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Association between stimulant and non-stimulant ADHD medications and completed suicide in adolescents and adults: A population-based nested case-control study

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ABSTRACT

Introduction: ADHD has been linked to an increased risk of completed suicide. The aim of this study was to assess the relationship between ADHD medication use and completed suicide.
Methods: This nested case-control study included individuals aged 12–49 in Quebec, Canada, diagnosed with ADHD and/or dispensed ADHD medication. Suicide cases ($n = 472$) between 2000 and 2021 were matched with 5 controls each ($n = 2360$) on date of birth, sex, and continuous public drug insurance coverage for at least 365 days before suicide death (index date). Multivariable conditional logistic regression was used to estimate the association between ADHD medication use and completed suicide. The association between specific ADHD medication types and completed suicide was also assessed.
Results: After controlling for potential confounders, no significant association was found between ADHD medication use and completed suicide in the overall sample, in individuals aged 12–24 and 25 to 49 years, and those with a prior ADHD physician diagnosis. No significant differences were found when comparing the use of non-stimulants only (aOR 1.27; 95 % CI: 0.62, 2.63), stimulants and non-stimulants (aOR 1.01; 95 % CI: 0.33, 3.08), and ADHD consultation without medication (aOR 0.94; 95 % CI: 0.69, 1.28) against stimulant-only use.
Conclusion: Both stimulants and non-stimulants were not associated with the risk of completed suicide. These findings can inform clinical decision-making.

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1. Introduction

Suicide is associated with a significant burden, resulting in premature loss of years of life (Naghavi, 2019). Recent evidence indicates suicide is responsible for twice the number of years of life lost compared to SARS-CoV-2 (Ljung et al., 2022). Attention-deficit/hyperactive disorder (ADHD) is the most common neurodevelopmental disorder affecting up to 7.2 % of school-aged children (Thomas et al., 2015) and 2.5 % of adults (Song et al., 2021). A systematic review showed a significant association between ADHD, suicidal behaviors and increased risk of completed suicide, after controlling for comorbid psychiatric conditions (Austgulen et al., 2023; Sheftall et al., 2022). Available genome-wide association studies (GWAS) have also shown a genetic association between suicide attempts and ADHD (Docherty et al., 2023). The presence of comorbid psychiatric disorders among individuals who died by suicide is well documented, and among these disorders, ADHD has been shown to be most prevalent among the youngest suicide decedents (Sheftall et al., 2022).

Although efficacious and tolerable pharmacological options exist for the treatment of ADHD, such as methylphenidate-based, or amphetamine-based stimulants and non-stimulants, including atomoxetine, guanfacine (Intuniv Extended Release Tablets) or viloxazine (Cortese et al., 2018; Jaeschke et al., 2021), there are concerns about their safety, including possible suicidal risk. In 2015, Health Canada advised for a black box warning on the risk of suicidal behaviors associated with ADHD medications (Government of Canada, 2015; Lesage et al., 2015). However, a systematic review found no statistically significant difference in suicidal attempts or ideations between individuals with ADHD using methylphenidate or atomoxetine and healthy controls (Kim et al., 2023). A more recent national registry cohort study including individuals with ADHD aged 16 to 65 years showed a decreased risk of suicide attempts and/or completed suicide among those using certain stimulants (dexamphetamine, lisdexamphetamine and methylphenidate) when comparing periods of use to periods of non-use (Taipale et al., 2024). On the contrary, the use of non-stimulants was associated with increased risk (Taipale et al., 2024).

To our knowledge, only one pharmacovigilance study (Wei et al., 2023) and three observational studies have specifically reported on the effect of ADHD medication use on the risk of completed suicide (Li et al., 2024; McCarthy et al., 2009; Rice et al., 2024). Conclusions on causality based on signals of completed suicide with methylphenidate and amphetamine in children and adolescents cannot be drawn from pharmacovigilance data, as the adverse event of completed suicide may be attributable to the medication, ADHD itself, or other comorbid mental disorders (Wei et al., 2023). An earlier retrospective study using general practice registry data indicated an increased risk of suicide among young patients aged 11 to 14 years who were prescribed ADHD medications when compared to the general population. The study, however, did not include a comparable control group with ADHD diagnosis (McCarthy et al., 2009). A more recent study focused on adult ADHD patients over a three-year period and found a decreased risk of suicide during months when individuals were using methylphenidate (Rice et al., 2024). However, the findings are limited in generalizability because the study cohort primarily consisted of male veterans who were predominantly white and had a high prevalence of comorbid major depression and trauma-related disorders (Rice et al., 2024). Additionally, many of these individuals were likely to be treated with other psychotropic medications during the months they used ADHD medications (Rice et al., 2024). This last study did not investigate the relationship between non-stimulant ADHD medications and suicide risk. The third observational study emulated a trial with a per-protocol analysis to estimate the risk of mortality associated with stimulant and/or non-stimulant medication use among individuals newly diagnosed with ADHD. The study, with a follow-up period ranging between two and five years, found no association between stimulant and non-stimulant medication use and death from suicide (Li et al., 2024). However, it is important to note that the generalizability of findings is limited to the per-protocol analysis of ADHD stimulant and non-stimulant medication use, which may not reflect real world patterns of ADHD medication use. Additionally, the investigation of the death by suicide was considered an exploratory subgroup analysis.

