Whole Body Health: Genestra HMF Probiotic Innovations and Evidence supporting GI, Immune and the Aging Brain

Presented by Dr. Nigel Plummer, Ph.D.
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Speaker Disclosure

Dr. Nigel Plummer, PhD

I am a paid advisor to Atrium Innovations. I have no other conflicts of interest to disclose.

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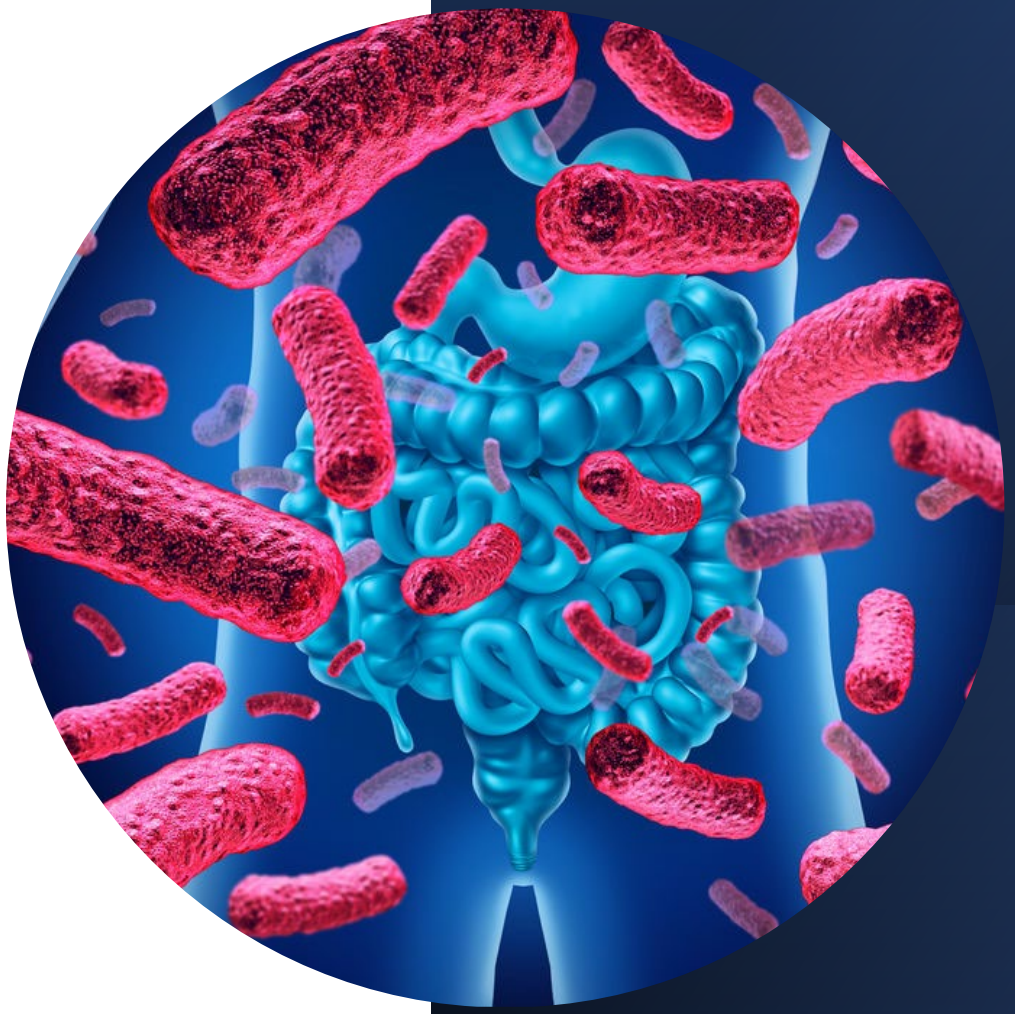
The Microbiome/ Microbiota – the other “Organ” in the Intestine



Our amazing microbiota – a constant companion and friend throughout our lives, without which, we would become ill and probably die within 5 years of birth!

The Gut Microbiome – The Small/Large Intestinal Split

SMALL INTESTINE

20 ft long - fast transit time (2-4 hours)

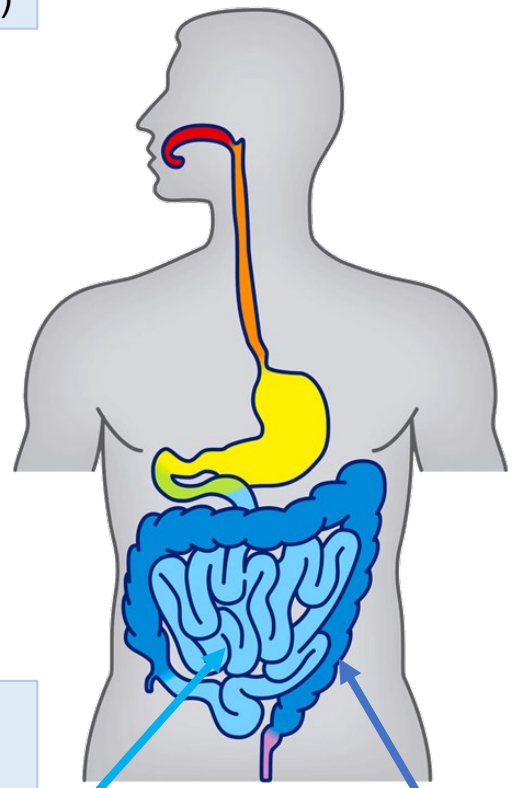
Site of major absorptive processes

Site of major immune, endocrine and enteric neural functionality

Site of major disruption of microbiome by antibiotics

Low microbial numbers dominated by facultative types (e.g Lactobacilli, Coliforms)

Site of most activity of most probiotics (2-25 billion)



4 ft long – slow transit time (18-90 hours)

LARGE INTESTINE

Minimal absorptive function

Site of some immune, endocrine, and neural functionality

Less disruption by most antibiotics

Huge microbial numbers dominated by obligate anaerobes (e.g Bacteroides)

Very high potency probiotics required to yield effect (100 billion – 2000 billion)

Site of major activity of prebiotics

Distribution of Physiological Systems Across the Intestine

Immune System

- 70-80% of the immune system is in the gut
- Present within:
  - epithelial layer (intraepithelial lymphocytes) every 4th cell is an IEL.
  - lamina propria (below epithelial layer)
  - mesenteric lymph nodes and Peyer's patches in ileum
- Distribution based on surface area and absorptive function – so circa 80% of gut immune system is in small intestine

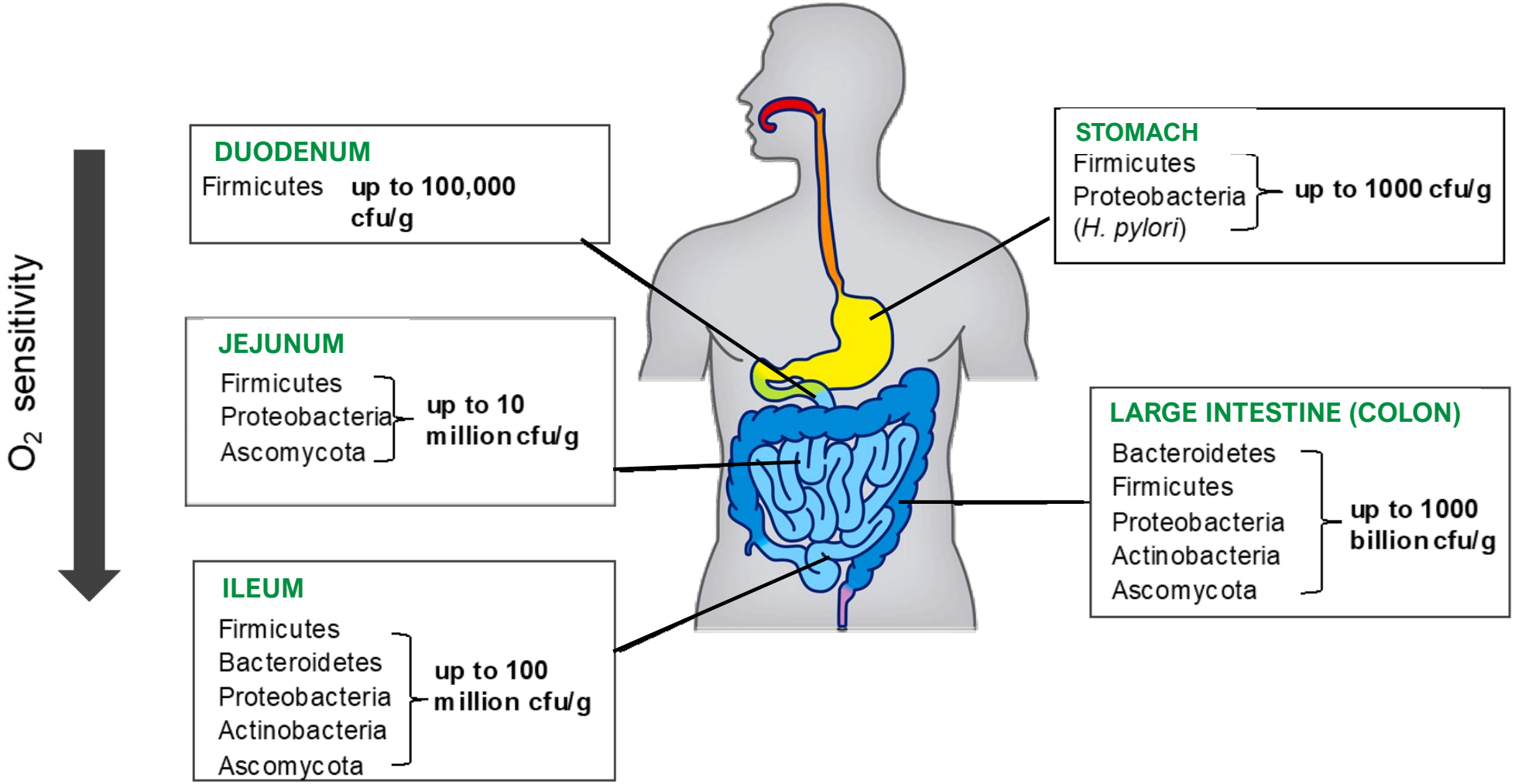
Enteric Neural System

- Second largest neural system in the body after the CNS
- 200-600 million neurones throughout gut – evenly distributed along gut length – so over 80% ENS in the small intestine

Enteric Endocrine System

- Functions to control appetite, sugar metabolism, etc
- Largest endocrine organ in the body in terms of numbers of cells
- Enteroendocrine cells are in the epithelial layer at 1/1000 cells
- Over 75% of enteroendocrine activity is in the small intestine

Typical Microbiota of the Adult Gastrointestinal Tract



Total number of microbiota: 100 – 200 billion
Total weight of microbiota: 2 - 5g

Total number of microbiota: up to 100,000 billion
Total weight of microbiota: 1000-1500g

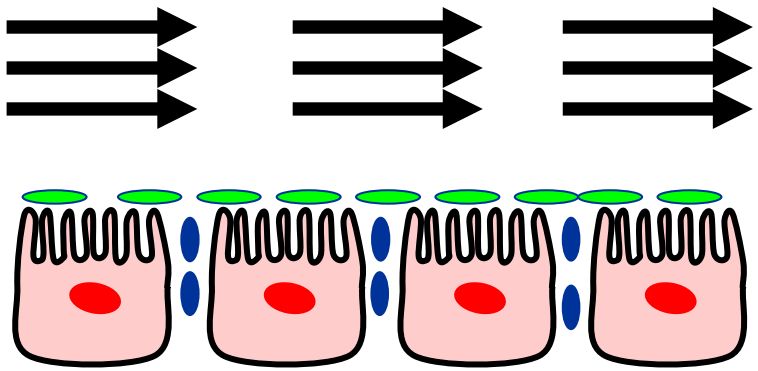
Why are there such major differences in small intestinal and large intestinal numbers of microbes?

Duodenum/ Jejunum

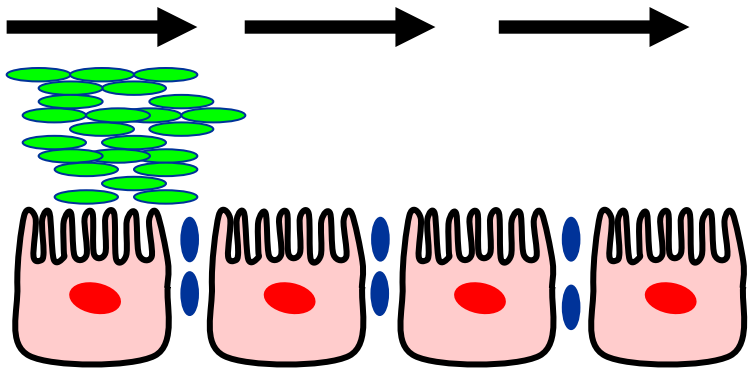
- Flow rate faster than replication rate
- Attachment compulsory for colonisation
- Bacterial layer one cell thick

Colon

- Flow rate slower than replication rate
- Attachment not necessary for colonisation
- Bacterial layer in mucous up to 200 cells thick

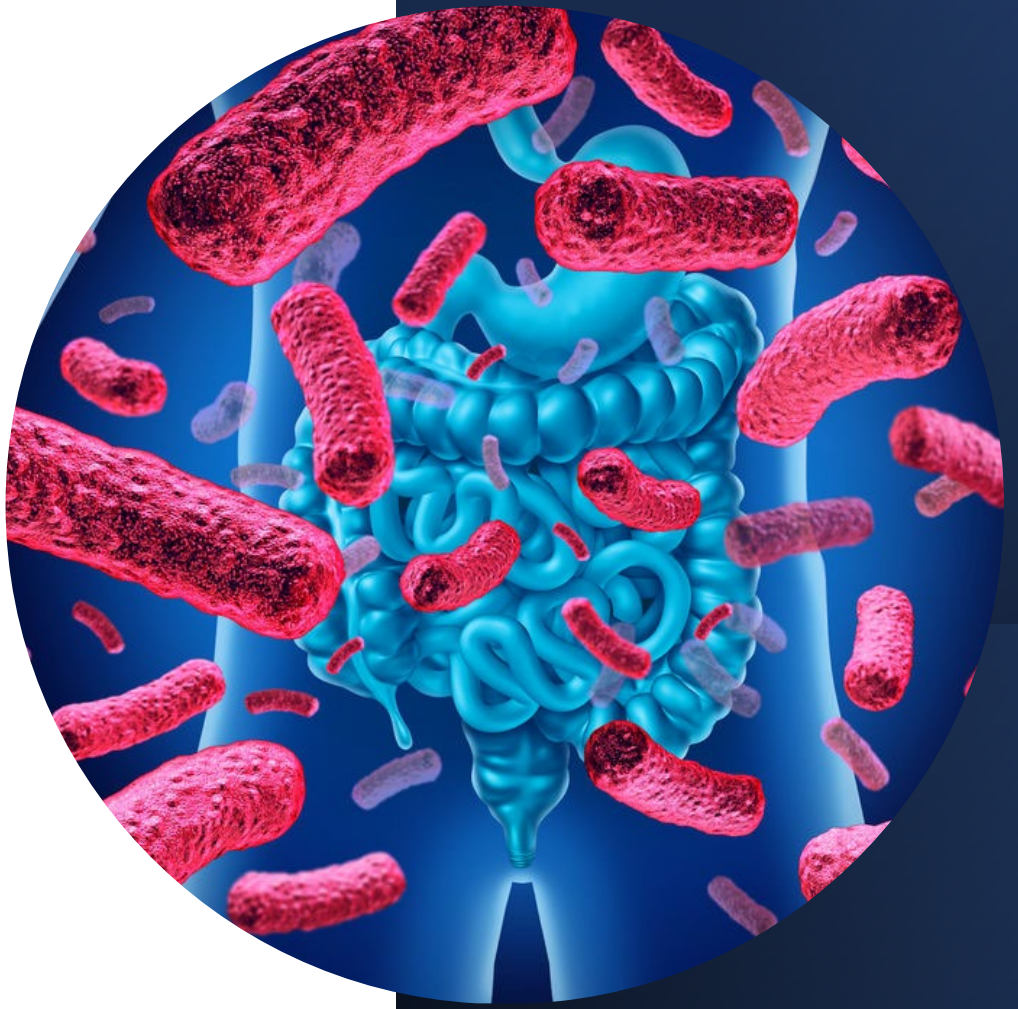


FAST FLOW



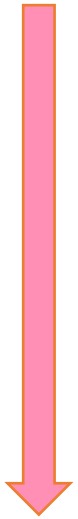
SLOW FLOW

Antibiotics: The Most Prevalent and Potent Disruptors of the Microbiome



Antibiotics: the Greatest Medical Advance of the 20th Century

1928: Penicillin discovery (Sir Alexander Fleming, 'Mould Juice')
1940s-1960s: Golden Age - Discovery of a number of antibiotics



- Pneumonia, staph infections, TB, infectious diarrhoea etc
- Wound and battlefield infections
- Surgical infections
- Childbirth complications
- etc

Antibiotics

….now antibiotic resistance is probably the biggest global threat to human healthcare in the 21st century

By 2050

- Global cumulative cost of antibiotic resistance will reach
  100 trillion US Dollars
- **10 million people** dying every year due to antibiotic resistance

(O'Neill J, Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations 2014)

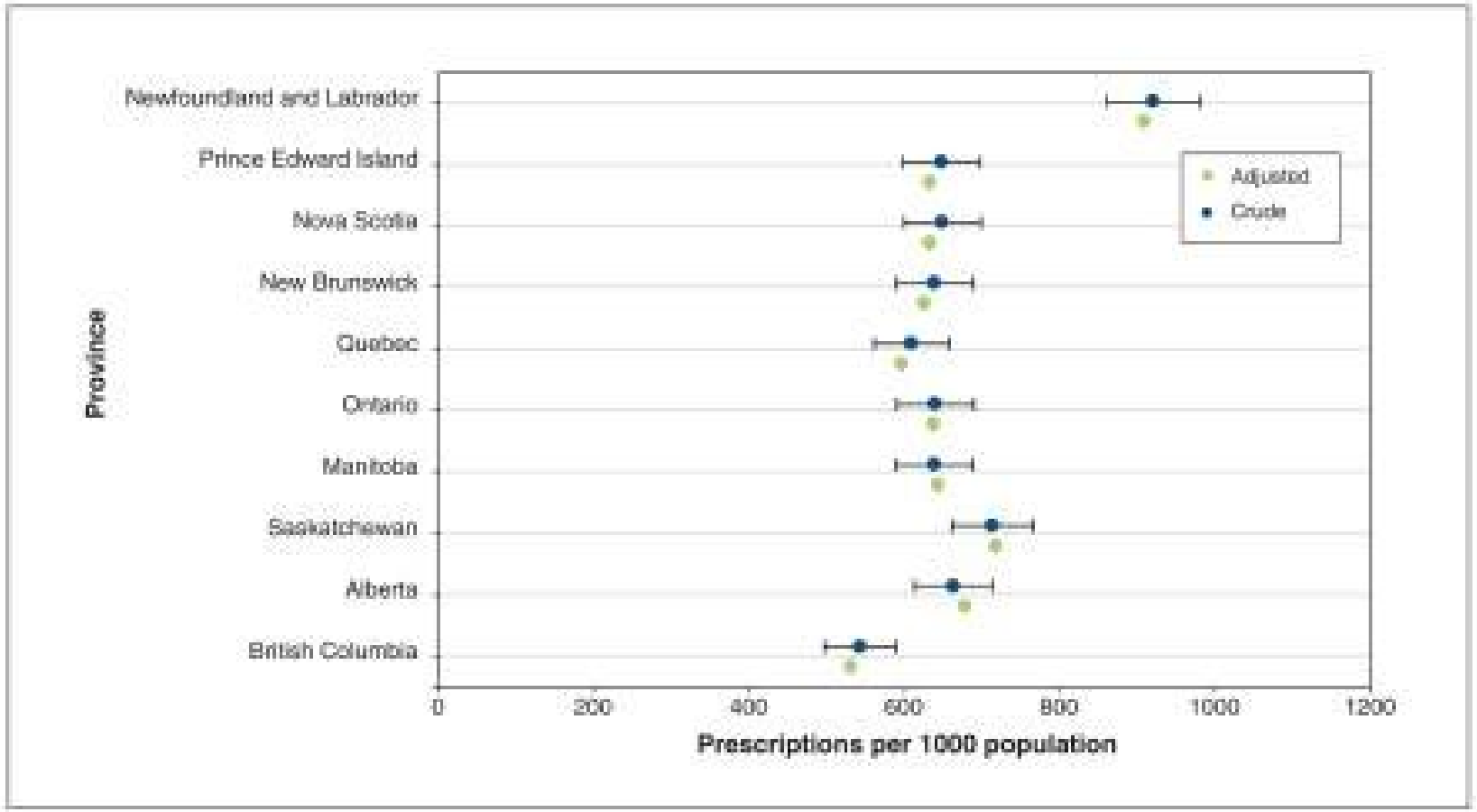
The Threat of Antibiotic Resistance – Carbapenem Resistant Enterobacteriaceae (CRE's) – The 'Nightmare Infection'

- E.coli and Klebsiella pneumonieae are main threats
- Carbapenem resistance first discovered in 2000
- In USA 9000 infections and 600 deaths per year
- In Greece and Italy – 10-25% of invasive Klebsiella are CRE's – less in N.Europe
- CRE's are typically resistant to all antibiotics with the exception of colistin
- Without colistin CRE blood infections have a fatality rate of over 50%.
- In May 2016 the first human carrier of the MCR-1 resistance gene carried on plasmids was found in a USA woman. This gene confers resistance to colistin, This resistance was traced to agricultural use of polymyxins.

CDC: Antibiotic Resistance Threats in the USA Report 2019

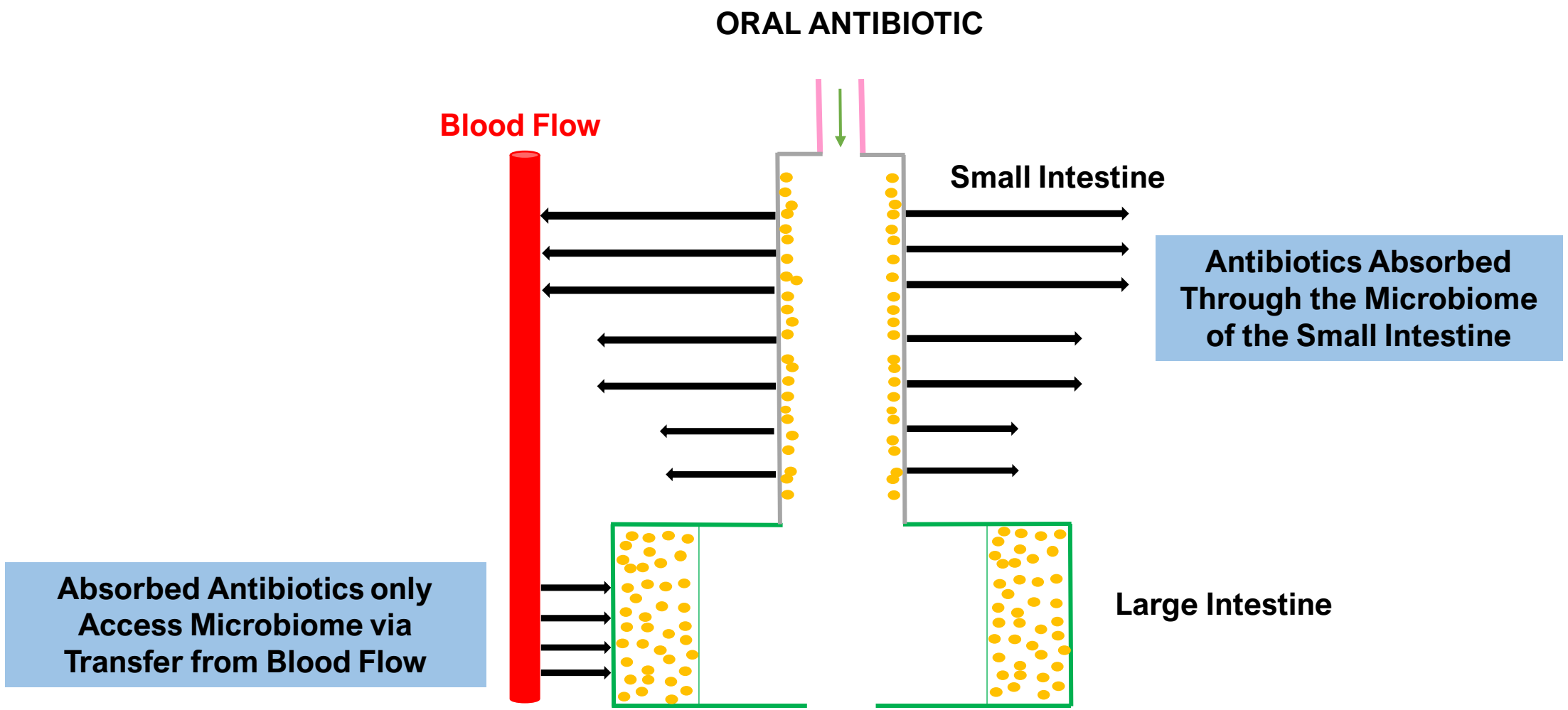
ECDC – Carbapenum resistant Enterobacteriaceae – second update Sept 2019

Antibiotic Use Across Canada in 2019



- **Total of 23,406,640 outpatient scripts**
- **Average of 627 scripts per 1000 population**
- **Newfoundland and Labrador nearly at one script per year.**

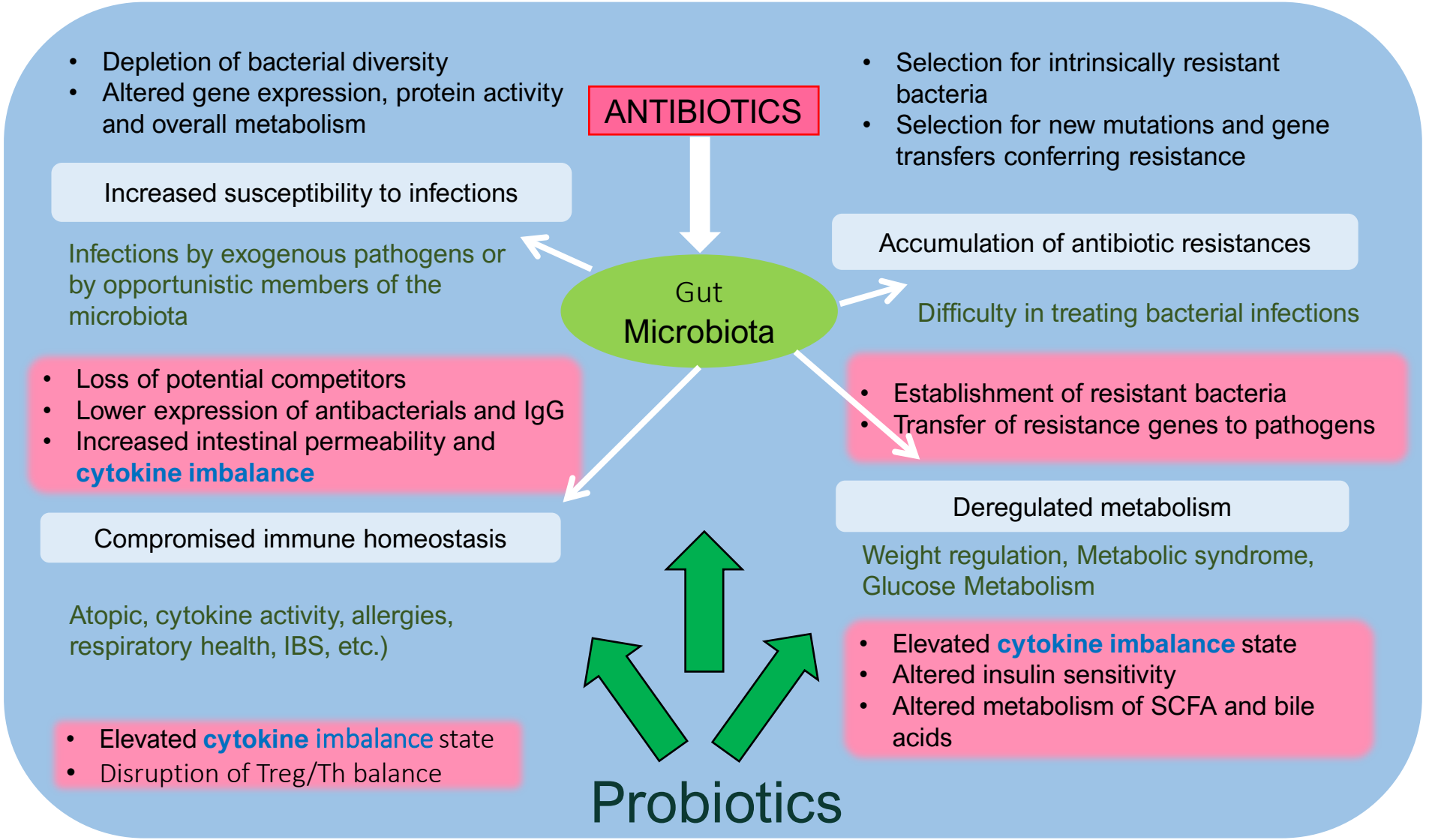
Differential Effects of Antibiotics on the Intestinal Microbiome



