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August 7, 2025

QUANT3: A New Machine Learning Model for Fentanyl Quantification

The BCCSU Drug Checking Program has adopted a new model for estimating the amounts of fentanyl and fluorofentanyl in submitted drug checking samples. As of July 2025, the new QUANT3 model will be used for BCCSU drug checking data sharing and reporting. It has been applied retrospectively for presenting trends.

The following document describes the rationale for using this new quantification model, over the previous QUANT2 model.

Rationale for new quantification modelling

To enhance the precision of fentanyl quantification in drug checking and results reporting, the BCCSU, in collaboration with the Hein Lab at the University of British Columbia, developed a new machine learning model trained on FTIR spectra validated against gold-standard confirmatory testing provided by Health Canada's Drug Analysis Service. The model is designed to improve fentanyl concentration estimates, making them more reliable for real-world harm reduction applications and data sharing.

Why are aggregate fentanyl concentrations lower with QUANT3 compared to QUANT2?

The implementation of QUANT3 has resulted in noticeably lower monthly median fentanyl concentrations in unregulated opioid samples, compared to those previously reported using the QUANT2 model. This difference can be attributed to several key factors related to improvements in model performance and classification.

1. Improved classification of fluorofentanyl

QUANT3 can distinguish between fentanyl hydrochloride and fluorofentanyl hydrochloride, whereas QUANT2 was unable to do so. As a result, samples that previously had their entire fentanyl-class signal attributed to fentanyl are now correctly classified between fentanyl and fluorofentanyl.

This has meaningful consequences for quantification. For example, if a sample contained only fluorofentanyl, the QUANT2 model would still return a fentanyl concentration—say, 8% fentanyl—even though no fentanyl HCl was present. The QUANT3 model, by comparison, would return 0% fentanyl and 8% fluorofentanyl, accurately reflecting the composition of the sample.

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This distinction matters because fluorofentanyl has increased in prevalence of unregulated opioid samples since 2022. As a result, the QUANT2 model likely overestimated fentanyl concentrations in mixed or analogue-positive samples, inflating both individual readings and aggregated metrics such as monthly medians. By more accurately classifying and quantifying each compound, the QUANT3 model yields lower fentanyl values in samples containing fluorofentanyl, which when aggregated over time leads to a downward shift in monthly median fentanyl concentrations.

2. Reduction in low-concentration overestimation

An analysis of the QUANT2 model revealed a systematic tendency to overestimate fentanyl at low concentrations. This bias artificially inflated many readings that fall below or near the median range. This was first reported when the QUANT2 model data was implemented in 2021.[1] The QUANT3 model corrects for this issue, producing more accurate low-end estimates and, as a result, lowering the overall monthly median (Figures 1 and 2).

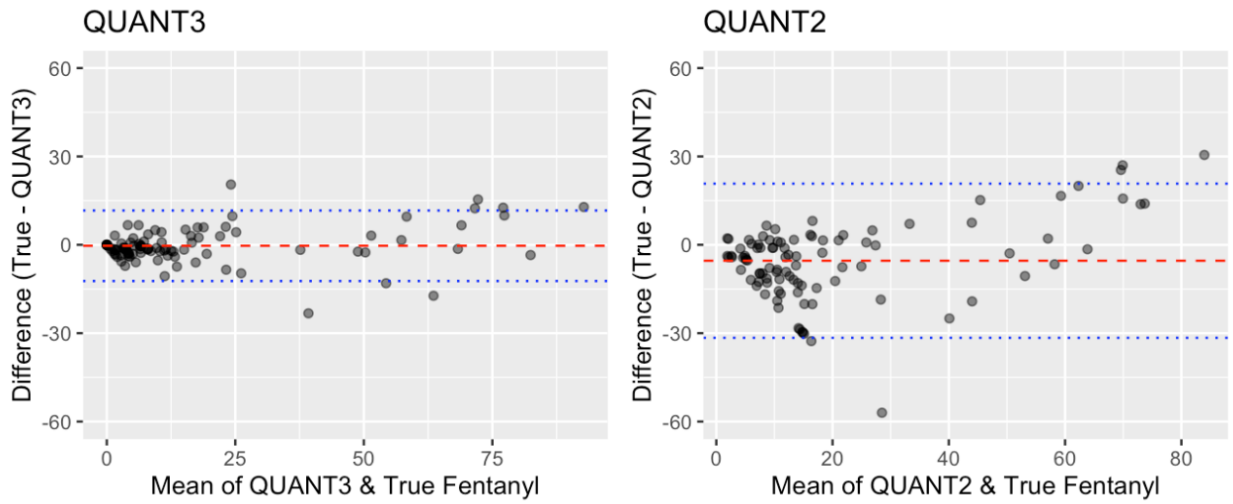

Figure 1. Bland-Altman plots comparing QUANT3 and QUANT2 fentanyl quantification models to Health Canada's confirmed results. The charts use the same drug samples for analysis.

