

# **The Effect of Probiotics and Fecal Transplantations on Crohn's Disease Symptoms**

Kiran Bengard

The background of the slide is a light gray network graph. It consists of numerous nodes, represented by small circles, some of which are solid gray and others are hollow with a gray outline. These nodes are interconnected by a web of thin, light gray lines representing edges. The overall appearance is that of a complex, interconnected system or data structure.

# Introduction

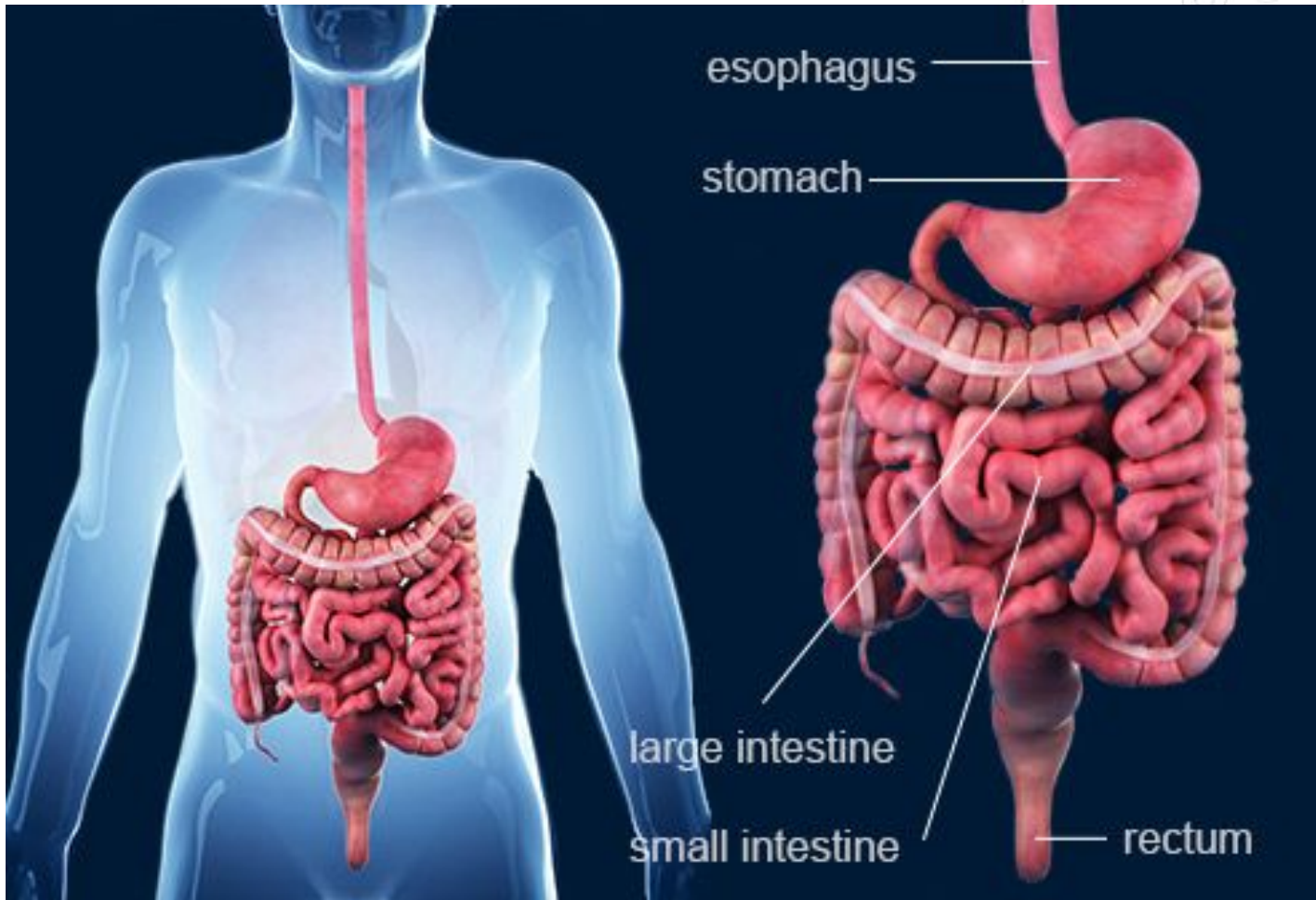


Figure 1. Diagram of parts of the body affected by Crohn's disease

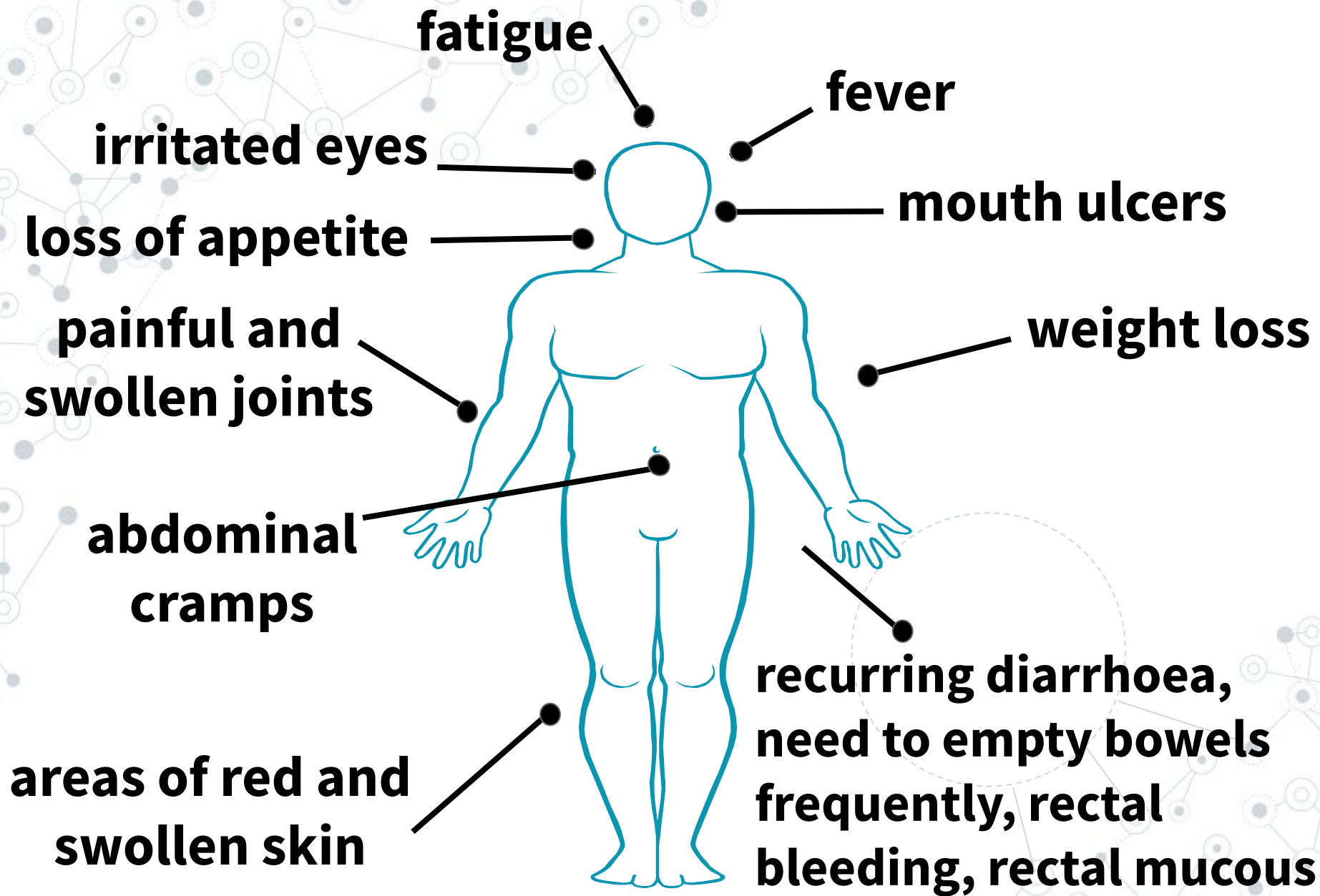


Figure 2. Diagram of the symptoms of Crohn's disease



**1,600,000**

People live with Crohn's disease worldwide



A decorative background consisting of a network of interconnected nodes and lines, resembling a molecular or biological structure, in shades of gray and blue.

