

# Antidepressant adherence and its predictors in immigrants with depression

## A population-based study

Suhyun Jang, PhD<sup>a</sup>, Hyemin Cho, MSc<sup>a</sup>, Cino Kang, MPH<sup>b</sup>, Sunmee Jang, PhD<sup>a,\*</sup>

### Abstract

Immigrants in Korea are relatively vulnerable in terms of medication self-management and have low levels of medication adherence. We aimed to evaluate antidepressant adherence and its patterns in immigrants and to identify predictors of nonadherence.

In this matched cohort study using the National Health Insurance claims database, immigrants who were newly prescribed antidepressants were identified ( $n=2,398$ ). The immigrants were matched with native-born Koreans in a 1:1 ratio. Antidepressant adherence was measured by the medication possession ratio at monthly intervals. Logistic regression was performed to compare antidepressant nonadherence between immigrants and native-born Koreans, and to identify factors affecting immigrants' nonadherence.

The average medication possession ratio of immigrants was 27.1%, which was lower than that of native-born Koreans (30.9%) ( $P=.038$ ). Immigrants had a lower likelihood of adherence than native-born Koreans (odds ratio [OR] 0.76, 95% confidence interval [CI] 0.3–0.92). Older age, visiting a psychiatrist for the first diagnosis of depression (OR 2.24, 95% CI 1.60–3.13), achieving appropriateness of care (OR 3.54, 95% CI 2.51–4.98), and having a usual source of care (OR 1.69, 95% CI 1.25–2.27) were associated with a higher likelihood of adherence in immigrants.

This study showed that antidepressant adherence of immigrants was lower than that of native-born Koreans. However, it appears that visiting a psychiatrist, achieving appropriateness of care, and having a usual source of care might increase antidepressant adherence among immigrants. Further research that focuses on cultural and/or linguistic factors affecting immigrants' adherence and healthcare utilization is suggested as a way to increase adherence.

**Abbreviations:** AOC = appropriateness of care, CCI = Charlson Comorbidity Index, CI = confidence interval, KNHI = Korean National Health Insurance, MPR = medication possession ratio, OR = odds ratio.

**Keywords:** antidepressant adherence, immigrants, matched cohort, medication possession ratio, native-born Koreans, population-based study

### 1. Introduction

The number of immigrants residing in South Korea has steadily grown, increasing by 50.6% since 2008 to reach 1.7 million, or 3.3% of the population, in 2018.<sup>[1]</sup> Most immigrants in South Korea are from Asian countries such as China (50.5%), Vietnam (12.3%), and other Asian countries (29.2%).<sup>[2]</sup> In particular, the number of permanent immigrants—a category that includes

marriage immigrants, permanent residents, and naturalized citizens—increased by 30.3% from 2013 to 2018 (from about 343,000 to 447,000).<sup>[3,4]</sup> Of those immigrants, 70% were marriage immigrants. In general, immigrants must live in Korea for 5 years or longer to apply for naturalization, but marriage immigrants can apply for naturalization 2 or 3 years after marriage.

Editor: Wen-Wei Sung.

This study used National Health Insurance Service claims data. These third-party data were obtained from the Korean National Health Insurance Service (KNHIS). The authors had no special access privileges to the data. Interested, qualified researchers can apply for access to the data by contacting the National Health Insurance Sharing Service (<https://nhiss.nhis.or.kr/bd/ab/bdaba001cv.do>).

This research was funded by the Basic Science Research Program through the National Research Foundation of Korea (NRF) (2017R1D1A1B03034121). However, the funding body had no influence on conducting the research or writing the manuscript.

The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

The authors have no conflicts of interest to disclose.

<sup>a</sup> College of Pharmacy and Gachon Institute of Pharmaceutical Sciences, Gachon University, Incheon, <sup>b</sup> Department of Biostatistics and Epidemiology Graduate School of Public Health, Seoul National University, Seoul, Republic of Korea.

\* Correspondence: Sunmee Jang, Address: College of Pharmacy and Gachon Institute of Pharmaceutical Sciences, Gachon University, 191 Hambakmoero, Yeonsu-gu, Incheon, 21936, Republic of Korea (e-mail: [smjang@gachon.ac.kr](mailto:sjang@gachon.ac.kr)).

Copyright © 2020 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Jang S, Cho H, Kang C, Jang S. Antidepressant adherence and its predictors in immigrants with depression: a population-based study. *Medicine* 2020;99:51(e23308).

Received: 4 April 2020 / Received in final form: 26 September 2020 / Accepted: 21 October 2020

<http://dx.doi.org/10.1097/MD.00000000000023308>

Studies of the health status of immigrants have shown inconsistent results; some research has reported that immigrants are less healthy than native-born inhabitants,<sup>[5]</sup> while other research has found immigrants to be healthier than natives (known as the healthy immigrant effect).<sup>[6]</sup> A meta-analysis found that the health of immigrants depends on their country of origin, socioeconomic background, and immigration status (citizenship, permanent residence, etc.).<sup>[7]</sup> However, in many previous studies,<sup>[8–10]</sup> it has been reported that immigrants receive less medical and preventive care than their native-born counterparts. Systematic literature reviews have found that the causes of these disparities include limited language skills, cultural differences, and a poor understanding of the health care system in the host country.<sup>[11]</sup> In addition, financial difficulties<sup>[5]</sup> and acculturative stress<sup>[12]</sup> are known to be barriers to immigrants' healthcare utilization. These barriers reduce healthcare accessibility for immigrants, which can lead to the deterioration of health outcomes.

