PATOLOGIA INTESTINALE

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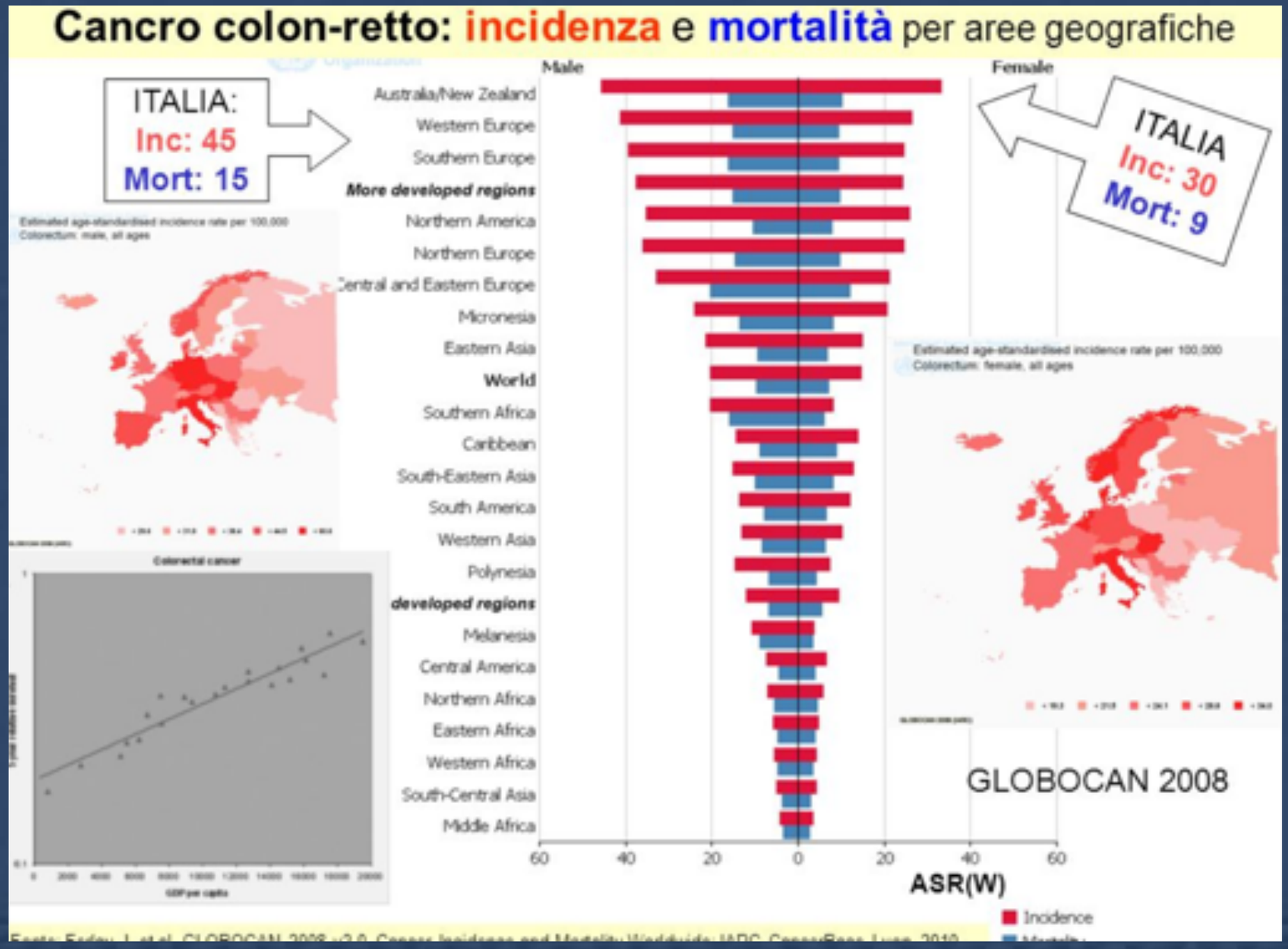
CANCRO COLON RETTO



Epidemiologia

WHO stima 945.000 nuovi casi/anno di CCR

ITALIA 1997: 35.185 nuovi casi di CCR

- 50 casi/100.000 abitanti/anno tra i 30 e i 50 anni
- 100 casi/100.000 abitanti/anno tra i 50 e i 70 anni
- 250 casi/100.000 abitanti/anno > i 70 anni

I tassi di incidenza maggiori si registrano nelle regioni centro-settentrionali

- Il 60% dei pazienti con CCR appartiene allo stadio II-III e quindi è trattabile con intenti curativi
- La sopravvivenza a 5 anni è strettamente correlata allo stadio della neoplasia al momento della diagnosi:

