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Purity of street-level cocaine across Denmark from 2006 to 2019: Analysis of seized cocaine

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A B S T R A C T

Cocaine-related emergency department admissions are increasing, and cocaine seizures are at an all-time high in Europe. Our aim was to investigate the trends in purity and adulterants over time in cocaine available to cocaine users at street level in Denmark. We used a representative sample of cocaine seized at street level and analyzed by the national departments of forensic medicine between 2006 and 2019 (n = 1460). Latent profile analysis was used to classify the samples based on cocaine, levamisole, and phenacetin content. Low purity cocaine comprised most of the cocaine seizures in early years, but its share began to decline in 2013, and from 2016 to 2019, the high purity profile was dominant. While the total number of samples containing adulterants decreased, levamisole remained a common and dangerous adulterant. The findings underline the need to inform the public, medical doctors, and service providers for people with drug use disorders about the higher potency of street cocaine.

1. Introduction

Cocaine is a fast-acting psychomotor stimulant made from the leaves of the coca plant, Erythroxylum coca [1]. The majority of coca cultivation and cocaine production takes place in Colombia, Bolivia, and Peru [2,3]. Cocaine is most commonly available as a crystalline powder, hydrochloride (COC), and as freebase, which consists of COC converted to molecular ('crack' cocaine) that is crystal- or rock-like in form and practically insoluble in water [4]. It has been reported that cocaine cultivation and production may be at the highest level recorded globally, and that the peace treaty in Colombia in 2016 has contributed to the upsurge in cocaine production, as the government no longer sprays herbicides over coca fields and no longer destroys crops by hand [5]. Further, cocaine seizures have increased globally and in Europe [6].

Cocaine is among the most commonly used illicit drugs globally, and recent trends have indicated that cocaine use may be increasing; the number of people using cocaine has approximately doubled in the U.S. [7] and the number of fatal overdoses has nearly tripled [8,9]. A number of factors may have contributed to the dramatic increase in overdoses, including psychosocial risk factors and increasingly poor health conditions among drug users [8]. Furthermore, cocaine is often used with alcohol, tobacco, marijuana, or opioids to increase subjective reinforcing effects, and this polysubstance use is associated with greater severity of use, more admissions to hospital, worse treatment outcomes [10,11], as well as a higher likelihood of overdose, especially due to concomitant use of synthetic opioids such as fentanyl [12]. However, another potential factor is the purity of the cocaine itself, as higher levels of cocaine concentrations in cocaine samples have been linked to more cocaine-related emergency room visits [13], suggesting that higher purity leads to more harm.

Only a few years ago, cocaine purity seemed to vary considerably by country and region, with higher purity closer to the areas where the coca leaves were grown [14]. However, the purity of cocaine has increased globally in recent years [15,16]. For example, there is some evidence that the purity of cocaine is increasing in Europe, as drugs

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seized for personal use are becoming purer in Italy [17], and the amount of cocaine in waste water is increasing in Holland, although the population of treatment-seeking patients is stable [18]. For instance, in Queensland, Australia, cocaine has a relatively low purity and a high degree of adulterants compared to other places in the world [19], indicating that global variability of drug purity still exists.

In Denmark, cocaine is the second most commonly used illegal drug, and the second most frequently seized substance after cannabis [20]. While last month use of amphetamine has decreased since 2000 among Danish youth below 25 years, last month use of cocaine has increased [6]. In 2019, 3.9% of young adults in Denmark reported having used cocaine last year, which is the third highest prevalence among countries submitting data to the EMCDDA. Furthermore, the number of primary cocaine clients entering treatment for the first time and emergency room contacts due to cocaine-related poisonings, have increased markedly since 2015 [21,22]. Thus, cocaine use is a growing problem in Denmark, and it is unclear to what extent it is linked with an increased purity of street level cocaine.

