

Intrinsically Connected: Prebiotics and Metabolic Function

Microbiota Management: A One Health Perspective Towards Metabolic Syndrome by Olaf Larsen



Microbiota Management: A One Health Perspective towards metabolic syndrome

Dr. Olaf Larsen

Prebiotics and Metabolic Health webinar, 8 June 2022

The information presented is only intended for healthcare professionals, scientists, and journalists

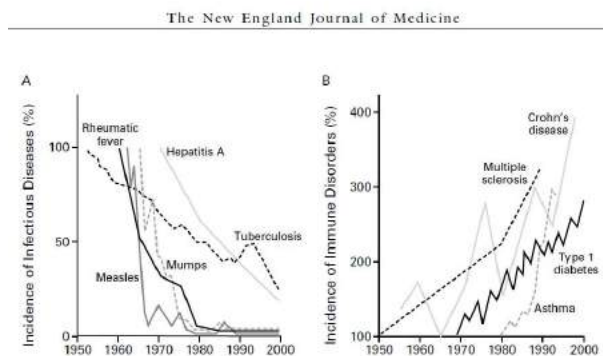
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Conflicts of interest



- Asst. Professor @ Athena Institute, Vrije Universiteit Amsterdam (0.2 FTE)
- Senior Manager Science @ Yakult Nederland B.V.

The fall of infectious disease vs. the rise of autoimmune disease

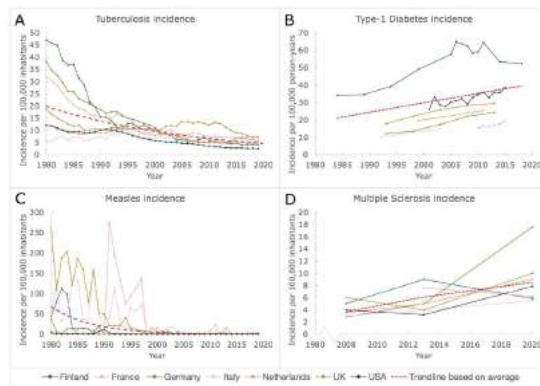


Bach, J. F. (2002). New England Journal of Medicine, 347(12), 911-920.

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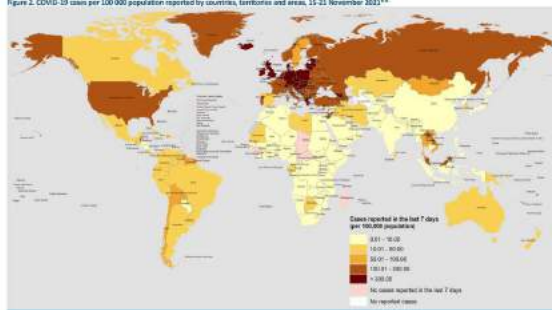
The trend continues....



Larsen, Olaf FA, Maike Van Der Grint, Cato Wiegers, and Linda HM van de Burgwal. "The Gut Microbiota: Master of Puppets Connecting the Epidemiology of Infectious, Autoimmune, and Metabolic Disease." *Frontiers in Microbiology* (2022): 1604.

The rise of infectious disease

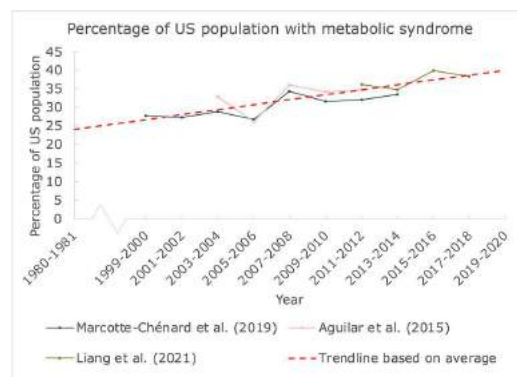
Figure 2. COVID-19 cases per 100,000 population reported by countries, territories and areas, 15-22 November 2021**



WHO: COVID-19 Weekly Epidemiological Update

https://www.who.int/health-topics/monkeypox#tab=tab_1

The rise of metabolic disease

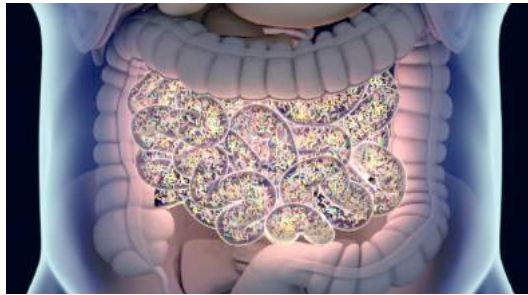


Larsen, Olaf FA, Maike Van Der Grint, Cato Wiegers, and Linda HM van de Burgwal. "The Gut Microbiota: Master of Puppets Connecting the Epidemiology of Infectious, Autoimmune, and Metabolic Disease." *Frontiers in Microbiology* (2022): 1604.

