1. Medical condition proposed: Please be specific.

gastric ulcer

2. Provide justification for why this medical condition should be included as a qualifying debilitating medical condition for the use of medical marihuana.

Other state medical marijuana programs have inflammatory bowel disease as a qualifying condition, including Maine, New Jersey, New York, Ohio and Pennsylvania. https://medicalmarijuana.procon.org/view.resource.php?resourceID=000881

Crohn's Disease is an inflammatory bowel disease which is already a qualifying condition under the MMMA. Crohn's Disease shares many similar inflammatory symptoms of Ulcerative colitis and IBS. These and other digestive tract diseases are frequently mis-diagnosed and misunderstood, sometimes producing mild to moderate nausea, but not "severe nausea" required to qualify under the MMMA.

In a study of 1,655 medical marijuana patients in California, researchers found 13% were using medical marijuana to treat symptoms of gastrointestinal disorders.

> Gastrointestinal disorders
> Nausea and vomiting 7.4%
> Anorexia 4.6%
> Abdominal pain 2.9%
> Gastritis and GERD 2.5%
> Irritable bowel syndrome 1.1%
> Any of these gastrointestinal disorder ICDs 13.3%

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3673028/

In a study of over 2000 medical marijuana patients in the UK, researchers found 3.92% of patients were treating their Gastrointestinal symptoms.

Gastrointestinal 84 patients.

https://www.ncbi.nlm.nih.gov/pubmed/15857325

The US Department Of Health And Human Services has determined through thorough medical research and analysis that the cannabinoids including THC and CBD specifically from the marijuana plant can be used safely in the treatment and prophylaxis of wide variety of oxidation associated diseases, such as ischemic, age-related, inflammatory and autoimmune diseases.

> Oxidative associated diseases include, without limitation, free radical associated diseases, such as ischemia, ischemic reperfusion injury, inflammatory diseases, systemic lupus erythematosis, myocardial ischemia or infarction, cerebrovascular accidents (such as a thromboembolic or hemorrhagic stroke) that can lead to ischemia or an infarct in the brain, operative ischemia, traumatic hemorrhage (for example a hypovolemic stroke that can lead to CNS hypoxia or anoxia), spinal cord trauma, Down's syndrome, *Crohn's disease*, autoimmune diseases (e.g. rheumatoid arthritis or diabetes), cataract formation, uveitis, emphysema, gastric ulcers, oxygen toxicity, neoplasia, undesired cellular apoptosis, radiation sickness, and others.

http://www.google.com/patents/US6630507

The Institute of Medicine in a 1999 report, the same report that the people of Michigan cited when creating the MMMA and declaring marijuana to be a medicine, stated that cannabinoids from the marijuana plant could be useful for patients who have nutrient malabsorption in the intestine.

https://www.nap.edu/catalog/6376/marijuana-and-medicine-assessing-the-science-base

> *The many reasons for decreased food intake among AIDS patients include mouth, throat, or esophageal infections or ulcers (oropharyngeal and esophageal pathology); adverse effects of medications; diarrhea; enteric infection; malabsorption; serious systemic infection; focal or diffuse neurological disease; HIV enteropathy; depression; fatigue; and poverty. Nutrient malabsorption is often the result of microorganism overgrowth or infection in the intestine, especially in the later stages of AIDS.*
>
> *Anecdotes abound that smoked marijuana is useful for the treatment of HIV associated anorexia and weight loss. Some people report a preference for smoked marijuana over oral THC because it gives them the ability to titrate the effects, which depend on how much they inhale. In controlled laboratory studies of healthy adults, smoked marijuana was shown to increase body weight, appetite, and food intake. Unfortunately, there have been no controlled studies of the effect of smoked marijuana on appetite, weight gain, and body composition in AIDS patients. At the time of this writing, Donald Abrams, of the University of California, San Francisco, was conducting the first clinical trial to test the safety of smoked marijuana in AIDS patients, and the results were not yet available.*

It seems cruel and unusual, arbitrary and capricious and against the Equal Protection Clause to allow medical marijuana use for patients who have digestive tract issues if they have AIDS or Crohn's, but deny other patients who have digestive tract diseases just because they do not have AIDS or Crohn's. People with IBD or Ulcerative Colitis are not able to use medical marijuana because the MMMA only specifies Crohn's disease as a qualifying condition. This petition would allow those patients who have a digestive tract disorder to use medical marijuana

if the panel and department approve of the condition, and a doctor recommends that medical marijuana may benefit the treatment of their disease.

Minnesota has completed a survey of 1500+ patients enrolled in the first year of its medical marijuana program. It details the benefits that patients with Crohn's Disease have when using medical marijuana. Adding other digestive tract disorders to the MMMA will help those patients who are currently not protected from the prohibition of marijuana and its schedule 1 placement in the controlled substances law of Michigan.