Of particular note, a meta-analysis of the mental health of immigrants reported that they were at a high risk of developing psychiatric diseases due to trauma experienced in the immigration process and stress from adjusting to immigration, but their medical use was relatively low.<sup>[13]</sup> The most common mental disorder among immigrants is depression, which is present in 20% to 44% of immigrants.<sup>[14]</sup> According to the World Health Organization, depression is the third-leading cause of moderate and severe disability and is more common among those aged 0–59 years than those aged 60 and older;<sup>[15]</sup> furthermore, the burden of depression is expected to increase further by 2030.<sup>[16]</sup>

Antidepressant adherence is important for managing depression. Gaynes et al. (2009) confirmed that taking antidepressants properly is one of critical components of treatment<sup>[17]</sup> and medication nonadherence increased the likelihood of relapse and/or recurrence, emergency department visits, and hospitalization according to a systematic review.<sup>[18]</sup> A meta-analysis reported a 1.76-fold higher risk of nonadherence among patients with depression; moreover, it is difficult for immigrants to properly manage this disease due to low health literacy.<sup>[19,20]</sup> Studies have reported high nonadherence rates, ranging from 56% to 87.6%.<sup>[21–23]</sup>

Immigrants are relatively vulnerable in terms of medication self-management due to language and cultural differences; these factors cause them to experience difficulties with antidepressant medication, for which sustainability is important. However, little research has been conducted on antidepressant adherence in immigrants, especially in Asian countries. Under these circumstances, it is vital to compare antidepressant adherence between immigrants and their nonimmigrant counterparts and to identify predictors of adherence.

The purpose of this study was to characterize differences in antidepressant adherence between immigrants and native-born Koreans, to analyze the patterns of adherence, and to identify predictive factors of low antidepressant adherence among immigrants.

## 2. Methods

### 2.1. Data

The Korean National Health Insurance (KNHI) covers all citizens and foreigners who have lived in Korea for more than 6 months. The KNHI provides benefits for inpatient care, outpatient care, and prescription drugs.<sup>[24]</sup> The KNHI collects data including eligibility information, healthcare utilization, and pharmacy

dispensation information for all subjects, making it possible to obtain comprehensive information on all medical use and dispensed prescriptions for immigrants who are registered in the KNHI system. The KNHI also gathers data on diagnoses, tests, drugs, treatments, and surgery. The data to be analyzed were constructed by integrating the 2011–2012 KNHI data for all immigrants, including permanent residents, marriage immigrants, and naturalized citizens. To protect privacy, the data were integrated after a third party deleted personally identifiable information.

### 2.2. Patients and study design

This matched cohort study analyzed immigrants who were over 20 years old and were newly prescribed antidepressants upon their first diagnosis with a depressive disorder (Korean Classification of Diseases, 10th revision [KCD-10]: F32, F33, F34.1, F41.2) in 2012. Although utilization of mental healthcare among immigrants' children and adolescents could have influenced their perspectives, parents' perspectives also count.<sup>[25]</sup> As such, we only focused on adult patients. In particular, we focused on patients who were newly prescribed antidepressants because prompt treatment is important for treating depression.<sup>[26,27]</sup> To exclude patients who were already undergoing treatment for depression, patients who were diagnosed with depression or prescribed antidepressants within 6 months before the index date were excluded. We also excluded patients who died within 1 year after the first prescription in order to analyze antidepressant adherence for a period of 1 year. It was also necessary for subjects to have visited a physician at least twice in the 1-year study period.

The matching group was created by selecting native-born Koreans with the same inclusion and exclusion criteria as applied to immigrants. The immigrants and native-born Koreans were matched 1:1 by sex, age, and Charlson Comorbidity Index (CCI) score.

### 2.3. Medication adherence

Medication adherence was measured by the medication possession ratio (MPR), which is often used to indirectly measure medication adherence using administrative claims data.<sup>[21,28]</sup> The MPR was calculated as follows:

$$MPR(\%) = \frac{\text{Total days supplied}}{\text{Days of study period (until 1 year from the index date)}} \times 100$$

The MPR was measured at monthly intervals up to 1 year after the index date, and it was assumed that the patients were taking their prescription medicines. The adherent group was defined as those with an MPR of over 80%, with reference to previous studies.<sup>[29]</sup> Those with an MPR of less than 80% were classified as nonadherent. Discontinuation was defined as no medication being prescribed for 30 days after the last prescription. Monthly adherence was calculated to identify adherence patterns. In instances of discontinuation, if the patients had re-started taking the antidepressants after 30 days, adherence was re-evaluated from the month when the medication was re-started.

### 2.4. Covariates

We considered the following variables as covariates: age, sex, type of insurance, residential region, insurance contribution,

number of household members, CCI score, psychiatric comorbidities, number of antidepressants, the physician's specialty at the first diagnosis, the presence of a usual source of care and appropriateness of care (AOC). In addition, immigration status was considered.

Patients were classified into six age groups: 20 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, and 70 years and older.

Type of insurance was classified as Medical Aid and KNHI. Medical Aid is a medical assistance program for low-income individuals. The beneficiaries of Medical Aid pay lower out-of-pocket costs than KNHI subscribers, who pay out-of-pocket for approximately 30% of expenditures.

The KNHI contribution used as a proxy for income, since it is calculated based on income using a predefined method (a fixed percentage of salary for employees and a score calculated based on assets for the self-employed). The KNHI contribution was divided into quintiles, with the fifth quartile corresponding to the highest income.

The number of household members was classified as one, two or three, and four and over.

The CCI was used to evaluate the severity of comorbidities based on diagnostic codes.<sup>[30]</sup> The diseases included in the CCI are as follows<sup>[30,31]</sup>: HIV/AIDS, cerebrovascular diseases, congestive heart failure, chronic pulmonary disease, dementia, diabetes, hemiplegia, liver diseases, any malignancy, myocardial infection, peripheral vascular diseases, peptic ulcer disease, rheumatologic diseases and renal diseases. A weighted score was assigned to each of the comorbidities based on the relative risk of 1-year mortality. CCI scores were categorized into three groups (0, 1, and 2+ points).

Psychiatric comorbidities included psychotic disorders, manic diseases, bipolar disorder, other affective disorders, anxiety, eating disorders, sleep disorders, personality disorders, or compulsive behavior disorder. These conditions were defined on the basis of a primary diagnosis with the following KCD-10 codes: F07, F09, F10, F20, F21, F22, F23, F25, F28, F29, F30, F31, F32, F33, F34, F38, F39, F40, F41, F42, F43, F44, F45, F48, F50, F51, F60, F63, F64.

The number of antidepressants was determined based on the first prescription and dichotomized as 1 active ingredient and 2 or more active ingredients.

The physician's specialty at the first diagnosis was classified as psychiatry and others.

According to clinical guidelines published in Korea<sup>[32]</sup> and an article on depression management from the United States (US),<sup>[33]</sup> AOC in the acute phase was defined as at least three prescriptions of antidepressants within 12 weeks from the index date.