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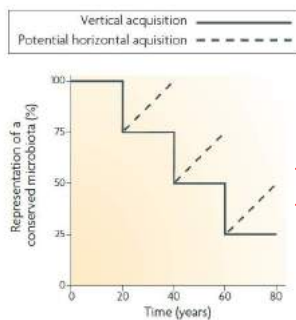
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The gut microbiota: Master of Puppets



Larsen, Olaf FA, Maike Van Der Grint, Cato Wiegers, and Linda HM van de Burgwal. "The Gut Microbiota: Master of Puppets Connecting the Epidemiology of Infectious, Autoimmune, and Metabolic Disease." *Frontiers in Microbiology* (2022): 1604.

Loss of old friends: on the verge of a catastrophic collapse?



→ What are the critical determinants for ecosystem structure and stability?

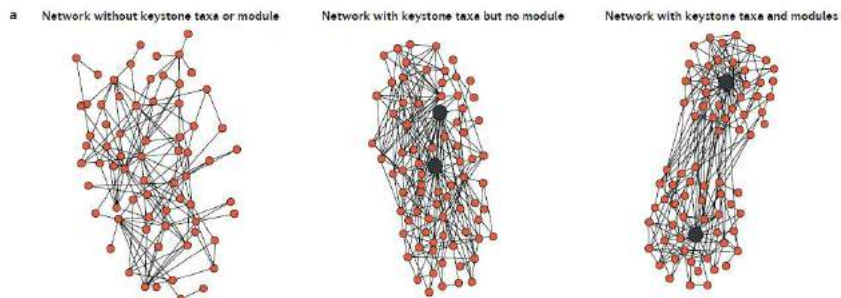
→ What are the associated functionalities of the ecosystem?

→ What are the critical inter-ecosystem determinants?

→ How to revitalize / replenish?

Picture: Blaser, Martin J., and Stanley Falkow. *Nature Reviews Microbiology* 7.12 (2009): 887-894.

Keystone taxa: drivers of structure & functionality



Banerjee, Samiran, Klaus Schlaeppi, and Marcel GA van der Heijden. *Nature Reviews Microbiology* 16.9 (2018): 567-576.

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Microbial guilds in the human GI tract

Wu et al. *Genome Medicine* (2021) 13:22
<https://doi.org/10.1186/s13073-021-00840-y>

Genome Medicine

OPINION

Open Access

Guild-based analysis for understanding gut microbiome in human health and diseases

Guojun Wu^{1,2,3*}, Nana Zhao^{1,4*}, Chenhong Zhang^{1,5}, Yan Y. Lam^{1,3,6} and Liping Zhao^{1,3,6*}

MICROBIOTA

Gut bacteria selectively promoted by dietary fibers alleviate type 2 diabetes

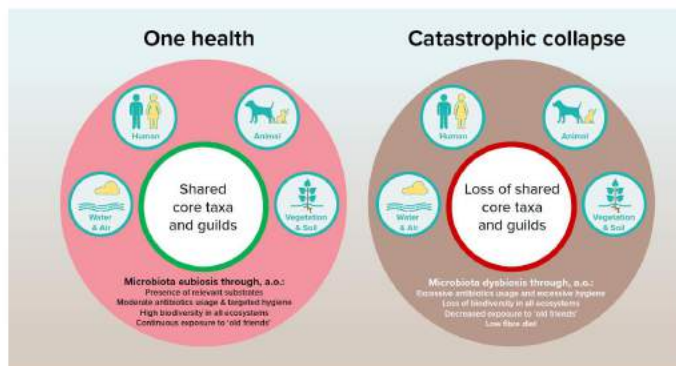
Liping Zhao,^{1,2,*} Feng Zhang,^{3,*} Xiaoying Ding,^{3,*} Guojun Wu,^{1,3} Yan Y. Lam,^{2,*} Xuejiao Wang,³ Huiqing Fu,¹ Xinhe Xue,¹ Chunhua Lu,³ Jilin Ma,³ Lihua Yu,³ Chengmei Xu,³ Zhongying Ren,³ Ying Xu,³ Songmei Xu,³ Hongli Shen,³ Xiuli Zhu,³ Yu Shi,³ Qingyun Shen,³ Weiping Dong,³ Rui Liu,³ Yuxia Ling,³ Yue Zeng,³ Xingpeng Wang,³ Qianpeng Zhang,³ Jing Wang,³ Linghua Wang,³ Yanglin Wu,¹ Benhua Zeng,³ Hong Wei,³ Menghui Zhang,³ Yongde Peng,^{1,2} Chenhong Zhang¹

