

Comparing Medical Comorbidities Between Opioid and Cocaine Users: A Data Mining Approach

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Original Article

Abstract

Background: Prescription drug monitoring programs (PDMPs) are instrumental in controlling opioid misuse, but opioid users have increasingly shifted to cocaine, creating a different set of medical problems. While opioid use results in multiple medical comorbidities, findings of the existing studies reported single comorbidities rather than a set, and furthermore, those findings are often conflicting because of the lack of controlling for other substances in the analysis when combined use of substance creates synergistic effects. On the other hand, the findings from cocaine use are mainly related to kidney and heart problems, which lack specificity. Because medical comorbidities from opioid and cocaine use are very different, it is imperative to investigate medical comorbidities from opioids and cocaine in order to minimize negative effects from PDMPs. Therefore, this study attempts to discover sets of medical comorbidities from opioid and cocaine use by controlling for other substances in the analysis.

Methods: A data mining technique, association rule mining algorithm, was employed to discover sets of medical comorbidities using electronic medical records. This method is ideal to discover co-occurring medical comorbidities.

Findings: Opioid use was associated with a set of [high diastolic blood pressure (DBP), abnormal specific gravity], [high body mass index (BMI), low blood gas] among others. Cocaine use correlated with [high creatine kinase (CK), high blood urea nitrogen (BUN)], [high CK, cardiopulmonary] among others.

Conclusion: The findings of this study addresses some of the conflicting findings by eliminating multidrug and reports sets of medical comorbidities from opioid and cocaine use.

Keywords: Cocaine; Data mining; Electronic health records; Comorbidity; Opioids

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Introduction

Opioids, which have been widely misused, are the representative legal prescription drug for pain. The Substance Abuse and Mental Health Services Administration (SAMHSA) reported that 11.8 million people misuse opioids,¹ and prescription opioid overdoses almost quadrupled from 1999 to 2011: 1.4 deaths per 100000 people to 5.4 deaths per 100000 people.² In order to combat this problem, 49 states have implemented prescription drug monitoring programs (PDMPs) to control the misuse of opioids and other prescription drugs.³ PDMPs are statewide electronic databases that store controlled drug dispensing information; this information is housed in regulatory, administrative, or law enforcement agencies.³ Those agencies then distribute the collected data to authorized individuals; this data allows the authorized individuals to gain access to controlled substances for legitimate medical use.³ Through the system, those individuals can check patient information and the exact number of drugs prescribed to the designated patient. Therefore, patients are prevented from doctor/pharmacy shopping. These programs have reduced prescription drug-related deaths in several states of the United States including Oklahoma, Kentucky, Tennessee, and New York.^{2,4} As an example, after the implementation of the program, deaths from drug overdoses in Oklahoma fell by 8% from 2012 to 2016.⁴ Furthermore, in Oklahoma prescriptions for controlled substances fell to 9.3 million in 2016, a 700000 decrease from 2013.⁴ This example clearly shows the success of a PDMP in reducing prescribed drug misuse. Unfortunately, while PDMPs can control and reduce prescription-related drug deaths, growing evidence shows that misusers of prescription opioids in Oklahoma are transitioning to illegal drugs.⁵ In 2016, 40% of drug deaths were attributable to street-drugs.⁵ This unfortunate trend is not limited to Oklahoma; it is occurring in every state as well.^{6,7}

As such, PDMPs inadvertently increased the use of illegal drugs, such as cocaine.⁸ Cocaine overdose deaths involving opioids sharply increased from 29.4% in 2000 to 63.0% in 2015.⁹ Additionally, cocaine use disorder was a significant risk factor for both prescription opioid use disorder and heroin use.¹⁰ The combination of

opioid and heroin use may be attributable to users combining cocaine (stimulant) and heroin (depressant); this combination, which is referred to as a "speedball," is believed to cancel out the negative effects of each drug.¹¹ Speedball led to increased cocaine use following the implementation of PDMPs. Lab submittal cases for cocaine increased to 35.3% between the years 2016 and 2017.⁸

Since users have the tendency to inject drugs, the use of illegal drugs leads to a different set of medical comorbidities, such as hepatitis C virus (HCV) and human immunodeficiency virus (HIV).^{12,13} As such, when PDMPs are implemented, it is imperative to understand medical comorbidities from illegal drug use, so serious negative consequences can be minimized.

The representative drugs selected for this research were based on impact and relevancy to current public health threats. First, opioids represent legal prescription drugs because of the national opioid epidemic and its effects. Second, cocaine represents illegal drugs in this research because of an increase in cocaine use and cocaine-related deaths following the implementation of PDMPs. Furthermore, cocaine use is the leading cause of drug misuse-related visits to emergency departments;¹⁴ the use of cocaine accounts for 31% of all visits to the emergency department.¹⁵

While medical comorbidities from opioid use have been reported, the findings have been inconsistent and often contradictory.¹⁶ A few examples are high blood pressure (BP), high hemoglobin A1c (HbA1c), kidney problem, etc.; however, these findings are often conflicting:^{17,18} opioid use elevates, lowers, or has no impact on BP;^{16,19-21} opioid use elevates, lowers, or has no impact on HbA1c;¹⁹⁻²² opioid use elevates, lowers, or has no impact on body mass index (BMI);^{17,19,20,23} opioid use increases white blood cells (WBCs), platelet, neutrophil, and monocyte counts, while lymphocyte counts are significantly lowered,²⁴ while other studies found that opioids elevate WBC, lymphocytes, and red blood cells (RBCs).²⁵ Kidney damage is also reported due to elevated BPs.²⁶⁻²⁸