Deleterious effects of adulterants in cocaine may also contribute to harm and morbidity. Historically, cocaine has been adulterated or "cut" with a number of substances that mimic the effect of the drug, or "diluted" with inactive substances such as starch or sugar [23]. Ten years ago, the drugs that were most commonly used as adulterants in cocaine were lidocaine, caffeine, and phenacetin, of which phenacetin is likely the most problematic due to its toxicity [2]. In recent years, levamisole, diltiazem, caffeine, procaine, lidocaine, and phenacetin have commonly been found [24,25]. Levamisole and caffeine have a stimulant effect on the central nervous system, which may enhance the effect of cocaine, while diltiazem may be added in an attempt to counteract cardiac adverse effects [26]. Procaine and lidocaine both have similar anesthetic properties as cocaine [23,27]. We consider phenacetin and levamisole as the most important adulterants to focus on in relation to the potential harm of adulterants in cocaine due to their potential toxicity and frequent appearance in cocaine seizures [28,29]. Furthermore, we believe that the composition of street-level cocaine gives the best picture of the cocaine consumed by the users, because the content of street cocaine is more likely to be adulterated to increase profits [30].

1.1. Aims and hypotheses

The aim of our study was to examine potential changes over time in the composition of street cocaine samples confiscated by the Danish police and sent for forensic analysis from 2006 to 2019 by examining: (a) cocaine concentration and (b) presence of phenacetin and levamisole. Based on recent international reports, we hypothesized that the purity of street cocaine in Denmark would increase over time ([6], p. 14).

2. Methods

2.1. Origin of sample material

The data used in this study consist of all samples collected for the large annual surveillance program "Drugs at street-level in Denmark" from 2006 to 2019. The national surveillance program covers a range of illegal drugs, including cocaine, and is conducted by the Danish Health Authority, the Danish National Police, and the three regional forensic laboratories in Denmark [20]. The surveillance program includes small drug seizures from five police districts in Denmark (Eastern, Western, Central, Southern, and Northern Denmark) that are sampled according to a set of well-defined selection criteria (see below). Only drug seizures between 0.03 g and 1 g were included in the program to reflect the prevalence and quality of the cocaine at street level.

Table 1
Descriptive statistics (N = 1460).

	Mean	95% confidence interval
Percent cocaine base	39.8	38.5, 41.1
Number of adulterants	1.3	1.29, 1.41
Adulterant	**Percentage**	
Levamisole	52.1%	49.5, 54.6
Phenacetin	38.6%	36.0, 41.1
Caffeine	18.4%	16.5, 20.5
Lidocaine	14.4%	12.7, 16.3
Procaine	3.8%	2.9, 5.0
Paracetamol	3.7%	2.8, 4.8
Diltiazem	1.8%	1.2, 2.6
Hydroxyzine	1.6%	1.1, 2.4
Salicylic acid	0.0%	0.0, 0.0
Ephedrine	0.0%	0.0, 0.0

Sampling in the program was conducted randomly among available seizures on a weekly basis by the police in Eastern Denmark (Copenhagen), Western Denmark (Aarhus), and Central Denmark (Odense). Specifically, the first seizure made each week after Monday at 8.00 AM is included. In the police districts in Southern Denmark (Esbjerg) and Northern Denmark (Aalborg), sampling was performed once every second week, and of these, the first seizure made every second week after Monday at 8.00 AM was included. The number of seizures by region is shown in supplementary material, Table 1.

In total, 1461 seizures contained cocaine and were included in the dataset. Of these, one seizure had to be excluded due to missing data on purity. As regards to the location of the seizures, 59.8% took place outdoors, 17.5% in cafés or bars, and 22.7% elsewhere. The median weight of the seized samples was 0.38 g (inter-quartile range [IQR]=0.37).

2.2. Chemical analysis

The samples were subjected to both qualitative and quantitative analyses to determine the cocaine concentration and the presence of all common organic small molecules, including the adulterants caffeine, paracetamol, diltiazem, ephedrine, hydroxyzin, levamisole, phenacetin, lidocaine, procaine, and salicylic acid. Diluents such as sugars, starch, creatine, boric acid, and inorganic compounds could, however, not be identified by the analytical methods used. Sample purity is provided as percent base (w/w).

