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## REPLY TO BECKSON *ET AL*. (2019): CANNABIS, CRASHES, AND BLOOD: CHALLENGES FOR OBSERVATIONAL RESEARCH

We thank Beckson *et al*. for their thoughtful comments [1], and agree with the need for more research on cannabis, especially with respect to driving. Our goal was to provide an unbiased, policy-relevant estimate of the risk of crashing associated with tetrahydrocannabinol (THC) levels obtained within a realistic time after a collision. We aimed to minimize or eliminate many of the biases found in previous research. The responsibility analysis design minimizes the problem of differential ascertainment of THC in cases versus controls. Unlike some previous studies, we adjusted for multiple confounders (age, sex, other substance use). We measured THC in blood obtained for clinical purposes with waiver of consent, eliminating potential bias from high refusal rates common in previous research, and minimizing the time from collision to blood draw. Despite the limitations that Dr Beckson correctly indicates, blood THC levels are more meaningful than urine or oral fluid cannabis tests, which is why we chose this biological sample.

We acknowledge that the THC levels in our study are less than at time of crash. THC levels decline rapidly in during the first hour after smoking, as THC distributes into the body tissue, and then decline more slowly as THC is eliminated. In our study the median time from crash until blood draw was 84 minutes, and 76% of samples were obtained within 2 hours, a significant improvement over previous research [2–5]. For drivers smoking cannabis in the vehicle, THC levels in our study would be lower than at time of collision. However, if there was a delay of more than an hour between smoking and collision, THC levels would decline more slowly and the drop in THC between collision and blood draw would be less. Most importantly, it is unlikely that blood samples could be obtained more quickly for law enforcement purposes than for medical reasons. Hence, our risk estimates are based on THC levels obtained within a feasible time after collision and are relevant to evaluating enforceable *per se* limits.

Beckson states, without reference, that postmortem THC concentrations more accurately reflect concentration at time of crash 'because circulation and metabolism ceases with death'. This statement is misleading, and we disagree strongly with the implication that postmortem studies yield more meaningful results; in fact, the opposite

is probably true. People may survive for hours following a collision and there will be ongoing distribution and metabolism of THC during that time. In the Vancouver region, where many of our cases came from, 50% of trauma deaths occur more than 6 hours after injury [6]. Beckson cites a postmortem study by Drummer *et al.* [10] that yielded an odds ratio (OR) of 6.1 for drivers with THC > 5 ng/ml. That study included drivers who survived up to 4 hours after the collision [7,8]. Equally importantly, THC undergoes significant postmortem redistribution as it diffuses from body stores into blood. The extent of postmortem distribution depends on the time from death until blood is obtained and on the body site where blood is obtained from [9,10]. As such, THC levels in postmortem blood correlate poorly with THC concentration at time of death [9], and antemortem hospital samples, when available, are more reliable [10]. We also point out that studying non-fatal crashes is important, because the vast majority of collisions are non-fatal and the likelihood of surviving a collision has increased substantially with advances in automotive safety (crumple zones, airbags) and improvements in trauma systems and care.

Beckson describes our study as underpowered. This might be said of virtually every study with a modest association and no statistical significance. The important questions are whether our methods were valid and the findings meaningful. We analyzed blood THC levels in a large sample (1825) of crash involved drivers with determinate crash responsibility. For drivers with THC < 5 ng/ml ($n$ = 145), confidence intervals were narrow and there was no evidence of increased risk. Only 20 drivers (1.0%) had THC > 5 ng/ml and the OR was not significant for those drivers. In contrast, risk was substantially elevated (OR = 6.0; $P < 0.01$) in the 241 drivers (13.2%) with BAC > 0.08%.[11] Hence our conclusion that the impact of cannabis on road safety is relatively small. Compared with alcohol, this is a fair conclusion. Beckson also criticizes our use of pre-legalization data. We see no plausible reason that the collision risk associated with cannabis will change following legalization. As discussed in the paper, we acknowledge that the overall road safety impact of cannabis may increase if more people drive after using cannabis, especially if they also use alcohol. We are collecting post-legalization data using identical methods to test for this possibility.

### Declaration of interests

None.

**Keywords** Alcohol, cannabis, epidemiology, motor vehicle collisions, per se limits, tetrahydrocannabinol.

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