

Supplmentary Figure Captions.

Supplementary Figure 1.: Time trends of cannabinoid concentrations in Federal seizures by cannabinoid.

Supplementary Figure 2.: Trends of unadjusted congenital anomaly rates against tobacco exposure by congenital anomaly type.

Supplementary Figure 3.: Trends of unadjusted congenital anomaly rates against tobacco exposure by congenital anomaly type.

Supplementary Figure 4.: Trends of unadjusted congenital anomaly rates against tobacco exposure by congenital anomaly type.

Supplementary Figure 5.: Trends of unadjusted congenital anomaly rates against tobacco exposure by congenital anomaly type.

Supplementary Figure 6.: Trends of unadjusted congenital anomaly rates against tobacco exposure by congenital anomaly type.

Supplementary Figure 7.: Trends of unadjusted congenital anomaly rates against tobacco exposure by congenital anomaly type.

Supplementary Figure 8.: Trends of unadjusted congenital anomaly rates against tobacco exposure by congenital anomaly type.

Supplementary Figure 9.: Trends of ETOPFA-corrected congenital anomaly rates against tobacco exposure by congenital anomaly type.

Supplementary Figure 10.: Trends of ETOPFA-corrected congenital anomaly rates against tobacco exposure by congenital anomaly type.

Supplementary Figure 11.: Trends of ETOPFA-corrected congenital anomaly rates against tobacco exposure by congenital anomaly type.

Supplementary Figure 12.: Trends of ETOPFA-corrected congenital anomaly rates against tobacco exposure by congenital anomaly type.

Supplementary Figure 13.: Volcano plot of significance level (as negative P-value) against the minimum E-value for congenital anomalies significantly positively related to tobacco exposure.

Supplementary Figure 14.: Volcano plot of significance level (as negative P-value) against the minimum E-value for congenital anomalies significantly positively related to AUD exposure.

Supplementary Figure 15.: Volcano plot of significance level (as negative P-value) against the minimum E-value for congenital anomalies significantly positively related to $\Delta 9$ THC exposure.

Supplementary Figure 16.: Volcano plot of significance level (as negative P-value) against the minimum E-value for congenital anomalies significantly positively related to cannabidiol exposure.

Supplementary Figure 17.: Categorical boxplots comparing extreme quintile exposures for ETOPFA-corrected congenital anomaly rates by tobacco exposure.

Supplementary Figure 18.: Categorical boxplots comparing extreme quintile exposures for ETOPFA-corrected congenital anomaly rates by AUD exposure.

Supplementary Figure 19.: Categorical boxplots comparing extreme quintile exposures for ETOPFA-corrected congenital anomaly rates by cannabis exposure.

Supplementary Figure 20.: Categorical boxplots comparing extreme quintile exposures for ETOPFA-corrected congenital anomaly rates by $\Delta 9$ THC exposure.

Supplementary Figure 21.: Categorical boxplots comparing extreme quintile exposures for ETOPFA-corrected congenital anomaly rates by analgesic exposure.

Supplementary Figure 22.: Categorical boxplots comparing extreme quintile exposures for ETOPFA-corrected congenital anomaly rates by cocaine exposure.

Supplementary Figure 23.: Summary of key epidemiological metrics from categorical analyses. (A) number of anomalies showing elevated lower relative risk bounds, (B) number of anomalies showing elevated lower attributable fraction in the exposure lower bounds, (C) number of anomalies demonstrating elevated lower bounds of the population attributable risk,

(D) total negative exponents of P-values, (E) number of anomalies with elevated lower minimum E-values and (F) total exponents of lower bounds of minimum E-values. In each case $\Delta 8\text{THC}$ is noted to be in the highest category.

Supplementary Figure 24.: Summary metrics for the additive panel model summarized in eTable 25 by covariate. (A) Number of significantly positive congenital anomalies, (B) log of the mean minimum E-values, (C) log of the total of the exponents of the minimum E-values, (D) log total negative P-value exponents.

Supplementary Figure 25.: Summary metrics for the interactive panel model summarized in eTable 28 by organ system. (A) Percentage of significantly positive congenital anomalies, (B) log of the total of the exponents of the minimum E-values, (C) total of the negative exponents of the P-values, (D) total average marginal effect.

Supplementary Figure 26.: Summary metrics for the interactive panel model at two temporal lags summarized in eTable 31 by covariate. (A) Number of significantly positive congenital anomalies, (B) median minimum E-Values, (C) log of the total of the exponents of the minimum E-values, (D) total of the negative exponents of the P-values.

Supplementary Figure 27.: Summary average marginal effects (AME) metrics for the interactive panel model at two temporal lags summarized in eTable 31 by covariate. (A) Mean AME, (B) median AME, (C) total AME and (D) ratio of the mean to standard error of the mean as a measure of AME variability.

Supplementary Figure 28.: Summary measures by organ system for interactive panel model lagged by two years shown in eTable 31. (A) percentage of anomalies in each organ system, (B) total exponent of minimum E-values by organ system, (C) total of exponents of minimum E-values and (D) total AME by organ system.

Supplementary Figure 29.: Summary metrics for interactive panel model lagged to four years shown in eTable 36 by covariate. (A) number of significantly positive anomalies by covariate, (B) median minimum E-values, (C) log of total minimum E-value exponents and (D) log total negative P-value exponents.

Supplementary Figure 30.: Summary metrics for interactive panel model lagged to four years shown in eTable 36 by average marginal effect (AME). (A) mean AME, (B) median AME, (C) total AME and (D) mean to standard error of the mean ratio as a measure of AME variability.

Supplementary Figure 31.: Summary metrics for interactive panel model lagged to four years shown in eTable 36 by organ system. (A) percentage of significant positive anomalies by

organ system, (B) total exponent of minimum E-values by organ system, (C) total negative exponents of P-values by organ system and (D) total AME by system.