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The association between regular cocaine use, with and without tobacco co-use, and adverse cardiovascular and respiratory outcomes

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Abstract

Background: Understanding the potential impact of cocaine use on health is increasingly important as cocaine use rises in the U.S.

Objectives: This study evaluated the associations of regular cocaine use, with and without tobacco co-use, with cardiovascular and respiratory outcomes.

Methods: Analysis of a limited dataset obtained through IBM Watson Health Explorys, a platform integrating electronic health record data. Matched controls were defined for: 1) cocaine-using patients (n=8,244; 44% female); and subgroups of cocaine-using patients: 2) with an encounter diagnosis for tobacco use disorder (TUD; n=4,706); and 3) without a TUD diagnosis

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Contributors

TW, JT, DCK, and DL contributed to the conception or design of the work. TW, JT, DCK, and DL contributed to the acquisition, analysis, or interpretation of data for the work. TW drafted the manuscript. TW, JT, DCK, and DL critically revised the manuscript. All authors contributed to and have approved the final manuscript.

Author Disclosure for: *The association between regular cocaine use, with and without tobacco co-use, and adverse cardiovascular and respiratory outcomes*

Conflict of Interest

TW, JT, and DL declare no conflicts of interest. DCK is the Chief Medical Informatics Officer of the MetroHealth System. In exchange for contributing de-identified data to the Explorys network, the MetroHealth System receives access to the Explorys Cohort Discovery tool, which was used to conduct this study. Neither DCK nor the MetroHealth System have any direct financial ties to Explorys (IBM Watson Health).

(non-TUD; n=3,538). Patients had at least one documented medical evaluation in the MetroHealth System (Cleveland, Ohio). Cocaine-using patients had an encounter diagnosis of cocaine abuse/dependence and/or ≥2 cocaine-positive drug screens. Control patients, with no documented cocaine-use, were matched to the cocaine-using patients on demographics, residential zip code median income, body mass index, and, for the total sample, TUD-status. Outcomes were encounter diagnosis (yes/no) of cerebrovascular accident, heart arrhythmia, myocardial infarction, subarachnoid hemorrhage, asthma, chronic obstructive pulmonary disease (COPD), pneumonia, and all-cause mortality.

Results: TUD-patients had the greatest prevalence of cardiovascular and respiratory disease, regardless of cocaine-use indication. In the total sample, TUD, and non-TUD subgroups, regular cocaine use was significantly associated with greater risk for cerebrovascular accident, arrhythmia, myocardial infarction, asthma, COPD, pneumonia and mortality.

Conclusions: Cocaine use is associated with significantly greater risk of adverse cardiovascular and respiratory diagnoses and all-cause mortality.

Keywords

Cocaine; cardiovascular; respiratory; electronic health record (EHR); mortality

1. INTRODUCTION

Heart disease is the leading cause of death in the U.S. (Xu et al., 2018), and respiratory diseases, including asthma (Centers for Disease Control and Prevention, 2018), chronic obstructive pulmonary disease (COPD) (Heron, 2018; World Health Organization, 2018), and pneumonia (Heron, 2018; World Health Organization, 2018) account for significant morbidity and mortality. Cocaine use and cocaine use disorder (CocUD) has increased significantly in the U.S. in recent years (John and Wu, 2017; Kerridge et al., 2019). In 2018, approximately 1.9 million Americans ≥12 years of age used cocaine within the past month, and approximately 977,000 had a CocUD in the prior year (Substance Abuse and Mental Health Services Administration, 2019). Although harmful cardiovascular and respiratory health effects of cocaine are widely recognized (Havakuk et al., 2017; Tseng et al., 2014), reviews on the topic acknowledge important weaknesses with existing clinical research literature. These weaknesses include: use of samples that are less likely to show cocaine-induced harm (e.g., small samples, younger participants, infrequent cocaine users); cross-sectional rather than longitudinal data collection; reliance on self-reported cocaine use; and failure to adjust for important confounders, such as tobacco use (Degenhardt et al., 2011; Havakuk et al., 2017; Sordo et al., 2014; Tashkin, 2001; Tseng et al., 2014). The latter is of importance since tobacco smoking is a primary cause of cardiovascular and respiratory disease (Banks et al., 2019; U.S. Department of Health and Human Services, 2010) and there is a high prevalence of tobacco smoking among people with CocUD with estimates of 56–70% (Liu et al., 2019; Parker et al., 2019).

