

MetLife

GUT HEALTH: FOCUSING ON OUR INNER ECONOMY

A new approach to employees' health and wellness



Contents

The most important health issue you've never heard of: gut microbes	3
Let's dive into our gut (and see who's home)	4
Interesting facts about our gut bacteria	6
Our evolving gut microbiome	7
Gut bacteria: our body's busiest workers	9
Aiding digestion	9
Supporting our immune system	10
Manufacturing vitamins	10
Augmenting our brain	10
Affecting depression, anxiety and other mental conditions	11
Affecting obesity and diabetes	12
Regulating body mass index and cardiovascular disease	12
Affecting drug efficacy	12
Gut bacteria: big breakthroughs from little critters	13
Inflammatory bowel disorders	13
Obesity	13
Cancer treatments	13
Recurrent Clostridium difficile infection	14
Prebiotics and probiotics	14
Diabetes	14
Tips for individuals and organisations to cultivate a friendship with our microbiomes	15
A few final thoughts	22

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The most important health issue

you've never heard of:

gut microbes



Scientists have made major breakthroughs to understand and manage the gut microbiome to improve our health, moods and well-being. These developments could revolutionise the way we approach and treat diseases.⁴

What if there were a multifunctional organ inside every person that the scientific community only recently started to acknowledge? What if this organ held the key to improved health and wellness – and taking care of it was one of the best ways to stay healthy and fight diseases?

What if that organ inside us weren't even human?

Well, it's not. We're talking about the microbiome, the vast colonies of bacteria and other microorganisms living on and in our bodies. 95% of these cells can be found in our gut and it's a multi-trillion-strong population of microbes that fulfils an incredible array of roles.¹

In a very real way, then, it's an additional organ inside our gut.

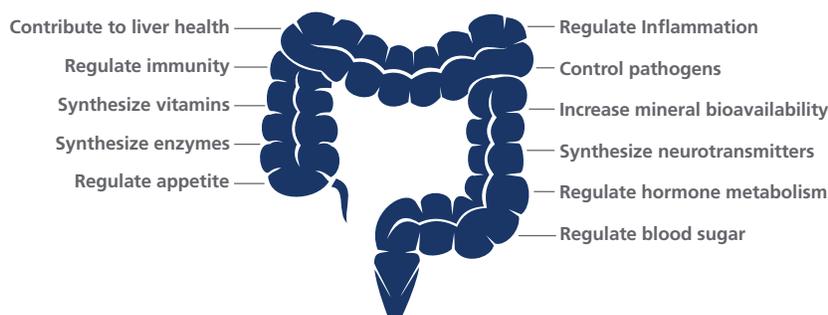
A growing body of research is now telling us that these gut microbes play a crucial role in regulating our moods, helping us adapt to our environment, giving us energy and, most importantly resisting disease. Even simple guidance around maintaining healthy gut microbes – through diet and behaviour – could drastically improve resistance to chronic disease, acute illness and stress, as well as wakefulness, energy and overall well-being.^{2,3}

The impact of these developments for both individuals and organisations could be profound. Within 24 hours of changing diet and behaviour, our gut microbiome can show signs of improvement – so anyone can take steps for immediate results.⁵

Over time, this could result in a happier, healthier workforce with lower incidence of both acute and chronic illness – driving down medical costs, and increasing engagement at work.

So let us explore the gut a little deeper – and see exactly how and why the microbiome is reshaping medical thinking.

FUNCTIONS OF THE GUT FLORA



Let's dive into our gut

(and see who's home)

While you were right to think that stress, sleep and exercise were important to wellness, you will want to add gut health to your list of good health priorities.

Microbes live all over our bodies. Some are passive; others have helpful or harmful effects on us. They live on our skin, inside our mouth and nose, in our urinary tract and, of course, in our intestines.

Inside our 7.6 metres of gut, we see legions of simple creatures – bacteria, fungi, viruses and protozoa. They contribute so much to human biology that it is difficult to say where the body ends and the microbes begin. That is why several initiatives, such as the Human Microbiome Project, are on a mission to characterise the human microbiota in its entirety.⁶

No wonder experts now consider the microbiome to be an 'organ'. It is an 'acquired' organ however: babies are born sterile. Intestine colonisation starts at birth and evolves as we grow.⁷ Each person's microbiome is influenced by genetics, age, sex, diet and lifestyle – and is unique to them.

Microbes all over our body turn out to be critical in arranging a person's unique attributes. For example, mosquitoes bite some people more often than others. One of the reasons for this has been attributed to the microbes on our skin. One study found that a diverse colony of microbes on our skin actually seem to *repel* mosquitoes, whereas a high density of just a small number of certain microbes seems to *attract* them.⁸ So, it's true that some people's unique skin bacteria actually drive mosquitos away!

Gut microbes can even alter the way genes work in the gastro-intestinal tract. Scientists have found that gut microbiota calibrate many functions particularly those that are involved in immunity, nutrient absorption, energy metabolism and intestinal barrier function.⁹

When our microbial communities are disturbed, we can see a big increase in disease susceptibility.¹⁰ Studies have shown links between this imbalance in the gut and chronic inflammation and metabolic disorders, which can lead to obesity and diabetes.¹⁰ Changes to the gut microbiome have been associated with infections, inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS).¹⁰

In other words, it's becoming apparent that there may be a direct link between the health of the gut and resistance to disease, how we process food, how alert and energetic we are – and how well our bodies keep out pathogens.

Jargon Buster



GUT MICROBIOTA (also called 'gut flora' or 'gut microbiome') are the legions of simple creatures – bacteria, fungi, viruses, archaea and protozoa (also called the ecological community) that share our body space.¹



PREBIOTICS are fibres or carbohydrates which perform the direct role of nourishing gut bacteria. While probiotics introduce good bacteria into the gut, prebiotics act as a fertilizer for the good bacteria that's already there. They help our good bacteria grow, improving the good-to-bad bacteria ratio. This ratio has been shown to have a direct correlation to our health and overall well-being, from our stomach to our brain.¹¹



PROBIOTICS are live micro-organisms which, when administered in adequate amounts, can confer a health benefit on the host.¹¹ Some examples are *Lactobacillus* and *Bifidobacterium*.