As stimulants and non-stimulant medications have different mechanisms of action (Cortese, 2020), it is possible that they are associated with different risks in terms of suicide. Therefore, the current study aimed to evaluate, over a 20-year period, the effect of ADHD medication use, including both stimulants and non-stimulants, as well as each class separately, on the risk of completed suicide among adolescents, young adults, and adults who were covered under a public drug insurance plan in Quebec, Canada.

2. Methods

2.1. Source population

Data were obtained from the Quebec Integrated Chronic Diseases Surveillance System (QICDSS), which links the health insurance registry, vital statistics death registry, medical physician claims registry, hospitalization registry, and pharmaceutical registry (data on prescriptions filled in outpatient settings). In Quebec, drug insurance is mandatory for residents, and coverage must be provided through either a private drug plan or the province's public drug plan. The QICDSS database records data on all prescriptions filled for residents who are insured under the public drug plan. As of the latest available information, in the 2022–2023 fiscal year, nearly 46 % of Quebec residents were covered under the provincial public drug plan (Régie de l'assurance maladie du Québec, 2023). The use of the QICDSS and linked health administrative databases was approved by the Public Health Ethics Committee and the *Commission d'accès à l'information du Québec,* Quebec's information and privacy commission. This study is part of the continuous chronic disease surveillance mandate granted to the National Public Health Institute of Quebec *"Institut national de santé publique du Québec"* by the provincial minister of health and social services. All surveillance activities of this mandate are approved by the provincial Ethics Committee of Public Health. No informed consent was required.

We conducted a population-based nested case-control study within a cohort of individuals aged 12 to 49 years of age, covered under the Quebec provincial health insurance plan (*Régie de l'assurance-maladie du Québec* - RAMQ) and either diagnosed with ADHD (ICD-9 code: 314; ICD-10-CA codes: F900, F901, F908, F909) or with at least a prescription filled for ADHD medication between April 1, 2000, and March 31, 2021. ADHD medications included amphetamine or methylphenidate-based stimulants and non-stimulants (atomoxetine and guanfacine). Individuals were considered at risk from the time of entry into the study until the end of the study period, emigration, death, or the age of 50 years.

2.2. Study population

There were 886 cases of completed suicides identified by the presence of ICD-10 codes X60–X84 and Y87.0 in the database and confirmed by the Coroner's report and registered in the vital statistics death registry between 2000 and 2021. Of the 886 confirmed suicide cases, 414 cases did not have continuous public drug insurance coverage in the year prior to their suicide. Therefore, there were 472 eligible suicide cases insured under the provincial public drug plan for at least 365 days in the period immediately preceding the date of completed suicide (or index date) and included for analyses. A sample of controls who were alive at the date of death of the case's was selected from the risk set, excluding all suicide cases, using a matching algorithm. We used a 5:1 matching, where for each case, five controls were matched based on the following confounders: duration of public drug insurance coverage (i.e. at least as long as the case's duration of coverage under public drug plan,

before the index date), sex, and date of birth within one year.