These inconsistent findings may be derived from the lack of eliminating multiple drug use in the analysis. It is necessary to eliminate polydrug use in the analysis, as opioid users consume multiple substances: benzodiazepine (BZD)

(53.4%), cocaine (30.0%), crack cocaine (18.9%), and heroin (8.7%).⁶ Concomitant use of multiple substances can be deadly because of synergistic effects.²⁹ For example, concurrent use of opioids and BZD has the potential to increase the respiratory depressant effects of opioids; similarly, alcohol and opioids together increase respiratory depressant effects.²⁹ The combined use of cocaine and heroin (aka speedball) can result in high BP and strong or irregular heartbeat.³⁰

In addition to conflicting findings, it is unclear whether opioid use associates with one comorbidity or multiple comorbidities. More specifically, does opioid use cause high BP, high HbA1c, or both high BP and high HbA1c? Finding sets of comorbidities may assist evidence-based treatments as substance use is likely to cause multiple co-occurring medical comorbidities.

Like other drugs, cocaine is metabolized in the kidneys and liver, and thus cocaine damages both organs.^{26,31-33} Thus, cocaine users have problems including proteinuria, leukocytosis, elevated serum creatinine, and elevated creatine kinase (CK) levels.^{34,35} The damaged kidney cannot properly control BP or make erythropoietin (EPO), which is vital for RBC production;³⁶ damaged kidney, in turn, elevates BPs and lowers RBC. One study showed that eighty-nine percent (49/55 or 89%) of cocaine users had a diagnosis of hypertensive end-stage renal disease (ESRD), and cocaine users' estimated ESRD development time was much shorter than non-users.³⁷ In fact, cocaine use was the biggest medical problem among African American dialysis patients.³⁸ Cocaine-induced renal infarction can also result in fever and night sweats.^{39,40} As such, cocaine use should be considered as a cause of ESRD in patients without a clear cause for renal failure.³⁷

The kidneys and heart are also damaged by cocaine through coronary vasoconstriction, elevated BPs, and rhabdomyolysis.^{33,41} This increases myocardial oxygen demand by increasing heart rate and BP, decreasing oxygen supply via coronary vasoconstriction, and accelerating narrowing arteries while hardening them with plaque buildup on the artery wall.^{15,31,42} As such, cocaine is the leading cause for drug misuse-related visits to emergency departments and most of them are due to cardiovascular problems.¹⁴

As shown, findings from opioid studies are conflicting due to the lack of controlling for other

substances in the analysis, and medical comorbidities from cocaine use lack specificity. Furthermore, opioid and/or cocaine use accompany multiple medical comorbidities. Therefore, the purposes of this research are as follows: first, identifying sets of medical comorbidities from sole opioid use; second, finding sets of medical comorbidities from sole cocaine use; and third, comparing significantly different medical comorbidities from opioid and cocaine use.

Methods

The data: The data was drawn from multiple hospitals in the United States. Data extraction was based on the International Classification of Diseases, 9th Revision (ICD-9). The data for this research consisted of year 2012 patient records, which were retrieved in 2016. This data extraction strategy was chosen for two reasons: first, medical comorbidities from substance misuse, such as opioids, do not differ with or without diabetes,^{17,18,43} and second, this strategy can prevent problems with model overfitting. If the total number of opioid and cocaine users were extracted, the number would be very large and would contribute to model overfitting.

The total number of retrieved diabetic patients' records (i.e., encounters) was 1038499. Among those records, only opioid user and outpatient records were filtered in, because opioids are legally used for pain control and inpatient opioid users will have many compounding factors such as surgeries or acute illness, and blood count will be influenced by their various procedures. The unit of analysis for association rule mining algorithm is transactions.⁴⁴ In this research context, the number of patients' hospital visits (not a unique patient) was the unit of analysis. The following example provides context for this unit of analysis: if a patient visited the hospital five times in 2012, the patient's records would be five. The logic for this unit of analysis is that when a patient goes back to the hospital, one can expect the patient's health to be improved (or deteriorated); the changes of health may result in a different lab result; however, if the lab results are the same for different visits, the finding will be filtered out because of redundancy. Among outpatient records, the total number of visits was 563816. The number of opioid and cocaine user

records totaled 21107: sole opioid users were 18046 and sole cocaine users were 3061. The combined users were not included in the analysis. All medical comorbidities in the database were included: a total of 1980 medical comorbidities. Opioid and cocaine use was based on urine tests at the time of the patients' hospital visits.

Association rule mining: Apriori association rule mining algorithm, a branch of data mining techniques, was the employed analytical strategy. This method is widely used when researchers attempt to discover a set of itemsets (comorbidity in this study) in a large dataset.⁴⁵ Often this method is referred to as market basket analysis, as it is widely used in the marketing field.⁴⁵ The following example illustrates the use of this method in marketing: marketers want to know what items customers are likely to co-purchase with milk. The expression for this association is written as {milk} \rightarrow {bread, butter}, and it is referred to as one association rule. Note that this relationship is an association, not a causal relationship. Here, marketers may only be interested in frequently co-occurring items (e.g., bread and milk); co-occurrence is measured by support level. The marketers may want to validate the strength of the co-occurrence; strength is measured by confidence level.⁴⁴ An itemset is the collection of purchased items for a specific market visit.⁴⁴ For example, if a customer visited a market and bought beer, diapers, and milk, these three items would be referred to as a 3-itemset for the transaction.

