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- Assess medication adherence and factors that influence it among older patients with major depressive disorder and other illnesses

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Adherence to Selective Serotonin and Serotonin-Norepinephrine Reuptake Inhibitor Prescriptions Affects Overall Medication Adherence in Older Persons: Evidence From the Italian Nationwide OsMed Health-DB Database

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ABSTRACT

Objective: This study aimed to evaluate prevalence of prescription of and adherence to selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) and whether adherence to these classes of drugs affects overall medication adherence in older persons.

Methods: In a cross-sectional analysis of administrative data comprehensive of all prescribed drugs reimbursed by the Italian national health care system, new prescriptions of SSRIs and SNRIs to persons aged 65 years or older were analyzed (n = 380,400 in 2011; 395,806 in 2012; 409,741 in 2013, from a total sample of 3,762,299 persons aged 65 years or older) as well as prescriptions of antihypertensives, statins, other psychiatric drugs, antidiabetics, antiplatelets, anticoagulants, drugs for chronic obstructive pulmonary disease, and antiosteoporotics. Adherence was estimated by calculating the proportion of days covered by drugs dispensed during a period of 365 days. Adherence was defined as a proportion of days covered of more than 80%.

Results: Prevalence of SSRI and SNRI prescriptions varied from 11.4% in 2011 to 12.1% in 2013. Adherence to SSRI and SNRI prescriptions ranged from 31.2% in persons aged ≥ 95 years in 2011 to 41.8% in persons aged 75–84 years in 2013. Persons adherent to SSRI and SNRI prescriptions were more likely to be adherent to the other medications, after adjustment for age, gender, and number of drugs prescribed. The highest association was found for adherence to psychiatric drugs (OR = 1.9; 95% CI, 1.8–2.0).

Conclusions: Adherence to SSRI and SNRI prescriptions is poor in older persons. However, people adherent to these classes of antidepressants are more likely to be adherent to the other medications they are prescribed. Studies are needed to evaluate the reasons for and the potential benefits of increasing adherence to antidepressants on overall adherence.

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Poor adherence to treatment of chronic diseases is a worldwide problem of great magnitude. Adherence to long-term therapy for chronic illnesses in developed countries averages 50% and is even poorer in developing countries,¹ and poor adherence has a negative impact on health outcomes, quality of life, and health care costs. Data from the United States estimated that more than \$100 billion is spent each year on avoidable hospitalizations due to poor adherence.² The origin of poor adherence is multifactorial, including social and economic factors, health systems organization, and behavior of professionals, as well as specific characteristics of diseases, individual patients, and therapies.³ Until now, interventions aimed at improving adherence have shown a limited efficacy.⁴

Though nonadherence is a general public health problem, it is particularly relevant in older adults, since they are more often prescribed several treatments simultaneously as a consequence of frequent chronic multimorbidity. The resulting polypharmacy is a well-recognized problem for many elderly patients, as it implies an increased risk of both adverse drug reactions and reduced adherence.⁵ Moreover, some barriers to adherence are more common in older patients and warrant particular attention in the clinical practice. For example, although forgetting one's medication may occur at any age, in older patients memory difficulties may be exacerbated by other medications or by concomitant cognitive impairment or depression.

Depression is very frequent in older persons. A recent meta-analysis⁶ of individuals aged 50 years and older found a rate of 3.2% for current and 16.5% for lifetime major depression and an even higher (19.4%) prevalence of depressive symptoms. The estimated prevalence of major depression in persons aged 65 years and older is 9.8%.⁷ Symptoms may vary in severity, ranging from an isolated and mild episode through recurrent episodes of moderate severity to chronic and persistent severe illness. For patients with a definite diagnosis of depression, guidelines advocate that drug treatment should continue for at least 6 months following remission of symptoms. Furthermore, long-term preventive treatment is suggested for patients with 2 or more episodes of clinically significant depression within 5 years.⁸ The level of adherence to antidepressant medications is positively correlated with treatment outcomes in depressed patients, independent of type of drug used.⁹ Adherence to recommended antidepressants is reported to range from 40% to 70%,¹⁰ with approximately 25% of patients not informing their physician of drug withdrawal.¹¹

