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Article

Association Rule Mining for Identifying High-Risk Drug Combinations in Overdose Fatalities: A Comparative Analysis of Apriori and FP-Growth Algorithms

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Abstract: Accidental fatal overdose is more often seen where the use of several substances occurs concurrently, e.g., opioids and stimulants. Association rule mining techniques in this research have been used to determine the high-frequency and highly probable fatal pairs of drugs based on an overdosage death database. In research, use of both the Apriori and FP-Growth algorithms used to identify patterns, quantify the association by utilizing support, confidence, and lift measures. Results show strong affinity, particularly for Xylazine and Fentanyl, with 99% confidence and 1.48 lift, representing a large co-occurrence that occurs over chance. Though Apriori has greater computational cost, it worked flawlessly due to sparsity in the data. FP-Growth, for its part, demonstrated its advantage in scalability as well as pattern discovery when its optimization was enabled. Comparative analysis not only reflects on methodological robustness and limitations but also provides useful suggestions to public health officials, forensic examiners, and policymakers. Some recommended suggestions are developing AI-driven early warning systems, enhancing forensic monitoring, and using gamified learning to raise awareness among youth. The findings highlight the importance of evidence-informed responses to stem the burgeoning epidemic of polysubstance overdoses.

Keywords: Polysubstance Overdose; Association Rule Mining; Apriori Algorithm; FP-Growth; Drug Pair Analysis; Xylazine; Fentanyl; Support-Confidence-Lift; Public Health

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1. Introduction

The sobering acceleration of drug overdose fatalities, particularly with polysubstance use, has emerged as a primary public health concern. Overdose is often caused by complex polypharmacy involving opioids, stimulants, depressants, and newer synthetic drugs, most of which synergize in fatal combinations. The Centers for Disease Control and Prevention (CDC) indicate that over 100,000 drug overdose deaths occurred in the United States in 2022, with synthetic opioids like fentanyl playing a leading role in the increase [1]. The increasing prevalence of xylazine—a veterinary sedative not approved for use in humans—being combined with fentanyl has been alarming, with extremely high morbidity and mortality rates [2]

Understanding the trends and combinations of these drugs is essential to the development of effective harm reduction strategies, policymaking, and emergency response protocols. Traditional methods of analyzing drug toxicity in forensic science and public health surveillance are not scalable and lack the capacity to detect patterns. This is where association rule mining—a data mining technique originally popularized in market basket analysis—becomes useful. It allows for the identification of statistically significant correlations of co-occurring items, in this instance, drugs, in large datasets [3-4].

In this research, two well-known association rule mining algorithms, Apriori and FP-Growth, are applied to a cleaned dataset of overdose deaths. The algorithms are applied to find frequent item sets and derive rules indicating the most common drug combinations implicated in deaths. The Apriori algorithm produces frequent drug item set systematically using iterative support thresholds, while the FP-Growth algorithm improves performance by condensing the dataset into a tree structure to prevent candidate generation [5]. The primary goal of this report is to identify and analyze high-risk drug combinations responsible for overdose deaths based on these data mining approaches. In doing so, we aim to assist healthcare professionals, forensic scientists, and policymakers in recognizing dangerous trends and taking proactive measures to avoid additional loss of life.

2. Literature Review

Polysubstance use and overdose mortality are growing public health problems, particularly in the context of the growing synthetic opioid and novel psychoactive substance problem. Simultaneous administration of drugs like fentanyl, heroin, cocaine, xylazine, and ethanol has profoundly increased the risk of accidental death from volatile pharmacodynamic drug interactions [6]. As forensic toxicology has become increasingly data-intensive, older analysis methods are wanting to uncover the hidden, complex interdependencies among substances. This has made data mining processes such as association rule mining necessary to analyze large data sets of drug-related fatalities and pull-out useful information[7-8].

Association rule mining, initially developed for market basket analysis, has gained greater traction in healthcare analytics to uncover drug-drug interactions and side effects. Techniques like Apriori and FP-Growth are suitable to identify frequent item sets—collections of drugs that co-appear often—and derive association rules with measures such as support, confidence, and lift [9-10]. Apriori algorithm identifies frequent patterns through iterative scanning of the database, while FP-Growth provides scalability using the construction of a prefix-tree to effectively mine frequent item sets [11].

Recent research vindicates the significance of such algorithms in data analysis of overdoes. For instance, applied association rule mining on electronic health records to determine risky combination drugs that led to adverse outcomes. The study showed that rule mining had the potential to contribute significantly to predictive power in clinical systems to detect unsafe interactions[12].

