Pharmacologic Response to Depressive Disorders Among Adolescents

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Objectives: **The purpose of this study was to identify determinants of use of psychoactive medication and receipt of selective serotonin reuptake inhibitors (SSRIs) among adolescents with a diagnosis of new-onset depression.** ***Methods:*** **A population-based retrospective cohort study was conducted among 447 adolescents enrolled in the Quebec drug plan who had new episodes of depression diagnosed between October 2000 and March 2001 by pediatricians, general practitioners, or psychiatrists. The main outcomes were use of psychoactive medication in the year after diagnosis and receipt of SSRIs at the first visit during which pharmacotherapy was prescribed. Receipt of SSRIs was assessed by the initial psychoactive dispensing claim following the diagnosis of depression.** ***Results:*** **In the year after diagnosis, 258 adolescents (58 percent) received psychoactive medications, of whom 135 (52 percent) initially received SSRIs. Diagnosing pediatricians were the least likely to prescribe psychoactive medication. Patients of psychiatrists were less likely than those of primary care physicians to receive antidepressants for dysthymia or adjustment disorder accompanied by depressed mood (26 percent compared with 42 percent). Being female, having a diagnosing general practitioner or pediatrician, and having the same diagnosing and treating physician were associated with higher odds of receiving SSRIs. Being a welfare recipient and living in a rural area rather than an urban area were associated with lower odds.** ***Conclusions:*** **Adolescent males, those receiving welfare, and those living in rural areas were less likely to receive treatment that was recommended at the time of the study and thus may need special attention from mental health care providers. (*Psychiatric Services* 56:1089–1097, 2005)**

Major depressive disorder is a highly prevalent mood disorder that affects up to 28 percent of adolescents by the age of 19 years (1,2) and is associated with cigarette smoking, substance abuse, early pregnancy, poor school performance, impaired work and social functioning, suicidal behavior and ideation, and increased use of medical and mental health services (1,3–9). Depressive symptoms and disorders among youths are associated with increased risk of recurrent depressive disorders (10–12) and other affective (13) and non–mood disorders (14) in adulthood. Gender differences emerge around the age of 13. Compared with boys, girls have higher rates of major depression (10) and higher levels of depressive symptoms (7,15); girls are also more likely to have recurrent depression (14), to receive treatment for depression (16), and to experience depressive symptoms in the month before suicide completion (17).

Given the prevalence and impact of adolescent depression, it is imperative to advocate effective treatment. Until 2003, treatment guidelines recommended psychotherapy with or without pharmacotherapy as first-line treatment (6,18,19) for moderate and severe depression among adolescents (6,19); pharmacotherapy was considered insufficient as a single treatment (6,18). However, during that year evidence emerged that brought into question the efficacy and safety of antidepressant treatment among depressed youths (20–22), although not all studies found links between use of antidepressants and increased risk of suicidal ideation and behavior (23).

Nonetheless, treatment of adolescent depression with antidepressants is currently controversial. In October 2004, the U.S. Food and Drug Administration (FDA) ordered all antidepressant manufacturers to post "black box" warnings of increased risk of suicidal tendencies on their prod-

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ucts (24). The FDA did not restrict the use of antidepressants, because untreated depression may pose a greater risk of suicide than antidepression treatment. In one study of 13- to 21-year-old suicide completers, only 3 percent had detectable levels of psychoactive medication (25).

At the time of the study reported here, guidelines from the United States, Canada, and the United Kingdom considered selective serotonin reuptake inhibitors (SSRIs) as first- and second-line treatments for adolescent depression (6,18,19). Second-generation antidepressants were considered second-line treatment by Canadian guidelines (18), and tricyclic antidepressants were not a subclass of choice because of possible cardiac problems, lethality of overdose, sudden unexplained death (6,19,20,26,27), and lack of efficacy (28). Little was known about which psychoactive medications were given for adolescent depression, because investigations of psychoactive prescribing patterns did not indicate a link between medication use and diagnosis (29–36) and did not specify which psychoactive medications were used (9,37).

