Drug checking to detect fentanyl and new psychoactive substances

Joseph J. Palamar, Alberto Salomone, and Monica J. Barratt

Purpose of review
Drug checking services invite drug consumers to anonymously submit drug samples for chemical analysis and provide feedback of results. Drugs are tested for strength/dose and/or presence of adulterants. Drug checking appears to be more common in recent years in response to increases in fentanyl-related deaths and the proliferation of new psychoactive substances (NPS). We aim to provide information regarding the current state of drug checking in relation to analysis methods, adulteration rates, and behavioral responses to results.

Recent findings
Various technologies are being used to detect the presence of fentanyl, its analogs, and other NPS in drug samples. Proxy drug checking, which we define as biospecimen testing for drug exposure postconsumption, is also becoming common. However, there appears to be a dichotomy between research focusing on populations at high risk for fentanyl exposure and to exposure to NPS such as synthetic cathinones.

Summary
Drug checking research and services largely focus on opioid consumers and nightclub and dance festival attendees, but more focus may be needed on the general population. Drug checking results can inform surveillance efforts, and more research is needed to overcome barriers to drug checking and to focus on whether test results indeed affect behavior change.

Keywords
adulterants, drug checking, ecstasy, fentanyl, heroin

INTRODUCTION
Drug checking services invite members of the public to anonymously submit psychoactive drug samples for chemical analysis and then provide individualized feedback of results and counseling as appropriate [1**]. Such services have been operating for over 50 years and have been known as drug checking, street drug analysis, pill testing, adulterant screening, multiagency safety testing, and drug safety testing [1**,2]. Drug checking services operate as a harm reduction service, aiming to help people who intend to use illegal drugs understand their contents and their dose/strength so they can adjust their drug-taking practices to reduce risks. These services are also a source of data for drug trend surveillance, aiming to detect misrepresented substances, particularly high-strength/dose samples, unexpected drug combinations, or new psychoactive substances (NPS), which are new drugs designed to mimic common drugs. Test results help facilitate rapid public health responses.

ANALYSIS METHODS FOR TESTING OF DRUG PRODUCT PRECONSUMPTION: DRUG CHECKING
Many recent studies have focused on traditional drug checking, in which drug products (e.g., pills, powders) are directly analyzed. Three recent studies focused mainly or exclusively on fentanyl testing. The most comprehensive study compared the efficacy of BTNX immunoassay fentanyl test strips, TruNarc, ThermoFisher Scientific, Waltham, MA (Raman
KEY POINTS

- Various technologies are being used to detect the presence of fentanyl, its analogs, and other new NPS in drug samples and quantify a wide range of illegal drugs.
- Proxy drug checking, defined as biospecimen testing for drug exposure postconsumption, is becoming common.
- There appears to be a dichotomy between research focusing on populations at high risk for fentanyl exposure and to exposure to NPS such as synthetic cathinones.

spectroscopy), and Bruker Alpha [Fourier-transform infrared spectroscopy (FTIR)] in detecting presence of fentanyl or its analogs in drug product [3**]. Test strips were found to have higher sensitivity and specificity than Raman and Bruker Alpha, and strips were also better able to detect smaller amounts of fentanyl and fentanyl analogs. Another study used FTIR and fentanyl test strips (to balance the low sensitivity of FTIR) to test various drugs [4*]. The authors presented results on the basis of FTIR or test strips; however, specific results from FTIR were not reported. Another article [5] focused on fentanyl detection used paper spray–mass spectrometry (MS) and proposed this as a point-of-care screening tool to be used before or in combination with more conventional techniques [e.g., liquid chromatography (LC)–MS]. The authors report simplicity, low-cost, potential high sample throughput, and high sensitivity and specificity, but specific estimates were not reported.