Comparison studies on both Apriori and FP-Growth algorithms have shown variable performance based on the dataset characteristics. Apriori is simpler to comprehend but falls under inefficiency when dealing with a large amount of the database because it uses process-repeated candidate generation. On the other hand, FP-Growth is scalable because it avoids candidate generation[13-14].

According to the performance evaluation, FP-Growth was consistently better than Apriori on executing time and memory requirement, even more during case of processing high-dimensional toxicology data for the experiments. It can also yield results in a lesser amount of time for smaller or sparse datasets, as reflected in the findings of this report[15-17].

Most crucial, more than computational efficiencies, is the use of association rule mining applications for public health and forensic purposes. Specifically, it allows real-time detection of toxic combinations, as well as the monitoring of emerging trends in drug usage and early intervention mechanisms. Forensic laboratories are now adopting these algorithms for automated detection of patterns in toxicology reports so that their ability to follow distribution trends and relay relevant information to law enforcement increases [18-19].

3. Methodology

This work uses a data mining approach to identify frequent pairs of drugs and dangerous associations responsible for overdose deaths. Data preprocessing, using two popular association rule mining algorithms, Apriori and FP-Growth, followed by comparing the performance of both algorithms based on accuracy, comprehensibility, and computational complexity, is accomplished[20-22].

3.1. Data Source and Preprocessing

The data employed in this study is the publicly available "Accidental_Drug_Related_Deaths.csv", which contains detailed toxicology reports of overdose deaths. In order to enable a focused and efficient analysis, some preprocessing was done. Demographic and geographic information were eliminated first to restrict the focus to only substances consumed in deaths. Next, only columns related to drugs were retained, eliminating any unnecessary attributes. These values were further translated into binary values, such that the "Y" indicating the presence of a drug was substituted with "1" and the absence or blank records were substituted with "0." Binary conversion is important because association rule mining algorithms necessitate them. Moreover, missing values were taken as zeros in order to be consistent across the dataset. The processed and formatted data were saved as "processed_drug_data.xlsx" for future analysis.

3.2. Implementation of the Apriori Algorithm

The implementation of the Apriori algorithm was initiated to identify frequent drug combinations responsible for overdose deaths. Minimum support was set at 0.05 (5%) and minimum confidence at 0.60 (60%), ensuring that only statistically significant patterns were considered for analysis. The algorithm worked with repeated scans of the dataset to find frequent itemsets, generate candidate itemsets, and finally, establish association rules through the thresholds set in advance. The most relevant rules obtained from the Apriori algorithm are summarized below:

Antecedents	Consequents	Support	Confidence	Lift
(Xylazine)	(Fentanyl)	0.0896	99%	1.48
(Cocaine)	(Fentanyl)	0.2772	72%	1.08
(Heroin/Morph/Codeine)	(Fentanyl)	0.1149	63%	0.95
(Ethanol)	(Fentanyl)	0.1814	67%	1.01

Interpretation: Among the rules found, the strongest was Xylazine → Fentanyl, with confidence of 99% and a lift of 1.48, showing strong and significant co-occurrence that is not by chance.

3.3. FP-Growth Algorithm Implementation

The FP-Growth algorithm was implemented to increase performance and efficiency. The same support and confidence levels were used as Apriori. FP-Growth builds a Frequent Pattern Tree (FP-Tree), and so it bypasses candidate itemset generation and mines frequent patterns directly[23-24]. The algorithm produced the highest co-occurring drug substances in the dataset, which are described below:

Fentanyl: 67.16%
Cocaine: 38.21%
Heroin: 29.86%
Fentanyl + Cocaine: 27.72%
Fentanyl + Heroin: 16.86%

According to these frequent trends, the FP-Growth algorithm developed the below significant association rules:

Antecedents	Consequents	Support	Confidence	Lift
(Xylazine)	(Fentanyl)	0.0896	99.63%	1.48
(Ethanol)	(Fentanyl)	0.1815	67.93%	1.01
(Heroin + Fentanyl)	(Heroin/Morph/Codeine)	0.1132	67.17%	3.73

Consistent with the expectations of Apriori, the association of Xylazine → Fentanyl was validated by the FP-Growth algorithm. There was a significant three-way dependency between

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Heroin, Fentanyl, and prescription opioids with a lift score of 3.73, indicating a very strong, significant, and predictive set.

3.4. Algorithm and Execution Time Comparison

To determine computational efficiency, execution times for both algorithms were compared before and after optimization techniques. First, Apriori was more efficient due to the sparsity of the data, where there were fewer overlapping sets of combinations. But after noise (introduced complexity) was introduced to Apriori and optimization techniques (like removing infrequent items) were applied to FP-Growth, the latter was more efficient[25-26].

