INFLAMMATION AND THE GUT

With Dr Will Bulsiewicz

Why the integrity of our barriers matters, and what food does to them.

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DISCLOSURES

38TERA

Simon Hill and Dr Will Bulsiewicz are co-founders of 38TERA, a company that formulates and sells medical-grade supplements targeting the gut.

DR WILL BULSIEWICZ

Sells online courses on gut health and nutrition, and books.

SIMON HILL

Sells a book; all proceeds are donated to charity. The Proof podcast is supported by paid sponsors.

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TISSUE WE CALLED STERILE

Bacteria aren't staying in the gut. They have been found in places we were taught nothing lived.

Presence, not proof of cause.
Each of these is association plus a plausible mechanism.



CORONARY PLAQUES

Mouth bacteria living inside the arteries of people who died of heart attacks.



ALZHEIMER'S BRAINS

A gum bacterium and its toxins, tracking with the damage.



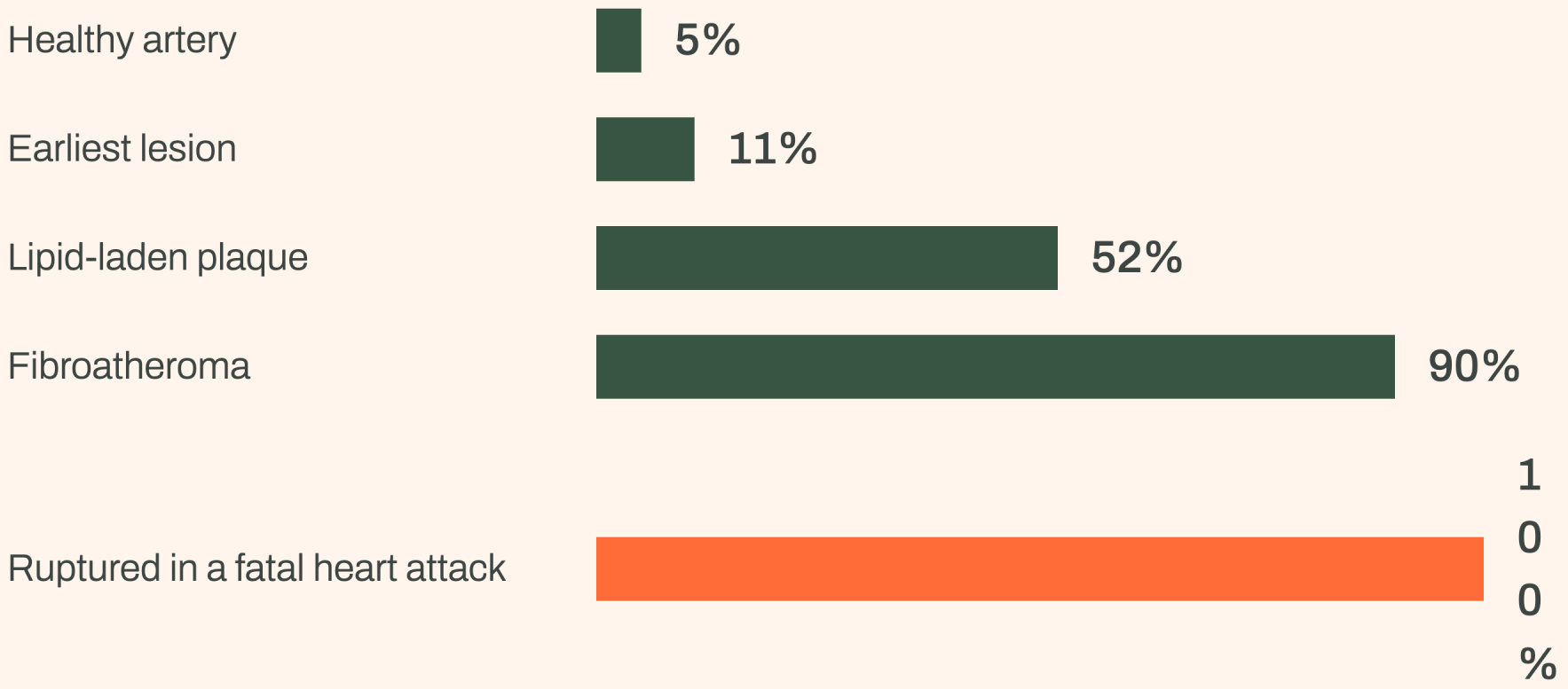
BOWEL TUMOURS

A mouth bacterium that travels with the cancer when it spreads to the liver.

