Food matrix effects: the case of calcium

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Conflict of Interest Disclosure

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CALCIUM:

- Essential micronutrient involved in many physiological processes
- Most abundant mineral in the human body
- Calcium is stored in our bone, which contains about 1.2 kg of calcium
- Must be obtained from the diet

OSTEOPOROSIS:

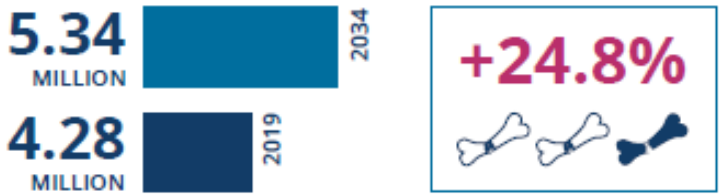
- A bone disease characterized by a reduced bone mineral density
- Defined as bone mineral density of 2.5 standard deviations below peak bone mass, relative to the age and sex-matched average (WHO)

OSTEOPOROSIS - A SOCIETAL ISSUE

Osteoporosis in people aged >50

Cost of osteoporosis-related healthcare

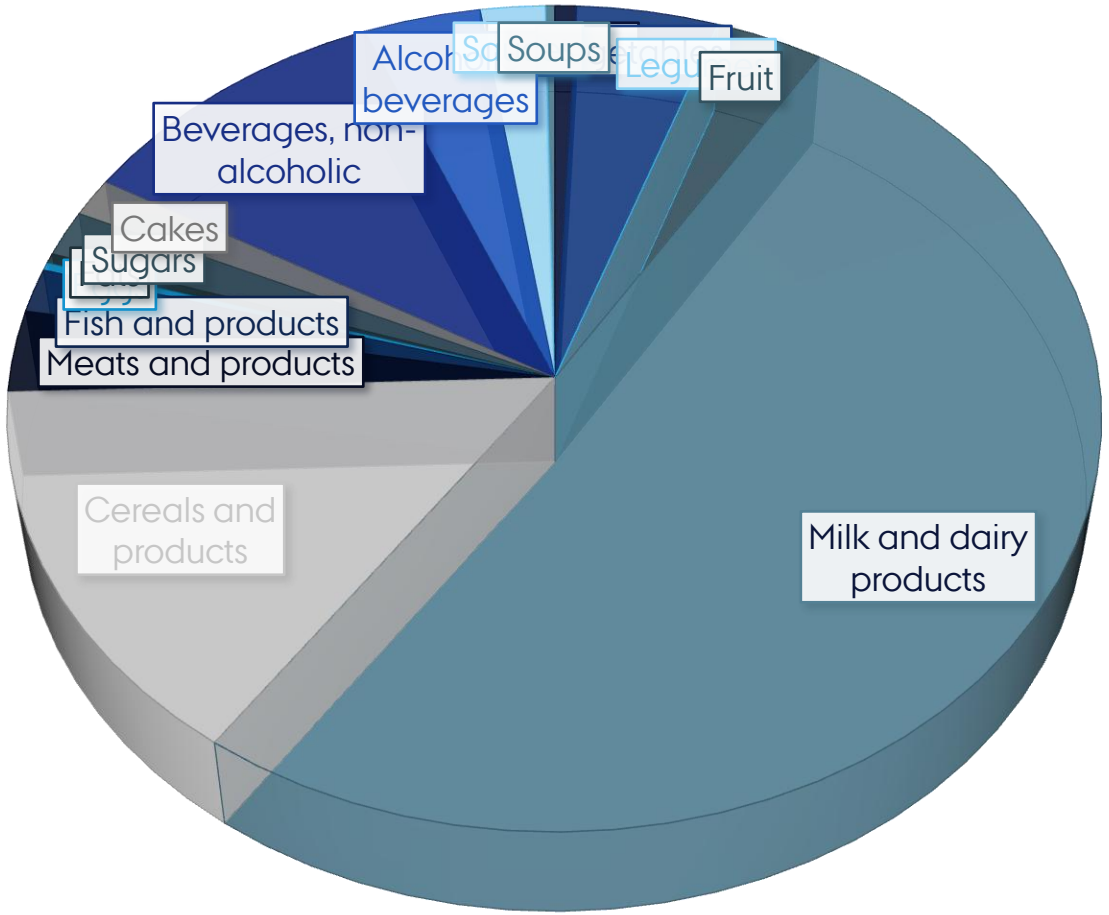
Demographic changes is a challenge ahead – increase in fragility fractures



Kanis, J.A., Norton, N., Harvey, N.C. *et al. Arch Osteoporos* **16**, 82 (2021).

