# Incidence of Cardiac Events among Children and Young Adults Exposed to Psychopharmacological Treatment (2006-2018) - A Nationwide Register-Based Study.

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What is already known?

* Findings regarding cardiac safety of psychopharmacological treatment are inconsistent in young people.
* Recently, both psychopharmacological treatment and cardiac event admissions have increased among those young population.

What this study adds?

* **The mean annual incidence of cardiac events in young patients exposed to psychopharmacological treatment in Sweden was** 0.98% in 2006–2018.
* **Female** teenagers and patients with polypharmacy had the highest incidence of cardiac events.
* The incidence of cardiac events increased significantly over time.

*Abstract*

Aim: To assess cardiac event incidence and trends by sex and age in young patients on psychopharmacological treatment in Sweden.

Methods: This nationwide incidence study encompassed data from Swedish registers (2006–2018). Patients aged 5–30 years were exposed to one or more psychotropic medications (attention deficit hyperactivity disorder medications, antihistamines, selective serotonin reuptake inhibitors, other antidepressants, anxiolytics, antipsychotics, hypnotics/sedatives). Annual incidences, trends, and mean incidences of cardiac events (cardiac arrest, arrhythmias, fainting/collapse, sudden death) and recurrent events were calculated.

Results: Among those exposed (n=875,430, 2,647,957 patient-years, 55% female), 26,750 cardiac events were identified. The mean annual incidence of cardiac events and first-ever events were 0.98% and 0.80%, respectively, showing significant upward annual trends of 4.26% and 2.48%, respectively (p<0.001). The highest incidences were among females aged 15–19 years (1.50%) and those exposed to polypharmacy (1.63%), anxiolytics (1.53%), or antihistamines (1.27%). The mean annual incidences of cardiac arrest and arrythmias, for both sexes, were 0.01% and 0.51%, respectively. Fainting/collapse accounted for about half of all events, occurring more often in females. The pattern of rising annual incidence remained after excluding fainting/collapse. In all, 21.1% of events were recurrent. Sudden death occurred in thirteen patients.

Conclusions: The mean annual incidence of cardiac events among young patients receiving psychopharmacological treatment was low, 0.98%, with an upward trend of 4.26% annually. Incidence was highest in females and patients exposed to polypharmacy. Our study highlights the need for more knowledge regarding the possible association between exposure to psychopharmacological treatment and cardiac events.

Introduction

Psychopharmacological treatments, including attention deficit hyperactivity disorder (ADHD) medications, selective serotonin reuptake inhibitors (SSRIs), anxiolytics, antipsychotics, and hypnotics, exhibit inconsistent findings regarding cardiac safety in young people 1-14. Sweden, like many other countries, has had rising prescription rates of these medications, and a shift to newer medications and polypharmacy in children, adolescents, and young adults in recent decades 15-19. Concurrently, there has been a growing trend of young patients admitted to hospitals with cardiac symptoms 20. This could indicate a knowledge gap regarding drug safety for young people exposed to modern psychopharmacological therapy.

Unlike in the adult population, arrhythmias and cardiac arrests are rare in young people, in the range 1-13/100,000. Some psychotropic medications may contribute to torsade’s de pointes, which can lead to lethal arrythmia 21-26. Syncope, which occurs more often in females than in males, may be caused by a physiological reaction or a serious cardiac event 21-23,27-29. The trend in arrhythmia incidence shows a clear rise in both sexes in recent years, with males demonstrating higher rates 30. Females face a higher risk of drug-induced adverse events, particularly with concurrent use of multiple psychotropic medications 31-34**.** Age-related pharmacokinetic and pharmacodynamic changes have been described but have not been found to raise cardiac risks related to psychopharmacological treatments 2,32,35.

Despite the abundance of research on psychopharmacological treatments in the young 36, it remains unclear if and to what extent this exposed population has experienced an upward trend in cardiac events. In addition, there is insufficient evidence on differences by sex, age, medication, and type of cardiac events 2,37. To address these knowledge gaps and provide valuable insights for clinical and public health disciplines, we conducted a register-based study in Sweden from 2006 to 2018. The study aimed to investigate cardiac event incidence and trends among 5–30-year-olds exposed to psychopharmacological treatment by sex, age, medication type, medication number, and event type.

