

**THE CORRELATION BETWEEN DISRUPTED GUT MICROBIOME TO MENTAL AND GASTROINTESTINAL DISORDERS
(HUBUNGAN ANTARA KETIDAKSEIMBANGNYA MIKROBIOTA USUS DENGAN GANGGUAN MENTAL SERTA PENCERNAAN)
STUDY OF DIFFERENCES BETWEEN GUT MICROBIOME UNDER VARIOUS CIRCUMSTANCES
STUDI MENGENAI PERBEDAAN MIKROBIOTA USUS DALAM BERBAGAI KONDISI**

Kristania Gunawan¹
[kristinatwins07@gmail.com¹](mailto:kristinatwins07@gmail.com)
Tjandrayani

Article Info

Article history:

Published July 30, 2024

Kata Kunci:

Mikrobioma Usus Terganggu, Gangguan Jiwa, Saluran Cerna, Kesehatan Usus, Poros Usus-Otak.

Keyword:

Disrupted gut microbiome, mental disorders, gastrointestinal, healthy gut, gut-brain axis.

ABSTRAK

Gangguan mikrobioma usus dan beberapa gangguan mental saling mempengaruhi satu sama lain. Selain itu, mikrobioma usus yang terganggu tidak akan mampu mempertahankan tubuh terhadap patogen secara efektif, sehingga menyebabkan masalah pencernaan karena ‘gut-brain axis’ yang memicu gangguan mental. Dalam studi ini, kami menganalisa and membandingkan beberapa pencarian mengenai hipotesis yang telah dibahas sebelumnya agar dapat mengembangkan sebuah pemahaman kohesif mengenai mikrobioma usus dalam berbagai kondisi dan pengertian dari dari usus sehat. Sebuah usus sehat terdiri akan sebuah komposisi seimbang antara berbagai macam bakteri yang masing-masing memiliki pekerjaan penting bagi kerjanya tubuh manusia. Mikrobioma usus juga sangat sensitive kepada perubahan dimana komposisinya mudah berubah.

ABSTRACK

Disrupted gut microbiome and several mental health disorders interplay with one another. Likewise, disrupted gut microbiome becomes ineffectual in defending the body against the invasion of pathogens, resulting in gastrointestinal problems, which, in accordance with the gut-brain axis, in return triggers mental disorders. In this study, we both analyse and compare various findings regarding the aforementioned hypothesis to create a cohesive understanding of the gut microbiome under various circumstances and elaborate on the definition of a ‘healthy’ gut. A healthy gut consist of a balanced composition of a large diversity of bacteria with each having an important role for the human body. The gut microbiome is also very sensitive to changes where its composition may easily change.

PENDAHULUAN

A healthy gut can be defined as having a gut microbiome with higher nutrient absorption rate. In order to maintain it, high quality and large variety of nutrients should be consumed; any drastic dietary changes may alter the microbiome.²The biodiversity of the gut microbiome changes naturally in every stage of life, with distinguishable patterns in each age group, depending on the factors for which it is exposed, such as mode of birth of infants, dietary changes from liquid to solid food in toddlers.. The gut microbiome is different for every person because of the differences in their microbiota's responsiveness towards diet, lifestyle, environment, mode of birth, drugs consumed, etc.

The gut microbiome, although most often interchangeable with the terms microbiota⁽¹⁾ and microflora⁽²⁾, has quite a different meaning. ³The microbiome refers to the overall coterie of mostly bacterias, with other minor microbes, such as fungi, viruses and archaea. The microbiome residing in a pouch of the large intestine(bowel), called cecum, may be the most influential bacteria coterie as it is the most densely inhibited inside the human body, ⁴with approximately 1,000 to 2,000 different variations of bacterias that have been classified taxonomically⁽³⁾. Besides, the gut microbiome undertakes possibly the most critical job, in which it plays a huge role in maintaining the human metabolism, immune functions, homeostasis and physiology. ⁵Therefore, any imbalances in the gut microbial composition, or referred to as dysbiosis, may lead to several complications such as intestinal permeability, type 2 diabetes, cancer, Irritable Bowel Syndrome, gut motility, including the development of a mental disorder. ⁵Furthermore, It was proven that IBS⁽⁴⁾ patients have a higher risk of depression and anxiety compared to healthy individuals.