This analytical strategy has been used for medical comorbidity studies.⁴⁶⁻⁴⁸ This association rule strategy was applied to the current study to discover frequently co-appearing sets of medical comorbidities with opioid (or cocaine) use. As shown, apriori association rule mining uses support and confidence to filter frequently appearing candidate itemsets (comorbidities from opioid or cocaine). This is achieved through the following formulas:

$$\text{Support } (X \rightarrow Y) = \sigma(X \cup Y) / N$$

$$\text{Confidence } (X \rightarrow Y) = \sigma(X \cup Y) / \sigma(X)$$

N is the number of total transactions, X and Y are items, and σ is the sum. The support of an itemset measures the percentage of the transactions in the database that carries the itemset. The confidence of a rule measures

between two frequent itemsets, X and Y , and the strength of rule is measured by the percentage of the transactions that contain X that also contain Y .⁴⁴

The following example contextualizes the use of support and confidence:

A database recorded the cases of different kinds of medical comorbidities from opioid use. Researchers set the minimum support at 20% and minimum confidence at 80%. If the discovered rule obtained from the association rule mining algorithm is (opioid use) \rightarrow (high BP, high glucose), 20% of the cases recorded in the dataset contain both high BP and high glucose (support) with opioid use, and the probability to have high BP given high glucose (confidence) is a minimum of 80%.

This study further employed lift, the "interestedness" of a rule, to ensure validity of the finding.⁴⁵ Lift is the measure of how many times more often XX and YY occur together than would be expected if they were statistically independent. If the lift value is 1, items X and Y are independent (not associated); if the lift value is greater than 1, items X and Y have a positive association; and if the lift value is less than 1, items X and Y have a negative association.⁴⁵ For instance, if the finding includes (opioids) \Rightarrow (high BP, high glucose), the value of lift is "1," opioid use and high BP and high glucose are not associated. P represents percentage. The lift of X and Y can be measured by computing:

$$\text{Lift } (X, Y) = P(X \cup Y) / P(X)P(Y)$$

Analytical parameters: This dataset has 1980 possible medical comorbidities. The typical opioid user will have a very small fraction of medical comorbidities from those 1980; in other words, the support level is likely to be very low. Because data-driven research does not select variables based on hypothesis or pre-conceived knowledge in order to discover new knowledge, this strategy uses all the variables in the analysis. On the other hand, certain medical comorbidities associated with opioid use are highly likely to occur together (e.g., elevated BP); therefore, the confidence level can be set high. Accordingly, the pruning criterion for the confidence level is set to 80% and for the support level is 0.002%. Since the support level measures co-occurrence, it is common that the level is low when a lot of variables are in the analysis.⁴⁹

The pruning criteria of confidence and support levels can serve as validation. In addition to

pruning association rules, this study added the value of lift, which measures the quality of the discovered association rules. In this study, all discovered rules for the lift values were positively high (i.e., over 10). As such, the report is not included in tables 1 and 2.

As noted, substance users tend to use multiple drugs.²⁶ If analysis is performed without eliminating multiple substances, the finding will be confounded due to additive and synergistic effects. As such, examination of substances commonly co-used with opioids and cocaine is required in order to identify comorbidities only from opioids or cocaine.

Eliminating polydrug in the analysis: In order to minimize the effects from combined use of opioid and cocaine, this manuscript split the cases to sole opioid and sole cocaine user groups and ran analysis separately. First, the opioid records showed that the most frequently co-occurring substances used with opioids were BZD (44.09%), marijuana (19.73%), cocaine (7.65%), and alcohol (7.55%). As such, records associated with these substances were removed from the analysis. Second, the cocaine group analysis showed that tobacco records occupied 13.46% and opioid records were 8.65%; therefore, those records were removed from the cocaine group. Eliminating those drugs were expected to minimize confounding effects from combined use of opioid and cocaine. Using the support of 0.002% and the confidence of 80%, 7 association rules were discovered for the opioid group and 10 association rules were discovered for the cocaine group.

Results

Table 1 shows the sets of medical comorbidities likely to co-occur with opioid use. Left-hand side (LHS) means that this analysis is used only for

opioid records to discover associated medical comorbidities, which are displayed on the right-hand side (RHS). The relationship between LHS and RHS is an association, not a causal relationship.

Rule 1 indicates that individuals who use opioids are likely to have a set of [high diastolic BP (DBP), abnormal specific gravity], and its support level is 0.0071% and the confidence is 100%. As noted, support is extremely low because co-occurrence of [high DBP, abnormal specific gravity] out of the 1980 variables is low. When the creatine is less than 20, the lab automatically runs a specific gravity test as another measure of concentration.⁵⁰ If specific gravity is greater than 1.003 with creatine less than 20, it is reported as abnormal.⁵⁰ Rule 5 adds one more comorbidity, cough, to Rule 1. Coughing could be the result of opioids often being used to soothe coughing,^{51,52} or it could be the lack of oxygen due to kidney damage or reduced breathing.⁵³ This finding certainly addressed the conflicting findings of BPs. The use of opioids elevates BPs, but this study further discovered that it was DBP that caused more harm than systolic BP (SBP), in terms of accompanying other comorbidities.

Opioids must be excreted via the liver and kidneys; therefore, opioid users can experience organ damage. Rule 2 reveals that [low albumin, high lymphocyte, high BMI] are likely to co-occur. Low albumin could be a sign of liver and/or kidney issues,⁵⁴ and lymphocyte is a type of WBC that fights infection. Based on Rule 2, one can claim that the use of opioids is highly associated with kidney and liver diseases and high BMI. Rule 3 shows a set of [elevated HbA1c, cardiopulmonary] among opioid users. This discovered rule addresses the conflicting finding of HbA1c.