Methods

*Data Source*

This nationwide register-based study retrieved data from Swedish national registers. Information on the exposure (psychotropic medications) was retrieved from the Swedish Prescribed Drug Register (SPDR), which includes information on type of prescribed drug based on the Anatomical Therapeutic Chemical classification, as well as age, sex, and number of prescriptions for each patient 38. Information on cardiac events was retrieved from the National Patient Register (NPR). Both the SPDR and the NPR have good national coverage 38-40. Information on deaths was retrieved from the Swedish Cause of Death Register (CDR) 41.

The National Board of Health and Welfare linked the SPDR, NPR, and CDR using the unique 12-digit personal identity number assigned to each Swedish inhabitant 39,41. Registrations of health care admittances, diseases, prescriptions, and death are supported in law (1988: 543). This study was approved by The Swedish Ethical Review Board (D nr 2019-04467 and D nr 2020-05889) 42.

*Study Design*

This incidence study included all individuals aged 5–30 years who were dispensed psychotropic medications in Sweden in 2006–2018. Each exposed patient was included from the first day of a recorded drug prescription each year.

*Exposure*

Sex, age, type of psychotropic medication, and number of medications were recorded for each exposed patient each calendar year. Age at inclusion was calculated by subtracting the birthyear of the participant from the year of the drug exposure for each calendar year studied and was stratified into five age groups: 5–9, 10–14, 15–19, 20–24, and 25–30 years. Psychotropic medications were stratified into seven groups based on the following Anatomical Therapeutic Chemical codes: ADHD drugs (N06BA & C02A), antihistamines (R06A) for systemic use, SSRIs (N06AB), other types of antidepressants (N06AA & others, see eTable1), anxiolytics/benzodiazepines (N05BA), antipsychotics (N05A), and hypnotics and/or sedatives (N05BB, N05BE & N05C). Exposure to three or more medications during the same calendar year was defined as polypharmacy. Further information is presented in the supplementary appendix (eTable1).

*Outcomes*

Information on cardiac events were captured in the NPR based on the International Statistical Classification of Diseases and Related Health Problems, 10th version (ICD-10). Only cardiac events that occurred after the exposure and within the same calendar year were included. On an annual basis, each cardiac event, except sudden death, was treated as a new event. Each patient’s earliest event in the study was considered a first-ever cardiac event, whereas recurrent events refer to instances where a patient experienced more than one event during the study period. Information on death was separately retrieved from the CDR. Cardiac events were stratified into seven categories based on ICD-10 codes: sudden death (sudden unexpected death, R96.0, and sudden cardiac death, I46.1) , cardiac arrest (unspecified with successful resuscitation, I46.9), atrial arrhythmia (I49.5, I49.5A, I49.5C), supraventricular tachycardia (I47.1), ventricular tachycardia (I47.0, I47.2, I47.2C, I47.2, I49.0, I49.1, I49.3), other rare and undefined arrythmias (I49.8, I49.8C, I49.9, R00.00), and fainting and/or collapse (R55.9). Further information on ICD-10 codes is described in the supplementary appendix (eTable1).

*Statistical analysis*

Each patient was included at most once per calendar year. Stratifications were made by sex, age group, and type of medication. Number of cardiac events, except for sudden death, was assessed among those exposed and stratified by type of event, sex, and age group. The overall annual incidence of cardiac events was calculated. Mean annual incidence by sex and age group were assessed and stratified. The mean incidence for each type of cardiac event was assessed by sex, age group, and type of medication. A second analysis was performed by excluding fainting and/or collapse (R55.9). The annual and mean incidence of first-ever cardiac event were estimated, as well as the number of recurrent evets (subsequent events). Sudden death was stratified by type and number of medications, sex, and age group. Linear regression was used to assess the significance of possible changes in linear secular trends (ln (incidence)~year). The analysis was performed using the analytical software Stata version 18 (College Station, TX: Stata Press).

Results

During the study period, 2006–2018, a total of 875,430 unique individuals (2,647,957 patient-years, 45% male, 55% female) received psychopharmacological treatment, of whom 66% were aged 20 years or older. An upward annual trend of 9.8% (p < 0.05; Figure 1) could be seen. Male were more often exposed to ADHD medications, whereas females were more often exposed to antidepressants and polypharmacy (Table1).

In total, 26,750 cardiac events (excluding sudden death) were identified in those exposed. Most events occurred in females (64%), in the age group 15–30 years. The most common events were fainting and/or collapse (50% of all events) and undefined arrhythmias (42% of all events). The number of unique patients experiencing recurrent events was 2409 (0.28% of the exposed), representing 5655 events (21.1% of all events) (eFigures 1 and 2).