In the Italian Medicines Agency, the National Observatory on the Use of Medicines (OsMed) is responsible for national monitoring of pharmaceutical consumption and expenditure. In this context, OsMed Health-DB is the largest Italian database that prospectively collects information on prescription drugs. This study aims to evaluate the prevalence of prescription of and adherence to selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) in persons aged 65 years of age or older and to analyze whether

- Poor adherence to long-term therapy for chronic diseases is the single most important modifiable factor that compromises treatment outcome, but not all potential factors affecting adherence were considered in previous studies.
- In older persons, depression is frequent and commonly coexists with other chronic diseases. In this part of the population, adherence to antidepressant drugs is associated with higher overall adherence to medications for other chronic illnesses.

adherence to antidepressants affects overall adherence to medications.

METHODS

The Nationwide OsMed Health-DB Database was used. This database includes 35 Italian Local Health Units (LHU) and about 18 million subjects (30% of the Italian population), with a uniform distribution in the North (28.7%), Central (33.7%), and South (29.8%) regions of Italy and a historical series from 2009. The mean age in the sample is 43.5 years versus 43.3 years in the overall Italian population, and the percentage of men is 48.5%, in accordance with the national data.

The Italian Medicines Agency (AIFA—Agenzia Italiana del Farmaco) is the national competent authority responsible for the regulation of medicine use. Inside AIFA, the OsMed monitors national use of medicines in Italy and, since 2012, has started to prospectively analyze data collected per patient with the technical support of CliCon. CliCon was delegated by AIFA for data warehousing and data analysis activities of information voluntarily provided by LHUs and stored in their own local administrative databases. In order to comply with privacy legislation (Legislative Decree n. 196 of 2003, and following amendments), patient ID code was anonymized by LHUs. Using this database, the OsMed report on drug use in Italy (www.agenziafarmaco.gov.it/it/content/rapporti-osmed-luso-dei-farmaci-italia) is published yearly by the AIFA with the following objectives: (a) to describe drug consumption at a national level, (b) to examine changes in drug use over time, (c) to benchmark drug consumption across different Italian regions, and (d) to evaluate appropriate use of drugs and adherence to treatment.

For each LHU, the following current administrative databases have been captured: demographic database (including deaths), outpatient pharmaceutical prescriptions database, inpatient pharmaceutical prescriptions database, "per conto" (distribution on behalf) pharmaceutical prescription database, and hospital discharge database. Data included are gender, birth and death date, Anatomical Therapeutic Chemical (ATC) code, prescription date, number of prescribed packages, price per package (both the community and the direct distribution price), admission and discharge date, type of admission (eg, ordinary, day hospital),

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discharge data (eg, discharged, moved), principal diagnosis (*International Classification of Diseases*, 9th Revision [ICD-9]), secondary diagnosis (ICD-9), main procedure (ICD-9), secondary procedures (ICD-9), and reimbursement per hospital stay (hospital discharge records).

Italian Pharmaceutical Reimbursement System

The Italian pharmaceutical reimbursement system covers the treatment of all relevant diseases, providing pharmaceutical coverage to the whole population. The general conditions of the reimbursement system are established by the Italian Medicines Agency at the national level. Reimbursed drugs (known as Class A) include essential drugs and drugs for serious, acute, and chronic diseases (eg, antihypertensive drugs, antibiotics, hypoglycemic agents, antibiotics, antidepressants, antiplatelet agents, anticoagulants, antiparkinson drugs). Nonreimbursed drugs (known as Class C) include drugs for less relevant disease or minor ailments, drugs whose use is discouraged, and drugs not requiring a medical prescription (eg, antispasmodics, topical treatments). The present analysis is limited to reimbursed medications (Class A).

