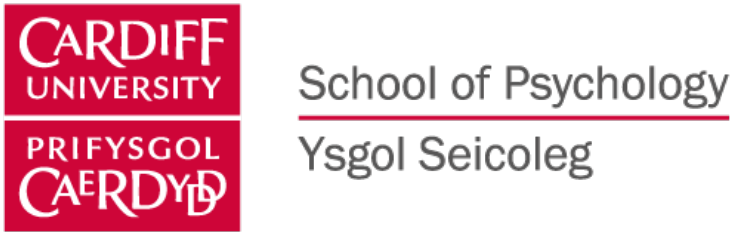

A Systematic Review of Anxiety, Depression and Medication Adherence in Inflammatory Bowel Disease, and an Empirical Study of Factors Predicting Psychological, Behavioural and Medical Outcomes in Home Parenteral Nutrition

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Preface

This research is presented in two parts: a systematic literature review and an empirical paper. The systematic literature review examined the relationship between anxiety, depression and medication nonadherence in inflammatory bowel disease (IBD). IBD encompasses one of the conditions (Crohn's disease) that is a common underlying reason for intestinal failure requiring home parenteral nutrition (HPN)—the topic of the empirical paper. The empirical study explored the role of psychological flexibility and self-compassion in predicting psychological, behavioural and medical outcomes in people on HPN.

IBD encompasses a variety of autoimmune non-infectious conditions involving chronic inflammation of the gastrointestinal tract, with the two most common forms being ulcerative colitis and Crohn's disease. At present there is no cure and therefore treatment focuses on helping people live well with the disease and is often managed with medication. Medication adherence, the extent to which medication taking corresponds with agreed recommendations by a health care provider, is associated with improved outcomes in IBD. Therefore, understanding factors associated with nonadherence is important to support patients. Anxiety and depression are common in IBD, and previous research suggests they may be associated with medication nonadherence. The systematic review examined whether anxiety and depression were associated with medication nonadherence in adults diagnosed with IBD. Searches on relevant databases found 18 studies that met inclusion criteria. Methodological quality of the included studies was assessed, and results pertaining to anxiety and depression, and medication adherence were summarised through narrative synthesis.

Results were mixed across studies, however a number of studies found a significant association between depression and medication nonadherence, with effect sizes ranging from very small to large. Studies that utilised objective measures of adherence consistently found significant associations with depression compared to self-report. The current evidence does

not support an association between anxiety and medication nonadherence. Study quality was found to vary across studies, impacting on the validity of findings. Potential explanations for the relationship between depression and nonadherence, and the challenges around measuring adherence are discussed. Suggestions for future research are provided, with a focus on increasing methodological rigour. The review highlights the importance of health professionals working with individuals with IBD to be alert to symptoms of depression, both to support their patients' mental wellbeing, and to facilitate conversations in relation to their treatment.

The empirical paper reports on the role of two psychological processes in predicting outcomes in home parenteral nutrition (HPN) from a cross-sectional, observational study. HPN is a type of nutrition feed provided directly to the bloodstream when a person is unable to absorb sufficient nutrients through their intestines. It poses significant challenges to daily activities, can impact a person's quality of life and psychological wellbeing, and requires meticulous adherence to line care procedures to prevent potentially life-threatening infection. Current understanding about psychological processes that affect outcomes in HPN is limited. Psychological flexibility and self-compassion have been identified as important processes in other health populations. Psychological flexibility is the ability to be in the present moment with awareness and openness to one's experience, and to take action guided by one's values. Self-compassion is the ability to connect to one's suffering, with feelings of kindness and caring, along with an understanding and non-judgemental attitude towards oneself, whilst acknowledging suffering as part of humanity. Sixty-six adults on HPN completed an online survey assessing psychological flexibility, self-compassion, psychological distress (depression, anxiety and stress), wellbeing, QOL, line care adherence and line infections.

Results indicated that higher psychological flexibility and self-compassion were significantly correlated with all outcomes in the predicted directions, except for line

infections. Psychological flexibility uniquely predicted lower total distress, lower anxiety, better wellbeing and higher QOL. Self-compassion uniquely predicted lower total distress, depression and stress. Despite some limitations, this study contributes to a gap in the literature around understanding psychological processes that contribute to outcomes in HPN. Interventions aimed at improving psychological flexibility and self-compassion may be beneficial to support the emotional wellbeing and quality of life of individuals on HPN. Further research would benefit from prospective designs and consideration of objective measures of infection. Additionally, a measure of line care adherence was developed for the study and future validation of this measure would help determine its usefulness for screening for line care adherence.

Overall, the systematic review contributes to the literature considering risk factors for medication nonadherence in IBD and emphasises the importance of a holistic, integrated care approach to caring for people with IBD. The empirical study highlights the role of two psychological processes in predicting psychological, behavioural and medical outcomes in HPN, and provides a rationale for further research examining psychological interventions that may help better support the wellbeing of people on HPN.

The Association Between Anxiety and Depression, and Medication Adherence in Adults with Inflammatory Bowel Disease: A Systematic Literature Review

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This manuscript has been prepared in accordance with author guidelines for the journal: Inflammatory Bowel Diseases (Appendix A). AMA 11th formatting has been used throughout in line with journal guidelines (correspondence with journal to confirm 11th edition of AMA). Tables and figures have been embedded in the main body, however, these will be placed at the end of the manuscript for journal submission.

Abstract

Adherence to medication is associated with improved outcomes in inflammatory bowel disease (IBD). Understanding factors associated with nonadherence is important to support patients. Anxiety and depression are common in IBD, however their relationship with adherence is unclear. This systematic review examined whether anxiety and depression were associated with medication nonadherence in IBD. *Methods*: Systematic searches were completed on Embase, Medline, Psych info, Web of Science, Scopus and CINAHL databases for primary, quantitative studies related to medication adherence, IBD, and anxiety or depression, from inception to September 2021. Included studies examined medication adherence and anxiety or depression in adults. Twenty-five percent of full texts were independently screened by a second reviewer. Eighteen papers were included. Study quality was assessed using the National Institutes of Health quality assessment tool and data were analysed by means of narrative synthesis. *Results*: Study quality was poor (n=4) to fair (n=12) with two studies rated good quality. Five out of 14 studies reported significant associations between anxiety and nonadherence, and 10 out of 17 studies reported significant associations between depression and nonadherence. Studies that utilised objective measures of adherence consistently found significant associations with depression compared to self-report. Effect sizes ranged from very small to large. *Conclusions*: There is evidence of an association between depression and adherence. The findings of this review do not support an association between anxiety and adherence. Further high-quality studies are required with consideration of measurement of adherence. It is important for clinicians to be alert to patients' mental health.

Keywords: Inflammatory bowel disease, medication adherence, depression, anxiety

Introduction

Inflammatory bowel disease (IBD) encompasses a variety of autoimmune non-infectious conditions involving chronic inflammation of the gastrointestinal tract.[1] The two most common forms of IBD are ulcerative colitis and Crohn's disease, with a minority of cases of indeterminate colitis or IBD-unclassified.[2] IBD affects people worldwide, and recent estimates suggest at least 0.3% prevalence in Western countries.[3] The cause of IBD is not fully understood, but it is thought to be a combination of factors including genetics, environmental and problems with immune system functioning.[4,5] There is no cure, and those with the disease may experience a fluctuating course of active disease, remission and further relapse flares. Treatment focuses on helping people live well with the disease, including reducing inflammation, and usually requires medication, which broadly includes anti-inflammatory, immunosuppressant and biologic drugs. The prescribing guidelines in countries vary, however key variables in the treatment decisions include disease type and presentation, response to previous treatments, and whether the aim is to treat active disease or maintain remission.[2,6,7] There is a lot of complexity in the decision-making process around which medication someone is prescribed, and it does not necessarily relate in a linear way to the severity of their disease.

Effectiveness of treatment often relies on a person adhering with their medication-taking prescribed regime. The World Health Organisation (WHO) defines adherence as "the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider."[8] Medication nonadherence in IBD is a recognised problem and is associated with negative disease consequences including an increase in disease activity and relapse.[9,10] Nonadherence in IBD has also been associated with higher health care costs. For example, non-adherence to 5-aminosalicylic acid for ulcerative colitis was associated with increased costs in both

inpatient and outpatient services[11] and medical and hospitalisation costs were higher in Crohn's disease patients who were non-adherent to infliximab treatment.[12] Medication adherence may also vary depending on the type of medication, for example anti-TNF therapy ('biologics') might be expected to have higher rates of adherence than oral medication. Some biologics are administered through injection, usually by the patient at home, whereas others are administered by infusion in a clinic, by a clinician. One study in Australia indeed found individuals on biologic therapies as maintenance treatment had the highest medication adherence.[13] However, non-adherence to these treatments is still reported, with one recent review finding non-adherence rates to range between 38%-77%.[14]

Understanding non-adherence is important for health professionals when providing care for patients and planning interventions to improve adherence. This area of research has included psychosocial factors as predictors of adherence, such as anxiety and depression. Anxiety and depression may be particularly relevant psychosocial factors because prevalence of both is higher in IBD than the general population. Between one quarter and one third of people with IBD experience symptoms of depression and anxiety, respectively, with rates being even higher during active disease.[15] Depression has been found to be associated with an increased risk of developing IBD[16], and a considerable proportion of people develop depression following the onset of IBD.[17] This bidirectionality may be related to inflammatory processes, as there is evidence of inflammation leading to increased depression, and depression being considered pro-inflammatory and in turn negatively affecting IBD disease activity.[18] There is also emerging evidence of a bi-directional relationship between anxiety and disease activity.[19]

Although some existing systematic literature reviews have included studies examining anxiety and depression, they are often grouped together with other psychiatric diagnoses or psychosocial factors more broadly. Furthermore, reviews have often focused on either

adherence to oral medication[20,21] or biologics[22] separately. Jackson et al[20] reviewed various factors associated with non-adherence to oral medication, including demographic, clinical and treatment variables. They determined that 'psychological distress', which included depression, psychiatric diagnosis or chronic stress, was found to be associated with non-adherence. However, the authors highlighted that it was a minority of the primary studies that examined psychological factors and further research is warranted. Peel et al[21] completed an updated review of the literature and concluded that there was no overall association between mental health factors (including anxiety and depression) and oral medication adherence. Lopez et al[22] reviewed adherence to biologics and identified anxiety as one of the factors associated with nonadherence, however this finding was based on a single study. Another review found anxiety was associated with nonadherence to any IBD medication in only two of six studies reviewed.[23]

The relationship between anxiety and depression and nonadherence to IBD medication remains to be determined.[24] As discussed above, previous reviews have had inconsistent conclusions, some finding anxiety and depression to be amongst mental health variables associated with medication nonadherence and others finding no such association. Furthermore, these conclusions were based on a small number of primary studies, and additional studies examining factors associated with medication adherence have since been published. Therefore, a review of this relationship is warranted, as further understanding of this relationship would be important for clinicians working with IBD to better manage potential risk factors for nonadherence. For example, a relationship between these factors would highlight the importance of assessing for mental health and for professionals to consider how to support individuals with adhering to their treatment. The aim of the current systematic review was to determine whether there is an association between anxiety or depression and IBD medication adherence.

Method

The current review followed guidelines outlined by preferred reporting items for systematic review and meta-analysis[25] (PRISMA) and a protocol can be found on PROSPERO (Registration: CRD42021274573). The literature search was completed on 27th September 2021.

Study selection and literature search

A search of the literature was conducted via the following online databases: Ovid Embase, Ovid Medline, APA PsychINFO, Web of Science, Scopus and CINAHL, from their inception until September 2021. A search strategy was developed to identify relevant studies, using key terms relevant to the research question (specific search strings used can be found in Appendix B). Studies met criteria for inclusion if they:

- Included participants with a diagnosis of IBD
- Included adult participants (18+)
- Measured anxiety or depression specifically
- Measured adherence to IBD medication (any medication or route)
- Reported statistical tests of association between anxiety or depression and medication adherence
- Were published in a peer reviewed journal and available in English language

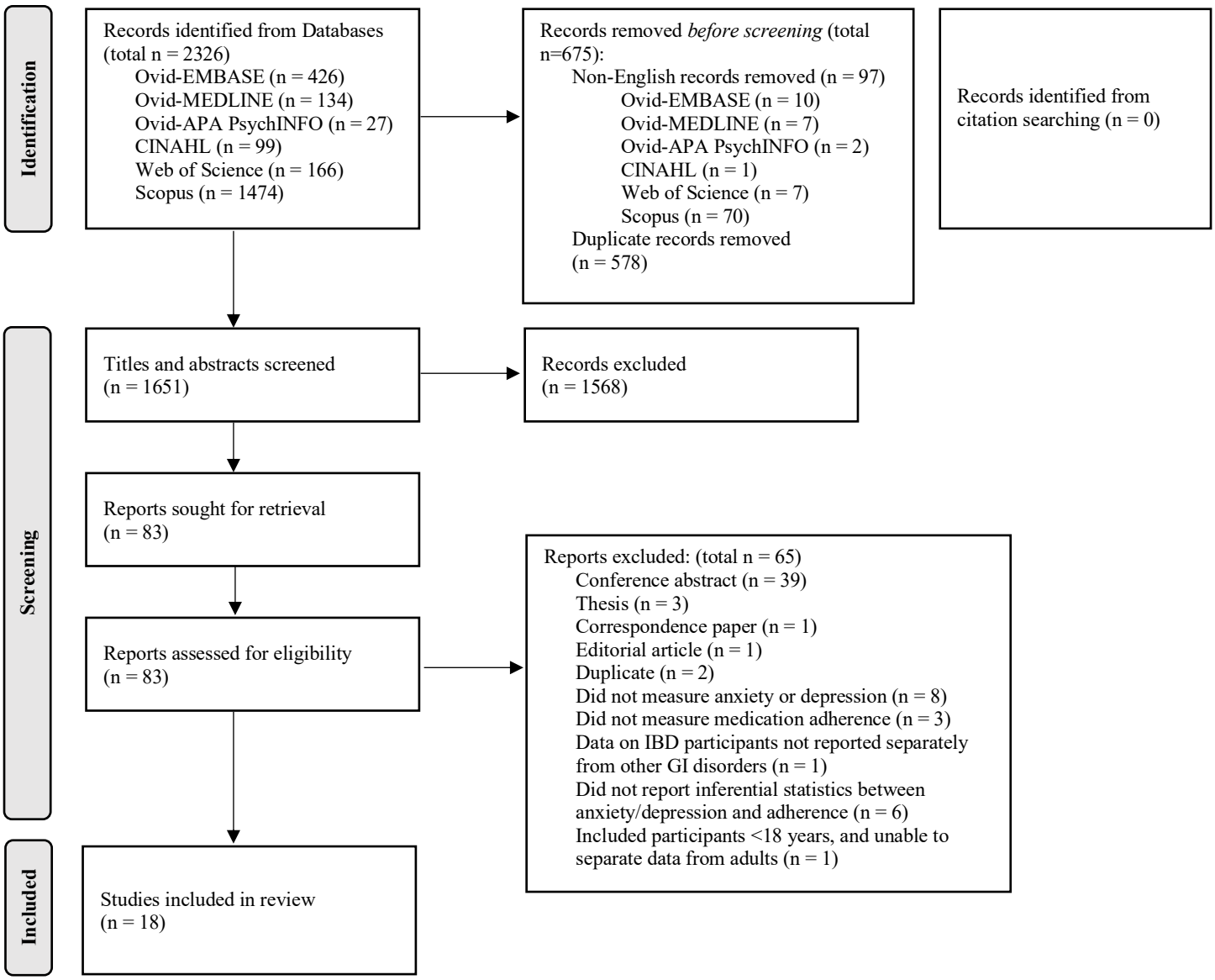
Studies were excluded if they were:

- Qualitative studies, case studies, editorials, reviews, or conference abstracts
- Did not specifically measure or report anxiety or depression (e.g., if only reported 'psychiatric history'), or adherence

Search results were collated in a reference database, duplicates were removed, and initial screening of titles and abstracts was completed for eligibility. The full texts were obtained and reviewed, and approximately 25% of full texts were screened by a second reviewer.

Initial agreement in ratings was 86.36% (κ=0.70), suggesting substantial inter-rater agreement.[26] Any disagreements were resolved through discussion. Reference lists of identified papers were also manually searched to identify any further suitable studies. This process resulted in the inclusion of 18 studies (Figure).

Figure. PRISMA Flow Diagram of Search Strategy



Data extraction and synthesis

Extracted data included study and population characteristics; research design; data sources and analyses; type and route of medications; prevalence of medication adherence;

methods of measuring anxiety, depression and medication adherence; relevant findings; and effect sizes. Narrative synthesis was used to analyse and present the data.

Quality assessment

Internal validity of the included studies was assessed using the National Institutes of Health (NIH) quality assessment tool for observational cohort and cross-sectional studies.[27] This tool was selected due to its applicability to both analytical cross-sectional and cohort study designs and has been identified as a recommended tool.[28] It is comprised of 14 items, and each study was given a quality rating of 'good', 'fair' or 'poor'. The NIH provides these rating categories and recommends applying them based on consideration of how each of the items would impact on a study's internal validity. In absence of specific score criteria, the following scores were applied: poor as 0-5, fair as 6-8 and good as 9-14. This was completed in addition to considering the risk of bias of each item, in attempt to increase objectivity of ratings. Ratings were used to inform data synthesis and report on risk of bias. When assessing study quality, consideration was given only to the aspects of the study relevant to the review question. An independent assessor (a trainee clinical psychologist) rated the quality of approximately 25% (n=5) of the studies. Initial agreement in ratings was 80% (weighted κ=0.615) indicating substantial agreement.[26] Any disagreements were resolved through discussion and through consultation with supervisors.

Results

Quality of studies

Individual study ratings are found in the Table and details regarding the specific items on the quality tool for each study are available in Appendix C. Studies have been grouped in the data table in accordance with their quality rating category. Overall, quality of studies was poor (n=4) to fair (n=12), and only two studies[29,30] were rated good quality. Data collection timeframes varied. Two cross-sectional studies had particularly long data collection periods

of 10 and 13 years.[31,32] Over such a wide time period, clinical guidance for treatment will have likely changed, which could introduce potential confounding variables. Some studies did not clearly state the study population, for example the age range included or time period of data collection. Only one study reported a sample size justification which was through power analysis.[33] Although this is more common for studies that may be exploratory in nature,[27] some studies might have been underpowered due to sample size requirements having not been calculated *a-priori*, and therefore it is possible some nonsignificant findings could be due to Type II error. Reporting of statistics was sometimes incomplete (for example missing coefficients), resulting in difficulty interpreting the findings and higher risk of reporting bias. There were also some studies that did not report effect sizes, which impacts on what clinically meaningful conclusions can be drawn. A significant issue relating to quality was the use of exposure and outcome measures that were not valid in a few studies. Only three studies were a longitudinal design, limiting causal conclusions between anxiety or depression and adherence.

Overview of studies / Study characteristics

Publication dates ranged from 2003 to 2021 with the majority of papers published in the last 10 years. Studies were located in a range of countries across Asia (n=4), Australia (n=1), Europe (n=7), North America (n=4), South America (n=1) and one study from both Australia and the UK (Table). Most studies used a cross-sectional design to examine the relationship between anxiety or depression and adherence. One study had a prospective cohort design[34] and two had a retrospective cohort design.[29,30]

There was considerable variation in sample sizes, ranging from 40 to 2612 (Table). Two thirds of studies had a higher proportion of women to men, although overall proportions were similar and ranged from to 35.8% to 61% men (Table). All studies were completed with adults, as per inclusion criteria, although one study included only older adults (65 years and

over)[35]. Ethnicity was reported in four studies[30,36-38] and these studies only reported white/Caucasian (82-100%) or non-white, therefore this was not included in the data table. Samples mainly consisted of outpatients from IBD clinics or other community samples (Table). Most studies included participants with Crohn's disease and ulcerative colitis, except for Wang and colleagues[31,32] who included participants with Crohn's disease only. Some studies also included a minority of participants with inflammatory bowel disease unspecified[38-42] (also known as indeterminate colitis), whereas for one study this was a specified exclusion criterion.[43] Ediger et al[37] included patients with indeterminate colitis, but then excluded them from the analyses specific to the current review question.

Two of the studies[31,32] appear to have overlapping datasets, based on the information available in the methodology. Both studies were retained in the current review, however it is to be noted that the significant findings in these studies may in part be a duplication.

Anxiety and depression

Most studies examined both anxiety and depression, however four studies examined depression only[29,30,35,36] and one measured health anxiety only.[37] The majority of studies examined anxiety or depression (or both) in addition to other potential variables that could be associated with adherence; only one study examined depression as the only independent variable.[29]

Anxiety and depression were assessed through self-reported questionnaires in all studies, most commonly the Hospital Anxiety and Depression Scale (HADS), although there were some differences of cut-off scores used, and in some cases, these were not specified (Table). All but three studies that measured anxiety utilised the HADS-anxiety subscale. For studies examining depression, the majority used the HADS-depression subscale. Four used other validated questionnaires (Table) and one study[36] used only a single question to assess

depression, rather than a validated depression questionnaire. Finally, Severs et al[34] used only a single item from a quality of life questionnaire to assess anxiety and depression together.

