In the Name of God

The Gut-Bone Axis: How Your Microbiome Shapes Your Skeleton

Presented by:

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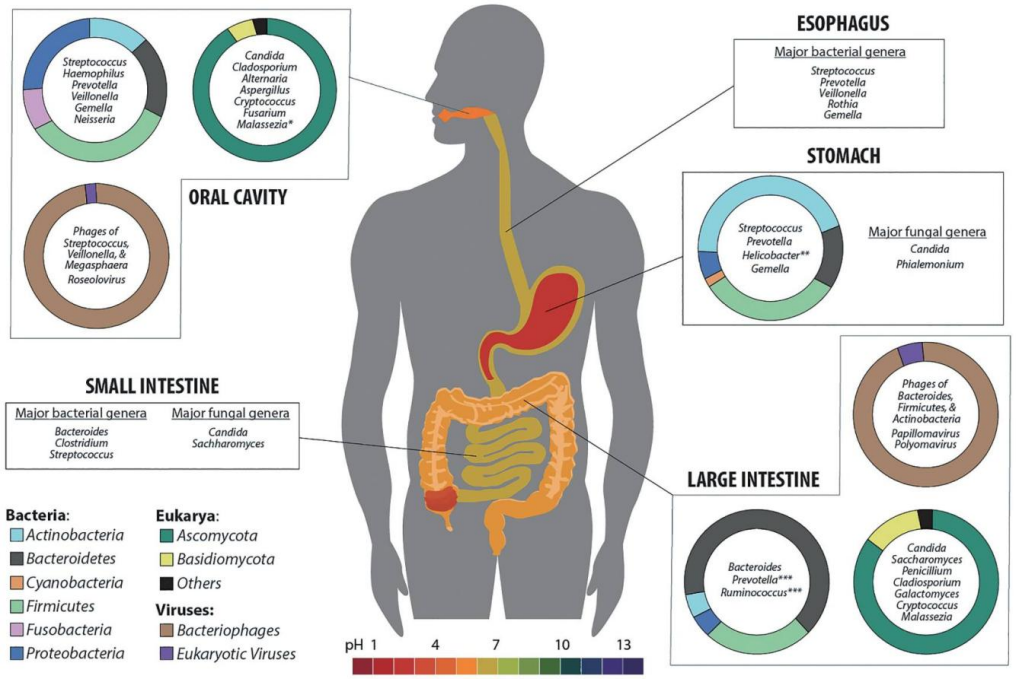
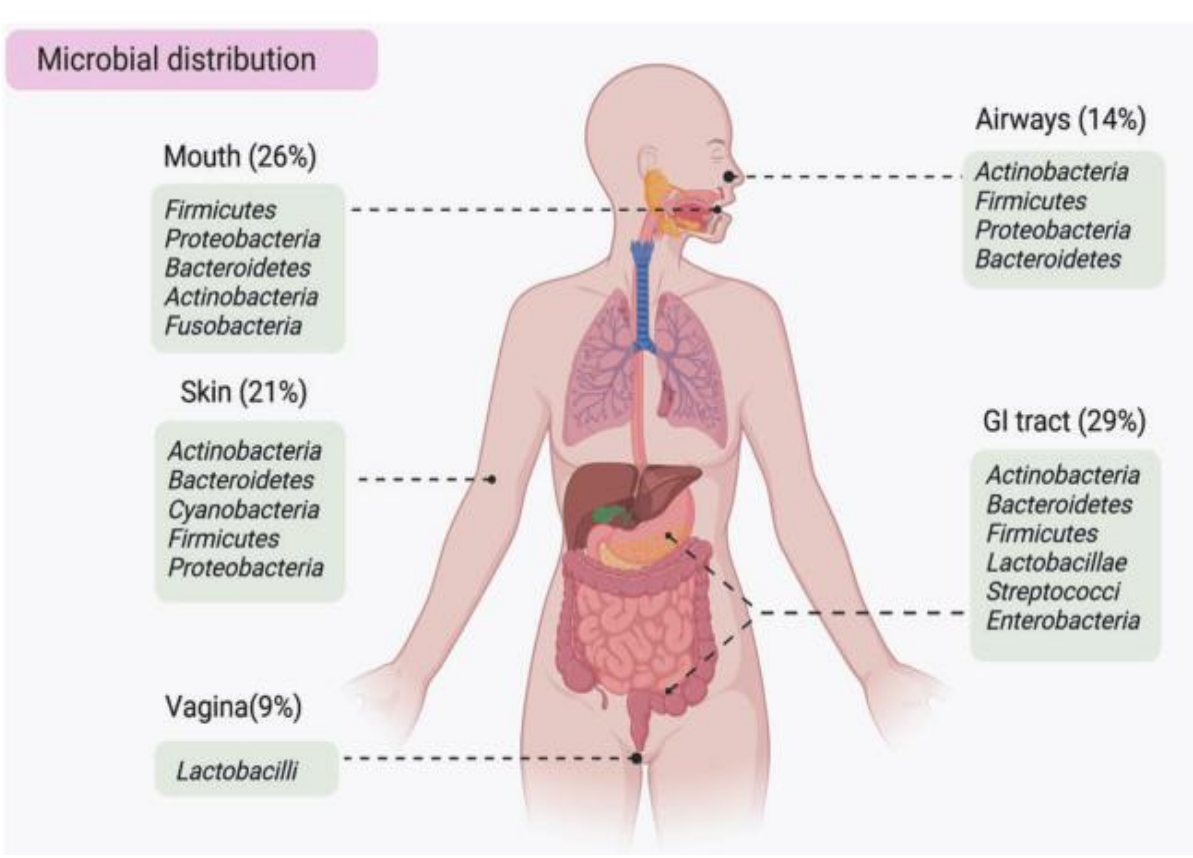
Introduction to human microbiota