Zhao et al., *Science* 359, 1151–1156 (2018)



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Microbiota management: a one health perspective

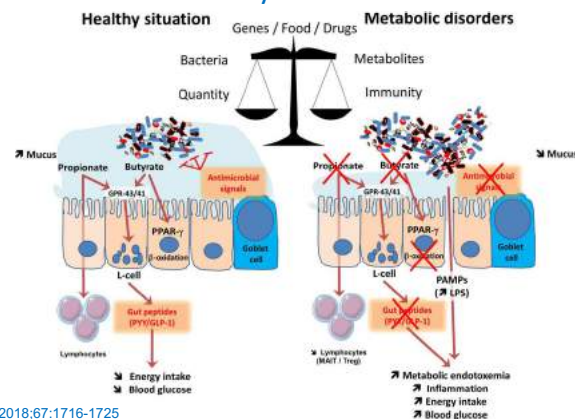


Larsen, O. F. A., & van de Burgwal, L. H. (2021). *Frontiers in Microbiology*, 12.



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Gut microbiota eubiosis & dysbiosis



Patrice D Cani *Gut* 2018;67:1716-1725

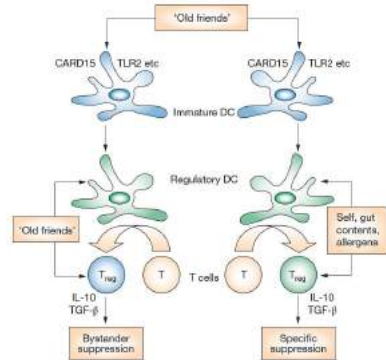


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Targeting metabolic syndrome by exposing to old friends



Guarner, F., et al. Nature clinical practice Gastroenterology & hepatology 3.5 (2006): 275-284.

<https://www.news-medical.net/health/What-are-Helminths.aspx>

The protective effect of helminths: metabolic syndrome

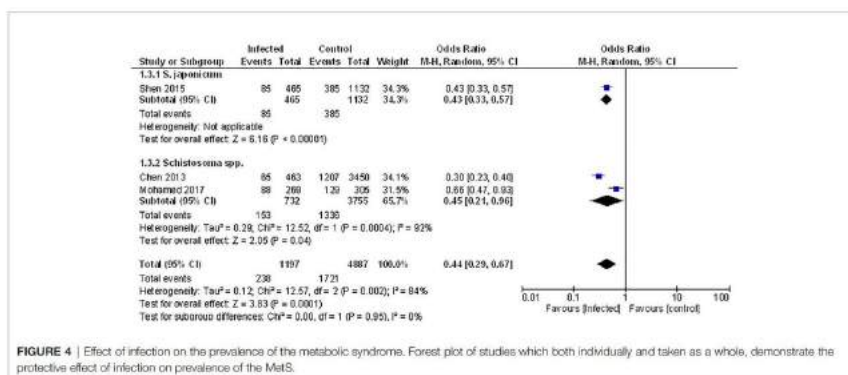


FIGURE 4 | Effect of infection on the prevalence of the metabolic syndrome. Forest plot of studies which both individually and taken as a whole, demonstrate the protective effect of infection on prevalence of the MetS.

Rennie et al. *Frontiers in endocrinology* (2021): 953.

Targeting metabolic syndrome by stimulating our friends: prebiotics



Table 1 | Prebiotics, (a.k.a. soluble fibers) improving growth of probiotic bacteria, as found in dietary components and milk ranked by quantitative availability.

Recovered oligosaccharides as % weight/weight fresh	
Chicory/endive stalks	15–20
Garlic	9–16
Black salsify and leek	4–10
Onion and artichoke	2–6
Asparagus	2–3
Wheat	1–4
Oats (and human breast milk)	0.5–1.5
Banana	0.3–0.7
Domestic/placental-mammal milk	0.01–0.1

Claassen, Eric. "Cost-benefit relation of diet and probiotics in iatrogenic bowel irregularity (IBI)." *Frontiers in Pharmacology* 5 (2014): 14.

