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The Influence of Diet on the Gut Microbiome

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Abstract: There is growing research that directly looks at the relationship between the human diet and the gut microbiome. This paper is a narrative review of the current literature on how the human diet can influence the gut microbiome. Without a healthy gut, bacterial imbalances can occur which have been linked to health complications. There are many factors that affect the gut microbiome such as diet, medications, and exercise. There is also limited research that looks at the macronutrients and their role in gut health. It is known that the type of food that people consume is a major influencer of the overall abundance and variety of bacteria in the microbiota.

Keywords: gut microbiome, diet, lifestyle, gut microbiota, health, and disease

Introduction: There are over 100 trillion bacteria that live in the human gut along with viruses, fungi, and protozoa that all work together to make up the human intestinal tract. [1-3] The gut microbiome is thought to have a role in prevention and treatment for a variety of diseases including obesity, Alzheimer's Disease, diabetes, and some types of cancer. [4-6] The research being done on the gut microbiome is increasing. We now know that gut microbiome can be influenced in many ways due to antibiotics, diet, birth mode, breastfeeding, exercise, ageing, and geography. [3 7] Although we know that the gut plays a role in a variety of ways, we lack an understanding as to what factors of a person's diet can influence the gut microbiome. Without the knowledge and understanding of how the diet can influence the gut microbiome millions of people will continue to suffer from diseases and conditions that can be treated though increased knowledge of how the diet can alter the gut microbiome.[8] The objective of this paper is to report the influence of diet on the gut microbiome from the current literature.

Methods: The primary database used for this literature review was PubMed. Articles were included if they met the criteria of pertaining to the human gut microbiome and were published within the last 20 years. No animal studies were included in this review paper. There were 17,681 search results of publications pertaining to the gut microbiome. Thirteen thousand four hundred forty-nine were excluded due to not pertaining to the diet. Two thousand two hundred seventy were excluded as they were not pertaining to humans. One thousand nine hundred sixty-four articles met the search criteria of pertaining to the human diet, gut microbiome, and published within the last 20 years. One thousand eight hundred eighty-nine articles were excluded based on titles and abstracts. Seventy-six articles were examined and compared. Forty-three articles were not included due not aligning with the objective of this paper and not being

able to retrieve access to the full article, thus the inclusion of 34 articles that were included in this literature review.

Literature Review

The gut microbiome

The microbial communities that colonize different regions of the human gut influence many aspects of health. In a healthy state, the bacteria aids in nutrient and energy fermentation of non-digestible dietary components within the large intestine. [9] The relationship of the microbiota and human health is becoming more recognized. We now know that a healthy gut flora plays a major role in the overall health of a human. [2 10] Without a healthy gut, bacterial imbalance can occur resulting in inflammation, infection, gastrointestinal disease, and possible contributions to diabetes mellitus and obesity. [9] There are numerous studies that have attempted to define the composition of a "normal" gut microbiome. However, it seems that many factors play a role in what is considered normal for each person. Microbial colonization occurs throughout the length of the gastrointestinal tract from the oral cavity to the rectum. The density of the colonization differs between areas due to host secretions, environmental conditions, and pH. [11] Based on studies that have been done researchers have been able to determine major taxonomy nodes rather than individual strains of bacteria due to the estimated gut microflora containing over 35,000 bacteria species. [10] The general gut microbiome is primarily made up of two phyla called Bacteroidetes and Firmicutes. [10 12] Actinobacteria and Proteobacteria are two other phyla that have a higher abundance of over 1% of the microbiome. *Bacteroides* include nine different species with seven of them having a great abundance found in over half of the 100 people that were tested, with *Bacteroides dorei* being the most abundant. [12] Having a wide

variety of bacteria in the human microbiome is essential due to bacteria being specialized in the

fermentation of different substrates.

Table 1. The gut microbiome references

Title	Author	Year Published	Objective	Primary outcomes
Metagenomic Analysis of the Human Distal Gut Microbiome	(1) Steven R. Grill et al.	2006	Comparison of the human genome with the average content of previously sequenced microbial genomes	Human intestinal microbiota is composed of 10^13 microorganisms
The influence of antibiotics and dietary components on gut microbiota	(2) Ruth K. Dudek-Wicher et al.	2018	Summarize the knowledge of regarding the impact of different antibiotics causing such long-term consequences as decreased microbial diversity	The microbiome that resides in the human GI tract compromises a dynamic community that changes throughout a lifespan. There is a body of evidence that suggests the gut microbiota has to potential to be an important factor in shaping human health
Systemic review on effects of diet on the gut microbiota in Relation to Metabolic Syndromes	(3) Katherine Wilson and Chen Situ	2017	Review the current literature on the effects of the diet on gut microbiome in relation to the development of MetS through determining how the diet influences the composition and functions of the microbiota. Evaluating the evidence of how this is linked with development of obesity and biomarkers for MetS, and to investigate the significance of diet diet-microbiota interactions in relation to obesity and MetS	Protein and amino acid fermentation provide the colonic microbes with nitrogen for growth. Herbivores showed enriched concentrations of enzymes involved in biosynthesis of amino acids and had a more diverse microbial community compared to carnivores
Influence of diet on the gut microbiome and implications for human health	(4) Singh et al.	2017	Evaluating the current data regarding the effects of several common dietary components on intestinal microbiota	This review suggests that diet can modify intestinal microbiome which has a profound impact on overall health. This impact can increase or decrease risk factors depending on lifestyle.
Influence of High-Fat diet on Gut Microbiota: A Driving Force for Chronic Disease Risk	(5) Murphy et al.	2016	This review examines the recent scientific literature surrounding high-fat-diet-induced alterations in the gut microbiota and subsequent development of obesity and chronic disease risk	Diets high in fat can alter the gut microbiome with alterations that have been linked to obesity and other chronic diseases.

