BRITISH COLUMBIA CENTRE ON SUBSTANCE USE
Networking researchers, educators & care providers

Vancouver Coastal Health

Drug Checking

A field assessment of Fourier Transform Infrared (FTIR) Spectroscopy and fentanyl immunoassay strips as point-of-care drug checking technologies

September 2019

Authors and Contributors

Brandon Yau, BSc, MD
PGY-1, Public Health and Preventative Medicine, Department of Medicine, University of British Columbia

Jaime Arredondo, PhD
Project Researcher, Drug Checking Services, British Columbia Centre on Substance Use;
Research Professor, Drug Policy Program, Centro de Investigacion y Docencia Económica

Samuel Tobias, MSc
Senior Drug Checking Operational Technician, British Columbia Centre on Substance Use

Cameron Grant, BSc
Data Analyst, British Columbia Centre on Substance Use

JinCheol Choi, MSc
Statistician, British Columbia Centre on Substance Use

Mark Lysyshyn, MD, MPH, FRCPC
Clinical Assistant Professor, School of Population and Public Health, University of British Columbia;
Medical Health Officer, Vancouver Coastal Health, British Columbia, Canada

Richard Laing, MSc
Manager Strategic Research & Science Development, Drug Analysis Service, Health Canada

Ekaterina Nosova, PhD
Associate Director Research Analytics & Senior Statistician, British Columbia Centre on Substance Use;
Adjunct Professor, Department of Medicine, University of British Columbia

Evan Wood, MD, PhD, ABIM, FASAM, FRCPC, ABAM Diplomat
Executive Director, British Columbia Centre on Substance Use;
Professor of Medicine, Department of Medicine, University of British Columbia

Lianping Ti, PhD
Research Scientist, British Columbia Centre on Substance Use;
Assistant Professor, Department of Medicine, University of British Columbia

Acknowledgements

The authors would like to express our sincere thanks to researchers and staff at the BC Centre on Substance Use, Fraser Health, Lookout Housing and Health Society, Portland Hotel Society, and Vancouver Coastal Health for their collaboration in providing drug checking services at the sites where this work was conducted. We would specifically like to thank Dr. Kenneth Tupper at the British Columbia Ministry of Health and Francine Chartier at the Drug Analysis Service (DAS), Health Canada, for their contributions to this work. Health Canada DAS provided confirmatory testing services; however, the findings reported here should in no way be taken as an endorsement by Health Canada of the specific point-of-care technologies that were used for this study.

Funding

The study was supported by a Health Canada Substance Use and Addictions Program grant to the BC Centre on Substance Use to implement and evaluate a drug checking pilot in British Columbia (Arrangement #: 1718-HQ-000024).

Table of Contents

Executive Summary

The current opioid overdose crisis in North America continues to pose a significant public health challenge, with many jurisdictions continuing to experience high rates of overdose and deaths.[1,2] In Canada, the opioid crisis has affected nearly every region in the country, with British Columbia (BC) and other Western provinces accounting for a disproportionate number of opioid related overdoses and deaths.[3] The introduction of illicitly manufactured opioids into the drug market (i.e. fentanyl, carfentanil) has been found to be largely responsible for the recent increase in opioid-related overdose deaths.[4,5] In response, a number of harm reduction approaches (e.g., expansion of opioid agonist treatment, take home naloxone programs, access to medically supervised safer injecting facilities and overdose prevention sites) have been implemented across the country.[6,7]

One novel harm reduction approach is the widespread provision of drug checking services. There are a range of drug checking technologies available with advantages and disadvantages in terms of applicability, from quick, simple and cheap point-of-care tests to more robust but expensive laboratory-based methods. While drug checking has been utilized as a harm reduction tool for close to 20 years, it has largely been implemented in festival and party settings among recreational drug users in parts of Europe, North and Latin America, and less so in street-entrenched settings.[8,9,10]

This report aims to assess the validity of two point-of-care drug checking technologies – Fourier Transform Infrared (FTIR) spectroscopy and fentanyl immunoassay strips – and to identify important emerging results from BC's drug checking program. It presents preliminary findings in which these point-of-care drug checking technologies were implemented in two supervised consumption sites in Vancouver and Surrey, BC. The validity of these two technologies were investigated in collaboration with Health Canada's Drug Analysis Service (DAS) laboratory, where a second sample of drugs tested with the point-of-care technologies were analyzed using laboratory reference standard drug analysis techniques of quantitative nuclear magnetic resonance (qNMR) spectroscopy and gas chromatography-mass spectrometry (GC-MS) technologies.

