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Article

From Bumps to Binges: Overview of Deaths Associated with Cocaine in England, Wales and Northern Ireland (2000–2019)

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Abstract

The UK, as the "cocaine capital of Europe," currently accounts for ∼75% of all cocaine-related hospital admissions in Europe. This study aims to analyze the trends in cocaine-related deaths in England, Wales and Northern Ireland over 20 years (2000–2019). Cases reported to the National Programme on Substance Abuse Deaths (NPSAD) occurring between 2000 and 2019 where cocaine was detected at post-mortem (PM) were extracted for analysis. A total of 5,339 cases were retrieved, with an increase in the rate of reporting over time. Cocaine was deemed a cause of death and quantified in PM blood samples along with its major metabolite benzoylecgonine in 685 cases. Of these 685 cases, 25% ($n = 170/685$) occurred following acute use, 22% ($n = 154/685$) following chronic/binge use, 40% ($n = 271/685$) in combination with morphine, 4% ($n = 29/685$) in drug packer/swallower circumstances and 9% ($n = 61/685$) in a suicide context. Cardiac complications were evident in 22% of cases ($n = 154/685$). The average concentration of cocaine detected in cardiac cases (900 ng/mL) was considerably lower than that detected in cases where acute (19,100 ng/mL) or chronic/binge (6,200 ng/mL) dosing was evident. This is the first cocaine-related mortality study in these geographical areas. Deaths following cocaine use continue to rise despite its Class A drug listing in the UK. While underlying and external risk factors including polydrug use, cardiac complications and mental health can all contribute to the incidence of fatal drug toxicity following cocaine use, this study demonstrates that the risk of a cocaine overdose cannot be attributed to a specific blood concentration range.

Introduction

Derived from *Erythroxylum coca* leaves, cocaine is one of the most consumed illicit drugs in the world (1–4). It is sought recreationally for its stimulant properties and has a high potential for drug abuse and addiction, with 5–6% of users becoming dependent within their first year of use (4). The European Drug Report indicates that the number and quantity of cocaine seizures currently stand at record levels, with the UK contributing to ∼75% of all reported treatment admissions related to cocaine abuse in Europe (3).

Individually, cocaine presents a significant overdose (OD) risk when large dosages of the drug are administered. This risk is further exacerbated in cases of polydrug use, particularly in combination with opiates and/or alcohol (5, 6). One of the chief risks of cocaine use is its impact on cardiac and circulatory function (7). Early-stage cocaine toxicity can manifest as elevated heart rate and blood pressure, which with increased dose and frequency can lead to late-stage toxic effects, including seizures, stroke and heart attack (8). Cocaine-induced vasoconstriction can lead to arterial spasm–mediated ventricular fibrillation and cardiac arrest, with the blocking of sodium and potassium channels forming the basis of several arrhythmic implications, including angina, cardiac inflammation and thrombosis-mediated myocardial infarction (9). Maladaptive architectural alterations of cardiac anatomy may develop following chronic cocaine use, including dilated cardiomyopathies, myofibril destruction and interstitial fibrosis (10). In addition to these physiological risks, cocaine users are also more likely to suffer from mental health issues, such as depression, schizophrenia and suicidal ideation (11–13).

Cocaine-related deaths can be broadly divided into two categories: acute toxicity and chronic toxicity. Acute toxicity is often associated with a single or a small number of drug administrations, with chronic toxicity, also known as binge use, being a result of frequent and repetitive cocaine dosing over a prolonged period (14). Identifying what constitutes acute or chronic toxicity is contentious: no upper blood concentration limit can reliably be attributed as fatal, while lower concentrations may be sufficient to cause myocardial infarction from coronary spasm, especially in individuals with underlying cardiac defects (15). It is however possible to estimate whether the administration was acute or chronic by examining the concentration ratio of cocaine to one of its major metabolites, benzoylecgonine (BZE), in blood (14). Furthermore, it is possible to delineate extreme accidental

administration of cocaine in supralethal doses as typically seen in "drug traffickers/packers," who smuggle illicit drugs in body cavities across jurisdictions, and "drug swallowers," who are typically local drug dealers swallowing drugs upon apprehension by the police. Cases of drug traffickers and drug swallowers carry a high risk of drug-induced fatalities, often as a result of ingested cocaine packages rupturing, instantly releasing a supralethal dose. In these cases, the deceased will typically display symptoms of cardiac standstill in addition to continuous seizures, intracranial bleeding, bowel ischemia, respiratory depression and death (14).

In this study, we have characterized trends in cocaine-related deaths in England, Wales and Northern Ireland over the past 20 years. Cases received by the National Programme on Substance Abuse Deaths (NPSAD) were analyzed based on the coroner's determination of the manner of death, comorbidities relating to cardiac and circulatory dysfunction and the ratio of BZE to cocaine as an indicator of binge/chronic and acute drug use, alongside co-detection of morphine and alcohol. Separate from recreational drug ODs, we have also described cases involving body packers and drug swallowers, and those concluded as suicide. Across all datasets, we have correlated the data to demographic factors of recreational drug users versus those involved in the distribution and smuggling of cocaine.