Screening and identification of cocaine and its adulterants were performed using gas chromatography with mass spectrometric detection (GC-MS). Subsequent quantitative analyses of cocaine concentrations were done using either liquid chromatography with UV or mass spectrometric detection or, alternatively, using gas chromatography with flame ionization detection (GS-FID). All analytical methods were validated and accredited according to ISO17025 by the Danish Accreditation Fund (DANAK).

Additional details of the methods used are provided in Supplementary Material, Table 2.

Table 2. Latent profile analysis for cocaine seizures from Denmark 2006–2019 (N = 1460).

	Low purity (n = 980)	High purity (n = 480)
Marginal means ± standard errors:		
Percent cocaine base	23.75 ± 0.41	72.57 ± 0.60
Proportion with levamisole	58.93% ± 0.02	38.03% ± 0.02
Proportion with phenacetin	54.62% ± 0.02	5.83% ± 0.01

2.3. Statistical analysis

Descriptive statistics are reported as means and standard deviations (SDs) for percentage of cocaine base and percentages for types of adulterants. In addition, we generated a count variable representing the total number of different adulterants identified in each sample, end report the means and standard deviations. All analyses were conducted using Stata/SE 15 for Windows [31].

2.3.1. Latent profile measurement model

Latent profile analysis (LPA) is a statistical method used to describe unobserved (i.e., latent) subgroups from patterns of observed variables. It is helpful for identifying clusters (subgroups) of observations that share patterns of characteristics.

We used the Stata generalized structural equation modelling module to identify latent profiles (LPA) of seizures based on three variables: percent cocaine base, the presence of phenacetin, and the presence of levamisole. Percent cocaine base was entered into the models as a continuous variable, and the presence of phenacetin and the presence of levamisole were entered as dichotomous variables using a logit link.[1]

As a sensitivity analysis, we conducted a latent profile analysis in which we included all adulterants that were present in more than 10% of seizures (i.e., phenacetine, levamisole, caffeine, and lidocaine). Finally, in another sensitivity analysis, we added the number of adulterants to the model using a negative binomial link (since the number of adulterants in a sample is a count variable). We compared these models with our original model using the Schwartz information criterion.

Following the LPA, we estimated the predicted class membership for each sample and then used estimated multinomial logistic regression coefficients for covariates (year of seizure and police district) predicting profile membership. Year of seizure was centered to have a mean of zero and an SD of one.

There is some debate about how best to determine the number of latent profiles in any given dataset: Some Monte Carlo simulation studies have been conducted to assess what statistics are the most useful in identifying the correct number of profiles [32,33]. Overall, the best indicator of the number of classes seems to be the Bayesian information criterion (BIC), also known as the Schwarz criterion. The Akaike information criterion (AIC) is another estimator of out-of-sample prediction error and thereby a measure of relative quality of statistical models for a given data set, based on information theory. A lower value of the criterion indicates a better fit, and two values based on the same dataset can be compared directly. The BIC criterion is also based on information theory but unlike the AIC, punishes increased model complexity [34].

3. Results

During the years 2006–2019, the proportion of all samples from the surveillance program that contained cocaine increased from less than 25% in 2006 to 57% in 2019 (See Fig. 1).

The mean purity of the cocaine was 39.8% (SD: 25.6, range: 0.1, 93.0, median 31%, IQR = 45). The mean number of adulterants was 1.3; levamisole was detected in 52.1% of the samples and phenacetin in 38.6% (see Table 1).

Of all samples, 383 or 26.2% had no active adulterants, and of those samples, 153 contained 80% or more cocaine, corresponding to 10.5% of all samples. Given that the purity is calculated as cocaine base rather than cocaine salts, these samples are for all intents and purposes samples that are completely pure cocaine, and have not been cut at all.