In fact, based on the global survey conducted by Magnus Simrén, a Professor of Gastroenterology, consisting of a huge sample of 73,000 people originating from 33 different countries, they were able to prove approximately 40% of the world's population, with women around 12% higher than men, suffer from a functional gastrointestinal disorder, FGID. ⁷Moreover, a Stanford University research conducted in 2011 with the intention of validating a hypothesis, 'the state of the gut determines the amount of stress a person experiences'. Where Fifty-six to seventy day old rats suffering from prior gastrointestinal disorders and those without, were exposed to depression markers test. The result subsequently proves that the rats with gastrointestinal issues have a higher likelihood of feeling depressed and anxious than those without. Thenceforth arriving with the conclusion that gastrointestinal problems bring about some changes to the brain, causing it to be in some ways permanently depressed and anxious. The gut-brain axis is responsible for the aforementioned hypothesis.

The gut-brain axis refers to the various connections between the central nervous system (CNS) of the brain and the gut, or the gastrointestinal (GI) tract, involving neurology with the enteric nervous system (ENS), metabolism, hormones and immunity. ⁹Although the way the Central Nervous System works has yet to be completely established, ¹⁰the neurological and metabolic connections are the only connections which have the direct influence in stimulating the sensory⁽⁵⁾ neurons of the ENS so that signals could be sent to the brain should any changes be detected in the gut. ¹¹However, it is known that any disturbances to the gut-brain axis leads to not only mental disorders, but also the release of gastric juices, bile and mucus that could change the composition of gut microbiome.

Although the gut microbiome had been discovered since the late 1600s, it was only for the past decade that gut microbiome became the subject of various intensive researches. Nevertheless, the knowledge regarding the gut microbiome is still vague to most people, including scientists and researchers. The reason behind the lack of knowledge regarding the gut microbiome is due to the various experimenting methods to obtain samples, such as carrying out endoscopy(6) , biopsy(7), luminal brush(8), catheter aspiration(9), analysing the bacterial composition of faeces, along with several other procedures that is faulty for several reasons. Firstly, the procured gut microbiome analysis from the aforementioned methods are shown to have different microbiota(3) composition from the one in the cecum, therefore not very accurate. Secondly, most of the methods involve an unavoidable risk of contamination or infections towards the existing gut microbiomes as bacterias from the other sites is brought to the intended sampling site by the surgical instrument. Thirdly, most of the procedures involve incongruous preparation through the use of harsh amount of laxatives, polyethylene glycol (PEG) or Sulphate to clean the intended sample site, resulting in noticeable changes in the gut microbiome as well as the disappearance of some bacterias, hence causing more harm than good. Fourthly, the above-stated procedures are highly inappropriate for healthy control(10), thus unable to provide any sort of comparison for the microbiota analysis.

With this in mind, we were able to gather scientific datas from various resources to prove and produce the cohesive understanding between the relationship of the state of the gut microbiome, gastrointestinal diseases and mental health under various circumstances, with a huge emphasis in differentiating the composition of the microbiota in distinct countries, LDC (less developed countries) and MDC (more developed countries), and their respective reported cases of mental and gastrointestinal diseases.

