Internal and Emergency Medicine
https://doi.org/10.1007/s11739-024-03555-1

EM - ORIGINAL

Acetaminophen overdose: analysis of 2018 US nationwide emergency database

Faria Sami[1] · Sarah Berg[2] · Augustine M. Manadan[3] · Mark B. Mycyk[4]

Received: 6 July 2023 / Accepted: 24 January 2024

Abstract

Introduction Recognized risk factors for acetaminophen overdose include alcohol, opioids, and mood disorders. The aim of this study is to assess additional risk factors for acetaminophen overdose evaluated in the emergency department (ED).

Methods A retrospective study was performed using the 2018 US Nationwide Emergency Department Sample (NEDS). All adult ED visits for acetaminophen overdose were included in the study group and those without it were taken as control. STATA, 16.1 was used to perform multivariable logistic regression analysis and adjusted odds ratios (ORadj) were reported.

Results We identified 27,792 ED visits for acetaminophen overdose. Relative to non-acetaminophen ED visits, this group was younger (median age 32 vs 47 years; $p < 0.0001$), more often female (66.1% vs 57.0%; $p < 0.0001$), had higher ED charges ($3,506 vs $2,714; $p < 0.0001$), higher proportion of alcohol-related disorders (15.8% vs 3.5%; $p < 0.0001$), anxiety disorders (30.2% vs 8.3%; $p < 0.0001$), cannabis use (8.7% vs 1.4%; $p < 0.0001$), hematology/oncology diagnoses (13.3% vs 10.9%; $p < 0.0001$), mood disorders (52.4% vs 7.9%; $p < 0.0001$), opioid-related disorders (4.1% vs 1.0%; $p < 0.0001$), and suicide attempt/ideation (12.2% vs 1.1%; $p < 0.0001$). Multivariable analysis showed alcohol-related disorders (ORadj 2.67), anxiety disorders (ORadj 1.24), cannabis (ORadj 1.63), females (ORadj 1.45), Income Q3 (ORadj 1.09), hematology/oncology diagnoses (ORadj 1.40), mood disorders (ORadj 10.07), opioid-related disorders (ORadj 1.20), and suicide attempt/ideation (ORadj 1.68) were associated with acetaminophen overdose.

Conclusion In addition to previously recognized risks, our study demonstrated that cannabis use and hematologic/oncologic comorbidities were more common among acetaminophen-overdose ED visits. These new findings are concerning because of rapid legalization of cannabis and the increasing incidence of cancer worldwide. Additional investigation into these risks should be a priority for clinicians, policymakers, and researchers.

Keywords Acetaminophen · Overdose · Toxicity · Poisoning · Cannabis

Introduction

Acetaminophen is among the most abundant and easily available medications in the United States. Though safe and effective when used appropriately, acetaminophen can cause significant morbidity and mortality in overdose. The ubiquity of acetaminophen means that it is one of the most frequently implicated pharmaceuticals in overdose in the United States [1]. Acetaminophen-containing products were responsible for 10% of fatalities from overdose reported to America's Poison Centers in 2020 and it is one of the most common substances reported to Poison Control Centers after intentional or unintentional misuse [2].

Acetaminophen poisoning is often unintentional, with repeated supratherapeutic dosing due to uncontrolled pain, mistakenly mixing acetaminophen-containing products with acetaminophen alone, and not adhering to recommended dosing. However, the most common cause of acetaminophen toxicity is still intentional overdose in suicide attempts [3]. Suicide rates are rising in the United States, and intentional poisoning is one of the most common methods of suicide in

✉ Faria Sami
faria.sami@cookcountyhealth.org

1 Department of Internal Medicine, Cook County Health, 1950 West Polk Street, Chicago, IL 60612, USA

2 Department of Emergency Medicine, Division of Medical Toxicology, Cook County Health, Chicago, USA

3 Division of Rheumatology, Cook County Health, Chicago, USA

4 Department of Emergency Medicine, Cook County Health, Chicago, USA

Published online: 06 March 2024

younger patients. It is widely known that individuals with concurrent alcohol use disorder are at increased risk for suicide. There appears to be a linear relationship between suicide rates and per-capita alcohol consumption [4]. Individuals with opioid-use disorder are also at risk for attempting and completing suicide and for suicidal ideation. People who use opioids are 14 times more likely to die by suicide compared to the general population, with an estimated lifetime suicide rate of 17–48% [5]. People with opioid-use disorder have elevated risk for lethal suicide attempts even after remission from their substance use. Individuals diagnosed with mood disorders are also at an increased risk of attempting or completing suicide [5].

