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Primary adherence to antidepressant prescriptions in primary health care: a population-based study in Sweden

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ABSTRACT

Background Medical adherence is important in the treatment of depression. Primary medical adherence, i.e. patients collecting their newly prescribed medications from pharmacies, is very different depending on the drug prescribed **Objective** To assess the rate of primary medical adherence in patients prescribed antidepressants and to identify characteristics that make patients less likely to pick up prescriptions. **Methods** An observational study was performed using primary health care data from Sweden on patients who were prescribed antidepressants. Univariate and multivariate logistic regression was used to determine differences in pick-up rate according to patient characteristics. **Main outcome** Pick-up rate, defined as collection of a prescription within 30 days. **Results** A total of 11 624 patients received an antidepressant prescription during the study period, and the overall pick-up rate was 85.1%. The pick-up rate differed according to country of birth: individuals born in the Middle East and other countries outside Europe had lower primary medical adherence than Swedes, with adjusted odds ratios (ORs) of 0.58 and 0.67, respectively. Patients at ages 64–79 years had a higher pick-up rate compared with those aged 25–44 years (OR 1.71). Divorced patients had a lower rate compared with married patients (OR 0.80). **Conclusion** Immigrants from the Middle East and other countries outside Europe and younger and divorced patients had lower primary medical adherence, which calls for clinical attention and preventive measures.

KEY POINTS

- Primary medical adherence is important in the treatment of depression.
- Are patient characteristics associated with primary medical adherence?
- The overall primary medical adherence rate was 85%.
- The rate differed by country of birth, age at diagnosis of depression, and marital status.
- Clinical attention is needed in patients who do not pick up their antidepressants.

Introduction

Adherence to prescribed medications is a key factor for effective management of many chronic disorders. It is of great importance that patients adhere to their prescriptions since treatment is beneficial for the patient, which in turn is beneficial for society.[1–3] Non-adherence constitutes a large problem for the healthcare system. It increases healthcare costs and is associated with greater morbidity and mortality in chronic disease.[4] Medical adherence usually refers to both primary adherence, which is the rate at which patients collect their newly prescribed medication from pharmacies, and secondary adherence, which is the correct intake of a prescribed medication.[2,5,6] The primary non-adherence rate has

been reported to range from 2.4% to 24%, depending on the drug prescribed.[7,8]

Antidepressant medications are important for the treatment of depression. However, some patients may not accept the treatment. Overall adherence to antidepressants is known to be low.[9,10] However, little is known about the primary adherence. One study that looked at primary adherence for all kinds of drugs found that the adherence rate based on 3476 prescriptions for antidepressant drugs was 70.5%.[1] Another study (including 153 young patients) showed that 86.3% of patients picked up their prescriptions at pharmacies.[11] No previous studies, to the best of our knowledge, have focused solely on primary non-adherence to

antidepressants and examined the associations with patients' clinical and sociodemographic characteristics.

In the current study, we use the Primary Health Care Database maintained at the Center for Primary Health Care Research, Lund University and corresponding pick-up information from the Swedish Drug Registry to examine primary adherence to antidepressant prescriptions. The combined database contains data from 75 primary health care centres located mainly in Stockholm County, and covers over one million individuals.

It is important to understand why non-adherence occurs. Research on adherence will hopefully identify patient subgroups that require intervention. Since the introduction of electronic prescriptions, more studies have focused on primary non-adherence and have attempted to identify clinical characteristics that make a patient fail to pick up his/her prescription. The results of one earlier study suggested that primary non-adherence occurs when patients perceive a lack of efficacy and have concerns about side effects. In addition, high cost and absence of symptoms may partly explain non-adherence.[14] Another study found that some patients thought there was no need for the prescription or did not know a prescription had been sent to their pharmacy.[8] Age, gender, socioeconomic status, and type of drug were also reported to play roles in primary adherence.[1,2,5,7,8,12–17] The aim of this study was to identify individual characteristics that are associated with low primary medical adherence to antidepressant prescriptions.

