**Table S1: List of constipation associated medications**

|  |  |
| --- | --- |
| **Medication group** | **Medication list** |
| Calcium channel blockers | Amlodipine, diltiazem, felodipine, isradipine, nicardipine, nifedipine, nisoldipine, verapamil |
| Anticholinergic medications | Diphenhydramine, trihexyphenidyl, benztropine, clomipramine, chlorpromazine, clozapine, fluphenazine, loxapine, olanzapine, perphenazine, pimozide, quetiapine, thioridazine, thiothixene, trifluoperazine, biperiden, belladonna, chloridiazepoxide,  dicyclomine, hyoscyamine |
| Opioids | Morphine, morphone, codeine, codone, methadone, meperidine, fentanyl, naloxone, pentazocine, naltrexone, dextromethorphan |
| Urinary urgency | Oxybutynin, , darifenacin, solifenacin, fesoterodine, tolterodine, trospium |
| Other gastrointestinal disorders: diarrhea, nausea, vomiting | Atropine, belladonna, dicyclomine, hyoscyamine, loperamide, promethazine, meclizine, scopolamine |
| Muscle relaxation | Cyclobenzaprine, dantrolene, carisoprodol, methocarbamol, orphenadrine, tizanidine |
| Antidepressants | Amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, nortriptyline, protriptyline, trimipramine |
| Antiseizure | Gabapentine, valproic, carbamazepine, phenobarbital, oxcarbazepine, phenytoin, primidone, levetiracetam, topiramate |
| Other medications | Ondansetron, pregabalin, calcium, iron |

**Table S2: Dietary characteristics of study participants by marijuana use, NHANES 2005-2010**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Marijuana (Cannabis) use** a. | | |  |
| **Food item** | | **Never Users (4,400)** | **Past Users (4,065)** | **Recent Users (1,180)** | **p-value** |
| Daily protein intake, % | |  |  |  | <0.0001 |
|  | Lowest quartile (<58.7gm/day) | 1225 (25.7%) | 866 (20.6%) | 238 (20.6%) |  |
|  | Second quartile (58.7-78.72gm/day) | 1135 (26.7%) | 959 (24.1%) | 268 (20.9%) |  |
|  | Third quartile (78.7-103.5gm/day) | 1075 (25.8%) | 1050 (25.8%) | 271 (24.3%) |  |
|  | Highest quartile (>103.5gm/day) | 885 (21.9%) | 1127 (29.5%) | 387 (34.2%) |  |
|  |  |  |  |  |  |
| Daily carbohydrate intake, % | |  |  |  | <0.0001 |
|  | Lowest quartile (<187.8gm/day) | 1170 (25.7%) | 910 (23.9%) | 237 (20.0%) |  |
|  | Second quartile (187.8-251.2gm/day) | 1118 (26.2%) | 1022 (26.4%) | 239 (19.9%) |  |
|  | Third quartile (251.2-328.8gm/day) | 1100 (26.1%) | 1017 (24.4%) | 267 (24.9%) |  |
|  | Highest quartile (>328.8gm/day) | 932 (22.0%) | 1053 (25.3%) | 421 (35.1%) |  |
|  |  |  |  |  |  |
| Daily kilocalorie intake, % | |  |  |  | <0.0001 |
|  | Lowest quartile (<1543.5kcal/day) | 1291 (27.1%) | 823 (20.5%) | 190 (15.7%) |  |
|  | Second quartile (1543.5-2043.5kcal/day) | 1177 (27.2%) | 970 (25.1%) | 212 (17.9%) |  |
|  | Third quartile (2043.5-2659.0kcal/day) | 1054 (25.8%) | 1048 (25.6%) | 287 (24.8%) |  |
|  | Highest quartile (>2659.0kcal/day) | 798 (19.9%) | 1161 (28.9%) | 475 (41.6%) |  |
|  |  |  |  |  |  |
| Daily fat intake, % | |  |  |  | <0.0001 |
|  | Lowest quartile (<16.2gm/day) | 1335 (26.7%) | 737 (18.2%) | 201 (16.6%) |  |
|  | Second quartile (16.2-24.0gm/day) | 1191 (27.5%) | 951 (23.4%) | 231 (20.0%) |  |
|  | Third quartile (24.0-33.9gm/day) | 982 (23.6%) | 1091 (27.1%) | 328 (27.0%) |  |
|  | Highest quartile (>33.9gm/day) | 812 (22.2%) | 1223 (31.3%) | 404 (36.5%) |  |
|  |  |  |  |  |  |
| Daily sugar intake, % | |  |  |  | <0.0001 |
|  | Lowest quartile (<72.3gm/day) | 1131 (25.6%) | 964 (26.3%) | 231 (20.3%) |  |
|  | Second quartile (72.3-109.0gm/day) | 1190 (27.5%) | 926 (23.9%) | 244 (21.0%) |  |
|  | Third quartile (109.0-156.9gm/day) | 1103 (25.8%) | 1016 (24.3%) | 270 (24.1%) |  |
|  | Highest quartile (>156.9gm/day) | 896 (21.1%) | 1096 (25.5%) | 419 (34.6%) |  |
|  |  |  |  |  |  |
| Daily caffeine intake, % | |  |  |  | <0.0001 |
|  | Lowest quartile (<26.5mg/day) | 1283 (25.5%) | 779 (15.3%) | 255 (18.5%) |  |
|  | Second quartile (26.5-93.0mg/day) | 1203 (24.6%) | 886 (19.5%) | 263 (20.8%) |  |
|  | Third quartile (93.0-205.5mg/day) | 1073 (26.7%) | 1003 (25.4%) | 294 (25.7%) |  |
|  | Highest quartile (>205.5mg/day) | 761 (23.2%) | 1334 (39.8%) | 352 (35.0%) |  |
|  |  |  |  |  |  |
| Daily fiber intake, % | |  |  |  | <0.0001 |
|  | Lowest quartile (<10.1gm/day) | 989 (22.0%) | 986 (22.5%) | 361 (30.1%) |  |
|  | Second quartile (10.1-14.7gm/day) | 1099 (25.7%) | 993 (24.7%) | 310 (25.0%) |  |
|  | Third quartile (14.7-20.6gm/day) | 1088 (26.5%) | 1043 (27.2%) | 233 (21.7%) |  |
|  | Highest quartile (>20.6gm/day) | 1144 (25.9%) | 980 (25.6%) | 260 (23.3%) |  |
|  |  |  |  |  |  |
| Daily liquid intake, % | |  |  |  | <0.0001 |
|  | Lowest quartile (<2004.7gm/day) | 1274 (24.8%) | 816 (16.8%) | 218 (15.9%) |  |
|  | Second quartile (2004.7-2691.9gm/day) | 1170 (26.9%) | 943 (23.2%) | 247 (17.7%) |  |
|  | Third quartile (2691.9-3584.2gm/day) | 1040 (26.2%) | 1073 (27.8%) | 291 (27.2%) |  |
|  | Highest quartile (>3584.2gm/day) | 836 (22.1%) | 1170 (32.1%) | 408 (39.1%) |  |