The Nationwide Emergency Department Sample (NEDS) is the largest all-payor emergency department patient database in the United States, yielding national estimates of hospital-owned ED visits. Because so much previous research examining risks associated with acetaminophen poisoning relied on toxicology-specific datasets such as the National Poison Data System (NPDS), the aim of this study was to examine characteristics of patients who present to EDs with acetaminophen poisoning using a large US database of emergency department patients.

Methods

Study design

We performed a retrospective study of acetaminophen overdose in NEDS (online at https://www.hcup-us.ahrq.gov). NEDS is part of a family of databases developed for the Healthcare Cost and Utilization Project (HCUP). A complete description of the HCUP databases of US is available at Nationwide HCUP website. Data in the NEDS registry include ED visits from 995 hospitals located in 40 States and the District of Columbia, approximating a 20-percent stratified sample of U.S. hospital-owned EDs. All discharges from these EDs were recorded and weighted to ensure that they were nationally representative. Diagnoses for each hospitalization were recorded utilizing the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10). In the NEDS, diagnoses are divided into a principal diagnosis and one or more secondary diagnoses; the principal diagnosis is the main reason for the ED visit. Secondary diagnoses are any ICD-10 codes other than the principal diagnosis. Use of the NEDS registry data for this study was deemed exempt by the CCH Institutional Review Board since all data are de-identified, anonymous, and publicly available. All authors completed the HCUP Data Use Agreement Training and followed all data use rules. Relevant to this specific project, cells of the tables containing hospitalization data between the values of 1 and 10 were not reported to protect hospital privacy per the HCUP data service agreement.

Inclusion criteria and study variables

All adult ED visits with a principal diagnosis of acetaminophen overdose were selected as the primary study population. Those without acetaminophen overdose as the principal diagnosis served as the reference population. We used the following ICD-10 codes to identify medical diagnoses:

T39.1 = poisoning by, adverse effect of, and overdosing of 4-aminophenol derivatives; F10 = alcohol-related disorders; C00-D49 and D50-D89 = hematology/oncology diagnoses; F11 = opioid-related disorders; F12 = cannabis-related disorders; F40, F41, F42, F43, F44, F45, and F48 = anxiety disorders; F30, 31, F32, F33, F34, and F39 = mood disorders; T14.91 and R45.851 = suicide attempt/ideation. Study variables included age, gender, total charges, median household income, and ED mortality. Median household income by zip code was divided into quartiles: Q1 = $1—45,999; Q2 = $46,000—58,999; Q3 = $59,000—78,999; Q4 > $79,000.

Outcomes

The outcomes studied in adult ED visits included (1) a description of the demographics and comorbidities of patients with acetaminophen overdose versus patients without acetaminophen overdose (2) an identification of variables associated with acetaminophen overdose, listed as secondary diagnoses for all APAP-related ED visits.

Statistical analysis

Analyses were performed using STATA, version 16.1. Descriptive statistics included weighted counts, percentages, medians, and interquartile ranges (IQR). Univariate analysis was used to calculate unadjusted odds ratios (ORs) for predictors of acetaminophen-overdose ED visits. All variables with p values ≤ 0.20 were included in a multivariable logistic regression model and were reported as an adjusted odds ratio (OR_{adj}). p values < 0.05 were considered significant in the multivariable analysis.