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FURTHER IN, MORE OF THEM

Coronary arteries from 121 people who died suddenly, stained for mouth streptococci. The further the disease had progressed, the more of them were found.



All 24 of the plaques that ruptured had them.

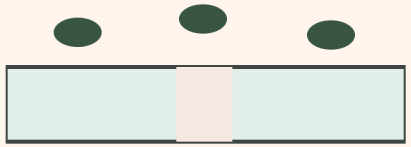
Karhunen et al., JAHA, 2025. Association plus a plausible mechanism – not proof. Largely one research group; independent replication outstanding.

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THE BUG NEEDN'T BE IN THE JOINT

Rheumatoid arthritis works differently from the heart. The provocation happens at a barrier, and the damage lands somewhere else entirely.

Bacterial DNA and cell-wall fragments do turn up in arthritic joints. A living community there has not been shown.



1. PROVOKED

At the gut wall, or at inflamed gums.



2. ANTIBODIES

The immune system makes them, and they travel.



3. THE JOINT

Takes the hit, with no bacteria living in it.

In people with rheumatoid arthritis and gum disease, oral bacteria spill into the blood again and again – and those bacteria are targets of the same antibodies.

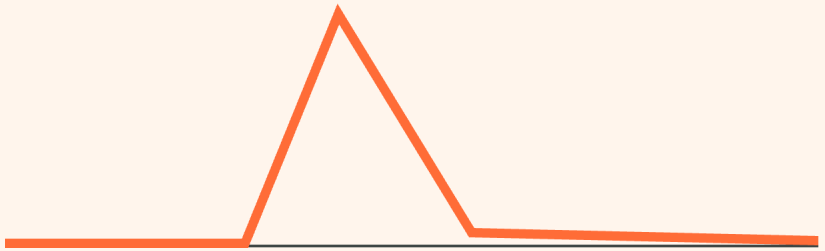
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TWO KINDS OF INFLAMMATION

Whether it helps or harms is context dependent. The shape over time is the difference.

Illustrative shapes, not data.

ACUTE



A sprained ankle, a cold, a cut. It rises fast, does its job, and switches off.