Studies differed on whether they treated anxiety and depression as dichotomous categorical variables in their analyses (anxious/depressed vs. not anxious/depressed) or continuous variables. Seven studies analysed them as categorical variables[29,34-37,41,43] and 10 studies entered them into analyses as continuous variables. In one study it was not clear.[44]

Medication Adherence

All studies reported how medication nonadherence was assessed, however the definition of medication nonadherence and the way this was measured varied widely between studies (Table). The majority of studies utilised self-report measures to assess adherence, including the Morisky Medication Adherence Scale (MMAS-8, n=7), the Medication Adherence Report Scale (MARS 4 item; n=3), MARS-5 (n=2), Visual Analogue Scales (VAS; n=3), or questions developed for the study (n=1). In addition to self-report, two studies included urine samples[42,44] and Nahon et al[41] recorded missed pills. Finally, Calloway et al[29] utilised interruption of medication (defined as not filling anti-TNF prescription if injectable or not getting infliximab infusion for 30 days beyond needed date for continuation) and Shah et al[30] used the medication possession ratio (MPR; the total sum of days' supply for each medication refill divided by the number of days in the observation period).

The current review included studies examining adherence to any type of medication used to treat IBD through any route (i.e. oral, injection, intravenous or rectal). Studies varied on what types of medication were included. Four studies evaluated adherence to only one medication (although participants may have still been taking concurrent medications), both of which were oral administration: azathioprine[31,32,45] and mesalazine (Asacol).[42] Conversely, other studies included multiple medications, or medication type was not reported (Table). Of those studies that reported multiple medications, seven included the proportions of

participants on each type. From these seven studies, it was still difficult to determine participants' medication profiles, as different combinations of the included medications were possible, and it would be impractical for authors to report all possible combinations. For some studies the route(s) of medication could be determined, either due to the type of medication included or because this was explicitly stated by the authors. In other instances, however, it was not clear, such as when the medications included could have been administered by multiple routes and the route was not specified. Details of the specific medications examined within each study are further outlined in the Table.

The proportion of participants categorised as nonadherent varied a great deal between studies, with a range across the 16 studies that reported extent of nonadherence of 10.4%[41] to 72%.[44] Most studies reported one figure for overall self-reported nonadherence, however two studies distinguished between intentional and nonintentional adherence.[44,45] Similar to overall adherence, definitions of these terms were not consistent between studies. Two studies collected urine samples in addition to self-report measures. Shale et al[42] completed urine analysis for all participants, and reported 12% complete non-compliance and 18% partial non-compliance, which also allowed them to report on how well-matched self-reporting of adherence was to an objective measure. Self-reported nonadherence correctly identified 66% of those considered non-adherent based on urine analysis.[42] San Roman et al[44] also used urine samples for a subset of their participants (n=15) and found 13% had no detectible drug levels, indicating complete nonadherence. It was not clear in this study how the researchers related these findings to the self-reported adherence.

Relationship between anxiety or depression and adherence

There were five studies that reported significant associations between anxiety and nonadherence, and 10 studies with significant associations between depression and nonadherence. Nine studies reported non-significant findings in relation anxiety and

adherence, and eight reported non-significant associations between depression and adherence (Table).

Where effect sizes were reported, the authors of the current review assigned qualitative labels according to criteria reported by Chen et al[46] (Odd's Ratio), Lu and Chen[47] (Hazard's Ratio) or Cohen[48] (correlation). Overall, effect sizes were very small to small, with the exception of Wang et al[32] where there was a medium effect size for anxiety and depression, and Shale and Riley[42] who found a large effect of depression on complete nonadherence, based on urine samples (Table).

From examination of effect sizes, three of the four studies that reported a statistically significant association between anxiety and self-reported nonadherence had very small effects[31,34,41] and Wang et al[32] found a medium effect. However, Severs et al[34] used only one item from the EQ-5D-3L as a measure of both anxiety and depression. The aforementioned studies with a significant association between anxiety and nonadherence also all reported associations between depression and nonadherence, except for Nahon et al[41] where no association between depression and nonadherence was found.

Of the ten studies reporting a statistically significant association between depression and nonadherence, effect sizes ranged, including large,[42] medium,[32] small[29,35,36,45] or very small[31,34] and two studies did not report effect size.[30,44] The majority of these studies relied on self-reported nonadherence, with the exception of three, where interruption to medication,[29] MPR[30] and urine analysis[42] were used, as described above. San Roman et al [44] and Shah et al[30] completed univariable analyses only for depression, whereas the other eight studies conducted multivariable analyses and determined depression as an independent predictor of adherence. The variables entered into these analyses differed between studies, however common variables controlled for included age,[29,31,32,45] gender[29,34,45] and disease type.[29,34] Full details of the variables controlled for across studies can be found in the Table.

Shale & Riley[42] examined adherence objectively through urine analysis; patients with undetectable urine samples (non-adherent) were more likely to be anxious or depressed, however only depression was an independent predictor of complete nonadherence. Conversely, anxiety and depression were not associated with objective partial non-compliance or self-reported nonadherence.[42] This was the only study to utilise a biological marker to measure adherence in relation to anxiety and depression.

Table. Overview of Included Studies

Author, year	Origin, Design and Sample (N)	Participant Characteristics	Measure of Anxiety (criteria used)	Measure of depression (criteria used)	Measure of Adherence (non-adherence criteria)	Type(s) of Medication evaluated (% if reported)	Route of medication (% if reported)	Extent of adherence	Results	Effect size interpr-etation	Quality rating
Calloway et al[29] 2017	Origin: USA Design: retrospective cohort Sample: outpatients from IBD clinic (246)	30% UC, 70% CD 38% M Age: 37	NA	PHQ-9 (score ≥10)	Interruption of medication[a]	Anti-TNF therapy: Infliximab (33%) Adalimumab (56%) Certolizumab (11%)	Injection infusion (infliximab)	13% non-compliant	Depressive symptoms at baseline were significantly associated with noncompliance in follow-up with a calculated hazards ratio 2.28 (CI 1.1–4.6, *P*<.05) when controlling for age, sex, psychiatric history and disease type	Small	Good
Shah et al[30] 2020	Origin: USA Design: retrospective cohort Sample: outpatients from IBD clinic (460)	14.6% UC; 85.4% CD 36.4% M Age: 40[b] (UC); 37[b] (CD)	NA	PHQ-9 (NR†)	Medication possession ratio (MPR)[c] (nonadherence MPR <0.86)	Biologic therapy: Certolizumab (18.5%) Adalimumab (73.5%) Golimumab (4.3%) Ustekinumab (3.7%)	Injection	31% non-adherence	Baseline depression scores were higher in nonadherent patients (median [range], 5, [2-10]) compared to adherent patients (3, [1-8]; *P*<.05)*	NR	Good
Bruna-Barranco et al[43] 2019	Origin: Spain Design: cross-sectional Sample: outpatients from IBD clinic (181)	54.7% UC, 45.3% CD 51% M Age: 47	GADS anxiety subscale (score >4)	GADS depression subscale (score >2)	MMAS-8[d]	Oral mesalamine (48.6%) Topical mesalamine (20.9%) Systemic steroids (3.3%) Topical steroids (3.3%) Thiopurine (29.3%) Metrotexate (1.7%) Anti-TNF (30.4 %) Antibiotics (3.3%)	Oral (52.5%) rectal (17.1%) intravenous (12.1%) subcutaneous or intramuscular (18.23%)	22.7% low adherence	Anxiety and depression were not associated with nonadherence (*P*=.21, *P*=.72, respectively)	NR	Fair

Author, year	Origin, Design and Sample (N)	Participant Characteristics	Measure of Anxiety (criteria used)	Measure of depression (criteria used)	Measure of Adherence (non-adherence criteria)	Type(s) of Medication evaluated (% if reported)	Route of medication (% if reported)	Extent of adherence	Results	Effect size interpr-etation	Quality rating
Campos et al[45] 2016	Origin: Portugal Design: cross-sectional Sample: outpatients from IBD clinic (112)	37.5% UC, 62.5% CD 41.7%M Age: 37.2	HADS-A (NR†)	HADS-D (NR†)	MMAS-8[e] (score <6)	Azathioprine (100%)	Oral (100%)	29.5% non-adherence[e]	Depression was an independent predictor of nonadherence (OR: 2.22; 95% CI: 1.36–3.62; *P*=.001)† when controlling for sex, age, smoking status and therapeutics complexity score No association between anxiety and adherence (*P*=.69)	Small NR	Fair
Ediger et al[37] 2007	Origin: Canada Design: cross-sectional Sample: Community sample (Manitoba IBD Cohort; 326)	45% UC, 50% CD, 5% IC[f] 40% M Age: 41	HAQ (categorised into high anxiety and low anxiety based on distribution of the sample)	NA	MARS-5 (score of ≤19)	5-ASA Immuno-suppressants Prednizone	NR [type indicates oral or rectal]	35% low adherence	High health anxiety was not associated with nonadherence (OR: 0.76; 95% CI: 0.33-2.22; *P*>.05)	Very small	Fair
Eindor-Abarbanel et al[39] 2018	Origin: Israel Design: cross-sectional Sample: IBD outpatients from 3 hospital clinics (311)	26% UC, 70.4% CD, 3.5% IBDU 37.6% M Age: 34.78[b]	HADS-A (score >10†)	HADS-D (score >10†)	MMAS-8[d] (score <6)	Topical 5-ASA Tablet 5-ASA Budesonide Prednisone Immuno-suppressive drugs Biologics	Mixed	40.5% low adherence	No correlation between anxiety (*P*=.61) or depression (*P*=.272) and adherence	NR	Fair

Author, year	Origin, Design and Sample (N)	Participant Characteristics	Measure of Anxiety (criteria used)	Measure of depression (criteria used)	Measure of Adherence (non-adherence criteria)	Type(s) of Medication evaluated (% if reported)	Route of medication (% if reported)	Extent of adherence	Results	Effect size interpr-etation	Quality rating
Freitas et al[33] 2015	Origin: Brazil Design: cross-sectional Sample: outpatients from gastroenterology service (147)	56.5% UC, 43.5% CD 42.9% M Age: 45.1	HADS-A (score ≥8†)	HADS-D (score ≥8†)	MMAS-8 (no criteria used)	NR	NR	NR	No association between anxiety (Beta=0.02, *P*=.848) or depression (Beta=0.14, *P*=.214) and adherence, as entered into multiple regression model with age, sex, race, religion, education, income, disease type, time since diagnosis, surgery, relapse rate, in remission, positive religious coping and negative religious coping	Very small	Fair
Jackson et al[40] 2018	Origin: Australia Design: cross-sectional Sample: outpatients from IBD clinic (81)	38% UC, 57% CD, 5% IBDU 51% M Age: 34	HADS-A (score ≥8†)	HADS-D (score ≥8†)	MMAS-8 (NR)	NR	NR	NR	No correlation between anxiety (CD: rho: 0.32, *P*>.05; UC: rho: -0.12, *P*>.05) or depression (CD: rho: 0.08, *P*>.05; UC: rho: 0.32, *P*>.05) and medication adherence	Very small-small	Fair
Long et al[35] 2014	Origin: USA Design: cross-sectional Sample: Community sample (Crohn's and Colits Foundation of America; 240)	37.5% UC[g], 62.5% CD[g] 37.9% M[g] Age: 70.2[gh]	NA	GDS (score ≥5)	MMAS-8 (score <8)	5-ASA (47.5%) Corticosteroids (25%) Immuno-modulators (25%) Biologic anti-TNF (22.5%)	Mixed	21.25% low adherence	Depression was significantly associated with reduced medication adherence (OR 2.18; 95% CI 1.04-4.57) when controlling for disease activity, education level, corticosteroid use and exercise (*P*-value NR)	Small	Fair

Author, year	Origin, Design and Sample (N)	Participant Characteristics	Measure of Anxiety (criteria used)	Measure of depression (criteria used)	Measure of Adherence (non-adherence criteria)	Type(s) of Medication evaluated (% if reported)	Route of medication (% if reported)	Extent of adherence	Results	Effect size interpr-etation	Quality rating
Selinger et al[38] 2013	Origin: Australia & UK Design: cross-sectional Sample: outpatients from IBD clinics (multiple sites; 356)	Australia: 50.7% UC, 39.7% CD, 5.3% IBDU, 4.3% unknown 45.4% M Age: 47.1 UK: 48.6% UC, 46.4% CD, 2.1% IBDU; 2.9% unknown 37.7% M Age: 46.8	HADS-A (score ≥8†)	HADS-D (score ≥8†)	MARS-4 item (score ≤16)	5-ASA: 80.4% (Aus); 67.4% (UK) Thiopurine: 32.1% (Aus); 43.3% (UK) Biological: 14.5% (Aus); 17.2% (UK)	Mixed	28.7% non-adherence	No differences in mean anxiety levels between adherent (7.35) and nonadherent (7.53) patients (*P*=.71) No difference in mean depression scores between adherent (4.67) and nonadherent (4.07) patients (*P*=.16)	NR NR	Fair
Severs et al[34] 2017	Origin: Netherlands Design: prospective cohort Sample: IBD patients from 7 medical centres and 7 general hospitals (multiple sites; 2612)	40.3% UC; 60.8% CD 50.0% M (UC); 36.8% M (CD) Age: 49.2 (UC); 46.9 (CD)	Anxiety/ depression domain (item) of the EQ-5D-3L (no problems vs. any problems)	Anxiety/ depression domain (item) of the EQ-5D-3L (no problems vs. any problems)	VAS rating 0-100 (Adherence ≥80%)	5-ASA (UC: 65.2%; CD:23.5%) Steroids (UC: 7.6%; CD: 10.2%) Immunosuppressive drugs (Aza/6 MP/MTX) (UC: 22.2%; CD: 35.4%) Anti-TNF (UC: 3.8%; CD: 22.9%)[i]	Mixed (rectal, oral, intramuscular, parenteral)	13.3% (UC); 12.1% (CD) non-adherence	Self-reported anxious or depressed feelings was an independent predictor of future nonadherence (adjusted OR 1.17; 95% CI 097-1.40, *P*=.11)[j] when controlling for disease type, sex, age at diagnosis, remission status and previous nonadherence	Very small	Fair

Author, year	Origin, Design and Sample (N)	Participant Characteristics	Measure of Anxiety (criteria used)	Measure of depression (criteria used)	Measure of Adherence (non-adherence criteria)	Type(s) of Medication evaluated (% if reported)	Route of medication (% if reported)	Extent of adherence	Results	Effect size interpr-etation	Quality rating
Shale & Riley[42] 2003	Origin: UK Design: cross-sectional Sample: outpatients from IBD clinics (multiple sites; 98)	63% UC; 27% CD; 10% IC 52% M Age: 49[b]	HADS-A (score ≥8†)	HADS-D (score ≥8†)	1. Self-report (0-100 rating; noncompliance <80%) 2. Urine sample	Mesalazine (Asacol) (100%)	Oral	43% non-compliance (self-reported) 12% complete non-compliance; 18% partial non-compliance (urinary sample)	Anxiety and depression were not associated with self-reported noncompliance Patients with undetectable urinary drug samples were more likely to be anxious (P <.01) or depressed (P <.001)* Depression was the only independent predictor of complete noncompliance (OR, 10.5; 95% CI, 1.8-79.0) when controlling for disease type, quality of life, and anxiety (P-value NR) Anxiety and depression did not predict partial non-compliance as measured by urinary drug levels	NR NR Large NR	Fair
Trindade & Ferreira[49] 2021	Origin: Portugal Design: cross-sectional Sample: online IBD patient groups (124)	31.9% UC; 68.1% CD 14.52% M Age: 39.93	HADS (NR†)	HADS (NR†)	Medication Adherence Report Scale (MARS-5; NR)	Immuno-suppressants, biologics, or corticosteroids	Mixed	NR (reported mean MARS score: 22.73)	No correlation between anxiety (r=-0.06, P>.05) or depression (r=-0.02, P>.05) and medication adherence	Very small	Fair

Author, year	Origin, Design and Sample (N)	Participant Characteristics	Measure of Anxiety (criteria used)	Measure of depression (criteria used)	Measure of Adherence (non-adherence criteria)	Type(s) of Medication evaluated (% if reported)	Route of medication (% if reported)	Extent of adherence	Results	Effect size interpr-etation	Quality rating
Wang et al[31] 2020a	Origin: China Design: cross-sectional Sample: outpatients and inpatients from hospital GI department (446)	100% CD 58.3% M Age:31.7	HADS-A (0-7 normal, 8-10 mild, 11-15 moderate, 16-20 severe†)	HADS-D (0-7 normal, 8-10 mild, 11-15 moderate, 16-20 severe†)	Medication Adherence Report Scale (MARS-4 item) (nonadherence MARS <17	Azathioprine (100%)	Oral	41.90%	Anxiety (OR: 1.549, 95% CI: 1.372–1.749; *P*<.001) and depression (OR: 1.190, 95% CI: 1.080–1.312; *P*<.001) were independent predictors of nonadherence when controlling for medication concern beliefs, education, medication knowledge and medication necessity beliefs	Very small	Fair
Banerjee et al[36] 2021	Origin: India Design: cross-sectional Sample: outpatients from IBD clinic (467)	59.7% UC, 40.3% CD 61.7 % M Age: 38.6	NA	Single Q: 'Have you felt mentally depressed due to medication / illness?' (yes = feeling depressed)	MMAS-8[d] (score <6)	Steroid use Thiopurine use 5-Amino salicylic acid use Biological use Topical therapy	Mixed	51% non-adherence	'Feeling depressed' was associated with adherence (adjusted OR: 0.43; 95% CI: 0.27-0.67; *P*<.001, for adherence) when controlling for perceived medication information, medication effectiveness belief, side effect worries, symptomatic remission, high-cost perception, comorbidities/underlying disease, social support, quality of life and physician-patient interactions Effect size (OR) for non-adherence = 2.32 (calculated for the purpose of the present review)	Small	Poor

Author, year	Origin, Design and Sample (N)	Participant Characteristics	Measure of Anxiety (criteria used)	Measure of depression (criteria used)	Measure of Adherence (non-adherence criteria)	Type(s) of Medication evaluated (% if reported)	Route of medication (% if reported)	Extent of adherence	Results	Effect size interpr-etation	Quality rating
Nahon et al[41] 2011	Origin: France Design: cross-sectional Sample: Community sample (French Association of IBD patients; 1663)	35% UC, 62.8% CD, 2.2% ID 35.8% M Age: 43.6	HADS-A (score >10)	HADS-D (score >10)	VAS rating 1-10 (Adherence ≥80%) Number of missed pills[k]	5 ASA (67.7%) Prednisolone (24.2%) Budesonide (0.9%) Thiopurines (53.8%) Methotrexate (9.8%) Anti-TNF therapy (34.55)	Mixed	10.40% non-adherence	Anxiety was significantly associated with adherence (OR 0.62, 95% CI 0.42-0.90, *P*=.013) when controlling for age, sex, smoking, flare, severe disease, surgery, Anti-TNF therapy, deprivation, depression, membership to patient organisation, and constraints related to treatment Effect size (OR) for non-adherence = 1.61 (calculated for the purpose of the present review) No association between depression and nonadherence (OR 1.22, 95% CI: 0.69-2.14, *P*=.48)	Very small Very small	Poor
San Roman et al[44] 2005	Origin: Spain Design: cross-sectional Sample: outpatients from IBD clinic (40)	30% UC, 70% CD 50% M Age: 39.4	HADS-A (NR)	HADS-D (NR)	Self-report (4 true/false items) Urine sample for subset of participants (N=15; 37.5%)[l]	Mesalazine 37.5% Others NR	NR	72% non-adherence[m] (self-report) 13% complete non-adherence (urine)	High depression scores were associated with self-reported intentional nonadherence (*P*=.01)* Anxiety results NR	NR	Poor

Author, year	Origin, Design and Sample (N)	Participant Characteristics	Measure of Anxiety (criteria used)	Measure of depression (criteria used)	Measure of Adherence (non-adherence criteria)	Type(s) of Medication evaluated (% if reported)	Route of medication (% if reported)	Extent of adherence	Results	Effect size interpr-etation	Quality rating
Wang et al[32] 2020b	Origin: China Design: cross-sectional Sample: NR (378)	100% CD 57.9% M Age: 31.01	NR†	NR†	Medication Adherence Report Scale (MARS-4 item) (nonadherence MARS<17)	Azathioprine (100%)	Oral	43.90%	Anxiety (OR 6.244, 95% CI 2.563–15.213, *P*<.001) and depression (OR 3.801, 95% CI 1.281–11.278, *P*=.016) were independent predictors of nonadherence when controlling for medication necessity beliefs, medication concerns beliefs and medication knowledge	Medium	Poor