Methods

NPSAD receives information from coroners across England, Wales and Northern Ireland on a voluntary basis on deaths related to drugs, as previously described (15). If a death has an unknown cause, is violent or unnatural, sudden or unexplained, occurred during an operation or before the person came out of an anesthetic or may have been caused by an industrial disease or poisoning, then it is referred to a coroner. Toxicology tests are requested at the discretion of the coroner, medical examiner or pathologist, dependent upon the circumstances of individual cases. A coroner reports a death to NPSAD if it features at least one of the following:

(i) Presence of one or more psychoactive substance(s) directly implicated in death
(ii) History of dependence or abuse of drugs
(iii) Presence of controlled drugs at post-mortem (PM).

The King's College London Biomedical and Health Sciences, Dentistry, Medicine and Natural and Mathematical Sciences Research Ethics Subcommittee have confirmed that NPSAD does not require research ethics review as all subjects are deceased. The General Data Protection Regulation and Data Protection Act do not apply to personal identifiable data once a person has died.

Case identification

A range of documents is contained in coronial inquest files, although this varies from case to case. Typically, the coroner has access to statements from witnesses, family and friends; general practitioner (GP) records (if the deceased is registered with one); reports from first responders (e.g., police and emergency services); hospital emergency departments and clinical ward reports; psychiatric and substance abuse team reports and PM and toxicology reports.

A retrospective study design was employed to identify cocaine-associated deaths occurring from 2000 to 2019 that were received by NPSAD by 22 April 2021. This was achieved by searching the drugs present in PM fields on the NPSAD database using the coded cocaine term and subsequently screening for the date of death.

All cases reported here have confirmatory evidence from toxicology reports indicating the presence of cocaine and/or its metabolites (e.g., BZE) in the decedents' blood samples, demonstrating that the decedent died following cocaine use.

Analysis of PM blood samples

One of the many challenges of assessing a large-scale dataset of PM toxicological findings in the UK is the variety of techniques employed by different laboratories in the analysis of these samples. The UK does not have a central laboratory or single testing organization that carries out PM toxicology testing, instead individual coroners enter commercial contracts and tenders with private and public (hospital) laboratories. Each of these laboratories differs in the range of analytes that they test for, the calibration range of each analyte, the sample preparation/extraction procedures and the analysis technique used to quantify the drug concentrations. In addition, there are no requirements for laboratories testing coronial samples to be accredited for this specific case type or to validate individual methods to any prescriptive criteria.

While there is a general expectation that these laboratories should comply with ISO 17,025 guidance, this is not mandatory. In recent years, a common request from coroners during the tender process is for laboratories to be ISO accredited, but accreditation is still not widespread. In toxicology laboratories in the UK, coronial samples are typically screened for drugs using an immunoassay or a multi-analyte liquid chromatography–mass spectrometry (LC–MS) screening technique. The samples then proceed to confirmatory testing using either an LC–MS/gas chromatography–mass spectrometry (GC–MS) or high-resolution accurate mass (HRAM) analysis (Table I), although the predominant testing method for cocaine and opiates is LC–MS (16). In forensic toxicology laboratories, alcohol analysis is performed using a dual column detector gas chromatography flame ionization detector) system.

The screening panel assesses samples for analytes of the antidepressant, opioid/opiate analgesic, antipsychotic, antihistamine, anxiolytics/hypnotic, non-opioid analgesic, anti-convulsant, antibiotic/fungal and non-steroidal anti-inflammatory drug classes. The panel also includes common recreational drugs such as cocaine, BZE, cocaethylene, amphetamine, methamphetamine-related drugs, piperazine derivatives, cannabinoids, ketamine, hallucinogens and benzodiazepine drugs. The extent to which testing can accurately identify emerging and novel new psychoactive substances (NPSs) is unknown. However, this capacity is thought to be quite low as NPSs are frequently not included in the standard drugs of abuse test. While some laboratories do retain the capacity for NPS testing, many others require the assistance of external specialist providers to detect these analytes.