Fig. 2 shows the distribution of the purity of cocaine in the samples. As can be seen, the cocaine concentration approximates a bimodal distribution, with one group with a mean cocaine content around 20% and a second group with a mean around 80%. Fig. 3 shows the proportion of seizures containing levamisole and phenacetin as a function of time. The most prevalent adulterant identified in our study was levamisole, which was, however, found in a decreasing number of samples from 2011 to 2018 followed by a small increase in 2019 (see Fig. 3).

3.1. Latent class analysis

The AIC favored a model with two profiles, and similarly, the BIC indicated that a two-profile model was more parsimonious. Two and three class models were conducted using all adulterants that were found in more than 10% of seizures. In addition, a sensitivity analysis was conducted using the number of adulterants as a count variable with a negative binomial link. All of these models had higher BIC than the two profiles model with levamisole and phenacetine, indicating that the latter model was the best fit for the data. Against this background, we retained the two-profile model for further analysis.

Profile 1 was the most common of the two, encompassing 67% of the samples. Samples in this profile had a low cocaine concentration (23.8%), and the majority contained the harmful adulterants levamisole (58.9%) and phenacetin (54.7%). This profile was labelled “Low purity”. Profile 2 was labelled “High purity” and comprised 33% of the samples, which were characterized by a high cocaine concentration (72.6%) and a lower proportion of levamisole (38%) and phenacetin (5.8%) (See Table 2).

Seizures with profile 2 occurred more frequently over time (see Table 3). The frequency of profile membership as a function of time is shown in Fig. 4. As can be seen, the proportion of seizures that falls into the “High purity” profile increased, especially after 2014.

Finally, we wanted to test if the results were similar for the different uptake areas in Denmark. A logistic regression with class membership as the dependent variable and the interaction between uptake area and time did not show any differences in trends over time. Fig. 5 shows the purity of the seized samples as a function of time stratified by uptake area.

4. Discussion

4.1. Summary of findings

Our findings indicate that cocaine at street level has become much more prevalent and much more pure over the past 14 years in Denmark. At the same time, the number of samples containing phenacetin and levamisole has fluctuated, with a decreasing trend in the last few years.

The increased proportion of seized cocaine samples with time is consistent with a recent reported increase in cocaine users in Denmark [21], which is a likely contributing factor to the marked increase in cocaine poisonings and drug treatment admissions with cocaine as the primary drug reported since 2015 [21,22]. The increase in purity of street cocaine is also in line with other studies from the US [15,16] and Europe [17]. It is very likely that the increase in purity is a contributing factor to the increase in admissions for cocaine treatment and cocaine poisonings, enlarging the risk of accidental overdose for the user unaware of the strength.

Interestingly, we found two profiles of cocaine samples distinguished by the level of cocaine purity. Thus, the cocaine that is distributed in Denmark falls into two classes, one of low and one of

[1] The Stata command used was gsem (procentbase1 <- _cons if procentbase1 <.) (phen leva <-, logit), family(gaussian) link(identity) lclass(A 2) nonrtolerance.