Interaction between diet composition and gut microbiota and its impact on gastrointestinal tract health	(6) Shahid Riaz Rajoka et al.	2017	Report a comprehensive study of interactions between how microbiota and food affect human physiology and this, generate useful information for the prevention of multiple diseases	Human-associated microbial communities are crucial for proper development. Type and amount of foods and the effect it has on the microbiome. Types of bacteria present based on the diet consumed.
Gut microbiome as a clinical tool in gastrointestinal disease managements: are we there yet?	(7) Eamonn M and M Quigley	2017	The status of microbiota signatures in the clinical arena will be critically assed and provide guidance toward future progress	Factors that affect the gut: birth mode, breastfeeding, diet, exercise, disease, ageing, drugs, and geography
The impact of Diet and Lifestyle on Gut Microbiota and Human Health	(8) Michael A. Conlon and Anthony R. Bird	2014	Explore the relevant literature to provide general perspective in this broad area of the gut microbiome	Nearly all of the bacteria in the human gut can be mapped to just two phyla (Bacteroidetes and firmicutes). Long- and short-term habits can influence the gut in different ways
The Role of the Gut Microbiota in Nutrition and Health	(9) Harry J. Flint et al.	2012	To review the complex interplay between the gut microbiota, diet, and health	Dietary intake especially of no digestible carbs alters the species composition of the gut microbiota both in the short and long term. The gut microbiota potentially influences the host's energy balance through multiple mechanisms.
Role of the normal gut microbiota	(10) Sai Manasa Jandhyala et al.	2015	Review the recent evidence on the functions of the normal gut microbiota and the mechanistic insights into the execution of these pro-health functions	The normal gut microbiota comprises of two major phyla. The gut microbiota of a child resembles that of an adult by age 3. Several factors play a role in shaping the normal gut microbiota. Composition of the normal gut microbiota.
Contribution of diet to the composition of the human gut microbiota	(11) Daniela Graf et al.	2015	The aim of the review was to summarize the recently published evidence from human in vivo studies on the gut microbiota-modulating effects of diet	Food components provide substrates for the intestinal microbial metabolism. Bacteria are specialized in fermentation of different substrates. The microbiota is influenced by general lifestyle, host genetics, early colonization, medication, and health/disease

Baseline human gut microbiota profile in healthy people and standard reporting template	(12) Charles H. King et al.	2019	Create a list of organisms and their abundances along with generating a collection of assembled contiguous sequences of metagenomics dark matter	Study participants recorded their dietary intake using a seven-day food journal and provided three fecal samples. N = 16. Bifidobacterium was positively correlated with dietary protein intake; specifically, vegetable protein

Prebiotics and Probiotics

The World Health Organization defines probiotics as live microorganisms that can provide benefits to human health when administered in adequate amounts. Certain strands of probiotic bacteria have been known to have an impact on gut barrier functions and immune health such as *Lactobacillus casei, Lactobacillus planatarum, Lactobacillus bulgaricus, Lactobacillus acidophilus, Bifidobacterium logum, Bifidobacterium infantis, Streptococcus thermophilus*, and *E. coli stran.* [10] These bacteria have been used as treatment in order to mimic the "good" bacteria in the gut to alleviate illnesses such as antibiotic associated diarrhea. [10] Prebiotics are defined as a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon and this improving the host's health. It is often thought of as prebiotics being the food for the probiotic bacteria. Combining a prebiotic with a probiotic is called a symbiotic which allows the fermentation by the gut bacteria resulting in the synthesis of short chain fatty acids and pro-health effects. [10]

Dietary Patterns

It has become clear that the human diet can have a major influence on the microbial community composition for both short and long term. Some studies have shown that the microbiome composition can change within a few days of altering the diet. However, we do

know that some bacteria take years to repopulate. [2 11] In a study that looked at the dietary patterns of 100 people over the course of 3 weeks noted that the bacteria *Bifidobacterium* was positively correlated with the consumption of dietary protein, specifically plant sources. Dietary soluble fiber from vegetables found in brussel sprouts, beans, peas, beans, and asparagus were thought to be a major contributing factor to increase the amount of *Bifidobacterium* in the gut after the 3-week period. *Akkermansia* was positively correlated with a consumption of saturated fat intake such as linoleic acid and negatively correlated with the total consumption of polyunsaturated fatty acids. *Bacteroides ovatus* was positively correlated with daily calorie intake as well as weight circumference and overall body weight in the participants. [12] This data shows us that diet plays a crucial role in the makeup of an individual's microbiome. Consuming a varied diet of simple and complex carbohydrates and a variety of fruits and vegetables can provide the bacteria with growth promoting and inhibiting factors. The end products of bacteria metabolism include vitamins and short-chain fatty acids (SCFA) which are vital for human health. [10]

While limited research is available that investigates the relationship between specific foods in the diet and gut microbiota, from the studies that have been done, it can give us an idea of what foods might contribute to gut health. However, there is not enough evidence to know to what extent they play a role. For example, recent studies have shown that artificial sweeteners such as saccharin, sucralose, aspartame, and acesulfame K can alter the microbial communities resulting in glucose intolerance in humans. [2] It is also important to note that it is suggested that the time of day along with the type of food that is being consumed can have an effect on the microbiome. One study, titled *Time of day and eating behaviors are associated with the composition and function of the human gastrointestinal microbiota,* looked at 77 fecal samples

from 28 healthy individuals. It was shown that circadian rhythms, or cycles of gene expression, metabolism, and behaviors created by an internal clock, can maximize an organism's metabolic efficiency. It was concluded that thirty five percent of bacteria were associated with time. Specifically, acetate, propionate, and butyrate concentrations were found to decrease throughout the day. Alternately, some bacteria were shown to increase throughout the day such as *Adlercreuzia, Eggerthella, Anaerotruncus, Oscillospria, Ruminococcus, Holdemeania, Descufovibrio,* and *Escherichia*. Interpretation of these results indicate that the human gastrointestinal microbiota can vary throughout the day based on early energy consumption which was defined as the percent of total kilocalories consumed before 1400 hours and overnight-fast duration. [13]

Carbohydrates are the most researched macronutrient when investigating the effect on the human gut microbiota. Carbohydrates are classified as simple or complex. Simple carbohydrates are often referred to as processed or simple sugars such as candy, and baked goods. Complex carbohydrates or whole grains are known for their high amount of fiber. It is recommended that humans consume 25-50 grams of dietary fiber each day from food sources, not supplements. Consumption of dietary fiber widely varies across the globe with an average intake of 12-18 grams in the United States and 16-29 grams per day in Europe. [14] Other countries in Africa are thought to have an intake of up to seven times more due to their fibrous plant consumption. Fiber is important for the human diet because our bodies do not have the enzymes that can digest and thus not absorbed. Instead, it is fermented in the gastrointestinal tract by bacteria which has an impact on the composition of bacterial communities such as the fermented end products. Diets that are higher in fiber are associated with increased gastrointestinal microbial diversity. [14]