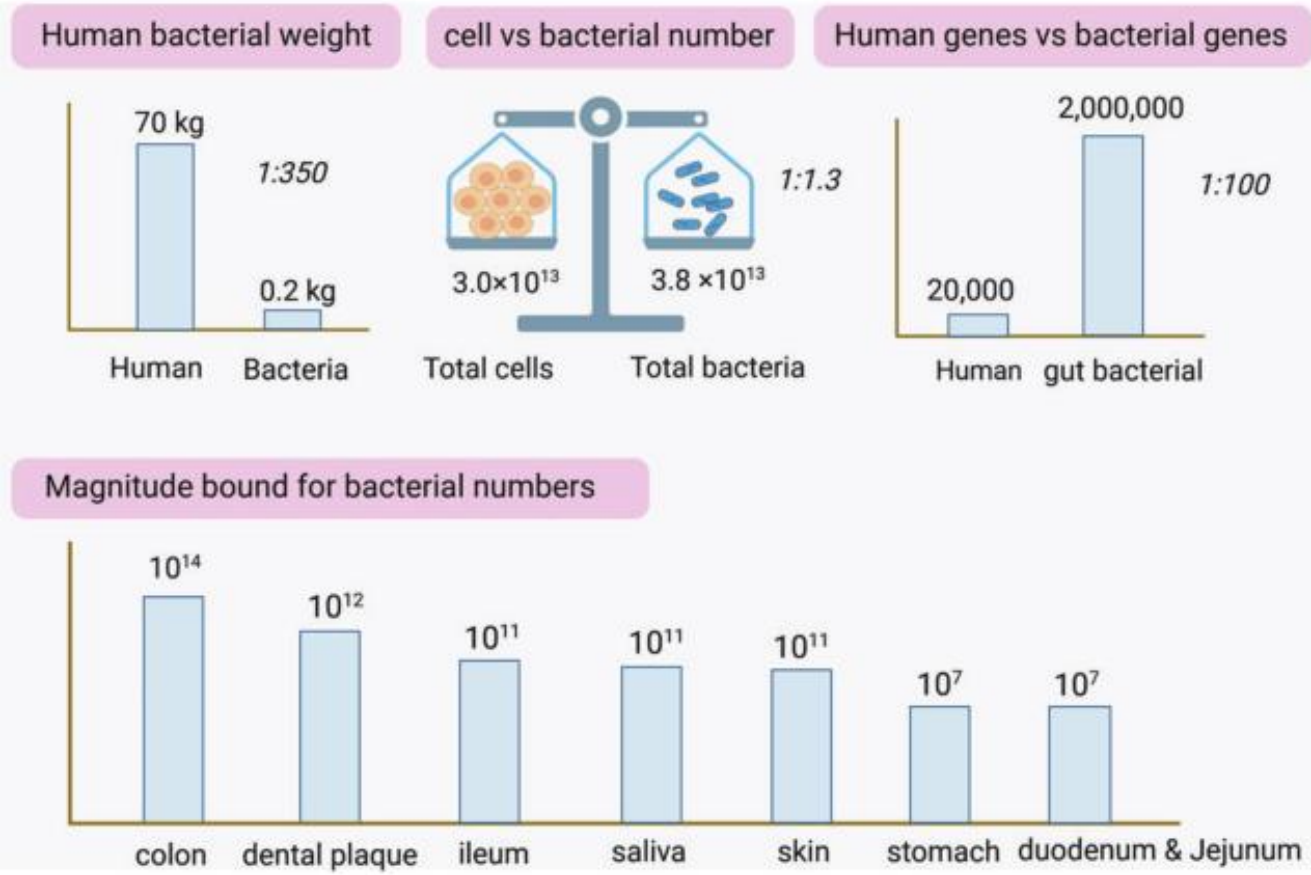
- Human microbiota consists of all of the microorganisms in the body; both on the surface and within the body.
- 99% of human genome is similar between individuals, whereas < 20% of microbial genome is similar.
- Majority are not harmful to their human host.
- Main sites:
  - Skin
  - Mouth
  - Gut
  - Conjunctiva
  - Vagina
  - Nasal / Respiratory tract