Therapeutic Categories

Information on each drug package, identified via ATC classification and ID package unique identifier codes, was tracked at the individual level. In the ATC system, antidepressants are coded N06A; in particular, SSRIs and SNRIs were searched with their specific coding (N06AB for SSRIs and N06AX16 and N06AX21 for SNRIs) for inclusion in the present analysis. The other therapeutic categories analyzed were antihypertensive drugs (ATC classification C02, C03, C07, C08, and C09), statins (C10AA and C10BA02), other psychiatric drugs (N03A and N05A), antidiabetics (A10), antiplatelets (B01AC), anticoagulants (B01A), drugs for chronic obstructive pulmonary disease (COPD) (R03), and antiosteoporotics (M05BA, M05BB, H05AA, H05BA, M05BX03, and G03XC01). Only medications prescribed and dispensed by a pharmacy are considered in the present analysis.

The total number of drugs was calculated as the number of different prescribed ATC codes independent of the number of doses.

Adherence Assessment

To calculate adherence, older adults who were newly prescribed one of the drugs of interest during years 2011, 2012, and 2013 were identified, and the date of first drug dispensing was defined as the index date. Patients were considered as newly treated if they had no dispensing of any drug of the same class over the 6 months before the index date. Adherence to antidepressants and to other chronic treatments, including antihypertensive drugs, statins, psychiatric drugs, antidiabetics, antiaggregants, anticoagulants, drugs for COPD, and antiosteoporotics, was estimated by calculating the proportion of days covered by drugs dispensed during a period of 365 days. The number of

days covered by each dispensing was calculated as the ratio between the total amount of active drug in each dispensed package and the recommended daily dose. In accordance with previously adopted thresholds, adherence was defined as a proportion of days covered more than 80%.^{12,13} Adherence was defined as adherence to the broad class of drugs (both SSRIs and SNRIs); this made it possible to calculate adherence even in the event of switching from one drug to another.

Data collection was in full compliance with the Italian law on personal data protection.

Statistical Analysis

Prevalence of SSRIs and SNRIs prescriptions was calculated across 4 age groups (65–74, 75–84, 85–94, and ≥95 years), gender, and 3 geographic areas (North, Central, and South Italy). Categorical and continuous variables were expressed as frequency and percentages, and as mean (SD), respectively. Multivariate logistic regression models were run to analyze the association of adherence to SSRIs and SNRIs with adherence to the other therapeutic categories in 2013. In these models, adherence to SSRIs and SNRIs, age, gender, and total number of prescribed drugs were independent variables.

RESULTS

During 2011, 2012, and 2013, a database was compiled of data collected on drug prescriptions. During 2013, the database included 17,846,127 individuals, who represented 30.0% of the Italian population ($n = 59,394,207$). Of these, 3,762,299 were aged 65 years or older (21.1% of the database sample).

Prevalence of SSRI and SNRI prescription ranged from 11.4 in 2011 to 12.1% of the whole sample in 2013 and was higher in the North than in the South of Italy across the 3 years (Table 1). The most frequently identified SSRIs and SNRIs in 2013 were paroxetine (25.6%), escitalopram (20.2%), sertraline (19.1%), citalopram (15.6%), venlafaxine (8.8%), duloxetine (7.5%), fluoxetine (2.6%), and fluvoxamine (0.6%).

Prevalence was more than double in women than in men. At analysis by age, the lowest prescription prevalence was found in the age group of ≥95 years (ranging from 8.6% to 8.9%) and the highest in the 2 age groups of 75–84 and 85–94 years (ranging from 13.1% to 15.6%) (Table 1). Table 2 presents characteristics of persons receiving a prescription of 1 or more SSRIs or SNRIs in 2013. Persons prescribed SSRIs or SNRIs were more likely to be women, younger, and prescribed a higher mean number of drugs (the mean [SD] number of drugs in persons prescribed with SSRIs and SNRIs was 8.5 [5.8], compared to 5.1 [4.9] in those not prescribed SSRIs and SNRIs) and a higher number of drugs of other therapeutic categories.

