

ANTIDEPRESSANT THERAPY DURING PREGNANCY: AN INSIGHT ON ITS POTENTIAL HEALTHCARE COSTS

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ABSTRACT

Background

Information on healthcare costs associated with poorly treated psychiatric disorders during and after pregnancy is limited.

Objective

To compare the direct healthcare costs, during and after pregnancy, between women who continue their antidepressant therapy during the whole gestational period and those who discontinue their treatment during the first trimester.

Methods

Data from a 'Medications and Pregnancy' registry were used. Eligible women were 1) aged 15 – 45, 2) insured by the Quebec drug plan for ≥ 12 months prior to, during, and ≥ 3 months after pregnancy, 3) had ≥ 1 diagnoses of psychiatric disorders before pregnancy, 4) used antidepressants for ≥ 30 days in the year before pregnancy, and 5) had delivered. Women who continued their antidepressant therapy throughout pregnancy (Group 1) were compared to those who discontinued during the first trimester (Group 2). Healthcare costs, expressed as mean total costs and cost ratios, were determined during and after pregnancy.

Results

In total, 2822 women met inclusion criteria. Of these, 501 (17.8%) were in Group 1, and 676 (23.4%) in Group 2. The median number of days of antidepressant use before pregnancy was higher in Group 1 (260 days vs. 144 days, $p < .01$); the proportion of women visiting a psychiatrist was also higher in Group 1 (33.7% vs. 26.8%, $p < .01$). The mean total cost during pregnancy in Groups 1 and 2 were \$2981.5 vs. \$1842.9 ($p < .01$), respectively, and after pregnancy were \$1761.2 vs. \$1024.9 ($p < .01$), respectively. When prescription costs were excluded, these differences in costs were no longer significant.

Conclusions

Women who use antidepressants during pregnancy are likely to have disorders of greater severity compared to those who discontinue during the first trimester. They incur significantly greater healthcare costs. However, this increased cost is attributable to higher prescription costs.

Key words: *Pregnancy; antidepressants; costs; psychiatric disorders*

Psychiatric disorders, such as depression, are common during the gestational period, affecting approximately 14% of women.¹ Pharmacotherapy, such as antidepressants, has been shown to be effective to treat psychiatric disorders, and their discontinuation around the

time of conception is associated with depression relapses,² which could be detrimental to both the mother and fetus.^{3,4} Furthermore, reinitiating an antidepressant therapy may take several weeks before the psychiatric condition is deemed to be under control.⁵ Therefore, discontinuing an

antidepressant therapy during gestation can potentially increase healthcare costs for services such as hospital stays, emergency department visits, community physician services, and prescriptions of other concurrent medications. In addition, it has been shown that untreated depression during the antenatal period can result in depression in the post-natal period,⁶ resulting in significant healthcare costs. Thus, women with moderate to severe psychiatric conditions may need to be treated adequately with antidepressants during the gestational period to maintain or improve their mental health, and consequently decrease cost of healthcare services associated with inadequate treatment of their condition.

The objective of the present study was to compare the direct healthcare costs, during and after pregnancy, between women who continue their antidepressant therapy during the whole gestational period and those who discontinue their treatment during the first trimester. A secondary objective was to identify determinants of costs during and after pregnancy.

Our hypotheses were that women diagnosed with psychiatric disorders before pregnancy and who continue their antidepressant therapy during gestation would:

1. be more likely to visit psychiatrists before pregnancy, probably indicating a more severe psychiatric disorder, and
2. have increased prescription-related costs, but,
3. have similar healthcare costs (excluding antidepressant prescriptions) than women who discontinued antidepressant therapy during the whole pregnancy suggesting the importance to be treated during gestation.