2.3. Exposure

ADHD medication use was identified from the QICDSS using DIN drug codes. Exposure to ADHD medication was defined as having used an ADHD medication (yes or no) as of the time of entry into the cohort. To examine the effect of the timing of ADHD medication exposure in relation to the index date, which was suicide death for cases and assigned matching date for controls, we analyzed exposure retrospectively from index date. This exposure was categorized as follows: ADHD medication use within 90 days of the index date; ADHD medication use from 91 to 365 days before the index date; ADHD physician diagnosis consultation within 365 days of the index date, without medication use; past ADHD medication use or diagnosis >365 days prior to the index date. Given the importance of assessing the effect of an individual's most recent exposure to ADHD medication before suicide, we used the category of medication use within 90 days of the index date as the reference group. We also examined the association between suicide and the type of ADHD medication used, including stimulants only, non-stimulants only, both stimulants and non-stimulants, and those having an ADHD diagnosis only. Additionally, we analyzed the duration of ADHD medication use based on the proportion of days covered during the 365 days prior to index date, categorized as follows: ≥80 %, 40 to <80 %, >0 to <40 %, 0 % (past use), 0 % (no use).

2.4. Covariates

The study variables considered as potential confounders were geographical area of residence and socioeconomic level of the area of residence based on social and material deprivation, assessed in the fiscal year of index date. The lifetime presence of an anxio-depressive disorder, intellectual disability, congenital anomalies, schizophrenia, organic psychosis, reactive and behavioral disorders, were also considered. The number of chronic physical conditions and substance abuse was assessed according to the presence of 2 ambulatory claims within 5 years or 1 hospital abstract summary code among a list of 30 medical conditions (Simard et al., 2018), of the index date, and categorized as 0, 1, 2, ≤3. The number of outpatient consultations in the past year and receipt of health care services while incarcerated prior to index date were also considered. Covariate definitions are presented in supporting material.

2.5. Statistical analyses

Descriptive statistics are presented as proportions and means (with their standard deviations (SD)) for categorical and continuous variables. Unadjusted conditional logistic regression analyses were used to calculate crude estimates of the association between study variables ADHD diagnosis, medication use, and suicide. Adjusted estimates were obtained from multivariable conditional logistic regression analyses controlling for all study covariates as potential confounders, and a reduced model controlling for lifetime presence of anxio-depressive disorders, intellectual disability, reactive and behavioral disorders in childhood and adolescence, organic psychosis, schizophrenia, and congenital anomalies. We conducted an additional analysis where we further categorised exposure to ADHD medication with and without a formal physician diagnosis. We also restricted the analyses to those who received a formal physician diagnosis of ADHD prior to the index date, as a formal diagnosis may not always be recorded in the QICDSS database since it is not mandatory for outpatient visits for reimbursement purposes and patients with ADHD but with a formal diagnosis may differ from those without it. We also restricted the analyses to individuals aged 12 to 24 years at the index date and 25 to 49 years, as the factors associated with ADHD medication use and completed suicide may differ by age group. We also carried out sensitivity analyses to assess the effect of any potential selection bias on study findings. For this, we restricted the analyses to individuals with public health insurance coverage of 730 days immediately prior to index date. This to include individuals with more consistent socioeconomic and employment status prior to completed suicide, as changes to public drug insurance coverage may influence ADHD medication use and completed suicide. We estimated odds ratios with their 95 % confidence intervals. Statistical analyses were performed with SAS Enterprise Guide 7.1 version 9.4 (SAS Institute).

3. Results

The study included 472 cases and 2360 matched controls. Characteristics of the study population are presented in Table 1. Cases and controls did not differ with respect to variables matched on. However, cases were more likely to have been diagnosed with comorbid mental and chronic physical disorders, have increased outpatient consultations in the year prior to index date and received health services while incarcerated any time prior to index date. Unadjusted estimates did not show an association between completed suicide and ADHD medication use and type of ADHD medication.

The conditional multivariable regression analysis indicated that overall, the use of ADHD medication was not significantly related to completed suicide in the total sample, nor in the samples categorized by age group or the presence of a formal physician diagnosis of ADHD (Table 2). Furthermore, the analyses did not show an association between the timing of ADHD medication exposure and completed suicide (Table 3). Specifically, as compared to individuals using ADHD medication within the 90 days before the index date, the odds of completed suicide were not different in individuals using an ADHD medication in the 91 and 365 days (aOR 1.31; 95 % CI: 0.85, 2.01) prior to index date, having an ADHD physician consultation only within the year prior to index date (aOR 1.43; 95 % CI: 0.74, 2.77), or no ADHD medication or physician consultation within the year (aOR 0.96; 95 % CI: 0.74, 1.24). The additional multivariable analyses showed similar results in the cohorts restricted to individuals aged between 12 and 24 years and 25 to 49 years, and individuals having obtained an ADHD physician diagnosis (Table 3). Furthermore, there was no statistically significant association between completed suicide and type of ADHD medication, and specifically as compared to the use of stimulants only within the year prior to index date, non-stimulants (aOR 1.27; 95 % CI: 0.62, 2.63) only, stimulants and non-stimulants (aOR 1.01; 95 % CI: 0.33, 3.08) within the year prior to index date, and no ADHD medication use (aOR 0.94; 95 % CI: 0.69, 1.28) (Table 3).

