

Post-Mortem Findings of ADHD Medications in Finland: Trends, Substance Use and Mortality Patterns in Medico- Legal Deaths, 2016–2024

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Research Article

Keywords:

Posted Date: October 11th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11084256/v1>

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Additional Declarations: No competing interests reported.

Abstract

Attention deficit hyperactivity disorder (ADHD) is associated with increased premature mortality, particularly from unnatural causes. As the use of stimulant medications has increased globally, more information is needed regarding their occurrence in medico-legally investigated deaths and their relationship with substance use and mortality. This retrospective observational study examined all medico-legal post-mortem (PM) cases in Finland between 2016 and 2024 in which methylphenidate or amphetamine was detected during forensic toxicological investigations.

A total of 271 methylphenidate-positive and 1,829 amphetamine-positive cases were identified. The annual number of methylphenidate-positive cases increased throughout the study period, paralleling increasing prescription rates, whereas fatal methylphenidate poisonings remained uncommon (2.6% of all cases positive for methylphenidate). Amphetamine-positive cases and fatal amphetamine poisonings increased until 2020 and subsequently stabilized; fatal amphetamine poisonings accounted for 19% of amphetamine-positive cases. Evidence of non-alcohol substance use was common, occurring in 76% of methylphenidate-positive cases and 97% of amphetamine-positive cases with documented ADHD medication use or diagnosis. Alcohol was detected in approximately one quarter of cases across all groups. Accidental deaths predominated, accounting for 46% of methylphenidate-positive and 49% of amphetamine-positive cases, while suicides accounted for 24% and 19% of deaths, respectively.

These findings indicate that PM detections of ADHD medications are strongly associated with substance-use comorbidity and premature unnatural mortality. Although methylphenidate findings increased substantially over time, fatal methylphenidate poisonings remained rare. The deceased individuals represented a particularly high-risk subgroup, highlighting the importance of substance-use and suicide prevention efforts among people with ADHD.

Introduction

Attention deficit hyperactivity disorder (ADHD) is a neuropsychiatric disorder that has been linked to substantially increased mortality, especially of non-natural causes and at a relatively young age [1–4]. The symptoms of ADHD include impulsivity, inattention and restlessness, which may lead to accident proneness and high-risk behaviours such as substance use [5–8], which may mediate this risk. Furthermore, ADHD is a risk factor for many psychiatric comorbidities in which suicide rates are significantly increased, such as major depressive disorder, bipolar disorder, and personality disorders [9–12]. Indeed, ADHD has repeatedly been found to be associated with increased risk of suicide, suicidal behaviour and intentional poisoning in both retro- and prospective settings [13–17]. ADHD patients are thus an important population in terms of potentially preventable early mortality.

Stimulant medications, such as methylphenidate and lisdexamphetamine, are the mainstay of pharmacological treatment of ADHD [5, 18]. The goal of such treatment is to alleviate symptoms, and thus potentially lessen the risk of unwanted outcomes including, indirectly, death. Among ADHD patients, receiving pharmacotherapy for ADHD has been found to correlate with lower risks of death, non-natural

death, accidents and need for medical treatment [19–21]. There is also some evidence that receiving pharmacotherapy for ADHD in childhood may alleviate risk of later substance use disorder (SUD) [22–24]. However, stimulant medications themselves have addictive and abuse potential, and can also induce psychotic states [25, 26], potentially mitigating or reversing their possible beneficial effects on mortality at least in some cases. How often stimulant medications might contribute to unnatural death in such indirect ways is still largely unknown. With regard to illicit drug use, amphetamine has long been the most prevalent stimulant drug in Finland, exceeding both cocaine and methamphetamine, and it is also the stimulant associated with the highest number of drug-induced deaths. [27].