Differential Effects of Antibiotics on the Intestinal Microbiome

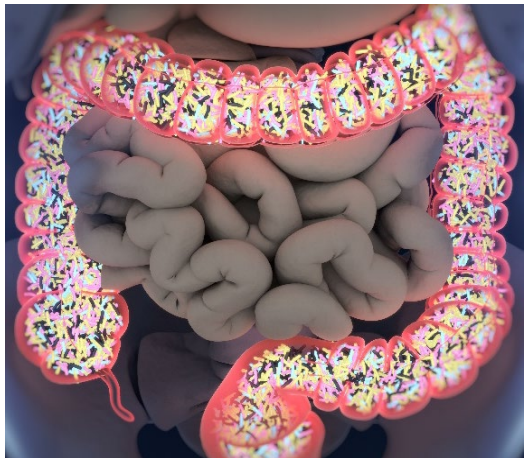
Antibiotic Administration	Disruption of Microbiome	
	Small Intestine	**Large Intestine**
Oral Absorbed Antibiotics	High	Low
Oral Non-absorbed Antibiotics	High	High
Intravenous Antibiotics	Moderate	Low

Microbial Balance and Potential Health Risks



(Francino MP 2016, Front Microbiol 6: 1543)

Conditions Associated with Dysbiosis



- NEC
- Allergy
- Obesity
- Type 1 Diabetes

Strong early life association

- AAD
- CDI
- IBD
- IBS
- Diabetes T2, Metabolic Syndrome
- CVD
- Abnormal Cell Growth
- Depression, Stress, Anxiety

Antibiotic Use Prenatally and in Early Life

- Loss of microbial diversity, increase of antibiotic resistance
- Antibiotic treatment for more than 5 days in premature infants is associated with an increased risk of late-onset sepsis, NEC and overall mortality
- Increased risk of infections, eczema, hay fever food allergy, asthma
- Increased risk of childhood obesity
- Increased risk of type 1 diabetes
- Increased risk of type 2 diabetes associated with repeated use
- Behavioural difficulties and greater number of depression symptoms

(Neuman et al, FEMS Microbiol Rev 2018; Langdon et al, Genome Medicine 2016)

Antibiotics in Early Life and Obesity

Philadelphia cohort study with 64,580 children:

- 69% children were exposed to antibiotics before age 24 months
- Mean of 2.3 episodes per child
- Cumulative exposure to antibiotics was associated with obesity at ages 24 to 59 months (RR=1.11, 95%CI: 1.02, 1.21 for ≥4 episodes)

(Bailey LC et al, JAMA Pediatr 2014)

In UK retrospective cohort study with 21,714 children:

- the administration of 3 or more courses of antibiotics prior to age 2 years is associated with an increased risk of obesity at 4 years
- 3-5 prescriptions: OR=1.41, 95%CI: 1.20, 1.65
- ≥6 prescriptions: OR=1.47, 95%CI: 1.19, 1.82

(Scott FI et al, Gastroenterology 2016)

The Need for Probiotics and The Repercussions of Microbial Imbalance

- The indigenous microbiota helps maintains normal function across a multitude of physiologies

- Microbial imbalance interrupts this beneficial homeostasis, with the potential to exacerbate existing conditions or cause adverse health situations

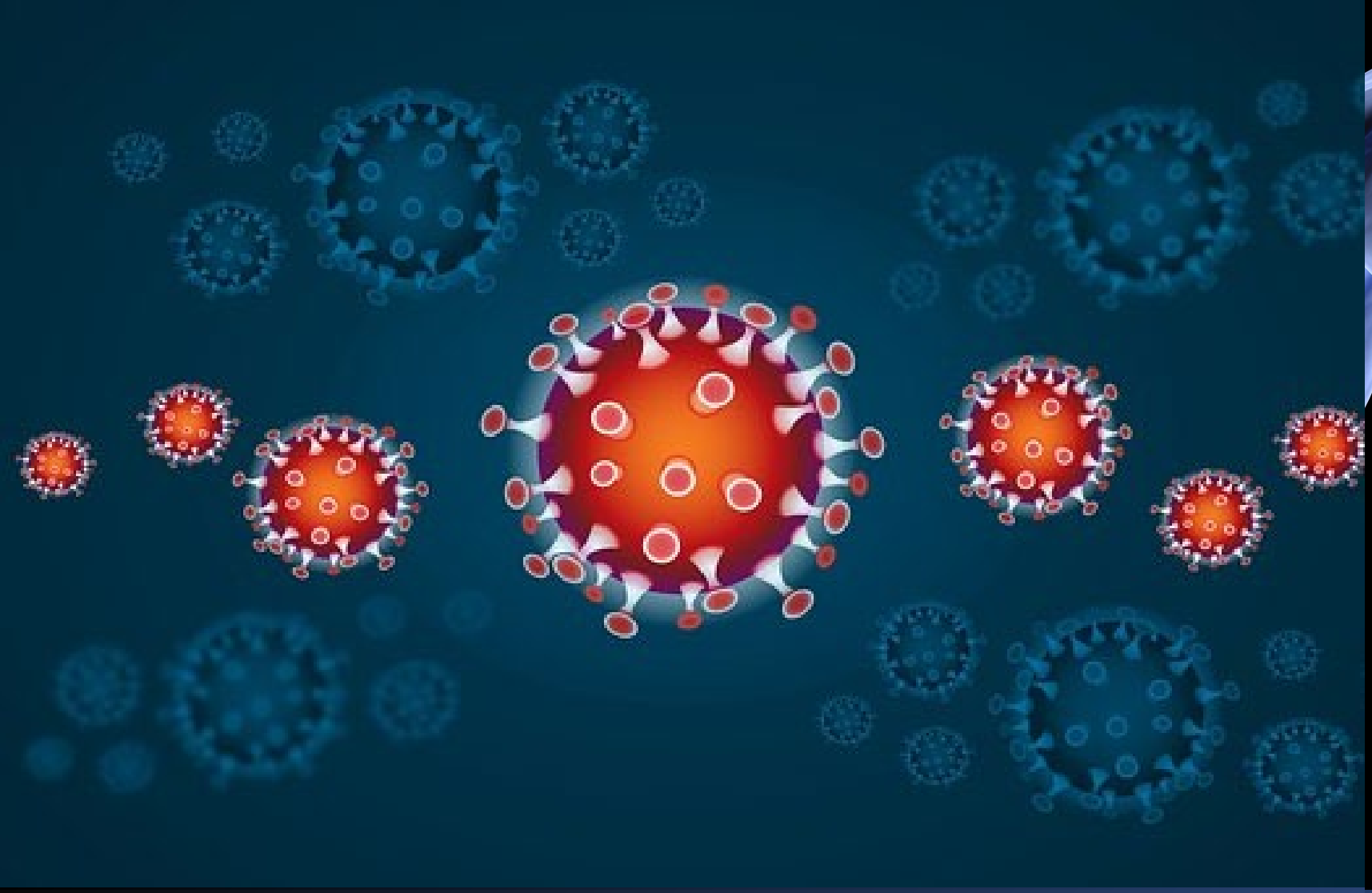
- Probiotics have the ability to:
  - prevent microbial imbalance from occurring e.g symptom of AAD
  - rectify a state of microbial imbalance and restore homeostasis e.g relief of IBS/IBD
  - create a more beneficial homeostasis e.g reduction of URTI in healthy individuals, athletic performance

Antibiotics and Associated Diarrhea

- The incidence rate of AAD ranges from 3.2% to 29% depending on antibiotic type and demographics
- Among all AAD cases, 10-20% are associated with CDAD
- The spectrum of CDAD varies from diarrhoea, pseudo-membranous colitis to toxic megacolon and death
- Individuals taking antibiotics are 7 to 10 times more likely to get *C. difficile* infection than people without antibiotic treatment *(CDC report 2017)*
- 15,000 deaths per year are caused by *C. difficile* infection *(CDC report 2017)*

(Elseviers et al, BMC Infect Dis 2015; Goldenberg et al, Cochrane Dat Syst Rev 2017)

Poll



CLINICAL EFFECTS OF HMF PROBIOTICS ON INTESTINAL HEALTH

The Cambridge Antibiotic Probiotic Trials

The Cambridge HMF Clostridium difficile Trial

AIM: Efficacy of HMF probiotics to prevent or reduce *Clostridium difficile* infection and associated diarrhoea in patients receiving antibiotics.

TRIAL DESIGN:

- Randomised, double blind, placebo-controlled study
- 138 patients initiating antibiotic therapy were randomly assigned to take daily either 25 billion HMF probiotics or placebo for 20 days with faecal samples taken at day 0 and 20

- Incidence of the following were monitored:
    1. Presence of *C.difficile*
    2. Presence of *C.difficile* toxin
    3. Incidence of *C.difficile* diarrhoea

The Cambridge HMF Clostridium difficile Trial - Results

1. Incidence of *C.difficile*:

   Placebo: 13.0%

   HMF: 15.9%

2. Incidence of *C.difficile* toxin:

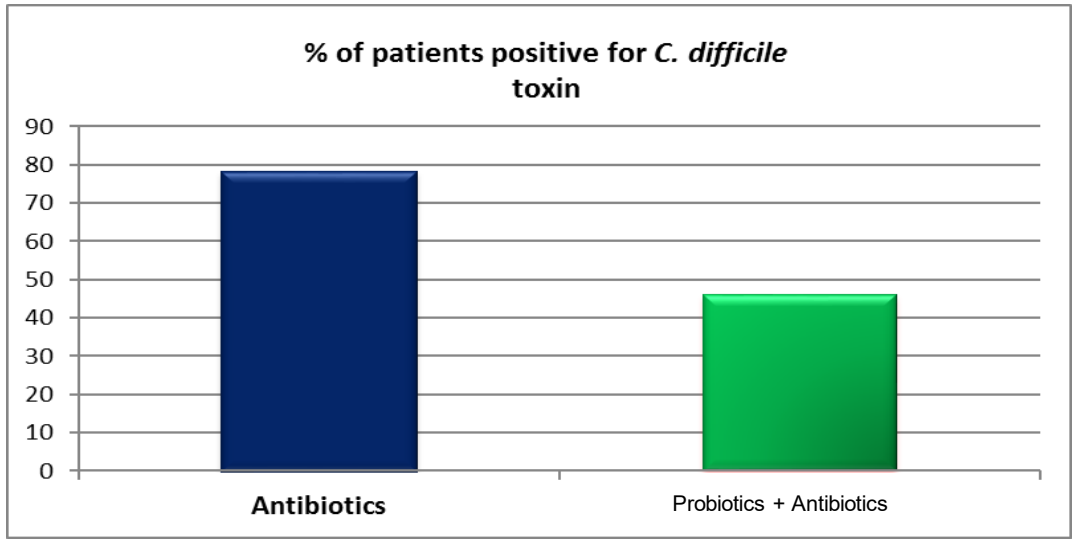
   Placebo: 78% of positives

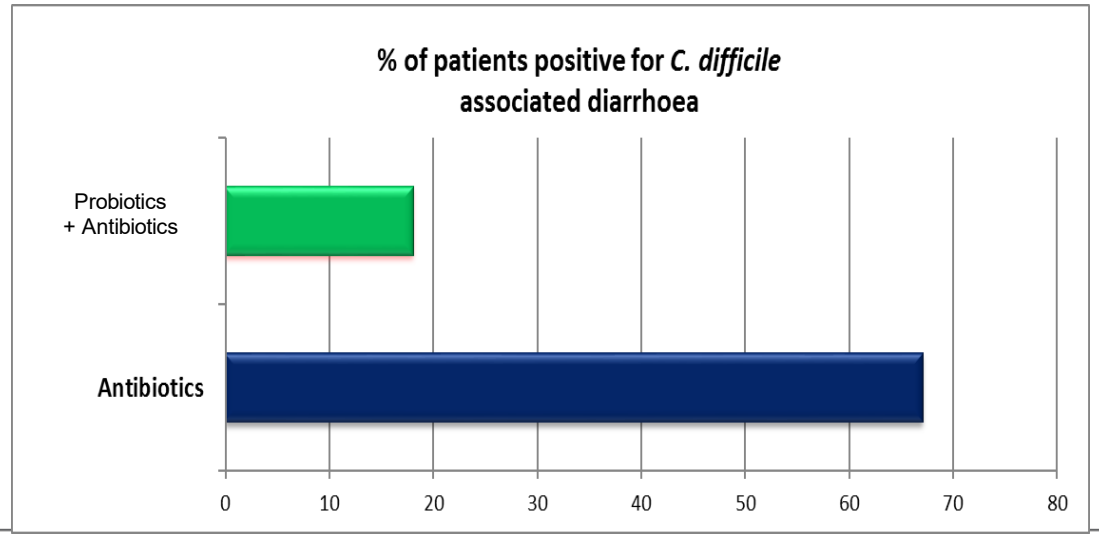
   HMF: 46% of positives

3. Development of *C.difficile* associated diarrhoea:

   Placebo: 67% of positives

   HMF: 18% of positives





Plummer et al 2005, Int J Antimicrob Agents 26; 69-74

The Cambridge HMF Antibiotic Trial 1

Opportunistic Pathogen Re-growth Following Antibiotic Therapy

Aim:

- To investigate the effect of antibiotics on re-growth of opportunistic pathogens
- To investigate the effect of HMF probiotics on this opportunistic pathogen re-growth

Trial Design:

	Treatment	Period (days)
	Antibiotics + Placebo	1 - 7
	Placebo	8 - 15
	Antibiotics + Placebo	1 - 7
	25 billion HMF probiotics	8 - 15
	Antibiotics + 25 billion HMF probiotics	1 - 7
	25 billion HMF probiotics	8 - 15

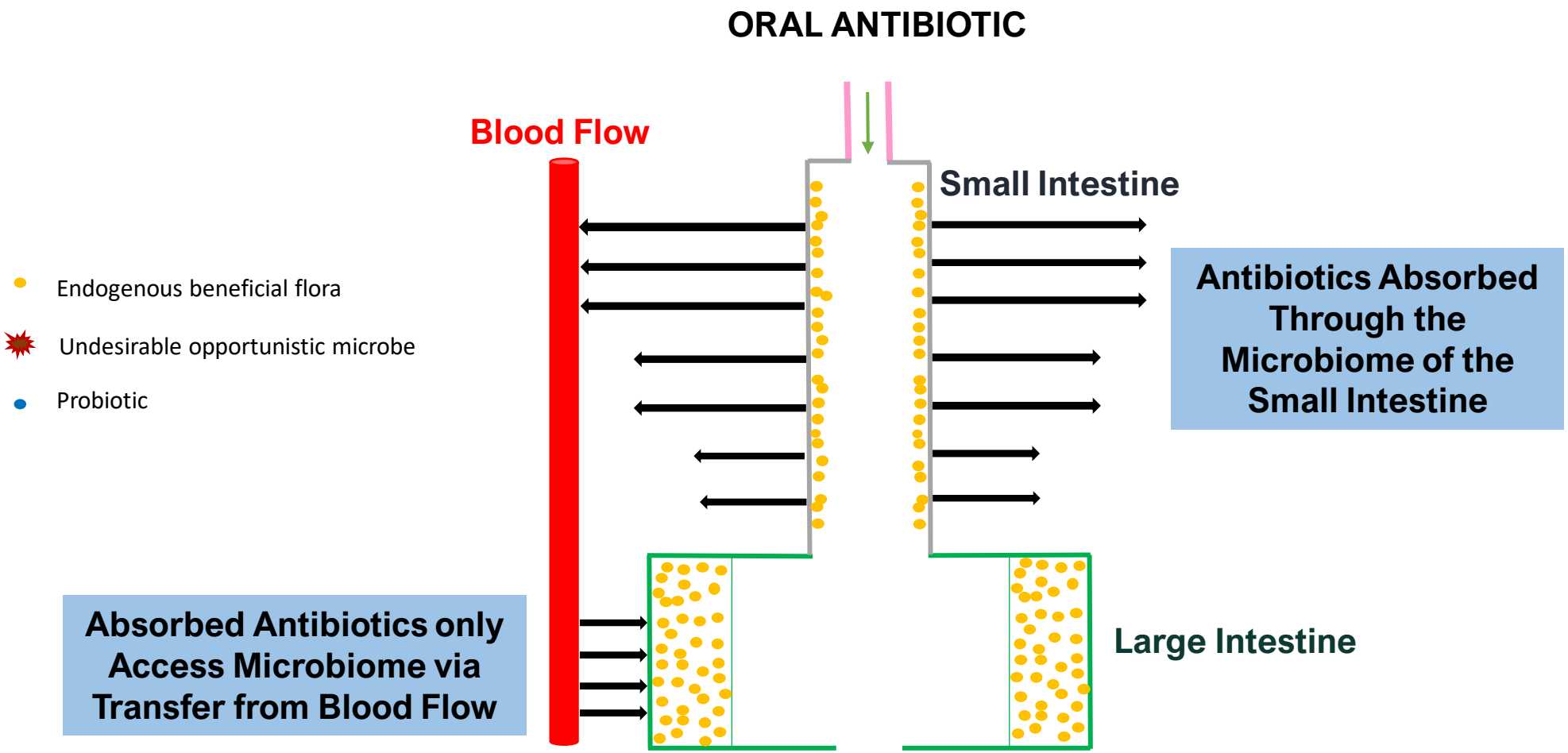
Samples collection: Days 1 (control), 7, 12, 17 and 27

Opportunistic pathogens measured:

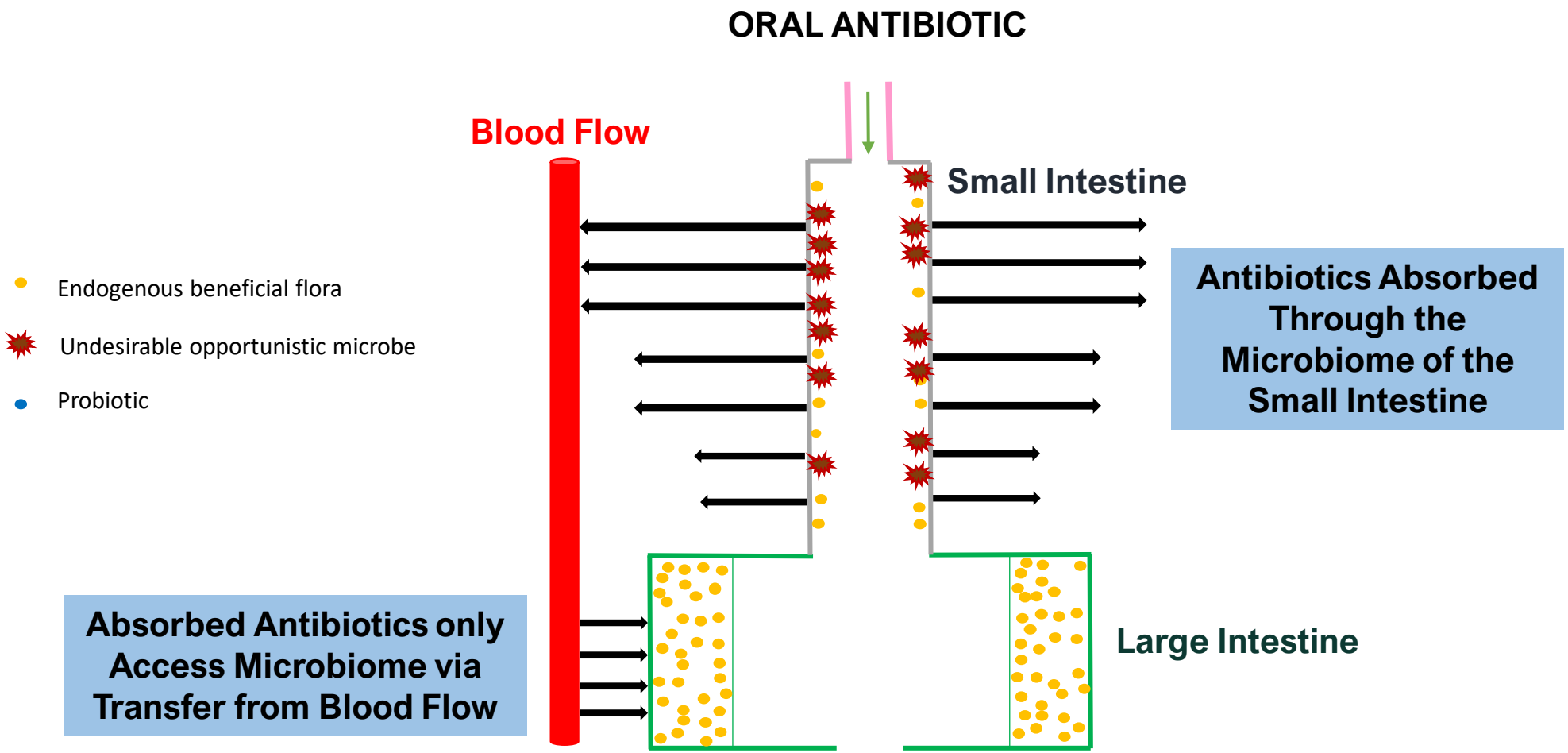
- Total facultative anaerobes
- Enterobacteria
- Enterococci
- Staphylococci

Madden et al 2005, Int Immunopharm 5; 1091-97

The Effect of Antibiotics on the Gut Flora



The Effect of Antibiotics on the Gut Flora



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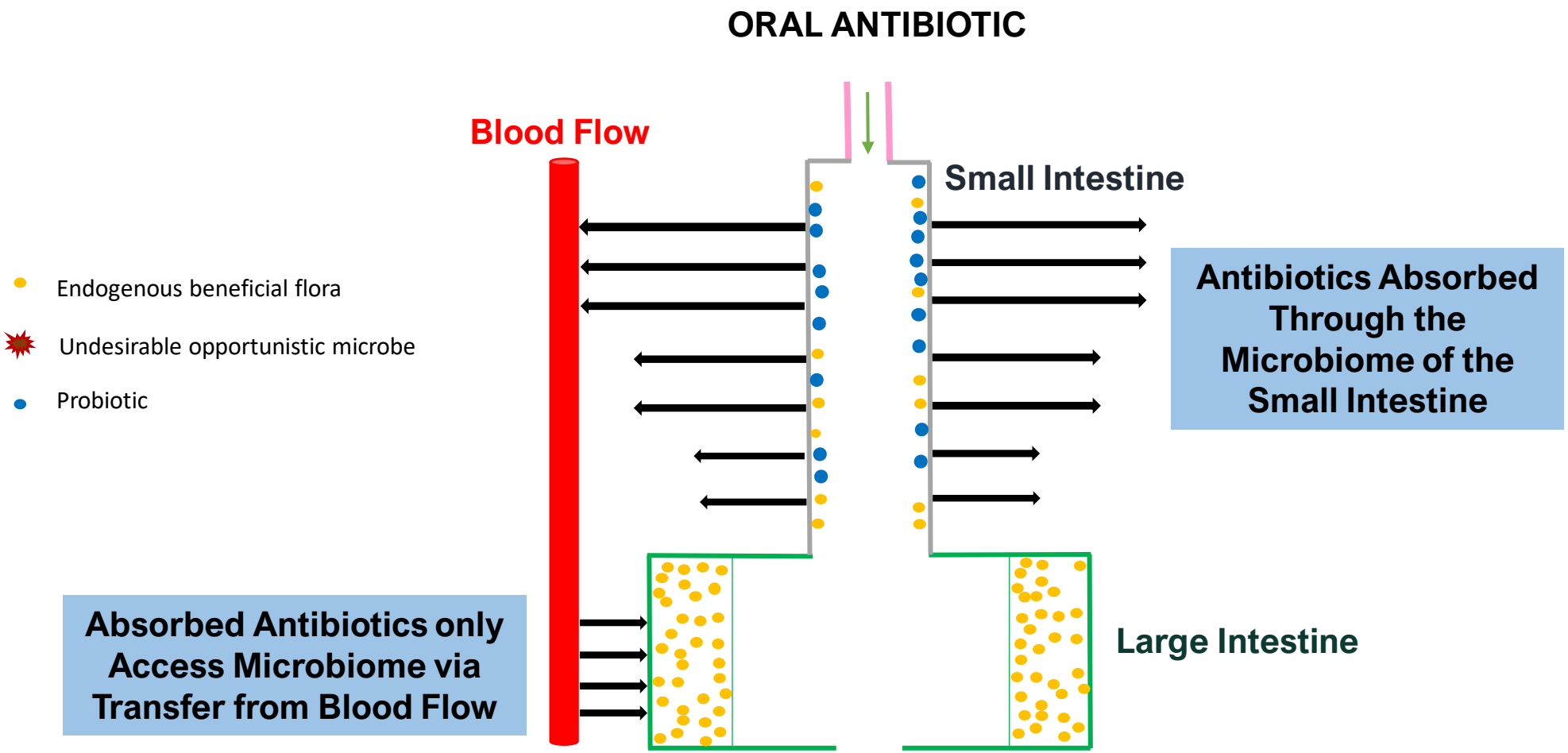
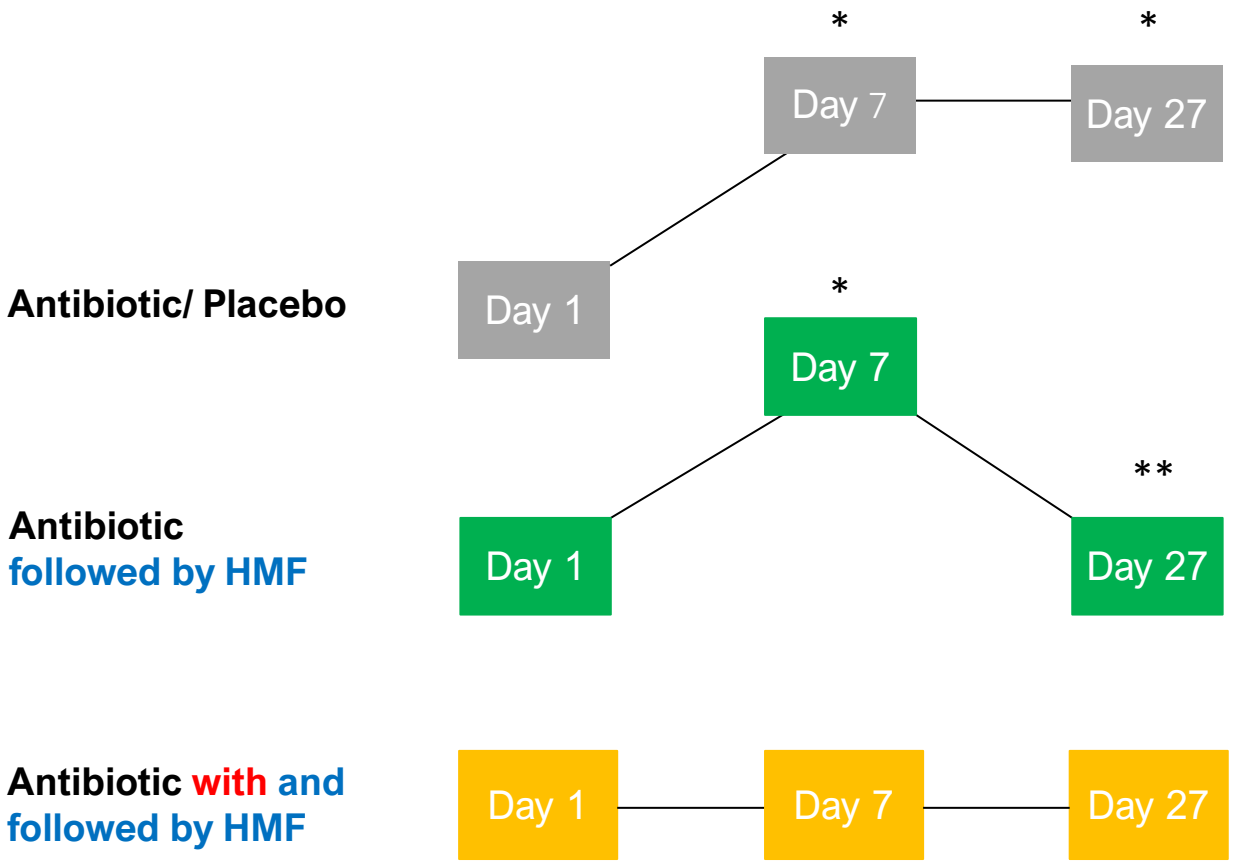
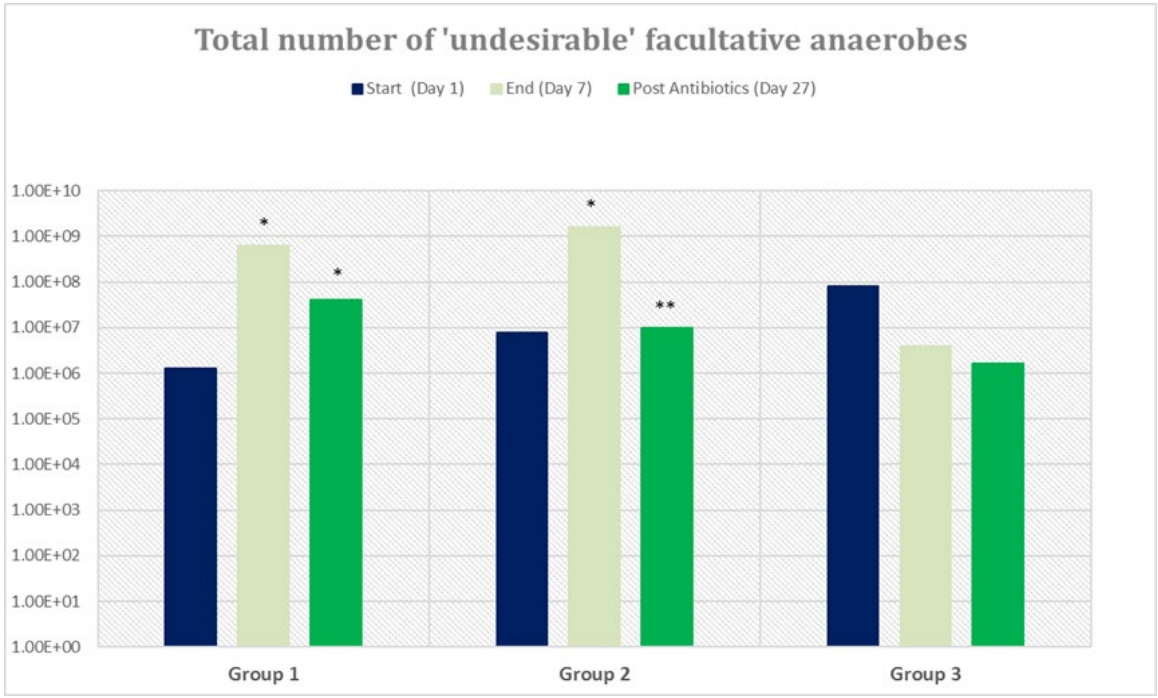


The Cambridge HMF Antibiotic Trial 1 - Results





Madden et al 2005, Int Immunopharm 5; 1091-97

Can Co-administration of Probiotics Alongside Antibiotics Reduce Antibiotic Resistance?