a.Recent MJ use was defined as the use of marijuana/hashish during the past 30 days. Past MJ use is defined as the use of marijuana/hashish more than 30 days ago.

b.All dietary factors were measured with a 24-hour dietary recall interview which consisted of detailed questions on over 60 food items/nutrients consumed during the preceeding 24-hour period. Two interviews were conducted 3-10 days apart, and the average was used as an estimate of daily nutrient consumption. Eight food items (protein, carbohydrate, kcal, fat, sugar, caffeine, fiber, liquid) related to bowel function were used in this study.

**Table S3: Fully adjusted multivariable models for factors associated with constipation, NHANES 2005-2010**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Effect of recent marijuana use (MJ)** a. | | **Odds ratio** | **Lower confidence limit** | **Upper confidence limit** | **p-value** |
| **compared to past/never users on constipation** | |
| Marijuana use | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.67 | 0.50 | 0.89 | 0.005 |
| Sex | |  |  |  |  |
|  | Female vs. Male | 2.67 | 2.20 | 3.31 | <0.0001 |
| Age | |  |  |  |  |
|  | Per 10 year increase | 0.87 | 0.8 | 0.96 | <0.0001 |
| Race/Ethnicity | |  |  |  | 0.0006 |
|  | Blacks vs. Whites | 1.29 | 1.03 | 1.61 | 0.024 |
|  | Hispanics vs. Whites | 0.91 | 0.74 | 1.12 | 0.39 |
|  | Others vs. Whites | 0.87 | 0.55 | 1.39 | 0.56 |
| Education level | |  |  |  | <0.0001 |
|  | Below vs. Above High School/GED | 1.5 | 1.17 | 1.91 | 0.001 |
|  | Completed vs. Above High School/GED | 1.6 | 1.33 | 1.93 | <0.0001 |
| Poverty level b. | |  |  |  |  |
|  | Below vs. Above 2 | 1.29 | 1.08 | 1.54 | 0.005 |
| Body Mass Index | |  |  |  | <0.0001 |
|  | Overweight (25.0-29.9 kg/m2) vs. Normal (<25.0 kg/m2) | 0.99 | 0.8 | 1.23 | 0.94 |
|  | Obese (>=30.0 kg/m2) vs. Normal (<25 kg/m2) | 0.6 | 0.48 | 0.75 | <0.0001 |
| Comorbidities c. | |  |  |  |  |
|  | One vs. None | 1.07 | 0.87 | 1.31 | 0.525 |
|  | Two vs. None | 1.23 | 0.93 | 1.62 | 0.15 |
|  | Three vs. None | 0.85 | 0.40 | 1.81 | 0.67 |
|  | Four or more vs. None | 1.59 | 0.75 | 3.38 | 0.23 |
| Diabetes mellitus d. | |  |  |  |  |
|  | Yes vs. No | 1.01 | 0.72 | 1.42 | 0.9538 |
| Depression e. | |  |  |  |  |
|  | Yes vs. No | 1.85 | 1.42 | 2.42 | <0.0001 |
| Constipating medications f. | |  |  |  |  |
|  | Yes (>=1) vs. None | 1.24 | 0.89 | 1.72 | 0.21 |
| Alcohol use g. | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.99 | 0.81 | 1.22 | 0.95 |
| Cigarette use g. | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.77 | 0.64 | 0.93 | 0.007 |
| Heroin use g. | |  |  |  |  |
|  | Recent users vs. Past/Never users | 2.61 | 0.42 | 16.18 | 0.304 |
| Cocaine use g. | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.92 | 0.49 | 1.73 | 0.792 |
| General health condition h. | |  |  |  |  |