Material and methods

Study population and data collection

Data from the Primary Health Care Register, which covers 75 health care centres in Stockholm and the middle part of Sweden, for the period 1 January 2001 to 30 June 2007 were linked to the Swedish Drug Register, which contains data on all prescriptions sent to and picked up at public pharmacies in Sweden between 1 July 2005 and 31 December 2008. Data were retrieved on patients who received a prescription for any SSRI or SNRI antidepressant (ATC code N06AB* or N06AX*) from their primary health care physicians between 1 July 2005 and 31 December 2007. Patients who had received a prescription for an antidepressant before the beginning of the study period were excluded from the study. Patients who had received an antidepressant prescription for the following conditions (main diagnoses) were included: F32 (depression), F41.0 (panic disorder), F41.1 (generalized anxiety disorder), and F41.9 (anxiety disorder, unspecified) (118 patients). Patients with a diagnosis code of F33 (recurrent depression) were not

included in this study because we explored here the pick-up rate of newly prescribed antidepressants among incident depressive patients. In all, 151 patients were excluded due to missing information for one or more variable(s). A total of 11 624 patients were included in the study. Information on gender, age, income, marital status, education, country of birth, and diagnoses was obtained from the Swedish Total Population Register at Statistics Sweden.

Study variables

The aim was to study the first-time antidepressant pick-up rate, i.e. primary adherence. Thus, only the first prescribed antidepressant was of interest. We use the terms "pick-up rate" and "primary adherence" commutatively in the text. If a patient was prescribed an antidepressant more than once, only the first prescription was included. Prescriptions picked up at the pharmacy within 30 days after receipt of an e-prescription from the primary health care centre were deemed to have been picked up.

The following study variables were analysed:

- *Gender*: Male or female.
- *Age*: <19 years, 19–24 years, 25–44 years, 45–64 years, 65–79 years, or 80 + years.
- *Income*: Low, middle, or high depending on individual disposable household income, which is the annual family income divided by the number of people in the family.
- *Marital status*: Married, not married, divorced, or widowed.
- *Education*: <10 years (compulsory school), 10–12 years (some or completed high school), >12 years (college/university).
- *Country of birth*: Sweden, other European countries (excluding Sweden), the Middle East, or other countries (those that do not belong in any other group).
- *Diagnosis*: Defined by the tenth revision of the International Classification of Diseases (ICD-10): depression (F32), panic disorder (F41.0), generalized anxiety disorder (F41.1), or anxiety disorder, unspecified (F41.9).

Analysis

The associations between the above-mentioned characteristics and medical adherence were examined by univariate logistic regression. Odds ratios (ORs) were calculated to compare the differences for different variables. Multiple logistic regression was performed to

calculate adjusted ORs after controlling for the effects of other variables. The two-sided level of significance was set at $p < 0.05$. STATA version 11™ (StataCorp LP, College Station, TX, USA) was used to handle the data and perform the analysis.

Results

A total of 11 624 patients were prescribed antidepressants between 1 July 2005 and 30 June 2007. Of these, 9896 (85.1%) picked up their first prescription within 30 days. Of those who did not, 598 (5.2%) picked it up at 31 to 365 days, and the remaining 1130 (9.7%) did not pick it up at all during the study period, which ran until 31 December 2008. Patients born outside Europe had a lower pick-up rate compared with those born in Sweden and other European countries. Older patients had a higher pick-up rate than younger ones and married patients had a higher pick-up rate than divorced patients. A middle or high income was associated with a higher pick-up rate compared with a low income (Table 1).

In Table 2 we present the OR and 95% CI from univariate and multivariate logistic regression analyses. From univariate logistic regression, we found that patients aged 65 + years showed a statistically significantly high pick-up rate as compared with patients aged 25–44 years at diagnosis. In addition, individuals born in Sweden had a statistically significantly high pick-up rate than those patients born in the Middle East and "Other countries". Individuals with high incomes had a significant high pick-up rate than those with low incomes.

Married individuals had a significantly higher pick-up rate than those who were divorced. We further calculated their associations using multiple logistic regression. After controlling for other confounding variables, the variables associated with medical adherence in univariate logistic regression retained their associations (see Table 2), with the exception of income.

The fact that the income variable showed a significant association in the univariate analysis but not in the multivariate analysis suggests that it was associated with other variables. We therefore performed a subgroup analysis. Individuals with low and middle incomes were more likely to have been born in the Middle East and other countries outside Europe (Table 3).

Discussion

The main findings of this study in primary health care were that younger and divorced patients and immigrants born in the Middle East and other countries

Table 1. Descriptive data for patients who were prescribed antidepressants.