Adherence to SSRI and SNRI prescription ranged from 40% in 2011 to 41% in 2013. Adherence was higher in the North and Central regions of Italy compared to the South (Table 3). It was also slightly higher in women than in men and lower in the oldest age group (Table 3 shows proportion of adherence to SSRIs and SNRIs during the 3 years).

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Table 1. Number and Percentage of Older Persons Prescribed SSRIs and SNRIs According to Age Group, Gender, and Geographic Area During 2011, 2012, and 2013

Variable	2011			2012			2013		
	n/N	%	P Value	n/N	%	P Value	n/N	%	P Value
Overall	380,400/3,348,656	11.4	...	395,806/3,365,484	11.8	...	409,741/3,382,396	12.1	...
Age group, y			<.001			<.001			<.001
65–74	161,327/1,678,084	9.6		166,540/1,686,517	9.9		168,342/1,694,992	9.9	
75–84	158,433/1,196,487	13.2		163,229/1,202,499	13.6		168,997/1,208,542	14.0	
85–94	57,853/442,746	13.1		63,321/444,971	14.2		69,592/447,207	15.6	
≥95	2,787/31,339	8.9		2,716/31,497	8.6		2,810/31,655	8.9	
Gender			<.001			<.001			<.001
Male	106,489/1,623,611	6.6		111,747/1,631,770	6.8		116,662/1,639,969	7.1	
Female	273,911/1,725,046	15.9		284,059/1,733,714	16.4		293,079/1,742,426	16.8	
Geographic area			<.001			<.001			<.001
North	197,117/1,558,537	12.6		200,911/1,566,368	12.8		206,691/1,574,240	13.1	
Central	83,654/700,694	11.9		85,070/704,215	12.1		88,574/707,754	12.5	
South	99,629/1,089,426	9.1		109,825/1,094,900	10.0		114,476/1,100,402	10.4	

Abbreviations: SNRI = serotonin-norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor.
Symbol: ... = not applicable.

Persons adherent to SSRI and SNRI prescription were more adherent to the other therapeutic categories (Table 4). Logistic regression models showed that adherence to antidepressants was associated with increased odds of adherence to all the other therapeutic categories with the exception of anticoagulants. Models were adjusted for age, gender, and total number of prescribed drugs (Table 4). The highest association was found between adherence to SSRIs and SNRIs and adherence to other psychiatric drugs (OR = 1.9; 95% CI, 1.8–2.0).

DISCUSSION

Principal Findings

Findings of this study on a large administrative database of older Italian persons showed that the prevalence of SSRI and SNRI prescription varied from 11.4% in 2011 to 12.1% in 2013. Adherence to SSRIs and SNRIs, calculated according to 4 age groups and during 3 years of observations, ranged from 31.2% in persons older than 95 years in 2011 to 41.8% in 75- to 84-year-old persons in 2013. Older persons adherent to these classes of antidepressants were more likely to be adherent to the other therapeutic categories for chronic diseases they were prescribed.

Comparison With Other Studies

Over the past few years, in both clinical and research settings, increasing attention has been devoted to the study of depression in the expanding population of older individuals, in whom a variety of topics, including prevalence, possible treatments, and consequences have been examined extensively. One of the most relevant issues in this area—the problem of nonadherence to antidepressants—still awaits further clarification.¹⁴ Although drugs are commonly considered a cornerstone in the treatment of depression, evidence from epidemiologic studies confirms that about 1 in 3 patients does not complete treatment.¹⁵ Previous studies showed that 50% of patients cease antidepressant treatment as early as within 3 months, a proportion peaking to over

Table 2. Characteristics of Older Persons According to the Prescription of SSRIs and SNRIs During 2013