Abbreviations: CD, Crohn's disease; GADS, Goldberg Anxiety and Depression Scale; GDS, Geriatric Depression Scale; HADS-A, Hospital Anxiety and Depression Scale-Anxiety subscale; HADS-D, Hospital Anxiety and Depression Scale-Depression subscale; HAQ, Health Anxiety Questionnaire; IBD, Inflammatory bowel disease; IC, Indeterminate colitis; IBDU, inflammatory bowel disease unclassified; UC, Ulcerative colitis; M, Male; MARS-5, Medication Adherence Report Scale; MMAS-8, Morisky Medication Adherence Scale; MPR, Medication Possession Raito; NA, Not applicable; NR, Not reported; PHQ-9, Patient Health Questionnaire-9; VAS, Visual Analogue Scale; 5-ASA, 5-aminosalicylic acid.
Ages reported as means unless stated. All participants ≥18 unless otherwise stated.
†Independent variables treated as continuous variables in the analyses
*Result based on univariate statistical test only

[a]Defined as not filling anti-TNF prescription if injectable, or not getting infliximab infusion for 30 days beyond needed date for continuation because the patient failed to get the prescription or could not get required maintenance health care
[b]Median age (mean not reported)
[c]MPR calculated as the total sum of days' supply for each medication refill divided by the number of days in the observation period
[d]Defined MMAS-8 adherence scores as: low = <6, medium = 6-7, high = 8
[e]Further divided into: intentional nonadherence (majority of answers indicated behaviour not related to forgetfulness; 42.4% of non-adherers) and nonintentional nonadherence (majority of answers indicated behaviours related to forgetfulness, 57.6% of non-adherers)
[f]IC was excluded from analyses on anxiety and depression in this study
[g]Demographic data reported based on wider sample that completed the Geriatric Depression Scale (N=359), as data not available for subsample that was included in adherence analyses (n=240)
[h]Participants ≥65
[i]Rates (%) measured at 3 month follow up time point
[j]Study used *P*-value of 0.157 for selection of independent predictors (through backwards selection), based on Akaike's Information Criterion
[k]Not clear how pill count was used for nonadherence
[l]Not stated how/if this was analysed in relation to self-reported nonadherence (no correlation reported). No analysis between urine sample results and anxiety and depression reported.
[m]67% endorsed at least some non-intentional nonadherence; 35% endorsed at least some voluntary nonadherence

Discussion

The systematic literature search identified 18 studies that examined an association between anxiety or depression and medication adherence in adults with IBD. Closer examination of the higher quality studies suggests an association between depression and nonadherence. Both of the good quality studies included in the current review found depression to be associated with nonadherence.[29,30] These were both retrospective cohort designs, therefore strengthening the evidence of the direction of this relationship. A prospective cohort study also found a significant association, however this study used only a single item to assess both anxiety and depression together.[34] Overall, studies that used objective measures of adherence consistently found an association with depression[29,30,42] whereas those that utilised self-report questionnaires were mixed, and there were no consistent patterns between the different questionnaires. In contrast, a previous meta-analysis of depression and medication adherence across a range of chronic diseases found that significant results were moderated by method of adherence measure, with pharmacy data resulting in significantly smaller correlations compared to self-report measures.[50] The finding in one study that depression was an independent predictor for complete nonadherence, but not partial nonadherence[42] was also the only result in the current review to have a large effect size. Further research into whether there are meaningful differences between complete and partial nonadherence is warranted.

Depression may be associated with nonadherence to medication for several reasons. For example, depression can negatively impact on motivation and self-care. Feelings of hopelessness are common in depression, and adherence may be affected if optimism for treatment is compromised.[51] Reductions in cognitive functioning associated with depression could also result in difficulties following agreed treatment plans.[51] Most studies did not differentiate between intentional (e.g. choosing to not take medication) and nonintentional

adherence (e.g. forgetting to take medication). San Roman et al[44] reported a significant association between depression and intentional nonadherence only, however this study was assessed as poor quality and caution should be taken regarding its conclusions. Campos et al[45] reported that 57.6% of their sample were non-intentional non-adherers, but they did not report separate analyses for different kinds of non-adherers. Compliance with medication treatment has been linked to social support, which can also be negatively impacted when someone is depressed as they may be more likely to withdraw and experience social isolation.[51] Knowing more about individuals' reasons for nonadherence could help to understand why depression may be a predictor of nonadherence, as well as to suggest targets for intervention and discussion with health practitioners.

The current review found no compelling evidence for an association between anxiety and adherence to IBD medication. The two studies assessed to be good quality examined depression only. Two of the four studies that found a significant relationship with anxiety and nonadherence were poor quality, and another assessed anxiety and depression together using only a single item.[34] One possible reason that anxiety was found not to be associated with medication adherence could be because the focus of anxiety differs from person to person. When anxiety relates to health concerns, this could conceivably increase adherence. Conversely, anxiety about medication side effects could decrease adherence. A combination of anxiety types could obscure trends at the group level. Most of the studies in the review examined anxiety more generally, whereas one assessed health anxiety specifically and found no association with adherence.[37]

The studies included in this review measured adherence in a variety of ways. There is no recognised gold standard measure of medication adherence. Measuring the level of drug metabolites in patient blood or urine samples is considered the only direct measure of adherence, which is expensive and may not be suitable for all types of medications.[24] In the

current review, two studies measured urine metabolite levels, however only Shale & Riley[42] utilised the results in relation to anxiety and depression. Indirect measures of adherence can entail professionals counting from the number of pills that patients have left over, obtaining data about number of pharmacy refill requests, using electronic devices that monitor whenever a medication bottle is opened, and patient self-report.[24] Patient self-report methods, such as administering adherence questionnaires, are the most common way of assessing adherence; they are simple and cost effective but prone to recall and social desirability bias. Studies within the current review most commonly used the MMAS-8, which has been validated within IBD populations against prescription claim data.[52] Pill count and pharmacy data were other indirect methods used by the reviewed studies, and whilst these have the advantage of being more objective than self-report, they are not a fail-safe measure of adherence. It has been suggested that using a combination of methods would be ideal for assessing adherence, for example using metabolite levels to verify self-report measures,[20] however this may not always be feasible due to time and financial constraints. In addition to the challenges around how to measure adherence, there is no universal cut-off for what is considered adequate adherence,[24] although around 80% is a figure commonly used for both questionnaires and pharmacy refill data. As previously discussed, there are also differences between complete nonadherence and partial nonadherence, with the latter being used in most studies.

The term ‘adherence’ is often used interchangeably with ‘compliance’. This is a recognised issue in the literature as the terms have different meanings. Most of the studies in the current review referred to adherence, however a minority utilised the term compliance. Compliance refers to the extent a patient’s behaviour matches the recommendations of the prescriber.[53] Rae[54] argued that this approach is paternalistic, as it holds the expectation of obedience and passivity from patients. Adherence still focuses on patient behaviour,

however, also incorporates agreement between practitioner and patient.[8,53] In their review, Rae[54] highlights that consensus has yet to be reached about the meaning of adherence, with some people considering it only slightly different to compliance, and others considering it similar to an additional construct, concordance. Within definitions of concordance however, the emphasis is on the relationship between practitioner and patient and a collaborative way of working, rather than the patient's medication taking behaviour.[53,54] Therefore, whilst concordance is recognised as an optimal way of working clinically, it has limitations for describing actual behaviour, and the concept itself is not as well operationalised.[53] This is relevant to anxiety and depression, as taking the individual's personal situation into consideration would include their mood and wellbeing. Future research should avoid using these terms interchangeably, and to make sure to define what is being assessed. Rae[54] advocates for the term adherence when examining behaviour, and concordance when considering the therapeutic relationship.

A strength of the current review was that it focused specifically on anxiety and depression as possible predictors of adherence, which allowed examination of these factors in more depth than previous reviews that included many potential factors related to adherence. This review also included all types of IBD medication, and it would have been useful to identify whether the relationship between anxiety or depression and adherence differs between medication types. The only two good quality studies in the current review examined medications administered through injection or infusion only, making it difficult to draw conclusions between medication routes. Although many studies conducted multivariate analyses to demonstrate whether anxiety or depression had an independent association with adherence, no studies completed any mediating or moderating analyses (for example type or route of medication). There were some studies that examined the association between type or route of medication and adherence more generally, however these results were outside the

scope of the current review question. Future research would also benefit from understanding more about potential interactions or mediations between anxiety and depression and medication nonadherence. For example, Chao et al[55] found that medication beliefs (including perceived side effect barriers and perceived general barriers), and self-efficacy mediated the association between depression and medication nonadherence within individuals with diabetes. Ecological Momentary Assessment (EMA), a methodology that utilises real time collection of experiences and behaviour throughout the day in an individual's natural environment,[56] would also be useful to better understand the relationship between anxiety and depression, and medication adherence. This would allow for monitoring of how anxiety and depression may affect medication adherence differently depending on context. It would also improve accuracy of mood assessment, which is normally impacted upon by recall bias.[56] EMA, along with a pill bottle monitoring system, has recently been used to explore medication adherence within human immunodeficiency virus (HIV) and was found to be an acceptable data collection method.[57]

There were no clear patterns in the data included in this review regarding sample characteristics or demographics that might indicate reasons for conflicting findings between studies. It would be interesting to see whether there are potential differences between ulcerative colitis and Crohn's disease, however studies generally analysed these together in relation to anxiety and depression. Wang and colleagues[31,32] were the only studies in the current review to look at Crohn's disease only, both of which reported a significant association between both anxiety and depression, and adherence; however, the quality of these studies was fair and poor, respectively. A previous review found that none of the frequently measured demographic, clinical and treatment variables were consistently associated with nonadherence, despite previous literature reporting some significant findings.[20] Although over half of the studies in the current review included multivariate

analyses, many of them did not consistently control for factors such as age, gender and disease type. Future studies examining anxiety and depression as predictors for nonadherence would benefit from controlling for these demographic factors, amongst others. Furthermore, within questionnaire studies the exact reasoning for why participants were prescribed certain medications is not provided, so there may be additional confounding factors that were unable to be accounted for.

This review has several clinical implications. Assessment of adherence is important in ongoing review of treatment. Gastroenterologists have been found to assess for high adherence well, however overestimation of adherence occurs more frequently than underestimation,[52] highlighting the importance of using other measures within clinical appointments. Incorporating the use of a VAS in appointments could be an efficient way of screening for nonadherence. If adherence was a concern, the MMAS-8 could then be used to help identify reasons for nonadherence to be further discussed with the individual. In their comparison study of self-report tools, Severs et al[58] found VAS to be the best way to self-assess overall adherence, and the MMAS-8 more useful for providing reasons for nonadherence. Identifying the reasons for nonadherence would help guide the support that is needed. Ghosh[59] outlines some practical suggestions to improve medication adherence depending on what reasons are relevant, including improving: patient-physician concordance, patient-physician relationships, patient's disease and medication knowledge, medication reminder strategies, and patient knowledge of available support. A recent review of interventions aimed to improve medication adherence in IBD concluded that multicomponent interventions were the most successful, and whilst these components varied between studies, they consistently included educational and behavioural components.[60]

It is important for clinicians working within gastroenterology and other medical settings to consider patients' mental health when agreeing treatment plans. This includes

having honest conversations with individuals about motivation to engage in treatment, as well as facilitating discussion about what the reasons may be for lower adherence, including unintentional factors that may negatively impact on adherence such as forgetting or having poorer self-care when depressed. The association between depression and medication nonadherence is also important for professionals who may be offering psychological therapy to be aware of so they can include the physical health consequences of depression in their assessments and formulation of the person's difficulties. Together, this emphasises the importance of a holistic, integrated team approach to caring for people with IBD. It has been well established that an integrated care model that involves multidisciplinary teams is the most effective model of care for individuals with IBD.[61] Furthermore, integrative care models have been shown to decrease direct and indirect costs of IBD compared to patient-physician models.[61] Both IBD patients and health care professionals have also expressed a need for biopsychosocial healthcare integration through a multidisciplinary care approach.[62] Despite these recommendations being in best practice guidelines,[63] barriers such as access to resources mean this is not always available across services. Integrative care could also better facilitate the team collaboratively targeting adherence behaviours and depressive symptoms, rather than either one in isolation. This approach has been suggested in other diseases such as cardiovascular disease, where it has been recognised that treating depression in isolation is unlikely to resolve the medication adherence due to it being a complex relationship likely involving moderating factors.[64]

Limitations

This review did not include a meta-analysis, limiting our ability to draw conclusions about average effect sizes. The review did not include unpublished data and consequently is at higher risk of publication bias; however, it was deemed important to maximise the quality of included studies. Importantly, the review did include numerous studies that reported non-

significant findings, reducing the risk of publication bias impacting on the conclusions. Most of the included studies were cross-sectional, and therefore this limits causal conclusions that can be drawn for the association between depression and nonadherence. Only studies in English were included, therefore it is possible that results from non-English publications could have been missed. Most primary papers did not report ethnicity, and where they did, the majority of participants were Caucasian, potentially limiting the generalisability of the results, although due to lack of reporting this is difficult to say for certain. Finally, this review is limited to adults only and its findings would potentially be less relevant for younger groups, where additional factors such as parental support with adherence would likely be especially important.

Conclusions

Overall, the findings of this review suggest evidence for an association between depression and medication nonadherence, however, there remain some conflicting findings and further research is needed to strengthen this conclusion. In particular, additional longitudinal study designs would help determine depression as a risk factor for nonadherence. Careful consideration of how adherence is assessed is needed, and potential mediators, moderators and interactions with other known risk factors warrant exploration. It is important for health professionals working with individuals with IBD to be alert to symptoms of depression, both to support their patients' mental wellbeing, and to facilitate conversations in relation to their treatment. Future research would benefit from exploring the possible mechanisms of why depression is associated with adherence. The current evidence does not support an association between anxiety and medication adherence. Future studies may benefit from considering the reasons driving anxiety, in order to better understand a possible association with medication adherence. Further higher quality studies are also needed.

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Psychological Flexibility and Self-compassion in People on Home Parenteral Nutrition: Psychological, Adherence and Medical Outcomes

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Abstract

Home parenteral nutrition (HPN) is an often life-saving nutritional treatment. However, it requires meticulous adherence to line care procedures and poses challenges to daily activities which can impact a person's quality of life (QOL) and psychological wellbeing. Less is understood about psychological processes that affect outcomes in HPN. Psychological flexibility (PF) and self-compassion (SC) have been identified as important processes in other health populations. This study aimed to examine the unique role of PF and SC in predicting psychological distress, wellbeing, QOL, line care adherence and line infections in adults on HPN. This cross-sectional, observational study was completed online. The sixty-six participants were primarily from the UK. Higher PF and SC were significantly correlated with the following outcomes in the predicted directions: lower psychological distress, higher wellbeing, higher QOL and increased line care adherence. Multiple linear regression models explained a significant proportion of the variance in all outcomes, except for line infections. PF was uniquely associated with lower total distress, lower anxiety, better wellbeing and higher QOL after controlling for SC, gender and age. Whereas SC was uniquely associated with lower total distress, depression and stress when controlling for PF, gender and age. Interventions aimed at improving PF and SC may be beneficial to support the emotional wellbeing and QOL in individuals on HPN. A measure of line care adherence was developed for the study, although additional validation is required. Further research would benefit from prospective designs and consideration of objective measures of infection.

Keywords: home parenteral nutrition, psychological flexibility, self-compassion, psychological distress, quality of life, adherence

Background

Home parenteral nutrition (HPN) is a type of nutrition therapy provided through intravenous administration for patients living at home (Cederholm et al., 2017). It is administered through a central venous catheter, or sometimes a peripherally inserted central venous catheter. HPN is most commonly used to treat patients with chronic intestinal failure (e.g., due to conditions such as short bowel syndrome or Crohn's disease), which means they are unable to absorb nutrients through their intestine. However, in some cases it is used to treat or prevent malnutrition in patients whose intestines are still functional (Pironi et al., 2020). Total parenteral nutrition (TPN) refers to when all nutritional needs are met through parenteral nutrition, and intravenous delivery is the only route via which nutrition is delivered. In contrast, partial parenteral nutrition (PPN) is when parenteral nutrition is provided in addition to any route other than intravenously (Cederholm et al., 2017). HPN is often a lifelong treatment, although it can be temporary depending on the underlying reason. It is a treatment that requires meticulous attention to line care practices, such as observing strict aseptic procedures when connecting and disconnecting the nutritional feed to prevent possibly life-threatening catheter-related bloodstream infections (CRBSI; Pironi et al., 2020).

Impact of Home Parenteral Nutrition

HPN poses many challenges to patients in terms of disruption to, or cessation of, daily activities including work, changes to social roles, and relationships. Infusions are generally given over a 10-to-12-hour period, often overnight, however this is dependent on the individual's treatment plan. Patients on HPN have been found to have lower quality of life (QOL) than the general population and individuals who have intestinal diseases not requiring HPN (Winkler, 2005). In particular, the physical functioning element of QOL appears lower in patients on HPN compared to the general population (Sowerbutts et al., 2021), which is perhaps unsurprising given the impact on physical health. In contrast, the impact of HPN on

the psychological element of QOL is less clear. One study found psychological QOL worse compared to the general population (Blüthner et al., 2019), whereas other studies found QOL no different to the general population (Schliefert & Carey, 2013), or that it improved over time (Chambers et al., 2005). QOL is viewed as an important outcome to monitor during treatment, both to be able to observe potential improvement in QOL and as an indicator of quality of care (Pironi et al., 2020). There is increasing research into understanding factors that impact QOL when on HPN.

Understanding the relationship between QOL and HPN is complicated, as it is difficult to differentiate between the impact of the physical effects of the underlying disease and the impact of HPN treatment itself. Persoon et al. (2005) found that despite individuals reporting multiple physical symptoms related to their underlying condition, it was psychosocial difficulties (such as changes in mood, restricted social lives, being dependant and lack of freedom) that participants expressed as having the largest negative impact on their daily lives. Huismann-de Waal et al. (2007) highlighted that patients with chronic gastrointestinal problems adjusted better to HPN treatment than patients with acute gastrointestinal trauma. Similarly, people on lower volumes of HPN had better QOL, with decreased severity of underlying disease suggested as a potential reason for this finding (Sowerbutts et al., 2021). In their recent review of QOL in HPN, Sowerbutts et al. (2021) concluded that the certainty of evidence within this literature is poor, and therefore confidence in current understanding of QOL is limited.

HPN requires good adherence to the procedures around caring for one's line, to prevent complications including CRBSI. Therefore, understanding psychological processes that may influence adherence behaviours is important. Psychosocial factors including depression, lower QOL, social impairment and fatigue were associated with higher incidence of venous access device related complications, including CRBSI (Huisman-de Waal et al.

2011). In another study, diagnoses of anxiety and depression were more common in patients who experienced central line associated bloodstream infections, however, these variables were not retained as significant predictors in a regression model (Xue et al., 2020).

Depression and anxiety are commonly reported by individuals on HPN (Huisman-de Waal et al., 2007). In patients with chronic intestinal failure, 56% have been found to have clinical levels of anxiety or depression (Ablett et al., 2018) and in another sample, 41.7% were prescribed antidepressants for their mental health (Cloutier et al., 2021). The need for psychosocial support for patients has been recognised within these studies. Although QOL and wellbeing can be negatively impacted, many individuals on HPN normalise their responses and cope well (Winkler & Smith, 2014). Indeed, in qualitative studies individuals on HPN described the treatment as improving their QOL compared to the impact of their underlying condition prior to starting HPN, despite the restrictions it imposed (Tsang & Carey, 2015; Winkler et al. 2010). HPN has also been found to improve QOL in patients with cancer (e.g. Culine et al., 2014; Girke et al., 2016). Although various factors affecting QOL and wellbeing have been identified, there is a dearth of research examining potential protective or moderating factors, including psychological processes, that may affect QOL and distress outcomes in HPN populations. Understanding these potential processes is crucial for implementing support and service improvement. There are psychological processes that have been found to predict coping in other health populations, including psychological flexibility (PF) and self-compassion (SC).

Psychological Flexibility

Psychological flexibility is the ability to be in the present moment with awareness and openness to one's experience, and to take action guided by one's values (Hayes et al., 2006). Increasing PF is the main aim of Acceptance and Commitment Therapy (ACT; Hayes et al., 2011a), and is underpinned by six processes: acceptance (awareness and willingness to

experience distressing internal experiences), cognitive defusion (distancing from thoughts and recognition that thoughts are not literal truth), contact with the present moment (e.g. through mindful non-judgemental experience), self-as-context (the perspective of being consciously aware of thinking and feeling, rather than the content of thoughts and emotions themselves), values (chosen qualities that provide meaning to one's life) and committed action (actions taken, informed by values; Hayes et al., 2006). Hayes et al. (2011b) described how these six processes can be grouped into three overarching processes: openness to experience, self-awareness and perspective taking, and valued action.