Variable	No.	Pick-up rate (%)
Gender		
Male	3875	85.6
Female	7749	84.9
Country of birth		
Sweden	8534	86.3
Europe (excluding Sweden)	1207	85.1
Middle East	1094	78.7
Others	789	80.9
Age (years)		
<19	65	83.1
19–24	754	84.2
25–44	4677	83.2
45–64	3970	85.4
65–79	1377	90.2
80+	791	87.6
Income		
High	2465	86.5
Middle	6329	85.6
Low	2830	82.9
Education (years)		
>12	3189	84.8
10–12	4740	85.1
<10	3695	85.5
Marital status		
Married	4410	86.3
Not married	4277	84.3
Divorced	2139	83.5
Widowed	798	87.5
Diagnosis		
Depression	8872	85.3
Panic disorder	801	84.9
Generalized anxiety disorder	192	81.3
Anxiety disorder, unspecified	1759	84.8
Total	11,624	85.1

outside Europe had lower primary medical adherence to antidepressants.

In this study we found that primary adherence to antidepressants prescribed at primary health care centres was 85%. A previous study from New Zealand on 153 young patients [11] found a pick-up rate of 86.3%. However, an American study [1] reported that the rate of collection of new e-prescriptions of antidepressants was 70.5% among patients aged 19 and over, which was somewhat lower than that in our study, probably because of the higher medication costs in the USA and/or limitations of the study design.[18]

Compared with patients born in Sweden, individuals born outside Europe had lower medical adherence, which is interesting and important, given that there are more than one million immigrants in Sweden, and 25% of these immigrants come from Middle Eastern countries. One possible explanation is that immigrants have a low trust in Swedish health care. In addition, mental disease may be unacceptable due to cultural differences or not understood because of language barriers.[19,20] It might improve our understanding as to whether language barriers contributed to the low rate of medical adherence among immigrants if we had more

Table 2. Odds ratios from univariate and multivariate logistic regression.

Variable	Univariate logistic regression			Multivariate logistic regression		
	Odds ratio	95% CI	p	Odds ratio	95% CI	p
Gender						
Male	1			1		
Female	0.95	0.85–1.06	0.37	0.95	0.85–1.07	0.4
Country of birth						
Sweden	1			1		
Europe (excluding Sweden)	0.91	0.77–1.08	0.26	0.88	0.74–1.05	0.13
Middle East	0.58	0.50–0.68	<0.0001	0.61	0.51–0.73	<0.001
Others	0.67	0.55–0.81	<0.0001	0.71	0.59–0.87	<0.001
Age (years)						
<19	0.99	0.52–1.91	0.98	0.98	0.50–1.91	0.96
19–24	1.07	0.88–1.33	0.46	1.07	0.85–1.33	0.54
25–44	1			1		
45–64	1.19	1.06–1.34	0.003	1.18	1.04–1.34	0.01
64–79	1.86	1.53–2.26	<0.0001	1.71	1.37–2.12	<0.001
80+	1.42	1.14–1.79	0.002	1.28	0.96–1.70	0.08
Income						
High	1			1		
Middle	0.93	0.81–1.07	0.3	0.98	0.85–1.12	0.77
Low	0.76	0.65–0.89	0.0004	0.89	0.75–1.05	0.16
Education (years)						
>12	1			1		
10–12	1.02	0.90–1.16	0.76	1.03	0.90–1.17	0.72
<10	1.05	0.92–1.20	0.43	1	0.86–1.16	0.8
Marital status						
Married	1			1		
Not married	0.85	0.76–0.96	0.009	0.86	0.75–0.98	0.02
Divorced	0.8	0.69–0.92	0.002	0.78	0.67–0.90	<0.001
Widowed	1.11	0.88–1.39	0.37	0.82	0.64–1.05	0.27
Diagnosis						
Depression	1			1		
Panic disorder	0.97	0.79–1.18	0.74	1.01	0.82–1.23	0.98
GAD	0.75	0.52–1.08	0.11	0.7	0.48–1.01	0.06
Anxiety disorder, unspecified	0.96	0.83–1.10	0.55	0.95	0.82–1.09	0.43

Table 3. Income and pick-up rate according to country of birth.

	Income								
	Low			Mid			High		
Country of birth	No.	%	Pick-up rate (%)	No.	%	Pick-up rate (%)	No.	%	Pick-up rate (%)
Sweden	1685	19.7	84.9	4791	56.1	86.7	2058	24.1	86.7
Europe (excluding Sweden)	292	24.2	82.2	684	56.7	85.8	231	19.1	87.0
Middle East	558	51.0	78.3	463	42.3	79.1	73	6.7	79.5
Others	295	37.4	81.0	391	49.6	79.5	103	13.1	85.4
All countries	2830	24.3	82.9	6329	54.4	85.6	2465	21.2	86.5

Note: % = percentage of patients from specific countries according to income.

information on whether these immigrants used an interpreter when they visited primary health care centres, or whether they understand the Swedish language. Unfortunately, such information was not available in our database. Further studies should address this issue.