The Minnesota Department of Health report found:

> Number of liquid/soft stools per day decreased by ≥30% for 51.2% of patients with at least five liquid/soft stools per day at baseline. Among patients who achieved ≥30% reduction, 57% (29.3% of patients included in analysis at baseline) retained that level of improvement over the next four months.
>
> Severity of abdominal pain improved for 53.4% of patients with moderate or severe abdominal pain at baseline. Among patients who reported an improvement in abdominal pain, 36% (19.2% of patients included in analysis at baseline) retained that improvement over the next four Months.
>
> General well-being improved for 46.7% of patients who described their baseline well-being as "Very Poor" or "Terrible" at baseline. Among patients who reported an improvement in general well-being, 29% (13.3% of patients included in analysis at baseline) retained that improvement over the next four months.
>
> On the combined Crohn's activity measure (number of liquid/soft stools, abdominal pain, general well-being), 51.0% of Crohn's Disease patients achieved ≥30% improvement. Among patients who achieved ≥30% reduction, 42% (21.6% of patients included in analysis at baseline) retained that level of improvement over the next four months.
>
> An increase of at least 3% in body weight was reported by 20.6% of patients. Among the patients who achieved ≥3% increase in body weight, 57% (11.8% of patients included in analysis at baseline) retained that increase over the next four months.

http://www.health.state.mn.us/topics/cannabis/about/firstyearreport.html

A safety profile of Medical Marijuana can be found in the first year report of the Minnesota medical marijuana program. The Minnesota Department of Health surveyed 1500+ patients enrolled in the program.

> Adverse Side Effects: At this point, the safety profile of the medical cannabis products available through the Minnesota program seems quite

favorable. Approximately 20-25% of enrolled patients report negative physical or mental side effects of some kind, with the majority – around 60% - reporting only one and 90% reporting three or fewer. The vast majority of adverse side effects, around 90%, are mild to moderate in severity. An assessment of the 30 patients reporting severe side effects, meaning “interrupts usual daily activities,” found no apparent pattern of patient age, medical condition, or type of medical cannabis used. **The most common adverse side effects are dry mouth, drowsiness, and fatigue.** Fortunately, up to the present no serious adverse events (life threatening or requiring hospitalization) have been reported.

http://www.health.state.mn.us/topics/cannabis/about/firstyearreport.html

Medical Marijuana's mild to moderate side effects of dry mouth, drowsiness and fatigue are easily tolerated by the vast majority of patients. The side effects of popular prescription drugs for ulcerative colitis and other digestive tract diseases are more severe, toxic, and even deadly compared with non-toxic and safe medical marijuana.

https://www.drugs.com/lialda.html
https://www.drugs.com/prednisone.html
https://www.drugs.com/remicade.html

Lialda side effects

Get emergency medical help if you have signs of an allergic reaction to Lialda: hives; difficulty breathing; swelling of your face, lips, tongue, or throat.
Stop using Lialda and call your doctor at once if you have:

● severe stomach pain, cramping, bloody diarrhea;
● fever, headache, skin rash;
● bloody or tarry stools, coughing up blood or vomit that looks like coffee grounds;
● kidney problems - little or no urination, painful or difficult urination, swelling in your feet or ankles, feeling tired or short of breath; or
● liver problems - loss of appetite, upper stomach pain, tiredness, easy bruising or bleeding, dark urine, clay-colored stools, jaundice (yellowing of the skin or eyes).

Common Lialda side effects may include:

● nausea, stomach pain, diarrhea, constipation;
● runny or stuffy nose, sinus pain, sore throat;
● flu-like symptoms;
● headache, back pain;

- rash; or
- abnormal liver function tests.

Prednisone side effects

Get emergency medical help if you have any of these signs of an allergic reaction to prednisone: hives; difficult breathing; swelling of your face, lips, tongue, or throat.

Call your doctor at once if you have:

- blurred vision, eye pain, or seeing halos around lights;
- swelling, rapid weight gain, feeling short of breath;
- severe depression, feelings of extreme happiness or sadness, changes in personality or behavior, seizure (convulsions);
- bloody or tarry stools, coughing up blood;
- pancreatitis (severe pain in your upper stomach spreading to your back, nausea and vomiting, fast heart rate);
- low potassium (confusion, uneven heart rate, extreme thirst, increased urination, leg discomfort, muscle weakness or limp feeling); or
- dangerously high blood pressure (severe headache, blurred vision, buzzing in your ears, anxiety, confusion, chest pain, shortness of breath, uneven heartbeats, seizure).

Other common prednisone side effects may include:

- sleep problems (insomnia), mood changes;
- increased appetite, gradual weight gain;
- acne, increased sweating, dry skin, thinning skin, bruising or discoloration;
- slow wound healing;
- headache, dizziness, spinning sensation;
- nausea, stomach pain, bloating; or
- changes in the shape or location of body fat (especially in your arms, legs, face, neck, breasts, and waist).

Remicade side effects

Some side effects may occur during the injection. Tell your caregiver right away if you feel dizzy, nauseated, light-headed, itchy or tingly, swollen, short of breath, or have a headache, fever, chills, muscle or joint pain, pain or tightness in your throat, chest pain, or trouble swallowing during the injection. Infusion reactions may also occur within 1 or 2 hours after injection.

Get emergency medical help if you have signs of an allergic reaction to Remicade: hives; chest pain, difficult breathing; fever, chills, severe dizziness; swelling of your face, lips, tongue, or throat.

Serious and sometimes fatal infections may occur during treatment with Remicade. Call your doctor right away if you have signs of infection such as: fever, extreme tiredness, flu symptoms, cough, or skin symptoms (pain, warmth, or redness).