Given the burden of cardiovascular and respiratory disease and recent increases in cocaine use, the present study evaluated the association between regular cocaine use, with and without tobacco co-use, and cardiovascular and respiratory outcomes using a method that

addresses many of the limitations of past research (Winhusen et al., 2019). This approach included using electronic health record (EHR) data, rather than self-report measures, of cocaine use and adverse outcomes, use of a multi-year dataset, which allows detection of effects that may take several years to develop, large sample sizes, and the use of rigorous matching and analytic procedures to control for potential confounding factors (e.g., age, race, ethnicity, socioeconomic status, other substance use, etc.). We predicted that a positive association would be found between regular cocaine use, with or without tobacco-co-use, and adverse outcomes.

2. METHODS

2.1 Setting

The study data were derived from the Explorys (IBM Watson Health; Cleveland, OH) technology platform, which utilizes a health data gateway server behind the firewall of each participating healthcare organization. The server collects data from a variety of health information systems (e.g., EHR, billing systems, lab/tests systems, etc.). The data are then de-identified and passed into the Explorys data grid, which is a private cloud-based data store, and are standardized and normalized (Kaelber et al., 2012). The Explorys dataset has been validated in past research (Kaelber et al., 2012; Pfefferle et al., 2014). Our analytic approach, in which substance-using patients are “matched” to patients without evidence of substance use to decrease the possibility of study confounds (Winhusen et al., 2019), requires individual patient-level data, available to us as a limited dataset derived from the MetroHealth System Explorys dataset. MetroHealth is an integrated healthcare system in Northeast Ohio that consists of one tertiary care academic medical center, four emergency departments, and over 24 ambulatory clinics, seeing approximately 25,000 inpatients per year, with over 1.2 million outpatient visits annually. A data use agreement between the MetroHealth System and the University of Cincinnati (UC) was established to allow the use of limited datasets. This study was deemed not to be human subjects research by the UC institutional review board.

2.2 Study Population

The Explorys Cohort Discovery tool was used to identify adult patients (age ≥18) in the MetroHealth System who received a medical evaluation as evidenced by having at least one recorded blood pressure measurement and at least one blood chemistry lab result. At the time of Explorys query, the MetroHealth System included 426,112 patients meeting these criteria and covered the years of 1999–2018.

2.2.1 Cocaine-use group—The a priori definition of the cocaine-using group, which was designed to identify regular cocaine users, was patients having: 1) at least one encounter diagnosis code for cocaine abuse or dependence (see Supplement, Table S1 for ICD-9/10 codes), indicating CocUD; and/or 2) at least two cocaine-positive drug screens. The rationale for this definition is that having at least one CocUD diagnosis suggests that the patient has experienced a period of regular cocaine use. On the other hand, a single cocaine-positive drug screen could occur for an infrequent cocaine user. Our consensus was that two or more such positive results are indicative of regular use (i.e., on multiple separate

occasions, a clinician ordered this testing to be done, and it was positive at least twice). The cocaine-use group included 8,244 patients. To further elucidate the potential impact of cocaine use, with and without tobacco use, the cocaine-using group was divided into patients who had at least one encounter diagnosis code for tobacco use disorder or nicotine dependence (see Supplement, Table S1 for ICD-9/10 codes), referred to as the tobacco use disorder (TUD) subgroup (n=4,706) and patients who did not have any TUD encounter diagnoses, referred to as the non-TUD subgroup (n=3,538).

2.2.2 Control groups—For each of the three groups (total sample, TUD subgroup, non-TUD subgroup), a control group was identified. To be included as a potential control participant, a patient could not have any encounter diagnoses with a cocaine-related ICD-9/10 code and could not have any cocaine-positive drug screen results; 3,261 patients had a single cocaine-positive drug screen result and were thus excluded. In accordance with our prior research with cocaine-using cohorts (Winhusen et al., 2019), we excluded an additional 403 patients with other encounter diagnosis ICD codes indicating stimulant (e.g., amphetamine) use disorder from selection into the control group. The potential control group included 414,204 patients. Because cocaine-using patients may differ from patients without evidence of cocaine use on a variety of factors that could impact cardiovascular health, we created a control group that was matched to the cocaine-use group. Matching variables included: age, sex, race, ethnicity, median income of zip code of residence, and average body mass index (BMI), and, for the total sample, TUD status (yes/no).

The Ohio Valley Node (OVN) matching programs, which are SAS macros (version 9.4; Cary, NC) created by one of the authors (DL), were used; they are open-source and can be used free of charge (Winhusen et al., 2019). The OVN matching program uses Mahalanobis Distance within Propensity Score Calipers as the distance measure (Hintze, 2007) and allows for two matching methods: “optimal” and “greedy”. For this study, we utilized optimal 1:1 matching, which matches patients from the cohort of interest (e.g., cocaine-use group) to respective control patients so as to minimize the sum of the distances over all pairs (Stuart, 2010).