Variable	Prescribed SSRIs and SNRIs, n (%)	Not Prescribed SSRIs and SNRIs, n (%)	P Value
All	409,741 (100)	3,352,558 (100)	
Age group, y			<.001
65–74	168,342 (41.1)	1,541,581 (46.0)	
75–84	168,997 (41.2)	1,141,981 (34.1)	
85–94	69,592 (17.0)	534,213 (15.9)	
≥95	2,810 (0.7)	134,782 (4.0)	
Gender			<.001
Male	116,662 (28.5)	1,503,216 (44.8)	
Female	293,079 (71.2)	1,849,342 (55.2)	
No. of drugs			<.001
0–4	100,628 (24.6)	1,750,095 (52.2)	
5–9	152,225 (37.2)	1,005,821 (30.0)	
≥10	156,888 (38.3)	596,642 (17.8)	
Therapeutic categories			
Antihypertensives	312,368 (76.2)	1,962,891 (58.5)	<.001
Statins	140,392 (34.3)	809,937 (24.2)	<.001
Other psychiatric drugs	67,838 (16.6)	168,289 (5.0)	<.001
Antidiabetics	64,051 (15.6)	405,676 (12.1)	<.001
Antiaggregants	169,494 (41.4)	949,277 (28.3)	<.001
Anticoagulants	69,648 (17.0)	391,873 (11.7)	<.001
COPD drugs	89,076 (21.7)	483,695 (14.4)	<.001
Antiosteoporotics	43,925 (10.7)	187,910 (5.6)	<.001

Abbreviations: COPD = chronic obstructive pulmonary disease, SNRI = serotonin-norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor.

70% at 6 months.¹⁶ Trifirò and colleagues¹⁷ reported that 27.5% of Italian general practitioner adult patients who were prescribed antidepressants discontinued therapy during the first year, mostly within 3 months. In a secondary analysis of results of the Clinical Outcomes in Measurement-Based Treatment (COMET) trial, Chang and colleagues¹⁸ showed the importance of the frequency of monitoring of symptoms in depressive disorders. More frequent measurement of depression symptoms was associated with greater medication persistence; this finding may explain the lower adherence that we observed among those aged ≥95 years, since this patient population may be less likely and able to be monitored frequently.

Table 3. Percentage of Older Persons Adherent to SSRI and SNRI Prescriptions During 2011, 2012, and 2013 According to Age Group, Gender, and Geographic Area

Variable	Adherence to SSRIs and SNRIs, n/N (%)		
	2011 (N=348,880)	2012 (N=380,400)	2013 (N=395,806)
Overall	128,916/321,916 (40.0)	152,490/380,400 (40.1)	162,306/395,806 (41.0)
Age group, y			
65–74	54,710/138,804 (39.4)	63,448/161,327 (39.3)	67,018/166,540 (40.2)
75–84	54,910/134,842 (40.7)	64,610/158,433 (40.8)	68,152/163,229 (41.8)
85–94	18,589/46,001 (40.4)	23,544/57,853 (40.7)	26,197/63,321 (41.4)
≥95	707/2,269 (31.2)	888/2,787 (31.9)	939/2,716 (34.6)
Gender			
Male	34,700/89,908 (38.6)	41,038/106,489 (38.5)	43,899/111,747 (39.3)
Female	94,216/232,008 (40.6)	111,452/273,911 (40.7)	118,407/284,059 (41.7)
Geographic area			
North	66,505/158,845 (41.9)	83,509/197,117 (42.4)	86,943/200,911 (43.3)
Central	29,902/71,094 (42.1)	35,178/83,654 (42.1)	36,188/85,070 (42.5)
South	32,509/91,977 (35.3)	33,803/99,629 (33.9)	39,175/109,825 (35.7)

Abbreviations: SNRI = serotonin-norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor.