Compared with laboratory reference standards, the results indicated FTIR spectroscopy to have a sensitivity and specificity for detecting fentanyl or its analogues of 72.1% and 99.0%, respectively. The positive predictive value for FTIR spectroscopy was 99.4% and the negative predictive value 59.9%, with a false negative rate of 27.9%. In contrast, fentanyl immunoassay strips had a sensitivity of 87.5% and a specificity of 95.2% for detecting fentanyl or its analogues. The positive predictive value for fentanyl immunoassay strips was 98.1% and the negative predictive value 73.4%, with a false negative rate of 12.5% when compared to highly-sensitive qNMR/GC-MS confirmation. Furthermore, the limit of detection for these technologies to consistently identify fentanyl in samples were 10% and 5% for FTIR spectroscopy and fentanyl immunoassay strips, respectively. In a comparative analysis of the percentage concentrations of fentanyl between FTIR spectroscopy and qNMR, findings suggest that the quantitative model from FTIR readings was more accurate when the percent of fentanyl concentration from the qNMR

reading was between 5% and 15%. The median difference in fentanyl concentration between FTIR and qNMR was 0.8% (quartile[Q1]-Q3: -1.1 – 2.2%).

These results have shown that the use of FTIR spectroscopy, in tandem with fentanyl immunoassay strips, to be a valid methodology to detect the presence of fentanyl as well as provide quantitative analysis for fentanyl in the point-of-care setting. Future research is needed to confirm the clinical relevance, if any, of false negatives on immunoassay strips as laboratory methods may be detecting pharmacologically irrelevant fentanyl presence. These results demonstrate that point-of-care drug checking services can provide accurate information to clients and public health authorities and provides support that they should be further investigated as harm reduction and surveillance intervention to help address the opioid overdose emergency.

Background

In Canada, death rates from opioid-related overdoses have risen from 9.3 per 100,000 population in 2016 to 11.2 per 100,000 population in 2018.[1] The introduction of illicitly-manufactured fentanyl and its analogues into the illicit drug market is largely responsible for the increased rate of overdose deaths observed in Canada.[4,5] British Columbia (BC) has been the province most affected by this epidemic, with the highest opioid-related overdose death rate in the country (31 per 100,000 population).[1] Provincial coroner's data suggests that fentanyl was detected (alone or in combination) in 85% of illicit drug overdose deaths in 2018.[11] To respond to this epidemic, BC declared a province-wide public health emergency in 2016.[12]

The declaration of the public health emergency, alongside continued challenges in reducing opioid-related deaths, has generated increased interest in novel approaches to addressing the crisis. Drug checking services have emerged as a harm reduction tool that chemically analyzes drug samples and provides timely results of drug composition and purity back to people who use drugs (PWUD).[8] Drug checking has been implemented primarily in countries across Europe since the early 1990s at party and festival settings for recreational drug users.[8,13,14] Results from European studies have demonstrated that drug checking services are often a first point of contact for many PWUD, with these individuals more likely to adopt risk reduction strategies (e.g. discarding drugs) if their drugs were found to contain harmful or unexpected substances.[15,16]

A variety of drug checking technologies are available to analyze the chemical composition of unknown substances, with advantages and disadvantages in terms of applicability and cost.[5,8] For example, stand-alone central laboratory services utilize robust, expensive technologies and are not limited by using non-destructive techniques, the length of time required to analyse the sample, the technical expertise required to operate the technology, and the portability of the technology. Alternatively, point-of-care drug checking services (e.g., fentanyl immunoassay strips, FTIR spectroscopy) are quick, simple, and cheap but often have decreased sensitivity and specificity and a higher limit of detection in comparison to gold standard central laboratory services.[8] The challenge is to provide a service that can combine the best features of laboratory and point-of-care services, with a quick, easy to operate, portable and reliable technology.