With regard to testing of a wider range of drugs, one study [6*] used Raman to test drug samples outside of nightclubs [and used gas chromatography (GC)–MS or LC–MS/MS to later test unidentified samples]. MDMA, ketamine, cocaine, and amphetamine were the most common drugs detected. Raman identified nine NPS and fentanyl was not detected. A similar study at music festivals used FTIR in combination with fentanyl strips to increase detection power [7]. Most samples submitted were psychostimulants and psychedelics. Very few samples tested positive for NPS and only one sample (an ‘unknown pill’) tested positive for fentanyl. Another study [8] tested low-voltage paper spray ionization quadrupole time-of-flight (QTOF)–MS and was able to detect NBOMe, DOB, and 4-F-α-PVP. The authors believe this method can be used to enhance the performance of other methods; for example, it can be used as a qualitative screening before MS. Another study [9] used thin-layer chromatography (TLC) and reagent testing to detect the presence of adulterants in drugs at dance festivals. Reagents were used for preliminary screening and spot confirmation after TLC. The majority of samples tested were purported MDMA or LSD, 10 and 12% of these drugs, respectively, tested positive for other drugs (mainly NPS such as synthetic cathinones and NBOMe).

BIOSPECIMEN TESTING POSTCONSUMPTION: PROXY DRUG CHECKING

Although traditional drug checking entails testing of drug product, we located many studies that tested for exposure, postuse, via biospecimen testing. This method of postconsumption drug checking can help consumers and researchers learn what drug(s) individuals have already been exposed to, especially when there are legal concerns about direct testing of drugs submitted by consumers. With regard to testing for fentanyl exposure, ultra-high performance LC (UHPLC)–MS/MS [10**] was used in one study to detect (unintentional) exposure to fentanyl, its analogs, opioid NPS, and fentanyl biomarkers/metabolites among past-month heroin consumers in detoxification. Almost all (98%) hair samples tested positive for one or more of these compounds. However, the authors determined in this study and in a similar study [11] that fentanyl analogs and/or other opioid NPS were always accompanied with a positive fentanyl test result. Therefore, if any fentanyl exposure is the outcome of interest, testing for analogs and opioid NPS may not be necessary.

With regard to urine testing, one study conducted enzyme immunoassay testing [12] to test for fentanyl exposure, with confirmatory testing among those initially positive (using triple quad LC–MS/MS) and 91% of heroin consumers tested positive for fentanyl. Another study [13] tested rudimentary flow strips developed to separate fentanyl from biofluids to be examined using surface-enhanced Raman spectroscopy. The remaining studies focused on fentanyl testing only used test strips to test urine of heroin injectors [14], opioid consumers [15], and cocaine and opioid consumers [16]. In some studies, drug consumers were provided test strips to test either their own urine or drug product [17–20].

Although most studies focused mainly or solely on fentanyl testing, one study [21] collected biospecimens from dance festival attendees to test for NPS exposure. The researchers used LC–QTOF MS to test saliva samples, and positive screen results were later confirmed using LC–MS/MS.

We believe testing of drug product and biospecimens each provide valuable drug-checking or drug exposure-related information. Although both direct
and proxy drug checking studies are valuable from a surveillance perspective (e.g., to triangulate findings), only direct drug checking can provide information to consumers prior to consumption. Consumers may not always have the opportunity to receive their results from biospecimen testing, and dissemination may be at the aggregate level when the study is completed.

**COMPARISON OF TESTING METHODS**

Of all methods discussed above, when the main concern is fentanyl, test strips may be most ideal for nonlaboratory settings. They are highly sensitive and specific, they are able to cross-react with multiple fentanyl analogs, and they can detect smaller amounts compared with portable machine tests (i.e., Raman, Bruker Alpha). Test strips can also be utilized anywhere and they are inexpensive (~$1 each). However, fentanyl test strips are qualitative so they cannot measure the amount present in samples and cannot differentiate between fentanyl analogs. Fentanyl test strips were also not originally designed to test drug product [22], and BNX single drug test strips cannot detect drugs other than fentanyl and some of its analogs [23]. They may also be too sensitive, testing positive in response to trace amounts of drug, which may leave some consumers who test positive believing they can now handle fentanyl exposure [22].

Raman, FTIR, LC–MS, and other technologies mentioned above are all expensive machinery, and some equipment requires a laboratory. Portable Raman and FTIR have limited sensitivity, but good specificity. Although they can easily detect the most abundant molecule, any other compounds (i.e., adulterants or cutting agents) might go undetected. A benefit regarding Raman, however, is that researchers do not have to touch the substance (which helps avoid potential legal risk). Methods such as MS, although expensive, provide quantitative results with low pg-to-ng-level detection. Portable versions are becoming available, but at the moment, MS testing is still mostly conducted in laboratories. Finally, although colorimetric reagents are indeed helpful for detecting adulterants, these tests are not always the most accurate and findings are not always easy to interpret [22,24]. When MS is unavailable or infeasible, a combination of techniques discussed above appears to help balance limitations of each separate test.