Stimulants, including medically used ones, such as methylphenidate and lisdexamphetamine, have profound effects on e.g., the central nervous and circulatory systems, and overdoses are potentially lethal [28]. The literature contains case reports on fatal methylphenidate poisonings, without involvement of other substances [29–32]. Most of these cases involved intravenous or intranasal, non-medical, use. However, in a study on nonlethal prescription stimulant overdoses from Hong Kong, 60% of individuals had an ADHD diagnosis, and 70% did not involve other substances than prescription stimulants [33]. Studies examining ADHD medication findings in forensic toxicology have to this date been few. A 2025 Australian research letter by Darke and colleagues reported on all deaths over 25 years in which prescription stimulants were implicated ($n = 64$) [34]. Of these, the majority involved multiple substances, and 20% were judged to be intentional. More studies are clearly needed of characteristics of deaths in which ADHD medications are found, and of the role of these medications also when not directly contributing to mortality.

Over the last decades, there has been a global increase in ADHD diagnosis and stimulant treatment, especially in adults [35, 36]. The genetic component of ADHD proneness, as represented by the polygenic risk score, is lower among more recently diagnosed individuals, which could indicate that less severe presentations than earlier receive a diagnosis and stimulant pharmacotherapy [37]. This could theoretically lead to less benefit and thus a relatively larger burden of adverse outcomes from medication use. Fitting into this pattern, the association between ADHD pharmacotherapy and real-world benefits were found to decrease in Sweden between 2000 and 2016 [38], while the rate of reported paediatric ADHD medication poisonings in the U.S. increased by ca. 60% from 2000 to 2014 [39]. In the U.S., there has been a large increase in stimulant-related mortality 2010–2017, and although medical stimulants represented a small minority of cases, this trend affected them as well [40]. Studies of how often ADHD medications are found in forensic toxicology or determined to be contributing to mortality would shed further light on this matter and inform patients and prescribers in making treatment choices.

For these reasons, in this retrospective observational study, we examined all cases in which ADHD medications, specifically methylphenidate or dexamphetamine (either prescribed directly or detected as a metabolite of lisdexamfetamine), were identified in toxicological analyses conducted as part of medico-legal death investigations in Finland between 2016 and 2024. Our specific aims were to investigate, in this population:

1. Trends in the frequency of such findings over time
2. The frequency of substance use preceding death
3. The manner of death and frequency of fatal poisonings
4. The way in which ADHD and use of ADHD medications was documented in the toxicology laboratory referral and the death certificate.

Material and methods

In Finland, a medico-legal investigation is initiated by the police whenever a death is sudden or unexpected. More specifically, such investigation is required when the death is not known to have resulted from disease, when the deceased was not under a physician's care during their final illness, when the death was caused by accident, suicide, homicide, poisoning, occupational disease, or medical treatment, or when there is reason to suspect any of these circumstances. A medico-legal autopsy is performed in most such cases, and comprehensive forensic toxicological analyses are routinely conducted on samples collected at autopsy.

Forensic toxicological screening was performed in urine, vitreous humour or blood using ultra-high-performance liquid chromatography coupled with high-resolution quadrupole time-of-flight mass spectrometry (UHPLC-QTOF-MS). The analytical procedure used in post-mortem (PM) cases has been described in detail elsewhere [41]. All amphetamine findings were quantitatively confirmed in blood and urine by gas chromatography-mass spectrometry (GC-MS) [42]. Methylphenidate was quantified using an ultra-high-performance liquid chromatography method equipped with two consecutive detectors, a photodiode array detector and a corona-charged aerosol detector (UHPLC-DAD-CAD), as part of an extensive toxicological screening panel [43]. The lower limits of quantification were 0.04 mg/L for amphetamine and 0.1 mg/L for methylphenidate.

Whenever amphetamine was identified during TOF screening, quantitative analysis was performed in femoral blood and urine or, when necessary, in other available PM specimens, as described previously [42]. Briefly, samples were prepared using a single-step alkaline liquid-liquid extraction with toluene as the extraction solvent and derivatised with heptafluorobutyric anhydride. Instrumental analysis was performed using an Agilent 6890N gas chromatograph coupled to a 5975C mass spectrometer operating in electron ionisation (EI) mode (Agilent Technologies, Santa Clara, CA, USA). Chromatographic separation was achieved using an Agilent DB-5MS fused-silica capillary column (12.5 m × 0.20 mm i.d., 0.33 µm film thickness; Agilent Technologies) under a rapid temperature-ramp programme.