Table 1. Medical comorbidities from opioid use

Rule number	LHS	RHS	Support	Confidence
1	Opioid	High DBP, abnormal specific gravity	0.0071	1.00
2	Opioid	High BMI, low albumin, high lymphocyte	0.0070	1.00
3	Opioid	High HbA1c, cardiopulmonary	0.0052	1.00
4	Opioid	High BMI, low blood gas, low RDW	0.0022	0.80
5	Opioid	High DBP, abnormal specific gravity, cough	0.0020	1.00
6	Opioid	Low calcium, low HDL	0.0020	0.80
7	Opioid	Low BUN, high MPV, abnormal UA nitrate	0.0020	0.80

LHS: Left-hand side; RHS: Right-hand side; DBP: Diastolic blood pressure; BMI: Body mass index; HbA1c: Hemoglobin A1c; RDW: Red cell distribution width; HDL: High-density lipoprotein; BUN: Blood urea nitrogen; MPV: Mean platelet volume; UA: Urine analysis

Table 2. Medical comorbidities from cocaine use

Rule number	LHS	RHS	Support	Confidence
1	Cocaine	High CK, high BUN	0.0082	1.00
2	Cocaine	High SBP, high CK	0.0082	1.00
3	Cocaine	High DBP, low MCHC, shortness of breath	0.0080	1.00
4	Cocaine	Low lymphocyte, neurological problems, abnormal UA blood	0.0079	0.80
5	Cocaine	Low BUN, abnormal UA blood, high BNP	0.0056	0.80
6	Cocaine	High DBP, abnormal protein	0.0031	1.00
7	Cocaine	High CK, low hemoglobin	0.0020	1.00
8	Cocaine	High CK, cardiopulmonary, high anion gap	0.0020	1.00
9	Cocaine	High DBP, abnormal protein, night sweats	0.0020	0.80
10	Cocaine	High DBP, shortness of breath, high anion gap	0.0020	0.80

LHS: Left-hand side; RHS: Right-hand side; CK: Creatine kinase; BUN: Blood urea nitrogen; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MCHC: Mean corpuscular hemoglobin concentration; UA: Urine analysis; BNP: B-type natriuretic peptide

The use of opioids elevates HbA1c. As such, the conflicting finding might have been attributed to multidrug synergistic effects. This rule additionally reveals that elevated HbA1c and cardiopulmonary are likely to co-occur among opioid users.

Kidney damage from opioid use is further evidenced by Rules 4 and 7, in addition to Rules 1 and 2, in that the damaged kidney cannot properly make EPO, which is vital for RBC and the lack of RBC will lower blood gas. High values of mean platelet volume (MPV) and abnormal urine analysis (UA) nitrate are observed among patients with chronic kidney disease (CKD).⁵⁵ Kidney problems can be blamed for these medical comorbidities appearing in Rules 4 and 7. Rule 6 shows that opioid users are likely to have a set of [low calcium, low high-density lipoprotein (HDL)]. This may be attributable to the fact that opioid users tend to have poor diets.⁵⁶

While studies tend to treat SBP and DBP as one BP measure, finding of this study shows that DBP is specifically the one that accompanies other comorbidities. Damage to the kidneys could be responsible for low red cell distribution width (RDW) and high lymphocytes, as such damage would hinder production of RBCs and WBCs.³⁸ The present study did not find "respiratory depression," which commonly occurs among heavy opioid users. This may be due to the dataset being composed of outpatients, whose opioid use may not be at critical levels.

Medical comorbidities from cocaine use: Cocaine, as the representative illegal drug, creates a unique set of medical comorbidities. Table 2 shows the discovered rules for the sets of medical comorbidities among cocaine users. As with opioids, cocaine is metabolized in the kidneys and

liver, and the lung is the primary organ that processes cocaine. Accordingly, medical comorbidities will be associated with those organs.

The use of cocaine elevates BPs through coronary vasoconstriction and accelerated atherosclerosis which narrows and builds up plaque on the vessels.^{57,58} The narrowed vessels increase heart rate, cannot deliver oxygen sufficiently, and result in low carbon dioxide (CO₂). Also, the narrowed vessels will cause additional damage to the heart, liver, and kidneys. The act of smoking cocaine can exacerbate liver and lung problems.^{31,59}

The discovered rules are consistent with major organ damage; however, these findings offer specific medical comorbidities. Frequently appearing medical comorbidities due to kidney diseases include high BUN, high anion gap, abnormal protein, and abnormal UA blood. The comorbidities due to heart-related problems are cardiopulmonary, high CK, high B-type natriuretic peptide (BNP), shortness of breath, low Hb, and low mean corpuscular hemoglobin concentration (MCHC). Low BUN may be due to liver problems. Elevated BP might be associated with heart and/or kidney problems.

In table 2, Rule 1 shows that the use of cocaine damages the heart and kidney, which is commonly reported in existing studies. Rule 1 reveals specific medical comorbidities related to heart and kidney diseases which are [high CK, high BUN]. Coronary vasoconstriction and accelerated atherosclerosis from cocaine might have resulted in the comorbidities in Rules 2 and 3, because coronary vasoconstriction and accelerated atherosclerosis elevate BPs and reduce oxygen level (low MCHC), which causes shortness of breath and heart damages. While coronary vasoconstriction elevates

BPs, specific medical comorbidities associated with DBP and SBP are different.

