Journal of Affective Disorders 299 (2022) 528–535

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Antidepressant use among immigrants with depressive disorder living in Finland: A register-based study

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ARTICLE INFO

Keywords:
transients and migrants
antidepressive agents
depression

ABSTRACT

Background: : The aim of this study was to examine differences in the initiation and discontinuation of antidepressants between immigrants and the Finnish-born population diagnosed with depression in specialized health care.

Methods: : The study utilized register-based data, which includes all immigrants living in Finland at the end of 2010 and matched Finnish-born controls. For this study, we selected individuals who had received a diagnosis of depression during 2011–2014 (immigrants $n = 2244$, Finnish-born $n = 2773$). Their antidepressant use was studied for a one-year period from initiation. A logistic regression was used to predict initiation and a Cox regression was used to predict discontinuation.

Results: : Immigrants were more likely to initiate the use of antidepressants than the Finnish-born controls (adjusted OR = 1.25, 95% CI = 1.07–1.46), but they also discontinued the medication earlier than the Finnish-born controls (adjusted HR = 1.48, 95% CI = 1.31–1.68). Immigrants from Sub Saharan Africa, the Middle East and Northern Africa were most likely to discontinue antidepressants earlier. More severe depression, a longer length of residence in Finland and more intensive psychiatric treatment were associated with decreased risk of discontinuation.

Limitations: : The registers do not provide information on the perceived reasons for the discontinuation.

Conclusions: : Immigrants with depression initiate antidepressants more often than the Finnish-born population, but they also discontinue them earlier. Early discontinuation may be a sign of insufficient treatment suggesting that there could be a need for improvement in mental health care for immigrants in Finland.

1. INTRODUCTION

Immigrants, refugees in particular, are at high risk of developing depressive disorders(Bas-Sarmiento et al., 2017; Close et al., 2016; Fazel et al., 2005), although the prevalence rates have varied greatly between studies (Lindert et al., 2009). There are many factors which may predispose immigrants to depressive disorders, including problems in acculturation, possible traumatic background, and downward social mobility (Das-Munshi et al., 2012; Steel et al., 2009). In Finland, immigrants in general have a lower risk of being diagnosed with depression compared to the Finnish-born population, but immigrants of Middle Eastern and Northern African origin have a higher risk (Markkula et al.,

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https://doi.org/10.1016/j.jad.2021.12.071
Received 21 June 2021; Received in revised form 9 November 2021; Accepted 19 December 2021
Available online 22 December 2021

2017). Another Finnish study showed that immigrants of Kurdish origin, and immigrant women of Russian origin, have a notably higher risk of experiencing symptoms of depression as compared to the general population (Rask et al., 2016).

Antidepressant medication is a central form of treatment for depression. It has been shown to be effective especially for the treatment of severe depression (Fournier et al., 2010). According to the Finnish current care guidelines for depression, antidepressants should be continued for six months after the acute phase to prevent relapses, and maintenance treatment should be considered after three lifetime episodes (Depression: Current Care Guidelines Abstract, 2021).

Despite equal or higher levels of depression, many studies have shown that immigrants tend to initiate antidepressant medication less often than native populations (Brendler-Lindqvist et al., 2014; Cruz et al., 2010; Freccero et al., 2016; Taipale et al., 2021; Wallach-Kildemoes et al., 2014). Immigrants are also more likely to discontinue antidepressants (Cruz et al., 2012; Geffen et al., 2009; Hansen et al., 2004; Wallach-Kildemoes et al., 2014). However, the results have differed between different immigrant groups (Gimeno-Feliu et al., 2016; Termorshuizen et al., 2018). Immigrants of non-Western origin seem to use antidepressants less compared to other migrant groups (Cruz et al., 2010; Geffen et al., 2009). In a Norwegian study, refugees were more likely to use antidepressants compared to other immigrant groups (Straiton et al., 2017). A previous study from Finland reported that immigrants from the Nordic countries, North Africa and the Middle East were more likely to purchase antidepressants than the Finnish-born population, but immigrants from Russia and the former Soviet Union, Western countries, Sub Saharan Africa and Asia were less likely to purchase antidepressants (Lehti et al., 2020). Similar findings of a higher likelihood of purchasing antidepressants by immigrants from Northern Africa and the Middle East have been published in another Finnish study (Bosqui et al., 2019).

Many of the earlier studies have focused on specific ethnic groups (Brendler-Lindqvist et al., 2014; Termorshuizen et al., 2018; Wallach--Kildemoes et al., 2014), and have measured the use of antidepressant as a simple dichotomic variable not accounting for changes in the duration of the medication (Brendler-Lindqvist et al., 2014; Cruz et al., 2010; Freccero et al., 2016). They have also not been limited to individuals with diagnosed depression (Brendler-Lindqvist et al., 2014; Cruz et al., 2012, 2010; Hansen et al., 2004). Studies that examine the differences in the patterns of use of antidepressant medication in more depth between immigrants and native-born population are lacking.

2. Aims of the Study

The aim of this study is to examine differences in the patterns of antidepressant use between immigrants living in Finland and Finnish-born population diagnosed with depression in specialized health care. We aim to study differences in the initiation and the discontinuation of the use of antidepressants, and to study the factors related to the initiation and discontinuation of the antidepressants, including sociodemographic, treatment-related, and immigration-related factors.

3. METHODS

This study uses a register-based sample maintained by the Finnish Institute for Health and Welfare (THL). The study has been approved by the Ethics Committee of the THL (589/2013, 798/2018). The data-keeping organizations have given their permission for the use of confidential register data.

4. Sample

The original sample includes all immigrants who were over 15 years old and residents in Finland on December 31st, 2010 (n = 185 605) and Finnish-born controls (n = 185 605). Immigrants were identified from the Finnish Digital Agency by country of birth and mother tongue. Asylum seekers or recent migrants are not included since they lack the personal identity code which is necessary for the data linkages. The Finnish-born controls were matched by sex and age so that they were born in the same year and month as the studied migrants and matched by the municipality of residence on December 31st, 2010. Both cases and controls were followed until death, emigration, or December 31st, 2015.