**70,000** new cases

Of IBD per year in the US

**\$19,000** annual cost


Of medical care for Crohn's disease patients

**15 to 35** median age

For those diagnosed

# Treatments

A decorative network diagram in the top right corner, consisting of interconnected nodes and lines, rendered in a light blue and grey color scheme.

- ⊙ Nonsteroidal anti-inflammatory drugs
  - ⊙ Steroids
  - ⊙ Immunosuppressive drugs
  - ⊙ Antibiotics
  - ⊙ Surgery
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- A decorative network diagram in the bottom left corner, consisting of interconnected nodes and lines, rendered in a light blue and grey color scheme.

# Current Standard Approach: “Bottom-Up”

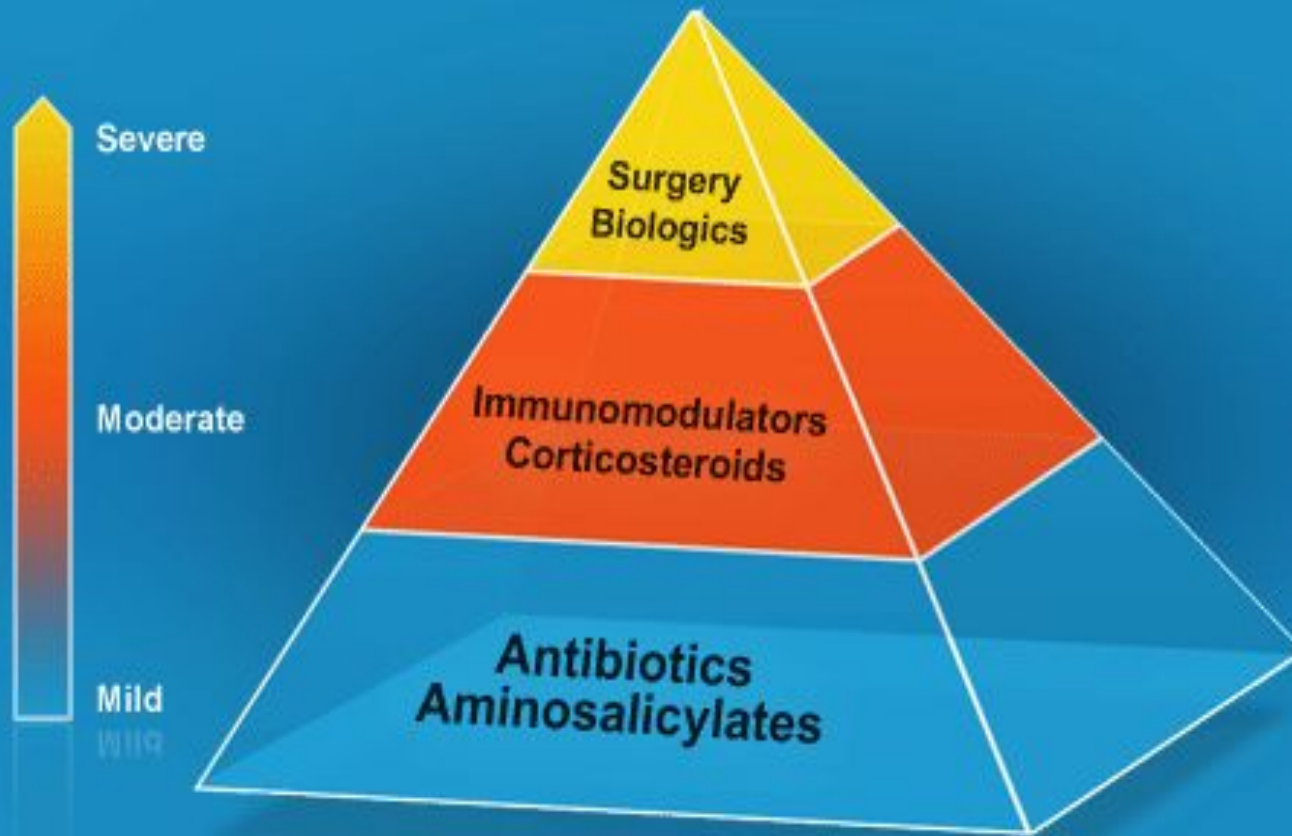


Figure 3. Diagram of the different treatments used for Crohn's disease depending on symptom severity



# Causes of Crohn's Disease




- ◎ Exact cause is unknown

Further developed by:

- ◎ Heredity
- ◎ Malfunctioning immune system

Associated with:

- ◎ Intestinal bacterial composition
  - ◎ Dysbiotic gut microbiota
  - ◎ Lower microbial diversity
- 

# Gut Microbiota

- ◎ Tens of trillion of microorganisms
- ◎ Over 1,000 species of bacteria
- ◎ Accounts for nearly 70% of all microbes



Figure 4. Diagram of the gut microbiota

# Probiotics

- ⦿ Live microorganisms
- ⦿ Replace bacteria
- ⦿ Balance good and bad bacteria
- ⦿ Most common type:  
*Lactobacillus*



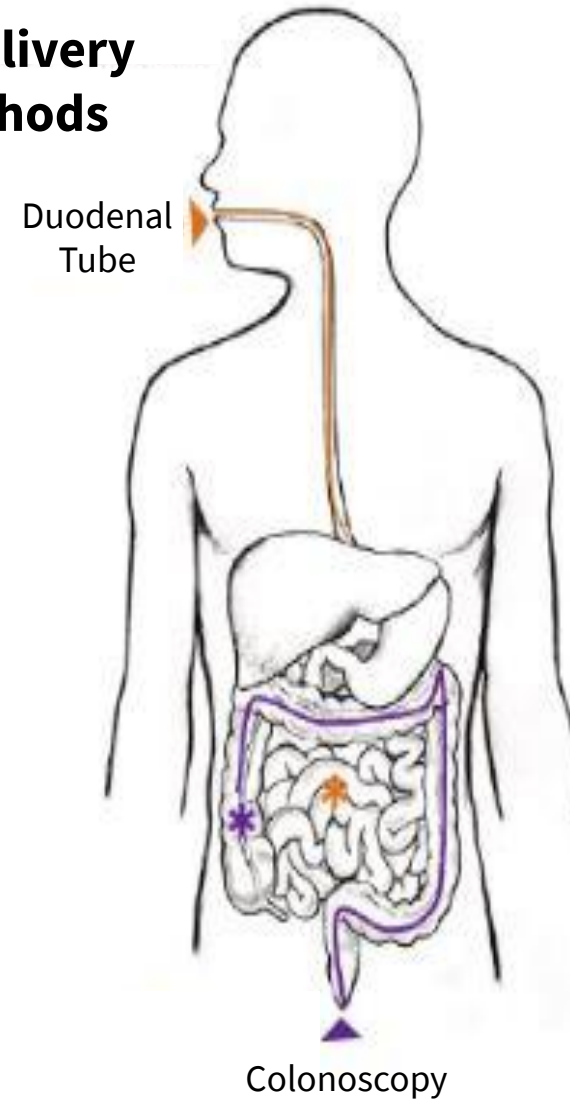
Figure 5. Pictures of examples of probiotics

# Fecal Transplantations

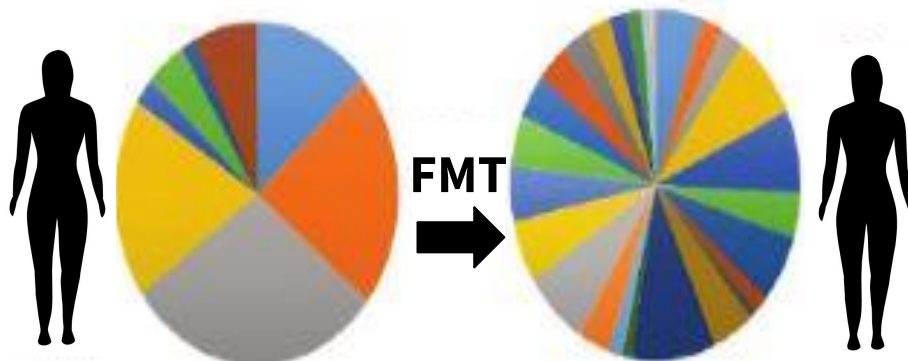
## a) Sample Preparation



## b) Delivery Methods



## c) Metagenomic Diversity Increases





*Do fecal transplantations have a greater effect on the symptoms of Crohn's disease than probiotics?*

# Hypotheses



## **Alternative**

Fecal transplants have a greater effect on the symptoms of Crohn's disease than probiotics

## **Null**

Fecal transplants do not have a greater effect on the symptoms of Crohn's disease than probiotics



The background of the slide is a complex network diagram. It consists of numerous nodes, represented by small circles, some of which are solid grey and others are hollow with a grey outline. These nodes are interconnected by a web of thin, light grey lines, some of which are solid and others are dashed, creating a dense, interconnected pattern that fills the entire frame.

# Methods

## Data Search

-Science Direct, PLOS, Pubmed, NCBI, Google Scholar, Research Gate, EbscoHost, JSTOR, etc.

