D-5L, and 'effect of underlying illness on QoL' of HPN/ITx-QOL). Many improvements do not occur for at least 6 months post-operatively, but many continue to improve out to 12-24 months and beyond. Notably, the ability to eat and drink (an important component of everyone's QoL) improves as early as 3 months following transplant. This is in keeping with the intended aim of ITx, to negate the further need for intravenous fluid/nutrition support, so it is encouraging to see this occurring at the earliest stage. Of concern is the apparent negative financial impact of ITx on patients and this probably represents a combination of increased travel required to attend follow up in national centres and time lost from employment. There appears to be little, if any change, in SF-36 emotional function following ITx. This suggests an ongoing adverse effect of illness on these patients, although a comparator healthy population or IF cohort was not included in this study. The extent to which this is an issue specific to ITx is therefore unclear. Perhaps surprisingly, there was no effect of ITx on body image.

Our data using EQ-5D-5L demonstrates that patients with IF who are assessed for ITx have a mean utility score of 0.42 and VAS 41.3. This is lower than that experienced by patients with many other chronic diseases. Adults with cystic fibrosis, who often require central venous access and numerous hospital admissions, have been shown to have a utility score of 0.67 and an average VAS of 71.9³⁵. Patients with mild heart failure exhibit mean utility scores of 0.78 whereas those with New York Heart Association class III-IV show a similar degree of impairment of QoL to our cohort (mean 0.51)³⁶. Another group requiring long-term central venous access are those on renal dialysis. Here, VAS scores are 60.4 for haemodialysis and 61.2 for peritoneal dialysis³⁷ which is similar to our IF cohort (VAS 62.7). Amongst UK patients awaiting renal transplant, utility scores are 0.77, improving to 0.83 six months following transplant³⁸. Given these data for other conditions, it is therefore encouraging that following ITx, mean utility score improves to 0.75 and VAS 73.6 although there is still work to be done to improve QoL to levels seen with renal transplantation for instance. The findings with SF-36 are similar to those with EQ-5D-5L. Across all domains, patients assessed for ITx exhibit lower QoL than patients with cystic fibrosis³⁹, and a number of other conditions including congestive heart failure, chronic lung disease, diabetes mellitus or arthritis⁴⁰. The group with greatest similarity are patients undergoing renal dialysis where studies have previously demonstrated an appreciable effect on QoL with a beneficial effect of renal transplant^{41,42}. Likewise, the effect of ITx in our cohort is to improve QoL across all domains although not to the same levels as renal transplantation. This likely reflects not only the conditions for which ITx is indicated but also the greater burden of the surgery on our patients.

The key strengths of our study are that we have used multiple, mainly validated, instruments to measure QoL both at the generic and disease-specific level. Comparable results between different instruments provides reassurance for our conclusions that QoL improves following ITx. We have compared not only pre- versus post-ITx but also assessed the effect of time-after-transplant on different domains. Comparison with a cohort of patients stable on HPN provides a meaningful comparator for clinical practice. Our cohort sizes both for IF and ITx are comparable to or larger than other published reports. This study adds to the UK experience of ITx. Other published UK data, from

a centre undertaking full multivisceral transplantation, demonstrated a trend to improved QoL in about 50% of patients, with QoL continuing to improve with time following transplant¹⁹.

There are, however limitations to this study: QoL responses were lacking for many of our patients undergoing ITx. It is possible that those who did not respond had a worse QoL, skewing our data towards demonstrating improved outcomes. Anecdotally, however, this appears unlikely from comments made in clinic and our data appears to reflect overall experience. Because there were few datasets tracking individual patients from pre- to post-ITx, data are presented as grouped data. It is not possible, therefore, to draw conclusions on QoL outcomes depending on the underlying cause of IF. Prospective, structured, longitudinal data collection is in progress.

Despite the massive undertaking for patients that is ITx, the fact that QoL improved following surgery is credible. Patients are no longer reliant upon central venous catheters and the time to infuse PN, providing greater freedom and more flexibility. It is, nevertheless, essential that the ITx community develops specific tools to analyse QoL and other PROMs using a common language, similar to PNIQ for patients with IF. Mandatory reporting of long-term QoL through local and national databases could help better understand the impact of HPN and ITx on our patients.

This study shows that ITx returns QoL to a similar level to patients who are well and stable on HPN. Both the VAS component of the generic EQ-5D-5L QoL questionnaire and the ‘effect of underlying illness on QoL’ of the HPN-QoL/ITx-QoL, show that QoL after ITx becomes better than observed by patients on HPN. There are improvements in pain and stoma/bowel function, but financial pressures are greater following ITx. However, given that many QoL measures post-ITx are only restored to, and do not exceed, QoL in patients stable on HPN, our findings may raise questions about poor QoL on HPN alone as an indication for ITx. Importantly, many patients on HPN with poor QoL also have other indications for ITx such as loss of vascular access or venous thromboses and therefore cannot necessarily be grouped within the ‘stable IF’ cohort. As more patients are transplanted internationally for QoL issues in the absence of other complications, tracking of QoL will be essential

361 to determine whether we can improve longer term QoL in this cohort through ITx or whether, indeed,
362 ITx should be reserved only for those patients experiencing vascular or hepatic complications of long
363 term PN.
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365 Stable IF patients and those undergoing ITx represent different patient groups along a spectrum of
366 disease. A more systematic application of the instruments used in this study, none of which have been
367 validated for the ITx population, may not necessarily identify important effects on QoL as patients
368 progress along this spectrum. A disease-specific QoL tool that covers the journey of patients from IF
369 through ITx needs to be developed using state of the art methodology to ensure not only validity, but
370 also reliability and responsiveness.

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Statement of Authorship

TA: Formal Analysis, Data Curation, Writing – Original Draft, Writing – Review and Editing.
LH, AS, HH: Investigation, Resources, Writing – Review and Editing.
LV, GV, SR, HG, SPLT, PJF: Resources, Writing – Review and Editing.
PJA: Conceptualisation, Methodology, Formal Analysis, Resources, Writing – Review and Editing, Supervision.
All authors approved the final manuscript.

