Title: **Factors associated with discontinuation of antidepressant treatment after a single prescription among patients aged 55 or over: evidence from English primary care**

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ABSTRACT

Purpose

Antidepressants are frequently prescribed to older people with depression but little is known on predictors of discontinuation in this population. We therefore investigated factors associated with early discontinuation of antidepressants in older adults with new diagnoses or symptoms of depression in English primary care.

Methods

Data from a nationally representative cohort of patients aged 55 and over were used to evaluate the association between discontinuation of antidepressant medication after a single prescription and potential explanatory variables, including socio-demographic factors, polypharmacy and age-related problems such as dementia.

Results

Overall, during the study period we observed 34,715 new courses of antidepressant treatment initiated after recorded symptoms or diagnoses of depression. Antidepressant discontinuation after a single prescription was more common in people with depressive symptoms (32%) than in those with diagnosed depression (21.6%). In those diagnosed with depression and in women with depressive symptoms we found that, after adjusting for confounders, the odds of early discontinuation significantly increased after age 65 with a peak at around age 80 and then either levelled or reduced thereafter. Early discontinuation was also significantly less common in people with dementia and in those with diagnosed depression living in more rural areas.

Conclusions

Early discontinuation of antidepressants increases in the post retirement years and is higher in those with no formal diagnosis of depression, those without dementia and those with diagnosed depression living in urban areas. Alternative treatment strategies, such as non-drug therapies, or more active patient follow-up should be further considered in these circumstances.

INTRODUCTION

Antidepressants are a well-established and effective treatment for depression in primary care [1]. Similar effectiveness is also seen in general populations aged 60 years and over [2], although the evidence in those older than 85 years is less clear as few studies include the oldest old. The volume of antidepressant medication has been rising in the last decade [3] and initiation of antidepressants is very common for older people (65 years and over) with new episodes of diagnosed depression or depressive symptoms in primary care [4]. A meta-analysis of studies on people aged 75 and over reported prevalence rates ranging from 4.6% to 9.3% for major depression and from 4.5% to 37.4% for depressive disorders [5].

In the UK depression management guidelines on prescribing antidepressants recommend a maintenance period of at least six months following the resolution of symptoms [6]. However, evidence suggests that in clinical practice, outside of trials, early discontinuation rates for antidepressants in the general adult population can be very high, with between one-third and one-half of patients discontinuing within the first 3 months [7]. This may be due to a reluctance to start antidepressants in the first place (i.e. they are issued but never taken) and a mismatch in treatment preference between the patient and the GP [8]. Alternatively, there may be poor tolerability or early adverse effects from the medication, a perceived lack of treatment response or decisions to try alternative treatments instead (e.g. psychological therapy) [8]. Patients may

also stop early as they quickly "feel better" [9], indicating possible prescribing for milder depression, natural improvement in mood or a placebo effect.

Studies on the relationship between early discontinuation of antidepressants and patient's characteristics (e.g. sex, age and socio-economic status) have led to mixed results and have involved various definitions of discontinuation. For instance, Hansen et al. identified early discontinuation as no purchase of antidepressants during the 6 months following the first prescription. Their study showed that patients of low socio-economic status were more likely to discontinue the antidepressant therapy early but no significant differences were observed in terms of sex and age [10]. Van Geffen et al. argued that declining a first-time antidepressant prescription, by either not filling it at the pharmacy or by stopping after a single fill in, was more common in people aged 60 years and over after adjusting for confounders [7]. A Scottish study that investigated factors influencing the continuation of newly initiated antidepressant treatment beyond 30, 90 and 180 days reported wide inter-practice variability and found that the strongest predictor of treatment duration was prescribing of antidepressants by GPs with corresponding entry of diagnosis of depression [11]. Most past research has been in the general population and we know less about factors predicting discontinuation in older populations (people aged 65 years and over), including polypharmacy and age-related problems such as cognitive impairment and dementia. This study therefore explores the factors associated with early discontinuation of antidepressants in those with new depression diagnoses or symptoms and treated with antidepressants in a nationally representative sample of older adults in England.

METHODS

Study design

Cohort study utilising routinely collected primary care data.

