





## ORIGINAL ARTICLE

# The relation between psychological distress and medication adherence in lung transplant candidates and recipients: A cross-sectional study

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## Abstract

**Aims and objectives:** To explore the prevalence of psychological distress such as anxiety, depression and post-traumatic stress disorder and its associations with medication adherence in lung transplant patients.

**Background:** Psychological distress after lung transplantation may impact clinical outcomes by associated behaviours such as non-adherence to medication. Evidence about the relation between psychological distress and medication adherence in lung transplant patients is limited and not well explained.

**Design and methods:** We conducted a single-centre study with a cross-sectional design in 73 lung transplant candidates and 116 recipients. Questionnaires were the Brief Symptom Inventory, Impact of Event Scale and Basel Assessment of Adherence to Immunosuppressive Medications Scale. The STROBE checklist was monitored.

**Results:** In candidates, 39.7% reported (sub)clinical symptoms of depression, in recipients this was 21.6%. We observed suicidal ideation in recipients (8.6%), and candidates (5.5%). The prevalence of (sub)clinical symptoms of anxiety was 38.3% in candidates and 33.7% in recipients. After lung transplantation, 12% of the recipients reported clinical symptoms of PTSD related to the transplantation. Symptoms of anxiety and medication adherence were significantly and positively related in transplant recipients. We found no association between depressive or post-traumatic stress symptoms, and medication adherence.

**Conclusions:** In lung transplant patients, we found a high prevalence of symptoms of depression and anxiety. Recipients had high levels of post-traumatic stress symptoms related to the transplantation. The prevalence of suicidal ideation was unexpectedly high in recipients. After lung transplantation, higher levels of anxiety were related to better medication adherence. We propose that LTX recipients are very anxious to develop dyspnoea and therefore take their medication more conscientiously.

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**Relevance to clinical practice:** The clinical nurse specialist can play a key role in identifying and addressing psychological and behavioural problems. More prospective research on the role of anxiety and dyspnoea in lung transplant recipients is recommended.

**KEYWORDS**

anxiety, depression, lung transplantation, medication adherence, post-traumatic stress disorder, suicidal ideation

## 1 | INTRODUCTION AND BACKGROUND

Lung transplantation is a successful treatment option for patients with various forms of end-stage lung disease. The median survival after lung transplantation is 6.7 years, and 8.8 years after surviving the first year (Chambers et al., 2019). This is shorter compared to other solid organ transplantations.

The transplant trajectory is complex and intensive, and patients usually experience this period as extremely stressful. Lung transplant candidates have to deal with functional impairment and face an imminent death when time is running out. After transplantation, lung transplant recipients may struggle with new uncertainties such as fear of infection or rejection (Dew et al., 2015,2018; Kugler et al., 2013).

Due to the intense period before and after transplantation, psychological distress such as depression, anxiety and post-traumatic stress is common (Dew et al., 2015). Reported prevalence rates in lung transplant candidates vary between studies. Parekh et al. (2003) found that 25% of the candidates awaiting lung transplantation had at least one current mood or anxiety disorder. In other studies, prevalence rates are described from 14.6% up to 40.9% for depressive disorders and 18.4% up to 25.3% for anxiety disorders (Courtwright et al., 2016; Rosenberger et al., 2016). In lung transplant recipients, prevalence rates of 30% are described for depression disorder, 22% for anxiety disorders and 15% for transplant related post-traumatic stress disorder (PTSD), during the first two years after lung transplantation (Dew et al., 2012).

Depression, anxiety and PTSD are potential risk factors for morbidity and mortality, both in the general population and in (lung) transplant recipients (Cuijpers et al., 2014; Dew et al., 2015,2018; Eaton et al., 2008; Smith et al., 2017). Prior studies observed that higher levels of depression and general distress after lung transplantation were associated with increased mortality in lung transplant recipients, independent of the patient's background characteristics and medical predictors (Smith et al., 2016,2017). This relation was not found for anxiety (Smith et al., 2016).