Stadio I: 80-90%

Stadio II: 65-75%

Stadio III: 25-60%

Stadio IV: 0-7%

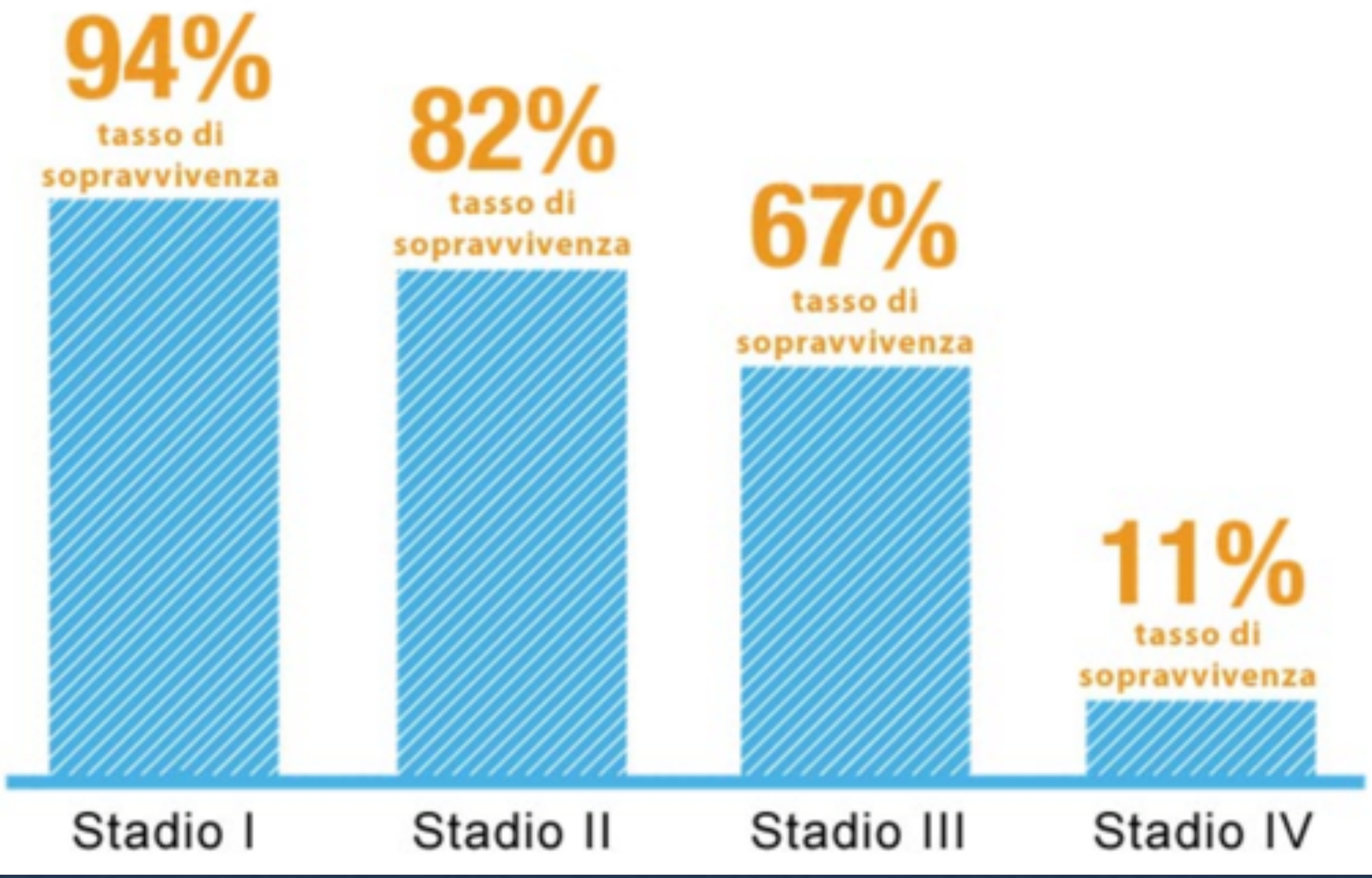
ASCO, J Clin Oncol 1999; 17:1312-1321

ASSR, Linee guida sul CCR, Roma 2002

Weitz J et al Lancet 2005; 365:153-65

Linee guida CNR-MIUR 2004

Tumore al colon: sopravvivenza
in base allo stadio al momento della diagnosi

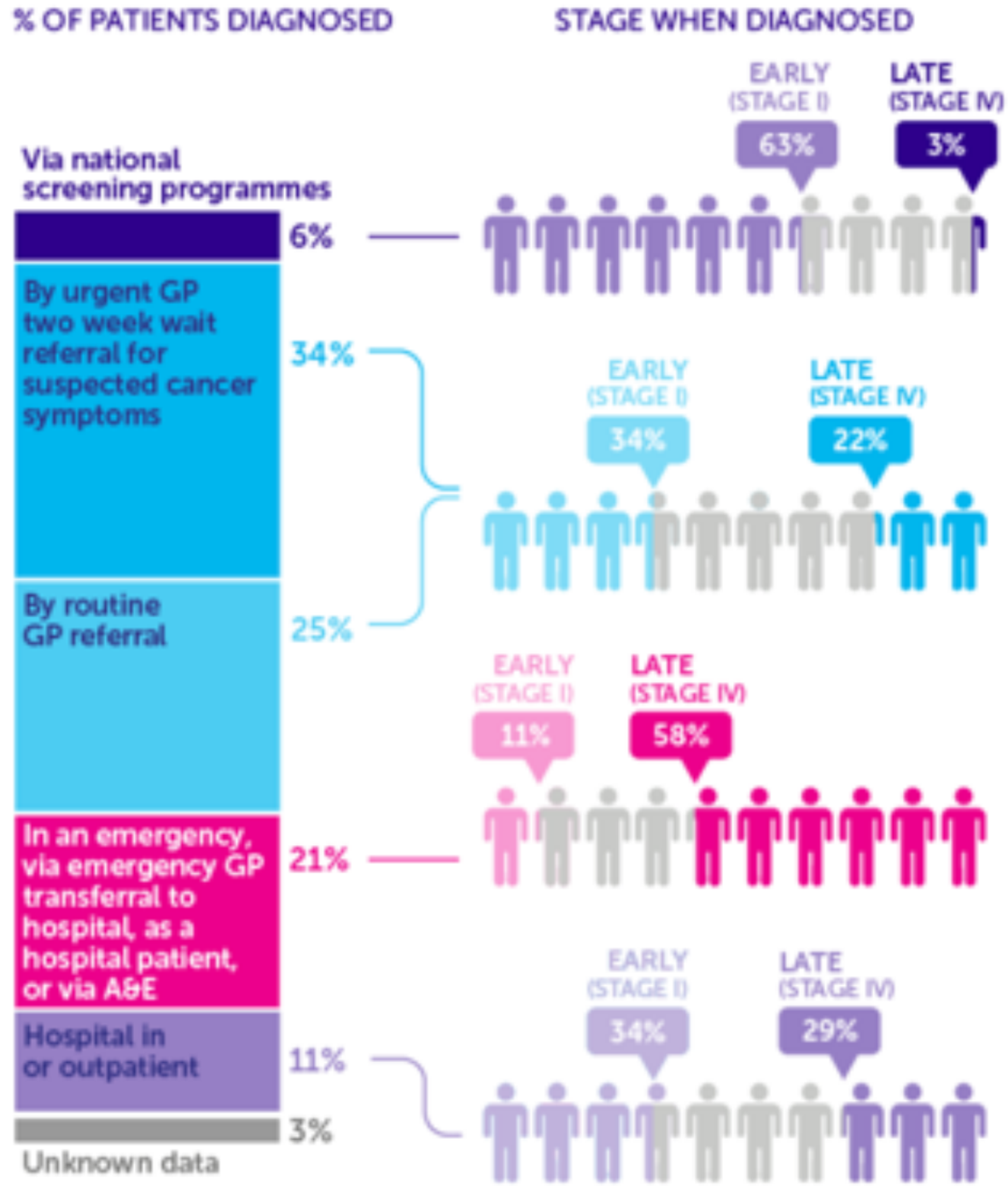


L'intestino crasso: cancro

- Sintomi: sangue (occulto) nelle feci, anemizzazione, astenia, dolore, occlusione, perforazione, massa addominale
- Diagnosi: colonscopia (endoscopica o virtuale), biopsia, PET-TC
- Fattori di rischio: familiarità, alcol, grassi, carne, colite ulcerosa, poliposi
- Terapia: resezione intestinale laparoscopica/tomica, terapia medica, radioterapia

❖ Prevenzione: alimentazione vegetariana, attività fisica, fibre, frutta e verdura, possono ridurre il rischio del 70%