Data source

We extracted data from The Health Improvement Network (THIN) UK primary care database, which contains the medical records of nearly 12 million patients from across the UK. It includes information on consultations, symptoms, diagnoses, investigations, health measurements, demographics, prescriptions, surgical procedures and referrals. In the UK General Practitioners (GPs) are responsible for drug prescriptions issued in the community within the NHS, so information on antidepressant prescribing is well recorded. Data on medical conditions are entered using Read Codes [12], a hierarchical coding system including diagnoses and symptom codes. GPs record depression in different ways, using both diagnostic codes and symptom codes (e.g. "low mood"). Indicators of area deprivation and type of neighbourhood were retrieved by linking the THIN database to UK Census data via the patients' postal (zip) code. We restricted our sample to the English GP practices where standard data quality criteria were met [13] and information on the linked Index of Multiple Deprivation score (IMD) [14] was available.

Study population

We selected all patients aged 55 years or older who were permanently registered with a participating practice between 1st January 2009 and 31st December 2013, were recorded with new symptoms or diagnoses of depression and had at least one new episode of antidepressant prescribing whose onset fell between January 2009 and June 2013. Patients were included from age 55 years to allow for the investigation of pre- and post-retirement changes in antidepressant discontinuation.

An entry in the database for an antidepressant prescription was treated as the onset of a new episode of antidepressant prescribing if in the prior 12 months ("washout" period) the patient was not prescribed any antidepressant drug. Only the episodes with contemporary symptoms or diagnoses of depression recorded during the washout period were retained for analysis. Code lists for symptoms and diagnosis of depression were created using standard methods [15] and approved by a general practitioner and psychiatrist. Records for depression symptoms were

identified using Read codes that were related to depression but too vague or uncertain to be considered as diagnoses, such as for example "low mood" or "C/O – feeling depressed".

The start of the follow-up was the latest of the following: 1st January 2009, 6 months after the patient's date of registration with the practice, the patient's 55th birthday and the date the practice achieved an acceptable level of data quality [13]. The end of the follow-up was the earliest of 31st December 2013, the patient's date of death, the patient's transfer out of the practice or the last date the practice contributed data to THIN. The records entered during the 6 months immediately after a new registration with a GP were excluded to avoid historical incident cases to be treated as truly new recordings of diagnosed depression or depressive symptoms [16].

Records for antidepressant prescriptions were extracted using the codes in sub-chapter 4.3 of the British National Formulary (BNF) [17]. Prescriptions of amitriptyline for less than 50 mg per day were excluded as low doses of this drug are usually indicated for chronic pain rather than for treating depression.

Outcome

For each of the new courses of antidepressant prescribing that met the inclusion/exclusion criteria we checked whether or not the patient received further prescriptions for antidepressant drugs during the three months following the episode onset. If a patient received only the prescription that initiated the episode, it is likely that either she/he did not commence therapy or had very early discontinuation. GPs will typically give a 28-day supply of antidepressant medication in one prescription, though longer prescriptions may be issued once people are stable long term, and at initiation short supplies of e.g. 14 days may be given. National UK guidelines recommend an early review of people newly diagnosed with an episode of depression within 2 weeks [6], and this is common practice in the UK. It is very unlikely that a GP would prescribe more than a 3-month supply of antidepressant medication at the first issue, due to concerns regarding suicidal risk.

The outcome of interest was defined as a binary variable comparing those who had a one-off prescription (i.e. the patient received no further antidepressant prescription during the 3-month follow-up post episode onset) with those who received 1 or more additional prescription for antidepressants within the 3-month period.

Explanatory variables

The regression models were adjusted for gender, age, class of antidepressant, polypharmacy (co-prescribing index), socio-economic status, type of neighbourhood and history of cognitive impairment (dementia, cognitive decline or memory loss). As a measure of polypharmacy, i.e. the concomitant use of multiple medications by an individual, we used a prescribing index created by counting the number of BNF codes (with the exclusion of antidepressants, vaccines and anaesthesia) from which patients received prescriptions the year before the episode onset. This has been shown to be a good indicator of morbidity [18]. Socio-economic status was defined using the quintiles of the Index of Multiple Deprivation (IMD) [14], a measure at the small area level based on 38 separate indicators across several domains of deprivation – income, employment, health, education, barriers to housing and, access to services, living environment and crime. Type of neighbourhood was classified into 3 categories: urban, town/fringe and rural (village, hamlet or isolated dwelling). Information on whether or not the patient had a history of cognitive impairment was retrieved by searching the patient's medical and therapy records for entries related to dementia, cognitive impairment or memory loss prior to the antidepressant prescribing episode. This search was performed on the records that met standard criteria of data quality and not further back than year 2000. These explanatory variables were selected on the basis of past research or clinical insights.