In lung transplant recipients, the mechanisms underlying the relation between psychological distress and morbidity or mortality are not well understood. Psychological distress may impact clinical outcomes by associated behaviours such as non-adherence to medication (Dew et al., 1999, 2015). Lifelong adherence to

### What does this paper contribute to the wider global clinical community?

- After lung transplantation, higher levels of anxiety symptoms are related to better medication adherence
- Patients after lung transplantation presumably are anxious to develop dyspnoea and therefore take their medication more conscientiously.
- After lung transplantation patients may experience suicidal ideations, which reflects the necessity of ongoing systematic screening on psychological distress

immunosuppressive medication is crucial for all solid organ transplant recipients, since non-adherence is related to rejection of the transplanted organ, need for re-transplantation and even death (Belaiche et al., 2017; Dew et al., 2018; Griva et al., 2012; Myaskovsky et al., 2018). In lung transplant recipients, adherence is especially important because lung transplantation is accompanied with greater risk of infection, and acute or chronic rejection, and patients have a limited access to re-transplantation (Bertram et al., 2019; Dew et al., 2008).

In lung transplant recipients, non-adherence to medication rates ranging from 2.3% to 72.2% are described in a systematic review including 13 studies (Hu et al., 2017). This wide range reflects that rates of non-adherence to immunosuppressive regimens vary highly, depending on used measures and criteria.

Studies on the relation between psychological distress and medication non-adherence in lung transplant recipients specifically are limited. A recent follow-up study of Chu et al. (2020) in 236 lung transplantation recipients, observed that depressive symptoms after lung transplantation and out of range immunosuppressive through levels, which are markers of medication adherence, are independently associated with adverse clinical outcomes. Although depression was expected to be associated with medication non-adherence to immunosuppressive medication, it did not mediate the association between depression and clinical outcomes (Chu et al., 2020). A systematic review of Hu et al. (2017) described that non-adherence to the medication regimen after lung transplantation was not consistently associated with any single risk factor. To our knowledge more evidence about the relation between

symptoms of anxiety or PTSD, and medication non-adherence in lung transplant recipients is lacking.

In other solid organ transplant recipients however, more extensive evidence was found regarding the existence of a relation between psychological distress and medication adherence (Annema et al., 2018; Dew et al., 1999, 2015; DiMatteo et al., 2000; Dobbels et al., 2009; de Geest et al., 2014). Depression may lead to poor adherence to the immunosuppressive medication regimen of heart, kidney and liver transplant recipients, and symptoms of anxiety are also related to medication non-adherence in these transplant populations (Annema et al., 2018; Denhaerynck et al., 2005; Reber et al., 2016). Furthermore, in heart transplant recipients, PTSD related to the transplantation (i.e. intrusive symptoms) has been associated with reduced medication adherence (Favaro et al., 2011). Despite the studies mentioned above, other studies did not find a relation between depression or anxiety and non-adherence in solid organ recipients (Dew et al., 2008; Griva et al., 2012; Weng et al., 2013).

The impact of psychological distress and its associations with medication adherence in solid organ transplant patients is frequently explored. However, evidence in lung transplant patients and the role of depression, anxiety and PTSD symptoms in relation to medication adherence is limited and not well explained. Therefore we will investigate both the prevalence of psychological distress (depression, anxiety and PTSD) and the association between psychological distress and medication adherence, in lung transplant candidates and recipients.

## 2 | MATERIALS AND METHODS

### 2.1 | Patients

All adults who were on the waiting list for their first lung transplantation or had received their first lung transplantation were eligible for this study. The exclusion criteria were: age below 16 years; re-transplantation; and inability to complete questionnaires. Inclusion took place between January 2016 and February 2020. During this period, 76 candidates were on the waiting list for lung transplantation and 129 recipients received follow-up after lung transplantation. We asked all these patients to participate in this study. Of the 76 candidates, one was excluded because a language barrier that prevented completing questionnaires. The remaining 75 candidates consented to participate, although two did not return the questionnaires (response rate 97%), resulting in 73 candidates that participated in the study. Of the 129 recipients, seven were excluded because of: re-transplantation ( $n = 2$ ); inability to complete questionnaires due to low cognitive functioning ( $n = 2$ ); and interference with current trauma therapy ( $n = 3$ ). Of the remaining 122 recipients, 121 gave informed consent, but 5 did not return the questionnaires. This resulted in 116 recipients that participated in this study (response rate 96%).

### 2.2 | Procedure

The study was exempt from the Medical Research Involving Human Subjects Act according to the Institutional Review Board of the University Medical Center. All participants provided written informed consent. We performed a single-centre study with a cross-sectional design, including all lung transplant candidates and recipients in our centre. Candidates and recipients were asked to fill out several questionnaires related to psychological functioning. We integrated the questionnaires used in this study with clinical care in order to monitor psychological health and refer patients for psychological treatment if necessary. We used the EQUATOR research reporting checklist STROBE as guideline in this study (see for Strobe Statement File S1).

