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data from a randomized controlled trial
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Factors affecting adherence to psychotropics in trauma-affected refugees: data from a randomized controlled trial

Hinuga Sandahl, Laura Glahder Lindberg, Erik Lykke Mortensen, Jessica Carlsson

ABSTRACT

Non-adherence to psychotropic drugs may reduce treatment effectiveness and may cause exacerbation of illness. Among migrant populations, studies have identified low adherence to psychotropic drugs. This study aimed to identify factors that were associated with the three basic components of adherence: non-initiation, non-implementation (blood sample), and discontinuation in a clinical sample of trauma-affected refugees diagnosed with posttraumatic stress disorder. The data for this study is derived from a randomized controlled trial (n = 108). Based on existing literature, individual sociodemographic and clinical candidate predictor variables that may affect the initiation, continuation, and implementation to psychotropics were selected as exposure variables. Logistic regression was used to assess the risk relation between non-initiation, non-implementation, discontinuation, and the individual sociodemographic and clinical factors. Three factors – level of education, turn-up rate for medical doctor sessions, and discomfort in relation to the psychotropics – were associated with non-initiation, non-implementation, or discontinuation. The relatively small sample size poses a limitation. Furthermore, factors not examined in the current study may have affected non-initiation, non-implementation, and discontinuation. The study identified level of education, turn-up rate for medical doctor sessions, and discomfort in relation to medicine as important factors in relation to treatment with psychotropics in trauma-affected refugees. Factors contributing to a low turn-up rate, and factors that are consequences of a low turn-up rate, as well as communication and trust in the patient-provider interaction need further research attention. Furthermore, there is a need for research on interventions addressing adherence for refugees with mental illness.

1. Introduction

The World Health Organization (WHO) estimates that merely 50% of patients with chronic illness are adherent to their prescribed medications (World Health Organization, 2003). The 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’ (World Health Organization, 2003). Adherence is crucial for the success of any treatment – not least psychotropic medication (Gast and Mathes, 2019).

Non-adherence to psychotropic drugs may reduce treatment effectiveness and may cause exacerbation of illness (Semahegn et al., 2020). It may result in inappropriate utilization of healthcare resources and is associated with higher use of emergency psychiatric services as well as a higher risk of and longer duration of hospitalization (Semahegn et al., 2020; Higashi et al., 2013). Furthermore, non-adherence may impact the patient’s quality of life and well-being (Pisani et al., 2022). A meta-analysis found non-adherence in 49% of patients with major psychiatric disorders (Semahegn et al., 2020).

Among migrant populations, studies have identified fewer initiators of psychotropic drugs after diagnosis of a mental illness, more frequent early discontinuation of treatment, and poor adherence to psychotropic drugs (Brendler-Lindqvist et al., 2014; Forcada et al., 2013; Kieseppa et al., 2022; Taipale et al., 2021; Lehti et al., 2021; van Geffen et al., 2009; Frecce et al., 2016; Wallach et al., 2014).

Refugees, who have been forcibly displaced from their country of origin, are a vulnerable population with a high prevalence of mental illness compared to host country populations (Priebe et al., 2016; Giacco
et al., 2018; Norredam et al., 2009; Bustamante et al., 2017; Kirmayer et al., 2011; Skamperlit, 2019; Nguyen et al., 2022). Despite the high prevalence of mental illness, studies on refugees show inappropriate use and underutilization of mental healthcare services in host countries, suggesting barriers in access to healthcare services (Satinsky et al., 2019) and a gap between the mental health needs of refugees and the treatment received (Kiesepa et al., 2022). A study of refugee youth has shown that refugees were at higher risk of discontinuing treatment with antidepressants after diagnosis of posttraumatic stress disorder (PTSD), depression, or anxiety compared with Swedish-born youth (Taipale et al., 2021). But overall, studies specifically on adherence, non-initiation, and discontinuation in refugees are scarce (Sacha et al., 2021; Bellamy et al., 2019; Kroll et al., 1990).