Statistical analysis

All new episodes of antidepressant prescribing with symptoms or diagnosis of depression recorded the year before were identified, including those initiated on the same day as the diagnosis or symptom was first registered. These episodes were then grouped into 2 categories depending on whether the previous year the patient had

1) one or more depressive symptoms recorded but no formal diagnosis of depression

2) at least one recorded diagnosis of depression

Since depression is a re-occurring condition, some of the patients had more than one new episode during the study period. Observations from individuals attending the same general practice are also likely to be correlated due for example to shared environmental factors or common clinical management of health conditions. An assumption of independence between observations was therefore untenable in this context and data clustering had to be adjusted for. Specifically, we used a generalized estimating equations (GEE) approach with a logistic link function and a working independence correlation structure [19] and we accounted for the lack of independence between observations by using robust standard errors [20,21]. Since this approach is based on quasi-likelihood estimation, popular likelihood-based model selection criteria such as AIC (Akaike's Information Criterion) [22] or BIC (Bayes Information Criterion) [23] could not be used. Model selection was therefore carried out using the quasi-likelihood under the independence model criterion (QIC), an AIC-type information criterion proposed by Pan [24] and suitable for GEE analyses.

The continuous predictors (age and polypharmacy) were handled using restricted cubic splines, i.e. a mathematical tool that allows the modelling of complex non-linear relationships. In brief, cubic splines are functions defined by a set of piecewise cubic polynomials that join together at pre-defined points, called knots, and that satisfy certain conditions to ensure that the overall curve is smooth. Restricted splines impose the additional constraint that the function must be linear beyond the boundary knots, i.e. the first and last knots. More details can be found for example in Durrleman and Simon [25] and Harrell [26].

A small proportion (around 4%) of the antidepressant episodes had less than 3 months of follow-up after the onset: 1.9% due to the patient's death, 1% because the patient left the study although alive (e.g. by moving GP practice) and 1.2% because the practice withdrew from THIN. Older patients were more likely not to have follow-up data but we assumed that after adjusting for age and the other covariates included in our model the missing values did not depend on the outcome. Under this assumption and given the small percentage of missing values, complete records analyses are expected to deliver valid results. We therefore restricted out attention to the episodes with complete 3-month follow-up.

All the analyses were carried out using Stata, version 14 [27].

RESULTS

Within the period 01/01/2009 to 30/06/2013 we observed 34,715 new courses of antidepressant prescribing in 33,288 patients who were 55 years or older, had at least 3 months of follow-up after the treatment initiation and had symptoms or diagnoses of depression the year before. Of these 34,715 new antidepressant treatments, 19,344 (55.7%) had a recorded diagnosis of depression and 15,371 (44.3%) had recorded depressive symptoms but no diagnosis of depression in the prior 12 months. One-off prescriptions (i.e. no further antidepressant prescription during the 3-month follow-up) were observed in 32% of treatment courses in the symptoms group and 21.6% in the diagnosis group. Most people were initiated to treatment with a Selective Serotonin Reuptake Inhibitor (SSRI) (86.4% of treatment courses for depressive symptoms and 89.6% for diagnoses). In particular, citalopram was the most commonly prescribed antidepressant at episode onset (54.5% for symptoms and 50.8% for diagnoses), followed by fluoxetine (16.7% for symptoms and 21.6% for diagnoses) and sertraline (13% for symptoms and 14.6% for diagnoses). The most frequently prescribed non-SSRI drug was mirtazapine (7.3% for symptoms and 6.1% for diagnoses). Summary statistics by gender and type of episode are reported in Table 1.

[Table 1 around here]

The covariates for polypharmacy and age were included in the regression models using restricted cubic splines with respectively 4 and 5 knots [26]. For those with depressive symptoms we observed a significant interaction between gender and age, so to simplify the interpretation and reporting of results we stratified our analyses by gender. Since the null hypothesis of a linear relationship between the log odds of early discontinuation and polypharmacy was not rejected for both symptoms (p=0.6 for males and p=0.4 for females) and diagnosis (p=0.1 for males and p=0.2 for females), polypharmacy was included in our final models as having a linear effect. A log transformation of polypharmacy was also considered but it did not improve the model fit and was therefore not applied.