Call your doctor at once if you have:

- skin changes, new growths on the skin;
- pale skin, easy bruising or bleeding;
- delayed allergic reaction (up to 12 days after receiving infliximab) - fever, sore throat, trouble swallowing, headache, joint or muscle pain, skin rash, or swelling in your face or hands;
- liver problems - upper stomach pain, tiredness, loss of appetite, dark urine, clay-colored stools, jaundice (yellowing of the skin or eyes);
- lupus-like syndrome - joint pain or swelling, chest discomfort, feeling short of breath, skin rash on your cheeks or arms (worsens in sunlight);
- nerve problems - numbness or tingling, problems with vision, or weak feeling in your arms or legs;
- new or worsening psoriasis - skin redness or scaly patches, raised bumps filled with pus;
- signs of heart failure - shortness of breath with swelling of your ankles or feet, rapid weight gain;
- signs of lymphoma - fever, night sweats, weight loss, stomach pain or swelling, chest pain, cough, trouble breathing, swollen glands (in your neck, armpits, or groin); or
- signs of tuberculosis - fever, cough, night sweats, loss of appetite, weight loss, feeling constantly tired.

Common Remicade side effects may include:

- stuffy nose, sinus pain;
- sore throat, cough
- headache; or
- stomach pain.

The Mayoclinic website has assembled dosage information on Medical Marijuana.

http://www.mayoclinic.org/drugs-supplements/marijuana/dosing/hrb-20059701

Drugs and Supplements
Marijuana (Cannabis sativa)

Dosing

The below doses are based on scientific research, publications, traditional use, or expert opinion. Many herbs and supplements have not been thoroughly tested, and safety and effectiveness may not be proven. Brands may be made differently, with variable ingredients, even within the same brand. The below doses may not apply to all products. You should read product labels, and discuss doses with a qualified healthcare provider before starting therapy.

Adults (18 years and older)

To treat amyotrophic lateral sclerosis (nerve cell disease), 10 milligrams of THC has been taken by mouth daily for two weeks.

To prevent nausea and vomiting caused by chemotherapy, five milligrams per meter squared of dronabinol (Marinol®) has been taken by mouth 1-3 hours before chemotherapy, then every 2-4 hours after chemotherapy, for a total of 4-6 doses daily. A dose of two milligrams of nabilone has been taken by mouth the night before chemotherapy, 1-3 hours before and after chemotherapy. A dose of 2-3 milligrams of nabilone has been taken by mouth 2-4 times daily. A dose of three milligrams of nabilone has been taken by mouth three times daily as a one-time dose, a four-day duration, and the duration of two cycles of chemotherapy. Cannabinoids have been taken by mouth over a 24-hour period as follows: 1-8 milligrams of nabilone daily as 1-4 milligrams daily, one milligram 3-5 times daily, or two milligrams 2-4 times daily or 24-50 milligrams per meter squared of dronabinol daily as 10 milligrams per meter squared 4-5 times daily, 12 milligrams per meter squared twice daily, or 15 milligrams twice daily. A dose of one milligram of nabilone has been taken by mouth 8-12 hours before chemotherapy, followed by 0.5-2 milligrams of nabilone 2-3 times daily after chemotherapy, depending on body weight. A dose of 10 milligrams per meter squared of THC has been taken by mouth two hours before and four, eight, 16, and 24 hours after chemotherapy. Cannabinoids have been injected into the muscle over the course of 24 hours in the form of 0.5-1 milligrams of levonantradol three times daily.

To treat atopic dermatitis (itchy, scaly skin rashes), hemp seed oil has been taken by mouth for 20 weeks.

To increase appetite in people with cancer, 2.5 milligrams of THC has been taken by mouth with or without one milligram of CBD for six weeks.

To treat chronic pain, cannabinoids have been taken by mouth in the form of capsules or sprayed into the mouth as THC, benzopyranoperidine (BPP), cannabidiol (CBD), nabilone, dronabinol, or synthetic nitrogen THC analogs (NIB), with doses of 2.5-20 milligrams for an average of 25 days. Cannabis-based medicines have been used for 1-6

weeks. Ajulemic acid has been used for one week. Doses of nabilone of 0.25-2 milligrams have been used daily for 4-6 weeks. Doses of smoked cannabis of 1-9.4 percent have been used for six hours to 14 days. Cannabis has been smoked 3-4 times daily for five days. Doses of dronabinol of 10-20 milligrams have been used daily for six hours to six weeks. In people with cancer, 5-20 milligrams of delta-9-THC has been taken by mouth daily, as have the following doses: 2-8 milligrams of nabilone by mouth daily; 0.25-1 milligram of nabilone by mouth daily for four weeks; 1-2 milligrams of nabilone twice daily for a year; 1-2 milligrams of nabilone twice at an eight-hour interval; and 0.5 milligrams of nabilone twice daily for seven days, followed by two milligrams daily for three weeks. A dose of 0.5-1 milligrams of nabilone has been taken twice daily. A dose of 10 milligrams of THC has been taken by mouth, increasing to a maximum tolerated dose for six weeks. A mouth sprayhas been used in divided doses of 2.5-120 milligrams for two weeks. Doses of Sativex® have been sprayed into the mouth, up to 48 sprays daily, for 1-2 weeks, then 10-15 sprays daily, or 4-8 sprays, with eight being the maximum one-time dose or within a three-hour period.

To improve appetite in people with cystic fibrosis (mucus buildup in the organs), a dose of 2.5 milligrams of dronabinol has been taken by mouth, increasing to a maximum of 10 milligrams daily for 1-6 months.

To treat dementia, 2.5 milligrams of dronabinol has been taken by mouth twice daily for six weeks.

To treat eating disorders, 7.5-30 milligrams of THC has been taken by mouth daily for four weeks.

To treat epilepsy, 200-300 milligrams of CBD has been taken by mouth daily for up to 4.5 months.