Results

After weighting, there were 114,823,417 adult ED visits in the 2018 NEDS; 27,792 of those had a principal diagnosis of acetaminophen overdose (Table 1). The reference adult population without the principal diagnosis of acetaminophen overdose was 114, 795, 625. Relative to the non-acetaminophen group, the acetaminophen group was younger

Table 1 Hospital characteristics of acetaminophen-overdose compared to non-acetaminophen-overdose ED visits

Adult ED visit characteristics	Acetaminophen overdose ($n=27,792$)	Non-acetaminophen overdose ($n=114,795,625$)	p value
Age, median (IQR) in years	32 (22–47)	47 (32–65)	< 0.0001
Female (%)	18,362 (66.1%)	65,411,386 (57.0%)	< 0.0001
Median household income			
Q1 ($1–45,999)	9,099 (32.7%)	40,444,247 (35.2%)	0.0027
Q2 ($46,000–58,999)	7,288 (26.2%)	31,013,918 (27.0%)	0.2462
Q3 ($59,000–78,999)	6,123 (22.0%)	22,770,133 (19.8%)	0.0001
Q4 (≥ $79,000)	4,614 (16.6%)	18,474,732 (16.1%)	0.4471
Overdose risk factors (%)			
Alcohol-related disorders	4379 (15.8%)	3,978,094 (3.5%)	< 0.0001
Anxiety disorders	8401 (30.2%)	9,568,243 (8.3%)	< 0.0001
Cannabis	2408 (8.7%)	1,633,024 (1.4%)	< 0.0001
Hematology/oncology	3691 (13.3%)	12,464,275 (10.9%)	< 0.0001
Mood disorders	14,555 (52.4%)	9,120,461 (7.9%)	< 0.0001
Opioid-related disorders	1139 (4.1%)	1,164,640 (1.0%)	< 0.0001
Suicide attempt/ideation	3386 (12.2%)	1,303,118 (1.1%)	< 0.0001
Died in ED, *n* (%)	≤ 10 (NR)	181,292 (0.2%)	–
Total hospital charges ED, median (IQR)	$3506 (2236–5,80)	$2714 (1421–5209)	< 0.0001

ED emergency department, *IQR* interquartile range, *n* number, *NR* not reported since below permitted reporting threshold, *Q* quartile

(median age 32 vs 47 years; $p < 0.0001$), were more likely to be female gender (66.1% vs 57.0%; $p < 0.0001$), had higher median total ED charges ($3,506 vs $2,714; $p < 0.0001$), higher proportion of alcohol-related disorders abuse (15.8% vs 3.5%; $p < 0.0001$), higher proportion of anxiety disorders (30.2% vs 8.3%; $p < 0.0001$), higher proportion of cannabis use (8.7% vs 1.4%; $p < 0.0001$), higher proportion of hematology/oncology diagnoses (13.3% vs 10.9%; $p < 0.0001$), higher proportion of mood disorders (52.4% vs 7.9%; $p < 0.0001$), higher proportion of opioid-related disorders (4.1% vs 1.0%; $p < 0.0001$), and higher proportion of suicide attempt/ideation (12.2% vs 1.1%; $p < 0.0001$). Mortality for acetaminophen was below the permitted HCUP reporting threshold.

Univariable analysis

Univariable analysis showed the following variables had an increased odds of ED visit for acetaminophen overdose (Table 2): alcohol-related disorders, anxiety disorders, cannabis, female gender, Income Q3, hematology/oncology diagnoses, mood disorders, opioid-related disorders, and suicide attempt or ideation.

Table 2 Univariate regression analysis for acetaminophen-overdose-related ED visits

Variable	Odds ratio	p value	95% C.I
Age	0.96	< 0.001	0.961–0.964
Alcohol-related disorders abuse	5.21	< 0.001	4.805–5.650
Anxiety disorders	4.77	< 0.001	4.447–5.106
Cannabis	6.57	< 0.001	5.926–7.291
Female	1.47	< 0.001	1.385–1.560
Income Q1	0.89	0.003	0.832–0.962
Income Q2	0.96	0.246	0.896–1.029
Income Q3	1.14	< 0.001	1.068–1.221
Income Q4	1.04	0.447	0.943–1.142
Hematology/oncology	1.26	< 0.001	1.159–1.365
Mood disorders	12.74	< 0.001	11.918–13.619
Opioid-related disorders	4.17	< 0.001	3.626–4.798
Suicide attempt/ideation	12.08	< 0.001	10.870–13.430