HOW AND WHEN CANCER PATIENTS ARE DIAGNOSED



Source: National Cancer Intelligence Network, data for England 2012-2013

LET'S BEAT CANCER SOONER
cruk.org

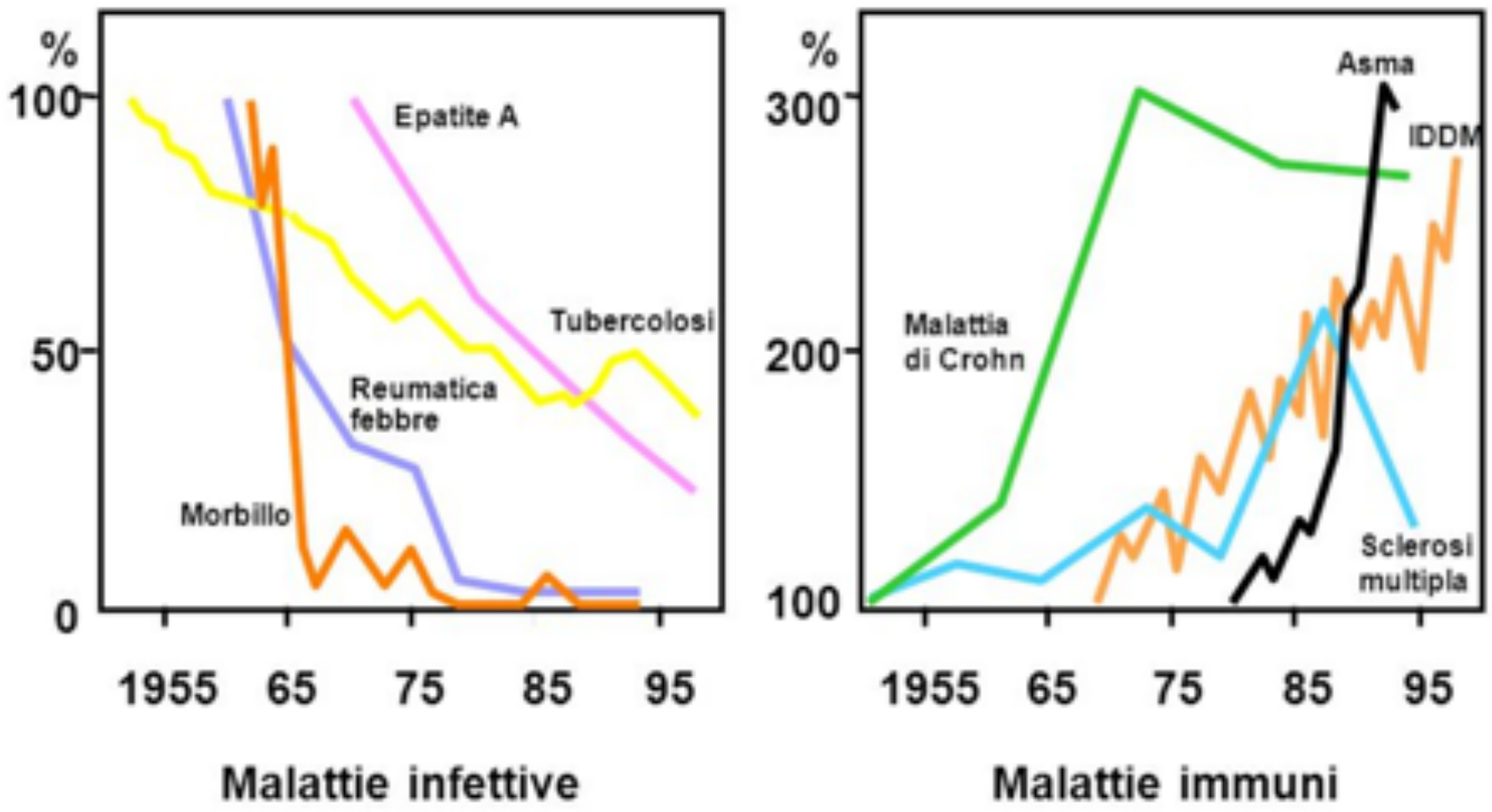
CANCER RESEARCH UK

Morbo di Crohn

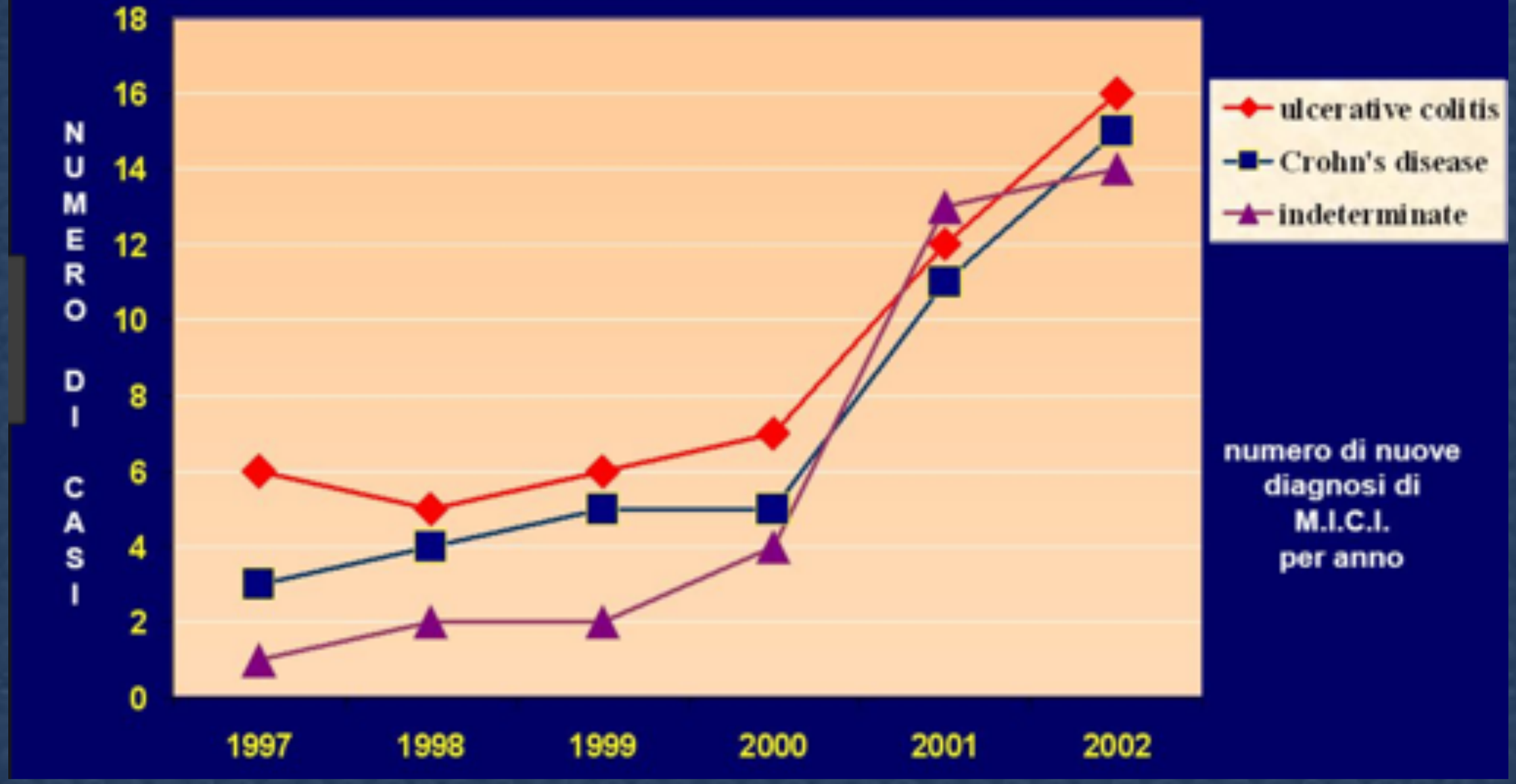
In Italia

- Incidenza 5-7 casi/100.000 l'anno
- Prevalenza 50-54 casi/100.000
- Maggiormente colpito il sesso femminile
- 55% dei casi prima dei 35 anni d'età

Nel corso delle ultime 4 decadi l'incidenza di malattie infettive si è ridotta mentre quella delle malattie immuno-mediate è aumentata.



Epidemiologia



Epidemiologia

a) 25-30% dei pz. con M.C.
   20% dei pz. con R.U.
   } esordio < 20 anni

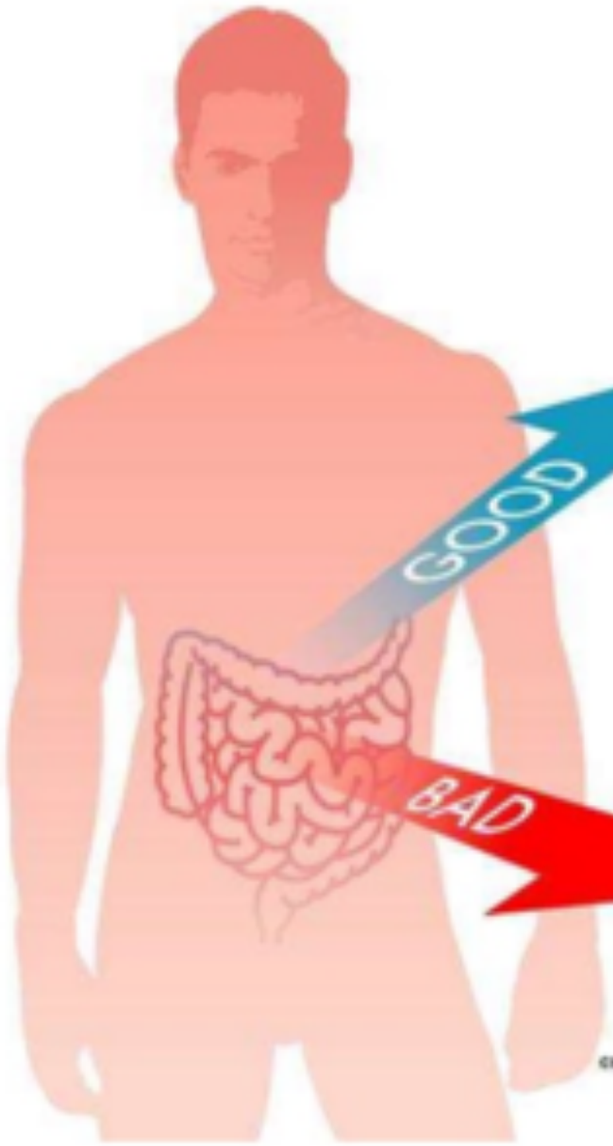
b) 60% tra 16-20 a. ; 30% tra 11-15 a. ; 10% < 10a.
   4% < 5a.

c) 15-40% dei pz. con M.I.C.I. ha un parente di 1° grado affetto da M.I.C.I.

d) aumento delle M.I.C.I. (= R.U., ↑ M.C.)

e) difficile precisare l'incidenza di ognuna delle M.I.C.I. (più frequenti nei paesi "ricchi" e nella razza bianca)

Good and Bad Bacterial Flora



BIFIDOBACTERIA
The various strains help to regulate levels of other bacteria in the gut, modulate immune responses to invading pathogens, prevent tumour formation and produce vitamins.

ESCHERICHIA COLI
Several types inhabit the human gut. They are involved in the production of vitamin K2 (essential for blood clotting) and help to keep bad bacteria in check. But some strains can lead to illness.

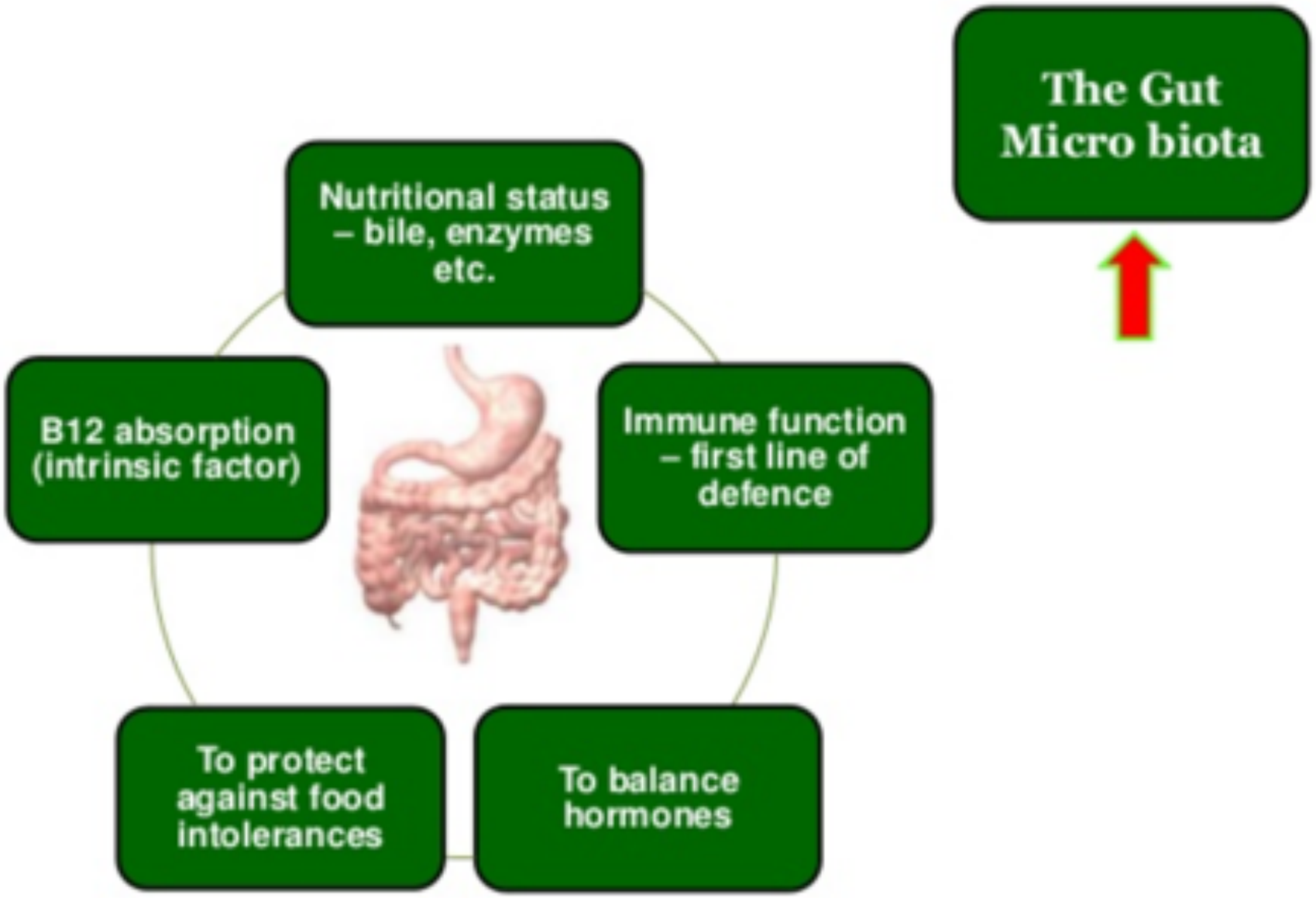
LACTOBACILLI
Beneficial varieties produce vitamins and nutrients, boost immunity and protect against carcinogens.

CAMPYLOBACTER
C Jejuni and C coli are the strains most commonly associated with human disease. Infection usually occurs throught the ingestion of contaminated food.

ENTEROCOCCUS FAECALIS
A common cause of post-surgical infections.

CLOSTRIDIUM DIFFICILE
Most harmfull following a course of antibiotics when it is able to proliferate.

The importance of gut health



The Gut Microbiota

Micro biota
The microorganisms that live in an established environment
Microbiome = a complex "organ"
The full complement of microbes, their genes, and genomes in a particular environment

Complex community of microbes estimated to contain

1- 200 trillion cells
2- > 1000 diverse microbial species
3- 10 x the number of human cells in our body
4- Gut Microbiome is 150 x larger than the human genome
5- 100 to 1,000 times more DNA than ours!!!
6- 20,000 functions *& make 100's of thousands of biochemicals*
7- Genes for making hormones, enzymes, etc. (Humans = 23,000 - Microbes = 4.5 million)
8- Found in "sterile" zones (e.g. lungs & womb)

Gut Microbiota

the next-gen frontier in preventive & therapeutic medicine?