Factors that affect adherence have been categorized as individual, clinical, as well as healthcare system-related (Semahegn et al., 2020). The inclusion of meso and macro-level factors is particularly important in cross-cultural settings, where culturally shaped illness explanations and medical traditions are at play, and where economic and health inequalities affecting minority patients may impact adherence (Gault et al., 2019). A thorough investigation of factors affecting adherence to psychotropic drugs among refugees is vital to understand the complexity of facilitators and barriers to adherence in mental health care, and to design and develop effective treatment interventions for this specific, vulnerable population (Semahegn et al., 2020).

Most studies on adherence are based on register data. Register data allow an analysis of indirect adherence, based on medication dispensed from pharmacies (i.e. the number of packs prescribed), pick-up rate (initiation), and discontinuation rate. However, this method has some serious limitations regarding the measurement of adherence, as the assumption is that medication dispensed from pharmacies is actually taken and that prescription directions are accurately followed, thereby potentially overestimating adherence (Anghel et al., 2019). Medication dispersal is as such only a proxy measurement for adherence. It does not provide knowledge on whether the patient uses the medication and does not allow for an examination of possible causes of non-adherence.

Clinical studies provide other options for measuring adherence. WHO suggests Medication Event Monitoring System (electronic monitoring of bottle openings) as the standard measurement of adherence (World Health Organization, 2003; van den et al., 2011). Pill counts, self-report, healthcare provider/caregiver rating, and direct methods measuring drug or metabolite levels in blood or urine have been used in various clinical studies to measure adherence (El et al., 2016).

Analysis of quantitative data from clinical studies may provide knowledge regarding the three basic components of adherence - initiation, implementation, and discontinuation (Vrijens et al., 2012) - and further insight regarding important factors influencing adherence at the patient level. Qualitative studies may provide a better understanding of factors, such as diverging explanatory models of illness, cultural belief systems, and treatment preferences in the patient-provider interaction as well as an insight into the patients’ everyday-life practices with medicine.

In a randomized controlled trial (RCT) on trauma-affected refugees performed at the Competence Centre for Transcultural Psychiatry (CTP), blood samples measuring concentration of psychotropic medication were taken after 2–3 months of treatment and at the end of the treatment course. Blood samples showed that respectively 46 % and 52% of the group of participants that the medical doctor had registered as taking the agreed recommended psychotropic medication did not take this medication (Sandahl et al., 2021). This around 50% discrepancy between registration from the medical doctor concerning the agreed recommended psychotropic medication and the direct measure of the concentration of the psychotropic in a blood sample calls for further analysis of the complex factors that impact adherence in trauma-affected refugees.

The data for the current study is derived from the above-mentioned RCT and is part of an explanatory sequential mixed-method design. The larger mixed-methods study on adherence will explore personal and contextual factors at the individual patient level, at the clinical level, at the patient-provider interaction level as well as at the healthcare system level. The present quantitative analysis focuses on sociodemographic and clinical factors. In a second phase, this analysis will be supplemented with in-depth qualitative patient interviews as well as observations of patient-provider encounters, to further explore cultural and behavioural factors of non-adherence.

Our choice of the mixed-method design is driven by a need for a more comprehensive and thorough understanding of the multitude of factors affecting adherence, including the patient perspectives.

As a foundation for the subsequent qualitative study, this current study aimed to identify factors that were associated with adherence in a clinical sample of trauma-affected refugees diagnosed with PTSD. Specifically, we aimed to identify sociodemographic and clinical factors that were associated with the three basic components of adherence: non-initiation, non-implementation, and discontinuation.

Our ambition with the mixed-method study was to inform the development of patient-centered interventions for refugees with mental illness that can be implemented in clinical settings in order to enhance treatment outcomes.

2. Methods

2.1. Study design and participants

The data for the current study is derived from an RCT (n = 108) performed at the CTP in the period 2016–2019 (Sandahl et al., 2017, 2021). The RCT was approved by the Ethics Committee of the Capital Region of Denmark (H-15014503), the Danish Medicines Agency (EudraCT: 2015-004153-40) and the Danish Data Protection Agency (2012-58-0004) and was registered at ClinicalTrials.gov ID (NCT02761161).