Having a usual source of care is an important factor influencing the accessibility and continuity of health care services. Generally, the surveys have been used to measure whether patients visited particular medical institutions or doctors.<sup>[34]</sup> However, this study defined a patient as having a usual source of care if he or she visited only one medical institution for depressive disorder in 2012.

## 2.5. Statistical analysis

To evaluate the statistical significance of differences between immigrants and native-born Koreans, the chi-square test was used for categorical variables and 1-way ANOVA for continuous variables. Multivariable logistic regression was performed to

compare the antidepressant adherence rate between immigrants and native-born Koreans, and to identify socioeconomic and medical predictors affecting immigrants' adherence. The variance inflation factor is used to detect the presence of linear relationships (ie, collinearity).<sup>[35]</sup> The variance inflation factor values were around 1, indicating that it was appropriate to proceed with logistic regression.<sup>[36]</sup> The odds ratios (ORs) for antidepressant adherence and the corresponding 95% confidence interval (CIs) were estimated, adjusting for possible covariates. Data management and analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

## 2.6. Ethics approval

This study was approved by the Gachon University Institutional Review Board (IRB No. 1044396-201710-HR-169-10).

## 3. Results

### 3.1. Characteristics of immigrants

The number of immigrants who were prescribed antidepressants for the first time in 2012 was 2,398. Native-born Koreans were matched by sex, age, and CCI score with the immigrants. The general characteristics of the immigrants and native-born Koreans are presented in Table 1.

By immigration status, naturalized citizens accounted for the greatest proportion of immigrants (63.7%), followed by marriage immigrants (20.1%) and permanent residents (16.2%) (Table 1). There were many more women (82.8%) than men (17.2%), and the most common age group was 40–49 years (28.5%), followed by 50 to 59 years (25.1%). The overwhelming majority (92.2%) of immigrants lived in cities, and 47% of them lived in households with two or three members. The proportion of the immigrants who were in the first quintile of KNHI contributions, corresponding to the lowest income level, was 33.1% and 7.6% of immigrants were Medical Aid beneficiaries. Slightly fewer than half (43.8%) of the patients had a CCI score of 1 or higher, and 6.8% of them had a psychiatric comorbidity other than depressive disorder. Furthermore, 9.4% of them were prescribed two or more antidepressants, and 52% of them achieved AOC in the acute phase within the initial 12 weeks.

### 3.2. Antidepressant adherence of immigrants compared to native-born Koreans

The first-year average MPR of immigrants who received antidepressants for the first time was 27.1%, which was significantly lower than the MPR of 30.9% observed for Korean natives ( $P=.038$ ). Only 10.1% of immigrants were adherent (defined as achieving an MPR of at least 80% for antidepressants), whereas 14.6% of native-born Koreans were adherent ( $P<.001$ , Table 2).

Multivariable logistic regression showed that immigrants were less likely to be adherent with antidepressants than native-born Koreans. After adjusting for the type of insurance, residential region, insurance contribution, number of household members, psychiatric comorbidities, number of antidepressants, physician's specialty at the first diagnosis, AOC within 12 weeks, and the presence of a usual source of care, the likelihood of adherence among immigrants was 0.76 times lower than that of native-born Koreans (OR 0.76, 95% CI 0.63–0.92) (Table 3).

**Table 1**  
**Characteristics of immigrants and matched native-born Koreans.**

		Immigrants		Native-born Koreans*		P-value†
		N	%	N	%	
Total		2398	100	2398	100	
Immigration status	Permanent resident	389	16.2			
	Marriage immigrant	482	20.1			
	Naturalized citizen	1527	63.7			
Sex	Male	413	17.2	412	17.2	.969
	Female	1985	82.8	1986	82.8	
Age group (yr)	20–29	202	8.4	202	8.4	1
	30–39	374	15.6	374	15.6	
	40–49	684	28.5	684	28.5	
	50–59	602	25.1	602	25.1	
	60–69	308	12.8	310	12.9	
	70 and over	228	9.5	226	9.4	
Type of insurance	NHI	2215	92.4	2244	93.6	.101
	Medical Aid	183	7.6	154	6.4	
Residential region	Urban	2211	92.2	2160	90.1	.010
	Rural	187	7.8	238	9.9	
Insurance premium, quintile	1	794	33.1	587	24.5	<.0001
	2	695	29.0	356	14.8	
	3	490	20.4	396	16.5	
	4	256	10.7	442	18.4	
	5	163	6.8	617	25.7	
Number of household members	1	786	32.8	567	23.6	<.001
	2–3	1127	47.0	920	38.4	
	4 and over	485	20.2	911	38.0	
CCI	0	1,347	56.2	1,346	56.1	.997
	1	663	27.6	662	27.6	
	2 and over	388	16.2	390	16.3	
Psychiatric comorbidities	No	2236	93.2	2148	89.6	<.001
	Yes	162	6.8	250	10.4	
Number of antidepressants	1	2172	90.6	2136	89.1	.086
	2 and over	226	9.4	262	10.9	
Physician's specialty at first diagnosis	Psychiatry	730	30.4	876	36.5	<.001
	others	1668	69.6	1522	63.5	
Usual source of care	No	1275	53.2	1261	52.6	.686
	Yes	1123	46.8	1137	47.4	
AOC (within 12 weeks)	No (<3)	1150	48.0	1088	45.4	.073
	Yes (>=3)	1248	52.0	1310	54.6	

AOC = appropriateness of care, CCI = Charlson Comorbidity Index, NHI = National Health Insurance.

\* Native-born Koreans were matched to each case by sex, age, and CCI score.

† P-value was determined using chi-square test.

**3.3. Patterns and predictors of antidepressant adherence in immigrants**

Changes in adherence over time after the first antidepressant prescription were analyzed. In the first month, 44.5% of patients were adherent (MPR ≥ 80%) but this proportion decreased to 29.5% in the second month. Over time, the proportion of

adherent patients gradually decreased, with only 14.0% continuing to be adherent at 12 months. The proportion of nonadherent patients (0 < MPR < 80%)—excluding those who discontinued medication—also steadily decreased from 55% in

**Table 2**  
**Mean MPR and proportion of adherence among immigrants and native-born Koreans.**

	Immigrants	Native-born Koreans	P-value†
Mean MPR (%)	27.1	30.9	.038
Adherence (% of patients)	10.1	14.6	<.001
Nonadherence* (% of patients)	89.9	85.4	

MPR = medication possession ratio.