Front. Med., 23 June 2014 | https://doi.org/10.3389/fmed.2014.00015

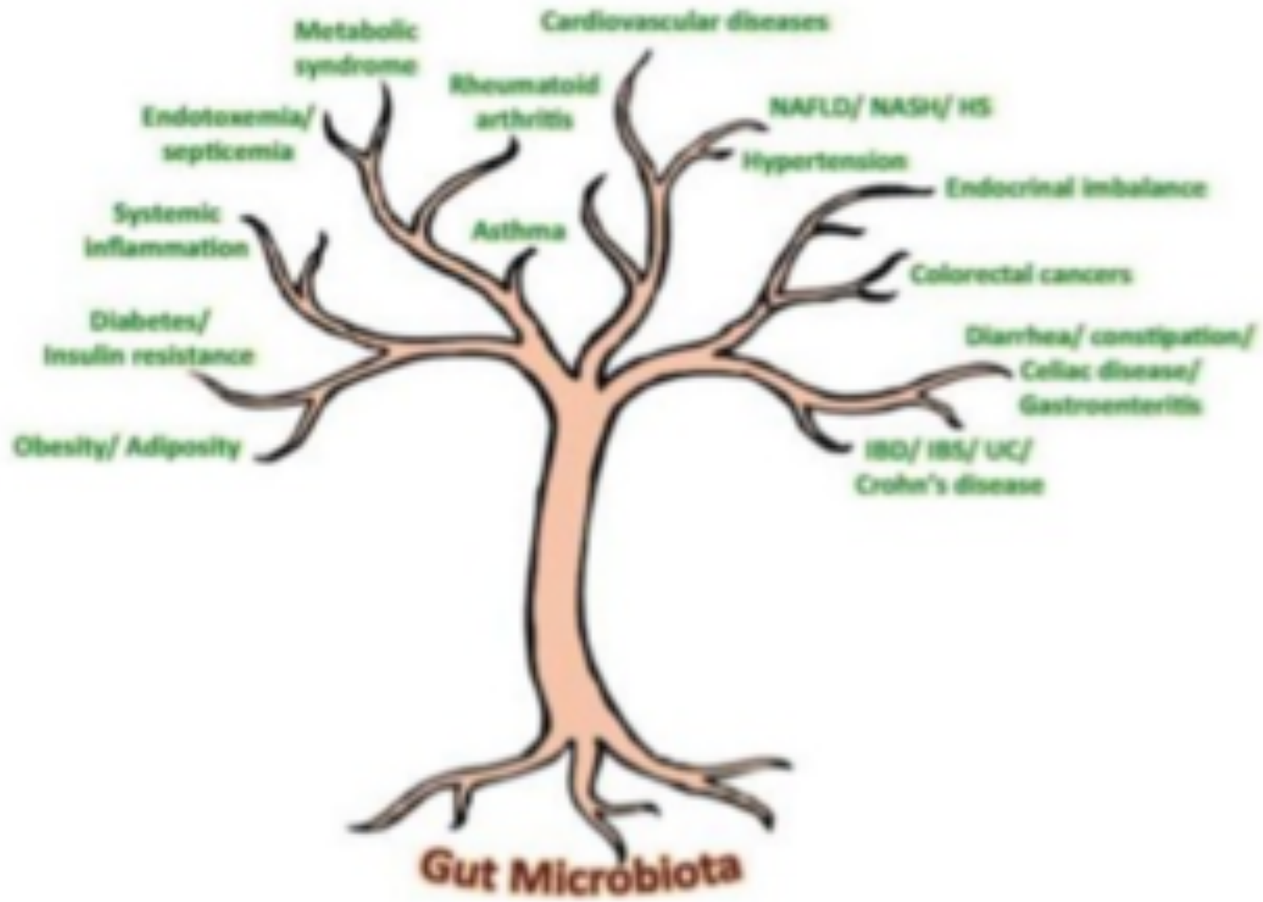


Figure 1. Speculated health implications of gut microbiota. NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; HS, hepatic steatosis; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; UC, ulcerative colitis.

What can damage Gut Flora

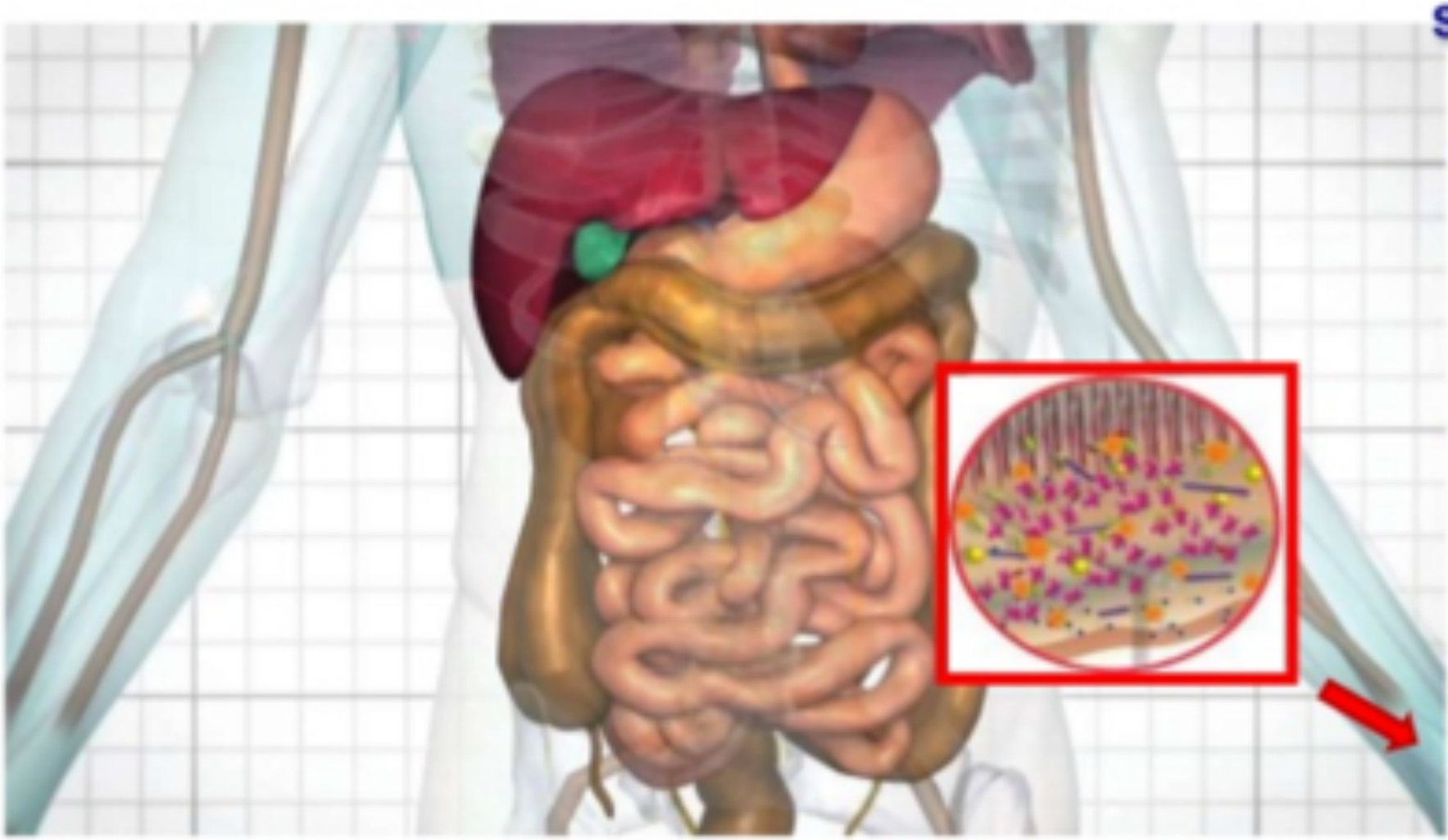
Dysbiosis: Microbial Imbalance Inside the Body

- Antibiotics
- Steroids, The Pill
- Other Drugs
- Stress
- Poor Diet
- Infections
- Disease
- Bottle Feeding
- Old Age
- Pollution
- Radiation
- Alcohol
- Toxic Chemicals
- Dental Work
  (mercury)

The Leaky Gut Syndrome

Permeable gut lining Vs. Inflamed digestive tract

(↑ Intestinal Permeability 2nd to inflamed digestive tract)