2.3 Cardiovascular and Respiratory Outcomes

The cardiovascular and respiratory outcomes were selected a priori and defined by ICD-9/10 encounter diagnoses. Four cardiovascular outcomes were evaluated: 1) cerebrovascular accident; 2) heart arrhythmia; 3) myocardial infarction; and 4) subarachnoid hemorrhage. Three respiratory outcomes were evaluated: 1) asthma; 2) chronic obstructive pulmonary disease (COPD); and 3) pneumonia. The ICD-9/10 codes used for each outcome, along with the number of patients having each code, are provided in the supplementary material (Table S2). While the data are correlational in nature (i.e., patients are not randomized to cocaine-use and control groups), our approach helped to ensure that the outcome encounter diagnoses occurred after the patient’s first indication of cocaine use (i.e., either CocUD diagnosis or cocaine-positive drug screen) and, thus, that cocaine use could have played a role in developing the condition. To this end, patients were scored as: 1) positive for the condition if the initial outcome encounter diagnosis date was later than the initial cocaine-use indication date (controls were assessed using the age-corrected initial cocaine-use

indication date of their respective matched cocaine-use patient); 2) negative for the condition if they did not have the outcome encounter diagnosis; or 3) missing if the initial outcome encounter diagnosis date was not later than the initial cocaine-use indication date. The rationale for using the missing code is based on the potential for patients to have a condition prior to it being entered into the EHR. For example, a patient could be using cocaine for years before a drug screen is completed. Hence, there is no way to ascertain whether an outcome diagnosis preceding the initial cocaine-use indication date reflects the outcome actually preceding the patient using cocaine or simply reflects the outcome diagnosis preceding the cocaine-use indication being added to the EHR. The missing code reflects the unknown temporal relationship.

2.4 All-Cause Mortality

Social Security Death Index data are linked to Explorys patient information, and the Explorys system provides a patient's year of death, if applicable. Mortality, unlike the morbidity outcomes described above, does not have the potential problems of temporal order (i.e., if a patient has died, we presume that all the encounter diagnoses of interest were made prior to the death). Patients with no indication of death were assumed to be alive at the time of data retrieval.

2.5 Data Analysis

All analyses were completed using SAS, Version 9.4. Statistical tests were defined a priori and were conducted at an α level of 0.05 (two-tail) for all measures. Logistic generalized mixed-model regressions (with a random effect to account for matched patient pairs) were used to evaluate whether cocaine-using status was significantly associated with each of the outcomes. For each planned regression, all possible models (i.e., all combinations of covariates) were estimated. The covariates considered for inclusion were other substance use disorders (opioid, cannabis, and alcohol; see Supplement, Table S3 for ICD 9/10 codes) and the matching covariates; the variable indicating cocaine-use group vs. control group was included in all models. The model with the covariates resulting in the best corrected Akaike Information Criterion (AIC-C) was selected; Tables S4–S6 list the covariates included in each regression. The proportion of data coded as missing (i.e., when initial outcome encounter diagnosis date was not later than the initial cocaine-use indication date) ranged from a minimum of 0.4% (subarachnoid hemorrhage) to 10.1% (asthma). The median proportion of missing data was 4.7%.

3. RESULTS

As can be seen in Table 1, the matching procedure created very comparable matched groups, with no significant difference on demographics. Table 2 displays the results of the comparisons between the cocaine-use group and its matched control for each of the evaluated outcomes. The crude odds ratio (OR) results were yielded by the comparison of the cocaine-use group with its matched control without controlling for additional variables (i.e., other substance use disorders including opioid, cocaine and alcohol; time since the earliest observation/diagnosis in the EHR; and demographics including age, sex, race, ethnicity, median income of zip code of residence, and BMI). The adjusted odds ratio (aOR)

reflects the results from a logistic regression comparing the cocaine-use group with its matched control using AIC-C to determine inclusion of additional variables. Discrepancies between the OR and aOR results may reflect the more precise control provided by the logistic regression analysis and/or may reflect complicating factors such as the relatively low prevalence of an outcome and the number of variables selected by AIC-C in the statistical model. The most conservative interpretation of the findings is to consider a cocaine-use-control group comparison to be significant based on the results of the logistic regression (i.e., as indicated by the aOR column in Tables 2 and 3) and to judge the degree to which the difference is clinically meaningful based on the aOR or crude OR value, whichever is closer to 1.0 (shaded in Tables 2 and 3); the summary of findings in this section reflects this conservative approach.