The Cambridge HMF Antibiotic Trial 2

Antibiotic Resistance in the Re-growth Microbiota

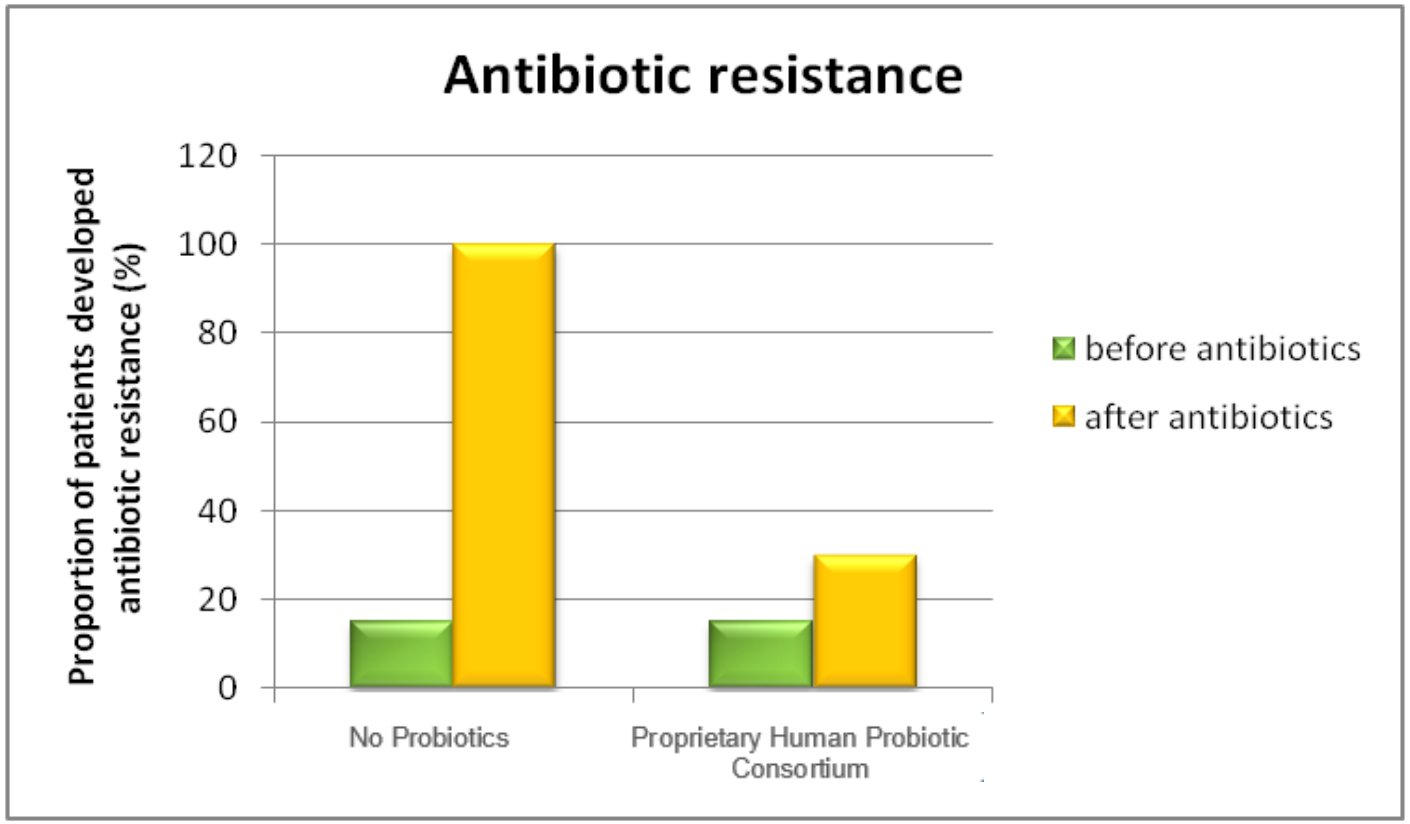
AIM: The effect of HMF probiotics on the antibiotic resistance in the re-growth gut microbiota following antibiotic therapy.

TRIAL DESIGN:

- Randomised, double blind, placebo-controlled study
- 155 patients requiring antibiotic therapy were randomly assigned to take daily either 25 billion HMF probiotics or placebo for 21 days in conjunction with antibiotics
- Sample collection: day 1 (start), day 7 (the end of antibiotic treatment) and day 35 (4 weeks post antibiotic treatment)
- Gut microbiota disruption and antibiotic resistance were investigated

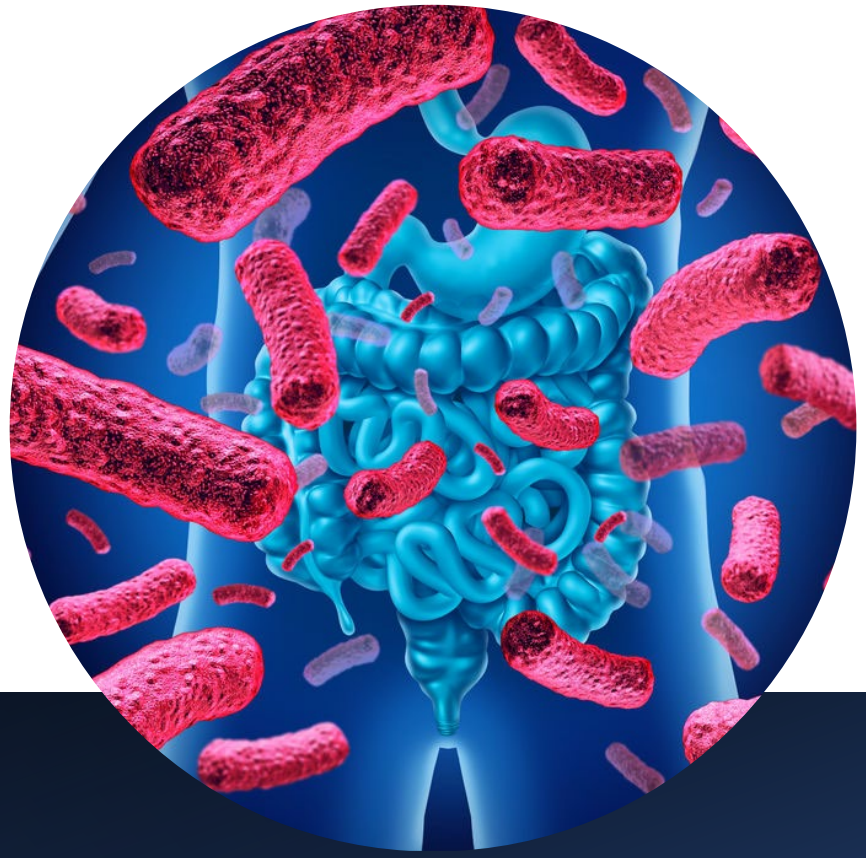
Plummer et al 2005, Int J Antimicrob Agents 26; 69-74

The Cambridge HMF Antibiotic Trial 2 - Results



- The types measured were the Enterococci
- At the start, about 18% of patients had detectable levels of antibiotic resistant Enterococci.
- After the trial, the control group 100% of patients developed detectable levels of antibiotic resistant Enterococci, whereas only 30% of the probiotic group had detectable levels of antibiotic resistant Enterococci

The FANTIB Study



HMF Travel

Overview

HMF® Travel combines five probiotic strains to support gastrointestinal health when travelling. The shelf-stable convenient capsule format is ideal for your vacation!

Benefits

- 35 billion CFU per day in a shelf-stable format
- Helps to reduce the risk of traveller's diarrhoea and occasional diarrhoea*
- Includes *Saccharomyces boulardii* plus four proprietary probiotic strains
- Potency guaranteed through expiration

GMO Non GMO · Gluten Free · Soy Free · Dairy Free · FOS No FOS · Vegan

Medicinal Ingredients

EACH TABLET CONTAINS:

Probiotic Consortium.....17.5 billion CFU
Lactobacillus acidophilus (CUL-60 & Cul-21).....9.375 billion CFU
Saccharomyces boulardii (CNCM-I-1079).....5 billion CFU
Bifidobacterium animalis subsp. Lactis (CUL-34)
& Bifidobacterium bifidum (CUL-20).....3.125 billion CFU

*Antibiotic-associated diarrhoea

Does Co-administration of Probiotics Alongside Antibiotics Reduce Antibiotic Resistance?

THE FANTIB STUDY

TRIAL DESIGN:

- Randomised, double-blind, placebo-controlled trial
- 50 adults receiving oral antibiotics for 5 to 10 days with or without probiotic supplementation of HMF-T Consortium for 10 days.
  - HMF Consortium-T is a combination of:
    - 25 billion CFU of the HMF Consortium - 25 BILLION CFU
    - And 10 billion CFU of Saccharomyces bouladrii (CNCM-I-1079) for 10 days.

(Clinical study undertaken in Bulgaria)

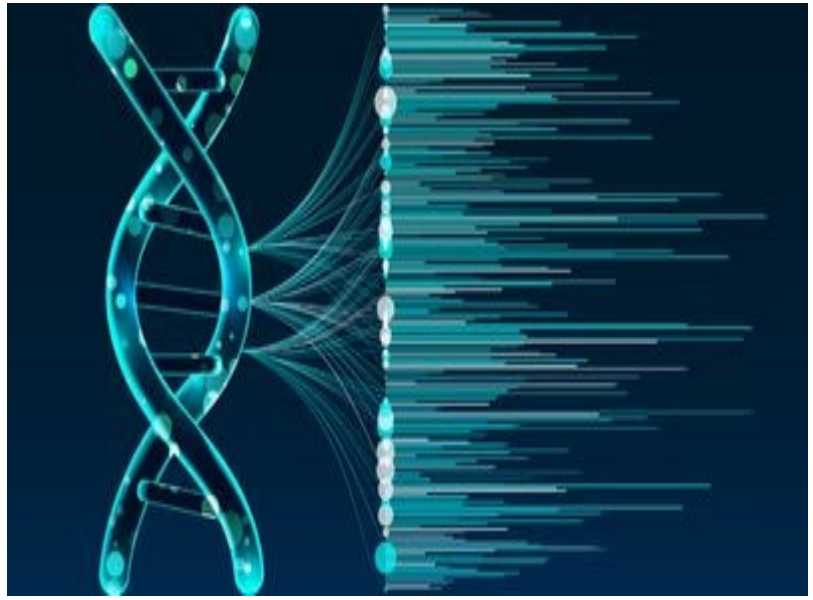
		Placebo (n=25)	Probiotic (n=25)
Antibiotic Class			
	β-Lactams	13 (52%)	14 (56%)
	Macrolides	12 (48%)	11 (44%)
Antibiotic			
	Amoxicillin	5 (20%)	5 (20%)
	Cephalosporins	8 (32%)	9 (36%)
	Azithromycin	5 (20%)	7 (28%)
	Clarithromycin	6 (24%)	3 (12%)
	Clindamycin	0 (0%)	1 (4%)
	Spiramycin	1 (4%)	0 (0%)
Length (Days)			
	5	15 (60%)	14 (56%)
	6	4 (16%)	3 (12%)
	7	5 (20%)	6 (24%)
	8	0 (0%)	1 (4%)
	9	0 (0%)	0 (0%)
	10	1 (4%)	1 (4%)

Does Co-administration of Probiotics Alongside Antibiotics Reduce Antibiotic Resistance?

THE FANTIB STUDY

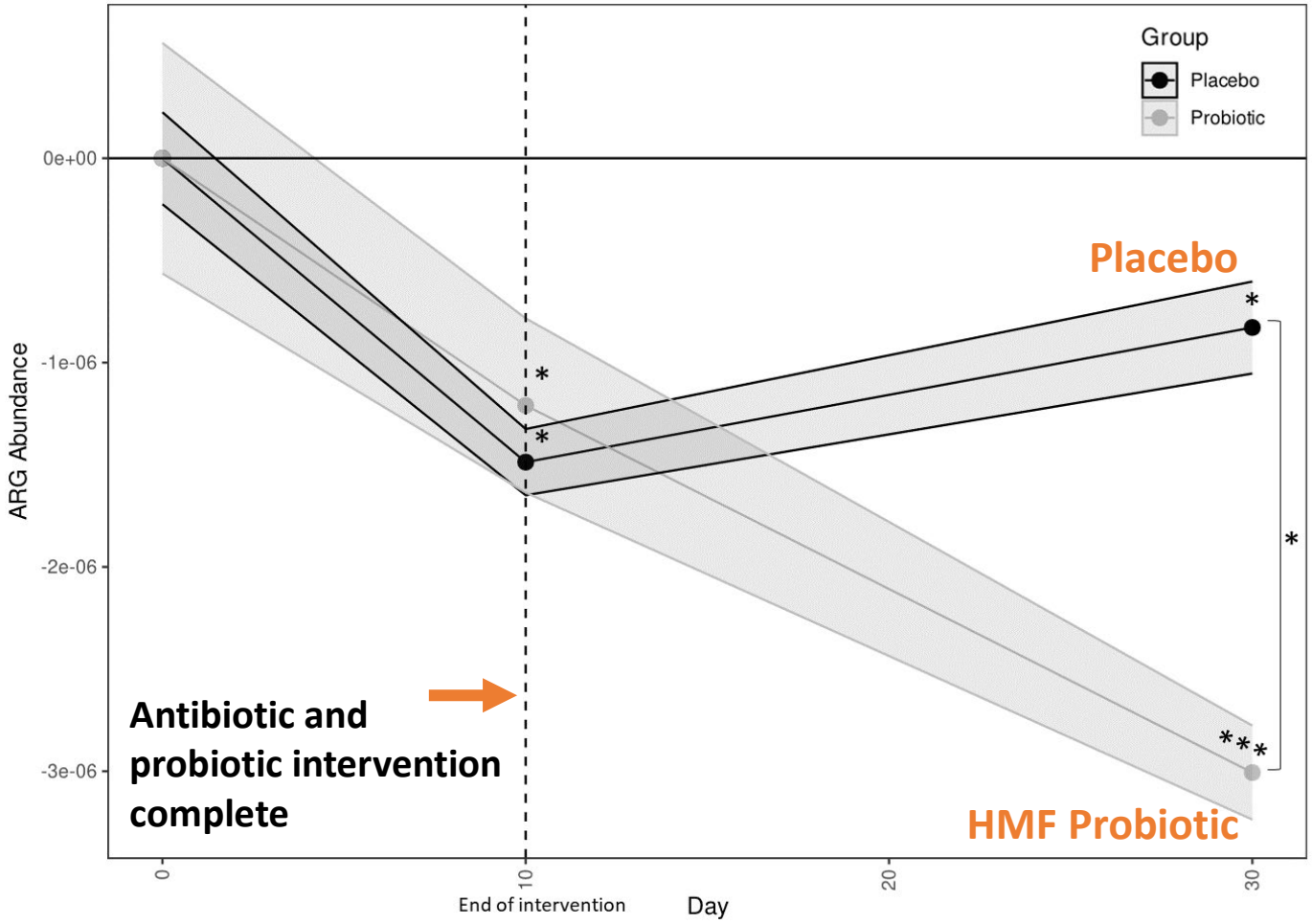
TRIAL METHODS:

- Faecal samples were taken at T0 (baseline), T10, and T30.
- Microbial DNA was extracted from all 150 faecal samples. These samples underwent Shotgun metagenomic sequencing.
- Shotgun sequencing allows:
  - Identification and visualisation of microbial diversity
  - Quantification of total levels of antibiotic resistant genes (ARG's), and resistance to individual antibiotic types



Results and Conclusions

‘HOT OFF THE PRESS’ RESULTS



THE FANTIB STUDY

- The total level of antibiotic resistant genes in the microbiota decreased in both the probiotic and placebo groups during the intervention period.
- This is due to the total numbers of bacteria in the gut being reduced including the partially resistant bacteria still being sensitive to the antibiotic and hence the total
- Following the end of intervention, the total ARG levels increased in the placebo group but decreased in the probiotic group
- HMF-T Consortium Probiotic supplementation significantly reduced total antibiotic resistance in patients taking antibiotics. HMF-T Consortium is a a combination of HMF Consortium - 25 BILLION CFU and 10 billion CFU of Saccharomyces bouladrii (CNCM-I-1079)
- **This effect was clear at 30 days (20 days after final intervention, and so is likely to be a PERMANENT effect.**

Summary

Antibiotic resistance is probably the biggest global threat to human healthcare in the 21st century

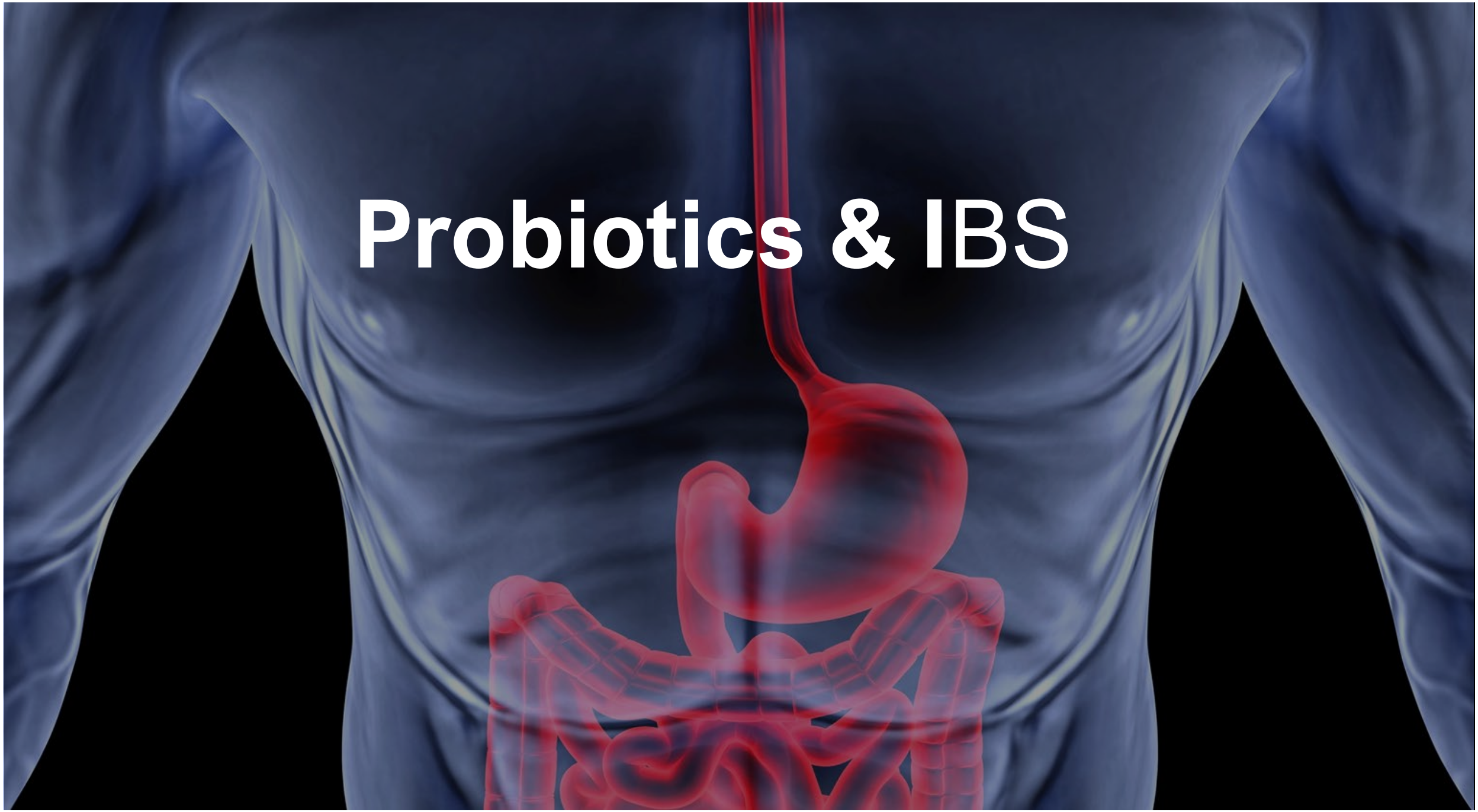
By 2050

- Global cumulative cost of antibiotic resistance will reach **100 trillion US Dollars**
- **10 million people** dying every year due to antibiotic resistance

(O'Neill J, Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations 2014)

- This is the second study where HMF Probiotics have demonstrated the ability to reduce levels of antibiotic resistance in the regrowth microbiota following co-administration with antibiotic therapy.
- **This is the only proactive intervention that has been shown to potentially decelerate the progression of antibiotic resistance. Everything else is based upon limitation of antibiotic use.**
- **If this can be demonstrated to be a consistent effect, then it provides a compelling rationale for probiotics to become a compulsory adjunctive therapy alongside antibiotics.**

Poll


Probiotics & IBS

The Sheffield IBS Studies

HMF Intensive / HMF IBS Relief

25 Billion CFU per capsule formulation of Genestra HMF Probiotics
Consisting of the **exact 4 core strains included in the most broadly studied consortium**

Clinically proven to:

- Promote favorable gut flora and support gastrointestinal health
- Effectively crosstalk with many parts of our physiology, supporting:
  - Immune health and function in adults
  - Cognitive function in adults
  - Significant reduction in symptoms of Irritable Bowel Syndrome in IBS sufferers and athletes
  - Reduction in the incidence of antibiotic resistance
  - Prevention antibiotic associated diarrhea (AAD) in adults
  - Athletic performance in endurance athletes
  - Reduction in intestinal permeability in adult athletes

Refrigerated Options

Shelf-stable Options

Probiotic Consortium/ Consortium probiotique	25 billion CFU/ milliards d'UFC
Lactobacillus acidophilus (CUL-60 & CUL-21)	19 billion CFU/ milliards d'UFC
Bifidobacterium animalis subsp. *lactis* (CUL-34) & *Bifidobacterium bifidum* (CUL-20)	6 billion CFU/ milliards d'UFC

Owen L et al Proceedings of the Nutrition Society 2014, 73: E29

Williams EA et al, Aliment Pharmacol Ther 2009, 29:97-103

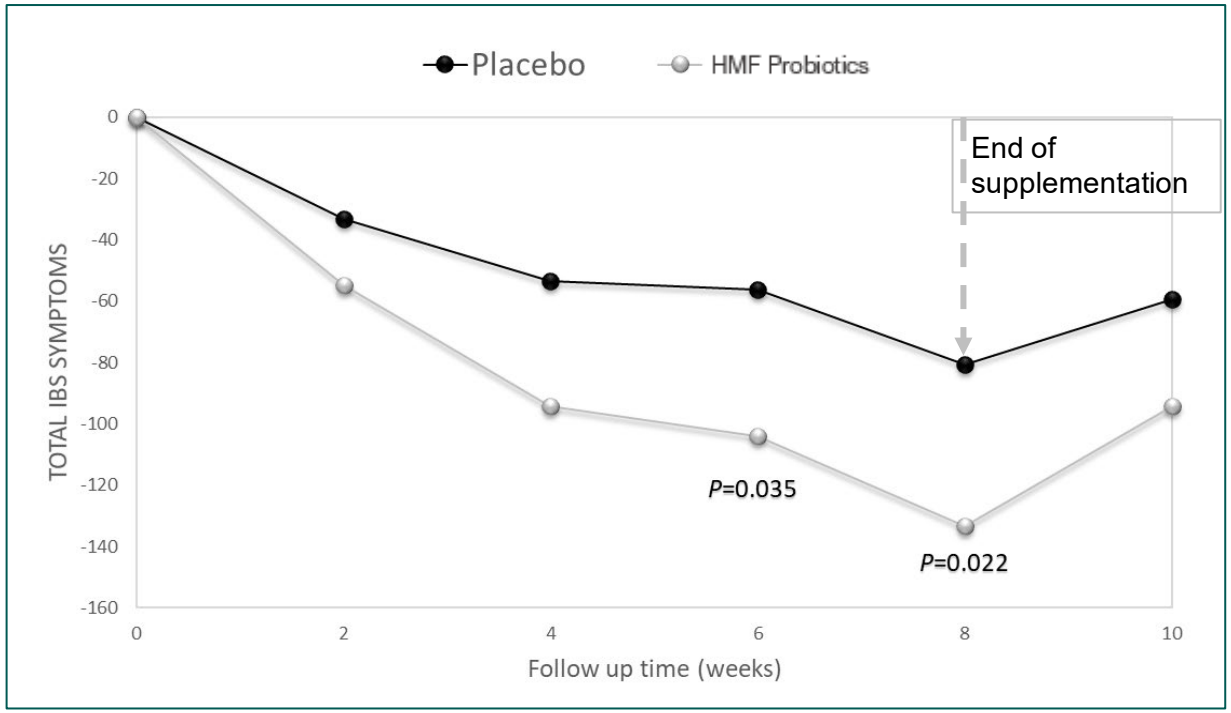
Plummer et al 2005, Int J Antimicrob Agents 26; 69-74

Pugh JN et al Eur J Appl Physiol 2019, 119 (7): 1491-1501

Effective formulation for IBS symptom relief (adults and children 11 years and older)
Perfect for anyone requiring a daily therapeutic dose, and/or who may be sensitive to fructooligosaccharides (FOS).