Practice guidelines will be revised as evidence accumulates. Thus it is important to elucidate patient, physician, and pattern-of-care characteristics associated with not receiving recommended treatment in order to improve patient outcomes, including reduction of the psychosocial consequences of depression, unnecessary use of health services, and, eventually, the prevalence of mood disorders in adulthood. The aims of the study reported here were to identify the psychoactive medications used to treat depression and to determine the predictors of receiving SSRIs as the initial pharmacotherapy after a diagnosis of depression in a sample of adolescents in Quebec, Canada. We aimed to answer the question of how the pharmacotherapy dispensed compared with guidelines in effect at the time (2000 to 2002).

Methods

Study design and data source

A population-based retrospective cohort design was used to explore the pharmacologic treatment of adolescents with diagnosed depression in Quebec, the second largest Canadian province (population 7.4 million). Data were obtained from the Quebec health insurance board (RAMQ), which remunerates physicians for their services and administers the Quebec Public Prescription Drug Insurance Plan. The public drug insurance plan covers about 3 million residents, who can be classified into three groups: welfare recipients and their dependents, persons without private or group insurance, and persons aged 65 years or older (who were not relevant for this study).

Three RAMQ databases were linked at the patient level by using unique encrypted numbers for both patients and physicians to maintain anonymity. The beneficiaries database, which includes all Quebec residents, provided information about patients' age, gender, and region of residence. The medical services database, which also includes all residents, provided data on diagnosis, the specialty of the diagnosing physician, and the facility at which the diagnosis was made. The pharmaceutical database, which includes residents insured by the public drug plan, is based on prescription claims for drugs dispensed and has been shown to be reliable and valid (38). This database provided information about drug name, type of medication, quantity and concentration, the date the prescription was filled, patient and physician identification numbers, and the prescribing physician's specialty. Patients who were not in the public drug plan were not included in the study.

Identification of study participants

During a six-month case identification period (October 1, 2000, to March 31, 2001), all beneficiaries aged 12 through 16 at study entry who had a new diagnosis of depressive disorder from a general practitioner, a pediatrician, or a psychiatrist were identified. Eligible beneficiaries had to be registered with the RAMQ public drug plan for the entire study period (October 1, 1999, to March 31, 2002). Information for all pharmaceutical records for this period was obtained. For each patient enrolled, two observation periods were created. The first was a follow-up one-year period from the date of the first diagnostic coding of depression (only those who remained alive were eligible for study participation). The second was an antecedent one-year period from the date of the first diagnostic coding of depression during which all beneficiaries with a diagnosis of possible depression were excluded in order to retain only patients with new-onset disorders.

Definition of depression

Diagnosis was based on the first diagnostic coding of depressive disorder during the six-month case identification period. One diagnosis per physician visit was provided, regardless of whether medication was prescribed. Whereas the RAMQ uses *ICD-9* (39) diagnostic codes, some physicians may have used *DSM-IV* (40) codes, which are more detailed for mental disorders. To compensate for this discrepancy, we created an algorithm to retain patients with probable depression. Our physician experts identified 21 diagnostic codes that might have been used to diagnose depression. A list of these codes is available from the authors on request. Of the 21 codes, we selected for inclusion the codes for which the corresponding diagnoses were common to both *ICD-9* and *DSM-IV*: 300.4, 309.0, 311.0, and 311.9. These diagnoses have been used previously to identify adolescent depression (9).

Study drugs

Psychoactive medications were identified on the basis of a comprehensive list of medications used by the RAMQ and were assigned to one of eight classes: antidepressants, benzodiazepines, anxiolytics, stimulants, tranquilizers, anticonvulsants, lithium, and others (for example, levodopa and sumatriptan). Anticonvulsants (12 patients), lithium (two patients), and others (one patient) were grouped into one category because of their small numbers. Antidepressant subgroups included SSRIs, tricyclic and second-generation antidepressants (bupropion, nefazodone, trazodone, and venlafaxine), and

monoamine oxidase inhibitors. Medication use was defined as having at least one prescription claim for a study drug. Two time intervals were created for studying use of psychoactive medications: the 365 days before diagnosis and the 365 days after diagnosis. New users of antidepressants were defined as not having any antidepressant claims in the 365 days before diagnosis.