\* Including both nonadherence and discontinuation.

† P-value: t-test for continuous variables (mean MPR), chi-square test for categorical variables.

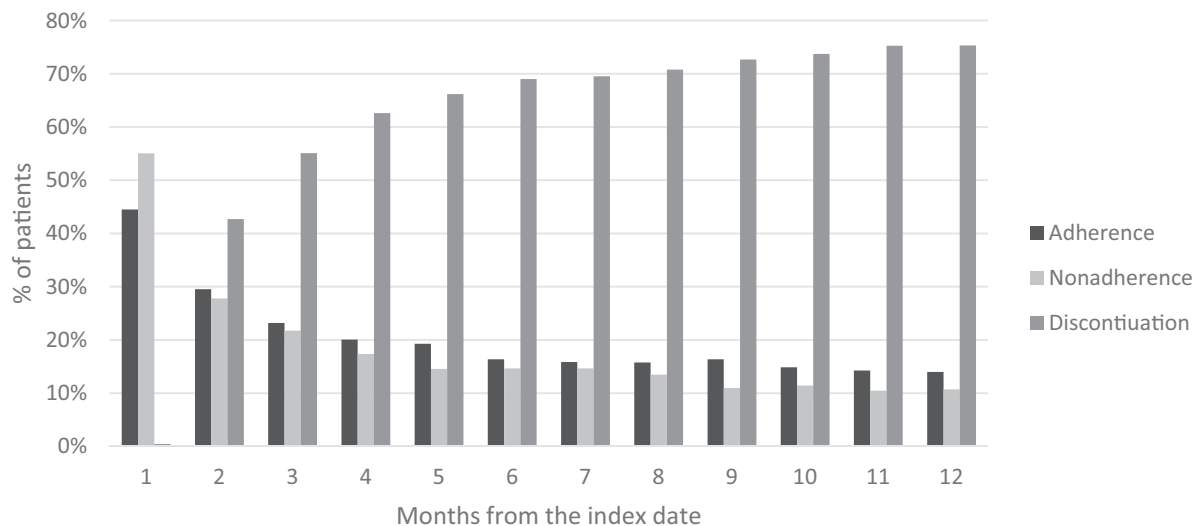
**Table 3**  
**Multivariable logistic regression for the antidepressant adherence among immigrants compared to native-born Koreans.**

	Category	Adjusted OR*	95% CI
Patient origin	Native-born Korean†	1	
	Immigrant	0.76	0.63–0.92

AOC = appropriateness of care, CCI = Charlson Comorbidity Index, CI = confidence interval, OR = odds ratio.

\* Adjusted for type of insurance, residential region, insurance premium quintiles, number of household members, psychiatric comorbidities, number of antidepressants, doctor's specialty at first diagnosis, AOC, and usual source of care.

† Native-born Koreans were matched for each case by sex, age, and CCI score. Therefore, we have excluded the variables used for the matching from the estimation of the adjusted OR.



**Figure 1.** Medication adherence patterns for antidepressants among immigrants (% of patients). Adherence: MPR  $\geq$  80%, Nonadherence: 0% < MPR < 80%, Discontinuation: no medication being prescribed for 30 days after the last prescription.

the first month to 10.7% at 12 months. Meanwhile, in the second month, medication discontinuation rapidly increased to account for 42.7% of all patients, and the proportion of patients who discontinued their medication continued to increase up to 5 months after the first prescription (Fig. 1).

In Table 4, the predictors of antidepressant adherence are presented. As age decreased, the likelihood of being adherent decreased (20–29 years: OR 0.22, 95% CI 0.10–0.46; 30–39 years: OR 0.27, 95% CI 0.15–0.50; reference group: 70 and over).

Being a KNHI beneficiary (OR 2.16, 95% CI 1.30–3.57), having a higher number of household members, having psychiatric comorbidities (OR 2.80, 95% CI 1.81–4.31) and taking two or more antidepressants (OR 2.45, 95% CI 1.67–3.61) were associated with a higher likelihood of adherence. In addition, immigrants who were initially diagnosed by a psychiatrist (OR 2.24, 95% CI 1.60–3.13), who achieved AOC within 12 weeks (OR 3.54, 95% CI 2.51–4.98), and who had a usual source of care (OR 1.69, 95% CI 1.25–2.27) were more likely to be adherent. Immigration status did not significantly affect medication adherence. Sex, residential region, CCI score, and insurance contribution (as a proxy for income) were likewise not associated with adherence.

#### 4. Discussion

This study analyzed medication adherence with antidepressants for all registered immigrants using KNHI data. The main findings of this study were that immigrants with depression residing in South Korea had lower antidepressant adherence than native-born Koreans with depression after adjusting for socioeconomic factors, comorbidities, and healthcare accessibility. The majority of immigrants who were newly prescribed antidepressants were women aged between 40 and 59 years. Compared to Korean-born depression patients, immigrants with depression had a relatively low income and were mostly single-person households.

The average annual MPR of the immigrants who were prescribed antidepressants for the first time was 27.1%, and only

10.1% were adherent (with an MPR of 80% or higher). The absolute difference in the adherence rate between immigrants and native-born Koreans was small, but significant (10.1% vs 14.6%,  $P < .001$  in Table 2). Non-adherence may increase the impact of under-treatment because non-adherence with antidepressants has been shown to result in negative outcomes in patients with depression, causing an economic burden in addition to its effects on mental health. The response rate to antidepressants was lower in the non-adherent group.<sup>[37,38]</sup> The relative risk of hospitalization or emergency department visit was higher in the non-adherent group.<sup>[39,40]</sup> In addition, non-adherence led to an increase in medical costs.<sup>[21,41]</sup> Antidepressant adherence was very low compared with medication adherence for other chronic diseases; for instance, the average MPR for type 2 diabetes was reported to be 75.3%,<sup>[42]</sup> and 45.2% of patients were found to be nonadherent with antihypertensive drugs.<sup>[43]</sup> Hunot et al (2007) similarly found that the adherence rate of patients who received antidepressants for the first time was only 19%, and the reason for this low rate was complex concerns about potential dependence or stigma.<sup>[44]</sup>