### 2.3 | Materials

We used clinical diagnostic instruments to screen patients for anxiety, depression and PTSD symptoms.

The Brief Symptom Inventory (BSI) was used to assess symptoms of anxiety and depression. BSI is the short version of the Symptom Checklist (SCL-90). This questionnaire is used to assess the nature and severity of psychological problems. Participants rate the extent to which they have been bothered (0 = 'not at all' to 4 = 'extremely') in the past week by various symptoms. The BSI consists of 53 items and has nine subscales designed to assess individual symptom groups, of which only anxiety and depression were used in this study. The BSI includes one question on suicidal thoughts and recommends to interpret this question separately as a signal for suicidality and thus a risk factor for depression. Dutch BSI scores are normed on the general Dutch population and range from 1 to 7 (based on 1662 individuals). High scores refer to psychological problems; score 6 is classified as 'subclinical' and score 7 as 'clinical', corresponding to the 80<sup>th</sup> and 95<sup>th</sup> percentile (Derogatis L.R., 1993). Normed scores were used in the analyses.

PTSD symptoms associated with the lung transplantation were measured with the Dutch version of the Impact of Event Scale (Ploeg van der et al., 2004). This questionnaire consists of 15 items, with 7 items referring to symptoms of intrusion and 8 items referring to avoidance symptoms. For every statement, the respondent answers on a 4-point Likert scale whether this was present, with 0 (not at all), 1 (rarely), 3 (sometimes) or 5 (often) during the past seven days. A strong or severe reaction (score  $\geq 26$ ) on the transplant experience (avoiding and intrusion score together) is clinically relevant. In clinical populations, the 70<sup>th</sup> percentile (raw score  $\geq 26$ ) is classified as 'subclinical' and the 93<sup>th</sup> percentile (raw scores  $\geq 44$ ) is classified as 'clinical' (Ploeg van der et al., 2004).

The Basel Assessment of Adherence to Immunosuppressive Medications Scale (BAASIS<sup>®</sup>) is a self-report instrument and was used to assess adherence to immunosuppressive medication during the previous four weeks (Dobbels et al., 2010). Adherence

was defined as 'the process by which patients take their medication as prescribed' (Dobbels et al., 2010; Vrijens et al., 2012). The BAASIS<sup>®</sup> is operationalised to measure four domains of adherence with multiple-choice questions: taking (taking the prescribed immunosuppressive medication), timing (taking the immunosuppressive drugs every 12 h +/- two hours), drug holidays (skipping the immunosuppressive medication 24 h or more) and dose reduction (changing immunosuppressive medication from the prescribed dose). Patients who report non-adherence to one of the four domains are considered non-adherent. Scoring is intentionally strict due to the assumption of underreporting of non-adherence (Dobbels et al., 2010). We assessed adherence before and after transplantation with the BAASIS<sup>®</sup>. For medication used by candidates, we adapted the BAASIS<sup>®</sup> for medication used while on the waiting list.

In addition to these psychological questionnaires, medical and demographic data were retrieved from medical records. Education level was classified into low, middle and high according to the International Standard Classification of Education ('Standaard Onderwijs Indeling, 2016').

## 2.4 | Statistical analysis

The relations between adherence, and depression, anxiety and PTSD, were analysed using Fisher's exact. To relate the PTSD dimensions avoidance and intrusion to adherence, Spearman's rho was used since avoidance and intrusion lacked a clinical cut-off and could therefore not be dichotomised. To show differences in demographic characteristics between candidates and recipients, the Mann-Whitney *U* test was used for not normally distributed continuous variables, Cramer's *V* for nominal variables with more than two categories, and Fisher's exact for dichotomous variables. Data were not imputed. *p*-values <.05 were considered statistically significant. SPSS version 25.0 was used for all analyses (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

## 3 | RESULTS

### 3.1 | Patient characteristics

Demographic characteristics of candidates and recipients are presented in Table 1. Candidates and recipients were similar in age, ethnicity and history of psychiatric diagnosis. The groups differed significantly on education level, employment and primary lung disease. In contrast to recipients, fewer candidates had a high educational status, paid work or voluntary work. Among the candidates, chronic obstructive pulmonary disease (COPD) was most prevalent, while in the group of recipients, the majority of patients were diagnosed with cystic fibrosis (CF). Gender did not significantly differ between the groups, but we observed a trend towards more females in the group of candidates.

