

Commentary – Heroin purity and adulteration: an updated snapshot from the Italian Early Warning System

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Heroin is the most commonly used opiate with 29.2 million users in 2017 worldwide, which represents a more than twofold increase of the estimated global consumption compared to 2008^{1,2}. By contrast, only a slight increase from 1.3 to 1.4 million drug users was observed in Europe over the last decade^{3,4}. The recent discovery of illicit heroin laboratories in Bulgaria, Czech Republic, Spain, and the Netherlands and the increase in drug seizures in Europe suggest that a percentage of street heroin is now produced closer to the European drug market⁵.

In Italy, the latest national report on drug abuse to Parliament indicated that the number of high-risk heroin users substantially increased by 35% from 2008, representing approximately 285,000 users in 2018⁶. Concurrently, with the increase of heroin users, a 10% increase in the number of drug-related deaths was reported in 2017, in Italy; in most cases, heroin was involved, either alone or in combination with other psychotropic substances⁶⁻⁹. Different causes have been suggested to explain this increase in heroin-related overdose fatalities: a potential change in adulterants composition^{10,11}, a simultaneous use of new psychoactive substances (NPS) (especially new synthetic opioids), the illicit sale of fentanyl or/and analogues as cutting agents or in place of heroin, and a possible increase in heroin purity in street preparations^{5,12}.

In this concern, we sought to explore the variability of heroin purity in products seized by the police forces in Italy from 2013 to 2019 and reported by the Italian Early Warning System (IEWS) on classic drugs and new psychoactive substances. The data highlight a fluctuating trend increase in drug purity from 2013 to 2018 with a significant rise in 2019 all over the country,

especially in northern regions of Italy (Table I). The average heroin purity was lower than 30% in 2013 (range: 15.0-51.5%), was 33.9% (range: 21.1-59.1%), 32.2% (range: 20.2-48.7%), 33.1% (range: 24.3-49.1%), 35.0% (range: 14.5-51.5%), and 30.7% (range: 13.9-42.4%) from 2014 to 2018, and reached 48% in 2019 (range: 32.2-74.5%) (Figure 1). Between 2013 and 2019, most products were seized in northern regions (86.2%), whereas 9.2% seizures were made in southern Italy and 4.6% in central Italy (Table I). Interestingly, caffeine was the most common adulterant (55.4% cases), followed by methorphan (52.3% cases) and paracetamol (36.9% cases); information on adulterants was not available in 24% cases. Caffeine and paracetamol¹³ are indeed the most frequently reported adulterants in street heroin¹⁴. It has been suggested that caffeine induces additional synergistic effects when smoked, improving opiate uptake¹⁵ and slightly enhancing drug effects¹⁶; levamisole has been widely used as an adulterant in cocaine seizures for similar reasons^{17,18}. By contrast, paracetamol is used as a cheap and readily available cutting agent since it has a melting point similar to that of heroin. Methorphan, an opium alkaloid, refers to a racemic mixture of two stereoisomers: dextromethorphan, an over-the-counter cough and cold medicine also used as a recreational drug for its dissociative and psychedelic effects¹⁹, and levomethorphan, a potent narcotic agent of the morphinan family that has never been commercialized. Methorphan use as heroin adulterant has not been reported by other countries, suggesting a specific feature of the Italian drug market²⁰.

Generally speaking, only limited information is currently available on the presence and

Table I. Heroin purity and adulterants in products seized in Italy between 2013 and 2019.