Krishna SB, Dubey A, Malla MA. Integrating microbiome network: establishing linkages between plants, microbes and human health. Open Microbiol J 13: 330–342.

Microbial distribution in our body



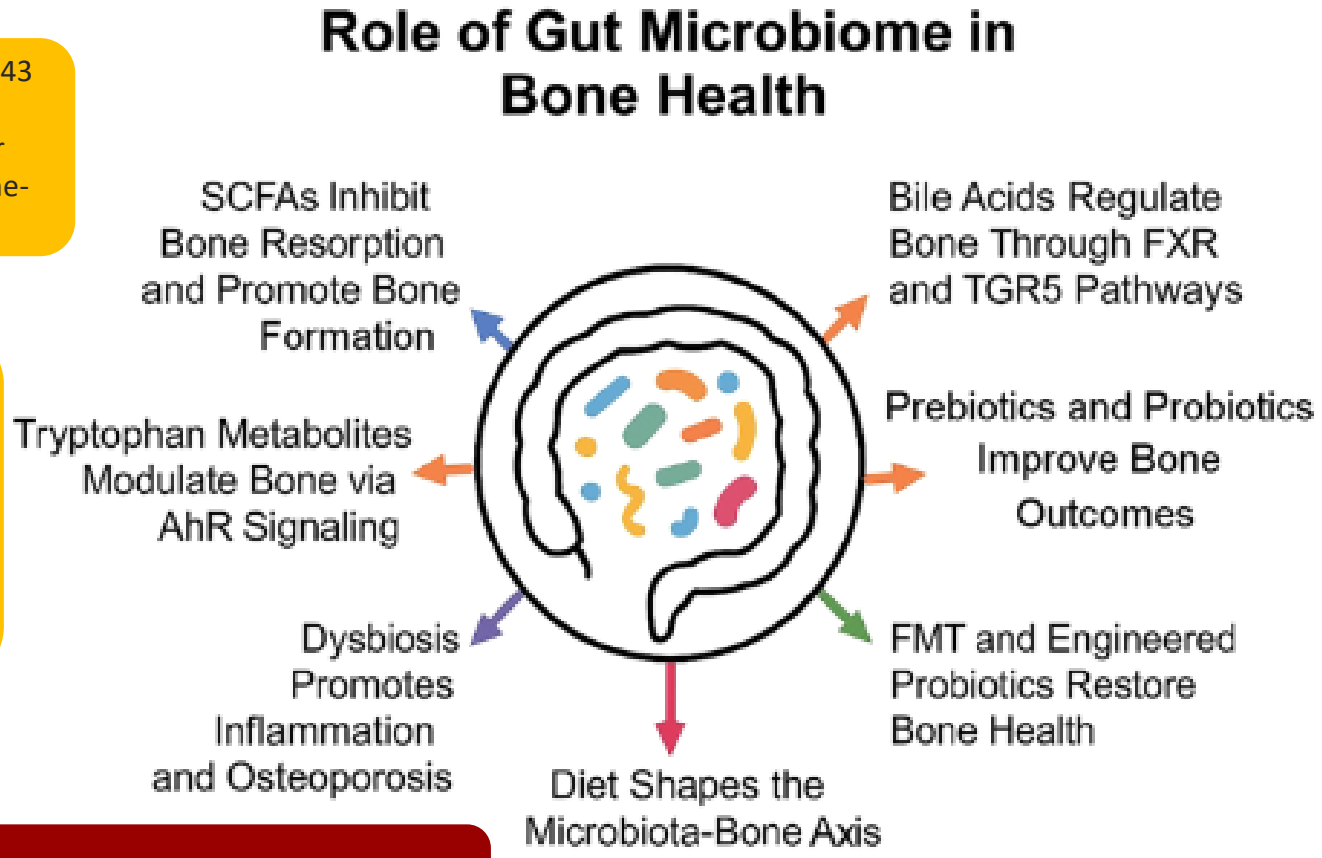


We're Only About 43% Human!