The additional analyses categorizing ADHD medication use based on the presence of an ADHD physician diagnosis indicated no statistically significant association between completed suicide and this regardless of the presence of a formal diagnosis of ADHD or the timing of ADHD medication use relative to the index date (Table S1 in supplement). The sensitivity analysis restricting the cohort to individuals with at least 730 days of coverage under the public drug insurance plan prior to completed suicide also did not show a significant association between ADHD medication use and completed suicide in the overall sample, except for a marginally significant association between ADHD medication use during the period between 366 and 730 days before the index date (Table S2 in supplement). No significant association was observed between ADHD medication use and completed suicide when restricting the analyses to the cohort of individuals aged 12 to 24 years, 25 to 49 years, and those with an ADHD physician diagnosis (Table S2 in supplement).

Regarding ADHD medication use, cases and controls did not differ with respect to the number of days of ADHD medication use within the 90 days (0 days 73.7 % vs. 75.8 %, 1 – 35 days: 7.8 % vs. 7.5 %; 36–90 days: 18.4 % vs. 16.7, X^2=0.96, $p = 0.62$) and the 91 to 365 days (0 days: 66.7 % vs. 68.9 %; 1–120 days: 12.5 % vs. 11.7 %; 121–274 days: 20.8 % vs. 19.4 %, X^2=0.85, $p = 0.65$) prior to index date. For the sensitivity analyses restricted to those with at least two years of coverage under the

Table 1
Characteristics of study population and crude associations between ADHD medication use and covariables, and the risk of suicide.

	Cases, $n = 472$	Controls, $n = 2360$	
Variables matched on	n (%)	n (%)	
Date of birth ± 1 year			
Age [Mean ± SD]	31.7 ± 9.3	31.6 ± 9.3	
12–24	116 (24.6)	580 (24.6)	
25–50	356 (75.4)	1780 (75.4)	
Sex			
Female	136 (28.8)	680 (28.8)	
Male	336 (71.2)	1680 (71.2)	
Years continuously covered under public drug insurance plan [Mean ± SD]	6.8 ± 5.0	6.8 ± 5.0	
			Crude OR (95 % CI)
Exposure to ADHD medications in the 365 days before index date*			
Yes	175 (37.1 %)	801 (33.9 %)	1.16 (0.94, 1.43)
No	297 (62.9 %)	1559 (66.1 %)	Reference
Timing of exposure to ADHD medications in the 365 days before index date			
ADHD medication ≤ 90 days before index date	132 (28.0)	631 (26.7)	Reference
ADHD medication 91–365 days before index date	43 (9.1)	170 (7.2)	1.22 (0.83, 1.80)
ADHD diagnosis consultation ≤ 365 days before index date	17 (3.6)	73 (3.1)	1.13 (0.63, 2.02)
No ADHD medication or physician consultation ≤ 365 days before index date	280 (59.3)	1486 (63.0)	0.89 (0.71, 1.13)
Type of ADHD medication			
Stimulants only ≤ 365 days before index date	156 (33.1)	738 (31.3)	Reference
Non-stimulants only ≤ 365 days before index date	14 (3.0)	43 (1.8)	1.55 (0.82, 2.92)
Both stimulants and non-stimulants ≤ 365 days before index date	5 (1.1)	20 (0.9)	1.19 (0.44, 3.23)
Past ADHD medication use (any type) > 365 days before index date	192 (40.7)	988 (41.9)	0.92 (0.72, 1.16)
ADHD Diagnosis only (no ADHD medication use)	105 (22.3)	571 (24.2)	0.87 (0.66, 1.14)
Duration of ADHD medications in the 365 days before index date as proportion of days covered			
≥ 80 %	52 (11.0)	244 (10.3)	1.17 (0.81, 1.69)
40 % to <80 %	49 (10.4)	245 (10.4)	1.10 (0.76, 1.59)
>0 % to <40 %	74 (15.7)	312 (13.2)	1.30 (0.93, 1.82)
0 % (past ADHD medication use)	192 (40.7)	988 (41.9)	1.06 (0.81, 1.37)
0 % (no ADHD medication use)	105 (22.3)	571 (24.2)	Reference
Lifetime comorbidities, prior to date of index date			
Anxio-depressive disorders			
No	47 (10.0)	614 (26.0)	Reference
Yes	425 (90.0)	1746 (74.0)	3.18 (2.32, 4.36)
Intellectual disability			
No	396 (83.9)	1916 (81.2)	Reference
Yes	76 (16.1)	444 (18.8)	0.83 (0.63, 1.08)
Reactive disorders			
No	160 (33.9)	1357 (57.5)	Reference
Yes	312 (66.1)	1003 (42.5)	2.64 (2.14, 3.25)
Behavioral disorder in childhood and adolescence			
No	168 (35.6)	1603 (67.9)	Reference
Yes	304 (64.4)	757 (32.1)	3.83 (3.11, 4.71)
Organic psychosis			
No	247 (52.3)	1952 (82.7)	Reference
Yes	225 (47.7)	408 (17.3)	4.36 (3.53, 5.38)
Schizophrenia			
No	353 (74.8)	2136 (90.5)	Reference
Yes	119 (25.2)	224 (9.5)	3.21 (2.51, 4.12)
Congenital anomalies			
No	404 (85.6)	1996 (84.6)	Reference
Yes	68 (14.4)	364 (15.4)	0.92 (0.70, 1.22)
Number of chronic physical and other psychiatric conditions (5 years prior to index date)			
0	200 (42.4)	1652 (70.0)	Reference
1	118 (25.0)	429 (18.2)	2.27 (1.77, 2.92)