Systemic Disease
Endotoxemia
Autoimmunity

↑

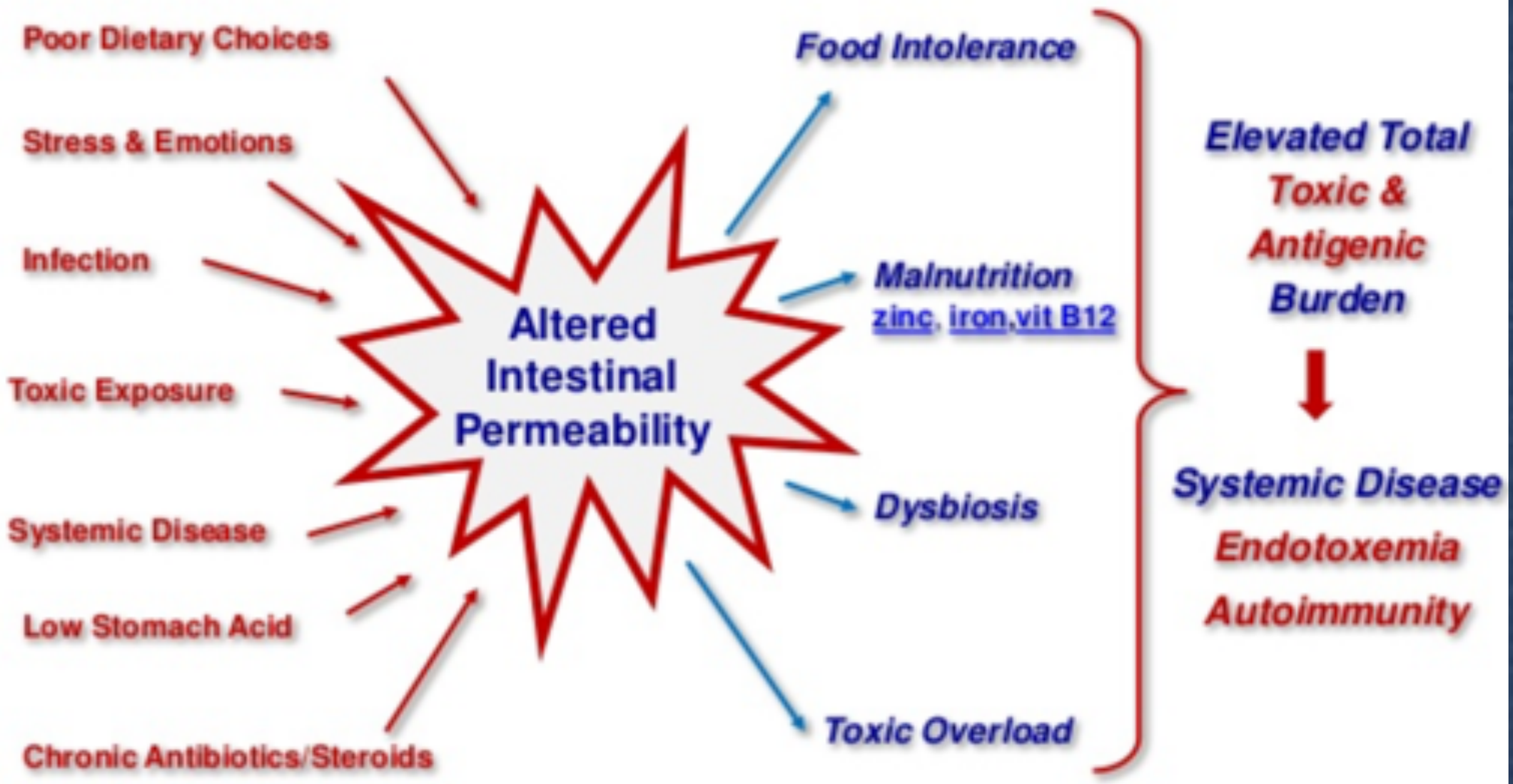
Elevated Total
Toxic & Antigenic
Burden

↑

Undigested food
Pathogens
& Toxins

↑ Intestinal Permeability

Pathophysiology



The Leaky Gut Syndrome

Leaky gut syndrome is a rapidly growing condition

Millions of people are struggling with and don't even know it

We might think leaky gut syndrome only affects the digestive system, but in reality it can lead to many other health conditions

Food allergies, low energy, joint pain, thyroid disease, autoimmune conditions and slow metabolism could be leaky gut symptoms

What is the Leaky Gut Syndrome?

The lining of digestive tract like a net with extremely small holes, only allow specific small substances to pass through
Gut lining as a barrier it keep out big particles that can damage our system

With a leaky gut (*increased intestinal permeability*), the "net" in the digestive tract gets damaged. Bigger holes developed in the net

Things that normally can't pass through, are now be able to
Proteins like gluten
Bad bacteria
Undigested foods particles
Toxic waste leak from the inside of intestinal wall into blood stream

Causing an immune reaction

Diagnosis of a leaky gut

symptoms

Leaky Gut leads to inflammation throughout our systems

Digestive symptoms

- Bloating
- Diarrhoea
- Pain
- Stomach cramps after eating
- Food sensitivities as bread

Other symptoms

- Sinusitis
- Skin issues like rosacea and acne
- Eczema
- Migraine & Headaches
- Thyroid conditions
- Joint pains
- Chronic fatigue
- Weight gain
- Syndrome X

Other symptoms

A leaky gut may not only present itself as digestive discomfort

Other symptoms relating to a leaky gut include:

- **Hormone imbalances causing mood swings**
- **Headaches**
- **Skin breakouts**
- **Tiredness and fatigue**
- **Joint pains associated with inflammation and intolerances**
- **Depression and anxiety**

Health issues linked to gut permeability

Conditions may increase gut permeability

- Inflammatory bowel diseases IBD
  - ulcerative colitis
  - Crohn's disease

- Irritable bowel syndrome IBS

Signs and symptoms are uncomfortable

IBS - doesn't cause changes in bowel tissue or increase risk of colorectal cancer

unlike ulcerative colitis and Crohn's disease, which are forms of inflammatory bowel disease

- Gastritis (inflammation of the stomach – several causes)

- HIV / AIDS

- Type 1 diabetes

Diagnosis of a leaky gut

Tests

- A digestive stool analysis can test secretory IgA (Immunoglobulin A) levels

- IgA is an antibody used by the immune system to identify and fight off unwanted objects such as infectious bacteria; this specific type of antibody is produced in mucosal linings (the gut wall)

- As unwanted undigested food particles may pass through the gut lining, an immune reaction involving high levels of IgA antibodies may suggest a permeable gut lining

- Test for food intolerances: if IgG antibodies are produced, a leaky gut is very likely

What Causes Leaky Gut?

The role of chronic inflammation

Chronic inflammation causes continuous breakdown of cells

Excess inflammation can damage mucosal cells' tight junctions

Inflammation may be a result of an inflammatory diet or medication

Inflammation exacerbates pain and sensitivity to foods

Too much inflammation stalls the healing process

- Possible causes
  - chronic inflammation
  - nutritional deficiencies
  - fatty acid deficiencies
  - improper digestion
  - high intake of commonly aggravating foods
  - Chronic stress
- Other possible causes
  - parasites
  - pathogenic bacteria
  - yeast infections

What Causes Leaky Gut?

Improper digestion

- Low stomach acid = improper breakdown of proteins

- Low production of bile = improper breakdown of fats

- Low levels of digestive enzymes = larger undigested food particles

- Possible causes
  - chronic inflammation
  - nutritional deficiencies
  - fatty acid deficiencies
  - improper digestion
  - high intake of commonly aggravating foods
  - Chronic stress

- Other possible causes
  - parasites
  - pathogenic bacteria
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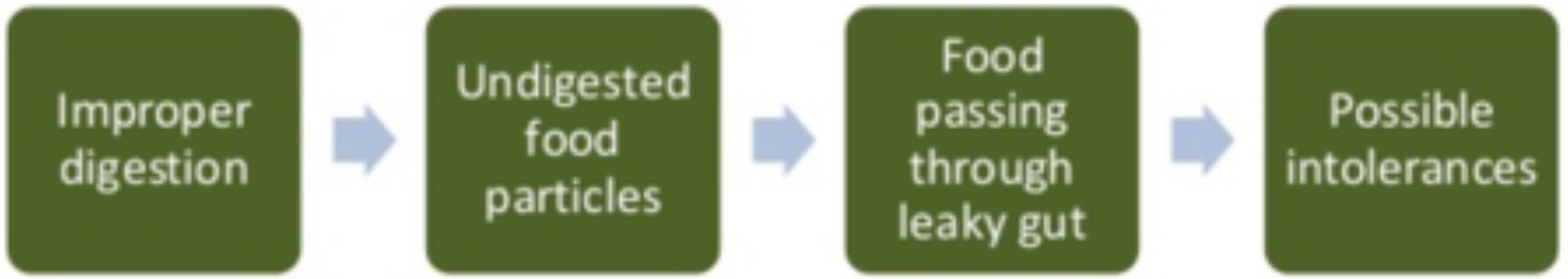

What Causes Leaky Gut?

Fatty acid deficiencies

- A deficiency in omega-3 fatty acids may increase inflammation

- A low omega-3 index may also reduce fluidity of cell membranes

- Low levels of omega-3 may also shrink cells (less plumped up) leading
  to possible gaps between mucosal cells

- Imbalanced ratio of omega-6 to omega-3 fatty acids may lead to inflammation

- Possible causes
  - chronic inflammation
  - nutritional deficiencies
  - fatty acid deficiencies
  - improper digestion
  - high intake of commonly aggravating foods
  - Chronic stress

- Other possible causes
  - parasites
  - pathogenic bacteria
  - yeast infections

Digestive symptoms

- Digestive symptoms are often not a priority to clients
- Clients may want to concentrate on other goals such as
  - overcoming fatigue (associated with leaky gut)
    - Diarrhoea
    - Constipation
    - Burning sensation in the stomach
    - Passing a stool shortly after eating
    - Pain after drinking alcohol or spicy food
    - Stomach cramps
    - Gas

The 4-Step Plan to Heal Leaky Gut

The good news is there's a solution to successfully healing leaky gut

There is a four (4R)-step process that includes:

1- Remove foods and factors that damage the gut

2- Replace with healing foods

3- Repair with specific supplements

4- Rebalance with probiotic

3- Repair with specific supplements

Top 5 Supplements for Healing Leaky Gut

l-glutamine, probiotics, digestive enzymes, aloe vera juice, quercetin, NAG and licorice root.

1- Probiotics are the most important supplement to take because it helps replenish good bacteria and crowds out bad bacteria. I recommend getting probiotics in both food and supplement form. I see people all the time only follow part of the protocol in healing their leaky gut syndrome by removing the damaging irritants. But the part they often leave out is re-inoculating their gut with beneficial bacteria that will keep bad bacteria at bay.

So load up on BOTH probiotic-rich foods and take AT LEAST 50 billion units of probiotics daily from a high-quality brand.

2- Digestive enzymes (one or two capsules at the beginning of each meal) ensure that foods are fully digested, decreasing the chance that partially digested foods particles and proteins are damaging your gut wall.

