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Children and Young Adults Who Used Medication for Attention Deficit Hyperactivity Disorder Faced Increased Cardiac Risks

Howaida Elmowafi[1] | Jenny M. Kindblom[2,3] | Linda Halldner[4,5] | David Gyllenberg[6,7] | Estelle Naumburg[1]

[1]Department of Clinical Sciences, Pediatrics, Umeå University, Umeå, Sweden | [2]Department of Drug Treatment, Sahlgrenska University Hospital, Gothenburg, Region Västra Götaland, Sweden | [3]Institute of Medicine, Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden | [4]Department of Clinical Sciences, Child and Adolescent Psychiatry, Umeå University, Umeå, Sweden | [5]Department of Medical Epidemiology and Biostatistics, Karolinska Institute, Stockholm, Sweden | [6]Department of Adolescent Psychiatry, Helsinki University Hospital, Helsinki, Finland | [7]Research Centre for Child Psychiatry and INVEST-Flagship, University of Turku, Turku, Finland

Correspondence: Howaida Elmowafi (howaida.elmowafi@umu.se)

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Keywords: arrhythmia | attention deficit hyperactivity disorder | cardiac arrest | fainting | medication

ABSTRACT

Aim: There have been concerns about links between medication for attention deficit hyperactivity disorder (ADHD) and cardiac events in children and young people. Our aim was to identify any associations.

Method: This Swedish case–control study used national register data to identify individuals aged 5–30 years who received their first diagnosis of a cardiac arrest, arrhythmia, fainting or collapse in 2006–2018. Each case was matched with five controls, by age, sex and region. Associations between ADHD medication and cardiac events were assessed using adjusted odds ratios (aORs) with 95% confidence intervals (CIs). Adjustments were made for concomitant medications and comorbidities, including congenital heart disease (CHD).

Results: We studied 112 605 cases (57.9% female), with a median age of 20 years (range 5–30), and 563 024 matched controls. Using ADHD medication was associated with cardiac events (aOR 1.63, 95% CI 1.47–1.81) across sexes and age groups. Undefined arrhythmias had the strongest association (aOR 2.66, 95% CI 2.27–3.13). Cardiac arrests and defined arrhythmias had no associations. Long-term medication was associated with an increased risk (aOR 1.20, 95% CI 1.12–1.28). CHD had no impact.

Conclusion: ADHD medication was associated with cardiac events, particularly undefined arrhythmias. CHD did not increase the risk.

1 | Introduction

Attention deficit hyperactivity disorder (ADHD) affects around 8% of children globally and it is characterised by persistent inattentiveness, hyperactivity and impulsiveness. Although studies have shown that ADHD medication, including stimulants and non-stimulants, can mitigate symptoms, potential cardiac risks have prompted safety concerns [1, 2].

Many observational and experimental studies have investigated both the long-term and the short-term cardiovascular risks of ADHD medication [2–5]. However, some studies have excluded

Abbreviations: ADHD, attention deficit hyperactivity disorder; aOR, adjusted odds ratio; CHD, congenital heart disease; CI, confidence interval.

Summary

- This national register study assessed the risks of cardiac events in individual aged 5–30 years who used medication for attention deficit hyperactivity disorder (ADHD).
- Comparing these Swedish cases with matched controls revealed an association between ADHD medication use and an increased risk of cardiac events, particularly undefined arrhythmias.
- No increased risks of cardiac events were seen in those with congenital heart disease.

fainting, which can be a sign of a cardiac event [6]. Others have not considered confounding factors [2, 4, 7], such as congenital heart disease (CHD), despite the fact that these factors have frequently been linked to cardiac arrhythmias [8].

The risk estimate can be biased by some physical, mental and neurological disorders that often occur at the same time as ADHD or heart conditions. For example, epilepsy has a well-established connection with ADHD and cardiac events, such as arrhythmias, and this is possibly due to shared genetic or non-genetic factors [9, 10]. This highlights a gap in the knowledge about specific cardiac risks related to ADHD medication use.

Certain medications, including antiepileptics, theophylline, oral steroids, levothyroxine and beta-adrenoceptor agonists [11–13], could influence the risk of cardiac events. Antiepileptics may affect the ion channels in the heart [11], while theophylline and beta-adrenoceptor agonists may initiate supraventricular or ventricular tachycardia [12, 13]. The risks of arrhythmias and a prolonged QTc interval are known to vary with both sex and age [14]. However, the associations between cardiac events and ADHD medication by sex and across childhood, adolescence and early adulthood are unknown.

The aim of this nationwide, register-based study was to assess the associations between different cardiac events and exposure to ADHD medication in patients aged 5–30 years.

2 | Methods

This Swedish study was based on a nationwide case–control study design that used data from 2006 to 2018. The design was selected due to the rarity of the outcome, namely cardiac events, in the target age group of 5–30 years. Associations between the risk of cardiac events and ADHD medication use were assessed. Age and sex, together with potential confounding factors such as cardiac, somatic and psychiatric comorbidities and concomitant medication, were considered. Associations between cardiac events and types of ADHD medication and duration of use were also assessed.

2.1 | Data Sources

Data were obtained from Swedish national registers. These were the Swedish National Patient Register, for inpatient and specialised outpatient care, the Swedish Prescribed Drug Register and the Swedish Population Register. The first two include detailed information on disease diagnoses and prescribed medication, respectively, and demographic data. Both have been recognised for their good national coverage. The Swedish Population Register, which was established in 1961, provides information on births, households, residence status and citizenship changes [15–17].

2.2 | Study Population and Inclusion Criteria

2.2.1 | Identification of Cases and Controls

Cases were identified from the Swedish National Patient Register. They comprised all individuals in Sweden aged 5–30 years who received an incident diagnosis of a cardiac event between 1 January 2006 and 31 December 2018. Cardiac events included cardiac arrests, defined and undefined cardiac arrhythmias, fainting and collapse. The date of the cardiac event was used as the index date. If a patient received a diagnosis of a cardiac arrest or defined arrhythmia, it was classified as such. A diagnosis of undefined arrhythmia, but not defined arrhythmia, was classified as undefined arrhythmia. A diagnosis of fainting or collapse, but not defined or undefined arrhythmia, was classified as fainting. The diagnoses were based on the International Classification of Diseases, Tenth Revision, Swedish version (ICD-10-SE) (Table S1). Patients were only excluded if they were outside the age range or study dates.

Controls were identified from the Swedish Population Register and each one was used only once during the study period. Five controls were matched with each case, based on age, sex and region of residence at the time of the index date. The controls were selected after all cases had been removed from the population pool and no replacements were used.