Interpretation of PM results

Reports are typically issued to the coroner with an overview of the effects of the drug and a guideline on whether the

Table I. List of Analytical Techniques Employed by Private and Public/Hospital Laboratories in the Testing of PM Samples

Laboratory	Technique used
Private Forensic Toxicology Laboratory 1	LC–MS-MS and High-Performance Liquid Chromatography Diode-Array Detection (HPLC DAD)
Private Forensic Toxicology Laboratory 2	LC–MS-MS and HPLC–DAD
Private Forensic Toxicology Laboratory 3	LC–MS-MS, HRAM and HPLC–DAD
Private Forensic Toxicology Laboratory 4	LC–MS-MS, GC–MS,
Private Forensic Toxicology Laboratory 5	LC–MS-MS
Hospital Laboratory 1	LC–MS-MS
Hospital Laboratory 2	GC–MS
Hospital Laboratory 3	LC–MS-MS, HRAM MS
Hospital Laboratory 4	LC–MS-MS, GC–MS
Hospital Laboratory 5	LC–HRAM MS

concentrations are consistent with toxicity or lethality. Concentrations are typically provided in mg/L with annotations of concentrations detected outside of calibration range. As with the testing techniques employed, there are considerable variations in the interpretation and the detail provided. Blood concentrations of cocaine detected by one laboratory may be interpreted as lethal or a significant contributor to cause of death; the same concentrations detected by another laboratory may be considered consistent with recreational or non-fatal use. Typical interpretative statements from cases where suspected cocaine OD occurred can include reference to cardiovascular complications associated with cocaine. "The results are consistent with the abuse of cocaine by the deceased relatively recently prior to his death. Furthermore, as stated above, the regular abuse of cocaine may also exacerbate or lead to cardiovascular events such as myocardial infarction and stroke. However, these adverse effects do not necessarily correlate with blood concentrations." Other laboratories may provide less detail and merely state that a cocaine concentration consistent with recreational use has been detected and that "as cocaine induces tolerance, there is great variation in both recreational and fatal concentrations." The detail of these reports is variable from case to case and provider to provider as is the interpretative scope.

Data analysis

Data analysis

Data analysis and statistical tests (Student's *t*-test and chi-square) were performed using IBM® SPSS™ Statistics for Windows version 25 and Microsoft Excel 365.

2019 projection

The average time between death and coronial inquest conclusion where cocaine was present is 7–10 months, although this time delay has been extended due to the impact of the national UK lockdowns as a result of the coronavirus disease of 2019 pandemic. Further deaths occurring in 2019 but reported after 22 April 2021 are therefore anticipated to be received. Based on jurisdiction reporting trends, the number of cocaine-related deaths expected to be received by NPSAD has been projected.

Cause of death

Circumstances that lead to death are categorized on the death certificate issued by the coroner, as follows:

Cause 1a: The immediate cause of death (and underlying if no 1b or 1c cited)
Cause 1b: Any disease/circumstance underlying Cause 1a
Cause 1c: Any disease/circumstance underlying Cause 1b
Cause 2: Any disease/circumstance that did not cause the death but contributed in some way.

It is not a requirement for a Cause 1b, 1c or 2 to be cited for all deaths (29).

Cardiac text detection

All cause of death fields of identified cocaine-related cases were searched for the text of keywords associated with cardiac and hematological function and dysfunction (aneury*, aortic, arrythm*, arter*, atheroma*, cardi*, coronary, haem*, heart, hypertens*, hypotens*, ischae*, thromb*, vein, ventric*). Identified cases were then manually screened with cases where text detected was not relevant to cardiac/hematological functions removed (e.g., "quarter" by the "arter" term).

Results

A total of 5,339 cases where cocaine was detected in PM blood samples were extracted from the NPSAD database. On average, the number of deaths where cocaine was detected increased by 3.8% for each year of the study (Figure 1). When normalized against total NPSAD reporting over the same period, this increase in cocaine-related deaths remains, demonstrating that there has been a proportional rise in their occurrence (data not shown).

PM concentrations of cocaine and BZE

In 1,018 cases, the blood concentrations of cocaine and BZE were quantified. In 333 cases, the quantifications indicated

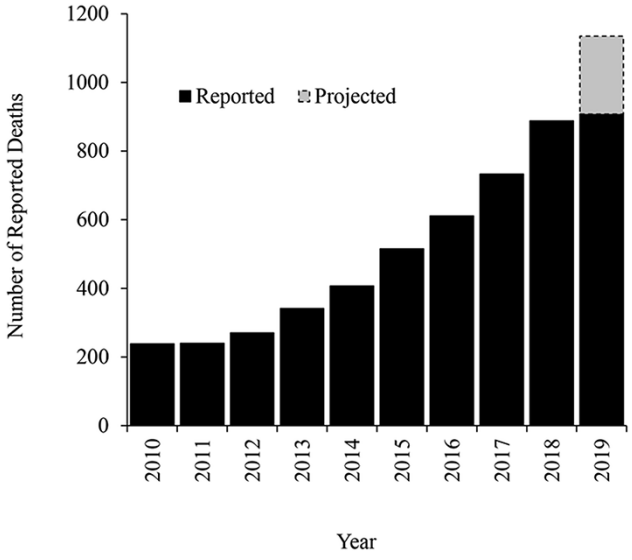

Figure 1. Number of deaths reported to NPSAD with cocaine detected at PM. Proportion of deaths reported to NPSAD where cocaine was detected in PM blood samples.