Chiral analysis of amphetamine enantiomers was performed upon request by the forensic pathologist or when amphetamine was detected in the TOF screening, ADHD diagnosis or medication was documented in the laboratory referral, and sufficient sample material was available. In cases with lisdexamphetamine medication, the substance detected in the analysis is its metabolite dexamphetamine. In the chiral analysis, sample preparation and instrumental analysis were identical to those used for routine

amphetamine quantification, except that derivatisation was performed using the chiral reagent (R)-(-)- α -methoxy- α -(trifluoromethyl)phenylacetyl chloride (Supelco, Bellefonte, PA, USA).

For the present study, all PM cases positive for methylphenidate and/or amphetamine were retrieved from the Forensic Toxicology Database maintained by the Finnish Institute for Health and Welfare. In addition to analytical findings, the database contains information extracted from death certificates, including the cause and manner of death and a brief description of the circumstances surrounding death.

The study was conducted under research permit THL/4310/6.02.00/2025 granted by the Finnish Institute for Health and Welfare.

Results

Findings of ADHD medications in PM toxicology

Between 2016 and 2024, methylphenidate was quantitatively detected in femoral blood in 271 PM cases. The annual number of methylphenidate-positive cases increased during the study period; however, no corresponding trend was observed in the number of fatal methylphenidate poisonings (Fig. 1).

The mean (range) age of methylphenidate-positive individuals was 34.3 (18–55) years, and 82% were male.

During the study period, 1,829 PM cases were positive for amphetamine. Chiral analysis of amphetamine enantiomers was performed in 16 cases. Dexamphetamine without detectable levoamphetamine was identified in 10 cases, whereas both enantiomers were detected in six cases.

The annual numbers of both amphetamine-positive cases and fatal amphetamine poisonings increased until 2020, after which they appeared to stabilise. Dexamphetamine was first identified in a PM case in 2020 (Fig. 1).

The mean (range) age was 34.6 (15–90) years among all amphetamine-positive cases and 35.6 (21–53) years among cases that underwent chiral analysis. Males accounted for 83% and 82% of these groups, respectively.

Methylphenidate and dexamphetamine were detected concurrently in three cases.

Documentation of ADHD diagnosis and medication

Information regarding prescribed medication was not available for all cases at the time of autopsy.

Among methylphenidate-positive cases, ADHD medication and/or an ADHD diagnosis was documented in the laboratory referral or in the death certificate in 99 cases (37%). The corresponding figure was 105

cases (5.7%) among all amphetamine-positive cases and 100% among cases subjected to chiral amphetamine analysis. The number increased for both methylphenidate and amphetamine over the study period (Fig. 1).

Methylphenidate was recorded as the underlying cause of death in seven cases. In two of these cases, methylphenidate was the sole substance implicated, whereas in the remaining cases it was listed together with other drugs. In addition, methylphenidate toxicity was recorded as a contributory cause of death in a further seven cases.

Among cases in which ADHD medication or diagnosis was documented, amphetamine was implicated in the underlying cause of death in 27 cases (26%). In all but two cases, additional drugs were implicated alongside amphetamine. Amphetamine toxicity was recorded as a contributory cause of death in a further 26 cases.

Non-alcohol substance use among ADHD cases

Evidence of substance use other than alcohol was identified in 207 methylphenidate-positive cases (76%). Benzodiazepines were detected in 67% of cases, amphetamine in 47%, buprenorphine in 42%, and cannabis in 32%. Antidepressants or antipsychotics were detected in 37% and 30% of cases, respectively.

Of the cases positive for methylphenidate, drug use paraphernalia were analysed in addition to biological specimens in 21 cases and methylphenidate was detected in three of them. Of the cases positive for amphetamine, the number of analysed paraphernalia was 119 and of them amphetamine was detected in 23. For cases in which ADHD medication and/or diagnosis was recorded the numbers were 10 and 3, respectively.