CHRONIC

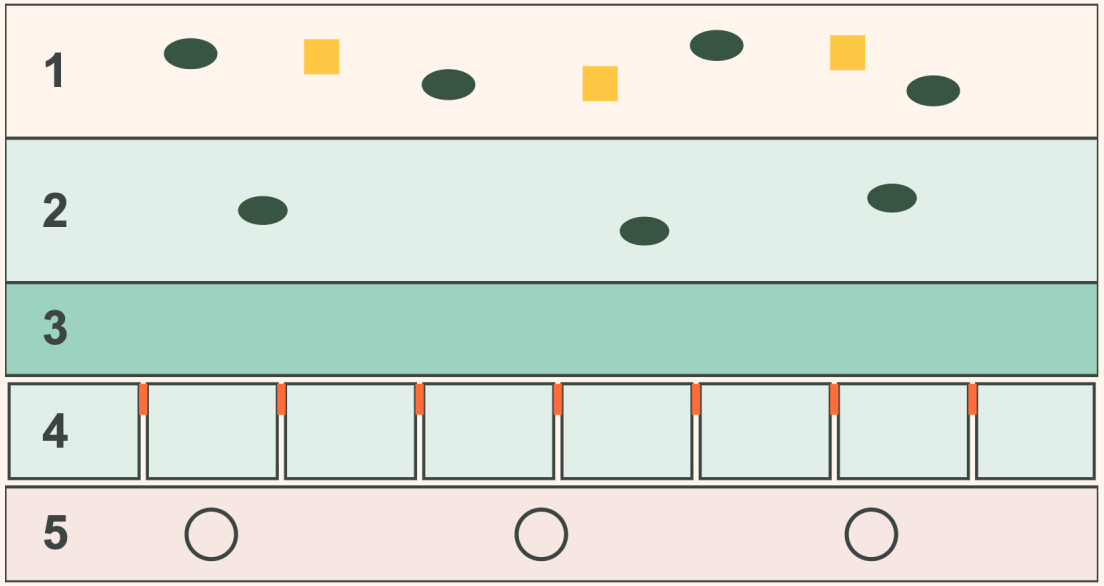


No injury, no infection. The alarm stays on quietly for years, and you feel very little of it.

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ONE CELL THICK

The surface separating the outside world from your bloodstream is the size of a studio apartment, and a single cell deep.



Two mucus layers, one layer of cells, and then your bloodstream. The orange marks are the tight junctions.

1. THE LUMEN

Trillions of microbes, and everything you ate.

2. OUTER MUCUS

Loose, and deliberately colonised. Bacteria live here.

3. INNER MUCUS

Dense and kept sterile. This is the real front line.

4. THE LINING

One cell thick, stitched together by tight junctions.

5. IMMUNE TISSUE

Most of the body's immune cells sit directly beneath.

Schematic. Not to scale.

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IT ISN'T USUALLY THE WHOLE BUG

Four different things cross the gut lining and meet the immune system. They are not equally well understood.

LPS: lipopolysaccharide, a piece of the outer membrane of gram-negative bacteria.

LIVE BACTERIA

The version everyone pictures, and the rarest. Mostly the bug itself stays put.

FRAGMENTS – LPS

The best-studied route. A piece of dead bacterial wall is enough to set the immune system off.

FOOD PROTEINS

Coeliac disease is the clearest version: gluten fragments reaching immune cells that react to them.

METABOLITES

TMAO and others. These are absorbed on purpose, not leaked – a different story from the first three.

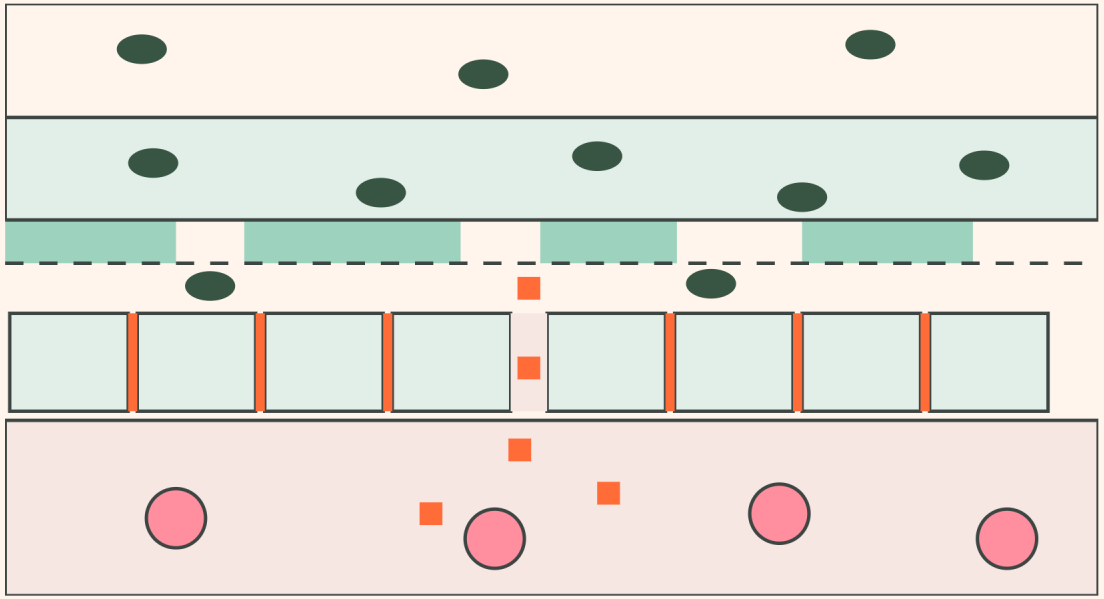
1/2 People carrying a gene variant that dulls the immune response to LPS were around half as likely to have carotid atherosclerosis – a hint that the response to the fragment, not just the fragment, is what matters.