Rule 4 proposes that opioid users are likely to have a set of {low lymphocyte, neurological problems, abnormal UA blood}. While not many studies have reported neurological problems from cocaine use, one study reported correlations between long-term cocaine use and neurological alteration.⁶⁰ The present study found that neurological problems frequently co-occur with low lymphocyte and abnormal UA blood. Low lymphocytes indicate low WBC that fight infections among opioid users with neurological and kidney issues. Rule 5 proposes that the use of cocaine frequently causes a set of {low BUN, abnormal UA blood, high BNP}. Low BUN can be derived from protein malnutrition or liver problems;^{54,61} abnormal UA blood can be from liver and/or kidney problems,⁶² and high BNP can be attributed to heart problems.

Rules 6 and 9 further give evidence to the relationship between the use of cocaine and kidney damages. Cocaine-induced renal infarction can cause night sweats.^{39,40} The sets of medical comorbidities discovered in Rules 7, 8, and 10 are associated with heart and kidney problems, which are highly correlated with elevated BPs. As noted, heart problems can increase oxygen demand by increasing heart rate and BP,^{15,41} which is captured in these three rules. Also, high anion gap can be derived from damaged kidney.⁶³

While existing studies reported organ damage from coronary vasoconstriction and associated medical comorbidities, this finding further identified specific medical comorbidities. Also, very few studies have reported low MCHC, night sweats, and neurological problems. Another finding, which differs from existing studies, is that elevated SBP and DBP have been inconsistent. For example, some studies reported that cocaine users had both elevated SBP and DBP compared to non-users,⁵⁷ while some other studies reported that only SBP was elevated with no significant difference with DBP between the control and cocaine-user groups.⁵⁸ The findings of the present study showed that the use of cocaine elevated BPs, but the medical comorbidities associated with DBP and SBP were different.

Discussion

The use of either opioids or cocaine harms organs;

however, the sets of medical comorbidities from these legal and illegal drugs are very different. A notable difference between the two is that opioid users have high BMI and DBP, low HDL, and kidney-related diseases. These findings address some of the conflicting findings of existing studies such as elevated BPs, HbA1c, and BMI. Interestingly, the pruned rules did not include SBP. Some studies reported low HDL and low calcium, while others did not. The findings of this study showed that the use of opioids was associated with both low HDL and low calcium.

The use of cocaine clearly elevates BPs and shows strong evidence of damaging the major organs such as the kidney, heart, and liver, more so than the use of opioids. Also, elevated SBP and DBP accompany different medical comorbidities. Consequently, these two BPs should be investigated as different independent variables rather than treating as one BP.

Based on the findings, major organ damage from cocaine use is more serious than that of opioid use. One can surmise that this is because opioids are legal drugs and administered by doctors, while cocaine is an illegal drug that users take without supervision. Given the serious organ damage from cocaine use, it is important to consider the impacts of cocaine when it comes to enforcing PDMPs.

Conclusion

The findings of the current study contribute to the field in the following ways: first, by eliminating polydrug use in the analysis, this research attempted to discover medical comorbidities solely derived from opioid or cocaine use. The finding shows that opioid use is associated with elevated DBP and BMI, and lowered calcium and HDL. As such, existing studies' conflicting findings might have been attributed to the lack of eliminating multidrug use records in the analysis. For cocaine use, existing studies reported that cocaine use would damage the major organs. Indeed this study confirmed the claim, but further still this study discovered specific medical comorbidities associated with cocaine use and discovered that SBP and DBP were associated with different medical comorbidities; second, this study discovered frequently appearing sets of medical comorbidities, which could assist evidence-based treatment for simultaneously co-

occurring medical comorbidities; and third, this research compared medical comorbidities derived from opioid and cocaine use; such comparison can assist policy makers by informing them about different sets of medical problems when PDMPs are enforced.

Limitations: The limitations of this study were as follows: first, this study chose the most popular legal and illegal drugs to compare medical comorbidities. Future studies are recommended to compare legal opioids with illegal opioids (e.g., heroin, fentanyl, other synthetic opioid drugs); second, this study used all population groups for analysis; however, different ethnic and socioeconomic groups differ in the amount and types of substances used, so the investigation of subgroup populations is recommended; third, this study's dataset was cross-sectional; some of the organ damage can take longer time to be associated with opioid (or cocaine) use. Also, some patients might have prior medical conditions. As such, it is recommended to use sequential association rule mining alongside association rule mining.