There are two types of fiber, soluble and insoluble. Soluble fiber is found in oats, beans, and other legumes along with some fruits and vegetables. It dissolves in water to form a gel-like material. [15] Soluble fiber can be classified in two different ways. The first form of fiber is defined as edible carbohydrate polymers that are naturally occurring in foods as consumed, such as pectin found in fruit. [14] The second form is edible carbohydrate polymers which have been obtained from raw food materials by physical, enzymatic, and chemical means and are shown to have a benefit to physiological processes such as inulin found in bananas. [14 15] Insoluble fiber can be found in whole wheat flour, bran, nuts, beans and vegetables. It does not dissolve in water and promotes movement of material through the digestive tract and increases stool bulk. [15]

Several studies have looked at the influence of whole grain breakfast cereals and their effect on the gut microbiota composition. [16-18] One study showed that after 3 weeks of a maize-based whole grain breakfast cereal consumption the *bifidobacteria*l levels had increased in the feces. *Lactobacillus/Enterococcus* group also had increased levels in the stool compared to the group that consumed a wheat/bran-based cereal. [16 17] Prebiotics, as mentioned previously, play a role in this as they are considered the food ingredients that contain the non-digestible oligosaccharides. [10] A majority of prebiotics can be classified as fiber, although not all fiber is considered a prebiotic. Therefore, having a variety of dietary fibers such as cellulose, hemicellulose, pectin, gums, fructans, and resistant starches in the diet can further support a varied microbiome community compared to a diet that is lower in these products. [14]

Although fruit, nut, vegetable, and legume are sources of carbohydrates, there have been fewer research studies focusing on consumption of these foods and the microbiota composition. One study investigated the consumption of a wild blueberry drink for six weeks showed that there was an increased amount of *Bifidobacterium spp*. as well as *lactobacillus acidophilus*. [19]

The increase in *Bifidobacterium genus* was also observed in a study where it was increased after consumption of red wine and de-alcoholized red wine. There was also an increase in *enterococcus, Eggerthella lenta,* and *phylum Fuso-bacteria*. These results indicate that alcohol may have a synergistic effect in combination with other red wine constituents containing polyphenols such as tea, coffee, and chocolate. [20]

To date, little is known about whether fat quality or quantity have an influence on the gut microbiome. [11] Preliminary studies suggest that dietary fat indirectly modulates the composition via bile acid secretion and composition. One study reported that the *Bacteroides enterotype* is positively correlated with the intake of saturated fats while the *Prevotella enterotype* is inversely associated with the total intake of dietary fat. [21] This shift in enterotypes is thought to be associated with obesity and subsequent development of chronic diseases. High fat diets have been associated with modifications of the microbial profile with decreased diversity in the gut. [5] The gut microbiome has been shown to have an impact on lipid metabolism by suppressing the inhibition of lipoprotein lipase acidity in adipocytes. *Bacteroides thetaiotomicron* is thought to play a role in the efficiency of lipid hydrolysis by up regulating the expression of colipase that is needed for lipid digestion. [10]

The effect of protein on microbiota composition has been studied to a minor extent. A diet high in protein and low in carbohydrates was shown to affect the gut microbiota and fatty acid profiles in obese men. After a 4-week period, the high protein diet resulted in an increase in branched chain fatty acids, decrease in *butyrate*, and decrease in *Roseburial Eubacterium*. It is unknown whether or not these changes are linked to increased or decreased benefits. However, high levels of butyrate within the body has been shown to have health benefits. It is thought that the decrease in butyrate is due to consuming a low carbohydrate diet and low fiber intake. [22]

Dietary protein provides colonic microbes with nitrogen which is necessary for growth, absorption of carbohydrates, and the production of short chain fatty acids. [3] Protein fermentation by the gut contributes to the metabolite pool in the large intestine and can contribute to the amino acid balance. However, it is not known the role these amino acids may have in the gut. [23] There are some factors that affect the amino acid fermentation process such as heat processing of the food product and the number of compounds that inhibit proteolysis which can determine the amount of protein that reaches the colon. Amino acid fermentation, although not as favorable as carbohydrates, can result in a large range of metabolites and gases such as amines, phenols, and branched chain fatty acids which can be potentially harmful to human cells. Regardless, microbiota health is determined by the type of dietary protein and its interaction with other dietary components. [23] For example, red meat consumption is shown to increase concentrations of *trimethylamine-N-oxide (TMAO),* a small colorless amine oxide generated from choline, betaine, and carnitine by the gut microbial metabolism. Elevated plasma levels of TMAP has been shown to have a positive correlation with increased risk for adverse cardiovascular events due to alterations in cholesterol and bile acid metabolism and activation of inflammatory pathways. [24] High protein and low carbohydrates diets are shown to have a decreased production of *butyrate* and *Bifidobacterium* levels compared to those who consume high carbohydrate, high fiber, and low fat diet. [3] Diets that promote microbial protein synthesis are shown to have a more diverse microbiome due to being more efficient at converting amino acids and excreting more nitrogen in the feces which reduce plasma nitrogen levels. This may indicate that the dietary protein response with other dietary products is an important factor in influencing how the microbiota will respond to the dietary protein that is being consumed. [3]

Specific nutrients such as vitamin K and components of vitamin B are considered a major metabolic function of the gut microbiota. Having a healthy microbiome shows increased concentrations of pyruvic acid, citric acid, fumaric acid, and malic acid which are indicators of a high energy metabolism. Polyphenolic metabolites can be found in a variety of plant products such as tea and wine as flavanols, flavanones, flavan-3-ols, anthocyanidins, isoflavones, flavones, tannins, lignans, and chlorogenic acids which are absorbed in the small intestine. [10]

The type of food that people consume is a major influencer of the overall abundance and variety of bacteria in the microbiota. It is difficult to track the specific components of the human diet because people consume a wide variety of foods and prepare foods in various ways. Non-dietary lifestyle factors also play a role in the gut microbiome. Factors such as smoking and exercise can greatly impact the large bowel and microbiota composition. [8] Because of this, few studies directly relating to the human diet have been done because controlling the diet in a human along with their lifestyle factors is difficult. Participants can be non-compliant in feeding studies and consume additional food or beverages. Accurate tracking of portion sizes and nutrient content of foods are difficult to analyze based on food records and can contain recall bias. Sample size in feeding studies are typically low, and people may not recall or track their diet history correctly. [8]

