

SUPPLEMENTARY TABLES AND FIGURES

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Supplementary Table S1. Sociodemographic Variables, Drug Use and Cannabinoid Exposure

Variable	Value
Sample Size	961
Country (%)	
Belgium	80 (8.3)
Bulgaria	80 (8.3)
Croatia	64 (6.7)
Finland	35 (3.6)
France	80 (8.3)
Germany	80 (8.3)
Hungary	21 (2.2)
Italy	80 (8.3)
Netherlands	72 (7.5)
Norway	80 (8.3)
Poland	80 (8.3)
Portugal	80 (8.3)
Spain	80 (8.3)
Sweden	49 (5.1)
Year (Range)	2010: 2019
Anomaly (%)	
Annular pancreas	122 (12.7)
Ano-rectal atresia and stenosis	122 (12.7)
Atresia of bile ducts	122 (12.7)
Atresia or stenosis of other parts of small intestine	122 (12.7)
Digestive system	107 (11.1)
Duodenal atresia or stenosis	122 (12.7)
Hirschsprung's disease	122 (12.7)
Oesophageal atresia with or without tracheo-oesophageal fistula	122 (12.7)
Anomaly_Rate (mean (SD))	3.02 (5.29)
Tobacco (mean (SD))	22.78 (5.46)
Alcohol (p.c.L/Yr) (mean (SD))	10.77 (1.83)
Amphetamines (% Use) (median [IQR])	0.60 [0.30, 0.80]
Cocaine (% Use) (median [IQR])	0.72 [0.40, 1.20]
Last_Month_Cannabis (% Use) (mean (SD))	0.04 (0.02)
Cannabis_Herb_THC_Content (%) (mean (SD))	0.09 (0.03)
Cannabis_Resin_THC_Content (%) (mean (SD))	0.16 (0.09)
%_Daily_Cannabis_Use (mean (SD))	0.01 (0.01)
%_Daily_Cannabis_Use_Interpolated (mean (SD))	0.01 (0.01)
Last_Month_Cannabis_x_Herb_THC_Content (mean (SD))	0.04 (0.03)
Last_Month_Cannabis_x_Resin_THC_Content (mean (SD))	0.13 (0.12)

Last_Month_Cannabis_x_Herb_THC_Content_x_Daily_Use_Interpolated (median [IQR])	0.02 [0.00, 0.06]
Last_Month_Cannabis_x_Resin_THC_Content_x_Daily_Use_Interpolated (median [IQR])	0.03 [0.01, 0.13]
Trend_in_Daily_Cannabis_Use = Increasing (%)	696 (72.4)
Mean_Annual_Household_Income (mean (SD))	30180.35 (17329.31)

Supplementary Table S2. Raw Data for Daily Cannabis Drugs Use

[illegible]

Supplementary Table S3. Interpolated Data for Daily Cannabis Drugs Use

[illegible]

Supplementary Table S4. Correlations between Substance and Selected Gastrointestinal Congenital Anomalies.

[illegible]

Supplementary Table S5. Significance Levels of the Correlations Shown in Previous Table.

Covariate	Tobacco	Annual_Alcohol	Daily_Cannabis_Interpolated	Log_Amphetamine	Log_Cocaine	Digestive system	Oesophageal S/A	Duodenal S/A	Small Intestine S/A	Ano-rectal S/A	Hirschsprungs	Bile duct A	Annular Pancreas
Tobacco	0	0.0000	0.2012	0.0724	0.0546	0.0812	0.0133	0.5516	0.8253	0.0076	0.0007	0.0504	0.0107
Annual_Alcohol	0.0000	0	0.1001	0.1776	0.0225	0.7834	0.0893	0.7088	0.7570	0.6293	0.2576	0.6436	0.9604
Daily_Cannabis_Interpolated	0.2012	0.1001	0	0.2893	0.0000	0.0013	0.0157	0.2161	0.0431	0.1486	0.0000	0.0000	0.0045
Log_Amphetamine	0.0724	0.1776	0.2893	0	0.0164	0.9858	0.7138	0.4740	0.8635	0.3354	0.0153	0.1010	0.0027
Log_Cocaine	0.0546	0.0225	0.0000	0.0164	0	0.0000	0.0000	0.6740	0.0213	0.0019	0.0000	0.0000	0.0000
Digestive system	0.0812	0.7834	0.0013	0.9858	0.0000	0	0.0005	0.0000	0.0001	0.0000	0.0000	0.0000	0.0004
Oesophageal S/A	0.0133	0.0893	0.0157	0.7138	0.0000	0.0005	0	0.3870	0.0002	0.0073	0.0001	0.0006	0.0042
Duodenal S/A	0.5516	0.7088	0.2161	0.4740	0.6740	0.0000	0.3870	0	0.0687	0.4649	0.2371	0.2266	0.3002
Small Intestine S/A	0.8253	0.7570	0.0431	0.8635	0.0213	0.0001	0.0002	0.0687	0	0.7214	0.0175	0.0587	0.0812
Ano-rectal S/A	0.0076	0.6293	0.1486	0.3354	0.0019	0.0000	0.0073	0.4649	0.7214	0	0.0008	0.0058	0.0591
Hirschsprungs	0.0007	0.2576	0.0000	0.0153	0.0000	0.0000	0.0001	0.2371	0.0175	0.0008	0	0.0000	0.0031
Bile duct A	0.0504	0.6436	0.0000	0.1010	0.0000	0.0000	0.0006	0.2266	0.0587	0.0058	0.0000	0	0.0002
Annular Pancreas	0.0107	0.9604	0.0045	0.0027	0.0000	0.0004	0.0042	0.3002	0.0812	0.0591	0.0031	0.0002	0

Supplementary Table S6. Pearson Correlation Coefficients Between Cannabinoids and
Selected Gastrointestinal Congenital Anomalies .

Covariates	LM_Cannabis	Herb	Resin	Daily_Cannabis_Interpolated	LM_Cannabis_x_Herb	LM_Cannabis_x_Resin	Log (LM_Cannabis_x_Herb_x_Daily.Interp)	Log (LM_Cannabis_x_Resin_x_Daily.Interp)	Digestive system	Oesophageal S/A	Duodenal S/A	Small Intestine S/A	Ano-rectal S/A	Hirschsprungs	Bile duct A	Annular Pancreas
LM_Cannabis	1	0.031	0.035	0.851	0.804	0.659	0.809	0.728	0.034	0.149	-0.157	0.025	-0.030	0.285	0.336	0.183
Herb	0.031	1	0.505	0.031	0.548	0.343	0.262	0.250	0.394	0.249	0.199	0.247	0.329	0.272	0.218	0.128
Resin	0.035	0.505	1	-0.049	0.304	0.691	0.179	0.387	0.155	0.077	0.091	0.146	0.300	0.063	-0.023	0.052
Daily_Cannabis_Interpolated	0.851	0.031	-0.049	1	0.687	0.498	0.875	0.754	0.225	0.180	-0.155	0.111	0.091	0.453	0.400	0.242
LM_Cannabis_x_Herb	0.804	0.548	0.304	0.687	1	0.783	0.864	0.812	0.235	0.205	0.004	0.150	0.093	0.366	0.374	0.160
LM_Cannabis_x_Resin	0.659	0.343	0.691	0.498	0.783	1	0.712	0.866	0.140	0.121	0.023	0.099	0.153	0.236	0.217	0.163
Log (LM_Cannabis_x_Herb_x_Daily.Interp)	0.809	0.262	0.179	0.875	0.864	0.712	1	0.929	0.231	0.154	-0.046	0.152	0.033	0.417	0.364	0.162
Log (LM_Cannabis_x_Resin_x_Daily.Interp)	0.728	0.250	0.387	0.754	0.812	0.866	0.929	1	0.222	0.167	0.000	0.148	0.098	0.394	0.336	0.202
Digestive system	0.034	0.394	0.155	0.225	0.235	0.140	0.231	0.222	1	0.261	0.411	0.270	0.459	0.428	0.383	0.307