For the present study, all the individuals who had received a diagnosis of a single episode of major depressive disorder (F32) or recurrent major depressive disorder (F33) in specialized health care between January 1st, 2011 and June 30th, 2014, and who had no prior diagnosis of a depressive disorder during the preceding four years, were included. In addition, we excluded all individuals who had received a diagnosis of manic episodes (F30), bipolar disorder (F31) or schizophrenia, schizotypal, delusional, or other non-affective psychotic disorders (F20-F29) between 2011 and 2015. The psychiatric diagnoses were based on the 10th version of the International Classification of Diseases and Related Health Problems (ICD-10) criteria, which are used in Finland. This selection yielded a sample of 2244 immigrants and 2773 Finnish-born controls.

5. Background characteristics

The background characteristics included age, sex, marital status, socioeconomic status, region of origin, length of residence in Finland, severity of depression, psychiatric hospital treatment (yes/no) and the intensity of psychiatric treatment. Information on the socioeconomic status was derived from Statistics Finland and information on the other variables was derived from the Finnish Digital Agency. *Marital status* was classified into two groups: (1) married or in a registered partnership and (2) any another status (single, divorced, or separated, including those cohabiting without marriage or a registered partnership). The *socioeconomic status* was based on the occupation (or lack thereof) in 2010 and, in this study, it was classified into five groups: (1) entrepreneurs and farmers, (2) upper white-collar workers (such as leaders or experts), (3) lower white-collar workers (such as office workers), (4) blue-collar workers (manual work), and (5) any another status (people not in employment, such as students, the unemployed, homemakers, etc.).

The *region of origin* was classified into five groups: (1) the European Union/European Free Trade Association (EU/EFTA), United Kingdom, North America, and Australia, (2) Eastern Europe (including Russia and the former Soviet Union), (3) the Middle East and Northern Africa, (4) Sub Saharan Africa, and (5) Asia. The number of immigrants from other countries was so small that no separate category was formed for them, and they were thus excluded in the analyses related to the region of origin. The *length of residence in Finland* was classified into three groups: (1) less than five years, (2) five to fifteen years, and (3) over fifteen years.

The information on psychiatric diagnoses and psychiatric services was obtained from the hospital discharge register, which is maintained by THL. The *severity of depression* was based on a diagnosis and categorized into four groups: (1) mild (F32.0 and F33.0), (2) moderate (F32.1 and F33.1), (3) severe (F32.2 and F33.2) (4) psychotic (F32.3 and F33.3). If the severity was unspecified then the severity was coded as missing. The *hospital treatment* included information on whether or not the individual had received psychiatric hospital treatment during the year after the diagnosis was given and was coded as yes/no. The *treatment intensity* included information on treatment visits to psychiatric specialized health care units (possible hospital treatment periods were coded as one visit) during the year after the diagnosis. The number of visits to mental health care units, including the visit the diagnosis was given on, were categorized as follows: (1) *low intensity* (one to three visits), (2) *moderate intensity* (four to ten visits), and (3) *high intensity* (eleven visits or more). A description of the rationalization for this categorization can be found elsewhere.(Kieseppä et al., 2020). *Comorbidity* included the number of comorbid psychiatric diagnoses that were

given during 2011-2014. The following psychiatric diagnoses were included: (1) alcohol-use disorders (F10), (2) other psychoactive substance-use disorders (F11–F19), (3) other mood disorders (F34–F39), (4) phobic disorders and other anxiety disorders, and obsessive-compulsive disorders (F40–F42), (5) post-traumatic stress disorder (F43), (6) dissociative and somatoform disorders (F44–F45), (7) eating disorders (F50), (8) personality disorders (F60), and (9) mental disorder, not otherwise specified (F99).

6. Antidepressant medication

Information on the purchases of antidepressant medication was collected from the National Prescription Register, which is maintained by the Social Insurance Institution of Finland (Kela). All drugs in the ATC (Anatomical Therapeutic Chemical) class N06A were included. The antidepressants at initiation were categorized into the following groups: five separate medication groups: (1) mirtazapine (N06AX11), (2) serotonin-norepinephrine reuptake inhibitors (SNRIs) (N06AX16, N06AX17, N06AX21), (3) selective serotonin reuptake inhibitors (SSRIs) (N06AB), (4) tricyclics (N06AA04, N06AA06, N06AA09, N06AA10, N06AA12), and (5) other, as well as polytherapy (6) with at least two medication groups.

The medication had to be initiated at the earliest six months before the diagnosis was first given and at the latest six months after the diagnosis, as our aim was to study the antidepressant treatment period most likely associated with the depression diagnosis. There was no wash-out period associated with the medication use. We included medication initiated up to six months prior to the diagnosis because typically, antidepressant medication is prescribed already in primary care, and it can take several months before the person is diagnosed in specialized health care. If the medication had been initiated before the diagnosis, it was required that the participant was still using it at the moment the diagnosis was given. To ensure there was no immortal time bias, we also performed the analyses including all who had initiated the use of the medication at earliest six months before the diagnosis and at latest six months after the diagnosis. We followed up the medication use for 12 months after initiation. If during those 12 months the participant moved abroad, died or had over 90 days of hospital care, they were censored.

The duration of antidepressant medication use was modeled using the PRE2DUP method(Tanskanen et al., 2015). The method analyzes personal drug purchasing behavior separately for each ATC code by calculating sliding averages of the defined daily doses. The method takes into account hospital care periods (as drugs used during hospital care are not recorded in the register), stockpiling of drugs, variation in purchase events, and changing doses. Construction of drug use periods is controlled with expert-defined parameters for each drug package and these define clinically meaningful upper and lower limits for daily dose (i.e. gap in drug use is formed if daily dose drops below lower limit).

7. Statistical analysis

Chi-square tests of independence were used to study the effect of the immigrant status, sociodemographic factors, region of origin, length of residence and treatment-related factors on the duration of categorized antidepressant medication use. The effect of psychiatric comorbidity on the medication use was studied with a one-way analysis of variance. For these analyses, antidepressant use was divided into three categories: (1) did not initiate, (2) initiated but discontinued within 180 days, (3) initiated and continued over 180 days.