(*continued on next page*)

Table 1 (*continued*)

	Cases, $n = 472$	Controls, $n = 2360$	
2	66 (14.0)	166 (7.0)	3.28 (2.38, 4.53)
≥3	88 (18.6)	113 (4.8)	6.43 (4.70, 8.81)
Sociodemographic covariates			
Region of residence			
Census metropolitan area of Montreal	151 (32.0)	917 (38.9)	Reference
Census metropolitan area with ≥ 100,000 inhabitants	142 (30.1)	581 (24.6)	1.48 (1.15, 1.91)
Census metropolitan area with 10,000 – 99,999 inhabitants	78 (16.5)	335 (14.2)	1.41 (1.05, 1.91)
Rural areas ≤9999 inhabitants	98 (20.8)	514 (21.8)	1.16 (0.88, 1.53)
Missing	–	–	NR
Material and social deprivation			
Quintile 1 (Least deprived)	40 (8.5)	271 (11.5)	Reference
Quintile 2	66 (14.0)	375 (15.9)	1.19 (0.78, 1.82)
Quintile 3	97 (20.6)	462 (19.6)	1.42 (0.96, 2.12)
Quintile 4	91 (19.3)	485 (20.6)	1.27 (0.85, 1.90)
Quintile 5 (Most deprived)	147 (31.1)	646 (27.4)	1.54 (1.06, 2.25)
Missing	31 (6.6)	121 (5.1)	1.74 (1.04, 2.91)
Health service utilization			
Receipt of health services during incarceration (lifetime)			
No	436 (92.4)	2276 (96.4)	Reference
Yes	36 (7.6)	84 (3.6)	2.24 (1.49, 3.35)
Ambulatory consultations in the year prior to index date [Mean ± SD]	10.1 ± 12.8	5.1 ± 8.0	1.05 (1.04, 1.07)

*Index date for suicide cases correspond to date of suicide; and assigned matching date for controls. NR: not reported, low cell count

public drug insurance plan, there was no difference in cases and controls with respect to the duration of ADHD medication use during the period 366 to 731 days (0 days: 69.3 % vs. 68.6 %; 1–120 days: 10.8 % vs. 13.9 %; 121–365 days: 19.9 % vs. 17.4 %, X^2=4.28, $p = 0.12$) prior to the index date.

Additionally, the analysis revealed that the duration of ADHD medication use, measured as the proportion of days covered during the observation period, was not linked to completed suicide in the overall cohort, nor in the subgroups for ages 12 to 24 and 25 to 49 years, or those with a physician diagnosis of ADHD (Table 3). Furthermore, the sensitivity analyses restricting the cohort to individuals with at least 730 days of coverage under a public drug insurance plan prior to completed suicide, did not show a significant association between completed suicide and duration of ADHD medication use, as defined by the proportion of days covered, in the overall sample and in the age-restricted cohorts or those with an ADHD physician diagnosis (Table S3 in supplement).