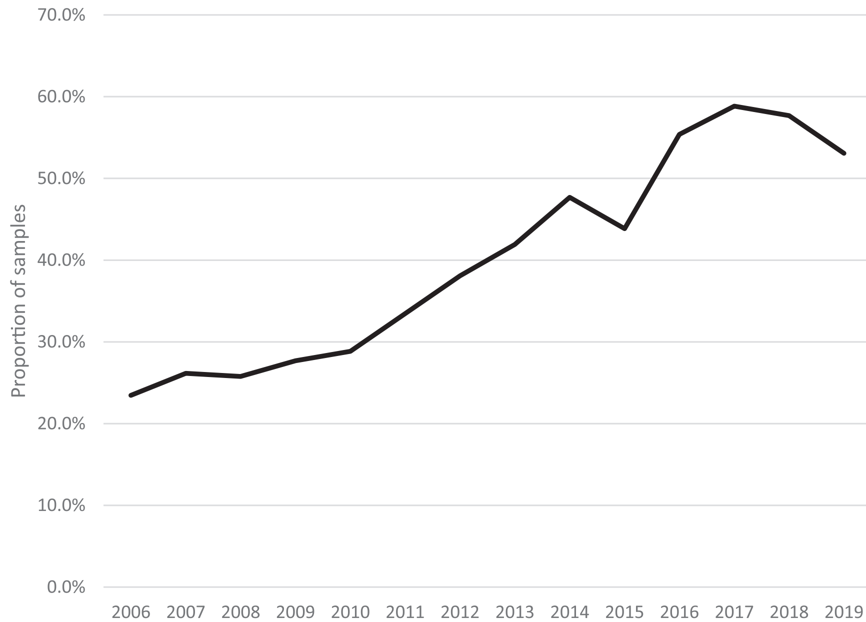

Fig. 1. Proportion of all seizures that are cocaine as a function of years.

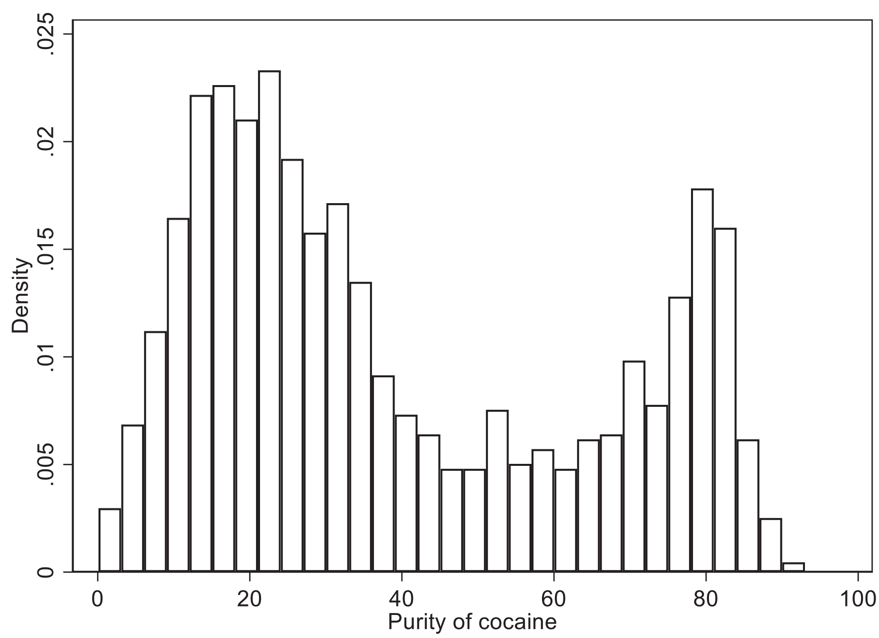

Fig. 2. Observed distribution of purity of cocaine in seizures.

high purity, and over the last years, high purity has all but overtaken the market.

4.2. Impact on cocaine use

It is unclear how the increase in purity influences the hazards of cocaine use. A previous study on composition, purity, and perceived quality of street cocaine showed that although users of cocaine were able to detect samples with an extremely high cocaine content, they were rarely able to tell the difference between adulterated cocaine and relatively pure cocaine [35]. Thus, if a user is consistently supplied with cocaine with the same profile, the risk of overdose is probably limited, while if a user is shifted unknowingly from low to high purity cocaine, it could have serious consequences. Further, besides the shifts in purity, adulterants [36], concomitant use of other drugs, general health factors [37] and mental disorders may also make it harder for the user to assess the strength of cocaine.

4.3. Implications of levamisole and phenacetin

Levamisole is a synthetic imidazothiazole derivate used to treat parasitic worm infections. It is no longer used to treat humans due to its toxicity [38]. Chronic toxicity of levamisole is characterized by bone marrow toxicity, leukoencephalopathy, and vasculitis. Furthermore, the active metabolite aminorex can induce pulmonary hypertension [28]. The forensic institutes in the Netherlands found that the content of levamisole in cocaine samples was most often 1–10% but in some samples, up to 30% or more. The authors of a thorough review of levamisole's adverse effects in cocaine users [28] suggested that average use of cocaine (0.63 g/day) with a levamisole