1. *Incidence and trend of cardiac events (all, first-ever, excluding fainting and/or collapse)*

The total mean annual incidence for cardiac events was 0.98% and that for first-ever events was 0.80%, with significant upward annual trends of 4.26% and 2.48%, respectively (p < 0.001; Figure 2). The cardiac event incidence was highest in females (1.17%), particularly those aged 15–19 years (1.50%) (Table 2, Figure 2). The incidence of recurrent events was 0.21%.

The mean incidence of cardiac events, excluding fainting and/or collapse, was 0.51%, rising with an annual percentage change of 4.52% (p < 0.001). The mean incidence was 0.53% for females and 0.49% for males. Peaks were seen at age 20–24 years for both sexes, and males showed a slightly higher incidence than females in this age group. The incidence of fainting and/or collapse had an annual percentage increase of 3.89% (p < 0.001). The occurrence rate among females (0.64%) was double that among males (0.32%) (Figure 3, Table 2, eTable 2).

1. *Incidence by type of psychopharmacological treatment*

The incidence of cardiac events was higher among those exposed to anxiolytics (1.53%), antihistamines (1.27%), or hypnotics and/or sedatives (1.17%) (Table 2). Patients exposed to polypharmacy had a higher mean annual incidence (1.63%) than those not exposed to polypharmacy (0.90%) (p < 0.05; Figure 2). The incidence of cardiac events was higher in females aged 15 years and older than in males or other age groups. Arrhythmias were more prevalent with polypharmacy than other cardiac events, in both sexes, particularly in individuals aged 15 years or older (eTable 3).

1. *Incidence by type of cardiac event (Table2 and eTable3)*

Cardiac arrest: The mean annual incidence of cardiac arrest was 0.01%, and higher in males exposed to anxiolytics (0.1%) or antipsychotics (0.04%) compared with other types of medications, or with females.

Atrial arrhythmias: The mean annual incidence of atrial arrhythmias was 0.001%, and higher in males aged 15 years or older exposed to anxiolytics (0.02%).

Supraventricular tachycardia (SVT): The mean annual SVT incidence was 0.04%, higher in males aged 5–9 years using SSRIs (0.12%), aged 15–19 years using antihistamines (0.08%), or aged over 19 years using anxiolytics (0.07%). Females aged 20–24 years using anxiolytics or ADHD medications had higher incidence than was seen for other medications or age groups.

Ventricular tachycardia (VT): The overall mean annual incidence was 0.03%. This incidence was higher in males aged 10–14 years exposed to other antidepressants (0.13%), and in females exposed to anxiolytics or antihistamines in the oldest age groups, at 0.08% and 0.05%, respectively.

Rare and undefined arrhythmias: The mean annual incidence was 0.43%. Females on ADHD medications displayed an average incidence of 0.50%.

Fainting and/or collapse: The mean annual incidence was 0.49%, and highest in females aged 15–19 years on anxiolytics (1.72%).

Sudden death: Thirteen cases of sudden death occurred during the study period, mainly in males aged over 19 years and exposed to hypnotics and/or sedatives, anxiolytics, SSRIs, or antipsychotics, corresponding to an incidence of 0.0005%.

Discussion

In this nationwide register-based incidence study, more than 800,000 young patients and over 2.6 million person-years were exposed to psychopharmacological treatment in 2006–2018. Among these patients, more than 26,000 cardiac events and thirteen sudden cardiac deaths occurred. The overall mean annual incidence of all cardiac events was 0.98%, and first-ever events was 0.80%, with a significant upward trend over the study period. We found that a fifth of recurrent events could be attributed to a small subset of exposed patients. The rising trend remained also after exclusion of fainting and/or collapse events. The rising trend of young patients admitted to hospitals for cardiac events coincided with an increase in the use of psychotropic medications in this group.

*1.Sex and age*

Like other researchers 43, we found that females had a higher mean incidence of cardiac events than males, also after exclusion of fainting and/or collapse (Table 2, eTable 2). Sex may have an impact on pharmacokinetics and pharmacodynamics, which may, in turn, have an impact on adverse outcomes 44. . Further, fainting and/or collapse occurred twice as often in females (0.64%) as in males (0.32%) (Table 2), a finding that aligns with those of another study 28. The highest incidence of cardiac events was found in female teenagers (1.50%) (Figure 2). This could be explained by higher help-seeking behavior among young females compared with young males or by the sex-based difference in pharmacokinetics, parasympathetic activity, and hormonal changes during puberty 45-47. Upon exclusion of fainting and/or collapse, the peak of incidence shifted from age 15–19 years to age 20–24 years for both sexes, with males showing slightly higher rates than females in the latter age group (Figure 3). This underscores the importance of carefully assessing fainting and/or collapse in patients on psychopharmacological treatment.