**EPIDEMIOLOGY OF DRUG CHECKING AND DISSEMINATION OF FINDINGS**

For the first time, in 2019, the European Drug Report [25] presented data from drug checking, obtained from the Trans-European Drug Information (TEDI) Project. TEDI obtains results from many drug checking organizations throughout Europe with each using different testing methods, including LC with diode array detection (LC-DAD) and GC–MS, TLC with GC–MS and ultraviolet (UV) spectrophotometry, and/or mobile HPLC devices equipped with DAD/UV–Vis spectrometers and autosamplers [26]. MDMA, cocaine, and amphetamine were the most common drugs submitted for testing, and <5% of samples tested positive for NPS (mainly synthetic cathinones). Regarding estimates of who tests their drugs, a survey of ecstasy-using nightclub and festival attendees also recently estimated that 23% have had their ecstasy tested in the past year, although tests were most likely conducted using reagents [27].

With respect to distribution of drug checking, a recent survey of 31 drug checking services around the world [11] found that 48% use one or more MS or LC method, 35% use at least one spectroscopy method (e.g., FTIR, Raman), 42% use TLC, and 52% use reagent tests. Of those using reagents, 25% only used this method.

**PREVALENCE OF FENTANYL/NPS DETECTION: ADULTERANTS IN DRUGS AND UNKNOWN EXPOSURE**

There was somewhat of a dichotomy between studies testing for fentanyl and studies testing for a wider range of substances. With regard to testing of party drugs (e.g., ecstasy), most studies tested drugs or collected biospecimens for testing at dance festivals. A study examining biospecimens of festival attendees [21] reported that 30% of ecstasy consumers tested positive for NPS (mainly synthetic cathinones) after denying use. With regard to direct testing of drug product, drug testing at a festival [9] determined that 9% of ecstasy submitted was adulterated, mainly with synthetic cathinones, and a study testing drugs at festivals [28] determined that 4% tested positive for NPS (mainly synthetic cathinones).

The other studies focused mainly or solely on fentanyl detection and detected high prevalence of fentanyl. A recent study in Canada [4] determined that 91% of purported heroin samples tested positive for fentanyl, and 6 and 2% of (meth)amphetamine and cocaine, respectively, also tested positive for fentanyl. No psychedelics or other party drugs (e.g., ecstasy) tested positive for fentanyl. At a supervised injection facility [29], 84% of those testing heroin detected fentanyl (in drug product or in urine). Urine-tested postconsumption, however, was more likely to be positive for fentanyl compared with those checked drug product preconsumption (83 vs. 77%). This suggests that testing for exposure...
postuse is more likely to detect fentanyl exposure, albeit after use.

With regard to studies testing biospecimens for fentanyl exposure postconsumption, a recent study hair-tested past-month heroin consumers in detoxification [10**] and determined that 98% of participants (72% of whom reported no known fentanyl use) tested positive for fentanyl, and often fentanyl analogs and/or other opioid NPS. Another study [15] found that 91% of people reporting opioid use had at least one fentanyl-positive urine sample, yet only 18% reported using fentanyl. Another study that urine-tested individuals in a withdrawal management program [12] found that of those reporting they had never been exposed to fentanyl, two-thirds tested positive for fentanyl. It should be noted that some studies [16,29] utilized fentanyl testing but did not compare results with self-report that limits understanding regarding unknown exposure.

Differential Risk of Exposure Across Populations

As noted above, there appears to be somewhat of a dichotomy between drug-using populations currently at high risk for fentanyl exposure and low risk for exposure, and published studies appear to focus largely on one population or the other. Specifically, most studies focusing mainly or solely on fentanyl exposure have focused on injectors (usually of heroin/opioids, but some participants who report cocaine use and not opioid use) [14,18,29], those reporting prescription opioid and/or cocaine use [17], heroin consumers in detoxification or opioid withdrawal management [10**,12]; and samples mainly consisting of heroin consumers – many of which were homeless [3**,19,30]. At festivals and nightclubs, however, participants almost solely submit party drugs (e.g., ecstasy, LSD) for analysis [6*,7,28], and fentanyl is almost never detected in samples.

