Using a Bayesian Approach to Estimate Chronic and Acute Cannabis Consumption

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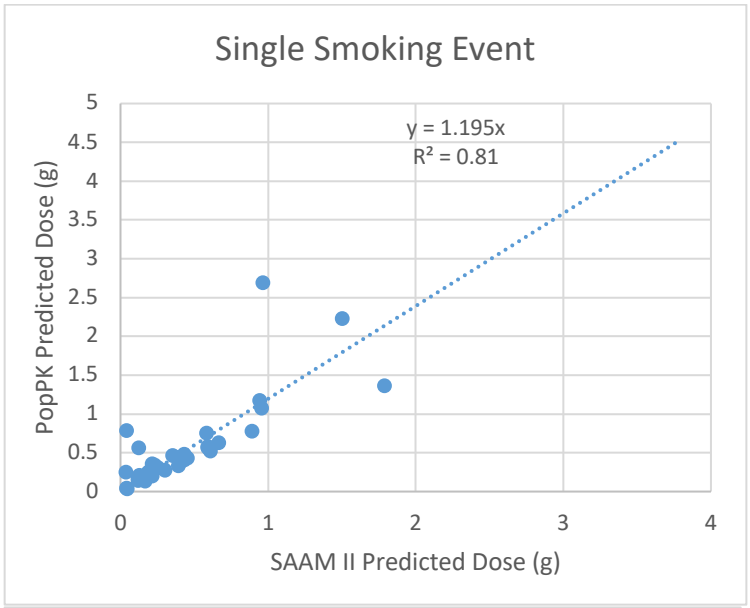
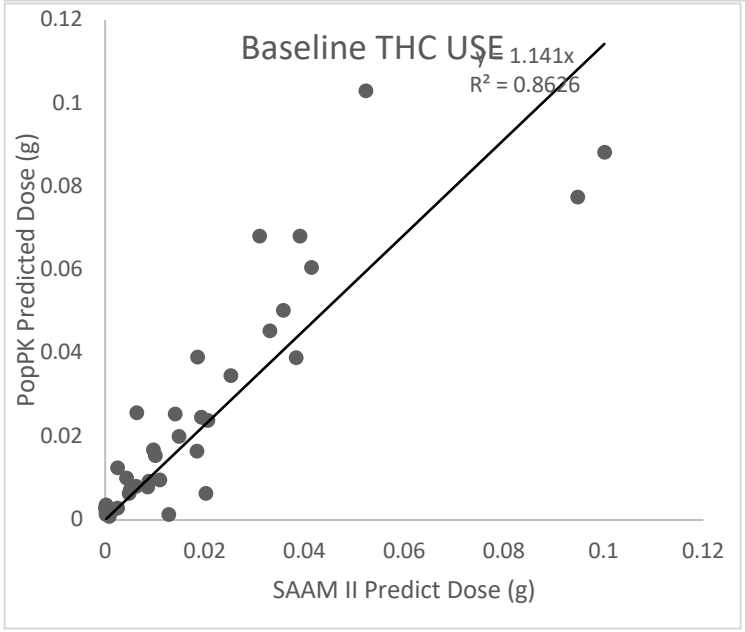
Introduction/Background: Cannabis for medicinal and recreational use is widespread and increasing. We have developed a popPK model of THC and two of its metabolites from Phase 1-like THC clinical trial studies. We previously used this popPK model to analyze THC and metabolite concentration versus time data from regular users of cannabis in Colorado in order to estimate the amount each individual used on both a daily basis (based on a single baseline blood sample) and smoked in a single an 'at home' episode that was not witnessed by investigators. These popPK-derived 'dose' estimates were statistically significantly correlated to detailed cannabis use questionnaire results at baseline and the weighed cannabis burned amount 'at home'. In order to interpret single or serial blood samples in clinical, forensic, or athletic event settings in an individual, a Bayesian prediction approach is needed. We hypothesized that estimates of daily and single cannabis use estimates obtained in one individual at a time, from THC and metabolite concentration data using a Bayesian approach, would be highly correlated to those obtained from full popPK modeling.

Methods: Thirty-seven regular users of cannabis from a larger study involving psychomotor testing were selected on the basis of indicating smoking as their primary method of cannabis consumption. Blood samples were obtained at recruitment, in a mobile lab immediately before smoking in their home, upon returning to the mobile lab and then again one hour later for analysis of THC/metabolites by LC-MS/MS. These data were analyzed with the Bayesian prior from our previous Phase 1-like popPK analysis (Pheonix NMLE, 8.1, Certara, Princeton, NJ). The same Bayesian prior estimates were used for fitting of each individual's data using SAAM2's Bayesian module. The individual fitting results were compared to the population posthoc values provided by Phoenix NLME results.

Results: There was a statistically significant correlation between the estimated THC baseline 'steady-state' cannabis usage determined with a population approach and with Bayesian forecasting approach utilizing just one individual's data ($r^2 = 0.73$, $p<0.01$) with a slope of 1.14. Additionally, there was a statistically significant correlation between the estimated THC consumed on a one-time smoking event ($r^2 = 0.63$, $p<0.01$) with a slope of 1.19.

Conclusions: The current study indicates that daily and single event cannabis usage can be estimated with plasma THC and metabolite concentration data from a single individual using Bayesian forecasting principles. Results are nearly identical to those obtained performing a popPK analysis of the data from all 37 individuals. There was a slight tendency for the individual Bayesian fits to under-predict doses compared to the popPK approach. While these results suggest that a well-characterized popPK model of THC and metabolites can be used to interpret observational or naturalistic concentration results, more robust popPK models of larger populations with the inclusion of covariates would likely improve accuracy and relevance.


Single Smoking Event
y = 1.195x
R² = 0.81
PopPK Predicted Dose (g)
SAAM II Predicted Dose (g)
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
0
1
2
3
4


Baseline THC USE
y = 1.141x
R² = 0.8626
PopPK Predicted Dose (g)
SAAM II Predict Dose (g)
0
0.02
0.04
0.06
0.08
0.1
0.12
0
0.02
0.04
0.06
0.08
0.1
0.12