Binomial logistic regression models were used to predict the initiation of the medication with the explanatory variables of interest. We separately performed analyses with the entire sample, with a subsample including only the immigrants, and with a subsample including only the Finnish-born population. All the variables of interest were included in the models. In addition, we performed unadjusted analyses for each individual predictor separately. The results of the unadjusted analyses can be found in the supplementary material (Supplementary Table 1).

Cox regression models were used to predict the time to the discontinuation of the medication with explanatory variables of interest. Analyses were performed separately for the entire sample, for a subsample including only the immigrants, and for a subsample including only the Finnish-born population. All the predictors were included in the models. In addition, unadjusted analyses for each individual predictor were performed. The results of the unadjusted cox regression models can be found in the supplementary material (Supplementary Table 2).

The results of the analyses which include all individuals who initiated the use of antidepressants during the six months before a diagnosis are available in the supplementary material (Supplementary Tables 3-5). The trends of the results remained very similar.

8. RESULTS

Table 1 shows descriptive statistics of the sample by immigrant status. The immigrants were on average slightly older (mean age 37.4 years (SD = 12.9), vs. 35.0 years (SD = 12.3)), had a lower socioeconomic status and were more often married or in a registered partnership compared to the Finnish-born population. There were no gender differences between the immigrants and Finnish-born populations, but there were more women than men in both groups. Immigrants had more often more severe depression, received less intensive psychiatric treatment and had lower psychiatric comorbidity than the Finnish-born population. Both groups received most often SSRIs as the first medication, although Finnish-born more often than immigrants.

Table 2 shows the categorized initiation/duration of antidepressant medication according to different background characteristics. The immigrants both initiated and discontinued medication more often than the Finnish-born population. All the background characteristics of

Table 1
Descriptive characteristics by immigrant status

	Immigrant (%)	Finnish-born (%)	p
Sex (female)	1336 (59.5)	1674 (60.4)	0.570
Age			**<0.001**
15-29	735 (32.8)	1097 (39.6)	
30-44	862 (38.4)	1078 (38.9)	
45-59	572 (25.5)	525 (18.9)	
>60	75 (3.3)	73 (2.6)	
SES			**<0.001**
Entrepreneurs and farmers	113 (5.7)	135 (5.1)	
Upper white-collar workers	136 (6.8)	298 (11.3)	
Lower white-collar workers	279 (14.0)	725 (27.6)	
Blue collar workers	418 (21.0)	468 (17.8)	
Other (students, unemployed, etc.)	1046 (52.5)	1001 (38.1)	
Marital status (married/registered partnership)	973 (46.8)	787 (28.4)	**<0.001**
Severity of depression			**<0.001**
Mild	140 (8.5)	246 (11.9)	
Moderate	738 (44.7)	1065 (51.6)	
Severe	645 (39.1)	671 (32.5)	
Psychotic	127 (7.7)	83 (4.0)	
Hospital treatment (yes)	299 (13.3)	393 (14.2)	0.409
Treatment intensity			**<0.001**
Low	870 (38.8)	930 (33.5)	
Moderate	732 (32.6)	816 (29.4)	
High	642 (28.6)	1027 (37.0)	
Comorbidity (mean(sd))	0.57 (0.78)	0.77 (0.92)	**<0.001**
Antidepressant			**<0.001**
Mirtazapine	247 (18.9)	218 (14.9)	
SNRI	222 (16.9)	205 (14.0)	
SSRI	698 (53.3)	859 (58.7)	
Tricyclic	18 (1.4)	24 (1.6)	
Other	53 (4.0)	104 (7.1)	
2 or more	72 (5.5)	54 (3.7)	

Information on the sociodemographic variables is from 2010.

Table 2
Duration of antidepressant medication use by background characteristics (initiated -6/+6 months from the diagnosis).

	Did not initiate	Discontinued, < 180 days	Continued ≥180 days	p
Immigrant status (%)				**<0.001**
Immigrant	934 (41.6)	623 (27.8)	687 (30.6)	
Finnish-born	1309 (47.2)	492 (17.7)	972 (35.1)	
Sex (%)				**0.002**
Men	896 (44.6)	491 (24.5)	620 (30.9)	
Women	1347 (44.8)	624 (20.7)	1039 (34.5)	
Age (%)				0.266
15–29	812 (44.3)	442 (24.1)	578 (31.6)	
30–44	869 (44.8)	403 (20.8)	668 (34.4)	
45–59	496 (45.2)	236 (21.5)	365 (33.3)	
≥ 60	66 (44.6)	34 (23.0)	48 (32.4)	
SES (%)				**<0.001**
Entrepreneurs and farmers	94 (37.9)	68 (27.4)	86 (34.7)	
Upper white-collar workers	202 (46.5)	76 (17.5)	156 (35.9)	
Lower white-collar workers	434 (43.2)	180 (17.9)	390 (38.8)	
Blue collar workers	344 (38.8)	231 (26.1)	311 (35.1)	
Others	968 (47.3)	470 (23.0)	609 (29.8)	
Marital status (%)				**0.019**
Married or in a registered partnership	742 (42.2)	417 (23.7)	601 (34.1)	
Others	1426 (46.1)	654 (21.2)	1012 (32.7)	
Region of origin (%)				**<0.001**
EU/EFTA, North America, Australia	277 (44.0)	132 (21.0)	221 (35.1)	
Eastern Europe, Russia, former SU	230 (41.0)	148 (26.4)	183 (32.6)	
Middle East and Northern Africa	258 (38.6)	230 (34.4)	181 (27.1)	
Sub Saharan Africa	71 (48.3)	47 (32.0)	29 (19.7)	
Asia	71 (40.6)	47 (26.9)	57 (32.6)	
Length of residence (%)				**0.003**
< 5 years	309 (43.4)	212 (29.8)	191 (26.8)	
5-15 years	346 (40.4)	253 (29.5)	258 (30.1)	
>15 years	207 (38.3)	133 (24.6)	201 (37.2)	
Antidepressant (%)				**<0.001**
Mirtazapine		256 (55.1)	209 (44.9)	
SNRI		168 (39.3)	259 (60.7)	
SSRI		564 (36.2)	993 (63.8)	
Tricyclic		16 (38.1)	26 (61.9)	
Other		65 (41.4)	92 (58.6)	
2 or more		46 (36.5)	80 (63.5)	
Severity of depression (%)				**<0.001**
Mild	210 (54.4)	79 (20.5)	97 (25.1)	
Moderate	795 (44.1)	388 (21.5)	620 (34.4)	
Severe	468 (35.6)	301 (22.9)	547 (41.6)	
Psychotic	72 (34.3)	47 (22.4)	91 (43.3)	
Hospital treatment (%)				**<0.001**
No	1995 (46.1)	951 (22.0)	1379 (31.9)	
Yes	248 (35.8)	168 (24.3)	276 (39.9)	
Treatment intensity (%)				**<0.001**
Low	958 (53.2)	426 (23.7)	416 (23.1)	
Moderate	675 (43.6)	376 (24.3)	497 (32.1)	
High	610 (36.5)	313 (18.8)	746 (44.7)	
Comorbid diagnoses (mean(sd))	0.69 (0.88)	0.63 (0.85)	0.70 (0.86)	0.106