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Table 1

Baseline patient demographics of patients in the ITx and IF cohorts. Data are displayed as n(%) or mean (range). The two groups were recognised to be unrelated cohorts and therefore no statistical analysis was applied to the demographic data. CRBSI = catheter-related blood stream infection; IFALD = intestinal-failure associated liver disease; QoL = quality of life.

^aOther includes conditions such as encapsulating peritoneal sclerosis, neuroendocrine tumours, Ehlers-Danlos type 3, autoimmune polyendocrinopathy, candidiasis and ectodermal dysplasia syndrome (APECED), ulcerative colitis, radiation enteropathy, and other causes of short/ultra-short bowel.

^b14 patients in this group received PN for an unknown duration prior to ITx.

^cOne patient did not receive PN before ITx.

^dThese patients were all referred to another centre to receive a liver graft in addition to intestine.

^eData only available for 23/42 patients in this group.

^fData only available for 38/43 patients in this group.

	ITx cohort (assessed but not transplanted) (n=42)	ITx cohort (assessed and transplanted) (n=43)	IF cohort (n=42)
Age (years)	48.1 (21-69)	42.0 (23-73)	53.0 (21-86)
Gender (M)	17 (40)	25 (58)	22 (52)
Causes of IF			
<i>Crohn's disease</i>	9 (21)	8 (19)	22 (52)
<i>Dysmotility</i>	6 (14)	6 (14)	3 (7)
<i>Mesenteric ischaemia</i>	12 (29)	8 (19)	4 (10)
<i>Surgical complications</i>	4 (10)	5 (12)	3 (7)
<i>Desmoid</i>	2 (5)	4 (9)	0 (0)
<i>Pseudomyxoma peritonei</i>	6 (14)	8 (19)	1 (2)

<i>Other^a</i>	23 (55)	4 (9)	9 (21)
Months on PN	86 (1-240) ^b	42 (0-198) ^c	55 (3-186)
PN-related complications			
<i>CRBSI</i>	10 (24)	15 (35)	18 (43)
<i>Thrombosis</i>	15 (36)	17 (40)	1 (2)
<i>IFALD (cholestasis alone, bilirubin > 17.1 μmol/l)</i>	7 (17)	5 (12)	12 (29)
<i>IFALD (impending liver failure, bilirubin > 54 μmol/l)</i>	3 (7)	2 (5)	1 (2)
<i>IFALD (overt liver failure)</i>	3 (7) ^d	0 (0)	0 (0)
<i>IFALD (unknown)</i>	0 (0)	0 (0)	1 (2)
Primary indication(s) for ITx assessment			
<i>CRBSI</i>	0 (0)	1 (2)	Not applicable
<i>Thrombosis</i>	4 (10)	5 (12)	Not applicable
<i>IFALD</i>	5 (12)	0 (0)	Not applicable
<i>Ultra-short bowel syndrome</i>	11 (26)	10 (23)	Not applicable
<i>Intra-abdominal malignancy (desmoid, neuroendocrine tumour, pseudomyxoma peritonii)</i>	9 (21)	13 (30)	Not applicable
<i>QoL</i>	3 (7)	4 (9)	Not applicable
<i>Chronic rejection</i>	0 (0)	1 (2)	Not applicable
<i>Visceral neuromyopathy</i>	2 (5)	3 (7)	Not applicable
<i>Mucosal disease</i>	1 (2)	6 (14)	Not applicable
<i>Other</i>	2 (5)	0 (0)	Not applicable
<i>Unknown</i>	5 (12)	0 (0)	Not applicable
Marital status			