Participants were recruited, and data collected at CTP. All patients referred to CTP were screened in a 2-3-h pre-treatment assessment by a medical doctor. Patients received oral and written information about the study. If a patient was eligible to participate, the patient provided written informed consent for study participation at the pre-treatment assessment. Participants were adult refugees diagnosed with PTSD. The participants were randomised to mianserin (a sedative antidepressant) and/or Imagery Rehearsal Therapy, added to treatment as usual (TAU), compared to TAU alone. The sample for this current study consists of only participants randomised to treatment with mianserin (n = 108).

All participants received TAU, consisting of a 10–12-months treatment program including 16 sessions of psychotherapy, 8 sessions of physiotherapy, 1–2 sessions of social counselling, and 10 sessions of psychopharmacotherapy and psychoeducation. Psychotropics were provided free of cost at the clinic. Experienced interpreters were present in sessions, if needed, and during the conduction of ratings, as required. All written materials were available in Danish, English, Farsi, and Arabic.

Further details are presented in the trial protocol (Sandahl et al., 2017), and the main results of the trial are presented in Imagery Rehearsal Therapy and/or mianserin in treatment of refugees diagnosed with PTSD: results from a randomized controlled trial (Sandahl et al., 2021).

2.2. Variable selection

2.2.1. Outcomes

In every session in the randomized controlled trial, the medical doctor interviewed the participant regarding the use of the antidepressant mianserin and registered whether the participant had initiated, continued, or discontinued the antidepressant mianserin as planned. After 2–3 months of treatment and at the end of the treatment course a blood sample was taken to measure the concentration of the
antidepressant mianserin. Implementation was defined as a plasma level of the antidepressant mianserin above 0. If the participant had informed the medical doctor that medication had been discontinued blood sample was not taken due to ethical reasons. In the current study, the following four binary variables were chosen as outcome variables: non-initiation/ initiation, non-implementation/implementation (for blood samples 1 and 2 respectively), and discontinuation/continuation.

2.2.2. Exposure variables

Based on existing literature we selected several individual sociodemographic and clinical candidate predictor variables that may affect the initiation, implementation, and continuation of psychotropics. Individual sociodemographic variables for the patient included age, gender, education, affiliation to the labour market, number of years in Denmark, and the need for an interpreter (World Health Organization, 2003; Semahegn et al., 2020; Kieseppä et al., 2022; Frecceero et al., 2016; Wallach et al., 2014; Sacha et al., 2021; Schepers, 2006). Patient motivation for treatment and chronic pain were selected as baseline clinical factors (World Health Organization, 2003; Semahegn et al., 2020; Lewis et al., 2013; Stromme et al., 2021; Sonne et al., 2016).

Furthermore, we selected clinical factors related to the treatment course, including patient-reported discomfort in relation to medication and the turn-up rate to planned sessions with the medical doctor (World Health Organization, 2003; Semahegn et al., 2020; Kieseppä et al., 2022).

Sociodemographic information and baseline clinical data were collected in the initial assessment interview by a medical doctor. Motivation and chronic pain were assessed by the medical doctor with an index (the CTP Predictor Index (Sonne et al., 2016)) developed by clinical researchers at CTP with the purpose of assessing predictors of treatment outcomes. With the CTP predictor index, the medical doctor assessed five potential predictors with a score ranging from 0 to 4 on a Likert scale (4 being the best score) according to pre-defined criteria (please see Fig. 1) (Sonne et al., 2016). Only two of the five predictors, namely motivation and chronic pain, were deemed relevant and thus chosen for analyses in the current study. Turn-up to sessions was documented and information regarding discomfort to medication was collected throughout the study period.

2.2.3. Statistical analysis

To describe the sample characteristics, means, and standard deviations were calculated for continuous variables, and percentages were calculated for categorical variables. The proportion of participants showing non-initiation, non-implementation, and discontinuation was reported.