3.1 Total Sample

3.1.1 Characteristics—The total sample was approximately 56% male and 51% African American, and participants were a mean age of 53 years. The average number of years of EHR data available for all patients was 17.0 years (SD=9.3). The average number of years of EHR data available following initial cocaine-use indication was 8.9 (SD=5.5) in the cocaine-use patients. The prevalence of a cocaine use disorder (CocUD) encounter diagnosis within the cocaine-use group was 86.6%; the remainder of the cocaine-use group met the cocaine-positive drug screen criterion described in Methods.

3.1.2 Outcomes—Table 2 provides the total sample logistic regression results for cardiovascular outcomes, which revealed significantly higher prevalence in the cocaine-use, compared to control, group for cerebrovascular accident (3.6% vs. 2.4%, OR=1.53 (1.27 – 1.84)), heart arrhythmia (26.6% vs. 18.1%, aOR=1.26 (1.15 – 1.38)), and myocardial infarction (3.1% vs. 2.0%, OR=1.58 (1.30 – 1.94)). There was no significant difference in prevalence of subarachnoid hemorrhage (0.6% vs. 0.5%. aOR=1.14 (0.50 – 2.59)). The regression results revealed significantly higher prevalence of all-cause mortality in the cocaine-use, compared to control, group (8.5% vs. 5.3%, OR=1.66 (1.47 – 1.88)).

Table 3 provides the total sample logistic regression results for respiratory outcomes, which revealed significantly higher prevalence in the cocaine-use, compared to control, group for asthma (11.8% vs. 8.2%, OR=1.49 (1.34 – 1.66)), COPD (14.1% vs. 9.3%, OR=1.61 (1.46 – 1.78)), and pneumonia (9.5% vs. 5.5%, OR=1.79 (1.58 – 2.02)).

3.2 TUD Subgroup

3.2.1 Characteristics—The TUD subgroup was approximately 53% male and 52% African American, and participants were a mean age of 54 years. The average number of years of EHR data available for TUD patients was 17.9 years (SD=9.4). The average number of years of EHR data available following initial cocaine-use indication was 8.7 (SD=5.4) in the cocaine-use patients. The prevalence of a CocUD encounter diagnosis within the cocaine-using TUD subgroup was 88.6%.

3.2.2 Outcomes—Table 2 provides the TUD subgroup logistic regression results for cardiovascular outcomes, which revealed significantly higher prevalence in the cocaine-use,

compared to control, group for cerebrovascular accident (4.6% vs. 3.1%, OR=1.52 (1.23 – 1.89)), heart arrhythmia (33.4% vs. 22.6%, aOR=1.48 (1.33 – 1.64)), and myocardial infarction (4.3% vs. 2.7%, OR=1.59 (1.27 – 2.00)). There was no significant difference in prevalence of subarachnoid hemorrhage (0.6% vs. 0.5%. aOR=0.74 (0.28 – 1.96)). The regression results revealed significantly higher prevalence of all-cause mortality in the cocaine-use, compared to control, group (8.0% vs. 5.9%, OR=1.39 (1.18 – 1.63)).

Table 3 provides the TUD subgroup logistic regression results for respiratory outcomes, which revealed significantly higher prevalence in the cocaine-use, compared to control, group for asthma (15.6% vs. 11.2%, aOR=1.32 (1.13 – 1.55)), COPD (21.7% vs. 14.9%, aOR=1.35 (1.18 – 1.54)), and pneumonia (12.8% vs. 7.6%, aOR=1.46 (1.23 – 1.73)).

3.3 Non-TUD Subgroup

3.3.1 Characteristics—The non-TUD subgroup was approximately 60% male and 50% African American, and participants were a mean age of 52 years. The average number of years of EHR data available for non-TUD patients was 15.8 years (SD=8.9). The average number of years of EHR data available following initial cocaine-use indication was 9.2 (SD=5.7) in the cocaine-use patients. The prevalence of a CocUD encounter diagnosis within the cocaine-using non-TUD subgroup was 84.0%.

3.3.2 Outcomes—Table 2 provides the non-TUD subgroup logistic regression results for cardiovascular outcomes, which revealed significantly higher prevalence in the cocaine-use, compared to control, group for cerebrovascular accident (2.2% vs. 1.3%, OR=1.71 (1.18 – 2.47)), heart arrhythmia (18.0% vs. 12.6%, aOR=1.20 (1.02 – 1.41)), and myocardial infarction (1.6% vs. 1.1%, OR=1.41 (0.93 – 2.13)). The regression modeling of subarachnoid hemorrhage in this subgroup was unsuccessful due to insufficient prevalence, and the crude OR did not demonstrate a significant difference (0.6% vs. 0.4%, OR=1.51 (0.76 – 2.97)). The regression results revealed significantly higher prevalence of all-cause mortality in the cocaine-use, compared to control, group (9.1% vs. 4.7%, OR=2.02 (1.67 – 2.45)).