Of the cases in which the chiral separation of amphetamine enantiomers was performed, substance use was identified in 15 (94%). Of the amphetamine-positive cases in which ADHD medication or diagnosis was documented, 102 (97%) showed evidence of substance use. Benzodiazepines were detected in 86% of the amphetamine-positive cases, buprenorphine in 44%, and cannabis in 46%. Antidepressants or antipsychotics were detected in 32% and 23% of cases, respectively.

Of the three cases in which both methylphenidate and dexamphetamine were detected, evidence of substance use was present in two.

Alcohol use

Alcohol was detected in 78 methylphenidate-positive cases (29%), with a mean (range) blood alcohol concentration (BAC) of 1.1 (0.2–2.5) ‰. Alcohol contributed to fatal poisoning, in combination with other substances, in 19 cases (7.0%). An alcohol-related disease was identified as the underlying cause of

death in five additional cases (1.9%), while chronic excessive alcohol use or alcohol intoxication was recorded as a contributory cause of death in 50 cases (18%).

Among amphetamine-positive cases, alcohol was detected in 464 cases (25%), with a mean (range) BAC of 1.2 (0.2–4.3) ‰. Alcohol, either alone or in combination with other substances, contributed to fatal poisoning in 141 cases (7.7%). An alcohol-related disease was recorded as the underlying cause of death in 39 additional cases (2.1%), and chronic excessive alcohol use or alcohol intoxication was listed as a contributory cause of death in 250 cases (14%).

In amphetamine-positive cases with documented dexamphetamine medication or an ADHD diagnosis, alcohol was detected in 18 cases (17%). The mean (range) BAC in these cases was 1.0 (0.21–2.5) ‰. Alcohol contributed to fatal poisoning, together with other substances, in seven cases (6.7%). No deaths were attributed to an alcohol-related disease as the underlying cause, whereas chronic excessive alcohol use or alcohol intoxication was recorded as a contributory cause of death in six cases (5.7%).

Among cases for which chiral separation of amphetamine enantiomers had been performed (N = 16), alcohol was detected in four cases (25%), with a mean (range) BAC of 1.8 (1.3–2.5) ‰. Alcohol was identified as one of the intoxicants in a fatal poisoning in one case (6.3%). Chronic excessive alcohol use or alcohol intoxication was recorded as a contributory cause of death in two cases (13%).

Cause and manner of death

Of all cases positive for methylphenidate, seven (2.6%) were fatal methylphenidate poisonings: Two of these deaths were mono-intoxications and five poly-drug poisonings with methylphenidate among the substances implicate into the cause of death.

Among methylphenidate-positive cases, 46% of deaths were classified as unintentional, 24% as suicides, and 20% as natural deaths.

There were 345 fatal amphetamine poisonings among the studied cases (19%). Of these, three were among individuals with a PM toxicology finding of dexamphetamine (19% of all dexamphetamine findings) and 26 in cases with ADHD medication or diagnosis documented (25% of cases with such a mention).

Among all amphetamine-positive cases, 49% of deaths were classified as unintentional, 19% as suicides, and 20% as natural deaths. Among cases in which ADHD medication or diagnosis had been documented, 55% of deaths were classified as unintentional, 20% as suicides, and 19% as natural deaths.

Discussion

In this retrospective observational study examining all medico-legal PM cases in Finland between 2016 and 2024 in which methylphenidate or amphetamine was detected during forensic toxicological

investigations, there was a clear increase in the number of methylphenidate-positive PM cases during the study period. This finding is consistent with the substantial increase in methylphenidate consumption in Finland during recent years. National consumption statistics expressed as Defined Daily Doses (DDD) increased from 6.21 in 2021 to 10.51 in 2024 [44]. Despite the increasing frequency of methylphenidate findings, no corresponding increase was observed in the number of fatal methylphenidate poisonings. This suggests that the growth in PM detections is likely driven primarily by increased exposure within the population rather than by an increasing toxicity burden attributable to the drug itself. Our findings do not indicate that lethal intoxications have become more common in Finland over time, which is opposite to trends seen in the U.S. [39, 40].