METODE PENELITIAN

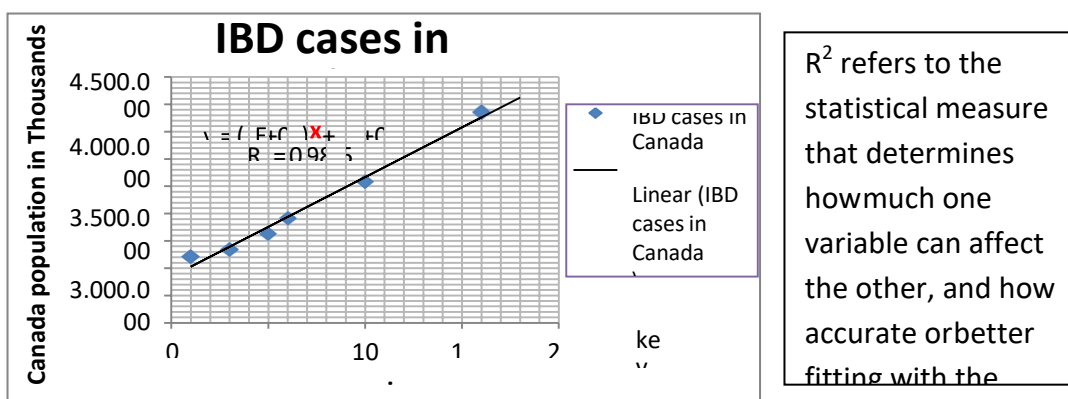
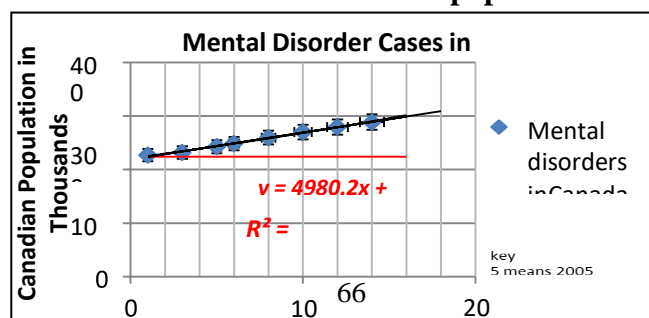


Figure 1 (a) The graph above shows the trend of IBD cases in Canada over the years, from 2002 to 2018 as the Canadian population increases.



(57%)

Number of mental disorders in female and male

- * Studies have proven that the lowest-income groups of Canadians are much more likely to develop from a mental disorder than those in the higher income groups.
- * The high mortality rate of Inuit (indigenous) Canadians living in Nunavut is due to increased suicides of those ages 15-24 caused by childhood abuse, family background of depressive disorders, major depressive disorders, drug abuse. (the suicidal rates of indigenous people is tentimes higher than the urban Canadians)
- *the social reasons for the suicides includes, colonization, sedentarization, relocations and forced to adopt the other cultures in residential schools.

Limitations:

- * Canada is one of the highest among other countries with incidence (meaning the development over a period of time) of IBS over the past decade.
- * Studies have proven that the children developing in rural areas are less likely to develop IBS rather than children in the urban areas.
- CL(1) - means that probability that a measurement of statistical parameter exists within the confidence interval
- * 100,000 patients and IRR (incident rate ratio(2)) counted using Poisson Regression

Table 2. Number of people suffering from gastrointestinal diseases in Canada

Number of people suffering from gastrointestinal diseases

The overall number of Canadians suffering from IBD In 2018	the number of Canadians suffering from IBD is 270,000 (0.728% of total population)	²⁶ Approximately 32 % have affective disorders, 27 % have gastroesophageal reflux disease and anxiety disorder while 71% often experience anxiety. 24 % have sleep disorders and 83% of the population have IBS that restricts their food choices
Canadian regions	Western/ Urban Canada	Inuit (indigenous) / Rural Canada
²⁵ IBD (Irritable Bowel Disease) From overall 45,567 IBD patients	33.16/100000 (95%) From 38,905 people	30.72/ 100000 (95%) From 6,662 people
²⁷ Birth cohort during the period of study (1-5 years of life)	No provided information	Lower risk of IBD during (IRR 0.075 – 0.78)

*limitation: Although the table above provides the data for both Inuit and Urban Canada, because there weren't any further information for Inuit Canada because the prior rural areas in Canada has converted to urban, hence we were only able to find about the IBD prevalence over the years for western Canada.