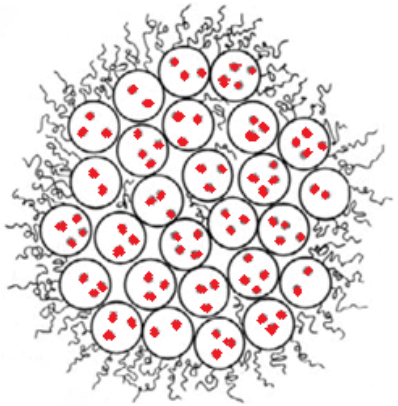
Salari, N., et al. (2021) *J Ortho Surg Res*, *16*:1-21.

DAIRY IS THE MOST IMPORTANT SOURCE OF DIETARY CALCIUM



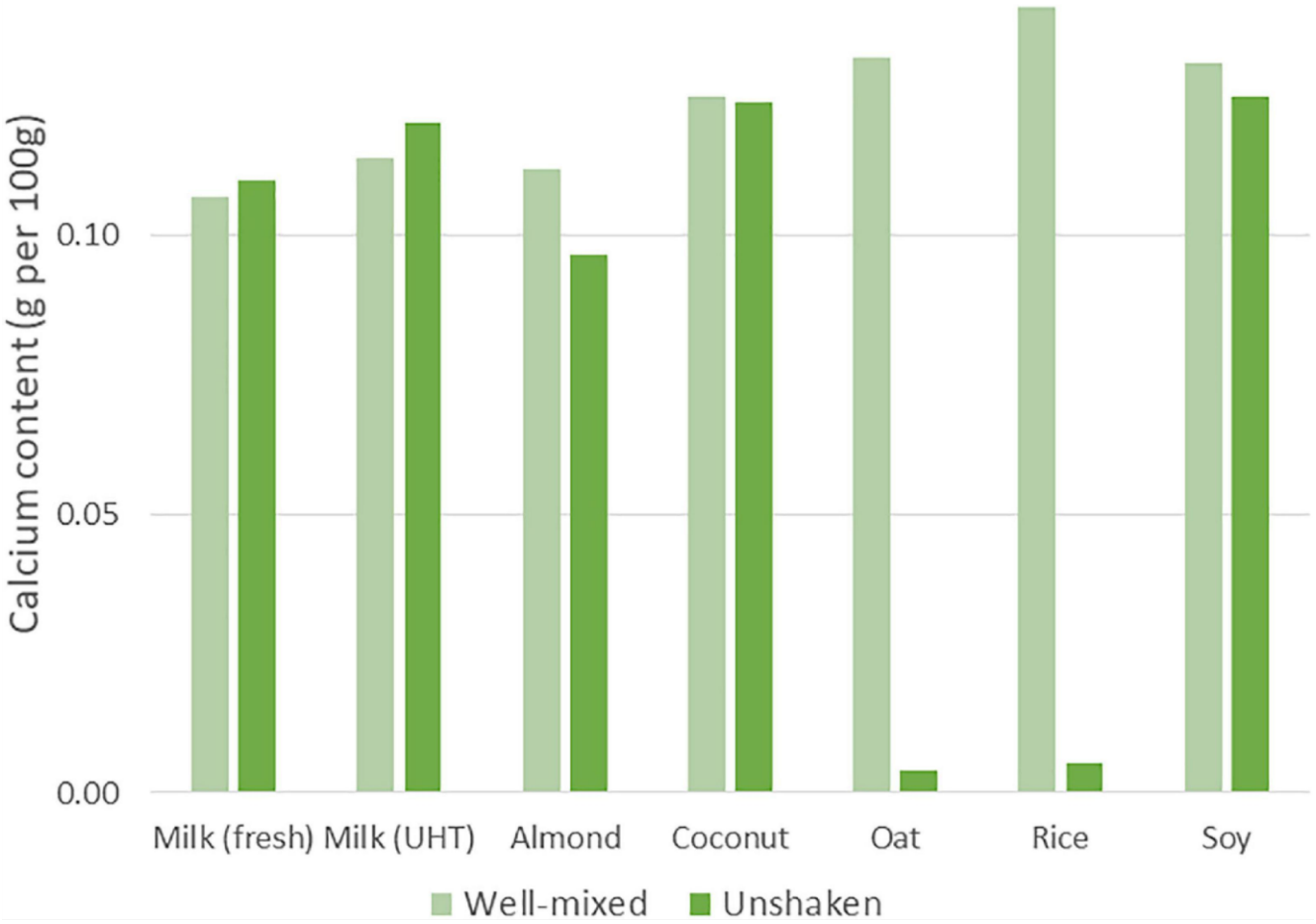
Welch et al. (2009). Eur J Clin Nutr 63, S101–S121