Logistic regression was used to assess the risk relation between non-initiation, non-implementation, and discontinuation and the individual sociodemographic and clinical factors. The Odds Ratio (OR) and its 95% CI were calculated (with a significance level of 5%). Data were analysed using STATA 17.0.

3. Results

The sociodemographic characteristics of the participants are shown in Table 1. Participants had a mean age of 43 years, and a mean length of stay in Denmark of 12 years. The participants originated from many different countries among other Syria, Iraq, Afghanistan, Iran, and Lebanon.

A total of 51% were women; 61% needed a language interpreter in sessions with the medical doctor; 33% had an affiliation with the labour market or were students; and 39% had an education level above primary school. Concerning clinical factors 41% experienced discomfort in relation to the psychotropics, the participants had a mean chronic pain score of 1.88 (0–4, 4 being the best score indicating low levels of pain), a mean motivation score of 3.41 (0–4, 4 being the highest motivation score), and a turn-up rate of 0.68.

The overall incidence of non-initiation of psychotropics was 6% (7/101). The incidence of non-implementation in blood sample 1 was 46% (31/37), and 52% (24/22) in blood sample 2. The incidence of

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motivation</td>
<td>The patient clearly expresses no interest in treatment or feels compelled to seek treatment e.g., by public bodies.</td>
<td>The patient expresses great doubt regarding treatment efficacy or concerns about practical issues such as transport, and therefore has limited motivation for starting treatment.</td>
<td>The clinician and/or the patient doubts whether treatment has interest. Perhaps the patient expresses motivation for trying out treatment but doubts that it will help.</td>
<td>The patient clearly expresses a desire for change and hope regarding treatment with certain reservations, e.g., a bit of scepticism about some parts of the treatment.</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>Has &gt; 2 years suffered such severe pain that it constitutes a significant interference with daily life, preventing the patient from coping with shopping, cooking, etc.</td>
<td>Has &gt; 2 years had constant pain in many parts of the body and/or constant severe headache, but yet still cope with activities of daily living.</td>
<td>Has moderately bothered by pain but the duration or scope is less than 0 and 1.</td>
<td>Has only limited pain problems in a single area of the body, such as a knee or hip, and no significant reduction of functional capacity.</td>
</tr>
</tbody>
</table>

Fig. 1. CTP predictor Index.
treatment initiation compared to 41.5% of Swedish-born youth (Taipale Health Organization, 2003; Semahegn et al., 2020). In a meta-analysis of patients with major psychiatric disorders (World Health Organization, 2008), the discontinuation rate was 49%. However, the low implementation rate of around 50% correlated with adherence: non-initiation, non-implementation, and discontinuation. Participants who had educational levels above primary school were less prone to non-implementation. Participants who reported discomfort in relation to psychotropics were more prone to discontinuing their psychotropics (OR 613.58, p < 0.001). Turn up rate to sessions with the medical doctors was associated with higher discontinuation (OR 278.01, p < 0.055). Participants who reported discomfort in relation to psychotropics 

### Table 1

<table>
<thead>
<tr>
<th>Characteristics of sample.</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)¹</td>
<td>42.73 (10.12)</td>
</tr>
<tr>
<td>Years since arrival in Denmark²</td>
<td>12.33 (9.50)</td>
</tr>
<tr>
<td>Female³</td>
<td>55 (51)</td>
</tr>
<tr>
<td>Male³</td>
<td>53 (49)</td>
</tr>
<tr>
<td>Psychosocial status</td>
<td>61 (67)</td>
</tr>
<tr>
<td>Needing interpreter during medical doctor sessions⁴</td>
<td>33 (37)</td>
</tr>
<tr>
<td>Affiliation to the labor market/studying⁴</td>
<td>39 (40)</td>
</tr>
<tr>
<td>Education above primary school⁴</td>
<td>41 (50)</td>
</tr>
<tr>
<td>Discomfort in relation to psychotropics⁴</td>
<td>0.68 (0.19)</td>
</tr>
<tr>
<td>Motivation for treatment⁴</td>
<td>3.41 (0.75)</td>
</tr>
<tr>
<td>Chronic pain⁴</td>
<td>1.88 (1.10)</td>
</tr>
</tbody>
</table>

SD, standard deviation. Motivation and chronic pain assessed on CTP predictor Index (0–4, 4 being the best score). Turn up rate calculated as number of sessions attended/number of sessions planned.