PF may be particularly relevant for people on HPN. For example, increased engagement with valued activities through committed action could potentially help mitigate the significant limitations arising from HPN. A willingness to be open to internal experiences through acceptance and defusion may also lessen the impact of psychological distress that can be an understandable response to the challenges associated with HPN. Although not yet explored in HPN populations, there is evidence of a role for PF within chronic illnesses.

Meta-analyses indicate that higher levels of PF are associated with better QOL and psychological outcomes, across general, mental health and physical health populations (Dochat et al., 2021; Hayes et al., 2006). More specifically, PF has been found to be associated with decreased rates of depression for patients with chronic kidney disease (Iida et al., 2020), lower diabetes related distress in Type 1 diabetes (Nicholas et al., 2021), and better wellbeing in Type 2 diabetes (Maor et al., 2021). PF also predicted increased life satisfaction and lower anxiety over four months within individuals with muscle disorders (Graham et al., 2016a). A recent review of meta-analyses concluded that ACT is an efficacious intervention across various presentations (Gloster et al., 2020). Within chronic pain populations, ACT interventions have improved functioning and distress (Du et al., 2021; Hann & McCracken, 2014; Hughes et al., 2017). A recent review also found improved outcomes for pain

interference, disability, depression and QOL, with PF as a mediator (McCracken et al., 2022). Emerging research also suggests that ACT interventions are associated with improved outcomes across other long-term health conditions, although higher quality studies are required (Graham et al., 2016b). Furthermore, there is growing evidence of a relationship between PF and behavioural and physical health outcomes. For example, PF was associated with improved glycated haemoglobin (HbA1c) levels in Type 1 diabetes (Nicholas et al., 2021). The impact of factors such as age or gender on PF is limited and inconclusive. Gloster et al. (2011) found no association between PF and age or gender. However, more recent studies suggest a possible gender difference for PF, with women having lower PF than men (Sanchez-Puertas et al., 2022; Bermejo-Franco et al., 2022). Furthermore, Edwards et al. (2019) found older age to independently predict lower cognitive fusion, one of the processes of PF.

Self-compassion

Self-compassion (SC) is the ability to connect to one's suffering, with feelings of kindness and caring, along with an understanding and non-judgemental attitude towards oneself, whilst acknowledging suffering as part of humanity (Neff, 2003a). Neff (2003b) further defined six components of SC as: self-kindness vs. self-judgement, common humanity vs. isolation, and mindfulness vs. overidentification. These facets of SC influence each other, whilst also being conceptually distinct (Neff 2003b). There are some plausible reasons SC may be important in HPN. Self-kindness may promote help-seeking, as well as improved self-care related to line care. Mindfulness aspects of SC might also be related to improved line care practices. SC may also help protect against self-criticism which could be easily triggered by the challenges and frustrations of adhering to a strict healthcare regime. A sense of common humanity could be related to increased social support, which has been shown to be an important factor influencing psychological distress within HPN (Ablett et al., 2018).

More generally, SC has been found to mediate the positive relationship between perceived social support and psychological wellbeing (Wilson et al., 2020).

Across numerous studies in clinical and nonclinical samples, SC has been negatively associated with psychopathology (Muris et al., 2017), including depression, anxiety and stress (MacBeth & Gumley, 2012). Zessin et al. (2015) found SC had a causal relationship with greater wellbeing. Within health populations, SC was associated with decreased depression and diabetes related distress in Type 1 and Type 2 diabetes (Friis et al., 2016) and better QOL in individuals with celiac disease (Dowd & Jung, 2017). Furthermore, SC was associated with lower stress, directly and indirectly through greater use of adaptive coping and reduced use of maladaptive coping, in individuals with inflammatory bowel disease (IBD) and arthritis (Sirosis et al., 2015). A recent review concluded that SC-based interventions improved SC within patients with chronic physical health conditions, and increased SC was associated with improved wellbeing outcomes such as depression (Kiliç et al., 2021). There is also evidence of a relationship between SC on behavioural and physical health outcomes. SC predicted stricter dietary adherence within celiac disease (Dowd & Jung, 2017). SC also indirectly predicted dietary adherence, with self-regulatory efficacy (i.e., the confidence to self-manage their behaviours to achieve a desired outcome) mediating this relationship (Dowd & Jung, 2017). Similarly, to PF, SC has also been associated with improved glycated haemoglobin (HbA1c) levels in Type 1 and Type 2 diabetes (Friis et al., 2016). Research also suggests an association between SC and gender, with men having slightly higher SC than women (Yarnell et al., 2015). Other studies have found SC increases with age (e.g. Neff & Vonk, 2009; Souza & Hutz, 2016) and that the positive relationship between SC and wellbeing has been found to be moderated by age (Hwang et al., 2016).

Identifying potential psychological factors associated with QOL, distress, adherence to line care and medical outcomes (infections) would have important clinical implications.

Positive findings would provide a rationale for treatment approaches underpinned by PF or SC, to support people on HPN to improve their QOL and health adherence behaviours. Better adherence is likely to result in fewer line infections, and therefore if higher levels of PF and SC help people better adhere to their line care this could have an indirect effect on infections. This could also have potential cost saving implications if infections requiring hospital care could be reduced (Buetti et al., 2022). To the author's knowledge, there have been no studies examining PF or SC within HPN populations.

Conceptual overlap between PF and SC

Both PF and SC have previously been associated with distress, QOL and health behaviours, as described above. There is also conceptual overlap between SC and PF, and the therapeutic approaches that they underpin (Neff & Tirch, 2013). In both models mindfulness processes are emphasised (Yadavaia et al., 2014). Relatedly, willingness to be open to painful experiences (in contrast to attempting to avoid, suppress or change these) is considered important in both PF and SC (Davey et al., 2020). Acceptance, central to PF, could also be considered in relation to compassionate self-kindness, as openness to difficult experiences is essential for self-understanding, and may help a person feel more validated in their experiences (Yadavaia et al., 2014). Perspective taking is present in SC in the context of taking the perspective of the 'compassionate other' and facilitates empathy (Neff & Tirch, 2013), whereas within PF, self-as-context involves being able to take an observer's perspective of one's own experiences. Finally, acting in accordance with one's values, which is central to PF, is also relevant to SC. For example, Neff (2003a) suggests SC may provide motivation to engage in actions that improve wellbeing, even when these actions are difficult. Consistent with theoretical similarities, there is emerging research that PF and SC are positively associated with one another in various settings. These include general student populations (Marshall & Brockman, 2016; Woodruff et al., 2014), women survivors of

interpersonal violence (McLean et al., 2018) and physical health populations (Davey et al., 2020; Kiliç et al., 2022). Therefore, it seems beneficial to explore both together, and this conceptual overlap forms the theoretical rationale for including them both in the current study. Furthermore, studies examining psychotherapeutic interventions for gastroenterological conditions incorporating both ACT and compassion-based approaches are currently being trialled (Trindade et al., 2021). Davey et al. (2020) considered whether it is appropriate to examine PF and SC as distinct processes, or whether they should be combined under an integrated model. Within the context of chronic pain, they determined that, despite being correlated, PF and SC are distinct enough to provide unique information, furthering the rationale to examine both their shared and unique predicative value. The authors based this on Campbell and Fiske's (1959) criteria of a correlation coefficient <0.85 to indicate adequate discriminant validity (Davey et al., 2020).

Aims of the current study

The aim of the current study was to examine the unique role of PF and SC in predicting psychological distress (depression, anxiety and stress), wellbeing and QOL in individuals on HPN. The study also aimed to determine if PF and SC were associated with improved line care adherence and decreased rates of line infections requiring hospital admission. As summarised, age and gender could be associated with PF and SC. As there is some evidence that age and gender may also be associated with depression, anxiety, and QOL (Baxter et al., 2013; Fryback et al., 2007; Salk et al., 2017) it was deemed important to assess the contribution of PF and SC whilst controlling for these variables.

Hypothesis 1: higher PF would be independently associated with decreased distress, increased wellbeing and increased QOL. Hypothesis 2: higher SC would be independently associated with decreased distress, increased wellbeing and increased QOL. Hypothesis 3: higher PF would independently predict increased line care adherence and a lower number of

infections. Hypothesis 4: SC would independently predict increased line care adherence and a lower number of infections. Hypothesis 5: the relationship between higher SC, or higher PF, and fewer infections would be mediated by better adherence to line care.

Method

Study Design and procedure

The study was a cross-sectional, observational questionnaire design with data collected online through convenience sampling. Participants provided online consent, confirmed eligibility for the study, and accessed the study questionnaire through the Qualtrics platform (Qualtrics, Provo, UT). Participant forms can be found in Appendices E-G. Data collection was completed between 17th May 2021 and 17th February 2022. The study questionnaire was advertised on online platforms including Facebook support groups and Reddit boards for individuals on parenteral nutrition, artificial nutrition or groups aimed at relevant health conditions (e.g. short bowel syndrome, IBD). It was also shared on Twitter. Crohn's and colitis third sector organisations in Australia, Canada, Portugal, United States and the United Kingdom (UK) shared the study on their websites and/or social media pages. The organisation PINTT (Patients on Intravenous and Naso-gastric Nutrition Treatment), based in the UK, shared the study in their newsletter and through email to members.

A service user receiving HPN was consulted throughout the study. They provided advice regarding questionnaire development and recruitment, assisted with study dissemination, and provided insight into living with HPN treatment. The study was approved by Cardiff University Ethics Committee (reference number: EC.20.04.14.6006A, Appendix H).

Participants

Participants were adults (18 years or older) and currently on HPN. There were no other exclusion criteria.

Measures

Demographic information

Participants were asked to indicate their age, gender, country of residence, who they live with, their relationship status, and level of education. They were also asked what health condition led to them requiring HPN, how long they had been on HPN, how many days a week they were on HPN, and whether they received TPN or PPN.

Psychological Flexibility

PF was measured using the Comprehensive assessment of Acceptance and Commitment Therapy processes (CompACT; Francis et al., 2016; Appendix I). The questionnaire includes 23 items each rated on a 7-point scale (0=strongly disagree; 6=strongly agree), with 12 items reverse-scored. This questionnaire contains three subscales: openness to experience, behaviour awareness and valued action. Items include statements such as: “one of my big goals is to be free from painful emotions”, “I rush through meaningful activities without being really attentive to them” and “I can identify the things that really matter to me in life and pursue them”. A total score is obtained by summing all items, ranging from 0 to 138, with higher scores indicating greater PF. The scale and its three-factor structure has been evaluated as a reliable and valid measure of PF (Bayliss, 2018). Cronbach’s alpha for the current study was 0.91.

Self-compassion

The Self-Compassion Scale short-form (SCS-SF; Raes et al., 2011; Appendix J) was used to measure SC. The questionnaire has been found to have a near perfect correlation with the original, long-form version and is recommended for research use (Neff, 2003b). It contains 12 items, six of which are reverse scored. Each question is rated on a 5-point scale (1=almost never; 5=almost always) and a total score is obtained by calculating a mean from all items following reverse scoring of negative items. Questions include statements such as “I

try to see my failings as part of the human condition" and "I'm disapproving and judgmental about my own flaws and inadequacies". The SCS-SF has been found to have good internal consistency and is a valid and reliable measure of SC. It has previously been used within various chronic health samples (e.g. Sirois, 2020). In the current study, Cronbach's alpha was 0.88.

Psychological Distress

The Depression Anxiety Stress Scale short-form (DASS21; Henry & Crawford, 2005; Appendix K) is a general measure of psychological distress, which also measures three separate constructs: depression, anxiety and stress. It was developed based on the validated, 42-item version of the DASS (Lovibond and Lovibond, 1995). Each of the 21 items is rated on a 3-point scale (0=did not apply to me at all; 3=applied to me very much or most of the time over the past week). Higher scores indicate greater levels of distress. Scores are derived by summing the seven items for each subscale and then multiplying by two. The total score is obtained by a sum of the three subscales. Development and normative data for the DASS21 was carried out in non-clinical samples and it is well suited for research use. Internal reliability estimated by Cronbach's alpha ranged from to 0.82 to 0.93 for the three subscales and total score (Henry & Crawford, 2005). In the current study, Cronbach's alphas were: 0.95, 0.93, 0.87 and 0.88 for total distress, depression, anxiety and stress scales, respectively.

Wellbeing

Wellbeing was assessed using the Short Warwick Edinburgh Mental Wellbeing Scale (SWEMWBS; Stewart-Brown et al., 2009; Appendix L). The questionnaire includes seven positively phrased items, such as "I've been feeling optimistic about the future" rated on a 5-point scale (1=none of the time; 5=all of the time). The SWEMWBS is scored by first summing the scores for each of the seven items, and then transforming the total raw scores into metric scores using a conversion table. Scores range from 7 to 35, with higher scores

indicating higher positive mental wellbeing. It has been validated in both the general adult population (Ng Fat et al., 2017) and clinical samples (Shah et al., 2021), and demonstrates good psychometric properties. Cronbach's alpha was 0.86 in the current study.

Quality of Life

The World Health Organization Quality of Life-bref (WHOQOL-BREF; Whoqul Group, 1998; Appendix M) was used to measure QOL. The questionnaire comprises of 24 items related to four domains: physical health (7 items), psychological health (6 items), social relationships (3 items) and environment (8 items), and two additional items pertaining to overall perception of QOL and health, which are not included in the domain scores. Item scores range from 1 to 5, and higher scores indicate better QOL. Domain scores are obtained by multiplying the average score of domain items by four, followed by conversion to a 0-100 scale to result in the final transformed score (WHO, 1996). The WHOQOL-BREF does not produce an overall total score. The WHOQOL-BREF has good to excellent psychometric properties, and it has been extensively evaluated across cultures and in many settings including within sick and well populations (Skevington et al., 2004). It has been recommended for use in research where a brief assessment of QOL is required. In the current study, Cronbach's alphas were: 0.84, 0.82, 0.69 and 0.82 for the physical, psychological, relationships and environment subscales, respectfully.

Line care adherence

To the author's knowledge, there is no existing measure of line care adherence for individuals on HPN, therefore a questionnaire was developed for the current study. The questionnaire items were developed through review of other treatment adherence questionnaires, such as the asthma routines questionnaire (Fiese et al., 2005) and Morisky medication adherence questionnaire (Morisky et al., 1986), and clinical knowledge of a clinical psychologist working within an intestinal failure service. A service user on HPN also

examined the original items and provided feedback on wording and relevancy to line care routine. Participants were asked to indicate their agreement to statements such as “it doesn’t really matter if I miss out the occasional step when following my line care procedure” and “I can be careless about line care”. Each of the items were rated on a 5-point Likert scale (1=strongly disagree; 5=strongly agree or 1=never; 5=always). A total score was calculated by summing the items after reverse coding negative questions. The original questionnaire consisted of 12 items, six related to thoughts and feelings and six related to behaviour. Following principal component analysis, nine items were retained, and all items loaded onto a single factor. Scores therefore ranged from 9 to 45, with higher scores indicating better line care adherence. Full details of the final 9-item version of the questionnaire used in analyses can be found in Appendix N. As this questionnaire was developed for the current study, it has not been previously validated. Cronbach’s alpha with the current sample was 0.80. Participants were also asked to indicate whether they currently, or in the past, received help looking after their line care at home, however these items were not part of the adherence score.

Line infections

Participants self-reported the number of line infections they had in the previous five years that required hospitalisation.

Sample size

There are no known studies that have used the variables of interest with the outcomes of the current study in this population, therefore in the absence of a previous effect size from the literature, a medium effect size was used in the power calculations. *A priori* power calculation for multiple regression analysis, completed using G*Power (Faul, et al. 2009), indicated for a medium effect size of Cohen’s f^2 (0.15), statistical power level of 0.80 and *p* value of .05, a minimum sample size of 68 was required to detect significant unique

contributions of PF and SC, on all outcomes. Subsequent power analyses were calculated based on up to four predictors, to include gender and age, indicating a minimum sample size of 85. To determine the minimum sample size required for a mediation analysis, recommendations by Fritz and MacKinnon (2007) indicated a sample size of 71 to detect a medium effect size.

Statistical Analyses

Data were analysed using SPSS Statistics 27. The study hypotheses were tested by bivariate correlations and multiple linear regression analyses. Independent variables were entered into the regression simultaneously, as there is currently not sufficient empirical or theoretical reasoning for whether PF or SC would be more predictive of the outcomes. Age and gender were entered into the regression analyses to control for their possible confounding effects on the outcomes.

Regression analyses were run following completion of assumption testing for normality, linearity, homoscedasticity, multicollinearity, and outliers, leverage values and influential points. These assumptions were met unless otherwise stated. When heteroscedasticity was found, robust standard errors and their associated confidence intervals were reported, rather than the standard error of the coefficients (Hayes & Cai, 2007). Where outliers were detected (by casewise diagnostics and deleted studentized residuals), these were examined, however they were retained as they were valid data points and did not have a large leverage value (assessed as less than 0.2; Huber, 1981) or large influence (measured by Cook's distance less than 1).

Results

Sample data

Participants that did not complete the full Qualtrics survey were excluded from the analysis. Twenty-six participants were excluded because they did not progress past informed

consent (n = 11) or provided demographic information only (n = 15). Three participants answered only the first questionnaire (CompACT). One participant was excluded from analysis following examination of their responses, which indicated they were not receiving HPN. The final number of participants included was 66. There was one participant that did not identify as man or woman, and therefore this participant was excluded from any analyses that included gender (n = 65).

Data was checked for any missing values; no data was missing except for two participants who did not record their age. Mean substitution method was used for these two data points (Field, 2013).

Sample characteristics

Participants were predominantly women (71.21%) and from the UK (86.36%). The mean age was 47.78. Only 19.7% of participants lived alone, the remaining lived with others, and over half (59.09%) had a pet. Fifty percent of the sample were married. Highest level of education varied, with the majority having undertaken some form of post-secondary education (69.18%). Common reasons for receiving HPN included a shortened or damaged small bowel (e.g., short bowel syndrome or surgical complications), Crohn's disease, and disordered movement of the small bowel (e.g., Gastroparesis or Ehlers Danlos Syndrome). Most participants were on TPN (81.82%), for at least five or more days of the week (83.33%) and 72.72% had been on HPN for at least three years. About a third (28.79%) of participants indicated that they receive help with some aspect(s) of their line care. A t-test was run to determine if there was a difference in line care adherence scores between individuals receiving help and no help. Although individuals receiving no help with their line care had a slightly higher mean line care adherence score (41.23 ± 4.28 vs. 39.58 ± 6.06), this difference was not statistically significant ($t(25.57) = 1.10$, $p = .28$). Full details of sample characteristics can be found in Tables 1 and 2.

Table 1

Sample characteristics (N = 66)

	Mean (SD) or *n* (%)
Age	49.78 (15.10)
Gender	
Women	47 (71.21%)
Men	18 (27.27%)
Did not identify as man or woman	1 (1.52%)
Country of residence	
United Kingdom	57 (86.36%)
Australia	3 (4.55%)
Ireland	1 (1.52%)
Netherlands	1 (1.52%)
Switzerland	1 (1.52%)
United States	3 (4.55%)
Living situation	
Alone	13 (19.70%)
With spouse or partner	33 (50%)
With family	16 (24.24%)
With others, not family	1 (1.52%)
Other	3 (4.55%)
Pet (yes)	39 (59.09%)
Marital status	
Single	21 (31.82%)
Married	33 (50%)
Living as married or cohabiting	4 (6.06%)
Separated	3 (4.55%)
Divorced	2 (3.03%)
Widowed	3 (4.55%)
Highest level of education	
Primary	1 (1.52%)
Secondary up to 16	11 (16.67%)
Completed secondary	9 (13.64%)
Undergraduate	26 (39.39%)
Postgraduate	11 (16.67%)
Trade/Vocational	8 (12.12%)
Reason for HPN[a]	
Blockage of the intestine	2 (3.03%)
A leak from a fistula or a false passage	1 (1.52%)
Disordered movement of the small bowel	15 (22.73%)
A shortened or otherwise damaged small bowel	23 (34.85%)
Crohn's disease (with no other information)	19 (28.79%)
Unable to classify[b]	6 (9.09%)
Number of years on HPN	
Less than 1 year	6 (9.09%)
1 year	4 (6.06%)
2 years	7 (10.61%)
3 years	10 (15.15%)

4 to 9 years	19 (28.79%)
10-19 years	11 (16.67%)
20 years or more	8 (12.12%)
Number of days on HPN/week	
2 days	1 (1.52%)
3 days	5 (7.58%)
4 days	5 (7.58%)
5 days	7 (10.61%)
6 days	9 (13.64%)
7 days	39 (59.09%)
HPN treatment	
Total (TPN)	54 (81.82%)
Partial (PPN)	10 (15.15%)
Unsure	2 (3.03%)
Currently receiving help with line care	19 (28.79%)

[a]Participants indicated their response as free text, which were classified into categories

[b]Reason stated could have fit into multiple categories (e.g. genetic condition, intestinal failure).