Behavior Change in Response to Test Results

Many studies assessed participants’ intention to change their behavior if learning their drug was adulterated. With regard to testing of party drugs, 95% of individuals who had their drug tested at a festival [9] reported that they would throw out their drug if adulterants were detected, and another study found that two-thirds of individuals learning their drug were adulterated disposed of the drug [28]. In a survey study focused on nightclub and festival attendees [27], most ecstasy consumers reported that they would be less likely to use again upon learning their ecstasy contained ‘bath salts’ (synthetic cathinones; 55%) or methamphetamine (54%), and another survey of festival attendees [31] found that the majority of people testing their drug would not use if found to contain methamphetamine, ‘bath salts’, ketamine, or other drugs.

With regard to studies focusing mainly or only on fentanyl exposure, one study [3**] found that 70% of respondents learning that their drugs contained fentanyl would reportedly modify their behavior. Behaviors included not using the drug, using more slowly, and using with others who possess naloxone. Similarly, a hair-testing study [10**] found that upon participants learning they have been exposed to fentanyl, most (75%) said they would try to stop using heroin; 68% would take test doses, 65% would ensure that someone is nearby with naloxone, and 58% reported that they would seek out a more trustworthy dealer. Some other studies, however, found lower prevalence of intention to change their behavior. For example, a study of injectors testing positive for fentanyl [29] found that 36% reported planning to reduce their drug dose and only 11% planned to dispose their drug.

Actual behavior changes after fentanyl exposure appear to be lower than intended behavior changes. For example, one study [20] found that 43% of those exposed to fentanyl changed their behavior with 32% of those exposed reportedly using less of drug than usual, 17% performing tester shots, 10% snorting instead of injecting, and 9% pushing the plunger more slowly. Another study [17] found that among those receiving a positive fentanyl test, 45% used less, 39% used with someone else around, 42% went slower, 36% used a test dose, 10% disposed of the drug, 10% sold the drug, and 7% gave the drug away.

BARRIERS

Since handling (possessing) scheduled drugs is illegal, it may be difficult for researchers to acquire institutional review board approval or federal funding to conduct drug checking studies. Research currently suggests that there is concern about legal liability and testing attracting law enforcement officials [3**]. Key informants have identified additional issues about the implementation of drug checking services, including security risks (such as attracting law enforcement), especially at the point of service [3**]. Some studies found that having to visit a specific place at a specific time could limit interest in testing [32,33]. Some target populations may also not be willing to wait more than a few minutes for test results [32].

Conclusion

Many recent studies have utilized drug checking, and a variety of methodologies were used across a
range of populations. We recommend that drug checking research and services expand beyond opioid consumers and nightclub and dance festival attendees. This would allow us to determine the risk of exposure to adulterants (e.g., in the general population) and help determine whether high-risk populations should indeed remain the main/only focus. We believe drug checking should be included in surveillance efforts, and more research is needed to overcome barriers to drug checking and to further assess the impact of test results on behavior change.

Acknowledgements

None.

Financial support and sponsorship

Research reported in this publication was supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Numbers K01DA038800 (J.J.P.) and R01DA044207 (J.J.P.). The National Drug and Alcohol Research Centre is supported by funding from the Australian Government under the Drug and Alcohol Program. The content is solely the responsibility of the authors and does not necessarily represent the official views of the funders.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