### 3.2 | Depression, anxiety and PTSD symptoms

The prevalence rates of symptoms of depression, anxiety and PTSD symptoms are presented in Table 2. The prevalence of candidates with clinical symptoms of depression was four times higher than in the general population, according to test normed scores. In recipients, the prevalence of clinical symptoms was higher than in the general population. Regarding suicidal thoughts, three candidates (4.1%) disclosed having 'few thoughts' about ending their life and one candidate (1.4%) disclosed having 'quite a lot thoughts' about ending his/her life. Eight recipients (6.9%) disclosed having 'few thoughts' and two recipients (1.7%) disclosed having 'quite some thoughts' about ending their life.

The prevalence of patients with clinical and subclinical symptoms of anxiety was higher than in the general population, both before and after lung transplantation. In candidates the prevalence of anxiety symptoms was 4 times higher than in the general population; in recipients it was almost 3 times higher. The prevalence of subclinical symptoms of PTSD was comparable to the general population, but the prevalence of clinical symptoms of PTSD was almost twice higher than the general population. With respect to the two dimensions of PTSD, symptoms of intrusion in recipients (median = 3, IQR 0–9) were more prevalent compared to avoidance symptoms (median = 0, IQR 0–4).

Since depression, anxiety and PTSD are not mutually exclusive diagnoses, overlap of symptoms in recipients is explored. In general, it turned out that comorbidity is more prevalent than singular psychological problems. A combination of both anxiety and PTSD symptoms was most prevalent in recipients (*n* = 15; 13.2%). Twelve recipients (10.6%) reported symptoms above the (sub)clinical threshold of all three psychological problems.

### 3.3 | Medication adherence in lung transplant candidates and recipients

In candidates, we observed 36% non-adherence. Of the recipients, 41% was categorised as non-adherent to medication (see Table 3). Problems with adherence were mostly related to timing adherence. None of the patients before or after transplantation had persistence problems, that is stopped the intake of (immunosuppressive) medication completely without telling their professional.

### 3.4 | Depression, anxiety and PTSD and association with medication adherence

Presence of (sub)clinical anxiety symptoms and medication adherence were significantly related in recipients (Fisher's exact = 4.05, *p* = .048). Recipients with (sub)clinical symptoms of anxiety were two times more likely to be adherent to medication compared to non-anxious recipients. This was not the case

	Candidates of LTX (n = 73)	Recipients of LTX (n = 116)	<i>p</i> <sup>a</sup>
Age, years, median (IQR)	55 (45–61)	50 (35–61)	.140
Female, n (%)	47 (64%)	57 (49%)	.051
Caucasian, n (%)	68 (93%)	114 (98%)	.110
Education, n (%)			.017 <sup>a</sup>
High educated	10 (14%)	37 (32%)	
Middle educated	28 (38%)	38 (33%)	
Low educated	35 (48%)	41 (35%)	
Employed, n (%)			<.001
Paid work	9 (12%)	35 (30%)	
Volunteering	3 (4%)	22 (19%)	
Not employed	61 (84%)	59 (51%)	
Medical diagnosis, n (%)			<.001 <sup>a</sup>
Cystic Fibrosis	15 (21%)	58 (50%)	
COPD and A1ATD	36 (49%)	27 (23%)	
Interstitial lung disease	20 (27%)	22 (19%)	
Other	2 (3%)	9 (8%)	
Transplant type, n (%)			–
Unilateral	–	15 (13%)	
Bilateral	–	101 (87%)	
LAS score, median (IQR)	33.24 (32.00–34.60)	–	–
Time on waitlist, median days (IQR)	522 (314–869)	421 (120–799)	.101
Time since LOTX, median days (IQR)	–	1,781 (2,658)	–
History of psychiatric diagnosis, n (%)	12 (16%)	22 (19%)	.711

<sup>a</sup>We tested whether there was an overall difference between groups.

\*Mann-Whitney U test for not normally distributed continuous variables, Fischer's exact for dichotomous variables, Chi squared for nominal variables.