Table 2

Outcome measure scores (N = 66)

	Mean (SD)
Psychological Flexibility	80.45 (22.68)
Self-compassion	2.88 (0.79)
Psychological distress score	41.88 (28.78)
Wellbeing score	20.81 (3.45)
QOL	
Physical domain	44.60 (19.94)
Psychological domain	47.35 (17.21)
Social domain	50.13 (23.14)
Environmental domain	57.39 (17.61)
Line care adherence	40.74 (4.90)
Number of infections	1.43 (2.75)[a]

[a]Range = 0-16; see Appendix O for further details of number of infections.

Principal Component Analysis

The Line Care Routine Questionnaire (LCRQ) was developed for the current study to assess for line care adherence. A principal components analysis (PCA) was run on the original 12-item questionnaire. The suitability of PCA was assessed prior to analysis. The overall Kaiser-Meyer-Olkin (KMO) measure was 0.73, considered ‘middling’ according to

Kaiser (1874). There were two individual KMO measures below <0.5, however these items were later removed based on the component matrix results. Bartlett's test of sphericity was statistically significant ($p < .001$), indicating that the data was likely factorizable.

Determination of how many factors to retain was completed by visual inspection of the scree plot (Cattell, 1966; Appendix P) and through parallel analysis. Percentile eigenvalues were generated for parallel analysis using Vivek et al. (2017) parallel engine. On these bases, only one factor was retained. No rotation was employed as all items loaded onto a single factor. Nine of the 12 items loaded onto this factor, using a 0.4 cut off value. Therefore, the three items that did not load were removed from the questionnaire. The component matrix can be found in the Appendix Q. The 9-item line care routine questionnaire was used for all subsequent analyses examining line care adherence.

Bivariate associations between study variables

PF, SC, distress, wellbeing, QOL and line care adherence were significantly intercorrelated with each other. In particular, PF and SC had a significant large correlation with each other ($r = .79$, $p < .01$). Conversely, number of line infections in the last five years was not correlated with any of the other variables (Table 3).

Table 3

Pearson product moment correlations between predictor and outcome variables

	CompACT	SCS	DASS-21-D	DASS-21-A	DASS-21-S	DASS-21-T	SWEMWS	WHOQOL-Ph	WHOQOL-Ps	WHOQOL-R	WHOQOL-E	LCA†	Infection	Gender‡	Age
SCS	.79**	-													
DASS21-D	-.56**	-.60**	-												
DASS21-A	-.47**	-.39**	.53**	-											
DASS21-S	-.52**	-.56**	.82**	.60**	-										
DASS21-T	-.59**	-.59**	.91**	.79**	.92**	-									
SWEMWS	.58**	.53**	-.71**	-.40**	-.64**	-.67**	-								
WHOQOL-Ph	.34**	.17	-.55**	-.48**	-.54**	-.60**	.44**	-							
WHOQOL-Ps	.60**	.54**	-.80**	-.56**	-.70**	-.79**	.70**	.60**	-						
WHOQOL-R	.37**	.37**	-.55**	-.49**	-.57**	-.61**	.50**	.39**	.62**	-					
WHOQOL-E	.29*	.20	-.47**	-.56**	-.42**	-.55**	.43**	.65**	.64**	.47**	-				
LCA	.26*	.29*	-.37**	-.16	-.34**	-.34**	.13	.12	.42**	.24	.16	-			
Infection†	-.15	-.02	.08	-.24	.14	.07	-.07	-.09	-.01	.04	.16	-.10	-		
Gender‡	-.04	-.06	-.02	.07	-.01	.01	.08	-.25*	-.07	.06	-.02	.19	.22	-	
Age	.02	.004	-.12	-.17	-.25*	-.20	-.07	.33**	.23	.003	.18	-.14	-.24	-.30*	-

Note. CompACT = Comprehensive assessment of Acceptance and Commitment Therapy processes; SCS = SC; DASS21 = Depression Anxiety Stress Scale (D = depression, A = anxiety, S = stress subscales); SWEMWS = Short Warwick–Edinburgh Mental Wellbeing Scale; WHOQOL = World Health Organization Quality of Life questionnaire-Bref (Ph = physical, Ps = psychological; R = relationship, E = environment domain subscales); LCA = Line care adherence. $n = 65$.

†Spearman's rank correlation was computed due to infection failing parametric assumptions

‡Point-biserial correlation was computed due to gender being a dichotomous variable.

*p<.05, **p<.01

Multiple linear regression

A series of multiple linear regressions were conducted, each including the following predictors entered simultaneously into the model: age, gender, PF, and SC. The outcomes that were separately assessed were psychological distress and each of its subcomponents (depression, anxiety, and stress), wellbeing, the subcomponents of QOL (physical, psychological, relationship and environment), line care adherence, and line infections.

Psychological distress (depression, anxiety and stress)

The multiple regression model statistically significantly predicted distress as measured by the total DASS21, $F(4, 64) = 11.64$, $p < .001$, and explained 40% of the variance. PF ($B = -0.39$, $p = .05$), SC ($B = -12.36$, $p = .03$) and older age ($B = -0.42$, $p = .04$) were significant unique predictors of decreased distress (Table 4).

The multiple regression models for the subscales of the DASS21 were also significant (Table 4). The model explained 36% of the variance in depression scores and higher SC was the only independent predictor of lower depression ($B = -6.36$, $p = .01$). For anxiety, the model explained 20% of the variance with PF as the only independent predictor of lower anxiety scores ($B = -0.19$, $p = .02$). The model explained 36% of the variance in stress scores. Both SC ($B = -5.49$, $p = .01$) and older age ($B = -0.20$, $p = .01$) uniquely predicted lower stress.

Table 4

Multiple regression results for total distress, depression, anxiety and stress

	Total distress		Depression[a]		Anxiety[a]		Stress	
	B (SE)	β	*B (SE)*	β	*B (SE)*	β	*B (SE)*	β
PF	-0.39 (0.20)*	-0.32*	-0.13 (0.08)	-0.24	-0.19 (0.08)*	-0.44*	-0.08 (0.07)	-0.18
SC	-12.36 (5.65)*	-0.35*	-6.36 (2.49)**	-0.42**	-0.52 (2.54)	-0.04	-5.49 (2.10)*	-0.43*
Gender	-5.57 (6.41)	-0.09	-2.76 (2.99)	-0.10	-0.01 (2.41)	0.00	-2.82 (2.38)	-0.13
Age	-0.42 (0.20)*	-0.22*	-0.12 (0.07)	-0.15	-0.10 (0.06)	-0.15	-0.20 (0.07)*	-0.28*
R^2	0.44***		0.40***		0.25**		0.40***	
Adj. R^2	0.40***		0.36***		0.20**		0.36***	
F	11.64***		9.98***		4.97**		10.08***	

Note. Model "Enter" method in SPSS Statistics. PF = Psychological Flexibility; SC = Self-compassion; *B* = unstandardized regression coefficients; *SE* = standard error of the coefficient; β = standardized coefficient; R^2 = coefficient of determination; Adj. R^2 = adjusted R^2.

[a]Robust standard error of the coefficient reported.

*p<.05; **p<.01; ***p<.001.

Wellbeing

The multiple regression model statistically significantly predicted wellbeing as measured by the SWEMWS, $F(4, 64) = 8.48$, $p < .001$, and explained 32% of the variance in scores. PF was the only independent predictor of increased wellbeing ($B = 0.06$, $p = .02$; Table 5).

Table 5

Multiple regression results for wellbeing

	Wellbeing	
	B (SE)	β
PF	0.06 (0.03)*	0.42*
SC	0.88 (0.74)	0.20
Gender	0.67 (0.84)	0.09
Age	-0.01 (0.03)	-0.06
R^2	0.36***	
Adj. R^2	0.32***	
F	8.48***	

Note. Model "Enter" method in SPSS Statistics. PF = Psychological Flexibility; SC = Self-compassion; *B* = unstandardized regression coefficients; *SE* = standard error of the coefficient; β = standardized coefficient; R^2 = coefficient of determination; Adj. R^2 = adjusted R^2.

*p<.05; ***p<.001

Quality of Life

The multiple regression models were statistically significant for both the physical and psychological domains of QOL, $F(4, 64) = 5.56$ $p < .001$ and $F(4, 64) = 11.16$, $p < .001$, respectfully. The model predicted 22% of the variance in the physical domain of QOL with PF ($B = 0.48$, $p < .01$) and older age ($B = 0.37$, $p = .02$) independently predicting increased QOL. PF ($B = 0.34$, $p < .01$) and older age ($B = 0.27$, $p = .03$) were also unique predictors for increased QOL on the psychological domain, and model predicted 39% of the variance in psychological QOL scores. The regression model was significant for the relationship domain,

however none of the predictors were uniquely significant. The regression model did not significantly predict the environment domain of QOL (Table 6).

Table 6

Multiple regression results for quality of life domains

	Physical		Psychological		Social		Environmental	
	B (SE)	β	*B (SE)*	β	*B (SE)*	β	*B (SE)*	β
PF	0.48 (0.16)**	0.55**	0.34 (0.12)**	0.45**	0.21 (0.20)	0.21	0.27 (0.15)	0.34
SC	-7.03 (4.56)	-0.28	4.10 (3.49)	0.19	5.91 (5.64)	0.20	-1.48 (4.40)	-0.07
Gender	-7.29 (5.17)	-0.16	1.02 (3.96)	0.03	4.26 (6.39)	0.08	1.76 (4.99)	0.05
Age	0.37 (0.37)*	0.27*	0.27 (0.12)*	0.23*	0.04 (0.20)	0.02	0.23 (0.15)	0.19
R^2	0.27***		0.43***		0.16*		0.12	
Adj. R^2	0.22***		0.39***		0.10*		0.06	
F	5.56***		11.16***		2.81*		2.06	

Note. Model "Enter" method in SPSS Statistics. PF = Psychological Flexibility; SC = Self-compassion; *B* = unstandardized regression coefficients; *SE* = standard error of the coefficient; β = standardized coefficient; R^2 = coefficient of determination; Adj. R^2 = adjusted R^2.

*p<.05; **p<.01; ***p<.001

Line care adherence

The multiple regression model was significant for line care adherence, $F(4, 64) = 5.58$ $p < .001$, and accounted for 22% of the variance in adherence scores (Table 7). Only older age and gender ($B = 0.11$, $p < .01$) uniquely predicted adherence, with increased adherence in women ($B = 4.17$, $p < .01$).

Table 7

Multiple regression results for line care adherence

	Line care adherence[a]	
	B (SE)	β
PF	0.01 (0.04)	0.06
SC	1.66 (1.02)	0.27
Gender	4.17 (1.10)***	0.38***
Age	0.11 (0.04)**	0.34**
R^2	0.27***	
Adj. R^2	0.22***	
F	5.57***	

Note. Model "Enter" method in SPSS Statistics. PF = Psychological Flexibility; SC = Self-compassion; *B* = unstandardized regression coefficients; *SE* = standard error of the coefficient; β = standardized coefficient; R^2 = coefficient of determination; Adj. R^2 = adjusted R^2.

[a]Robust standard error of the coefficient reported.

**p<.01; ***p<.001.

Line infections

The multiple regression model for number of line care infections was not significant (Table 8). This model violated the assumption of linearity, and therefore a series of exploratory quantile regression analyses were performed.

Table 8

Multiple regression results for line infections

	Line infections[a]	
	B (SE)	β
PF	-0.01 (0.02)	-0.10
SC	-0.43 (0.76)	-0.11
Gender	1.07 (0.49)	0.15
Age	-0.04 (0.02)	-0.20
R^2	0.12	
Adj. R^2	0.06	
F	2.01	

Note. Model "Enter" method in SPSS Statistics. PF = Psychological Flexibility; SC = Self-compassion; *B* = unstandardized regression coefficients; *SE* = standard error of the coefficient; β = standardized coefficient; R^2 = coefficient of determination; Adj. R^2 = adjusted R^2.

[a]Robust standard error of the coefficient reported.

Quantile regressions for line infections

Quantile regression analyses were performed to explore whether the predictor variables were associated with line infections at different quantiles of the outcome variable. Parameter estimates were computed for each 10th percentile. Neither of the predictors, PF, SC or covariates, age or gender, significantly predicted number of infections at any of the quantiles. Details can be found in Appendix R.

Mediation analysis

A simple mediation analysis was performed through the PROCESS macro (Hayes, 2017) to test whether line care adherence mediated a relationship between either of the two independent predictors (PF or SC) and number of line infections. Bootstrapping was used to generate confidence intervals around the indirect effects. This is a nonparametric sampling procedure that allows for analyses without the assumption for normality (Preacher & Hayes, 2008). For the current study a bootstrap sample of 5000 was used. Through this procedure,

95% confidence intervals are produced for the indirect effect. If the lower and upper bound of the 95% confidence interval do not contain zero, then the variables mediate the relationship (Preacher & Hayes, 2008). Mediation analyses do not require a significant total effect, as an indirect effect can still be found (Agler & De Boeck 2017).

Both the direct effect of PF on infections and the indirect effect with line care as a mediator were not significant. The direct effect of SC on infections, and the indirect effect with line care as a mediator, were also not significant. Details of the models can be found in Appendix S.

Discussion

This study aimed to test the association of PF and SC with psychological, behavioural and medical outcomes of individuals on HPN. Higher PF and SC were significantly correlated with the following outcomes in the predicted directions: lower psychological distress, higher wellbeing, higher QOL and increased line care adherence. The only variable which was not correlated with both PF and SC was number of infections, and SC was not correlated with the physical and emotional QOL domains. PF and SC were highly correlated with each other, consistent with previous research (e.g., Marshall & Brockman, 2016; Davey et al., 2020). The large correlation between PF and SC in the present study (r = .79) was very similar to the values observed in Kiliç et al. (2022).

Regression models included four predictors (age, gender, PF, and SC) and were significant for all psychological outcomes, except for environmental QOL. Regression analyses indicated that PF uniquely predicted lower total distress as measured by the DASS21, lower anxiety, higher wellbeing and higher physical and psychological QOL. SC also uniquely predicted lower total distress in the regression model. In contrast, SC was found to be a unique predictor for lower depression and lower stress, whereas PF was not. The finding that PF was associated with anxiety but not depression is consistent with the

longitudinal findings of a previous study in muscle disorders, which found the same pattern prospectively, when controlling for baseline levels of anxiety, depression and life satisfaction (Graham et al., 2016a). Although in their cross-sectional analysis, PF was also independently associated with depression (Graham et al., 2016a).

Two other studies have examined PF and SC simultaneously within physical health populations. Consistent with the current study, Davey et al. (2020) found that SC uniquely predicted lower depression when age, gender, pain intensity, and PF were included in the model. However, they also found the openness facet of PF (in this case pain acceptance) to uniquely predict lower depression. Indeed, pain acceptance was consistently the facet of PF associated with better outcomes including pain inference and work and social adjustment, whereas the other two components of PF (awareness and engagement) were not significant (Davey et al., 2020). In a longitudinal study within Type 2 diabetes, PF independently predicted depression at six months (Kiliç et al., 2022). These findings somewhat conflict with those of the current study, where only SC was uniquely associated with depression. The way depression is measured may be important. For instance, the aforementioned studies finding PF to predict lower depression utilised the Patient Health Questionnaire (PHQ-9; Kroenke et al., 2001) which includes somatic items. This may have distorted findings due to overlapping symptoms of the physical health condition and may be a possible explanation for the discrepancy in findings. Future studies might wish to carefully consider the measures that are used in health populations to measure mood. Consistent with the current study, within Type 2 diabetes PF independently predicted anxiety at six and 12 months, whereas SC did not (Kiliç et al., 2022). Kiliç et al. (2022) also found PF (and not SC) to uniquely predict QOL at 12-months. Collectively, these findings suggest that PF and SC are associated with distress and QOL in distinct ways, with PF being a somewhat more consistent predictor.

It could be hypothesised that PF's positive relationship with QOL could be a factor in the inconsistent findings in relation to QOL within HPN populations. For example, components of PF such as increased acceptance and viewing HPN as helpful in aiding the ability to live a meaningful life, may promote better QOL. These types of mediational analyses are an important area to explore in future studies. Some studies have started to explore possible mediators in the relationship between PF or SC and wellbeing outcomes. For example, Pyszkowska and Ronnlund (2021) examined the role of a balanced time perspective—an ability to mentally switch between orientations in time in an adaptive way—in mediating the positive relationship between each PF and SC, and wellbeing. They found that reduced deviations from a balanced time perspective did indeed mediate these relationships in a non-clinical, community sample, with Past Positive, Past Negative, and Present Fatalistic dimensions being most important (Pyszkowska & Ronnlund, 2021).

The current study also examined adherence behaviours and line infection outcomes. Although the regression model was significant, neither PF nor SC were independently associated with line care adherence. Harrison et al. (2021) had similar findings in relation to medication adherence, as PF was not uniquely associated with improved adherence to antiretroviral therapy in people with human immunodeficiency virus (HIV). Quantile regression results for the number of line infections were also not significant, indicating no association between PF or SC and line infections in the current sample. Finally, the hypothesis that line care would mediate a relationship between each PF and SC, and number of line infections was not supported, as there were no significant indirect effects. These nonsignificant findings could be due to a lack of variability in number of line infections, as over half of the sample reported zero line infections and very few participants reported more than three infections. Caution should be taken interpreting these results due to the limitations in measurement of line care and infections (discussed below).

Strengths and Limitations

This was the first study to examine PF and SC as predictors of distress, wellbeing, QOL, adherence and medical outcomes within individuals on HPN. The robustness of the analyses was strengthened by controlling for the possible confounding effects of age and gender, which have previously been shown to be associated with PF, SC and many of the outcomes. The use of the CompACT to measure PF is a strength of the current study, as it was developed to include all six underlying processes (Francis et al., 2016). In contrast, the Acceptance and Action Questionnaire-II (AAQ-II; Bond et al., 2011), the most commonly used questionnaire in ACT and PF studies, does not encompass all six ACT processes and has been shown to have poor discriminative validity in relation to general distress (Tyndall et al., 2019; Wolgast, 2014).

The results from the current study need to be interpreted in the context of its limitations. A generic measure of QOL was used in the current study. Whilst this measure has been successfully used within health populations (Skevington & McCrate, 2011), generic measures also miss potential factors that are specific to individuals on HPN (Baxter et al., 2005). Measures specific to HPN treatment have been developed more recently, including: Home Parenteral Nutrition QOL questionnaire (HPN-QOL ; Baxter et al., 2008; Baxter et al., 2010), Home Parenteral Nutrition Patient Reported Outcome questionnaire (HPN-PROQ, Miller et al., 2017), New QOL questionnaire (New-QOL, Thellia et al., 2017), and Parenteral Nutrition Impact Questionnaire (PNIQ, Wilburn et al., 2018). For the current study, we were unable to obtain permissions to utilise the PNIQ or the HPN-QOL. The HPN-PROQ was not used as it was developed for use in clinical settings (Miller et al., 2017). It was also deemed advantageous to use a QOL measure with well-established psychometric properties, and consideration was given to response fatigue effects if two measures of QOL were to have been used. Nonetheless, future research would benefit from including one of the HPN

specific QOL measures; the HPN-QOL tool in particular has been increasingly used (Chen et al., 2022).

As there was no existing measure of line care adherence, the LCRQ was developed for the current study. Cronbach's alpha of 0.8 indicated good reliability and PCA revealed that the measure loaded onto a single factor. However, validation studies of this measure are needed to determine if it is a suitable measure of line care adherence. If it is valid, it could be a useful way to screen for adherence behaviours, and to explore with patients any potential barriers to adherence. Assessing adherence to health-related behaviours is a challenge more widely, as subjective reporting is liable to social desirably and recall biases, and more likely to overestimate adherence (Stirratt et al., 2015).

The present study utilised self-reported number of line infections. A more objective measure of infections, such as medical records, would improve the validity of medical outcome data. However, this poses a separate challenge as due to the low number of people on HPN in any given hospital, this would likely need to be coordinated across multiple sites and was not feasible for the current study.

The analyses were based on cross-sectional data, therefore, temporal causation between the variables cannot be inferred. Future studies would benefit from longitudinal designs where PF, SC and the outcomes are assessed at various points over time. Despite extensive recruitment efforts, the required sample size was not achieved and therefore the study was potentially underpowered. This may have contributed to an underestimation of effect. Notwithstanding, we still found PF and SC to be uniquely associated with some of the outcomes. It is plausible that there could be other important confounding factors that were not controlled for in the current study, for example the underlying reason for HPN treatment and differing treatment regimes. These factors were not entered into the current regression analyses because additional variables would have further decreased the power. However

future research would benefit from exploring their potential influence. Effect sizes found in this study could be used as a guide for more precise sample size calculations in the future.

The study recruited internationally, although the Qualtrics questionnaire was only available in English. Results indicated that most respondents were from the UK, and therefore findings may not be generalisable beyond this population. The study was also subject to self-report bias. It is unknown whether there are differences between individuals choosing to take part in the study versus those who do not.