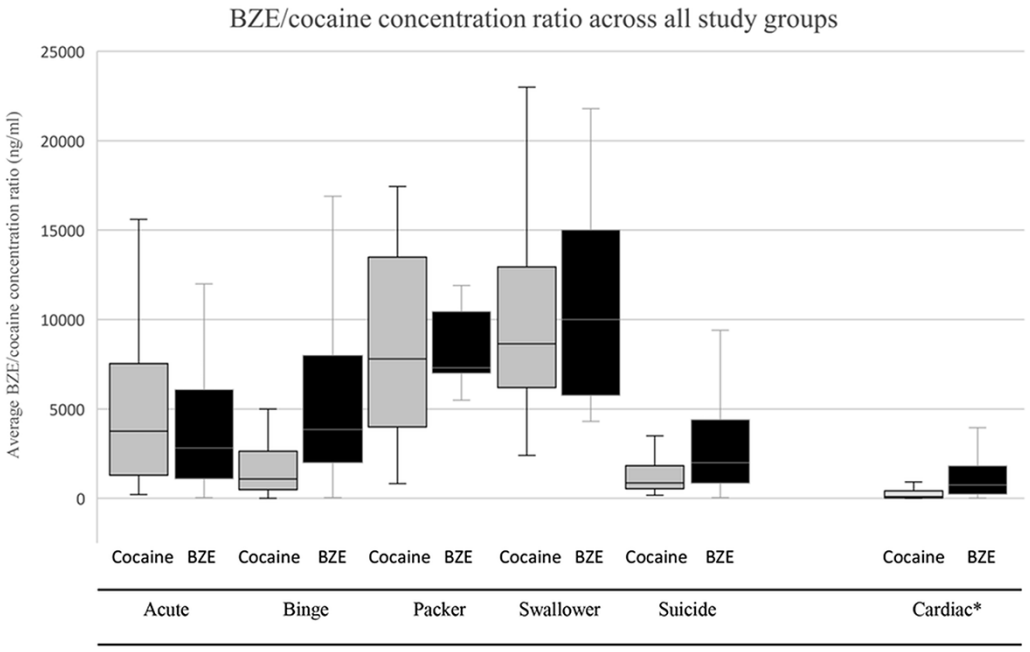

Figure 2. BZE/cocaine concentration ratio in cocaine-related drug OD cases between 2000 and 2019. Cocaine-related cardiac complications recorded the lowest range of cocaine and BZE concentration with the highest BZE/cocaine concentration ratio. However, ∼40% of the recorded cardiac cases had cocaine concentrations of ≤60 ng/mL, concentration not typically associated with an OD. The lowest average cocaine concentration was recorded in cardiac cases of 879 ng/mL. Contrarily, the highest recorded average cocaine concentration was reported in packer cases, at 12,373 ng/mL. Box plot graph representing median (line) of cocaine and BZE, respectively, across all studied overdose groups. *Cardiac cases were derived from acute, binge, swallower, packer, suicide and opiate co-administration cases.

the use of cocaine in the days preceding death, but not in the immediate hours preceding death (very low cocaine, low BZE), and were excluded from further analysis. The remaining 685 cases were categorized according to the circumstance of death, with recreational use cases further delineated by the BZE/cocaine ratio and co-use of morphine, as follows:

(i) Recreational use
  (a) Acute use ($n = 170/685$)
  (b) Binge/chronic use ($n = 154/685$)
  (c) Cocaine–morphine co-administration ($n = 271/685$)
(ii) Drug packer or swallower cases ($n = 29/685$)
(iii) Suicides ($n = 61/685$).

Cases were individually categorized based on the criteria for assessing repetitive cocaine dosing as described by Jufer et al. (17). Cardiac data were derived from acute, binge, swallower, packer, suicide and opiate co-administration cases. Other prescription and illicit substances were detected though in low quantities and unlikely to have contributed to the cause of death.

Acute and binge/chronic use

Acute use cases were defined as those with higher blood concentrations of cocaine than of BZE. Chronic "binge" use cases were defined as those with high blood concentrations of both cocaine and BZE (17). Acute and binge use represented 47% ($n = 324/685$) of total cases with cocaine/BZE quantifications. Acute cases (25%, $n = 170/685$) had a low BZE to cocaine concentration ratio (0.71), with >40% ($n = 69/170$) found to have cocaine concentrations >5,000 ng/mL (Figure 2, Table II); binge cases (22%, $n = 154/685$) had an average BZE to cocaine concentration ratio of 11.66, with <12% ($n = 18/154$) of cases >5,000 ng/mL (Figure 2, Table II). Decedents in both acute dose and binge cases were predominantly white males, with a history of drug abuse (Table III).