CLOSTRIDIUM PERFRINGENS is a spore-forming bacterium that is found in many environmental sources as well as in the intestines of humans and animals. Commonly found on raw meat and poultry, it prefers to grow in conditions with very little or no oxygen, and under ideal conditions can multiply very rapidly. Some strains produce a toxin in the intestine that causes illness.¹²



DYSBIOSIS happens when there's a microbial imbalance inside the body. Good species of microbes can become under-represented and other (often bad) microbes dominate.¹³



ENTERIC NERVOUS SYSTEM (ENS), or the 'second brain', is embedded in the lining of the gastrointestinal system and can operate independently of the brain and the spinal cord.¹⁴



PATHOGENS are bad microorganisms that can cause disease. A healthy gut microbiome helps crowd these critters out and fights their effects.¹⁵



SHORT CHAIN FATTY ACIDS (SCFA) are created by gut microbes and are key sources of energy, as well as helping maintain gut tissue.¹⁶



TRIMETHYLAMINE N-OXIDE (TMAO) is a compound produced by bacteria that appears to correlate with risk of heart disease.¹¹

Interesting facts

about our gut bacteria

A huge quantity (hundreds of trillions) of bacteria and other microorganisms inhabit our intestines fulfilling key functions for our health and well-being.¹⁷

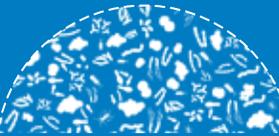
Gut microbiota's weight can reach up to



95% of our bacteria are located in the gastrointestinal (GI) tract



There are up to 100 trillion bacteria living in our gut.¹⁸

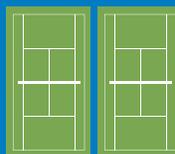


At least 1,000 unique species of bacteria can be found in the human gut.¹⁸

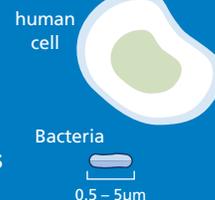
A gut microbiome contains 3 million genes – 150 times more unique genes than its human host.¹⁹



The GI tract surface is as big as 2 tennis courts
400 m²



Bacteria are **10 to 50** times smaller than human cells



The composition of our gut microbiota is **unique** to each individual, just like our fingerprints.



Laid end to end, our body's bacteria would circle the Earth **2.5 times**



Cell densities in the colon are the highest recorded for any known ecosystem.²⁰



Altering our diet changes the balance of our gut microbiome within hours.²¹



The gut microbiome has a direct effect on the central nervous system, creating what scientists call a 'gut-brain axis'. This enteric nervous system (ENS) contains more neurons than the human spinal column or central nervous system itself.²²

Our evolving gut microbiome



Although behaviours – like eating and sleeping well – are important, the make-up of an individual's gut bacteria starts very early and is affected by a range of factors.

The gut microbiome is a complex and highly influential organ that is a crucial player in how often and how seriously we're affected by a range of both acute and chronic conditions. But what do we know about how to build and support a balanced and diverse gut microbiome?

Here's a quick run-down of natural behaviours that influence life in our gut – and where we might support new behaviours to improve gut health.



The womb

Babies are born 'sterile', but maternal diet, infection, prenatal stress and microbial infections during pregnancy have been associated with neurodevelopmental disorders such as autism, attention deficit hyperactivity disorder (ADHD) and schizophrenia.²³ Maternal health plays a key role in microbiota development and in neurodevelopment in babies.²³



Mode of birth

A study of infants delivered by Caesarean section revealed a lack of one of the major groups of gut bacteria compared with the babies who were born vaginally.²⁴ The total range of bacteria among infants delivered by C-section was also lower. These infants also had lower levels of Th1 cells in their blood, which are critical for defense against microbial infections and immune responses, making them more susceptible to developing allergies as well as asthma, gastrointestinal disorders, obesity and diabetes.²⁵ In early 2016, researchers began experiments to offset this effect using a swab in the birth canal that can be applied to the baby after C-section to kick-start their microbiome.²⁶



Breastfeeding

Robust gut microbiota build up the immune system.²⁷ Oligosaccharides present in breast milk promote the growth of *Lactobacillus* and *Bifidobacterium*, which can strengthen or promote development of the immune system and may help prevent conditions such as eczema and asthma.²⁶



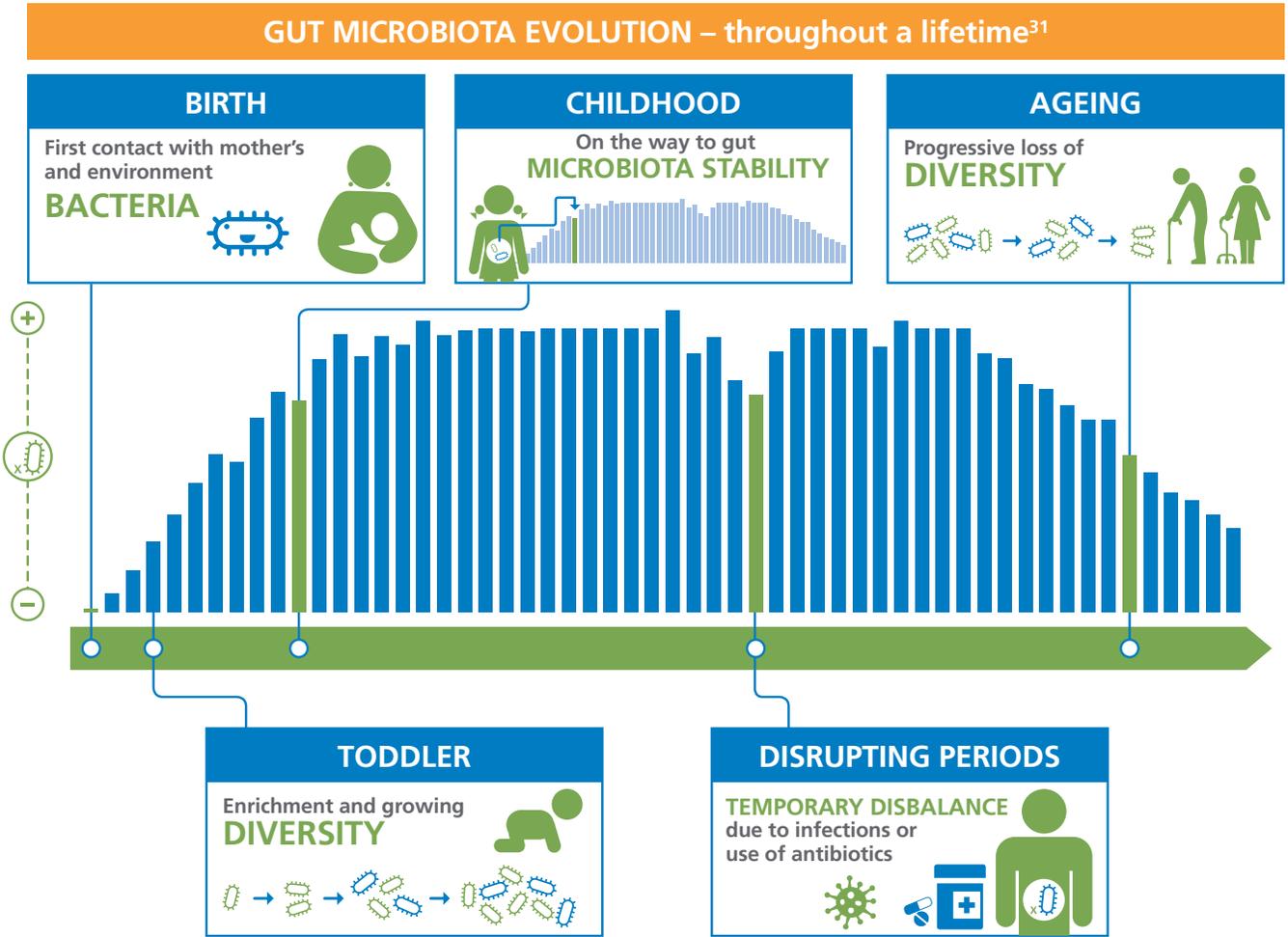
Life events

Major life events – like puberty, the ovarian cycle, pregnancy and menopause – can affect gut bacteria. Increasing amounts of data are beginning to show a clear link between the gut microbiome and skin conditions, such as acne.²⁷ A Canadian study found that alterations to the gut microbiota during puberty can influence the development to the brain and may contribute how various psychiatric illnesses are manifested.²⁸