The basis of the human diet can be broken down into two generalized groups with multiple sub-groups. There are varying levels of each group due to the inclusion or exclusion of certain types of foods within each group which can make it difficult to distinguish. However, the two general groups are those who consume animal products and those who do not. Thus, vegans, who consume no animal products, vegetarians, who may consume some animal products such as dairy or fish and omnivores, who consume animal products, have distinct microbiomes. [2 3 8

25] The western diet is typically low in fiber and consists of a high amount of fat, refined carbohydrates, and red meat. [8 26] Total counts of *Bacteroides spp., Bifidobacterium spp., Escherichia coli, and Enterobacteriaceae spp.* were higher in this group compared to individuals who consumed a vegetarian or vegan diet. [2] Bacteria such as *E. coli biovars, Klebsiella spp., Enterobacter spp, other forms of Enterobacteriaceae, Enterococcus spp., Lactobacillus spp., Citrobacter spp., and Clostridium spp.* did not differ between groups. Animal based diets have shown an increase in the abundance of bile-tolerated microorganisms such as *Alistipes, Biophilia,* and *Bacteroides* and a decreased level of *Firmicutes* which help metabolize dietary plant polysaccharides. Overall, a western style diet can lead to a decrease in total bacteria and a decrease in specific bacteria such as *Bifidobacterium* and *Eubacterium* which are considered beneficial bacteria, thus potentially leading to adverse health effects. [2]

A vegetarian/vegan diet can be broken down into different sub-groups but is primarily composed of plant products. This makes it difficult to track the diets of those who identify as vegetarian because there are different forms of vegetarianism. Semi-vegetarian occasionally consumes fish, red meat, and poultry, lacto-ovo-vegetarianism includes eggs and dairy; lacto-vegetarian consume dairy; ovo-vegetarian consumes eggs, and vegan diets do not include any animal products or animal byproducts. [27] It has been shown that those who consume a vegan or vegetarian style diet have significantly lower stool pH levels and counts of E. coli and Enterobacteriaceae. This is thought to be related to increased consumption of short chain fatty acids within the diet compared to other dietary patterns. [2] Based on studies that have been done, the microbiota of omnivores has a higher level of *Clostridium cluster XIVa* which are butyrate producing bacteria. Because of this there is an indication of an increased production of butyrate which has been associated with health benefits. The major drawback from this study is

that it was conducted in rural southern India and thus the results may not be generalizable to other populations. Researches are unaware if the changes in microbiota are due to the diet or from the region in which the study was taken place. [11, 28] Overall, herbivores showed to have an enriched concentration of enzymes that are involved in biosynthesis of amino acids and a more diverse microbial community compared to those who consumed animal-based food products. These enzymes are involved in the biosynthesis of amino acids and produce a more diverse microbiota compared to carnivores. [3]

Butyrate is considered the least abundant short chain fatty acid that is produced in the body, although it is considered one of the major energy sources for colonocytes. Butyrate has been found to play an important role in modulating immune and inflammatory responses and intestinal barrier function. [29] There is increasing evidence that butyrate plays a role in the brain through the gut-brain axis due to changes in butyrate-producing bacteria modulating the peripheral and central nervous system as well as having the capability of crossing the blood-brain barrier, thus activating the vagus nerve and hypothalamus allowing it to affect the appetite and eating behavior. [29 30] Butyrate is found in the intestinal barrier and is capable of upregulating Mucin-2 which is the most prominent mucin that is responsible for reinforcing the mucus layer which can lead to the enhanced protection against luminal pathogens. [31] Butyrate is produced from dietary fibers through bacterial fermentation via two metabolic pathways. The first pathway allows butyryl-CoA to be phosphorylated to form butyryl-phosphate which transforms to butyrate via butyrate kinase. The second pathway the CoA of butyryl-CoA is transferred to acetate via butyryl-CoA: acetate CoA transferase, which forms butyrate and acetyl-CoA. [31] Overall, butyrate can influence a person's immune response by affecting the immune cell migration, adhesion, and cellular functions such as proliferation and apoptosis and prevent the

accumulation of toxic metabolic by-products such as D-lactate which if not excreted can lead to

D-lactic acidosis, a rare neurologic syndrome, causing altered mental status, slurred speech, and

ataxia. [10]

Table 2. Dietary patterns and probiotics references

Title	Author	Year Published	Objective	Primary outcomes
The influence of antibiotics and dietary components on gut microbiota	(2) Ruth K. Dudek-Wicher et al.	2018	Summarize the knowledge of regarding the impact of different antibiotics causing such long-term consequences as decreased microbial diversity	The microbiome that resides in the human GI tract compromises a dynamic community that changes throughout a lifespan. There is a body of evidence that suggests the gut microbiota has to potential to be an important factor in shaping human health
Systemic review on effects of diet on the gut microbiota in Relation to Metabolic Syndromes	(3) Katherine Wilson and Chen Situ	2017	Review the current literature on the effects of the diet on gut microbiome in relation to the development of MetS through determining how the diet influences the composition and functions of the microbiota. Evaluating the evidence of how this is linked with development of obesity and biomarkers for MetS, and to investigate the significance of diet diet-microbiota interactions in relation to obesity and MetS	Protein and amino acid fermentation provide the colonic microbes with nitrogen for growth. Herbivores showed enriched concentrations of enzymes involved in biosynthesis of amino acids and had a more diverse microbial community compared to carnivores
Influence of High-Fat diet on Gut Microbiota: A Driving Force for Chronic Disease Risk	(5) Murphy et al.	2016	This review examines the recent scientific literature surrounding high-fat-diet-induced alterations in the gut microbiota and subsequent development of obesity and chronic disease risk	Diets high in fat can alter the gut microbiome with alterations that have been linked to obesity and other chronic diseases.
The impact of Diet and Lifestyle on Gut Microbiota and Human Health	(8) Michael A. Conlon and Anthony R. Bird	2014	Explore the relevant literature to provide general perspective in this broad area of the gut microbiome	Nearly all of the bacteria in the human gut can be mapped to just two phyla (Bacteroidetes and firmicutes). Long- and short-term habits can influence the gut in different ways