MILK MATRIX SUPPORTS CALCIUM DELIVERY



Casein micelle with calcium phosphate
→ Protect against low gastric pH in stomach
→ Enhances solubility of calcium in the small intestine

SOLUBILITY - MATRIX MATTERS

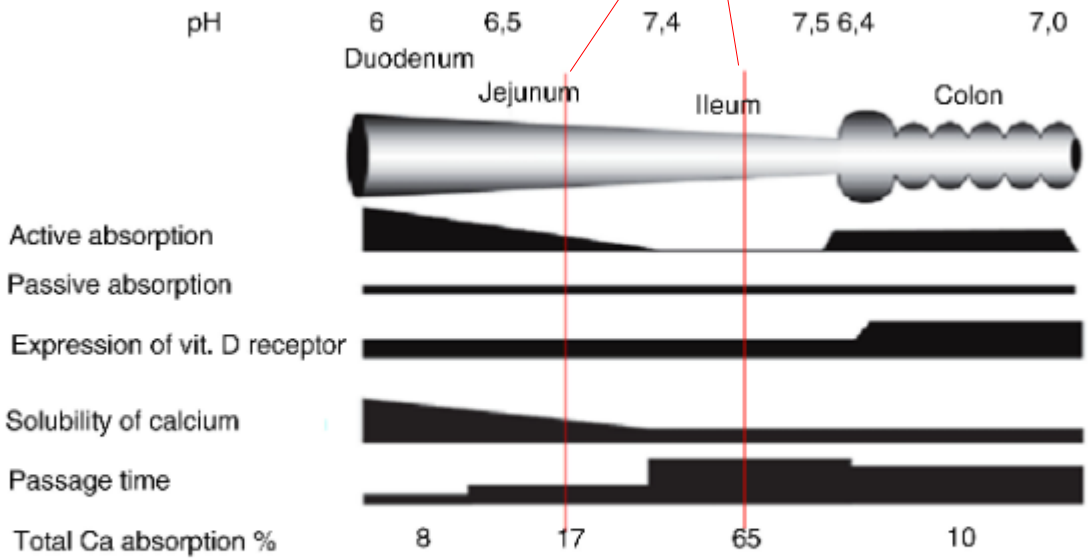


Smith et al. (2022). Front. Nutr.

CALCIUM ABSORPTION IN GUT

65 % of the total calcium absorption

Robert Y. van der Velde et al.



65% of the total calcium absorption takes place in the ileum (between the red lines).

Fig. 2. Calcium absorption, solubility of calcium, contribution of active and passive absorption of calcium and pH in the various segments of the small and large intestine (19, 22, 23).

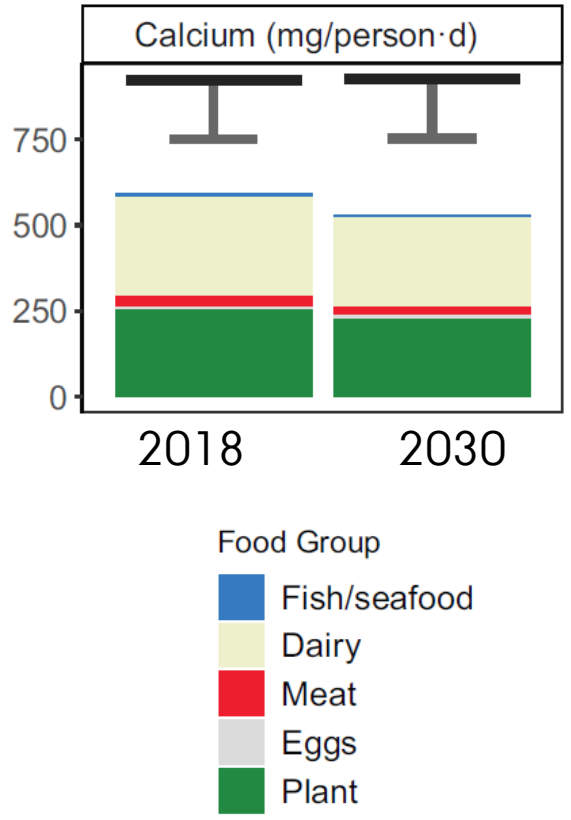
Active transcellular process regulated by active vitamin D (1,25(OH)2D3)