Growing old

Essential *Bacteroidetes* tend to dominate the gut microbiome during youth, but numbers decline significantly in older adults.²⁹ Although the consequences and reason for this change are not yet clear, research indicates that microbial populations could be impacted by the way elderly live.²⁹ One study of residents in long-term care facilities found a high prevalence of *Clostridium perfringens* (*C. perfringens*), potentially toxic bacteria, and a low prevalence of *Bifidobacterium* and *Lactobacillus*, identified as 'good bacteria'.²⁹ The elderly living in long-term care facilities were generally found to have a reduced microbial diversity compared to those living at home or in a 'mainstream' community.³⁰



Gut bacteria: our body's busiest workers



Let's look at the most important roles our gut bacteria plays.



Aiding digestion

Beneficial bacteria help manage with foods that stomach and small intestine haven't yet digested. They also can correct pH balance in the gut, break down foods and help prevent the build-up of harmful bacteria. The most plentiful bacteria type in the small intestine, *Lactobacillus*, helps ferment indigestible carbohydrates and break down sugars. *Lactobacillus* also produce lactic acid, which supports our immune system. The *Bifidobacterium* group does a similar job in the large intestine, or colon.

Fermentation of fibre and protein by large bowel bacteria produce short chain fatty acids (SCFA) which act as key sources of energy, and help maintain gut tissue integrity.¹⁶ Microbes are vital for breaking down nutrients, particularly complex polysaccharides like cellulose (an essential dietary fibre).¹⁶ For example, specific bacteria are how specific acids in grains are broken down, releasing minerals such as magnesium and phosphate that build tissues such as bone.¹⁶

The gut microbiome plays a crucial role in the gastrointestinal (GI) tract. It helps support the balance in our immune systems and regulates our energy levels.⁷

Stop when you're full

One of the simplest dieting tips is 'stop eating when you're full'. It's harder than it sounds, especially when people are juggling busy lives and reacting to a wide-set of social and environmental factors – and not listening to their bodies. Or, perhaps more accurately, their gut microbiome.

We now know that when animals eat, gut bacteria numbers spike. The rise in this bacteria then sends signals to their host to stop eating. Researchers have reported that *E. coli* bacteria, often thought of as bad bacterium, produce proteins that stimulate the release of so-called satiety hormones that curb eating in mice and rats.³² This suggests that the growth and activity of the microbiome might specifically *regulate* appetite and feeding behaviour. Maintaining a healthy gut microbiome – and listening to it – may be a great way to eat healthier.



Psychological factors have an impact upon physical factors, such as:

- the movements and contractions of the GI tract.³⁵
- causing inflammation, pain, and other bowel symptoms.³⁵



Supporting our immune system

Microbes act as a physical barrier, protecting our gut, plugging holes in the lining and joining together against encroaching pathogens. If SCFA (which are extremely useful, but only within the gut) reach our circulation, for example, they reduce immune function and inflame sensitive tissues.¹⁷

Many bacteria (some *E. coli* strains, for example) can produce toxins or cause diarrhoea.¹⁶ But usually good gut bacteria keep them in check. Others, such as *Faecalibacterium prausnitzii*, may produce anti-inflammatory compounds called 'butyrates', which can stop colon cells from eating themselves or dying off.³³



Manufacturing vitamins

By producing various metabolites, gut microbes help with the production of some vitamins – particularly vitamin K (needed for blood clotting) and the group of B vitamins (needed for keeping our nervous system healthy and turning food into energy).³⁴



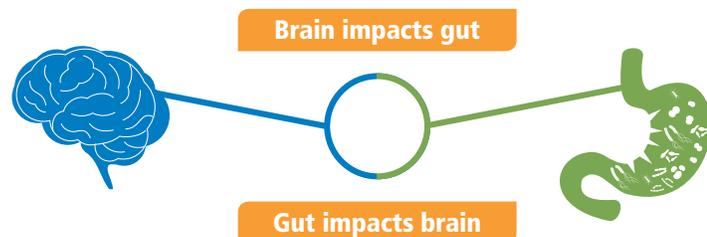
Augmenting our brain

Most of us can relate to the experience of having butterflies in our stomach or a visceral gut-wrenching feeling. We are even told not to ignore our 'gut-instinct' when making a decision. Our gut microbiota play a vital role in our physical and psychological health via a neural network: the enteric nervous system (ENS), a complex system of about 100 million nerves found in the lining of the gut.¹⁴

The ENS is sometimes called the 'second brain', and it actually arises from the same tissues as our central nervous system (CNS) during foetal development. Therefore, it has many structural and chemical parallels to the brain. In a miraculously orchestrated symphony of hormones, neurotransmitters, and electrical impulses through a pathway of nerves, both 'brains' communicate back and forth.¹⁴

The ENS produces a lot of neurotransmitters, which are chemicals released by nerve cells to send signals to other nerve cells, as well as about 95% of our serotonin and half of our dopamine.

Given how closely the gut and brain interact, it is becoming clear that emotional and psychosocial factors like stress can trigger symptoms in the gut. This is especially true in cases when the gut is acting up and there are no obvious physical causes.





Affecting depression, anxiety and other mental conditions

Poor gut health has been implicated in neurological and neuropsychiatric disorders.³⁶ Disturbances in gut health have been linked to multiple sclerosis, autistic spectrum disorders, and Parkinson's disease.^{37, 38, 39} This is potentially related to pro-inflammatory states caused by gut microbial imbalance.

Further, there is new research that throws light on depression as an inflammatory disorder mediated by poor gut health. Scientists discovered that mice with some features associated with autism had much lower levels of a common gut bacterium called *Bacteroides fragilis* (*B. fragilis*) than did normal mice. They were stressed, antisocial, and had the same gastrointestinal symptoms often associated with autism.⁴⁰ Interestingly enough, when the scientists fed the mice *B. fragilis*, they found that the mice's symptoms reversed.

By tinkering with the gut's bacterial residents, scientists have changed the behaviour of lab animals and human test groups.

In fact, multiple animal studies have shown that manipulating the gut microbiota in some way can produce behaviours related to anxiety and depression.



SOCIAL

Anxious mice became bold and shy mice became social when fed *B. fragilis*.²⁵



DEPRESSION

Rats inoculated with bacteria from depressed people developed signs of depression themselves.⁴¹



BRAIN ACTIVITY

Eating specific kinds of bacteria may change brain activity and ease anxiety.²⁶

Though preliminary, such results suggest that the right bacteria in our gut could brighten mood and perhaps even help combat mental disorders including anxiety and depression. Scientists are amassing evidence that they hope will lead to 'psychobiotics'-bacteria-based drugs made of live organisms that could improve mental health.