Discontinuation was 49% (50/49). See Table 2.

Several factors were associated with higher or lower odds of non-initiation, non-implementation, or discontinuation, see Table 3. Education above primary school was associated with lower odds of non-implementation in blood sample 1 (OR 0.25, p = 0.015). A low turn-up rate to sessions with the medical doctors was associated with higher odds of non-initiation (OR 613.58, p = 0.001) and with a higher risk of non-implementation in blood sample 2 (OR 278.01, p = 0.055). Participants who reported discomfort in relation to the psychotropics were more prone to discontinuing their psychotropics (OR 5.21, p = 0.001).

### 4. Discussion

This study identified three factors – level of education, turn-up rate, and discomfort in relation to the psychotropics – that were associated with adherence: non-initiation, non-implementation, and discontinuation. Participants who had educational levels above primary school were less prone to non-implementation. Participants who had a low turn-up rate to sessions with their medical doctor were more likely to not initiate psychotropics and of non-implementation. Participants who reported discomfort in relation to the psychotropics were more likely to discontinue the prescribed psychotropics.

The study identified a non-implementation rate of respectively 46% and 52% for blood samples 1 and 2 in this sample of trauma-affected refugees diagnosed with PTSD. Furthermore, the discontinuation rate was 49%. However, the low implementation rate of around 50% corresponds to the rate reported by the WHO concerning adherence to treatment against chronic illness as well as the adherence rate reported in a meta-analysis of patients with major psychiatric disorders (World Health Organization, 2003; Semahgen et al., 2020).

A register-based study has shown that 68.7% of refugee youth discontinued antidepressant treatment during the first six months after treatment initiation compared to 41.5% of Swedish-born youth (Taipale et al., 2021), and a clinical study has shown non-adherence in 53% of refugees in treatment with antidepressants in the USA (Kroll et al., 1990). No other studies with a refugee sample are available for comparison regarding the rates of non-initiation, non-implementation or discontinuation (Taipale et al., 2021). A few studies have examined different aspects of treatment with psychotropics in diverse migrant populations. A study found that 70.5% of migrants compared to 61.2% of natives in Spain withdrew less than 80% of prescribed antidepressants from the pharmacy over a four month period (Cruz et al., 2012). Two studies on antipsychotics found, respectively, that 34.4% of a migrant population in Finland discontinued antipsychotic medication during the first year after being diagnosed with a psychotic disorder (Lehti et al., 2021), and that 80.9% of a migrant population in Spain withdrew less than 80% of their prescribed antipsychotic drugs from the pharmacy (Forcada et al., 2013). One key difference between the three above-mentioned studies and the current study is that psychotropics in our study were provided free of cost at the clinic. The fact that there was no out-of-pocket expense for the participants diminished possible financial barriers to acquiring psychotropics. The fact that medication was delivered at the treatment facility reduced other potential barriers related to purchasing psychotropics at a pharmacy, such as transportation issues or stigma. Possible factors related to non-initiation, non-implementation, and discontinuation identified in the current study will be discussed below.