*2. Type of psychopharmacological treatment*

*2.1 Psychopharmacological monotherapy*

In our study, individuals exposed to anxiolytics had a higher mean incidence of cardiac events (1.53%) compared with individuals on hypnotics and/or sedatives (1.17%) or other psychotropic medications (Table 2). This is consistent with another study, where anxiolytics showed a higher risk of cardiac events than hypnotics 4. Patients on ADHD medications had the lowest incidence of cardiac events (0.73%) (Table 2), even lower than in other studies 34,48. This might be related to growing awareness of the cardiac risks with ADHD medications, and good compliance with guidelines on assessing and monitoring cardiac risks in the context of these medications.

*2.2 Psychopharmacological polypharmacy*

Patients exposed to polypharmacy had a higher mean incidence, at 1.63%, compared with patients on fewer medications (0.90%), a result which aligns with other findings 34. Polypharmacy may induce pharmacodynamic and/or pharmacokinetic interactions and can extend half-life, which may further increase cardiac risks 31,34,49-51. We found that incidence was higher in females aged 15 years or older with polypharmacy (Figure 2d, eTable 3). Female sex and polypharmacy may increase the risk of drug-induced adverse events, possibly due to immunological, hormonal, or dosage factors 32,44.

*3. Types of cardiac event*

*3.1 Cardiac arrest*

The incidence of cardiac arrest is low in pediatric patients 26 , which was seen in our study of young patients exposed to psychotropic medications. Males had a higher incidence of cardiac arrest than females, especially if exposed to antipsychotics or anxiolytics (eTable 3). This is in line with other studies reporting that ventricular arrhythmias are linked to antipsychotic medications 13, and that anxiolytics (diazepam) can cause cardiovascular collapse 52. Thus, we recommend careful individual risk evaluation of young male patients before exposure to psychotropic medications.

*3.2 Arrhythmias*

In our study, the incidence of arrhythmias was higher than the reported incidence of childhood arrhythmias 21-23 , and nearly the same in both sexes (Table 2, eTable 3). This is not in line with other authors’ findings of drug-induced life-threatening arrhythmias specifically in females 44. The incidence rates of SVT and VT at ages 15 years and older in both sexes, as well as in male patients exposed to SSRIs and other antidepressants, align with the findings of others 11,12,14,53. This may relate to drug-induced inhibition of Na+, Ca2+, and K+ channels 54, which may affect pathways in the cardiac conduction system. Further, our study found a notable incidence of arrhythmias in individuals exposed to antihistamines, which are pharmacologically similar to tricyclic antidepressants and are known to cause arrhythmias in children 55,56. Females exposed to ADHD medications showed a higher incidence of rare and undefined arrhythmias than males, in line with findings of other studies 33. Taken together, the findings suggest that age and sex are important factors to considered when assessing the cardiac safety of psychopharmacological treatments.

*3.3 Fainting and/or collapse*

The incidence of fainting and/or collapse was 0.49% in our study (Table 2), with the highest incidence in females on anxiolytics (1.72 %) (eTable 3). This was higher than the reported incidence of syncope in young people 27. Syncope is common in this age group and can be a natural physiological response 29. However, fainting can also be a sign of a medically induced cardiac event 52,57 . Harmful fainting must be distinguished from benign events in all patients, especially those on psychopharmacological treatment. We argue for careful assessment and awareness of the potential for pharmacologically induced fainting.

*3.4 Sudden death*

The incidence of sudden death was low (5/1,000,000) – lower than the reported incidence of sudden death in the general population in the same age groups 24,25. Some psychotropic medications, such as hypnotics 3,4, antipsychotics, and SSRIs 5,6, have been considered to protect against death in young adults, as well as against suicide at all ages. However, these medications, as well as anxiolytics, have been reported to increase the risk of sudden death in children, adolescents, and young adults **10-14**. Patients who died suddenly in our study were exposed to hypnotics and/or sedatives, anxiolytics, antipsychotics, and /or SSRIs. The well-known risk of death and sudden death linked to any underlying psychiatric disease must sometimes carry more weight in the decision-making process concerning treatment risks.