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"LEAKY GUT" IS INCREASED INTESTINAL PERMEABILITY

The same wall as the slide before, degraded. Not a hole – a seal that stops holding.

Schematic. Not to scale.



Some permeability is normal and necessary. The question is how much, where, and what gets through.

1. MUCUS THINS

The inner layer goes patchy, and bacteria reach the cell surface.

2. A JUNCTION OPENS

One seal between two cells loosens – the orange stitching, missing in a single spot.

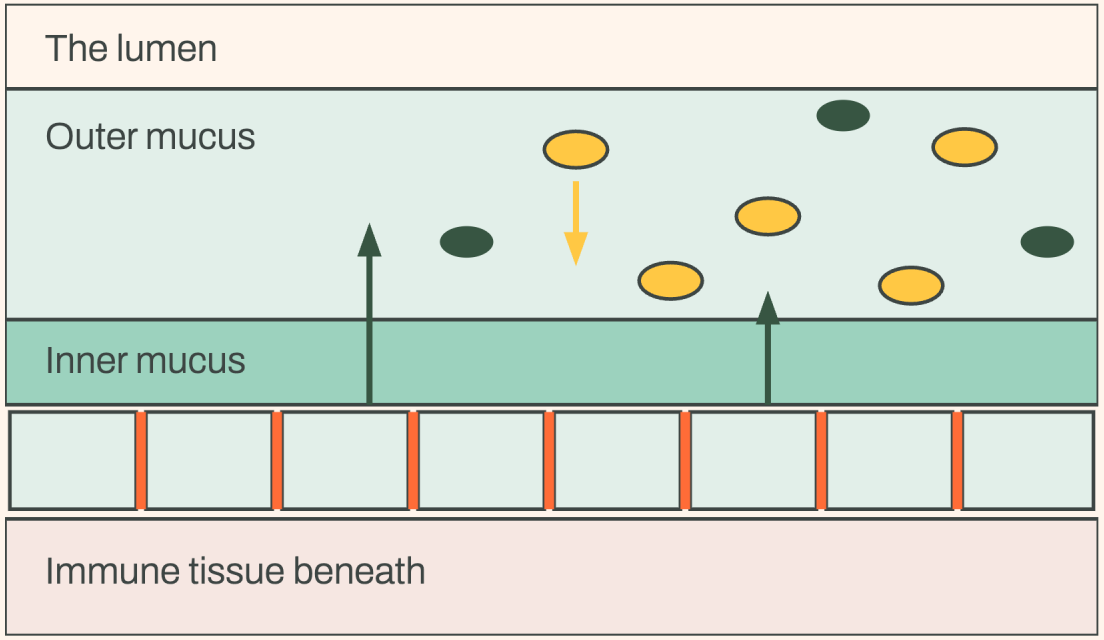
3. FRAGMENTS CROSS

Pieces of bacterial wall, LPS among them, reach the immune cells beneath.

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IT LIVES IN THE MUCUS IT HELPS MAINTAIN

Akkermansia sits in the outer mucus, eats the mucin, and the lining responds by making more of it.



Yellow: Akkermansia. Green: other bacteria. Schematic, not to scale.

WHERE IT SITS

In the loose outer mucus – the layer that is meant to be colonised – not the sterile inner one.

WHAT IT EATS

Mucin, the mucus itself. The yellow arrow. It is a consumer of the barrier.

WHAT HAPPENS NEXT

The lining answers by secreting more – the green arrows – and the layer ends up thicker, not thinner.

A bacterium that eats your mucus and leaves you with more of it. That is the part that sounds wrong and isn't.