BACTERIA THAT MAKE BRAIN CHEMICALS⁴²

TYPE OF BACTERIA	NEURAL MESSENGERS
BACILLUS	Dopamine, norepinephrine
BIFIDO-BACTERIUM	Gamma-aminobutyric acid (GABA)
ENTEROCOCCUS	Serotonin
ESCHERICHIA	Norepinephrine, serotonin
LACTOBACILLUS	Acetylcholine, GABA
STREPTOCOCCUS	Serotonin



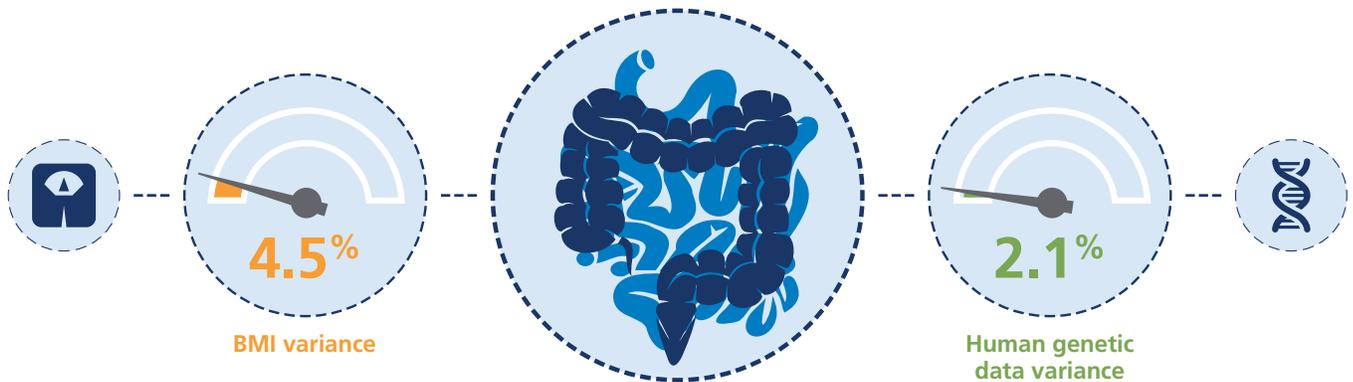
Affecting obesity and diabetes

According to the World Health Organization (WHO), obesity has nearly doubled worldwide since 1980.⁴³ Every year, it kills 3.4 million people.⁴⁴ New evidence suggests gut bacteria may alter the way we store fat, how we balance glucose levels and even how we respond to hormones that make us feel hungry or full. The wrong mix of microbes might actually set us up for obesity and diabetes. Studies have found that the gut microbiome in lean people is plentiful and diverse enough to seem like an internal rain forest, brimming with many species. In obese people, however, the gut microbiome is less diverse – more like a stagnant pond where relatively few species survive or are dominant.⁴⁵



Regulating body mass index (BMI) and cardiovascular disease

Researchers have found a connection between gut microbiota and cardiovascular disease – namely abnormal blood lipid levels and high BMI. In a study of 893 subjects, gut microbiota was shown to explain a 4.5% variance in BMI while human genetic data only explained 2.1% of the variance. This supports the notion that the gut microbiota should be a 'partner' in helping manage metabolic syndrome which is associated with developing cardiovascular disease and type 2 diabetes.⁴⁶



Affecting drug efficacy

We now know that gut bacteria is involved in the processing of over 30 U.S. Food and Drug Administration (FDA)-approved medicines.⁴⁷ That means a healthy gut microbiome ensures drugs work as they are supposed to – and an imbalance in gut bacteria can change that effectiveness. Similarly, certain drugs can themselves bring about a change to the composition of the gut microbes. An animal study from the Perelman School of Medicine at the University of Pennsylvania showed that indomethacin, a non-steroidal anti-inflammatory drug (NSAID) similar to ibuprofen and naproxen, changed the composition of gut microbes, which in turn reduced its own effectiveness.⁴⁸

Gut bacteria: big breakthroughs from little critters



Microbiologists are excited by the opportunity recent studies in this area present, including the food and pharmaceutical industries, as gut microbiology potentially offers huge impacts in a number of areas. Here are a few areas where today's ground-breaking research could make a big difference tomorrow:



Inflammatory bowel disorders (IBD)

Imbalanced bacterial microbiota are now thought to be a major factor in IBD. *B. fragilis*, for example, protects animals from colitis caused by the bacterium *Helicobacter hepaticus*. We might soon be able to harness molecules that modify the immune response via the gut microbiome for therapies for human inflammatory disorders.⁴⁹



Obesity

A family of microbes called *Christensenellaceae* was found to be more abundant in low weight people than in obese people, and in experiments has even helped protect mice from weight gain. In theory, these bacteria could be used as a probiotic in elementary vehicles such as yoghurt to prevent weight gain. Scientists at Vanderbilt University carried out a study with rodents in which they modified a strain of probiotic bacteria to produce high amounts of a hormone called NAPE, which sends a message of feeling full to the brain.⁵⁰ Treated mice ate less, gained less weight and even had fewer markers for diabetes.



Cancer treatments

The presence of certain types of gut microbes in mice can boost the anti-tumour effects of cancer immunotherapy, according to two published studies.^{51,52} Patients' responses to cancer immunotherapies vary, but we haven't been sure why. Studies show that certain types of gut microbes in mice can boost the anti-tumour effects of these treatments – and the gut microbiota could be critical for regulating the immune system to encourage it to fight cancer.⁵¹

Studies show that certain types of gut microbes in mice can boost the anti-tumour effects of these treatments – and the gut microbiota could be critical for regulating the immune system to encourage it to fight cancer.⁵¹

Link between gut bacteria and breast cancer⁵³

Did you know there are bacteria living in women's breast tissue that may affect their health? Researchers found that women with breast tumours had a different mix of bacteria living in their breast tissue compared with woman who did not have tumours. By isolating the microbes found in the diseased breast tissue, researchers proved that these microbes could cause DNA damage to normal breast tissue DNA. DNA damage can lead to breast cancers.

After giving women probiotics, a study found the types of bacteria contained in probiotics in the women's breast tissue. It is thought that immune cells in the gut may pick up the probiotics and transport them to the breast.

Research exploring the bacteria of the breast and how they may impact women's breast cancer risk is still in its infancy, but promises new breakthroughs in our fight against breast cancer.