There is a paucity of evidence on the use of point-of-care drug checking as a harm reduction tool in the context of the opioid overdose crisis.[8,9,17] Less is known about the validity of point-of-care drug checking technologies outside of festival and party settings. Moreover, the benefits of drug checking for the purposes of disseminating near-real time public health alerts, monitoring novel or dangerous substances in the illicit drug market, and the impact of these services on preventing overdose deaths remains hypothetical.[8,17] The overall aim of the report is to provide preliminary evidence to validate results obtained through drug checking to provide support for drug checking as a harm reduction tool in the context of the opioid overdose crisis as well as provide evidence for using various specific drug checking technologies.

Objectives

The objectives are to examine the accuracy of various components of two point-of-care drug checking technologies, FTIR spectroscopy and fentanyl immunoassay strips, against laboratory reference standards. Specifically, we will: (1) validate the use of the point-of-care technologies by estimating their sensitivity and specificity for detecting fentanyl or its analogues; (2) determine the limit of detection of fentanyl or its analogues using the two point-of-care technologies; and (3) assess the accuracy of FTIR spectroscopy in quantifying the fentanyl composition of drug samples in a point-of-care setting.

Methodology

Point-of-care drug checking service

The provision of drug checking services is a collaboration between the British Columbia Centre on Substance Use (BCCSU), regional health authorities, and various levels of government. The harm reduction service being evaluated in this report, involves the implementation of point-of-care technologies using FTIR spectroscopy in conjunction with fentanyl immunoassay strips at several supervised consumption sites in Vancouver and Surrey, BC where PWUD anonymously provide samples for testing. These sites were chosen as they had legal exemptions that allowed clients to be in possession of controlled substances, and typically engage with a street-entrenched clientele who live with proportionally high rates of homelessness, substance use disorder, psychiatric co-morbidities and above all, a high risk of overdose.[18,19]

Prior studies on point-of-care testing have found that FTIR spectroscopy has the capacity to rapidly detect and quantify the amount of a variety of compounds, including fentanyl. This technology relies on reference libraries of drugs spectra to accurately identify various substances that may be present. While previous studies have demonstrated that FTIR spectroscopy can detect and quantify fentanyl with high sensitivity (83%) and specificity (90%), the reported 3-4% detection limit may result in failure to detect some fentanyl analogues (e.g., carfentanil) at concentrations that can produce severe toxicity.[5] On the other hand, fentanyl immunoassay strips have shown to have the lowest detection limit (0.13mcg/ml) and the highest sensitivity and specificity.[5] However, there are concerns around the strips being able to detect and distinguish between fentanyl analogues, as well as the inability to provide quantitative information on drug concentrations.[4,5] Taken together, there is evidence to suggest that the use of both technologies in tandem may improve the validity of these methods for detecting fentanyl and its analogues.

The drug checking services provided in BC currently utilizes a combination of *Bruker ALPHA* FTIR spectroscopy and *BTNX* fentanyl immunoassay strips. The drug checking process involves an experienced technician collecting a small 1-2mg drug sample to first test with the FTIR spectrometer. The same portion of the sample is then dissolved in a small amount of water and tested with the fentanyl immunoassay strip. The technician records the results, which includes the percent composition of the primary compounds detected, in average three to four principal components. The client is then informed of the results of the test and offered harm reduction advice

about risk reduction according to what was found via the point-of-care tests. The inherent limitations of the testing methods (i.e. detection limit, inclusion in reference spectra library) are described to the client before and after they are informed of the results.