Metabolic intersections: microbiome and bone health

SCFAs: activate GPR41 and GPR43 receptors on osteoclast precursors→ preventing their differentiation into mature bone-resorbing osteoclasts

Gut microbiota metabolizes tryptophan into various indoles, such as indole-3-acetic acid and indole-3-aldehyde, which might be the ligands of the aryl hydrocarbon receptor pathway in mediating bone health



The gut microbiota converts primary bile acids into secondary forms

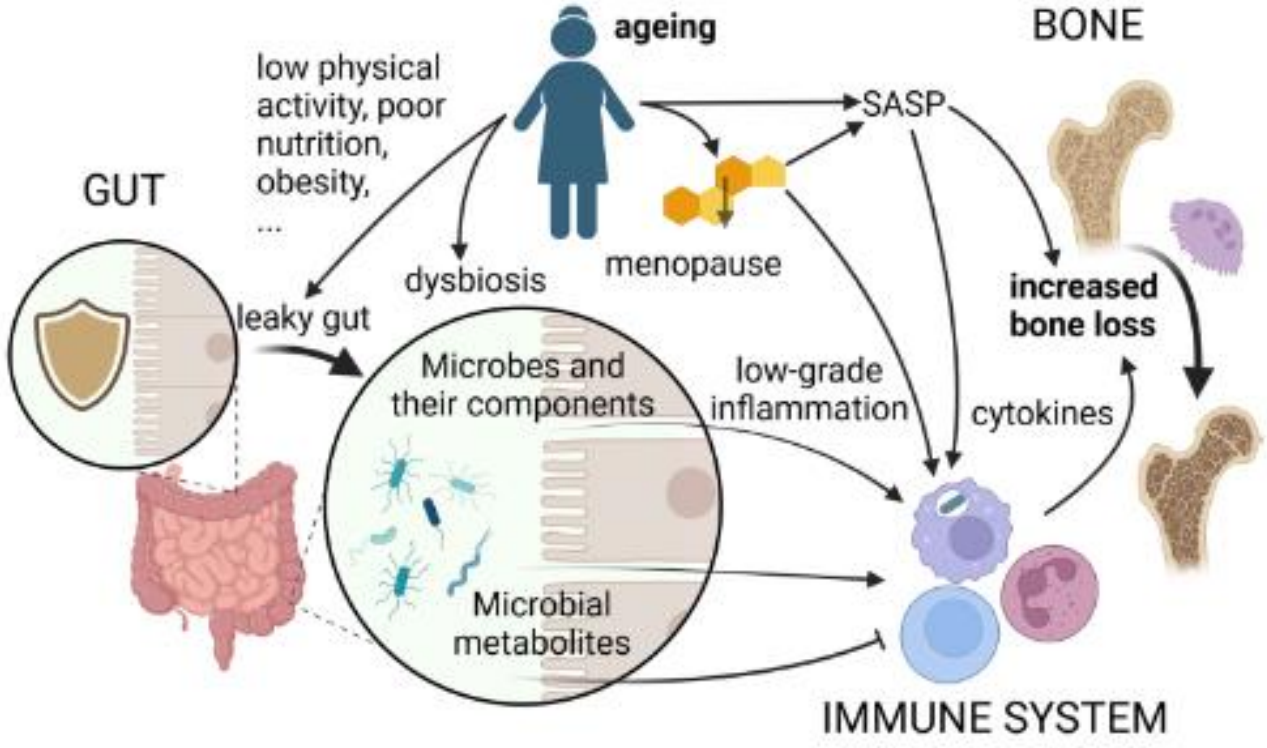
Microbiota-modulating interventions

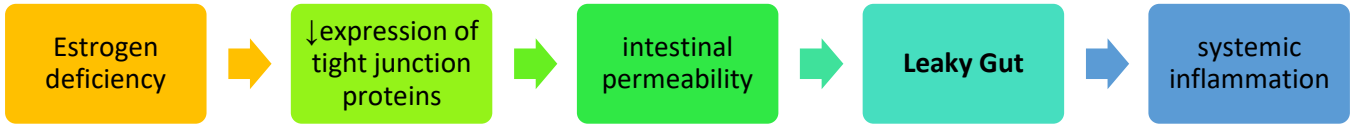
leaky gut may be associated with systemic inflammation and osteoporosis

Hwang D, et al. Deciphering the gut microbiome's metabolic code: pathways to bone health and novel therapeutic avenues. Frontiers in Endocrinology. 2025;16:1553655.