In contrast, both amphetamine-positive cases and fatal amphetamine poisonings increased between 2016 and 2020, after which the numbers appeared to stabilise. A plausible explanation for this pattern is the disruption of amphetamine availability following a major international drug seizure in February 2021 following a period of general increase in amphetamine use. This event removed a substantial amount of amphetamine from the illicit drug market and was reflected in decreased population-level consumption estimates based on wastewater monitoring data [45]. The parallel levelling of both amphetamine findings and fatal poisonings observed in the present study is consistent with a reduced availability of the drug during this period.

Prescription use of dexamphetamine and lisdexamphetamine also increased during the study period according to national DDD statistics, with dexamphetamine increasing from 0.17 in 2021 to 0.29 in 2024 and lisdexamphetamine from 1.84 to 5.00 over the same period [44]. However, comparatively few dexamphetamine findings were identified in the present material. The low number of confirmed cases limits conclusions regarding temporal trends but may reflect the still relatively modest use of amphetamine-based ADHD medications compared with methylphenidate in Finland. It is also possible that cases involving prescribed dexamphetamine remained unidentified owing to the limited availability of medication data and the selective use of chiral amphetamine analysis. Overall, however, the mortality-based data reported here are likely to reflect primarily non-medical amphetamine use patterns.

Another noteworthy finding was the increasing frequency with which ADHD medication use or diagnosis was documented in the laboratory referral and the death certificate over time. This trend may reflect growing awareness of adult ADHD among healthcare professionals and forensic practitioners, increasing prescription rates, or improvements in the recording of medical background information during medico-legal death investigations. Nevertheless, documentation remained incomplete in a substantial proportion of cases, highlighting the challenges of obtaining accurate medication histories in PM investigations.

Substance use was extremely common among the studied cases, with evidence of non-alcohol substance use identified in 76% of methylphenidate-positive cases and in 97% of amphetamine-positive cases in which ADHD medication and/or diagnosis had been documented. These proportions are somewhat higher than reported in deaths related to methylphenidate and dexamphetamine toxicity in

Australia [34] and greatly exceed those reported in ADHD populations in general [46], suggesting that the deceased individuals identified in this study represent a particularly vulnerable subgroup of patients with ADHD. Rather than reflecting the average individual receiving ADHD pharmacotherapy, the present material is likely to include persons with severe psychiatric comorbidity, SUD, social disadvantage, and other risk factors associated with premature mortality. Consequently, these findings should not be interpreted as representative of the broader ADHD population.

Alcohol was found in roughly 25% of samples, similarly across studied groups. Although this is a high number, it is lower than what was found (i.e., 37.5%) in a forensic toxicological study of all Finnish suicide deaths 2016–2018 in an earlier government report [46]. Nevertheless, the mean BAC was 1.0‰ or more in all groups, which is enough to significantly affect functioning, and additionally, in the clear majority of our cases, there was a causal link between alcohol use and death. This means that interventions aimed at reducing alcohol use could potentially alleviate the mortality risk in persons using ADHD medications.

In both the methylphenidate-positive and amphetamine-positive groups, accidental deaths were the largest category, constituting nearly half of deaths in both groups. This pattern closely resembles that reported in populations with problematic substance use, in whom fatal poisonings, injuries and other accidental causes account for a substantial proportion of mortality [48, 49]. Given the established associations between ADHD, impulsivity, risk-taking behaviour and SUD, it is likely that these factors interacted to contribute to the predominance of accidental deaths observed in the present material. The proportion of suicides was also high, accounting for approximately one fifth of deaths in both medication groups. This observation is consistent with previous evidence demonstrating increased risks of suicidal behaviour and completed suicide among individuals with ADHD [13]. The proportion of suicides was the same as reported in an earlier study on fatalities among people who had used ADHD medication [34]. In our study, the proportion appears higher than that reported in Finnish studies of deceased persons with evidence of illicit drug use before death, although direct comparisons are limited by methodological differences between studies [50]. Nevertheless, the findings emphasise the substantial psychiatric burden among the individuals represented in this material and highlight suicide as an important contributor to premature mortality in this population. Previous research has shown a correlation between SUD and risk of suicidal behaviour in ADHD, and our study supports the notion that this relationship may also affect suicide mortality [14, 16].