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WHAT PULLS THE OTHER WAY

Two columns worth keeping apart. One is where the human evidence sits. The other is where the headlines are.

Column placement reflects the weight of human evidence, not the size of the effect.

STRONGEST SIGNAL

- A diet low in fibre and plant variety
- Alcohol
- Antibiotics, and how often they are used

EMERGING, MOSTLY ANIMALS

- Emulsifiers in ultra-processed foods
- Some artificial sweeteners
- Poor sleep and sustained stress

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WHAT FEEDS THE LINING

You don't feed the gut wall directly. You feed the microbes, and they make the thing that feeds it.

The mucus-eating finding below comes from animal work. Polyphenols, fermented foods and plant fats reach the lining by their own routes, covered later.

1

FIBRE, AND VARIETY

Beans, whole grains, vegetables, fruit, nuts, seeds.

2

MICROBES FERMENT IT

Different fibres feed different species. That is why variety does something range alone cannot.

3

SHORT-CHAIN FATS

Butyrate and propionate are among the products of that fermentation.

4

FUEL, SEAL, SIGNAL

Butyrate fuels the colon cells, helps tighten the junctions between them, and calms the immune cells underneath.

Starve the microbes of fibre and, in animal work at least, some of them start eating the mucus layer instead.

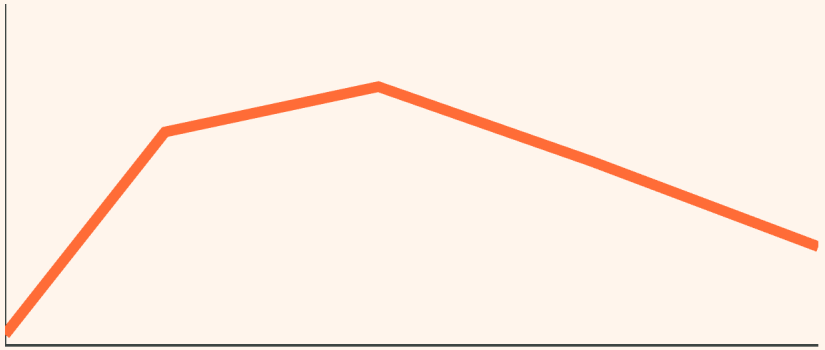
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TWO BREAKFASTS

A meal heavy in saturated fat raises endotoxin in the blood for hours afterwards. Add 30 g of fibre to the same meal and that rise is prevented.

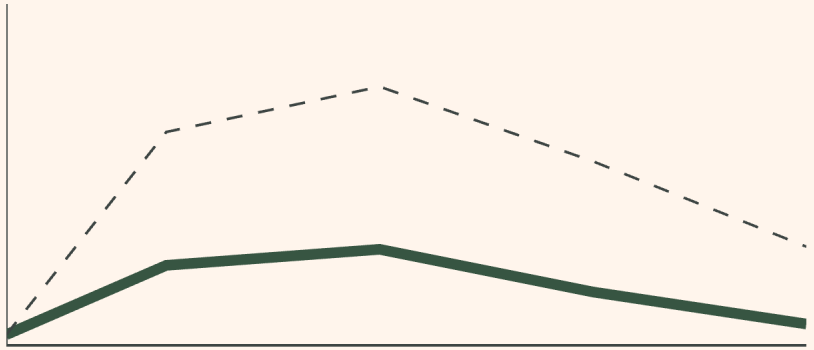
Ghanim et al., J Clin Endocrinol Metab, 2017 – ten people, the same meal with and without fibre on two visits. Direction of effect, not measured values.

FAT ALONE



Cream, butter, a fatty processed meal. Endotoxin climbs and stays up.

SAME MEAL, PLUS FIBRE



The same high-fat meal with 30 g of fibre added, in the same ten people. The dashed line is the meal without it.

The immune system is not recognising the fat itself. The fat is the vehicle – it helps endotoxin get absorbed along with the meal.

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TWO DIETS, TWO DIFFERENT JOBS

36 healthy adults, 10 weeks, randomised to fermented foods or high fibre.