Trazodone in daily doses less than 150 mg was classified as psychoactive medications but not as antidepressants, because low-dose trazodone is used to aid sleep. The total dose of antidepressant was calculated as the quantity of drug prescribed multiplied by the unit of concentration. Daily dose was calculated as the total dose divided by the duration. When there was more than one prescription claim for the same antidepressant per patient, the daily dose was calculated as total dose 1 + total dose 2) / (duration 1 + duration 2).

Outcomes

Use of psychoactive medications in the year after diagnosis was defined as having at least one prescription claim for a study drug during this time interval. Receipt of an SSRI was defined as having a dispensing claim for an SSRI at the first prescribing visit (6,18,19) to encompass the Canadian, American, and European recommendations in effect at the time (6,18,19). Insofar as psychotherapy may have been the treatment of choice, receipt of SSRIs was evaluated only among adolescents for whom psychoactive medications were dispensed.

Approval from the University of Montreal Faculty of Medicine's research ethics committee was obtained before the study began.

Statistical analysis

The analyses were conducted with use of the Statistical Analysis System (SAS) for Windows 8.02 (41). Descriptive statistics were used to characterize the study sample. Participants were compared by gender with use of t tests and chi square tests, as appropriate. Type of psychoactive medication was compared by gender by using chi square tests.

To account for the possible effect of different patients having the same physician, a generalized estimating equation (GEE) approach (42) was used for the binary indicators of psychoactive medication use and receipt of SSRIs. This method accounts for clustered data as well as for the unbalanced structure of the data—that is, for the fact that the number of patients varied across physicians. Analyses were performed with use of the SAS procedure GENMOD (43), which indicated 204 distinct physician clusters ranging in size (number of patients) from one to five. The compound symmetry, known as exchangeable structure, of the covariance of errors was assumed a priori and was validated against alternative structures with use of Akaike's Information Criterion (AIC) (44).

In 2003 evidence emerged that brought into question the efficacy and safety of antidepressants for depressed youths, although not all studies found links between use of antidepressants and increased risk of suicide.

To arrive at the final models, we screened all independent variables for statistical significance ($p<.05$) in separate bivariate GEE analyses. Then, all variables were entered into one multivariate model, and a backward elimination was performed to identify the independent determinants of psychoactive medication use and receipt of SSRIs. The likelihood was estimated from the odds ratios calculated by using the SAS GENMOD procedure. Potential determinants of psychoactive medication included patients' age, sex, region of residence (urban, intermediate, rural, or distant), diagnosis (depression not otherwise specified, dysthymia, or adjustment disorder with depressed mood), facility at which the diagnosis was made (outpatient clinic, emergency department, or hospital), type of insuree (welfare recipients, adherents, or, in the case of those who changed status during the study period, "both"), and diagnosing physician's specialty (general practitioner, pediatrician, or psychiatrist). Potential determinants of receipt of SSRIs included these variables and two additional binary variables: having the same diagnosing and prescribing physician and receiving the medication within 31 days of diagnosis. Two-tailed p values less than .05 were considered statistically significant.

Results

Patient characteristics

A total of 447 adolescents aged 12 to 16 had a new episode of depression that was diagnosed by a general practitioner, a pediatrician, or a psychiatrist during the case identification period. The average age of the patients was 14.6±1.31 years, and two-thirds were female (Table 1). Depressive disorders were diagnosed and treated by more general practitioners than pediatricians or psychiatrists. Most adolescents received their diagnoses in outpatient clinics rather than hospitals or emergency departments. Approximately 22 percent of patients were given psychoactive medication before receiving a diagnosis of depression, and 58 percent were given medication after the diagnosis. A majority of adolescents received psychoactive medications within 31 days of diagnosis, received the diagnosis and treatment from the same physician, and did not have private or group insurance. Compared with

Table 1

Characteristics of adolescents with a diagnosis of new-onset depressive disorder, by gender