To improve fatty acid status, hemp seed oil has been taken by mouth.

To treat movement problems caused by Huntington's disease, 1-2 milligrams of nabilone has been taken by mouth daily for five weeks. A dose of 10 milligrams per kilogram of CBD has been taken by mouth daily for six weeks.

To treat sleep disorders, 40-160 milligrams of CBD has been taken by mouth.

To treat multiple sclerosis symptoms, 2.5 milligrams of dronabinol (Marinol®) has been taken by mouth daily, increasing to a maximum of 10 milligrams daily for three weeks. A dose of 15-30 milligrams of cannabis extract capsules has been taken by mouth in five-milligram increments, based on tolerance, for 14 days. Cannabis extracts, including Cannador®, have been taken by mouth for 2-4 weeks. Cannabis plant extracts containing 2.5-120 milligrams of a THC-CBD combination have been taken by mouth

daily for 2-15 weeks. A mouth spray (Sativex®, containing 2.7 milligrams of THC and 2.5 milligrams of CBD) has been used at a dose of 2.5-120 milligrams in divided doses for up to eight weeks. Eight sprays within any three hours, up to 48 sprays in a 24-hour period, have been used. Sativex® has been sprayed into the mouth for 6-14 weeks.

As a nutritional supplement, 15-30 milliliters of hemp oil has been taken by mouth daily.

To treat schizophrenia, 40-1,280 milligrams of CBD has been taken by mouth daily for up to four weeks.

To treat Tourette's syndrome, gelatin capsules containing 2.5-10 milligrams of THC have been taken by mouth as a single dose. A dose of 2.5 milligrams of THC has been taken by mouth daily, increasing to 10 milligrams daily in 2.5-milligram intervals over a four-day time period for six weeks.

To treat rheumatoid arthritis, up to six sprays of Sativex® have been used once daily 30 minutes before bed for five weeks.

In the peer reviewed scientific research (24) “Impact of cannabis treatment on the quality of life, weight and clinical disease activity in inflammatory bowel disease patients: a pilot prospective study.” (doi: 10.1159/000332079) the conclusions speak for themselves.

> Three months' treatment with inhaled cannabis improves quality of life measurements, disease activity index, and causes weight gain and rise in BMI in long-standing IBD patients.

Marijuana improves bladder function and urine voiding according to anecdotal and historical sources.

There are anecdotal reports that some Cannabis preparations may be useful for bladder dysfunctions.

https://www.ncbi.nlm.nih.gov/pubmed/26197538

NIDA finds it difficult to put the words together, but finally admits there is no gateway theory of marijuana use.

These findings are consistent with the idea of marijuana as a "gateway drug." However, the majority of people who use marijuana do not go on to use other, "harder" substances.

https://www.drugabuse.gov/publications/research-reports/marijuana/marijuana-gateway-drug

NIDA also finds it very difficult to backtrack on the propaganda research they grant. When other researchers tried to duplicate the results of the first study on marijuana and IQ points, they were unable to find any IQ loss due to marijuana use. I hope that any knowledge you have on marijuana is up to date, and that you are paying attention when NIDA's biased research grants backfire on them, over and over again.

> In a recent study sponsored by NIDA and the National Institute of Mental Health, teens who used marijuana lost IQ points relative to their nonusing peers. However, the drug appeared not to be the culprit. The new findings contribute to an ongoing scientific exploration of the drug's impact on users' cognition.

https://www.drugabuse.gov/news-events/nida-notes/2016/08/study-questions-role-marijuana-in-teen-users-iq-decline

3. Provide a summary of the evidence that the use of medical marihuana will provide palliative or therapeutic benefit for this medical condition or is a treatment for this condition.

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4126607/
Prospective cohort survey study of marijuana use patterns in patients with IBD at an academic medical center.
A total of 292 patients completed the survey; 12.3% of patients were active marijuana users, 39.0% were past users, and 48.6% were never users. Among current and past users, 16.4% of patients used marijuana for disease symptoms, the majority of whom felt that marijuana was "very helpful" for relief of abdominal pain, nausea, and diarrhea.
In addition, the majority of patients who used marijuana for symptom relief were not also using narcotics, suggesting that marijuana may have a separate therapeutic benefit.
Half of never users expressed an interest in using marijuana for symptom control, when it is legally available. Marijuana may, therefore, be expected to become a common adjunct to patients' therapeutic regimens if current legislative trends continue.
Our findings suggest that patients with UC may also benefit from the use of medicinal marijuana although the 11 states that have legalized medical marijuana have only approved its use for only patients with CD. Lawmakers should consider adding this condition to the list of acceptable diseases that may be treated with medicinal marijuana.

2. https://www.ncbi.nlm.nih.gov/pubmed/26317379
Studies also show that cannabis significantly reduces chronic pain (see Lynch and Campbell 2011), *inflammatory bowel disease (Allegretti et al. 2013)*, post traumatic stress disorder (Greer, Grob, and Halberstadt 2014), and seizure disorders (Lorenz 2004).

3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1262744/

Up to 35 other conditions/symptoms were listed, most commonly post traumatic stress disorder (PTSD) (5%) and *irritable bowel syndrome (4%).*
When asked to rate the overall effects of cannabis on a Likert scale ranging from "I feel a lot worse" to "gives me great relief", cannabis was perceived to provide "great relief" (86%) or a little relief (14%). No one believed it had been detrimental to their condition or symptoms.