*Strengths and limitations*

The prospectively retrieved data and the well-documented national coverage and validation of data in the Swedish national registers, along with the large number of included exposed patients, strengthen the study. This is an incidence study, which of course lacks a control group, making it impossible to compare with an unexposed population. This is a limitation of the study. Further, the method of analysis, with an annual cycle, may have led to loss of events where a patient was prescribed medication late in one year if they occurred the subsequent year. Patient adherence to the prescribed medications was unknown, as this is not recorded in the registers. The study did not cover all psychotropic or non-psychotropic medications, such as non-legal substances. Nor did it cover non-cardiac adverse events, or other medications and diseases. Further, the NPR does not contain diagnoses from non-specialized outpatient care, and thus there is a risk of underestimating the incidence rates of cardiac events. Studies in real-world settings assessing the association between psychotropic medications and cardiac events are needed to identify confounding factors.

*Conclusions*

This nationwide register-based study found that young patients on psychopharmacological treatment had a 0.98% mean annual incidence of cardiac events, which increased over the period 2006–2018. Exclusion of fainting and collapse events did not alter the rising trend. Incidence were highest among those aged 15–19 years, those exposed to anxiolytics, antihistamines, or polypharmacy. A small group of patients contributed a fifth of all cardiac events. Our findings suggest the need for more studies to assess the possible association between exposure to psychotropic medications and cardiac events.

Authors contributions: Howaida Elmowafi: Study design, statistical analysis, data interpretation and drafting of the manuscript. Estelle Naumburg: Protocol development and analytical framework, study design and in-depth reviewing of the manuscript. Linda Halldner, David Gyllenbergand Jenny M Kindblom: Critical reviewing of the study design and the manuscript.

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# Data availability statement: The data that support the findings of this study are available from Socialstyrelsen (the Swedish National Board of Health and Welfare; [https://bestalladata.socialstyrelsen.se/](https://eur01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fbestalladata.socialstyrelsen.se%2F&data=05%7C02%7Chowaida.elmowafi%40umu.se%7C6d6f40afc3c94a9f0e8d08dc733356b9%7C5a4ba6f9f5314f329467398f19e69de4%7C0%7C0%7C638511911529270849%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C0%7C%7C%7C&sdata=PBfOX%2FoeG%2F1VyBrxQzkVWsYurdmY%2F0EYBhiw1U0rEbI%3D&reserved=0) (Swedish)), but restrictions apply to their availability. The data were used under license for the current study and are not publicly available.

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**Table 1. Characteristics of Patients Aged 5–30 Years Exposed to Psychopharmacological Treatment During 2006–2018, in Patient-Years.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **2006–2018** | **Male**  **n = 1,191,717**  **n (%)** | **Female**  **n = 1,456,240**  **n (%)** | **Total**  **N = 2,647,957**  **n** | **Patient-Years Contributed by Each Age and Medication Category,**  **%** |
| Age groups | | | | |
| 5–9 y a | 71,143 (67.25) | 346,48 (32.75) | 105,791 | 4.00% |
| 10–14 y | 180, 851(67.86) | 85,649 (32.14) | 266,500 | 10.06% |
| 15–19 y | 240, 999 (46.70) | 275, 040 (53.30) | 516, 039 | 19.49% |
| 20–24 y | 277, 627 (40.17) | 413, 578 (59.83) | 691, 205 | 26.10% |
| 25–30 y | 421, 097 (39.41) | 647, 325 (60.59) | 1, 068, 422 | 40.35% |
| Type of psychotropic medication | | | | |
| ADHD medications a | 323, 729 (69.26) | 143, 665 (30.74) | 467, 394 | 17.65% |
| Antihistamines | 54, 845 (26.68) | 150, 718 (73.32) | 205, 563 | 7.76% |
| SSRIs a | 251, 794 (34.54) | 477, 101 (65.46) | 728, 895 | 27.53 % |
| Other anti-depressants | 102, 069 (42.57) | 137, 721(57.43) | 239, 790 | 9.06% |
| Anxiolytics | 63, 254, (44.79) | 77 975 (55.21) | 141, 229 | 5.33% |
| Antipsychotics | 66, 478 (58.71) | 46 761 (41.29) | 113, 239 | 4.28% |
| Hypnotics and/or sedatives | 329, 548 (43.83) | 422 299 (56.17) | 751, 847 | 28.39% |
| Polypharmacy b | | | | |
| No (<three medications) | 1, 019, 419 (85.54) | 1, 212, 916 (83.29) | 2, 232,335 | 84.30% |
| Yes (three or more medications) | 172, 298 (14.46) | 243, 324 (16.71) | 415, 622 | 15.70% |
| a Abbreviations: y: years, ADHD: attention deficit hyperactivity disorder, SSRIs: selective serotonin reuptake inhibitors.  b Polypharmacy = three or more psychotropic medications.  Note: Number of unique individuals = 875,430 during the study period 2006–2018, totaling 2,647,957 patient-years.  Further information on coding presented in eTable 1 | | | | |