interest except age and psychiatric comorbidity were significantly associated with the initiation/duration of medication.

Table 3 shows the results of fully adjusted logistic regression models predicting initiation with immigrant status and the background characteristics of interest. The immigrant population were more likely to initiate antidepressant medication than the Finnish-born population (OR = 1.23, 95% CI = 1.05–1.43). Compared to those not in employment, blue collar workers were more likely to initiate medication. Those with more severe depression and those who had received hospital treatment were more likely to initiate medication. Those who received less intensive psychiatric treatment and those with higher psychiatric comorbidity were also less likely to initiate medication. Immigrants who had lived in Finland for less than five years were less likely to initiate medication compared to those who had lived in Finland for over fifteen years. Generally, the trends of the associations remained quite similar between the subsamples including only the immigrants and only the Finnish-born population. The results of the unadjusted regression models are available in the supplementary material (Supplementary).

Results of the fully adjusted Cox regression models predicting medication discontinuation are shown in Table 4. Immigrants were more likely to discontinue medication compared to the Finnish-born population (HR = 1.48, 95% CI = 1.31–1.68). Sociodemographic factors did not have any significant effects on discontinuation, except within the subsamples. Within the immigrant subsample, as compared to those not in employment, blue collar workers were more likely to discontinue the medication, and those who were married or in a registered partnership were less likely to discontinue the medication than those who were not. Within the Finnish-born subsample, lower white-collar workers were less likely to discontinue medication as compared to those not in employment.

When other antidepressants at initiation were compared to the SSRIs, mirtazapine (HR = 1.61, 95% CI = 1.37–1.90), SNRI (HR =1.28, 95% CI = 1.08–1.52) and the "other antidepressant" group (HR = 1.40, 95% CI = 1.09–1.80) were most likely to be discontinued. The effects were even stronger when only immigrants were considered, and nonsignificant (except for mirtazapine) when only Finnish-born were considered. The more severe the depression was, the less likely the participants were to discontinue the use of the medication, although these associations were not significant when only Finnish-born were considered. A lower number of psychiatric treatment visits predicted discontinuation significantly.

In the model including only the immigrants, different regions of origin were compared to Western countries. Immigrants from Sub Saharan Africa (HR = 1.83, 95% CI = 1.21–2.76) and the Middle East and Northern Africa (HR = 1.47, 95% CI = 1.13–1.92) were the most likely to discontinue the use of antidepressants. Immigrants who had lived in Finland for less than five years (HR = 1.53, 95% CI = 1.17–1.99)

Table 3
Initiation of antidepressant medication predicted by immigrant status and background characteristics.

	All OR (95% CI)	Only immigrants OR (95% CI)	Only Finnish-born OR (95% CI)
Immigrant status (ref. Finnish)			
Immigrant	**1.23 (1.05–1.43)**		
Sex (ref. Male)			
Female	0.86 (0.74–1.00)	0.91 (0.71–1.18)	**0.81 (0.66–0.98)**
Age (ref. 60 or more)			
15-29	1.14 (0.72–1.81)	1.29 (0.57–2.92)	1.00 (0.52–1.88)
30-44	0.91 (0.57–1.44)	1.30 (0.58–2.91)	0.67 (0.35–1.27)
45-59	0.83 (0.52–1.32)	1.08 (0.48–2.42)	0.63 (0.32–1.21)
SES (ref. not in employment)			
Entrepreneurs	1.38 (0.99–1.93)	1.32 (0.76–2.34)	1.49 (0.97–2.30)
Upper white-collar workers	1.09 (0.85–1.41)	0.66 (0.40–1.07)	**1.43 (1.04–1.98)**
Lower white-collar workers	1.16 (0.96–1.40)	1.34 (0.92–1.95)	1.17 (0.92–1.49)
Blue collar workers	**1.43 (1.17–1.75)**	**1.44 (1.04–2.00)**	**1.46 (1.11–1.93)**
Marital status (ref. others)			
Married	1.09 (0.93–1.27)	1.12 (0.87–1.45)	1.01 (0.82–1.25)
Region of origin (ref. Western countries)			
Eastern Europe, Russia, former SU		1.10 (0.79–1.54)	
Middle East and Northern Africa		1.37 (0.97–1.94)	
Sub-Saharan Africa		1.12 (0.64–1.98)	
Asia		0.98 (0.61–1.59)	
Length of residence (ref. > 15 years)			
< 5years		**0.65 (0.46–0.92)**	
5-15 years		0.94 (0.70–1.27)	
Severity (ref. Mild)			
Moderate	**1.41 (1.11–1.79)**	1.31 (0.83–2.06)	**1.50 (1.12–2.02)**
Severe	**1.65 (1.27–2.15)**	1.60 (0.99–2.59)	**1.74 (1.26–2.41)**
Psychotic	**1.52 (1.01–2.30)**	1.44 (0.76–2.75)	**1.89 (1.05–3.47)**
Hospital (ref. No)			
Yes	**1.56 (1.24–1.97)**	1.39 (0.95–2.06)	**1.71 (1.27–2.31)**
Treatment intensity (ref. high)			
Low	**0.53 (0.44–0.64)**	**0.47 (0.34–0.65)**	**0.57 (0.45–0.72)**
Moderate	**0.79 (0.66–0.94)**	**0.62 (0.46–0.84)**	0.94 (0.75–1.18)
Comorbidity	**0.90 (0.83–0.98)**	0.93 (0.79–1.10)	**0.87 (0.79–0.97)**