Estimates of the adjusted odds ratios (ORs) and their 95% confidence intervals (CIs) are reported stratified by gender in Table 2 and Figure 1. After adjusting for confounders, the overall association between age and early discontinuation was highly significant for females with depressive symptoms and both males and females with diagnoses of depression (p<0.001) but not for males with depressive symptoms (p=0.1). For females in the symptoms group the relationship between age and the log odds of discontinuation after a single prescription was strongly non-linear (p<0.001), steeply increasing after age 65 up to a peak at just under 80 years and decreasing afterwards (adjusted OR for age 80 vs 65 = 1.59, 95% CI: 1.41 to 1.80). In patients with diagnosed depression the adjusted odds of early discontinuation increased with age in the age interval 65-80 and then levelled off in females or slightly went down in males. Our results also showed that the adjusted odds of early discontinuation were significantly lower in people with dementia than in those without dementia (for example, adjusted OR=0.31 with 95% CI: 0.22 to 0.44 in females with symptoms of depression when comparing those with dementia against those without) and in people with diagnosed depression living in more rural areas. Evidence of a significant association between early discontinuation and polypharmacy was found only for female patients with

diagnosed depression (adjusted OR=1.01, 95% CI: 1.004 to 1.02). The overall effect of IMD, after controlling for the other exploratory variables, was non-significant (p=0.8 and p=0.2 for respectively males and females with depressive symptoms; p=0.09 and p=0.3 for respectively males and females with diagnosed depression). Table 3 reports the adjusted odds ratios and 95% CIs estimated at selected values of age.

[Table 2 around here]

Fig. 1 *Multivariable adjusted odds ratios of early discontinuation and 95% confidence intervals for age (reference age value=65). The vertical axis is displayed on the log scale.*

[Figure 1 around here]

[Table 3 around here]

DISCUSSION

Summary of the main findings

This study investigated factors influencing discontinuation of antidepressant treatment after a single prescription. In a large nationally representative sample of 33,288 patients we found that more than one in five people with depression diagnoses who started on an antidepressant received a single prescription and this increases to nearly a third of those prescribed antidepressants where depression symptoms (e.g. low mood) only were recorded. This is in line with the poor adherence to treatment observed for other medical conditions [28,29]. Various definitions of early discontinuation have been used in the literature, in our study we focussed on one-off antidepressant prescriptions within the first 3 months' time window. In such cases it is likely that either the patient did not commence therapy or had very early discontinuation due to adverse effects of the medication, or an alternative non-antidepressant treatment plan was followed.

There has been little previous work on factors affecting discontinuation in an older population. Evidence on the influence of age on early discontinuation is mixed, with some studies reporting no association [10] and others finding a clear effect. For example, van Geffen et al. [7] found that the odds of declining treatment were almost twofold higher in patients aged 60 and over when compared with their younger counterparts. On the other hand, Aikens et al. [30] argued that older patients are more likely to continue antidepressant therapy as they have a greater perceived need for medication. Some of the discrepancies observed in the literature on the role played by age on early antidepressant treatment may be explained by differences in the way age was accounted for in the analyses. To the best of our knowledge, this is the first study to model the relationship between age and early discontinuation of antidepressants using a flexible smoothed non-linear function, thus avoiding the bias that could arise from an incorrect assumption of linearity or an arbitrary categorization of age. After adjusting for all the other variables included in the model, we observed a strong non-linear relationship between the log odds of early discontinuation and age in female patients with symptoms of depression. However, no evidence of significant age differences was found for male patients with depressive symptoms. For both males and females with diagnosed depression and for females with symptoms of depression the odds of early discontinuation increases after age 65 with a peak at around age 80 and then either levels off or reduces thereafter.

Consistent with our previous findings on treatment initiation by deprivation [4], we found no evidence of a significant impact of deprivation on early discontinuation. Our earlier work did not however show differences in initiation of antidepressants in rural areas, but in this study we show that fewer people with diagnosed depression living in those areas discontinue their treatment. Possible explanations may be more restricted access to psychological therapy services, limiting alternative treatment options for older people in more rural neighbourhoods or socio-cultural differences in attitudes to antidepressants between urban and rural areas [31].

In our investigation patients with dementia had significantly lower odds of discontinuing treatment after the first prescription. There has been little previous work on adherence to antidepressant treatment in people with dementia, and so the reasons for this are unclear. It may be explained, for example, by increased adherence where medicines are administered (and decisions to continue are made) by a caregiver or reduced reporting of adverse effects that might precipitate early discontinuation. We found no consistent influence of polypharmacy on discontinuation with evidence of polypharmacy being associated with early discontinuation only for females with diagnosed depression, though it is possible that in general people with polypharmacy continue with antidepressants but have less consistent adherence over time.

