Sampling strategy and analysis of cannabis, alcohol and nicotine biomarkers in pregnant women pre- and post-legalization in Alberta, Canada

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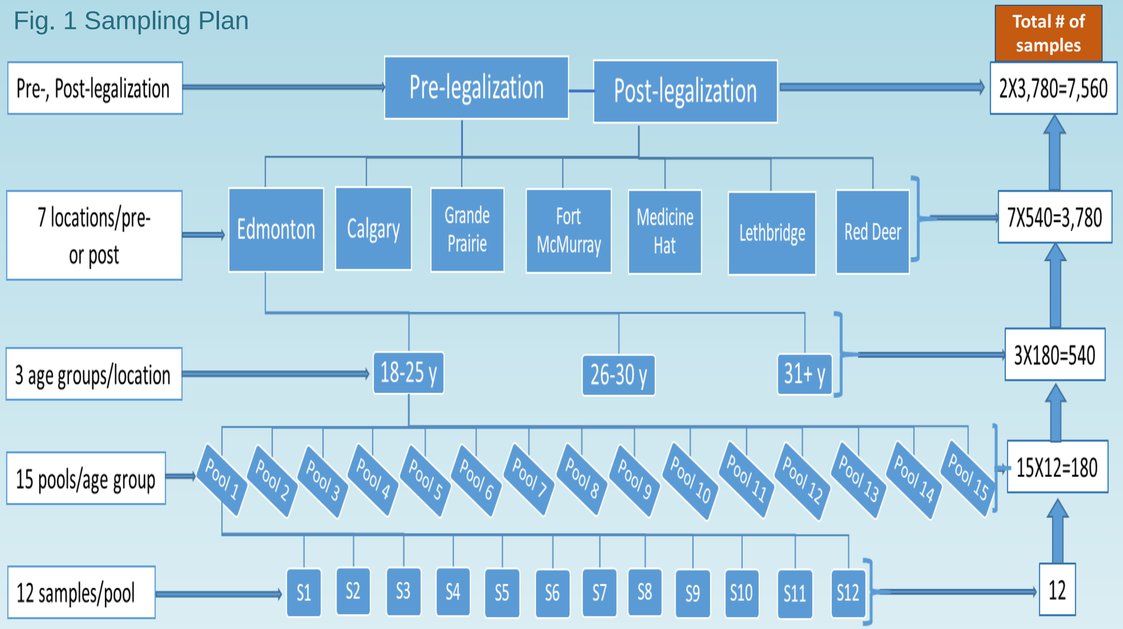
BACKGROUND

Pregnancy is a very sensitive and vital time point in human development. The developing fetus is the most sensitive life stage and can be exposed to chemicals that cross the placenta. Research has demonstrated that co-exposure to cannabinoids and alcohol increases the risk of birth defects. Recreational cannabis use was legalized in Canada on October 17th, 2018. ACFT is conducting a biomonitoring survey to measure biomarkers of cannabis, alcohol and nicotine in the serum of pregnant women in Alberta pre and post cannabis legalization. The data will indicate the degree of use and any change of use of these substances in this population. However, one of the challenges for the survey was to collect large numbers of valid samples to ensure statistical significance, especially the samples from pre-legalization. Establishing sensitive and cost effective analytical methods that are suitable for the survey was another challenge as the volumes of valid samples are limited.

SAMPLING STRATEGY & ANALYTICAL METHODS

Fig.1 shows the sampling plan for the study. In order to provide sufficient statistical power for the determination of statistically significant differences between pre- and post-legalization, a total of 7,560 maternal blood samples are required, among which 3,780 were collected before legalization and 3,780 were collected 6 months after legalization. The blood samples were spun down and the serum was pooled. 180 individual sample yielded 15 pools/age group/region.

Fig. 1 Sampling Plan



Some samples are from the previous Alberta Biomonitoring Program. The majority of samples are leftovers from the routine prenatal assessment screening samples requested from the Provincial Public Health Laboratory in Edmonton.

Table 1 lists biomarkers for monitoring the exposure of cannabis, alcohol and nicotine. Liquid chromatography tandem mass spectrometry (LC-MS/MS) methods were chosen for sensitive and reliable analysis of the biomarkers.

Table 1: LOD/LOQ of the LC-MS/MS Methods

Chemicals	Biomarker	LOD/LOQ(ng/mL)
Cannabis	THC-COOH	1/1
	THC-COOH-glucuronide	1/1
Alcohol	Ethyl glucuronide	10/10
	Ethyl sulfate	1/1
Nicotine	Cotinine	0.1/0.1

RESULTS & DISCUSSION

Thus far, ACFT has prepared 315 pools from 3780 samples collected before legalization. Post-legalization pools are in progress.

It would have been time-consuming, labor-intensive and very costly to recruit this large number of pregnant women from different age groups and geographic locations to collect samples. Further, it was impossible for us to collect pre-legalization samples after legalization. For this study, we proposed to utilize leftover samples that would otherwise be discarded from previous study and the Provincial Public Health Laboratory. Pooling these samples provides enough volume for the analysis of the biomarkers of interest and maintains statistical significance

Three LC-MS/MS methods have been developed for analysis. The LOD/LOQ achieved for each biomarker fits the biomonitoring purposes.

CONCLUSION

Biomonitoring studies require a large number of samples. Using leftover samples collected for routine patient screening and from the previous study offers great advantages. It is cost effective and simplifies sample procurement. The biomarkers will highlight any differences in the use of cannabis, alcohol, and nicotine pre- and post-legalization of cannabis.

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