Immigrants with depression were 0.76 times less likely to be adherent with antidepressants than native-born Koreans with depression. Similarly, in a Swedish study,<sup>[45]</sup> immigrants showed a lower likelihood of adherence, with an OR of 0.61 for migration from the Middle East and an OR of 0.67 for migration from other countries. Another study conducted in Denmark found that immigrants had a higher risk of a low pick-up rate of prescriptions than native-born Danes, with a hazard ratio of 1.55.<sup>[46]</sup> It is an important finding that immigrants' adherence with medication is significantly lower than that of their native-born counterparts, even after adjusting for demographic, socioeconomic, and predisposing factors. In South Korea, 70% of permanent migrants were found to be marriage migrants, and multicultural families accounted for 1.58% of all households and 5.2% of all births.<sup>[47]</sup> For this reason, it is important to take note of research showing that the health of second-generation immigrants may also be at higher risk. US-born Latinos were found to have a higher risk of mental disorders than immigrants who emigrated to a new country,<sup>[48]</sup> and the first generation of

**Table 4**  
**Factors associated with antidepressant adherence among immigrants.**

Variables	Category	OR	95% CI
Immigration status	Naturalized citizen	1	
	Permanent resident	0.87	0.56–1.36
	Marriage immigrant	1.27	0.85–1.88
Sex	Male	1	
	Female	0.96	0.66–1.41
Age group (yr)	20–29	0.22	0.10–0.46
	30–39	0.27	0.15–0.50
	40–49	0.37	0.22–0.60
	50–59	0.41	0.25–0.69
	60–69	0.55	0.34–0.9
	70 and over	1	
Type of insurance	NHI	2.16	1.30–3.57
	Medical Aid	1	
Residential region	Urban	1	
	Rural	1.19	0.68–2.08
Insurance premium, quintile	1	1.73	0.91–3.26
	2	0.70	0.36–1.35
	3	1.15	0.60–2.22
	4	1.19	0.58–2.45
	5	1	
Number of household members	1	1	
	2~3	1.51	1.07–2.14
	4 and over	1.58	0.99–2.53
CCI	0	1	
	1	1.05	0.75–1.48
	2 and over	1.12	0.75–1.67
Psychiatric comorbidities	No	1	
	Yes	2.80	1.81–4.31
Number of antidepressants	1	1	
	2 and over	2.45	1.67–3.61
Physician's specialty at first diagnosis	Psychiatry	2.24	1.60–3.13
	Others	1	
AOC (within 12 wk)	No (<3)	1	
	Yes (≥3)	3.54	2.51–4.98
Usual source of care	No	1	
	Yes	1.69	1.25–2.27

AOC = appropriateness of care, CCI = Charlson Comorbidity Index, CI = confidence interval, NHI = National Health Insurance, OR = odds ratio.

immigrant women was found to be healthier than the second generation.<sup>[49]</sup> Furthermore, US-born Asian children have been reported to be at a higher risk in terms of physical and mental health than US-born white children.<sup>[50]</sup> When mental illness occurs, challenges such as financial problems, lack of information, discrimination, language barriers, and feeling unheard by service providers can limit immigrant children's access to medical care.<sup>[51]</sup>

A monthly breakdown of the pattern of medication adherence among immigrants showed that the proportion of adherent patients was only 44.5% even in the first month and declined to less than 30% in the second month. The proportion of patients who stopped taking their medication surged to 42.7% in the second month, and subsequently increased over time. These results are in line with the findings of Cruz et al. (2012) that the median time to discontinuation of antidepressant medication was 2 months and the risk of discontinuation was higher among immigrants than among their native-born counterparts, with a hazard ratio of 1.28 (95% CI 1.16–1.42).<sup>[52]</sup> In situations where pharmacological treatment is required, discontinuation of

medication within the first 3 months significantly reduces the clinical usefulness of antidepressant use. This is reflected in clinical guidelines for antidepressant medication, which indicate that at least 3 months of drug use is required in the acute phase, and that long-term drug use is generally required for 1 to 2 years.<sup>[53]</sup> Early treatment is very important because its failure causes repetition and deterioration of symptoms. A previous study showed that the achievement of AOC among immigrants who were prescribed antidepressants for the first time was significantly lower than that of native-born Koreans.<sup>[54]</sup> A possible explanation is that low AOC may have acted as a barrier for medication adherence among immigrants.

No significant difference in adherence was found according to immigration status, although the Korean proficiency of naturalized citizens is relatively high and their residence period is long.<sup>[55]</sup> These results differ from those of other studies, which reported that higher language proficiency<sup>[11,56]</sup> or acculturation<sup>[57]</sup> increased mental health service use. In this study, administrative data were used to classify naturalized citizens, permanent residents, and marriage immigrants according to visa type. However, Korean-Chinese (known as *joseon-jok*) account for approximately half of permanent residents and naturalized citizen, as well as 22% of marriage immigrants.<sup>[58]</sup> Most Korean-Chinese are proficient in Korean.

Younger patients had a lower likelihood of being adherent. The OR of adherence was 0.22 for patients in their 20s and 0.27 for those in their 30s. These results are similar to those of previous studies that reported higher adherence in older patients.<sup>[59,60]</sup> A possible explanation may be that older people are more accustomed to taking medicine. Alternatively, immigrants aged 60 or older may have a relatively long residence period. The mean age of migrant women in Korea is 33 years old, and 75% of them are aged 31 or younger at the time of migration.<sup>[61]</sup> Therefore, this finding may support the importance of acculturation. In other words, it can be inferred that language proficiency and understanding of the health system had positive effects on medication adherence.