Linking Estrogen, Gut, and Bone

- Aging and increasing bone loss are linked via dysbiosis of the intestinal microbiota, a leaky gut, low-grade inflammation and immune system
- A "leaky gut" allows the translocation of microbial components and the migration of pro-inflammatory immune cells (especially Th17 cells) from the gut to the bone marrow. There, they produce cytokines (IL-17, TNF-α) that stimulate bone-resorbing osteoclasts.
- The gut microbiota (the "estrobolome") produces enzymes (β-glucuronidases) that deconjugate estrogens, allowing their reabsorption into circulation.



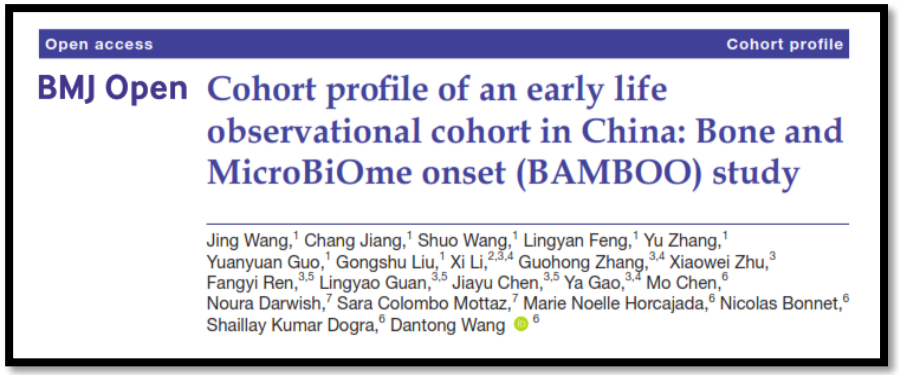


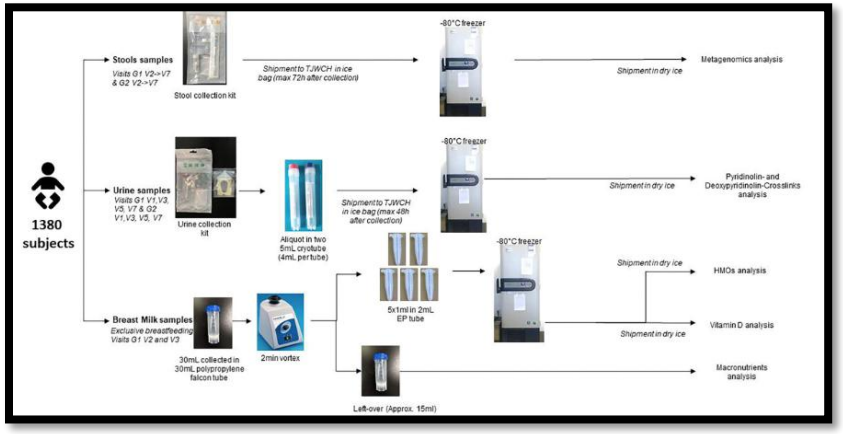
Kverka M, Stepan JJ. Associations among estrogens, the gut microbiome and osteoporosis. Current Osteoporosis Reports. 2025;23(1):2.

Ongoing cohort study on bone and microbiome

- **BAMBOO (Bone And MicroBiOme Onset) study**
- A large, prospective, observational cohort study in Tianjin, China
- **Aim**: establish age-appropriate trajectories for gut microbiome maturation and bone development in children from 0 to 3 years old and to investigate the influence of dietary factors on these processes
- Group 1: 690 infants recruited at birth and followed until 12 months.
- Group 2: 690 infants recruited at 6 months and followed until 36 months.

- A preliminary analysis of 20 stool samples showed that the infant gut microbiome at the species level was primarily composed of ***Bacteroides dorei, Bacteroides vulgatus***, **and** ***Escherichia coli***.