Oesophageal S/A	0.149	0.249	0.077	0.180	0.205	0.121	0.154	0.167	0.261	1	-0.115	0.292	0.220	0.325	0.279	0.248
Duodenal S/A	-0.157	0.199	0.091	-0.155	0.004	0.023	-0.046	0.000	0.411	-0.115	1	0.153	0.050	0.095	0.094	0.087
Small Intestine S/A	0.025	0.247	0.146	0.111	0.150	0.099	0.152	0.148	0.270	0.292	0.153	1	-0.040	0.164	0.099	0.125
Ano-rectal S/A	-0.030	0.329	0.300	0.091	0.093	0.153	0.033	0.098	0.459	0.220	0.050	-0.040	1	0.284	0.225	0.157
Hirschsprungs	0.285	0.272	0.063	0.453	0.366	0.236	0.417	0.394	0.428	0.325	0.095	0.164	0.284	1	0.441	0.259
Bile duct A	0.336	0.218	-0.023	0.400	0.374	0.217	0.364	0.336	0.383	0.279	0.094	0.099	0.225	0.441	1	0.324
Annular Pancreas	0.183	0.128	0.052	0.242	0.160	0.163	0.162	0.202	0.307	0.248	0.087	0.125	0.157	0.259	0.324	1

Supplementary Table S7. Significance Levels of Correlation Coefficients of Previous Table

Covariates	LM_Cannabis	Herb	Resin	Daily_Cannabis_Interpolated	LM_Cannabis_x_Herb	LM_Cannabis_x_Resin	Log (LM_Cannabis_x_Herb_x_Daily.Interp)	Log (LM_Cannabis_x_Resin_x_Daily.Interp)	Digestive system	Oesophageal S/A	Duodenal S/A	Small Intestine S/A	Ano-rectal S/A	Hirschsprungs	Bile duct A	Annular Pancreas
LM_Cannabis	0	7.61E-01	7.32E-01	2.70E-28	3.33E-23	2.25E-13	1.13E-23	2.96E-17	7.41E-01	1.45E-01	1.24E-01	8.07E-01	7.73E-01	4.67E-03	7.81E-04	7.35E-02
Herb	7.61E-01	0	1.30E-07	7.63E-01	6.21E-09	5.81E-04	9.55E-03	1.35E-02	6.63E-05	1.39E-02	5.09E-02	1.48E-02	9.86E-04	7.14E-03	3.15E-02	2.12E-01
Resin	7.32E-01	1.30E-07	0	6.37E-01	2.43E-03	4.47E-15	7.97E-02	8.89E-05	1.29E-01	4.55E-01	3.73E-01	1.55E-01	2.79E-03	5.39E-01	8.22E-01	6.11E-01
Daily_Cannabis_Interpolated	2.70E-28	7.63E-01	6.37E-01	0	7.83E-15	2.15E-07	1.01E-31	4.69E-19	2.68E-02	7.83E-02	1.30E-01	2.79E-01	3.77E-01	3.09E-06	5.01E-05	1.67E-02
LM_Cannabis_x_Herb	3.33E-23	6.21E-09	2.43E-03	7.83E-15	0	2.66E-21	5.33E-30	6.48E-24	2.07E-02	4.35E-02	9.70E-01	1.43E-01	3.63E-01	2.25E-04	1.60E-04	1.17E-01
LM_Cannabis_x_Resin	2.25E-13	5.81E-04	4.47E-15	2.15E-07	2.66E-21	0	2.77E-16	2.75E-30	1.72E-01	2.38E-01	8.25E-01	3.36E-01	1.35E-01	1.97E-02	3.24E-02	1.10E-01
Log (LM_Cannabis_x_Herb_x_Daily.Interp)	1.13E-23	9.55E-03	7.97E-02	1.01E-31	5.33E-30	2.77E-16	0	9.26E-43	2.30E-02	1.33E-01	6.56E-01	1.38E-01	7.47E-01	2.10E-05	2.47E-04	1.14E-01

Log (LM_C annabi s_x_Re sin_x_ Daily.I nterp)	2.96E- 17	1.35E- 02	8.89E- 05	4.69E- 19	6.48E- 24	2.75E- 30	9.26E- 43	0	2.87E- 02	1.03E- 01	9.97E- 01	1.47E- 01	3.41E- 01	6.50E- 05	7.78E- 04	4.67E- 02
Digesti ve system	7.41E- 01	6.63E- 05	1.29E- 01	2.68E- 02	2.07E- 02	1.72E- 01	2.30E- 02	2.87E- 02	0	9.92E- 03	2.83E- 05	7.57E- 03	2.23E- 06	1.23E- 05	1.09E- 04	2.25E- 03
Oesop hageal S/A	1.45E- 01	1.39E- 02	4.55E- 01	7.83E- 02	4.35E- 02	2.38E- 01	1.33E- 01	1.03E- 01	9.92E- 03	0	2.63E- 01	3.69E- 03	3.06E- 02	1.17E- 03	5.66E- 03	1.43E- 02
Duode nal S/A	1.24E- 01	5.09E- 02	3.73E- 01	1.30E- 01	9.70E- 01	8.25E- 01	6.56E- 01	9.97E- 01	2.83E- 05	2.63E- 01	0	1.36E- 01	6.29E- 01	3.56E- 01	3.58E- 01	3.98E- 01
Small Intestin e S/A	8.07E- 01	1.48E- 02	1.55E- 01	2.79E- 01	1.43E- 01	3.36E- 01	1.38E- 01	1.47E- 01	7.57E- 03	3.69E- 03	1.36E- 01	0	7.00E- 01	1.09E- 01	3.33E- 01	2.21E- 01
Ano- rectal S/A	7.73E- 01	9.86E- 04	2.79E- 03	3.77E- 01	3.63E- 01	1.35E- 01	7.47E- 01	3.41E- 01	2.23E- 06	3.06E- 02	6.29E- 01	7.00E- 01	0	4.75E- 03	2.70E- 02	1.26E- 01
Hirsch sprung s	4.67E- 03	7.14E- 03	5.39E- 01	3.09E- 06	2.25E- 04	1.97E- 02	2.10E- 05	6.50E- 05	1.23E- 05	1.17E- 03	3.56E- 01	1.09E- 01	4.75E- 03	0	6.03E- 06	1.05E- 02
Bile duct A	7.81E- 04	3.15E- 02	8.22E- 01	5.01E- 05	1.60E- 04	3.24E- 02	2.47E- 04	7.78E- 04	1.09E- 04	5.66E- 03	3.58E- 01	3.33E- 01	2.70E- 02	6.03E- 06	0	1.22E- 03
Annula r Pancre as	7.35E- 02	2.12E- 01	6.11E- 01	1.67E- 02	1.17E- 01	1.10E- 01	1.14E- 01	4.67E- 02	2.25E- 03	1.43E- 02	3.98E- 01	2.21E- 01	1.26E- 01	1.05E- 02	1.22E- 03	0

Supplementary Table S8. Regression Coefficients from Regression Lines Shown in Figures 1 and 2.