Adjusted Odds Ratios (ORs) and 95% Confidence Intervals (95% CI). All the variables were included in a single model (fitted separately for all and only immigrants). The unadjusted associations are reported in Supplementary table 1.

or five to fifteen years (HR = 1.30, 95 % CI = 1.04–1.63) were more likely to discontinue the use of antidepressants than those who had lived in Finland longer. The results of the unadjusted models are available in the supplementary material (Supplementary).

Table 4
Results of the fully adjusted Cox regression models predicting the discontinuation of antidepressant medication.

	All HR (95% CI)	Only immigrants HR (95% CI)	Only Finnish-born HR (95% CI)
Immigrant status (ref. Finnish)			
Immigrant	**1.48 (1.31–1.68)**		
Sex (ref. Male)			
Female	0.91 (0.80–1.03)	0.84 (0.69–1.02)	0.95 (0.80–1.14)
Age (ref. 60 or more)			
15-29	1.21 (0.83–1.77)	0.90 (0.46–1.73)	1.33 (0.77–2.29)
30-44	0.91 (0.62–1.33)	0.68 (0.35–1.32)	1.00 (0.57–1.73)
45-59	0.97 (0.66–1.43)	0.82 (0.43–1.59)	1.02 (0.58–1.80)
SES (ref. not in employment)			
Entrepreneurs	1.13 (0.88–1.47)	1.37 (0.93–2.01)	1.03 (0.72–1.49)
Upper white-collar workers	1.01 (0.81–1.26)	1.27 (0.83–1.94)	0.96 (0.72–1.28)
Lower white-collar workers	0.87 (0.74–1.03)	1.23 (0.93–1.64)	**0.78 (0.63–0.98)**
Blue collar workers	1.04 (0.88–1.21)	**1.40 (1.11–1.76)**	0.90 (0.71–1.14)
Marital status (ref. others)			
Married	0.90 (0.79–1.02)	**0.81 (0.67–0.99)**	0.84 (0.69–1.02)
Antidepressant (ref. SSRI)			
Mirtazapine	**1.61 (1.37–1.90)**	**1.67 (1.32–2.12)**	**1.51 (1.19–1.90)**
SNRI	**1.28 (1.08–1.52)**	**1.47 (1.14–1.89)**	1.05 (0.82–1.35)
Tricyclic	1.27 (0.77–2.09)	1.04 (0.43–2.55)	1.48 (0.81–2.72)
Other	**1.40 (1.09–1.80)**	**1.71 (1.11–2.65)**	1.26 (0.91–1.74)
2 or more	1.09 (0.81–1.47)	1.01 (0.65–1.59)	1.16 (0.77–1.75)
Severity (ref. Mild)			
Moderate	**0.79 (0.64–0.98)**	**0.67 (0.47–0.96)**	0.89 (0.67–1.17)
Severe	**0.79 (0.63–0.99)**	**0.62 (0.43–0.90)**	0.89 (0.66–1.21)
Psychotic	**0.66 (0.47–0.92)**	**0.47 (0.28–0.78)**	0.76 (0.46–1.25)
Hospital (ref. No)			
Yes	0.99 (0.83–1.19)	0.97 (0.73–1.29)	1.11 (0.87–1.40)
Treatment intensity (ref. High)			
Low	**1.63 (1.39–1.91)**	**1.73 (1.35–2.22)**	**1.49 (1.20–1.85)**
Moderate	**1.43 (1.24–1.65)**	**1.41 (1.12–1.76)**	**1.36 (1.12–1.66)**
Comorbidity	0.99 (0.92–1.06)	1.00 (0.89–1.13)	0.97 (0.89–1.07)
Region of origin (ref. Western)			
Eastern Europe, Russia, former SU		1.29 (0.99–1.68)	
Middle East and Northern Africa		**1.47 (1.13–1.92)**	
Sub-Saharan Africa		**1.83 (1.21–2.76)**	
Asia		1.20 (0.83–1.74)	
Length of residence (ref. > 15 years)			
< 5years		**1.53 (1.17–1.99)**	
5-15 years		**1.30 (1.04–1.63)**	

Adjusted Hazard Ratios (HRs) and 95% Confidence Intervals (95% CI). All the variables were included in a single model (fitted separately for all and only immigrants). The unadjusted associations are reported in Supplementary table 2.

9. DISCUSSION

In general, immigrants with depression initiated antidepressant medication more often than the Finnish-born population, but they also discontinued the medication earlier than the Finnish-born population. Approximately half of the immigrants who initiated antidepressants stopped the medication within six months of the initiation, whereas approximately a third of the Finnish-born population stopped medication within six months of the initiation. Immigrants from Sub Saharan Africa and the Middle East and Northern Africa were most likely to discontinue the medication early. More severe depression, a longer length of residence in Finland and more intensive psychiatric treatment made discontinuation less likely.

Adequate treatment of depression includes psychotherapy and/or antidepressant medication, so a lack of the use of antidepressants does not necessarily imply less adequate treatment. However, the early discontinuation of medication can increase the risk of recurrence of the symptoms(Kato et al., 2021). In addition, the role of medication is more central the more severe the depression is, and individuals who have been referred to specialized health care typically have more severe symptoms. In our sample, immigrants generally had more severe depression than the Finnish-born population. It is also known that immigrants receive less psychotherapy than Finnish-born individuals(Castaneda et al., 2020), and also in our sample earlier discontinuation was associated with less psychiatric treatment. This indicates that the high discontinuation rates among immigrants might be a sign of insufficient treatment.