C.I. confidence interval, *Q* quartile

Multivariable analysis

Multivariable analysis showed the following variables had an increased odds of ED visit for acetaminophen overdose (Table 3): alcohol-related disorders ($OR_{adj} = 2.67$; 95% C.I. 2.444–2.9313), anxiety disorders ($OR_{adj} = 1.24$; 95% C.I. 1.140–1.340), cannabis ($OR_{adj} = 1.63$; 95% C.I. 1.468–1.811), female gender ($OR_{adj} = 1.45$; 95% C.I. 1.355–1.542), Income Q3 ($OR_{adj} = 1.09$; 95% C.I. 1.007–1.176), hematology/oncology ($OR_{adj} = 1.40$; 95% C.I. 1.281–1.521), mood disorders ($OR_{adj} = 10.07$; 95% C.I. 9.200–11.027), opioid-related disorders ($OR_{adj} = 1.20$;

Table 3 Multivariable regression analysis for acetaminophen-overdose-related ED visits

Variable	Odds ratio	*p* value	95% C.I
Age	0.96	< 0.001	0.955–0.959
Alcohol-related disorders	2.67	< 0.001	2.444–2.913
Anxiety disorders	1.24	< 0.001	1.140–1.340
Cannabis	1.63	< 0.001	1.468–1.811
Female	1.45	< 0.001	1.355–1.542
Income Q1	0.90	0.007	0.826–0.971
Income Q3	1.09	0.032	1.007–1.176
Hematology/oncology	1.40	< 0.001	1.281–1.521
Mood disorders	10.07	< 0.001	9.200–11.027
Opioid-related disorders	1.20	0.017	1.032–1.393
Suicide attempt/ideation	1.68	< 0.001	1.488–1.907

C.I. confidence interval, *Q* quartile

95% C.I. 1.032–1.393), and suicide attempt or ideation ($OR_{adj} = 1.68$; 95% C.I. 1.488–1.907).

Discussion

Acetaminophen overdose is the second most common reason for liver transplant worldwide. It also remains one of the leading causes of calls to poison control centers. Therefore, understanding the epidemiology and risk factors associated with acetaminophen toxicity remains crucial. The most novel findings of the current study, not previously reported, are the use of cannabis and history of hematology/oncology comorbidities as independent risk factors for acetaminophen-overdose-related ED visits.

There was a higher prevalence of history of hematology/oncology comorbidities among ED visits for acetaminophen overdose compared to all other ED visits. Hematology/oncology comorbidities were found to be an independent risk factor for APAP-related ED visits. There could be several potential reasons to speculate for this. Acetaminophen remains a crucial part of chronic pain control regimens for cancer patients as either easily available over-the-counter medicine or prescription medicine in combination with other pain control medications [6]. A study done on ED visits in the US from 2006 to 2007 finds that about 56% of patients with therapeutic misadventures leading to acetaminophen overdose took higher doses for medicinal analgesic effect [7]. Uncontrolled cancer pain remains a potential risk factor for cancer patients for this type of overdose. Based on a study done in the US using the National Poison Data System (NPDS), acetaminophen in combination with opioids, medications commonly used to control cancer pain, hold a greater risk of both minor and severe hepatic injury [8]. Willy et al. studied analgesic-related ED visits from 2005 to 2006 and report that the highest rate at 64% of ED visits attributed to acetaminophen-related adverse events was for narcotic-acetaminophen combination products [9]. While several acetaminophen combination medications are used to control cancer-related pain, prior literature has hinted that combination medications may hold a greater risk of an acetaminophen-related adverse event. It is also crucial to highlight the risk of suicide in cancer patients. A large population-based cohort study done over 16 years in the US finds an overall elevated risk of suicide in cancer patients [10]. A literature review in a nursing cancer journal published over 10 years ago concluded that the risk of suicide is approximately twofold higher in patients with cancer than the general population [11]. As mentioned above, acetaminophen overdoses have already been linked to suicide attempts; notably however, the risk in patients with history of hematologic or oncologic comorbidity was independent of history of suicide attempt. This raises the concern of underreported and underrecognized suicidal ideation among cancer patients that could potentially contribute to the findings. Further studies are needed to explore other possibilities as well. This is particularly important during these times as an up-going trend in the incidence of cancers is seen, and by the year 2040, the number of new cancer cases per year is expected to rise to 29.5 million.