METHODS

Data Sources

We used three administrative databases of the province of Quebec (Canada): the Régie de l'Assurance Maladie du Québec (RAMQ), Med-Echo, and the Fichier des événements démographiques du Québec (birth and death registries) managed by the Institut de la

Statistique du Québec (ISQ). The RAMQ database contains information on medical services (diagnoses and procedures) received by all Quebec residents. All diagnoses are classified according to the International Classification of Diseases, Ninth revision (ICD-9).⁷ Although the RAMQ covers all Quebec residents for the cost of physician visits, hospitalisations and procedures, it covers only a portion of residents for the cost of medications. The RAMQ drug plan covers individuals 65 years or older, recipients of social assistance (welfare recipients), and workers and their families (adherents) who do not have access to a private drug insurance program, accounting for approximately 43% of the overall Quebec population.⁸ It is also estimated that 30% of women between 15 and 45 years of age in Quebec are covered by the RAMQ drug plan for their medications (RAMQ data); the remainder are covered by private insurance plans. The Med-Echo database is a provincial database which records acute care hospitalisation data for all Quebec residents, including data on deliveries. The Fichier des événements démographiques du Québec (ISQ) provides demographic information on the mother, father and baby.

The linkage between the RAMQ, Med-Echo, and ISQ was done using an encrypted 'Numéro d'Assurance Maladie' (NAM), which is a unique identifier for all Quebec residents (between RAMQ and Med-Echo), and using mothers' and babies' dates of birth, first names and family names (between RAMQ and ISQ). This linkage allowed the construction of the 'Medications and Pregnancy' registry that contains data on all pregnancies that occurred in Quebec between January 1, 1998 and December 31, 2002.

Data recorded in the medication database of the RAMQ have been suitably evaluated and found to be comprehensive and valid.⁹ The same was found for certain medical diagnoses recorded in the Med-Echo database.¹⁰ The 'Medications and Pregnancy' registry has been used extensively for the study of risks and benefits of medication use during pregnancy.¹¹⁻¹⁵

This study was approved by the CHU Sainte-Justine Ethics Committee. The linkage

between administrative databases was approved by the Commission d'Accès à l'Information (CAI) of Quebec.

Study Population

Women eligible for the present study were selected from the 'Medications and Pregnancy' registry, according to the following criteria:

1. 15 – 45 years of age on the first day of gestation,
2. insured by the Quebec drug plan for ≥ 12 months prior to, during, and ≥ 3 months after pregnancy,
3. received at least one diagnosis for a psychiatric disorder (ICD- 9 codes: 290 – 319) before pregnancy,
4. used antidepressants for at least 30 days in the year before pregnancy, and
5. had a pregnancy ending with a delivery.

Women with diagnoses of psychotic/non-psychotic conditions, or mental retardation that were not indications for the use of antidepressants were excluded (ICD-9 codes: 290 – 295, 297 – 299, 302, 303, 305 – 308, 312, 314 – 319). Finally, in the event of multiple pregnancies for a given woman during the study period (between 1998 and 2002), only the first pregnancy meeting eligibility criteria was considered for analysis.

Study Groups

Two study groups were identified within the cohort described above. The first group consisted of continued antidepressant users throughout pregnancy and was defined as women who filled at least one prescription for antidepressants during each trimester of pregnancy or had a treatment course covering each trimester (Group 1). To insure that only women with moderate to severe psychiatric conditions were considered, the second group (the discontinued users) was defined as women who were exposed to antidepressant therapy during the first trimester, but who did not fill any other prescriptions for these agents during the remainder of their pregnancy (Group 2). Women who did not meet these criteria for psychiatric severity were excluded from the analyses. For example, women who

discontinued their antidepressant therapy during the first trimester but who refilled a prescription during the third trimester were not considered in the analyses; women who discontinued their therapy in the second or the third trimester were also excluded from analyses.

Components of Costs

Costs related to healthcare services were assessed from the perspective of the provincial health insurance system (RAMQ/Government of Quebec). Five cost components were considered for each woman in each study group: direct inpatient hospital costs, emergency department (ED) visit costs, community physician (excluding psychiatrist) visit costs, psychiatrist visit costs, and pharmacy costs.

Recorded Healthcare Use and Costs

Data on the quantity of resources used (days spent in hospital, number of ED visits, number of procedures performed by physicians, and number of medications dispensed) were obtained from the RAMQ or Med-Echo databases. The costs of medical procedures incurred during outpatient visits were determined from the amount charged by the physician (as recorded in RAMQ database). Prescription costs are recorded in the RAMQ, and include the cost of the medication plus the cost of the professional fees, minus the co-payment from the patient (as recorded by RAMQ).