Initial Execution Time:

Algorithm	Execution Time (s)
Apriori	~2.3
FP-Growth	~3.6

After Optimization:

Algorithm	Execution Time (s)
Apriori (with added noise)	~6.2
FP-Growth (optimized)	~1.8

Insights:

- Apriori is more efficient on smaller and denser datasets with fewer candidate item sets generated.
- FP-Growth, although initially slower, handles larger datasets better when optimized with faster execution and deeper pattern exploration.
- These findings suggest that the choice of algorithm must be driven by the data structure and the analysis goals, with FP-Growth better optimized for scalability and performance on more complex datasets.

Implementation of Apriori Algorithm

The **Apriori algorithm** is a foundational technique in the field of data mining, particularly useful for uncovering associations among items within large datasets. Its primary strength lies in its ability to identify co-occurring elements—such as drugs—in complex records, and generate meaningful association rules. The algorithm works by performing multiple scans over the dataset to identify recurring combinations of drugs implicated in overdose fatalities. Through its systematic pattern discovery, Apriori allows analysts to identify potentially lethal substance combinations, guiding forensic investigations and public health interventions (GeeksforGeeks, 2018).

Steps for Apriori Algorithm Implementation

Apriori algorithm implementation in this research is guided by an ordered set of procedures. To begin with, the dataset is passed through to extract frequent itemsets—drug pairs that occur simultaneously in overdose incidents. These are then filtered for statistical significance against a minimum support threshold. For example, if Heroin and Fentanyl tend to co-occur together, then they represent a valid candidate itemset. Next, the algorithm generates candidate item sets by growing these frequent pairs to include larger sets, such as Heroin + Cocaine + Fentanyl. Sets with less than minimum support is discarded in a process known as pruning, which reduces computational overhead and focuses analysis on high-impact interactions[27-29].

Following itemset generation, the algorithm produces association rules from residual frequent combinations. The rules are evaluated against crucial measures:

- Support how frequently a combination appears
- Confidence, the probability that one drug appears given the presence of the other
- Lift, how much more frequently drugs co-appear than by chance
- This generation of the rule offers valuable information on the most lethal pairings of drugs that commonly lead to death.

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Analysis of Apriori Algorithm

In an effort to generate meaningful association rules, support and confidence threshold values were set. A minimum support of 0.05 (5%) was set so that a set of drugs needs to occur in at least 5% of the overdose cases in order to be considered. A minimum confidence of 0.60 (60%) was also set so that any rule has to have at least 60% precision in predicting the presence of one drug when the other is present. These thresholds balance between discovering beneficial rules and avoiding spurious relations that may occur randomly.

Frequent Itemset Generation

The algorithm was also used to identify frequent drug pairs at the defined support threshold. For instance, combinations such as Fentanyl + Cocaine and Fentanyl + Heroin were identified with high frequency among overdoses. Such findings provide the bottom level for rule generation and help determine which of the drugs are more likely to be ingested together in fatal scenarios.

Association Rule Extraction

Association rules were derived by examining frequent item sets with the association_rules() function. Rules show how the presence of some drugs signifies the presence of others. Rules were filtered according to the set confidence threshold to only retain those with 60% or higher confidence. The most significant measures displayed in the final output are:

- Antecedents: The combinations of drugs that were seen
- Consequents: The drugs that were predicted to be present
- Support: Combination prevalence
- Confidence: Predictive performance of the rule
- Lift: Strength of association above random chance, i.e., lift > 1 and statistically significant.

The most confident rule found was Xylazine → Fentanyl with 99% confidence and a lift of 1.48, showing an extremely strong and non-chance-dependent association. These findings map directly to revealing high-risk drug combinations that may warrant policy and clinical attention.

Results Interpretation:

The Apriori algorithm extracted key association rules which reveal a strong correlation between the drugs used in overdose cases. The following table listing some of the top rules according to lift and confidence values:

Antecedents	Consequents	Support	Confidence	Lift
(Heroin/Morph/Codeine)	(Fentanyl)	0.1149	63%	0.95
(Cocaine)	(Fentanyl)	0.2772	72%	1.08
(Heroin/Cocaine)	(Fentanyl)	0.0586	61%	0.91
(Ethanol)	(Fentanyl)	0.1814	67%	1.01
(Xylazine)	(Fentanyl)	0.0896	99%	1.48

FP-Growth Algorithm Implementation

The FP-Growth algorithm serves as a scalable, efficient alternative to traditional association rule mining algorithms such as Apriori. Because FP-Growth does not do multiple scans of the database and does not generate extensive candidacies, it eliminates the inefficiencies attributed to Apriori's high computational costs. Instead, FP-Growth compresses the dataset into a compact structure, known as a Frequent Pattern Tree (FP-tree), enabling direct mining of frequent itemsets without generating candidate sets. This property makes FP-Growth well-suited for large databases and cases where mining for frequent itemsets must occur with minimal overhead.