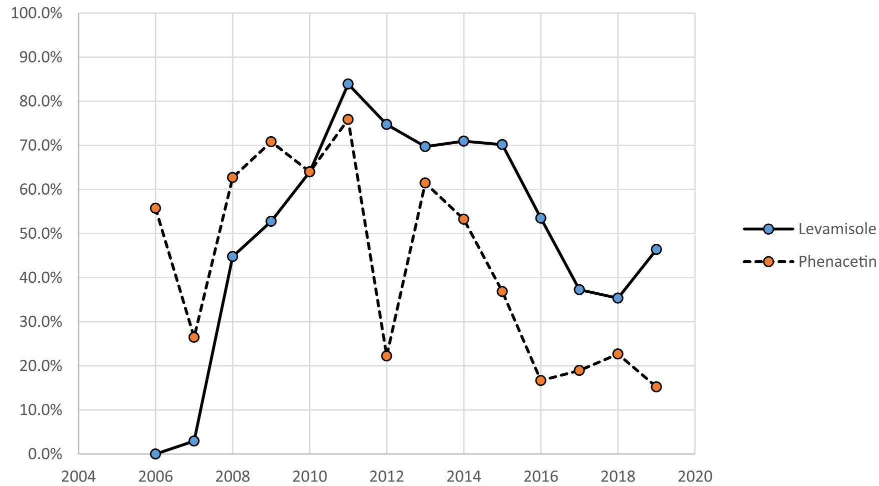

Fig. 3. Proportion containing levamisole and phenacetin as a function of year of seizure.

Table 3
Predictors of high purity class membership.

Predictors	Mean ± standard error Low purity	High purity	Odds ratio	P-value	Adjusted odds ratio	P-value
Year of seizure	2012 ± 0.12	2016 ± 0.68	6.19 ± 0.65	0.000	9.11 ± 2.08	0.000
Year of seizure squared	–	–	–	–	1.07 ± 0.22	0.741
Weight of seizure	1.68 ± 0.88	0.40 ± 0.01	1.00 ± 0.00	0.171	1.00 ± 0.00	0.578

Notes: Adjusted odds ratios estimated with random effects for uptake area (coefficients not shown).

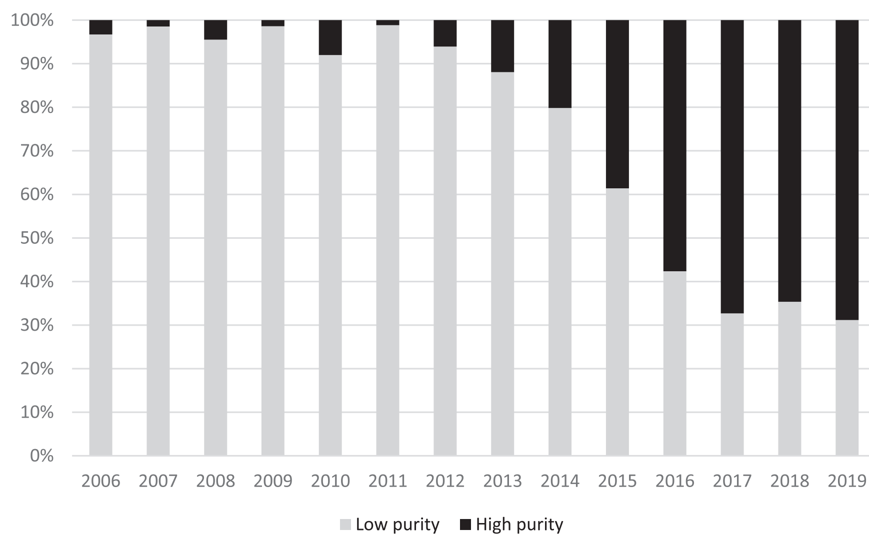

Fig. 4. Predicted profile membership as a function of year of seizure.

content of 10% would result in a levamisole exposure below the toxic levels known from clinical studies. However, due to the variation of levamisole content, average cocaine use may pose a risk for chronic toxicity. Levamisole may also contribute to acute cocaine toxicity due to an ability to increase monoamine levels [28], enhancing the effects of cocaine. However, the impact of levamisole on the risk of acute cocaine poisoning requiring emergency room contact is hard to determine since levamisole dose in relation to such emergencies is unknown. Altogether, a contributing role of levamisole in cocaine-related emergencies cannot be excluded, but levamisole toxicity is an unlikely explanation for the increase in cocaine-related emergency room contacts due to the decreasing prevalence of levamisole in seizures.