Cases with morphine co-administration

Denotation of heroin in the NPSAD database is referred to collectively as morphine/diamorphine or 6-MAM. Diamorphine is rapidly metabolized to 6-monoacetylmorphine and then morphine after administration, and it is impossible to ascertain whether heroin or morphine was administered if diamorphine-specific metabolites or common street heroin contaminants are not tested for. Morphine was co-detected and quantified in 40% of cases ($n = 271/685$). Morphine concentrations were most commonly found to be between 2 and 800 ng/mL (56% of cases $n = 152/271$; data not shown). The overall average morphine to cocaine concentration ratio was 16.96, with a BZE to cocaine concentration ratio of 8.88 (Figure 2, Table II). Morphine–cocaine co-administration cases had the highest proportion of decedents who had a known history of drug abuse and the lowest employment (Table III).

Drug packers and swallowers

Drug packing and swallowing cases were defined as those with supralethal doses of cocaine detected, and where narratives indicating packing/swallowing circumstances were provided, representing <5% of cases with quantifications ($n = 29/685$). The most common blood concentrations of cocaine in drug packer cases were >20,000 ng/mL, with 65% ($n = 11/17$) of cases falling within this range. While drug swallower cases

Table II. Frequency Table of Cocaine Concentrations Detected at PM and BZE/Cocaine Concentration Ratio in Studied Groups

	Cardiac[a]	Acute	Binge	Packer	Swallower	Suicide	Opiate
Average BZE/cocaine concentration ratio	18.34	0.71	11.66	1.38	1.55	3.02	8.88
2–200 ng/mL	88	0	19	0	0	1	48
201–400 ng/mL	21	5	5	0	0	3	16
401–800 ng/mL	17	23	41	0	0	22	88
801–2,000 ng/mL	8	31	41	2	0	20	57
2,001–5,000 ng/mL	5	42	30	4	1	7	21
5,001–20,000 ng/mL	13	58	12	0	9	7	31
>20,001 ng/mL	2	11	6	11	2	1	10
Concentration not quantified	232	0	0	0	0	1	0
Total	386	170	154	17	12	62	271

Highest BZE/cocaine concentration ratio identified in cardiac cases with 400–800 ng/mL being the most commonly recorded concentration range. Interestingly, acute cocaine OD cases recorded the lowest BZE/cocaine concentration ratio possibly due to cocaine not metabolizing into BZE before the individual's death. Acute OD cases often are a result of fewer but higher and thus more lethal doses. [a]Cardiac cases were derived from acute, binge, swallower, packer, suicide and opiate co-administration cases.

Table III. Demographic Data Presented across All Cocaine Death–Related OD Cases between 2000 and 2019

	Cardiac[a]	Acute	Binge	Packer	Swallower	Suicide	Opiate
Age (mean)	42	36	35	37	35	35	38
Gender							
Male	333	146	129	12	11	49	224
Female	53	24	25	5	1	13	48
Ethnicity							
White	233	101	97	1	6	34	158
Black	7	9	1	12	1	0	1
South Asian	5	3	1	0	0	0	2
Chinese	0	0	1	0	0	0	0
Other	3	2	2	2	0	2	3
Unknown	138	55	52	2	5	26	108
Employment	74%	57%	50%	53%	27%	55%	24%
History of drug abuse	N/A	63%	56%	24%	33%	57%	77%

Our results indicate that the dominant gender and ethnicity in the study is Caucasian males with an average age of 35–42 years. The lowest employment and highest history of drug abuse was noted in opiate/cocaine OD cases with 24% and 77%, respectively. [a]Cardiac cases were derived from acute, binge, swallower, packer, suicide and opiate co-administration cases.

on average had comparatively lower cocaine blood concentrations, 92% ($n = 9/12$) of cases were still found within the 5,000–20,000 ng/mL range (Figure 2, Table II). These cases were identified by case information provided by authorities and medical personnel. Drug packers were predominantly black males, while drug swallowers were typically white males (Table III), with both groups recording the lowest percentage of decedents with a known history of drug abuse.

Please note that this study was unable to differentiate between *in vitro* and *in vivo* cases of spontaneous hydrolysis of cocaine (18).

Cases concluded as suicide

A total of 302 deaths with cocaine detected were concluded by the coroner as suicide, with cocaine and BZE concentrations quantified in 20% ($n = 61/302$) of cases. Blood concentrations of cocaine were most commonly found between 2 and 800 ng/mL, with the highest cocaine concentration detected at 56,000 ng/mL (Figure 2, Table II). Cases with cocaine concentrations between 2 and 800 ng/mL also presented with the highest BZE/cocaine concentration ratios, indicating prolonged cocaine use through repeated dosing. The BZE/cocaine concentration ratio decreased to 0.63 with increasing cocaine concentration >20,000 ng/mL, suggesting a recent but lethal dose of cocaine. The most commonly noted cause of death was hanging (53%, $n = 32/61$) followed by acute drug toxicity (26%, $n = 16/61$). These results indicate that the predominant cause of death in suicide cases was asphyxiation through hanging, with cocaine/BZE detected in the PM samples but not at concentrations indicative of a drug OD. Antidepressant medications were listed as prescribed to the deceased in 26% of cases ($n = 16/61$), which is comparable to the proportion of all cases with cocaine/BZE quantifications and antidepressants prescribed (39%, $n = 266/685$, $P > 0.05$).