The left chart shows the Bland-Altman plot for the QUANT3 model; the right shows the same for the QUANT2 model. Each point represents a drug sample with confirmed fentanyl concentration by confirmatory testing at Health Canada's Drug Analysis Service. The x-axis displays the mean of the model-predicted and true fentanyl concentration, while the y-axis shows the difference between the predicted and true value. The red dashed line indicates mean bias, and the blue dotted lines represent the limits of agreement. Compared to QUANT2, the QUANT3 model exhibits

substantially lower bias and narrower limits of agreement, with reduced overestimation at low concentrations and fewer extreme deviations

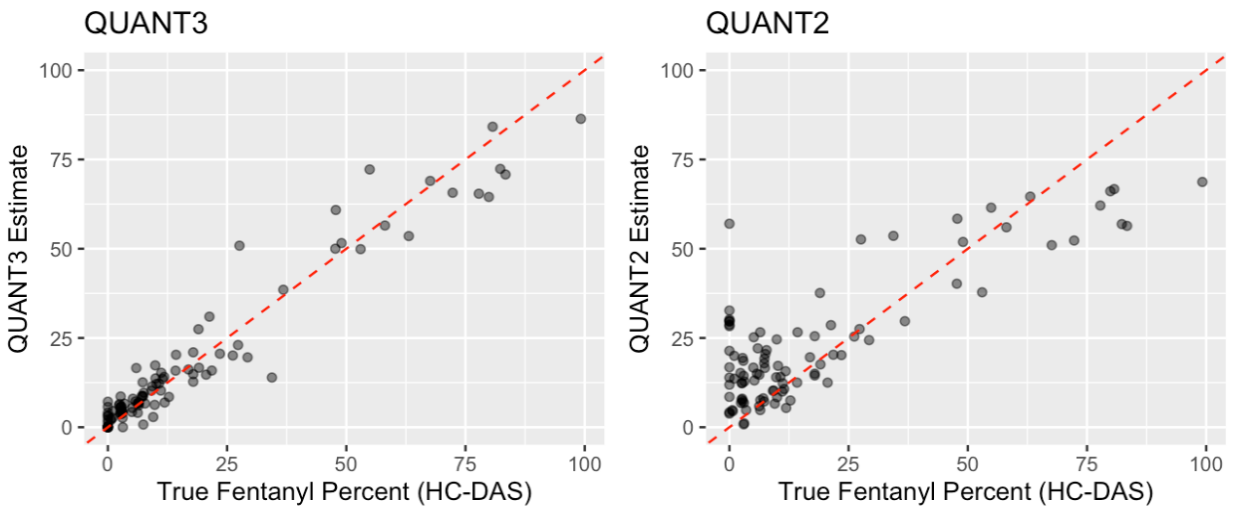

Figure 2. Scatter plots depicting the relationship between the true fentanyl percentage (DAS) and the QUANT3 model (left) and QUANT2 model (right). The red dashed line is *y=x*. The charts use the same drug samples for analysis.

Each point represents a drug sample and its quantification results from Health Canada's Drug Analysis Service and the respective FTIR quantification model. Notice how in the QUANT2 chart there is clustering in the lower left corner; this suggests an overestimation by the QUANT2 model compared to the true fentanyl results. Looking at the QUANT3 chart, this clustering does not exist, and instead the points are more closely aligned with the red line which indicates perfect agreement.

3. Correction of high-concentration outliers

QUANT2 also exhibited high variability and produced extreme overestimates at the upper end of the concentration range, particularly when fentanyl analogues were present. These outliers can disproportionately increase the median in small or skewed sample distributions. The QUANT3 model, with lower mean squared error and root mean squared error, better controls for these outliers, thus stabilizing and slightly lowering monthly central tendency measures.

4. Improved handling of complex or low-quality spectra

QUANT3 benefits from being trained on a more diverse and representative dataset than QUANT2. It likely handles degraded or mixed spectra more accurately, resulting in fewer

erroneous high estimates. This improved handling narrows the distribution and reduces the median.

Accreditation

QUANT3 was developed by Sara Guzman and Samuel Tobias. Data were derived from drug checking samples checked at point of care sites then submitted to Health Canada's Drug Analysis Service for confirmatory testing.

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