Irritable Bowel Syndrome Study 1 – 2009 (IBS Related Outcomes)

IBS sufferers randomly assigned to take daily either 25 billion HMF Probiotics or a matching placebo for 8 weeks. IBS symptoms assessed every two weeks during the study period and again at 10 weeks (2 weeks after taking the HMF Probiotics/placebo).



Total IBS symptoms:

- Frequency of pain
- Severity of pain
- Bloating
- Satisfaction with bowel habit
- Quality of Life

THE SHEFFIELD IBS TRIAL:
HMF Consortium - 25 BILLION CFU

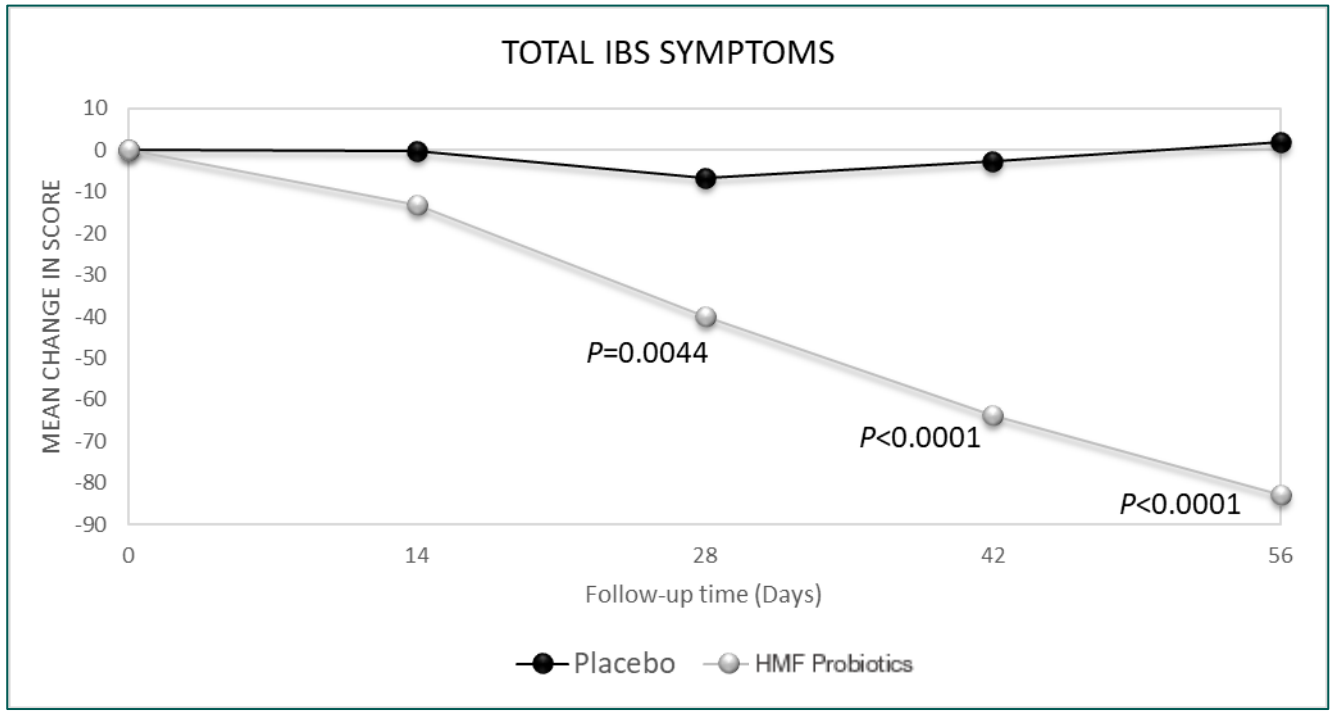
Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34

Significant difference observed in the probiotic group despite strong placebo effect
Continuous supplementation is necessary to sustain the effect.

Williams EA et al, Aliment Pharmacol Ther 2009, 29:97-103

Irritable Bowel Syndrome Study 2 – 2022 (IBS Related Outcomes)

Female IBS sufferers randomly assigned to take daily either 25 billion HMF Probiotics probiotics or a matching placebo for 8 weeks. IBS symptoms assessed every two weeks during the study period (days 0, 14, 28, 42 and 56).



THE SHEFFIELD IBS TRIAL:
HMF Consortium - 25 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34

Significant reductions in IBS scores with HMF Probiotic supplementation
Two probiotic studies demonstrated the beneficial effect of HMF Probiotics in the management of IBS

Michael DR et al, manuscript submitted

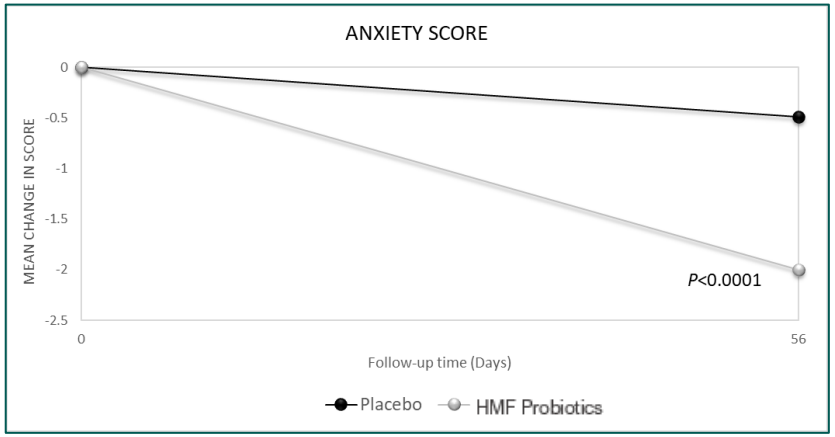
Irritable Bowel Syndrome Study 2 – 2022 (Mental Health Related Outcomes)

Female IBS sufferers randomly assigned to take daily either 25 billion HMF Probiotics or a matching placebo for 8 weeks. The HADS and IBS-BRQ questionnaires were completed at days 0 and 56.

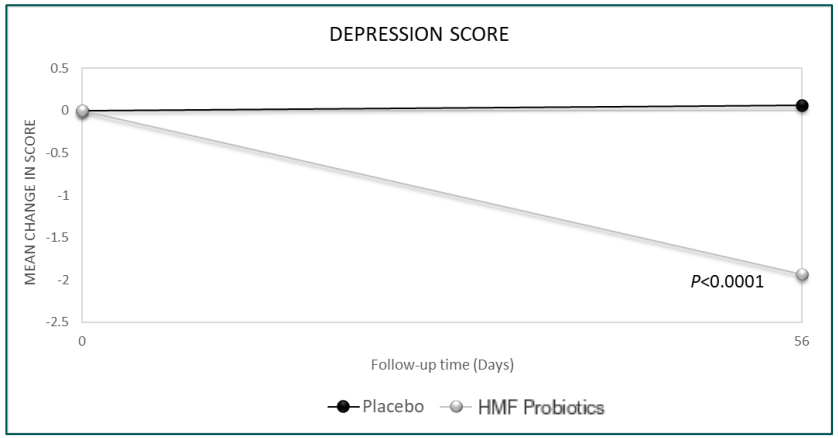
HMF Consortium - 25 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34

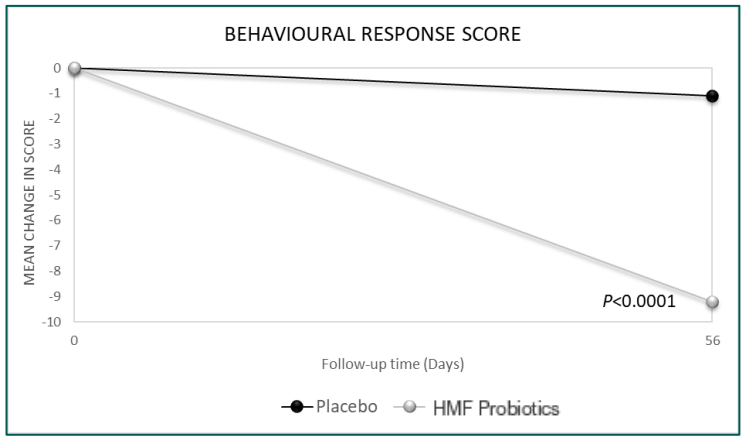
ANXIETY



DEPRESSION



AVOIDANCE BEHAVIOUR



HMF Probioticsb4 supplementation has a beneficial impact on the mental health of IBS sufferers

Michael DR et al, manuscript submitted

The Cambridge IBS Study

Effects of probiotics on the caecal and faecal microbiota of irritable bowel syndrome patients receiving antibiotics: A pilot study

Effect of Probiotic on Fungal Overgrowth in the Caecal Flora of IBS Patients Receiving Antibiotic Therapy

AIM:

- To investigate the role of antibiotics and probiotic on the:
  - Caecal mucosal microbiota (from biopsy)
  - Caecal lumen microbiota (from biopsy)
  - Faecal microbiota

First ever microbiota trial conducted on human caecal tissue.

1. Biopsy samples taken on day 0 and 14
2. Faecal samples taken on days 0,14, and 28
3. Antibiotics given days 7-14
4. HMF Consortium - 25 billion CFU per day given from days 0 -14
5. 6 patients in each group- ethical approval!

Plummer S, et al 2013 Effects of probiotics on the caecal and faecal microbiota of Irritable Bowel Syndrome patients receiving antibiotics: a pilot study. Short Communication. ENGIHR, Valencia, Spain, 18-20th September 2013, pg183-6

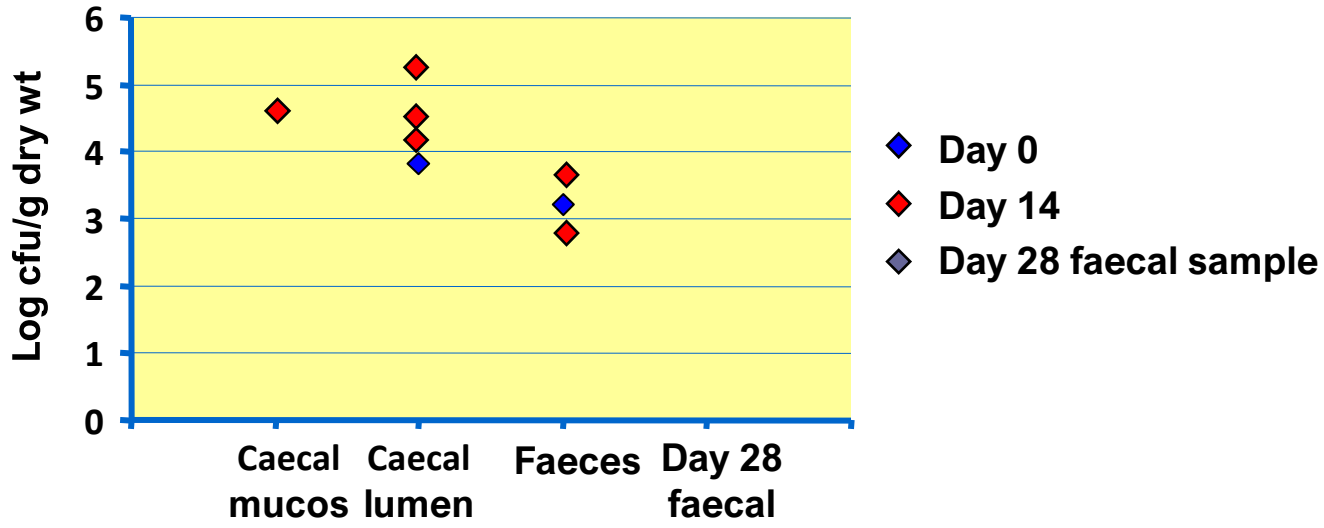
Caecal Trial Design

	DAY 0	DAY 7	DAY 14	DAY 28
Group 1 (6 patients)	B+F	No treatment	Antibiotics	B+F	F
Group 2 (6 patients)	B+F	HMF Probiotics	Antibiotics + HMF Probiotics	B+F	F

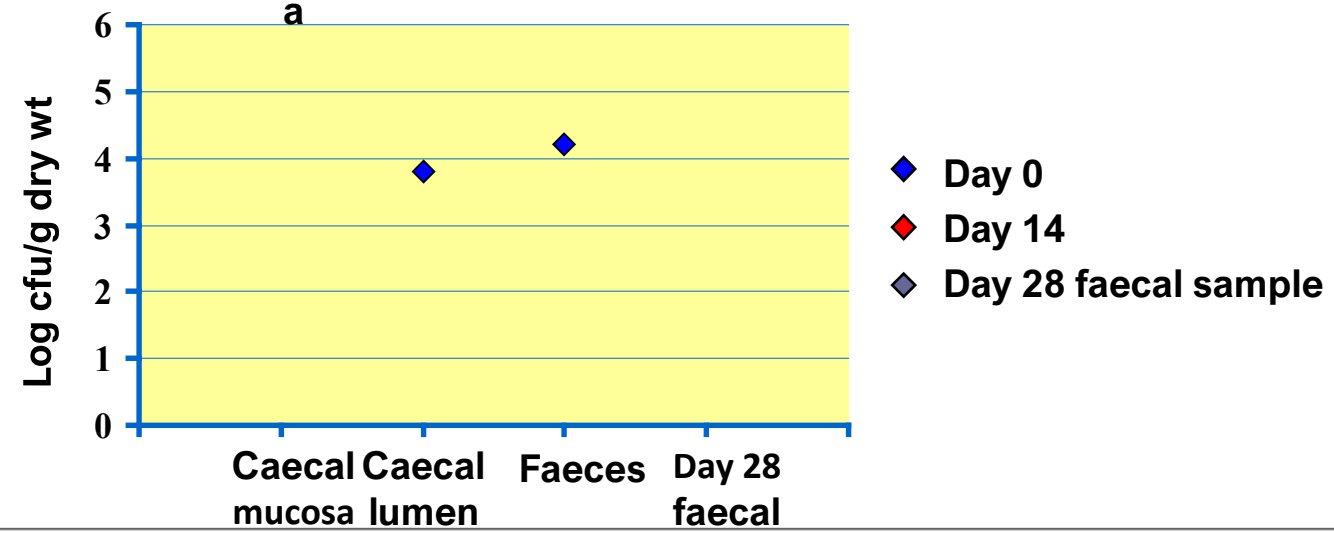
Plummer S, et al 2013 Effects of probiotics on the caecal and faecal microbiota of Irritable Bowel Syndrome patients receiving antibiotics: a pilot study. Short Communication. ENGIHR, Valencia, Spain, 18-20th September 2013, pg183-6

Effects of Antibiotics Alone and with HMF Probiotics on the Incidence of *Candida albicans* in IBS Patients

Antibiotics Only



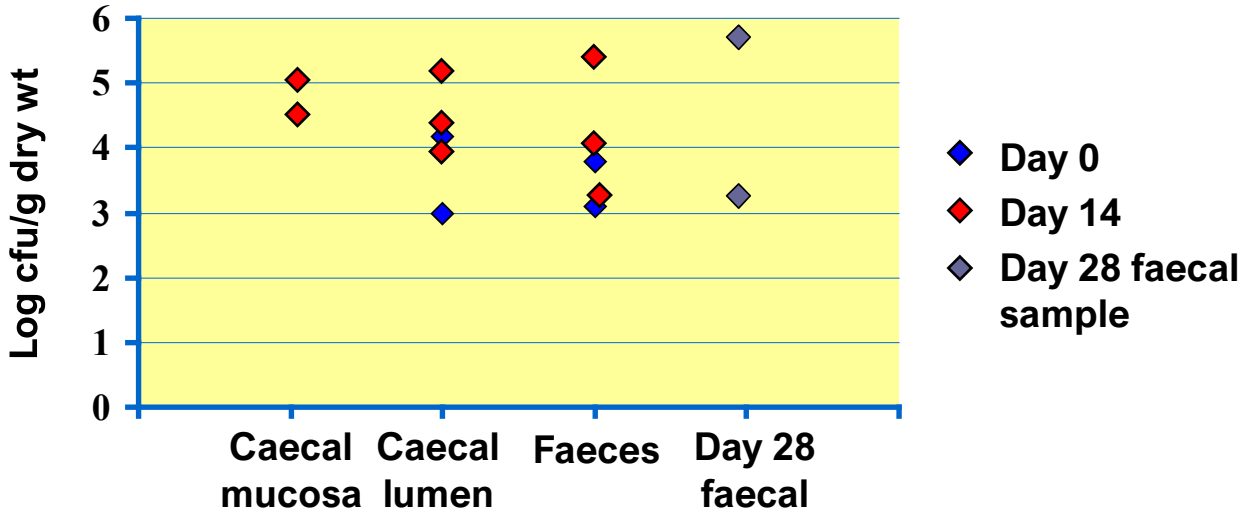
Antibiotics with Simultaneous HMF Probiotic supplementation



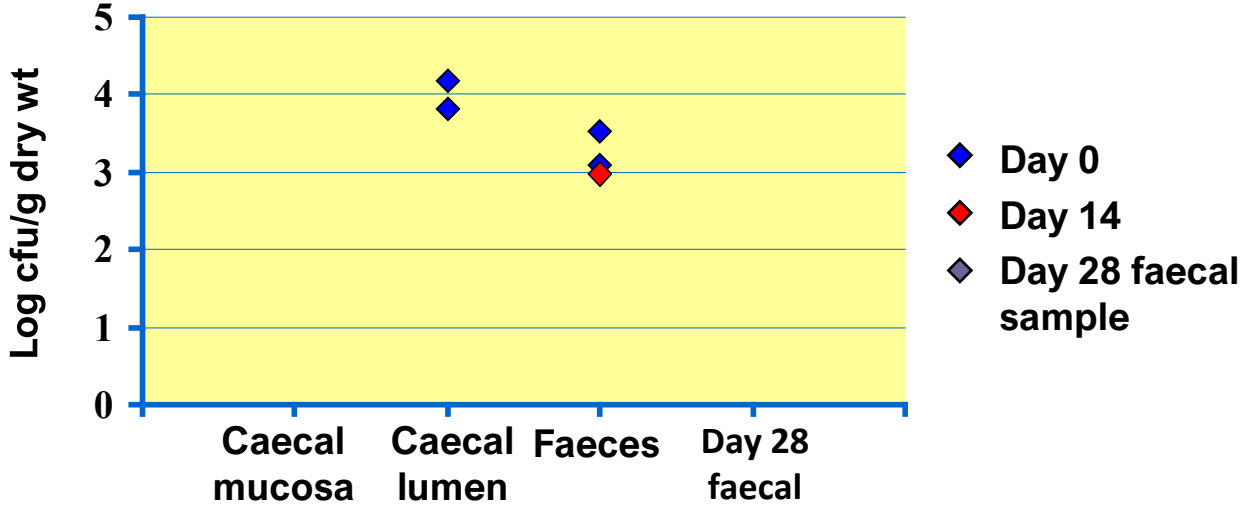
Plummer S, et al 2013 Effects of probiotics on the caecal and faecal microbiota of Irritable Bowel Syndrome patients receiving antibiotics: a pilot study. Short Communication. ENGIHR, Valencia, Spain, 18-20th September 2013, pg183-6

Effects of Antibiotics Alone and with HMF Probiotics on the Incidence of Total Yeast Infection *in IBS* Patients

Antibiotics only



Antibiotics with simultaneous HMF Probiotic supplementation



Plummer S, et al 2013 Effects of probiotics on the caecal and faecal microbiota of Irritable Bowel Syndrome patients receiving antibiotics: a pilot study. Short Communication. ENGIHR, Valencia, Spain, 18-20th September 2013, pg183-6

HMF Antibiotic Care and HMF Replenish

100 Billion CFU of Genestra HMF Probiotic Strains per Capsule

Probiotic for during and post-antibiotic care

It provides **100 billion CFU per capsule** of Genestra HMF probiotics

Provides a higher potency than the therapeutic dose utilized in the clinical trial delivers superior support

Proven to supplement the normal intestinal microbiota following antibiotic therapy

Contains a small quantity of Fructooligosaccharides (FOS)

Use during antibiotic use, and for 14 days post antibiotics to maximize the benefit of supplementation; then transition to a maintenance formulation (HMF Intensive or HMF Forte/Super Powder)

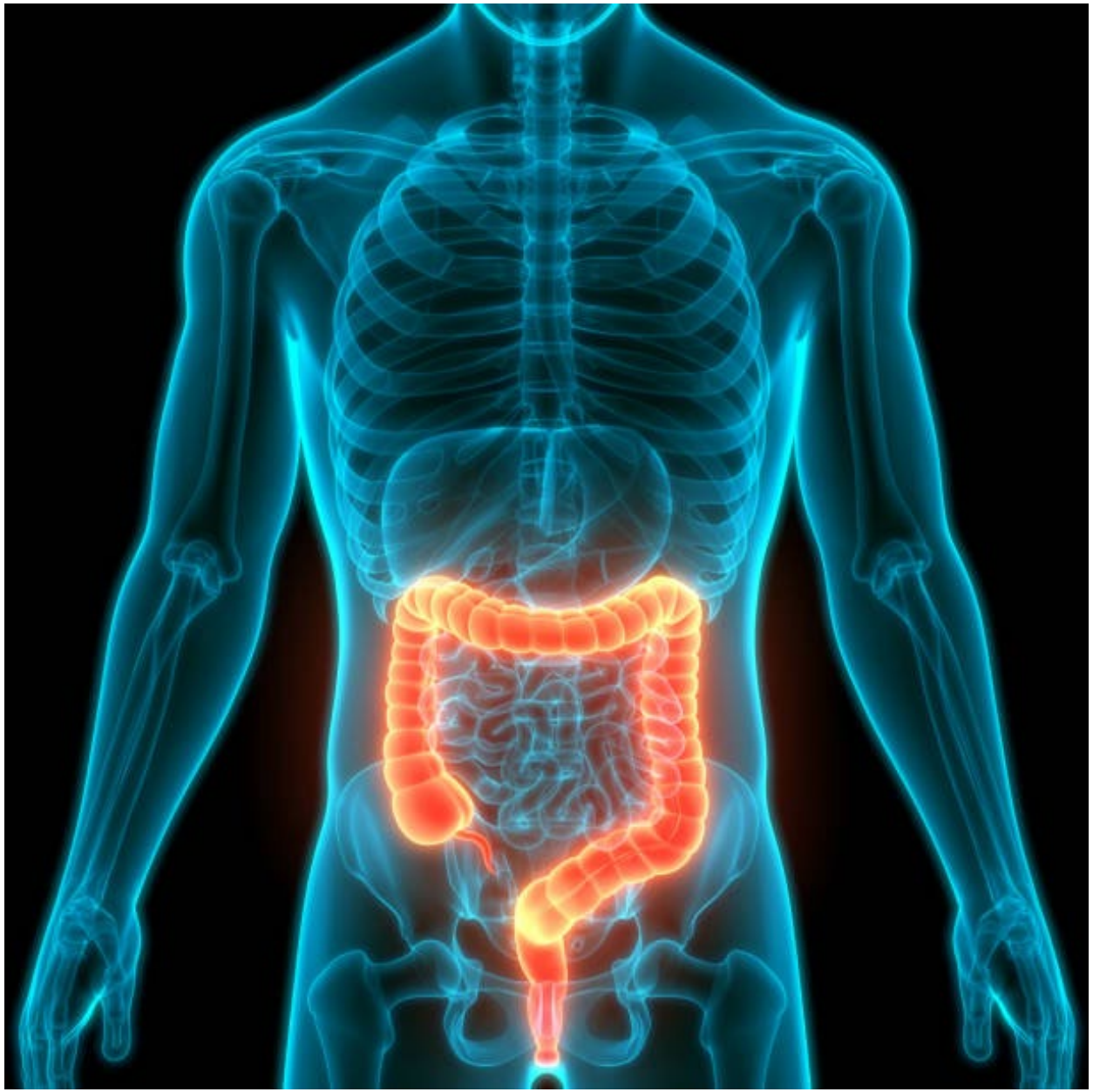
EACH CAPSULE CONTAINS:

Probiotic Consortium	100 billion CFU
Lactobacillus acidophilus (CUL-60 & CUL-21)	50 billion CFU
Bifidobacterium animalis subsp. *lactis* (CUL-34) & *Bifidobacterium bifidum* (CUL-20)	25 billion CFU
Lactobacillus salivarius (CUL-61)	25 billion CFU

When you need to target the large intestine

or

Need a stronger option with some antimicrobial action



HMF Intensive 500

500 Billion **CFU per sachet formulation of Genestra HMF Probiotics**

At 500 billion CFU per sachet/dose of five clinically studied proprietary Genestra HMF probiotic strains, **HMF Intensive 500** provides the **highest concentration of CFU per dose available in Canada.**

Among many functions, this once-daily powdered format probiotic formulation is effective in:

- Supplementing the normal gastrointestinal microbiota following antibiotic therapy
- Improving symptoms of irritable bowel syndrome (IBS) within six weeks

HMF Intensive 500 is vegan friendly, and Gluten, Dairy, Soy and GMO free

EACH SACHET (5 g) CONTAINS:

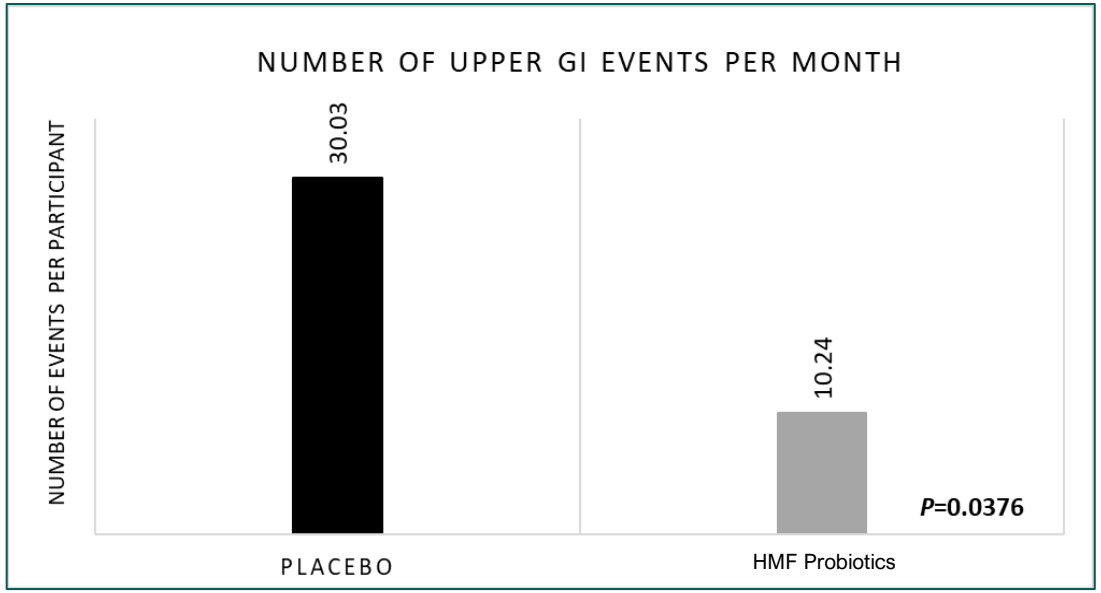
Probiotic Consortium	500 billion CFU
Bifidobacterium animalis subsp *lactis* (CUL-34)	285 billion CFU
Bifidobacterium bifidum (CUL-20)	15 billion CFU
Lactobacillus salivarius (CUL-61)	100 billion CFU
Lactobacillus acidophilus (CUL-60)	50 billion CFU
Lactobacillus acidophilus (CUL-21)	50 billion CFU

The Probiotics & Healthy Adults Study

Intestinal Health in Healthy Adults – 1. Upper GIT Symptoms

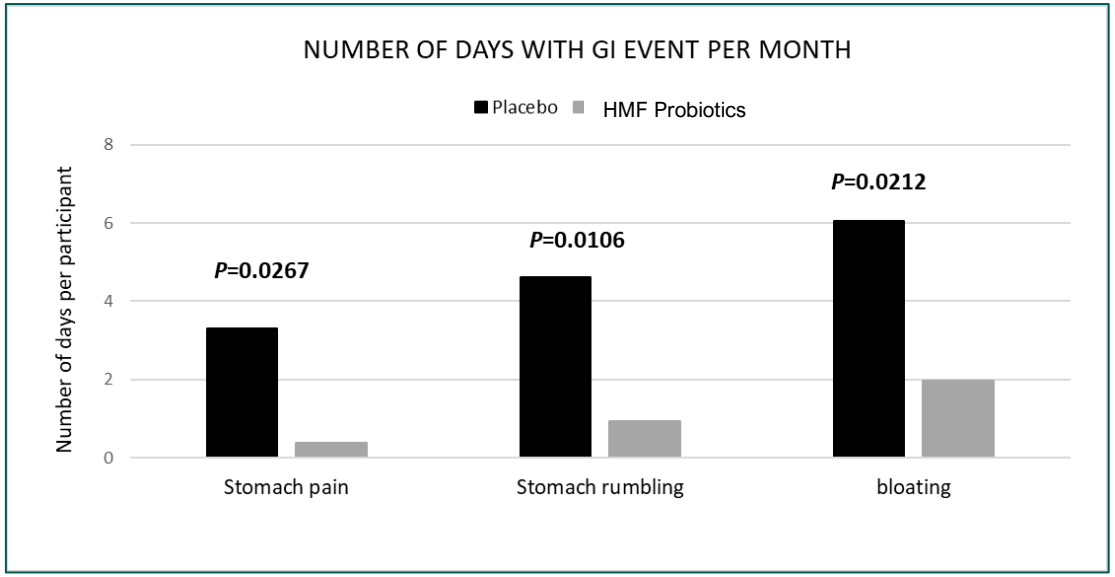
(The Probiotics & Healthy Adult Study)

INCIDENCE OF GI EVENTS



Significant reduction in the incidence of GI events in adults supplemented with HMF Probiotics.