	FERMENTED FOODS	HIGH FIBRE
19 inflammatory proteins	**All decreased**	None decreased
Microbiome diversity	**Increased steadily**	Stable
Immune signalling	**Lower in four cell types**	Split three ways, below



Lowest starting diversity. Immune signalling rose.



Middling diversity. Signalling came down.



Highest diversity. Signalling came down here too.

An argument for building fibre up slowly, not an argument against fibre.

Wastyk et al., Cell, 2021. Clusters, not tertiles – the authors gave no group sizes. Direction only, not magnitudes.

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TAKE IT, OR FEED IT?

Three routes to more Akkermansia, and the trial evidence does not rank them the way the shelf does.

?

PASTEURISED

Beat the live form on insulin sensitivity and cholesterol, and changed the microbiome not at all. Not the same as heat-killed, which did nothing.

LIVE

Only took hold in people who started low. Where levels were already high, it largely passed through.

FED

Fibre, polyphenols and fermented foods have all shifted its abundance, though by how much varies by person.

If the heat-killed form works, it is acting as a signal to the lining rather than as a bug that moves in – which changes what you would even be buying.

Depommier, Nature Medicine, 2019 (pasteurised form) · Zhang, Cell Metabolism, 2025. Small trials, metabolic endpoints, not gut-barrier ones.

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MOST OF IT NEVER GETS IN

Polyphenols are poorly absorbed, which turns out to be the point. They reach the colon, and the microbes do the work.

Whole foods are what the evidence is built on. Isolated extracts are a different exposure.

WHERE THEY ARE

Extra virgin olive oil, berries, cocoa, tea, coffee, herbs, red onions, pomegranate.

MICROBES CONVERT THEM

Into metabolites the body can use – and which ones depends on who is living in your colon.

THE LAYER RESPONDS

Several polyphenol-rich foods raise Akkermansia and mucus thickness in the work done so far.

THE CATCH WORTH KNOWING

Two people eating identical pomegranate can end up with completely different metabolites, because they are carrying different microbes. It is one of the clearest examples of why personalised advice is hard and variety is the safer bet.

Not a supplement story. A reason to eat colour and bitterness.

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WHEN DRUGS TARGET INFLAMMATION

Cardiology has run the experiment. Lowering the marker turns out not to be the same as lowering the risk.

TRIAL	TARGET	RESULT
CANTOS	IL-1 beta	Heart attacks and strokes down about 15%, with no change in cholesterol – but more fatal infections, and no drop in overall deaths.
Colchicine	Broad anti-inflammatory	Benefit in two large trials, and none in a third in people treated straight after a heart attack.
ZEUS	IL-6	Free IL-6 and hs-CRP fell exactly as expected, and major cardiovascular events did not move at all – hazard ratio 0.99.

Which is an argument for treating the causes rather than chasing a single molecule.

CANTOS, NEJM 2017 · ZEUS headline results, 2026. Full ZEUS data still to be presented.

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WHAT ACTUALLY MOVES IT

There is no single lever. The effect is in doing several of these, for long enough to matter.

Movement belongs on this list too. It is off the grid for space, not for want of evidence.

FIBRE, DAILY

Beans, whole grains, vegetables, fruit, nuts, seeds – built up slowly if you bloat.

PLANT VARIETY

Different fibres feed different species. Variety beats any one superfood.

FERMENTED FOODS

Yoghurt, kefir, kimchi, sauerkraut. A different job from fibre, on the trial evidence.

PLANT FATS

Olive oil, nuts, seeds, avocado, omega-3s – the fats that arrive with polyphenols and fibre.

INFLAMMATION



LESS ALCOHOL

One of the clearer disruptors of the lining and the microbes living in it.

SLEEP

Short and broken sleep shows up in inflammatory markers, and in what you eat the next day.

STRESS, CONNECTION

Loneliness and chronic stress sit alongside food here, not beneath it.

ANTIBIOTICS

Necessary medicines, not casual ones. The microbiome takes time to recover.

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SOURCES

The papers behind the figures on screen.

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Full reference list and every study discussed: theproof.com

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