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Targeting metabolic syndrome: prebiotics



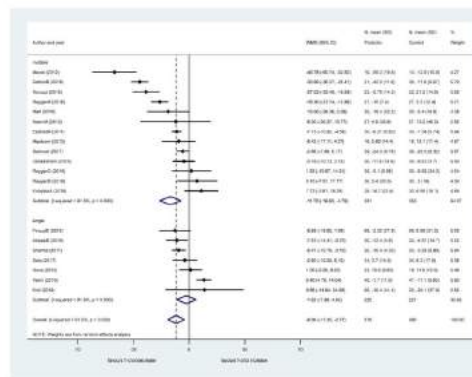
Fiber	Duration	Population: M/F	Study design	Results	Ref.
Oligofructose-enriched maize (0.5 g/day)	10 weeks	42 subjects 24M/18F	Single center, double-blind, placebo-controlled	Reduced body weight z-score, percent body fat, percent trunk fat, and serum level of interleukin-6	Nicolini et al ¹⁰
Low-calorie diet + inulin (0.5 g)	12 weeks	39 female subjects	Randomized, controlled, longitudinal	Reduced triglycerides and improved intake of macronutrients	Toussaint et al ¹¹
Galacto-oligo-saccharide (5.5 g)	12 weeks	43 subjects; 50M/20F	Double-blind, randomized, placebo-controlled, crossover	Decreased fasting insulin, TC, TG, CRP, fecal calprotectin	Valero-Cabré et al ¹²
Inulin (10 g)	4 weeks	49 female subjects	Randomized, triple-blind controlled	Decreased FPG, A1c, malondialdehyde, increased antioxidant defense	Gargari et al ¹³
Inulin (10 g)	4 weeks	49 female subjects	Randomized controlled	Reduction in FPG, HbA1c, total cholesterol, triglyceride, LDL-C, LDL-C/HDL-C ratio, and TC/HDL-C ratio, increased HDL-C	Dehghan et al ¹⁴
Oligofructose-enriched maize (10 g)	4 weeks	32 female subjects	Triple-blind randomized controlled	Decreased fasting plasma glucose, glycosylated hemoglobin, interleukin-6, tumor necrosis factor- α and plasma lipoprotein-cholesterol	Dehghan et al ¹⁵
Glucosamine Capsule (0.42 g)	4 weeks	63 subjects	Double-blind crossover; placebo-controlled	Reduced total cholesterol, LDL-C, triglyceride, and systolic BP	Arruti et al ¹⁶
Glucosamine Capsule (2 g/d)	4 weeks	40 subjects; 20M/20F	Randomized controlled	Reduced plasma total cholesterol and LDL-C	Martinez et al ¹⁷
Glucosamine Capsule (2 g/d)	4 weeks	40 subjects; 19M/21F	Randomized, double-blind, placebo-controlled	Reduced total cholesterol and LDL-C	Martinez et al ¹⁸
Glucosamine Capsule (2 g/d)	4 weeks	40 subjects; 19M/21F	Randomized, double-blind	Decrease of alpha-lipoprotein, increase of pre-beta-lipoprotein and triglycerides	Vidal et al ¹⁹
Glucosamine Capsule (5 g/d)	4 weeks	43 subjects; 22M/21F	Randomized, placebo double-blind, crossover	Reduced body mass, fat mass, total cholesterol, and LDL-C	Kraemer et al ²⁰
Glucosamine Capsule (5 g/d)	12 weeks	38 subjects; 19M/19F	Double-blind, placebo controlled	Reduced total cholesterol and LDL-C	Vieques et al ²¹

Ferrarese, R., et al. Eur Rev Med Pharmacol Sci 22.21 (2018): 7588-605.

