BRITISH COLUMBIA CENTRE ON SUBSTANCE USE

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Drug Checking

An Assessment of the Accuracy of Fentanyl Quantification Results Reported by Drug Checking Technicians

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Land Acknowledgement

The BC Centre on Substance Use would like to respectfully acknowledge that the land on which we work is the unceded ancestral homelands of the xwmekwey'em (Musqueam), Skwxwú7mesh (Squamish), and sel'ílweta| (Tsleil-Waututh) Nations.

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Summary

In British Columbia (BC), many drug checking technicians use point-of-care Fourier-transform infrared (FTIR) spectroscopy to provide an estimated range of fentanyl concentrations to people accessing drug checking services. However, little is known about how accurate point-of-care drug checking technologies are in their quantification results. We sought to assess the accuracy of reported point-of-care quantification results by comparing them to a laboratory reference standard, quantitative nuclear magnetic resonance (qNMR). Our results showed that 81.5% of the time, point-of-care results delivered by technicians in an estimated range (eg. 10-15%) do not contain the actual fentanyl concentration identified by qNMR. We observed that when inaccurate ranges were reported, they generally tended to overestimate fentanyl concentrations (63.9% of the time) by 8.2%, on average. Although the point-of-care FTIR technology does, at times, underreport fentanyl concentrations (17.6%), the average margin of error is minimal (3.2%). Further investigation into quantification accuracy when other potentially dangerous drug components are present (e.g., non-fentanyl opioids and fentanyl analogues) is warranted. As FTIR drug checking is subjective on the part of trained drug checking technicians, a firmer understanding of the limitations of fentanyl quantification with FTIR will allow technicians to interpret and deliver results to service users more accurately. Amid a worsening overdose epidemic driven by an unpredictable unregulated drug market, we must strive to ensure that drug checking services are a reliable source of life-saving information for people who use drugs.

Background

Drug checking has emerged as an evidence-based harm reduction initiative in response to the ongoing overdose epidemic fuelled by the toxic, unregulated drug supply in BC. Community-based drug checking allows people to learn what is in their drugs and make informed decisions about their drug use.

Currently, drug checking technicians in BC rely on point-of-care methods like Fourier-transform infrared (FTIR) spectroscopy,[1,2] as it is a relatively affordable option and can return results quickly with minimal sample preparation.[3–5] While laboratory-based techniques (e.g., quantitative nuclear magnetic resonance spectroscopy (qNMR), gas chromatography-mass spectrometry) are the "gold standard" for detecting components with high sensitivity and specificity,[4–6] they are costly, time-consuming, and generally impractical to use in point-of-care settings. Quantification methods using FTIR spectroscopy are currently limited and have mostly relied on manufacturer-provided mixture analysis methods. Once the number of components present in a sample based on its absorbance of infrared light are identified, the estimated concentration of each compound relative to others can be produced. Generally, technicians avoid using mixture analysis alone to quantify fentanyl due to its lack of ability to detect unknown compounds and those present in low concentrations. Other methods used to refine mixture analysis results include QUANT 2, a validated prediction model which has shown to estimate fentanyl concentrations more accurately. In addition, fentanyl test strips can confirm the presence of fentanyl in a sample with high sensitivity and specificity. These methods, when used in combination, allow trained drug checking technicians to determine an estimate of how much fentanyl (or other drug of interest) is present in a sample. However, these methods can be variable depending on a number of factors, including technician expertise.[7] To account for FTIR's lack of precision, technicians have been encouraged to report the estimated fentanyl value using a range.[8] An example of the results a technician might report is: "This sample contains caffeine, mannitol, and between 5% and 10% fentanyl." A technician who is more confident in reporting quantification results may feel more comfortable to provide a narrower range of estimated values, such as between 6% and 9% fentanyl.

Now that fentanyl is almost ubiquitous in the unregulated opioid supply, it is more important than ever to provide individuals who access drug checking with accurate and reliable quantification results, particularly when the drug in question is as potent as fentanyl. Quantification information is used by drug checking service users not only as a safety measure but also as accountability for drug sellers in the context of a toxic unregulated drug supply. If people can receive a clear estimate of how much fentanyl their drugs contain, they can better harness that information to make informed decisions about their drug use.

As drug checking services expand across the province to address the worsening public health crisis, we must ensure that the current point-of-care drug checking quantification techniques are accurate. Identifying how often the ranges generated reflect a sample's true fentanyl concentration serves to provide technicians with important feedback, which can then be used to revise how they report quantification results and help improve the information they give to people who use drugs.