3- Repair with specific supplements

Top 5 Supplements for Healing Leaky Gut

3- L-Glutamine is critical for any program designed to heal leaky gut. **Glutamine powder** is an essential amino acid supplement that is anti-inflammatory and necessary for the growth and repair of your intestinal lining. L-glutamine benefits include acting as a protector: coating your cell walls and acting as a repellent to irritants. Take 2–5 grams twice daily.

4- Licorice Root (DGL) is an adaptogenic herb that helps balance cortisol levels and improves acid production in the stomach. DGL supports the body's natural processes for maintaining the mucosal lining of the stomach and duodenum. This herb is especially beneficial if someone's leaky gut is being caused by emotional stress. Take 500 milligrams twice daily.

5- Quercetin has also been shown to improve gut barrier function by sealing the gut because it supports creation of tight junction proteins. It also stabilizes mast cells and reduces the release of histamine, which is common in food intolerance. New studies have also shown its effectiveness in healing ulcerative colitis. Take 500 milligrams three times daily with meals.

If you can follow the above protocol, you are well on your way to successfully treating your gut for good.

PERSPECTIVE ARTICLE

Front. Med., 23 June 2014 | https://doi.org/10.3389/fmed.2014.00015

Gut microbiota: the next-gen frontier in preventive and therapeutic medicine?

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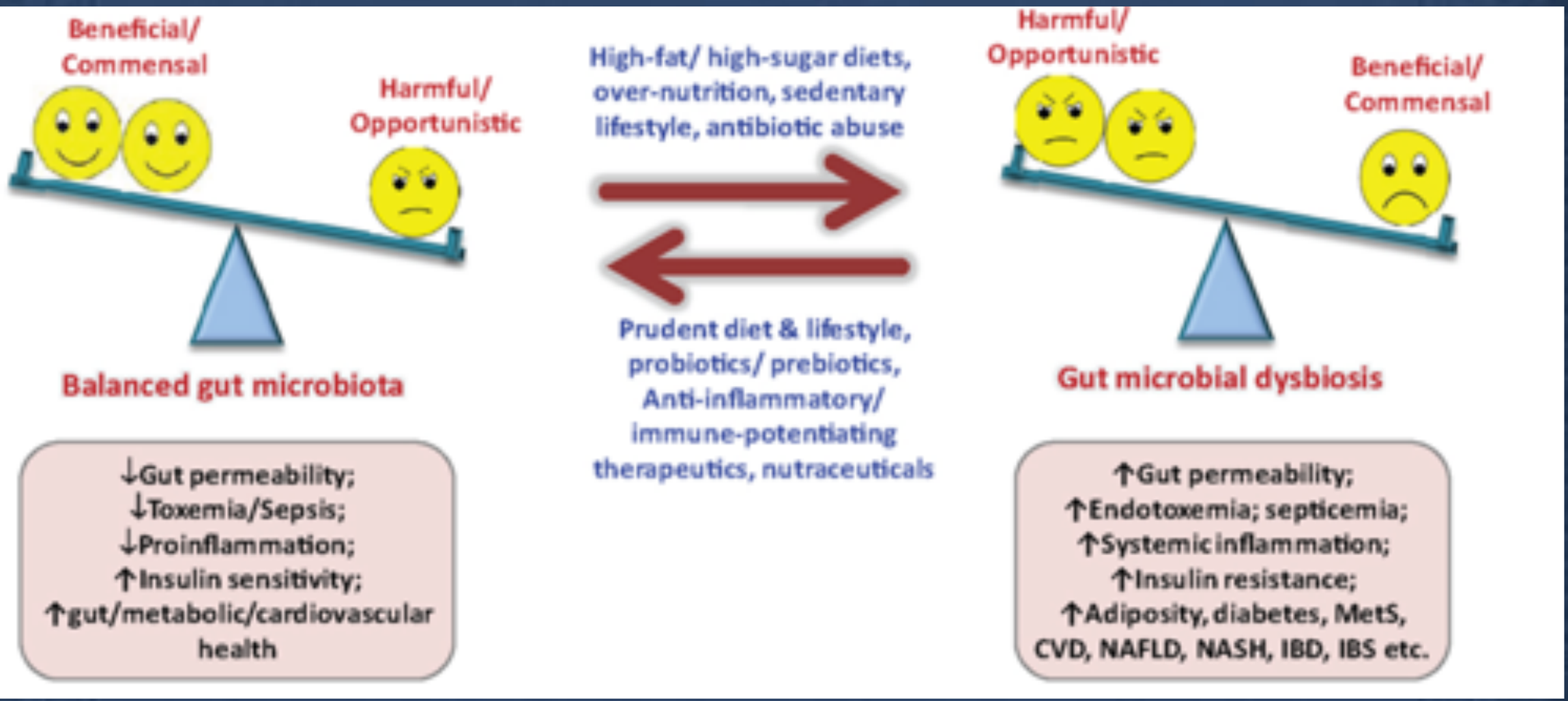
[3]ReGenera Research Group for Aging Intervention, Milan, Italy

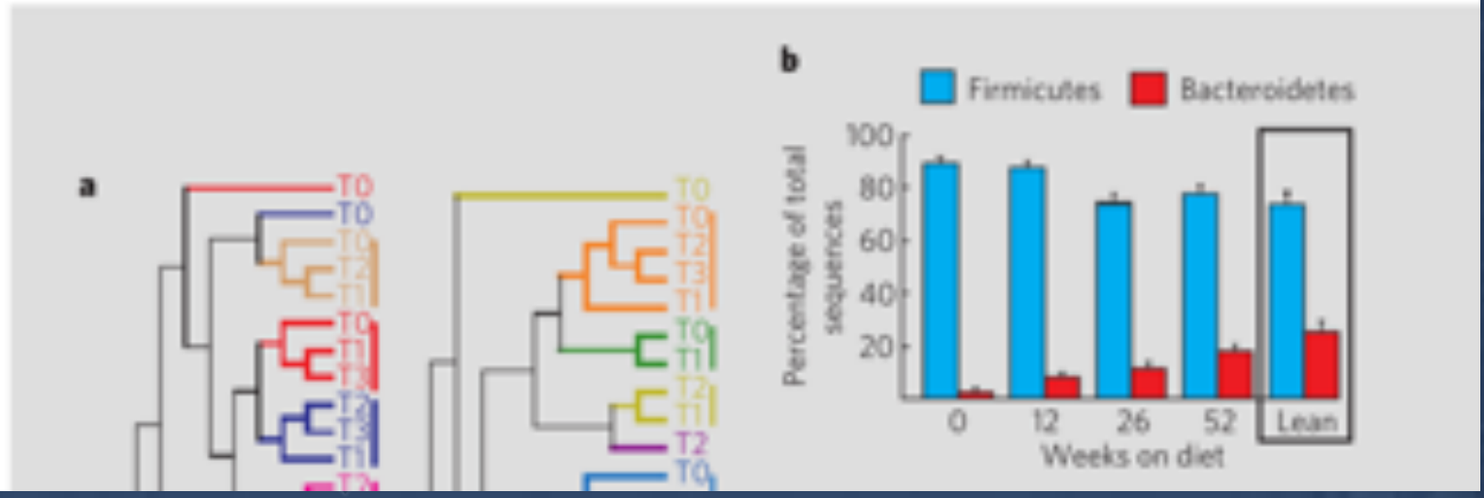

Beneficial/
Commensal
Harmful/
Opportunistic
Balanced gut microbiota
↓Gut permeability;
↓Toxemia/Sepsis;
↓Proinflammation;
↑Insulin sensitivity;
↑gut/metabolic/cardiovascular health
High-fat/ high-sugar diets, over-nutrition, sedentary lifestyle, antibiotic abuse
Prudent diet & lifestyle, probiotics/ prebiotics, Anti-inflammatory/ immune-potentiating therapeutics, nutraceuticals
Harmful/
Opportunistic
Beneficial/
Commensal
Gut microbial dysbiosis
↑Gut permeability;
↑Endotoxemia; septicemia;
↑Systemic inflammation;
↑Insulin resistance;
↑Adiposity, diabetes, MetS, CVD, NAFLD, NASH, IBD, IBS etc.

MICROBIAL ECOLOGY

Human gut microbes associated with obesity

Two groups of beneficial bacteria are dominant in the human gut, the Bacteroidetes and the Firmicutes. Here we show that the relative proportion of Bacteroidetes is decreased in obese people by comparison with lean people, and that this proportion increases with weight loss on two types of low-calorie diet. Our findings indicate that obesity has a microbial component, which might have potential therapeutic implications.