2.2.2 | Main Medication Exposure

Data on medication were drawn from the Swedish Prescribed Drug Register for the period 2006–2018. We selected individuals aged 5–30 years who had received at least one dispensed ADHD medication in the year before their index date. This was defined as current use. No dispensed medication for any other psychotropic medication during this time span was included. The Anatomical Therapeutic and Chemical codes that were included were for the stimulants methylphenidate (N06BA04), dexamphetamine (N06BA02) and lisdexamphetamine (N06BA12) and the non-stimulants atomoxetine (N06BA09) and guanfacine (C02AC02) (Table S1).

2.2.3 | Potential Confounders and Covariates

We retrieved potential confounders and covariates from the Swedish National Patient Register and the Swedish Prescribed Drug Register. Only occurrences that preceded the index date for the cardiac event in the case were considered. We included the cardiac comorbidities, CHD, long QT syndrome and Brugada's syndrome as covariates. Other covariates that were included were somatic diseases, like chronic obstructive pulmonary

disease, epilepsy, chronic kidney disease, sleep disorders and primary adrenocortical insufficiency. Neurodevelopmental and psychiatric disorders were also included. We considered some concomitant medications as confounding factors. These included the systemic use of asthma medication, steroids, thyroxine, certain antihypertensives, such as doxazosin, and medication for Parkinson's disease or epilepsy. Further details are available in Table S1.

2.3 | Statistical Analysis

Conditional logistic regression was used to compute the crude odds ratios and adjusted odds ratios (aORs) for all cardiac events. Separate analyses were also carried out for cardiac arrests or arrhythmias and fainting or collapse. Subgroup analyses were carried out for sex, cases under 15 years versus 15 years or older, and undefined versus defined arrhythmias. The latter subgroup included atrial arrhythmias and supraventricular or ventricular tachycardia. The level of significance was assessed using 95% confidence intervals (CIs). Six multivariable models were used for the stepwise adjustments. In Model I, crude odds ratios of cardiac events relative to ADHD medication were assessed, based on the matching variables of age, sex and region. In Model II, adjustments for cardiac comorbidities were carried out and these are presented as adjusted odds ratios (aOR). Model III used adjustments for cardiac comorbidities and neurodevelopmental disorders. In Model IV, adjustments for cardiac comorbidities, neurodevelopmental disorders and somatic diseases were carried out. Model V used adjustments for cardiac comorbidities, neurodevelopmental disorders, somatic diseases and concomitant medications. All the aforementioned covariates and other psychiatric disorders were adjusted in Model VI.

Five sensitivity analyses were conducted to check the robustness of the association between ADHD medication and the risk of cardiac events. First, the analysis was restricted to individuals who had used ADHD medication at any time, and this was compared with those who had not used medication. Second, ADHD medication use was categorised into three groups: no medication use, former use or current use. Former use was defined as before the index date, but not in the 1-year period before the cardiac event. This was the reference group, and it allowed us to compare the cardiac event risks between current and former users.

Third, we carried out a subgroup analysis to assess the association between cardiac events and stimulant versus non-stimulant ADHD medication. The fourth sensitivity analysis explored the association between the duration of exposure to ADHD medication and incident cardiac events. The duration of ADHD medication use was categorised into four subgroups: no medication use, short-term use of 2 years or less, intermediate use of 2–5 years and long-term use of 5–13 years. The aim of these categories was to improve the statistical power and enable comparisons between different exposure thresholds. The fifth sensitivity analysis was carried out to determine whether psychiatric disorders served as mediators rather than confounders in the study protocol.

2.4 | Ethics

The study was approved by the Swedish Ethical Review Board (numbers 2019-04467 and 2020-05889) [18]. The Swedish National Board of Health and Welfare and Statistics Sweden linked the datasets using the unique personal identity numbers assigned to all the legal residents. Data were then pseudonymised and securely delivered [19].

3 | Results

We matched each case from the Swedish National Patient Register with five controls from the Swedish Population Register and applied the inclusion and exclusion criteria. This meant that 112 605 cases (57.9% females) and 563 024 controls (57.9% females) from 2006 to 2018 were included in the final analysis. The median age (interquartile range) at baseline was 20 years (15–25 years) for all cases. The mean age was 22 years (17–26 years) for the combined category of cardiac arrests and arrhythmias, and it was 18 years (14–24 years) for fainting and collapse (Figure 1, Table 1).

The most common types of cardiac events among our cases were fainting and collapse (57.5%), followed by undefined arrhythmias (37.4%) (Table S2). Overall, cardiac, somatic and psychiatric comorbidities and concomitant medication use were more common among cases than controls (Table 1).

Table 1 shows that more than twice as many cases as controls currently used ADHD medication (0.5% vs. 0.2%). Methylphenidate was the most frequently dispensed medication (89.8%), followed by atomoxetine (8.2%) and lisdexamphetamine (1.7%). In the full cohort, current ADHD medication use was more strongly associated with cardiac events than no medication (aOR 1.63 [95% CI 1.47–1.81]). The aOR for the combined category of cardiac arrests and arrhythmias was 2.54 (95% CI 2.17–2.96). The risk of cardiac events with ADHD medication was almost similar across the age groups. For those aged 5–14 years the aOR was 1.60 (95% CI 1.35–1.92) and for those aged 15–30 years it was 1.55 (95% CI 1.36–1.77). An association between fainting and collapse and current ADHD medication was only found in the younger age group (aOR 1.35, 95% CI 1.07–1.71). These associations remained unchanged when we adjusted for CHD, but were attenuated when we included neurodevelopmental disorders (Table 2).

Current ADHD medication use was more common among the cases than controls and was associated with cardiac events in both sexes, compared with no medication. For females, the aOR was 1.56 (95% CI 1.33–1.83) and for males it was 1.69 (95% CI 1.47–1.94). There was a slightly higher risk of the combined category of cardiac arrests and arrhythmias in females, with an aOR of 2.60 (95% CI 2.01–3.37). No association between fainting or collapse and current use of ADHD medication was observed in either sex (Table 3).

Current ADHD medication use was associated with undefined arrhythmias (aOR 2.66, 95% CI 2.27–3.13), but not with defined arrhythmias (Table 4).