NUMBER OF DAYS WITH THE INDIVIDUAL GI EVENT

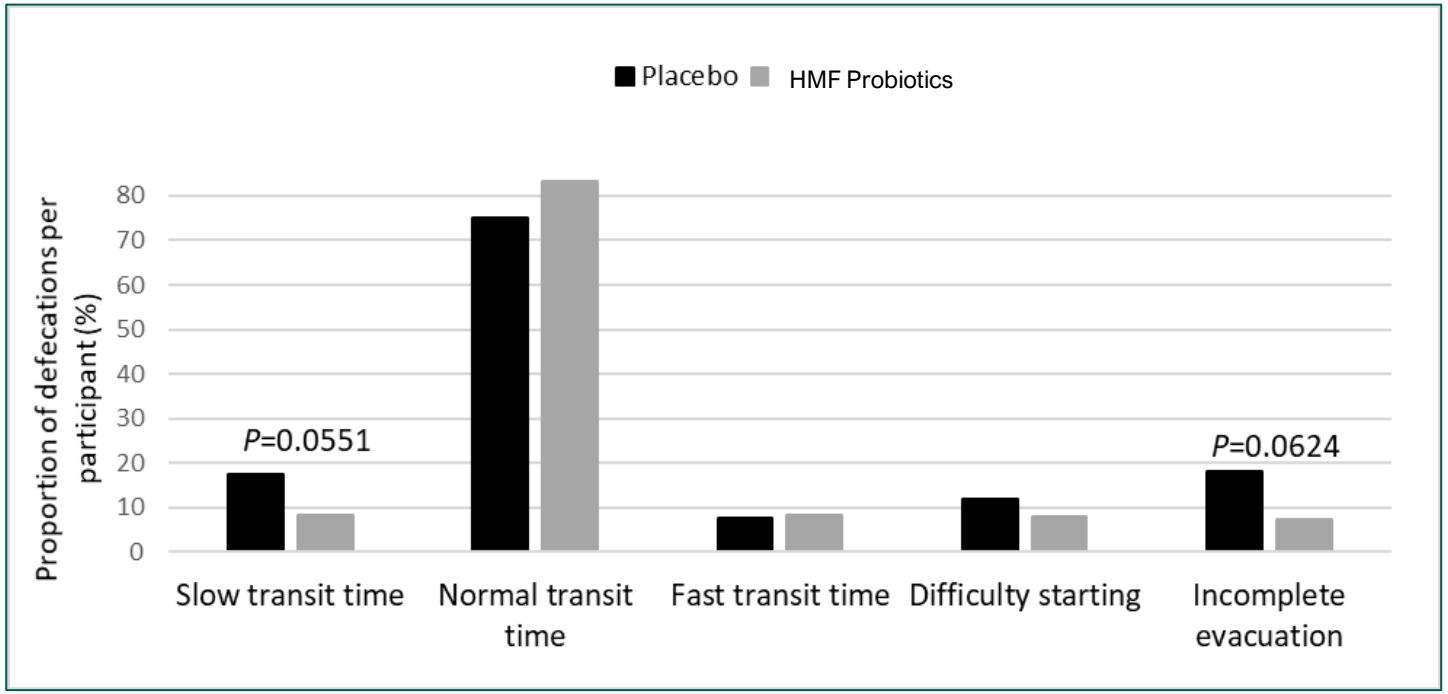


Stomach pain: 88.2% significant reduction.
Stomach rumbling: 79.5% significant reduction.
Bloating : 67.7% significant reduction.

Mullish B et al, Beneficial Microbes 2023

Intestinal Health in Healthy Adults – 2. Bowel Habits

(The Probiotics & Healthy Adult Study)



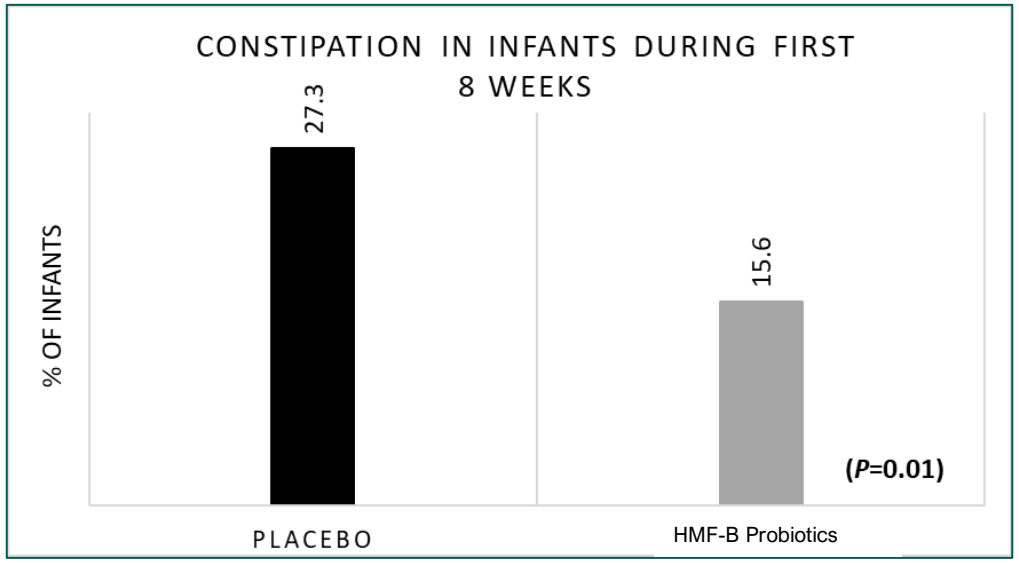
HMF Probiotic supplementation modulates bowel habits:

- Reduced proportion of slow transit defecations (hard stools),
- Increased normal defecation rates,
- Reduced defecation with difficulty starting,
- Reduced incompleteness.

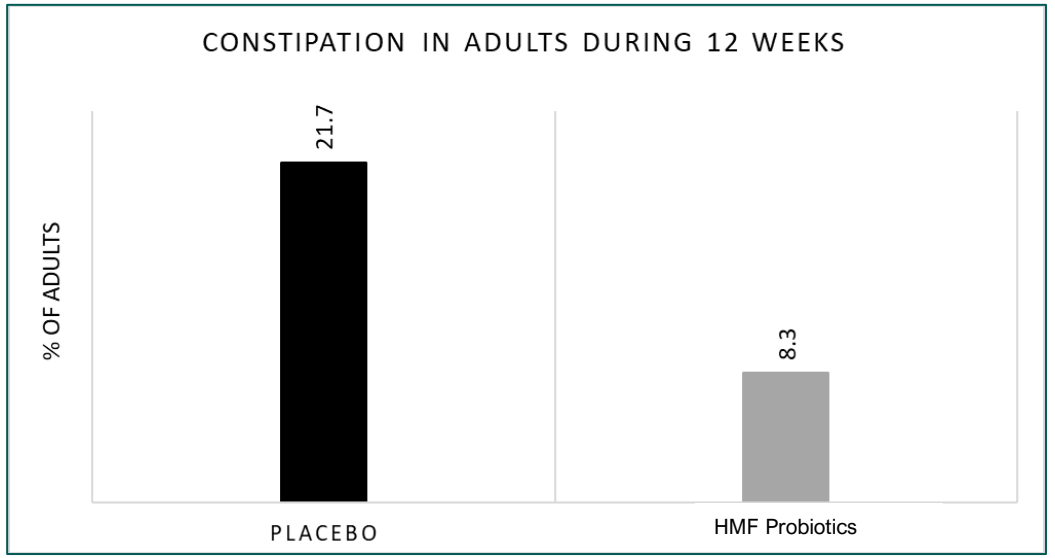
Mullish B et al, Beneficial Microbes 2023

Anti-constipation Effects in Infants and Adults

INFANTS
THE SWANSEA BABY STUDY



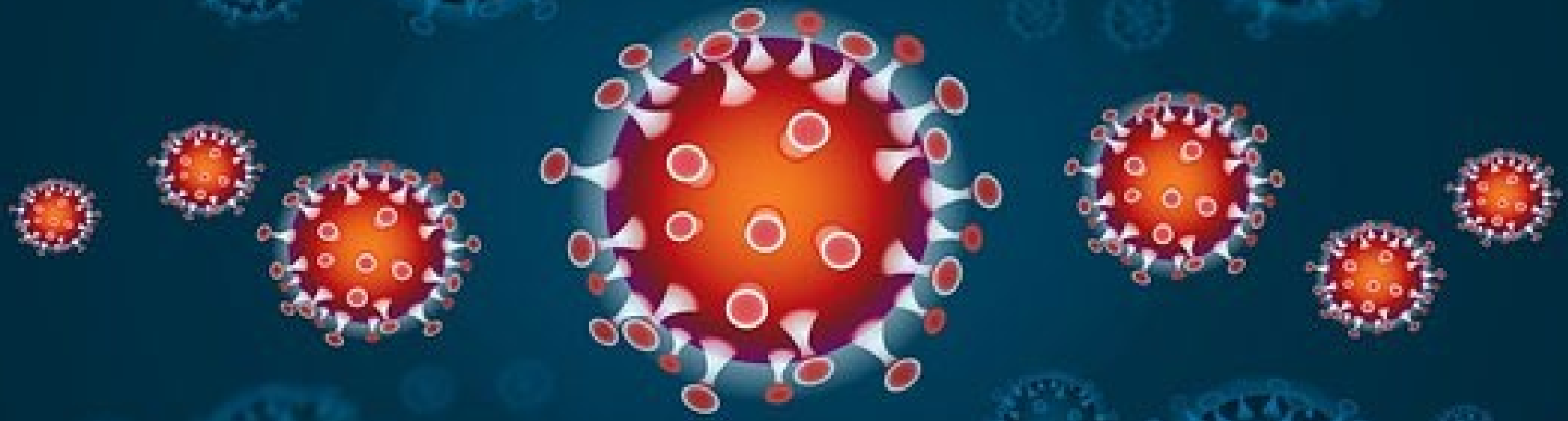
ADULTS
THE PROBIOTICS & HEALTHY ADULT STUDY



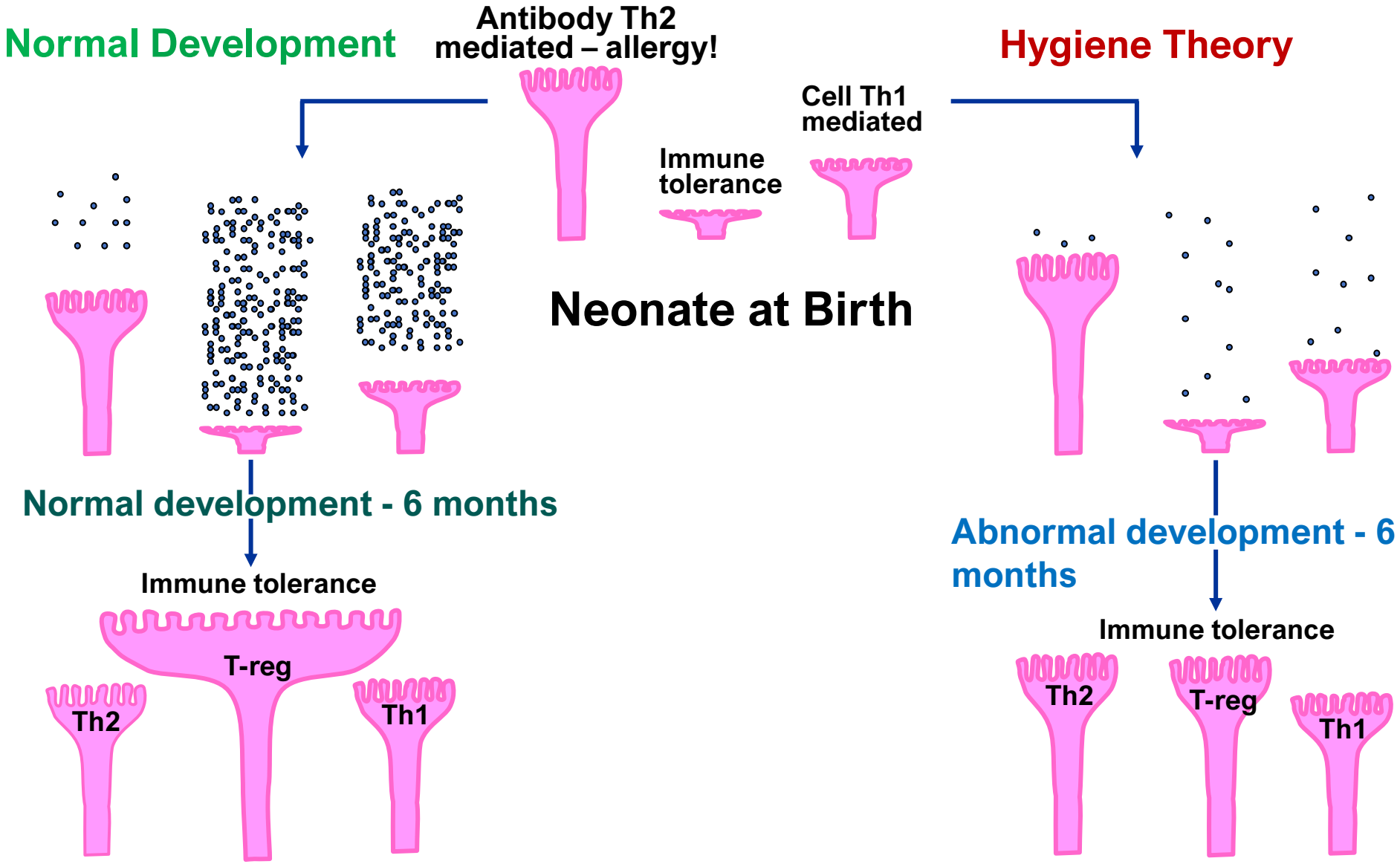
Significant reduction in constipation in infants supplemented with HMF-B and in adults supplemented with HMF probiotics.

Allen SJ et al, Arch Dis Child 2014; Mullish B et al, Beneficial Microbes 2023

CLINICAL EFFECTS OF HMF PROBIOTICS ON IMMUNE HEALTH



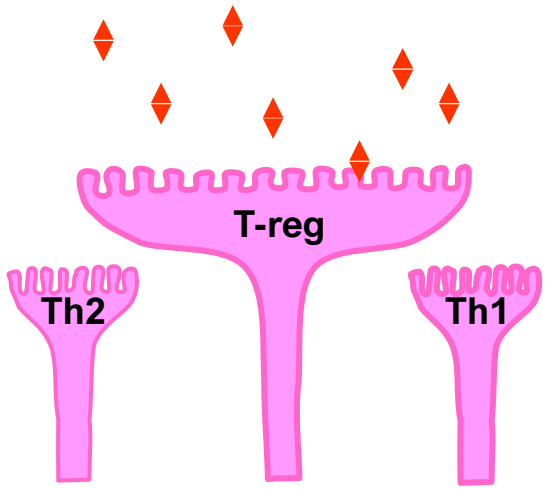
Allergy Development, The Hygiene Theory and Probiotics



Allergy Development, The Hygiene Theory and Probiotics

Normal pathway

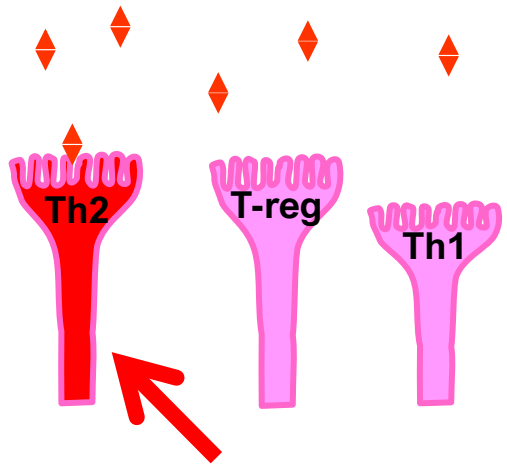
Processing by immune tolerance pathway (high likelihood) – no allergy



Normal

Hygiene theory pathway

Processing by allergy (antibody) pathway - high likelihood



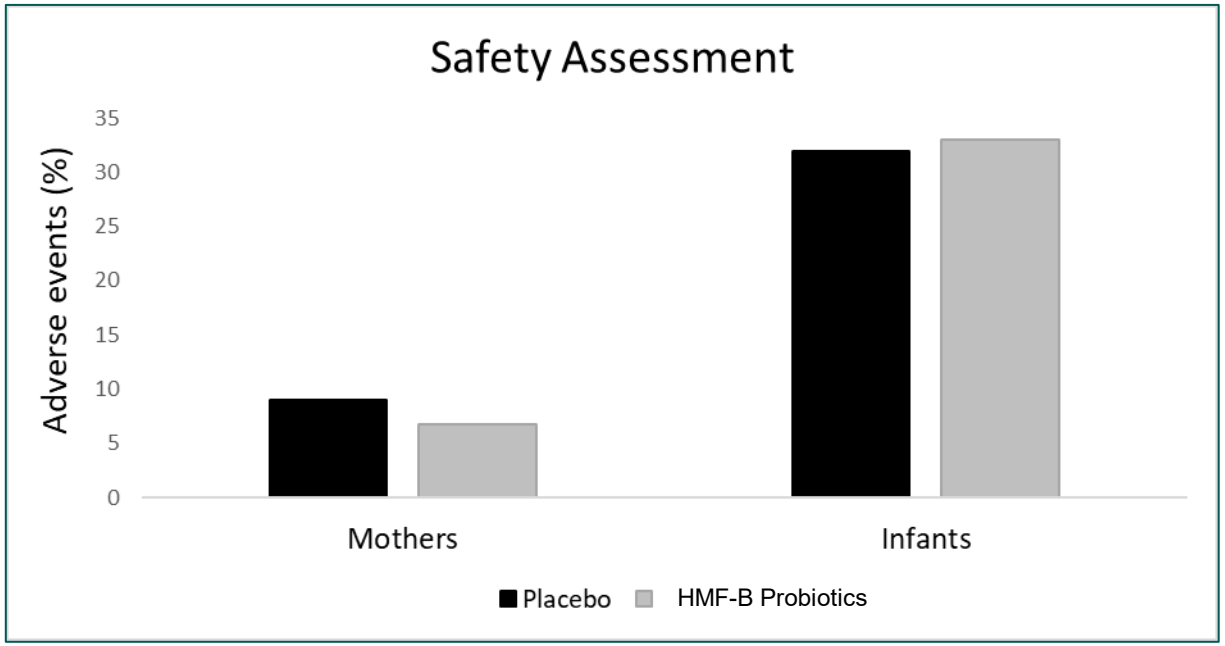
Allergy!

The Swansea Baby Trial

The Swansea Baby Trial

HOW SAFE ARE PROBIOTICS IN PREGNANCY AND FOR NEWBORN BABIES?

The Swansea Baby Study: 454 mothers took daily either 10 billion HMF-B Consortium Probiotics or a matching placebo during the last month of pregnancy and gave the same to their newborn babies every day for 6 months following birth.



THE SWANSEA BABY TRIAL,
THE SWANSEA "SAFETY IN NEWBORNS STUDY":
HMF-B Consortium - 10 BILLION CFU

Lactobacillus salivarius	CUL61
Lactobacillus paracasei	CUL08
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34

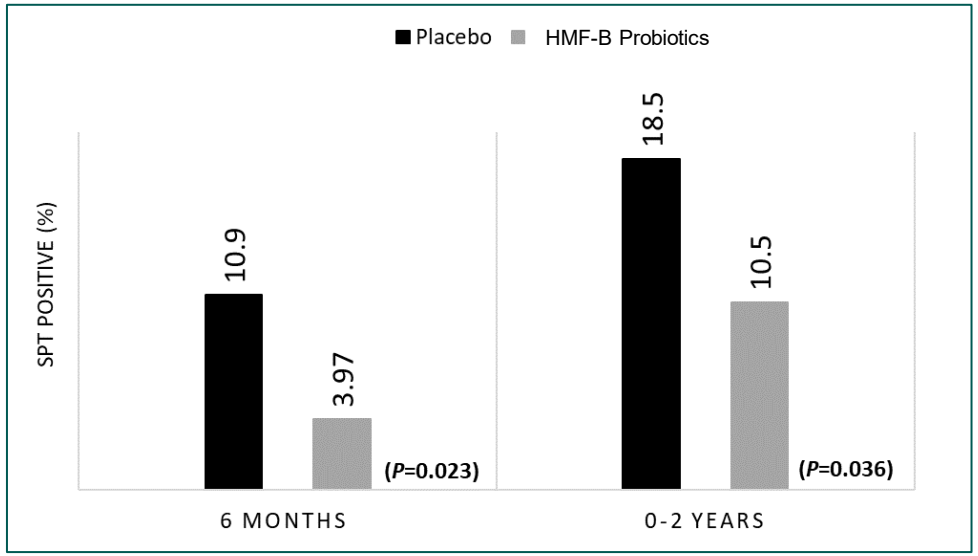
HMF-B Probiotic administration was not associated with adverse events in mothers or their infants.
No Lactobacilli or Bifidobacteria infections were identified.

Allen SJ et al, J Nutr 2010

The Swansea Baby Trial: Allergy Prevention

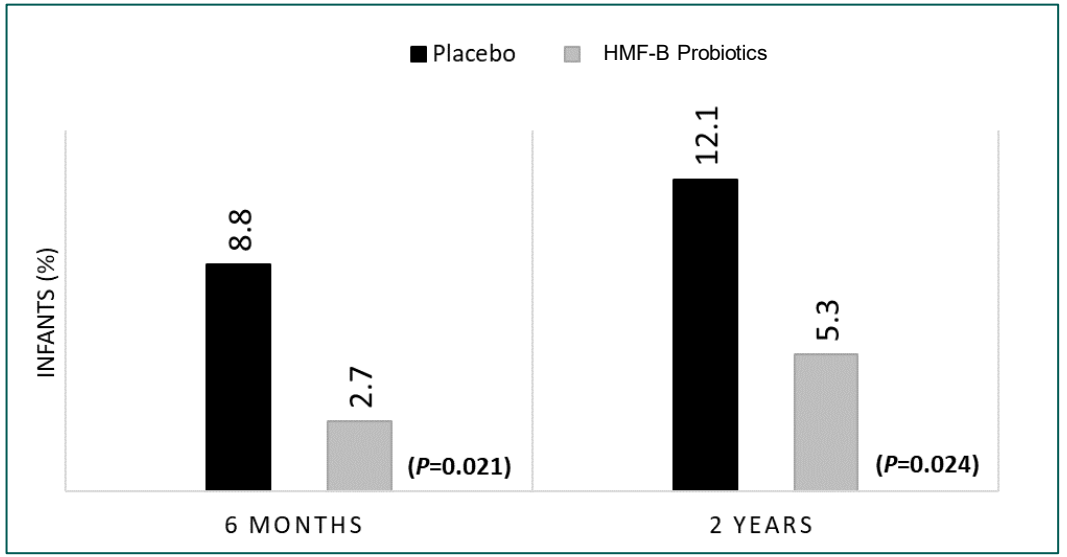
The Swansea Baby Study: 454 mothers took daily either 10 billion HMF-B Consortium Probiotics or a matching placebo during the last month of pregnancy and gave the same to their newborn babies every day for 6 months following birth. Atopic sensitisation measured by SPT reaction to one or more of following allergens: cows milk, egg, grass pollen, house dust mite, cat dander.

ATOPIC SENSITIZATION



44% significant reduction in frequency of atopic sensitization with HMF-B Probiotic.

ATOPIC ECZEMA



57% significant reduction in frequency of atopic eczema with HMF-B Probiotic.