1. of special interest
2. of outstanding interest

1. Barratt MJ, Kowalski M, Maier LJ, Ritter A. Global review of drug checking services operating in 2017. In: Drug policy modelling program bulletin no. 24. Sydney, Australia: National Drug and Alcohol Research Centre, UNSW Sydney; 2018. The bulletin provides a comprehensive description of drug checking services operating worldwide.
2. Rentfrow JL, MDMA on the street: analysis anonymous. J Psychoactive Drugs 1986; 18:363–369.
3. Bloomberg American Health Initiative. Fentanyl overdose reduction checking analysis study. Baltimore, MD: Johns Hopkins Bloomberg School of Public Health; 2018. To our knowledge, this is the first comprehensive study to compare methods for detecting fentanyl and/or its analogs. This study also provides and compares statistics on sensitivity and specificity of each method.
4. Tupper W, McCrae K, Garber I, et al. Initial results of a drug checking pilot program to detect fentanyl adulteration in a Canadian setting. Drug Alcohol Depend 2018; 190:242–245. The study in particular demonstrates that common psychedelics and party drugs (e.g., ecstasy) are currently unlikely to contain fentanyl. However, alarmingly, some samples of purported (meth)amphetamine and cocaine indeed contained fentanyl.
5. Vandergriff GW, Hessels AJ, Palaty J, et al. Paper spray mass spectrometry for the direct, semi-quantitative measurement of fentanyl and norfentanyl in complex matrices. Clin Biochem 2018; 54:106–111.
6. Gerace E, Seganti F, Luciano C, et al. On-site identification of psychoactive drugs by portable Raman spectroscopy during drug-checking service in electronic music events. Drug Alcohol Rev 2019; 38:50–56. The article presents the first field testing activity on the basis of a portable Raman instrument.