Health Canada's Drug Analysis Service Laboratory

We used convenience sampling to choose a proportion of drugs that were checked in two point-of-care settings, and then sent for confirmatory analysis to Health Canada's Drug Analysis Service (DAS) laboratory. As per protocol for analyzing drug samples, the DAS laboratory utilizes qNMR spectroscopy as a first-line test when suitable. The qNMR spectroscopy provides a quantitative assessment of compounds and an assessment of impurities and adulterants by comparing qNMR signal intensities against a reference.[20] For samples that are non-water-soluble or samples with trace amounts of a certain compound that may not be captured by qNMR, a second-line test using GC-MS was applied. GC-MS involves the separation of compounds by gas chromatography followed by detection using a mass spectrometer. Qualitative results are reported. For each sample, data on the compound(s) present, as well as the percent concentration of each compound present using qNMR spectroscopy (%) were recorded.

Findings

Fentanyl positivity

Of the 331 samples sent for confirmatory analysis at Health Canada's DAS laboratory that tested positive for fentanyl or its analogues, FTIR spectroscopy identified 169 (51.1%) of these samples to be positive for fentanyl or its analogues, whereas fentanyl immunoassay strips identified 207 (62.5%) of these samples to be positive for fentanyl or its analogues. The concentrations of fentanyl in the samples tested ranged from 1% to 91% by weight, with a median fentanyl concentration of 7.4% (quartile [Q]1 – Q3: 5.5 – 12%).

Confirmatory testing of point-of-care technologies

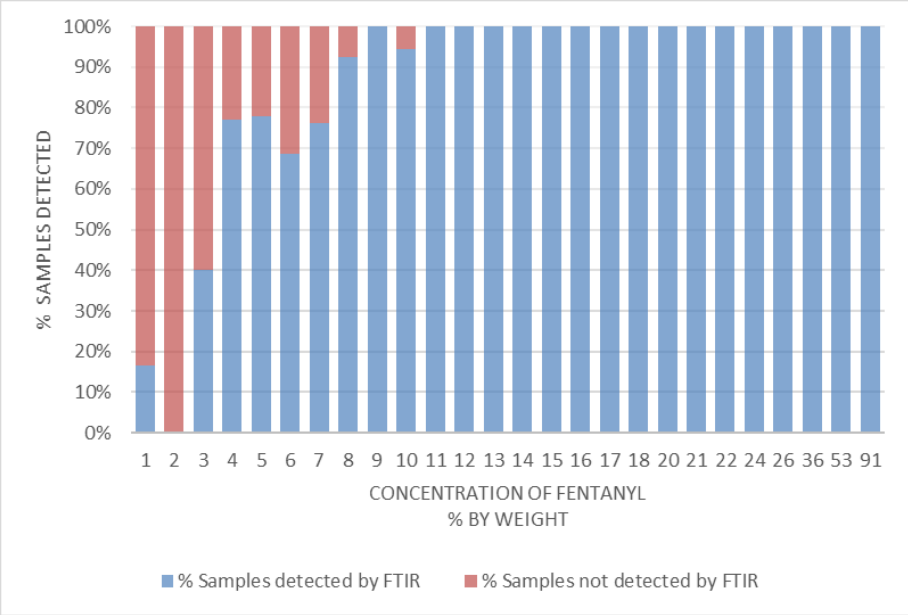
Validation of the point-of-care technologies was provided by analysis of the 331 samples sent to Health Canada's DAS laboratory for confirmatory testing using the qNMR and GC-MS procedures as described above. The findings revealed that FTIR spectroscopy had a sensitivity and specificity for detecting fentanyl or its analogues of 72.1% and 99.0%, respectively, with a false negative rate of 27.9%. The positive predictive value and negative predictive value for FTIR spectroscopy was 99.4% and 59.9%, respectively. In contrast, fentanyl immunoassay strips had a sensitivity and specificity for detecting fentanyl or its analogues of 87.5% and 95.2%, respectively, with a false negative rate of 12.5% when fentanyl was detected at any level by GC-MS. The positive predictive value and negative predictive value for fentanyl immunoassay strips was 98.1% and 73.4%, respectively. When compared to qNMR only as the reference standard, we found a lower false negative rate of 17.7% and 2.3% by FTIR and fentanyl immunoassay strips,