#### 4.1. Individual sociodemographic factors and non-initiation, non-implementation and discontinuation

Looking at individual sociodemographic factors, this study did not find that factors specifically related to the participants’ refugee background, such as the number of years since arrival in Denmark or the need for interpretation in sessions with a medical doctor, were associated with non-initiation, non-implementation, or discontinuation. These results are divergent from the following previous studies, where a short duration of formal residency in Sweden was associated with a higher frequency of discontinuation among refugee youth (Taipale et al., 2021); where rates of dispensed psychotropic drugs among refugees increased with duration of residence among adults in Sweden (Brendler-Lindqvist et al., 2014); or where a shorter length of residency in Finland was associated with a higher frequency of discontinuation among migrants (Kiesseppi et al., 2022; Lehti et al., 2021). These findings of an association between high frequencies of discontinuation and short durations of stay in reception countries in refugee and migrant populations have been explained by barriers in access to health care services. These barriers, including low levels of knowledge regarding the organization of the health care system as well as economic barriers, are likely to be more dominant in newly arrived refugees. Likewise, it is possible that more time in the reception country will increase refugees’ knowledge about the health care system and their language skills and that cultural differences regarding concepts and explanatory models for health and illness may diminish (Brendler-Lindqvist et al., 2014). Some of the above-mentioned barriers related to economy and language may have been eliminated in our study where psychotropics were provided free of cost at the clinic and interpreters were present free of cost for the patient. Furthermore, participants in our study had a mean of 12 years of stay in Denmark. This fairly long duration of stay in Denmark could have shaped the participants’ cultural understandings of health and illness towards that of the Danish medical doctors. It is known, that low cultural congruence and impaired communication and understanding between patient and medical doctor may cause misdiagnosis (Schim et al., 2021).

### Table 2

<table>
<thead>
<tr>
<th>Non-initiation, non-implementation, and discontinuation.</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-initiation (n = 108)</td>
<td>7 (6)</td>
</tr>
<tr>
<td>Non-implementation blood sample 1 (n = 68)⁴</td>
<td>31 (46)</td>
</tr>
<tr>
<td>Non-implementation blood sample 2 (n = 46)⁴</td>
<td>24 (52)</td>
</tr>
<tr>
<td>Discontinuation (n = 101)</td>
<td>50 (49)</td>
</tr>
</tbody>
</table>

¹ Data only available for participants registered to take medication.

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1 In our study, participants were exempted from the amendment to the Danish Health Care Act passed in 2018 making it a requirement for patients not proficient in Danish to pay for interpretation services in health care settings (Ældreministeriet, 2018).
Doorenbos, 2010), which may lead to incorrect treatment plans, ineffective prescription of psychotropics, and thus a lack of health improvements which can contribute to non-adherence (Forcada et al., 2013; Cruz et al., 2012) and poorer treatment (Davidsen et al., 2022). Consequences related to impaired mutual understanding caused by a lack of trained interpreters, which is seen in other studies, may have been reduced in our study.

In line with the previously mentioned study on refugee youth, our study did not find that age, gender, and attachment to the labour market (work disability in the refugee youth study) were associated with discontinuation (Taipale et al., 2021). Education above primary school, however, was associated with a lower probability of discontinuation (Taipale et al., 2021). Education above primary school, motivation and chronic pain assessed on CTP predictor Index (0 = 2, continuous variable. Non-initiation/initiation coded 0/1, Non-implementation/implementation coded 0/1, Discontinuation/continuation coded 0/1 (b), binary variable, coded yes = 1, no = 2(c), continuous variable.

Motivation and chronic pain assessed on CTP predictor Index (0–4, 4 being the best score). Turn up rate calculated as number of sessions attended/number of sessions planned. Statistically significant correlations are indicated in bold and *. Treatment in a mental health unit; to the patients’ social surroundings such as competing obligations or a lack of supportive network; and to a societal level, such as geographic availability of health services and public transportation costs. A low turn-up rate may also reflect factors in the patient-provider interaction, such as diverging explanatory models of illness and treatment preferences and, lack of mutual trust in the encounter. In addition to factors that cause a low turn-up rate, the consequences of a low turn-up rate are less time to establish rapport and a trustful relations and to discuss explanatory models of illness and treatment preferences, and less time for the medical doctor to provide thorough information regarding psychotropics as well as on potential discomfort and side effects the patient should expect in relation to treatment. These consequences highlight the importance of discussing turn-up with patients to identify and anticipate possible modifiable factors impacting turn-up for the individual patient.