Almost two thirds (62%) of respondents claimed that they decreased or discontinued their use of other medicines when they started using cannabis medicinally. This was more common in males (65% vs. 58% of females) and older participants (aged 50 years +) (70% vs. 59% among younger participants). For some people this was a substantial change, representing a shift away from chronic, high-dose medication use.

Perhaps not surprisingly, cannabis was typically perceived as superior to other medications in terms of undesirable effects, and the extent of relief provided. Thus, cannabis was rated to produce equivalent (8%) or worse side effects (3%) by a minority of therapeutic users. It was considered to work "a bit" or "much better" than other medicines, or to be the only source of relief, by more than three quarters (82%).

4. 10.1080/02791072.2013.805976
The survey was completed by 953 participants, of whom 614 (64%) were male and 339 (36%) were female. The mean age was 40.7 years old (range 14–76).
The majority of subjects in our study were current users who had a health professional involved in the management of their illness, and were using CBMs for at least several years
13 patients reported using medical marijuana for Irritable bowel syndrome.
17 patients reported using medical marijuana for Crohn's disease or ulcerative colitis.

5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4636852/
CD is an inflammatory bowel disease (IBD) that has no cure; treatment targets include reducing inflammation and secondary symptoms. Between 16 percent and 50 percent of patients use marijuana to relieve symptoms of IBD [34-36], and patients using marijuana for 6 months or longer are five times more likely to have had surgery for their IBD [34]; whether marijuana exacerbates disease progression or more severe disease results in self-medication is unclear. Only one placebo-controlled study of the effects of marijuana in patients with CD has been conducted [37]. This study found that there was no difference between placebo and smoked marijuana on CD remission (defined as a CD Activity Index (CDAI) of less than 100), and that marijuana was superior to placebo in promoting clinical response (a decrease in CDAI score greater than 100), reducing steroid use, and improving sleep and appetite [37]. Importantly, this study did not include objective measurement of inflammatory activity, and there was no significant difference in placebo and treatment groups 2 weeks after treatment cessation [37]. Until clinical trials with objective measurement of treatment effects over an extended period of time are conducted to examine the safety and efficacy of marijuana for the treatment of IBD, there is insufficient evidence for the use of marijuana for the treatment of IBD.

6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5193087/

A significant portion of IBD patients, particularly those with severe disease, use cannabis to relieve symptoms of pain, nausea, and appetite and to improve their overall mood. The significant morbidity seen in patients with severe disease emphasizes the limited number of conventional therapies for symptomatic control of IBD, a disorder still poorly understood. Patients with IBD have increased rates of psychiatric disease, pain, and malnutrition, and thus the use of adjunctive therapies or CAM to treat poorly controlled symptoms may improve patient morbidity. However, cannabis use, as discussed above, raises concerns of legality, side effects, and preparation, and its use in human trials has failed to provide objective evidence of therapeutic efficacy on endoscopy, biopsy, and inflammatory marker levels.58 Concerns regarding the possible profibrotic effects of cannabis need further study, as such possible side effects could have consequences in patients with stricturing disease.

The safety profile of cannabis is still not established despite acknowledged detrimental effects. However, current options for IBD management, including corticosteroids, immunomodulators, and biologic agents, carry risks for long-term side effects such as malignancy and infection.

7. https://www.ncbi.nlm.nih.gov/pubmed/21910367
Of the 30 patients 21 improved significantly after treatment with cannabis. The average Harvey Bradshaw index improved from 14 +/- 6.7 to 7 +/- 4.7 ($P < 0.001$). The need for other medication was significantly reduced. Fifteen of the patients had 19 surgeries during an average period of 9 years before cannabis use, but only 2 required surgery during an average period of 3 years of cannabis use.

This is the first report of cannabis use in Crohn's disease in humans. The results indicate that cannabis may have a positive effect on disease activity, as reflected by reduction in disease activity index and in the need for other drugs and surgery. Prospective placebo-controlled studies are warranted to fully evaluate the efficacy and side effects of cannabis in CD.

8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3947743/
In summary, the survey by Ravikoff Allegretti et al. strongly suggests that in patients with IBD, self-medication with Cannabis may improve abdominal pain and nausea and may be a promising option for alternative IBD treatment.1 However, all aforementioned studies have limitations by being uncontrolled or too small. As the authors point out, clinical trials are warranted to determine efficacy, safety and side effects of a Cannabis-based treatment and this survey study will help to identify the ideal patient selection. With the legalization of medical marijuana in several states of the US and the observation that almost half of non-Cannabis users in the present survey would be interested to participate in a trial, Cannabis has become a realistic and feasible therapeutic possibility for IBD. Presently though, Cannabis can not be recommended for the treatment of symptoms associated with IBD but from a medical perspective, clinical trials exploring such opportunities are wanted.

9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3423254/

Cannabinoids have been used to treat various disorders of the gastrointestinal tract, such as vomiting, anorexia, abdominal pain, gastroenteritis, diarrhoea, intestinal inflammation and diabetic gastroparesis (Coutts and Izzo, 2004,Duncan *et al*., 2005; Sanger, 2007; Izzo and Camilleri, 2008). Many of these digestive disorders are associated with acute or chronic inflammatory processes, and with alterations in intestinal permeability. Our data show that cannabinoids have the ability to both positively and negatively modulate permeability through the CB1 receptor. Specifically, endocannabinoids seem to be involved in the increase in permeability associated with the development of inflammation, while phytocannabinoids can inhibit or restore increased permeability after cytokine application.

10. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2697772/
In dogs, Δ9-THC dose-dependently inhibited TLESRs and reduced acid reflux rate. SR141716A significantly reversed the effects of Δ9-THC on TLESRs. **Similarly, in healthy volunteers, Δ9-THC significantly reduced the number of TLESRs and caused a non-significant reduction of acid reflux episodes in the first postprandial hour.** In addition, lower oesophageal sphincter pressure and swallowing were significantly reduced by Δ9-THC.

11. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1574910/
Early studies showed that delta9-THC slowed the rate of gastric emptying and small intestinal transit in mice and in rats (Shook & Burks, 1989). The ability of cannabinoids to decrease motor activity in the stomach (Krowicki *et al*., 1999) and decrease gastric emptying (Izzo *et al*., 1999a) were confirmed.

Similar findings have also been reported in healthy volunteers given delta9-THC, confirming that the drug delays gastric emptying of a radiolabeled solid food (McCallum *et al*., 1999).
Delta9-THC also decreased intragastric pressure in rats (Krowicki *et al*., 1999) and, by using a miniaturized rigid cylinder barostat, it was shown that this resulted in an increase in intragastric volume (Ball *et al*., 2001).

An early study showed that delta9-THC (5–10 mg kg) reduces diarrhea associated with naloxone-precipitated withdrawal from morphine in rats (Hine *et al*., 1975).

The beneficial effects of CB1R activation in animal models include reduction of transient lower esophageal sphincter relaxations, increased compliance of the proximal stomach, reduced acid secretion, reduction of GI transit, reduced intestinal fluid secretion in response to secretogogues and reduced large intestinal propulsive activity are all aspects that could be beneficial in functional bowel disorders such as IBS.

12. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4445116/
First line medical treatment (nitrites) and second line surgical treatment and pneumatic dilatation failed in preventing long time symptoms return; **cannabis consumption was described by the patient as facilitating food and weight intake.**

13. http://www.health.state.mn.us/topics/cannabis/about/firstyearreport.html
Number of liquid/soft stools per day decreased by =30% for 51.2% of patients with at least five liquid/soft stools per day at baseline. Among patients who achieved =30% reduction, 57% (29.3% of patients included in analysis at baseline) retained that level of improvement over the next four months.

On the combined Crohn's activity measure (number of liquid/soft stools, abdominal pain, general well-being), 51.0% of Crohn's Disease patients achieved =30% improvement. Among patients who achieved =30% reduction, 42% (21.6% of patients included in analysis at baseline) retained that level of improvement over the next four months.

An increase of at least 3% in body weight was reported by 20.6% of patients. Among the patients who achieved =3% increase in body weight, 57% (11.8% of patients included in analysis
at baseline) retained that increase over the next four months.

14. https://www.ncbi.nlm.nih.gov/pubmed/24969296
In an observational study in 30 patients with Crohn's disease (CD), we found that medical cannabis was associated with improvement in disease activity and reduction in the use of other medications. In a more recent placebo-controlled study in 21 chronic CD patients, we showed a decrease in the CD activity index >100 in 10 of 11 subjects on cannabis compared to 4 of 10 on placebo. Complete remission was achieved in 5 of 11 subjects in the cannabis group and 1 of 10 in the placebo group.

15. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1575197/
Botanical preparations of *Cannabis sativa* (Indian hemp) have been widely used in the past to treat a variety of disorders including those affecting the digestive tract.
The potential therapeutic value of such findings seems to be relevant. Activation of CB2 receptors represents a novel mechanism for the re-establishment of normal gastrointestinal transit after an inflammatory stimulus.

16. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4630406/

Cannabis sativa (Cannabaceae) has been long employed for the treatment of different diseases, especially for chronic pain and different neurological conditions [81, 82]. Moreover, this botanical drug has treated different gastrointestinal conditions including anorexia, emesis, abdominal pain, diarrhea, and diabetic gastroparesis [83]. It has been reported to contain over 60 different cannabinoid compounds, which are responsible for the biological activities reported for *Cannabis sativa* [84]. In addition, experimental evidence suggests that the endogenous cannabinoid system is involved in most of the major immune events, including those located in the gastrointestinal tract [85, 86]. For this reason, it was proposed that the activation of this system by cannabinoids might have a therapeutic role in human IBD [87]. However, and

although its use is common in IBD patients, there are few controlled studies that evaluate the exact role of cannabis in IBD [22, 23, 88] (Table 1).

The mechanisms involved in the intestinal anti-inflammatory effects of cannabis can be related to the capacity of cannabinoids to downregulate the production and release of different proinflammatory mediators including TNFα, IL-1β, and nitric oxide, thus restoring the altered immune response that occurs in IBD [89]. Most probably, these effects would be related to cannabinoid receptors type 1 (CB1) activation that mediates essential protective signals and counteracts proinflammatory pathways, since it has been reported that the severity of two different experimental models of colitis, induced by the intrarectal infusion of 2,4-dinitrobenzene sulfonic acid (DNBS) or by oral administration of DSS, are higher in CB1-deficient mice (CB1(−/−)) than in wild-type [90]. Lack of CB1 receptors rendered mice more sensitive to inflammatory insults, indicating a protective role of the CB1 receptors during inflammation induction. Consistently, the administration of a specific CB1 antagonist to these wild-type mice before colitis induction resulted in a similar degree of intestinal damage to that seen in CB1(−/−) mice, whereas the administration of a cannabinoid receptor agonist protected from DNBS-induced colitis in mice [90]. Supporting these observations, both Δ-tetrahydrocannabinol (THC) and cannabidiol (CBD) (Figure 6), two of the main components of cannabis, were able to exert beneficial effects in the TNBS model of acute colitis in rats, with a similar efficacy to that shown by sulphasalazine, which was used as a positive control [91]. Particularly, treatment with THC and combined treatment with CBD was able to reduce macroscopic damage score. Both alone and in combination, THC and CBD reduced the MPO activity similarly to treatment with sulphasalazine [91].

17. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2275439/
Targeting the endocannabinoid system might thus offer novel therapeutic strategies in the treatment of gastric motility diseases and has potential for the treatment of diabetic obese patients with dyspepsia.

18. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1856409/
The inhibitory effects of cannabinoids on intestinal inflammation, as well as on intestinal motility and secretory diarrhoea, observed in preclinical studies, increase the potential for their use in the treatment of IBD. In fact, based on these data in animal studies, a clinical study with *Cannabis* in patients with relapse of crohnic intermittent Crohn's disease has been started at the University Hospital of Munich.41

19. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5053383/
The patient was prescribed 1 g per day of a cannabis strain containing 9% THC and 13% CBD to be administered by a vaporizer. At 60 days of follow-up, the patient’s pain was lowered to a weekly average of 3/10 on a numerical rating scale. The patient also indicated he did not see a need for pregabalin, and had begun the process of lowering his daily dose. **Surprisingly, the patient also reported far fewer symptoms of his irritable bowel syndrome, claiming near-remission.**

20. https://www.ncbi.nlm.nih.gov/pubmed/18924447
The plant Cannabis has been known for centuries to be beneficial in a variety of gastrointestinal diseases, including emesis, diarrhea, inflammatory bowel disease and intestinal pain.

21. https://www.ncbi.nlm.nih.gov/pubmed/22414698
The data of this study indicate that in addition to intraperitoneal application, intrarectal delivery of cannabinoids may represent a useful therapeutic administration route for the treatment of colonic inflammation.

22. https://www.ncbi.nlm.nih.gov/pubmed/23756391
Orally, but not systemically administered MFF dose-dependently reduced the severity of naproxen-induced gastric damage, and a CB1 antagonist reversed this effect. MFF prevented gastric distention-induced visceral pain via a CB2-dependent mechanism. **These results demonstrate that a simple extract of medicinal cannabis can significantly enhance resolution of inflammation and injury, as well as prevent injury, in the gastrointestinal tract.** Interestingly, different cannabinoid receptors were involved in some of the effects. MFF may serve as the basis for a simple preparation of cannabis that would produce beneficial effects in the GI tract with reduced systemic toxicity.

23. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2931570/

Sulphasalazine, THC and CBD proved beneficial in this model of colitis with the dose–response relationship for the phytocannabinoids showing a bell-shaped pattern on the majority of parameters (optimal THC and CBD dose, 10 mg·kg−1). THC was the most effective drug. The effects of these phytocannabinoids were additive, and CBD increased some effects of an ineffective THC dose to the level of an effective one. THC alone and in combination with CBD protected cholinergic nerves whereas sulphasalazine did not.

In this model of colitis, THC and CBD not only reduced inflammation but also lowered the occurrence of functional disturbances. Moreover the combination of CBD and THC could be beneficial therapeutically, via additive or potentiating effects.

24. https://www.ncbi.nlm.nih.gov/pubmed/22095142

Three months' treatment with inhaled cannabis improves quality of life measurements, disease activity index, and causes weight gain and rise in BMI in long-standing IBD patients.

25. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2832623/
The endocannabinoid system has important physiological functions not only in the central nervous system but also in peripheral tissues. The activation of central CB1 receptors, particularly in hypothalamic nuclei and in the limbic system, is involved in the regulation of feeding behavior, and especially in the control of the intake of palatable food. In the periphery,

cannabinoid receptors are present in adipocytes, skeletal muscle, gastrointestinal tract and liver, modulating energy metabolism.

26. https://www.ncbi.nlm.nih.gov/pubmed/23648372
Although the primary end point of the study (induction of remission) was not achieved, a short course (8 weeks) of THC-rich cannabis produced significant clinical, steroid-free benefits to 10 of 11 patients with active Crohn's disease, compared with placebo, without side effects.

27. https://www.ncbi.nlm.nih.gov/pubmed/19377043
In a study on 768 HIV positive patients, they reported that marijuana worked slightly better for diarrhea than imodium.
Comparing Paired Strategies' Effectiveness for Each Symptom and for Total Symptoms
Effectiveness Symptom Paired Strategy (n) Ratings, Mean (SD) t Test (df) p Value
Diarrhea
Over-the-counter 6.57 (3.30) −0.242 (22) .811 (OTC)-imodium
Marijuana 6.70 (3.48) (23)

28. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4076530/
In summary, in agreement with the ancient use of Cannabis in intestinal disturbances and one decade of animal research, Cannabis was shown in a clinical trial to reduce symptoms in patients with CD. This elegant translation should be followed by larger trials confirming these results and by trials establishing the involved mechanisms to open a promising direction for future treatment of IBD.