Key bacterial genera and their roles in bone health

Fiber-rich diet

Mediterranean diet

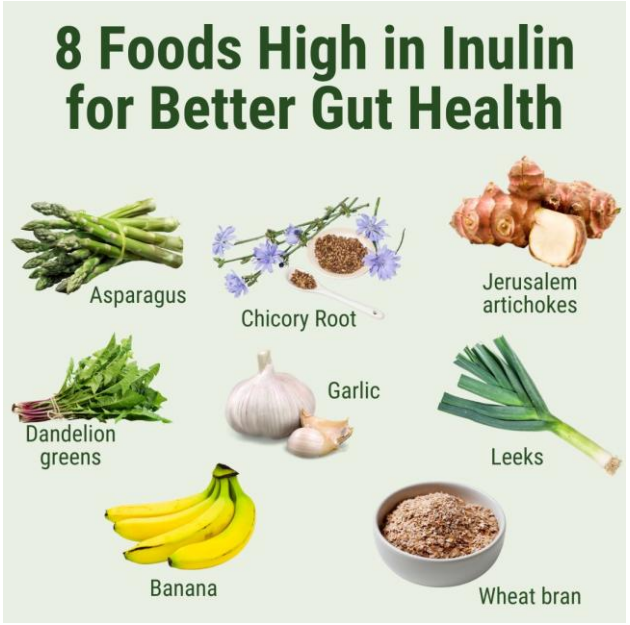
probiotic supplements

inulin supplementation

Diet rich in resistant Starch, prebiotics and polyphenols

↑ SCFA Producers

- ***Lactobacillus***
- ***Bifidobacterium***
- ***Roseburia***
- ***Faecalibacterium***
- ***Akkermansia***



- Reduce inflammation

- Enhance gut barrier function

- Improve calcium absorption

leading to stronger bones

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Key bacterial genera and their roles in bone health

High-fiber low-fat diet

Bile acids metabolizing bacteria: *Bacteroides* *Prevotella*

Metabolize bile acids modulate FXR and TGR5 signaling

- Regulate calcium absorption
- Regulate activity of osteoblasts
- Increase bone remodeling

High protein diet, tryptophan supplementation

Tryptophan metabolizing bacteria: *Clostridium*

Activate AhR and modulate immune responses

- Reduced bone resorption
- increased osteoblast differentiation

Tryptophan sources: Poultry, Meat, Seafood, Dairy, Nuts

Western diet

Pathogenic bacteria: *Escherichia coli*

Produces toxins, impairs gut barrier function

- Increased bone resorption

Targeting the **Gut-Bone Axis** using advanced microbiome-based interventions

Clinical Evidence for Probiotics

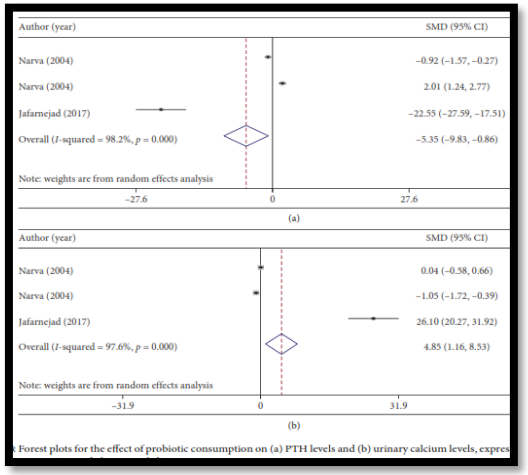
- In clinical trials, probiotic consumption affects bone health parameters such as serum calcium levels (3.82; 95% CI: 1.05, 6.59 mmol/l), urinary calcium levels (4.85; 95% CI: 1.16, 8.53 mmol/l), and parathyroid hormone (PTH) levels (−5.53; 95% CI: −9.83, −0.86 ng/l).
- In most studies, *Lactobacillus* species such as *L. helveticus, L. reuteri,* and *L. casei* were consumed
- Spinal and total hip bone mineral density (BMD) was not affected significantly by probiotic consumption.

Hindawi
Evidence-Based Complementary and Alternative Medicine
Volume 2021, Article ID 3582989, 35 pages
https://doi.org/10.1155/2021/3582989

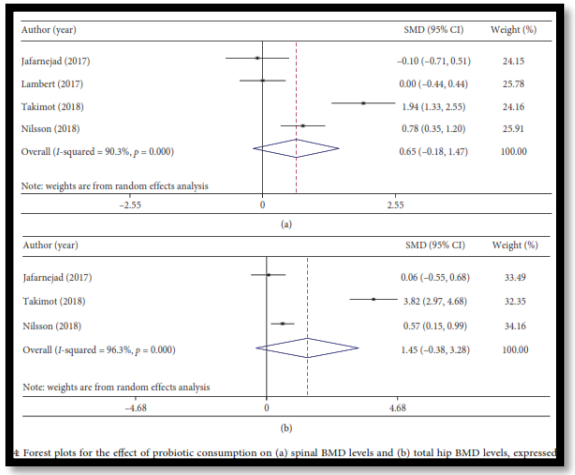
Review Article

Probiotics as a New Regulator for Bone Health: A Systematic Review and Meta-Analysis