Table 3 provides the non-TUD subgroup logistic regression results for respiratory outcomes, which revealed significantly higher prevalence in the cocaine-use, compared to control, group for asthma (7.1% vs. 4.4%, OR=1.64 (1.32 – 2.02)), COPD (5.0% vs. 2.3%, OR=2.23 (1.70 – 2.92)), and pneumonia (5.2% vs. 3.2%, OR=1.70 (1.33 – 2.17)).

4. DISCUSSION

With the increasing use of cocaine by adults in the U.S., it is important to understand the potential impact of cocaine use on health. The present study used an approach designed to address some of the limitations of past research. This approach included utilizing multi-year EHR data to evaluate the associations between documented cocaine use and adverse health outcomes using a rigorous procedure to define matched controls. Controls were matched to a sample of cocaine-using patients and subgroups of cocaine-using patients with and without tobacco use disorder (TUD). The results suggest that cocaine use is associated with a

significantly greater risk of some adverse outcomes (cerebrovascular accident, heart arrhythmia, myocardial infarction, asthma, COPD, and pneumonia) and all-cause mortality.

The present analyses evaluating adverse cardiovascular events revealed significantly worse outcomes for cocaine-using, relative to control, participants on three of the four outcomes evaluated: cerebrovascular accident, heart arrhythmia, and myocardial infarction. The present results revealed that cerebrovascular accident was significantly more prevalent in cocaine-using, relative to control, patients in the total sample, which controlled for TUD status, and in the TUD and non-TUD subgroups. Past studies evaluating the association between cocaine use and stroke have generally found significant associations (Cheng et al., 2016; Gunja et al., 2018; Westover et al., 2007). However, an analysis of 18–45 year-old respondents to the third National Health and Nutrition Examination Survey found no such association (Qureshi et al., 2001), which could be explained by the researchers' definition of "frequent" cocaine use (> 10 times in lifetime), low prevalence of stroke (0.33%), and/or their reliance on self-reported data. In contrast, our results are based on a large sample of adults with documented cocaine use (n=8,244; 87% of whom had a CocUD encounter diagnosis), and outcomes were determined by encounter diagnoses documented in the EHR.

Consistent with animal studies and human case reports (Hoffman, 2010; Lange and Hillis, 2001; Schwartz et al., 2010), our study found greater heart arrhythmia encounter diagnoses in cocaine-using patients, in the total sample, and the TUD and non-TUD subgroups. To the best of our knowledge, the only other clinical study evaluating arrhythmia as a function of cocaine use was an analysis of hospital patients with drug screen results being treated for cerebrovascular accident (n=262), which found that patients with cocaine-related cerebrovascular accidents had significantly greater prevalence of in-hospital arrhythmia than patients with non-cocaine-related cerebrovascular accidents (Bhattacharya et al., 2011). Our results are comparable to those of Bhattacharya and colleagues, and were found in a large sample from a general patient population. Thus, our analysis of the association between cocaine use and arrhythmias is a significant contribution to the literature given the dearth of large-scale, systematic studies addressing this question (Wood and Dargan, 2010). The present finding of significantly greater prevalence of myocardial infarction encounter diagnoses in cocaine-using patients, in the total sample, and TUD and non-TUD subgroups, is consistent with the results of past studies (Aslibekyan et al., 2008; Gunja et al., 2018; Mittleman et al., 1999; Qureshi et al., 2001). The present finding of no significant increase in subarachnoid hemorrhage encounter diagnoses among cocaine-using patients, in the total sample, and TUD and non-TUD subgroups, is discrepant with a prior case-control study that identified recent (past 3 days) cocaine use as a risk factor for aneurysmal subarachnoid hemorrhage (Broderick et al., 2003). One factor that may play a role in the lack of a statistically significant association in the present study is the extremely low prevalence of subarachnoid hemorrhage diagnoses (0.5%; n=85) in our data. Broderick and colleagues note that their study's ability to detect the cocaine-subarachnoid hemorrhage association was aided by the relatively large number of aneurysmal subarachnoid hemorrhage cases (n=312), who were recruited from 44 hospitals in 6 states.