Interestingly, immigrants (30.4%) visited psychiatrists for the first diagnosis less frequently than their native-born Korean counterparts (36.5%) ( $P < .001$ ). Meanwhile, visiting a psychiatrist for the first diagnosis was associated with a significantly higher likelihood of adherence (OR 2.24; 95% CI 1.60–3.13) among immigrants. A possible explanation for this is linked to patients' awareness of mental illness and concerns about stigma. In Asian countries, mental illness is still regarded as a personal weakness and there is a great deal of family stigma.<sup>[62]</sup> Stigma<sup>[63]</sup> and negative attitudes of patients<sup>[64,65]</sup> are important factors that inhibit medication adherence and healthcare utilization. In particular, the perceptions of mental illness in China and Vietnam, which account for the majority of immigrants, were relatively negative. For instance, 80% of psychiatric patients experienced discrimination and 69% of the patients believed that illness would affect their job position in China,<sup>[62]</sup> and similar perceptions were reported in Vietnam.<sup>[66]</sup> In contrast, mental health care utilization has recently improved in Korea. The mental health care utilization rate increased from 15.3% in 2011 to 22.2% in 2016, while visits to psychiatrists increased by 30.6% during the same period.<sup>[67]</sup>

Another meaningful finding was that having a usual source of care significantly increased the likelihood of adherence (OR 1.69, 95% CI 1.25–2.27). Jung et al (2016) reported a significantly lower level of medication nonadherence in patients with a usual

source of care (OR 0.61).<sup>[68]</sup> The presence of a usual source of care has also been shown to have a positive effect on the pharmacological treatment and management of other chronic diseases such as diabetes,<sup>[34]</sup> and hypertension.<sup>[69]</sup>

The fact that visiting a psychiatrist, achieving AOC, and having a usual source of care greatly increased the likelihood of antidepressant adherence is a sign of the importance of trust between patients and physicians. This is because health care providers play a very important role in encouraging patients to learn about their diseases, to manage chronic diseases, and to maintain good health.<sup>[70]</sup> Insufficient patient education about the disease leads to poor adherence, and the patient-physician relationship is a major predictor of adherence (with a negative provider-patient relationship associated with low adherence).<sup>[71,72]</sup> This relationship is very important for achieving therapeutic goals. The fear of not being understood by health care providers and the lack of understanding of cultural differences among health care providers further impedes the use of mental healthcare by immigrants.

A major strength of this study is that representative national insurance data were used to investigate antidepressant adherence among all registered immigrants. Because of the use of claims data, the risk of selection bias or recall bias for all variables was low, including the adherence data that were analyzed. Above all, there have been few studies on the factors affecting antidepressant adherence among immigrants. In addition to the effects of demographic factors, socioeconomic factors, and predisposing factors on antidepressant adherence, policy implications were provided to improve future adherence, including the need to foster the establishment of a usual source of care, improved access to psychiatric care, and the importance of early treatment. Our findings suggest that there is a need for improved access to mental health care for immigrants and families of immigrants, as well as support for the continuity of mental health care.

There are several limitations worth noting. First, undocumented immigrants who had entered Korea illegally or were unable to afford health insurance were excluded from this analysis. Medication adherence among these undocumented immigrants is expected to be lower than among legal immigrants. However, since the Korean health insurance system was changed in 2019 to make it mandatory for foreigners living in Korea for more than 6 months to register, it is expected that more foreigners will benefit from health insurance in the future. Second, the data did not reflect services that did not generate claims, such as psychological counseling services that were not covered by insurance. In addition, it was not possible to distinguish whether the discontinuation reflected the clinician's medical judgment due to symptom improvement or the patient's arbitrary discontinuation. Nevertheless, attention to medication adherence is still important. because the medication discontinuity rate exceeded 40% within 2 months of the first dose, whereas clinical guidelines and clinicians state that patients should take medicines for at least 4 to 6 months.<sup>[53,73]</sup> Third, MPR is an indirect measurement of adherence, because it depends on the assumption that patients take their prescription medicines. However, it is unknown whether patients actually did so. Fourth, this study could not assess the linguistic and cultural factors that influenced antidepressant adherence among immigrants, such as language barriers and country of origin. This suggests that in-depth follow-up studies are needed to investigate factors affecting immigrants' medical use and medication adherence in addition to demographic and medical factors.

## 5. Conclusion

Antidepressant adherence is important for managing depression, but this study showed that it is difficult for immigrants to achieve proper adherence and that of adherence rate of immigrants was lower than that of native-born Koreans. However, it appears that visiting a psychiatrist, achieving AOC, and having a usual source of care might increase antidepressant adherence among immigrants. This suggests the need for policies in the healthcare system that promote access to mental healthcare and ensure continuity of care for immigrants with depression. Further research is suggested, with a focus on cultural and/or linguistic factors affecting immigrants' adherence and healthcare utilization to increase adherence and to ensure immigrants' access to mental health care.

## Acknowledgments

The authors would like to thank the National Health Insurance Service for cooperation.

## Author contributions

SHJ and SMJ conceived and designed the study. HC and CK analyzed the data. SHJ wrote the paper. SMJ participated in drafting the article or revising it critically for content.

**Conceptualization:** Suhyun Jang, Sunmee Jang.

**Data curation:** Hyemin Cho, Cino Kang.

**Formal analysis:** Hyemin Cho, Cino Kang.

**Supervision:** Sunmee Jang.

**Writing – original draft:** Suhyun Jang.

**Writing – review & editing:** Sunmee Jang.

## References

- [1] Korea Immigration Service. Korea Immigration Service Statistics 2018. In: Ministry of Justice, ed. Korea 2018.
- [2] Survey on Immigrant's Living Conditions and Labour Force. 2018. Available at: [http://kosis.kr/statHtml/statHtml.do?orgId=101&tblId=DT\\_2FF001F&conn\\_path=I3](http://kosis.kr/statHtml/statHtml.do?orgId=101&tblId=DT_2FF001F&conn_path=I3).
- [3] Korean Statistical Information Service. Statistics of Arrivals and Departures. In: Ministry of Justice, ed. Korea 2018.
- [4] Ministry of justice. Fact Check 2019; Available at: <http://www.immigration.go.kr/immigration/2536/subview.do?enc=Zm5jdDF8QEB8JTJGYmJzJTJGaW1taWdyYXRpb24lMkY0MjllMkY1MTYzMDMlMkZhenRjbfZpZXcuZG8lM0Y%3D>. Accessed 20 Feb, 2020.
- [5] Vicol M-C, Loue S, Sajatovic M. Barriers to Care. *Encyclopedia of Immigrant Health* New York, NY: Springer New York; 2012;260–3.
- [6] Aldridge RW, Nellums LB, Bartlett S, et al. Global patterns of mortality in international migrants: a systematic review and meta-analysis. *Lancet* 2018;392:2553–66.
- [7] Derr AS. Mental health service use among immigrants in the United States: a systematic review. *Psychiatr Serv* 2016;67:265–74.
- [8] Ku L, Matani S. Left out: immigrants' access to health care and insurance. *Health Affairs* 2001;20:247–56.
- [9] Chen J, Vargas-Bustamante A. Estimating the effects of immigration status on mental health care utilizations in the United States. *J Immigr Minor Health* 2011;13:671–80.
- [10] Leinonen MK, Campbell S, Ursin G, et al. Barriers to cervical cancer screening faced by immigrants: a registry-based study of 1.4 million women in Norway. *Eur J Public Health* 2017;27:873–9.
- [11] Suphanchaimat R, Kantamaturapoj K, Putthasri W, et al. Challenges in the provision of healthcare services for migrants: a systematic review through providers' lens. *BMC Health Serv Res* 2015;15:390.
- [12] Whittal A, Lippke S. Investigating patients with an immigration background in Canada: relationships between individual immigrant attitudes, the doctor-patient relationship, and health outcomes. *BMC Public Health* 2016;16:23.