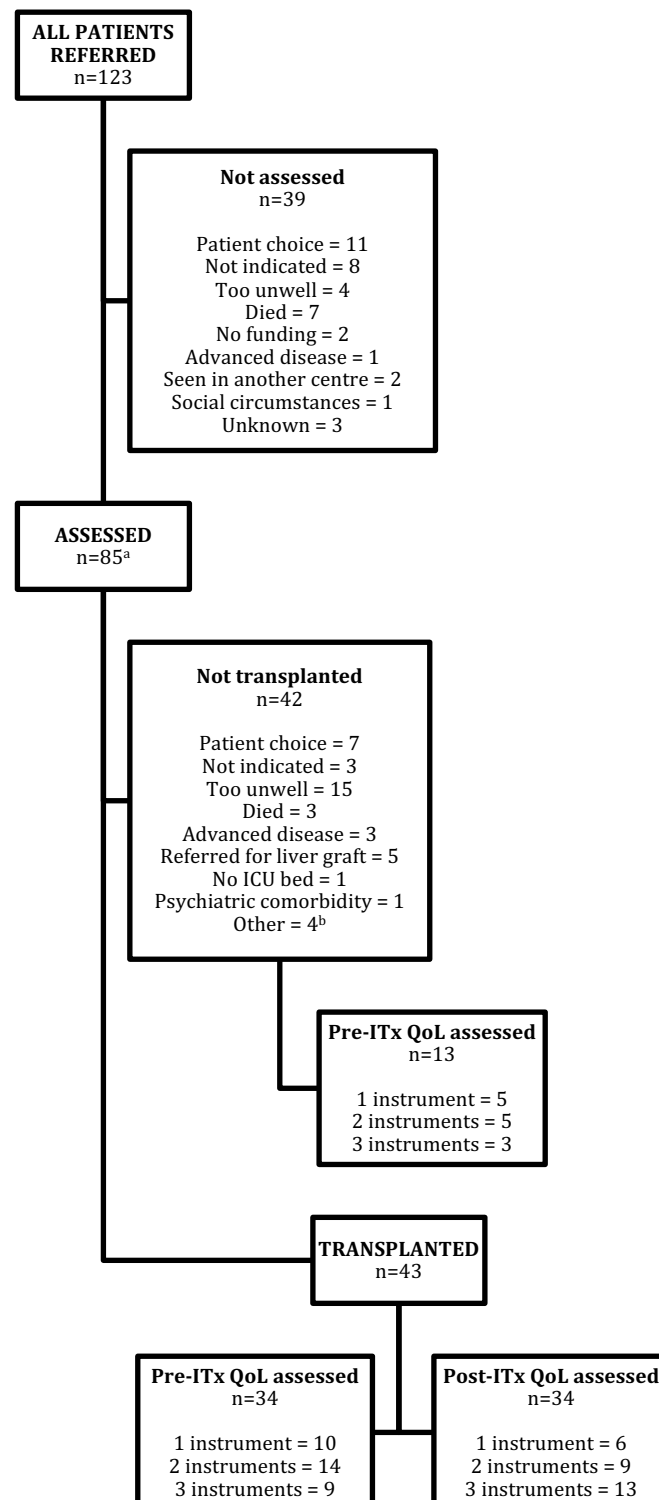
<i>Single</i>	9 (21)	13 (30)	14 (33)
<i>Married</i>	12 (29)	26 (60)	19 (45)
<i>Separated/Divorced</i>	4 (10)	3 (7)	3 (7)
<i>Widowed</i>	0 (0)	0 (0)	4 (10)
<i>Unknown</i>	17 (40)	1 (2)	2 (5)
Employment status			
<i>Employed/Self-employed full time</i>	2 (5)	4 (9)	6 (14)
<i>Employed/Self-employed part time</i>	2 (5)	9 (21)	12 (29)
<i>Retired</i>	2 (5)	5 (12)	9 (21)
<i>Unemployed</i>	7 (17)	21 (49)	13 (31)
<i>Full time education</i>	1 (2)	0 (0)	0 (0)
<i>Volunteer work</i>	1 (2)	0 (0)	0 (0)
<i>Unknown</i>	27 (64)	4 (9)	2 (5)
Living arrangements			
<i>Alone</i>	7 (17)	8 (19)	7 (17)
<i>With family</i>	21 (50)	32 (74)	23 (55)
<i>Unknown</i>	14 (33)	3 (7)	12 (29)
Highest educational attainment			
<i>School</i>	0 (0)	6 (14)	0 (0)
<i>College</i>	0 (0)	0 (0)	0 (0)
<i>Undergraduate</i>	0 (0)	2 (5)	0 (0)
<i>Postgraduate</i>	0 (0)	1 (2)	0 (0)
<i>Unknown</i>	42 (100)	34 (79)	42 (100)
Smoker (Yes)	8 (19) ^e	7 (16) ^f	6 (19)

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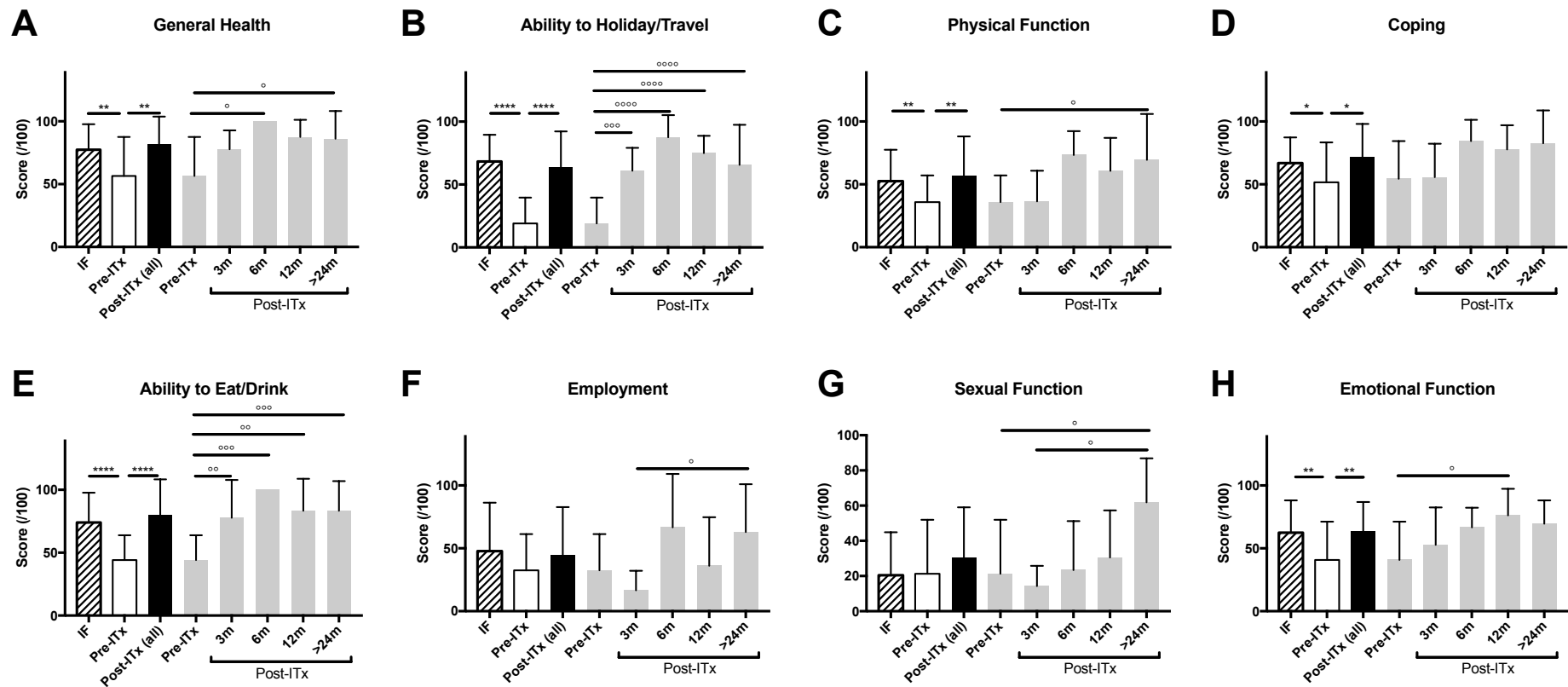
Figure 1

Flow of patients following referral and rates of completion of QoL instruments. ^a1 patient assessed and transplanted twice due to chronic rejection. ^b1 patient awaiting treatment with teduglutide, 1 underwent debulking surgery for pseudomyxoma peritonei, 2 underwent IF surgery to restore continuity. ICU = Intensive Care Unit, ITx = intestinal transplant, QoL = quality of life.