respectively. In all cases, the immunoassay strips were able to detect fentanyl or its analogues in all positive samples detected by FTIR spectroscopy (and more); thus, the use of both technologies in combination yielded the same sensitivity and specificity as the fentanyl immunoassay strips. Given that the use of these technologies in tandem provided the client with more fulsome results about the contents of their substance beyond fentanyl (i.e. proportion of main components), studies have shown higher utilization rates of the combination service.[21]

Limit of detection of point-of-care technologies vs. qNMR

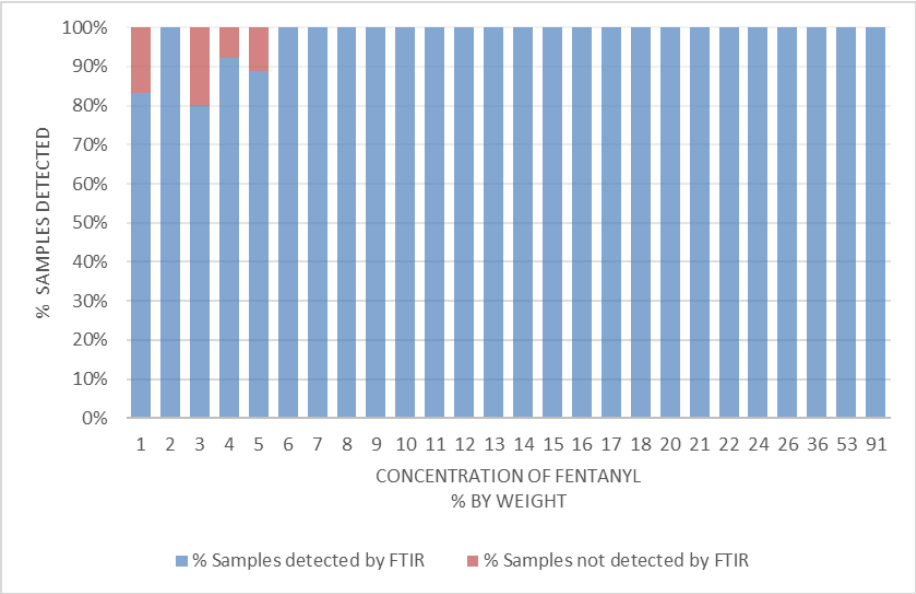
To determine the limit of detection for fentanyl in point-of-care technologies, qNMR quantification results were used as the reference standard. Figures 1a and 1b indicates that although both point-of-care technologies were able to detect the presence of fentanyl at concentrations as low as 1% in some samples, they were found to only be able to consistently (i.e., 100% of the time) detect fentanyl at levels of greater than 10% and 5% for FTIR spectroscopy and fentanyl immunoassay strips, respectively. These results corroborate prior studies which demonstrate that fentanyl immunoassay strips have a lower limit of detection for fentanyl than FTIR spectroscopy.[5]

FIGURE 1a. Prevalence of fentanyl detection, Fourier transform infrared spectroscopy versus quantitative nuclear magnetic resonance spectroscopy



FTIR: Fourier transform infrared spectroscopy

FIGURE 1b. Prevalence of fentanyl detection, fentanyl immunoassay strips versus quantitative nuclear magnetic resonance spectroscopy