Alcohol co-administration

Alcohol was co-detected and quantified in 39% of cases ($n = 264/685$; Figure 3). Alcohol was most commonly detected in cases with cardiac/circulatory causes of death (40%, $n = 153/386$, Table IV). Acute cocaine-related OD deaths recorded the highest co-detected alcohol concentration of 352 mg%. Over 50% ($n = 145/264$, Table IV) of cases had a quantified alcohol concentration between 10 and 80 mg%, exerting minimal physiological effects (19). Alcohol concentrations between 200 and 300 mg%, known to represent severe intoxication, were detected in only 11.7% ($n = 31/264$, Table IV) of total cases. A by-product of combined cocaine and alcohol intoxication, cocaethylene, was detected in ~9% of total cases ($n = 40/685$).

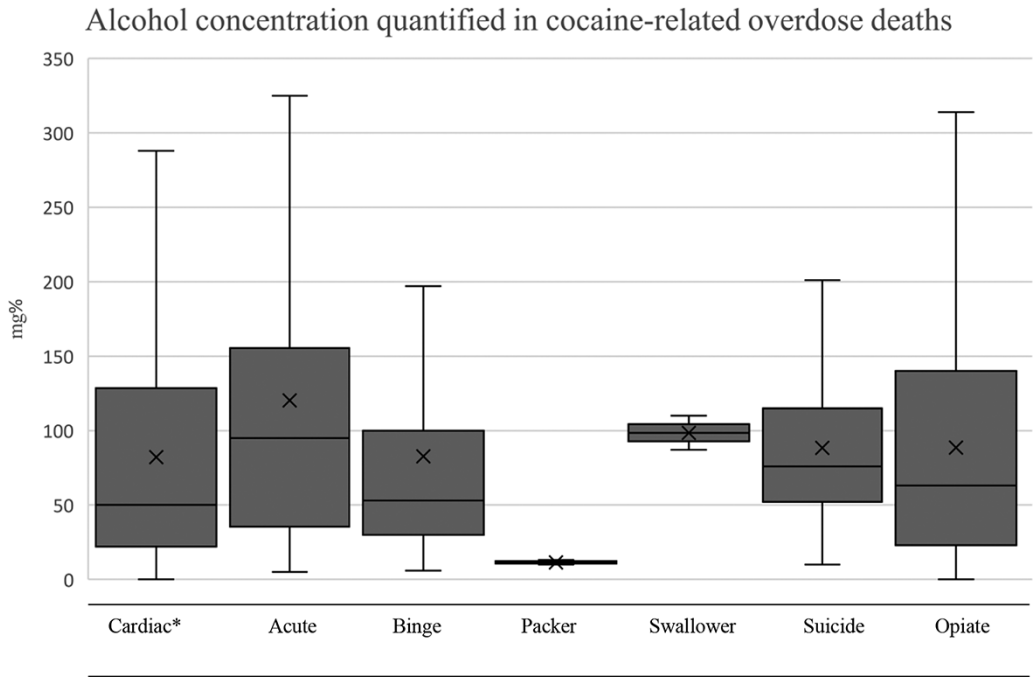

Figure 3. Alcohol concentrations in cocaine-related OD deaths. Alcohol was detected in 39.2% of cases ($n = 269/686$) and was quantified in 98.1% ($n = 264/269$) of those cases. Alcohol was detected in 39.6% of all cardiac cases ($n = 153/386$) and was quantified in 93.4% ($n = 143/153$) of those cases. Acute cocaine-related OD deaths recorded the highest detected alcohol concentration of 352 mg%. Drug packer and swallower cases recorded the lowest frequency of cases where alcohol was quantified alongside cocaine. Box plot graph representing median (line) and average (cross) concentrations of alcohol. *Cardiac cases were derived from acute, binge, swallower, packer, suicide and opiate co-administration cases.

Table IV. Frequency Table of Alcohol Concentration Detected at PM across All Studied Groups

	Cardiac[a]	Acute	Binge	Packer	Swallower	Suicide	Opiate
10–80 mg%	88	32	42	2	0	9	60
81–200 mg%	44	31	11	0	2	6	34
201–350 mg%	11	8	8	0	0	2	13
>351 mg%	0	4	0	0	0	0	0
Not quantified	10	1	1	0	0	2	1
Total	153	76	62	2	2	19	108

[a]Cardiac cases were derived from acute, binge, swallower, packer, suicide and opiate co-administration cases.