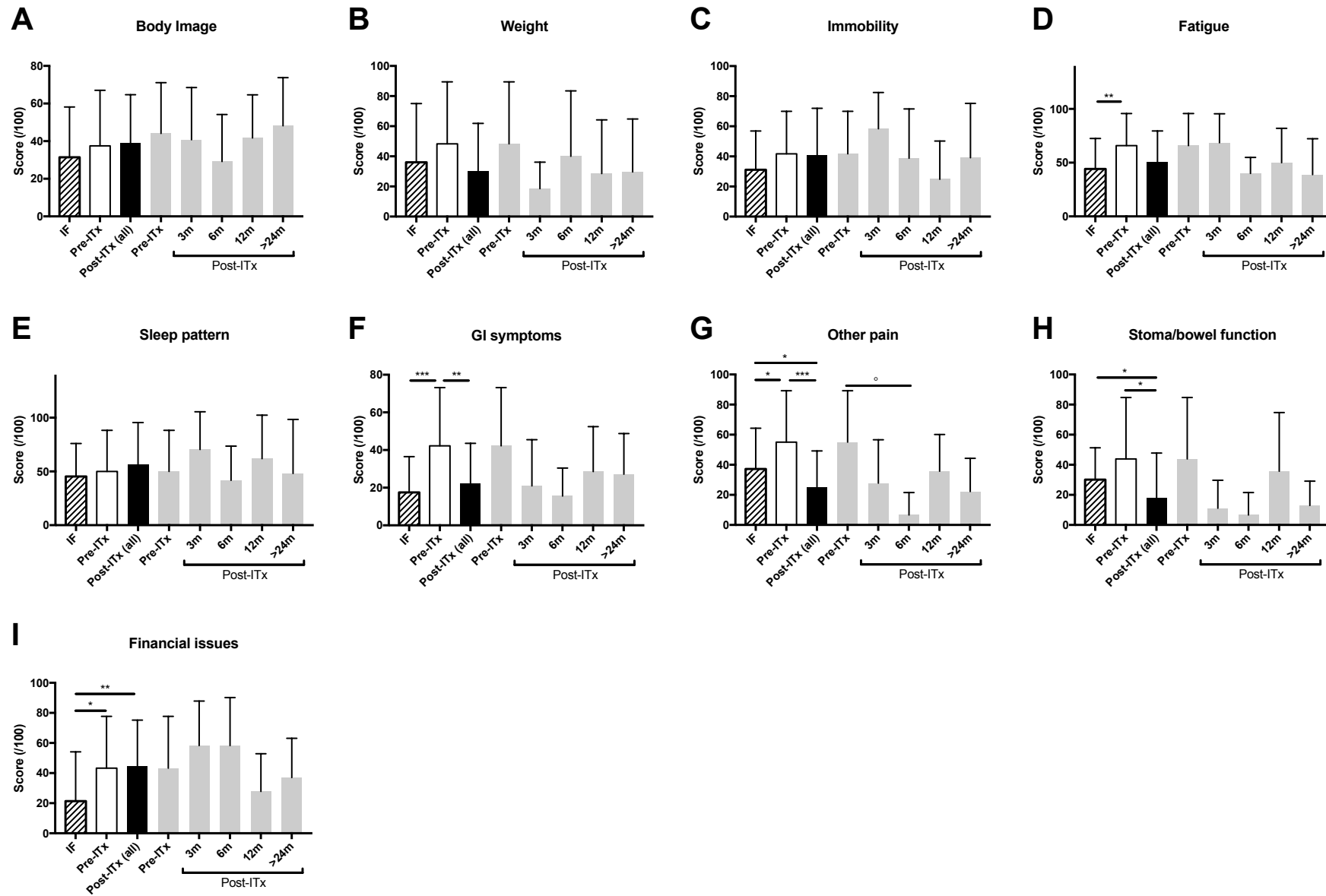
545 **Figure 2**

546 Functional scales and outcomes of the HPN-QOL and ITx-QOL. Improvements were seen across most domains following transplant (**A-E, H**) with some
547 improvements occurring at 3 months in ability to travel and with oral intake (**B, E**). Notably, issues such as employment and sexual function were late to
548 improve following transplant (**F, G**). Data is displayed as mean +/- standard deviation with higher scores indicative of better outcomes. Number of responses
549 in each category are IF (53), pre-ITx (20), post-ITx (all) (30), 3m (9), 6m (5), 12m (7), and >24m (9). Statistical comparisons are by unpaired, two-tailed t-test
550 (* p<0.0332, ** p<0.0021, **** p<0.0001) or one-way ANOVA with Bonferroni correction (° p<0.0332, °° p<0.0021, °°° p<0.0002). IF = intestinal failure;
551 ITx = intestinal transplant.