Finally, data collection occurred within the context of the Coronavirus (Covid-19) pandemic. Studies conducted during the pandemic indicate its negative impact on psychological wellbeing and QOL in people with gastrointestinal disorders such as IBD (Gavrilescu et al., 2022; Hayes et al., 2021; Sempere et al., 2022; Trindade & Ferreira, 2021). As some participants of the current study were likely on immunosuppressant medications for an underlying illness (e.g. Crohn's disease) this may have affected their adherence behaviours due to increased fear of infections or having to go into hospital. However, the impact of Covid-19 on adherence to line care is unknown. Findings related to medication adherence within IBD populations is mixed; with some reporting changes to their medication in response to the pandemic (El-Dallal et al., 2022) whereas Trindade & Ferreira (2021) found adherence to medication was high, and unrelated to fear of contracting Covid-19. Less has been examined about the impact of Covid-19 in relation to HPN populations specifically, however an international survey of professionals caring for individuals on HPN highlighted the adverse effect of the pandemic on supply shortages, reduced home care nurse availability, and psychological wellbeing (Allan et al., 2020). Differential timings of Covid-19 restrictions in various regions over the time period of the current study could differentially impact on results.

Clinical Implications

The results of this study provide a rationale for future research into psychological interventions with individuals on HPN to support their emotional wellbeing and QOL. Therapeutic interventions that aim to increase PF and SC, such as third wave cognitive behaviour therapy (CBT) approaches may be particularly appropriate. Third wave CBT interventions such as ACT and compassion-based approaches (e.g. compassion focussed therapy [CFT, Gilbert, 2014] or mindful self-compassion [MSC, Neff & Germer, 2013]) may be differentially effective depending on the presenting difficulty. For example, the tentative findings from the present study suggest that improving PF could positively impact those experiencing anxiety and lower QOL, whereas targeting SC may be more helpful for those with depression. However, the results from the current study need to be replicated, preferably employing longitudinal designs, to further understand the unique contributions of PF and SC.

There are encouraging findings on the applicability of ACT and CFT in other health conditions. For example, a recent randomised control trial (RCT) comparing a self-help ACT intervention to usual care found ACT improved QOL, mood, impact of symptoms on functioning, and the acceptance and committed action components of psychological flexibility, for individuals with muscle diseases (Rose et al., 2022). ACT was also associated with decreased stress and depression in people with IBD compared to treatment as usual (Wynne et al., 2019). Interestingly, this study found no difference in anxiety. This contrasts with what may be expected based on the current study's finding of PF's independent association with anxiety. Psychological flexibility also significantly improved over the 8-week intervention and was maintained at 20 weeks; these positive changes in psychological flexibility were significantly correlated with the reduction in stress (Wynne et al., 2019).

Kilic et al. (2022) proposed that due to the degree of correlation between PF and SC, interventions underpinned by either construct may improve the other as well. For example,

one RCT determined an ACT-based workshop significantly improved self-compassion compared to a waitlist control condition; furthermore, this change was mediated by psychological flexibility (Yadavaia et al., 2014). More recently, a study comparing the efficacy of brief, online ACT and CFT interventions found both were effective in reducing illness-related shame and uncompassionate self-responding, as well as increased valued living, within a chronic illness sample, with the most common illness being IBD (Carvalho et al., 2022).

Conclusions

This study sought to understand the independent associations of PF and SC with QOL, wellbeing, distress, line care adherence and infections within people on HPN. Findings indicated that PF and SC were strongly correlated to each other and were correlated with all outcomes other than number of infections. Whilst both PF and SC were independent contributors to the regression models, this differed across outcomes. Specifically, PF predicted total distress, anxiety, wellbeing and QOL, whereas SC predicted total distress, depression and stress. A measure for line care adherence was also developed for the current study, although validation studies are required before any conclusions can be made regarding its appropriateness for future use. This study has important limitations, and findings should be confirmed, particularly with longitudinal designs. However, it provides an encouraging rationale for exploring psychological therapies to improve emotional wellbeing and QOL amongst people on HPN.

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Appendix A

Author Guidance for submission to Inflammatory Bowel Diseases

Inflammatory Bowel Diseases

Instructions to Authors

Scope

Inflammatory Bowel Diseases® (IBD) supports the mission of the Crohn's & Colitis Foundation by bringing the most impactful and cutting-edge clinical topics and research findings related to inflammatory bowel diseases to clinicians and researchers working in IBD and related fields. The Journal is committed to publishing on innovative topics that influence the future of clinical care, treatment, and research. The Journal publishes peer-reviewed manuscripts and review articles in basic, translational, and clinical sciences, updates on clinical trials, reviews of the current literature, editorials, and other features.

General Submission Information

All manuscripts must be submitted through the Journal's online submission system. For questions on preparing manuscripts for submission to *IBD*, please contact ibd.editorialoffice@jjeditorial.com.

IBD complies with International Committee of Medical Journal Editors' Uniform Requirements for Manuscripts. Authors should observe high standards with respect to publication ethics as set out by the Committee on Publication Ethics (COPE).

Presubmission Language Editing

If you are not confident in the quality of your English, you may wish to use a language-editing service to ensure that editors and reviewers understand your paper. Oxford University Press partners with Enago, a leading provider of author services. Prospective authors are entitled to a discount of 30% for editing services at Enago, via the Specialist English Editing Services for Oxford University Press Authors page.

Enago is an independent service provider, who will handle all aspects of this service, including payment. As an author you are under no obligation to take up this offer. Language editing is optional and does not guarantee that your manuscript will be accepted. Edited manuscripts will still undergo peer review by the journal.

Graphical and Video Abstracts

Authors are encouraged to submit a graphical abstract and/or video abstract as part of the article, in addition to the text abstract. A template for graphical abstracts can be found here. The graphical/video abstract should clearly summarize the focus and findings of the article, and will be published as part of the article online and in PDF. The graphical/video abstract should be submitted for peer review as a separate file, selecting the appropriate file-type designation in the journal's online submission system. The file should be clearly named, e.g. *graphical_abstract.tiff*, *video_abstract.mp4*. See more manuscript resources for guidance on appropriate file format and resolution for graphics and videos. Video abstracts must be provided in mp4 files and graphical abstracts must be provided in tiff files with a resolution of 300 dpi or higher. Please ensure graphical abstracts are in landscape format.

Ethical Considerations

A submitted manuscript must be an original contribution not previously published (except as an abstract or preliminary report), must not be under consideration for publication elsewhere, and, if accepted, must not be published elsewhere in similar form, in any language, without the consent of the publisher. Deposition of manuscripts prior to submission on community preprint servers or on conference presentations online will not be considered prior publication and will not compromise potential publication in *IBD.* In the Editorial Manager submission process, authors are asked to disclose that the manuscript has been posted to a preprint server along with a link to the paper. Although the editors and referees make every effort to ensure the validity of published manuscripts, the final responsibility rests with the authors, not with the Journal, its editors, or the publisher.

Authorship

Each person listed as an author is expected to follow the authorship criteria put forth by the ICMJE. Deceased persons who meet the criteria for inclusion as coauthors should be so included, with an Author Information note indicating the date of death.

In submitting to *IBD*, authors are expected to honor all deadlines presented to them. Authors are expected to respond to all communication from the Editorial staff in a timely manner and should inform the Editorial staff promptly if they require an extension to complete their paper or if any unforeseen events prohibit them from writing their paper. The Journal reserves the right to not publish a paper if an author fails to meet their assigned deadlines or if the paper does not meet the Journal's standards of quality.

Plagiarism

All papers must be free of plagiarism. Plagiarism includes the unreferenced use of the author's own work or ideas or the work or ideas of others, either published or unpublished. It may occur at any stage of the development of a manuscript and it applies to print and electronic versions of the work. Authors should consult the Committee on Publication Ethics' (COPE) Guidelines on Good Publication Practice if they have questions about reuse of others' work.

The Editorial staff may subject submitted manuscripts to analysis using the iThenticate software program. If plagiarism is identified, the Editorial staff will request corrections or clarification from the author.

When a case of plagiarism is confirmed after publication, the Journal will publish a notice in a subsequent issue and possibly take further action according to Committee on Publication Ethics guidelines. Authors who have been found to be guilty of plagiarism after the appropriate institutional investigation will be banned from submitting to the Journal for a defined period of time.

Patient Anonymity and Informed Consent

It is the author's responsibility to ensure that a patient's anonymity be carefully protected and to verify that any experimental investigation with human subjects reported in the manuscript was performed with informed consent and following all the guidelines for experimental investigation with human subjects required by the institution(s) with which all the authors are affiliated. Patients' identity must be removed in all figures (e.g., x-rays, MRIs, charts, photographs, etc.). Written informed consent is required from any potentially identifiable patient or legal representative, and should be presented in either the Methods section or the Acknowledgments. Please use the Patient Consent Form.

Human Studies

Human experimentation must conform to ethical standards, and be approved by the appropriate Institutional Review Board (IRB). A statement concerning IRB approval and consent procedures must appear at the beginning of the Methods section. Any systematic data gathering effort in patients or volunteers must be approved by an IRB or adhere to appropriate local/national regulations. The Editors of *IBD* take IRB review and informed consent very seriously. Authors may be questioned about the details of consent forms or the consent process. On occasion, the Editors may request a copy of the approved IRB application from the author. Lack of appropriate consent or documentation may be grounds for rejection. Local IRB approval does not guarantee acceptability; the final decision will be made by the Editors.

Manuscripts that reveal the identity of any patient through figures, video, or audio files must be accompanied by written permission statement/release form signed by the identified adult or minor, or legal representative. The author may download and utilize the Patient Consent Form using the links above.

Animal Studies

Experimental work on animals must conform to the Guide for the Care and Use of Laboratory Animals, which is available from the National Academy of Science; a text-only version is available to download as a pdf. Adherence to all relevant regulations and/or approval of the appropriate institutional Animal Care Committee or governmental licensure of the investigator and/or laboratory must be obtained. A statement concerning such approval must be included at the beginning of the Methods section. The Editors of *IBD* are concerned about appropriate animal care. On occasion, the Editors may request a copy of the approved Animal Care Committee application from the author. Local committee approval does not guarantee acceptability; the final decision will be made by the Editors.

Observational Studies

The STROBE statement must be used when reporting observational research.

Registration of Clinical Trials

All clinical trials that involve investigational drugs supported by a pharmaceutical firm or investigational devices supported by a device manufacturer must be registered at the time that a manuscript is submitted to *IBD* for publication. The registry and registration number must be stated in the first paragraph of the Methods section of the manuscript.

Policies on Conflicts of Interest

IBD is committed to making transparent the Journal's policies on Conflict of Interest as they relate to authors, reviewers, and editors. Authors should familiarize themselves with the below points as well as COPE's Guidelines on Good Publication Practice before committing to working with the Journal.

Conflicts in regard to publication can occur when a competing interest may influence or be perceived to influence the judgment of author, reviewers, and editors. Conflicts of interest are considered relationships within three years prior to the authoring, reviewing, or editing of the given manuscript. Specifically, these relationships may include:

- Employment (including employment by the same institution)
- Mentoring
- Collaborating
- Research funding
- Consultancies
- Honoraria
- Stock or share ownership

- Grants received and pending
- Royalties
- Company support for staff
- Commercial interests
- Political or religious views
- Any other close personal relationship

Author Conflict of Interest

As part of the Editorial Manager submission process, authors are required to declare all potential conflicting interests — financial, personal, or otherwise — that might be perceived as influencing the information presented in their manuscript. All sources of funding should be acknowledged in the manuscript. All relevant conflicts of interest and sources of funding should be disclosed during the submission process in Editorial Manager and should be listed on the title page as well.

When in doubt, authors should seek advice from the Editors if they are unsure whether something constitutes a relevant conflict of interest. If there is no conflict of interest, this should also be explicitly stated as none declared.

In the event that a potential conflict of interest is apparent or suspected, the Journal Editorial staff will request clarification from the author. In the event that a conflict was not disclosed, the Journal may publish a notice in a subsequent issue and possibly take further action according to COPE guidelines.

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All clinical practice guidelines submitted for publication in *IBD* must adhere to the recommendations set forth by the National Academy of Medicine. Their recommendations include appointing committee chairs with no financial conflicts of interest and limiting guideline authors with financial conflicts of interest to less than 50% of the panel. Further detail on the recommendations can be found on the NCBI website.

Guidelines by Article Type

Basic, translational, and clinical articles submitted to *IBD* should be submitted as one of the following article types using the parameters below.

Review Articles

Review Articles should be classified as Basic Science, Translational, or Clinical and should present recent advances in a relatively narrow topic that have been made in cutting-edge research. Translational articles are those that bring science directly into clinical practice. They describe novel data at the intersection of basic science and clinical research/clinical care. Review articles should present a complete summary of important research areas that are now improving our understanding of Crohn's disease and ulcerative colitis. All Review Articles will be peer-reviewed. Pre-submission inquiries to the Editors in Chief on the

suitability of topics for Review Articles are highly suggested. Inquiries should be submitted to ibd.editorialoffice@jjeditorial.com.

Parameters

- Manuscript body: 6,000 words (not including references, figures, and tables). Authors must request permission from the Editors to increase the length.
- Tables and figures: No more than six (combined)
- References: No more than 100
- Supplemental data: Allowed, including tables and figures
- Abstract required

Original Articles

Original Articles should be classified as Basic Science, Translational, or Clinical, should add to the body of knowledge of Crohn's disease and ulcerative colitis, and should be in alignment with the scope of *IBD*. Translational articles are those that bring science directly into clinical practice. They describe novel data at the intersection of basic science and clinical research/clinical care Please review *IBD*'s mission statement for more information.

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- References: No more than 40
- Supplemental data: Allowed, including tables and figures
- Abstract required

Brief Reports

Brief Reports should be classified as either Basic Science, Translational, or Clinical and should be concise communications of original research. Translational articles are those that bring science directly into clinical practice. They describe novel data at the intersection of basic science and clinical research/clinical care. Brief Reports should add to the body of knowledge of Crohn's disease and ulcerative colitis as well as be in alignment with the scope of *IBD*. Please review *IBD*'s mission statement for more information.

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- Manuscript body: 1,500 words (not including references, figures, and tables). Authors must include Introduction, Methods, Results, and Discussion.
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- References: No more than 10
- Supplemental data: Not allowed, including tables and figures

- Abstract: An abstract should not be included

Case Reports

Case Reports should illustrate a novel clinical finding or pathogenetic mechanisms. Novel case series should be submitted as a case report.

Parameters

- Manuscript body: No more than 400 words
- Tables and figures: No more than one table or one figure
- References: No more than 10
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Letters to the Editor

Letters in response to articles published in the Journal are welcome. All Letters should start with the phrase "To the Editors," and be written as a letter. Letters must be submitted the end of the following calendar month (e.g. by the end of July, for letters referring to articles in the June print issue). All Letters to the Editor will be published online-only and the Journal only allows for one exchange between the initial letter writer and the responding author. Case reports or case series should NOT be submitted as a Letter to the Editor.

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- Manuscript body: No more than 400 words
- Tables and figures: No more than one table or one figure
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Commentaries

Commentaries focus on timely topics related to improving the career of the IBD physician including basic research, translational and clinical research, education, and career advice. Unsolicited commentaries with no more than three authors will be considered. Editors' Commentaries may be co-authored by one of *IBD's* Associate Editors. Invited Commentaries are invited by the Editors and must have no more than three authors.

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Preparation of Manuscript

Manuscripts that do not adhere to the following instructions will be returned to the corresponding author for technical revision before undergoing peer review.

Title Page

Include on the title page (a) complete manuscript title; (b) authors' full names, highest academic degrees, and affiliations; (c) name and address for correspondence, telephone number, and email address; and (d) sources of support that require acknowledgment. For both affiliations and postal addresses, please include the country.

The title page must also include disclosure of funding received for this work from any of the following organizations: National Institutes of Health (NIH); Wellcome Trust; Howard Hughes Medical Institute (HHMI); and others.

Authors' financial disclosures and conflicts of interest should be included on the title page. If there are no financial disclosures or conflicts of interest, this should be specifically noted as well.

A brief, 40-word summary of the article's main point is also required. This is separate from the article's abstract. Summaries are not needed for Letters to the Editor.

Abstract and Key Words

The abstract must be factual and comprehensive and should not exceed 250 words. Do not cite references in the abstract. Limit the use of abbreviations and acronyms, and avoid general statements (e.g., "the significance of the results is discussed"). It should be sectioned into Background, Methods, Results, and Conclusions. Three to five key words should also be provided. Review articles, editorials, and editors' commentaries do not require structured abstracts.

Key Messages

Please include the key messages of your article after your abstract using the following bullet points. This section should be distinct from the abstract and should be specific and accurate. There should be no more than one sentence per point. (Max 100 words)

- What is already known?
- What is new here?
- How can this study help patient care?

Text

For full-length research articles, please organize the manuscript in the following sequence:

- Abstract and Key Words
- Key Messages
- Introduction
- Materials and Methods
- Results
- Discussion
- Acknowledgments
- Ethical Considerations
- References
- Tables
- Figure Legends

Abbreviations

Non-standard abbreviations should be kept to a minimum. They should be defined at the first occurrence and introduced only where multiple use is made.

Style

Follow American Medical Association Manual of Style (10th edition). Stedman's Medical Dictionary (27th edition) and Merriam Webster's Collegiate Dictionary (10th edition) should be used as standard references. Refer to drugs and therapeutic agents by their accepted generic or chemical names, and do not abbreviate them. Use code numbers only when a generic name is not yet available. In that case, supply the chemical name and a figure giving the chemical structure of the drug. Capitalize the trade names of drugs and place them in parentheses after the generic names. To comply with trademark law, include the name and location (city and state in USA; city and country outside USA) of the manufacturer of any drugs, supplies, or equipment mentioned in the manuscript. Use the metric system to express units of measure and degrees Celsius to express temperatures, and use SI units rather than conventional units.

References

The authors are responsible for the accuracy of the references. Key the references (double-spaced) at the end of the manuscript. Cite the references in text in the order of appearance, including those references cited in tables and figure legends at the chronological citation of the tables and figures in text. Cite unpublished data, such as papers submitted but not yet accepted for publication, personal communications, in parentheses in the text. If there are more than three authors, only name the first three authors and then use et al. For abbreviations of journal names, you can access the National Library of Medicine catalog.

Sample references are given below:

Journal Article

1. Lutgens MW, van Oijen MG, van der Heijden GJ, et al. Declining risk of colorectal cancer in inflammatory bowel disease: an updated meta-analysis of population-based cohort studies. Inflamm Bowel Dis. 2013;19:789–99.

Book Chapter

2. Lee AM, Chan CLW, Ho AHY, et al. Improving the Quality of Life and Psychological Well-being of Patients with Colorectal Cancer. In: Lee MY, Ng S, Leung PPY, et al. Integrated Body-Mind-Spirit Social Work. 1st ed. New York, NY: Oxford University Press; 2009: 236-244.