## Paper Collection

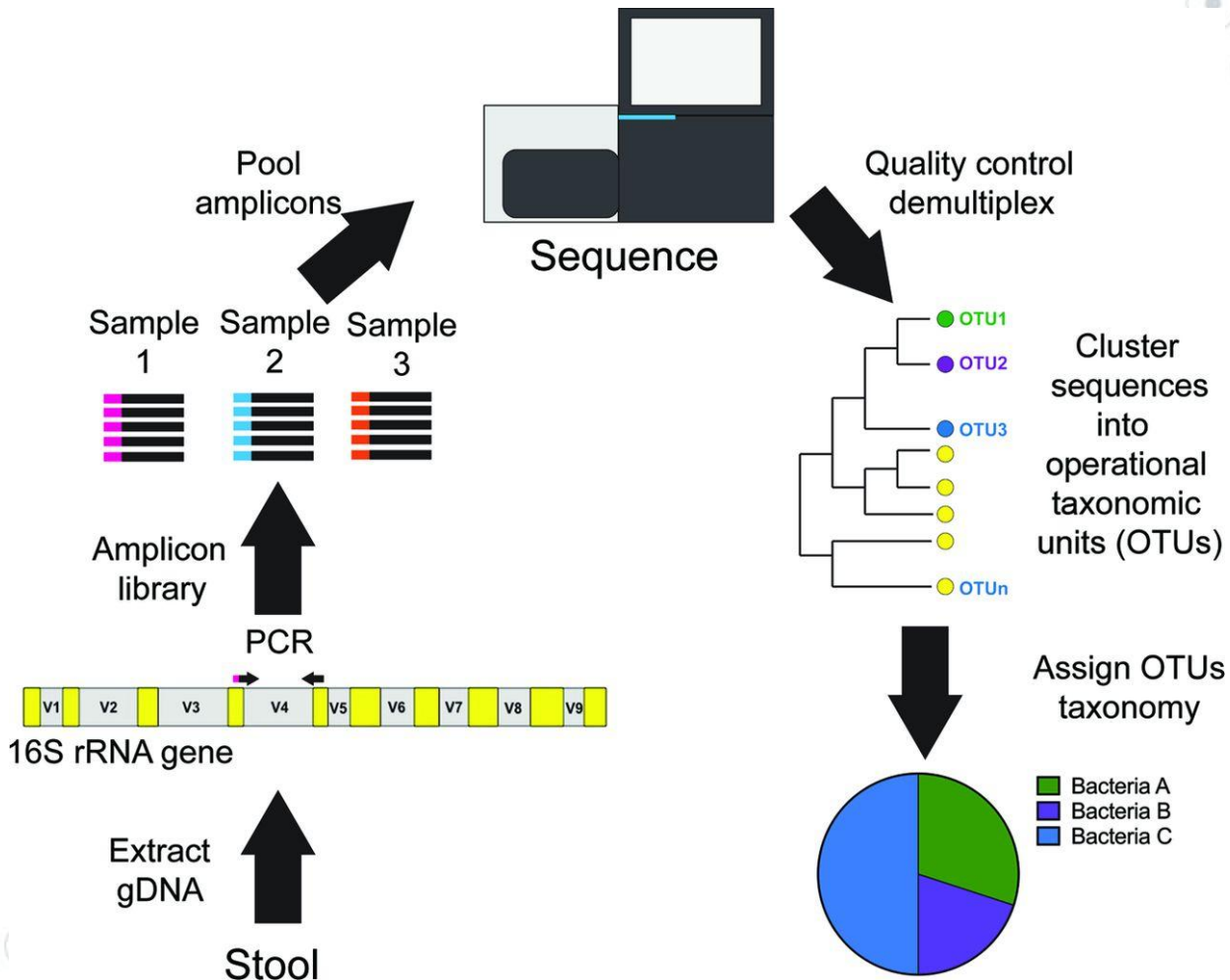
-Peer reviewed papers only

## Data Extraction

-Remission rates  
-Bacterial composition of gut microbiota




# 16s rRNA Gene Sequencing



# Remission

A decorative network diagram in the top right corner, consisting of various sized circles (nodes) connected by thin lines (edges). Some nodes are solid grey, while others are hollow with a grey outline. The connections form a complex, interconnected web.

- © Absence of symptoms
  - © 6 weeks after completion of treatment
- 
- A decorative network diagram in the bottom left corner, similar to the one in the top right, featuring a cluster of interconnected nodes and lines.

# Crohn's Disease Activity Index

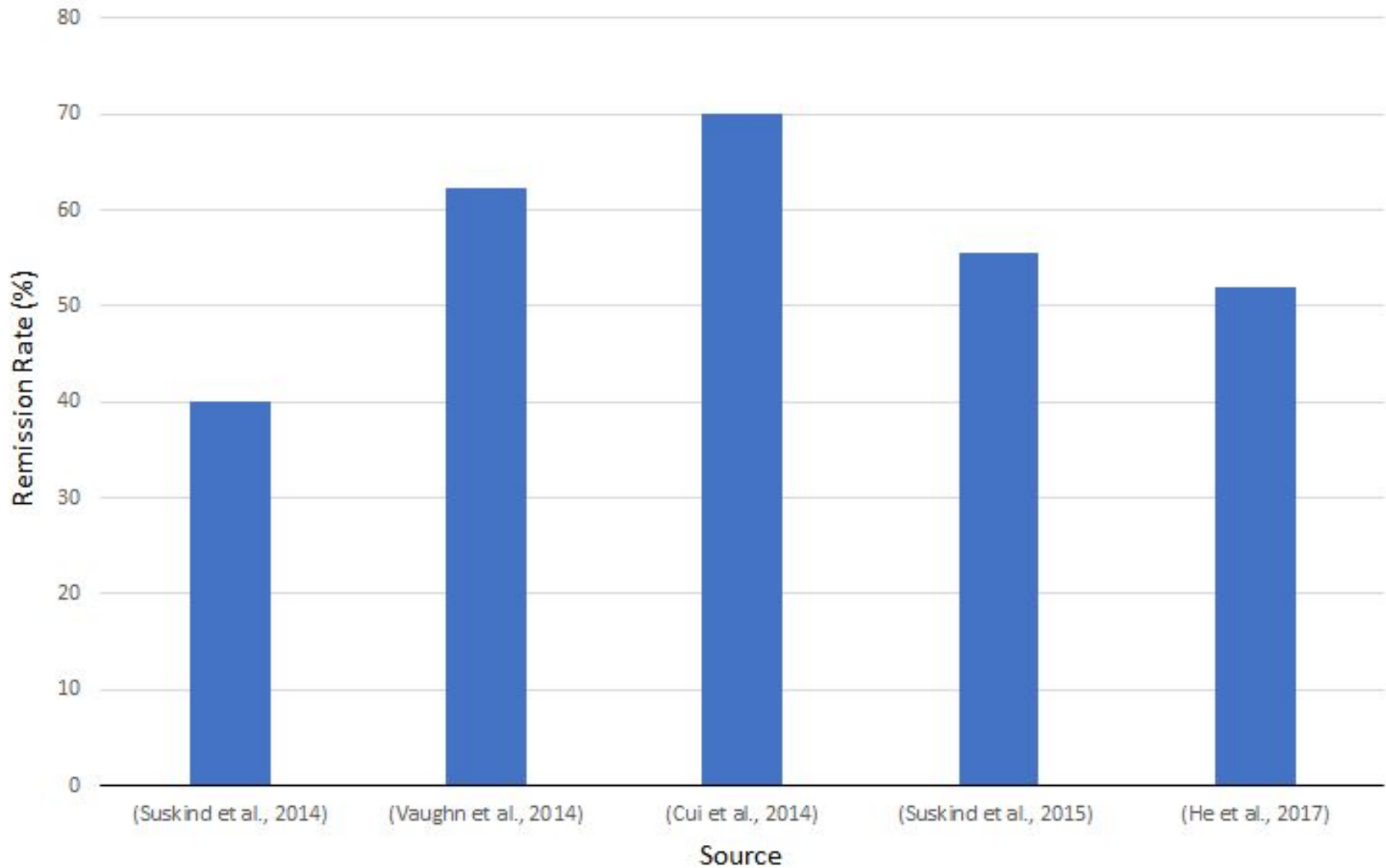
<i>Variable</i>	<i>Quantity</i>	<i>Multiple</i>	<i>Total</i>
Number of liquid or soft stools per day		2	
Abdominal pain (0 = none, 1 = mild, 2 = moderate, 3 = severe)		5	
General well being (0 = well, 1 = slightly under par, 2 = poor, 3 = very poor, 4 = terrible)		7	
Number of complications: arthralgias, iritis, erythema nodosum, pyoderma gangrenosa, aphthous ulcerations, anal fissure, anal fistula, anal abscess, fever > 37° past week, intestinal obstruction		20	
Opiates for diarrhea (no = 0, yes = 1,)		30	
Abdominal mass (no = 0, questionable = 2, yes = 5)		10	
Deviation from normal hematocrit (N = 42 for female, 47 for male)		6	
% deviation from standard weight		1	
<b>Total CDAI</b>			