Phenacetin was marketed as an analgesic and antipyretic drug in 1913 and was widely used until it was abandoned in the 1950 s based on studies showing that chronic ingestion was associated with cancer and interstitial nephritis [39,26,40]. Of note, cocaine abuse may induce renal injury per se by multifactorial mechanisms including e.g. sympathetic and platelet activation. Thus, the role of phenacetin in cocaine-related renal disease is difficult to isolate. It seems that the risk of cancer and interstitial nephropathy is associated with a relatively high amount of ingested phenacetin [26,40]. In our study, concentrations of phenacetin in cocaine seizures were not determined, and we were not able to find other data on the percent-wise content of phenacetin in cocaine seizures. Taken together with the great variation in cumulative doses of cocaine in

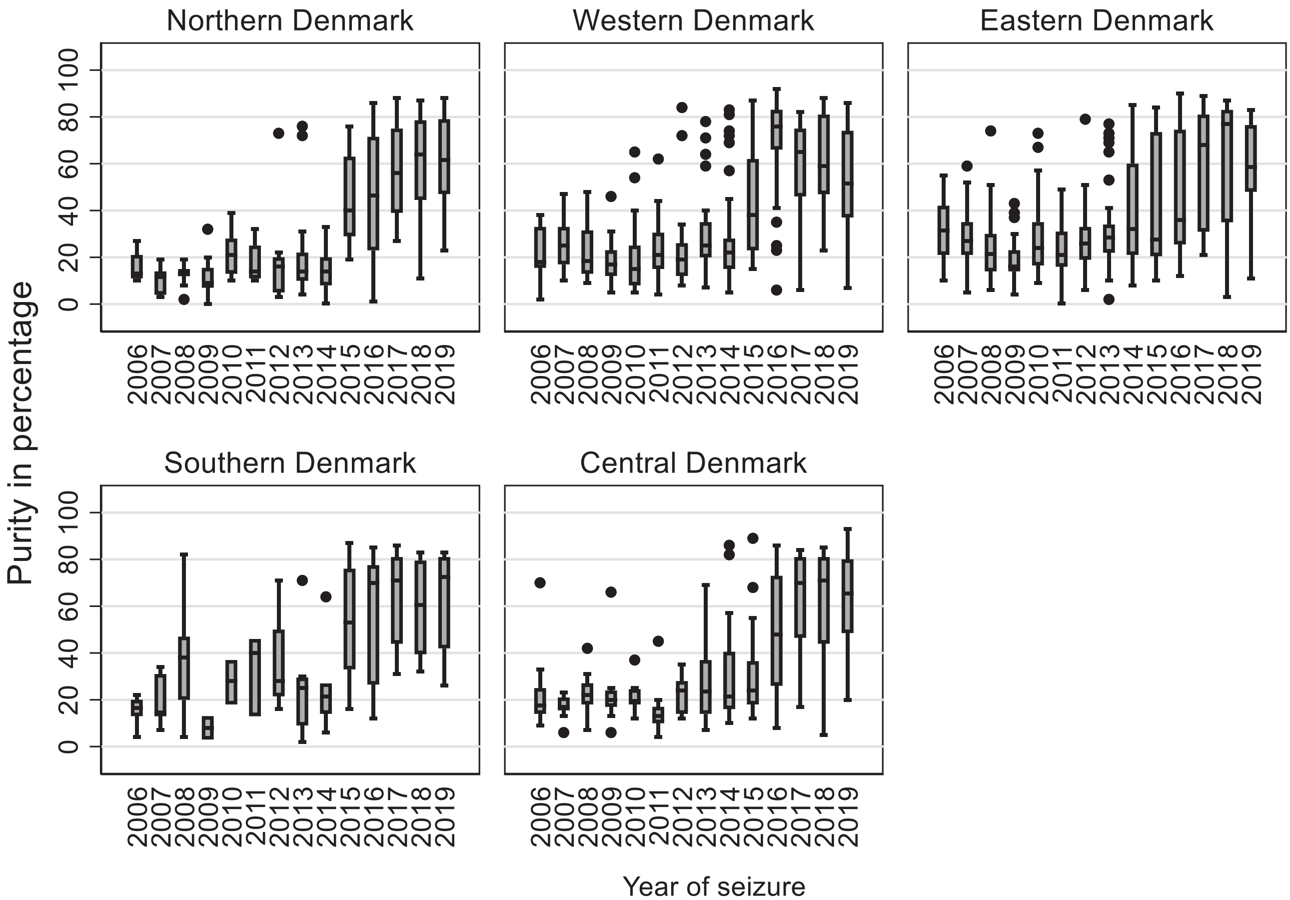

Fig. 5. Purity of seized samples as a function of year of seizure by uptake area. Note: the black lines in the middle of the boxes represent the median purity, the boxes the interquartile range, and the whiskers the non-outlier range. Black dots represent outliers.

different users, it is difficult to determine the risk of cocaine users being exposed to harmful amounts of phenacetin [40]. A recent study on cocaine-positive post-mortem blood samples and samples from impaired drivers found phenacetin concentrations within the therapeutic level range in 19% of the samples [41]. However, the amount of ingested phenacetin and cocaine in this study was not known. In our study, the samples containing phenacetin decreased over time and accounted for approximately 20% or less of the samples since 2016, which speaks against phenacetin as a main cause of the apparent increased cocaine-related burden in Denmark.

4.4. Limitations

Some limitations in this study must be acknowledged. Only confiscated cocaine could be included, and not all cocaine seizures were sent for analysis. However, the samples were randomly selected and are representative of the cocaine that reaches the buyers at street level in Denmark. Perhaps more important, not all adulterants were included in the analyses, and diluents such as sugars, starch, creatine, boric acid and inorganic compounds could not be identified by the analytical methods, which is why we chose to focus only on the most dangerous adulterants.