Anomaly	Substance	Mean Anomaly Rate	Estimate	Std.Error	Sigma	t_statistic	P_Value	E-Value Estimate	E-Value Lower Bound
Hirschsprungs	Daily.Interpol.	1.0261	27.7162	5.7170	0.5366	4.8480	4.01E-06	5.17E+20	3.00E+12
Bile duct A	Daily.Interpol.	0.2861	12.2756	2.9410	0.2761	4.1739	5.91E-05	7.50E+17	4.36E+09
Digestive system	Daily.Interpol.	16.2215	15.6512	4.7358	0.4332	3.3049	0.0013	3.81E+14	1.35E+06
Annular Pancreas	Daily.Interpol.	0.2394	8.4039	3.1319	0.2940	2.6834	0.0084	3.97E+11	2.31E+03
Digestive system	Herb	16.2215	5.3718	1.2704	0.4207	4.2284	5.04E-05	2.22E+05	1.03E+03
Digestive system	LMCannabis_Herb	16.2215	5.0475	1.6875	0.4369	2.9911	0.0035	7.36E+04	75.53
Bile duct A	LMCannabis_Herb	0.2861	3.0288	0.9811	0.2816	3.0871	0.0025	3.56E+04	71.65
Bile duct A	LM_Cannabis	0.2861	3.3413	1.1699	0.2831	2.8561	0.0051	9.22E+04	58.49
Hirschsprungs	LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	1.0261	2.8261	0.6376	0.5444	4.4321	2.17E-05	224.78	27.50
Bile duct A	LM.Cannabis_x_Herb.THC: LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	0.2861	1.2190	0.3279	0.2799	3.7173	3.15E-04	104.66	12.55
Hirschsprungs	LMCannabis_Herb	1.0261	4.9510	2.0147	0.5783	2.4574	0.0154	4.83E+03	9.27
Hirschsprungs	LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	1.0261	1.2355	0.2891	0.5409	4.2743	4.45E-05	15.47	5.63
Digestive system	LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	16.2215	1.5453	0.5190	0.4371	2.9775	0.0036	49.42	5.48
Ano-rectal S/A	Resin	3.2084	2.1278	0.7183	0.6457	2.9624	0.0038	39.62	4.98
Bile duct A	LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	0.2861	0.5219	0.1435	0.2686	3.6366	4.43E-04	11.20	3.96
Digestive system	Cocaine	16.2215	0.2633	0.0554	0.4128	4.7556	6.33E-06	2.97	2.16
Hirschsprungs	Cocaine	1.0261	0.3172	0.0679	0.5452	4.6723	7.85E-06	2.79	2.06
Bile duct A	LMCannabis_Resin	0.2861	0.5401	0.2296	0.2749	2.3520	0.0205	11.43	2.04
Annular Pancreas	Cocaine	0.2394	0.1521	0.0347	0.2788	4.3819	2.54E-05	2.67	1.96
Bile duct A	Cocaine	0.2861	0.1421	0.0340	0.2734	4.1736	5.70E-05	2.59	1.89
Annular Pancreas	Log(Amphetamine)	0.2394	0.1256	0.0359	0.2860	3.5018	6.50E-04	2.35	1.67
Oesophageal S/A	Cocaine	2.4957	0.2230	0.0706	0.5671	3.1573	0.0020	2.21	1.55

Digestive system	LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	16.2215	0.4925	0.2217	0.4128	2.2213	0.0287	5.37	1.54
Annular Pancreas	LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	0.2394	0.3478	0.1631	0.3052	2.1328	0.0354	5.09	1.40
Small Intestine S/A	LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	1.0052	1.3045	0.6589	0.5625	1.9799	0.0502	15.99	1.19
Ano-rectal S/A	Cocaine	3.2084	0.1748	0.0809	0.6499	2.1597	0.0328	1.87	1.18
Small Intestine S/A	Cocaine	1.0052	0.1404	0.0685	0.5505	2.0487	0.0427	1.84	1.11
Duodenal S/A	Log(Amphetamine)	1.3088	0.0056	0.0753	0.6005	0.0749	0.9404	1.10	1
Digestive system	Annual_Alcohol	16.2215	0.0065	0.0234	0.4550	0.2756	0.7834	1.13	1
Small Intestine S/A	Annual_Alcohol	1.0052	0.0094	0.0278	0.5598	0.3391	0.7351	1.14	1
Small Intestine S/A	Log(Amphetamine)	1.0052	0.0115	0.0702	0.5600	0.1644	0.8697	1.16	1
Oesophageal S/A	Log(Amphetamine)	2.4957	0.0300	0.0740	0.5898	0.4053	0.6860	1.27	1
Ano-rectal S/A	Log(Amphetamine)	3.2084	0.1395	0.0821	0.6546	1.6996	0.0918	1.72	1
Bile duct A	Resin	0.2861	0.0783	0.3137	0.2820	0.2495	0.8035	1.90	1
Ano-rectal S/A	LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	3.2084	0.2448	0.7872	0.6721	0.3110	0.7564	2.13	1
Ano-rectal S/A	LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	3.2084	0.3264	0.3643	0.6817	0.8958	0.3725	2.46	1
Oesophageal S/A	LMCannabis_Resin	2.4957	0.3251	0.4952	0.5930	0.6564	0.5130	2.68	1
Small Intestine S/A	LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	1.0052	0.4475	0.3007	0.5627	1.4884	0.1399	3.54	1
Small Intestine S/A	LMCannabis_Resin	1.0052	0.4456	0.4614	0.5525	0.9658	0.3364	3.59	1
Oesophageal S/A	Resin	2.4957	0.4795	0.6593	0.5927	0.7273	0.4686	3.60	1
Ano-rectal S/A	LMCannabis_Resin	3.2084	0.5546	0.5587	0.6690	0.9926	0.3232	3.67	1
Duodenal S/A	Herb	1.3088	0.5024	1.5437	0.6003	0.3254	0.7454	3.71	1
Oesophageal S/A	LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	2.4957	0.5138	0.3168	0.5927	1.6221	0.1080	3.83	1
Duodenal S/A	Resin	1.3088	0.5453	0.6828	0.6138	0.7986	0.4264	3.92	1
Hirschsprungs	Resin	1.0261	0.6290	0.6558	0.5895	0.9593	0.3396	4.72	1
Annular Pancreas	Resin	0.2394	0.3396	0.3412	0.3068	0.9952	0.3219	4.92	1
Digestive system	LMCannabis_Resin	16.2215	0.5046	0.3668	0.4192	1.3759	0.1721	5.43	1
Annular Pancreas	LMCannabis_Resin	0.2394	0.3965	0.2545	0.3047	1.5580	0.1222	5.99	1
Hirschsprungs	LMCannabis_Resin	1.0261	0.9275	0.4861	0.5821	1.9080	0.0591	7.99	1
Digestive system	Resin	16.2215	0.7446	0.4858	0.4182	1.5328	0.1286	9.58	1
Small Intestine S/A	Resin	1.0052	1.0183	0.6092	0.5477	1.6714	0.0976	10.34	1