Table 4. Number and Percentage of Persons Adherent to Other Single Therapeutic Categories According to SSRI and SNRI Adherence and Odds for Adherence to Single Therapeutic Categories Due to SSRI and SNRI Adherence

Therapeutic Category	Adherent to SSRIs and SNRIs, n (%)		
	SNRIs, n (%)	OR (95% CI) ^a	P Value
Antihypertensives	103,178 (63.6)	1.3 (1.3–1.4)	<.001
Statins	79,351 (48.9)	1.5 (1.5–1.6)	<.001
Other psychiatric drugs	23,762 (14.6)	1.9 (1.8–2.0)	<.001
Antidiabetics	106,586 (65.7)	1.2 (1.2–1.3)	<.001
Antiaggregants	76,917 (47.4)	1.3 (1.3–1.4)	<.001
Anticoagulants	10,793 (6.6)	1.0 (1.0–1.1)	.107
COPD drugs	37,054 (22.8)	1.2 (1.1–1.2)	<.001
Antiosteoporotics	77,777 (47.9)	1.1 (1.0–1.1)	<.001

^aModels adjusted for age, gender, and total number of prescribed drugs. Abbreviations: COPD = chronic obstructive pulmonary disease, SNRI = serotonin-norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor.

A comparison with previous studies on the association between adherence to antidepressants and adherence to other therapeutic categories for chronic diseases is not possible due to the lack of previous research in this field.

Strengths and Limitations

Assessment of adherence to treatment from administrative data is a potential key limitation to this study. Until now, several indicators of adherence have been proposed, each presenting advantages and limitations; rate of prescriptions has the advantage to be objective and relatively easy to measure. However, it has the limitation that a prescription is not equivalent to ingestion of medication. Thus, our findings may slightly overestimate the real adherence to treatment, though identification of repeated dispensing from pharmacy can be taken as an indirect proof that the drug is effectively ingested.¹⁹ Finally, we cannot exclude that our results might be explained by residual confounding. People adhering to antidepressants might have higher education, cultural status, and health literacy and for this reason be more likely to adhere to other treatments. In addition, adherence reflects individual and behavioral factors such as cognitive and functional status, self-efficacy, and motivation

for self-care as well as factors related to the nature of a condition or coexisting diseases, complexity and duration of the treatment regimen, possible adverse drug reactions, and cost of treatment. Studying factors associated with attrition during treatment for depression, Warden and colleagues²⁰ showed that patients' pretreatment concerns about continuing antidepressant treatment in the presence of side effects signals challenges to the completion of acute phase treatment. Social factors are also important, not only individual relationships, but also patient-provider relationship and different access to social support.²¹ Thus, the causal pathway of such an association cannot be explored in our study, and we might argue that higher adherence to antidepressants simply reflects an individual tendency toward

good of adherence in general. However, when we checked the association of adherence to categories of non-antidepressant drugs with all the other drugs, we did not find consistent results. For example, adherence to antihypertensive drugs was inversely correlated with adherence to other psychiatric drugs (OR=0.88); adherence to other psychiatric drugs and antidiabetics, with adherence to antiosteoporotics (OR=0.78 and 0.74, respectively); and adherence to antiplatelets, with adherence to anticoagulants (OR=0.50). Thus, despite these limitations, our results may suggest that adherence to drugs that reduce depressive symptoms translates into greater adherence to overall therapeutic prescriptions; in fact, depressed patients' improvement in motivation with treatment may lead to enhanced self-care and motivation to improve physical health. This hypothesis, to be proven in prospective trials, further reinforces the indication to actively treat depression in older persons to improve their quality of life and general state of health.

A strength of the study is the very high number of prescriptions evaluated over 3 years across different Italian regions. Another strength is the novelty of the topic, as no study has evaluated whether adherence to a specific class of drugs is associated with adherence to other chronically prescribed medications in older persons.

Conclusions and Policy Implications

The burden of illness in both the general and the elderly population has shifted from acute to chronic diseases, making the problem of poor adherence to long-term treatments of major concern to all stakeholders in the health care system. The risk of poor adherence increases with the duration and complexity of therapeutic regimens, which are by definition inherent to chronic diseases. Adherence is the single most important modifiable factor that compromises treatment outcome.