Income has been reported to be associated with medical adherence in previous studies, and we found that the pick-up rate was 3.5 percentage points lower in the low-income group compared with the high-income group (OR 0.76). However, the association was not significant after controlling for other variables in the multivariate analysis, indicating that income is

associated with other variables, notably the country of birth variable. When analysing pick-up rate according to country of birth and income, the difference between those with middle incomes compared with those with low incomes was modest: less than two percentage points for individuals born in Sweden and less than one percentage point for those born in the Middle East.

As shown by two other studies,[8,12] the elderly had better primary adherence. In our study 90.2% of those aged 65–79 years and 87.6% of those aged 80 + years picked up their prescriptions, compared with only 83.2% of those aged 25–44 years. Possible explanations for this age difference are that older patients may be more used

to taking medications and hence do not find it alarming to be prescribed another drug, or that they trust their doctors more than younger patients. In addition, older patients may live in nursing homes with special help with medications, which may lead to a higher rate of medical adherence. However, the pick-up rate for those aged 80 + years was somewhat lower than that for those aged 65–79 years, suggesting that other factors may affect medical adherence among these older patients.

Another significant finding is that divorced patients had a lower pick-up rate than married ones. It may be that married patients get more support from their spouses, feel under more pressure to do something about their disease, or receive help in picking up their medication. It is possible that divorced people may live with someone else without being married. This may have influenced the study results. Unfortunately, we cannot control for this as we have no data regarding this confounding factor. However, widowed individuals also showed a lower pick-up rate (OR = 0.82). This suggests that individuals who live alone, either divorced or widowed, could be an independent risk factor for low adherence.

There were almost no differences in pick-up rates between males and females or between individuals with high and low levels of education. These results differ from those of other studies, which showed that men have lower pick-up rates than women.[2,8,12] However, these previous studies did not only focus on antidepressant drugs. Medical diagnosis did not significantly affect the pick-up rate in this study. However, the pick-up rate for patients with general anxiety disorder was four percentage points lower than that for those with depression (OR 0.75), which suggests that there might actually be a difference and that the lack of statistical significance was due to the relatively low number of observations ($n = 192$). Such a difference could possibly be explained by patients' anxiety about going to the pharmacy or taking medicines.

Strengths of this study include the inclusion of a large number of patients and the exclusion of only a very small number of patients because of missing data, suggesting that the quality of the data is high. The prescription data are unique: as far as we know they come from the only primary health care database of such large size in Scandinavia. Also, we only studied primary adherence for antidepressant medications, which means that the results are specific. All the prescription and pick-up information was obtained from a national registry, avoiding selection and recall bias. One limitation is that we could not determine why some patients did not collect their prescriptions. Moreover, patients who were diagnosed and treated in hospital were not included. In addition, patient and/or physician factors, such as patient–physician communication and education regarding the importance of the prescription, were not assessed in the study. Most previous studies focused on secondary adherence to medication, whereas our study examined primary adherence. It is necessary to investigate whether patients collect their prescriptions as this is the first step in the process of adherence, and the first step towards effective interventions for improving medical adherence. It is also important for identifying key determinants of primary non-adherence and access to medication.

Conclusion

The pick-up rate for antidepressants in this study was 85%. While the pick-up rate varied according to age and marital status, country of birth had the largest effect. Our data did not show significant results for gender, income, education, or diagnosis. Further studies are needed to examine why 15% of patients do not pick up their prescribed antidepressants and why the pick-up rate differs depending on country of birth. A 100% pick-up rate is, however, a goal that is unrealistic to strive for. The 85% pick-up rate reminds physicians that a prescription is only a recommendation for the patient. At follow-up, it is important to determine whether or not the prescription has been followed as a step to continuing the treatment and looking out for side effects. In addition, future studies should examine the pick-up rates for other medications among patients with different countries of birth.

Acknowledgements

Ethical approval

This study was approved by the Regional Ethical Review Board of Lund University in Sweden.

Disclosure statement

No potential conflict of interest was reported by the authors.

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