	Candidates (n = 73)			Recipients (n = 116)		
	Median (IQR)	% subclinical	% clinical	Median (IQR)	% subclinical	% Clinical
Depression	5 (3–6)	23.3	16.4	3 (3–5)	14.7	6.9
Anxiety	5 (3–6)	17.8	20.5	4 (4–6)	19.0	13.8
PTSD				4 (0–13)	21.6	12.1

Note: General Dutch population norms for depression and anxiety are 15% subclinical and 5% clinical. Dutch norms in clinical populations for PTSD are 23% subclinical and 7% clinical.

for candidates (Fisher's exact = 0.27,  $p = .614$ ). In both candidates and recipients we found no significant relation between (sub)clinical symptoms of depression and medication adherence (candidates: Fisher's exact = 0.00,  $p = .999$ ; recipients Fisher's exact = 0.06,  $p = .999$ ). Neither did we find a significant relation between PTSD and medication adherence for recipients (Fisher's exact = 1.06,  $p = .325$ ). The PTSD dimensions avoidance and intrusion were also not significantly related to medication

adherence (avoidance: Spearman's rho =  $-0.10$ ,  $p = .288$ ; intrusion: Spearman's rho =  $-0.04$ ,  $p = .675$ ).

## 4 | DISCUSSION

The aim of this study was to investigate the prevalence of depression, anxiety and PTSD, and their association with medication adherence

TABLE 1 Demographic and disease characteristics of lung transplant candidates and recipients

TABLE 2 Symptoms of psychological distress in lung transplant candidates and recipients

TABLE 3 Medication adherence in lung transplantation candidates and recipients

	Candidates (n = 73) n (%)	Recipients (n = 116) n (%)
BAASIS		
1a. Taking dimension: missing a dose in the past 4 weeks	19 (26%)	27 (23%)
Once	8 (11%)	22 (19%)
Twice	9 (12%)	3 (2%)
Three times	0	2 (2%)
Four times	2 (3%)	0
More than four times	0	0
1b. Taking dimension: missing two or more doses behind each other in the past 4 weeks	0	1 (1%)
2. Timing dimension: taking medication more than 2 h before or after the prescribed dosing time in the past 4 weeks	19 (26%)	39 (34%)
Once	8 (11%)	19 (16%)
2–3 times	9 (12%)	15 (13%)
4–5 times	2 (3%)	3 (3%)
Every 2 to 3 days	0	0
Almost daily	0	2 (2%)
3. Reduction of dose: altering the prescribed amount of medication during the past 4 weeks without telling professional	4 (6%)	2 (2%)
4. Persistence: Stopped taking medication completely in the past 4 weeks without telling professional	0	0
Categorised as non-adherent	26 (36%)	48 (41%)

in lung transplant candidates and recipients. We found that symptoms of depression, anxiety and PTSD were more prevalent in both candidates and recipients compared to the Dutch general population (Derogatis, 1993). Furthermore, we have shown that in recipients, anxiety was positively related to medication adherence, whereas depression and PTSD were not related to medication adherence.

Although 21.6% of the transplant recipients disclosed (sub)clinical symptoms of depression and 39.7% of the transplant candidates, the prevalence of clinical symptoms of depression in recipients was still 1.5 times higher compared to the Dutch general population (Derogatis, 1993). Almost 9% of the lung transplant recipients experienced 'thoughts of ending his/her life', which is nearly 8 times more often than in the Dutch general population (Have et al., 2011). Surprisingly, suicidal thoughts occurred frequently in recipients. Because candidates make an explicit choice to wait for lung transplantation, their main focus may be on survival, which conflicts with suicidal ideation. In case of physical deterioration and waiting a long period to be transplanted, feelings of hopelessness and suicidal

thoughts are understandable. For recipients however, these suicidal thoughts are unexpected, because we assumed that these patients would be relieved and happy after receiving a new life and opportunities. However, frustration about unmet expectations of the transplantation may cause both depression and suicidal ideation (Rynar et al., 2018).