In general, women discontinued antidepressants less often than men. Blue collar workers and entrepreneurs and farmers initiated the medication and discontinued it within six months from initiation more often than others. Interestingly, we did not find any association between age and initiation or discontinuation of antidepressant medication.

The risk of discontinuation was especially high among immigrants from the Middle East, Northern Africa and Sub Saharan Africa. Other studies have shown that immigrants from the Middle East and Northern Africa purchased antidepressants more often than the Finnish-born population(Bosqui et al., 2019; Lehti et al., 2020). So even though these immigrants initiated antidepressant medication more often than others, the initiation led to earlier discontinuation.

Similar findings of low antidepressant use among immigrants from these areas have been reported in other studies. A Swedish study found that refugees from the Middle East and Africa used less antidepressants than the Swedish-born population, although the effect decreased with the time from immigration(Brendler-Lindqvist et al., 2014), similarly as we found. Studies from Spain have shown that immigrants from Sub Saharan Africa consume less antidepressants (Cruz et al., 2010) and quit antidepressant medication more quickly than others (Cruz et al., 2012). A study from Denmark found that non-Western immigrants were more likely to discontinue antidepressant medication prematurely than the general population (Wallach-Kildemoes et al., 2014).

Those who started with mirtazapine or SNRIs were more likely to discontinue the medication compared to those who started with SSRIs. The effects were even stronger when only immigrants were considered. This could result from the fact that these drugs are not only prescribed to treat depressive symptoms but also insomnia and pain symptoms. Previous studies have shown that SSRI medication is typically least likely to be discontinued (Sundell et al., 2013). Several studies have reported tricyclic medication to be the most likely to be discontinued (Hansen et al., 2004; Sundell et al., 2013). We did not observe such association here, but it should be noted that in our sample tricyclics were very rarely prescribed: only 24 of the Finnish-born population (1.6%) and 18 immigrants (1.4%) received tricyclics.

10. What causes the discontinuation of the antidepressants?

There are many possible reasons for the earlier discontinuation of antidepressants among immigrants. One explanation could be less severe symptoms. An earlier Finnish study showed that immigrants of Kurdish origin, and immigrant women of Russian origin, have a notably higher rate of clinically significant depressive symptoms compared to the general population (Rask et al., 2016), and a study on the health of asylum seekers in Finland had similar findings: refugees from the Middle East and Africa had especially high levels of significant depressive symptoms (Skogberg et al., 2019). As these were the groups with the highest discontinuation rates, lower symptom levels are unlikely to explain the earlier discontinuation. We have also found that these same immigrant groups receive less intensive psychiatric treatment when accessing psychiatric specialized health care (Kieseppä et al., 2020), which suggests that there is a gap between the mental health needs and the treatment received.

Another explanation could be the cost of the medication. In Finland, the Social Insurance Institution provides reimbursements for medicine expenses, but it does not cover the total cost (the basic reimbursement level was 35-40% during the study period until the maximum annual co-payment of around 600-700 €). Co-payment could be a more significant barrier for immigrants, as in our sample immigrants had a lower socioeconomic status compared to the Finnish-born population—although the effect of socioeconomic status on discontinuation was unclear. The discontinuation of antidepressants was associated with a low socioeconomic status in a Danish study of general practice patients (Hansen et al., 2004) and with a lower level of education in Sweden (Sundell et al., 2013).

Different conceptions of depression and appropriate treatment for it could also lead to discontinuation. There is some evidence that there are more negative attitudes towards psychopharmacology among ethnic minorities (Thorens et al., 2008). A study from the United States found that ethnic minorities, particularly African Americans, preferred psychotherapy over medication as treatment for depression and antidepressant medication was often believed to be addictive(Givens et al., 2007). An Australian study comparing the accounts of depression and appropriate treatments for it between the Australian-born population and East-African refugees with depressive symptoms found that depression was viewed quite differently in these groups: the African-born participants stressed the importance of social and structural factors and believed social-based solutions to be most effective in treating depression, whereas the Australian-born population believed depression to be something inherently individual (Kokanovic et al., 2008). A Ugandan study on conceptions of depression among lay people found that depressive symptoms were typically recognized as “illness of thoughts”, which was not believed to be treatable by Western medicine (Okello and Ekblad, 2006).

Difficulties could also arise in the health care system. A qualitative study from Sweden focusing on general practitioners’ experiences of treating foreign-born patients highlights difficulties in recognizing, understanding and treating depressive symptoms among individuals with a different cultural background(Lehti et al., 2009). Antidepressant medication was found to be less beneficial among the foreign-born population than among Swedish-born patients, yet medication was still prescribed as many of the doctors felt they lacked other tools to treat the patients’ distress. Our finding of Middle Eastern and Northern African immigrants both initiating and discontinuing antidepressants at a high rate could reflect problems in communication between the patient and the clinician, or even misdiagnosis.

Another explanation for the discontinuation could be adverse side effects from the antidepressants. There is some evidence that there are genetic differences between different ethnic groups in response to pharmacotherapy (Schraufnagel et al., 2006). This could lead to differences in sensitivity and efficacy of psychotropic drugs. It is possible that some ethnic groups might experience stronger side effects from the

antidepressants, which could lead to discontinuation, especially if the risk of the side effects has not been discussed with the patient.

As antidepressant medication should be continued for at least over six months to ensure its efficacy, early discontinuation can be a sign of insufficient treatment. Discontinuation might reflect cultural issues, such as different conceptions of and attitudes towards depression and psychotropic medication, or structural issues, such as the high cost of the medication or a lack of cultural competence among mental health care professionals. The results indicate that there may be a need for improvement in the mental health care of immigrants. More research is needed to investigate the causes of the discontinuation of antidepressants among immigrants living in Finland.

11. Strengths and limitations

The strengths of this study include the large quantity of nation-wide register-data which covers all immigrants living in Finland at the end of 2010, so there is no selection bias. The PRE2DUP method allowed us to model the duration of antidepressant use reliably for different antidepressant groups. By limiting this study to participants who were diagnosed with depression we were able to study the use of antidepressants specifically for the treatment of depression.