Estimated Hospitalisation Costs

Unlike the RAMQ databases, the Med-Echo databases do not provide any data on costs. We therefore obtained the average per diem costs, for any given hospital department, from five major hospitals in the province of Quebec.¹⁶ Thus, the average per Diem costs for the following hospital departments were: obstetrics [obstetric ante-partum (\$889) and obstetric post-partum (\$195)], psychiatry (\$121), intensive care (\$716), general medicine (\$206), anaesthesia/reanimation (\$787), and ED (\$121). Hospitalisation costs for the delivery procedure were not considered since all women in both groups had this procedure, and furthermore, this procedure was independent of the patients' co-morbidities. The RAMQ does not provide data on medications taken during hospitalisations.

We therefore added \$56 to each admission, which corresponds to the average cost of prescriptions during hospitalisations.¹⁶ Costs derived from the RAMQ databases applied to the year the resource utilisation took place. For hospitalisation costs, we used an average cost over the years of the study (1998 – 2002). All costs are expressed in Canadian dollars.

Determinants of Cost

We investigated whether socio-demographic and psychiatric-related characteristics were determinants of higher cost during and after pregnancy. The characteristics examined were maternal age, having a diagnosis of psychiatric disorders, being a recipient of social assistance (welfare recipient), marital status, level of education, and place of residence (urban vs. rural dwelling).

Statistical Analysis

Descriptive statistics were reported for socio-demographic and psychiatric-related variables of women in the year before pregnancy and on the first day of gestation. Student t-tests and Chi-squared tests were used to examine differences between continuous and categorical data, respectively. For data not normally distributed, the Wilcoxon non-parametric test was used. The mean total healthcare costs, and individual component costs, were determined for both study groups. In order to investigate the relative costs of the two groups for healthcare utilisation as an indicator of morbidity, total costs were also analyzed without the medication cost component. The bootstrap method with 1000 replications was performed to estimate 95% confidence intervals (CI) for the mean total and component healthcare costs.¹⁷

Total healthcare costs were also expressed as a ratio together with corresponding 95% CI by constructing generalized linear models. The models employed a gamma distribution and a log link function.¹⁸ The option 'offset' was used to adjust for the follow-up time during and after pregnancy.¹⁹ Generalized linear models were also constructed to identify the socio-demographic determinants of healthcare costs. All analyses were two-tailed and $p < .05$ was considered significant. SAS version 8.2 (SAS

Institute Inc., Cary, NC) was used to perform analyses.

RESULTS

A total of 152,107 pregnant women were identified between January 1, 1998 and December 31, 2002. Of these, 2822 met eligibility criteria for the study. There were 501 (17.8%) women in Group 1 and 676 (23.4%) in Group 2.

Table 1 displays socio-demographic and psychiatric-related characteristics of the study groups during the year before pregnancy, and on the first day of gestation. Women in Group 1 were greater users of healthcare services than women in Group 2. Furthermore, Group 1 also had a greater number of days of antidepressant use in the year before pregnancy, and a higher proportion of visits to a psychiatrist, suggesting that they had more severe psychiatric disorders. During pregnancy, the median follow-up among women in both Groups 1 and 2 was 39.0 weeks. After pregnancy, the median follow-up of women in Group 1 was 1048.5 days compared to 964.0 days for women in Group 2 ($p > .05$).

Table 2 displays the five most frequently diagnosed psychiatric disorders during and after pregnancy in each study group. The percentage of different psychiatric disorder diagnoses is similar in both study groups.