Year	Region	Color	Purity (%)	Other opiates	Adulterants
2019, September	Puglia	Beige	74.5	–	–
2019, June	Trentino-Alto Adige	Beige	32.9	–	Caffeine, paracetamol
2019, May	Lombardia	Beige	50.3	–	–
2019, April	Puglia	Beige	44	–	Caffeine, paracetamol
2019, March	Lazio	Beige	51.4	–	Paracetamol
2019, February	Lazio	Beige	48.6	–	–
2019, January	Lombardia	Brown	34.5 (*)	Methorphan, morphine, 6-monoacetylmorphine	Caffeine, paracetamol
2018, November	Lombardia	Beige	38.8	6-monoacetylmorphine, acetyl codeine	–
	Veneto	Beige	13.9	6-monoacetylmorphine (5.12%), acetyl codeine	Caffeine, paracetamol
2018, October	Trentino-Alto Adige	Beige	26.5	Methorphan	Caffeine, paracetamol
2018, August	Veneto	Beige	20.5	6-monoacetylmorphine, acetyl codeine	Caffeine, paracetamol (10.6%)
2018, July	Trentino-Alto Adige	--	41.8	Methorphan	Caffeine
2018, May	Trentino-Alto Adige	Beige	30.6	–	Phenacetin, caffeine, paracetamol
2018, April	Trentino-Alto Adige	Beige	17.7	–	Dimenhydrinate, caffeine, paracetamol
2018, March	Lazio	Beige	41	Methorphan, 6-monoacetylmorphine	Caffeine
	Campania	Beige	42.4(*)	Methorphan, 6-monoacetylmorphine (4.5%)	Caffeine
	Veneto	Beige	23.8	acetyl codeine, 6-monoacetylmorphine (11.7%)	Caffeine, paracetamol
2018, February	Veneto	Beige	33.8	Methorphan, codeine, acetyl codeine, 6-monoacetylmorphine	Paracetamol
2017, March-August	Veneto	Beige/Yellow ocher	51(*)	Methorphan	Caffeine, paracetamol
			37.5(*)		
			30(*)		
			51.5(*)		
			40(*)		
			44.5(*)		
			26(*)		
			14.5(*)		
			22(*)		
15.5(*)					
2017, February	Lombardia	Beige	51.2	6-monoacetylmorphine (7.7%)	–
	Veneto	Beige	50.8	Meconin, acetyl codeine, 6-monoacetylmorphine (8.6%)	–
2017, January	Trentino-Alto Adige	Beige	21	Metorphan, 6-monoacetylmorphine, morphine	–
2016, May	Trentino-Alto Adige	–	24.3(*)	Methorphan	Caffeine, paracetamol
	Emilia-Romagna	--	49.1	Methorphan	Caffeine

Continued

Table 1 (continued). Heroin purity and adulterants in products seized in Italy between 2013 and 2019.

Year	Region	Color	Purity (%)	Other opiates	Adulterants
2016, April	Trentino-Alto Adige	–	25.8	Methorphan	Caffeine, paracetamol
2015, December	Trentino-Alto Adige	–	20.2	–	–
2015, October	Veneto	–	30.1	–	–
2015, September	Trentino-Alto Adige	–	32.8	–	–
2015, July	Lombardia	–	48.7	–	–
2015, May	Piemonte	–	36.7	–	–
2015, March	Veneto	–	21.7	–	–
2015, January	Trentino-Alto Adige	–	35.8	–	–
2014, September	Trentino-Alto Adige	–	59.1	Codeine, thebaine, noscapine	
2014, March	Veneto	–	30.1	Acetyl codeine, methorphan	Paracetamol, caffeine, mannitol
			32.4	Acetyl codeine, methorphan	Paracetamol, caffeine, mannitol
2014, February	Veneto	–	21.1	Methorphan	Caffeine, paracetamol
			47.6	Methorphan	Caffeine, mannitol
			32.5	Methorphan	Caffeine, paracetamol
			44.6	Methorphan	Caffeine
	Piemonte	–	38.5	Methorphan	Caffeine
			21.4	Methorphan	Caffeine, paracetamol
	Campania	–	22.1	Methorphan	Caffeine, lidocaine, paracetamol
2014, January	Piemonte	–	24.2	Methorphan	Caffeine, lidocaine, paracetamol
2013, November	Veneto	–	47.6	Methorphan	Caffeine, paracetamol
	Trentino-Alto Adige	–	51.5	Methorphan, 6-monoacetylmorphine	Caffeine
	Campania	–	24.3	Methorphan	Caffeine
			21.8	Methorphan	Caffeine
	Piemonte	–	28.1	Methorphan	Caffeine
			29.1	Methorphan	Caffeine
2013, September	Trentino-Alto Adige	–	28.9	Methorphan	Caffeine
			36.4	Methorphan	Caffeine
			29.2	Methorphan	Caffeine, paracetamol
			29.6	Methorphan	Caffeine, paracetamol
	Piemonte	–	15	Methorphan	Lidocaine
	2013, June	Trentino-Alto Adige	–	16.3	Methorphan
–			31.3	Methorphan	–