Oesophageal S/A	LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	2.4957	1.0996	0.6890	0.5883	1.5959	0.1133	10.43	1
Oesophageal S/A	LM_Cannabis	2.4957	1.1847	2.4364	0.5897	0.4862	0.6277	11.92	1
Annular Pancreas	LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	0.2394	0.6263	0.3502	0.2990	1.7883	0.0764	12.93	1
Small Intestine S/A	LM_Cannabis	1.0052	1.2445	2.3112	0.5594	0.5385	0.5912	14.63	1
Oesophageal S/A	Herb	2.4957	1.4142	1.5125	0.5881	0.9350	0.3517	17.32	1
Annular Pancreas	Herb	0.2394	0.8060	0.7687	0.2989	1.0485	0.2965	22.76	1
Bile duct A	Herb	0.2861	0.8016	0.7489	0.2912	1.0703	0.2866	23.98	1
Oesophageal S/A	LMCannabis_Herb	2.4957	2.0509	2.0477	0.5878	1.0016	0.3186	47.36	1
Hirschsprungs	Herb	1.0261	2.2365	1.5106	0.5874	1.4806	0.1413	63.45	1
Ano-rectal S/A	Herb	3.2084	2.8155	1.6842	0.6549	1.6717	0.0972	99.54	1
Annular Pancreas	LMCannabis_Herb	0.2394	1.3203	1.0390	0.2983	1.2707	0.2063	111.82	1
Small Intestine S/A	Herb	1.0052	2.4883	1.4223	0.5530	1.7495	0.0828	119.50	1
Digestive system	LM_Cannabis	16.2215	2.0964	2.1109	0.4530	0.9931	0.3229	134.37	1
Small Intestine S/A	Daily.Interpol.	1.0052	3.0240	1.9314	0.5544	1.5657	0.1201	285.68	1
Annular Pancreas	LM_Cannabis	0.2394	1.7605	1.2302	0.2977	1.4311	0.1550	433.99	1
Hirschsprungs	LM_Cannabis	1.0261	3.9413	2.4224	0.5863	1.6270	0.1064	907.04	1
Ano-rectal S/A	Daily.Interpol.	3.2084	6.4243	7.1376	0.6700	0.9001	0.3700	1.23E+04	1
Small Intestine S/A	Daily.Interpol.	1.0052	10.9181	6.0085	0.5640	1.8171	0.0719	8.95E+07	1
Oesophageal S/A	Daily.Interpol.	2.4957	11.8979	6.2377	0.5855	1.9074	0.0590	2.15E+08	1
Digestive system	Log(Amphetamine)	16.2215	-0.0010	0.0588	0.4551	-0.0178	0.9858	1.05	NA
Annular Pancreas	Annual_Alcohol	0.2394	-0.0008	0.0149	0.3003	-0.0565	0.9550	1.05	NA
Bile duct A	Annual_Alcohol	0.2861	-0.0022	0.0146	0.2926	-0.1485	0.8822	1.09	NA
Small Intestine S/A	Tobacco	1.0052	-0.0058	0.0093	0.5591	-0.6217	0.5353	1.11	NA
Duodenal S/A	Annual_Alcohol	1.3088	-0.0075	0.0299	0.6004	-0.2496	0.8033	1.12	NA
Duodenal S/A	Tobacco	1.3088	-0.0121	0.0099	0.5969	-1.2164	0.2262	1.16	NA
Ano-rectal S/A	Annual_Alcohol	3.2084	-0.0145	0.0329	0.6619	-0.4402	0.6606	1.16	NA
Digestive system	Tobacco	16.2215	-0.0137	0.0078	0.4486	-1.7605	0.0812	1.20	NA
Duodenal S/A	LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	1.3088	-0.0300	0.3343	0.6255	-0.0898	0.9286	1.26	NA
Bile duct A	Tobacco	0.2861	-0.0137	0.0047	0.2828	-2.9069	0.0043	1.26	NA
Oesophageal S/A	Tobacco	2.4957	-0.0297	0.0094	0.5672	-3.1521	0.0020	1.28	NA
Annular Pancreas	Tobacco	0.2394	-0.0156	0.0048	0.2877	-3.2651	0.0014	1.28	NA
Ano-rectal S/A	Tobacco	3.2084	-0.0349	0.0106	0.6342	-3.3037	0.0013	1.28	NA

Hirschsprungs	Annual_Alcohol	1.0261	-0.0350	0.0293	0.5892	-1.1928	0.2353	1.30	NA
Hirschsprungs	Tobacco	1.0261	-0.0398	0.0092	0.5510	-4.3427	2.96E-05	1.34	NA
Oesophageal S/A	Annual_Alcohol	2.4957	-0.0512	0.0290	0.5827	-1.7662	0.0799	1.38	NA
Bile duct A	Resin	0.2861	-0.0319	0.0366	0.2917	-0.8722	0.3848	1.44	NA
Ano-rectal S/A	LMCannabis_Herb	3.2084	-0.0866	2.3077	0.6624	-0.0375	0.9701	1.50	NA
Duodenal S/A	Cocaine	1.3088	-0.0952	0.0743	0.5965	-1.2818	0.2024	1.58	NA
Hirschsprungs	Log(Amphetamine)	1.0261	-0.1100	0.0736	0.5873	-1.4932	0.1380	1.66	NA
Duodenal S/A	LMCannabis_Resin	1.3088	-0.1515	0.5140	0.6154	-0.2948	0.7687	1.81	NA
Duodenal S/A	LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	1.3088	-0.5096	0.7116	0.6075	-0.7162	0.4753	3.71	NA
Duodenal S/A	LMCannabis_Herb	1.3088	-2.3470	2.0811	0.5974	-1.1278	0.2617	70.90	NA
Ano-rectal S/A	LM_Cannabis	3.2084	-3.1167	2.7223	0.6589	-1.1449	0.2545	147.60	NA
Duodenal S/A	LM_Cannabis	1.3088	-6.2253	2.4153	0.5846	-2.5774	0.0112	3.23E+04	NA
Duodenal S/A	Daily.Interpol.	1.3088	-11.5891	6.3943	0.6002	-1.8124	0.0726	8.55E+07	NA

Supplementary Table S9. Forest Regression and Variable Importance Table
- Esophageal Stenosis and Atresia

Variable	Importance
Income	7.4817
Tobacco	5.7847
Resin	3.1387
Cocaine	2.9261
Daily.Interpol.	2.7509
LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	2.6959
LM.Cannabis_x_Resin.THC	2.5971
Daily.Interpol.	2.5685
Alcohol	2.0999
LM.Cannabis_x_Herb.THC	1.9033
LM.Cannabis	1.8734
Herb	1.7290
Amphetamines	1.5916