TABLE 1 Characteristics of women diagnosed with psychiatric disorders before pregnancy

Variables	Study Group 1* (n = 501)	Study Group 2* (n = 676)	P-Value
Measured on the first day of gestation:			
Socio-demographic related			
Maternal age, years, mean (SD) ^a	29.3 (5.6)	28.2 (5.9)	<.01
Welfare recipient, n (%) ^b	272 (54.3)	307 (45.4)	<.01
Urban resident, n (%) ^b	391 (78.0)	521 (77.1)	0.69
Living alone, n (%) ^b	170 (33.9)	183 (27.1)	<.05
Education (>12), n (%) ^b	186 (37.1)	249 (36.8)	0.92
Measured in the year before pregnancy:			
Psychiatric-related variables			
Days of antidepressant utilisation, median (interquartile range) ^c	260.0 (165.0 – 334.0)	144.0 (71.0 – 261.0)	<.01
Number of different psychiatric disorders, n (%) ^b			
≤ 1	267 (53.5)	367 (54.3)	0.08
> 1	234 (46.5)	309 (47.1)	
≥ 1 visit to the psychiatrist, n (%) ^b	169 (33.7)	181 (26.8)	<.01
Co-morbidities related			
Number of different medications other than antidepressants, n (%) ^b			
0 -4	271 (54.1)	367 (54.3)	0.95
≥ 5	230 (45.9)	309 (45.7)	
*Study Group 1: Women who continued their antidepressant therapy during the whole gestational period. *Study Group 2: Women who discontinued their antidepressant therapy during the first trimester of pregnancy. ^a - Student t-test; ^b - Chi squared test; ^c -Wilcoxon test.			

TABLE 2 Description of different psychiatric diagnosed disorders

	Study Group 1*	Study Group 2*
During pregnancy (n, %)	(n = 711)	(n = 526)
Anxiety states (ICD-9: 300.0)	146 (20.5%)	133 (25.3%)
Depressive disorders (ICD-9: 311.9)	100 (14.1%)	91 (17.3%)
Dysthymic disorders (ICD-9: 300.4)	58 (8.2%)	50 (9.5%)
Unspecified non-psychotic mental disorder (ICD-9: 300.9)	27 (3.8%)	16 (3.0%)
Unspecified personality disorder (ICD-9: 301.9)	21 (3.0%)	16 (3.0%)
After pregnancy (n, %)	(n = 715)	(n = 624)
Anxiety states (ICD-9: 300.0)	171 (23.9%)	180 (28.8%)
Depressive disorders (ICD-9: 311.9)	121 (16.9%)	119 (19.1%)
Dysthymic disorders (ICD-9: 300.4)	55 (7.7%)	45 (7.2%)
Unspecified non-psychotic mental disorder (ICD-9: 300.9)	41 (5.7%)	19 (3.0%)
Unspecified personality disorder (ICD-9: 301.9)	26 (3.6%)	22 (3.5%)
Abbreviation: ICD-9, International Statistical Classification of Diseases, ninth revision.		
*Study Group 1: Women who continued their antidepressant therapy during the whole gestational period.		
*Study Group 2: Women who discontinued their antidepressant therapy during the first trimester of pregnancy.		

Mean costs and CI associated with each type of healthcare service are given in Table 3. Data are also stratified according to study groups and study periods (figure 1 and figure 2). With the exception of prescription medications during and after pregnancy, the two study groups had similar utilisation profiles and average costs for all other healthcare services.

By considering all healthcare costs (including prescription medication costs), for both study periods (during and after pregnancy), the mean total healthcare cost for women in

Group 1 was 1.6 (95% CI: 1.4 – 1.8) times greater than for women in Group 2. Once prescription medication costs were excluded, the mean total cost for women in Group 1 during pregnancy was 1.4 (95% CI: 1.0 – 1.6) times greater than for women in Group 2. After pregnancy, mean total costs were 1.1 (95% CI: 1.0 – 1.3) times greater in Group 1 compared to Group 2.