The present report compares point-of-care fentanyl quantification results reported to people accessing a drug checking service by trained technicians against a laboratory reference standard (i.e., qNMR).

Methods

The data for the present report was extracted from a centralized database of over 1,000 confirmed drug checking samples in BC between February 2021 and March 2022.

Samples were included in the analysis if a technician had recorded a contemporaneous estimate of fentanyl quantification based on point-of-care results into the provincial drug checking data repository. Technicians were instructed to only enter percentages of detected components that were reported to individuals using the service, in order for later analysis to be representative of what percentages were shared with community members. Fentanyl percentages were recorded in the database as a range, with a low and high end of estimated concentration. Additionally, samples included in the study must have been sent to Health Canada's Drug Analysis Service for confirmatory qNMR analysis to provide a true, gold-standard quantification of fentanyl. This report focused only on assessing quantification information for fentanyl hydrochloride and no other analogues (e.g., carfentanil).

First, we compared fentanyl hydrochloride concentrations reported in ranges by drug checking technicians against the actual values as identified by qNMR. Each sample was categorized based on whether the qNMR value was within or outside the range of fentanyl concentrations reported by technicians.

Second, we distinguished whether the technicians had overreported or underreported the fentanyl concentration for the samples where technicians reported inaccurately. Overreporting errors were defined as when the lower bound of the technician-reported range was higher than the qNMR result (Figure 1). Underreporting errors were defined as when the upper bound of the technician-reported was lower than the qNMR result (Figure 1).

Third, we sought to characterize how much technicians overreported and underreported fentanyl concentrations. We calculated the average difference between the lower bound and qNMR results for all the samples where technicians had overreported fentanyl concentration (Figure 1). Similarly, we calculated the average difference between the upper bound and qNMR results for all the samples that technicians had underreported fentanyl concentration (Figure 1).

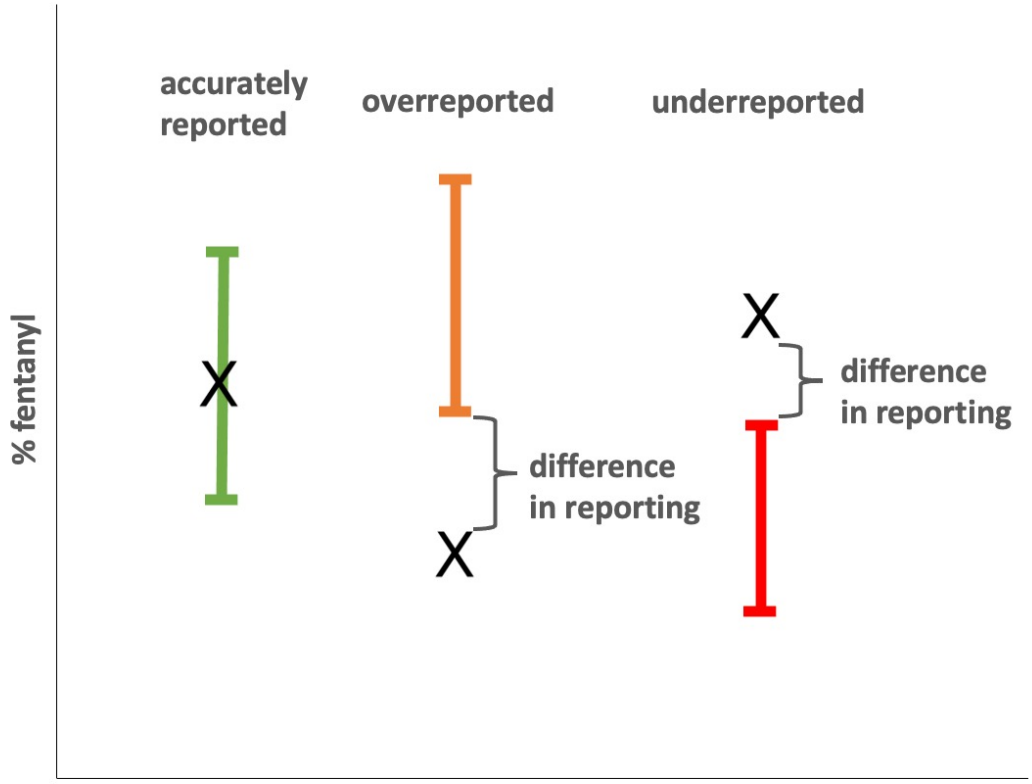

Figure 1. A plot showing how the accuracy of drug technician-reported ranges was assessed in this report. The x depicts the true fentanyl concentration as identified by qNMR confirmatory testing.