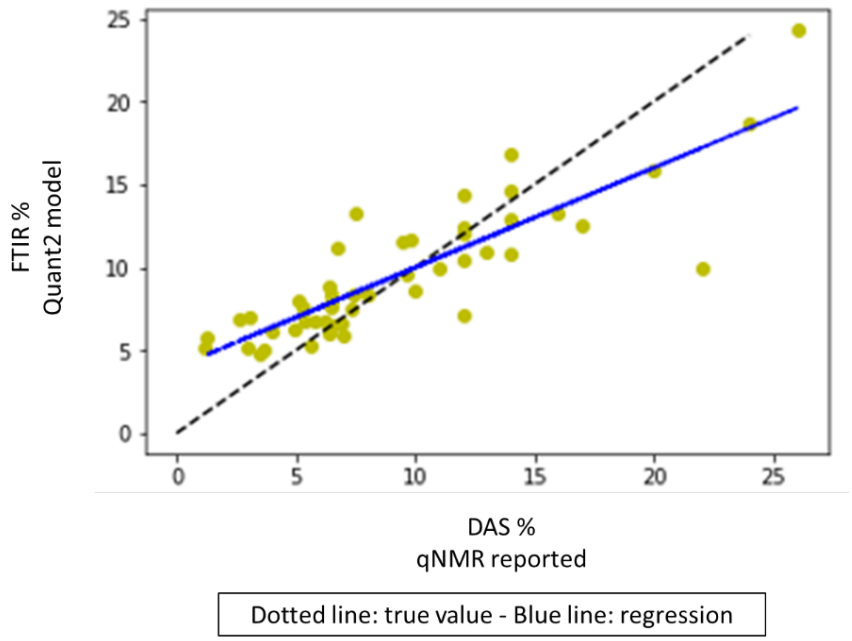
FTIR: Fourier transform infrared spectroscopy

Percent concentration of FTIR spectroscopy vs. qNMR

An advantage of FTIR technology is the capacity to rapidly quantify components of drug samples at point-of-care. Specifically, the *OPUS analysis software* from the *Bruker ALPHA* allows technicians to derive the percent concentration of respective components using a mixture analysis of the reported spectrum. One important limitation of this method is the potential for inter-rater variability, as technicians have to determinate a priori the number of principal components using manual interpretation of the spectroscopy signals. Using 100 samples with known fentanyl concentrations derived from qNMR, we were able to create a new quantification model (BCCSU Quant 2) that provides an automated approximation of fentanyl concentrations in a given sample.

In a comparative analysis, the Quant 2 model calculated a median fentanyl concentration of 8.4% (quartile [Q]1 – Q3: 6.7 – 12.2%), while the laboratory qNMR method reported a median fentanyl concentration of 7.4% (quartile [Q]1 – Q3: 5.5 – 12%) for all samples analyzed by qNMR. As indicated in Figure 2, the Quant2 model tends to overestimate fentanyl concentrations at lower percentages (~5% or less) and underestimate fentanyl concentrations at higher percentages (~15% or more). The difference in fentanyl concentrations between the Quant2 model and qNMR ranged from -12.1% to 21.2%, with a median difference of 0.8% (quartile [Q]1 – Q3: -1.1 – 2.2%).

FIGURE 2. BCCSU Quant2 Model versus qNMR: Fentanyl Concentration Percentages



Limitations

There are several limitations to consider. First, the use of a convenience sampling methodology for confirmatory laboratory analysis may have resulted in selection bias. The relatively small number of samples sent for confirmatory testing (around 10% of samples submitted for drug checking at these sites) and the limited number and location of sites where drug samples were collected, makes the generalizability of the results to the broader drug market challenging. As the drug checking service is completely anonymous, we were unable to record whether some clients were checking their drugs multiple times per day or per week. There is also a possibility that the small sample provided for drug checking (2-10mg) may not represent or contain the same concentration of fentanyl as in the larger drug sample, which could lead to misleading results. Finally, the inter-rater variability among technicians may affect the detection of fentanyl in lower concentrations, possibly affecting the overall sensitivity of the FTIR.

Conclusion

The study found that compared to laboratory reference standards, fentanyl immunoassay strips performed with high sensitivity and specificity for detecting fentanyl or its analogues, while FTIR spectroscopy had poor sensitivity despite the technology's high specificity. The high false negative rate in FTIR spectroscopy is concerning, and these findings suggest that this technology should not be used in isolation. However, the advantage of utilizing FTIR spectroscopy in

combination with immunoassay strips is its ability to detect and quantify the main components of a sample beyond just fentanyl.