Supplementary Table S10. Forest Regression and Variable Importance Table
- Bile Duct Atresia

Variable	Importance
Income	2.1659
Tobacco	0.9401
Daily.Interpol.	0.7664
Cocaine	0.7149
Alcohol	0.7062
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	0.6995
LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	0.6529
Amphetamines	0.6441
LM.Cannabis	0.5538
LM.Cannabis_x_Resin.THC	0.5272
LM.Cannabis_x_Herb.THC	0.4930
Resin	0.4393
Herb	0.4119

Supplementary Table S11. Forest Regression and Variable Importance Table
- Small Intestinal Stenosis and Atresia

Variable	Importance
Income	4.3228
Tobacco	4.2394
Daily.Interpol.	3.2878
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	3.2707
LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	2.6342
LM.Cannabis_x_Resin.THC	2.4123
Herb	2.3969
Resin	2.3410
Cocaine	2.0365
Amphetamines	2.0189
LM.Cannabis_x_Herb.THC	1.9242
LM.Cannabis	1.8381
Alcohol	1.6612

Supplementary Table S12. Forest Regression and Variable Importance Table
- Large Intestinal Stenosis and Atresia

Variable	Importance
Income	10.7345
Tobacco	7.9453
Resin	3.7489
Herb	3.5230
LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	3.0013
Daily.Interpol.	2.8507
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	2.8467
LM.Cannabis	2.6059
LM.Cannabis_x_Herb.THC	2.5638
Cocaine	2.5331
Alcohol	2.3779
LM.Cannabis_x_Herb.THC: LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	2.3016
LM.Cannabis_x_Resin.THC	2.2129

Supplementary Table S13. Forest Regression and Variable Importance Table
- Hirschprungs Disease / Congenital Megacolon

Variable	Importance
Income	9.3342
Resin	6.1273
Daily.Interpol.	3.6838
Cocaine	2.8498
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	2.7871
LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	2.6591
Alcohol	2.3730
LM.Cannabis_x_Herb.THC	2.0344
LM.Cannabis	1.8889
LM.Cannabis_x_Resin.THC	1.7612
Amphetamines	1.7370
Herb	1.4887
Resin	1.3853

Supplementary Table S14. Panel Regression Table for Esophageal Stenosis and Atresia

Parameters			Model Parameters	
Term	Estimate (C.I.)	P-Value	Parameter	Value
<i>Additive</i>				
<i>(LANomRt ~ TobRt + AlcRt + LpmHerbDailyInt + LpmResinDailyInt + pm.Daily.Intpltd + pmResin + LAmph + LCocc + MHY)</i>				
Alcohol	-0.1 (-0.15, -0.05)	0.0001	Adj.R.Squared	0.0345
Daily.Interpol.	11.36 (6.37, 16.34)	1.83E-05	Statistic	11.7614
			Deg.Freedom	2,119
			P-Value	2.18E-05
<i>Interactive</i>				
<i>Rate ~ Tobacco * Daily.Interpol. + Resin + LM.Cannabis_x_Resin.THC_x_Daily.Interpol. + LM.Cannabis_x_Herb.THC_x_Daily.Interpol. * LM.Cannabis_x_Resin.THC + Alcohol + Amphetamines + Cocaine + Income</i>				
Tobacco	-0.02 (-0.04, -0.01)	0.0047	Adj.R.Squared	0.1165
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	0.6 (0.04, 1.16)	0.0381	Statistic	9.288
LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	-0.53 (-0.98, -0.07)	0.0256	Deg.Freedom	2,119
Cocaine	0.16 (0.06, 0.26)	0.0019	P-Value	1.80E-03
<i>2 Lags</i>				
<i>Rate ~ Tobacco * Daily.Interpol. + LM.Cannabis_x_Resin.THC_x_Daily.Interpol. * LM.Cannabis_x_Herb.THC_x_Daily.Interpol. + Resin + Alcohol + Amphetamines + Cocaine + Income</i>				
Resin	-1.59 (-2.96, -0.22)	0.0232	Adj.R.Squared	0.1271
LM.Cannabis_x_Resin.THC	2.57 (1.18, 3.96)	0.0003	Statistic	6.1838
Income	0 (0, 0)	0.0008	Deg.Freedom	2,91
			P-Value	3.00E-03

Supplementary Table S15. Panel Regression Table for Bile Duct Atresia

Parameters			Model Parameters	
Term	Estimate (C.I.)	P-Value	Parameter	Value
<i>Additive</i>				
<i>Rate ~ Tobacco + Alcohol + LM.Cannabis_x_Herb.THC_x_Daily.Interpol. + LM.Cannabis_x_Resin.THC_x_Daily.Interpol. + LM.Cannabis_x_Resin.THC + Daily.Interpol. + Amphetamines + Cocaine + Income</i>				
Alcohol	0.13 (0.07, 0.19)	4.03E-05	Adj.R.Squared	0.1516
LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	-0.42 (-0.72, -0.13)	0.0054	Statistic	10.9696
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	0.48 (0.15, 0.8)	0.0046	Deg.Freedom	5,116
Daily.Interpol.	-14.8 (-30.01, 0.41)	0.0589	P-Value	1.16E-08
Amphetamines	-0.15 (-0.29, -0.01)	0.0341		
Cocaine	0.36 (0.13, 0.58)	0.0028		
Income	0 (0, 0)	0.0069		
<i>Interactive</i>				
<i>Rate ~ Tobacco * Daily.Interpol. * LM.Cannabis_x_Resin.THC_x_Daily.Interpol. + LM.Cannabis_x_Herb.THC_x_Daily.Interpol. + LM.Cannabis_x_Resin.THC + Alcohol + Amphetamines + Cocaine + Income</i>				
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	0.22 (0.05, 0.39)	0.0116	Adj.R.Squared	0.1516
LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	-0.2 (-0.36, -0.03)	0.0239	Statistic	10.9696
Alcohol	0.09 (0.04, 0.15)	0.0008	Deg.Freedom	5,116
Cocaine	0.13 (0.05, 0.21)	0.0013	P-Value	1.16E-08
Income	0 (0, 0)	0.0011		
<i>2 Lags</i>				
<i>Rate ~ Tobacco * LM.Cannabis_x_Herb.THC_x_Daily.Interpol. + Daily.Interpol. * LM.Cannabis_x_Resin.THC_x_Daily.Interpol. + LM.Cannabis_x_Resin.THC + Alcohol + Amphetamines + Cocaine + Income-Income</i>				
Cocaine	0.18 (0.08, 0.27)	0.0003	Adj.R.Squared	0.1154
Daily.Interpol.: LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	8.08 (2.91, 13.26)	0.0029	Statistic	13.5844
			Deg.Freedom	2,91
			P-Value	6.88E-04

Supplementary Table S16. Panel Regression Table for Small Intestinal Stenosis and Atresia