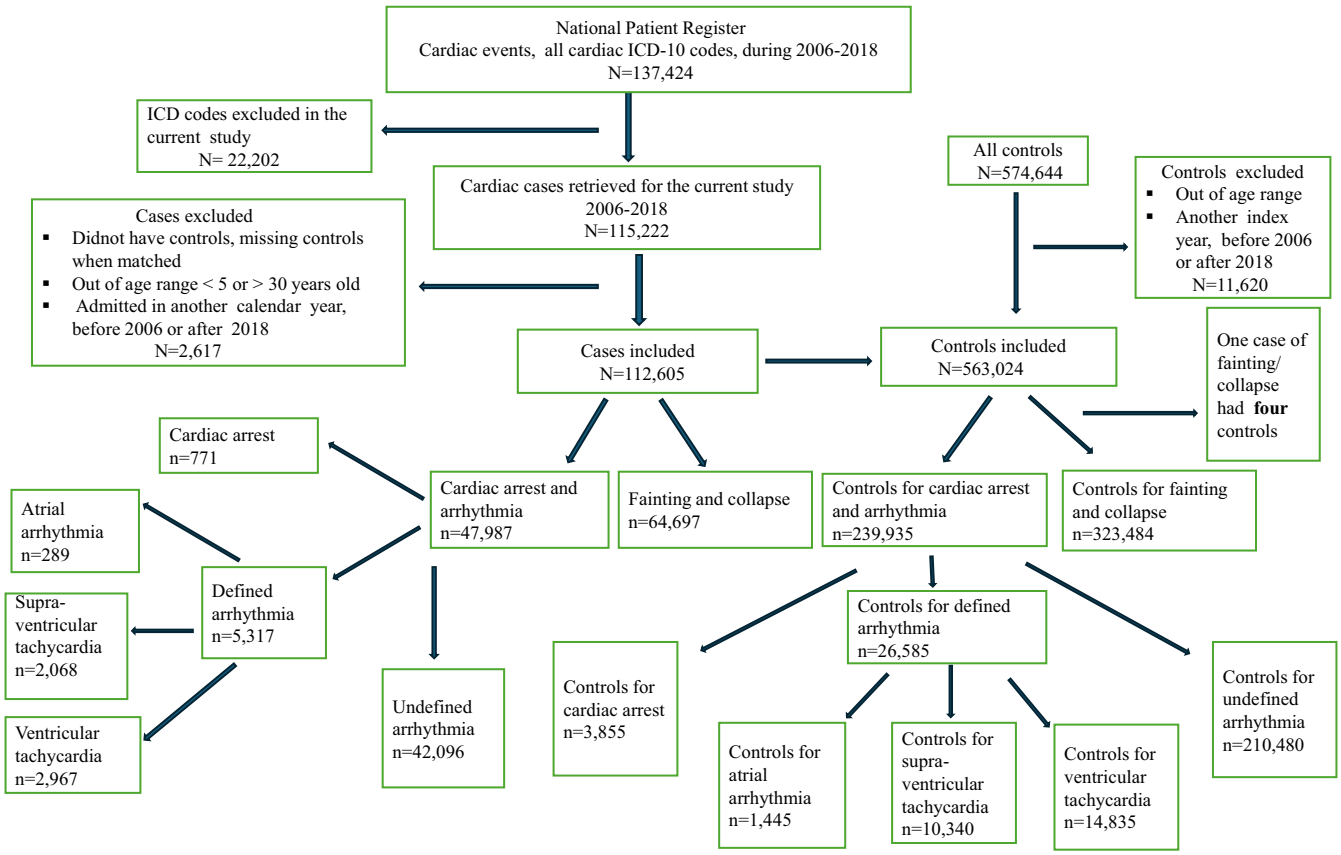

FIGURE 1 | Identification of cases and matched controls. Cases were individuals aged 5–30 years old who received an incident diagnosis of a cardiac event, cardiac arrest, arrhythmia, fainting or collapse, between 2006 and 2018. They were retrieved from the Swedish National Patient Register. Controls were identified from the Swedish Population Register. The controls, who had no cardiac events, were included only once during the study period (2006–2018).

3.1 | Results of Sensitivity Analyses

The use of ADHD medication at any time was associated with cardiac events (Table S3). There was a stronger association between cardiac events and current use of ADHD medication than former use (aOR 1.56, 95% CI 1.40–1.75). This was also the case for the separate analyses of cardiac arrests and arrhythmias (aOR 2.49, 95% CI 2.11–2.94). No difference in fainting and collapse was found when current and former use of ADHD medication were compared (Table S4).

When we carried out the subgroup analysis by type of ADHD medication, we found similar associations between cardiac events and stimulants versus non-stimulants (Table S5). We found an increased risk of cardiac events with long-term use, namely 5–13 years, compared with no medication (aOR 1.20, 95% CI 1.12–1.28) or shorter use (Table S6). The aOR remained significant when only psychiatric illnesses that occurred before the exposure were included.

4 | Discussion

This nationwide case–control, register-based study identified a small but significant association between the use of ADHD medication and an increased risk of cardiac events. This increased risk was significant for all age groups and both sexes when it was compared with individuals who had not used ADHD medication. The primary contributor was an increased risk of undefined arrhythmias. There was no significant association between using ADHD medication and cardiac arrests or defined arrhythmias. Using ADHD medication for 5 years or more was associated with a greater risk of cardiac events.

To our knowledge, only one previous study [20] had assessed the risk of cardiac events related to current ADHD medication use as psychopharmacological monotherapy. This study considered arrhythmias and CHD.

We found an increased risk of the combined category of cardiac arrests, arrhythmias and fainting, and current ADHD medication use (Table 2). This agreed with the findings of two other studies [21, 22], but was lower than the risk reported by a study that assessed adults aged 18 years plus who used ADHD medication [23]. This may have been due to acquired comorbidities or differences in the lifestyles of older adults [24], compared to our younger study population.

ADHD medication use was associated with undefined arrhythmias. To our knowledge, these have rarely been studied, apart from in one incidence study by our group [25]. Most of the previous research has focused on the associations between

TABLE 1 | Baseline characteristics of cases and matched controls.