There are several limitations associated with this study. We had no information on possible psychotherapy received aside or instead of antidepressants, so conclusions about the adequacy of the treatment cannot be drawn. In addition, we did not have any information on the participants' perceived reasons for the discontinuation, which limits us from drawing further conclusions about the mechanisms behind these patterns.

12. Author Statement

12.1. Funding

This work has been supported by grants from Juho Vainio Foundation and Social Insurance Institution of Finland. Minna Holm was supported by a grant from the Academy of Finland (#310295).

12.2. Contributors

Authors Kieseppä, Lehti, Markkula, Taipale and Suvisaari designed the study. Author Lehti managed the literature searches and author Kieseppä managed the analyses and wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Declaration of Competing Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Acknowledgments

Marjut Graigner is acknowledged for data management.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2021.12.071.

References

Bas-Sarmiento, P., Saucedo-Moreno, M.J., Fernández-Gutiérrez, M., Poza-Méndez, M., 2017. Mental Health in Immigrants Versus Native Population: A Systematic Review of the Literature. Arch. Psychiatr. Nurs. 31, 111–121. https://doi.org/10.1016/j.apnu.2016.07.014.

Bosqui, T., Väänänen, A., Buscariolli, A., Koskinen, A., O'Reilly, D., Airila, A., Kouvonen, A., 2019. Antidepressant medication use among working age first-generation migrants resident in Finland: an administrative data linkage study. Int. J. Equity Health 18, 157. https://doi.org/10.1186/s12939-019-1060-9.

Brendler-Lindqvist, M., Norredam, M., Hjern, A., 2014. Duration of residence and psychotropic drug use in recently settled refugees in Sweden - a register-based study. Int. J. Equity Health 13. https://doi.org/10.1186/s12939-014-0122-2.

Castaneda, A.E., Çilenti, K., Rask, S., Lilja, E., Skogberg, N., Kuusio, H., Salama, E., Lahti, J., Elovainio, M., Suvisaari, J., Koskinen, S., Koponen, P., 2020. Migrants Are Underrepresented in Mental Health and Rehabilitation Services—Survey and Register-Based Findings of Russian, Somali, and Kurdish Origin Adults in Finland. Int. J. Environ. Res. Public. Health 17, 6223. https://doi.org/10.3390/ijerph17176223.

Close, C., Kouvonen, A., Bosqui, T., Patel, K., O'Reilly, D., Donnelly, M., 2016. The mental health and wellbeing of first generation migrants: a systematic-narrative review of reviews. Glob. Health 12, 47. https://doi.org/10.1186/s12992-016-0187-3.

Cruz, I., Serna, C., Real, J., Rué, M., Soler, J., Galván, L., 2010. Comparison of the consumption of antidepressants in the immigrant and native populations in a Spanish health region: an observational study. BMC Public Health 10, 255. https://doi.org/10.1186/1471-2458-10-255.

Cruz, I., Serna, C., Rué, M., Real, J., Soler-Gonzalez, J., Galván, L., 2012. Duration and compliance with antidepressant treatment in immigrant and native-born populations in Spain: a four year follow-up descriptive study. BMC Public Health 12, 256. https://doi.org/10.1186/1471-2458-12-256.

Das-Munshi, J., Leavey, G., Stansfeld, S.A., Prince, M.J., 2012. Migration, social mobility and common mental disorders: critical review of the literature and meta-analysis. Ethn. Health 17, 17–53. https://doi.org/10.1080/13557858.2011.632816.

Depressio, 2021. Käypä hoito -suositus. Suomalaisen Lääkäriseuran Duodecimin ja Suomen Psykiatriyhdistys ry:n asettama työryhmä. Helsinki: Suomalainen Lääkäriseura Duodecim [WWW Document]. URL. https://www.kaypahoito.fi/hoi50023 (accessed 5.18.21).

Fazel, M., Wheeler, J., Danesh, J., 2005. Prevalence of serious mental disorder in 7000 refugees resettled in western countries: a systematic review. The Lancet 365, 1309–1314. https://doi.org/10.1016/S0140-6736(05)61027-6.

Fournier, J.C., DeRubeis, R.J., Hollon, S.D., Dimidjian, S., Amsterdam, J.D., Shelton, R. C., Fawcett, J., 2010. Antidepressant drug effects and depression severity: A patient-level meta-analysis. JAMA - J. Am. Med. Assoc. 303, 47–53. https://doi.org/10.1001/jama.2009.1943.

Freccero, C., Sundquist, K., Sundquist, J., Ji, J., 2016. Primary adherence to antidepressant prescriptions in primary health care: a population-based study in Sweden. Scand. J. Prim. Health Care 34, 83–88. https://doi.org/10.3109/02813432.2015.1132884.

Geffen, E.C.van, Gardarsdottir, H., Hulten, R.van, Dijk, L.van, Egberts, A.C., Heerdink, E. R., 2009. Initiation of antidepressant therapy: do patients follow the GP's prescription? Br. J. Gen. Pract. 59, 81–87. https://doi.org/10.3399/bjgp09X395067.

Gimeno-Feliu, L.A., Calderón-Larrañaga, A., Prados-Torres, A., Revilla-López, C., Diaz, E., 2016. Patterns of pharmaceutical use for immigrants to Spain and Norway: a comparative study of prescription databases in two European countries. Int. J. Equity Health 15. https://doi.org/10.1186/s12939-016-0317-9.

Givens, J.L., Houston, T.K., Van Voorhees, B.W., Ford, D.E., Cooper, L.A., 2007. Ethnicity and preferences for depression treatment. Gen. Hosp. Psychiatry 29, 182–191. https://doi.org/10.1016/j.genhosppsych.2006.11.002.

Hansen, D.G., Vach, W., Rosholm, J.-U., Søndergaard, J., Gram, L.F., Kragstrup, J., 2004. Early discontinuation of antidepressants in general practice: association with patient and prescriber characteristics. Fam. Pract. 21, 623–629. https://doi.org/10.1093/fampra/cmh608.