Motive was not significantly associated with non-initiation, non-implementation or discontinuation in this study. We have not identified other studies examining motivation as a predictor of non-initiation, non-implementation, or discontinuation in a refugee or migrant population. However, interventions using motivational interviewing to improve adherence have shown promising effects for improving antidepressant adherence in different populations (Vannachavee et al., 2016a; Higgins et al., 2004a; Interian et al., 2013). These interventions have focused on, among other things, concerns regarding antidepressant treatment, exploring previous episodes of non-adherence, anticipations, and barriers to adherence, as well as the patient’s motivation to overcome symptoms (Interian et al., 2013; Vannachavee et al., 2016b; Higgins et al., 2004b). Research is needed on interventions using motivational interviewing in the specific population of trauma-affected refugees.

Discomfort in relation to the psychotropics was associated with higher odds of discontinuation and borderline associated with a higher likelihood of non-adherence. This replicates findings from a meta-analysis on adherence to psychotropics, identifying numerous studies showing an association between non-adherence and psychotropic-related side-effects (Semahgcn et al., 2020). Likewise, a study of refugees in the USA found an association between side-effects and non-adherence/discontinuation and suggests that refugees tend to react to early side-effects to psychotropics by discontinuing rather than

### Table 3

<table>
<thead>
<tr>
<th>Non-initiation</th>
<th>Non-implementation 1</th>
<th>Non-implementation 2</th>
<th>Discontinuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR [95% CI]</td>
<td>OR [95% CI]</td>
<td>OR [95% CI]</td>
<td>OR [95% CI]</td>
</tr>
<tr>
<td>Age (c)</td>
<td>1.02 (0.94-1.09)</td>
<td>1.00 (0.95-1.05)</td>
<td>0.89 (0.80-1.02)</td>
</tr>
<tr>
<td>Male (b)</td>
<td>0.77 (0.63-1.35)</td>
<td>0.73 (0.91-3.26)</td>
<td>0.841 (0.52-5.40)</td>
</tr>
<tr>
<td>Years since arrival in Denmark (c)</td>
<td>1.04 (0.95-1.13)</td>
<td>0.407 (0.92-1.04)</td>
<td>0.472 (0.88-1.02)</td>
</tr>
<tr>
<td>Needing interpreter during medical doctor sessions (b)</td>
<td>1.25 (0.23-6.85)</td>
<td>0.797 (1.43 (0.45-5.54)</td>
<td>0.546 (1.17 (0.26-5.24)</td>
</tr>
<tr>
<td>Education above primary school (b)</td>
<td>0.74 (0.13-4.27)</td>
<td>0.739 (0.25 (0.08-0.77)</td>
<td>0.095* (0.59 (0.17-2.06)</td>
</tr>
<tr>
<td>Attachment to labour market/ studying (b)</td>
<td>0.55 (0.06-5.54)</td>
<td>0.614 (1.65 (0.56-4.88)</td>
<td>0.362 (0.77 (0.20-3.01)</td>
</tr>
</tbody>
</table>

**Clinical factors**

| Motivation for treatment (c) | 0.30 (0.04-2.30) | 0.248 (1.77 (0.83-3.77) | 0.138 (0.99 (0.45-2.20) | 0.985 (1.73 (0.95-3.14) |
| Chronic pain (c) | 0.73 (0.30-1.79) | 0.488 (1.53 (0.92-2.52) | 0.098 (1.32 (0.78-2.27) | 0.303 (0.98 (0.66-1.46) |
| Turn up rate for medical doctor sessions (c) | 613.58 | 0.001* (43.29) | 0.089 (279.01) | 0.055* (11.08) |
| Discomfort in relation to psychotropics (b) | – | – | 0.86 (0.29-2.48) | 0.776 (3.08 (0.81-1.16) |

| OR [95% CI] | OR [95% CI] | OR [95% CI] | OR [95% CI] |
| 0.86 (0.29-2.48) | 0.776 (3.08 (0.81-1.16) | 0.098 (5.21 (1.97-3.75) | 0.001* |

3. The level of education may reflect health literacy, defined as “knowledge, motivation, and competences to access, understand, appraise and apply health information in order to make judgements and take decisions in everyday life concerning health care” (Health Organization, 2013). Research is needed on the role of patients’ health literacy and equally on the cultural competencies of the health care providers who inform, obtain information from, and communicate with the patient. We hypothesise that interventions targeted at improving health care providers’ cultural competencies and refugee patients’ health literacy could positively influence adherence to psychotropics (Fox et al., 2022).

