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A geospatiotemporal and causal inference epidemiological exploration of substance and cannabinoid exposure as drivers of rising US pediatric cancer rates

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Abstract

Background: Age-adjusted US total pediatric cancer incidence rates (TPCIR) rose 49% 1975-2015 for unknown reasons. Prenatal cannabis exposure has been linked with several pediatric cancers which together comprise the majority of pediatric cancer types. We investigated whether cannabis use was related spatiotemporally and causally to TPCIR.

Methods: State-based age-adjusted TPCIR data was taken from the CDC Surveillance, Epidemiology and End Results cancer database 2003-2017. Drug exposure was taken from the nationally-representative National Survey of Drug Use and Health, response rate 74.1%. Drugs included were: tobacco, alcohol, cannabis, opioid analgesics and cocaine. This was supplemented by cannabinoid concentration data from the Drug Enforcement Agency and ethnicity and median household income data from US Census.

Results: TPCIR rose while all drug use nationally fell, except for cannabis which rose. TPCIR in the highest cannabis use quintile was greater than in the lowest (β-estimate = 1.31 (95%C.I. 0.82, 1.80), $P = 1.80 \times 10^{-7}$) and the time:highest two quintiles interaction was significant (β-estimate = 0.1395 (0.82, 1.80), $P = 1.00 \times 10^{-14}$). In robust inverse probability weighted additive regression models cannabis was independently associated with TPCIR (β-estimate = 9.55 (3.95, 15.15), P = 0.0016). In interactive geospatiotemporal models including all drug, ethnic and income variables cannabis use was independently significant (β-estimate = 45.67 (18.77, 72.56), P = 0.0009). In geospatial models temporally lagged to 1,2,4 and 6 years interactive terms including cannabis were significant. Cannabis interactive terms at one and two degrees of spatial lagging were significant (from β-estimate = 3954.04 (1565.01, 6343.09), P = 0.0012). The interaction between the cannabinoids

THC and cannabigerol was significant at zero, 2 and 6 years lag (from β-estimate = 46.22 (30.06, 62.38), P = 2.10 × 10^{-8}). Cannabis legalization was associated with higher TPCIR (β-estimate = 1.51 (0.68, 2.35), P = 0.0004) and cannabis-liberal regimes were associated with higher time:TPCIR interaction (β-estimate = 1.87 × 10^{-4}, (2.9 × 10^{-5}, 2.45 × 10^{-4}), P = 0.0208). 33/56 minimum e-Values were > 5 and 6 were infinite.

Conclusion: Data confirm a close relationship across space and lagged time between cannabis and TPCIR which was robust to adjustment, supported by inverse probability weighting procedures and accompanied by high e-Values making confounding unlikely and establishing the causal relationship. Cannabis-liberal jurisdictions were associated with higher rates of TPCIR and a faster rate of TPCIR increase. Data inform the broader general consideration of cannabinoid-induced genotoxicity.

Keywords: Acute leukaemia; Cannabigerol; Cannabinoid; Cannabis; Genotoxicity; Pediatric cancer; Δ9-tetrahydrocannabinol.

Figures

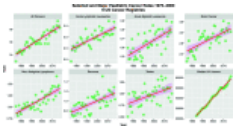

Fig. 1 Pediatric Cancers 1975–2017, CDC SEER...

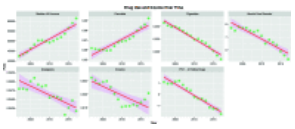

Fig. 2 Drug use over time. Data...

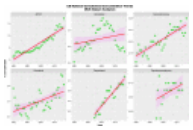

Fig. 3 Cannabinoid concentrations in Federal Seizures...

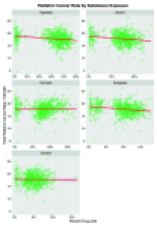

Fig. 4 Total pediatric cancer incidence rate...

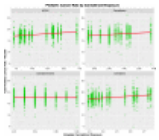

Fig. 5 Total pediatric cancer incidence rate...

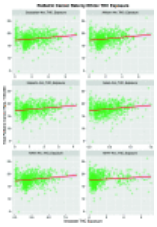

Fig. 6 Total pediatric cancer incidence rate...

All figures (10)

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