Role of the normal gut microbiota	(10) Sai Manasa Jandhyala et al.	2015	Review the recent evidence on the functions of the normal gut microbiota and the mechanistic insights into the execution of these pro-health functions	The normal gut microbiota comprises of two major phyla. The gut microbiota of a child resembles that of an adult by age 3. Several factors play a role in shaping the normal gut microbiota. Composition of the normal gut microbiota.
Contribution of diet to the composition of the human gut microbiota	(11) Daniela Graf et al	2015	The aim of the review was to summarize the recently published evidence from human in vivo studies on the gut microbiota-modulating effects of diet	Food components provide substrates for the intestinal microbial metabolism. Bacteria are specialized in fermentation of different substrates. The microbiota is influenced by general lifestyle, host genetics, early colonization, medication, and health/disease
Baseline human gut microbiota profile in healthy people and standard reporting template	(12) Charles H. King et al.	2019	Create a list of organisms and their abundances along with generating a collection of assembled contiguous sequences of metagenomics dark matter	Study participants recorded their dietary intake using a seven-day food journal and provided three fecal samples. N = 16. Bifidobacterium was positively correlated with dietary protein intake; specifically, vegetable protein
Time of day and eating behaviors are associated with the composition and function of the human gastrointestinal microbiota	(13) Jennifer Kaczmarek et al.	2017	The goal was to determine whether human GI microbiomes and bacteria metabolites were associated with time of day or behavioral factors including eating frequency, percentage of energy consumed early in the day, and overnight-fast duration.	Acetate, protonate, and butyrate concentrations decreased throughout the day. Included 77 fecal samples from 28 participants. 7-day diet record.
Dietary Fiber and prebiotics and the gastrointestinal microbiota	(14) Hannah D. Holscher	2017	Review the current knowledge of the impact of fiber and prebiotic consumption on the composition and metabolic function of the human GI microbiota	Cross-sectional studies of human populations across the globe reveal that greater dietary fiber intake is associated with increase GI microbial diversity.
Determination of the in vivo prebiotic potential of a maize-based whole grain breakfast cereal: a human feeding study	(16) Andrew L. Carvalho-Wells et al.	2010	Determine the prebiotic potential of a breakfast cereal enriches with who grain derived from maize and to determine the impact of whole grain maize on colonic metabolic output bowel habit and on the fasted lipid profile	32 participants aged 20-51 with a BMI range of 20-30. after consumption of the WGM there was an increase in bifidobacterial. Increase in lactobacillus/Enterococcus during intervention and control. Non-significant increase after consumption of the control compared to baseline.

Whole-grain wheat breakfast cereal has a prebiotic effect on the human gut microbiota	(17) Adele Costabile et al.	2007	To determine the impact of whole grain wheat on the human intestinal microbiota compared to wheat bran	N=32. Double blind, randomized, placebo-controlled crossover study. Fecal samples were collected 5 different times over a 73-day period. Numbers of bifidobacterial were significantly higher during the ingestion of the whole grain compared to the whole bran treatment period. There was a significant increase in Bifidobacterium spp. numbers during whole grain intake compared to pre-whole grain.
Gut Microbiome composition is linked to whole grain-induced immunological improvements	(18) Ines Martinez et al.	2012	Characterize the impact of the incorporation of whole grains to an otherwise unrestricted diet on gut microbial ecology in healthy human subjects and to investigate whether a connection with metabolic and immunological improvements exist	Participants received one of three test meals with varying amounts of whole grains. A total of 28 participants were in the study. Whole grains have a measurable effect on gut microbiota composition. All three treatments received significantly increased the bacterial diversity. These results indicated an increase in community evenness, but not in total species richness.
Six-Week Consumption of a Wild Blueberry Powder Drink Increases Bifidobacterial in the Human Gut	(19) Stefano Vendrame et al.	2011	Repeated crossover dietary intervention on human subjects to observe the effects of while blueberry drink versus a placebo drink in modulating the intestinal microbiota.	Wild blueberries are a rich source of polyphenols and other compounds that are highly metabolized in the gut. Bifidobacterium spp. Significantly increased following the blueberry treatment. Lactobacillus acidophilus increased after both treatments.
Influence of red wine polyphenols and ethanol on the gut microbiota ecology and biochemical biomarkers	(20) Maria Isabel Queipo-ortuno et al.	2012	Evaluate the effect of a moderate intake of red wine polyphenols on select gut microbial groups implicated in host health benefits	Included ten healthy adult men between 45-50y. Fecal samples were taken at baseline and after the washout period at the end of each 20-day period (4 samples taken total per person)
Linking Long-Term Dietary Patterns with Gut Microbial Enterotypes	(21) Gary D. Wu et al.	2011	To determine the microbiome composition, change after 24 hours of initiating a high-fat/low-fiber diet	Enterotypes were strongly associated with long-term diets particularly protein and animal fat versus carbohydrates. 10 subjects participated in a controlled feeding study showed that the biome changed within 24 hours of a high fat/low fiber or low fat/high fiber diet.

High-protein, reduced-carbohydrate weight-loss diets promote metabolite profiles likely to be detrimental to colonic health	(22) Wendy R Russell et al.	2011	Assess the effect of diets with reduced carbohydrate and increased protein contents on metabolites considered to influence long-term colonic health, in particular the risk of colorectal disease	Diets that were high in protein and reduced carbs and fiber resulted in a decrease in fecal cancer-protective metabolites and increased concentrations of hazardous metabolites.
Microbial Fermentation of Dietary Protein: An important factor in Diet	(23) Natalie E. Diether and Benjamin P. Willing	2019	Focus on the compartment-specific effects of proteolytic fermentation in different segments of the intestine along with metabolites such as ammonia, p-cresol, and amines that may shape health	The effects of increased protein fermentation are not entirely clear, but high protein/low carbohydrate diets for weight loss have been shown to increase the proportions of phenylacetic acid from phenylalanine degradation and N-nitroso compounds, raising questions about the long-term effects of these diets on colonic health
Trimethylamine N-Oxide: The Good, the Bad and the Unknown	(24) Manuel T. Velasquez et al.	2016	To look into how Trimethylamine N-Oxide affects humans and contributes to other health conditions.	This paper discusses high plasma levels of TMAO show an increased risk of cardiovascular events and deaths being reported. TMAO levels increase with decreasing levels of kidney function.
The influence of diet on the gut microbiota	(25) Karen P. Scott et al.	2012	To understand the rapid progress towards understanding how diet can be used to modulate the composition and metabolism of the gut microbiota, allowing researchers to provide informed advice, that should improve long-term health status	This paper discusses the influence of short-term diet changes and antibiotic exposure. Relationship between birth route and microbiome makeup. Resistant starches and pre/probiotics.
The Impact of Dietary Fiber on Gut Microbiota in Host Health and Disease	(26) Kassem Makki et al.	2018	How dietary fiber impacts gut microbial ecology, host physiology, and health by specifically focusing on mechanisms by which a low-fiber diet disrupts the microbial ecosystem and leads to a predisposition to chronic inflammatory disease	This study compares the long-term intake of foods and the comparison of industrialized and non-industrialized human populations. This study also looked at the microbiome in children as well as specific nutrients.