Allen SJ et al, Arch Dis Child 2014

HMF Maternity, HMF Baby B & HMF Baby F

10 Billion CFU of Genestra HMF Probiotic organisms per Capsule

10 Billion CFU of Genestra HMF Probiotic organisms per scoop

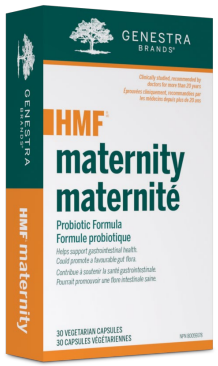
Organisms proven to be **safe** for use **during pregnancy**

Contains the same **organisms and potency** as utilized in the **Swansea Baby Trial**

Vegan friendly, Gluten, Dairy, Soy, FOS and GMO free

HMF **Baby B** provides ease of use for **breast fed** babies
Contains 100 mg of GOS per scoop and no FOS

HMF **Baby F** developed for **formula fed** babies
Contains 600mg of GOS to provide prebiotic oligosaccharides generally present in breast milk, and 75 mg of FOS per scoop



EACH CAPSULE CONTAINS:

Probiotic Consortium	10 billion CFU
Lactobacillus salivarius (CUL-61)	6.25 billion CFU
Bifidobacterium animalis subsp. *lactis* (CUL-34) & *Bifidobacterium bifidum* (CUL-20)	2.5 billion CFU
Lactobacillus paracasei (CUL-08)	1.25 billion CFU

EACH SCOOP (200 mg) CONTAINS:

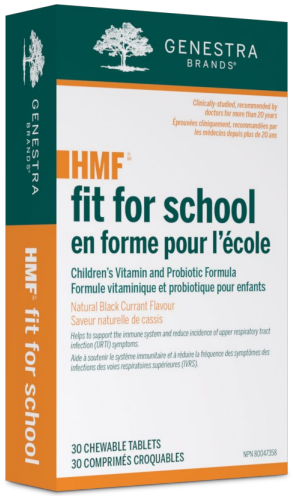
Probiotic Consortium	10 billion CFU
Bifidobacterium bifidum (CUL-20)	0.125 billion CFU
Bifidobacterium animalis subsp. *lactis* (CUL-34)	2.375 billion CFU
Lactobacillus salivarius (CUL-61)	6.25 billion CFU
Lactobacillus paracasei (CUL-08)	1.25 billion CFU

EACH SCOOP (1.1 g) CONTAINS:

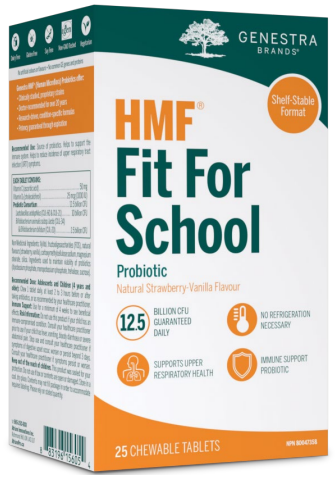
Probiotic Consortium	10 billion CFU
Bifidobacterium bifidum (CUL-20)	0.125 billion CFU
Bifidobacterium animalis subsp. *lactis* (CUL-34)	2.375 billion CFU
Lactobacillus salivarius (CUL-61)	6.25 billion CFU
Lactobacillus paracasei (CUL-08)	1.25 billion CFU

The ProChild Studies

HMF Fit for School



Refrigerated Options



Shelf-stable Option

GMO Non GMO · Gluten Free · Soy Free · Dairy Free · Vegetarian

Medicinal Ingredients

EACH TABLET CONTAINS:

Vitamin C (ascorbic acid).....50 mg
Vitamin D_3 (cholecalciferol).....25 mcg (1000 IU)
Probiotic Consortium.....12.5 billion CFU
Lactobacillus acidophilus (CUL-60 & Cul-21).....10 billion CFU
Bifidobacterium animalis subsp. Lactis (CUL-34)
& Bifidobacterium bifidum (CUL-20).....2.5 billion CFU

The ProChild Study 1 – 2015 (URT-related & non-health parameter outcomes)

Objective of the Double-blind Placebo Controlled Study:

To assess the impact of specific proprietary human probiotic strains in combination with Vitamin C, on Upper Respiratory Tract health function in pre-school aged children

Design of the studies:

57 children in the **3–6-year age range** (preschoolers) participated

Participants received **1 tablet** containing **12.5 billion** proprietary human probiotics and 50mg of Vitamin C daily

Duration and intervention:
6 months, with a focus on indicators of respiratory health

Probiotic Consortium Utilized:

THE PROCHILD STUDY:
HMF Consortium - 12.5 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34

Outcome of the studies:

49% REDUCTION — Total number of days with URTI symptoms (sneezing, sore throat, cough, runny/blocked nose)

33% REDUCTION — Frequency of occurrence of URTI symptoms

Doctor visits — **43%** REDUCTION

30% REDUCTION — Absence from preschool ("non-health parameter")

Oral antibiotic usage — **40%** REDUCTION

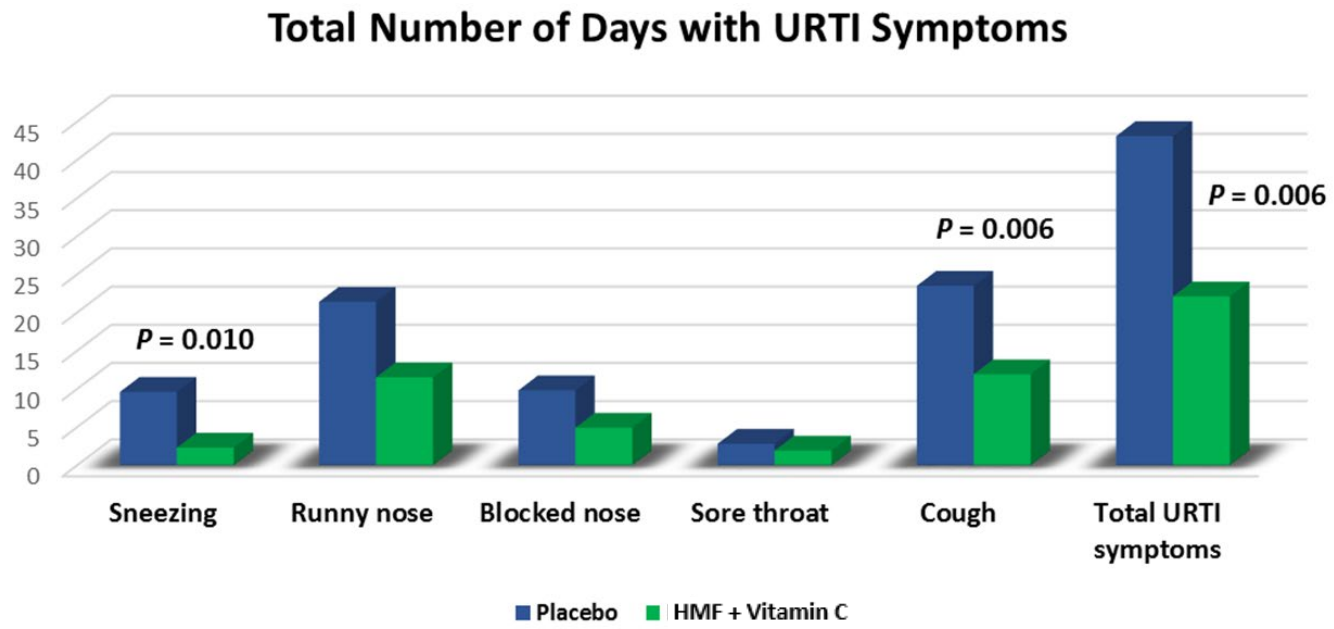
Supplementation with this specific proprietary human probiotic (HMF Consortium -12.5 billion CFU) and 50mg of Vitamin C daily showed **significant improvement in Upper Respiratory Tract Health in children**

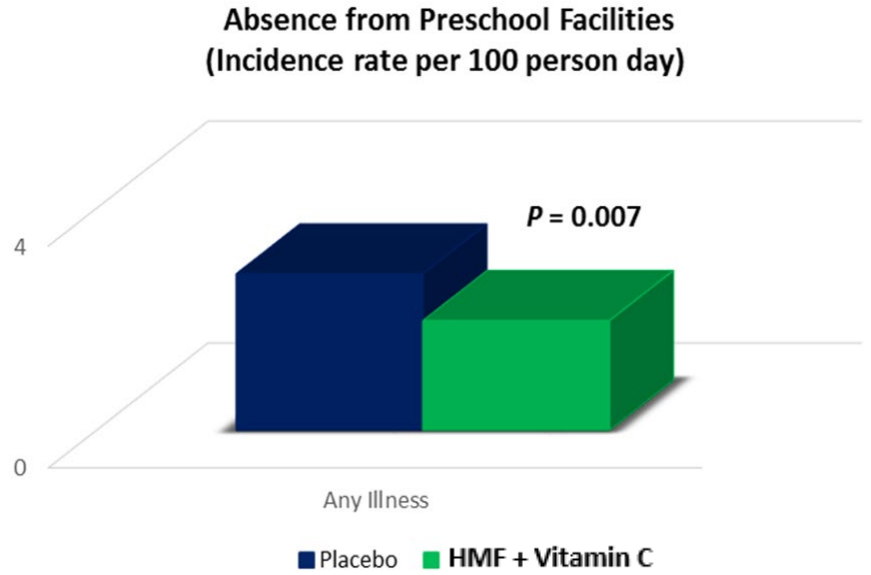
Garaiova, et al. Eur J Clin Nutr. 2015

The ProChild Study 1 – 2015 (URT-related outcomes)

Objective of the Double-blind Placebo Controlled Study:

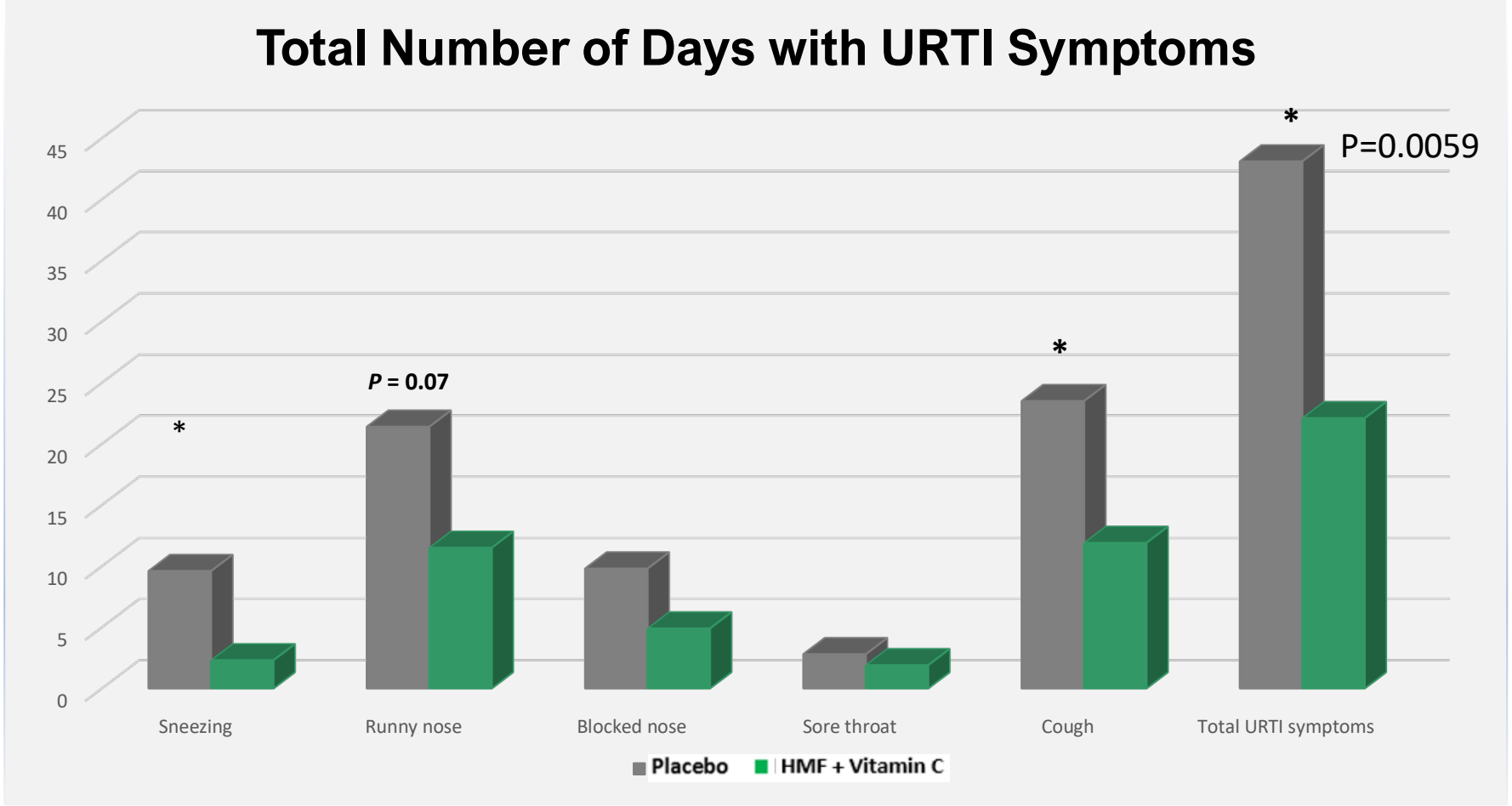
To assess the impact of specific proprietary human probiotic strains in combination with Vitamin C, on Upper Respiratory Tract health function in pre-school aged children



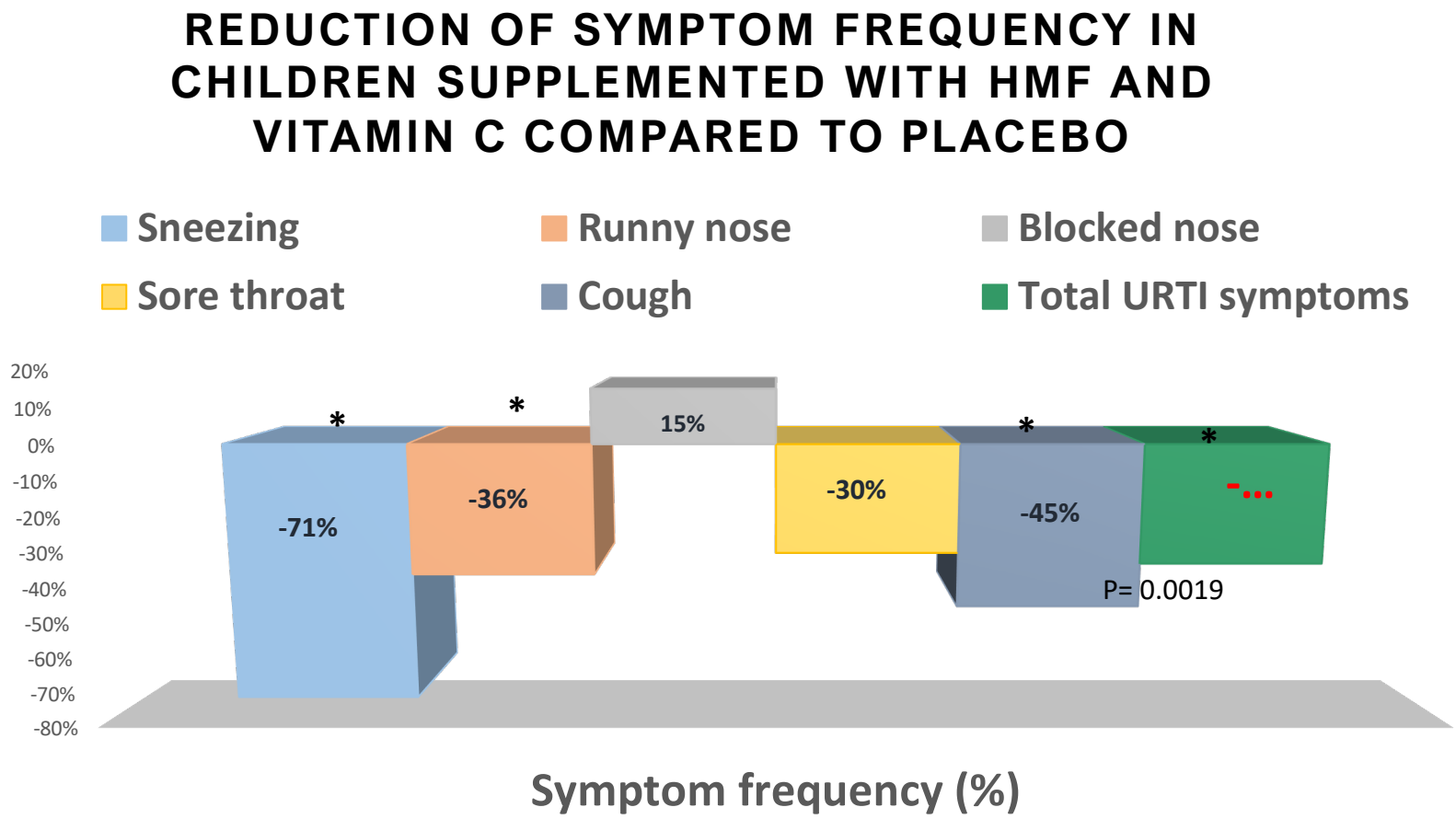


Garaiova I et al Eur J Clin Nutr 2015, 69: 373-379

Reduction in Duration of UTRI Symptoms by almost 50%

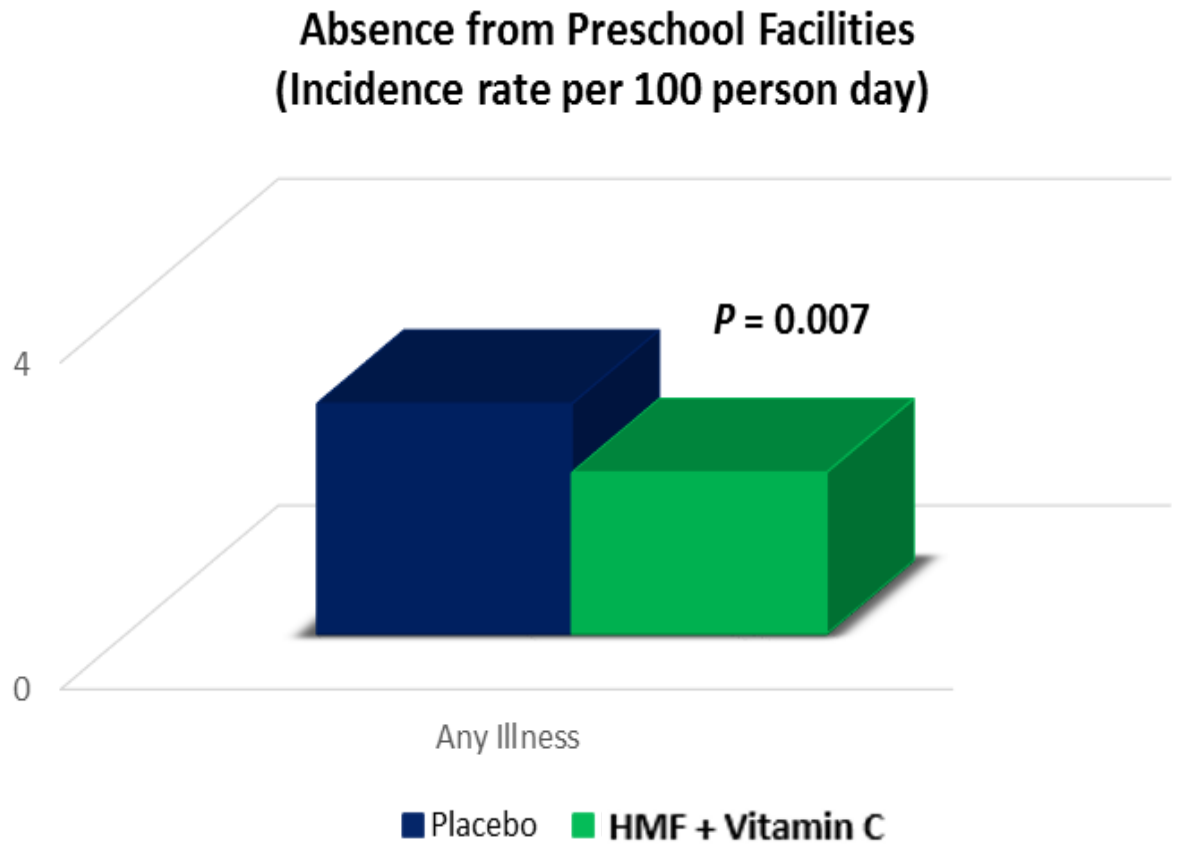


Reduction in Incidence of UTRI Symptoms by 33%



Garaiova I et al Eur J Clin Nutr 2015, 69: 373-379

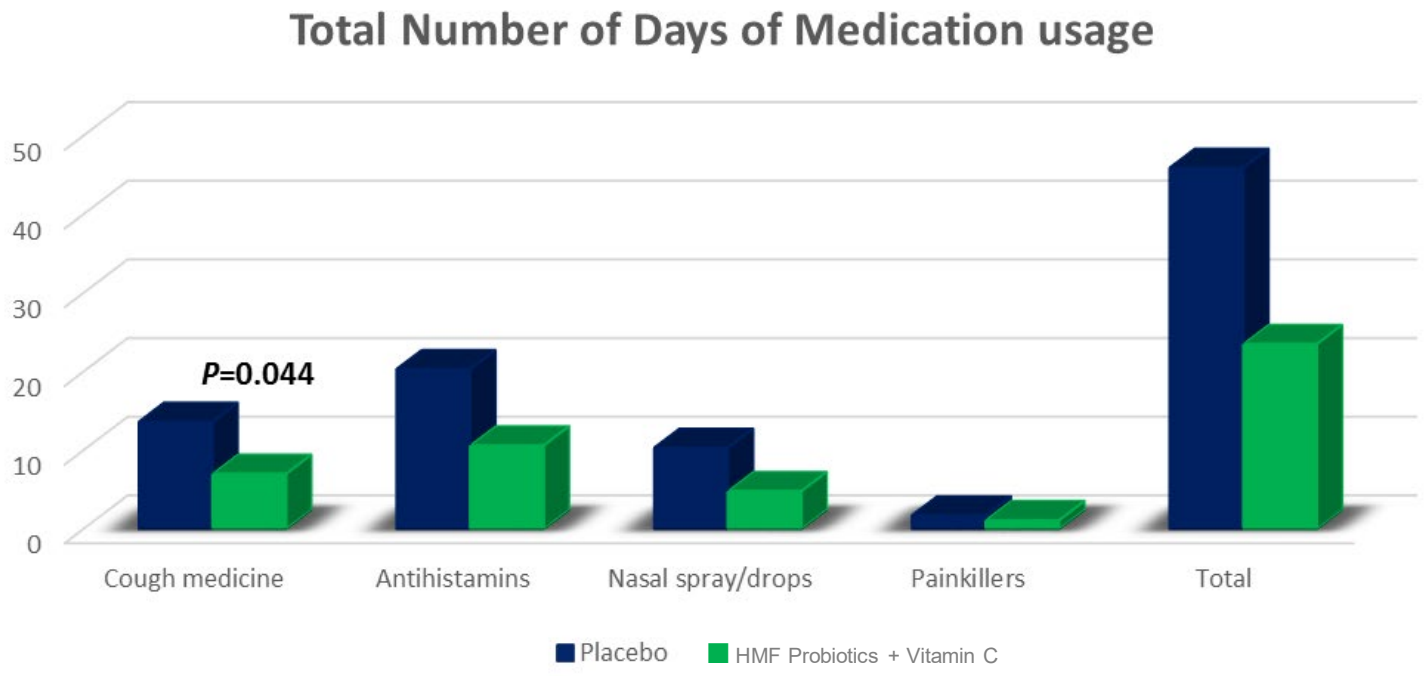
Reduction in Absence from School



30% significant reduction in the incidence of absenteeism from preschool

Garaiova I et al Eur J Iin Nutr 2015, 69: 373-379

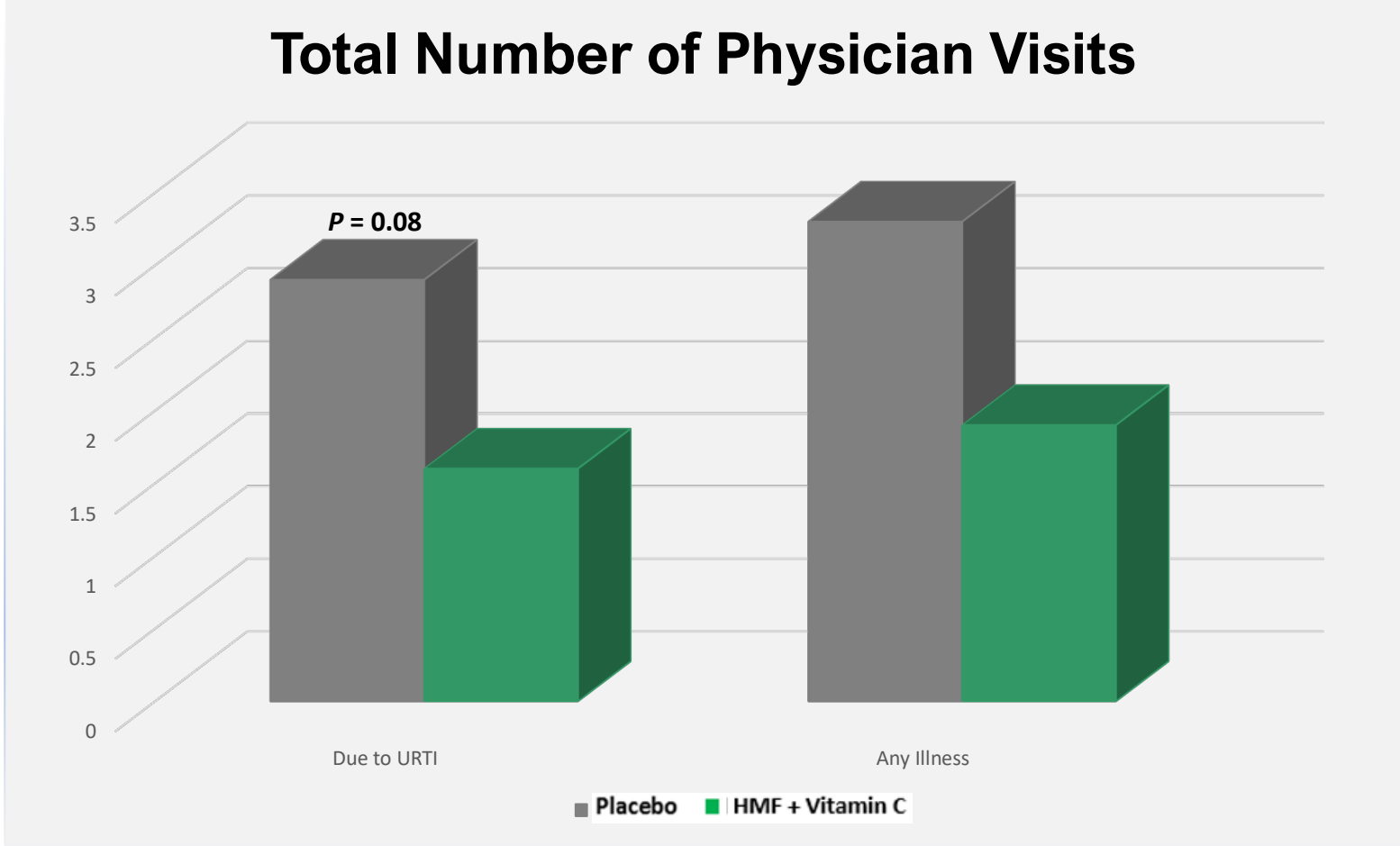
Antibiotics and Medication Usage



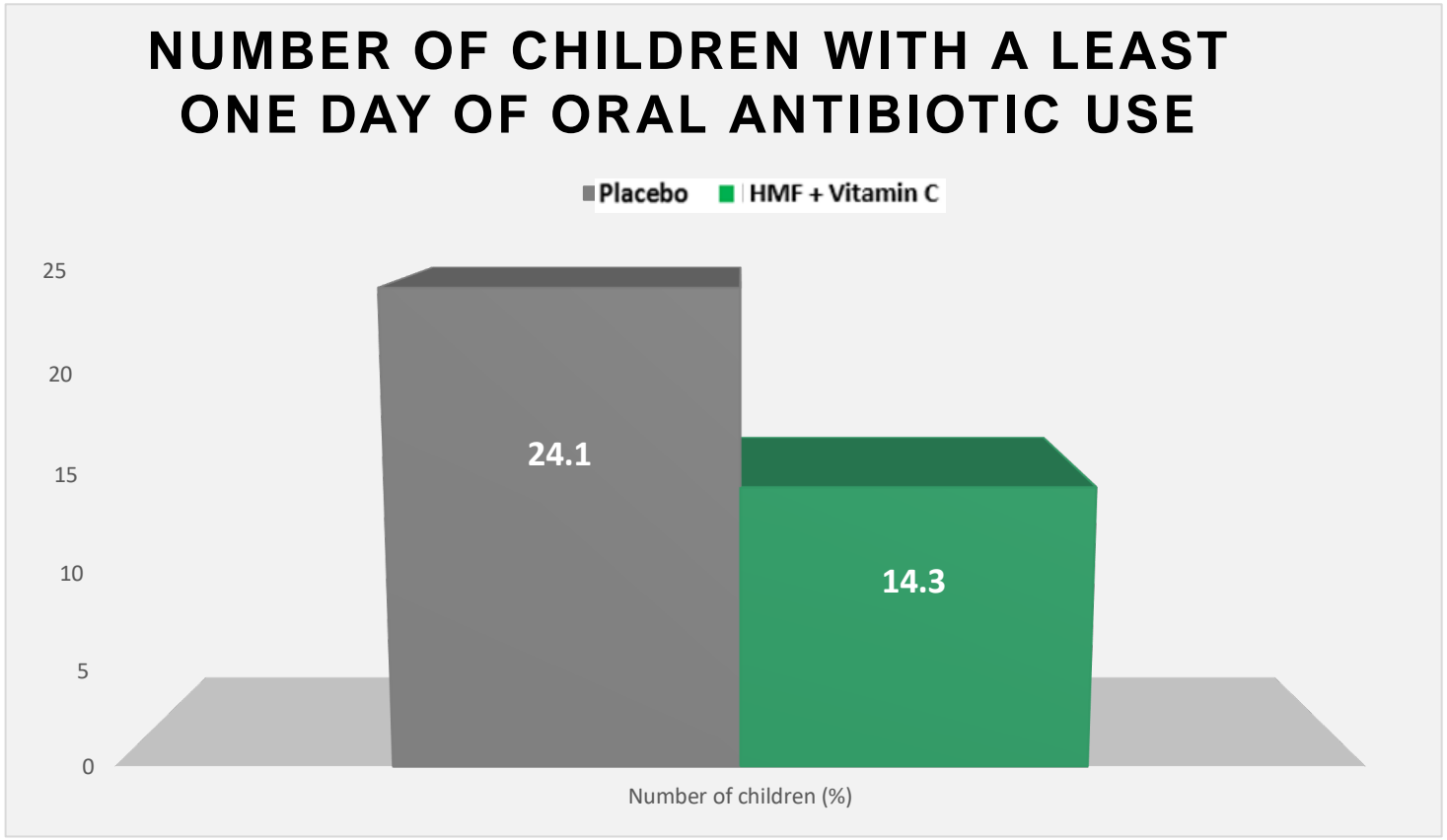
Significant reduction in the use of cough medicine

Garaiova I et al Eur J Clin Nutr 2015, 69: 373-379

Visits to Physician Reduced by almost 50%



Reduction of Antibiotic Use by 40%



The ProChild Study 2 – 2021 (URT-related, non-health parameter & GI-related outcomes)

Objective of the Double-blind Placebo Controlled Study:

To assess the impact of specific proprietary human probiotic strains in combination with Vitamin C, on Upper Respiratory Tract health function in children aged 3-10 yrs.