References

1. Substance Abuse and Mental Health Services Administration. SAMHSA/HHS: An Update on the Opioid Crisis [Online]. [cited 2018 Mar 14]; Available from: URL: https://www.samhsa.gov/sites/default/files/aatod_2018_final.pdf
2. Haffajee RL, Jena AB, Weiner SG. Mandatory use of prescription drug monitoring programs. *JAMA* 2015; 313(9): 891-2.
3. U.S. Department of Justice, Drug Enforcement Administration. State Prescription Drug Monitoring Programs [Online]. [cited 2016 Jun]; Available from: URL: https://www.deadiversion.usdoj.gov/faq/rx_monitor.htm#4
4. Raymond J, Bryant M. In Search of New Ways to Tame Opioid Crisis. *Alva Review-Courier* [Online]. [cited 2017 Sep 17]; Available from: URL: <https://www.alvareviewcourier.com/story/2017/09/17/regional/in-search-of-new-ways-to-tame-opioid-crisis/20690.html>
5. Oklahoma Attorney General. The Oklahoma Commission on Opioid Abuse Final Report [Online]. [cited 2018 Jan 23]; Available from: URL: <http://www.oag.ok.gov/Websites/oag/images/Oklahoma%20Commission%20on%20Opioid%20Abuse%20Final%20Report.pdf>
6. Cicero TJ, Kurtz SP, Surratt HL, Ibanez GE, Ellis MS, Levi-Minzi MA, et al. Multiple determinants of specific modes of prescription opioid diversion. *J Drug Issues* 2011; 41(2): 283-304.
7. Inciardi JA, Surratt HL, Lugo Y, Cicero TJ. The diversion of prescription opioid analgesics. *Law Enforc Exec Forum* 2007; 7(7): 127-41.
8. Oklahoma Bureau of Narcotics and Dangerous Drugs. 2018 Oklahoma Drug Threat Assessment [Online]. [cited 2018 Sep 12]; Available from: URL: <https://www.ok.gov/obndd/documents/Oklahoma%20Drug%20Threat%20Assessment%202018%20FINAL.pdf?fbclid=IwAR2gb1u5vnscBpONc0acP8Eu4HEq7-BZb9leu2IUVymhbimEbegqKIZFE0M>
9. McCall JC, Baldwin GT, Compton WM. Recent increases in cocaine-related overdose deaths and the role of opioids. *Am J Public Health* 2017; 107(3): 430-2.
10. Muhuri PK, Gfroerer JC, Davies MC. Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States [Online]. [cited 2013 Aug]; Available from: URL: <https://www.samhsa.gov/data/sites/default/files/DR006/DR006/nonmedical-pain-reliever-use-2013.htm>
11. Addiction Center. Polydrug Use [Online]. [cited

Conflict of Interests

The Authors have no conflict of interest.

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Authors' Contribution

YM K, organized study, collected the data, performed statistical analysis, literature review, wrote the first draft of the article, writing the final draft of manuscript, and overseeing the final writing and editing of the manuscript.

- 2018 Sep 4]; Available from: URL: <https://www.addictioncenter.com/addiction/polydrug-use/>
12. Havens JR, Lofwall MR, Frost SD, Oser CB, Leukefeld CG, Crosby RA. Individual and network factors associated with prevalent hepatitis C infection among rural Appalachian injection drug users. *Am J Public Health* 2013; 103(1): e44-e52.
 13. Vickerman P, Hickman M, May M, Kretzschmar M, Wiessing L. Can hepatitis C virus prevalence be used as a measure of injection-related human immunodeficiency virus risk in populations of injecting drug users? An ecological analysis. *Addiction* 2010; 105(2): 311-8.
 14. Havakuk O, Rezkalla SH, Kloner RA. The cardiovascular effects of cocaine. *J Am Coll Cardiol* 2017; 70(1): 101-13.
 15. Schwartz BG, Rezkalla S, Kloner RA. Cardiovascular effects of cocaine. *Circulation* 2010; 122(24): 2558-69.
 16. Mallappallil M, Sabu J, Friedman EA, Salifu M. What do we know about opioids and the kidney? *Int J Mol Sci* 2017; 18(1).
 17. Bayani M, Nazemi S, Khosroosiniaki M, Ramezani M, Khani A. Opium consumption and lipid and glucose parameters in diabetic patients with acute coronary syndrome: A survey in northern Iran. *Tunis Med* 2014; 92(7): 497-500.
 18. Sanli DB, Bilici R, Suner O, Citak S, Kartkaya K, Mutlu FS. Effect of different psychoactive substances on serum biochemical parameters. *Int J High Risk Behav Addict* 2015; 4(2): e22702.
 19. Rahimi N, Gozashti MH, Najafipour H, Shokoohi M, Marefati H. Potential effect of opium consumption on controlling diabetes and some cardiovascular risk factors in diabetic patients. *Addict Health* 2014; 6(1-2): 1-6.
 20. Roohafza H, Talaei M, Sadeghi M, Haghani P, Shokouh P, Sarrafzadegan N. Opium decreases the age at myocardial infarction and sudden cardiac death: A long- and short-term outcome evaluation. *Arch Iran Med* 2013; 16(3): 154-60.
 21. Gautam S, Franzini L, Mikhail OI, Chan W, Turner BJ. Longitudinal analysis of opioid analgesic dose and diabetes quality of care measures. *Pain Med* 2015; 16(11): 2134-41.
 22. Rose AJ, Hermos JA, Frayne SM, Pogach LM, Berlowitz DR, Miller DR. Does opioid therapy affect quality of care for diabetes mellitus? *Am J Manag Care* 2009; 15(4): 217-24.
 23. Mysels DJ, Sullivan MA. The relationship between opioid and sugar intake: review of evidence and clinical applications. *J Opioid Manag* 2010; 6(6): 445-52.
 24. Haghpanah T, Afarinesh M, Divsalar K. A review on hematological factors in opioid-dependent people (opium and heroin) after the withdrawal period. *Addict Health* 2010; 2(1-2): 9-16.
 25. Shahabinejad G, Sirati-Sabet M, Kazemi-Arababadi M, Nabati S, Asadikaram G. Effects of opium addiction and cigarette smoking on hematological parameters. *Addict Health* 2016; 8(3): 179-85.
 26. Leeman RF, Sun Q, Bogart D, Beseler CL, Sofuoglu M. Comparisons of cocaine-only, opioid-only, and users of both substances in the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *Subst Use Misuse* 2016; 51(5): 553-64.
 27. Novick T, Liu Y, Alvanzo A, Zonderman AB, Evans MK, Crews DC. Lifetime cocaine and opiate use and chronic kidney disease. *Am J Nephrol* 2016; 44(6): 447-53.
 28. Asgary S, Sarrafzadegan N, Naderi GA, Rozbehani R. Effect of opium addiction on new and traditional cardiovascular risk factors: do duration of addiction and route of administration matter? *Lipids Health Dis* 2008; 7: 42.
 29. Gudin JA, Mogali S, Jones JD, Comer SD. Risks, management, and monitoring of combination opioid, benzodiazepines, and/or alcohol use. *Postgrad Med* 2013; 125(4): 115-30.
 30. Bellum S. Real Teens Ask About Speedballs [Online]. [cited 2013 Jun 26]; Available from: URL: <https://teens.drugabuse.gov/blog/post/real-teens-ask-about-speedballs>
 31. Antai-Otong D. Medical Complications of cocaine addiction: clinical implications for nursing practice. *J Addict Nurs* 2006; 17(4): 215-25.
 32. Churchwell MD, Mueller BA. Selected pharmacokinetic issues in patients with chronic kidney disease. *Blood Purif* 2007; 25(1): 133-8.
 33. Steele MR, Belostotsky V, Lau KK. The dangers of substance abuse in adolescents with chronic kidney disease: a review of the literature. *CANNT J* 2012; 22(1): 15-22.
 34. Edmondson DA, Towne JB, Foley DW, Abu-Hajir M, Kochar MS. Cocaine-induced renal artery dissection and thrombosis leading to renal infarction. *WMJ* 2004; 103(7): 66-9.
 35. Weber JE, Chudnofsky CR, Boczar M, Boyer EW, Wilkerson MD, Hollander JE. Cocaine-associated chest pain: how common is myocardial infarction? *Acad Emerg Med* 2000; 7(8): 873-7.
 36. National Kidney Foundation. Anemia and Chronic Kidney Disease [Online]. [cited 2015]; Available from: URL: www.kidney.org/atoz/content/what_anemia_ckd
 37. Norris KC, Thornhill-Joynes M, Robinson C, Strickland T, Alpers BL, Witana SC, et al. Cocaine use, hypertension, and end-stage renal