Faecal microbiota composition in vegetarians: comparison with omnivores in a cohort of young women in southern India	(28) Jayakanthan Kabeerdoss et al.	2011	Compare the faecal microbiota of vegetarian and omnivorous young women in southern India	There was a total of 32 vegetarian and 24 non-vegetarian women who participated. There were not significant differences in background, BMI, and age between the groups. Total energy intake of complex carbs and Ca were higher in the omnivore group. Fecal levels of C. cocoides-E rectale and butyl-CoA CoA-transferase gene levels were higher in the omnivore group. All other microbial groups tested were similar between the two groups.
Butyrate: A Double-Edged Sword for Health?	(29) Hu Liu et al.	2018	Summarize the current knowledge on butyrate, especially its potential effects and possible mechanisms of action in relation to host gastroenteric health and obesity	Numerous in vitro and vivo studies have shown that butyrate plays an important role in modulating immune and inflammatory responses and intestinal barrier function. Butyrate is produced from dietary fibers through bacterial fermentation via 2 metabolic pathways. Butyrate can influence the immune response by affecting immune cell migration, adhesion, and cellular functions such as proliferation and apoptosis
Microbiota-Gut-Brain Axis: Modulator of Host Metabolism and Appetite	(30) Marcel van de Wouw et al.	2017	Focus on the diverse mechanisms through which the gut microbiota influences host metabolism, feeding behavior, and appetite as a crucial piece of the puzzle in conditions wherein food intake and body weight are dysregulated	A growing body of evidence indicates that there is a critical role for the microbiota in regulating different aspects of eating-related behavior, as well as behavioral comorbidities of eating and metabolic disorders
Formation of propionate and butyrate by the human colonic microbiota	(31) Petra Louis and Harry J. Flint	2017	To emphasize the important role played by cross-feeding of intermediary metabolites (in particular lactate, succinate, and 1,2-propanediol) between different gut bacteria	Acetate is a net fermentation product for most gut anaerobes that is also produced by reductive acidogenesis and almost invariably achieves the highest concentrations among the SCFA in the gut lumen. Butyrate is produced from carbohydrates via glycolysis from the combination of two molecules of acetyl-CoA to form acetoacetyl-CoA, followed by stepwise reduction to butyryl-CoA

Impact on Infants and Children

Several studies have been done that show differences in gut microbiota in children as young as 6 months of age. One study compared US Americans to African or South Americans. [11 32] The study found that regardless of age, the gut microbiota was different based on the regions where people were from. African children had a higher prevalence of Prevotella compared to European children. The Prevotella bacterium possesses a high fiber degrading potential which is important due to the typical diet of rural African population being high in fiber and complex carbohydrates. [32] It is widely believed that the gut begins colonizing immediately after birth, however emerging evidence is showing that an infant gut could begin colonizing by organisms in utero, although the biggest microbiota profile is shaped by the mode of delivery of the infant. Infants born vaginally are initially colonized by organisms of the maternal vagina such as Lactobacillus and Prevotella. Infants born through cesarean contain more of the maternal skin flora such as *Streptococcus, Corynebacterium*, and *Propionibacterium*. Another influencer of the infant microbiome is the infant diet. Breastmilk contains several bioactive compounds that are not available in infant formula. These compounds have a significant role in the nutrient digestion and absorption, immune protection, and anti-microbial defense. Human milk oligosaccharides provide a unique advantage for *Bifidobacterium sp.* which ferment the oligosaccharides resulting in health promoting short chain fatty acids such as butyrate. Regardless of the mode of delivery and infant diet, a child's microbiome is 40-60% similar to that of an adult by the age of three. [10] Creating a balance of the gut microbial composition can be done though symbiosis which promotes immune systems and protects against diseases. This can be achieved through the consumption of a balanced diet. Dysbiosis can happen due to an imbalanced diet and can cause dysregulation of the immune system which puts bodies at risk for inflammation and diseases. [6]

Medications

One major factor that affects the microbiota is the use of medications such as antibiotics. Antibiotics have different microbial spectrums that can affect the balance of bacteria in a variety of ways. In young children, the microbiota is still developing and therefore, the use of antibiotics can potentially have permanent negative effects on the microbiota. In adults it was found that the microbiota can be restored within one month of taking antibiotics. However, some strains of bacterial growth take years to recover which may have a lasting impact on human health. [11 33 34] Prescription medication such as those used to treat diabetes have been shown to have beneficial effects on the host microbiome, particularly metformin and berberine. It was shown that both medications shifted the overall gut microbiota reverting the effects of a high fat diet induced structural changes of the gut. The diversity of the gut was significantly reduced, but short chain fatty acid producing bacteria such as *Allobaculum, Bacteroides, Blautia, Butyricioccus,* and *Pharscolarctobacterium* were increased in individuals taking metformin and berberine. [2]

Table 3. Medications and impact on children references

Title	Author	Year Published	Objective	Primary Outcomes
The influence of antibiotics and dietary components on gut microbiota	(2) Ruth K. Dudek-Wicher et al.	2018	Summarize the knowledge of regarding the impact of different antibiotics causing such long-term consequences as decreased microbial diversity	The microbiome that resides in the human GI tract compromises a dynamic community that changes throughout a lifespan. There is a body of evidence that suggests the gut microbiota has to potential to be an important factor in shaping human health