2006–2018	Full sample		Cardiac arrest and arrhythmias		Fainting and collapse	
	Cases	Controls	Cases	Controls	Cases	Controls
	n = 112 605	*n* = 563 024	*n* = 47 987	*n* = 239 935	*n* = 64 697	*n* = 323 484
Variable	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Sex						
Male	47 465 (42.15)	237 325 (42.15)	23 737 (49.47)	118 685 (49.47)	23 763 (36.73)	118 815 (36.73)
Female	65 140 (57.85)	325 699 (57.85)	24 250 (50.53)	121 250 (50.53)	40 934 (63.27)	204 669 (63.27)
Age in years, median (IQR)	20 (15–25)	20 (15–25)	22 (17–26)	22 (17–26)	18 (14–24)	18 (14–24)
ADHD medication, current use						
Yes	577 (0.51)	1180 (0.21)	330 (0.69)	399 (0.17)	247 (0.38)	782 (0.24)
Cardiac comorbidities						
Congenital heart disease (CHD)						
Mild CHD	447 (0.40)	938 (0.17)	237 (0.49)	373 (0.16)	210 (0.32)	567 (0.18)
Severe CHD	776 (0.69)	1016 (0.18)	503 (1.05)	422 (0.18)	275 (0.43)	594 (0.18)
Long QT	8 (0.01)	0 (0.00)	7 (0.01)	0 (0.00)	2 (0.00)	0 (0.00)
Psychiatric comorbidities						
Anxiety and depressive disorders						
Unipolar disorders	5339 (4.74)	13 012 (2.31)	2324 (4.84)	6015 (2.51)	3019 (4.67)	7011 (2.17)
OCD	604 (0.54)	1617 (0.29)	307 (0.64)	732 (0.31)	297 (0.46)	887 (0.27)
Other anxiety disorders	5046 (4.48)	9740 (1.73)	2558 (5.33)	4546 (1.89)	2495 (3.86)	5208 (1.61)
Other emotional disorders	138 (0.12)	409 (0.07)	65 (0.14)	161 (0.07)	73 (0.11)	250 (0.08)
Substance use disorders						
Alcohol use disorders	2463 (2.19)	6530 (1.16)	1250 (2.60)	3153 (1.31)	1216 (1.88)	3384 (1.05)
Other substance use	2261 (2.01)	3854 (0.68)	1280 (2.67)	1943 (0.81)	981 (1.52)	1918 (0.59)
Psychotic and bipolar disorders						
Schizophrenic disorders	188 (0.17)	370 (0.07)	117 (0.24)	220 (0.09)	71 (0.11)	150 (0.05)
Other psychotic disorders	532 (0.47)	1122 (0.20)	299 (0.62)	598 (0.25)	233 (0.36)	525 (0.16)
Bipolar and mania disorder	847 (0.75)	1647 (0.29)	420 (0.88)	801 (0.33)	428 (0.66)	847 (0.26)
Neurodevelopmental disorders						
ADHD	4822 (4.28)	11 155 (1.98)	2510 (5.23)	4747 (1.98)	2318 (3.58)	6419 (1.98)
Autism spectrum disorders	1476 (1.31)	4619 (0.82)	687 (1.43)	1961 (0.82)	793 (1.23)	2663 (0.82)
Intellectual disorders	722 (0.64)	2216 (0.39)	269 (0.56)	929 (0.39)	454 (0.70)	1290 (0.40)

(Continues)

TABLE 1 | (Continued)

2006–2018	Full sample		Cardiac arrest and arrhythmias		Fainting and collapse	
	Cases	Controls	Cases	Controls	Cases	Controls
	n = 112 605	*n* = 563 024	*n* = 47 987	*n* = 239 935	*n* = 64 697	*n* = 323 484
Variable	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Tic disorders	180 (0.16)	548 (0.10)	79 (0.16)	224 (0.09)	101 (0.16)	324 (0.10)
Learning/speech disorders	342 (0.30)	1208 (0.21)	135 (0.28)	443 (0.18)	208 (0.32)	768 (0.24)
Other psychiatric disorders						
Conduct disorders	487 (0.43)	1033 (0.18)	202 (0.42)	410 (0.17)	286 (0.44)	625 (0.19)
Eating disorders	1489 (1.32)	3396 (0.60)	680 (1.42)	1385 (0.58)	811 (1.25)	2015 (0.62)
Neurotic and personality disorders	6322 (5.61)	13 110 (2.33)	2806 (5.85)	6093 (2.54)	3525 (5.45)	7035 (2.17)
Somatic comorbidities						
Epilepsy	1185 (1.05)	3160 (0.56)	389 (0.81)	1342 (0.56)	796 (1.23)	1820 (0.56)
Sleep disorders	743 (0.66)	1696 (0.30)	366 (0.76)	769 (0.32)	377 (0.58)	928 (0.29)
COPD	10 (0.01)	21 (0.00)	6 (0.01)	9 (0.00)	4 (0.01)	12 (0.00)
Chronic kidney diseases	109 (0.10)	158 (0.03)	54 (0.11)	65 (0.03)	55 (0.09)	93 (0.03)
Adrenal insufficiency	57 (0.05)	141 (0.03)	26 (0.05)	44 (0.02)	31 (0.05)	97 (0.03)
Concomitant medications						
Antiepileptic	4142 (3.68)	8847 (1.57)	1919 (4.00)	4056 (1.69)	2224 (3.44)	4801 (1.48)
Antiparkinsonian	402 (0.36)	721 (0.13)	223 (0.46)	376 (0.16)	179 (0.28)	347 (0.11)
Steroids	11 626 (10.32)	40 197 (7.14)	5451 (11.36)	17 712 (7.38)	6184 (9.56)	22 510 (6.96)
Bronchial asthma medication	1997 (1.77)	8094 (1.44)	712 (1.48)	2694 (1.12)	1285 (1.99)	5406 (1.67)
Antithyroid medications	2209 (1.96)	6174 (1.10)	1191 (2.48)	2902 (1.21)	1020 (1.58)	3274 (1.01)
Doxazocin	56 (0.05)	92 (0.02)	29 (0.06)	54 (0.02)	27 (0.04)	38 (0.01)

Note: Further details on ICD-10 & ATC codes for the included covariates presented in Table S1.
Abbreviations: ADHD = attention deficit hyperactivity disorder, COPD = chronic obstructive pulmonary disease, IQR = interquartile range, OCD = obsessive compulsive disorder.

ADHD medication and severe cardiovascular diseases [26, 27] or all types of cardiac events [2, 4]. A diagnosis of undefined arrhythmia is often applied when a specific arrhythmia is suspected, but not confirmed by clinicians or echocardiography. Sometimes an undefined arrhythmia can be defined and treated at a later date, but diagnosing them can take time.

Our study relied on registry data, which meant that undefined arrhythmias could not become defined, leaving us with limited knowledge of their characteristics and clinical consequences. In addition, individuals on ADHD medication are more likely to be referred to specialised clinics than non-medicated individuals, even if they do not have more severe arrhythmias. Furthermore, we lacked data on those who only visited primary care services or did not seek medical care due to undefined events. Taken together, these factors may have contributed to inflated associations in our results.