Among the acetaminophen-overdose-related ED visits, cannabis use was significantly more common than ED visits for other diagnoses. This is a relatively new and pertinent finding for clinical consideration. A study done between 1996 and 1998 reported chronic marijuana use was a risk factor for hepatotoxicity alone or in combination with other drugs [12]. A few animal studies have been undertaken to study the effects of cannabis with acetaminophen to gauge the consequences in humans. One such study reports that cannabis significantly potentiates the acetaminophen hepatotoxicity in rats [13]. Cannabis use is increasing in the United States, especially since the recreational use of cannabis was legalized in 21 states, medicinal use is legal in 37 states, and several other states are discussing legalization [14]. About 43.5 million Americans over age 12 used reported using cannabis in 2018, and that number increased to 52.5 million in 2021 [15, 16]. In a recent study of cannabis users in the state of Washington, almost half reported substituting their prescription medications with cannabis [17]. It is imperative to understand the long-term health outcomes of cannabis use and drug interactions as the use of cannabis continues to become widespread.

Other findings from our study were consistent with earlier literature that showed female gender, mood disorders, anxiety disorder, suicide attempt/ideation, alcohol-related disorders, and opioid-related disorders are significantly more prevalent in patients with acetaminophen poisoning-related ED visits. The present study's epidemiological findings for

the population with APAP overdose are in concordance with findings in published literature including the 2006–2010 NEDS database study of US population by Altyar et al. [18]. Altyar et al. also find that the acetaminophen-overdose patients commonly had behavioral and mental health comorbidities as well as alcohol abuse history. Similarly, Li and Martin conducted an analysis of ED visits for acetaminophen overdose in 2011 and noticed that behavioral and mental health comorbidities were common among these patients. This included depression, psychosis, drug abuse, and alcohol abuse [19]. The linkage between psychiatric disorders, suicidality, and acetaminophen poisoning has been observed across other works as well [20–23].

To emphasize, it can be estimated from the findings in our study that an increasing number of patients are at risk for acetaminophen toxicity as patients have easier access to cannabis and rate of hematologic diagnoses continues to increase globally, especially cancers. While acetaminophen will expectedly remain a primary choice of non-opioid pain control medication by clinicians, it is crucial to be aware of the at-risk population when exposing them to the drug. Whereas our study included data from NEDS 2018, it is difficult to ignore the dramatic socioeconomic and healthcare changes that followed with the COVID-19 pandemic. There was a concurrent psychiatric pandemic of mental health disorders and increasing use of alcohol and other illicit drugs [24, 25]. It is reasonable to argue that estimates of APAP-overdose-related ED visits in the future could be worse than estimated through this present study, due to increasing exposure to the risk factors identified. Prevention strategies should be implemented, and additional research should be undertaken for strategic implementation of policies and guidelines to avoid potentially preventable harm.