Characteristic	Total sample (N=447)		Boys (N=148)		Girls (N=299)		p[a]
	N	%	N	%	N	%	
Age (years)							.001
12	44	10	27	18	17	6	
13	61	14	25	17	36	12	
14	81	18	17	12	64	21	
15	126	28	38	26	88	29	
16	135	30	41	28	94	31	
Region							.167
Urban	159	36	56	38	103	35	
Rural	146	33	53	36	93	31	
Intermediate	115	26	28	19	87	29	
Distant	26	6	11	7	15	5	
Unknown	1	1	0	—	1	—	
Diagnosis							.003
Depression not otherwise specified	224	50	60	41	164	55	
Dysthymia	159	36	69	47	90	30	
Adjustment disorder with depressed mood	64	14	19	13	45	15	
Diagnosing physician							.001
General practitioner	235	53	60	41	175	59	
Pediatrician	45	10	9	6	36	12	
Psychiatrist	167	37	79	53	88	29	
Facility where diagnosis was made							.773
Hospital inpatient	26	6	9	6	17	6	
Emergency department	87	20	26	30	61	20	
Outpatient clinic	334	75	113	76	221	74	
Psychoactive medication							
Before diagnosis	97	22	47	32	50	17	.001
After diagnosis	258	58	93	63	165	55	.123
Medication dispensed within 30 days of diagnosis	168	65	63	68	105	64	.507
Prescribing physician (N=258)							.293
General practitioner	148	57	46	50	102	62	
Pediatrician	23	9	10	11	13	8	
Psychiatrist	80	31	34	37	46	28	
Other	7	3	3	3	4	2	
Same diagnosing and prescribing physician	139	54	49	53	90	56	.724
Type of drug plan insuree							.783
No private or group insurance	270	60	86	58	184	63	
Welfare recipient	86	19	30	20	56	19	
Both	91	20	32	22	59	20	

[a] Chi square test for comparison of boys and girls

boys, girls with new-onset depressive disorders were older (t=–2.94, df=244 [unequal variance], p=.004), received psychoactive medication less often in the year before diagnosis (χ^2=13.17, df=1, p=.001), more often received their diagnosis from general practitioners (χ^2=24.78, df=2, p=.001), and more often received a diagnosis of depression not otherwise specified (χ^2=11.98, df=2, p=.003).

Psychoactive medication use

Figure 1 shows dispensing of psychoactive medications in the years before and after diagnosis. Before diagnosis, stimulants and antidepressants were the most frequently dispensed drugs. Boys received more major tranquilizers (Fisher's exact p=.018) and stimulants (χ^2=44.59, df=1, p=.001) than girls. After diagnosis, use of all medications except anxiolytics increased. Girls received significantly more antidepressants than boys (χ^2=11.81, df=1, p=.001) and fewer major tranquilizers (χ^2=21.56, df=1, p=.001) and stimulants (χ^2=44.55, df=1, p=.001). Psychoactive medication was dispensed to more patients of diagnosing general practitioners and psychiatrists than pediatricians (61 percent and 59 percent compared with 36 percent; χ^2=10.34, df=2, p=.006).

Use of psychoactive medications in the year following diagnosis did not differ by diagnostic category (χ^2=.5398, df=2, p=.764). Compared with patients of primary care physicians, patients of psychiatrists received fewer antidepressants (48 percent and 34 percent, respectively; χ^2=8.78, df=1, p=.003) and benzodiazepines (15 percent and 8 percent; χ^2=4.63, df=1, p=.031) and more major tranquilizers (4 percent and 11 percent; χ^2=8.15, df=1, p=.004) and stimulants (5 percent and 23 percent; χ^2=33.95, df=1, p=.001) (data not shown).

Table 2 presents the results of the univariate and multivariate models for psychoactive medication dispensing during the year after diagnosis. In the univariate analysis, diagnosing pediatricians were less likely than psychiatrists to prescribe psychoactive medications (z=–2.51, p=.012). This relationship was slightly weaker (z=–2.03, p=.028) in the multivariate analysis after we controlled for age, gender, diagnosis, type of insuree, and facility at which the diagnosis was made. Region of residence was unrelated to psychoactive medication in univariate and multivariate analyses (data not shown).