Results

Of the 119 samples included in the analysis, the true fentanyl concentrations identified using qNMR ranged from 1.0% to 87.4%. The mean concentration of fentanyl in these samples was 22.2% and the median was 13.4%.

The true fentanyl concentration was outside the range (either overreported or underreported) for 97 (81.5%) samples reported by drug technicians. Specifically, drug checking technicians overreported fentanyl concentration for 76 (63.9%) samples. On average, the lower bound of the range of possible values drug checking technicians provided to people were 8.2% higher than the fentanyl concentration found through qNMR analysis. There were 23 instances where a fentanyl range was provided and the lower bound of the range was more than 10% above the true value of fentanyl.

Drug checking technicians underreported fentanyl concentration for 21 (17.6%) samples. The maximum fentanyl concentration that drug checking technicians provided to people were, on average, 3.2% lower than the value from qNMR analysis.

The remaining 22 (18.5%) samples analyzed were found to have qNMR values that fell within the range of possible fentanyl concentrations reported by drug checking technicians.

The range width (interval) reported by technicians had a minimum of 0 (e.g., 17–17%) a median and mode of 5 (e.g., 5-10%, 15-20%).

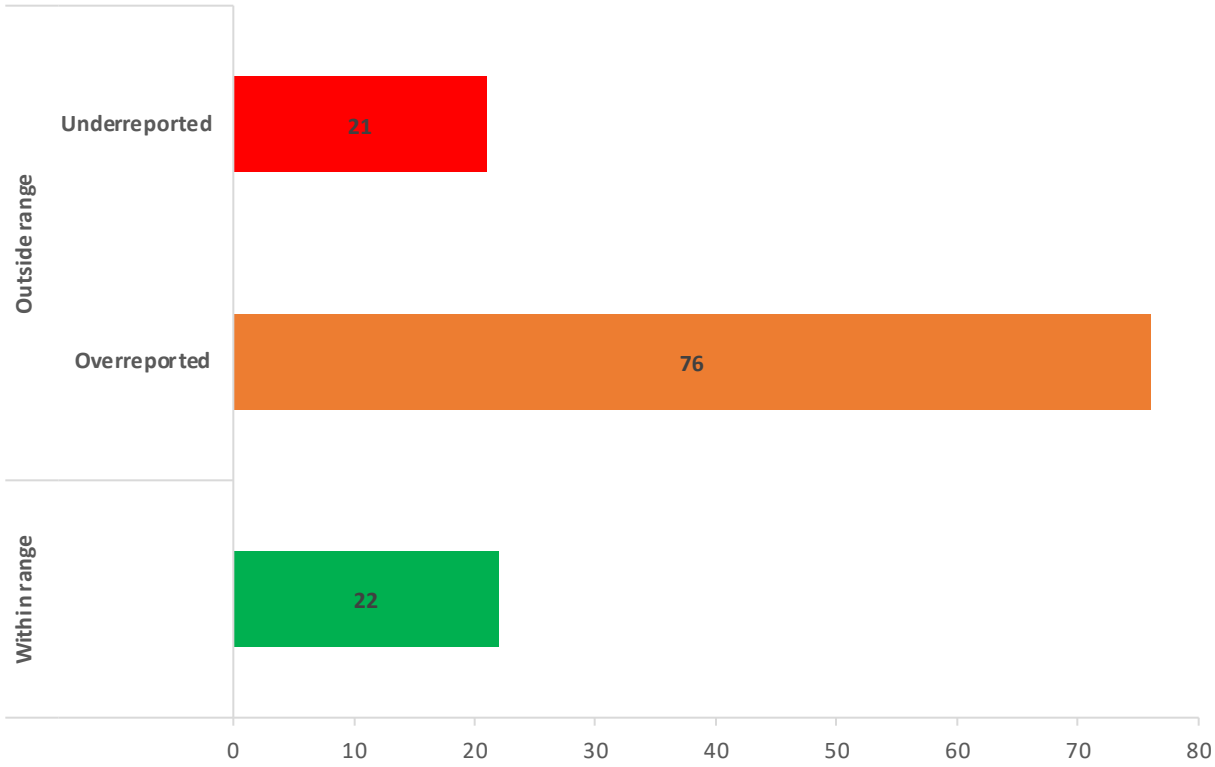

Figure 2. Stacked bar graph depicting the number of drug checking samples whose fentanyl concentrations were accurately reported by technicians (green, n=22). Of those that were inaccurately reported, underreporting errors are shown in red (n=21), and overreporting errors are shown in orange (n=76).