|  | Excellent/very good/good vs. fair/poor | 0.71 | 0.55 | 0.91 | 0.007 |
| Regular rigorous physical activity i. | |  |  |  |  |
|  | Yes vs. No | 0.97 | 0.79 | 1.2 | 0.79 |
| Emotional problems j. | |  |  |  |  |
|  | Yes vs. No | 1.57 | 1.01 | 2.44 | 0.04 |
| Daily protein intake | |  |  |  | 0.68 |
|  | Second vs. First quartile (58.7-78.7gm/day vs. <58.7gm/day) | 1.16 | 0.88 | 1.55 |  |
|  | Third vs. First quartile (78.7-103.5gm/day vs. <58.7gm/day) | 1.19 | 0.87 | 1.61 |  |
|  | Highest vs. First quartile (>103.5gm/day vs. <58.7gm/day) | 1.14 | 0.66 | 1.96 |  |
| Daily carbohydrate intake | |  |  |  | 0.31 |
|  | Second vs. First quartile (187.7-251.3gm/day vs. <187.7gm/day) | 1.32 | 0.92 | 1.89 |  |
|  | Third vs. First quartile (251.2-328.8gm/day vs. <187.7gm/day) | 1.44 | 0.91 | 2.29 |  |
|  | Highest vs. First quartile (>328.8gm/day vs. <187.7gm/day) | 1.45 | 0.79 | 2.68 |  |
| Daily kilocalorie intake | |  |  |  | 0.47 |
|  | Second vs. First quartile (1543.5-2043.5kcal/day vs. <1543.5kcal/day) | 0.88 | 0.66 | 1.16 |  |
|  | Third vs. First quartile (2043.5-2659.0kcal/day vs. <1543.5kcal/day) | 0.74 | 0.46 | 1.19 |  |
|  | Highest vs. First quartile (>2659.0kcal/day vs. <1543.5kcal/day) | 0.69 | 0.33 | 1.44 |  |
| Daily fat intake | |  |  |  | 0.05 |
|  | Second vs. First quartile (16.2-24.0gm/day vs. <16.2gm/day) | 1.01 | 0.77 | 1.33 |  |
|  | Third vs. First quartile (24.0-33.9gm/day vs. <16.2gm/day) | 0.95 | 0.69 | 1.32 |  |
|  | Highest vs. First quartile (>33.9gm/day vs. <16.2gm/day) | 0.99 | 0.65 | 1.5 |  |
| Daily sugar intake | |  |  |  | 0.31 |
|  | Second vs. First quartile (72.3-109.0gm/day vs. <72.3gm/day) | 1.02 | 0.74 | 1.4 |  |
|  | Third vs. First quartile (109.0-156.9gm/day vs. <72.3gm/day) | 1.24 | 0.83 | 1.86 |  |
|  | Highest vs. First quartile (>156.9gm/day vs. <72.3gm/day) | 1.62 | 1 | 2.63 |  |
| Daily caffeine intake | |  |  |  | 0.88 |
|  | Second vs. First quartile (26.5-93.0mg/day vs. <26.5mg/day) | 0.92 | 0.7 | 1.2 |  |
|  | Third vs. First quartile (93.0-205.5mg/day vs. <26.5mg/day) | 0.87 | 0.66 | 1.15 |  |
|  | Highest vs. First quartile (>205.5mg/day vs. <26.5mg/day) | 0.99 | 0.74 | 1.32 |  |
| Daily fiber intake | |  |  |  | 0.006 |
|  | Second vs. First quartile (10.1-14.7gm/day vs. <10.1gm/day) | 0.77 | 0.62 | 0.96 |  |
|  | Third vs. First quartile (14.7-20.6gm/day vs. <10.1gm/day) | 0.72 | 0.55 | 0.94 |  |
|  | Highest vs. First quartile (>20.6gm/day vs. <10.1gm/day) | 0.52 | 0.38 | 0.72 |  |
| Daily liquid intake | |  |  |  | <0.0001 |
|  | Second vs. First quartile (2004.7-2691.9gm/day vs. <2004.7gm/day) | 0.87 | 0.69 | 1.1 |  |
|  | Third vs. First quartile (2691.9-3584.2gm/day vs. <2004.7gm/day) | 0.57 | 0.43 | 0.75 |  |
|  | Highest vs. First quartile (>3584.2gm/day vs. <2004.7gm/day) | 0.54 | 0.4 | 0.73 |  |