Cases with cardiac causes of death

Morphological alterations of the cardiac structure were identified in 7% of total cases ($n = 386/5{,}339$, Table II). Cocaine and BZE concentrations were quantified in 40% of these cases ($n = 154/386$). Cardiac cases presented with the highest BZE/cocaine ratio of 18.34% (Figure 2, Table II). In relation to cocaine blood concentrations, 82% of cases ($n = 126/154$) were found to be between 2 and 800 ng/mL. Of these 154 cases, 40% ($n = 60/154$) had cocaine concentrations of $\leq$60 ng/mL. In addition, there were several cases in which structural alterations of the heart were evident with ischemic heart disease (17%, $n = 26/154$), left ventricular hypertrophy (7%, $n = 12/154$) and coronary artery atheroma (4%, $n = 7/154$) as the most prevalent (20). While cardiac case decedents were majority male and on average older at the time of death than other case categorizations (26% were aged 35–42 years, $n = 40/154$; Table III), this is significantly lower than the average age typically associated with cardiac events such as cardiorespiratory arrest (21).

Discussion

Our results show that year on year, there has been an increase in cocaine-related deaths; in a 10-year period from 2010, there has been a six-fold increase in the detection of cocaine in NPSAD cases. As of 2019, cocaine was detected in ~50% of NPSAD cases. While there is a consensus that cocaine usage has increased worldwide, the UK is still considered to be the primary center of cocaine use in Europe (22–28). Increased trafficking of cocaine to the UK has risen by over a third since 2011 (20). This is reflected in an increase in cocaine usage of ~300% within the last decade, with the number of deaths from cocaine use concomitantly rising, as demonstrated in this study (29). The price of cocaine and its average purity are thought to be key contributory factors to these trends, with the price decreasing, while the purity has increased year on year since 2008—estimated to be as high as 44% in 2018 (27, 29). Our findings provide confirmation of the growing use of cocaine within the UK.

The concentration at which cocaine is considered toxic is widely debated within the field of forensic toxicology, with several studies suggesting that long-term users with morphological changes in the brain and heart tissues are more vulnerable to ODs at low cocaine concentrations (4). This is particularly pertinent when considering cardiac and circulatory pathophysiologies; our results suggest that on average, a 900 ng/mL blood concentration of cocaine can prove fatal in individuals with underlying cardiac and/or circulatory abnormalities. Significantly, this cocaine concentration is considerably lower than the average concentrations detected in deaths associated with acute (19,100 ng/mL) or binge cases (6,200 ng/mL) in non-cardiac-comprised individuals (30). In addition, in our study, the average age of individuals presenting cardiac irregularities was 42 years, a reduction of 13 years compared to non-drug abuse subjects in other studies (21).

Chronic cocaine users are more vulnerable to a range of cardiac morphology alterations (8, 9, 31); the most frequently encountered in this study were structural changes of the cardiac architecture including ischemic heart disease due to narrowing of the coronary arteries, left ventricular hypertrophy characterized by increased ventricular mass index, cardiac wall thickness and left ventricular failure. Left ventricular hypertrophy has previously been identified as a symptom of long-term cocaine use and may act as a substrate facilitating the development of myocardial ischemia and/or arrhythmias in cocaine abusers (23). We found that in ∼40% of the cases where cardiac complications were evident and cocaine concentration was quantified, cocaine was detected at concentrations <60 ng/mL—concentrations well below those typically associated with an acute OD. Collectively, the presented data identify individuals with a history of cocaine abuse and cardiac pathophysiology as being at an increased risk of death following cocaine use, even at doses routinely considered non-toxic. While it is not possible to attribute the morphological alterations of the cardiac architecture solely to cocaine use or to distinguish them from underlying cardiac deficiencies, in the context of cardiac tissue remodeling, the cases in this investigation are supportive of previously proposed links between cocaine use and long-term pathological cardiac injury (8, 31–37). It should be noted that many of the morphological and structural changes of the heart identified in this study are irreversible; therefore, even after cessation of cocaine abuse, previously chronic or long-term users should still be considered a high-risk category for cardiac failure and myocardial ischemia. Previous history of cocaine use should be considered when screening for cardiac defects and during regular GP appointments, even years after termination of cocaine use.

The results of this study indicate that in cases of acute and binge ODs, most of the decadents were male, of white ethnicity with approximately half of this cohort employed and with a history of drug abuse. By contrast, cases involving body packers were predominantly of black ethnicity with a limited history of drug abuse. In the case of drug swallowers, low-level drug distributers who have swallowed small wraps of cocaine, this category displayed the highest degree of unemployment but a significantly lower history of drug abuse than cases classified as binge or acute use. Furthermore, studies have shown that unemployment is a significant risk factor in relapse into substance abuse and has a greater prevalence and impact on communities of lower socioeconomic status (38).