4. Discussion

This study is one of the few that examines the relationship between completed suicide and the use of ADHD medications, including stimulants, non-stimulants, and the combined use of both, in adolescents and adults covered under a public drug insurance plan. In this nested case-control study, no significant association was found between ADHD medication use including stimulants, non-stimulants, and both stimulants and non-stimulants, and completed suicide, even after controlling for important confounding factors.

Our main findings showed a lack of an association between completed suicide and type of ADHD medication use during the observation period, regardless of timing. These findings extend and complement those of a Swedish population-based cohort study that used a target trial emulation framework that showed no association between ADHD medication use within three months of ADHD diagnosis and the risk of completed suicide over a 2-year and 5-year period (Li et al., 2024). The study however was not powered to assess completed suicide and assess the effects of stimulants and non-stimulants separately (Li et al., 2024). In contrast, our findings differ from those of a study involving a Veterans Affairs cohort of adults actively being treated for ADHD. In that study, individuals experienced a lower risk of suicide during months when they were using stimulant medications compared to when they were not (Rice et al., 2024). Of note, this latter study included a cohort of individuals predominantly consisting of men with an average age of 39 years, a high prevalence of comorbid conditions such as depression, trauma-related disorders, substance use and personality disorders, as well as a cohort actively followed and treated for their ADHD in the Veterans Affairs Department. Therefore, these findings may not be generalizable to individuals with ADHD in the general population who are followed in regular primary care or specialty mental health services within public health care systems. Although these systems provide coverage for medical consultations, there are often long waiting lists for mental health specialists. The authors of the Veteran Affairs cohort study suggest that their findings may, in part, be explained by the increased follow-up of patients during treatment episodes with stimulants, even though their analyses controlled for both patient consultations and psychotropic medication use (Rice et al., 2024). Another population-based Scandinavian registry study found a decreased risk of suicide with the use of ADHD medication in individuals with borderline personality disorders also being diagnosed with comorbidities including depression, substance use disorders and ADHD (Lieslehto et al., 2023). Another study also found decreased all-cause mortality in individuals with the use of methylphenidate in individuals with amphetamine use disorder (Hartikainen et al., 2023). It is suggested that ADHD medication may help regulate the impulsivity often associated with substance use disorders or personality disorders in adults (Kozak et al., 2019).

To address the potential selection bias caused by non-continuous public drug insurance coverage, our sensitivity analyses examined

Table 2
The association between timing and type of ADHD medication use and completed suicide.

	Overall sample $N = 472$ cases $N = 2360$ controls	Restricted to individuals 12–24 years of age $N = 116$ cases $N = 580$ controls	Restricted to individuals 25–49 years of age $N = 356$ cases $N = 1780$ controls	Restricted to individuals with an ADHD physician diagnosis $N = 275$ cases $N = 1419$ controls
	Adjusted OR[a] (95 % CI)			
Overall ADHD medication use: Yes vs No	1.13 (0.89, 1.42)	0.77 (0.45, 1.30)	1.24 (0.96, 1.61)	1.12 (0.78, 1.62)
Timing of exposure to ADHD medication prior to index date*				
ADHD medication ≤ 90 days before index date	Reference	Reference	Reference	Reference
ADHD medication 91–365 days before index date	1.28 (0.84, 1.94)	1.16 (0.44, 3.07)	1.39 (0.87, 2.23)	1.70 (0.86, 3.36)
ADHD diagnosis physician consultation ≤ 365 days before index date	1.30 (0.68, 2.46)	0.90 (0.16, 5.15)	1.38 (0.69, 2.77)	1.49 (0.65, 3.41)
No ADHD medication or physician consultation ≤ 365 days before index date	0.92 (0.71, 1.19)	1.38 (0.77, 2.47)	0.84 (0.63, 1.12)	0.97 (0.65, 1.45)
	Adjusted OR[b] (95 % CI)			
Overall ADHD medication use: Yes vs No	1.09 (0.85, 1.38)	0.67 (0.38, 1.19)	1.18 (0.90, 1.55)	1.03 (0.70, 1.51)
Timing of exposure to ADHD medication prior to index date*				
ADHD medication ≤ 90 days before index date	Reference	Reference	Reference	Reference
ADHD medication 91–365 days before index date	1.31 (0.85, 2.01)	1.15 (0.41, 3.24)	1.44 (0.89, 2.35)	1.95 (0.94, 4.01)
ADHD diagnosis physician consultation ≤ 365 days before index date	1.43 (0.74, 2.77)	0.94 (0.16, 5.65)	1.62 (0.79, 3.33)	1.54 (0.63, 3.75)
No ADHD medication or physician consultation ≤ 365 days before index date	0.96 (0.74, 1.24)	1.58 (0.84, 2.97)	0.88 (0.66, 1.18)	1.09 (0.71, 1.66)
	Adjusted OR[b] (95 % CI)			
Type of ADHD medication use prior to index date				
Stimulants only ≤ 365 days before index date	Reference			
Non-stimulants only ≤ 365 days before index date	1.27 (0.62, 2.63)			
Both stimulants and non-stimulants ≤ 365 days before index date	1.01 (0.33, 3.08)			
Past ADHD medication user (any type) > 365 days before index date	0.94 (0.72, 1.24)			
ADHD diagnosis consultation only	0.94 (0.69, 1.28)			