There are many strengths to our analysis. It includes a large cohort sample from NEDS, representative of the national US population estimates for ED utilization during a single year. However, it is important to acknowledge limitations in our study. First, use of the NEDS registry includes limitations inherent in all registry data—rather than exact counts, the registry produces national US estimates using rigorous sampling methodology, and thus some data may be incomplete or lacking specific granularity. For example, we were unable to identify the clinical and therapeutic characteristics of the acetaminophen-related ED visits including quantity ingested, timing of ingestion prior to ED arrival, the severity of acetaminophen toxicity, if taken as a combination pill or with other medications, timing or reason for treatment strategies implemented, and other antidote requirements in the ED setting as the data was extracted using ICD-10 billing codes. Second, the data reflect total ED visits only and not individual patients, and for this reason, a single patient visiting an ED more than once for acetaminophen overdose during that same time period cannot be discerned. Third, errors during medical chart abstraction into the NEDS registry or miscoding of ED charts are possible. The rigor of HCUP's NEDS has been compared to the National Hospital Ambulatory Medical Care Survey (NHAMCS), CDC's National Electronic Injury Surveillance System, and other nationally representative data registries in the US, and all undergo annual reassessment of their reliability and quality to minimize these types of errors. Previous studies using NEDS have informed policymakers on emerging and evolving trends. Importantly, previously confirmed risks associated with acetaminophen poisoning using different study methodologies, such as alcohol-related disorders and depression, were also found in our study, and thus we believe the data in NEDS are reliable and provide important findings for future research to examine evolving risks for acetaminophen poisoning treated in emergency departments. Finally, since NEDS is limited to the ED visit, inpatient hospital data, transfers to other healthcare settings from the ED, and post-ED visit outcomes in these patients were unable to be assessed. Future research should examine the findings in NEDS in conjunction with other nationally representative registries for a more complete understanding of the burden of acetaminophen poisoning on the US healthcare system.

Conclusion

In addition to previously recognized risks, cannabis use and hematology/oncology comorbidities were more common among acetaminophen-overdose ED visits. These findings are concerning because of rapid legalization of cannabis and the increasing incidence of cancer worldwide. Additional investigation into these risks should be a priority association for clinicians, policymakers, and researchers.

Author contributions All authors contributed equally to this work. FS and SB drafted and wrote the manuscript. AMM designed and conducted the analysis. MBM was the principal investigator and supervised the project, proofread and edited for final submission. All authors discussed the results and implications and commented on the manuscript at all stages. All authors contributed extensively to the work presented in this paper.

Declarations

Conflict of interest All the authors confirm that the article or any part of this article has not been published and is not under consideration for publication elsewhere. There are no financial or other relationships that could lead to a conflict of interest to disclose.

Ethical approval and informed consent This study utilizes de-identifiable data publicly available (online at https://www.hcup-us.ahrq.gov) US National Emergency Database and does not require IRB approval.

Data availability statement Not applicable.