Parameters			Model Parameters	
Term	Estimate (C.I.)	P-Value	Parameter	Value
<i>Additive</i>				
<i>Rate ~ Tobacco + Alcohol + LM.Cannabis_x_Herb.THC_x_Daily.Interpol. + LM.Cannabis_x_Resin.THC_x_Daily.Interpol. + LM.Cannabis_x_Resin.THC + Herb + Daily.Interpol. + Amphetamines + Cocaine + Income</i>				
LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	-0.85 (-1.1, -0.6)	7.10E-10	Adj.R.Squared	0.01768
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	0.98 (0.73, 1.22)	3.55E-12	Statistic	31.7325
			Deg.Freedom	2,119
			P-Value	9.01E-12
<i>Interactive</i>				
<i>Rate ~ Tobacco * Daily.Interpol. + LM.Cannabis_x_Herb.THC_x_Daily.Interpol. * LM.Cannabis_x_Resin.THC_x_Daily.Interpol. * LM.Cannabis_x_Resin.THC + Alcohol + Herb + Amphetamines + Cocaine + Income</i>				
Tobacco	0.1 (0.05, 0.15)	8.43E-05	Adj.R.Squared	-0.0302
Daily.Interpol.	242 (129.89, 354.11)	4.59E-05	Statistic	18.9707
LM.Cannabis_x_Herb.THC: LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	-1.76 (-2.76, -0.76)	0.0007	Deg.Freedom	7,114
Amphetamines	-0.25 (-0.44, -0.06)	0.0115	P-Value	<2.2E-16
Income	0 (0, 0)	0.0005		
Tobacco: Daily.Interpol.	-9.48 (-13.91, -5.05)	5.51E-05		
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.: LM.Cannabis_x_Resin.THC	1.96 (1.18, 2.74)	2.84E-06		
<i>2 Lags</i>				

<i>LAnomRt ~ lag(TobRt,2) * lag(LpmResinDailyInt,2) + lag(pm.Daily.Intpltd,2) + lag(LpmHerbDailyInt,2) + lag(pmResin,2) + lag(AlcRt,2) + lag(LAmph,2) + lag(LCocc,2) + lag(MHY,2)</i>				
Tobacco	0.07 (0.03, 0.11)	0.0006	Adj.R.Squared	-0.0074
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	6.27 (3.84, 8.7)	2.29E-06	Statistic	20.8532
LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	-5.46 (-7.58, -3.34)	2.43E-06	Deg.Freedom	5,88
LM.Cannabis_x_Resin.THC	-5.74 (-8.8, -2.68)	0.0004	P-Value	1.09E-13
Income	0 (0, 0)	0.0036		

Supplementary Table S17. Panel Regression Table for Anorectal Stenosis and Atresia

Parameters			Model Parameters	
Term	Estimate (C.I.)	P-Value	Parameter	Value
<i>Additive</i>				
<i>Rate ~ Tobacco + Alcohol + LM.Cannabis_x_Herb.THC_x_Daily.Interpol. + LM.Cannabis_x_Resin.THC_x_Daily.Interpol. + Herb + Daily.Interpol. + Amphetamines + Cocaine + Income</i>				
LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	-0.64 (-0.97, -0.31)	0.0003	Adj.R.Squared	0.0442
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	0.71 (0.34, 1.08)	0.0003	Statistic	14.0779
Daily.Interpol.	-47.71 (-62.09, -33.33)	2.02E-09	Deg.Freedom	4,117
Cocaine	0.59 (0.36, 0.82)	2.72E-06	P-Value	2.08E-09
<i>Interactive</i>				
<i>Rate ~ Tobacco * Resin * LM.Cannabis_x_Resin.THC_x_Daily.Interpol. + Herb + LM.Cannabis_x_Herb.THC_x_Daily.Interpol. + Alcohol + Daily.Interpol. + Amphetamines + Cocaine + Income</i>				
Herb	-5.8 (-9.96, -1.64)	0.0071	Adj.R.Squared	0.1984
Alcohol	0.11 (0.04, 0.19)	0.0027	Statistic	14.9668
Daily.Interpol.	-41.7 (-56.58, -26.82)	2.31E-07	Deg.Freedom	6,115
Cocaine	0.59 (0.32, 0.86)	3.22E-05	P-Value	1.35E-12
Income	0 (0, 0)	0.0002		
Tobacco: Resin	0.12 (0.07, 0.17)	7.35E-06		
<i>2 Lags</i>				
<i>Rate ~ Tobacco * Daily.Interpol. + Resin * LM.Cannabis_x_Resin.THC_x_Daily.Interpol. + Herb + LM.Cannabis_x_Herb.THC_x_Daily.Interpol. + Alcohol + Amphetamines + Cocaine + Income</i>				
Tobacco	0.09 (0.02, 0.15)	0.0074	Adj.R.Squared	0.0131
Daily.Interpol.	213 (74.62, 351.38)	0.0035	Statistic	7.0592
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	-0.57 (-0.91, -0.23)	0.0015	Deg.Freedom	8,85
Herb	-4.44 (-8.56, -0.32)	0.0375	P-Value	4.10E-07
Alcohol	0.13 (0.04, 0.22)	0.0074		
Income	0 (0, 0)	4.82E-06		
Tobacco: Daily.Interpol.	-9.18 (-14.79, -3.57)	0.0019		
Resin: LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	4.98 (2.33, 7.63)	0.0004		

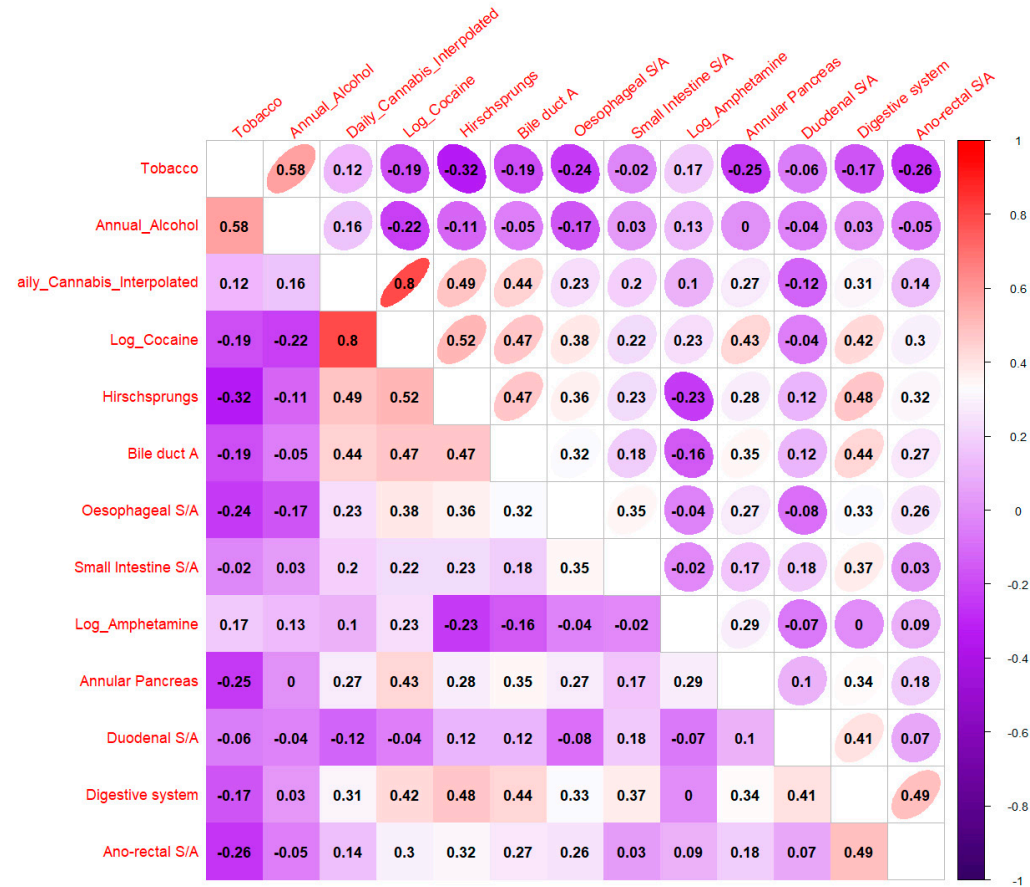
Supplementary Table S18. Panel Regression Table for Hirschprungs Disease