We did not observe any statistically significant increase in the risk of defined arrhythmias with current use of ADHD medication, in common with another study [2]. Although the risk was not statistically significant, it could not be ruled out, due to the limited cell numbers. However, we found it reassuring that there was no change in the association between defined serious arrhythmias and using ADHD medication.

TABLE 2 | Associations between risk of cardiac events and ADHD medication use, assessed using odds ratios.

	Cases	Controls	Model I (Crude)	Model II	Model III	Model IV	Model V	Model VI
	No. (%)	No. (%)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)
Cardiac events and ADHD medication, current use								
Full sample								
	112 605	563 024						
No	112 028 (99.49)	561 844 (99.79)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	577 (0.51)	1180 (0.21)	2.46 (2.22–2.72)	2.46 (2.23–2.72)	1.48 (1.33–1.64)	1.47 (1.32–1.63)	1.55 (1.40–1.72)	1.63 (1.47–1.81)
Cardiac arrest and arrhythmias								
	47 987	239 935						
No	47 657 (99.31)	239 536 (98.83)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	330 (0.69)	399 (0.17)	4.15 (3.58–4.80)	4.17 (3.60–4.83)	2.23 (1.92–2.61)	2.23 (1.91–2.60)	2.37 (2.03–2.76)	2.54 (2.17–2.96)
Fainting and collapse								
	64 697	323 484						
No	64 450 (99.62)	322 702 (99.76)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	247 (0.38)	782 (0.24)	1.59 (1.37–1.83)	1.58 (1.37–1.83)	1.10 (0.91–1.23)	1.05 (0.91–1.22)	1.10 (0.95–1.27)	1.14 (0.98–1.32)
Cardiac events, age groups, and ADHD medication, current use								
< 15 years old								
All < 15 years								
	24 491	122 455						
No	24 272 (99.11)	122 027 (99.65)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	119 (0.89)	428 (0.35)	2.58 (2.19–3.04)	2.59 (2.20–3.05)	1.58 (1.32–1.88)	1.57 (1.32–1.88)	1.59 (1.33–1.90)	1.60 (1.35–1.92)

(Continues)

TABLE 2 | (Continued)

	Cases	Controls	Model I (Crude)	Model II	Model III	Model IV	Model V	Model VI
	No. (%)	No. (%)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)
Cardiac arrest and arrhythmias								
	7355	36 775						
No	7244 (98.49)	36 659 (99.68)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	111 (1.51)	116 (0.32)	4.83 (3.72–6.27)	4.91 (3.78–6.38)	2.16 (1.62–2.87)	2.16 (1.62–2.87)	2.17 (1.62–2.89)	2.23 (1.67–2.97)
Fainting and collapse								
	17 142	85 710						
No	17 034 (99.37)	85 397 (99.63)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	108 (0.63)	313 (0.37)	1.74 (1.39–2.16)	1.73 (1.39–2.16)	1.33 (1.05–1.68)	1.33 (1.05–1.68)	1.34 (1.06–1.70)	1.35 (1.07–1.71)
≥ 15 years old								
All ≥ 15								
	88 114	440 569						
No	87 756 (99.59)	439 817 (99.83)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	358 (0.41)	752 (0.17)	2.39 (2.11–2.71)	2.39 (2.11–2.71)	1.43 (1.25–1.63)	1.42 (1.24–1.62)	1.50 (1.32–1.71)	1.55 (1.36–1.77)
Cardiac arrest and arrhythmias								
	40 632	203 160						
No	40 413 (99.46)	202 877 (99.86)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	219 (0.54)	283 (0.14)	3.89 (3.24–4.62)	3.88 (3.25–4.64)	2.13 (1.77–2.56)	2.12 (1.76–2.55)	2.26 (1.88–2.72)	2.42 (2.01–2.91)
Fainting and collapse								
	47 555	237 774						
No	47 416 (99.71)	237 305 (99.80)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	139 (0.29)	469 (0.20)	1.49 (1.23–1.80)	1.48 (1.23–1.80)	0.96 (0.79–1.17)	0.96 (0.79–1.16)	1.00 (0.82–1.22)	1.01 (0.82–1.23)

Note: Mode I: the crude model, including only the main exposure (ADHD medication use) with no covariates. Model II: adjusted for cardiac comorbidities covariates. Model III: adjusted for cardiac comorbidities covariates and neurodevelopmental disorders. Model IV: adjusted for cardiac comorbidities covariates, neurodevelopmental disorders and somatic diseases. Model V: adjusted for cardiac comorbidities covariates, neurodevelopmental disorders, somatic diseases and medications. Model VI: fully adjusted, adjusted for cardiac comorbidities covariates, somatic diseases, medications and all psychiatric disorders, including neurodevelopmental disorders.
Abbreviations: ADHD = attention deficit hyperactivity disorder, CI = confidence interval, No = no use of ADHD medication, Ref = reference group, Yes = use of ADHD medication.

TABLE 3 | Association of cardiac events with ADHD medication exposure, stratified by sex.

	Cases	Controls	Full sample		Cardiac arrest and arrhythmias		Fainting and collapse	
			Crude model[a]	Adjusted model[b]	Crude model[a]	Adjusted model[b]	Crude model[a]	Adjusted model[b]
Sex and ADHD medication, current use	No. (%)	No. (%)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)	Odds ratios (95% CI)
Male	47465	237325						
No	47136 (99.31)	236652 (99.72)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	329 (0.69)	673 (0.28)	2.46 (2.16–2.80)	1.69 (1.47–1.94)	3.81 (3.17–4.57)	2.52 (2.08–3.06)	1.58 (1.29–1.92)	1.13 (0.91–1.39)
Female	65140	325699						
No	64892 (99.62)	325192 (99.84)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Yes	248 (0.38)	507 (0.16)	2.46 (2.11–2.86)	1.56 (1.33–1.83)	4.81 (3.78–6.13)	2.60 (2.01–3.37)	1.60 (1.30–1.96)	1.15 (0.92–1.42)

Abbreviations: ADHD = attention deficit hyperactivity disorder, CI = confidence interval, No = no use of ADHD medication, Ref = reference group, Yes = use of ADHD medication.
[a]Crude model, adjusted by design, included only ADHD medication use, no other covariates.
[b]Adjusted model, fully adjusted for cardiac and somatic comorbidities, medications and all psychiatric disorders including neurodevelopmental disorders.