Antidepressant treatment

At the first prescribing visit after diagnosis, 171 adolescents (66 percent) were given antidepressants, of whom 144 (84 percent) were new users. The median number of days between diagnosis and new use of antidepressant was 8.5 (interquartile range=0 to 53.5); 93 adolescents (65 percent) received an antidepressant within the 31 days following diagnosis. Table 3 shows the antidepressants dispensed at the first prescribing visit. SSRIs

were the most commonly dispensed subclass, and paroxetine was the most commonly dispensed antidepressant. Median dosages were 20 mg for citalopram and paroxetine, 18 mg for fluoxetine, 50 mg for fluvoxamine and sertraline, 100 mg for bupropion, 400 mg for nefazodone, 75 mg for venlafaxine, 13 mg for amitriptiline, and 10 mg for nortriptiline (data not shown). At the first prescribing visit, 151 adolescents (88 percent) were given antidepressants alone, and 20 (12 percent) received antidepressants plus other psychoactive agents. Psychiatrists were significantly less likely than primary care physicians to prescribe antidepressants for adjustment disorder with depressed mood (18 percent compared with 44 percent, χ^2=3.83, df=1, p=.025) or dysthymia (26 percent compared with 42 percent; χ^2=3.83, df=1, p=.05) (data not shown).

Restricting the analysis to patients for whom psychoactive medications were dispensed, we found that antidepressants were given to proportionally more girls than boys (79 percent compared with 43 percent; χ^2=35.23, df=1, p=.001), to more adolescents who had the same (as opposed to different) diagnosing and prescribing physician (76 percent compared with 57 percent; χ^2=9.42, df=1, p=.002), to proportionally more patients with depression not otherwise specified compared with adjustment disorder and dysthymia (79 percent compared with 60 percent and 52 percent; χ^2=18.93, df=2, p=.001), and by proportionally more diagnosing pediatricians and general practitioners than psychiatrists (88 percent and 78 percent compared with 46 percent; χ^2=29.92, df=2, p=.001).

Receipt of SSRIs at the first prescribing visit

As can be seen in Table 3, SSRIs were initially dispensed to 135 adolescents, novel antidepressants to 25, and tricyclics to 11. Patients for whom SSRIs were dispensed at the first prescribing visit had an average of three dispensings in the following year, those for whom novel antidepressants were dispensed had an average of four dispensings, and those for whom tricyclics were dispensed had an average of two dispensings. Patients who received tricyclics were at least 14 years of age and received this medication only, and 46 percent received their diagnoses from a psychiatrist. Significantly more girls than boys received SSRIs (χ^2=13.36, df=1, p=.001).

Table 4 summarizes the results of the univariate and multivariate analy-

Figure 1

Use of psychoactive medication in a sample of 447 adolescents one year before and one year after diagnosis of new-onset depression

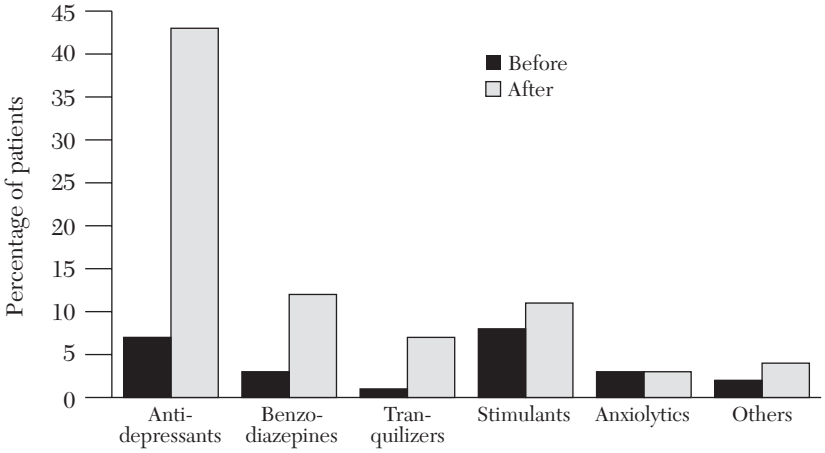

Table 2

Results of univariate and multivariate generalized estimating equation models for use of at least one psychoactive medication in the year after diagnosis in a sample of 447 adolescents with a diagnosis of new-onset depression