Table 3. The trend of IBD prevalence in Canada over the years.

Actual and Foreseen IBD cases in Canada Over the years

Years	2002	2004	2008	2010	2018	2030
<i>IBD cases</i>	1.215.952.257	1.336.250.748	1.630.210.498	1.912.263.584	2.584.096.971	3.858.787.202

Limitation: Provided that the real number of IBD in Canada is only present for the years below 2018, following it is only accurate prediction.

Table 4 The number of Canadian Population From year 2002 – 2022, (actual) and 2024-2030 (predicted)

³² Actual and Foreseen Canadian Population Over the years						
Years	2002	2004	2008	2010	2018	2030
Population size	31,178,263	31,815,494	33,337,638	34,147,564	37,074,562	40,833,727

Table 5. Percentage of numbers of microbiota in Canada

Percentage of number of microbiota	Firmicutes	Proteobacteria	Bacteroidetes	Actinobacteria	Clostridium
Canadian infants at 4 months old (24 infants)	43.8 %	7.4 %	0.0%	36.4%	0.1%
After 4 months of age	Decreases	Decreases	Decreases	Increases	Decreases

Limitations: The data doesn't classify the microbiota percentage into Inuit and Western Canada.

India

Table 6. Total number of people suffering mental disorders

India		
²⁹ Mental disorders	²⁸ 197.3 million (2017) / 1.339 billion	
	Female	Male
Stress	542.1 million / 1.39 billion (2017)	528.2 million / 1.39 billion (2017)
Depression	430.9 million / 1.39 billion (2017)	458.7 million / 1.39 billion (2017)
Anxiety	417 million / 1.39 billion (2017)	403.1 million / 1.39 billion (2017)

Table 7. Total number of adolescent suffering from functional gastrointestinal diseases

	Indian female adolescent	Indian male adolescent
Number of adolescent suffering from functional gastrointestinal diseases	54 female / 1115 children	58 male / 1115 children

³⁰This survey is conducted with 1115 students in the age of 10-17 years at four government schools of National Capital Territory (NCT) of Delhi. Based on the survey, around ten percent (112 students) suffered from gastrointestinal diseases from 1115 children in total.

Table 8. Comparison of microbiota composition in Northern and Southern India

³¹ Percentage of microbiota Phyla	Firmicutes	Proteobacteria	Bacteroidetes	Actinobacteria	Clostridium
Tribal adults in Northern India (millets-based diet)	85.9 %	7.1%	2.65%	1.2 %	32.7 %
Rural adults in Southern India, villagers, (rice-based diet)	63.5%	15.5%	0.45%	5.25%	4.8%

* following the 4 months of age, as the introduction of solid food begins, the infants around one years old, begin to have different genus/family/species of bacteria albeit from the same phylum, however, at this stage, their gut microbiome composition, especially later at the age of 2, begins to take after the gut microbiome of adults.

Table 9. Microbiota composition between Inuit and Western Canada

Inuit Canadians	Western Canadians
Prevotella	Bifidobacterium
Treponema	Ruminococcus
Succinivibrio	Faecalibacterium (firmicutes)
Cyanobacteria	Lactic Acid bacteria
<i>Prevotella / treponema</i> is present because of the inuit diet that is rich in natural fiber. Whereas the <i>succinivibrio bacteria</i> is rich among the Inuits because it is found in herbivorous animals ; the Cyanobacteria are coming from the waters, like the rivers, lakes and ocean.	The bacterias present in the urban population is generally due to the lifestyle, which is influenced by refined fats, high amount of sugars, drugs, extremity in hygiene and the relatively less healthy lifestyle in comparison to the Inuits.