Interaction between diet composition and gut microbiota and its impact on gastrointestinal tract health	(6) Shahid Riaz Rajoka et al.	2017	Report a comprehensive study of interactions between how microbiota and food affect human physiology and this, generate useful information for the prevention of multiple diseases	Human-associated microbial communities are crucial for proper development. Type and amount of foods and the effect it has on the microbiome. Types of bacteria present based on the diet consumed.
Role of the normal gut microbiota	(10) Sai Manasa Jandhyala et al.	2015	Review the recent evidence on the functions of the normal gut microbiota and the mechanistic insights into the execution of these pro-health functions	The normal gut microbiota comprises of two major phyla. The gut microbiota of a child resembles that of an adult by age 3. Several factors play a role in shaping the normal gut microbiota. Composition of the normal gut microbiota.
Contribution of diet to the composition of the human gut microbiota	(11) Daniela Graf et al.	2015	The aim of the review was to summarize the recently published evidence from human in vivo studies on the gut microbiota-modulating effects of diet	Food components provide substrates for the intestinal microbial metabolism. Bacteria are specialized in fermentation of different substrates. The microbiota is influenced by general lifestyle, host genetics, early colonization, medication, and health/disease
Impact of Diet in Shaping Gut Microbiota Revealed by a Comparative Study in Infants During the First Six Months of Life	(32) Wenguang Fan et al.	2014	To compare the fecal microbiota of breast-fed, formula fed, and mixed fed infants from Hebei Province, China	Proteobacteria was more abundant in FF and MF infants than BG infants. Firmicutes were highest in BF infants. Actinobacteria and Bacteroidetes were highest in BF infants and lowest in FF infants.
Resilience of the dominant human fecal microbiota upon short-course antibiotic challenge	(33) M.F. De La Cochetiere et al.	2005	Assess the ability of the human fecal microbiota to return to its original dominant species profile after a 5-day course of amoxicillin, one of the most prescribed antibiotics in Europe	Dominant species of the human fecal microbiota were markedly modulated within 2-3 days of an antibiotic treatment. The dominant fecal microbiota tended to return to its initial profile within 60 days following the 5-day treatment of 500mg/day. Individual responses varied.
The pervasive effects of an antibiotic on the human gut microbiota, as revealed by deep 16S rRNA sequencing	(34) Les Dethlefsen et al.	2008	To analyze the bacterial community composition in a time series of stool samples obtained from three healthy individuals before, during, and after a short course of the antibiotic ciprofloxacin	Ciprofloxacin treatment influenced the abundance of about 1/3 of the bacterial taxa in the gut, decreasing the taxonomic richness, diversity, and evenness of the community. The magnitude of this effect varied among individuals and some taxa showed interindividual variation in the response to ciprofloxacin

Long Term Goals: Going forward, the long-term goal is to learn how specific diets and lifestyle factors influence the gut microbiome. The purpose of this paper is to report the influence of diet on the gut microbiome from the current literature. This information is critical in gaining a better understanding of how the diet can influence the gut microbiome. Based on this information we are able to identify the gaps in understanding of this topic and where more research is needed. It is clear that the human diet can have a major influence on the gut microbiome as it continues to be the most important determinant in shaping the composition, diversity, and richness of the biome. Future research needs to include long term feeding studies that specifically look at all factors in a person's diet and lifestyle to see how the microbiome can be altered by specific foods. More research needs to be done on specific strains of bacteria and their role in a person's health and how the microbiome changes over the course of a person's life and other factors that can influence changes. In general, intake of a diet rich in fruits, vegetables, and fiber is associated with a higher level of diversity in the gut microbiota. Having a higher abundance of insoluble fiber containing carbohydrates creates higher levels of the Firmicutes phylum such as *Ruminococcin bromii, Roseburia,* and *Eubacterium rectale*. Even a short manipulation of the diet that includes animal-based produces resulted in a decrease in the abundance of the Firmicutes bacteria showing that dietary manipulation can have a substantial impact on the gut microbiome. [10] We can conclude that although the research surrounding the diet and its influence on the gut microbiome is growing, there is still a need for further research.

References:

1. Science. Metagenomic Analysis of the Human Distal Gut Microbiome Secondary Metagenomic Analysis of the Human Distal Gut Microbiome 2006. http://science.sciencemag.org/content/312/5778/1355.

2. Dudek-Wicher RK, Junka A, Bartoszewicz M. The influence of antibiotics and dietary components on gut microbiota. Prz Gastroenterol 2018;**13**(2):85-92 doi: 10.5114/pg.2018.76005[published Online First: Epub Date]|.

3. <Systematic Review on Effects of Diet on Gut Microbiota .pdf>.

4. Singh RK, Chang HW, Yan D, et al. Influence of diet on the gut microbiome and implications for human health. J Transl Med 2017;**15**(1):73 doi: 10.1186/s12967-017-1175-y[published Online First: Epub Date]|.

5. <Influrnce of High-Fat Diet on Gut Microbiota.pdf>. doi: 10.1097/MCO[published Online First: Epub Date]|.

6. Riaz Rajoka MS, Shi J, Mehwish HM, et al. Interaction between diet composition and gut microbiota and its impact on gastrointestinal tract health. Food Science and Human Wellness 2017;**6**(3):121-30 doi: 10.1016/j.fshw.2017.07.003[published Online First: Epub Date]|.

7. Quigley EMM. Gut microbiome as a clinical tool in gastrointestinal disease management: are we there yet? Nature Reviews Gastroenterology & Hepatology 2017;**14**(5):315-20 doi: 10.1038/nrgastro.2017.29[published Online First: Epub Date]|.

8. Conlon MA, Bird AR. The Impact of Diet and Lifestyle on Gut Microbiota and Human Health. Nutrients 2015;**7**(1):17-44 doi: 10.3390/nu7010017[published Online First: Epub Date]|.

9. Flint HJ, Scott KP, Louis P, Duncan SH. The role of the gut microbiota in nutrition and health. Nature reviews. Gastroenterology & hepatology 2012;**9**(10):577-89 doi: 10.1038/nrgastro.2012.156[published Online First: Epub Date]|.

10. Jandhyala SM, Talukdar R, Subramanyam C, Vuyyuru H, Sasikala M, Nageshwar Reddy D. Role of the normal gut microbiota. World J Gastroenterol 2015;**21**(29):8787-803 doi: 10.3748/wjg.v21.i29.8787[published Online First: Epub Date]|.