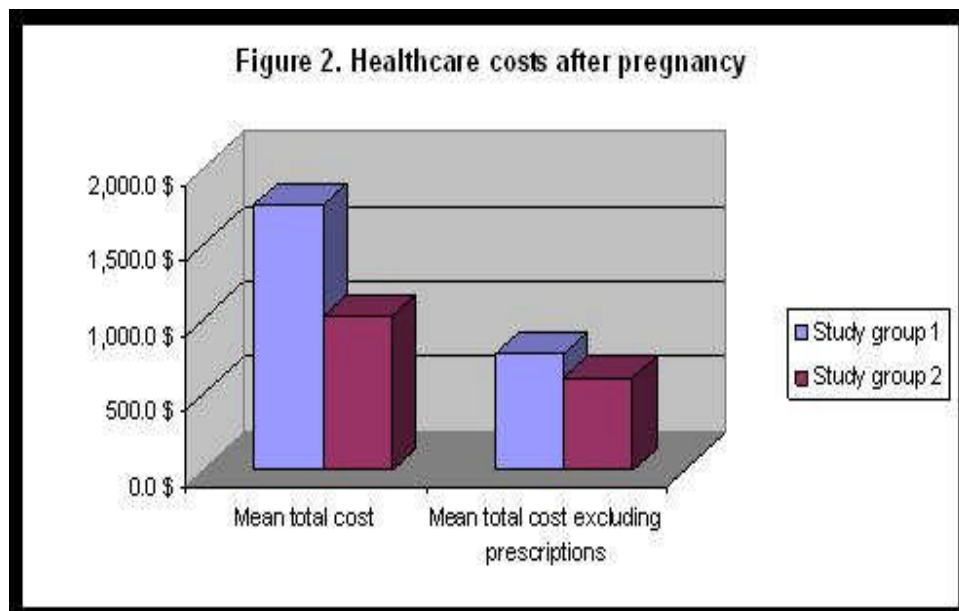
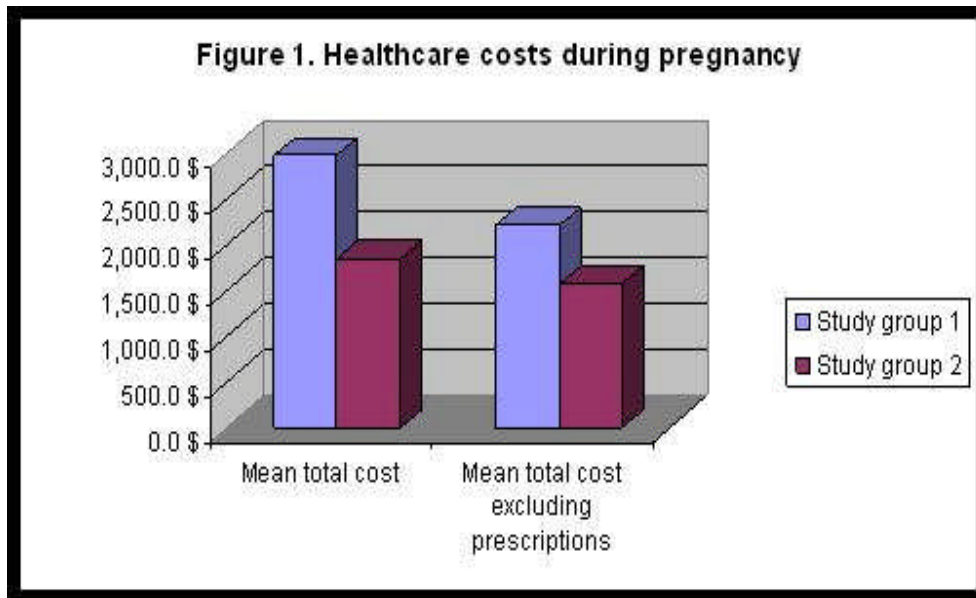