The present analyses found significantly greater prevalence of asthma encounter diagnoses among cocaine-using patients than control patients in the total sample, TUD subgroup, and

non-TUD subgroup. This finding is in accordance with prior research that reported a positive association of cocaine use with self-reported current asthma (Bender, 2007; Khandor and Mason, 2008), asthma symptoms (Osborn et al., 1997), and acute asthma exacerbations (Gaeta et al., 1996). The present analyses found significantly greater prevalence of COPD encounter diagnoses among cocaine-using patients than control patients in the total sample, TUD subgroup, and non-TUD subgroup. Prior research, though limited, has suggested an association between COPD and cocaine use (Burhan et al., 2019; Khandor and Mason, 2008; Seeram et al., 2012). The present analyses found significantly greater prevalence of pneumonia encounter diagnoses among cocaine-using patients than control patients in the total sample, TUD subgroup, and non-TUD subgroup. Previous research has suggested that cocaine use is associated with pneumonia infection and severity (Romney et al., 2008), particularly in people living with HIV (Caiaffa et al., 1994; Jolley and Welsh, 2019; Lamas et al., 2017). Several mechanisms by which cocaine use may enhance transmission of pneumonia-causing bacteria have been suggested, including the sharing of contaminated drug paraphernalia, crack-induced coughing, and negative effects on lung immune defenses (Romney et al., 2008). Our study, which used a large sample of patients with documented cocaine use, matched controls, and documented respiratory outcome diagnosis, lends further support to the suggestions that cocaine use is a risk factor for asthma, COPD, and pneumonia. The present results revealed that all-cause mortality was significantly more prevalent in cocaine-using, relative to control, patients in the total sample, and the TUD and non-TUD subgroups. This is consistent with past research finding an elevated mortality rate in cocaine users (DeFilippis et al., 2018; Degenhardt et al., 2011; Gunja et al., 2018; Qureshi et al., 2014).

The present study contributes additional evidence for understanding the potential associations between cocaine use and health. Of note, this study avoided many of the limitations of past research in this area (Degenhardt et al., 2011; Havakuk et al., 2017; Sordo et al., 2014). First, the definition of the cocaine-using group was based on documentation in the EHR and, thus, was not open to recall bias. Second, a longitudinal design was utilized, which allows the detection of effects that may take years to develop. Additional strengths include a large sample size (N=16,488) and the use of rigorous matching and analytic approaches.

This study also has important limitations. First, the findings are correlational in nature and, thus, cause and effect determinations cannot be made. Second, while the sample size was large, the sample was limited to patients being treated in the MetroHealth System, located in Northeast Ohio, and the extent to which the results are generalizable to the rest of the U.S. and other countries is unknown. Third, while the Explorys dataset has been validated in past research (Kaelber et al., 2012; Pfefferle et al., 2014) there is still the potential for data quality issues. For example, as is the case with medical conditions generally, the under-diagnosis, misclassification, or under-coding of substance use disorder by clinicians is possible (Wu et al., 2015). Some “control” participants may have been cocaine users despite not having had any cocaine-positive screens or cocaine diagnosis in the EHR; this would serve to weaken the associations observed in this study and, thus, the reported associations may be overly conservative. In addition, the ascertainment of tobacco use from EHR diagnosis codes has demonstrated high specificity, but notably lower sensitivity (Wiley et al.,

2013). Sub-optimal sensitivity would imply that some cigarette smokers may not have been given a TUD diagnosis and, thus, classified as non-smokers; such misclassification could reduce the accuracy of the subgroup-specific estimates. Another limitation entails the possibility that patients may have had a medical condition prior to the onset of cocaine use but that the diagnosis was not made until after the documentation of cocaine use in the EHR. If documentation of cocaine use systematically increases the likelihood of existing respiratory and cardiovascular problems being diagnosed then this would inflate the observed associations between cocaine use and respiratory and cardiovascular outcomes. The dataset also does not allow for the characterization of the cocaine-using patients in terms of severity, route, and frequency of use nor the longitudinal course of their use including remission and relapse cycles. Finally, there may have been other potential confounding factors that were not accounted for in the statistical models. With these limitations in mind, the present results suggest that regular cocaine use is associated with a significantly greater risk of adverse cardiovascular diagnoses and all-cause mortality. Future research to understand the potential impact of cocaine use on cardiovascular and respiratory health seems warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- As cocaine use rises in the US, it is critical to assess the potential health impact.
- Cardiovascular and respiratory disease are leading causes of morbidity and mortality.
- There are gaps in cocaine research about cardiovascular and respiratory disease.
- Our matching and analysis methods reduce potential confounds in health record data.
- We found regular cocaine use was associated with worse health outcomes and mortality.

Table 1.