- [13] Kirmayer LJ, Narasiah L, Munoz M, et al. Common mental health problems in immigrants and refugees: general approach in primary care. *CMAJ* 2011;183:E959–67.
- [14] Lindert J, Ehrenstein OS, Priebe S, et al. Depression and anxiety in labor migrants and refugees—a systematic review and meta-analysis. *Soc Sci Med* 2009;69:246–57.
- [15] Organization WH. The global burden of disease: 2004 update. 2008; World Health Organization,
- [16] Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *Plos Med* 2006;3:e442.
- [17] Gaynes BN, Warden D, Trivedi MH, et al. What did STAR\*D teach us? Results from a large-scale, practical, clinical trial for patients with depression. *Psychiatr Serv* 2009;60:1439–45.
- [18] Ho SC, Chong HY, Chaiyakunapruk N, et al. Clinical and economic impact of non-adherence to antidepressants in major depressive disorder: a systematic review. *J Affect Disord* 2016;193:1–0.
- [19] Eo YS, Kim JS. Associations of health belief and health literacy with Pap smear practice among Asian immigrant women. *Eur J Oncol Nurs* 2019;42:63–8.
- [20] Kreps GL, Sparks L. Meeting the health literacy needs of immigrant populations. *Patient Educ Couns* 2008;71:328–32.
- [21] Cantrell CR, Eaddy MT, Shah MB, et al. Methods for evaluating patient adherence to antidepressant therapy: a real-world comparison of adherence and economic outcomes. *Med Care* 2006;44:300–3.
- [22] Serna MC, Cruz I, Real J, et al. Duration and adherence of antidepressant treatment (2003 to 2007) based on prescription database. *Eur Psychiatry* 2010;25:206–13.
- [23] Sheehan DV, Keene MS, Eaddy M, et al. Differences in medication adherence and healthcare resource utilization patterns: older versus newer antidepressant agents in patients with depression and/or anxiety disorders. *CNS Drugs* 2008;22:963–73.
- [24] Lee J, Lee JS, Park S-H, et al. Cohort profile: the national health insurance service–national sample cohort (NHIS-NSC), South Korea. *Int J Epidemiol* 2016;46:e15–15.
- [25] Owens PL, Hoagwood K, Horwitz SM, et al. Barriers to children's mental health services. *J Am Acad Child Adolesc Psychiatry* 2002;41:731–8.
- [26] Oluboka OJ, Katzman MA, Habert J, et al. Functional recovery in major depressive disorder: providing early optimal treatment for the individual patient. *Int J Neuropsychopharmacol* 2018;21:128–44.
- [27] Siu AL, Bibbins-Domingo K, Grossman DC, et al. Screening for depression in adults: US Preventive Services Task Force recommendation statement. *JAMA* 2016;315:380–7.
- [28] Jacobs K, Julyan M, Lubbe MS, et al. Medicine possession ratio as proxy for adherence to antiepileptic drugs: prevalence, associations, and cost implications. *Patient Prefer Adherence* 2016;10:539–47.
- [29] Krueger K, Griese-Mammen N, Schubert I, et al. In search of a standard when analyzing medication adherence in patients with heart failure using claims data: a systematic review. *Heart Fail Rev* 2018;23:63–71.
- [30] Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;43:1130–9.
- [31] Kim KH. [Comparative study on three algorithms of the ICD-10 Charlson comorbidity index with myocardial infarction patients]. *J Prev Med Public Health* 2010;43:42–9.
- [32] Korean Medication Algorithm Project for Depression Disorder Task Force/Korean Medication Algorithm Project for Depression Disorder. Seoul, Korea: Korean Society for Affective Disorders; 2012.
- [33] Simon GE. Evidence review: efficacy and effectiveness of antidepressant treatment in primary care. *Gen Hosp Psychiatry* 2002;24:213–24.
- [34] DeVoe JE, Tillotson CJ, Wallace LS. Usual source of care as a health insurance substitute for U.S. adults with diabetes? *Diabetes Care* 2009;32:983–9.
- [35] Midi H, Sarkar SK, Rana S. Collinearity diagnostics of binary logistic regression model. *J Interdiscip Math* 2010;13:253–67.
- [36] Akinwande MO, Dikko HG, Samson A. Variance inflation factor: as a condition for the inclusion of suppressor variable (s) in regression analysis. *Open J Stat* 2015;5:754.
- [37] Akerblad AC, Bengtsson F, Ekselius L, et al. Effects of an educational compliance enhancement programme and therapeutic drug monitoring on treatment adherence in depressed patients managed by general practitioners. *Int Clin Psychopharmacol* 2003;18:347–54.
- [38] Akerblad AC, Bengtsson F, von Knorring L, et al. Response, remission and relapse in relation to adherence in primary care treatment of depression: a 2-year outcome study. *Int Clin Psychopharmacol* 2006;21:117–24.
- [39] Yau WY, Chan MC, Wing YK, et al. Noncontinuous use of antidepressant in adults with major depressive disorders - a retrospective cohort study. *Brain Behav* 2014;4:390–7.
- [40] Liu X, Tepper PG, Able SL. Adherence and persistence with duloxetine and hospital utilization in patients with major depressive disorder. *Int Clin Psychopharmacol* 2011;26:173–80.
- [41] White TJ, Vanderplas A, Ory C, et al. Economic impact of patient adherence with antidepressant therapy within a managed care organization. *Dis Manag Health Out* 2003;11:817–22.
- [42] Iglay K, Cartier SE, Rosen VM, et al. Meta-analysis of studies examining medication adherence, persistence, and discontinuation of oral anti-hyperglycemic agents in type 2 diabetes. *Curr Med Res* 2015;31:1283–96.
- [43] Abegaz TM, Shehab A, Gebreyohannes EA, et al. Nonadherence to antihypertensive drugs: a systematic review and meta-analysis. *Medicine* 2017;96:
- [44] Hunot VM, Horne R, Leese MN, et al. A cohort study of adherence to antidepressants in primary care: the influence of antidepressant concerns and treatment preferences. *Prim Care Companion J Clin Psychiatry* 2007;9:91–9.
- [45] Freccero C, Sundquist K, Sundquist J, et al. Primary adherence to antidepressant prescriptions in primary health care: a population-based study in Sweden. *Scand J Prim Health Care* 2016;34:83–8.
- [46] Wallach-Kildemoes H, Thomsen LT, Kriegabaum M, et al. Antidepressant utilization after hospitalization with depression: a comparison between non-Western immigrants and Danish-born residents. *BMC Psychiatry* 2014;14:77.
- [47] Korean Women's Development Institute. An Analysis on the National Survey of Multicultural Families 2018. In: Ministry of Gender Equality & Family, ed. Seoul 2019.
- [48] Alegría M, Canino G, Shrout PE, et al. Prevalence of mental illness in immigrant and non-immigrant US Latino groups. *American Journal of psychiatry* 2008;165:359–69.
- [49] Lau AS, Tsai W, Shih J, et al. The immigrant paradox among Asian American women: are disparities in the burden of depression and anxiety paradoxical or explicable? *J Consult Clin Psychol* 2013;81:901.
- [50] Huang KY, Calzada E, Cheng S, et al. Physical and mental health disparities among young children of Asian immigrants. *J Pediatr* 2012;160:331–336.e331.
- [51] Tulli M, Salami B, Begashaw L, et al. Immigrant mothers' perspectives of barriers and facilitators in accessing mental health care for their children. *J Transcult Nurs* 2020;1043659620902812.
- [52] Cruz I, Serna C, Rué M, et al. Duration and compliance with antidepressant treatment in immigrant and native-born populations in Spain: a four year follow-up descriptive study. *BMC Public Health* 2012;12:256.
- [53] National Institute for Health and Care Excellence. Depression in adults: recognition and management. Clinical guideline [CG90]. 2009.
- [54] Jeong S, Kang C, Cho H, et al. Socioeconomic determinants affecting the access and utilization of depression care services in immigrants: a population-based study. *PloS one* 2019;14:e0213020.
- [55] Survey on Immigrant's Living Conditions and Labour Force. 2019.
- [56] Kim G, Aguado Loi CX, Chiriboga DA, et al. Limited English proficiency as a barrier to mental health service use: a study of Latino and Asian immigrants with psychiatric disorders. *J Psychiatr Res* 2011;45:104–10.
- [57] Lorenzo-Blanco EI, Delva J. Examining lifetime episodes of sadness, help seeking, and perceived treatment helpfulness among US Latino/as. *Community Ment Health J* 2012;48:611–26.
- [58] Park K-S, Lee CW, Jiang M. Changes in the demographic structure of Korean-Chinese population and policy implications. *Migration Research & Training Centre* 2019.
- [59] McGettigan P, Kelly A, Carvahlo M, et al. Anti-depressants in primary care: analysis of treatment discontinuations. *Pharmacoepidemiol Drug Saf* 2000;9:521–8.
- [60] Robinson RL, Long SR, Chang S, et al. Higher costs and therapeutic factors associated with adherence to NCQA HEDIS antidepressant medication management measures: analysis of administrative claims. *J Manag Care Pharm* 2006;12:43–54.
- [61] Lee S, Kim D-S. Acculturation and self-rated health among foreign women in Korea. *Health and Social Welfare Review* 2014;34:453–83.
- [62] Zhang Z, Sun K, Jatchavala C, et al. Overview of stigma against psychiatric illnesses and advancements of anti-stigma activities in six Asian societies. *Int J Environ Res Public Health* 2019;17:
- [63] Sirey JA, Bruce ML, Alexopoulos GS, et al. Stigma as a barrier to recovery: perceived stigma and patient-rated severity of illness as