Characteristics	Univariate OR	Univariate 95% CI	Multivariate Adjusted OR	Multivariate 95% CI
Age (years)				
12 (referent)	1	—	1	—
13	.84	.40–1.76	.87	.41–1.86
14	.86	.44–1.66	.92	.46–1.83
15	.95	.51–1.76	1.03	.54–1.95
16	1.62	.85–3.11	1.67	.84–3.34
Gender, female	.74	.49–1.11	.75	.48–1.18
Diagnosis				
Depression not otherwise specified (referent)	1	—	1	—
Dysthymia	1.11	.71–1.72	1.39	.79–2.45
Adjustment disorder with depressed mood	.90	.51–1.60	.90	.49–1.64
Type of drug plan insuree				
No private or group insurance	1.08	.60–1.92	.99	.54–1.81
Welfare recipient	1.16	.72–1.88	1.01	.62–1.66
Both (referent)	1	—	1	—
Diagnosing physician's specialty				
Psychiatrist (referent)	1	—	1	—
Pediatrician	.38	.18–.81*	.44	.20–.97
General practitioner	1.14	.75–1.73	1.34	.76–2.35
Facility at which diagnosis was made				
Outpatient clinic (referent)	1	—	1	—
Hospital	1.24	.51–2.97	1.28	.45–3.28
Emergency department	1.01	.62–1.66	1.09	.65–1.81

*p<.05

Table 3

Medication dispensed at the first prescribing visit for adolescents with a diagnosis of depression

Medication	Total sample (N=258)		Boys (N=93)		Girls (N=165)		p
	N	%	N	%	N	%	
Antidepressant	171	66	40	43	131	79	.001
Selective serotonin reuptake inhibitor	135	52	28	30	107	65	.001
Citalopram	34	13	5	5	29	18	
Fluoxetine	11	4	2	2	9	5	
Fluvoxamine	8	3	1	1	7	4	
Paroxetine	64	25	16	17	48	29	
Sertraline	18	7	4	4	14	8	
Second-generation agent	25	10	9	10	16	10	.752
Bupropion	5	2	3	3	2	1	
Nefazodone	1	1	0	—	1	1	
Venlafaxine	19	7	6	7	13	8	
Tricyclic	11	5	3	3	8	5	.999
Amitriptiline	10	4	2	2	8	5	
Nortriptiline	1	1	1	1	0	0	
Major tranquilizer	23	9	17	18	6	4	.001
Stimulant	43	17	32	34	11	7	.001
Benzodiazepine	30	12	7	8	23	14	.123
Anxiolytic	7	3	2	2	5	3	.999
Anticonvulsant	5	2	3	3	2	1	.355
Lithium carbonate	2	1	2	2	0	—	.129
Other	1	1	0	—	1	1	.999

ses for receipt of SSRIs. In the univariate models, female gender (z=5.80, p=.001), diagnosis by a general practitioner (z=4.44, p=.001) or pediatrician (z=2.95, p=.003), and having the same diagnosing and prescribing physician (z=3.28, p=.001) were associated with a greater likelihood of receiving SSRI therapy. Adolescents aged 14 years (z=3.02, p=.002), 15 years (z=2.37, p=.018), and 16 years (z=3.26, p=.001) had a greater likelihood of receiving SSRIs compared with 12-year-olds. Having dysthymia (z=–3.39, p=.001) and living in a rural area (z=–2.58, p=.01) were associated with lower odds of receiving an SSRI. In the multivariate analysis, female gender (z=4.29, p=.001), diagnosis by a pediatrician (z=2.87, p=.004) or general practitioner (z=1.99, p=.05), and having the same diagnosing and prescribing physician (z=2.50, p=.012) were associated with a greater likelihood of receiving an SSRI. Living in a rural area (z=–2.42, p=.016) and being a welfare recipient (z=–2.03, p=.043) were associated with a lower likelihood of receiving an SSRI. Sixteen-year-olds received an SSRI more often than 12-year-olds, but the difference was not significant (p=.081).