TABLE 3 Healthcare utilisation and costs during and after pregnancy

Variables	During pregnancy		After pregnancy	
	Study Group 1* (n = 501)	Study Group 2* (n = 676)	Study Group 1* (n = 501)	Study Group 2* (n = 676)
Visits to community physician				
Median number, interquartile range	22 (17 – 29) ^{a,3}	22 (17 – 29)	9 (5.0 – 15.0) ^{a,3}	9 (5.0 – 16.0)
Mean cost, 95% CI	572.5 (543.5 – 605.3)	544.7 (522.5 – 573.9)	343.6 (318.0 – 373.4)	331.3 (310.9 – 358.5)
Visits to psychiatrist				
Median number, interquartile range	4 (2 – 9) ^{a,3}	4 (2 – 7)	5 (2 – 11) ^{a,3}	4 (2 – 9)
Mean cost, 95% CI	74.1 (56.3 – 99.6)	41.0 (30.0 – 59.3)	73.7 (57.7 – 95.8)	37.8 (28.7 – 50.8)
Prescriptions				
Median number, interquartile range	16.0 (10.0 – 27.0) ^{a,1}	5.0 (2.0 – 11.0)	22.0 (13.0 – 35.0) ^{a,1}	11.0 (4.0 – 20.5)
Mean cost, 95% CI	772.4 (693.2 – 855.3)	271.0 (228.9 – 322.3)	991.7 (875.6 – 1129.6)	408.1 (352.3 – 472.3)
Hospitalisations				
≥ 1 hospitalisation, n (%)	154 (30.7) ^{b,2}	160 (23.7)	95 (19.0) ^{b,3}	111 (16.4)
Mean cost, 95% CI	1561.6 (1148.8 – 2096.6)	985.4 (717.5 – 1336.8)	353.2 (244.7 – 477.6)	247.1 (162.7 – 353.7)
Emergency department visits				
≥ 1 visit, n (%)	0 (0)	0 (0)	1 (0.2)	1 (0.2)
Mean cost, 95% CI	N/A	N/A	N/A	N/A
Mean total cost, 95% CI	2981.5 (2537.6 – 3528.8)	1842.9 (1552.0 – 2180.4)	1761.2 (1564.8 – 1965.5)	1024.9 (901.9 – 1164.4)
Mean total cost excluding prescriptions, 95% CI	2209.1 (1751.0 – 2790.6)	1571.9 (1298.4 – 1887.0)	769.5 (649.9 – 904.5)	616.8 (514.1 – 732.0)
Abbreviations: SD, standard deviation; CI, confidence interval; N/A, non applicable. Costs expressed in Canadian dollars (1 CAD = 0.95 USD), rounded to nearest dollar. Total cost = medical procedures + prescriptions + hospitalisations + emergency department visits. *Study Group 1: Women who continued their antidepressant therapy during the whole gestational period; *Study Group 2: Women who discontinued their antidepressant therapy during the first trimester of pregnancy. ^a - Wilcoxon test; ^b - Chi squared test. ¹ - P <.0001. ² - P <.01. ³ - P ns.				

TABLE 4 Most frequently prescribed medications during and after pregnancy

Class of medications	During pregnancy		After pregnancy	
	Number of prescriptions in Study Group 1* (n = 2863)	Number of prescriptions in Study Group 2* (n = 3225)	Number of prescriptions in Study Group 1* (n = 3925)	Number of prescriptions in Study Group 2* (n = 4310)
Antidepressants (AHFS: 28.16.04), n (%)	627 (21.9)	728 (22.6)	623 (15.9)	378 (8.8)
Anti-emetics (AHFS: 56.22.00), n (%)	197 (6.9)	255 (7.9)	44 (1.1)	34 (0.8)
Penicillins (AHFS: 8.12.16), n (%)	163 (5.7)	220 (6.8)	175 (4.5)	238 (5.5)
Anxiolytics, sedatives and hypnotics (AHFS: 28.24.08), n (%)	146 (5.1)	177 (5.5)	173 (4.4)	188 (4.4)
Anticonvulsants (AHFS: 28.12.08), n (%)	125 (4.4)	91 (2.8)	116 (3.0)	91 (2.1)
Sympathomimetic (adrenergic) (AHFS: 12.12.00), n (%)	117 (4.1)	141 (4.4)	129 (3.3)	151 (3.5)
Anti-inflammatory agents (AHFS: 84.06.00), n (%)	115 (4.0)	95 (3.0)	153 (3.9)	187 (4.3)
Corticosteroids (AHFS: 68.04.00), n (%)	114 (4.0)	121 (3.8)	109 (3.0)	112 (2.6)
Antifungals (AHFS: 84.04.08), n (%)	80 (2.8)	134 (4.2)	113 (2.9)	157 (3.6)
Macrolids (AHFS: 8.12.12), n (%)	73 (2.6)	77 (2.4)	109 (2.8)	123 (2.9)
Miscellaneous analgesics (AHFS: 28.08.92), n (%)	73 (2.6)	87 (2.7)	161 (4.1)	221 (5.5)
Diabetes mellitus (AHFS: 36.26.00), n (%)	62 (2.2)	57 (1.8)	40 (1.0)	22 (0.5)
Iron preparation (AHFS: 20.04.04), n (%)	50 (1.8)	53 (1.6)	99 (2.5)	91 (2.1)
Anti-inflammatory (intranasal corticosteroids) (AHFS: 52.08.00), n (%)	49 (1.7)	50 (1.55)	51 (1.3)	73 (1.7)
Insulin (AHFS: 68.20.08), n (%)	49 (1.7)	43 (1.3)	36 (0.9)	28 (0.7)
Non-steroidal anti-inflammatory (AHFS: 28.08.04), n (%)	47 (1.6)	68 (2.1)	225 (5.7)	331 (7.7)