Trillions of microbes live in the human gut,



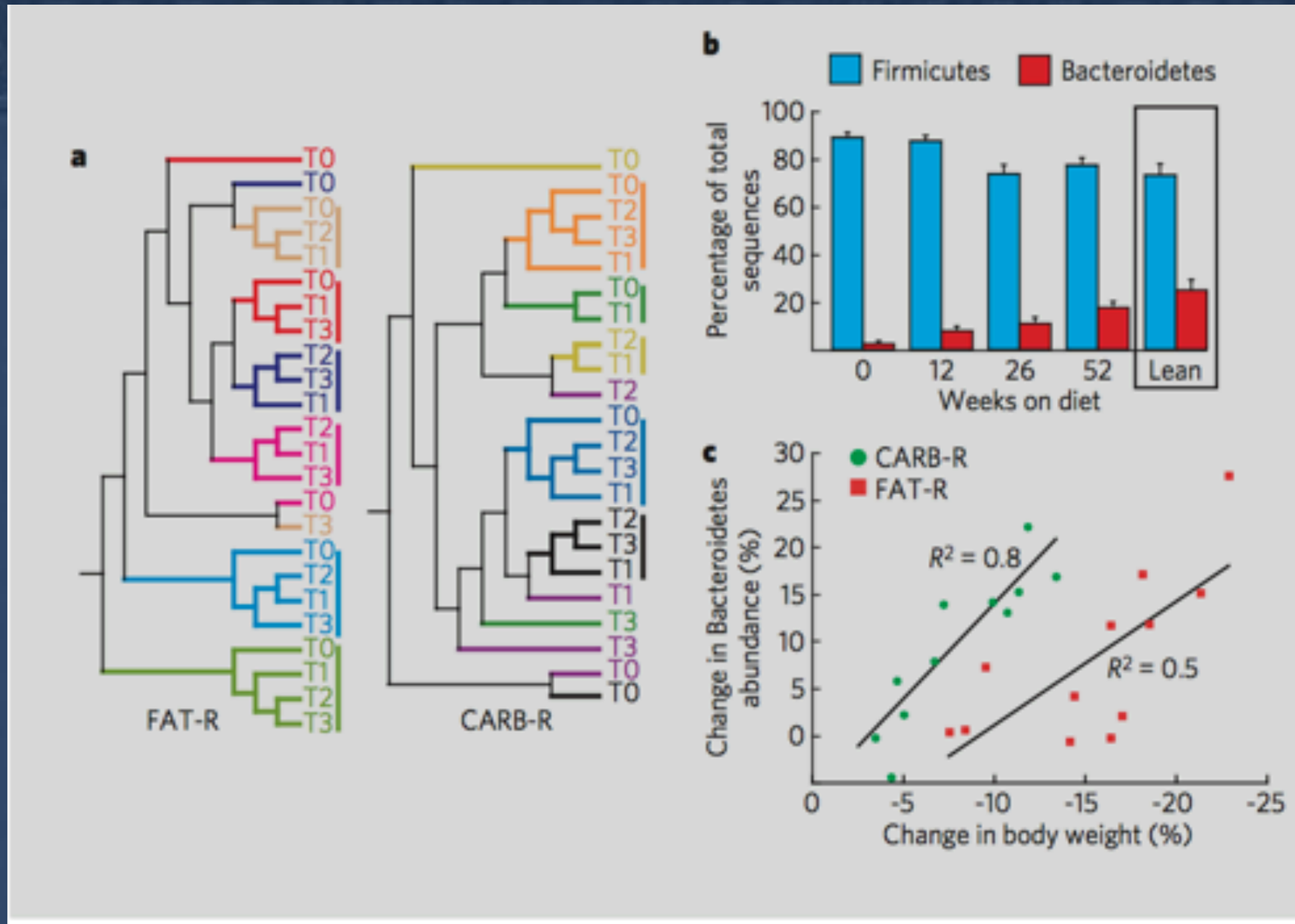


Figure 1 | Correlation between body-weight loss and gut microbial ecology. **a,** Clustering of 16S ribosomal RNA gene sequence libraries of faecal microbiota for each person (in different colours) and time point in diet therapy (T0, baseline; T1, 12 weeks; T2, 26 weeks; T3, 52 weeks) in the two diet-treatment groups (fat restricted, FAT-R; carbohydrate restricted, CARB-R), based on UniFrac analysis of the 18,348-sequence phylogenetic tree. **b,** Relative abundance of Bacteroidetes and Firmicutes. For each time point, values from all available samples were averaged (*n* was 11 or 12 per time point). Lean-subject controls include four stool samples from two people taken 1 year apart, plus three other stool samples[6]. Mean values ± s.e. are plotted. **c,** Change in relative abundance of Bacteroidetes in subjects with weight loss above a threshold of 2% weight loss for the CARB-R diet and 6% for the FAT-R diet.

REVIEW Open Access

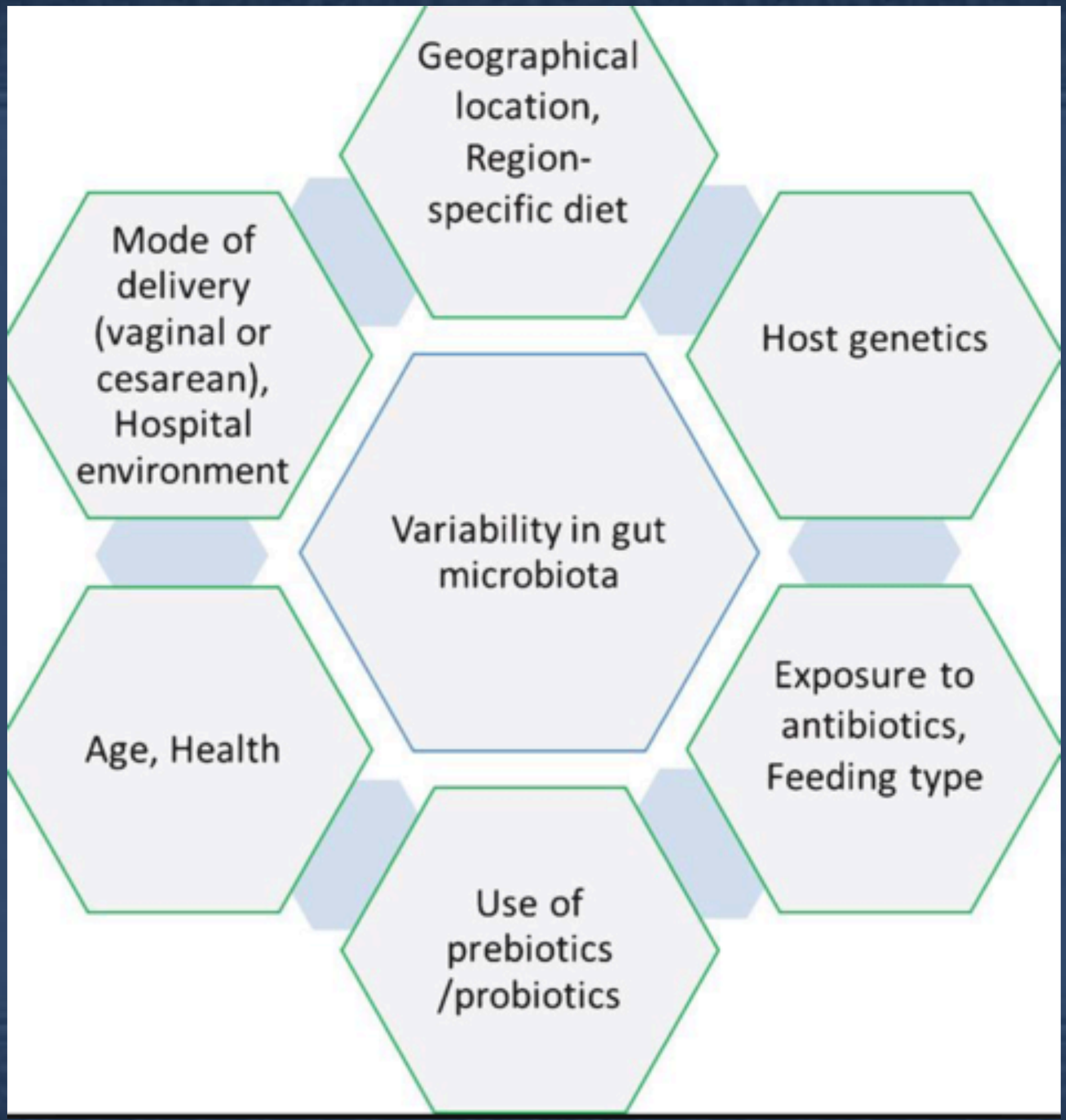
Physical exercise, gut, gut microbiota, and atherosclerotic cardiovascular diseases

Jingyuan Chen, Yuan Guo, Yajun Gui and Danyan Xu*

Abstract

Arteriosclerotic cardiovascular diseases (ASCVDs) are the leading cause of morbidity and mortality worldwide and its risk can be independently decreased by regular physical activity. Recently, ASCVD and its risk factors were found to be impacted by the gut microbiota through its diversity, distribution and metabolites. Meanwhile, several experiments demonstrated the relationship between physical exercise and diversity, distribution, metabolite of the gut microbiota as well as its functions on the lipid metabolism and chronic systematic inflammation. In this review, we summarize the current knowledge on the effects of physical exercise on ASCVD through modulation of the gut microbiota and intestinal function.

Keywords: Atherosclerosis, Physical exercise, Gut microbiota


Geographical location, Region-specific diet
Mode of delivery (vaginal or cesarean), Hospital environment
Host genetics
Variability in gut microbiota
Age, Health
Exposure to antibiotics, Feeding type
Use of prebiotics /probiotics

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Published online 2015 Sep 8. doi: 10.1053/j.seminoncol.2015.09.001

PMCID: PMC4789109
NIHMSID: NIHMS754339
PMID: 26970128

The Microbiome and Its Potential as a Cancer Preventive Intervention

Scott J. Bultman[1,*]

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Abstract

Go to:

It is becoming increasingly clear that microbiota which inhabit our body influence cancer predisposition and etiology. In addition to pathogens with oncogenic properties, our commensal and symbiotic microbiota have tumor-suppressive properties. Our diet and other environmental factors can modulate the abundance of certain members of microbial communities within our gastrointestinal tract and at other anatomical sites. Furthermore, some dietary factors are metabolized by commensal/symbiotic gut microbiota into bioactive food components believed to prevent cancer. For example, dietary fiber undergoes bacterial fermentation in the colon to yield butyrate, which is a short-chain fatty acid and histone deacetylase (HDAC) inhibitor that suppresses the viability and growth of colorectal cancer cell lines. A recent study utilizing gnotobiotic mouse models demonstrates that fiber can protect against colorectal tumorigenesis in a microbiota- and butyrate-dependent manner that involves the Warburg effect. This and other examples suggest that some of the inter-individual variation observed in epidemiology and intervention studies that have investigated associations between diet and cancer risk might be explained by differences in microbiota among the participants. Data from basic research studies also support the idea that probiotics and prebiotics could be plausible chemoprevention strategies that may be utilized to a greater extent in the future.