Additionally, future research is needed to confirm the clinical relevance, if any, of false negatives on immunoassay strips as laboratory methods may be detecting pharmacologically irrelevant fentanyl presence. Indeed, in the case of false negatives on immunoassay strips, second-line GC-MS testing detected suspected or indicated levels of fentanyl, which first-line qNMR testing failed to detect. These "trace" levels of fentanyl may be below the limit of detection indicated by the *BTNX* immunoassay strips. Moreover, the results of this study varied slightly with prior studies investigating the reliability of these technologies.[5] This variation may be the result of potential differences in the local drug markets that may have influenced point-of-care drug checking results (e.g., cuts and buffs that may mask the signal of fentanyl) and differences in the settings where analyses were conducted (e.g., laboratory versus real-world public health setting). In particular, caffeine is commonly used as a cutting agent for fentanyl in the BC illicit drug market. The fact that the two compounds share a carbonyl group may mask the fentanyl signal, making it more difficult to detect it in lower concentrations. It is important to mention that specialized training on the detection and recognition of fentanyl signal patterns might increase sensitivity in combination with more sophisticated quantification models.

While this research represents preliminary investigation of these services, they have already contributed to local public health surveillance, helping health authorities understand the changing dynamics of contamination in the local drug supply and provide timely health warnings to help reduce overdose risk in the community. Drug checking results have been used to generate public health alerts distributed via the Real-time Drug Alert and Response (RADAR) system.[22,23] Additionally, the collaboration with DAS laboratory has allowed for identification of new contaminants in the local drug supply, such as illicitly manufactured benzodiazepines and benzodiazepine-derivatives (e.g. etizolam), synthetic cannabinoids (e.g. AMB-FUBINACA, 5-fluoro-ADB) and carfentanil.

Overall, the findings on the validity of these technologies generally suggest that the use of FTIR spectroscopy in tandem with fentanyl immunoassay strips in a point-of-care setting may be a valid harm reduction tool in the context of the opioid overdose crisis. While fentanyl immunoassay strips have a lower limit of detection and a higher sensitivity in comparison to FTIR spectroscopy, FTIR spectroscopy has the added benefit of being able to detect a wide range of substances and can provide a quantitative analysis of fentanyl content and other psychoactive drugs, which has been used for public health surveillance of unusual or unexpected substances.[21] The results of this pilot study represent an important first step for investigating the use of point-of-care drug checking technologies for fentanyl and its analogues.

References

1. Health Canada. (2018, Dec 12). Health Canada. Retrieved March 27, 2019, from Overview of national data on opioid-related harms and deaths: https://www.canada.ca/en/health-canada/services/substance-use/problematic-prescription-drug-use/opioids/data-surveillance-research/harms-deaths.html
2. Centers for Disease Control and Prevention. (2018, December 19). Opioid Overdose: Understanding the epidemic. Retrieved April 7, 2019, from Centres for Disease Control and Prevention: https://www.cdc.gov/drugoverdose/epidemic/index.html
3. Belzak, L., & Halverson, J. (2018, June). Evidence synthesis – The opioid crisis in Canada: a national perspective. Health Promotion and Chronic Disease Prevention in Canada, 38(6), 224-233.
4. McGowan, C. R., Harris, M., Platt, L., Hope, V., & Rhodes, T. (2018). Fentanyl self-testing outside supervised injection settings to prevent opioid overdose: Do we know enough to promote it? International Journal of Drug Policy, 58, 31-36.
5. Sherman, S. G., Park, J. N., Glick, J., Christensen, T., Morales, K., Green, T. C., & McKenzie, M. (2018). *FORECAST Study Summary Report*. Johns Hokpins Bloomberg School of Public Health.
6. British Columbia Ministry of Mental Health and Addictions. (2018). *Responding to BC's illegal drug overdose epidemic: Progress update January 2018*. Retrieved April 7, 2019, from https://www2.gov.bc.ca/assets/gov/overdose-awareness/final_responding_to_bcs_opioid_overdose_epidemic_-_progress_updatejan_2018.pdf
7. Government of Canada. (2017). *Government of Canada Actions on Opioids 2016 and 2017*. Ministry of Health, Ottawa. Retrieved April 7, 2019
8. Kerr, T., & Tupper, K. (2017). *Drug Checking as a Harm Reduction Intervention*. British Columbia Centre on Substance Use.
9. Sage, C. (2017). Harm Reduction and Drug Checking: A wrap-around service for festivals - Case Study: Shambhala Music Festival /ANKORS Drug Checking Harm Reduction.
10. Mema, S. C., Sage, C., Yujui, X., Tupper, K. W., Ziemianowicz, D., McCrae, K., . . . Corneil, T. (2018). Drug checking at an electronic dance music festival during the public health overdose emergency in British Columbia. *Canadian Journal of Public Health, 109*(5-6), 740-744.
11. British Columbia Coroner's Service. (2019). *Illicit Drug Overdose Deaths in BC January 1, 2009 - January 31, 2019*. Ministry of Public Safety and Solicitor General. Retrieved March 27, 2019, from https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/deaths/coroners-service/statistical/illicit-drug.pdf