TABLE 4 | Association of cardiac events with ADHD medication use, stratified by type of cardiac event.

Cardiac event and ADHD medication, current use	Cases No. (%)	Controls No. (%)	Crude model[a] Odds ratio (95% CI)	Adjusted model[b] Odds ratio (95% CI)
Cardiac arrest	771	3855		
No	769 (99.74)	3853 (98.95)	1 (Ref)	1 (Ref)
Yes	2 (0.26)	2 (0.05)	5.00 (0.70–35.50)	9.38 (1.21–72.49)
Defined arrhythmias				
Defined arrhythmias, all	5317	26 585		
No	5303 (99.74)	26 543 (99.84)	1 (Ref)	1 (Ref)
Yes	14 (0.26)	42 (0.16)	1.66 (0.91–3.05)	1.29 (0.67–2.49)
Defined arrhythmias, separate groups				
1. Atrial arrhythmias	289	1445		
No	289 (100.00)	1443 (99.89)	1 (Ref)	1 (Ref)
Yes	0 (0.00)	2 (0.14)	NA	NA
2. SVT	2068	10 340		
No	2061 (99.66)	10 323 (99.84)	1 (Ref)	1 (Ref)
Yes	7 (0.34)	17 (0.16)	2.06 (0.85–4.96)	1.58 (0.61–4.11)
3. VT	2967	14 835		
No	2960 (99.76)	14 811 (99.84)	1 (Ref)	1 (Ref)
Yes	7 (0.24)	24 (0.16)	1.46 (0.63–3.38)	1.09 (0.44–2.71)
Undefined arrhythmias	42 096	210 480		
No	41 779 (99.25)	210 125 (99.83)	1 (Ref)	1 (Ref)
Yes	317 (0.75)	355 (0.17)	4.48 (3.85–5.21)	2.66 (2.27–3.13)

Abbreviations: ADHD = attention deficit hyperactivity disorder, CI = confidence interval, NA = not applicable, No = no use of ADHD medication, Ref = reference group, SVT = supraventricular tachycardia, VT = ventricular tachycardia, Yes = use of ADHD medication.
[a]Crude model, adjusted by design, included only current ADHD medication use, but no other covariates.
[b]Adjusted model, fully adjusted, to cardiac, somatic comorbidities, medications, and all psychiatric disorders including neurodevelopmental disorders.

The association between cardiac events and the current use of ADHD medication was similar across the age groups in our study. This agreed with the results of another study, but their findings were not statistically significant [2]. We found a small but significant association between the risk of fainting or collapse and children under 15 years of age using ADHD medication. This may have been influenced by changes related to their age or puberty, making them sensitive to drug-induced side effects [28–30]. We found that 8.7% of the cases and 7.9% of the controls under 15 years of age had used ADHD medication at some point. The proportion was higher in the older controls than in their matched cases. Atomoxetine, which is a selective norepinephrine reuptake inhibitor, accounted for 99.3% of the non-stimulant ADHD medication use by individuals in our study. The side effects of atomoxetine include syncope, orthostatic hypotension and long QT syndrome [31]. Atomoxetine metabolism is complex, primarily governed by cytochrome P450 2D6, with significant variations among individuals, races and ethnicities, due to genetic differences [31]. We speculate that the association was influenced by either atomoxetine metabolism or by help-seeking behaviour in these patients. Further research into personalised medication and age-related pharmacokinetics is recommended.

Our findings indicated that using ADHD medication posed a slight difference in cardiac event risks between the sexes. Females showed a slightly higher risk of the combined category of cardiac arrests and arrhythmias than males. This was in line with one study [2], but was contrary to another study, which indicated similar risks between the sexes [4]. Sex-based differences in pharmacokinetics [32] may result in varying responses to ADHD medication, and other studies have shown these in females [33]. This sex difference in cardiac risks may be counterbalanced by the benefits of ADHD medication, which can both alleviate symptoms and limit risky behaviours [34, 35].

The odds of cardiac events remained unchanged after adjusting for CHD. Although CHD has been associated with an increased risk of arrhythmias [8], using ADHD medication did not increase this risk, in common with results from other studies [22, 36, 37]. A study on children with CHD who used central stimulants for

ADHD reported no changes in cardiovascular parameters and highlighted notable improvements in ADHD symptoms [38]. We believe that, overall, the well-known cardiovascular risks associated with ADHD medication have raised awareness of the safety aspects when these are prescribed. This may be demonstrated by the low risks found in the current study and others. Consultations with specialist colleagues, and considering cardiac risks among children and young people with serious cardiac conditions, are essential when prescribing ADHD medication.

Neurodevelopmental and psychiatric disorders have been associated with cardiac risks. In our study, the association between ADHD medication and cardiac events was decreased by adjusting for neurodevelopmental disorders. The reason for this is unknown. Dysregulation of pathways, like the hypothalamic–pituitary–adrenal axis, or autonomic nervous system activity or inflammation, may play a role [10]. This highlights the need for full screening and early management of concomitant psychiatric and neurodevelopmental disorders in ADHD patients, in order to increase cardiac protection.

This study indicated a higher cardiac risk with long-term ADHD medication use, compared with no medication use, in line with previous findings [4]. A systematic review only identified two studies on ADHD medication use lasting more than 2 years. Neither of these studies showed significant results [2]. However, biases in those studies prevent ruling out long-term cardiovascular risks of ADHD medication.

4.1 | Strengths and Limitations

The register-based case–control study had a number of strengths. We minimised recall bias by using previously collected data that were retrieved from real-world settings, and this strengthened the study implications. The case–control design is particularly well-suited for studying rare outcomes, such as cardiac events in young individuals. This is because it increases statistical power and thereby strengthens the study's findings. However, sudden death was exceedingly rare in the death register, and was only recorded for nine cases aged 5–30 years. Only four of these could be matched with controls by Statistics Sweden. This indicates that some of the nine cases may have had a prior cardiac event and were already included in the study under other cardiac events.

We included individuals with preexisting cardiac syndromes and CHD, but excluded those with psychopharmacological polypharmacy. This approach enabled us to carry out a focused assessment of these cardiac conditions and provide specific insights into the effects of ADHD medication as a distinct exposure. The risk of selection bias was thereby decreased.

There were also some limitations. Socioeconomic factors and lifestyle behaviours were not accounted for in this study, as these were not available in national patient registers. The retrospective approach may have limited the study through the risk of selection, recall and attribution bias. Furthermore, the data used could not be controlled because it came from other sources. However, all the registries we used have been validated, with good coherence found between them and medical records [15, 16]. The associations assessed in this study could not establish causality, in common with all observational studies.