From Best *et al*<sup>22</sup>: CDAI < 150 = remission; > 450 = severely ill.

The background of the slide is a light gray network diagram. It consists of numerous small circular nodes connected by thin, light gray lines. Some nodes are solid gray, while others are hollow circles. The connections form a complex, interconnected web of lines across the entire page.

# Results

# Remission Rates of Crohn's Disease Patients After Fecal Transplantations



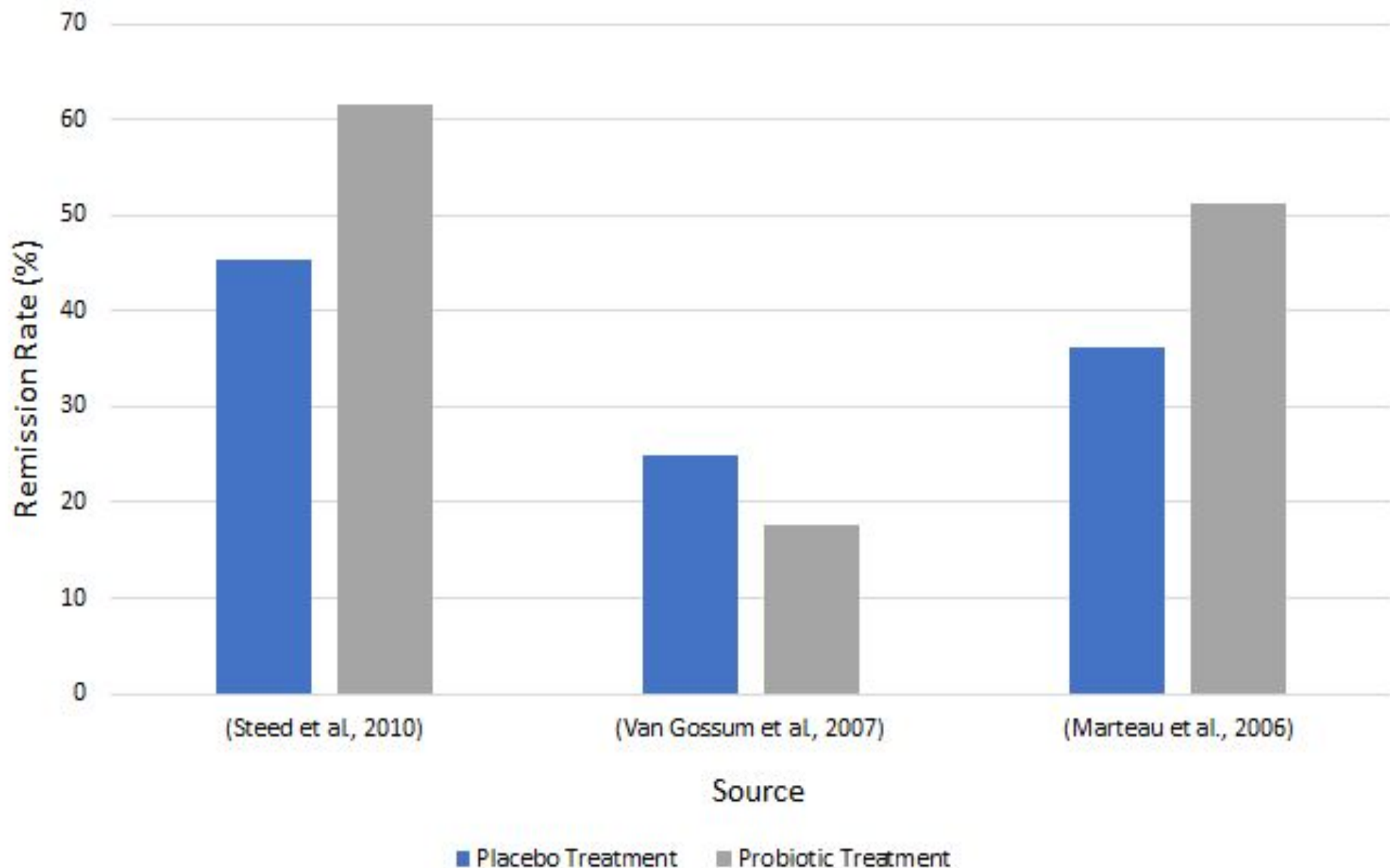
<i>t-Test: Paired Two Sample for Means</i>	<i>Before</i>	<i>After</i>
<b>Mean</b>	<b>0</b>	<b>55.96111</b>
<b>Variance</b>	<b>0</b>	<b>126.8131</b>
<b>Observations</b>	<b>5</b>	<b>5</b>
<b>Hypothesized Mean Difference</b>	<b>0</b>	
<b>df</b>	<b>4</b>	
<b>t Stat</b>	<b>-11.1119</b>	
<b>P(T&lt;=t) one-tail</b>	<b>0.000187</b>	
<b>t Critical one-tail</b>	<b>2.131847</b>	
<b>P(T&lt;=t) two-tail</b>	<b>0.000373</b>	
<b>t Critical two-tail</b>	<b>2.776445</b>	