a.Recent MJ use was defined as the use of marijuana/hashish during the past 30 days. Past MJ use is defined as the use of marijuana/hashish more than 30 days ago.

b.Poverty Income Ratio: Ratio of income to poverty threshold.

c.Comorbid medical diagnoses are self-reported and include chronic disorders of the thyroid, lung, and liver, as well as heart failure, coronary heart disease, stroke, cancer, and hypertension.

d.Diabetes mellitus was retrieved as having any of these: being told by health profession to have diabetes; taking diabetic medication or insulin; hemoglobin A1C ≥ 6.5.

e.Depression was captured using the patient health questionnaire.

f.Constipating medications: Medications that increase the risk of constipation (see **Table S1**).

g.Recent alcohol use was defined as the use of alcohol within the past 30 days, while past/never alcohol use was defined as either having no history of alcohol intake or alcohol use more than 30 days ago. Cigarete, heroin and cocaine use were defined similar to alcohol use.

h.General health condition was measured by reports from subjects on how they feel about their health status.

i.Regular vigorous activity was defined as regular participation in activities that cause heavy sweating, large increase in breathing, or increased heart rate either at work or during leisure time.

j.Emotional disturbance was captured in the NHANES data as report of depression, anxiety or other emotional problems for more than 3 days.

All dietary factors were measured with a 24-hour dietary recall interview which consisted of detailed questions on over 60 food items/nutrients consumed during the preceeding 24-hour period. Two interviews were conducted 3-10 days apart, and the average was used as an estimate of daily nutrient consumption. Eight food items (protein, carbohydrate, kcal, fat, sugar, caffeine, fiber, liquid) related to bowel function were used in this study.

**Table S4: Crude and adjusted models of the odds of constipation with marijuana use, NHANES 2005-2010, using BSFS as a measure of constipation.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Effect of recent marijuana use (MJ)** a. **compared to past/never users on constipation** b. | | **Odds Ratio** | **Lower confidence limit** | **Upper confidence limit** | **p-value** |
| Crude (MJ alone) | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.69 | 0.51 | 0.94 | 0.02 |
|  | Recent users vs. Never users | 0.62 | 0.45 | 0.84 | 0.02 |
| Adjusted (MJ + age) | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.64 | 0.47 | 0.87 | 0.005 |
|  | Recent users vs. Never users | 0.71 | 0.52 | 0.97 | 0.03 |
| Adjusted (MJ + demographics c.) | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.67 | 0.49 | 0.91 | 0.01 |
|  | Recent users vs. Never users | 0.70 | 0.50 | 0.96 | 0.03 |
| Adjusted (MJ + demographics + comorbidities d.) | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.72 | 0.52 | 1.00 | 0.05 |
|  | Recent users vs. Never users | 0.73 | 0.53 | 1.00 | 0.05 |
| Adjusted (MJ + demographics + comorbidities + diet e.) | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.74 | 0.53 | 1.03 | 0.07 |
|  | Recent users vs. Never users | 0.73 | 0.53 | 1.02 | 0.06 |

a.Recent MJ use was defined as the use of marijuana/hashish during the past 30 days.

b.Constipation defined by stool consistency (Bristol Types 1 and 2 as predominant stool forms) and/or frequency (<3 bowel movements/week).

c.Demographics includes: sex, ethnicity, education, body mass index, and socioeconomic status

d.Comorbidities include chronic disorders of the thyroid, lung, and liver, as well as heart failure, coronary heart disease, stroke, cancer, and hypertension. This model also includes depression, diabetes mellitus, constipating medications, substance use (alcohol, tobacco, heroin, cocaine), general health condition, level of physical activity and emotional disturbance.

e.Diet includes: fat, kilocalories, fibers, liquid, caffeine, sugar, carbohydrates, and proteins.