Kato, M., Hori, H., Inoue, T., Iga, J., Iwata, M., Inagaki, T., Shinohara, K., Imai, H., Murata, A., Mishima, K., Tajika, A., 2021. Discontinuation of antidepressants after remission with antidepressant medication in major depressive disorder: a systematic review and meta-analysis. Mol. Psychiatry 26, 118–133. https://doi.org/10.1038/s41380-020-0843-0.

Kieseppä, V., Torniainen-Holm, M., Jokela, M., Suvisaari, J., Gissler, M., Markkula, N., Lehti, V., 2020. Immigrants' mental health service use compared to that of native Finns: a register study. Soc. Psychiatry Psychiatr. Epidemiol. 55, 487–496. https://doi.org/10.1007/s00127-019-01774-y.

Kokanovic, R., Dowrick, C., Butler, E., Herrman, H., Gunn, J., 2008. Lay accounts of depression amongst Anglo-Australian residents and East African refugees. Soc. Sci. Med. 66, 454–466. https://doi.org/10.1016/j.socscimed.2007.08.019.

Lehti, A., Hammarström, A., Mattsson, B., 2009. Recognition of depression in people of different cultures: a qualitative study. BMC Fam. Pract. 10, 53. https://doi.org/10.1186/1471-2296-10-53.

Lehti, V., Suvisaari, J., Gissler, M., Markkula, N., 2020. Purchases of psychotropic drugs among the migrant population in Finland: a nationwide register-based cohort study. Eur. J. Public Health 30, 1152–1157. https://doi.org/10.1093/eurpub/ckaa117.

Lindert, J., Ehrenstein, O.S.von, Priebe, S., Mielck, A., Brähler, E., 2009. Depression and anxiety in labor migrants and refugees – A systematic review and meta-analysis. Soc. Sci. Med. 69, 246–257. https://doi.org/10.1016/j.socscimed.2009.04.032.

Markkula, N., Lehti, V., Gissler, M., Suvisaari, J., 2017. Incidence and prevalence of mental disorders among immigrants and native Finns: a register-based study. Soc. Psychiatry Psychiatr. Epidemiol. 52, 1523–1540. https://doi.org/10.1007/s00127-017-1432-7.

Okello, E.S., Ekblad, S., 2006. Lay Concepts of Depression among the Baganda of Uganda: A Pilot Study. Transcult. Psychiatry 43, 287–313. https://doi.org/10.1177/1363461506064871.

Rask, S., Suvisaari, J., Koskinen, S., Koponen, P., Mölsä, M., Lehtisalo, R., Schubert, C., Pakaslahti, A., Castaneda, A.E., 2016. The ethnic gap in mental health: A population-based study of Russian, Somali and Kurdish origin migrants in Finland. Scand. J. Public Health 44, 281–290. https://doi.org/10.1177/1403494815619256.

Schraufnagel, T.J., Wagner, A.W., Miranda, J., Roy-Byrne, P.P., 2006. Treating minority patients with depression and anxiety: what does the evidence tell us? Gen. Hosp. Psychiatry 28, 27–36. https://doi.org/10.1016/j.genhosppsych.2005.07.002.

Skogberg, N., Mustonen, K.-L., Koponen, P., Tiittala, P., Lilja, E., Omar, A.A.H., Snellman, O., Castaneda, A.E., 2019. Turvapaikanhakijoiden terveys ja hyvinvointi. Helsinki.

Steel, Z., Chey, T., Silove, D., Marnane, C., Bryant, R.A., van Ommeren, M., 2009. Association of Torture and Other Potentially Traumatic Events With Mental Health Outcomes Among Populations Exposed to Mass Conflict and Displacement: A Systematic Review and Meta-analysis. JAMA 302, 537–549. https://doi.org/10.1001/jama.2009.1132.

Straiton, M.L., Reneflot, A., Diaz, E., 2017. Mental Health of Refugees and Non-refugees from War-Conflict Countries: Data from Primary Healthcare Services and the Norwegian Prescription Database. J. Immigr. Minor. Health 19, 582–589. https://doi.org/10.1007/s10903-016-0450-y.

Sundell, K.A., Waern, M., Petzold, M., Gissler, M., 2013. Socio-economic determinants of early discontinuation of anti-depressant treatment in young adults. Eur. J. Public Health 23, 433–440. https://doi.org/10.1093/eurpub/ckr137.

Taipale, H., Niederkrotenthaler, T., Helgesson, M., Sijbrandij, M., Berg, L., Tanskanen, A., Mittendorfer-Rutz, E., 2021. Initiation of antidepressant use among refugee and Swedish-born youth after diagnosis of a common mental disorder: findings from the REMAIN study. Soc. Psychiatry Psychiatr. Epidemiol. 56, 463–474. https://doi.org/10.1007/s00127-020-01951-4.

Tanskanen, A., Taipale, H., Koponen, M., Tolppanen, A.-M., Hartikainen, S., Ahonen, R., Tiihonen, J., 2015. From prescription drug purchases to drug use periods – a second generation method (PRE2DUP). BMC Med. Inform. Decis. Mak. 15, 21. https://doi.org/10.1186/s12911-015-0140-z.

Termorshuizen, F., Heerdink, E.R., Selten, J.-P., 2018. The impact of ethnic density on dispensing of antipsychotic and antidepressant medication among immigrants in the Netherlands. Soc. Sci. Med. 211, 87–94. https://doi.org/10.1016/j.socscimed.2018.06.005.

Thorens, G., Gex-Fabry, M., Zullino, D.F., Eytan, A., 2008. Attitudes toward psychopharmacology among hospitalized patients from diverse ethno-cultural backgrounds. BMC Psychiatry 8, 55. https://doi.org/10.1186/1471-244X-8-55.

Wallach-Kildemoes, H., Thomsen, L.T., Kriegbaum, M., Petersen, J.H., Norredam, M., 2014. Antidepressant utilization after hospitalization with depression: a comparison between non-Western immigrants and Danish-born residents. BMC Psychiatry 14. https://doi.org/10.1186/1471-244X-14-77.