* Index date for suicide cases correspond to date of suicide; and assigned matching date for controls.

[a] Adjusted for study covariables: The presence of anxio-depressive disorders, intellectual disability, reactive disorders, behavioral disorder in childhood and adolescence, organic psychosis, schizophrenia, and congenital anomalies.

[b] Model further adjusted for number of chronic physical and other psychiatric conditions, region of residence, material and social deprivation, health service utilization while incarcerated, and consultations in year prior to suicide death.

Table 3
The association between ADHD medication use and duration and completed suicide among individuals with public drug insurance coverage in the 365 days prior to index date*.

	Overall sample *N* = 472 cases *N* = 2360 controls	Restricted to individuals 12–24 years of age *N* = 116 cases *N* = 580 controls	Restricted to individuals 25–49 years of age *N* = 356 cases *N* = 1780 controls	Restricted to individuals with an ADHD physician diagnosis *N* = 275 cases *N* = 1419 controls
	Adjusted OR[a] (95 % CI)			
Duration of ADHD medication use (proportion of days covered):	0.97 (0.65, 1.44)	0.95 (0.39, 2.30)	0.95 (0.60, 1.50)	1.08 (0.60, 1.93)
≥ 80 %	1.08 (0.72, 1.62)	0.66 (0.26, 1.68)	1.19 (0.75, 1.88)	0.70 (0.37, 1.32)
40 % to <80 %	1.35 (0.94, 1.94)	0.96 (0.43, 2.14)	1.50 (0.99, 2.27)	1.49 (0.87, 2.54)
> 0 % to <40 %	1.01 (0.76, 1.34)	1.20 (0.68, 2.12)	0.96 (0.68, 1.34)	0.89 (0.60, 1.31)
0 % (past ADHD medication use)	Reference	Reference	Reference	Reference
0 % (no ADHD medication use)				
	Adjusted OR[b] (95 % CI)			
Duration of ADHD medication use (proportion of days covered):	0.95 (0.63, 1.43)	0.80 (0.30, 2.09)	0.93 (0.58, 1.49)	1.03 (0.56, 1.91)
≥ 80 %	0.97 (0.64, 1.47)	0.59 (0.22, 1.58)	1.05 (0.65, 1.70)	0.55 (0.28, 1.09)
40 % to <80 %	1.33 (0.91, 1.93)	0.86 (0.36, 2.07)	1.49 (0.97, 2.28)	1.47 (0.82, 2.62)
> 0 % to <40 %	1.00 (0.74, 1.34)	1.18 (0.63, 2.20)	0.96 (0.68, 1.36)	0.87 (0.57, 1.32)
0 % (past ADHD medication use)	Reference	Reference	Reference	Reference
0 % (no ADHD medication use)				

* Index date for suicide cases correspond to date of suicide; and assigned matching date for controls.

[a] Adjusted for study covariables: The presence of anxio-depressive disorders, intellectual disability, reactive disorders, behavioral disorder in childhood and adolescence, organic psychosis, schizophrenia, and congenital anomalies.

[b] Model further adjusted for number of chronic physical and other psychiatric conditions, region of residence, material and social deprivation, health service utilization while incarcerated, and consultations in year prior to suicide death.

individuals who were covered by the public drug insurance plan for two years, rather than just one year. These analyses did not show a significant association between ADHD medication use and completed suicide, except for a marginally significant association where past ADHD medication use was associated with lower odds of completed suicide. Future prospective longitudinal studies on completed suicide in ADHD should aim to clarify the effect of a cumulative exposure to medications overall, timing of exposure, and temporal order of treatments including stimulant only, non-stimulant only, and combination stimulant and non-stimulant in individuals with ADHD and comorbid conditions.