29. https://www.ncbi.nlm.nih.gov/pubmed/23769745
Δ(9)-THC given i.p. was 2-3 orders of magnitude more potent in reducing diclofenac-induced gastric ulcers than in producing locomotor immobility, antinociception, hypothermia, and catalepsy, while the potency of ratio of p.o. Δ(9)-THC between each behavior measure was 7-18. These data indicate that the phytocannabinoid Δ(9)-THC protects against diclofenac-induced gastric inflammatory tissue damage at doses insufficient to cause common cannabinoid side effects.

30. https://www.ncbi.nlm.nih.gov/pubmed/22815234
This minireview highlights the importance of cannabidiol (CBD) as a promising drug for the therapy of inflammatory bowel diseases (IBD). Actual pharmacological treatments for IBD should be enlarged toward the search for low-toxicity and low-cost drugs that may be given alone or in combination with the conventional anti-IBD drugs to increase their efficacy in the therapy of relapsing forms of colitis. In the past, Cannabis preparations have been considered new promising pharmacological tools in view of their anti-inflammatory role in IBD as well as other gut disturbances. However, their use in the clinical therapy has been strongly limited by their psychotropic effects. CBD is a very promising compound since it shares the typical cannabinoid beneficial effects on gut lacking any psychotropic effects. For years, its activity has been enigmatic for gastroenterologists and pharmacologists, but now it is evident that this

compound may interact at extra-cannabinoid system receptor sites, such as peroxisome proliferator-activated receptor-gamma. This strategic interaction makes CBD as a potential candidate for the development of a new class of anti-IBD drugs.

31. https://www.ncbi.nlm.nih.gov/pubmed/12517253
A pharmacological modulation of the endogenous cannabinoid system could provide new therapeutics for the treatment of a number of gastrointestinal diseases, including nausea and vomiting, gastric ulcers, irritable bowel syndrome, Crohn's disease, secretory diarrhoea, paralytic ileus and gastroesophageal reflux disease. Some cannabinoids are already in use clinically, for example, nabilone and delta(9)-tetrahydrocannabinol are used as antiemetics.

32. https://www.ncbi.nlm.nih.gov/pubmed/21795981
Cannabis use is common amongst patients with IBD for symptom relief, particularly amongst those with a history of abdominal surgery, chronic abdominal pain and/or a low quality of life index. The therapeutic benefits of cannabinoid derivatives in IBD may warrant further exploration.

33. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5388177/
Cannabinoids could be helpful for certain symptoms of IBD, but there is still a lack of clinical studies to prove efficacy, tolerability and safety of cannabinoid-based medication for IBD patients, leaving medical professionals without evidence and guidelines.

34. https://www.ncbi.nlm.nih.gov/pubmed/25269802
In vivo, CBG inhibited the growth of xenograft tumours as well as chemically induced colon carcinogenesis. CBG hampers colon cancer progression in vivo and selectively inhibits the growth of CRC cells, an effect shared by other TRPM8 antagonists. CBG should be considered translationally in CRC prevention and cure.

35. https://www.ncbi.nlm.nih.gov/pubmed/24373545
CBD BDS attenuates colon carcinogenesis and inhibits colorectal cancer cell proliferation via CB1 and CB2 receptor activation. The results may have some clinical relevance for the use of Cannabis-based medicines in cancer patients.

36. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3533417/
In conclusion, the present results demonstrate that behaviorally active doses of exogenous cannabinoids also produce profound diuretic effects in female and male rats. These results suggest that diuresis may occur separately, yet simultaneously, with other measures of cannabinoid activity in laboratory animals and, perhaps, in humans.

37. https://www.ncbi.nlm.nih.gov/pubmed/21290238
Systemic cannabinoids have effects on the lower urinary tract that may be able to become clinically useful; however, a much greater understanding of the mechanisms of cannabinoid

receptors in control of the human lower urinary tract is necessary to facilitate development of novel cannabinoid drugs for treatment of pelvic disorders.

38. https://www.ncbi.nlm.nih.gov/pubmed/26197538
The rank order of efficacy was CBG=THCV>CBD>CBDV. In depth studies on CBG showed that the effect of this phytocannabinoid on acetylcholine-induced contractions was not affected by CB1 or CB2 receptor antagonists. Additionally, CBG also reduced acetylcholine-induced contractions in the human bladder.

39.
https://www.omicsonline.org/Cannabinoids-and-the-Urinary-Bladder-2161-0932.1000163.php?aid=17343
To date, a small number of open-label and placebo-controlled studies have demonstrated that oral administration of cannabinoids may alleviate OAB (Overactive Bladder Syndrome) /DO symptoms as first line. Most of these studies have been carried out on patients with advanced multiple sclerosis using preparations containing Δ9 -THC and/or CBD. One such study using Sativex, showed a reduction in urgency, number of incontinence episodes, frequency and nocturia in patients with multiple sclerosis.

40. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3673028/

Nausea and vomiting 7.4%
Anorexia 4.6%
Abdominal pain 2.9%
Gastritis and GERD 2.5%
Irritable bowel syndrome 1.1%
Any of these gastrointestinal disorder ICDs 13.3%

41. https://www.ncbi.nlm.nih.gov/pubmed/15857325
84 patients reported using medical marijuana for Gastrointestinal symptoms.

4. Provide articles published in peer-reviewed scientific journals reporting the results of research on the effects of marihuana on the medical condition or treatment of the medical condition and supporting why the medical condition should be added to the list of debilitating medical conditions under the Medical Marihuana Act. Attach a copy of all articles that are discussed in this section. Please do not attach articles that are not discussed in this section.

See enclosed.