Design of the studies:

234 children in the **3–10-year age range** randomized to participate.
171 completed the study (85 in placebo group & 86 in probiotic group)

Participants received **1 tablet** containing **12.5 billion** proprietary human probiotics and 50mg of Vitamin C daily

Duration and intervention:
6 months, with a focus on indicators of respiratory health

Probiotic Consortium Utilized:

THE PROCHILD STUDY:
HMF Consortium - 12.5 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34

Outcome of the studies:

16% REDUCTION — Total number of days with the URTI symptom of coughing

20% REDUCTION — Total number of days with the URTI symptom of sore throat

Doctor visits — **19%** REDUCTION

16% REDUCTION — Absence from school (“non-health parameter”)

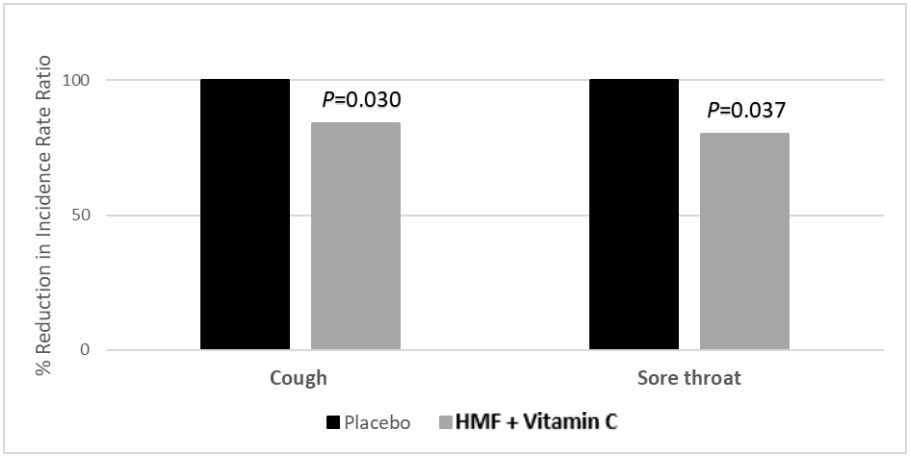
Total antibiotic usage — **27%** REDUCTION

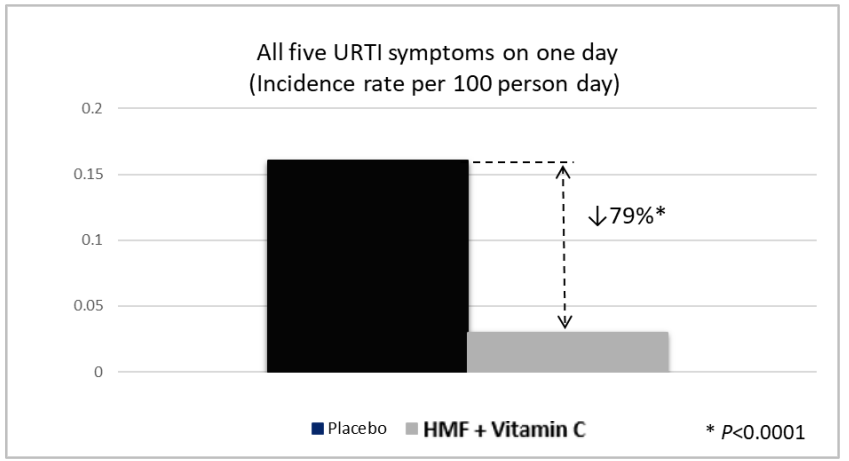
This clinical trial substantiated findings of the initial study, confirming that children supplemented with this specific proprietary human probiotic (HMF Consortium -12.5 billion CFU) and 50mg of Vitamin C daily experience **significant improvement in their Upper Respiratory Tract Health. Substantial improvement in intestinal health and normal bowel habit were found to be additional outcomes.**

Garaiova, et al Beneficial Microbes, 2021

The ProChild - 2 Study:
Prevention of URTI in Children aged 3 to 10 years

DBRPC study (ISRCTN 26587549): 171 children took daily either one chewable tablet comprising of 12.5 billion HMF Probiotics – (HMF Consortium 12.5 Billion CFU) and 50mg Vitamin C or placebo for 6 months



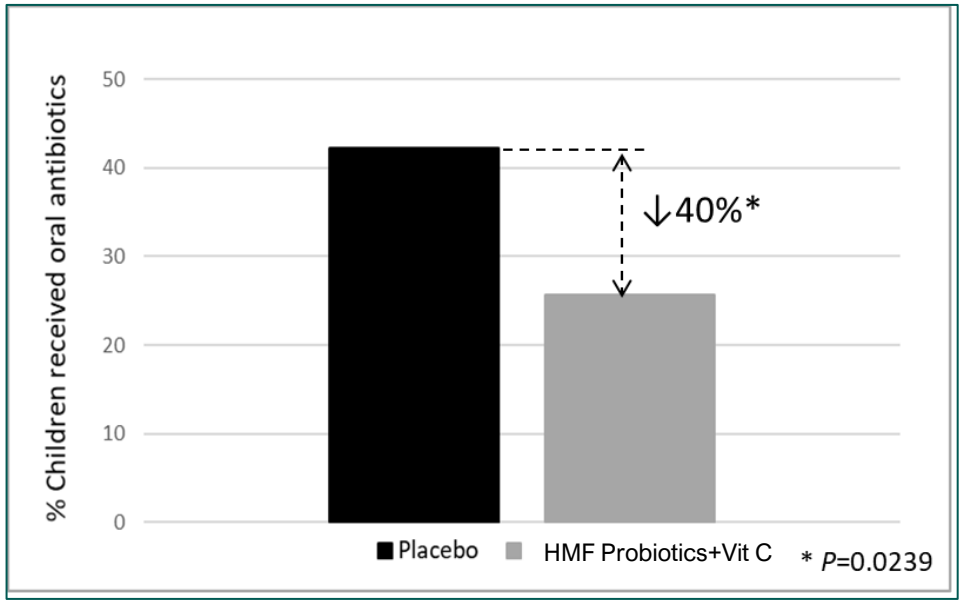


16% significant reduction in the incidence of coughing. 20% significant reduction in the incidence of sore throats.

79% significant reduction in the incidence of episodes with five URTI symptoms# on one day. #(cough, sore throat, sneezing, runny nose, blocked nose).

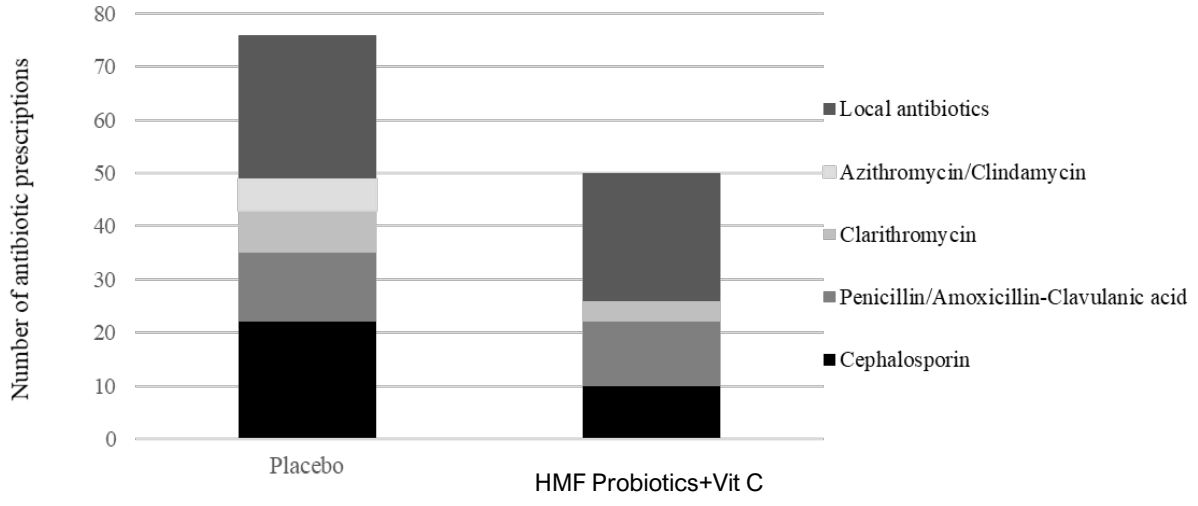
Reduction of Antibiotic Prescriptions (ProChild 2 Study)

PROPORTION OF CHILDREN WITH ORAL ANTIBIOTICS



42.3% children in placebo group were prescribed oral antibiotics compared to 25.6% children in HMF Probiotic group.

NUMBER OF ANTIBIOTIC PRESCRIPTIONS



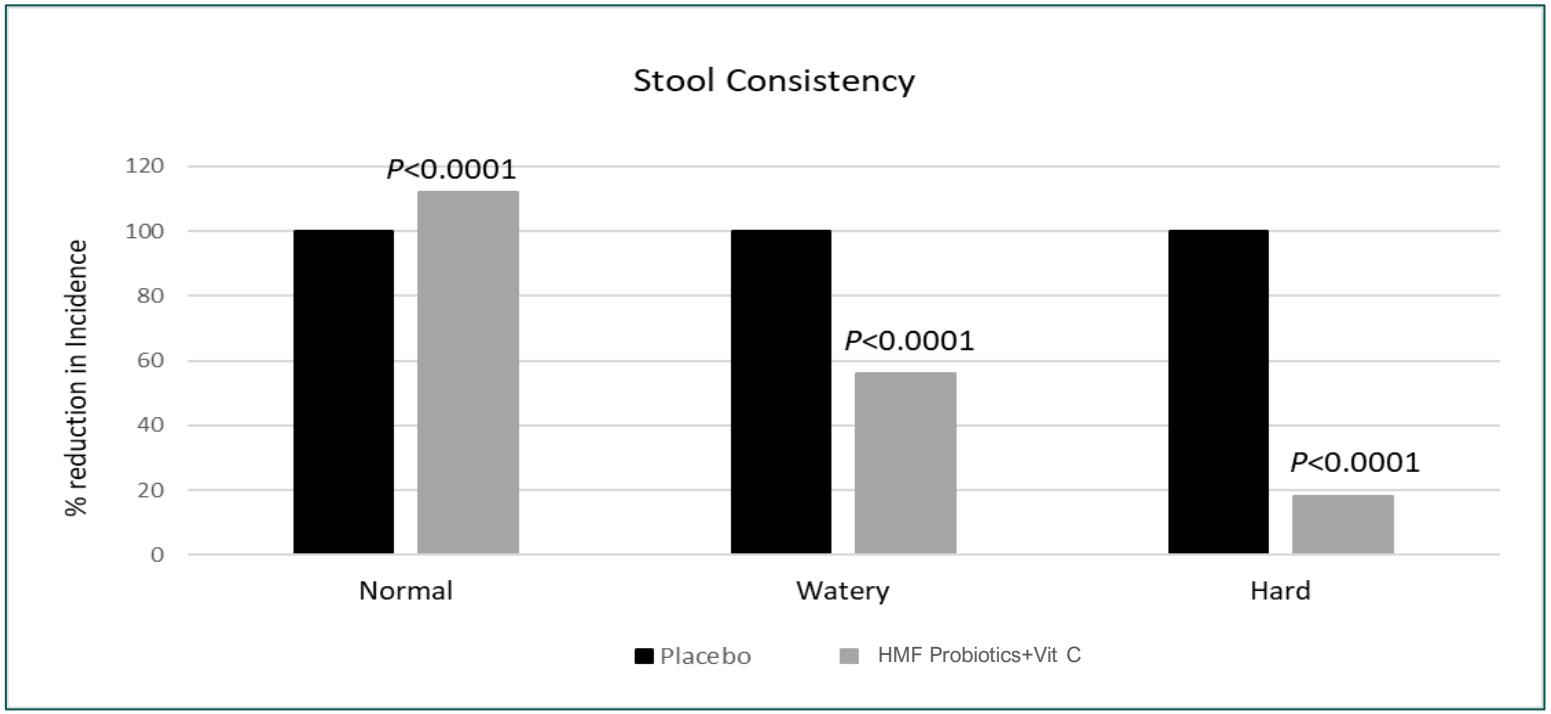
	Cephalosporin	Penicillin/Amoxicillin-Clavulanic acid	Clarithromycin	Azithromycin/Clindamycin	Local antibiotics
Placebo	22	13	8	6	27
Active	10	12	4	0	24

48% significant reduction in the incidence of total oral antibiotic prescriptions (*P*=0.0079).
55% significant reduction in the incidence of cephalosporin prescriptions (*P*=0.0360).

Garaiova I et al, J Functional Foods 2023

Intestinal Health in Children (ProChild 2 Study)

School children aged 3 to 10 years took daily either one chewable tablet comprising of 12.5 billion HMF Probiotics and 50mg vitamin C or a matching placebo for 6 months.



Significant improvement in the 'normal' stool consistency.
Significant reduction in the incidence of watery and hard stools.

Garaiova I et al, Beneficial Microbes 2021

A Probiotic That Delivers Full-body Health Outcomes

The Promagen Study

A landmark probiotic study which for the first time showed multiple and significant ‘unrelated’ health benefits simultaneously from the single intervention:

- **Weight loss**
- **Reduced upper respiratory tract infections**
- **Reduced body pain and headaches**
- **Improved Quality of Life**
- **Reduced LDL cholesterol**

HMF Metabolic

50 Billion

CFU of Genestra HMF Probiotic Strains per Capsule

Includes a combination of five proprietary strains clinically studied in adults

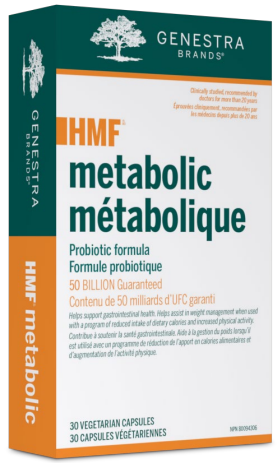
Supports **weight management, gastrointestinal health and several aspects of general health and well-being**

Contains the **HMF-P Probiotic consortium** (a combination of five proprietary strains clinically studied in adults)

Includes 16.5 Billion CFU of **Lactobacillus Plantarum (CUL-66)** per capsule

Vegan friendly, Gluten, Dairy, Soy and GMO free

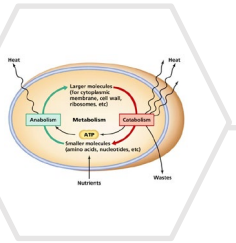
Contains no FOS



EACH CAPSULE CONTAINS/ CHAQUE CAPSULE CONTIENT:

Probiotic Consortium/ Consortium probiotique	50 billion CFU/ milliards d'UFC
Lactobacillus acidophilus (CUL-60 & CUL-21)	25.2 billion CFU/ milliards d'UFC
Lactobacillus plantarum (CUL-66)	16.5 billion CFU/ milliards d'UFC
Bifidobacterium animalis subsp. *lactis* (CUL-34) & *Bifidobacterium bifidum* (CUL-20)	8.3 billion CFU/ milliards d'UFC

The Promagen / Metabolic Study 1 – 2020 (Metabolic status & general health outcomes)



Objective of the Double-blind Placebo Controlled Study:

To Investigate the Impact of Probiotics on Metabolic Status and General Well-Being in an Overweight and Obese Population

Design of the studies:

220 healthy adults (BMI 25-35, waist circumference >89cm (>35'') for women or >100cm (>39'') for men) participated in **this 6-month study**

50 billion CFU of the proprietary human probiotic consortium was administered to participants **daily** with **no change in their diet or exercise regime**

Probiotic Consortium Utilized:

THE PROMAGEN / METABOLIC STUDY
HMF-P Consortium - 50 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34
Lactobacillus plantarum	CUL66

Outcome of the studies:

After 3 months there was improvement in Quality-of-Life parameters for the probiotic group:

- Improvement of Energy levels
- Mood
- and General wellness

After 6 months the probiotic group showed reduction in:

- Weight (3 lbs.)
- Waist circumference (1cm)
- BMI
- Upper respiratory tract infections
- Headaches
- Muscle pain

Sub-group analysis showed:

- Higher weight loss: in people who were overweight (BMI 25-30) (3.3 lbs. / 1.5 kg), in people over 50 years (4 lbs. / 1.8 kg) and in people with higher cholesterol (5 lbs. / 2.27 kg) compared to the placebo group
- Highest weight loss compared to placebo in people over 50 with higher cholesterol (7lbs / 3.21 kg)
- The most dangerous type of LDL cholesterol reduced in high cholesterol group

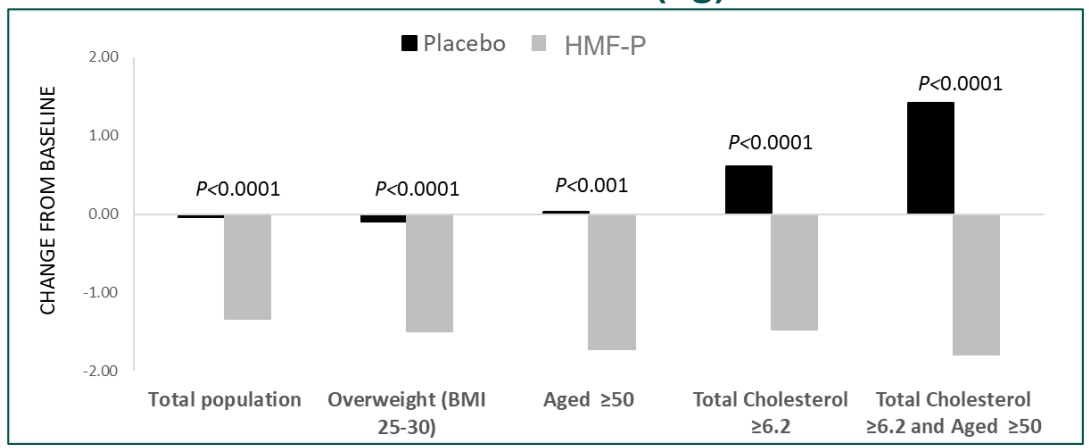
GENESTRA BRANDS® Garden of Life SiSU pure encapsulations DOUGLAS LABORATORIES UNDA Atrium Innovations Brands ATRIUM INNOVATIONS

D. R. Michael1, A. A. Jack1, G. Masetti1, T. S. Davies1, K. E . Loxley1, J. Kerry-Smith1, J. F . Plummer1, J. R. Marchesi2,3, B. H. Mullish 3, J. A. K. McDonald 4, T. R. Hughes5, D. Wang6, I. Garaiova1, Z. Paduchová7, J. Muchová7, M. A. Good8 & S. F . Plummer1 (2020) Scientific Reports*

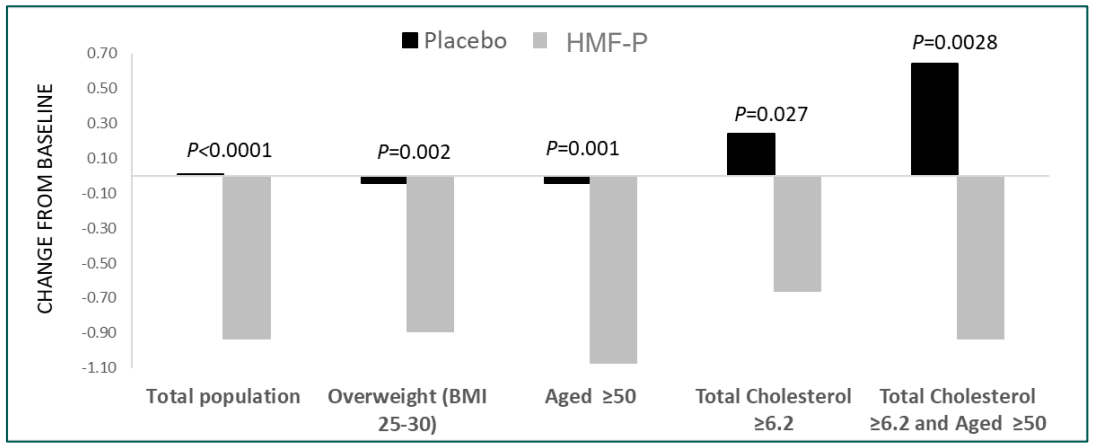
The Promagen Study: Weight Loss in Overweight and Obese Adults

Healthy volunteers (BMI 25-34.9) took either 50 billion HMF-P Consortium probiotics or placebo daily for 6 months and maintained a normal lifestyle.

BODY WEIGHT (kg)



WAIST CIRCUMFERENCE (cm)



Total population: 1.3kg (2.9lb), 0.94cm (0.37in)

Overweight participants: 1.4kg (3.1lb), 0.85cm (0.34in)

Over 50-year-olds: 1.8kg (4lb), 1.03cm (0.41in)

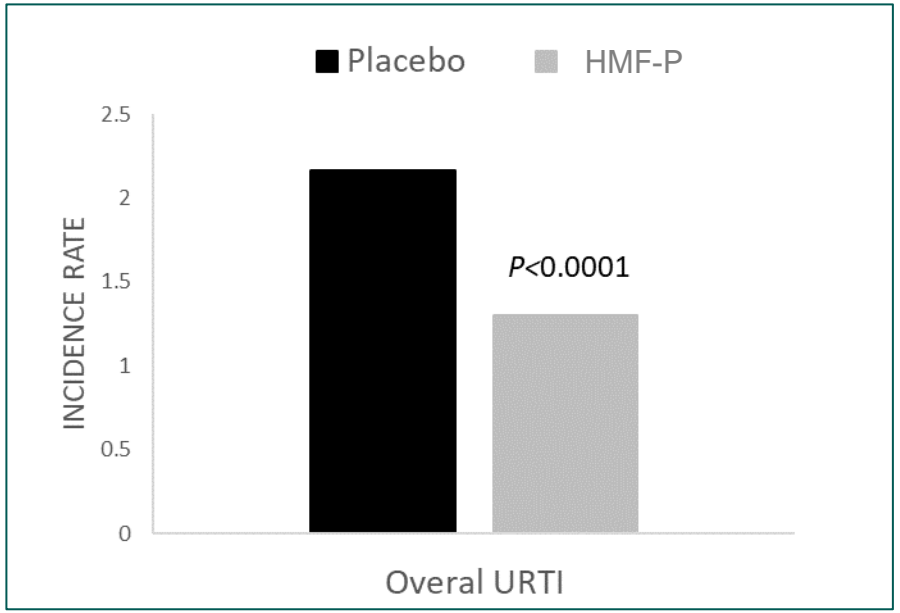
Hypercholesteraemic participants: 2.1kg (4.6lb), 0.90cm (0.35in)

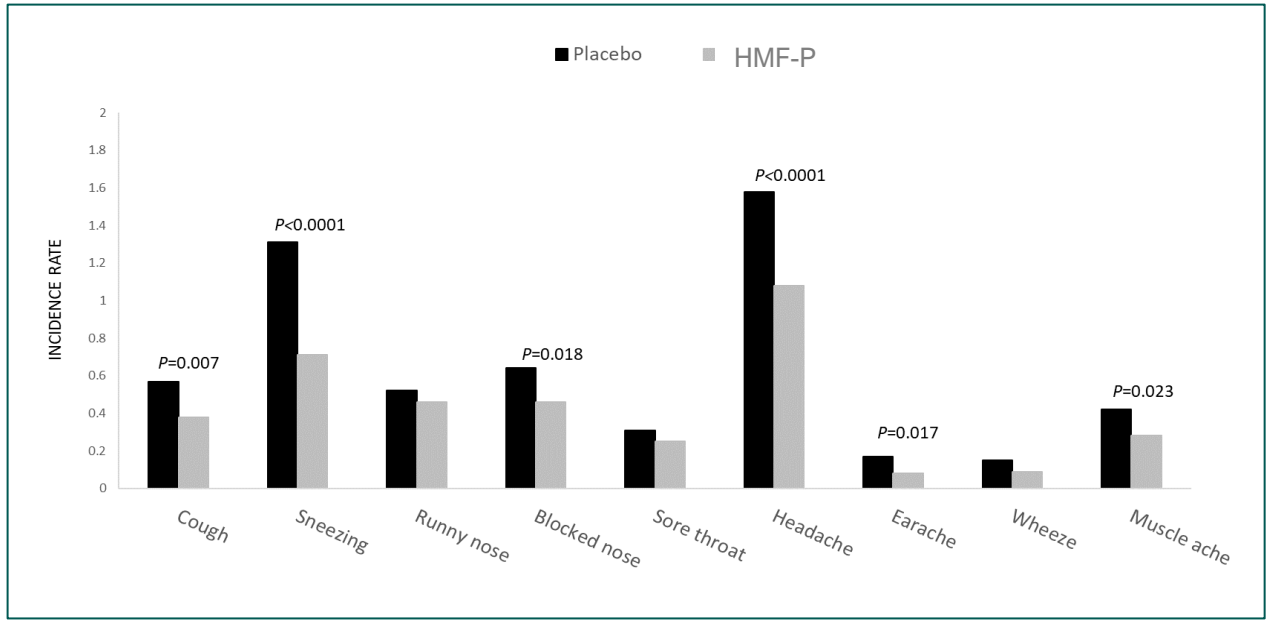
Hypercholesteraemic participants over 50 years old: 3.2kg (7.1lb), 1.57cm (0.62in)

Michael DR et al, Scientific Reports 2020

The Promagen Study: Prevention of Colds and Coughs in Adults

Overweight or obese adults (BMI 25-34.9) took daily either 50 billion HMF-P Consortium probiotics or a matching placebo for 6 months and maintained a normal lifestyle.





40% significant reduction in the incidence of URTI symptoms.

Michael DR et al, Scientific Reports 2020

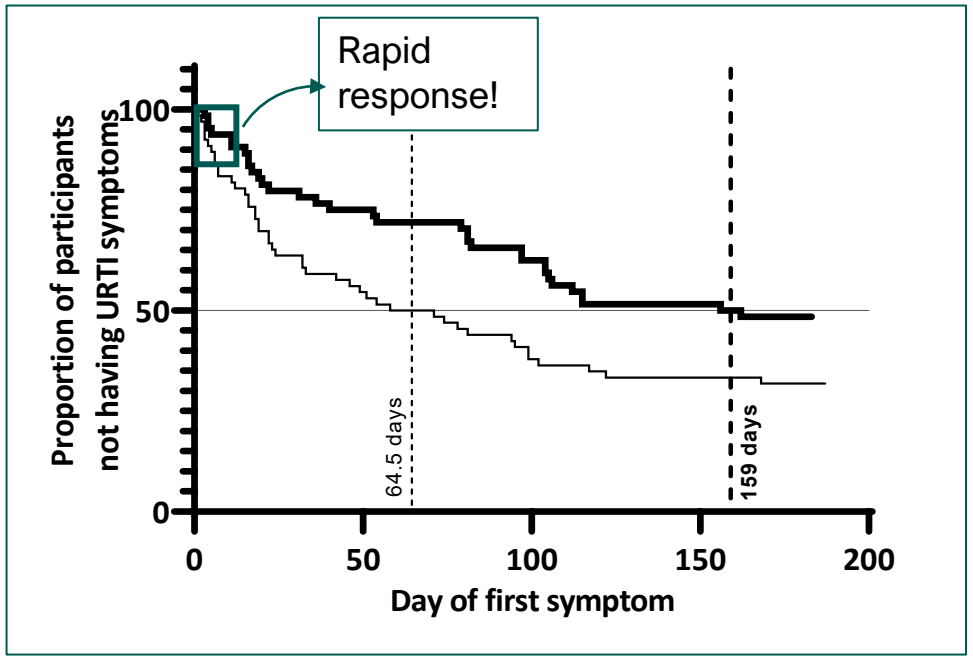
Prevention of Coughs & Colds in Adults

THE PROMAGEN / METABOLIC STUDY
HMF-P Consortium - 50 BILLION CFU

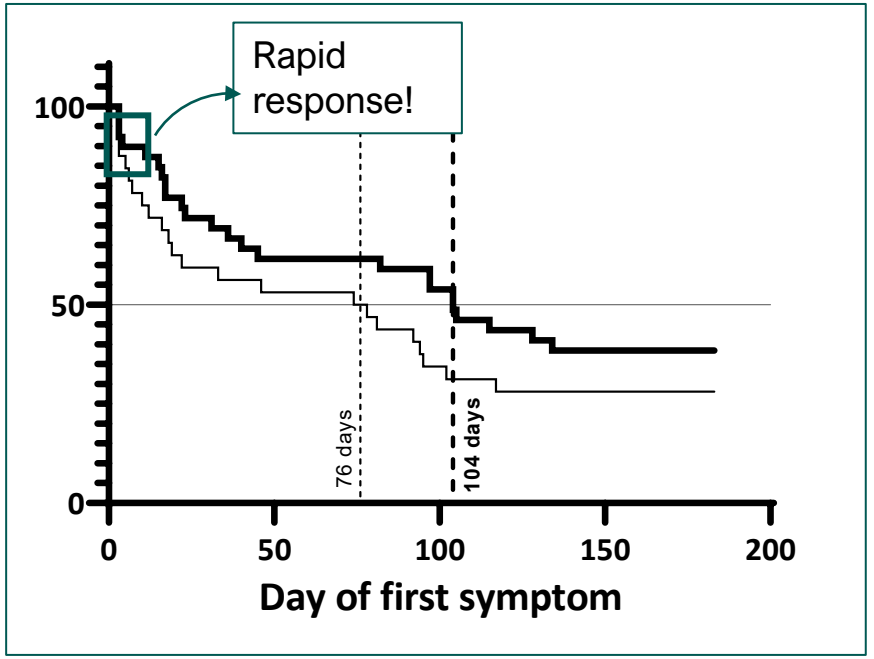
Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34
Lactobacillus plantarum	CUL66

Further analyses were carried to investigate the impact of the HMF-P Consortium probiotics on the occurrence of specific upper respiratory tract infections symptoms and the impact of age and BMI.