Entire Book

3. Fogen BS, Greenberg DB. Psychiatric Care of the Medical Patient. 3rd ed. New York, NY: Oxford University Press; 2016.

Software

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Online

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Database

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World Wide Web

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- Line art saved at a resolution of at least 1200 dpi.
- Images saved at a resolution of at least 300 dpi.
- Each figure is saved as a separate file and saved separately from the accompanying text file.
- Multi-panel or composite figures should be sent as one file with each part labeled the way it is to appear in print.
- Ensure that no artwork generated from office suite programs such as CorelDRAW, MS Word, Excel, or artwork downloaded from the Internet (JPEG or GIF files) is used.
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Appendix B

Search Terms Applied to Systematic Literature Review Database Searches

Database	Search strings applied
Ovid searches: Embase, Medline and APA PsychInfo	1 Colitis, Ulcerative/ 35073 2 ulcerative colitis.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 87851 3 Crohn Disease/ 95474 4 crohn*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 110620 5 inflammatory bowel disease*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 101284 6 Inflammatory Bowel Diseases/ 17695 7 1 or 2 or 3 or 4 or 5 or 6 199033 8 Depression/ 397310 9 Anxiety/ 230124 10 depress*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 850525 11 anxiety.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 409721 12 anxious.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 25614 13 psychological* distress*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 29883 14 psychological* challenge*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 671 15 mood disorder*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 61372 16 psychological disorder*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 5634

17 psycho* factors.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 38454
18 psychological health.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 8236
19 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 1111314
20 adhere*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 321372
21 complian*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 378260
22 comply.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 17158
23 concordanc*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 80163
24 nonadheren*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 14214
25 noncomplian*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 12946
26 non-adheren*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 19102
27 non-complian*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 14645
28 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 720005
29 medic*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 5070773
30 treat*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 8991577
31 therap*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word] 9300835
32 29 or 30 or 31 15846188
33 28 and 32 473712
34 Patient Compliance/ 139533
35 Medication Adherence/ 28762

	36	Directly Observed Therapy/ 1971
	37	33 or 34 or 35 or 36 489013
	38	7 and 19 and 37 426
Scopus	(TITLE-ABS-KEY (("ulcerative colitis") OR (crohn*) OR ("inflammatory bowel disease*"))) AND (TITLE-ABS-KEY (depress*) OR (anxiety*) OR (anxious) OR ("psychological* distress*") OR ("psychological* challenge*") OR ("mood disorder*") OR ("psychological disorder*") OR ("psycho* factors") OR ("psychological health")) AND ((((adhere*) OR (complian*) OR (comply) OR (concordanc*) OR (nonadheren*) OR (noncomplian*) OR ("non adheren*") OR ("non complian*")) AND ((medic*) OR (treat*) OR (therap*))) OR (("directly observed therap*")))	
CINAHL	(("ulcerative colitis") OR (crohn*) OR ("inflammatory bowel disease*")) AND ((depress*) OR (anxiety*) OR (anxious) OR ("psychological* distress*") OR ("psychological* challenge*") OR ("mood disorder*") OR ("psychological disorder*") OR ("psycho* factors") OR ("psychological health")) AND (("directly observed therap*") OR (((adhere*) OR (complian*) OR (comply) OR (concordanc*) OR (nonadheren*) OR (noncomplian*) OR ("non adheren*") OR ("non complian*")) AND ((medic*) OR (treat*) OR (therap*))))	
Web of Science	1	(“ulcerative colitis”) OR (crohn*) OR (“inflammatory bowel disease*”)
	2	(depress*) OR (anxiety*) OR (anxious) OR (“psychological* distress*”) OR (“psychological* challenge*”) OR (“mood disorder*”) OR (“psychological disorder*”) OR (“psycho* factors”) OR (“psychological health”)
	3	(“directly observed therap*”)
	4	(adhere*) OR (complian*) OR (comply) OR (concordanc*) OR (nonadheren*) OR (noncomplian*) OR (“non adheren*”) OR (“non complian*”)
	5	(medic*) OR (treat*) OR (therap*)
	6	#4 AND #5
	7	#3 OR #6
	8	#1 AND #2 AND #7

Appendix C

Quality Rating Item and Rating Scores from the National Institutes of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (NHLBI, 2014).

Author	Study Design	Criteria														Rater 1 Quality Rating	Rater 2 Quality Rating	Final Overall Quality Rating
		1	2	3	4	5	6	7	8	9	10	11	12	13	14			
Banerjee et al (2021).	cross-sectional	Y	N	Y	Y	N	N	N	NA	N	N	Y	NA	NA	Y	poor		poor
Bruna-Barranco, et al. (2019)	cross-sectional	Y	Y	Y	Y	N	N	N	N	Y	N	Y	NA	NA	N	fair		fair
Calloway, et al. (2017)	retrospective cohort	Y	Y	Y	Y	N	Y	Y	N	Y	N	Y	CD	NA	Y	good	good	good
Campos, et al. (2016)	cross-sectional	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	NA	NA	Y	fair	fair	fair
Ediger, et al. (2007)	cross-sectional	Y	Y	Y	Y	N	N	N	N	Y	N	Y	NA	NA	Y	fair		fair
Eindor-Abarbanel, et al. (2018)	cross-sectional	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NA	NA	Y	fair		fair
Freitas, et al. (2015)	cross-sectional	Y	N	Y	Y	Y	N	N	Y	Y	N	Y	NA	NA	Y	fair		fair

Jackson, et al. (2018)	cross-sectional	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	NA	NA	Y	fair	fair	fair
Long, et al. (2014)	cross-sectional	Y	Y	Y	Y	N	N	N	N	Y	N	Y	NA	NA	Y	fair		fair
Nahon, et al. (2011)	cross-sectional	Y	N	N	CD	N	N	N	N	Y	N	Y	NA	NA	Y	poor		poor
San Roman, et al. (2005)	cross-sectional	Y	N	NR	Y	N	N	N	CD	Y	N	N	NA	NA	N	poor		poor
Selinger, et al. (2013)	cross-sectional	Y	N	N	Y	N	N	N	Y	Y	N	Y	NA	NA	Y	fair	poor	fair
Severs, et al. (2017)	prospective cohort	Y	Y	N	Y	N	Y	Y	N	N	Y	Y	NA	N	Y	fair		fair
Shah, et al. (2020)	retrospective cohort	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	CD	NA	N	good		good
Shale & Riley, (2003)	cross-sectional	Y	N	NR	Y	N	N	N	Y	Y	N	Y	NA	NA	Y	fair		fair
Trindade & Ferreira (2021)	cross-sectional	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NA	NA	N	fair	fair	fair
Wang, et al. (2020a)	cross-sectional	Y	N	Y	N	N	N	N	Y	Y	N	Y	NA	NA	Y	fair		fair

Wang, et al (2020b)	cross-sectional	Y	N	NR	N	N	N	N	Y	NR	N	Y	NA	NA	Y	poor	poor

Notes. Y=Yes; N=No; CD=Cannot determine; NA=Not applicable; NR=Not reported

NIH Quality Assessment Tool Items:

1. Was the research question or objective in this paper clearly stated?
2. Was the study population clearly specified and defined?
3. Was the participation rate of eligible persons at least 50%?
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?
5. Was the sample size justification, power description or variance and effect estimates provided?
6. For the analyses in this paper were the exposure(s) of interest measured prior to the outcome(s) being measured?
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if existed?
8. For exposures that can vary in amount or level did the study examine the different levels of the exposure as related to the outcome (e.g. categories of exposure or exposure measured as continuous variable)?
9. Were the exposures (independent variables) clearly defined, valid, and reliable and implemented consistently across all study participants?
10. Was the exposure(s) assessed more than once over time?
11. Were the outcome measures (dependent variables) clearly defined, valid, and reliable and implemented consistently across all study participants?
12. Were the outcome assessors blinded to the exposure status of the participant?
13. Was the loss to follow up after baseline 20% or less?
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?

Appendix D

Author Guidance for submission to Journal of Contextual Behavioral Science

GUIDE FOR AUTHORS

Types of article

All manuscripts must clearly and explicitly be of relevance to CBS. You may find the JCBS article "Contextual Behavioral Science: creating a science more adequate to the challenge of the human condition" helpful in assessing whether your manuscript is likely to be of interest to readers of this journal.

Articles should fall into one of six categories: 1. Empirical research (up to 6000 words)
2. Brief empirical reports (up to 3000 words) 3. Review articles (up to 10,000 words)

4. Conceptual articles (up to 6000 words)
5. Practical innovations (up to 6000 words) 6. Commentaries (up to 3000 words)
7. Registered reports (see instructions below)

Word limits exclude references, tables and figures but include the abstract

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2. Brief empirical reports. Manuscripts in this section may report preliminary, provocative or replicated results. Empirically sound methodology and adequate power remain important considerations.

3. Review articles. Manuscripts reviewing a wide range of topics are encouraged as long as their content is directly relevant to CBS. Systematic reviews and meta-analyses are particularly welcome. For meta-analyses and systematic reviews, JCBS requires submissions follow PRISMA guidelines (http://www.prisma-statement.org/).

4. Conceptual articles. Manuscripts in this section should address conceptual or theoretical issues relevant to CBS. This may include papers that discuss relevant philosophical assumptions and traditions, or conceptual papers which explore aspects of or inconsistencies in contextual behavioral theory and science.

5. Practical innovations. Manuscripts in this section share innovative and practically useful descriptions of applications of CBS to a given problem area based on real world implementation, with preliminary data supporting the innovation directly (preferred) or indirectly through relevant conceptual and empirical references. Submissions are evaluated based on the degree to which they 1) provide information that is directly useful to applied work, 2) provide innovative information (e.g., a novel protocol, population, issue), 3) are

based on real world implementation/practice, and 4) are based on preliminary data reported in the manuscript, or a strong link to existing conceptual/empirical literature. Submissions that report empirical data should still primarily emphasize detailed descriptions of the intervention/training protocol and/or of the applied relevance of the findings (e.g., clarifying and problem solving how to address an applied challenge identified in the study).

6. Commentaries. In some circumstances, we will consider commentaries on other manuscripts that have been recently published in JCBS. Commentaries will be subjected to peer-review and will be held to the same standards of providing a notable contribution to our field to warrant publication. Authors will typically be informed when a commentary has been submitted on a manuscript they have published and will be given the opportunity to respond in print if the commentary is published. We encourage authors to contact the editor-in-chief prior to preparing a commentary to determine potential suitability for JCBS.

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Appendix E

Participant Information Sheet

Study title: Psychological correlates of distress, quality of life, adherence, and medical outcomes in patients receiving home parenteral nutrition (HPN)

Researcher: Sara Rea

You are being invited to take part in a research project that is being undertaken as part of a Doctorate in Clinical Psychology. Please read the information below carefully before deciding whether to take part. If you have any questions, please contact the researcher.

Why is the study being done?
This study is looking at psychological factors that might be related to individuals' distress and wellbeing, quality of life and line care when they are receiving HPN. It is hoped that this study will help us understand more about the impact of these psychological factors, and in doing so, better understand what kind of support might benefit the mental wellbeing of people receiving HPN.

Do I have to take part?
No, it is your choice whether to participate or not. If you do decide to take part, you are free to change your mind and withdraw from the study at any time during completion of the survey. However, once you have completed the survey you will not be able to withdraw from the study. This is because the data is anonymous and there is no way to link you to your responses.

What will happen if I decide to take part?
If you would like to participate in this study, you will be asked to indicate your consent and then answer some questions that will take approximately 20-25 minutes of your time.
The first questions will ask you some demographic information about yourself and the reason you are receiving HPN. There will then be a number of questions that ask about your thoughts, feelings, behaviours and experiences. Finally, there will be some questions that ask you about your line care and whether you have had any line infections.

What are the possible disadvantages of taking part?
There are minimal anticipated disadvantages to participating in the study. There is a small possibility that some of the questions may cause some emotional discomfort, as the questions ask you to think about your thoughts and feelings. You will be provided with information about sources of support if needed at the end of the survey.

What are the possible benefits of taking part?
Although you may not benefit personally, your participation will contribute to a study that may improve our understanding of what contributes to people's wellbeing, quality of life and line care behaviours when receiving HPN.

What will happen to the information I provide?
All information collected about you during the course of the research is anonymous. You will not be asked to provide any identifiable information. Data from the study will be kept on a secure device, and following the study will be kept for 7 years. All data will be held in

compliance with GDPR regulations. Cardiff University is the data controller and James Merrifield is the data protection officer (inforequest@cardiff.ac.uk).

What will happen when the study ends?
The results of the study will be written up and submitted to Cardiff University in order to fulfil the requirements for a Doctorate in Clinical Psychology. Reports may also be sent to a peer-reviewed journal for publication. You will not be identified in any reports or publications that follow this study.

Who has reviewed the study?
The study has been reviewed and approved by the School of Psychology Research Ethics Committee at Cardiff University.

Contact for further information?
If you would like any further information or have any queries, please contact:

Sara Rea
Trainee Clinical Psychologist
South Wales Clinical Psychology Doctoral Programme
Cardiff University
Tower Building, 70 Park Place, Cardiff, CF10 3AT
Tel: 02920870582

Research Supervisors:
Dr Marc Williams and Dr Victoria Samuel
South Wales Clinical Psychology Doctoral Programme
Cardiff University
Tower Building, 70 Park Place, Cardiff, CF10 3AT
Tel: 02920870582

Thank you for taking the time to read this information.

Kind regards,

Sara Rea
Trainee Clinical Psychologist

Appendix F

Participant Consent Form

Psychological correlates of distress, quality of life, adherence, and medical outcomes in patients receiving home parenteral nutrition

Consent Form

I confirm that I have read and understand the information sheet for the above study.

I understand that my participation in this project will involve answering some questionnaires about thoughts, feelings, behaviours, experiences and line care which will require approximately 20-25 minutes of my time.

I understand that participation in this study is entirely voluntary and that I can withdraw from the study at any time during completion of the survey. However, once I have completed the survey I will not be able to withdraw from the study. This is because the data is anonymous and there is no way to link you to your responses.

I understand that I am free to contact the researcher with questions or concerns.

I understand that at the end of the study I will be provided with additional information and feedback about the purpose of the study.

I understand that the research information provided by me will be held totally anonymously, so that it is impossible to trace this information back to me individually. I understand that this information will be retained for 7 years, and the data will be used for analyses for publications.

By selecting ‘I consent’ you agree to the above.

I consent

I do not consent

Appendix G

Participant Debrief Form

Psychological correlates of distress, quality of life, adherence, and medical outcomes in patients receiving home parenteral nutrition

Debrief Information Sheet

Thank you very much for taking the time to participate in this study.

The study aimed to explore two psychological factors and their possible relationship to level of distress, quality of life, line care adherence and line infections. One of these psychological factors was psychological flexibility, which is a person's ability to be in, and experience, the present moment (despite potential difficult thoughts, feelings and physical sensations) and engage in actions lead by their values. The other was self-compassion, the ability to connect to one's suffering, with feelings of kindness and caring, along with an understanding and non-judgemental attitude towards oneself, whilst acknowledging suffering as part of humanity. Previous research has suggested that increased psychological flexibility and self-compassion predict psychological wellbeing and quality of life, however it is not known if this is the case for individuals receiving HPN. We also sought to determine if these factors are associated with medical outcomes, specifically line care adherence and number of line infections.

You answered questions from two questionnaires that measure psychological flexibility and self-compassion. You also completed questionnaires assessing level of distress (depression, anxiety and stress), wellbeing and quality of life. Finally, you completed a questionnaire that asked about line care adherence, and a question about line infections.

If you have felt upset by any of the questions asked, please seek support. Your friends and family may be able to support you. Should you be worried about your mental health, please contact your general practitioner. You can also find some information on mental health on the following link: **https://www.nhs.uk/mental-health/**

If you are located in the United Kingdom, you can also contact the C.A.L.L helpline: 0800 132737or https://www.callhelpline.org.uk

Please be assured that your data will be kept strictly anonymous. Data from the study will be kept on a secure device and following the study will be kept for 7 years. All data will be held in compliance with GDPR regulations. Cardiff University is the data controller and James Merrifield is the data protection officer (inforequest@cardiff.ac.uk).
If you have any concerns about the research, please do not hesitate to contact the researchers.
Sara Rea
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Appendix H

Ethical Approval

From: **psychethics** psychethics@cardiff.ac.uk
Subject: Ethics Feedback - EC.20.04.14.6006A
Date: 9 December 2020 at 10:46
To: Sara Rea ReaS1@cardiff.ac.uk
Cc: Marc Williams WilliamsM93@cardiff.ac.uk

Dear Sara,

The Ethics Committee has considered the revised amendment to your PG project proposal: *Psychological correlates of distress, quality of life, adherence, and medical outcomes in patients receiving home parenteral nutrition (EC.20.04.14.6006A).*

The amendment has been approved.

Please note that if any changes are made to the above project then you must notify the Ethics Committee.

Best wishes,
Jo

School of Psychology Research Ethics Committee

Cardiff University Tower Building 70 Park Place Cardiff CF10 3AT	Prifysgol Caerdydd Adeilad y Tŵr 70 Plas y Parc Caerdydd CF10 3AT
Tel: +44(0)29 208 70360 Email: psychethics@cardiff.ac.uk http://psych.cf.ac.uk/aboutus/ethics.html	Ffôn: +44(0)29 208 70360 E-bost: psychethics@caerdydd.ac.uk

Please note that I do not expect a response to this email outside of your normal working hours
Nid wyf yn disgwyl ymateb i'r ebost hwn y tu allan i'ch oriau gwaith arferol

Appendix I

Comprehensive assessment of Acceptance and Commitment Therapy processes (CompACT; Francis et al., 2016)

CompACT

Name:	Date:

Please rate the following 23 statements using the scale below:

0 Strongly disagree	**1** Moderately disagree	**2** Slightly disagree	**3** Neither agree nor disagree	**4** Slightly agree	**5** Moderately agree	**6** Strongly agree

1. I can identify the things that really matter to me in life and pursue them	0	1	2	3	4	5	6
2. One of my big goals is to be free from painful emotions	0	1	2	3	4	5	6
3. I rush through meaningful activities without being really attentive to them	0	1	2	3	4	5	6
4. I try to stay busy to keep thoughts or feelings from coming	0	1	2	3	4	5	6
5. I act in ways that are consistent with how I wish to live my life	0	1	2	3	4	5	6
6. I get so caught up in my thoughts that I am unable to do the things that I most want to do	0	1	2	3	4	5	6
7. I make choices based on what is important to me, even if it is stressful	0	1	2	3	4	5	6
8. I tell myself that I shouldn't have certain thoughts	0	1	2	3	4	5	6
9. I find it difficult to stay focused on what's happening in the present	0	1	2	3	4	5	6
10. I behave in line with my personal values	0	1	2	3	4	5	6
11. I go out of my way to avoid situations that might bring difficult thoughts, feelings, or sensations	0	1	2	3	4	5	6
12. Even when doing the things that matter to me, I find myself doing them without paying attention	0	1	2	3	4	5	6
13. I am willing to fully experience whatever thoughts, feelings and sensations come up for me, without trying to change or defend against them	0	1	2	3	4	5	6
14. I undertake things that are meaningful to me, even when I find it hard to do so	0	1	2	3	4	5	6
15. I work hard to keep out upsetting feelings	0	1	2	3	4	5	6
16. I do jobs or tasks automatically, without being aware of what I'm doing	0	1	2	3	4	5	6
17. I am able to follow my long terms plans including times when progress is slow	0	1	2	3	4	5	6
18. Even when something is important to me, I'll rarely do it if there is a chance it will upset me	0	1	2	3	4	5	6
19. It seems I am "running on automatic" without much awareness of what I'm doing	0	1	2	3	4	5	6
20. Thoughts are just thoughts – they don't control what I do	0	1	2	3	4	5	6
21. My values are really reflected in my behaviour	0	1	2	3	4	5	6
22. I can take thoughts and feelings as they come, without attempting to control or avoid them	0	1	2	3	4	5	6
23. I can keep going with something when it's important to me	0	1	2	3	4	5	6

Appendix J

Self-Compassion Scale short-form (SCS-SF; Raes et al., 2011)

Running head: SELF-COMPASSION SCALE–Short Form (SCS–SF) 2

HOW I TYPICALLY ACT TOWARDS MYSELF IN DIFFICULT TIMES

Please read each statement carefully before answering. To the left of each item, indicate how often you behave in the stated manner, using the following scale:

Almost never				**Almost always**
1	**2**	**3**	**4**	**5**

_____1. When I fail at something important to me I become consumed by feelings of inadequacy.

_____2. I try to be understanding and patient towards those aspects of my personality I don't like.

_____3. When something painful happens I try to take a balanced view of the situation.

_____4. When I'm feeling down, I tend to feel like most other people are probably happier than I am.

_____5. I try to see my failings as part of the human condition.

_____6. When I'm going through a very hard time, I give myself the caring and tenderness I need.

_____7. When something upsets me I try to keep my emotions in balance.

_____8. When I fail at something that's important to me, I tend to feel alone in my failure

_____9. When I'm feeling down I tend to obsess and fixate on everything that's wrong.

_____10. When I feel inadequate in some way, I try to remind myself that feelings of inadequacy are shared by most people.

_____11. I'm disapproving and judgmental about my own flaws and inadequacies.

_____12. I'm intolerant and impatient towards those aspects of my personality I don't like.

Appendix K

Depression Anxiety Stress Scale short-form (DASS21; Henry & Crawford, 2005)

DASS21 *Name:* *Date:*

Please read each statement and circle a number 0, 1, 2 or 3 which indicates how much the statement applied to you *over the past week*. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

0 Did not apply to me at all
1 Applied to me to some degree, or some of the time
2 Applied to me to a considerable degree, or a good part of time
3 Applied to me very much, or most of the time

1	I found it hard to wind down	0	1	2	3
2	I was aware of dryness of my mouth	0	1	2	3
3	I couldn't seem to experience any positive feeling at all	0	1	2	3
4	I experienced breathing difficulty (eg, excessively rapid breathing, breathlessness in the absence of physical exertion)	0	1	2	3
5	I found it difficult to work up the initiative to do things	0	1	2	3
6	I tended to over-react to situations	0	1	2	3
7	I experienced trembling (eg, in the hands)	0	1	2	3
8	I felt that I was using a lot of nervous energy	0	1	2	3
9	I was worried about situations in which I might panic and make a fool of myself	0	1	2	3
10	I felt that I had nothing to look forward to	0	1	2	3
11	I found myself getting agitated	0	1	2	3
12	I found it difficult to relax	0	1	2	3
13	I felt down-hearted and blue	0	1	2	3
14	I was intolerant of anything that kept me from getting on with what I was doing	0	1	2	3
15	I felt I was close to panic	0	1	2	3
16	I was unable to become enthusiastic about anything	0	1	2	3
17	I felt I wasn't worth much as a person	0	1	2	3
18	I felt that I was rather touchy	0	1	2	3
19	I was aware of the action of my heart in the absence of physical exertion (eg, sense of heart rate increase, heart missing a beat)	0	1	2	3
20	I felt scared without any good reason	0	1	2	3
21	I felt that life was meaningless	0	1	2	3

Appendix L

Short Warwick Edinburgh Mental Wellbeing Scale (SWEMWBS; Stewart-Brown et al., 2009)

Short Warwick Edinburgh Mental Wellbeing Scale (S) WEMWBS

Below are some statements about feelings and thoughts.