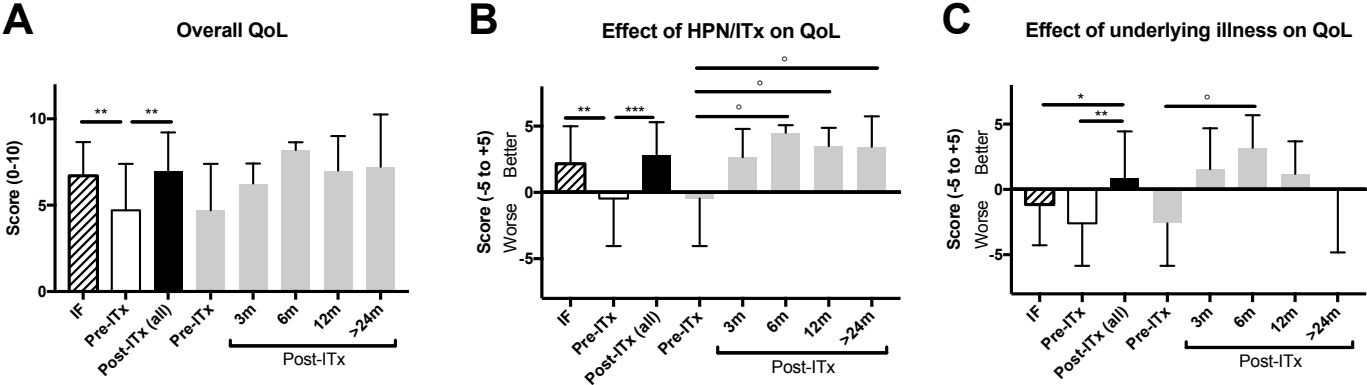


555 **Figure 3**

556 Symptom scales and outcomes of the HPN-QOL and ITx-QOL. Statistical improvement was seen for improvement in gastrointestinal symptoms (**F**), other
557 pain (**G**), and stoma/bowel function (**H**) following transplant but financial issues (**I**) persisted following transplant and were worse than in the IF cohort.
558 Fatigue was worse in those patients undergoing transplant assessment compared to the IF cohort not requiring transplant assessment (**D**). Data is displayed as
559 mean +/- standard deviation with higher scores indicative of worse symptoms. Number of responses in each category are IF (53), pre-ITx (20), post-ITx (all)
560 (30), 3m (9), 6m (5), 12m (7), and >24m (9). Statistical comparisons are by unpaired, two-tailed t-test (* $p<0.0332$, ** $p<0.0021$, *** $p<0.0002$) or one-way
561 ANOVA with Bonferroni correction ($^{\circ} p<0.0332$). IF = intestinal failure; ITx = intestinal transplant.



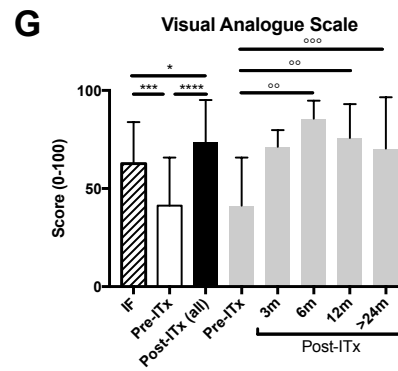
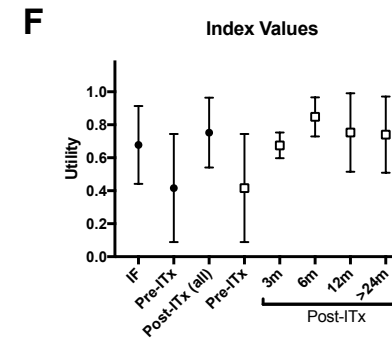
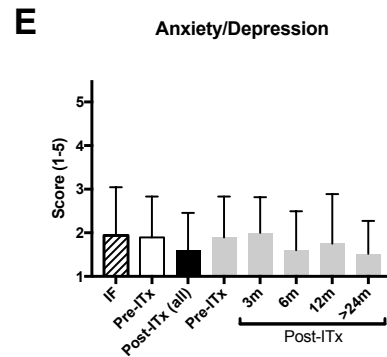
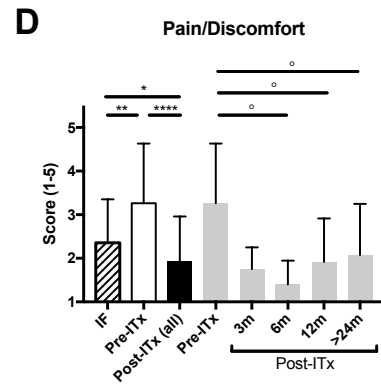
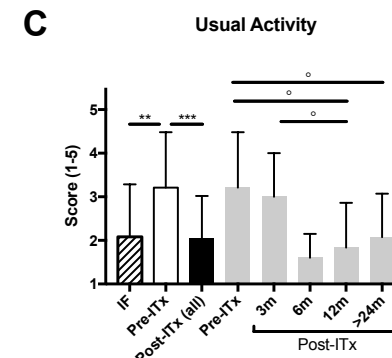
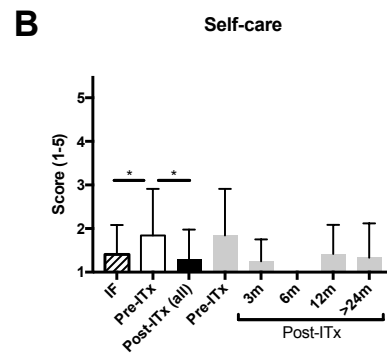
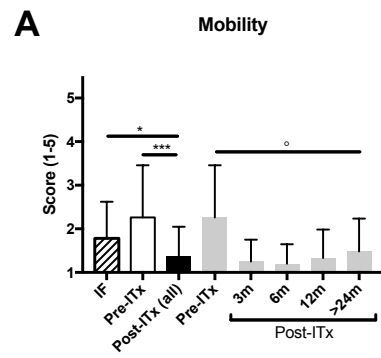
563 **Figure 4**
 564 Overall quality of life measures of the HPN-QOL and ITx-QOL. Quality of life improved across all domains following transplant (A-C) compared with pre-
 565 transplant. Data is displayed as mean +/- standard deviation with higher scores indicative of improved quality of life. Number of responses in each category
 566 are IF (53), pre-ITx (20), post-ITx (all) (30), 3m (9), 6m (5), 12m (7), and >24m (9). Statistical comparisons are by unpaired, two-tailed t-test (* $p < 0.0332$, **
 567 $p < 0.0021$, *** $p < 0.0002$) or one-way ANOVA with Bonferroni correction ($^{\circ} p < 0.0332$). IF = intestinal failure; ITx = intestinal transplant.
 568