1. Barratt MJ, Kowalski M, Maier LJ, Ritter A. Global review of drug checking services operating in 2017. In: Drug policy modelling program bulletin no. 24. Sydney, Australia: National Drug and Alcohol Research Centre, UNSW Sydney; 2018. The bulletin provides a comprehensive description of drug checking services operating worldwide.
2. Rentfrow JL, MDMA on the street: analysis anonymous. J Psychoactive Drugs 1986; 18:363–369.
3. Bloomberg American Health Initiative. Fentanyl overdose reduction checking analysis study. Baltimore, MD: Johns Hopkins Bloomberg School of Public Health; 2018. To our knowledge, this is the first comprehensive study to compare methods for detecting fentanyl and/or its analogs. This study also provides and compares statistics on sensitivity and specificity of each method.
4. Tupper W, McCrae K, Garber I, et al. Initial results of a drug checking pilot program to detect fentanyl adulteration in a Canadian setting. Drug Alcohol Depend 2018; 190:242–245. The study in particular demonstrates that common psychedelics and party drugs (e.g., ecstasy) are currently unlikely to contain fentanyl. However, alarmingly, some samples of purported (meth)amphetamine and cocaine indeed contained fentanyl.
5. Vandergriff GW, Hessels AJ, Palaty J, et al. Paper spray mass spectrometry for the direct, semi-quantitative measurement of fentanyl and norfentanyl in complex matrices. Clin Biochem 2018; 54:106–111.
6. Gerace E, Seganti F, Luciano C, et al. On-site identification of psychoactive drugs by portable Raman spectroscopy during drug-checking service in electronic music events. Drug Alcohol Rev 2019; 38:50–56. The article presents the first field testing activity on the basis of a portable Raman instrument.
7. McCrae K, Tobias S, Tupper K, et al. Drug checking services at music festivals: first events in a Canadian setting. Drug Alcohol Depend 2019; 205:107989.
8. Birks L, de Oliveira SEF, Mafra G, et al. A low-voltage paper spray ionization QTOF-MS method for the qualitative analysis of NPS in street drug blotter samples. Forensic Toxicol 2019; 38:227–231.
9. Valente H, Martins D, Carvalho H, et al. Evaluation of a drug checking service at a large scale electronic music festival in Portugal. Int J Drug Policy 2019; 73:88–95.
10. Palamar JJ, Salomone A, Bigiarini R, et al. Testing hair for fentanyl exposure: a method to inform harm reduction behavior among individuals who use heroin. Am J Drug Alcohol Abuse 2019; 45:90–96. This is among the first studies to detect fentanyl and its analogs in hair samples and a combination of surveys and hair analysis was used to highlight unknown past exposure to fentanyl.
11. Salomone A, Bigiarini R, Palamar JJ, et al. Toward the interpretation of positive testing for fentanyl and its analogs in real hair samples: preliminary considerations. J Anal Toxicol 2019. [Epub ahead of print]
12. Kenney SR, Anderson BJ, Conti MT, et al. Expected and actual fentanyl exposure among persons seeking opioid withdrawal management. J Subst Abuse Treat 2018; 86:65–69.
13. Shende C, Brouillette C, Farquharson S. Detection of codeine and fentanyl in saliva, blood plasma and whole blood in 5 min using a SERS flow-separation strip. Analyst 2019; 144:5449–5454.
14. Barratt MJ, Latimer J, Jauncey M, et al. Urine drug screening for early detection of unwitting use of fentanyl and its analogues among people who inject heroin in Sydney, Australia. Drug Alcohol Rev 2018; 37:847–850.
15. Jones AA, Jang K, Panenka WJ, et al. Rapid change in fentanyl prevalence in a community-based, high-risk sample. JAMA Psychiatry 2018; 75:298–300.
16. Momen SC, Sage C, Popoli S, et al. Expanding harm reduction to include fentanyl urine testing: results from a pilot in rural British Columbia. Harm Reduct J 2018; 18:19.
17. Goldman JE, Waye KM, Periera KA, et al. Perspectives on rapid fentanyl test strips as a harm reduction practice among young adults who use drugs: a qualitative study. Harm Reduct J 2019; 18:3.
18. Krieger MS, Goedel WC, Burton JA, et al. Use of rapid fentanyl test strips among young adults who use drugs. Int J Drug Policy 2018; 61:52–58.
19. Rouhani S, Park JN, Morales KB, et al. Harm reduction measures employed by people using opioids with suspected fentanyl exposure in Boston, Baltimore, and Providence. Harm Reduct J 2019; 16:39.
20. Peiper NC, Clarke SD, Vincent LB, et al. Fentanyl test strips as an opioid overdose prevention strategy: findings from a syringe services program in the Southeastern United States. Int J Drug Policy 2018; 69:122–128.
21. Krutulski AJ, Mohr ALA, Fogarty MF, Logan BK. The detection of novel stimulants in oral fluid from users reporting ecstasy, Molly and MDMA ingestion. J Anal Toxicol 2018; 42:544–553.
22. McGowan CR, Harris M, Platt L, et al. Fentanyl self-testing outside supervised injection settings to prevent opioid overdose: do we know enough to promote it? Int J Drug Policy 2018; 58:31–36.
23. Vandergriff GW, Gill CG. Paper spray mass spectrometry: a new drug checking tool for harm reduction in the opioid overdose crisis. J Mass Spectrom 2019; 54:729–737.
24. Palamar JJ, Acosta P, Sutherland R, et al. Adulterants and altruism: a qualitative investigation of ‘drug checkers’ in North America. Int J Drug Policy 2019; 74:160–169.
25. European Monitoring Centre for Drugs and Drug Addiction. European drug report 2019: trends and developments. Luxembourg: Publications Office of the European Union; 2019. To our knowledge, this is the first national or international report to include drug checking results. We highly recommend that drug checking be used as a form of surveillance as systematic data on drug purity trends are sorely needed.
26. Brunt TM, Nagy C, Bucheli A, et al. Drug testing in Europe: monitoring results of the Trans European Drug Information (TEDI) Project. Drug Test Anal 2016; 9:188–198.
27. Palamar JJ, Barratt MJ. Prevalence of reagent test-kit use and perceptions of purity among ecstasy users in an electronic dance music scene in New York City. Drug Alcohol Rev 2019; 38:42–49.
28. Measham FC. Drug safety testing, disposals and dealing in an English field: exploring the operational and behavioural outcomes of the UK’s first onsite ‘drug checking’ service. Int J Drug Policy 2019; 67:102–107.
29. Karamouzian M, Dohoo C, Forsting S, et al. Evaluation of a fentanyl drug checking service for clients of a supervised injection facility, Vancouver, Canada. Harm Reduct J 2018; 15:46.
30. Sherman SG, Morales KB, Park JN, et al. Acceptability of implementing community-based drug checking services for people who use drugs in three United States cities: Baltimore, Boston and Providence. Int J Drug Policy 2019; 68:46–53.
31. Day N, Criss J, Griffiths B, et al. Music festival attendees’ illicit drug use, knowledge and practices regarding drug content and purity: a cross-sectional survey. Harm Reduct J 2018; 15:1.
32. Sande M, Sabic S. The importance of drug checking outside the context of nightlife in Slovenia. Harm Reduct J 2018; 15:2.
33. Bardsell GB, Boyd J, Tupper KW, Kerr T. We don’t get that kind of time, man. We’re trying to get high! exploring potential use of drug checking technologies among structurally vulnerable people who use drugs. Int J Drug Policy 2019; 71:125–132.