4.1. Strengths and limitations

The strengths of the current study include the use of a population-based cohort of individuals with available linked health data, allowing the linkage of medical consultation claims and pharmaceutical claims in the province of Quebec, Canada, a province with a prevalence of ADHD medication use (Turgeon, 2017) and suicide rate higher than the national average (Public Health Agency of Canada, 2023). ADHD physician diagnosis and medication use were based on claim-based information from the QICDSS-linked medical and administrative databases, routinely used in similar studies (Diallo et al., 2022; Turgeon, 2017; Vasiliadis et al., 2017). Suicide deaths were confirmed by coroner's report.

The study findings need to be considered with the following limitations. First, while we matched cases and controls based on the year of birth, sex, and duration of insurance coverage, and controlled for several potential confounding factors, including sociodemographic and economic factors, the presence of psychiatric and physical conditions, and health service use, residual confounding cannot be ruled out. Second, the act of filling a prescription does not indicate that a medication was used, which introduces the possibility of misclassification bias. If cases are less likely than controls to take their medications, the association between ADHD medication use and completed suicide may be overestimated. Third, health service utilization in the current study was limited to information relating to physician medical claims and, therefore, does not include mental health services received by non-physicians (e.g., neuropsychologists) as well as, although rarer, mental health consultations in private settings. Fourth, although there was no difference in the duration of ADHD medication use between cases and controls examined within specific periods before the index date and measured with the proportion of days covered, we did not consider the persistent cumulative duration of ADHD medication use prior to suicide. Fifth, suicide is a rare event, and therefore, the study may have been limited by small cell sizes when examining the association between ADHD medication in subgroups. Future studies with larger sample sizes are needed to further elucidate the relationship between ADHD medication use and completed suicide in different subgroups. The current study focused only on completed suicide, and the findings may not apply to suicidal ideation and attempts. Finally, the findings of this study may be generalizable to individuals who are covered by public health plans for their medications, as well as health services. Quebec has the highest proportion of residents enrolled in the government-sponsored public drug insurance plan in Canada (Yang & Gupta, 2024). Canadians who are more likely to be covered by government-sponsored drug plans tend to be women, report five or more chronic conditions, and fall within the lowest income quintile (Yang & Gupta, 2024).

5. Conclusion

In conclusion, there was no significant association found between completed suicide and ADHD medication use overall. Despite Blackbox warnings for ADHD medications, Quebec and the rest of Canada have continued prescribing these medications to more youth and adults, even during the pandemic, according to an IQVIA survey of community pharmacies for privately or publicly insured individuals (IQVIA, 2024).

Meanwhile, Quebec's and Canada's suicide rates remain stable (Levesque, 2022; Public Health Agency of Canada, 2023). Future studies should consider including birth cohorts of individuals up to 30 years of age using national registers like QICDSS. This could help establish the trajectory of onset of ADHD and other comorbidities and utilization of psychotropic medication towards outcomes like overall mortality, suicide attempts, substance use disorders, hospitalization or emergency room visits for traumatic injuries (Vasiliadis et al., 2024) and health service utilization in the private health sector.

CRediT authorship contribution statement

Helen-Maria Vasiliadis: Writing – original draft, Methodology, Funding acquisition, Conceptualization. **Louis Rochette:** Writing – review & editing, Methodology, Funding acquisition, Formal analysis. **Victoria Massamba:** Writing – review & editing, Methodology, Funding acquisition, Conceptualization. **Alain Lesage:** Writing – review & editing, Methodology, Funding acquisition, Conceptualization. **Elham Rahme:** Writing – review & editing, Methodology, Funding acquisition, Conceptualization. **Martin Gignac:** Writing – review & editing, Funding acquisition, Conceptualization. **Fatoumata Binta Diallo:** Writing – review & editing, Funding acquisition, Conceptualization. **Alvine Fansi:** Writing – review & editing, Funding acquisition, Conceptualization. **Samuele Cortese:** Writing – review & editing, Conceptualization. **Carlotta Lunghi:** Writing – review & editing, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

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Martin Gignac: Served on advisory committee and declares conference honorarium and travel reimbursement from Takeda, Elvium and Kye pharmaceuticals.

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Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) used Grammarly for proofreading and editing. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

Supplementary materials

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