Age ≥ 45



BMI ≥ 30



40% reduction in incidence of URTI in people over 45 compared to placebo.
43% reduction in incidence of URTI in people with a BMI ≥30 compared to placebo.

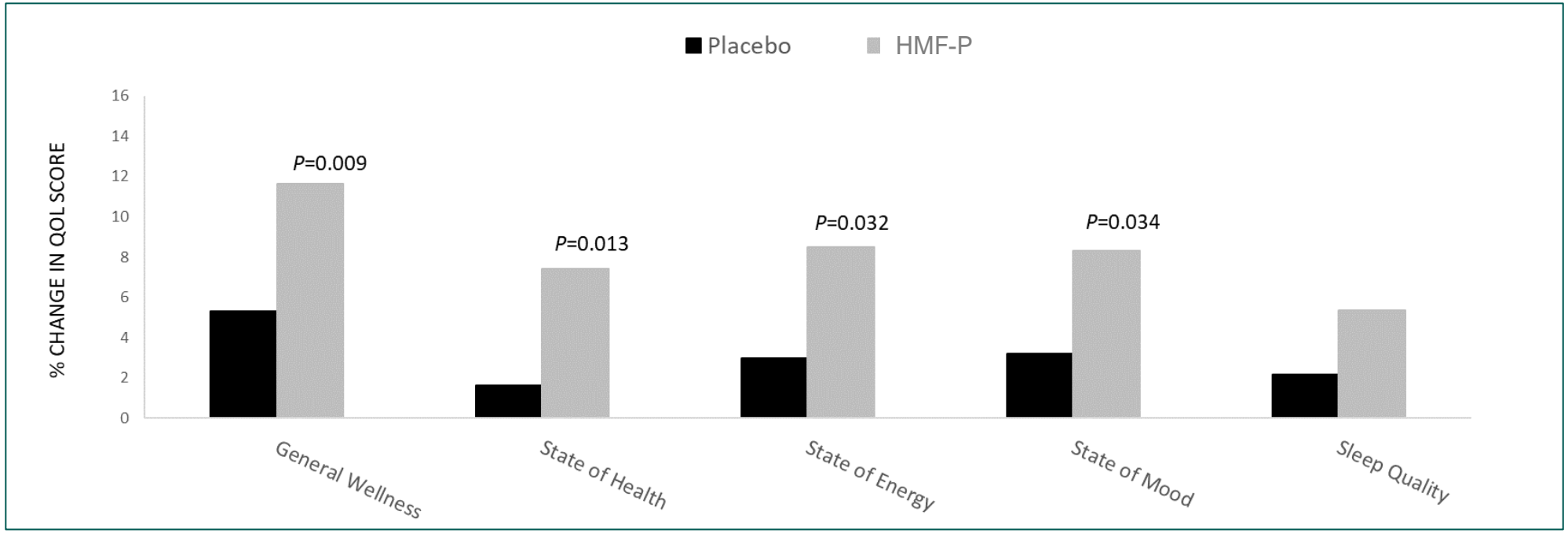
Mullish et al, Gut Microbes 2021

The Promagen Study: General Health

Overweight or obese adults (BMI 25-34.9) took daily either 50 billion HMF-P Consortium probiotics or a matching placebo for 6 months and maintained a normal lifestyle.

THE PROMAGEN / METABOLIC STUDY
HMF-P Consortium - 50 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34
Lactobacillus plantarum	CUL66



Supplementation of overweight and obese adults with HMF-P Probiotics resulted in a significant improvement of reported Quality of Life scores.

Michael DR et al, Scientific Reports 2020

The Promagen / Metabolic Study 2 – 2021 (Metabolic status & general health outcomes)

Objective of the Double-blind Placebo Controlled Study:
To Investigate the Impact of Probiotics on Metabolic Status and General Well-Being in an Overweight and Obese Population

Design of the studies:

70 healthy adults (BMI 25-29.9 and aged between 45-65) participated in **this 9-month study**

50 billion CFU of the proprietary human probiotic consortium was administered to participants **daily** with **no change in their diet or exercise regime**

Probiotic Consortium Utilized:

THE PROMAGEN / METABOLIC STUDY
HMF-P Consortium - 50 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34
Lactobacillus plantarum	CUL66

Outcome of the studies:

After 9 months:

- Weight loss of 7 lbs. (3kg)
- Reduction in waist measurement of 1.1 inches (3cm)
- Reduction in hip measurement of 1 inch (2.66 cm)
- Favorable changes in blood pressure values

Additional Findings:

In alignment with an assessment of 5% weight loss in a 6–12-month timeframe established by the American Heart Association (AHA) as a meaningful weight loss achievement, some additional findings were:

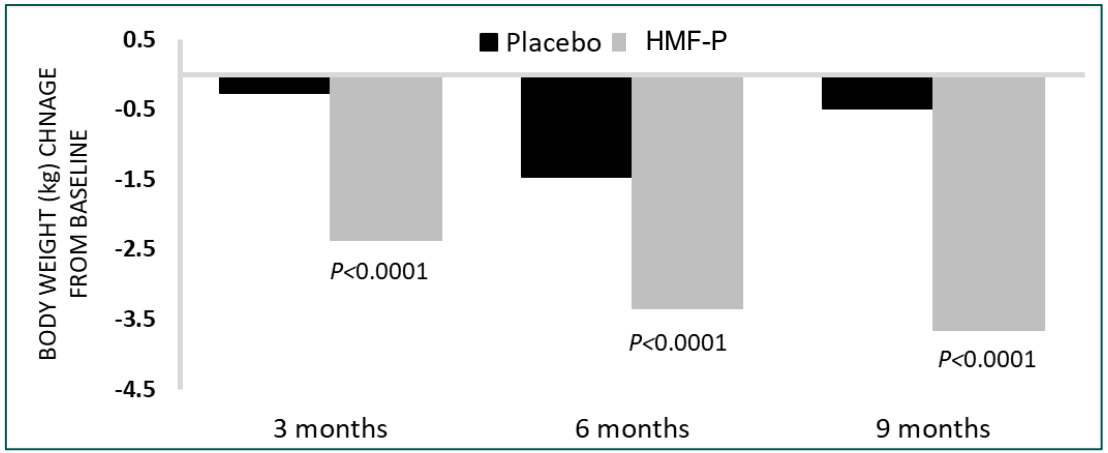
- At 6 months there was a 31% of participants in the probiotic group experienced a 5% weight loss, versus 6% in the placebo group
- At 9 months the percentage increased to 40% in probiotic group versus 3% in the placebo group

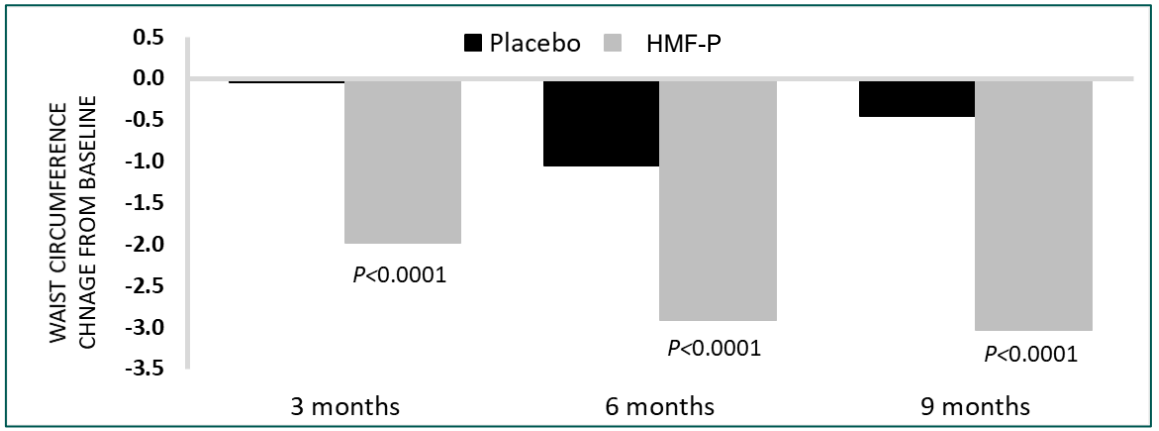
By the end of the study 71% of the participants in the probiotic group achieved a 3% reduction in weight versus 17% in the placebo group.

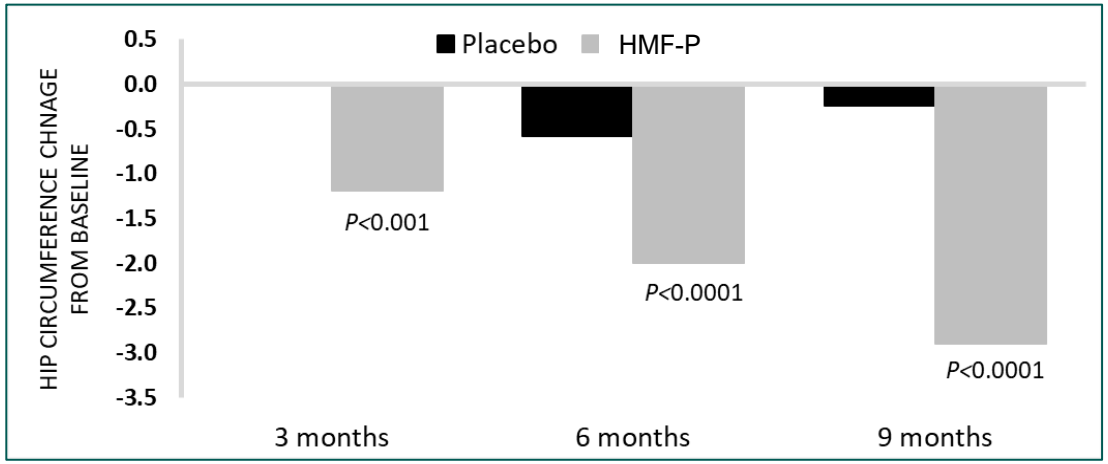
D. R. Michael, T. S. Davies, A. A. Jack, G. Masetti, J. R. Marchesi, D. Wang, B. H. Mullish & S. F. Plummer (2021) Scientific Reports

The Promagen 2 Study: Weight Loss in Overweight Adults

Overweight adults (BMI 25-29.9) aged 45-65 years took either 50 billion HMF-P Consortium probiotics or placebo daily for 9 months and maintained a normal lifestyle.





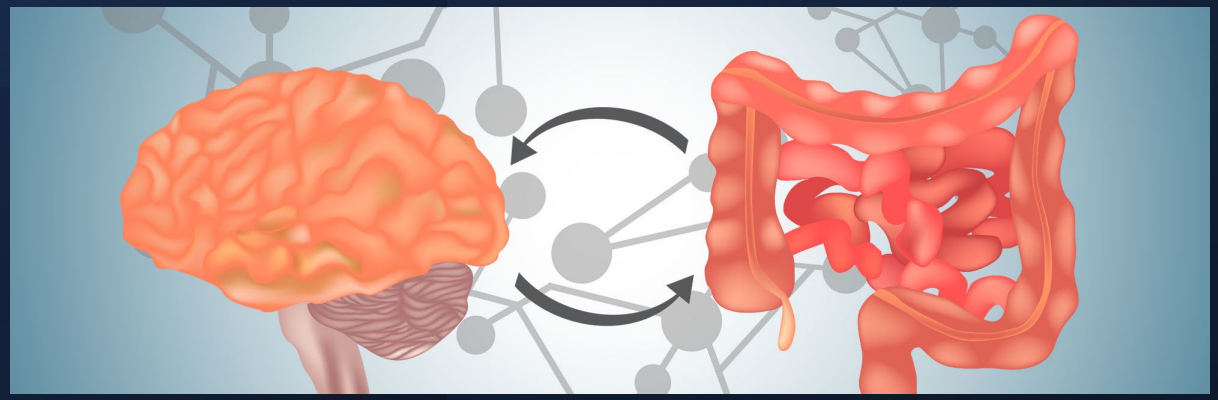


Weight loss: 3.2kg (7.1lbs)
Waist circumference: 2.6cm (1.02in)
Hip circumference: 2.7cm (1.06in)

40% of participants reached the desirable annual 5% weight loss beneficial for health and well-being.

Michael et al, Scientific Reports 2021

CLINICAL EFFECTS OF HMF PROBIOTICS ON THE BRAIN AND MENTAL HEALTH



The Keele Study

THE Effect of HMF Probiotics on Anxiety and Cognitive Function in Adults

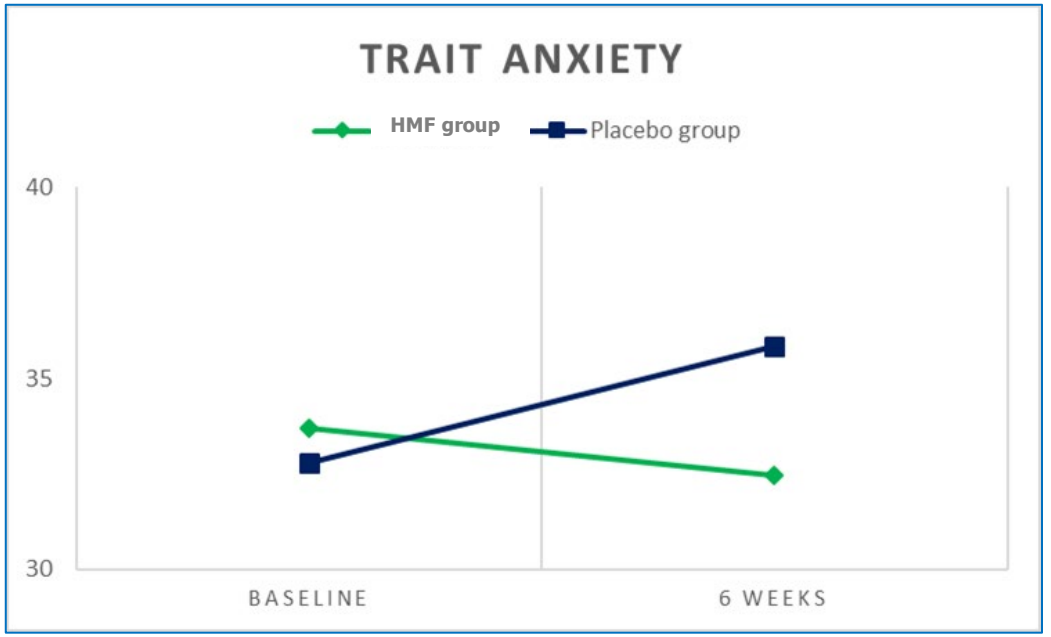
DBRPC study: 50 healthy volunteers aged 19-38 years took daily either 25 billion Proprietary Human Probiotic Consortium or or placebo for 6 weeks. Volunteers completed mood and anxiety questionnaires (Bond Lader Mood Scales, Stait Trait Anxiety Inventory) and comprehensive computerised cognitive battery of tests (COMPASS).

THE KEELE STUDY:
HMF Consortium - 25 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34

Trait' Anxiety: individual's tendency to experience anxiety in response to the anticipation of a future threat, how individuals felt over the previous 6 weeks

HMF probiotics significantly decreased 'trait' anxiety levels compared to placebo group (*P*=0.042).



'Continuity of attention': ability to focus and avoid distraction

Significantly increased in response to to the supplementation with Proprietary Human Probiotic Consortium and decreased in the placebo group (*P*=0.035)

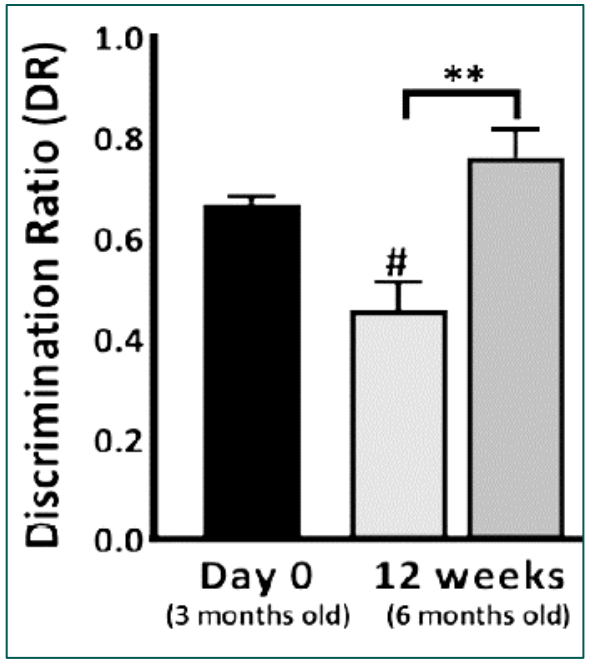
Owen L et al Proceedings of the Nutrition Society 2014

Probiotics and Their Therapeutic Potential in Alzheimer's Disease

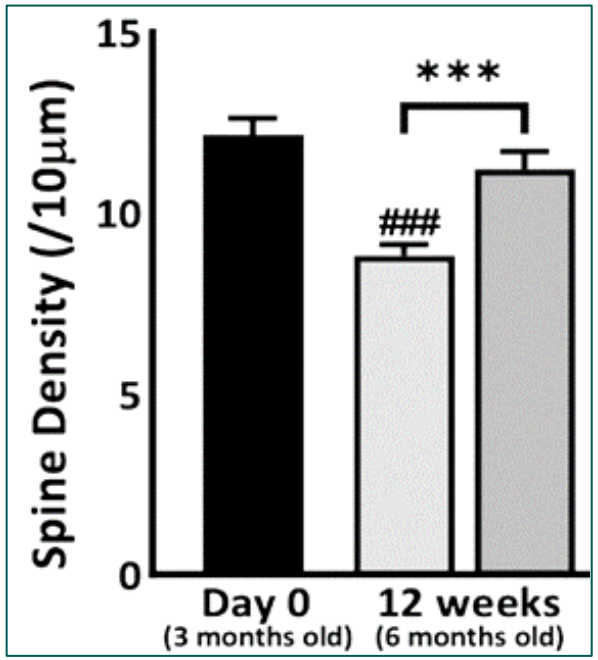
PRESENCE OF A 'METABOLIC' CHALLENGE

3xTG Alzheimer's mice were fed high fat diet supplemented with HMF-P Consortium Probiotics ($5x10^8$ cfu/mouse/day, 50 -100 billion/day equivalent human dose) or high fat diet alone for 12 weeks.

NOVEL OBJECT RECOGNITION



NEURONAL SPINE DENSITY



HMF-P Consortium - 50 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34
Lactobacillus plantarum	CUL66

BLB – 3xTG mice baseline
HFD-C – High fat diet control
HFD-P – High fat diet plus HMF-P

$^{**}P<0.01$ or $^{***}P<0.001$ vs. control
$^{\#}P<0.05$ or $^{\#\#\#}P<0.001$ vs. baseline

HMF-P Probiotics maintain cognitive performance and preserve the hippocampal neuronal architecture in presence of a metabolic challenge.

Webberley TS et al, Int J Mol Sci 2023

Poll

Clinically Proven Benefits of HMF Probiotic Strains

Cognitive Function - In healthy adults
HMF Consortium 25 Billion CFU

Immune Function - In adults
HMF Consortium 25 Billion CFU

Well being and Quality of Life
HMF-P Consortium – HMF Metabolic

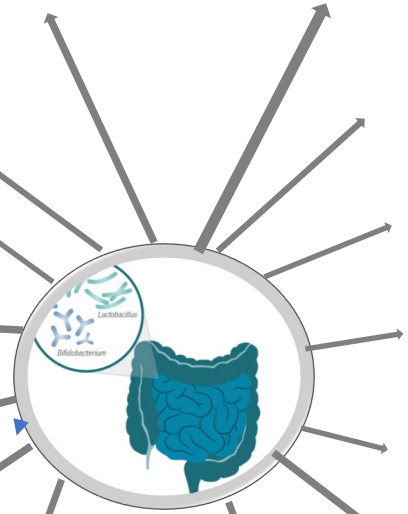
Athletic Performance - In endurance athletes
HMF Consortium 25 Billion CFU

Anxiety - In healthy adults
HMF Consortium – 25 Billion CFU

Diarrhoea - Antibiotic associated
HMF Consortium 25 Billion CFU – HMF Intensive

Allergy - in babies and children:
HMF-B Consortium

IBS - in IBS sufferers and athletes:
HMF Consortium 25 Billion CFU - HMF IBS Relief



Constipation in babies – HMF-B Consortium –
HMF Baby B / HMF Baby F

Antibiotic Resistance
HMF Consortium 25 Billion CFU – HMF Intensive

Intestinal Permeability
HMF Consortium 25 Billion CFU – HMF Intensive

Coughs and Colds
In children: HMF Consortium – 12.5 Billion CFU – HMF Fit For School
Adults: HMF-P Consortium

Weight Reduction
In overweight and obese adults:
HMF-P Consortium - HMF Metabolic

Cholesterol – LDL
HMF-P Consortium

All clinical trials are applicable to shelf-stable formulations that have an associated refrigerated version

Clinically Proven Benefits of HMF Probiotic Strains

THE PROCHILD STUDIES 1 & 2
HMF Consortium - 12.5 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34

- Upper Respiratory Tract Infections (URTI – coughs & colds) in children
- Reduced absenteeism from school
- Significant improvement in normal stool consistency

THE SHEFFIELD IBS TRIALS 1 & 2,
THE CAMBRIDGE PROBIOTIC / ANTIBIOTIC TRIALS, KEELE STUDY:
HMF Consortium - 25 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34

- Immune function in adults
- Irritable Bowel Syndrome (IBS) in IBS sufferers and athletes
- Antibiotic resistance in adults
- Antibiotic associated diarrhea in adults (AAD)
- Intestinal permeability in adult athletes
- Athletic performance in endurance athletes
- Anxiety
- Cognitive function in healthy adults
- Quality of life in healthy adults

THE METABOLIC STUDIES
HMF-P Consortium - 50 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34
Lactobacillus plantarum	CUL66

- Weight reduction in overweight and obese adults
- Reduction in URTI (coughs and colds) in adults
- Improved quality of life in adults (General wellness; and state of health, energy, mood and sleep quality)
- Cholesterol metabolism in adults – small dense LDL
- Reduction in headaches and muscle pain

THE SWANSEA BABY TRIAL,
THE SWANSEA "SAFETY IN NEWBORNS STUDY":
HMF-B Consortium - 10 BILLION CFU

Lactobacillus salivarius	CUL61
Lactobacillus paracasei	CUL08
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34

- Allergy and skin sensitivity in infants and children
- Constipation in infants
- Intestinal permeability in infants and children
- Safety in pregnancy and in neonates

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Atrium Innovations Brands ATRIUM INNOVATIONS

Major HMF Probiotic Consortiums are Backed by Research!

HMF Consortium – 12.5 BILLION CFU

Probiotic Consortium ..... 12.5 billion CFU
Lactobacillus acidophilus (CUL-60 & CUL-21)..... 10 billion CFU
Bifidobacterium animalis subsp. *lactis* (CUL-34)
& *Bifidobacterium bifidum* (CUL-20) ..... 2.5 billion CFU

THE PROCHILD STUDIES 1 & 2
HMF Consortium - 12.5 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34

HMF Consortium - 25 BILLION CFU

Probiotic Consortium ..... 25 billion CFU
Lactobacillus acidophilus (CUL-60 & CUL-21) ..... 19 billion CFU
Bifidobacterium animalis subsp. *lactis* (CUL-34)
& *Bifidobacterium bifidum* (CUL-20) ..... 6 billion CFU

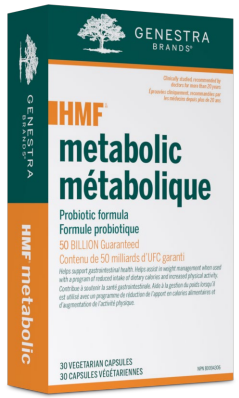
THE SHEFFIELD IBS TRIALS 1 & 2,
THE CAMBRIDGE PROBIOTIC / ANTIBIOTIC TRIALS, KEELE STUDY:
HMF Consortium - 25 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34

Major HMF Probiotic Consortiums are Backed by Research!

HMF-P Consortium- 50 BILLION CFU

Probiotic Consortium	50 billion CFU
Lactobacillus acidophilus (CUL-60 & CUL-21)	25.2 billion CFU
Lactobacillus plantarum (CUL-66)	16.5 billion CFU
Bifidobacterium animalis subsp. *lactis* (CUL-34) & *Bifidobacterium bifidum* (CUL-20)	8.3 billion CFU



THE METABOLIC STUDIES
HMF-P Consortium - 50 BILLION CFU

Lactobacillus acidophilus	CUL60
Lactobacillus acidophilus	CUL21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34
Lactobacillus plantarum	CUL66

HMF-B Consortium - 10 BILLION CFU

Probiotic Consortium	10 billion CFU
Lactobacillus salivarius (CUL-61)	6.25 billion CFU
Bifidobacterium animalis subsp. *lactis* (CUL-34) & *Bifidobacterium bifidum* (CUL-20)	2.5 billion CFU
Lactobacillus paracasei (CUL-08)	1.25 billion CFU

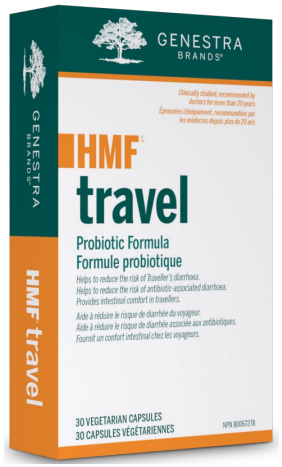
THE SWANSEA BABY TRIAL, THE SWANSEA "SAFETY IN NEWBORNS STUDY":
HMF-B Consortium - 10 BILLION CFU

Lactobacillus salivarius	CUL61
Lactobacillus paracasei	CUL08
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34

Major HMF Probiotic Consortiums are Backed by Research!

HMF-T Consortium - 35 BILLION CFU

Probiotic Consortium	17.5 billion CFU
Lactobacillus acidophilus (CUL-60 & CUL-21)	9.375 billion CFU
Saccharomyces boulardii (CNCM-I-1079)	5 billion CFU
Bifidobacterium bifidum (CUL-20) & *Bifidobacterium animalis* subsp. *lactis* (CUL-34)	3.125 billion CFU



THE FANTIB STUDY:
HMF-T Consortium - 35 BILLION CFU

Lactobacillus acidophilus	CUL-60 & CUL-21
Bifidobacterium bifidum	CUL20
Bifidobacterium animalis sbsp. lactis	CUL34
Saccharomyces boulardii	CNCM-I-1079

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