Demographics for cocaine use and matched control cohorts for the total, tobacco use disorder (TUD), and non-TUD samples

Total Sample	**Control (n=8244)**	**Cocaine Use (n=8244)**
Age, m (sd)	52.7 (11.0)	52.7 (11.1)
Female n (%)	3639 (44.1%)	3637 (44.1%)
Race n (%)		
Black / African American	4210 (51.1%)	4210 (51.1%)
White	3365 (40.8%)	3365 (40.8%)
Other †	669 (8.1%)	669 (8.1%)
Hispanic n (%)	232 (2.8%)	232 (2.8%)
Median income for the zip code of residence m (sd)	$35191.7 (13692.7)	$35199.7 (13753.8)
TUD n (%)	4706 (57.1%)	4706 (57.1%)
Average BMI m (sd)	28.9 (6.8)	28.9 (6.9)
TUD Subgroup	**Control** (n=4706)	**Cocaine Use** (n=4706)
Age, m (sd)	53.5 (10.6)	53.5 (10.6)
Female n (%)	2215 (47.1%)	2211 (47.0%)
Race n (%)		
Black / African American	2443 (51.9%)	2443 (51.9%)
White	1936 (41.1%)	1935 (41.1%)
Other †	327 (6.9%)	328 (7.0%)
Hispanic n (%)	130 (2.8%)	130 (2.8%)
Median income for the zip code of residence m (sd)	$34936.7 (13086.7)	$34949.1 (13149.9)
Average BMI m (sd)	28.8 (6.8)	28.8 (6.8)
Non-TUD Subgroup	**Control** (n=3538)	**Cocaine Use** (n=3538)
Age, m (sd)	51.7 (11.7)	51.7 (11.6)
Female n (%)	1428 (40.4%)	1426 (40.3%)
Race n (%)		
Black / African American	1767 (49.9%)	1767 (49.9%)
White	1429 (40.0%)	1430 (40.4%)
Other †	342 (9.7%)	341 (9.6%)
Hispanic n (%)	102 (2.9%)	102 (2.9%)
Median income for the zip code of residence m (sd)	$35513.7 (14391.9)	$35533.4 (14514.4)
Average BMI m (sd)	29.0 (6.8)	29.0 (6.9)

* Quantitative measures were tested with Wilcoxon rank-sum test; Categorical measures were tested with Pearson's chi-square test of independence.

†: "Other" race includes: American Indian / Alaska Native, Asian, Multiracial, Native Hawaiian / Pacific Islander, and "missing" (i.e., no race data available).

Table 2.

Cardiovascular outcome diagnosis prevalence and all-cause mortality in cocaine-using vs. matched control cohort and cocaine-use ORs for total, tobacco use disorder (TUD), and non-TUD samples.

a. Cerebrovascular accident			
Sample[†]	**Prevalence**[*]	**Odds Ratio (95% CI), p-value**	**aOR (95% CI), p-value**
Total Sample	3.6% vs. 2.4%	**1.53 (1.27 – 1.84), p<0.0001**	**2.50 (1.76 – 3.54), p<0.0001**
TUD[≠] Subgroup	4.6% vs. 3.1%	**1.52 (1.23 – 1.89), p=0.0001**	**2.46 (1.65 – 3.64), p<0.0001**
Non-TUD Subgroup	2.2% vs. 1.3%	**1.71 (1.18 – 2.47), p=0.0040**	**4.14 (1.89 – 9.06), p=0.0004**
b. Heart arrhythmia			
Sample[†]	**Prevalence**[*]	**Odds Ratio (95% CI), p-value**	**aOR (95% CI), p-value**
Total Sample	26.6% vs. 18.2%	**1.63 (1.51 – 1.76), p<0.0001**	**1.26 (1.15 – 1.38), p<0.0001**
TUD[≠] Subgroup	33.4% vs. 22.6%	**1.71 (1.55 – 1.88), p<0.0001**	**1.48 (1.33 – 1.64), p<0.0001**
Non-TUD Subgroup	18.0% vs. 12.6%	**1.52 (1.33 – 1.74), p<0.0001**	**1.20 (1.02 – 1.41), p=0.0241**
c. Myocardial Infarction			
Sample[†]	**Prevalence**[*]	**Odds Ratio (95% CI), p-value**	**aOR (95% CI), p-value**
Total Sample	3.1% vs. 2.0%	**1.58 (1.30 – 1.94), p<0.0001**	**2.92 (2.04 – 4.18), p<0.0001**
TUD[≠] Subgroup	4.3% vs. 2.7%	**1.59 (1.27 – 2.00), p<0.0001**	**2.70 (1.82 – 4.01), p<0.0001**
Non-TUD Subgroup	1.6% vs. 1.1%	1.41 (0.93 – 2.13), p=0.1294	**2.50 (1.07 – 5.86), p=0.0343**
d. Subarachnoid hemorrhage			
Sample[†]	**Prevalence**[*]	**Odds Ratio (95% CI), p-value**	**aOR (95% CI), p-value**
Total Sample	0.6% vs. 0.5%	1.24 (0.81 – 1.91), p=0.3216	1.14 (0.50 – 2.59), p=0.7502
TUD[≠] Subgroup	0.6% vs. 0.5%	1.04 (0.60 – 1.81), p=0.8787	0.74 (0.28 – 1.96), p=0.5455
Non-TUD Subgroup	0.6% vs. 0.4%	1.51 (0.76 – 2.97), p=0.2336	*Regression was not successful due to insufficient prevalence*
e. All-cause Mortality			
Sample[†]	**Prevalence**[*]	**Odds Ratio (95% CI), p-value**	**aOR (95% CI), p-value**
Total Sample	8.5% vs. 5.3%	**1.66 (1.47 – 1.88), p<0.0001**	**3.93 (3.04 – 5.09), p<0.0001**
TUD[≠] Subgroup	8.0% vs. 5.9%	**1.39 (1.18 – 1.63), p<0.0001**	**2.42 (1.82 – 3.22), p<0.0001**
Non-TUD Subgroup	9.1% vs. 4.7%	**2.02 (1.67 – 2.45), p<0.0001**	**8.44 (5.24 – 13.60), p<0.0001**