Our findings indicate that a significant proportion of the cases in this study (40%) had taken morphine along with cocaine before death. Our results suggest that the average concentrations of cocaine and BZE in opiate/cocaine polydrug deaths were 1,800 and 3,000 ng/mL, respectively, while the average concentrations of morphine were 800 ng/mL. Attributing a cause of death to an individual drug is frequently difficult in polydrug OD cases as it is often not feasible to identify which drug was the primary cause of mortality. Despite this, numerous studies have suggested that the risk of OD from opiates, chiefly heroin, presents a greater hazard than that of cocaine (5, 39–42). A US study by McCall Jones et al. over a 15-year period showed that the number of cocaine-related OD deaths involving opioids has increased from 0.37 per 100,000 population in 2000 to 1.36 in 2015. The authors concluded that the increase in supply/demand of opiates is responsible for the recent increase in cocaine-related OD deaths in the USA (5). By contrast, alcohol was co-detected in 40% of cases in this study, but critically at concentrations <80 mg%; concentrations not associated with significant impairment to an individual's behavior and sensory-motor coordination (43). A toxic by-product of alcohol and cocaine consumption is cocaethylene, the formation of which is associated with a greater elevation of heart rate and cardiotoxicity than cocaine alone (44). Cocaethylene was only detected in 9% of total cases, and despite the relevance of alcohol to drug ODs, it is difficult to ascertain from toxicological findings what role, if any, alcohol consumption had on the cause of death. It should also be noted that not all drug screen panels would have included cocaethylene as an analyte of interest. Overall, these findings corroborate previous studies that highlight polydrug as a substantial risk of fatal drug toxicity (4–6, 14, 39, 41, 42).

Our results suggest that most cocaine-positive suicide cases occurred following sustained or binge-like use of the drug, with a high BZE to cocaine concentration ratio concomitant with cocaine concentrations >800 ng/mL in 55% of cases with a further 58% of suicide victims having an admitted history of drug abuse/addiction. In the suicide cases assessed in this study, the primary cause of death was asphyxiation due to self-hanging, rather than by cocaine-induced drug OD. In addition, a considerable proportion of decedents in this study (39%) were listed as being prescribed an antidepressant medication at the time of death. While the causes of suicide are multifactorial and beyond the scope of this study, previous literature highlighted a link between cocaine abuse and increased suicide risk (45–49). Roy et al. demonstrated a strong correlation between childhood trauma/abuse and substance abuse translating into future suicide attempts, with a later study by the same authors identifying strong correlations in a drug-dependent patient group between attempted suicide and major depressive episodes (46, 49).

Limitations

The data collected in this study are based on voluntary reports submitted to NPSAD; in addition, coronial investigations are not carried out for all deaths, so the figures presented here almost certainly under-represent the true number of deaths following cocaine use in England, Wales and Northern Ireland. In addition, the panel of drug testing and the

methodologies used by different laboratories to test samples are varied with no consistent limits of detection or panel of drug screens for each coroner, resulting in a lack of consistency in results provided from the laboratories to the coroners. One of the major challenges in the interpretation of PM toxicology results is this lack of standardization and oversight of the analytical techniques, with further variation in the nature and extent of interpretation supplied by each laboratory. The lack of a requirement for any prescriptive validation or accreditation is a huge area of concern, as basic validation parameters such as uncertainty, matrix effect and specificity are frequently not taken into consideration in the analysis of PM samples. In the UK, toxicology testing of coronial samples is not under the jurisdiction of the Forensic Science Regulator (FSR) and therefore do not require testing laboratories to adhere to the FSR code of practice. In recent years, a number of coroner's offices have requested ISO accreditation during the tender of PM testing. This is a positive development, however, without a prescriptive and detailed framework on the requirements of testing techniques and interpretation standards; PM testing will still lack standardization across suppliers. The UK Accreditation Service has recently rolled out the implementation of Laboratory 51, specific guidance of the ISO 17,025 requirements targeted at toxicology testing. It is hoped that this should improve the consistency of and quality of testing across toxicology laboratories in the UK. Further improvements could be made by developing a national panel of drugs to be tested for in PM cases, possibly in conjunction with a working group from the UK and Ireland Association of Forensic Toxicologists.

For appropriate case segregation, this study relies on the case details provided by law enforcement, medical practitioners and coronial services all of which are independent and have a broad scope for interpretation of case outcomes. Despite this, the data provided to NPSAD are a significant source of information for the UK and international practitioners and highlight the requirement for a nationwide mandatory data repository that can provide a real-time and detailed itemization of the drug deaths in England, Wales and Northern Ireland.

Conclusion

This is the largest study investigating the role of cocaine in drug ODs in the UK. The data presented in this study indicate that there has been a year on year increase in the number of cocaine-related deaths in the UK. Our findings also suggest that cocaine use may lead to irreversible morphological changes in the cardiac architecture of cocaine users, which further predisposes them to increased risk of ischemia and myocardial infraction events. We have also delineated the data on the basis of acute and binge cocaine use with our investigations, suggesting that drug ODs of this nature are most common in white males aged between 35 and 40 years with a previous history of substance abuse. Our results also show that morphine is the most commonly co-detected drug in cocaine ODs and could play a significant role in increased toxicity, by contrast alcohol while frequently detected was commonly found at concentrations not associated with lethality or severe intoxication. This study also identified a number of suicide cases in which the cause of death was self-asphyxiation following prolonged cocaine use.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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