Recurrent *Clostridium difficile* (C. diff) infection

C. diff colitis is an infection of the colon by the bacterium *C. diff*, which produces toxins that can damage the lining of the colon bringing fever, diarrhoea and abdominal pain. It's common in those using antibiotics, which kill off the gut bacteria that keep *C. diff* in check. An alternative treatment could be faecal transplants, reintroducing a healthy diversity of bacteria via colonoscopy. In a 2014 study at Massachusetts General Hospital, frozen faecal matter cleared up diarrhoea in 18 out of 20 *C. diff* patients.⁵⁴



Prebiotics and probiotics

Prebiotics are dietary supplements that promote bacterial growth by providing an energy source indigestible by the host. They have been shown to change the composition of the gut microbiome, improve glucose tolerance and lower the levels of blood triglycerides and body fat in rodents.⁵⁵ They have a similar effect to gastric bypass surgery in increasing the number of microbes of the genus *Akkermansia*, which researchers are testing as a supplement in obese patients.⁵⁶



Fighting disease with yoghurt

Probiotics are live bacterial cultures embedded in pills or 'active' yoghurt. There is mounting evidence that selected probiotic strains can provide health benefits to their human hosts. They're also a new way to improve maternal metabolic and pregnancy outcomes – such as minimising gestational diabetes mellitus (GDM), one of the most frequent complications of pregnancy. Probiotics may be a new way of treating respiratory tract infections, too – although more work is needed to understand how.⁵⁷



Diabetes

A recent study found that microbial changes that occur before the onset of type 2 diabetes could be used for early diagnosis and intervention.⁵⁸ Shifts in the gut microbial communities prior to the full disease may be either causal or an early correlative indicator.



Tips for individuals and organisations to cultivate a friendship with our microbiomes



We can see that our gut bacteria can have a direct effect on health, energy levels and even happiness. We know that the make-up of those gut bacteria is shaped by many factors, from what we eat to the drugs we take. So why should this matter to us? What does it have to do with the workplace?

Everything, actually.

It's hard to think of any other single aspect of health – diet, exercise or even stress management – that on its own might have a more significant impact on employee happiness, energy and uptime than a healthy gut microbiome.

Great gut health can mean fewer days lost to illness and lower healthcare costs and gut health can be a yardstick for how well all those other factors are contributing to a healthy workforce.

So how might individuals be encouraged to care more about and cultivate their gut?



Watch our medicine intake⁵⁹

As we have seen that taking antibiotics and/or painkillers can disrupt our personal microbiome. While pharmaceuticals have proven to be modern miracles in medicine, it's important to understand their impact on our microbiome. Maybe we should reconsider whether taking an additional painkiller is really necessary, whenever we find ourselves reaching into our medicine cabinet.

- **Use antibiotics judiciously**

One of the unfortunate side effects of taking antibiotic drugs is that they are not selective in choosing which bacteria to kill. Good bacterial colonies in the gut die along with the bad.⁶⁰

According to a study by the Centers for Disease Control and Prevention (CDC), nearly a third of antibiotics in the United States are inappropriately prescribed.⁶¹

A study found that just one week-long course of antibiotics radically changed the gut microbiome, with some gut bacteria taking up to a year to recover from a course of antibiotics.⁶²



In the US, about **47 MILLION** patients received the wrong treatment for colds, sore throats, bronchitis and flu.⁶¹

Always consult a physician before changing medicine intake.



Antibiotic-resistant pathogens cannot discern between bacteria that are beneficial for us and those that are not. This problem is not limited to the US. Awareness campaigns on the risks of taking antibiotics for minor complaints can help reduce the number of inappropriately taken antibiotics, as the UK government showed in 2014.⁶³

Spanish scientists showed that prolonged exposure to antibiotics may lead to weight gain, obesity and even diabetes.⁶⁴ The study showed that people treated with antibiotics show metabolic behaviour similar to that of obese people or those with a high BMI. The direction of this research is interesting as it could one day lead to diets, including probiotic supplements, adjusted to each individual's gut microbiome to minimise the impact of antibiotics.

- **Reduce painkiller consumption**

Millions of us find relief with over-the-counter painkillers for aches and pains. Globally, NSAIDs are the most common group of drugs used to reduce pain associated with inflammation.⁶⁵ This could be the inflammation and pain related to premenstrual cramping, or it could be used to reduce chronic inflammation, such as arthritis.⁶⁶

Researchers have found, however, that taking NSAIDs for their beneficial anti-inflammatory effects could also affect us negatively by changing our gut bacteria.⁶⁵

NSAIDs inhibit the production of hormones – prostaglandins – which cause inflammation in the body. The prostaglandins being inhibited are in the body for an important reason – they provide protection from gastric ulcers. Researchers have found that both acute and chronic dosing of some pain relievers significantly altered the microbiome genomic structure such that it created a more pro-inflammatory architecture in the GI tract.⁶⁷ Therefore, a common side effect of short-term and long-term dosing of certain painkiller therapies (e.g. naproxen and ibuprofen) is gastric ulcers and even 'leaky gut'.⁶⁸

We should be aware that misuse of NSAIDs can cause the type of chronic and acute problems that will often keep them off work and cause other long-term health issues.



Why is leaky gut bad?

When toxic bacteria and food proteins 'leak' into our bloodstream through our gut wall, our immune system attacks, triggering inflammation that can lead to allergies, autoimmune disease, depression, obesity, type 2 diabetes, heart disease and even cancer.⁶⁹

So although antibiotics and painkillers are sometimes an essential part of the armoury against pain and other illnesses, people should be aware their effects go beyond alleviating aches and pains, and overuse and long-term use may have negative consequences.



Educate our immune system

Scientists studying the prevalence of autoimmune diseases – disorders that attack healthy tissues in the body like type 1 diabetes – have suggested that the shifts in our gut microbial communities may be driven by changes in what we eat, and that the quantity and type of microbes we're exposed to have increased our vulnerability to these diseases.⁷⁰ They also believe that these changes may have contributed to the rise of these disorders in the developed world. Research indicates that in order to develop properly and to avoid the hyper-reactive tendencies that underlie autoimmune and allergic diseases, the immune system needs a certain type of stimulation early in life.⁷¹ It needs an education. Scientists hypothesize that toughening the immune system early in life alters how we respond to 'hits' later in life.

The implication is that by delaying exposure to once-common infections (due to the improvements in societal hygiene) the prevalence of autoimmune diseases may have actually increased. Lifestyle seems to be the major determinant – the way you live guarantees (or prevents) exposure to a rich variety of microbes that favorably sculpt the immune system.



Healthcare workers who **routinely** used **hand sanitisers** increased their risk of developing **norovirus by 600%**.⁷²



Norovirus is a group of **viruses** that cause **inflammation** of the stomach and large intestine lining.⁷²

In addition, a study found that children whose parents cleaned their dirty pacifier by sucking on it instead of boiling it in water were less likely to have eczema.⁷³ So be picky about using hand sanitisers excessively and some cleaners used to disinfect the homes and workplace. Perhaps use natural alternatives that don't kill all bacteria (even the good ones) for lighter clean jobs, such as vinegar, castile soap or lemon juice.