11. Graf D, Di Cagno R, Fak F, et al. Contribution of diet to the composition of the human gut microbiota. Microb Ecol Health Dis 2015;**26**:26164 doi: 10.3402/mehd.v26.26164[published Online First: Epub Date]|.

12. King CH, Desai H, Sylvetsky AC, et al. Baseline human gut microbiota profile in healthy people and standard reporting template. PLoS One 2019;**14**(9):e0206484 doi: 10.1371/journal.pone.0206484[published Online First: Epub Date]|.

13. <(2) Time of Day and Eating Behaviors .pdf>. doi: 10.3945/[published Online First: Epub Date]|.

14. Holscher HD. Dietary fiber and prebiotics and the gastrointestinal microbiota. Gut Microbes 2017;**8**(2):172-84 doi: 10.1080/19490976.2017.1290756[published Online First: Epub Date]|.

15. <Guidelines on Nutrition Labeling.pdf>.

16. Carvalho-Wells AL, Helmolz K, Nodet C, et al. Determination of the in vivo prebiotic potential of a maize-based whole grain breakfast cereal: a human feeding study. The British journal of nutrition 2010;**104**(9):1353-6 doi: 10.1017/s0007114510002084[published Online First: Epub Date]|.

17. Costabile A, Klinder A, Fava F, et al. Whole-grain wheat breakfast cereal has a prebiotic effect on the human gut microbiota: a double-blind, placebo-controlled, crossover study. The British journal of nutrition 2008;**99**(1):110-20 doi: 10.1017/s0007114507793923[published Online First: Epub Date]|.
18. Martinez I, Lattimer JM, Hubach KL, et al. Gut microbiome composition is linked to whole grain-induced immunological improvements. The ISME journal 2013;**7**(2):269-80 doi: 10.1038/ismej.2012.104[published Online First: Epub Date]|.
19. Vendrame S, Guglielmetti S, Riso P, Arioli S, Klimis-Zacas D, Porrini M. Six-week consumption of a wild blueberry powder drink increases bifidobacteria in the human gut. Journal of agricultural and food chemistry 2011;**59**(24):12815-20 doi: 10.1021/jf2028686[published Online First: Epub Date]|.
20. Queipo-Ortuno MI, Boto-Ordonez M, Murri M, et al. Influence of red wine polyphenols and ethanol on the gut microbiota ecology and biochemical biomarkers. The American journal of clinical nutrition 2012;**95**(6):1323-34 doi: 10.3945/ajcn.111.027847[published Online First: Epub Date]|.
21. Wu GD, Chen J, Hoffmann C, et al. Linking long-term dietary patterns with gut microbial enterotypes. Science (New York, N.Y.) 2011;**334**(6052):105-8 doi: 10.1126/science.1208344[published Online First: Epub Date]|.
22. Russell WR, Gratz SW, Duncan SH, et al. High-protein, reduced-carbohydrate weight-loss diets promote metabolite profiles likely to be detrimental to colonic health. The American journal of clinical nutrition 2011;**93**(5):1062-72 doi: 10.3945/ajcn.110.002188[published Online First: Epub Date]|.
23. Diether NE, Willing BP. Microbial Fermentation of Dietary Protein: An Important Factor in Diet(-)Microbe(-)Host Interaction. Microorganisms 2019;**7**(1) doi: 10.3390/microorganisms7010019[published Online First: Epub Date]|.
24. Velasquez MT, Ramezani A, Manal A, Raj DS. Trimethylamine N-Oxide: The Good, the Bad and the Unknown. Toxins (Basel) 2016;**8**(11) doi: 10.3390/toxins8110326[published Online First: Epub Date]|.
25. Scott KP, Gratz SW, Sheridan PO, Flint HJ, Duncan SH. The influence of diet on the gut microbiota. Pharmacol Res 2013;**69**(1):52-60 doi: 10.1016/j.phrs.2012.10.020[published Online First: Epub Date]|.
26. Makki K, Deehan EC, Walter J, Backhed F. The Impact of Dietary Fiber on Gut Microbiota in Host Health and Disease. Cell Host Microbe 2018;**23**(6):705-15 doi: 10.1016/j.chom.2018.05.012[published Online First: Epub Date]|.
27. Society V. What is a Vegetarian? . Secondary What is a Vegetarian? 2016. https://www.vegsoc.org/definition.
28. Kabeerdoss J, Devi RS, Mary RR, Ramakrishna BS. Faecal microbiota composition in vegetarians: comparison with omnivores in a cohort of young women in southern India. The British journal of nutrition 2012;**108**(6):953-7 doi: 10.1017/s0007114511006362[published Online First: Epub Date]|.
29. Liu H, Wang J, He T, et al. Butyrate: A Double-Edged Sword for Health? Adv Nutr 2018;**9**(1):21-29 doi: 10.1093/advances/nmx009[published Online First: Epub Date]|.
30. van de Wouw M, Schellekens H, Dinan TG, Cryan JF. Microbiota-Gut-Brain Axis: Modulator of Host Metabolism and Appetite. J Nutr 2017;**147**(5):727-45 doi: 10.3945/jn.116.240481[published Online First: Epub Date]|.

31. Louis P, Flint HJ. Formation of propionate and butyrate by the human colonic microbiota. Environ Microbiol 2017;**19**(1):29-41 doi: 10.1111/1462-2920.13589[published Online First: Epub Date]|.

32. De Filippo C, Cavalieri D, Di Paola M, et al. Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa. Proceedings of the National Academy of Sciences of the United States of America 2010;**107**(33):14691-6 doi: 10.1073/pnas.1005963107[published Online First: Epub Date]|.

33. De La Cochetiere MF, Durand T, Lepage P, Bourreille A, Galmiche JP, Dore J. Resilience of the dominant human fecal microbiota upon short-course antibiotic challenge. Journal of clinical microbiology 2005;**43**(11):5588-92 doi: 10.1128/jcm.43.11.5588-5592.2005[published Online First: Epub Date]|.

34. Dethlefsen L, Huse S, Sogin ML, Relman DA. The pervasive effects of an antibiotic on the human gut microbiota, as revealed by deep 16S rRNA sequencing. PLoS biology 2008;**6**(11):e280 doi: 10.1371/journal.pbio.0060280[published Online First: Epub Date]|.