Please select the answer that best describes your experience of each over the last 2 weeks.

	None of the Time	Rarely	Some of the Time	Often	All of the Time
I've been feeling optimistic about the future	**1**	**2**	**3**	**4**	**5**
I've been feeling useful	1	2	3	4	5
I've been feeling relaxed	1	2	3	4	5
I've been dealing with problems well	1	2	3	4	5
I've been thinking clearly	1	2	3	4	5
I've been feeling close to other people	1	2	3	4	5
I've been able to make up my own mind about things	1	2	3	4	5

Appendix M

World Health Organization Quality of Life-bref (WHOQOL-BREF; Whoqul Group, 1998)

WHOQOL–BREF

UK VERSION

Department of Mental Health
World Health Organisation
Geneva

For Office Use Only

	Equations for computing domain scores	Raw score	Transformed score	
			4-20	0-100
Domain 1	(6-Q3) + (6-Q4) + Q10 + Q15 + Q16 + Q17+ Q18 □ + □ + □ + □ + □ + □ + □	=		
Domain 2	Q5 + Q6 + Q7 + Q11 + Q19 + (6-Q26) + (6-Q27) + Q28 □ + □ + □ + □ + □ + □ + □ + □	=		
Domain 3	Q20 + Q21 + Q22 □ + □ + □	=		
Domain 4	Q8 + Q9 + Q12 + Q13 + Q14 + Q23 + Q24 + Q25 □ + □ + □ + □ + □ + □ + □ + □	=		

ABOUT YOU

Before you begin we would like you to answer a few general questions about yourself: by **circling** the correct answer or by **filling in the space provided**.

What is your gender? **MALE** / **FEMALE**

What is your date of birth? **____/___/_____.** (day/month/year.)

What is the highest education you've received? **None at all**
Primary school
Secondary school
Tertiary

What is your marital status? **Single** **Separated**
Married **Divorced**
Living as married **Widowed**

Are you currently ill? **YES / NO**

If something is wrong with your health what do you think it is?
Please write your illness(s) or problem here:_____
_____

Instructions

This questionnaire asks how you feel about your quality of life, health and other areas of your life. **Please answer all the questions**. If you are unsure about which response to give to a question, **please choose the ONE** that appears most appropriate. This can often be your first response.

Please keep in mind your standards, hopes, pleasures and concerns. We ask that you think about your life **in the last two weeks**. For example, thinking about the last two weeks, a question might ask:

		Not at all	Not much	Moderate	A great	Complete
	Do you get the kind of support from others that you need?	1	2	3	4	5

You should **circle** the number that best fits how much support you got from others **over the last two weeks**. So you would circle the number 4 if you got a great deal of support from others as follows:

		Not at all	Not much	Moderate	A great	Complete
	Do you get the kind of support from others that you need?	1	2	3	4	5

You would circle the number 1 if you did not get any of the support that you needed from others in the last two weeks. Please read each question, assess you feelings, and **circle** the number on the scale for each question that gives the best answer for you.

2

		Very poor	Poor	Neither poor nor good	Good	Very good
1	How would you rate your quality of life?	1	2	3	4	5

		Very Dissatisfied	Dissatisfied	Neither Satisfied nor Dissatisfied	Satisfied	Very Satisfied
2	How satisfied are you with your health?	1	2	3	4	5

The following questions ask about **how much** you have experienced certain things **in the last two weeks.**

		Not at all	A little	A moderate amount	Very much	An extreme amount
3	How much do you feel that pain prevents you from doing what you need to do?	1	2	3	4	5
4	How much do you need medical treatment to function in your daily life?	1	2	3	4	5
5	How much do you enjoy life?	1	2	3	4	5

		Not at all	A little	A moderate amount	Very much	Extremely
6	To what extent do you feel life to be meaningful?	1	2	3	4	5
7	How well are you able to concentrate?	1	2	3	4	5
8	How safe do you feel in your daily life?	1	2	3	4	5
9	How healthy is your physical environment?	1	2	3	4	5

The following questions ask about **how completely** you experience or were able to do certain things **in the last two weeks**.

		Not at all	A little	Moderately	Mostly	Completely
10	Do you have enough energy for everyday life?	1	2	3	4	5
11	Are you able to accept your bodily appearance?	1	2	3	4	5
12	To what extent do you have enough money to meet your needs?	1	2	3	4	5
13	How available to you is the information that you need in your day-to-day life?	1	2	3	4	5
14	To what extent do you have the opportunity for leisure activities?	1	2	3	4	5

3

The following questions ask you to say **how good or satisfied** you have felt about various aspects of your life **over the last two weeks**.

		Very poor	Poor	Neither poor nor good	Good	Very good
15	How well are you able to get around?	1	2	3	4	5

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
16	How satisfied are you with your sleep?	1	2	3	4	5
17	How satisfied are you with your ability to perform daily living activities?	1	2	3	4	5
18	How satisfied are you with your capacity for work?	1	2	3	4	5
19	How satisfied are you with yourself?	1	2	3	4	5
20	How satisfied are you with your personal relationships?	1	2	3	4	5
21	How satisfied are you with your sex life?	1	2	3	4	5
22	How satisfied are you with the support you get from your friends?	1	2	3	4	5
23	How satisfied are you with the conditions of your living place?	1	2	3	4	5
24	How satisfied are you with your access to health services?	1	2	3	4	5
25	How satisfied are you with your transport?	1	2	3	4	5

The following question refers to **how often** you have felt or experienced certain things **in the last two weeks**.

		Never	Seldom	Quite often	Very often	Always
26	How often do you have negative feelings, such as blue mood, despair, anxiety, depression?	1	2	3	4	5

Did someone help you to fill out this form? **YES** / **NO**

THANK YOU FOR YOUR HELP

Appendix N

Line Care Routine Questionnaire

Screening Questions:
The following questions will ask you about your line care routine:

1. Are you currently having help looking after your line care at home (e.g. from family or home care staff)?

Yes No

2. In the past have you received help with looking after your line care when you are at home?

Never Rarely Sometimes Most of the time Always

Line care adherence questions:
Now thinking about when you are carrying out your own line care at home, please indicate how much you agree with the following statements:

Options:
1 = strongly disagree 2 = disagree 3 = neither agree nor disagree
4 = agree 5 = strongly agree

1. *It doesn't really matter if I miss out the occasional step when following my line care procedure*
2. *If someone hasn't had a recent line infection, then they don't need to be as strict with their line care*
3. *Sometimes I cannot be bothered to care for my line*
4. *I find it difficult to be honest with medical professionals about how well I'm looking after my line*

Options:
1 = Never 2 = Rarely 3 = Sometimes 4 = Most of the time 5 = Always

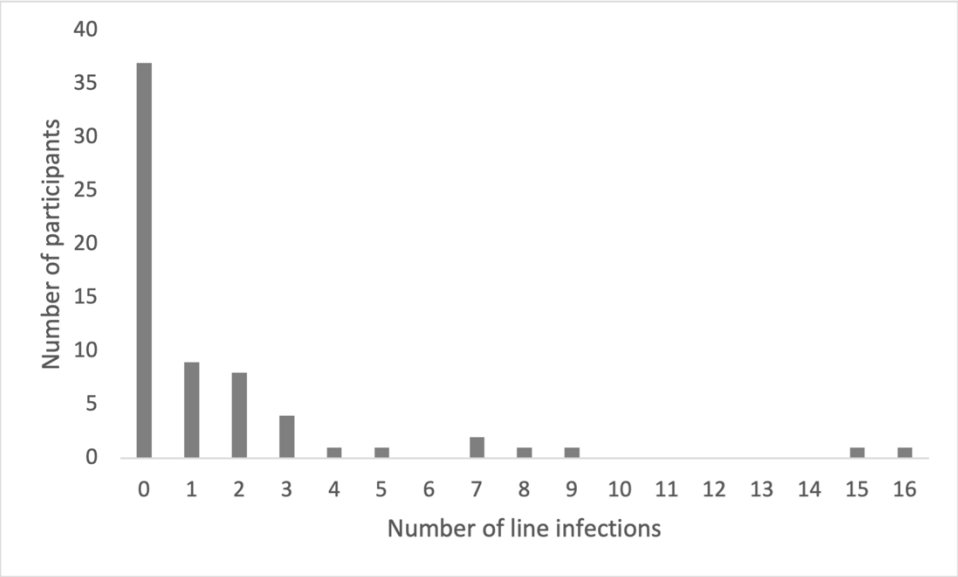
5. I follow a strict series of steps when connecting/disconnecting my line
6. *I am not as careful with my line care when I am feeling down or tired, or if am busy*
7. *I can be careless about line care*
8. *I miss out a step or two when connecting/disconnecting my line*
9. *I engage in activities that might accidentally lead to a line infection*

Scoring:
Sum all items (*reverse-scored items in italics)*
Higher scores indicate higher line care adherence.

Appendix O

Self-reported Line Infections

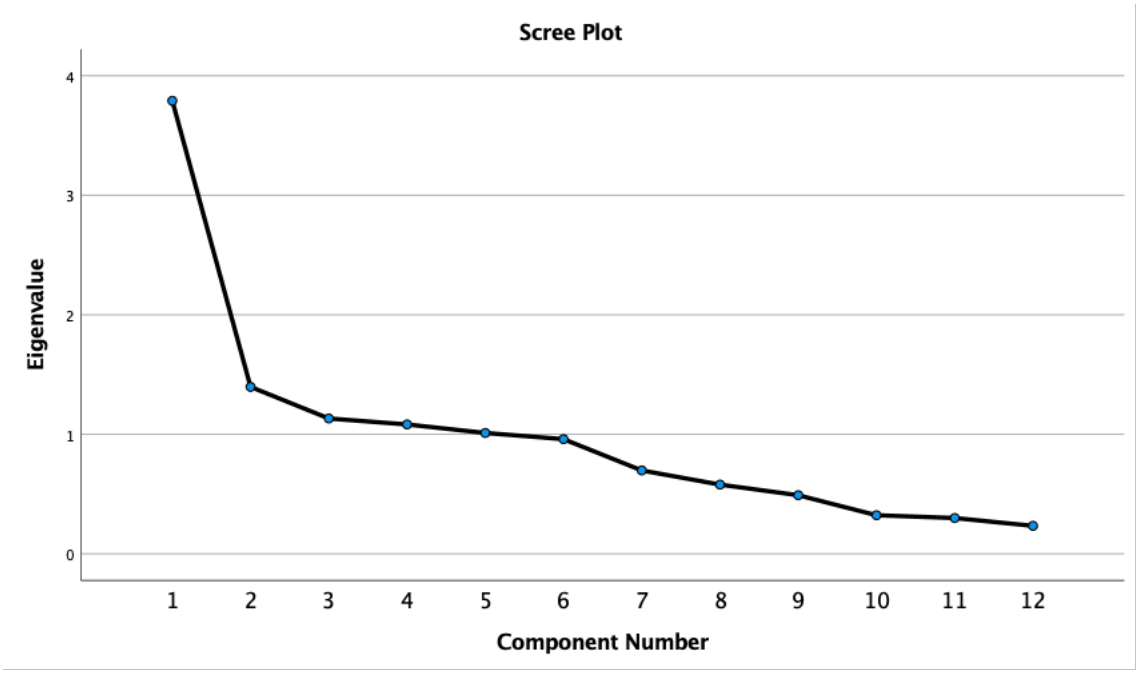
Number of line infections self-reported by participants



Appendix P

Scree Plot

Scree Plot for determination of how many factors to retain in Principal Components Analysis



Appendix Q

Principal Component Analysis Correlation and Component Matrices

Table Q1

Principal Component Analysis Correlation Matrix[a] for the Line Care Routines Questionnaire

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q8	Q10	Q11	Q12
Q2	0.537	-										
Q3	-0.081	-0.048	-									
Q4	0.315	0.141	-0.086	-								
Q5	0.316	-0.039	-0.028	0.457	-							
Q6	-0.147	-0.125	-0.019	-0.067	0.052	-						
Q7	0.267	0.284	-0.07	0.206	0.239	-0.299	-					
Q8	0.479	0.462	-0.071	0.5	0.338	-0.2	0.336	-				
Q9	0.528	0.382	0.028	0.465	0.373	-0.12	0.226	0.712	-			
Q10	0.111	0.099	0.02	0.035	0.057	-0.177	0.024	0.153	0.066	-		
Q11	0.352	0.377	-0.051	0.195	0.135	-0.13	0.378	0.454	0.5	-0.025	-	
Q12	0.247	0.124	0.052	0.082	0.127	-0.083	0.215	0.171	0.223	0.227	0.506	-

[a]Determinant = 0.028

Table Q2

Component Matrix[a]

	Component
	1
Q1. It doesn't really matter if I miss out the occasional step when following my line care procedure	0.724
Q2. If someone hasn't had a recent line infection, then they don't need to be as strict with their line care	0.593
Q3. It is important to follow the right steps in the right order when connecting and disconnecting my line to avoid infection	
Q4. Sometimes I cannot be bothered to care for my line	0.58
Q5. I find it difficult to be honest with medical professionals about how well I'm looking after my line	0.473
Q6. I give myself a hard time when I don't follow the line care procedure perfectly	
Q7. I follow a strict series of steps when connecting/disconnecting my line	0.534
Q8. I am not as careful with my line care when I am feeling down or tired, or if am busy	0.821
Q9. I can be careless about line care	0.801
Q10. I remind myself of the order of the steps in connecting/disconnecting my line	
Q11. I miss out a step or two when connecting/disconnecting my line	0.675
Q12. I engage in activities that might accidentally lead to a line infection	0.428

Extraction Method: Principal Component Analysis

[a]1 components extracted.

Appendix R

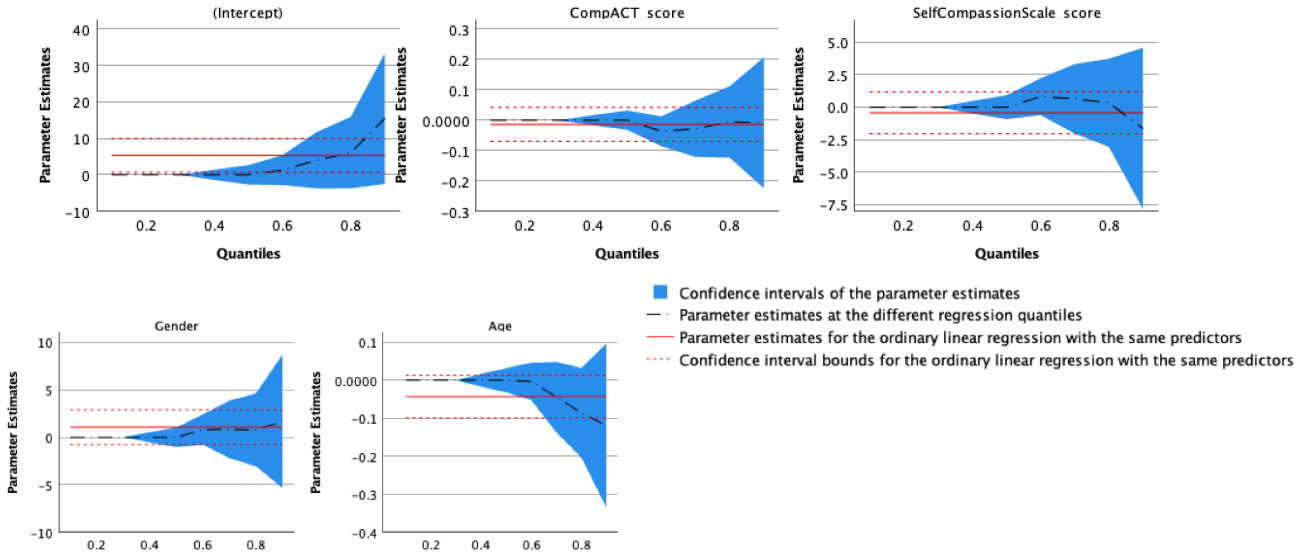
Quantile regression results

Results from the quantile regression analysis of PF, SC, age and gender (dependent variable line infections)

	Quantiles															
	60%				70%				80%				90%			
Variable	Coeff.	*SE*	*t*	Pseudo R^2	Coeff.	*SE*	*t*	Pseudo R^2	Coeff.	*SE*	*t*	Pseudo R^2	Coeff.	*SE*	*t*	Pseudo R^2
PF	-0.04	0.02	-1.49	0.04	-0.03	0.05	-0.60	0.08	-0.01	0.06	-0.10	0.11	-0.01	0.11	-0.08	0.27
SC	0.81	0.71	1.15		0.65	1.33	0.48		0.35	1.69	0.20		-1.63	3.10	-0.53	
Gender	0.82	0.80	1.02		0.83	1.51	0.55		0.78	1.92	0.41		1.69	3.51	0.48	
Age	0.00	0.02	-0.12		-0.04	0.05	-0.95		-0.09	0.06	-1.45		-0.12	0.11	-1.11	

Note. PF = Psychological Flexibility; SC = Self-compassion; Coeff = coefficient; *SE* = standard error of the coefficient; Pseudo R^2 = pseudo coefficient of determination. None of the predictors were statistically significant (p>.05).
Values for the 10-50% quantiles were all zero, and therefore are not reported here.

Ordinary Least Squares (OLS) and quantile regression estimates for line infections

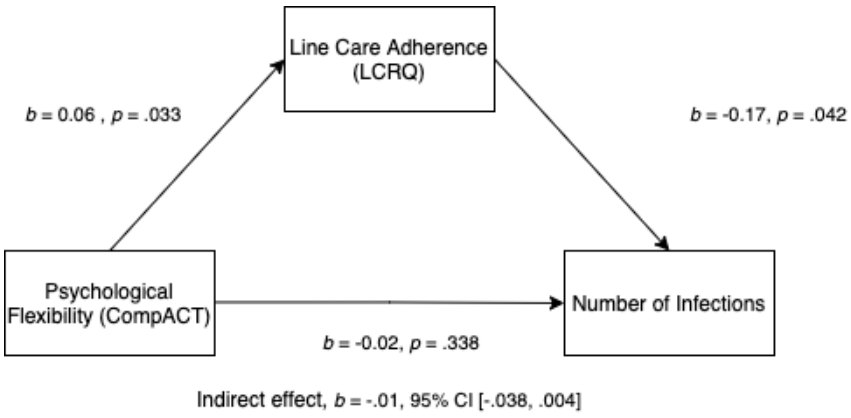


Appendix S

Mediation Analyses

Figure S1

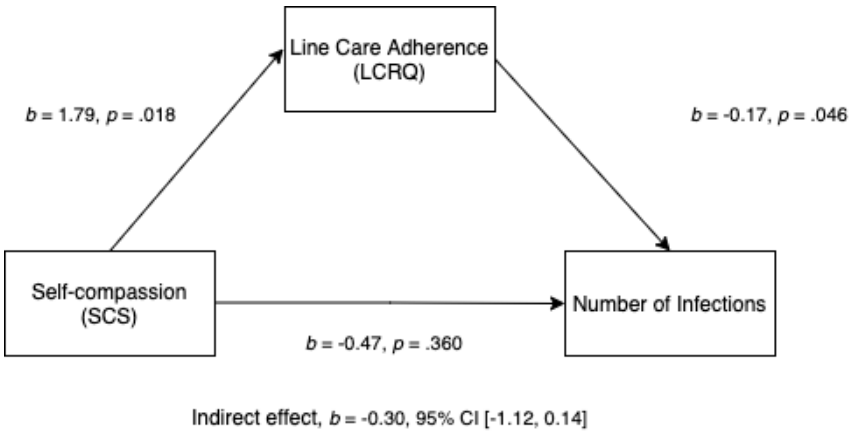
Mediation model of the hypothesised direct and indirect effects of PF on number of infections



Note. Model 1: Effect of PF on number of infections, with line care adherence as a predicted mediator. Higher PF directly predicted better line care adherence and better line care adherence directly predicted fewer infections. However, contrary to our hypothesis, both the direct effect of PF on infections and the indirect effect with line care as a mediator were not significant.

Figure S2

Mediation model of the hypothesised direct and indirect effects of PF on number of infections.



Note: Model 2: Effect of SC on number of infections, with line care adherence as a predicted mediator. Higher SC directly predicted better line care adherence and better line care adherence directly predicted fewer infections. The direct effect of SC on infections, and the indirect effect with line care as a mediator, were not significant.