Discussion

In this population-based study we examined psychoactive medication claims data of adolescents with newly diagnosed depressive disorders in Quebec, Canada, from 2000 to 2002. Psychoactive medications were dispensed for 58 percent of the adolescents, of whom 67 percent received medication within 31 days after diagnosis. Patients of pediatricians were the least likely to receive psychoactive medications, possibly because they were referred to mental health professionals. Patients of psychiatrists received antidepressants less often for mild depression—for example, adjustment disorder with depressed mood and dysthymia—than patients of primary care physicians.

Depressive disorders were more common among older adolescents and among girls, a result that corroborates the findings of other studies (1,3,9,31,45). Most adolescents were given their first prescription for a psychoactive agent by a general practitioner, a finding that mirrors results of DeBar and colleagues (9), who reported that most adolescent depression is identified and treated by primary care rather than mental health providers. Use of all psychoactive medications except anxiolytics increased after a diagnosis of depression. Antidepressants showed the largest increase, from 7 percent in the year before diagnosis to 43 percent the next year. Gender differences were found that showed that before diagnosis, boys and girls were equally likely to be given antidepressants, even though proportionally more boys than girls were given psychoactive medication. However, after diagnosis, the situation reversed—proportionally more girls than boys were given antidepressants, even though the boys and girls were equally likely to receive psychoactive medication.

Analysis of initial psychoactive dispensing showed that 52 percent of treated adolescents received SSRIs, 10 percent received novel antidepressants, 4 percent received tricyclics, and 34 percent (87 of 258) received agents other than antidepressants. Adolescents in older age groups were more likely to receive an SSRI than younger adolescents. Perhaps, because of the unknown risk of these medications and the evidence that cognitive-behavioral therapy reduces depressive symptoms among adolescents with depression (46,47), clinicians are less inclined to prescribe these medications for younger adolescents. Among treated patients, girls were nearly four times as likely as boys to receive SSRIs. This finding corroborates and extends that of DeBar and colleagues (9) in that gender differences, which were not found for use of psychoactive medications, emerged for receipt of SSRIs as the initial pharmacotherapy. Welfare recipients were the least likely to receive SSRIs, a finding that corroborates results from the United States of associations between lower socioeconomic status and lack of antidepressant treatment (37). Given that all Quebec public drug insurance plan beneficiaries under the age of 18 receive medication without charge, our findings suggest that there are acces-

sibility or acceptability issues related to unemployment.

Our study was constrained by several limitations. Administrative data do not permit validation of diagnosis. Dispensing claims were proxies for medication consumption and practitioners' prescribing. An algorithm was created to define depression, because diagnostic accuracy is a problem in claims databases. Up to three (of 11) patients may have begun tricyclic therapy before diagnosis, although sensitivity analyses showed that removing the data for these individuals did not meaningfully alter the results of the multivariate analyses. The generalizability of the study results may be limited by the fact that not all adolescents in Quebec with a diagnosis of depressive disorders were included. For example, adolescents had to be registered with the drug plan for the entire study period, an algorithm was created to retain study participants with depression, and the drug plan covered only 31 percent of the population aged 10 to 19 years who were registered with the RAMQ (in 2001) (48–50).

Despite these limitations, we included only patients with a diagnosis of depression because antidepressants may be prescribed for psychiatric disorders that are not addressed by depression practice guidelines (51). We also examined new episodes of depression and focused on the initial medications dispensed in order to evaluate predictors of receiving medication recommended at the time of the study. Another strength is that adolescents from all socioeconomic strata were included, because 60 percent of the study sample did not have private or group insurance and had similar socioeconomic profiles to those of the general population (52,53). Furthermore, although we did not have a code for major depression, in one study of depressed adolescents that included a code for major depression, only 8 percent received this diagnosis, and the remaining 92 percent had diagnoses of the three depressive disorders evaluated in the study reported here. In that study, a majority of adolescents received the diagnosis of depression not otherwise specified (9), which may have represented providers' uncertainty regarding the specific diagnostic criteria for major depression and dysthymia.