# t-test

Significance value= 0.05

P value= 0.000187

# Remission Rate of Crohn's Disease Patients After Probiotic or Placebo Treatment





<i><b>t-Test: Two-Sample Assuming Unequal Variances</b></i>	<i><b>Placebo Treatment</b></i>	<i><b>Probiotic Treatment</b></i>
<b>Mean</b>	<b>35.54158167</b>	<b>43.44852067</b>
<b>Variance</b>	<b>104.8934735</b>	<b>526.2130997</b>
<b>Observations</b>	<b>3</b>	<b>3</b>
<b>Hypothesized Mean Difference</b>	<b>0</b>	
<b>df</b>	<b>3</b>	
<b>t Stat</b>	<b>-0.545152068</b>	
<b>P(T&lt;=t) one-tail</b>	<b>0.311782711</b>	
<b>t Critical one-tail</b>	<b>2.353363435</b>	
<b>P(T&lt;=t) two-tail</b>	<b>0.623565422</b>	
<b>t Critical two-tail</b>	<b>3.182446305</b>	



# t-test

Significance value= 0.05

P value= 0.623565422

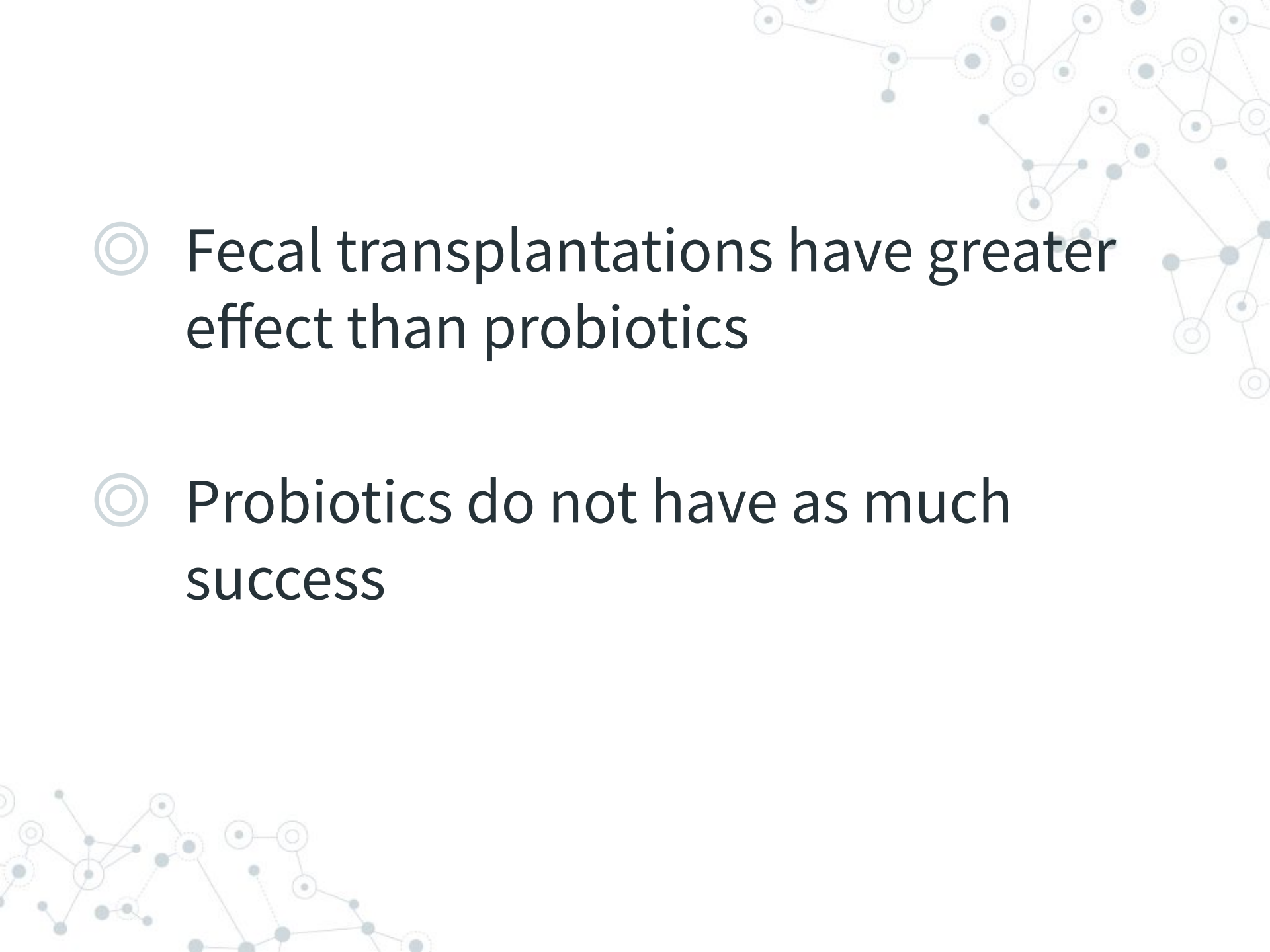
The background of the slide is a light gray network diagram. It consists of numerous small circular nodes, some of which are highlighted with a darker gray or blue color. These nodes are interconnected by thin, light gray lines, creating a complex web of connections that fills the entire page. The overall aesthetic is clean and technical, suggesting a focus on communication or data exchange.

# Discussion

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- ◎ Reject null hypothesis
  - ◎ No statistical significance of probiotics
  - ◎ Statistical significance of fecal transplants


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# Conclusion

- 
- ① Fecal transplantations have greater effect than probiotics
  - ① Probiotics do not have as much success


# Further work

A decorative network diagram in the top right corner, consisting of various sized circles (nodes) connected by thin lines (edges). Some nodes are solid grey, while others are hollow with a grey outline. The connections form a complex, interconnected web.

- ◎ Fecal transplantations
  - ◎ Mixed probiotics
  - ◎ Cost of Treatments
- 
- A decorative network diagram in the bottom left corner, similar to the one in the top right, featuring a cluster of interconnected nodes and lines.