Abbreviation: AHFS, American Hospital Formulary Service
 *Study Group 1: Women who continued their antidepressant therapy during the whole gestational period.
 *Study Group 2: Women who discontinued their antidepressant therapy during the first trimester of pregnancy.

Table 4 displays the most commonly prescribed medication classes during and after pregnancy. Antidepressants were the most frequently prescribed medications during and after pregnancy in Group 1. Multivariate generalized linear models showed that women in Group 1 had significantly greater healthcare costs (including prescription medication costs), both during and after pregnancy, than women in Group 2, after

adjusting for socio-demographic and clinical differences (Table 5). Independent determinants of cost during pregnancy were being on welfare, living in an urban area, and having a diagnosis of psychiatric disorders.

After pregnancy, independent determinants of cost were being a welfare recipient, having a higher education, and having a diagnosis of psychiatric disorders (Table 5).

TABLE 5 Determinants of cost during and after pregnancy

Variables	Crude cost ratio (95% CI) (n = 501)	Adjusted cost ratio* (95% CI) (n = 676)
During pregnancy:		
Exposure to antidepressants (continuing versus discontinuing)	1.63 (1.45 – 1.85)	1.40 (1.23 – 1.58)
Diagnoses of psychiatric disorders (≥ 1)	1.49 (1.35 – 1.69)	1.36 (1.21 – 1.53)
Maternal age (>28)	1.13 (1.00 – 1.28)	1.01 (0.90 – 1.14)
Welfare recipient	1.90 (1.69 – 2.14)	1.74 (1.53 – 1.98)
Urban area	1.20 (1.04 – 1.39)	1.17 (1.02 – 1.35)
Living alone	1.39 (1.22 – 1.59)	1.09 (0.95 – 1.25)
Education (>12)	0.83 (0.73 – 0.94)	0.92 (0.81 – 1.05)
After pregnancy:		
Exposure to antidepressants (continuing versus discontinuing)	1.56 (1.38 – 1.77)	1.47 (1.30 – 1.66)
Diagnoses of psychiatric disorders (≥ 1)	2.07 (1.84 – 2.34)	1.90 (1.69 – 2.14)
Maternal age (>28)	1.00 (0.88 – 1.14)	0.93 (0.82 – 1.04)
Welfare recipient	1.66 (1.47 – 1.88)	1.60 (1.41 – 1.82)
Urban area	1.26 (1.09 – 1.47)	1.09 (0.95 – 1.26)
Living alone	1.30 (1.13 – 1.48)	1.07 (0.94 – 1.23)
Education (>12)	1.10 (0.97 – 1.25)	1.17 (1.03 – 1.32)
Abbreviations: CI, confidence interval. *Adjusted for all other variables listed.		

DISCUSSION

In this population-based study, we compared healthcare costs between women treated with antidepressants during the whole gestation (Group 1) and women who discontinued their antidepressant treatment during the first trimester of pregnancy (Group 2). The mean total healthcare cost for women in Group 1 was 1.6 times greater than for women in Group 2.

Once costs associated with prescription medications were excluded, the cost ratios between both groups during and after pregnancy

were not statistically different. Moreover, we identified several socio-demographic and psychiatric-related determinants of higher cost, including being on welfare, living in an urban area, having a higher education level, and having a diagnosis of a psychiatric disorder. This study also provides some insight on the impact of moderate to severe psychiatric conditions on the use of the healthcare system. It also adds to the limited literature on the healthcare costs associated with the treatment of psychiatric disorders during and after pregnancy.