Parameters			Model Parameters	
Term	Estimate (C.I.)	P-Value	Parameter	Value
<i>Additive</i>				
<i>Rate ~ Tobacco + Alcohol + LM.Cannabis_x_Herb.THC_x_Daily.Interpol. + LM.Cannabis_x_Resin.THC_x_Daily.Interpol. + LM.Cannabis_x_Herb.THC + Daily.Interpol. + Amphetamines + Cocaine + Income</i>				
LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	-0.96 (-1.29, -0.62)	1.67E-07	Adj.R.Squared	0.3607
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	1.06 (0.7, 1.42)	8.72E-08	Statistic	35.4619
Daily.Interpol.	17.4 (8.7, 26.1)	0.0001	Deg.Freedom	4,117
Income	0 (0, 0)	0.0008	P-Value	<2.2E-16
<i>Interactive</i>				
<i>Rate ~ Tobacco * Daily.Interpol. * LM.Cannabis_x_Resin.THC_x_Daily.Interpol. + LM.Cannabis_x_Herb.THC_x_Daily.Interpol. + LM.Cannabis_x_Herb.THC + Alcohol + Amphetamines + Cocaine + Income</i>				
Daily.Interpol.	31.15 (21.15, 41.15)	1.50E-08	Adj.R.Squared	0.08198
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	-4.72 (-6.77, -2.67)	1.54E-05	Statistic	34.047
LM.Cannabis_x_Herb.THC	-11.12 (-18.11, -4.13)	0.0023	Deg.Freedom	8,113
Alcohol	-0.11 (-0.17, -0.05)	0.0003	P-Value	<2.2E-16
Amphetamines	-0.25 (-0.44, -0.06)	0.01073		
Tobacco: LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	0.2 (0.11, 0.29)	4.52E-05		
Daily.Interpol.: LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	631.85 (426.44, 837.25)	2.12E-08		
Tobacco: Daily.Interpol.: LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	-24.89 (-33.76, -16.01)	2.44E-07		

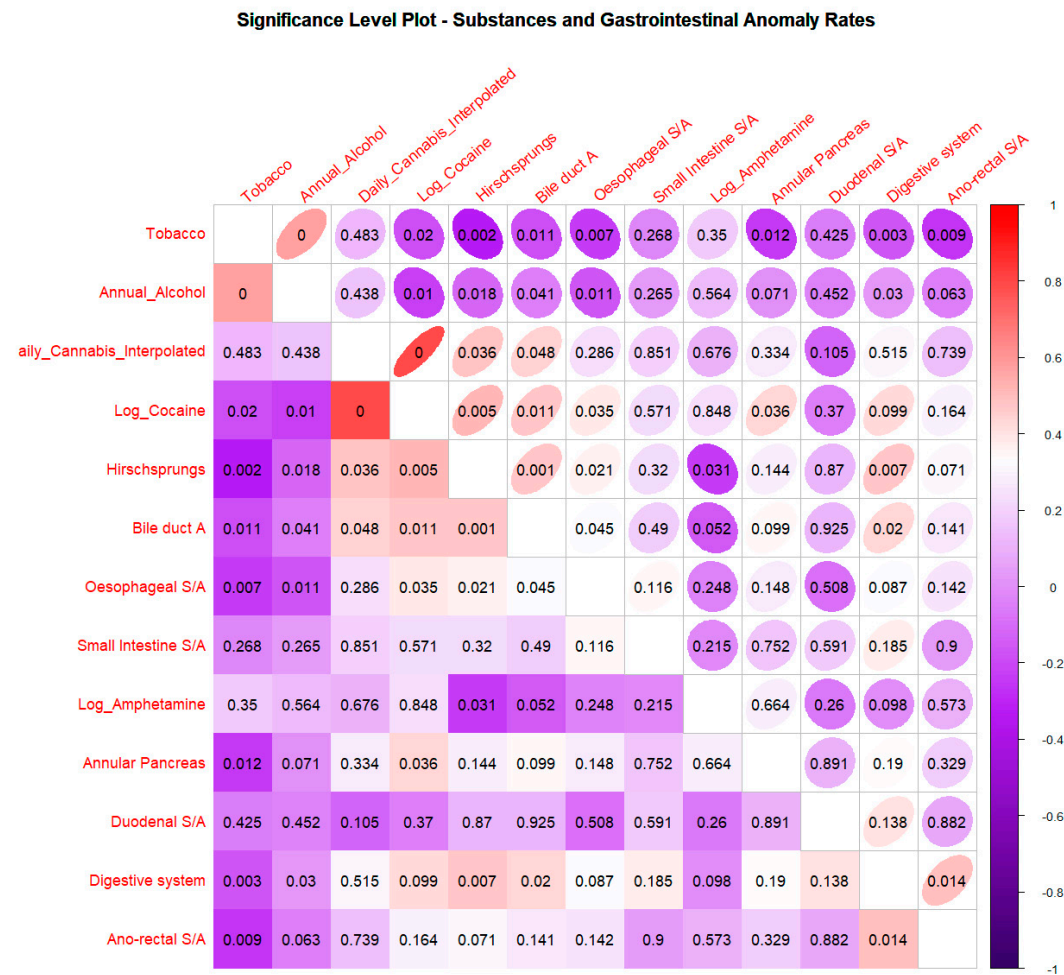
2 Lags				
Rate ~ Tobacco * LM.Cannabis_x_Herb.THC_x_Daily.Interpol. + LM.Cannabis_x_Resin.THC_x_Daily.Interpol. + Daily.Interpol. + LM.Cannabis_x_Herb.THC + Alcohol + Daily.Interpol. + Amphetamines + Cocaine + Income				
LM.Cannabis_x_Herb.THC_x_Daily.Interpol.	-1.5 (-1.87, -1.13)	5.60E-12	Adj.R.Squared	0.2067
LM.Cannabis_x_Resin.THC_x_Daily.Interpol.	1.62 (1.23, 2.01)	2.00E-12	Statistic	46.6245
Daily.Interpol.	31.77 (22.23, 41.31)	3.99E-09	Deg.Freedom	4,89
Alcohol	-0.14 (-0.21, -0.07)	0.0002	P-Value	<2.2E-16