[†]Total Sample: N=16,488 (n=8,244 in each cohort); TUD Subgroup: N=9,412 (n=4,706 in each cohort); Non-TUD Subgroup: N=7,076 (n=3,538 in each cohort).

[*]Prevalence is the prevalence of the diagnosis in the cocaine-using versus matched control cohorts. aOR=adjusted Odds Ratio; bold= statistically significant ($p < 0.05$) effect; see section 3.0 for discussion of effect size estimates.

[≠]Tobacco Use Disorder.

Table 3.

Respiratory outcome diagnosis prevalence and all-cause mortality in cocaine-using vs. matched control cohort and cocaine-use ORs for total, tobacco use disorder (TUD), and non-TUD samples

a. Asthma			
Sample[†]	**Prevalence**[*]	**Odds Ratio (95% CI), p-value**	**aOR (95% CI), p-value**
Total Sample	11.8% vs. 8.2%	**1.49 (1.34 – 1.66), p<0.0001**	**2.33 (1.91 – 2.85), p<0.0001**
TUD[ǂ] Subgroup	15.6% vs. 11.2%	**1.47 (1.29 – 1.67), p<0.0001**	**1.32 (1.13 – 1.55), p=0.0006**
Non-TUD Subgroup	7.1% vs. 4.4%	**1.64 (1.32 – 2.02), p<0.0001**	**3.34 (2.27 – 4.93), p<0.0001**
b. COPD			
Sample[†]	**Prevalence**[*]	**Odds Ratio (95% CI), p-value**	**aOR (95% CI), p-value**
Total Sample	14.1% vs. 9.3%	**1.61 (1.46 – 1.78), p<0.0001**	**2.46 (2.01 – 3.01), p<0.0001**
TUD[ǂ] Subgroup	21.7% vs. 14.9%	**1.58 (1.41 – 1.77), p<0.0001**	**1.35 (1.18 – 1.54), p<0.0001**
Non-TUD Subgroup	5.0% vs. 2.3%	**2.23 (1.70 – 2.92), p<0.0001**	**10.65 (5.70 – 19.91), p<0.0001**
c. Pneumonia			
Sample[†]	**Prevalence**[*]	**Odds Ratio (95% CI), p-value**	**aOR (95% CI), p-value**
Total Sample	9.5% vs. 5.5%	**1.79 (1.58 – 2.02), p<0.0001**	**2.93 (2.31 – 3.72), p<0.0001**
TUD[ǂ] Subgroup	12.8% vs. 7.6%	**1.79 (1.55 – 2.06), p<0.0001**	**1.46 (1.23 – 1.73), p<0.0001**
Non-TUD Subgroup	5.2% vs. 3.2%	**1.70 (1.33 – 2.17), p<0.0001**	**5.15 (3.25 – 8.15), p<0.0001**

[†]Total Sample: N=16,488 (n=8,244 in each cohort); TUD Subgroup: N=9,412 (n=4,706 in each cohort); Non-TUD Subgroup: N=7,076 (n=3,538 in each cohort).

[*]Prevalence is the prevalence of the diagnosis in the cocaine-using versus matched control cohorts. aOR=adjusted Odds Ratio; bold= statistically significant ($p < 0.05$) effect; see section 3.0 for discussion of effect size estimates.

[ǂ]Tobacco Use Disorder.