4.2. Clinical factors and non-initiation, non-implementation and discontinuation

In the current study, a low turn-up rate to sessions with the medical doctors was associated with higher odds of non-initiation and non-implementation. This finding replicates previous studies showing that turn-up rate and continuity in care are significantly related to adherence in treatment with psychotropics in migrant populations (Forcada et al., 2013; Lehtih et al., 2021). Qualitative studies could provide insight into the causes and consequences of a low turn-up rate. We hypothesise that the low turn-up rate may reflect barriers to accessing treatment facilities. Such barriers could be ascribed to the individual patient level, such as cognitive difficulties, severity of symptoms, or lack of motivation for
brining up the side-effects with the prescribing medical doctor (Kroll et al., 1990). Furthermore, the above-mentioned study suggested that the refugee population has difficulties in finding adequate and precise words for describing and separating side-effects from somatic complaints related to their mental illness, such as fatigue, weakness, and dizziness (Kroll et al., 1990). As discussed above regarding the low turn-up rate, the reasons for not discussing side-effects with the prescribing medical doctor may be based on miscommunication or lack of trust in the patient-provider interaction. These aspects need further studying.

The second qualitative part of the current mixed method study will consist of interviews with patients and observations of patient-provider encounters addressing specific factors and problem areas identified in the quantitative results. Factors contributing to a low turn-up rate, and factors that are consequences of a low turn-up rate, as well as communication and trust in the patient-provider interaction all require attention.

4.3. Strengths and limitations

The main strength of the current study is the longitudinal design of a clinical study and the combined use of clinical reports and blood samples to measure adherence: initiation, implementation and discontinuation.

Several limitations in the study need attention. Despite the longitudinal design of the study, the causal direction of associations needs to be interpreted with caution. The small sample size poses a limitation, which needs to be considered when interpreting the results. As discussed above regarding the turn-up rate, several factors not examined in the current study may have influenced the turn-up rate and thereby indirect adherence. Factors such as explanatory models of illness, cultural belief systems, and treatment preferences were not included in the current study. Presenting a limitation. However, these complex factors will be studied in the second qualitative part of the current mixed method study.

The RCT was not designed to collect data regarding reasons for non-initiation, non-implementation or discontinuation to treatment with psychotropics and some important aspects may not have been discussed based on the available data in the current study. Furthermore, the data collected regarding motivation for treatment was general and not specific on motivation for treatment with psychotropics. This poses a limitation regarding the interpretation on the role of motivation.

Lastly, the participants provided informed consent to participate in an RCT, and despite the pragmatic design of the RCT, factors related to the exclusion of participants who did not wish to participate in a trial with psychotropics may have impacted initiation, implementation, and continuation.

5. Conclusion

We identified a non-implementation rate of approximately 50% in this sample of trauma-affected refugees diagnosed with PTSD. WHO emphasises that interventions improving adherence “may have a far greater impact on the health of the population than any improvement in specific medical treatments.” (World Health Organization, 2003) There is a need for research on interventions addressing adherence for refugees with mental illness - interventions with a goal of not simply improving adherence but providing a platform for a trustful dialogue, which allows the patient to make decisions based on the knowledge provided and their own preferences. Further research on interventions addressing health literacy, motivation, shared decision-making, and cultural competencies is needed.

We identified the level of education, turn-up rate, and discomfort in relation to medicine as important factors in relation to treatment with psychotropics in trauma-affected refugees. These results raise several questions that need attention and prompt a need for further research.

Author statement

Hinuga Sandahl, Laura Glahder Lindberg and Jessica Carlsson designed and conducted the study. Hinuga Sandahl performed the statistical analysis and wrote the first draft of the manuscript. Erik Lykke Mortensen advised on methodological and statistical issues. All authors contributed to and have approved the final manuscript.

Data statement

The data supporting the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy and ethical restrictions.

Declaration of competing interest

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