571 **Figure 5**

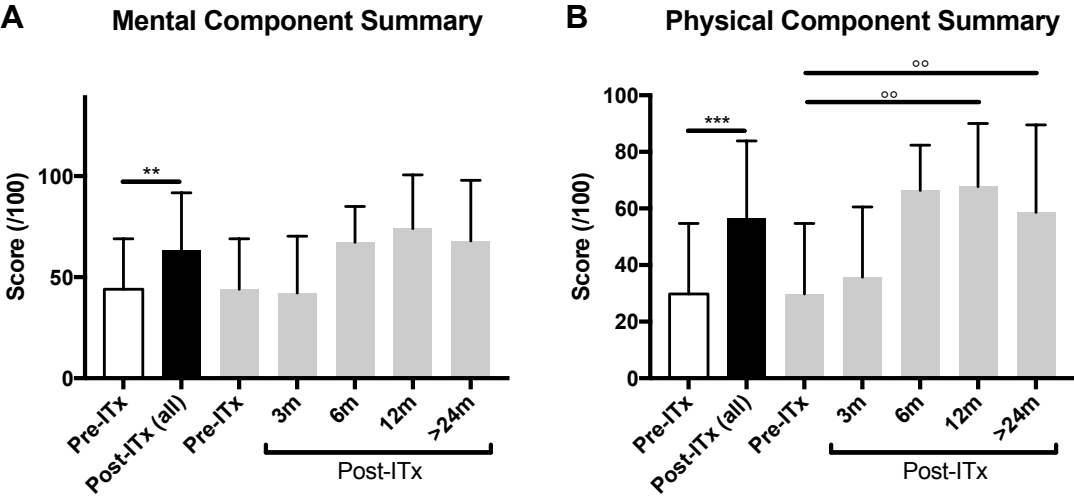
572 Responses to the EQ-5D-5L questionnaire between groups. Data demonstrated an improved overall quality of life following intestinal transplant comparable
573 with the IF cohort. The changes were predominantly after 6 months following transplantation but appear durable to beyond 24 months. Particular
574 improvement was seen within the usual activity (**C**) and pain/discomfort (**D**) domains. Scores for mobility (**A**), self-care (**B**), usual activity (**C**),
575 pain/discomfort (**D**), and anxiety/depression (**E**) are rated from 1-5 with 1 indicating the best health state within that category and 5 the worst. Index values
576 (**F**), calculating utility, is rated from 0-1 with higher utility reflective of increased quality of life. Visual analogue scale (**G**) is rated from 0-100 with higher
577 scores indicating a better health state. Data is displayed as mean +/- standard deviation. Number of responses in each category are IF (49), pre-ITx (19), post-
578 ITx (all) (50), 3m (4), 6m (5), 12m (12), and >24m (27). Statistical comparisons are by unpaired, two-tailed t-test (* $p<0.0332$, ** $p<0.0021$, *** $p<0.0002$,
579 **** $p<0.0001$) or one-way ANOVA with Bonferroni correction ($^{\circ}$ $p<0.0332$, $^{\circ\circ}$ $p<0.0021$, $^{\circ\circ\circ}$ $p<0.0002$). No statistics were performed on the index values.
580 IF = intestinal failure; ITx = intestinal transplant.

581



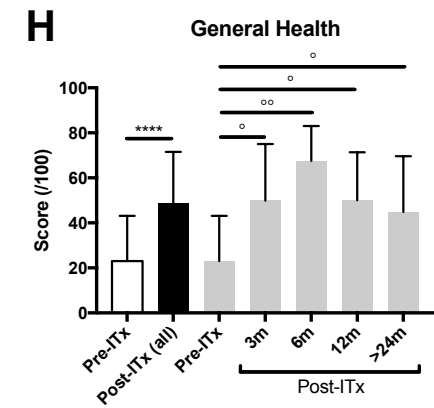
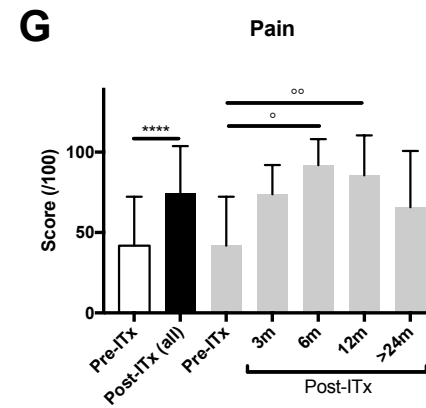
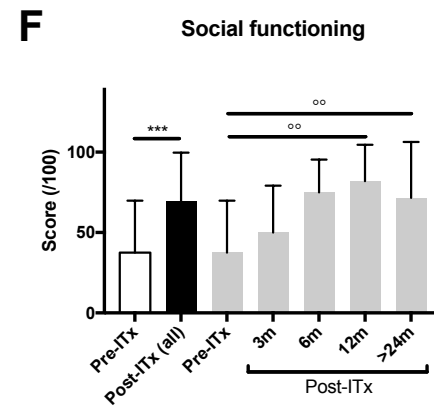
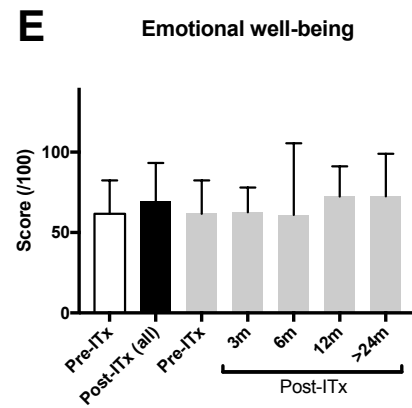
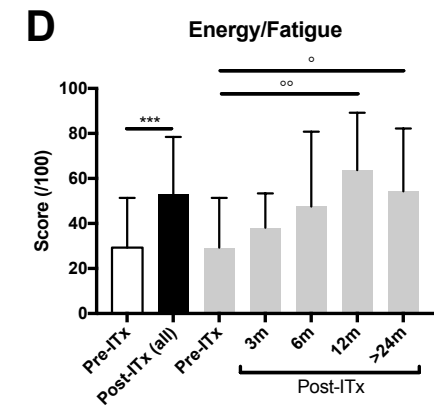
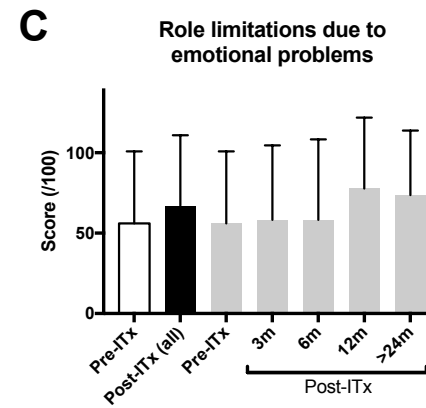
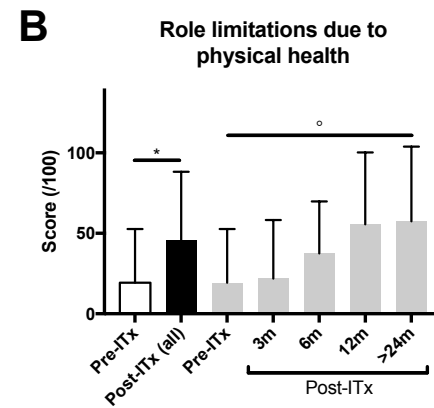
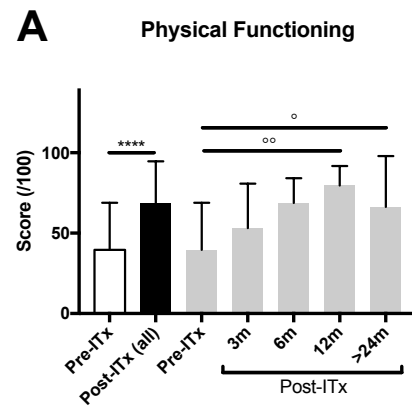
583 **Figure 6**