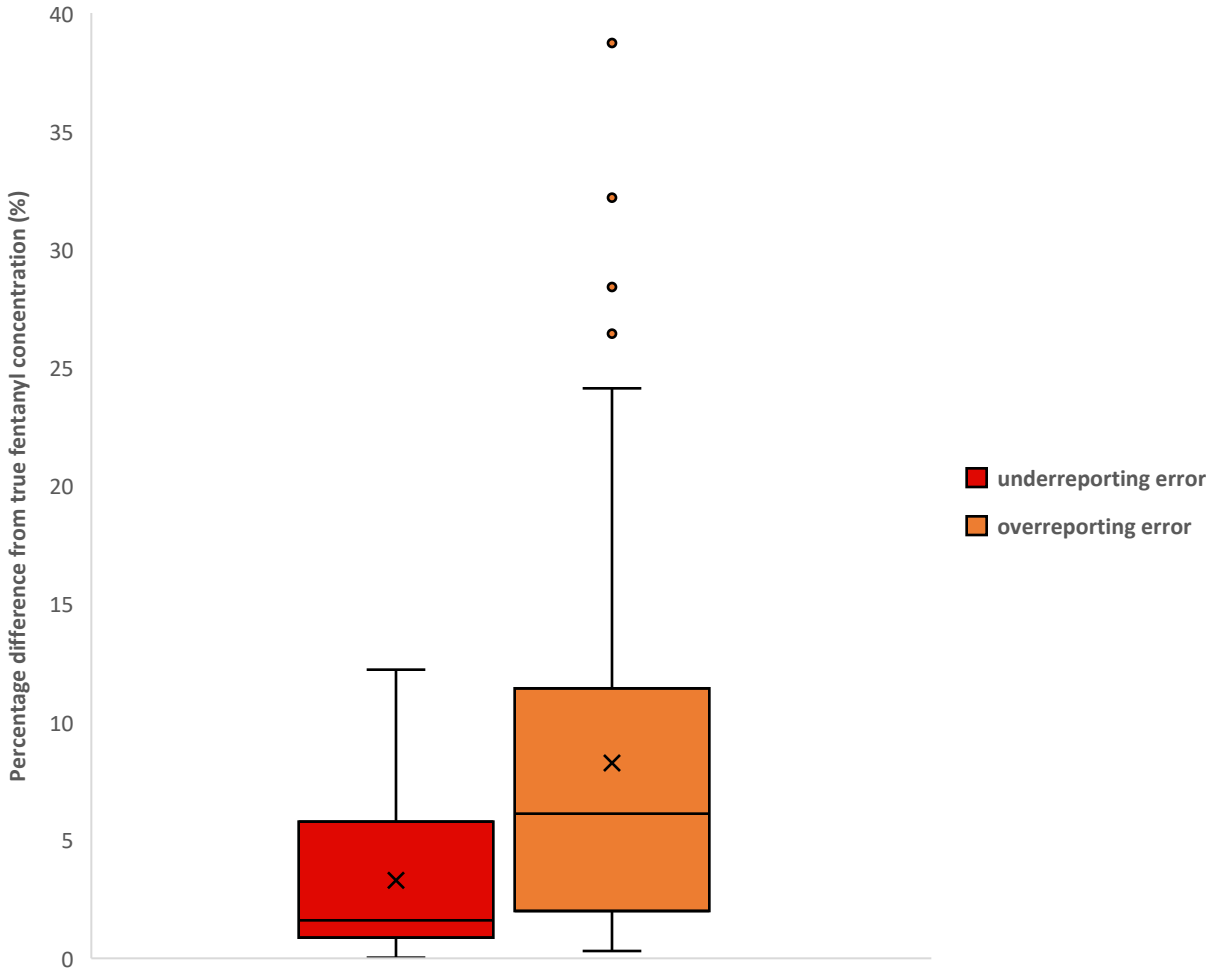

Figure 3. Box plots showing the average margin of error for all the drug checking samples for which technicians had underreported fentanyl concentration (red, 3.2%). The orange bar indicates the average margin of error for all the samples where technicians had overreported fentanyl concentration (orange, 8.2%).