A further limitation is that our only source of cocaine was the police. Therefore, the methods used by the police to identify individuals who were in possession of drugs influenced the types of samples that we had access to. If any meaningful changes to police strategies had occurred during the period covered, these could have potentially influenced the results. However, we are not aware of any such changes, and no new legislation came into force during the period covered.

5. Conclusions

During the years 2006–2019, Denmark saw a dramatic shift towards cocaine in the drugs that were seized at street level. At the same time, the purity of the cocaine at street level increased markedly, and levamisole remains a common and dangerous adulterant in the cocaine that is available to drug users. The extremely high potency of the cocaine seized is likely to lead to more adverse effects of cocaine, including more psychotic symptoms, more dependent users, and more adverse health effects. Services for people with mental health problems, substance use disorders, or the homeless should be aware of this challenge. The findings point to the usefulness of systematic routine collection of forensic data for monitoring of societal challenges, within and beyond the field of criminal offending.

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CRedit authorship Contribution statement

Morten Hesse: Conceptualization, Methodology, Formal analysis, Writing - original draft. **Kristine Rømer Thomsen:** Literature Review, Writing - review & editing **Birgitte Thylstrup:** Literature Review, Writing - review & editing **Charlotte Uggerhøj Andersen:** Literature Review, Writing-Review & editing **Lotte Ask Reitzel:**

Investigation, Writing - review & editing **Martin Worm-Leonhard:** Investigation, Writing - review & editing. **Christian Lindholst:** Conceptualization, Investigation, Writing - review & editing.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.forsciint.2021.111050.

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