A marked difference was observed between methylphenidate-positive and amphetamine-positive cases with regard to fatal poisonings. Only 2.6% of methylphenidate-positive cases were classified as fatal methylphenidate poisonings, whereas nearly one fifth of amphetamine-positive cases were fatal amphetamine poisonings. Several factors may account for this difference. The amphetamine-positive population included many individuals likely using illicit amphetamine outside a therapeutic context, often in conjunction with other psychoactive substances. Indeed, polydrug use was common in these cases. Findings may also reflect differences in pharmacological potency (and thus potentially toxicity) [51]. Although causal conclusions cannot be drawn from the present data, the findings indicate that

amphetamine detections in PM toxicology are substantially more often associated with poisoning mortality than methylphenidate detections.

The toxicological investigations also provided direct evidence of non-medical use of ADHD medication. In three methylphenidate-positive cases, methylphenidate was identified in drug-use paraphernalia submitted for laboratory analysis. The detection of methylphenidate in syringes strongly suggests intravenous administration, a route previously described in both fatal and non-fatal cases of methylphenidate misuse [29, 31]. Although uncommon, these findings demonstrate that parenteral misuse of prescribed stimulant medication occurs and may be identifiable through routine forensic toxicological investigations.

An important limitation of this study is the lack of comprehensive information on prescribed medications. In some cases, medication use had been recorded by the forensic pathologist in the laboratory referral or other available documents; however, such information was not consistently available and may not always have been up to date. Consequently, among amphetamine-positive cases, any mention of ADHD medication or diagnosis in the available forensic documentation was considered indicative of possible dexamphetamine/lisdexamphetamine treatment. Without chiral analysis, it is not possible to establish whether the detected amphetamine was attributable to therapeutic use or to illicit drug use. The approach used in our study may have resulted in both false-positive and false-negative interpretations, and some individuals receiving prescribed dexamphetamine/lisdexamphetamine may have remained unidentified. Future studies combining PM toxicological data with national prescription and healthcare registers would allow more accurate identification of treated ADHD patients and provide a more comprehensive understanding of the relationship between ADHD pharmacotherapy, substance use and premature mortality.

Conclusion

Post-mortem findings of ADHD medications in Finland were strongly associated with substance use, accidental deaths and, to a lesser extent, suicides. While methylphenidate findings increased over the study period in parallel with prescribing trends, fatal methylphenidate poisonings remained uncommon. The individuals represented in this material appear to constitute a particularly high-risk subgroup of patients with ADHD characterised by extensive substance-use comorbidity, which thus represent a critical population for preventing early unnatural death. Further research linking forensic toxicology findings with healthcare and prescription data is warranted to clarify the role of ADHD medications in premature mortality and to identify opportunities for targeted prevention.

Declarations

Competing Interests:

The authors have no competing interests to declare that are relevant to the content of this article.

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Ethical considerations

This is a retrospective register-based study. According to the Finnish legislation, no ethical approval is required in such studies on PM cases.

Funding

No funding was received for conducting this study.

Author Contribution

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by P.K. The first draft of the manuscript was written by J.S and P.K, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Acknowledgement

The authors would like to thank Anssi Kivinen for his assistance.

Data Availability

The data underlying this article cannot be shared publicly due to the terms of the research agreement.