FP-Growth Algorithm Fast Performance

The FP-growth algorithm was created to overcome the major drawbacks of Apriori: the excessive data scan and huge candidate itemsets generation. These causes could slow the processes, especially when it comes to large and complicated datasets[30-32]. Hence, the FP-growth algorithm addresses all these problems by providing a prefix-based tree structure called FP-tree, which retains all necessary compressed information about the frequent patterns. Hence, the algorithm can directly mine the itemsets stored in the tree, which minimizes the required computation, therefore making it faster and memory-efficient.

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3.2. Steps for the Implementation of FP-Growth Algorithm

The FP-growth algorithm works by a well-defined procedure ensuring its efficiency and scalability. The first step is data compression, where the entire dataset is converted to an FP-tree. The structure of this tree retains only the essential frequency information of itemsets and does away with the generation of candidates by exhaustion. Thereafter follows mining the FP-tree, where frequent itemsets are generated based on a set minimum support threshold. The tree is then recursively divided into smaller conditional FP-trees for each item for localized mining. Finally-in the third phase-frequent itemsets are derived and bounds representing statistically significant relationships between items are generated as association rules.

Analysis of the FP-Growth Algorithm:

The thresholds were established to extract only meaningful associations in the relevant data using the FP-Growth algorithm. Accordingly, a minimum support criterion level of 5% and a minimum confidence criterion level of 60% were set. The algorithm efficiently finds the most frequent and relevant drug combinations in the dataset based on parameters.

The analysis showed that Fentanyl accounted for the maximum support of 67.16%, with Cocaine and Heroin following at 38.21% and 29.86%, respectively. Two of the combinations, most important being Fentanyl plus Cocaine (27.72%) and Fentanyl plus Heroin (16.86%), have even higher co-occurrence values, indicating that this identifies critical dependency between them.

Association Rule Extraction

As soon as itemsets have been realized frequently, the following stage was association rule extraction using a minimum confidence threshold in order to select only statistically significant associations that aroused the need for obtaining a rule. The function association_rules served to analyze drug combinations and to derive interpretative rules with each rule comprising two segments' antecedents (existing drug combinations) and 'consequents': the drug predicted to appear alongside the antecedent. The following three measures rated the strength and relevance of these rules. Support records how often the drug combination occurs in the database. Confidence is the probability of finding the consequent drug when the antecedents are present. Lift evaluates the strength of the association beyond random chance — a value greater than 1 suggests a meaningful, nonrandom relationship. This set of metrics was further exploited to determine the most important combinations of substances causing overdose fatalities.

Results Interpretation

Following the application of FP-Growth algorithm, a list of association rules was derived that emphasized key drug associations in cases of overdose. The most relevant rules are given in the table below along with their corresponding support, confidence, and lift values:

Antecedents	**Consequents**	**Support**	**Confidence**	**Lift**
(Heroin/Morph/Codeine)	(Fentanyl)	0.1149	63.84%	0.95
(Cocaine, Heroin)	(Fentanyl)	0.0587	61.50%	0.91
(Ethanol)	(Fentanyl)	0.1815	67.93%	1.01
(Xylazine)	(Fentanyl)	0.0896	99.63%	1.48
(Heroin, Fentanyl)	(Heroin/Morph/Codeine)	0.1132	67.17%	3.73

Analysis of the Results

The rule (Heroin/Morph/Codeine) → (Fentanyl) showed a confidence level of 63.84%, indicating that in nearly two-thirds of the cases where these opioids were present, fentanyl was also detected. The lift value of 0.95 suggests that this association is just below the level of random chance, pointing to a weak predictive relationship. The combination (Cocaine, Heroin) → (Fentanyl) had a 61.50% confidence and a lift of 0.91. While the confidence is moderate, the lift being below 1 suggests that co-occurrence of cocaine and heroin does not significantly increase the likelihood of fentanyl being present, making it a weak association.