KESIMPULAN

The gut microbiome is different for every person to a great extent, however there are similarities in composition and pattern in the population of a particular country. Based on our extensive research we were able to discover differences in gut microbiome between Canada (MDC) and India (LDC), thus able to prove the relationship between gastrointestinal and mental health with the gut microbiome.

In the less developed country, India, 1314.73% of the population (2017) suffers from mental disorders, predominated by stress, followed by depression, then anxiety. 14Mental disorders in India are mostly caused by bullying, childhood sexual abuse, violence, loneliness, marital status, occupation and education (especially during covid period). Nonetheless, we have also found striking dissimilarities between the microbiota composition between two regions of India, Southern and Northern, due to their major differences in diet and lifestyle. Healthy tribal Northern Indians (NI) consumed pork meat daily but did not drink any milk(due to religious belief), whereas the healthy rural Southern Indians (RS) consumed meat only weekly. 15Although NI has a higher amount of firmicutes bacteria, both groups have relatively high abundance of the bacteria because of the high carbohydrates consumption; 16NI also has a higher number of Clostridium which are bacterias mainly found in raw meat. 17However, NI has a significantly lower amount of actinobacteria than RS due to their diet that doesn't include milk nor milk products. 18Both NI and RS have a comparatively low percentage of bacteroidetes - bacterias obtained from high fiber intake of fruits and legumes. 19Firmicutes and bacteroidetes are the two largest phyla occupying the gut and they form a ratio of 12 - 620. If the ratio isn't maintained, the gut microbiome will be imbalanced. An increase in firmicutes and a decrease in bacteroidetes can cause obesity while a decrease in firmicutes and increases in bacteroidetes can cause type 2 diabetes and other diseases.

In comparison, in the more developed country, Canada, has one of the highest incidence of IBS over the past decade, 20in which around 14.28% of the population (1 in

5) in 2017 as well as in any other year have a prevalence of mental disorders, in which the majority of those with mental disorders comes from the lower income group. The Canadians can be classified into two groups, which are the Inuits, indigenous hunter-gatherer living in the northern regions, and the Western, whose majority occupies Southern Canada. Although the two groups have completely different lifestyles and environments, the differences in microbiota composition is very minor. ²²This is because of the Inuit's gradual transition from their traditional diets, which has been for a millenia, low in carbohydrate, high in animal fats and protein, into highly processed, high carbohydrates typical western diets, which subsequently cause changes in their microbiota composition. As a result, the number of gastrointestinal patients from both areas are similar, with western Canadians 3% higher than the Inuits; however, the Inuits have lower risk of developing IBD compared to the Western in the first 5 years of life.

Due to the presence of a research gap for which data regarding the composition of bacterias in Canadian adults is absent, the bacterial composition of infants had to be taken instead. The composition of healthy Canadian infants provided above shows that compared to the Indians, the Canadians at 4 months old have less number of firmicutes, bacteroidetes, and Clostridium, but higher numbers of proteobacteria (in the case of TI) and Actinobacteria. However, approaching the age of 2, where the microbial composition starts to resemble the pattern of the adults, the numbers of the all aforementioned bacterias, except Actinobacteria, decreases.