- disease. *Am J Kidney Dis* 2001; 38(3): 523-8.
38. Kim YM, Kathuria P, Delen D. Uncovering different CKD-related medical issues among African American gender groups using Apriori. In: Hawamdeh S, Allen J, Alemneh D, editors. Knowledge discovery and data design innovation: Proceedings of the International Conference on Knowledge Management (ICKM 2017) (Innovation and Knowledge Management). River Edge, NJ: World Scientific Publishing Company; 2017. p. 27-45.
 39. Bemanian S, Motallebi M, Nosrati SM. Cocaine-induced renal infarction: Report of a case and review of the literature. *BMC Nephrology* 2005; 6: 10.
 40. Draper JC, McCance-Katz EF. Medical illness and comorbidities in drug users: implications for addiction pharmacotherapy treatment. *Subst Use Misuse* 2005; 40(13-14): 1899-8.
 41. Garg S, Hoenig M, Edwards EM, Bliss C, Heeren T, Tumilty S, et al. Incidence and predictors of acute kidney injury in an urban cohort of subjects with HIV and hepatitis C virus coinfection. *AIDS Patient Care STDS* 2011; 25(3): 135-41.
 42. McCord J, Jneid H, Hollander JE, de Lemos JA, Cercek B, Hsue P, et al. Management of cocaine-associated chest pain and myocardial infarction: A scientific statement from the American Heart Association Acute Cardiac Care Committee of the Council on Clinical Cardiology. *Circulation* 2008; 117(14): 1897-907.
 43. Najafipour H, Beik A. The impact of opium consumption on blood glucose, serum lipids and blood pressure, and related mechanisms. *Front Physiol* 2016; 7: 436.
 44. Tan P, Steinbach M, Kumar V. 1st ed. Introduction to data mining. Boston, MA: Pearson; 2005.
 45. Han J, Kamber M, Pei J. Data mining: Concepts and techniques. 3rd ed. San Francisco, CA: Morgan Kaufmann; 2012.
 46. Shen CC, Hu LY, Hu YH. Comorbidity study of borderline personality disorder: applying association rule mining to the Taiwan national health insurance research database. *BMC Med Inform Decis Mak* 2017; 17(1): 8.
 47. Huang YC. Mining association rules between abnormal health examination results and outpatient medical records. *Health Inf Manag J* 2013; 42(2): 23-30.
 48. Pattanaprteep O, McEvoy M, Attia J, Thakkinstian A. Evaluation of rational nonsteroidal anti-inflammatory drugs and gastro-protective agents use; association rule data mining using outpatient prescription patterns. *BMC Med Inform Decis Mak* 2017; 17(1): 96.
 49. McNicholas PD, Murphy TB, O'Regan M. Standardising the lift of an association rule. *Comput Stat Data Anal* 2008; 52(10): 4712-21.
 50. National Council of State Boards of Nursing. Toxicology 101: A Quick Reference Guide [Online]. [cited 2018]; Available from: URL: https://www.ncsbn.org/2018DCM_BLubin.pdf
 51. Marks S, Rosielle DA. Opioids for cough #199. *J Palliat Med* 2010; 13(6): 769-70.
 52. Morice AH, Menon MS, Mulrennan SA, Everett CF, Wright C, Jackson J, et al. Opiate therapy in chronic cough. *Am J Respir Crit Care Med* 2007; 175(4): 312-5.
 53. Perper JA, Van Thiel DH. Respiratory complications of cocaine abuse. *Recent Dev Alcohol* 1992; 10: 363-77.
 54. Skluzacek PA, Szewc RG, Nolan CR 3rd, Riley DJ, Lee S, Pergola PE. Prediction of GFR in liver transplant candidates. *Am J Kidney Dis* 2003; 42(6): 1169-76.
 55. Verdoia M, Barbieri L, Schaffer A, Bellomo G, Marino P, De LG. Impact of renal function on mean platelet volume and its relationship with coronary artery disease: A single-centre cohort study. *Thromb Res* 2016; 141: 139-44.
 56. Nabipour S, Ayu SM, Hussain HM. Burden and nutritional deficiencies in opiate addiction-systematic review article. *Iran J Public Health* 2014; 43(8): 1022-32.
 57. Akkina SK, Ricardo AC, Patel A, Das A, Bazzano LA, Brecklin C, et al. Illicit drug use, hypertension, and chronic kidney disease in the US adult population. *Transl Res* 2012; 160(6): 391-8.
 58. Kozor R, Grieve SM, Buchholz S, Kaye S, Darke S, Bhindi R, et al. Regular cocaine use is associated with increased systolic blood pressure, aortic stiffness and left ventricular mass in young otherwise healthy individuals. *PLoS One* 2014; 9(4): e89710.
 59. Ali SR, Krugar M, Houghton J. Upper airway obstruction and acute lung injury associated with cocaine abuse. *Int J Clin Pract* 2002; 56(6): 484-5.
 60. Buttner A. Neuropathological alterations in cocaine abuse. *Curr Med Chem* 2012; 19(33): 5597-600.
 61. Hosten AO. BUN and creatinine. In: Walker HK, Hall WD, Hurst JW, editors. Clinical methods: The history, physical, and laboratory examinations. 3rd ed. Boston, MA: Butterworths; 1990. p. 874-78.
 62. Medicine Plus. Blood in Urine: How do You Test for Blood in Urine? [Online]. [cited 2019 Apr 15]; Available from: URL: <https://medlineplus.gov/lab-tests/blood-in-urine/>
 63. Brubaker RH, Meseeha M. High anion gap metabolic acidosis. *StatPearls* [Online]. [cited 2019 Jun 4]; Available from: URL: <https://www.ncbi.nlm.nih.gov/books/NBK448090/>