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In the rule (Ethanol) → (Fentanyl), confidence reached 67.93% at a lift of 1.01, indicating an almost random relationship. Although ethanol is often found with fentanyl, its presence does not seem to work strongly as an indicator for fentanyl use, nor does it suggest a strong association. A highly significant rule was (Xylazine) → (Fentanyl), with confidence of 99.63% and lift of 1.48. Such a strong lift value is indicative of a meaningful relationship between the two substances and supports the concerns of public health agencies regarding their co-occurrence in overdose deaths. Finally, the rule (Heroin, Fentanyl) → (Heroin/Morph/Codeine) showed confidence at 67.17% with a particularly high lift of 3.73, thus suggesting that when heroin and fentanyl are both present, then there is a strong and non-random prospect that prescription opioids such as morphine or codeine are also involved. This rule emphasizes the complex interdependencies between synthetic, illicit, and prescription opioids in overdose situations.

Key Observations of Association Analysis

1. High-Risk Drug Pairs for Identification

Typical drug combinations have been identified through association rule mining which has critical operational application and using overdoses as an outcome mortality. High-risk interactions are indicated. The most striking patterns reveal the link between Xylazine and Fentanyl. The two had a confidence of 99% with a lift of 1.48, indicating strong and nonrandom co-occurrence. Cocaine and fentanyl similarly had 72% confidence and lift of 1.08, another common potentially lethal pair. The existence of those relationships shows certain drugs, in particular combinations, strongly increase the chances of dying.

They also discovered lethal combinations through association rule mining using electronic health records in subjects similar to Nazyrova et al. (2023). In many cases, according to the U.S. Drug Enforcement Administration (DEA, 2022), the increase in contamination by Xylazine presented as 23% of fentanyl powder and 7% of fentanyl pills in 2022, further signifying its looming danger. Therefore, such evidence validates the applicability of such algorithmically inferred patterns to real-world health public data and emphasizes the importance for more targeted surveillance on these high-risk drug mixtures.

High-Risk Drug Pair	Confidence	Lift
Xylazine → Fentanyl	99%	1.48
Cocaine → Fentanyl	72%	1.08

Execution speed of Apriori and FP-Growth algorithms

Comparison performance-wise between Apriori and FP-Growth algorithms shows that both these algorithms are good, but FP-Growth is superior to Apriori with an increasing dataset size. The merit of FP-Growth owes to the tree-based structure, which eliminates the diminished candidate itemset generation and testing —A major drawback in the design of Apriori lies. However, for small or sparse datasets like the one analyzed, at times Apriori ran faster due to a less frequent drug co-occurrence, hence limiting the complexity of candidate generation.

In their study, Mythili and Shanavas (2013) suggest that FP-Growth is highly favorable for high-dimensional datasets as it saves memory and execution time. The introduced complexity in Apriori and optimizations done in FP-Growth, thereby eliminating unnecessary iterations and rare ones, accounted for the significant reduction in execution time of FP-Growth. Their findings suggest that Apriori is useful for small and simple datasets, whereas FP-Growth is advantageous as a fast and scalable approach when optimization comes into play for complex and large-scale data.

Algorithm	Initial Time (s)	After Optimization (s)
Apriori	~2.3	~6.2
FP-Growth	~3.6	~1.8

Recommendations Based on Findings

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Based on the findings, a number of recommendations have been made for public health, forensic science, and future research. One priority for public health agencies should be to monitor high-risk drug combinations, especially Xylazine and Fentanyl, due to their overwhelming association with overdose fatalities. Informing people about combinations often seen with Fentanyl: Heroin, Cocaine, or Ethanol could lower accidents rates with these combinations. Governments ought to tighten up policies regarding emerging substances entering the drug market.

For forensic and law enforcement ranks, the use of association rule mining can help in the development of early detection of overdose patterns which will allow for timely intervention and hence prevent the illicit drug distribution networks from working further. Further development of an AI-based early warning system that includes inputs such as toxicology reports, social media posting, and dark web monitoring would assist in predicting what will become dangerous combinations, hence preventing large-scale destruction.

For the youth education, gamification approaches such as an interactive mobile application simulating the consequences of drug misuse can be used to effectively teach about polysubstance abuse and drugs. Finally, there is room for upcoming studies integrating a hybrid modeling approach that employs Apriori and FP-Growth algorithms with deep learning or graph-based neural networks for better accuracy to identify novel and counterintuitive drug interactions.

Recommendation Domain	**Actions Suggested**
Public Health	Monitor drug mixtures, especially Xylazine-Fentanyl
Forensics & Law	Use rule mining for trend detection and interventions
AI & Drug Surveillance	Develop predictive models for emerging combinations
Youth Education	Create gamified learning tools for substance abuse awareness
Research & Modeling	Explore hybrid models and advanced pharmacokinetics integration

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