**Table 2. Incidence of Cardiac Events Among Those Exposed** a **by Cardiac Event and Medication Type.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **2006­-2018** | **Male**  **Cardiac events**  **n= 9 641**  **n (%)** | | **Female**  **Cardiac events**  **n=17,109**  **n (%)** | | **Total**  **Cardiac events**  **n=26,750**  **n (%)** | |
| Type of psychotropic medication |  |  | |  | |
| ADHD medications  b | 1789 (0.55) | | 1612 (1.12) | | 3401 (0.73) | |
| Antihistamines | 633(1.15) | | 1977 (1.31) | | 2610 (1.27) | |
| SSRIs  b | 1762 (0.70) | | 4373 (0.92) | | 6135 (0.84) | |
| Other anti-depressant | 875 (0.86) | | 1588 (1.15) | | 2463 (1.03) | |
| Anxiolytics | 833 (1.32) | | 1321 (1.69) | | 2154 (1.53) | |
| Antipsychotics | 501 (0.75) | | 669 (1.43) | | 1170 (1.03) | |
| Hypnotics and/ or sedatives | 3248 (0.99) | | 5569 (1.32) | | 8817 (1.17) | |
| Type of cardiac event |  | |  | |  | |
| Cardiac arrest | 197 (0.02) | | 102 (0.01) | | 299 (0.01) | |
| Atrial arrhythmia | 37(0.002) | | 35 (0.001) | | 72 (0.001) | |
| SVT b | 391 (0.03) | | 679 (0.05) | | 1070 (0.04) | |
| VT  b | 295 (0.02) | | 433 (0.03) | | 728 (0.03) | |
| Undefined arrhythmia | 4871 (0.41) | | 6 479 (0.44) | | 11,350 (0.43) | |
| Fainting and/ or collapse | 3850 (0.32) | | 9381 (0.64) | | 13,231 (0.49) | |
| Mean overall incidence | 0.81% | | 1.17% | | 0.98% | |
| a Exposed are patients aged 5–30 years who received psychopharmacological treatment between 2006–2018 based on data in Swedish prescribed drug registers.  b Abbreviations:  N: number, Cardiac arrest: successfully resuscitated cardiac arrest, SVT: supraventricular tachycardia, VT: ventricular tachycardia, ADHD: attention deficit & hyperactivity disorder, SSRIs: selective serotonin reuptake inhibitors.  For detailed information on ICD codes and types of medication, please see supplementary table eTable 1. | | | | | | |

**Figure legends.**

**Figure 1.** Number of children, adolescents, and young adults aged 5–30 years on psychopharmacological treatment.

**Figure 2.** Incidence of cardiac events among those aged 5–30 years exposed to psychopharmacological treatment (2006–2018).

**A** Overall annual incidence.

**B** Annual incidence by sex.

**C** Mean overall incidence by sex and age.

D Mean overall incidence by polypharmacy and sex.

**Figure 3.** Incidence of cardiac events, excluding fainting and/or collapse among those exposed to psychopharmacological treatment (2006–2018).

**A** Annual incidence by sex.

**B** Mean overall incidence by sex and age.

**C** Annual incidence versus incidence of fainting and/or collapse.

**Appendices.**

1. **Supplementary eFigures**

* eFigure1. Number of cardiac events among patients exposed to psychopharmacological treatment in 2006–2018.
* eFigure2. Proportion of cardiac event types among patients exposed to psychopharmacological treatment (2006–2018).

1. **Supplementary eTables.**

* eTable1. ICD and ATC Codes.
* eTable2. Incidence of arrythmias (cardiac events excluding fainting and/or Collapse)
* eTable3. Incidence of different types of cardiac events for each psychotropic medication during 2006-2018