Exercise more

Exercise is of course a well-established part of any individual or organisational wellness programme. The fact that exercise helps support a healthy gut microbiome should be an added incentive to get active. The evidence is in: scientists at University College Cork in Ireland studied the faeces of 40 professional rugby players and found that the athletes' microbiomes were far more diverse than those of control groups.⁷⁴

A study conducted in Switzerland investigated the changes in subjects after smoking cessation, and discovered that there were profound shifts in the microbial composition with increased microbial diversity.⁷⁷



Reduce stress

It is well-known that stressed employees can be less engaged and productive at work.⁷⁵ Researchers have also found that stress can alter the balance of bacteria (lowering numbers of potentially beneficial *Lactobacillus*) that live in the intestine, leading to immune system problems.¹¹ Stress can also impact the movement and contractions of the GI tract causing inflammation, pain, and other bowel symptoms via the gut-brain axis.²² Stress may contribute to IBS, one of the most common functional bowel disorders, and the associated changes in microbial populations may influence brain activity, including mood, via the central nervous system (CNS).²² Stress reduction programmes, therefore, not only have the potential to improve employee engagement and productivity at the workplace but may help prevent and treat many gastrointestinal disorders.



Breathe clean air

A Canadian study revealed that airborne toxic particles can reach the large bowel via mucociliary clearance from the lungs; increased pollution associated with industrialisation could contribute to increases in IBD cases.⁷⁶ Hence, it's important to develop and implement a high air quality management plan at the workplace. Having the right ventilation system and high quality filters can be the first step to maintaining good air quality, as inside air can affect a person's health, comfort, and ability to work.

Importantly, air pollution is not the only inhaled environmental exposure that has been associated with gastrointestinal disease. Smoking also affects our gut microbiota adversely (smoking-induced changes in microbial populations could contribute to increased risk of Crohn's disease) and this is yet another reason to promote smoking cessation at the workplace and beyond.⁷⁷ Smoking cessation not only results in the health benefits we all know about but it also benefits gut microbiota.



Western diet vs. gut microbes

In a study that switched the nutrient composition of diets of a group of healthy African-Americans (with a high-fat, low-fibre diet) and Africans (consuming low-fat, high-fibre foods), biopsies showed significant suppression of inflammation and proliferation of cancer biomarkers in Americans, and increases in Africans.⁷⁸ The research suggests that the incidence of colon cancer changes within just one generation of westernisation of diet; that the mucosal changes associated with carcinogenesis change in just two weeks of switching – and that these changes are caused by colonic microbial metabolism. Time to cut back on red meats and processed foods, and get fresher, more high-fibre vegetable matter in our diets.



Maintain a healthy diet

An unhealthy diet (especially one high in fat) can prevent virtuous bacteria from flourishing in the gut. Saturated fats may increase numbers of inflammatory gut microbes. Research now suggests the gut microbiome affected by Western diets (typically high-fat, low-fibre) correlate to colorectal cancer, the third most common cancer in the world (predicted to rise to 2.4 million cases by 2035).⁷⁹

- **Reduce sugar, artificial preservatives and processed foods**

The research is in and, as we've seen, it's not good news for sugars and processed foods. These impair gut bacteria diversity, causing the gut microbiome to become hostile to its host and can create vicious cycles of chemical reactions that contribute to diabetes, obesity, depression and a host of other conditions.⁸¹

Artificial preservatives can increase the risk of inflammatory bowel diseases and metabolic disorders.⁸¹ Researchers at Georgia State University found healthy mice became obese and developed metabolic problems when fed common food emulsifiers, which are ingredients used to improve the texture and taste of many foods.⁸² Sugar substitutes, such as saccharin, might aggravate metabolic disorders by acting on bacteria in the gut, according to a study published by Nature in 2014.⁸³

- **Eat more plants and dietary fibre**

Gut experts may differ on whether fruits or grains help gut bacteria, but scientists all agree we should eat more plants, especially green leafy vegetables, which can build and maintain microbiota diversity.⁷⁴

- **Eat less red meat**

Harvard scientists had a group of volunteers go on a diet of meat and cheese. Within two days, the bacteria in the subjects' gut had changed, with more *Bilophila*, which has been found to cause inflammation and intestinal diseases in mice. And their gut microbiome was excreting more of trimethylamine N-oxide (TMAO), a compound that causes arteriosclerosis (the narrowing or obstruction of the arteries) and heart disease.⁸⁴

L-carnitine, an amino acid present in meat, can cause an increase in the bacteria that metabolises it, producing even greater amounts of TMAO.⁸⁴ A study carried out by researchers at the Cleveland Clinic has shown that this change in the bacteria living in the digestive tract resulting from meat consumption can also lead to an increase in TMAO.⁸⁴

A diet high in L-carnitine shifts our gut microbe composition and generates an increase in the bacteria that 'like' carnitine, which means that meat eaters are more susceptible to forming TMAO and its artery-clogging effects.⁸⁴ Meanwhile, vegans and vegetarians have a significantly reduced capacity to synthesise TMAO from carnitine, which may explain the cardiovascular health benefits of those diets.⁸⁴

Oregon State University also found that a diet high in sugar caused changes in the gut bacteria of mice, impairing their 'cognitive flexibility' – and negatively affected both long-term and short-term memories.⁸⁰

We are what we eat

Today's employee menu = healthier gut bacteria⁸⁵

Our microbes help define our health, energy levels and moods and food is one of the biggest determinants of gut microbiome health. So it's true: we really are what we eat.

The good news is that we cultivate a new microbiota in just 24 hours by changing our diet. Sticking to a gut bacteria diet over time can help form bacteria colonies that combat obesity, type 2 diabetes, heart disease, autoimmune disease, and even certain forms of cancer.

TRY THESE EIGHT SUPER-FOODS TO SUPER-CHARGE THE GUT MICROBIOME:

	WHAT?	WHY?
	Asparagus, jerusalem artichokes, leeks, and onions	These are high in inulin, which has strong prebiotic potential, and once they find their way to the colon, they ferment into healthy microbiota. Ease into Jerusalem artichokes: people with sensitive digestive tracts may notice increased gas.
	Bananas	These popular fruit may reduce gut inflammation, due to high levels of potassium and magnesium. Bananas work to maintain harmony among microbes in the bacterial community known as phyla. This is one reason bananas are a standard prescription for an upset stomach.
	Beans	Any legume will help release SCFAs that strengthen our intestine cells and help with weight loss. Packed with fibre protein, folate, and B vitamins, they play a role in regulating a healthy gut and a healthy brain. Researchers have recently proved legumes also improve weight loss by enhancing the feeling of being full.
	Blueberries	We're not sure if it's the antioxidants, vitamin K compounds or fibre that gives blueberries clout as a superfood, but studies show they may boost memory, improve our immune system and diversify gut bacteria.
	Broccoli and other cruciferous vegetables	Cruciferous vegetables such as broccoli, kale, cabbage and cauliflower feature sulphur-containing metabolites. These are broken down by microbes to release substances that reduce inflammation and reduce the risk of bladder, breast, colon, liver, lung, and stomach cancer. People who eat the most cruciferous vegetables reduce their risk of colorectal cancer by 18%.
	Fermented plant foods	Fermented foods – such as kimchi, sauerkraut, tempeh and soy sauce – directly inoculate our gut with healthy live micro-organisms that crowd out the unhealthy bacteria while increasing the absorption of minerals, and improve overall health. They improve the health of the intestinal cells and immune function, decrease allergies, reduce the risk of colon cancer, and treat diarrhoea.