# Limitations




- ◎ Available research on fecal transplantations and probiotics
  - ◎ Crohn's disease specific articles
- 



# Acknowledgements

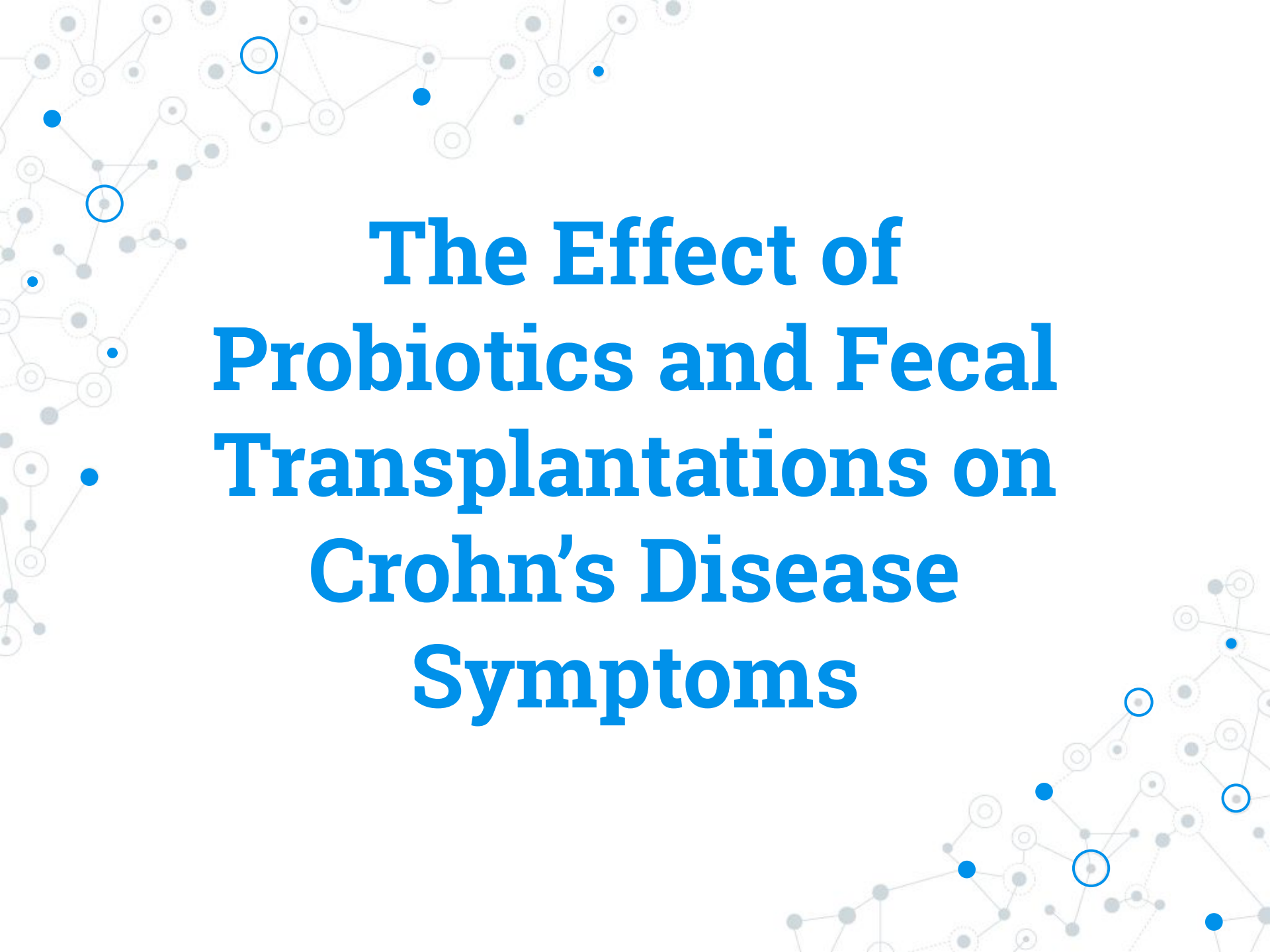


- ◎ Jonathan Braun MD, Ph.D.
  - ◎ Jonathan Hansen MD, Ph.D.
  - ◎ Nikki Malhotra Ph.D.
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# References

- Bamola, V. D., Ghosh, A., Kapardar, R. K., Lal, B., Cheema, S., Sarma, P., & Chaudry, R. (2017). Gut microbial diversity in health and disease: Experience of healthy indian subjects, and colon carcinoma and inflammatory bowel disease patients. *Taylor & Francis Group*, 28, 1322447. doi: 10.1080/16512235.2017.1322447.
- Baroja, M. L., Kirjavainen, P. V., Hekmat, S., & Reid, G. (2007). Anti-inflammatory effects of probiotic yogurt in inflammatory bowel disease patients. *Clinical and Experimental Immunology*, 149, 470-479. doi: 10.1111/j.1365-2249.2007.03434.x.
- Bousvaros, S., Guandalini, S., Baldassano, R., Botelho, C., Evans, J., Ferry, G., Goldin, B., Hartigan, L., Kugathasan, S., Levy, J., Murray, K., Oliva-Hemker, M., Rosh, J., Tolia, V., Zholudev, A., Vanderhoof, J., & Hibberd, P. (2005). A randomized, double-blind trial of lactobacillus GG versus placebo in addition to standard maintenance therapy for children with crohn's disease. *Inflammatory Bowel Disease*, 11(9), 833-839. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/16116318>
- Bull, M., Plummer, N. (2014). Part 1: The human gut microbiome in health and disease. *Integrative Medicine: A Clinician's Journal*, 13(6), 17-22. Retrieved from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4566439/>.
- Campbell, K., Galipeau, H., Hardy, A., & Mouw, M. (2017). Refractory crohn's disease with fecal microbiota transplantation. *Korean Association for the Study of Intestinal Diseases*, 15(2), 244-248. doi: 10.5217/ir.2017.15.2.244.
- Carding, S., Verbeke, K., Vipond, D. T., Corfe, B. M., & Owen, L. J. (2015). Dysbiosis of the gut microbiota in disease. *Microbial Ecology in Health and Disease*, 26, 1-9. doi: 10.3402/mehd.v26.26191.
- Cheifetz, A. S. (2013). Management of active crohn disease. *Journal of the American Medical Association*, 309(20), 2150-2158. doi: 10.1001/jama.2013.4466.
- Cui, B., Feng, Q., Wang, H., Wang, M., Peng, Z., Li, P., Huang, G., Liu, Z., Wu, P., Fan, Z., Ji, G., Wang, X., Wu, K., Fan, D., & Zhang, F. (2014). Fecal microbiota transplantation through mid-gut for refractory crohn's disease: Safety, feasibility, and efficacy trial results. *Journal of Gastroenterology & Hepatology*, 30(1), 51-58. <https://doi.org/10.1111/jgh.12727>
- Filteau, M., Matamoros S., Savard P., Roy, D. (2013). Molecular monitoring of fecal microbiota in healthy adults following probiotic yogurt intake. *PharmaNutrition*, 1(4), 123-129. <https://doi.org/10.1016/j.phanu.2013.05.002>.
- Goossens, D., Jonkers, D., Russel, M., Stobberingh, E., Van Den Bogaard, A., & StockbrÜgger, R. (2003). The effect of lactobacillus plantarum 299v on the bacterial composition and metabolic activity in faeces of healthy volunteers: A placebo -controlled study on the onset and duration of effects. *Alimentary Pharmacology and Therapeutics*, 18(5), 495-505. doi: 10.1046/j.0269-2813.2003.01708.x.
- He, Z., Li, P., Zhu, J., Cui, B., Xu, L., Xiang, J., Zhang, T., Long, C., Huang, G., Ji, G., Nie, Y., Wu, K., Fan, D., & Zhang, F. (2017). Multiple fresh fecal microbiota transplants induces and maintains clinical remission in Crohn's disease complicated with inflammatory mass. *Scientific Reports*, 7(4753), 1-10. doi:10.1038/s41598-017-04984-z