Our previous work demonstrated that older age groups had higher psychotropic prescribing and lower rates of referrals to psychological therapies services than their younger counter-parts [4]. This current study suggests that there is a corresponding increased rate of early discontinuation of antidepressants in older people, with rising rates of early discontinuation in people aged 65-80 years, though this stabilises or lowers again in the oldest age groups. This would support a hypothesis suggested in qualitative work that older people are being prescribed antidepressants through a perceived lack of suitable alternatives for depression in frailer older populations [32] and that this is potentially against their wishes [33], leading to higher discontinuation rates. The exception to this in our study was in women with depressive symptoms only (e.g. low mood), where early discontinuation rates fell in the oldest age groups (80 years or more), suggesting potentially greater adherence in this group.

Strengths and limitations of the study

The main strength of the study is the use of a large primary care data set which is broadly representative of the UK population in terms of patients' demographics and crude prevalences of major conditions [34]. In particular, information on antidepressant prescribing is well recorded as prescriptions are automatically entered into the computer system at the time of issuing. Another

strength is the use of restricted cubic splines rather than an arbitrary categorization of age when modelling the complex relationship between age and early discontinuation of antidepressants.

This study has several limitations. Our cohort of patients included people who had recorded symptoms or diagnoses of depression before being started on antidepressants. Thus, our findings may not be generalizable to patients who have depression but this was not recorded in their medical records. Our study used the GP's diagnosis of depression, which has been shown to have around 81% specificity against diagnostic instruments [35]. Prior work has demonstrated that depression tends to be under-recorded in general practice [35] and that antidepressant treatment rates, while lower than for diagnosed depression, are still high for those recorded as having depressive symptoms only [4]. In our study we found that early discontinuation was overall more common in people with recorded depressive symptoms rather than in those with diagnosed depression (32% vs 21.6%), supporting a hypothesis that those recorded with symptoms may have milder depression and are thus less inclined to persist with antidepressant treatment. However, a reliable measure of depression severity was not available in our data set. This lower treatment adherence for antidepressants in those recorded with depressive symptoms only would support that a better definition and recording of mild depression (or depression severity) is needed in UK General Practice. This would facilitate adherence to guidelines on treatments for those with mild depression, which generally recommend non-drug approaches at least initially. Some patients with depression may have concomitant anxiety symptoms and this might impact on discontinuation rates. Anxiety symptoms tend to be under recorded in primary care, and further research is needed to explore this. Our data were until 2013, and since this time some data have suggested that the prevalence of antidepressant prescribing may be increasing but not the incidence of new prescriptions, and it may be that early discontinuation rates have reduced in more recent years.

The THIN database contains well-recorded information on prescriptions issued in primary care but does not provide indication of whether prescriptions were filled at the pharmacy or medicines were actually taken by the patients. Therefore, it does not allow direct assessment of treatment

adherence or an exploration of the reasons behind treatment interruption. Prior studies found that more than half of the patients who decide to stop taking antidepressants early do not inform their GP about their decision [36] and those who interrupt antidepressant medication after a single prescription are unlikely to restart treatment in the following 12 months [37]. Further research would be needed to investigate depression outcomes in all those who discontinue antidepressants at a very early stage.

Conclusions

Given the significant risk of antidepressant discontinuation after a single prescription, GPs should engage with patients' preferences and attitudes and encourage therapy adherence from the very early stages of treatment. They should be aware that this is especially important with patients in the post retirement years, those with no formal diagnosis of depression, those without dementia and those with diagnosed depression living in urban areas. Alternative strategies, such as non-drug therapies, or more active patient follow-up should be further considered for these patients.

Ethical statement

Funding

Conflict of interest

The authors declare that they have no conflict of interest.