In the older population, depression is frequent and also commonly coexists with other chronic medical conditions requiring several co-prescriptions, and this association can be interactive. On the one hand, chronic diseases increase

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the risk of depression, with the prevalence of depression being up to 5 times higher in persons with chronic medical conditions.²² This strong association can be explained by the presence of disability, pain, and polypharmacy in older persons affected by multiple diseases. On the other hand, depression can delay diagnosis of other diseases and negatively affect adherence to medications and a healthy lifestyle that are needed to prevent other clinical conditions.²³ In this study, persons prescribed SSRIs and SNRIs were more likely to be prescribed a greater number of drugs, which indirectly confirms the association between depression and the burden of chronic diseases. Moreover, persons adherent to antidepressants were more likely to be adherent to the other drugs they were co-prescribed. A strong association has been shown between late-life depression and poor adherence to medical treatment for diabetes and cardiovascular disease.²⁴ Moreover, older adults with chronic depression with 80% or greater antidepressant adherence had significantly lower risk of hospitalizations for cardiovascular diseases than those with lower adherence.²⁵ The Prevention of Suicide in Primary Care Elderly Collaborative Trial (PROSPECT) project demonstrated that older adults with major depression provided with additional resources to intensively manage depression had a mortality risk lower than that observed in usual care and similar to that of older adults without depression.²⁶ Possible explanations for all of the previously described findings are that persons adherent to antidepressants have a higher rate of remission of depressive symptoms, which makes them more interested in and attentive to their global health status. They might also have more trust in other medical treatments and

have greater awareness of their diseases. Another hypothesis could be that persons who are adherent to antidepressants have a higher health literacy. The result of these attitudes and behaviors is the higher likelihood of being adherent to the overall therapeutic regimen.

Social and economic factors and factors related to the health care team/system, the characteristics of the disease, the type of therapies, and patient-related factors may all influence adherence. Indeed, patients' personal attributes are likely to have the strongest influence on adherence. No single intervention strategy or package of strategies has been shown to be effective in improving adherence across all patients, conditions, and settings. Consequently, interventions that target adherence must be tailored to the particular illness-related demands experienced by the patient. To accomplish this, health systems and providers need to assess not only adherence, but also those factors that influence it. Treatment guidelines for chronic conditions, for instance, should recommend screening for depression, which can be an indicator of poor adherence.²⁷ When benefits and harms in treating depression are balanced, adherence to treatment should be taken into account as a potential benefit.

Results from this study suggest the need for further evaluation of possible interventions aimed at increasing adherence to antidepressants, which may translate into improved overall adherence and patient outcomes, with potential substantial overall cost savings. Underdiagnosis and undertreatment of depression, which are very frequent in older adults,²⁸ should be considered as factors contributing to poor drug adherence in older persons.

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Drug names: citalopram (Celexa and others), duloxetine (Cymbalta), escitalopram (Lexapro and others), fluoxetine (Prozac and others), fluvoxamine (Luvox and others), paroxetine (Paxil, Pexeva, and others), sertraline (Zoloft and others).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration–approved labeling has been presented in this article.

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POSTTEST

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1. This study found what prevalence of new prescriptions of selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) in individuals aged 65 years or older?
 - a. 3–4%
 - b. 6–8%
 - c. 11–12%
 - d. 20–25%
2. Which of the following statements about adherence to SSRI and SNRI prescriptions in older persons is true, according to the results of this study?
 - a. Older persons adherent to these antidepressants were more likely to be adherent to other medications for chronic diseases
 - b. The rate of adherence to SSRIs and SNRIs was higher in the very old compared with those younger than 95 years
 - c. The rate of adherence to SSRIs and SNRIs was slightly lower in women than in men
 - d. Overall adherence to SSRIs and SNRIs for each of the 3 years studied was consistently about 70%
3. Mr X has been diagnosed with major depressive disorder. He was prescribed an SSRI 3 months ago. According to previous research, what is the probability that he is still taking the antidepressant drug?
 - a. 10%
 - b. 20%
 - c. 50%
 - d. 80%