- predictors of antidepressant drug adherence. *Psychiatric services* 2001;52:1615–20.
- [64] Jang Y, Chiriboga DA, Okazaki S. Attitudes toward mental health services: age-group differences in Korean American adults. *Aging Ment Health* 2009;13:127–34.
- [65] Mohamed S, Rosenheck R, McEvoy J, et al. Cross-sectional and longitudinal relationships between insight and attitudes toward medication and clinical outcomes in chronic schizophrenia. *Schizophr Bull* 2009;35:336–46.
- [66] Seeman N, Tang S, Brown AD, et al. World survey of mental illness stigma. *Journal of affective disorders* 2016;190:115–21.
- [67] Hong JP. *The Survey of Mental Disorders in Korea 2016*. Ministry of Health and Welfare, Samsung Medical Center; 2017.
- [68] Jung Y, Byeon J. The association between having a usual source of care and adherence to medicines in patients with chronic diseases. *Korean J Clin Pharm* 2016;26:128.
- [69] He J, Muntner P, Chen J, et al. Factors associated with hypertension control in the general population of the United States. *Arch Intern Med* 2002;162:1051–8.
- [70] Bodenheimer T, Lorig K, Holman H, et al. Patient self-management of chronic disease in primary care. *JAMA* 2002;288:2469–75.
- [71] Hansen MC, Cabassa LJ. Pathways to depression care: help-seeking experiences of low-income Latinos with diabetes and depression. *J Immigr Minor Health* 2012;14:1097–106.
- [72] Shigemura J, Ogawa T, Yoshino A, et al. Predictors of antidepressant adherence: results of a Japanese Internet-based survey. *Psychiatry Clin Neurosci* 2010;64:179–86.
- [73] Qaseem A, Snow V, Denberg TD, et al. Clinical Efficacy Assessment Subcommittee of American College of P. Using second-generation antidepressants to treat depressive disorders: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2008; 149:725–33.