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Table 1: *summary statistics of the new episodes.*

	Depressive symptoms		Diagnosed depression	
	Males	**Females**	**Males**	**Females**
No. of new treatment courses (row %)	5513 (35.9%)	9858 (64.1%)	7269 (37.6%)	12075 (62.4%)
Age at treatment onset				
median	66.7	69.2	63.8	65.6
IQR	[60, 77.3]	[61,79.6]	[59, 73]	[59.4,74.7]
No. of prescriptions				
one-off	1628 (29.5%)	3294 (33.4%)	1476 (20.3%)	2697 (22.3%)
> 1	3885 (70.5%)	6564 (66.6%)	5793 (79.7%)	9378 (77.7%)
Class of antidepressant at treatment onset				
SSRI only	4768 (86.5%)	8505 (86.3%)	6505 (89.5%)	10824 (89.6%)
TCA only	216 (3.9%)	492 (5.0%)	172 (2.4%)	363 (3.0%)
combination of drugs	13 (0.2%)	13 (0.1%)	9 (0.1%)	19 (0.2%)
others	516 (9.4%)	848 (8.6%)	583 (8.0%)	869 (7.2%)
Drug at treatment onset				
citalopram	2952 (53.5%)	5418 (55.0%)	3622 (49.8%)	6198 (51.3%)
fluoxetine	985 (17.9%)	1587 (16.1%)	1628 (22.4%)	2558 (21.2%)
sertraline	719 (13.0%)	1283 (13.0%)	1091 (15.0%)	1741 (14.4%)
mirtazapine	433 (7.9%)	685 (6.9%)	476 (6.6%)	712 (5.9%)
other antidepressants	424 (7.7%)	885 (9.0%)	452 (6.2%)	866 (7.2%)

Table 2: *multivariable* adjusted odds *ratios of early discontinuation of antidepressant medication and their 95% confidence intervals.*

The results for age are displayed in Figure 1.

	Depressive symptoms		Diagnosed depression	
	Males	**Females**	**Males**	**Females**
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Deprivation				
1 (lowest)	1	1	1	1
2	1.06 (0.88, 1.28)	1.11 (0.97, 1.27)	1.01 (0.84, 1.21)	1.05 (0.90, 1.21)
3	1.01 (0.85, 1.21)	1.11 (0.96, 1.28)	1.18 (0.97, 1.42)	1.01 (0.87, 1.17)
4	1.06 (0.88, 1.29)	1.19 (1.03, 1.38)	1.25 (1.04, 1.50)	1.10 (0.95, 1.27)
5 (highest)	1.13 (0.90, 1.41)	1.14 (0.97, 1.33)	1.22 (0.98, 1.53)	1.19 (1.00, 1.43)
Neighbourhood				
Urban	1	1	1	1
Town and fringe	1.00 (0.83, 1.20)	0.86 (0.76, 0.98)	0.93 (0.75, 1.16)	0.83 (0.69, 0.99)
Village, hamlet, isolated dwelling	1.01 (0.83, 1.23)	0.89 (0.76, 1.05)	0.72 (0.55, 0.95)	0.82 (0.69, 0.97)
Class of antidepressants				
SSRI	1	1	1	1
non-SSRI	0.90 (0.77, 1.05)	0.91 (0.80, 1.03)	0.92 (0.75, 1.13)	0.92 (0.80, 1.06)
Polypharmacy (prescribing index)	1.01 (1.00, 1.02)	1.00 (0.99, 1.01)	1.01 (0.99, 1.02)	1.01 (1.00, 1.02)[a]
Dementia	0.51 (0.32, 0.80)	0.31 (0.22, 0.44)	0.50 (0.28, 0.90)	0.42 (0.25, 0.69)
Cognitive impairment or memory loss	0.88 (0.69, 1.13)	0.80 (0.68, 0.95)	0.83 (0.64, 1.08)	0.83 (0.68, 1.02)
Age	see Figure 1 (a)	see Figure 1 (b)	see Figure 1 (c)	see Figure 1 (d)

[a] This 95% CI does not contain 1 as the lower bound is 1.004.

Table 3: *multivariable adjusted ORs of early discontinuation and their 95% CIs at selected values of age (reference value: age=65).*

	Depressive symptoms		Diagnosed depression	
	males	*females*	*males*	*females*
age				
55	0.96 (0.74, 1.26)	1.04 (0.85, 1.27)	1.14 (0.89, 1.46)	0.97 (0.82, 1.15)
65	1	1	1	1
80	1.15 (0.94, 1.41)	1.59 (1.41, 1.80)	1.44 (1.18, 1.77)	1.29 (1.11, 1.50)
95	1.31 (0.92, 1.88)	0.93 (0.75, 1.16)	1.33 (0.92, 1.92)	1.31 (1.03, 1.66)