WHAT?

WHY?



Polenta

This is rich in high-fibre complex carbohydrates, which ferment in the colon into many strands of gut bacteria. Corn, the base of polenta, earns credit for fostering a healthy gut. Polenta's insoluble fibre travels directly to the colon, where it ferments into multiple strands of gut flora. It's good to note that polenta, like kombucha, varies in fermentable components.⁸⁶



Probiotics

Every supermarket now stocks active yoghurts and probiotic drinks, and studies have shown that they really do work. In one study, healthy women consumed a fermented milk product that contained four probiotics and MRI tests revealed differences in the activity of brain regions that control emotion and sensation.⁸⁷ Another study found that healthy volunteers who consumed a mix of probiotic foods decreased their scores on measures of psychological distress.⁸⁸



A few final thoughts



We know from surveys of employers and their employees that wellness at work is a key consideration for many organisations today. The treatment of chronic conditions that impair energy levels, require short- or long-term absences, and make serious use of healthcare insurance, has become a top priority around the world.

Maintaining and promoting a healthy gut microbiome seems to be poorly understood by most people, but it could be beneficial to make it an important part of any wellness programme. The latest research showing a link between a healthy gut microbiome and chronic diseases is extremely compelling. Even with the mounting evidence we've seen in this report, scientists have only scratched the surface on the importance of healthy gut bacteria.

The more we learn, the more it's clear that how we live our lives shapes the diversity and robustness of the trillion-strong community of bugs in our guts. In turn, their health turns out to affect our own in very fundamental ways. They may help us live longer, give us more energy and help fight a variety of health conditions.



The right message

Many employers are getting the message out that exercise, sleep and stress are crucial to health and wellness at work. We urge employers to add gut health to that list.

Maintaining and promoting a healthy gut is more than just eating right and doing other good things like exercise and managing stress. It is also about ensuring that we have the right environment for a healthy gut; watching the way we work and live. We think if more people knew about the role their gut microbiome can play in how they feel and what ails them, the initiatives focused on other wellness issues could be reinforced and even amplified.



The right environment

How we clean our workplaces, protect employees from pollution, feed them in workplace canteens, manage the rhythms of the working day – these could all have definitive effects on gut bacteria and therefore our employees' health. We should respect these microscopic guests and help them to help us.