SUPPLEMENTARY FIGURES

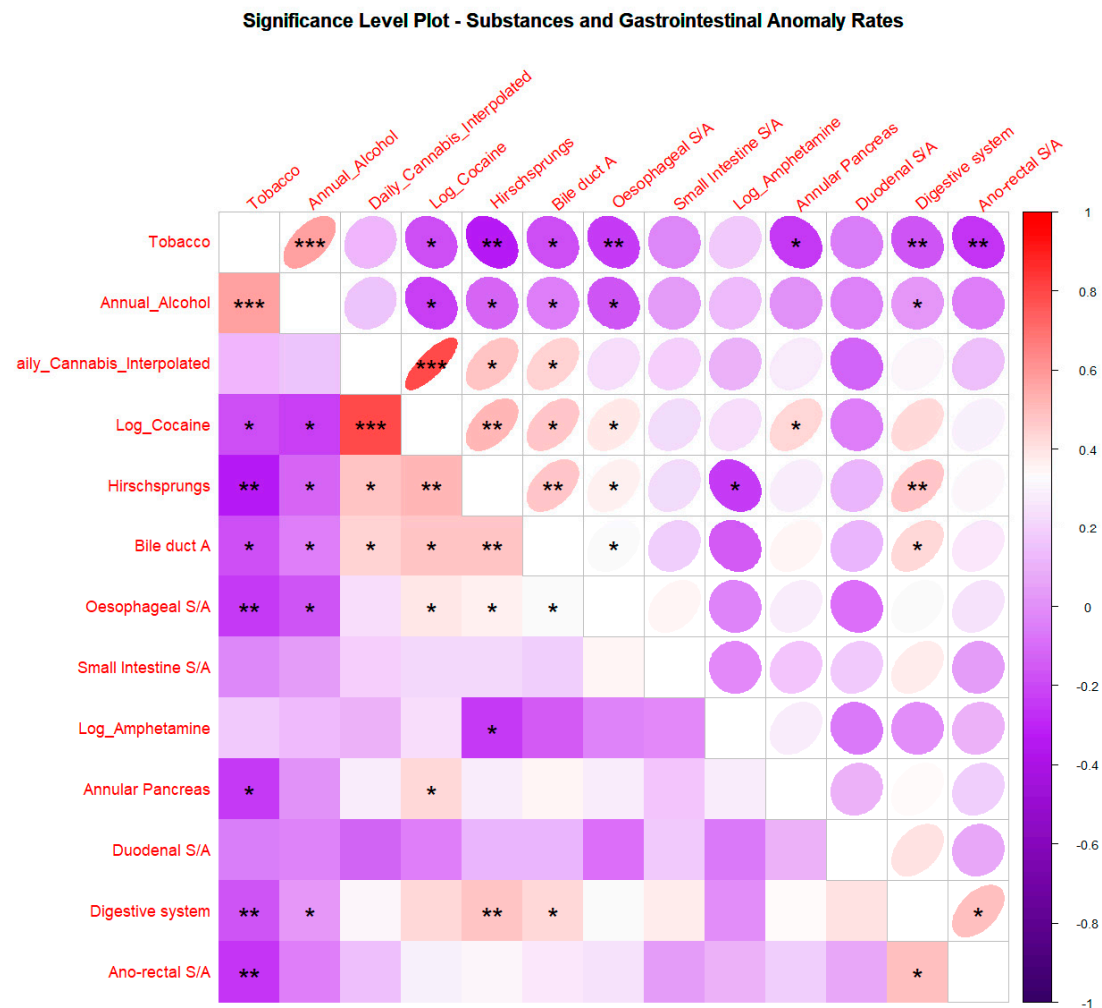
Correlation Plot - Substances and Gastrointestinal Anomaly Rates



Supplementary Figure S1. Pearson correlation coefficients between substance use and selected gastrointestinal anomalies.



Supplementary Figure S2. Significance levels of Pearson correlation coefficients between substance use and selected gastrointestinal anomalies shown in Supplementary Figure 1.

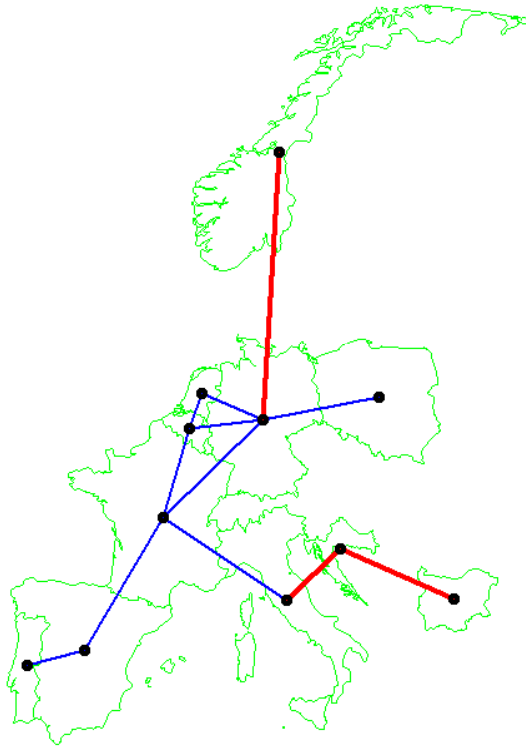


Supplementary Figure S3. Semi-quantitative significance levels of Pearson correlation coefficients between substance use and selected gastrointestinal anomalies shown in Supplementary Figure 1, shown as glyphs.

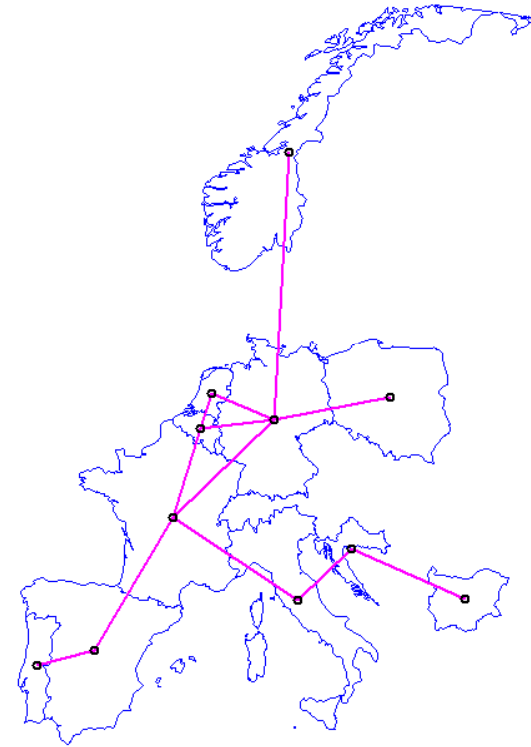


Supplementary Figure S4. Semi-quantitative significance levels of Pearson correlation coefficients shown in Figure 3 between metrics of cannabis exposure and selected gastrointestinal anomalies, shown as glyphs.

**Edited (Red) Links (Blue) to European Country
Neighbourhood Links for Gastrointestinal Anomalies Dataset**



**Final Country Neighbourhood Links for
European Gastrointestinal Anomalies Dataset**



Supplementary Figure S5. Links between nations used to define the sparse spatial weight matrix for geospatial modelling.