- Lewis, J. D., Chen, E. Z., Baldassano, R. N., Otley, A. R., Griffiths, A. M., Lee, D., . . . Bushman, F. D. (2015). Inflammation, antibiotics, and diet as environmental stressors of the gut microbiome in pediatric crohn's disease. *Cell Host Microbe*, 18(4), 489-500. doi: 10.1016/j.chom.2015.09.008.
- Lisko, D. J., Johnston, G. P., & Johnston, C. G. (2017). Effects of dietary yogurt on the healthy human gastrointestinal (GI) microbiome. *Microorganisms*, 5(1). doi: 10.3390/microorganisms5010006.
- Marteau, P., Lémann, M., Seksik, P., Laharie, D., Colombel, F., Bouhnik, Y., Cadot, G., Soulé, J., Bourreille, A., Metman, E., Lerebours, E., Carbonnell, F., Dupas, J., Veyrac, M., Coffin, B., Moreau, J., Abitbol, V., Blum-Sperisen, S., & Mary, J. (2005). Ineffectiveness of lactobacillus johnsonii LA1 for prophylaxis of postoperative recurrence in crohn's disease: A randomised, double blind, placebo controlled GETAID trial. *Inflammatory Bowel Disease*, 55(6), 842-847. doi:10.1136/gut.2005.085381
- MedlinePlus. (2018). Crohn's Disease [Data file]. Retrieved from: <https://medlineplus.gov/crohnsdisease.html>
- Kato-Kataoka, A., Nishida, K., Takada, M., Kawai, M., Kikuchi-Hayakawa, H., Kuda, K., . . . Rokutan, K. (2016). Fermented milk containing lactobacillus casei strain shirota preserves the diversity of the gut microbiota and relieves abdominal dysfunction in healthy medical students exposed to academic stress. *Applied and Environmental Microbiology*, 82(12), 3649-3658. doi: 10.1128/AEM.04134-15.
- Prantera, C., Scribano, M., Falasco G., Andreoli, A., & Luzi, C. (2002). Ineffectiveness of probiotics in preventing recurrence after curative resection for crohn's disease: A randomised controlled trial with Lactobacillus GG. *Gut*, 51(3), 405-409. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/12171964>
- Shadnough, M., Hosseini, R. S., Khalilnezhad, A., Navai, L., Goudarzi, H., & Vaezjalali, M. (2015). Effects of probiotics on gut microbiota in patients with inflammatory bowel disease: A double-blind, placebo-controlled clinical trial. *Korean J Gastroenterol*, 65, 215-221. doi: 10.4166/kjg.2015.65.4.215.
- Schultz, M., Timmer, A., Herfarth, H., Sartor, R., Vanderhoof, J., & Rath, H. (2004). Lactobacillus GG in inducing and maintaining remission of crohn's disease. *BMC Gastroenterology*, 4(5), 1-4. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/15113451>
- Steed, H., Macfarlane, G., Blackett, K., Bahrami, B., Reynolds, N., Walsh, S., Cummings, J., & Macfarlane, S. (2010). Clinical trial: The microbiological and immunological effects of synbiotic consumption - a randomized double-blind placebo-controlled study in active crohn's disease. *Alimentary Pharmacology and Therapeutics*, 32(7), 872-883. doi:10.1111/j.1365-2036.2010.04417.x.
- Suskind, D., Brittnacher, M., Wahbeh, G., Shaffer, M., Hayden, H., Qin, X., Singh, N., Damman, C., Hager, K., Nielson, H., & Miller, S. I. (2015). Fecal microbial transplant effect on clinical outcomes and fecal microbiome in active crohn's disease. *Inflammatory bowel diseases*, 21(3), 556-563. doi:10.1097/MIB.0000000000000307
- Suskind, D., Wahbeh, G., Vendetoulli, H., Singh, N., & Miller, S. (2014). Fecal microbial transplant in pediatric crohn's disease. *Gastroenterology*, 146(5), S-834. [https://doi.org/10.1016/S006-5085\(14\)63030-4](https://doi.org/10.1016/S006-5085(14)63030-4)
- Van Gossum, A., Dewit, O., Louis, E., Hertogh, G., Baert, F., Fontaine, F., Devos, M., Enslin, M., Paintin, M., & Franchimont, D. (2006). Multicenter randomized-controlled clinical trial of probiotics (Lactobacillus johnsonii, LA1) on early endoscopic recurrence of crohn's disease after ileo-caecal resection. *Inflammatory Bowel Diseases*, 13(2), 135-142. <https://doi.org/10.1002/ibd.200631>
- Vaughn, B., Gevers, D., Ting, A., Korzenik, J., Robson, S., & Moss, A. Fecal microbiota transplantation induces early improvement in symptoms in patients with active crohn's disease. (2014). *Gastroenterology*. 146(5), S-591-S-592. [https://doi.org/10.1016/S0016-5085\(14\)62143-0](https://doi.org/10.1016/S0016-5085(14)62143-0)

A decorative background featuring a network diagram with nodes and connecting lines. The nodes are represented by circles of varying sizes and colors, including light gray, dark gray, and blue. Some nodes are highlighted with a blue outline. The lines connecting the nodes are thin and light gray, creating a complex web-like structure.

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