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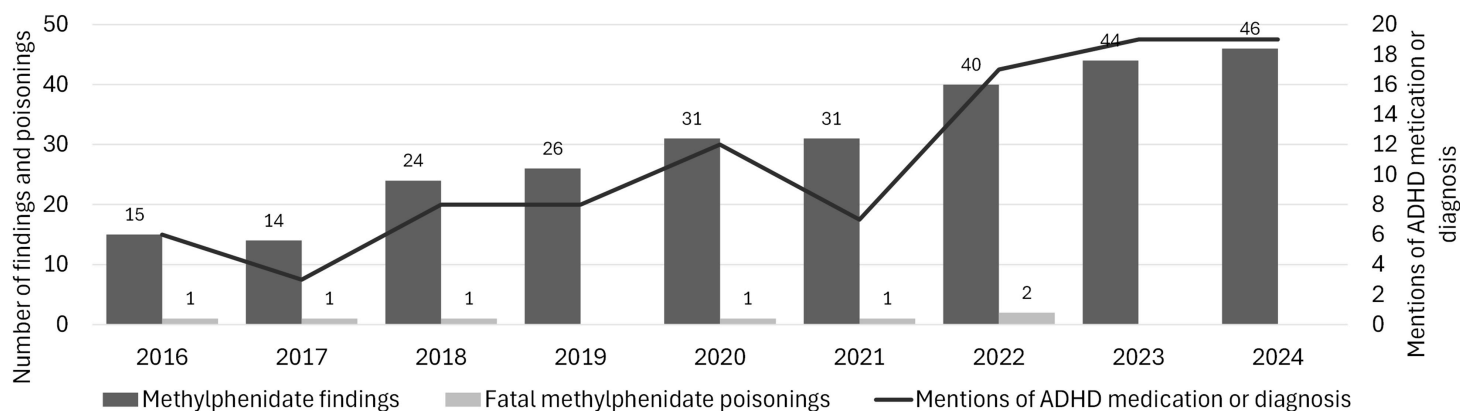
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Figures

A. Methylphenidate-positive cases



B. Amphetamine-positive cases

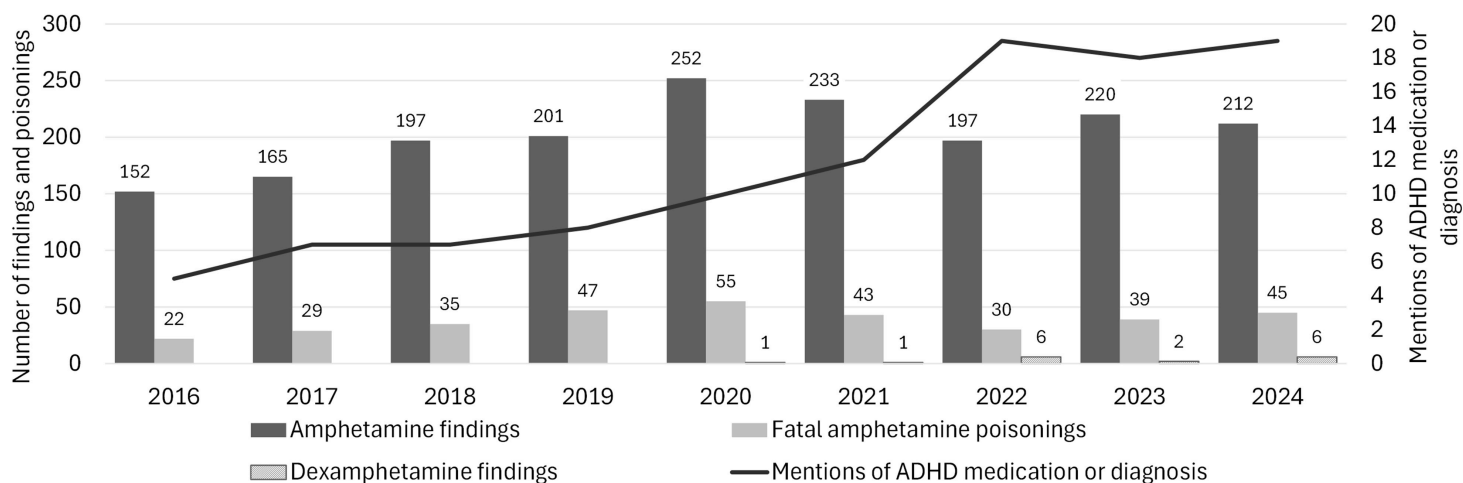


Figure 1

The yearly number of PM findings of methylphenidate (A), amphetamine (B) and dexamphetamine (B), the number of fatal poisonings by methylphenidate (A) and amphetamine (B), and the mentions of ADHD medication or diagnosis in cases positive for methylphenidate (A) and amphetamine (B) in the laboratory referral and/or the death certificate.