In our study, the prevalence of clinical anxiety symptoms after lung transplantation was 3–4 times higher compared to the Dutch general population. This may be largely attributed to the fear for dyspnoea, which is common in chronic lung disease and lung transplant patients (Brandl et al., 2018; ; Montserrat-Capdevila et al., 2018; Nevins et al., 2017; Quittner, Goldbeck, et al., 2014; Rosenberger et al., 2016). Although recipients experience improvement in physical functioning and quality of life after lung transplantation, the onset of complications such as infection, acute rejection and chronic lung allograft dysfunction is accompanied by recurrence of dyspnoea. This dyspnoea causes distress and can contribute to high levels of anxiety symptoms (Shahabeddin Parizi et al., 2018) Treatment with Prednisone, used as immunosuppressive medication after transplantation, can also contribute to an elevated level of anxiety symptoms (Warrington & Bostwick, 2006).

Clinical PTSD symptoms related to the lung transplantation were prevalent in 12.1% of the recipients. This prevalence is in accordance with other studies in lung transplant patients (Dew et al., 2012; Gries et al., 2013; Köllner et al., 2002). It reaches almost twice the rate of clinical population norms (Ploeg et al., 2004). The lung transplantation procedure itself can be potentially traumatic because of the experience of pain, delirium and hospitalisation on the intensive care unit with mechanical ventilation and/or extra corporal membrane oxygenation therapy (Needham et al., 2012; Rawal et al., 2017). As a result of these treatments former traumatic intrusions can re-occur for example in case of new episodes of dyspnoea due to infection or rejection and hospitalisation periods after the transplantation.

Besides the high prevalence of singular disorders, our results showed that at least one third of the recipients had symptoms of multiple psychological disorders. Comorbidity between anxiety, depression and PTSD is common and highly important since patients with multiple psychological disorders require more intensive psychological treatment (Kessler et al., 2015).

Similar to the high rates of psychological distress, medication non-adherence rates were high in both candidates (36%) and recipients (41%). Non-adherence rates are in line with other European studies which reported non-adherence rates after lung transplantation of respectively 54%, 7.7% and 27.4%. (Bosma et al., 2011; Drick et al., 2018; Lennerling et al., 2019) Our numbers of medication non-adherence are comparable with the results of Drick et al. (2018) and Lennerling et al. (2019), which may reflect the use of the same instrument to assess adherence. The BAASIS is very strict, to prevent underreporting of medication non-adherence. Additionally, our clinical experience is that medication adherence after lung transplantation indeed is very difficult to achieve. Lung transplant recipients are at risk to make unintentional mistakes in intake and timing because of regular changes in their complicated and comprehensive medication

regimen consisting of on average 10 different drugs to be taken on 4–5 specific moments each day. It is therefore obvious that medication adherence after lung transplantation requires a lot of effort from recipients, and it is therefore a continuing focus of attention and guidance from the clinical nurse specialist.

Non-adherence is especially problematic after transplantation since it is a potential risk factor for rejection, loss of the transplanted organ or increased mortality (Dew et al., 2008,2015; Smith et al., 2016,2017). In recipients, non-adherence may be caused by their inability to execute the complicated medication regimen. This involves at least three immunosuppressive medications that require strict intake times because of the narrow therapeutic ranges. Many recipients also report cognitive problems, which may further hinder their understanding and execution of the medication regimen (Cohen et al., 2014; Stillely et al., 2010). Finally, 50% of our recipients have cystic fibrosis, which is a known at risk population for non-adherence, especially during adolescence (Quittner, Zhang, et al., 2014). Although we did not include recipients beneath the age of eighteen, we do have a lot of young adults in our study population. From our experience we noticed that young adults often struggle with medication adherence. They do not have a regular life, and they often don't want to reveal their illness by taking medication in front of co-workers or friends.

We found that recipients with anxiety symptoms were more likely to be adherent. Patients suffering from a lung disease experience dyspnoea, which causes severe fear and may traumatise patients (Teixeira et al., 2015). We propose that lung transplant recipients are more adherent in order to prevent dyspnoea (by taking their medication accurately) while other organ transplant recipients may try to prevent being confronted with their transplantation (thus not taking their medication) (Favaro et al., 2011). We found limited evidence about the role of anxiety and its relation with adherence in patients with a chronic lung condition. The literature suggests that general anxiety may differ from dyspnoea-related fear (Janssens et al., 2011; Lavoie et al., 2006). The relation between anxiety, dyspnoea and medication adherence has been described in patients with asthma and may be associated with behavioural factors such as self-monitoring and treatment adherence (Lavoie et al., 2006). Lavoie et al. (2006) found that patients with an anxiety disorder, used their asthma medication better compared to patients without an anxiety disorder suggesting that patients with anxiety are likely to fear an exacerbation, and thus fearing dyspnoea, which is beneficial for medication adherence. Janssens et al. (2011), described a mediating effect of dyspnoea-related fear on the association between anxiety and exercise related dyspnoea. We therefore may assume that dyspnoea-related fear may also affect behaviour in lung transplant recipients. Dyspnoea-related fear may motivate patients to take their prescribed immunosuppressive medication more conscientiously. We suppose that the type of anxiety may discriminate between favourable effects of anxiety in case of dyspnoea-related fear (e.g. being more alert and conscientious with medication intake), and general anxiety for which referral to a psychologist or psychiatrist might be needed due to the burden of anxiety. Previous research