(*) average purity of heroin seized

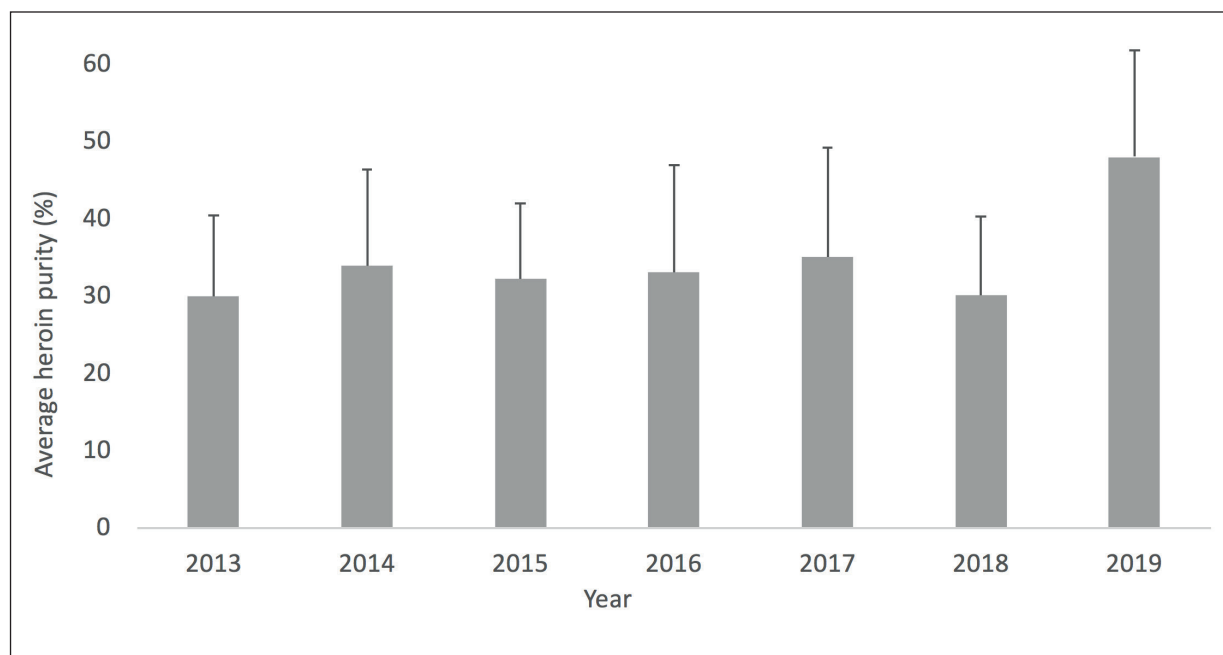


Figure 1. Purity of heroin products seized in Italy between 2013 and 2019. Bar are mean values with standard deviations.

concentration of drug adulterants in Italy. There is no standardized protocol to perform complete toxicological analysis of seizures, and concentrations of adulterants are rarely assessed. Testing of adulterants is not required by the judicial authorities and is generally not performed¹⁹. The absence of reports on the detection of NPS as heroin adulterants, which has been described in other countries, may be another consequence of this regulatory vacuum²¹. Additionally, certified standards of the newest NPS are rarely available and detection methodologies are not frequently adapted. For this reason, the IEWS promoted the “NPS-LABVEQ” project in 2019, aiming to improve the performance of laboratories for developing and validating analytical methodologies to identify NPS in non-biological and biological matrices²²⁻²⁴. Therefore, IEWS laboratories, including the police forces, have been encouraged to search for distributed NPS in upcoming seizures and in cases of intoxication and fatalities, including heroin-related overdoses.

The increase in opiate overdoses during the last two years have been improperly attributed to the so-called “yellow” or “cheese” heroin by the media²⁵. “Yellow” heroin is a street preparation of a black tar with a heroin purity

ranging from 2 to 8%, cut with paracetamol and diphenhydramine, an antihistaminic²⁶. It was first described in the United States, where it caused a high number of deaths among teenagers in Dallas between 2005 and 2007²⁷. In reality, only one single seizure of “yellow” heroin, containing a non-established amount of diphenhydramine, was reported in Italy during the last decade (central region of Umbria in 2018). This seizure was an isolated case and is not responsible for the rise of heroin-related overdose fatalities. Local media²⁸ hypothesized that this highly deadly heroin could be cut or totally replaced by illicit fentanyl and analogues. This hypothesis has not been confirmed by toxicological analyses and it was finally concluded that a continuous rise in heroin purity, demonstrated by the present data, is the probable cause of the rising number of heroin-related overdoses.

The diffusion of this higher-purity heroin, in Italy represents a significant public health problem that requires intensive coordination and collaboration between governmental institutions, law enforcement agencies, forensic laboratories, and the scientific community to raise awareness on the issue and alert health professionals involved in the care and cure of heroin addicts.

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Conflict of interest

The authors declare that they have no conflict of interests.

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