5 | Conclusion

This case–control study found that current use of ADHD medication was associated with cardiac events in individuals aged 5–30 years, especially undefined arrhythmias. This suggests that ADHD medication may be safer in terms of defined arrhythmias. Pre-existing CHD did not modify the risk of cardiac events, whereas neurodevelopmental disorders significantly influenced it. Further research is needed, and this should focus on individuals with neurodevelopmental disorders and those with undefined arrhythmias.

Author Contributions

Howaida Elmowafi: responsible for statistical analysis, data interpretation and drafting the manuscript. **Estelle Naumburg:** oversaw protocol development, contributed to the analytical framework and performed a comprehensive review of the manuscript. **Linda Halldner, David Gyllenberg and Jenny M. Kindblom:** offered critical feedback on the study design and provided detailed revisions to the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that supports the findings of this study are available in Swedish from Socialstyrelsen, the Swedish National Board of Health and Welfare, https://bestalladata.socialstyrelsen.se/, but restrictions apply. The data were used under licence for the current study and are not publicly available.

References

1. G. Ayano, S. Demelash, Y. Gizachew, L. Tsegay, and R. Alati, "The Global Prevalence of Attention Deficit Hyperactivity Disorder in Children and Adolescents: An Umbrella Review of Meta-Analyses," *Journal of Affective Disorders* 339 (2023): 860–866, https://doi.org/10.1016/j.jad.2023.07.071.

2. L. Zhang, H. Yao, L. Li, et al., "Risk of Cardiovascular Diseases Associated With Medications Used in Attention-Deficit/Hyperactivity Disorder: A Systematic Review and Meta-Analysis," *JAMA Network Open* 5, no. 11 (2022): e2243597, https://doi.org/10.1001/jamanetworkopen.2022.43597.

3. K. K. C. Man, A. Häge, T. Banaschewski, et al., "Long-Term Safety of Methylphenidate in Children and Adolescents With ADHD: 2-Year Outcomes of the Attention Deficit Hyperactivity Disorder Drugs Use Chronic Effects (ADDUCE) Study," *Lancet Psychiatry* 10, no. 5 (2023): 323–333, https://doi.org/10.1016/s2215-0366(23)00042-1.

4. L. Zhang, L. Li, P. Andell, et al., "Attention-Deficit/Hyperactivity Disorder Medications and Long-Term Risk of Cardiovascular Diseases," *JAMA Psychiatry* 81 (2023): 178–187, https://doi.org/10.1001/jamapsychiatry.2023.4294.

5. O. J. Storebo, E. Ramstad, H. B. Krogh, et al., "Methylphenidate for Children and Adolescents With Attention Deficit Hyperactivity Disorder (ADHD)," *Cochrane Database of Systematic Reviews* 2015, no. 11 (2015): CD009885, https://doi.org/10.1002/14651858.CD009885.pub2.

6. B. Reynisson, G. Tanghöj, and E. Naumburg, "QTc Interval-Dependent Body Posture in Pediatrics," *BMC Pediatrics* 20 (2020): 107, https://doi.org/10.1186/s12887-020-1959-8.

7. O. J. Storebø, N. Pedersen, E. Ramstad, et al., "Methylphenidate for Attention Deficit Hyperactivity Disorder (ADHD) in Children and Adolescents—Assessment of Adverse Events in Non-Randomised Studies," *Cochrane Database of Systematic Reviews* 5, no. 5 (2018): CD012069, https://doi.org/10.1002/14651858.CD012069.pub2.

8. D. Ntiloudi, S. Rammos, M. Karakosta, A. Kalesi, N. Kasinos, and G. Giannakoulas, "Arrhythmias in Patients With Congenital Heart Disease: An Ongoing Morbidity," *Journal of Clinical Medicine* 12, no. 22 (2023): 7020, https://doi.org/10.3390/jcm12227020.

9. H. C. Fan, K. L. Chiang, K. H. Chang, C. M. Chen, and J. D. Tsai, "Epilepsy and Attention Deficit Hyperactivity Disorder: Connection, Chance, and Challenges," *International Journal of Molecular Sciences* 24, no. 6 (2023): 5270, https://doi.org/10.3390/ijms24065270.

10. J. Bernardi, K. A. Aromolaran, and A. S. Aromolaran, "Neurological Disorders and Risk of Arrhythmia," *International Journal of Molecular Sciences* 22, no. 1 (2020): 188, https://doi.org/10.3390/ijms22010188.

11. G. Zaccara and S. Lattanzi, "Comorbidity Between Epilepsy and Cardiac Arrhythmias: Implication for Treatment," *Epilepsy & Behavior* 97 (2019): 304–312, https://doi.org/10.1016/j.yebeh.2019.05.038.

12. Z. Gluvic, M. Obradovic, A. J. Stewart, et al., "Levothyroxine Treatment and the Risk of Cardiac Arrhythmias—Focus on the Patient Submitted to Thyroid Surgery," *Frontiers in Endocrinology (Lausanne)* 12 (2021): 758043, https://doi.org/10.3389/fendo.2021.758043.

13. C. Huerta, S. F. Lanes, and L. A. García Rodríguez, "Respiratory Medications and the Risk of Cardiac Arrhythmias," *Epidemiology* 16, no. 3 (2005): 360–366, https://doi.org/10.1097/01.ede.0000158743.90664.a7.

14. V. Berger, L. Bromee, A. Lindam, et al., "Adolescents on Psychotropic Treatment Displayed Longer Corrected QT Intervals Than Unmedicated Controls When They Rose Rapidly From the Supine Position," *Acta Paediatrica* 113, no. 7 (2024): 1621–1629, https://doi.org/10.1111/apa.17206.

15. J. F. Ludvigsson, E. Andersson, A. Ekbom, et al., "External Review and Validation of the Swedish National Inpatient Register," *BMC Public Health* 11, no. 1 (2011): 450, https://doi.org/10.1186/1471-2458-11-450.

16. B. Wettermark, N. Hammar, C. M. Fored, et al., "The New Swedish Prescribed Drug Register—Opportunities for Pharmacoepidemiological Research and Experience From the First Six Months," *Pharmacoepidemiology and Drug Safety* 16, no. 7 (2007): 726–735, https://doi.org/10.1002/pds.1294.

17. "Population Register (RTB), Statistics Sweden (SCB)," accessed July 1, 2024, https://rut.registerforskning.se/metadatakatalog/register/5c4db9f3-5f04-4fb6-8696-e8e034382dc0/.