Hanieh Malmir,[1,2] Hanieh-Sadat Ejtahed,[1,3] Ahmad-Reza Soroush,[1] Amir Mohammad Mortazavian,[4] Noushin Fahimfar,[5] Afshin Ostovar,[5] Ahmad Esmaillzadeh,[1,2] Bagher Larijani,[3] and Shirin Hasani-Ranjbar[1,3]



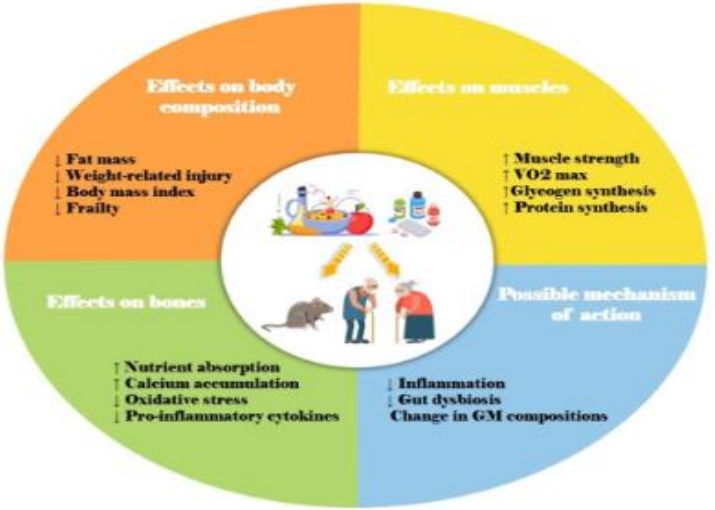
Forest plots for the effect of probiotic consumption on (a) PTH levels and (b) urinary calcium levels, expres



Forest plots for the effect of probiotic consumption on (a) spinal BMD levels and (b) total hip BMD levels, expressed

Probiotics and Age-related Musculoskeletal Disorders

- 20 clinical trials and 30 animal studies
- An improvement in physical performance, a decrease in frailty index, and a lower reduction in bone mineral density
- Body composition tends to increase in muscle ratio and muscle mass
- A decreasing trend of inflammatory markers such as IL1, IL6, IL17, T helper 17, and TNF-α
- Increasing absorption of Ca, P, and Mg



Probiotics and Antimicrobial Proteins (2025) 17:3495–3524
https://doi.org/10.1007/s12602-024-10306-3

RESEARCH

Evaluating the Role of Probiotics, Prebiotics, and Synbiotics Supplementation in Age-related Musculoskeletal Disorders in Older Adults: A Systematic Review

Narges Lashkarbolouk[1,2] · Mahdi Mazandarani[3] · Azin Pakmehr[4] · Hanieh-Sadat Ejtahed[1]

The Future: Next-Generation Probiotics

- ***Precision probiotics:***

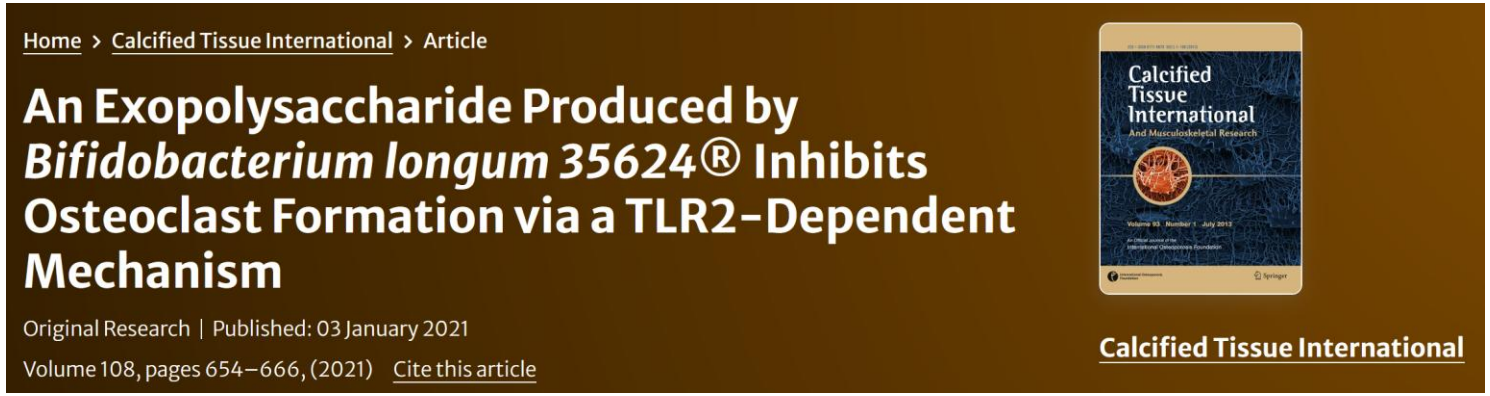
➢ **strain-specific molecular mechanisms**