found associations between symptoms of PTSD (i.e. avoidance and intrusion) and non-adherence; however, in our study we did not confirm the association of PTSD symptoms with adherence (Dew et al., 1999; Favaro et al., 2011; Gries et al., 2013). We presume that in lung transplant recipients, the relation between anxiety symptoms and adherence mediated by underlying fear for dyspnoea, prevails the relation between PTSD and adherence. We suggest prospective longitudinal research in order to explore the nature and presence of this relationship.

Prior research of Chu et al., and Smith et al. already proved that early depression and greater depressive symptoms shortly after lung transplantation was independently associated with mortality (Chu et al., 2020; Smith et al., 2017). Although we did not investigate the relation between depression and clinical outcomes, we did not find a relation between depression and medication non-adherence, which is in line with the assumption that medication non-adherence does not mediate the relation depression and worse clinical outcomes.

The strength of our study is the very high response rate. Patients visiting the outpatient clinic expressed that they considered this study to be very important. The high disclosure of mental problems and medication non-adherence may be the result of the fact that this study is performed by a clinical nurse specialist who is also working on the lung transplant outpatient department. As a consequence of the narrow therapeutic relation with the study population, patients probably feel safe and at ease to disclose their problems on mental health and adherence issues to a nurse. The high disclosure of psychological symptoms and non-adherence of the patients underscores the necessity of systematic screening. For example, on the questionnaires, patients disclosed problems they had not mentioned to the medical professionals before, because they probably felt it would be ungrateful if they were not happy after receiving a new lung. A limitation of our study is that we used screening instruments instead of diagnostic interviews, enabling us to report on symptoms of depression, anxiety and post-traumatic stress but not on actual psychiatric diagnoses. A second limitation is the cross-sectional design, which makes it impossible to investigate causal inferences. A third limitation is that we used a self-report instrument to assess adherence which may under or overestimate the actual problem of medication adherence. In future research a combination of different methods to assess medication non-adherence, for instance a combination with measuring through levels of medication in blood samples, is preferable. To keep the focus of this article clear, we did not choose to explore whether time on waiting list or time after transplantation changes over time affected the outcomes. In future longitudinal research it might be interesting to explore the course of psychological distress and medication adherence over time.

## 5 | CONCLUSION

In lung transplant patients, we found a high prevalence of symptoms of depression and anxiety. Recipients disclosed a high level of post-traumatic stress symptoms related to the transplantation and a high

prevalence of suicidal ideation. We also observed a high prevalence of medication non-adherence in both candidates and recipients, which may partly reflect our choice of our strict measurement instrument. After lung transplantation, higher levels of anxiety were related to better medication adherence. We presume that the fear for rejection, and thus dyspnoea-related fear, motivates lung transplant patients to be more adherent with medication. Dyspnoea, which is a common problem in patients with a chronic lung condition, may also be responsible for the high levels of anxiety before and after lung transplantation. We suggest more longitudinal research on the special role of anxiety and dyspnoea in lung transplant recipients in order to better understand the relation between anxiety and medication adherence and the underlying mechanism.

## 5.1 | Relevance to clinical practice

This study underscores the importance of systematic screening of psychological health and medication adherence after transplantation. Patients may hesitate to report serious mental health and non-adherence problems during consultation with their physician, unless they are explicitly invited to mention their psychological and behavioural issues. This is unfortunate since effective evidence based psychological treatment is available. Given the close relationship of the clinical nurse specialist with his/her patients, he/she can play a key role in identifying and addressing psychological and behavioural problems.


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### CONFLICT OF INTEREST

All authors have contributed to the manuscript and have approved the content of this manuscript. None of the authors has a conflict of interest. We received no funding for this study.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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