Adolescent depression treatment guidelines were derived from a limited knowledge base and continue to undergo revision in response to new evidence. In 2003–2004, drug regulators in Canada, the United States, and the United Kingdom recommended that paroxetine and venlafaxine not be prescribed to patients under the age of 18 because of mounting evidence against these drugs' safety and efficacy (54–57). In addition, nefazodone was discontinued in Canada because of adverse hepatic events (58) and pulled from the U.S. market by the manufacturer. Because these three medications accounted for 49 percent of antidepressants dispensed in our study, it is not surprising that use of antidepressants among children and adolescents dropped 18 percent in the year after the new drug regulations were released (59). Nevertheless, concern remains about the risk of suicidality from nonpharmacologically treated depression (24,60), especially in light of the findings that a combination of cognitive-behavioral therapy and fluoxetine was superior at reducing depressive symptoms among adolescents compared with either treatment alone (23).

Table 4

Results of univariate and multivariate generalized estimating equation models for receipt of selective serotonin reuptake inhibitors in a sample of 258 adolescents with a diagnosis of new-onset depression

Characteristics	Univariate		Multivariate	
	OR	95% CI	Adjusted OR	95% CI
Age (years)				
12 (referent)	1	—	1	—
13	3.02	.91–9.99	2.63	.51–13.62
14	5.78	1.85–18.10*	3.64	.76–17.35
15	4.04	1.28–12.83*	2.72	.58–12.78
16	6.14	2.06–19.14*	3.94	.85–18.36
Gender, female	4.28	2.61–6.97*	3.23	1.89–5.51*
Diagnosis				
Depression not otherwise specified (referent)	1	—	1	—
Dysthymia	.39	.23–.67*	.85	.40–1.83
Adjustment disorder with depressed mood	.73	.33–1.61	12.66	.50–3.22
Region of residence				
Urban (referent)	1	—	1	—
Rural	.43	.22–.82*	.40	.19–.84*
Intermediate	.92	.47–1.80	.80	.38–1.70
Distant	.79	.26–2.46	1.03	.30–3.49
Diagnosing physician's specialty				
Psychiatrist (referent)	1	—	1	—
Pediatrician	7.48	1.96–28.51*	5.01	1.67–15.07*
General practitioner	3.06	1.87–5.01*	2.07	1.01–4.23*
Facility at which diagnosis was made				
Outpatient clinic (referent)	1	—	1	—
Hospital	.94	.33–2.65	1.17	.42–3.30
Emergency department	1.00	.51–1.97	1.90	.84–4.30
Received medication within 31 days of diagnosis	1.64	.96–2.79	1.56	.83–2.95
Same diagnosing and prescribing physician	2.25	1.39–3.66*	2.45	1.21–4.93*
Type of drug plan insuree				
No private or group insurance	.66	.30–1.44	.57	.22–1.48
Welfare recipient	.57	.29–1.11	.43*	.19–.97
Both (referent)	1	—	1	—

*p<.05

Conclusions

This population-based study of adolescents with a diagnosis of depression showed that most received psychoactive medication and that a majority of treated patients initially received SSRIs. Our finding that male gender, receipt of welfare, and living in a rural area were associated with not receiving SSRIs may increase physicians' awareness of the patients who are at the most risk of not receiving recommended treatment. Inasmuch as psychiatrists prescribed antidepressants less often for mild depression than did primary care physicians, our findings may also raise concerns that nonpsychiatrists are diagnosing and initiating antidepressant therapy, because these medications should be prescribed only for moderate and severe depression and not in the absence of psychotherapy. ♦

Acknowledgment

Dr. Sewitch is supported as a Research Scientist of the Canadian Cancer Society through an award from the National Cancer Institute of Canada. During this study, she was supported as a Postdoctoral Fellow of the Canadian Institutes of Health Research. Dr. Rahme is supported by the Canadian Arthritis Society. The authors thank Michèle Paré.

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