12. British Columbia Ministry of Health. (2016, April 24). *Provincial health officer declares public health emergency*. Retrieved March 28, 2019, from Government of British Columbia: https://news.gov.bc.ca/releases/2016HLTH0026-000568

13. Karamouzian, M., Dohoo, C., Forsting, S., McNeil, R., Kerr, T., & Lysyshyn, M. (2018). Evaluation of a fentanyl drug checking service for clients of a supervised injection facility, Vancouver, Canada. *Harm Reduction Journal, 15*(46).

14. Brunt, T. (2017). *Drug checking as a harm reduction tool for recreational drug users: opportunities and challenges*. European Monitoring Centre for Drugs and Drug Addiction, The Netherlands.

15. Laing, M. K., Tupper, K. W., & Fairbairn, N. (2018). Drug checking as a potential strategic overdose response in the fentanyl era. *International Journal of Drug Policy, 62*, 59-66.

16. Hungerbuehler, I., Buecheli, A., & Schaub, M. (2011). Drug checking: A prevention measure for a heterogeneous group with high consumption frequency and polydrug use - evaluation of Zurich's drug checking services. *Harm Reduction Journal, 8*(16).

17. Leece, P. (2017). *Evidence Brief: Evidence on drug checking services as a harm reduction intervention*. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Toronto, ON: Queen's Printer for Ontario.

18. Linden, I. A., Mar, M. Y., Werker, G. R., Jang, K., & Krausz, M. (2012). Research on a Vulnerable Neighborhood - The Vanouver Downtown Eastside from 2001 to 2011. *Journal of Urban Health, 90*(3), 559-573.

19. Somers, J. M., Moniruzzaman, A., & Rezansoff, S. N. (2016). Migration to the Downtown Eastside neighbourhood of Vancouver and changes in service use in a cohort of mentally ill homeless adults: a 10-year retrospective study. *BMJ, 6*.

20. McCrae, K., Tobias, S., & Stunden, C. (2019). *Drug Checking: Operational Technician Manual*. British Columbia Centre on Substance Use, Vancouver.

21. Tupper, K. W., McCrae, K., Garber, I., Lysyshyn, M., & Wood, E. (2018). Initial results of a drug checking pilot program to detect fentanyl adulteration in a Canadian setting. *Drug and Alcohol Dependence, 190*, 242-245.

22. Vancouver Coastal Health (VCH). Overdose prevention & response. http://www.vch.ca/public-health/harm-reduction/overdose-prevention-response. (accessed June 2019).

23. British Columbia Centre on Substance Use (BCCSU). Drug Checking Reports. http://www.bccsu.ca/drug-checking/ (accessed June 2019).