584 Summary scores for the SF-36 questionnaire between groups. Data demonstrated an improved overall quality of life following intestinal transplant compared
585 to pre-transplant in both mental (A) and physical (B) component scores. This was significant for the physical component from 12 months after transplant but
586 durable to beyond 24 months. A similar absolute improvement was seen for the mental component but this did not meet statistical significance. Data is
587 displayed as mean +/- standard deviation with higher scores indicating a better quality of life. Number of responses in each category are pre-ITx (25), post-
588 ITx (all) (41), 3m (8), 6m (4), 12m (9), and >24m (16). Statistical comparisons are by unpaired, two-tailed t-test (** p<0.0021, *** p<0.0002) or one-way
589 ANOVA with Bonferroni correction (°° p<0.0021). IF = intestinal failure; ITx = intestinal transplant.



594 **Figure 7**

595 Scores for individual domains of the SF-36. Absolute scores for SF-36 increased across all domains following intestinal transplant although did not meet
596 statistical significance for role limitations due to emotional problems (**C**) or emotional well-being (**E**). Improved scores were seen particularly beyond 12
597 months after transplant although general health (**H**) improved as early as 3 months. Data is displayed as mean +/- standard deviation with higher scores
598 indicating a better quality of life. Number of responses in each category are pre-ITx (25), post-ITx (all) (41), 3m (8), 6m (4), 12m (9), and >24m (16).
599 Statistical comparisons are by unpaired, two-tailed t-test (* $p<0.0332$, *** $p<0.0002$, **** $p<0.0001$) or one-way ANOVA with Bonferroni correction (°
600 $p<0.0332$, °° $p<0.0021$). IF = intestinal failure; ITx = intestinal transplant.



601

602

603 **Supplementary Table 1**

604 Mean and standard deviation of responses to the HPN-QOL (IF and pre-ITx) or ITx-QOL (post-ITx) instruments. Number of responses in each category are

605 IF (53), pre-ITx (20), post-ITx (all) (30), 3m (9), 6m (5), 12m (7), and >24m (9). IF = intestinal failure; ITx = intestinal transplant; SD = standard deviation.

	General Health	Holiday & Travel	Physical Function	Coping	Eating & Drinking	Employment	Sexual Function	Emotional Function	Nutrition Team	Pump	Body Image
IF											
Mean	77.36	68.27	52.61	66.88	74.04	47.76	20.49	62.50	87.33	81.88	31.41
SD	20.37	21.22	24.92	20.46	23.67	38.49	24.37	25.65	21.18	26.95	26.74
Pre-ITx											
Mean	56.58	19.08	35.83	54.39	44.17	32.50	21.30	40.83	78.33	76.19	44.12
SD	31.00	20.57	21.31	30.07	19.70	28.85	30.68	30.34	29.17	27.51	26.97
Post-ITx (all)											
Mean	81.45	63.79	57.03	71.38	79.80	44.62	30.36	63.64	No data	No data	39.06
SD	22.33	28.42	31.04	26.65	28.49	38.10	28.71	23.28	No data	No data	25.61
3m											
Mean	77.78	60.94	36.46	55.56	77.78	16.67	14.29	52.78	No data	No data	40.74
SD	15.02	18.22	24.37	26.64	30.05	15.43	11.50	29.76	No data	No data	27.78
6m											
Mean	100.00	87.50	73.33	84.44	100.00	66.67	23.33	66.67	No data	No data	29.17
SD	0.00	17.68	19.00	16.85	0.00	42.49	27.89	15.59	No data	No data	25.00
12m											
Mean	87.50	75.00	60.71	77.78	83.33	36.11	30.56	76.19	No data	No data	41.67
SD	13.69	13.69	26.23	19.25	25.46	38.61	26.70	21.21	No data	No data	22.97
>24m											
Mean	86.11	65.63	69.44	82.72	83.33	62.96	61.90	69.44	No data	No data	48.15
SD	22.05	31.87	36.56	26.12	23.57	37.99	24.93	18.63	No data	No data	25.61