- *Lactobacillus helveticus* and *Bifidobacterium longum*-derived Runx2/BMP-2 upregulation to enhance osteogenesis
- *Lactobacillus plantarum* mediated elevation of vitamin D receptor coupled with promoting osteoblast activity
- *Faecalibacterium prausnitzii* reinforces intestinal barrier integrity via butyrate production, mitigating inflammatory conditions
- *Bacillus amyloliquefaciens* demonstrates anti-osteoporosis effects mediated by the increased IGF-1 levels

Wei J, et al. Next-generation probiotics and engineered BEVs for precision therapeutics in osteoporosis. Frontiers in Nutrition. 2025;12:1581971.

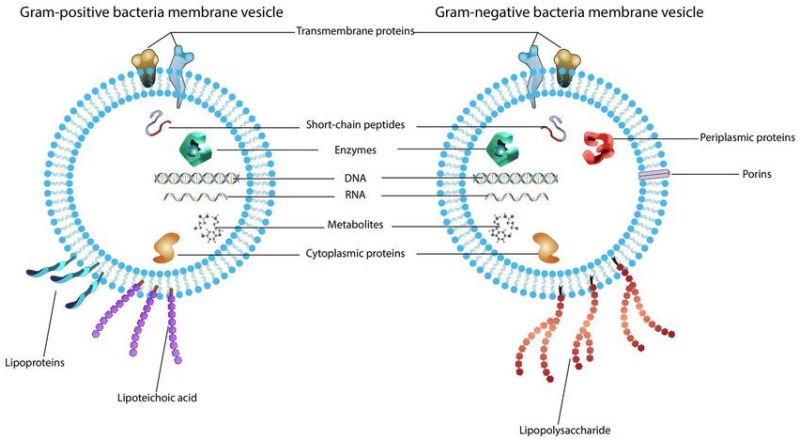
Engineered probiotics

- Exopolysaccharide (EPS) produced by the recombinant *Bifidobacterium longum* 35624 has been shown to inhibit osteoclast formation and thus increase bone formation in vitro experiments
- Orally administered *B. longum* 35624 could slow down bone loss in an ovariectomized mouse model
- A novel approach to prevent bone loss in inflammatory conditions such as post-menopausal osteoporosis
- If probiotics could be engineered by synthetic biology, they may prove more functional and potent in targeted delivery
- Safety and ethical issues



Bacterial Extracellular Vesicles as Postbiotics

- Natural, nano-sized lipid vesicles (40-200 nm) released by bacteria.



Advantages over Live Probiotics:

- **Cell-free:** No risk of uncontrolled colonization.
- **Biocompatible & Scalable:** Can be mass-produced.
- **Natural Nanocarriers**

Therapeutic Potential for Osteoporosis:

- Derived from beneficial bacteria, they can carry anti-osteoclastogenic signals.
- Can be engineered to **target bone tissue specifically**.

The Role of AI:

- **Strain Screening:** Identifying optimal probiotic candidates from vast datasets.
- **Predicting Host Response:** Analyzing microbiome data to predict which patients will benefit from specific probiotics.
- **Design Safe NGPs**

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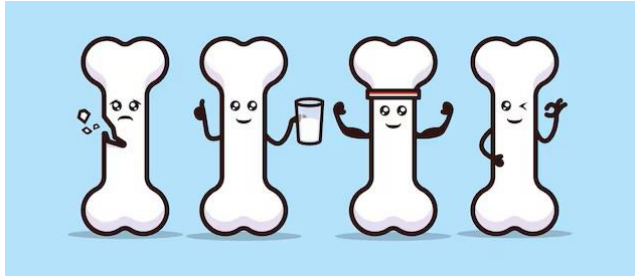
Dietary recommendations focused on modulating the gut microbiota for bone health

- Foods rich in diverse fibers (inulin, FOS, GOS): garlic, onions, leeks, bananas, artichokes, whole grains, and legumes
- Fermented foods (yogurt, kefir, kimchi, kombucha) and specific probiotic strains
- Most promising strains for bone:
  - *Lactobacillus reuteri*
  - *Lactobacillus casei*
  - *Bifidobacterium longum*
- Colorful fruits, vegetables, green tea, and dark chocolate rich in polyphenols
- The Mediterranean Diet
- Avoid Western-style diets (high in saturated fats, sugar, and ultra-processed foods)



Eat the rainbow to diversify your gut microbiome


Thanks for your attention