مقایسه اختلالات همراه بین مصرف‌کنندگان مواد مخدر و مصرف‌کنندگان کوکائین:

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مقاله پژوهشی

چکیده

مقدمه: برنامه‌های کنترل داروهای تجویزی در کنترل سوء مصرف مواد مخدر سودمند هستند، اما مصرف‌کنندگان مواد مخدر به استفاده از کوکائین روی آورده‌اند که این امر مجموعه متفاوتی از مشکلات پزشکی را ایجاد کرده است. در حالی که مصرف مواد مخدر منجر به بروز اختلالات پزشکی متعددی می‌شود، نتایج مطالعات موجود نه فقط مجموعه‌ای از بیماری‌ها، بلکه اختلالات همراه را نشان می‌دهد. همچنین، این نتایج اغلب به علت عدم کنترل مواد دیگر در تحلیل به ویژه زمانی که استفاده ترکیبی از مواد اثر هم‌افزایی ایجاد می‌کند، متناقض می‌باشد. از سوی دیگر، یافته‌های مربوط به مصرف کوکائین به طور عمده مشکلات کلیوی و قلبی را ایجاد می‌کند که اختصاصی نیست. از آنجایی که اختلالات همراه ناشی از مصرف مواد مخدر و کوکائین بسیار متفاوت هستند، بررسی این اختلالات پزشکی برای به حداقل رساندن تأثیرات منفی ناشی از برنامه‌های کنترل داروهای تجویزی ضروری به نظر می‌رسد. از این رو، پژوهش حاضر با هدف کشف و تحلیل مجموعه‌ای از اختلالات همراه ناشی از مصرف مواد مخدر و کوکائین با کنترل مواد دیگر انجام شد.

روش‌ها: از روش داده‌کاوی و الگوریتم کاوش قانون وابستگی، برای کشف مجموعه‌ای از اختلالات همراه با استفاده از سوابق پزشکی الکترونیکی استفاده شد. این روش برای کشف اختلالات پزشکی که هم‌زمان با هم اتفاق می‌افتد، مناسب است.

یافته‌ها: استفاده از مواد مخدر با مجموعه‌ای از علائم (فشار خون دیاستولیک بالا، چگالی نسبی غیر طبیعی) و (شاخص توده بدنی بالا و گاز خون پایین) همراه بود. مصرف کوکائین با علائمی مانند کراتین کیناز بالا، نیتروژن اوره خون بالا و کراتین کیناز بالا، مشکلات قلبی-ریوی ارتباط داشت.

نتیجه‌گیری: نتایج به دست آمده برخی یافته‌های متناقض را با حذف چندین ماده مخدر بررسی می‌کند و مجموعه‌ای از اختلالات همراه ناشی از مصرف مخدر و کوکائین را گزارش می‌دهد.

واژگان کلیدی: کوکائین، داده‌کاوی، مدارک الکترونیک سلامت، اختلالات همراه، مواد مخدر

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