After excluding the costs associated with prescription medications, there were no differences in healthcare costs, during and after pregnancy, between women in Groups 1 and 2. Assuming that women who need to continue antidepressant treatment during pregnancy are more likely to have a severe condition, this suggests that treatment with medications maintains their health status at a level similar to that of women with less severe or moderate psychiatric conditions. This emphasizes the need to adequately treat women with psychiatric disorders during pregnancy.

A major strength of this study was the large study population and the ability of the linked databases to provide accurate information on healthcare utilisation. Indeed, the administrative databases used provide accurate information on the names, dosages, quantities, and treatment duration of medications dispensed. They also provide accurate information on hospitalisations, ED visits, community physician visits, and psychiatrist visits. In addition, we had access to socio-demographic information that enabled us to create prediction models. Several variables were found to be determinants of higher healthcare costs during and after pregnancy. The cost determinants during pregnancy (being a welfare recipient, living in urban area) may be related to a greater reliance for support from the healthcare system by welfare recipients and accessibility to these services. The cost determinants after pregnancy (being a welfare recipient and having a higher education) may be related, as previously mentioned, to the greater need for support among welfare recipients, and an increased awareness of the need for medical interventions to avoid adverse outcomes in the post-partum period among those who are more educated.

This study was performed using the perspective of the payer, the provincial government. As such, the population investigated was adapted for this perspective, since it included subjects who were recipients of social assistance (welfare recipients), and workers (adherents) who did not have access to private drug insurance program (all other healthcare services are free for all Quebec residents). Therefore, both groups were covered for their healthcare services and medications by the Quebec government. However, Bérard et al.²⁰ have shown that socio-

economic status may act as an effect modifier. That is, these women may be more likely to use healthcare services and antidepressants than those covered by private medication insurance plans.

Despite these strengths, this study does have a few limitations. Adopting a broader, societal perspective would have allowed us to measure the direct non-medical costs (e.g. child care costs), indirect costs (e.g. lost productivity), and intangible costs (e.g. pain and suffering) attributable to psychiatric conditions. There were also limitations related to our costing procedures. Specialty per diem costs were used as they most accurately represented the average cost of hospitalisation in specific departments. While this is superior to using generic costs of a bed-day in hospital, a limitation of this approach is that it does not capture the cost differences that may exist between patients with specific comorbidities. Consequently, this could result in an underestimation of the true cost of hospitalisation. Furthermore, cost data were not available for all hospitals in the province. Using cost data from only five major hospitals may have underestimated some costs (larger hospitals would have lower operating costs due to economies of scale). Nevertheless, this approach accurately captured the relative costs between women who continued to be treated during the whole gestation and women who discontinued their pharmacotherapy during the first trimester. The presentation of cost ratios also provided more generalizable information on how one group compares to the other. Although we computed absolute point estimates of costs, the interpretation of the values and their generalizability is more limited than the information provided by cost ratios because of the specific costing strategies used in this study.^{18, 21} However, we used the bootstrap method to derive 95% confidence intervals for these costs to provide an idea of the possible range of total cost for a given woman. The Wilcoxon rank sum test could have been used to compare costs between the two study groups. This non-parametric test is often used where data, such as cost data have a highly skewed distribution.²² Since this test compares differences in location between two distributions (an effective test of differences of medians in two samples), and the primary comparator of interest in cost analyses is the

mean, the bootstrap method was considered more appropriate.^{17,22}

In conclusion, the prevention and treatment of mental health problems in the antenatal period and their deleterious consequences should be regarded as a public health priority. As expected, women treated with antidepressants during the gestational period had more severe psychiatric illnesses as determined by prior duration of antidepressant use and psychiatric visits and also had higher healthcare costs as compared to women who discontinued their treatment during the first trimester. However, after exclusion of the costs related to prescription medications, the difference in the mean total healthcare costs between the two groups was no longer statistically significant. Future economic studies, measuring cost-effectiveness for example, should be conducted to determine the value of antidepressant therapy during pregnancy and its impact on the overall healthcare system.

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