	Weight	Immobility	Fatigue	Sleep	Gastrointestinal symptoms	Other pain	Stoma & bowel function	Financial issues	QoL overall	QoL due to HPN/ITx	QoL due to underlying illness
IF											
Mean	36.05	31.11	44.12	45.33	17.52	37.18	30.13	21.38	6.71	2.17	-1.16
SD	38.99	25.74	28.45	30.68	18.97	27.14	21.14	32.75	1.95	2.83	3.12
Pre-ITx											
Mean	48.33	41.67	65.83	50.00	42.22	55.00	43.89	43.33	4.71	-0.47	-2.59
SD	41.15	28.27	29.85	38.24	30.93	34.24	40.82	34.37	2.69	3.58	3.26
Post-ITx (all)											
Mean	30.30	40.83	50.51	56.25	22.22	25.25	18.18	44.44	6.97	2.81	0.84
SD	31.58	31.12	29.01	39.20	21.34	23.98	29.57	30.74	2.24	2.50	3.61
3m											
Mean	18.52	58.33	68.52	70.37	20.99	27.78	11.11	58.33	6.25	2.67	1.56
SD	17.57	24.10	26.93	35.14	24.50	28.87	18.63	29.55	1.16	2.12	3.13
6m											
Mean	40.00	38.67	40.00	41.67	15.56	6.67	6.67	58.33	8.20	4.50	3.20
SD	43.46	32.80	14.91	31.91	14.91	14.91	14.91	31.91	0.45	0.58	2.49
12m											
Mean	28.57	24.76	50.00	61.90	28.57	35.71	35.71	27.78	7.00	3.50	1.20
SD	35.63	25.45	31.91	40.50	23.88	24.40	39.00	25.09	2.00	1.38	2.49
>24m											
Mean	29.63	39.17	38.89	48.15	27.16	22.22	12.96	37.04	7.22	3.44	-0.11
SD	35.14	36.07	33.33	50.31	21.60	22.05	16.20	26.06	3.03	2.30	4.70

606

607 **Supplementary Table 2**

608 Mean and standard deviation of responses to the EQ-5D-5L instrument. Index score is equivalent to utility score. Number of responses in each category are IF
 609 (49), pre-ITx (19), post-ITx (all) (50), 3m (4), 6m (5), 12m (12), and >24m (27). IF = intestinal failure; ITx = intestinal transplant; SD = standard deviation;
 610 VAS = visual analogue scale.

	Mobility	Self-care	Usual Activity	Pain & discomfort	Anxiety & depression	VAS	Index score
IF							
Mean	1.78	1.41	2.08	2.35	1.94	62.7	0.68
SD	0.84	0.67	1.20	1.00	1.11	21.2	0.24
Pre-ITx							
Mean	2.26	1.84	3.21	3.26	1.89	41.3	0.42
SD	1.19	1.07	1.27	1.37	0.94	24.5	0.33
Post-ITx (all)							
Mean	1.38	1.30	2.04	1.94	1.60	73.6	0.75
SD	0.67	0.68	0.98	1.02	0.86	21.6	0.21
3m							
Mean	1.25	1.25	3.00	1.75	2.00	71.3	0.68
SD	0.50	0.50	1.00	0.50	0.82	8.5	0.08
6m							
Mean	1.20	1.00	1.60	1.40	1.60	85.6	0.85
SD	0.45	0.00	0.55	0.55	0.89	9.2	0.12
12m							
Mean	1.33	1.42	1.83	1.92	1.75	75.8	0.75
SD	0.65	0.67	1.03	1.00	1.14	17.3	0.24
>24m							
Mean	1.48	1.33	2.07	2.07	1.52	70.4	0.74
SD	0.75	0.78	1.00	1.17	0.75	26.2	0.23

611

612 **Supplementary Table 3**

613 Mean and standard deviation of responses to the SF-36 instrument. Number of responses in each category are pre-ITx (25), post-ITx (all) (41), 3m (8), 6m (4),
 614 12m (9), and >24m (16). IF = intestinal failure; ITx = intestinal transplant; SD = standard deviation.

	Mental Component Score Summary	Physical Component Score Summary	Physical functioning	Role limitations due to physical health	Role limitations due to emotional problems	Energy & fatigue	Emotional well-being	Social functioning	Pain	General health
IF										
Mean	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
SD	No data	No data	No data	No data	No data	No data	No data	No data	No data	No data
Pre-ITx										
Mean	44.10	29.77	39.56	19.33	56.00	29.27	61.68	37.50	41.80	23.07
SD	24.96	24.95	29.32	33.40	44.85	22.15	20.71	32.27	30.53	20.08
Post-ITx (all)										
Mean	63.44	56.53	68.48	45.77	67.12	53.03	69.31	69.60	74.20	48.57
SD	28.34	27.38	26.25	42.49	43.78	25.46	24.01	30.04	29.57	22.99
3m										
Mean	42.10	35.70	53.13	21.88	58.33	38.13	62.63	50.00	73.75	49.84
SD	28.11	24.88	27.64	36.44	46.29	15.21	15.37	29.12	18.27	25.22
6m										
Mean	67.23	66.41	68.75	37.50	58.33	47.50	61.00	75.00	91.88	67.50
SD	17.78	15.99	15.48	32.27	50.00	33.29	44.47	20.41	16.25	15.55
12m										
Mean	73.97	67.69	79.63	55.56	77.78	63.70	72.44	81.94	85.56	50.00
SD	26.69	22.36	12.16	44.68	44.10	25.51	18.70	22.63	24.84	21.36
>24m										
Mean	71.39	61.52	70.20	61.05	78.25	57.03	75.05	75.22	68.41	46.43
SD	27.34	29.41	28.25	45.46	36.60	26.34	25.13	32.39	34.33	24.66

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