DAFTAR PUSTAKA

- 1Galland L. The gut microbiome and the brain. *J Med Food*. 2014 Dec;17(12):1261-72. doi: 10.1089/jmf.2014.7000. PMID: 25402818; PMCID: PMC4259177.
- 2Odamaki, T., Kato, K., Sugahara, H. et al. Age-related changes in gut microbiota composition from newborn to centenarian: a cross-sectional study. *BMC Microbiol* 16, 90 (2016). <https://doi.org/10.1186/s12866-016-0708-5>
- 3Patel, Venita. (2021). The gut microbiome. 10.1016/B978-0-12-821573-9.00015-1.
- 4Kovatcheva-Datchary, Petia & Tremaroli, Valentina & Bäckhed, Fredrik. (2013). The Gut Microbiota. 10.1007/978-3-642-30144-5_87.
- 5Canakis, Andrew; Haroon, Mustafa; Weber, H. Christian Irritable bowel syndrome and gut microbiota, *Current Opinion in Endocrinology & Diabetes and Obesity*: February 2020 - Volume 27 - Issue 1 - p 28-35 doi: 10.1097/MED.0000000000000523
- 6Simren, Magnus; Four of ten adults worldwide have functional gastrointestinal disorders: May 2020 - Four of ten adults worldwide have functional gastrointestinal disorders | University of Gothenburg (gu.se)
- 7Fredericks, R. Can Gastric Disorders Contribute to Anxiety and Depression? Retrieved from MentalHelp.net: An American Addiction Centers Resource.
- 8 Ways Gut Bacteria And Mental Health, Probiotics And Depression Are Linked. (July). Retrieved from Atlas Biomed Blog 2020.
- 9Zhu X, Han Y, Du J, Liu R, Jin K, Yi W. Microbiota-gut-brain axis and the central nervous system. *Oncotarget*. 2017 May 10;8(32):53829-53838. doi: 10.18632/oncotarget.17754. PMID: 28881854; PMCID: PMC5581153.
- 10Galland L. The gut microbiome and the brain. *J Med Food*. 2014 Dec;17(12):1261-72. doi: 10.1089/jmf.2014.7000. PMID: 25402818; PMCID: PMC4259177.

- 11Wettstadt, Sarah. #FEMSmicroBlog: Celebrating how your gut microbiome keeps you mentally healthy. 2021 June 27. <https://fems-microbiology.org/gut-microbiome-and-mental-health/>
- 12Qiang, T, Ge, J., Gang, W., Tianyu, L., Xiang, L., Bangmao, W., Hailong, C. 2020. Current Sampling Methods for Gut Microbiota: A Call for More Precise Devices. *Frontiers in Cellular and Infection Microbiology*.10. doi:10.3389/fcimb.2020.00151
- 13 Lavanya, L.; Selvamani, I.; Natarajan, V.; Raman, K..2020 Prevalence of depression, anxiety and stress symptoms and their association with quality of sleep and loneliness in the general population during the covid-19 pandemic in India. *International Journal of Research in Pharmaceutical Sciences*.
- 14India State-Level Disease Burden Initiative Mental Disorders Collaborators. The burden of mental disorders across the states of India: the Global Burden of Disease Study 1990-2017. *Lancet Psychiatry*. 2020 Feb;7(2):148- 161. doi: 10.1016/S2215-0366(19)30475-4. Epub 2019 Dec 23. PMID: 31879245; PMCID: PMC7029418.
- 15, 31Ramadass B, Rani BS, Pugazhendhi S, John KR, Ramakrishna BS. Faecal microbiota of healthy adults in south India: Comparison of a tribal & a rural population. *Indian J Med Res*. 2017 Feb;145(2):237-246. doi: 10.4103/ijmr.IJMR_639_14. PMID: 28639601; PMCID: PMC5501057.
- 162021, May 18. Prevent Illness From *C. perfringens*. Retrieved from CDC, Centers for Disease Control and Prevention.
- 17Ramadass, B., Rani, S., Srinivasan, P., John, Kr., Ramakrishna, B. 2017, Faecal microbiota of healthy adults in South India: Comparison of a tribal & a rural population. *Indian Journal of Medical Research*. 145(2):237-246 Doi: 10.4103/ijmr.IJMR_639_14
- 18Tomova, A., Bukovsky, I., Rembert, E., Yonas, W., Alwarith, J., Barnard, N., Kahleova, H. (2019) The Effects of Vegetarian and Vegan Diets on Gut Microbiota. *Frontiers in Nutrition*. Vol. 6, IS 2296-861X, doi: 10.3389/fnut.2019.00047
- 19Koliada A, Syzenko G, Moseiko V, Budovska L, Puchkov K, Perederiy V, Gavalko Y, Dorofeyev A, Romanenko M, Tkach S, Sineok L, Lushchak O, Vaiserman A. Association between body mass index and Firmicutes/Bacteroidetes ratio in an adult Ukrainian population. *BMC Microbiol*. 2017 May 22;17(1):120. doi: 10.1186/s12866-017-1027-1. PMID: 28532414; PMCID: PMC5440985.
- 20, 24Mental Illness and Addiction: Facts and Statistics. Retrieved from CAMH, The Centre for Addiction and Mental Health.
- 21Croissant, Morgane. (2021) 50% of Canadians Live South of This Line. News, Canada.
- 22Girard, C., Tromas, N., Amyot, M., Shapiro, J. (2017) Gut Microbiome of the Canadian Arctic Inuit. *American Society for Microbiology*. Vol 2, IS 1. doi: 10.1128/mSphere.00297-16
- 23Mental Illness in Canada – Infographic.(December 2020). Retrieved from Government of Canada
- 25Zimmerman, E. Inflammatory bowel disease rate higher among urban residents. (August 2017). FROM THE AMERICAN JOURNAL OF GASTROENTEROLOGY.
- 26Gastrointestinal society: 2016 Survey Results, Irritable Bowel Syndrome (IBS).