End Notes

- ¹ American Society for Microbiology, 'Humans Have Ten Times More Bacteria Than Human Cells: How Do Microbial Communities Affect Human Health?', June 2008
- ² Institute of Medicine, 'The Human Microbiome, Diet, and Health: Influence of the Microbiome on the Metabolism of Diet and Dietary Components', 2013
- ³ International Journal of Molecular Sciences, 'Impacts of Gut Bacteria on Human Health and Diseases', April 2015
- ⁴ Gail Hecht, MD, MD, MS, AGAF, 'The Power of the Microbiome', March 2013
- ⁵ Raphael Kellman MD, 'The Microbiome Diet: The Scientifically Proven Way to Restore Your Gut Health and Achieve Permanent Weight Loss', June 2015
- ⁶ National Institutes of Health, 'Human Microbiome Project'
- ⁷ ObedientLifestyle, 'Disease Begins in the Gut', January 2016
- ⁸ Verhulst et al, 'Composition of Human Skin Microbiota Affects Attractiveness to Malaria Mosquitoes', December 2011
- ⁹ Gut, 'Analysis of gut microbial regulation of host gene expression along the length of the gut and regulation of gut microbial ecology through MyD88', August 2012
- ¹⁰ Therapeutic Advances in Gastroenterology, 'Effects of probiotics on gut microbiota: mechanisms of intestinal immunomodulation and neuromodulation', January 2013
- ¹¹ Nature, 'Diet rapidly and reproducibly alters the human gut microbiome', April 2013
- ¹² Journal of Medical Microbiology, 'Prevalence and characterization of Clostridium perfringens from the faecal microbiota of elderly Irish subjects', March 2013
- ¹³ Doctors Health Press, 'Dysbiosis: Microbial Imbalance Inside the Body', April 2016
- ¹⁴ Nature Reviews Gastroenterology and Hepatology, 'The enteric nervous system and neurogastroenterology', May 2012
- ¹⁵ Nature Reviews Gastroenterology and Hepatology, 'The enteric nervous system and neurogastroenterology', May 2012
- ¹⁶ Justin Sonnenburg and Erica Sonnenburg, 'Good Gut: Taking Control of Your Weight, Your Mood, and Your Long-Term Health', May 2016
- ¹⁷ Gut Microbiota Worldwatch, 'Getting to know your gut microbiota'
- ¹⁸ FEMS Microbiology Reviews, 'The first 1000 cultured species of the human gastrointestinal', September 2014
- ¹⁹ Alcohol Research : Current Reviews, 'The Gastrointestinal Microbiome: Alcohol Effects on the Composition of Intestinal Microbiota', 2015
- ²⁰ Center for Genome Sciences, 'Extending Our View of Self: the Human Gut Microbiome Initiative (HGMI)', 2005
- ²¹ Scientific American, 'The Gut's Microbiome Changes Rapidly with Diet', December 2013
- ²² Trends in Neurosciences, 'Gut-brain axis: how the microbiome influences anxiety and depression', May 2013
- ²³ Trends in Molecular Medicine, 'Microbiota and neurodevelopmental: implications for brain', 2014
- ²⁴ Medical News Today, 'Fewer 'good gut' bacteria in C-section infants', August 2013
- ²⁵ Gut, 'Decreased gut microbiota diversity, delayed Bacteroidetes colonisation and reduced Th1 responses in infants delivered by caesarean section', April 2014
- ²⁶ Nature medicine, 'Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer', March 2016
- ²⁷ Nutrients, 'The Impact of Diet and Lifestyle on Gut Microbiota and Human Health', January 2015
- ²⁸ The Canadian Journal of Psychiatry, 'Reframing the Teenage Wasteland: Adolescent Microbiota-Gut-Brain Axis', April 2016
- ²⁹ Science, 'Host-gut microbiota metabolic interactions', June 2012
- ³⁰ Current Osteoporosis Reports, 'The Microbiome and Osteosarcopenic Obesity in Older Individuals in Long-Term Care Facilities', October 2015
- ³¹ Gut Microbiota Worldwatch, 'Gut microbiota evolution throughout lifetime'
- ³² Cell Metabolism, 'Gut Commensal E. coli Proteins Activate Host Satiety Pathways following Nutrient-Induced Bacterial Growth', November 2015
- ³³ PLoS ONE, 'Faecalibacterium prausnitzii Inhibits Interleukin-17 to Ameliorate Colorectal Colitis in Rats', October 2014
- ³⁴ Current Opinion in Biotechnology, 'Bacteria as vitamin suppliers to their host: a gut microbiota perspective', April 2013
- ³⁵ Health, 'The gut-brain connection', December 2015
- ³⁶ Molecular Psychiatry, 'From Gut Dysbiosis to Altered Brain Function and Mental Illness: Mechanisms and Pathways', June 2016
- ³⁷ Institute of Medicine, 'The Human Microbiome, Diet, and Health: Influence of the Microbiome on the Metabolism of Diet and Dietary Components', 2013
- ³⁸ International Journal of Molecular Sciences, 'Impacts of Gut Bacteria on Human Health and Diseases', April 2015
- ³⁹ World Journal of Gastroenterology, 'Brain-Gut-Microbiota Axis in Parkinson's Disease', October 2015
- ⁴⁰ Cell, 'The microbiota modulates gut physiology and behavioral abnormalities associated with autism', December 2014
- ⁴¹ Science News, 'Microbes can play games with the mind', March 2016
- ⁴² Journal of Psychiatric Research, 'Collective unconscious: How gut microbes shape human behavior', April 2015
- ⁴³ World Health Organization, 'Obesity and overweight', June 2016
- ⁴⁴ World Health Organization, 'Obesity', August 2014
- ⁴⁵ Scientific American, 'How Gut Bacteria Help Make Us Fat and Thin', June 2014
- ⁴⁶ Circulation Research, 'The Gut Microbiome Contributes to a Substantial Proportion of the Variation in Blood Lipids', September 2015
- ⁴⁷ eLife, 'Bidirectional interactions between indomethacin and the murine intestinal microbiota', December 2015
- ⁴⁸ National Heart, Lung, and Blood Institute, 'Bidirectional interactions between indomethacin and the murine intestinal microbiota', December 2015
- ⁴⁹ World Journal of Gastroenterology, 'Role of the Gut Microbiota in Inflammatory Bowel Disease Pathogenesis: What Have We Learnt in the Past 10 Years?' February 2014
- ⁵⁰ The Journal of Clinical Investigation, 'Incorporation of therapeutically modified bacteria into gut microbiota inhibits obesity', June 2014
- ⁵¹ Science, 'Anticancer immunotherapy by CTLA-4 blockade relies on the gut microbiota', November 2015
- ⁵² Science, 'Commensal Bifidobacterium promotes antitumor immunity and facilitates anti-PD-L1 efficacy', November 2015
- ⁵³ American Society for Microbiology, 'Beneficial bacteria may protect breasts from cancer', June 2016
- ⁵⁴ The Journal of the American Medical Association, 'Oral, Capsulized, Frozen Fecal Microbiota Transplantation for Relapsing Clostridium difficile Infection', November 2014
- ⁵⁵ The Scientist, 'Microbes', November 2015
- ⁵⁶ Cochrane Database of Systematic Reviews, 'Probiotics for preventing acute upper respiratory tract infections', February 2015
- ⁵⁷ Genome Medicine, 'Impact of the gut microbiota on inflammation, obesity, and metabolic disease', April 2016
- ⁵⁸ Genome Medicine, 'Sub-clinical detection of gut microbial biomarkers of obesity and type 2 diabetes', February 2016
- ⁵⁹ Always consult a physician before changing medicine intake.
- ⁶⁰ Neurogastroenterol & Motility, 'Gut Microbiota and Gastrointestinal Health: Current Concepts and Future Directions', December 2012
- ⁶¹ Centers for Disease Control and Prevention, 'CDC: 1 in 3 antibiotic prescriptions unnecessary', May 2016
- ⁶² mBio, 'Same Exposure but Two Radically Different Responses to Antibiotics: Resilience of the Salivary Microbiome versus Long-Term Microbial Shifts in Feces', November 2015
- ⁶³ www.gov.uk, 'European Antibiotic Awareness Day: evaluations', June 2014
- ⁶⁴ Gut Microbes, 'Functional consequences of microbial shifts in the human gastrointestinal tract linked to antibiotic treatment and obesity', August 2013
- ⁶⁵ Perelman School of Medicine at the University of Pennsylvania, 'Anti-inflammatory drug and gut bacteria have a dynamic interplay', January 2016
- ⁶⁶ Cleveland Clinic, 'Drugs, Devices & Supplements', April 2016
- ⁶⁷ eLife, 'Bidirectional interactions between indomethacin and the murine intestinal microbiota', December 2015
- ⁶⁸ Huffington Post, '5 Steps to Heal a Leaky Gut Caused By Ibuprofen', September 2014
- ⁶⁹ Clinical Reviews in Allergy & Immunology, 'Leaky gut and autoimmune diseases', February 2012
- ⁷⁰ Cell Host & Microbe, 'The Dynamics of the Human Infant Gut Microbiome in Development and in Progression toward Type 1 Diabetes', February 2015
- ⁷¹ Cell, 'Variation in Microbiome LPS Immunogenicity Contributes to Autoimmunity in Humans', April 2016
- ⁷² Centers for Disease Control and Prevention, 'Updated Norovirus Outbreak Management and Disease Prevention Guidelines', March 2011
- ⁷³ Pediatrics, 'Pacifier Cleaning Practices and Risk of Allergy Development' May 2013
- ⁷⁴ Gut microbiota, 'Exercise and associated dietary extremes impact on gut microbial diversity', June 2014
- ⁷⁵ Forbes, 'Workplace Stress Leads To Less Productive Employees', September 2014
- ⁷⁶ Gut Microbes, 'Air pollution effects on the gut microbiota: a link between exposure and inflammatory disease', March 2014
- ⁷⁷ Inflammatory Bowel Disease, 'Smoking cessation induces profound changes in the composition of the intestinal microbiota in humans', 2014
- ⁷⁸ Imperial College London, 'Diet swap has dramatic effects on colon cancer risk for Americans and Africans', April 2015
- ⁷⁹ International Agency for Research on Cancer, 'Cancer Incidence and Mortality Worldwide: IARC CancerBase', 2014
- ⁸⁰ Neuroscience, 'Relationships between diet-related changes in the gut microbiome and cognitive flexibility', May 2015
- ⁸¹ Nutrients, 'Diet-Induced Dysbiosis of the Intestinal Microbiota and the Effects on Immunity and Disease', August 2012
- ⁸² Nature, 'Dietary emulsifiers impact the mouse gut microbiota promoting colitis and metabolic syndrome', March 2015
- ⁸³ Nature, 'Sugar substitutes linked to obesity', September 2014
- ⁸⁴ Nature Medicine, 'A study carried out by researchers at the Cleveland Clinic has shown that this change in the bacteria living in the digestive tract resulting from meat consumption can also lead to an increase in TMAO', April 2013
- ⁸⁵ The Physicians Committee, 'Seven Foods to Supercharge Your Gut Bacteria', September 2014
- ⁸⁶ The Physicians Committee, 'Carbohydrates: Complex Carbs vs Simple Carbs', July 2015
- ⁸⁷ Gastroenterology, 'Consumption of Fermented Milk Product With Probiotic Modulates Brain Activity', June 2013
- ⁸⁸ British Journal of Nutrition, 'Assessment of psychotropic-like properties of a probiotic formulation (Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) in rats and human subjects', March 2011



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