Targeting metabolic syndrome by (re)introducing our friends: probiotics

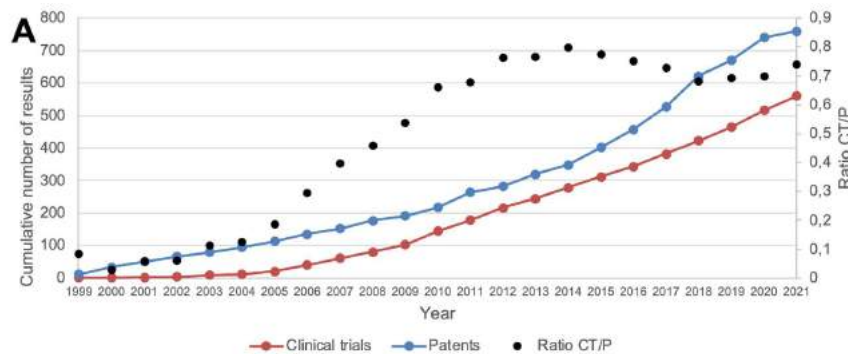
Life microorganisms which
when administered in adequate
amounts confer a health benefit
on the host

WHO/FAO



Kocsis, Ticia, et al. Scientific reports 10.1 (2020): 1-14.

Probiotics & infectious disease: what's the state-of-the-art?



Wiegiers, Cato, L. van de Burgwal, and O.F.A. Larsen. "Probiotics for the Management of Infectious Diseases: Reviewing the State of the Art." *Frontiers in microbiology* 13 (2022).

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Probiotics / prebiotics & metabolic syndrome: recognized potential



Multi preparations as a first step towards supplying guilds?

Digestive Diseases and Sciences (2021) 66:694–704
<https://doi.org/10.1007/s10620-020-06244-z>

REVIEW

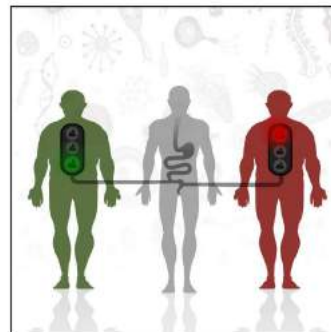


Efficacy of Single-Strain Probiotics Versus Multi-Strain Mixtures: Systematic Review of Strain and Disease Specificity

Lynne V. McFarland¹

“Choice of an appropriate probiotic should be based, not on the number of strains in the product, rather based on evidence-based trials of efficacy. In most cases, multi-strain mixtures were not significantly more effective than single-strain probiotics.”

The gut microbiota: one intervention fits all?



Applying probiotics and prebiotics in new delivery formats – is the clinical evidence transferable?

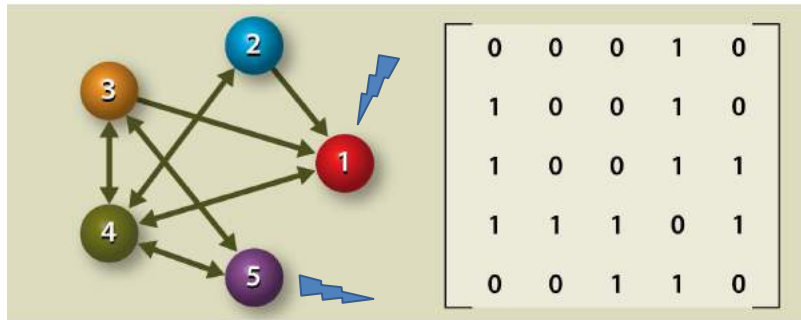
Marla Cunningham^{1,2}, Gabriel Vinderola³, Dimitris Charalampopoulos⁴, Sarah Lebeer⁵, Mary Ellen Sanders⁶, Robert Grinold⁷

Kootte, Ruud S., et al. Cell metabolism 26.4 (2017): 611-619

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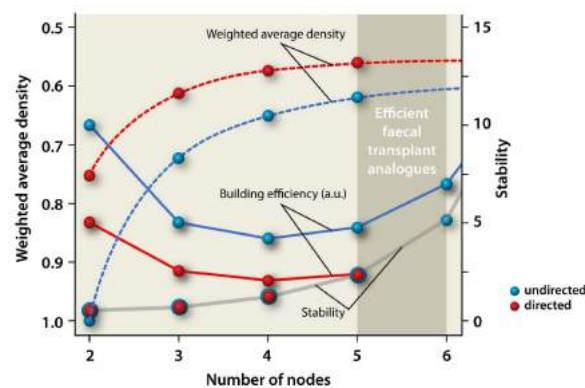
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Modelling microbial guilds



Larsen, Olaf FA, et al. "Towards a rational design of faecal transplant analogues." Scientific reports 9.1 (2019): 1-6.

Restoring a microbial guild: first ecological dimensions



Larsen, Olaf FA, et al. "Towards a rational design of faecal transplant analogues." Scientific reports 9.1 (2019): 1-6.