18. "Swedish Ethical Review Authority (Etikprövnings myndigheten)," accessed May 12, 2022, https://etikprovningsmyndigheten.se/en/.

19. J. Ludvigsson, P. Olausson, B. Pettersson, and A. Ekbom, "The Swedish Personal Identity Number: Possibilities and Pitfalls in Healthcare and Medical Research," *European Journal of Epidemiology* 24 (2009): 659–667, https://doi.org/10.1007/s10654-009-9350-y.

20. A. G. Winterstein, T. Gerhard, P. Kubilis, et al., "Cardiovascular Safety of Central Nervous System Stimulants in Children and Adolescents: Population Based Cohort Study," *BMJ* 345 (2012): e4627, https://doi.org/10.1136/bmj.e4627.

21. J. Y. Shin, E. E. Roughead, B. J. Park, and N. L. Pratt, "Cardiovascular Safety of Methylphenidate Among Children and Young People With Attention-Deficit/Hyperactivity Disorder (ADHD): Nationwide Self Controlled Case Series Study," *BMJ* 353 (2016): i2550, https://doi.org/10.1136/bmj.i2550.

22. M. Garcia-Argibay, P. C. Bürkner, P. Lichtenstein, et al., "Methylphenidate and Short-Term Cardiovascular Risk," *JAMA Network Open* 7, no. 3 (2024): e241349, https://doi.org/10.1001/jamanetworkopen.2024.1349.

23. L. Li, Z. Chang, J. Sun, et al., "Attention-Deficit/Hyperactivity Disorder as a Risk Factor for Cardiovascular Diseases: A Nationwide Population-Based Cohort Study," *World Psychiatry* 21, no. 3 (2022): 452–459, https://doi.org/10.1002/wps.21020.

24. A. Sinha, O. Lewis, R. Kumar, S. L. Yeruva, and B. H. Curry, "Adult ADHD Medications and Their Cardiovascular Implications," *Case Reports in Cardiology* 2016 (2016): 2343691, https://doi.org/10.1155/2016/2343691.

25. H. Elmowafi, J. M. Kindblom, L. Halldner, D. Gyllenberg, and E. Naumburg, "Incidence and Trend of Cardiac Events Among Children and Young Adults Exposed to Psychopharmacological Treatment (2006–2018): A Nationwide Register-Based Study," *British Journal of Clinical Pharmacology* 91, no. 3 (2024): 817–828, https://doi.org/10.1111/bcp.16321.

26. L. A. Habel, W. O. Cooper, C. M. Sox, et al., "ADHD Medications and Risk of Serious Cardiovascular Events in Young and Middle-Aged Adults," *Journal of the American Medical Association* 306, no. 24 (2011): 2673–2683, https://doi.org/10.1001/jama.2011.1830.

27. H. Schelleman, W. B. Bilker, B. L. Strom, et al., "Cardiovascular Events and Death in Children Exposed and Unexposed to ADHD Agents," *Pediatrics* 127, no. 6 (2011): 1102–1110.

28. A. M. Moyer, E. T. Matey, and V. M. Miller, "Individualized Medicine: Sex, Hormones, Genetics, and Adverse Drug Reactions," *Pharmacology Research & Perspectives* 7, no. 6 (2019): e00541, https://doi.org/10.1002/prp2.541.

29. N. Sato and S. Miyake, "Cardiovascular Reactivity to Mental Stress: Relationship With Menstrual Cycle and Gender," *Journal of Physiological Anthropology and Applied Human Science* 23, no. 6 (2004): 215–223, https://doi.org/10.2114/jpa.23.215.

30. L. R. Olde Nordkamp, N. van Dijk, K. S. Ganzeboom, et al., "Syncope Prevalence in the ED Compared to General Practice and Population: A Strong Selection Process," *American Journal of Emergency Medicine* 27, no. 3 (2009): 271–279, https://doi.org/10.1016/j.ajem.2008.02.022.

31. P. M. Kasi, R. Mounzer, and G. H. Gleeson, "Cardiovascular Side Effects of Atomoxetine and Its Interactions With Inhibitors of the Cytochrome p450 System," *Case Reports in Medicine* 2011 (2011): 952584, https://doi.org/10.1155/2011/952584.

32. M. Romanescu, V. Buda, A. Lombrea, et al., "Sex-Related Differences in Pharmacological Response to CNS Drugs: A Narrative Review," *Journal of Personalized Medicine* 12, no. 6 (2022): 907, https://doi.org/10.3390/jpm12060907.

33. F. M. Kok, Y. Groen, A. B. M. Fuermaier, and O. Tucha, "The Female Side of Pharmacotherapy for ADHD-A Systematic Literature Review," *PLoS One* 15, no. 9 (2020): e0239257, https://doi.org/10.1371/journal.pone.0239257.

34. Z. Chang, P. D. Quinn, L. O'Reilly, et al., "Medication for Attention-Deficit/Hyperactivity Disorder and Risk for Suicide Attempts," *Biological Psychiatry* 88, no. 6 (2020): 452–458, https://doi.org/10.1016/j.biopsych.2019.12.003.

35. O. J. Storebø, M. R. O. Storm, J. Pereira Ribeiro, et al., "Methylphenidate for Children and Adolescents With Attention Deficit Hyperactivity Disorder (ADHD)," *Cochrane Database of Systematic Reviews* 3, no. 3 (2023): CD009885, https://doi.org/10.1002/14651858.CD009885.pub3.

36. T. E. Wilens, J. Biederman, M. Lerner, and Group CS, "Effects of Once-Daily Osmotic-Release Methylphenidate on Blood Pressure and Heart Rate in Children With Attention-Deficit/Hyperactivity Disorder: Results From a One-Year Follow-Up Study," *Journal of Clinical Psychopharmacology* 24, no. 1 (2004): 36–41.

37. S. Berger, "Attention Deficit Hyperactivity Disorder Medications in Children With Heart Disease," *Current Opinion in Pediatrics* 28, no. 5 (2016): 607–612, https://doi.org/10.1097/mop.0000000000000388.

38. P. Trairatvorakul, J. Meinzen-Derr, H. Heydarian, K. Mason, and J. S. Anixt, "Stimulant Medication Treatment in Children With Congenital Heart Disease and Attention-Deficit/Hyperactivity Disorder: Cardiovascular Outcomes," *Journal of Developmental and Behavioral Pediatrics* 44, no. 1 (2023): e247–e254, https://doi.org/10.1097/dbp.0000000000001187.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.