Key Findings

In summary, we found that 18.5% of the time, drug checking technicians accurately quantified fentanyl for individuals who access drug checking by providing a range estimate that contained the true value of fentanyl. When the true concentration fell outside of the range technicians reported (81.5%), technicians tended to make the less grievous error of overreporting (78.4%) by an average of fentanyl concentration 8.2%. This means that technicians were correct in their estimations, or provide conservative estimations of fentanyl concentration 82.4% of the time.

It is a positive finding that drug checking technicians were more likely to overreport than underreport, given the concerns regarding potential adverse health harms (e.g., overdose) associated with fentanyl. When technicians underreported fentanyl concentration (17.6% of the samples), on average, technicians were only underreporting fentanyl concentrations by a small margin (3.2%).

These results are encouraging, but still suggest that drug checking technicians should be cautious, and ranges should be used to account for inaccuracies that may lead to negative health harms. We found that the modal range technicians reported was 5%. Given that little is known on this topic, it is difficult to determine whether this range is considered standard, and technicians may be reporting ranges of this size simply for convenience. There exists a trade-off between the obligation to be correct with ranges provided (provide a wide range encompassing the true value) and reporting a narrow range that allows a service user to make actionable harm reducing measures. While using a wider range is more likely to capture the true fentanyl value, wider ranges might limit the utility of the quantified information. Our data show that in several instances, technicians provided ranges narrower than 5% or no range at all; in every one of these instances, the true value of fentanyl was not captured in the narrow range.

Drug checking technicians in British Columbia are highly trained when it comes to interpreting the information generated by the FTIR. Given that, it remains puzzling to see how in some instances, the estimates of fentanyl concentration are drastically different than the true value determined by confirmatory testing. Further research will need to examine this phenomenon further, but we hypothesize that an FTIR measurement of a heterogenous mixture containing fentanyl may not be fully representative of the whole sample (commonly referred to as the chocolate chip cookie effect). When samples are sent to the confirmatory testing laboratory, they are pulverized and dissolved in a solution, leading to a truer measurement of fentanyl concentration by weight. In that sense, it is important to be clear that the fault of erroneous point-of-care estimations of fentanyl concentrations is not at the fault of the drug checking technician but is merely a limitation of the current spectroscopy method.

Given the need to provide accurate quantification information for those who access drug checking services, further research and training development is warranted. Future research should seek to explore different factors that can affect the accuracy of technician reporting, such as varying adulterating agents present in a sample or technician experience. As mixture analysis using FTIR spectroscopy is not suitable for identifying unknown compounds, future research could also investigate new point-of-care drug checking methods or technologies that can effectively identify and quantify novel drug components. Such advancements could be particularly useful in the context of a continuously evolving unregulated drug supply.

Limitations

There are some limitations to this report that should be considered. The samples included in our analysis largely came from drug checking sites in the Vancouver Downtown Eastside neighbourhood. The testing infrastructure, drug supply, and logistical challenges are quite unique to this specific area in BC, so our findings might not be representative of the province. Very few samples from other regions were collected because of relatively limited services and access to confirmatory testing over the study period. There were not enough samples to be able to make geographic or site-based difference calculations. Further research could explore inter-rater variation such as individual technician differences or differences across sites. Additionally, we limited our analysis to technician reporting of fentanyl hydrochloride concentrations; thus, our findings cannot be applied to other fentanyl analogues. Carfentanil is one example of a fentanyl analogue that can produce toxicity at very low concentrations and might be missed by point-of-care drug checking technologies.

Conclusion

It is important to provide individuals who access drug checking services with accurate, utilizable quantification information about what is in their drugs, as this can help reduce their risk of adverse events, including overdose. This report found that drug checking technicians are generally cautious with reporting fentanyl concentrations, tending to err on the side of overreporting. Our findings were only specific to fentanyl hydrochloride; thus, there is a need to investigate further the accuracy of point-of-care quantification for non-fentanyl opioids and fentanyl analogues that may also be present in drug samples. Future research could also explore different factors that affect the accuracy of quantification (e.g., varying adulterating agents, technician experience). Amid a worsening overdose epidemic driven by a dynamic unregulated drug supply, we must strive to ensure drug checking services are a reliable source of life-saving information for people who use drugs.

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