Retrieved from Canadian Society of Intestinal Research.

27Benchimol EI, Kaplan GG, Otley AR, Nguyen GC, Underwood FE, Guttman A, Jones JL, Potter BK, Catley CA, Nugent ZJ, Cui Y, Tanyingoh D, Mojaverian N, Bitton A, Carroll MW, deBruyn J, Dummer TJB, El-Matary W, Griffiths AM, Jacobson K, Kuenzig ME, Leddin D, Lix LM, Mack DR, Murthy SK, Sánchez JNP, Singh H, Targownik LE, Vutcovici M, Bernstein CN. Rural and Urban Residence During Early Life is Associated with Risk of Inflammatory Bowel Disease: A Population-Based Inception and Birth Cohort Study. *Am J Gastroenterol*. 2017 Sep;112(9):1412-1422. doi: 10.1038/ajg.2017.208. Epub 2017 Jul 25. Erratum in: *Am J Gastroenterol*. 2017 Sep;112(9):1485. PMID: 28741616; PMCID: PMC5596205.

28The burden of mental disorders across the states of India: the Global Burden of Disease Study 1990–2017. (December 2019). India State-Level Disease Burden Initiative Mental Disorders Collaborators. 7(2). [https://doi.org/10.1016/S2215-0366\(19\)30475-4](https://doi.org/10.1016/S2215-0366(19)30475-4)

29Kanwal, S. Share of mental health disorders among Indians in India in 2021, by gender. (June 2021).

Retrieved from Statista.

30Bhatia V, Deswal S, Seth S, Kapoor A, Sibal A, Gopalan S. Prevalence of functional gastrointestinal disorders among adolescents in Delhi based on Rome III criteria: A school-based survey. *Indian J Gastroenterol*. 2016 Jul;35(4):294-8. doi: 10.1007/s12664-016-0680-x. Epub 2016 Aug 24. PMID: 27554498.

31S Coward, F Clement, E I Benchimol, C N Bernstein, A Bitton, M W Carroll, G Hazlewood, S Jelinski, J Jones, E Kuenzig, D Leddin, K McBrien, S Murthy, G C Nguyen, A Otley, A Rezaie, J Pena-Sanchez, H Singh, L Targownik, G G Kaplan, A29 THE RISING PREVALENCE OF INFLAMMATORY BOWEL DISEASE IN

CANADA: ANALYZING THE PAST TO PREDICT THE FUTURE , *Journal of the Canadian Association of Gastroenterology*, Volume 1, Issue suppl_2, February 2018, Pages 47–

48, <https://doi.org/10.1093/jcag/gwy009.029>

32UN (World Population Prospects 2019).