**Table S5: Crude and adjusted models of the odds of constipation with marijuana use, NHANES 2005-2010, using weekly stool frequency as a measure of constipation.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Effect of recent marijuana use (MJ)** a. **compared to past/never users on constipation** b. | | **Odds Ratio** | **Lower confidence limit** | **Upper confidence limit** | **p-value** |
| Crude (MJ alone) | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.87 | 0.61 | 1.22 | 0.40 |
|  | Recent users vs. Never users | 0.85 | 0.57 | 1.28 | 0.40 |
| Adjusted (MJ + age) | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.78 | 0.55 | 1.10 | 0.16 |
|  | Recent users vs. Never users | 0.79 | 0.56 | 1.12 | 0.18 |
| Adjusted (MJ + demographics c.) | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.71 | 0.48 | 1.04 | 0.07 |
|  | Recent users vs. Never users | 0.68 | 0.46 | 1.00 | 0.05 |
| Adjusted (MJ + demographics + comorbidities d.) | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.66 | 0.45 | 0.98 | 0.04 |
|  | Recent users vs. Never users | 0.65 | 0.45 | 0.96 | 0.03 |
| Adjusted (MJ + demographics + comorbidities + diet e.) | |  |  |  |  |
|  | Recent users vs. Past/Never users | 0.73 | 0.50 | 1.06 | 0.10 |
|  | Recent users vs. Never users | 0.71 | 0.49 | 1.03 | 0.07 |

a.Recent MJ use was defined as the use of marijuana/hashish during the past 30 day.

b.Constipation defined by stool consistency (Bristol Types 1 and 2 as predominant stool forms) and/or frequency (<3 bowel movements/week).

c.Demographics includes: sex, ethnicity, education, body mass index, and socioeconomic status

d.Comorbidities include chronic disorders of the thyroid, lung, and liver, as well as heart failure, coronary heart disease, stroke, cancer, and hypertension. This model also includes depression, diabetes mellitus, constipating medications, substance use (alcohol, tobacco, heroin, cocaine), general health condition, level of physical activity and emotional disturbance.

e.Diet includes: fat, kilocalories, fibers, liquid, caffeine, sugar, carbohydrates, and proteins.

**Table S6: Frequency distribution of frequency of marijuana use (number of days) with bowel function among individuals using marijuana within the past 30 days, NHANES 2005-2010**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Number of days of marijuana use within the past 30 days** | | |  |
|  |  | **1-3 days (438)** | **4-19 days (368)** | **20-30 days (374)** | **p-value** |
| Bristol Stool Form Scale, % | |  |  |  | 0.14 |
|  | Constipation | 23 (4.8%) | 25 (5.3%) | 22 (5.6%) |  |
|  | Diarrhea | 25 (6.1%) | 19 (4.2%) | 33 (9.4%) |  |
|  | Normal | 389 (89.2%) | 324 (90.5%) | 317 (85.1%) |  |
| Bowel Movement per Week, % | |  |  |  | 0.03 |
|  | Constipation | 21 (4.6%) | 13 (3.4%) | 8 (1.4%) |  |
|  | Diarrhea | 2 (0.56%) | 11 (1.94%) | 5 (0.69%) |  |
|  | Normal | 412 (94.8%) | 343 (94.7%) | 359 (97.9%) |  |
| Both (Bristol & Bowel movement), % | |  |  |  | 0.17 |
|  | Constipation | 40 (8.3%) | 34 (7.4%) | 28 (6.5%) |  |
|  | Diarrhea | 25 (6.1%) | 25 (4.9%) | 35 (9.7%) |  |
|  | Normal | 370 (85.6%) | 309 (87.7%) | 308 (83.8%) |  |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |

Footnote: Constipation defined by stool consistency (Bristol Types 1 and 2 as predominant stool forms) and/or frequency (<3 bowel movements/week). Diarrhea defined by stool consistency (Bristol Types 6 and 7 as predominant stool forms) and/or frequency (>21 bowel movements/week).