References

1. Gunnell D, Murray V, Hawton K (2000) Use of paracetamol (acetaminophen) for suicide and nonfatal poisoning: worldwide patterns of use and misuse. Suicide Life Threat Behav 30(4):313–326
2. Gummin DD et al (2021) (2020) Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 38th Annual Report. Clin Toxicol 59(12):1282–1501
3. Rumack BH (1983) Acetaminophen overdose. Am J Med. https://doi.org/10.1016/0002-9343(83)90240-1
4. Roche SP, Rogers ML, Pridemore WA (2018) A cross-national study of the population-level association between alcohol consumption and suicide rates. Drug Alcohol Depend 188:16–23
5. Rizk MM, Herzog S, Dugad S, Stanley B (2021) Suicide risk and addiction: the impact of alcohol and opioid use disorders. Curr Addict Rep 8:194–207
6. Stockler M, Vardy J, Pillai A, Warr D (2004) Acetaminophen (paracetamol) improves pain and well-being in people with advanced cancer already receiving a strong opioid regimen: a randomized, double-blind, placebo-controlled cross-over trial. J Clin Oncol 22(16):3389–3394. https://doi.org/10.1200/JCO.2004.09.122
7. Budnitz DS, Lovegrove MC, Crosby AE (2011) Emergency department visits for overdoses of acetaminophen-containing products. Am J Prev Med 40(6):585–592. https://doi.org/10.1016/j.amepre.2011.02.026
8. Bond GR, Ho M, Woodward RW (2012) Trends in hepatic injury associated with unintentional overdose of paracetamol (Acetaminophen) in products with and without opioid: an analysis using the National Poison Data System of the American Association of Poison Control Centers, 2000–7. Drug Saf. https://doi.org/10.2165/11595890-000000000-00000
9. Willy M, Kelly JP, Nourjah P, Kaufman DW, Budnitz DS, Staffa J (2009) Emergency department visits attributed to selected analgesics, United States, 2004–2005. Pharmacoepidemiol Drug Saf 18(3):188–195. https://doi.org/10.1002/pds.1691
10. Hu X, Ma J, Jemal A, Zhao J, Nogueira L, Ji X, Yabroff KR, Han X (2023) Suicide Risk Among Individuals Diagnosed With Cancer in the US, 2000–2016. JAMA Netw Open. https://doi.org/10.1001/jamanetworkopen.2022.51863
11. Anguiano L, Mayer DK, Piven ML, Rosenstein D (2012) A literature review of suicide in cancer patients. Cancer Nurs 35(4):E14-26. https://doi.org/10.1097/NCC.0b013e31822fc76c
12. Borini P, Guimarães RC, Borini SB (2004) Possible hepatotoxicity of chronic marijuana usage. Sao Paulo Med J. https://doi.org/10.1590/s1516-31802004000300007
13. Abdel-Salam OME, Metwaly S, Sleem AA et al (2013) Cannabis sativa exacerbates hepatic injury caused by acetaminophen or carbon tetrachloride in rats. Comp Clin Pathol 22:209–218. https://doi.org/10.1007/s00580-011-1388-z
14. Cousins MM, Jannausch ML, Coughlin LN, Jagsi R, Ilgen MA (2021) Prevalence of cannabis use among individuals with a history of cancer in the United States. Cancer. https://doi.org/10.1002/cncr.33646
15. https://www.samhsa.gov/data/sites/default/files/reports/rpt39443/2021NSDUHFFRSubstance Abuse and Mental Health Services Administration. (2022). Key substance use and mental health indicators in the United States: Results from the 2021 National Survey on Drug Use and Health (HHS Publication No. PEP22-07-01-005, NSDUH Series H-57). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/report/2021-nsduh-annual-national-report
16. Substance Abuse and Mental Health Services Administration. (2019). Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health (HHS Publication No. PEP19–5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data/
17. Corroon JM Jr, Mischley LK, Sexton M (2017) Cannabis as a substitute for prescription drugs - a cross-sectional study. J Pain Res 2(10):989–998. https://doi.org/10.2147/JPR.S134330
18. Altyar A, Kordi L, Skrepnek G (2015) Clinical and economic characteristics of emergency department visits due to acetaminophen toxicity in the USA. BMJ Open. https://doi.org/10.1136/bmjopen-2014-007368
19. Li C, Martin BC (2011) Trends in emergency department visits attributable to acetaminophen overdoses in the United States: 1993–2007. Pharmacoepidemiol Drug Saf 20(8):810–818. https://doi.org/10.1002/pds.2103
20. Jiang T, Nagy D, Rosellini AJ, Horváth-Puhó E, Keyes KM, Lash TL, Galea S, Sørensen HT, Gradus JL (2021) Suicide prediction among men and women with depression: A population-based study. J Psychiatr Res 142:275–282. https://doi.org/10.1016/j.jpsychires.2021.08.003
21. Zyoud SH, Awang R, Sulaiman SA, Al-Jabi SW (2010) A cross-sectional observation of the factors associated with deliberate self-poisoning with acetaminophen: impact of gender differences and psychiatric intervention. Hum Psychopharmacol 6:500–508. https://doi.org/10.1002/hup.1140
22. Gyamlani GG, Parikh CR (2002) Acetaminophen toxicity: suicidal vs accidental. Crit Care. https://doi.org/10.1186/cc1475
23. Kjartansdottir I, Bergmann OM, Arnadottir RS, Björnsson ES (2012) Paracetamol intoxications: a retrospective population-based study in Iceland. Scand J Gastroenterol 47(11):1344–1352. https://doi.org/10.3109/00365521.2012.703236
24. Roberts A, Rogers J, Mason R, Siriwardena AN, Hogue T, Whitley GA, Law GR (2021) Alcohol and other substance use during the COVID-19 pandemic: A systematic review. Drug Alcohol Depend. https://doi.org/10.1016/j.drugalcdep.2021.109150
25. Hossain MM, Tasnim S, Sultana A, Faizah F, Mazumder H, Zou L, McKyer ELJ, Ahmed HU, Ma P (2020) Epidemiology of mental health problems in COVID-19: a review. Fresh 23(9):636