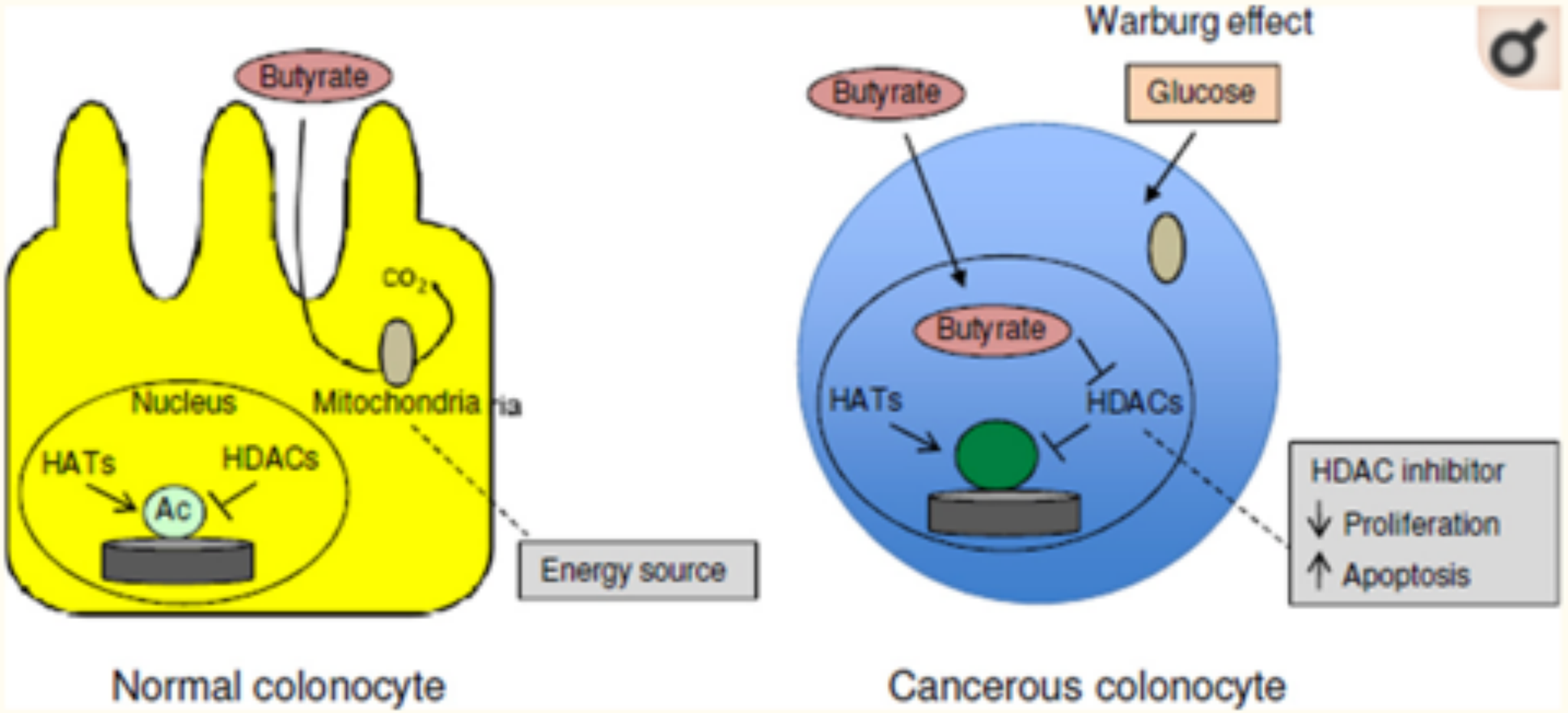

Figure 6

Mechanism of butyrate-mediated tumor suppression. In normal colonocytes (left), butyrate is utilized as the primary energy source and metabolized in the mitochondria so relatively little accumulates inside of the cell. In cancerous colonocytes (right), glucose is the primary energy source due to the Warburg effect. Butyrate is still transported into the cell via monocarboxylate transporters but is not metabolized in the mitochondria, which allows it to accumulate in the nucleus and function as an HDAC inhibitor to epigenetically regulate genes involved in cell proliferation and apoptosis.

Genomics, Proteomics & Bioinformatics

Volume 16, Issue 1, February 2018, Pages 33-49

open access

Review

Human Gut Microbiota and Gastrointestinal Cancer

Changting Meng [1, 2, a], Chunmei Bai [2, b], Thomas D. Brown [3, c], Leroy E. Hood [1, 3, d], Qiang Tian [1, 4] [e]

Show more

https://doi.org/10.1016/j.gpb.2017.06.002

Abstract

Human gut microbiota play an essential role in both healthy and diseased states of humans. In the past decade, the interactions between microorganisms and tumors have attracted much attention in the efforts to understand various features of the complex microbial communities, as well as the possible mechanisms through which the microbiota are involved in cancer prevention, carcinogenesis, and anti-cancer therapy. A large number of studies have indicated that microbial dysbiosis contributes to cancer susceptibility via multiple pathways. Further studies have suggested that the microbiota and their associated metabolites are not only closely related to carcinogenesis by inducing **inflammation** and immune dysregulation, which lead to genetic instability, but also interfere with the pharmacodynamics of anticancer agents. In this article, we mainly reviewed the

Bidirectional Interactions Between Dietary Curcumin and Gut Microbiota

Liang Shen [1 2 3], Hong-Fang Ji [1 2 3]

Affiliations + expand

PMID: 29781709 DOI: 10.1080/10408398.2018.1478388

Abstract

Curcumin is a polyphenolic compound with a long history of use as an herbal remedy, dietary spice, and food-coloring agent. Despite curcumin possesses a wide range of biological and pharmacological activities, it exhibits extremely poor bioavailability, which makes its pharmacology intriguing and also hinders its clinical application. In recent years, there is ample evidence supporting the associations between the alteration of gut microbiota and many diseases. Interestingly, after oral administration, curcumin shows its preferential distribution and accumulation in the intestine. In view of the above aspects, we reviewed the updated knowledge regarding the bidirectional interactions between curcumin and gut microbiota from two perspectives: (1) gut microbiota regulation by curcumin and (2) curcumin biotransformation by digestive microbiota. Besides the study deals with 3 potential pharmacological implications: (1) identification of metabolites being more active and bioavaliable than parent curcumin; (2) assessment of contribution of gut microbiota regulation of curcumin to its pharmacological effects and (3) development of gut microbiota regulation-based disease prevention/treatment strategy for curcumin in view of its clinical safety. This review is important to deepen our understanding of the mechanisms of action of curcumin and to provide future directions about how to use this natural compound to combat human diseases.

Keywords: Bioavailability; Curcumin; Gut microbiota; Interactions; Microbial biotransformation.

Similar articles

12 novembre 2015

IEO/Università Statale di Milano: Gli italiani scoprono il meccanismo che controlla la disseminazione batterica

Comunicato stampa - Science pubblica la ricerca dell'Istituto Europeo di Oncologia e dell'Università Statale di Milano che identifica una nuova struttura anatomica intestinale: si aprono nuove prospettive di cura per la celiachia, il diabete di tipo 2 e il danno epatico

Science, una delle più prestigiose riviste scientifiche al mondo, pubblica oggi lo studio di un gruppo di ricercatori dell'Istituto Europeo di Oncologia di Milano e dell'Università Statale di Milano, guidati da Maria Rescigno - Direttore del Programma di Immunoterapia allo IEO e professore del Dipartimento di Oncologia e Emato-Oncologia (DIPO) alla Statale - che, studiando l'origine delle malattie del tratto gastro-intestinale, ha scoperto una nuova struttura anatomica. Gli italiani hanno identificato una barriera vascolare (che hanno chiamato Gut Vascular Barrier, GVB) che impedisce ai batteri funzionali che risiedono nell'intestino di trasferirsi attraverso il sangue, al fegato e di invadere l'organismo. La scoperta apre prospettive finora insperate per la cura della celiachia, del diabete di tipo 2 e delle malattie caratterizzate da danno epatico.

"Negli individui sani - spiega Maria Rescigno - i batteri intestinali (che formano una comunità chiamata Microbiota) difficilmente accedono al fegato, alla milza o ad altri organi periferici. Alcuni batteri nocivi, invece, riescono a raggiungere il fegato ed attivare una risposta del sistema immunitario, provocando un'infezione. Si pensava che l'epitelio dell'intestino (la parte più esterna della parete intestinale) fosse l'unica protezione per evitare la "migrazione" batterica. Noi abbiamo dimostrato l'esistenza di un'ulteriore barriera (quella vascolare intestinale – gut vascular barrier -GVB) che funge da schermo contro i batteri quando essi superano l'epitelio. Questa barriera vascolare impedisce così l'accesso del microbiota al fegato e controlla il trasferimento di proteine e nutrienti nel sangue. La GVB può essere elusa invece da batteri aggressivi, come la Salmonella - l'agente responsabile del tifo - che hanno sviluppato dei sistemi per infrangerla e quindi diffondersi nell'organismo attraverso il sistema circolatorio".

I ricercatori hanno scoperto inoltre che nei celiaci i quali, pur non ingerendo glutine, hanno elevate quantità di transaminasi nel sangue (vale a dire circa il 50% della popolazione celiaca) la GVB è modificata, e hanno così dimostrato che l'inattività di questa barriera può essere causa del danno epatico. Lo studio del ruolo della GVB porterà dunque a una migliore comprensione dell'asse intestino-fegato, che è fondamentale per la salute di tutto il nostro organismo.
"L'impatto clinico della nostra scoperta - continua Rescigno - può essere significativo da subito per le malattie con danno epatico. Stiamo inoltre valutando la funzione della barriera nella formazione delle metastasi epatiche del carcinoma intestinale. Dal punto di vista del pensiero scientifico, l'identificazione della GVB conferma il parallelismo straordinario che esiste in natura fra cervello e intestino. Infatti una barriera analoga esiste anatomicamente anche a livello encefalico, con una differenza funzionale: la barriera encefalica è ancora più selettiva perché crea un ambiente immunoprivilegiato dove il sistema immunitario entra solo se danneggiata, la barriera intestinale invece deve permettere il passaggio di nutrienti al fegato, ma evitare la disseminazione batterica".

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