Passive para-cellular diffusion depends on vitamin D

MATRIX MATTERS – CALCIUM RESOURCES ARE LIMITED

TABLE 1 DELTA Model results using the 2018 food system to feed the 2018 population or the forecast 2030 population

	2018 population (7.6 billion)	2030 population (8.6 billion)
Total biomass production leaving farms/fisheries, billions of tons/y	10.58	10.58
Total food supply after waste, billions of tons/y	4.64	4.6
Amount of total biomass above used as animal feed, billions of tons/y	1.5	1.5
Energy supply (energy target), kcal/person· d	2502 (2160)	2244 (2166)
Protein supply (protein target), g/person· d	61 (45.4)	54.7 (46.1)
Fat supply (fat target), g/person· d	76.1 (60.1)	68.1 (60.3)
Nutrient gaps >5%, % of target daily intake		
Calcium	36	43
Vitamin E	31	42
Iron	—	11
Potassium	—	12
Riboflavin	—	6
Vitamin A	—	9
Vitamin B-12	—	6



Smith et al. (2021). *J Nutr* 151:3253-3261

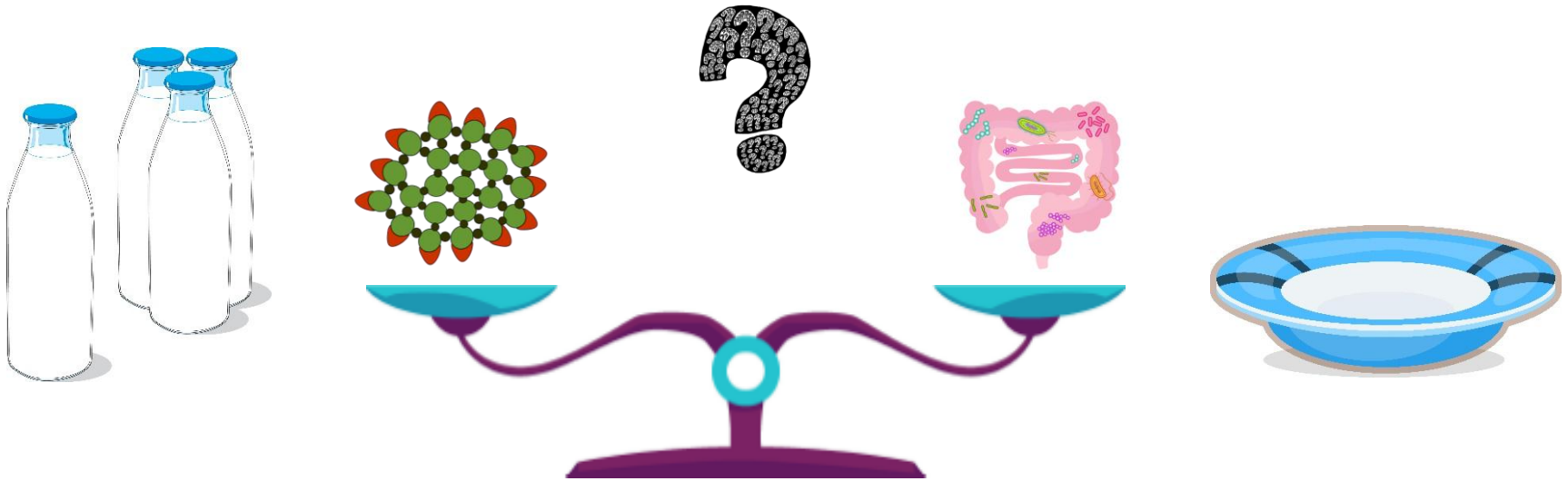
MILK VERSUS YOGHURT AS CALCIUM SOURCE

Milk:

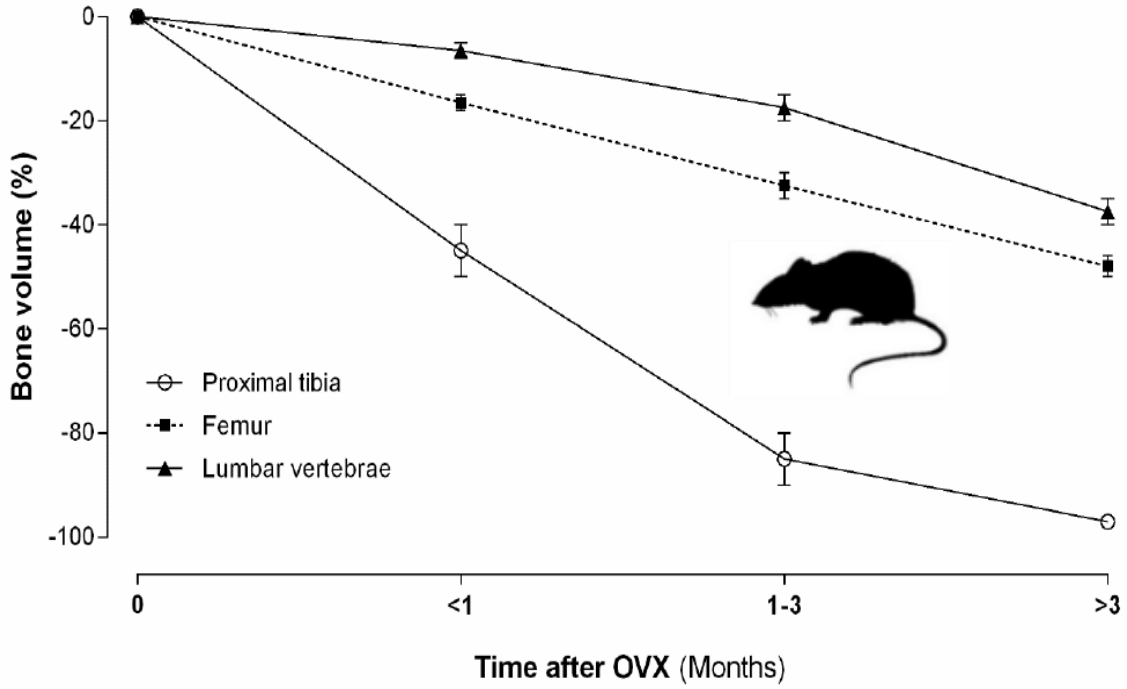
Casein micelles encapsulate calcium phosphate, protects against low gastric pH in the stomach and enhances solubility of calcium in the small intestine

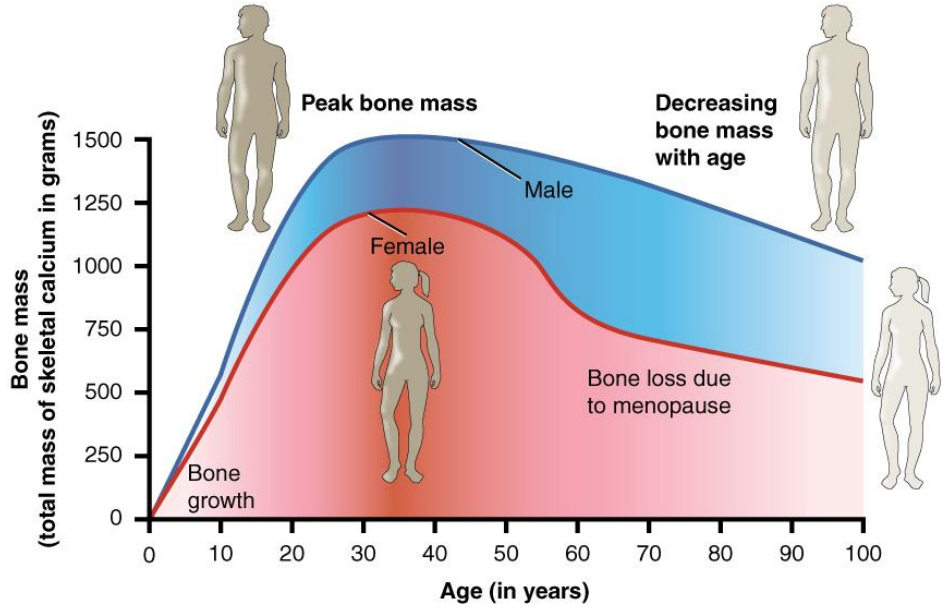
Yoghurt:

Yougurt contains starter cultures that promote a beneficial gut microbiome



OVARIECTOMIZED RAT MODEL FOR MENOPAUSE CONDITIONS





Yousefzadeh et al. EXCLI Journal 2020;19:89-107

RAT STUDY:

Ovariectomized rats (OVX)

- Negative control (12 mg Ca/day)
- MCa: Milk (90 mg Ca/day)
- YCa: Yogurt (90 mg Ca/day)
- YCa-In: Yogurt with 5% inulin (90 mg Ca/day)
- Positive control (90 mg Ca/day)

6 wks →

Analyses:

Whole body:

- DXA: Bone mineral density and content

Femur bone:

- Mechanical bone strength
- Bone structure (X-ray)

Intestinal content:

- pH
- 16sRNA sequencing
- Metabolomics

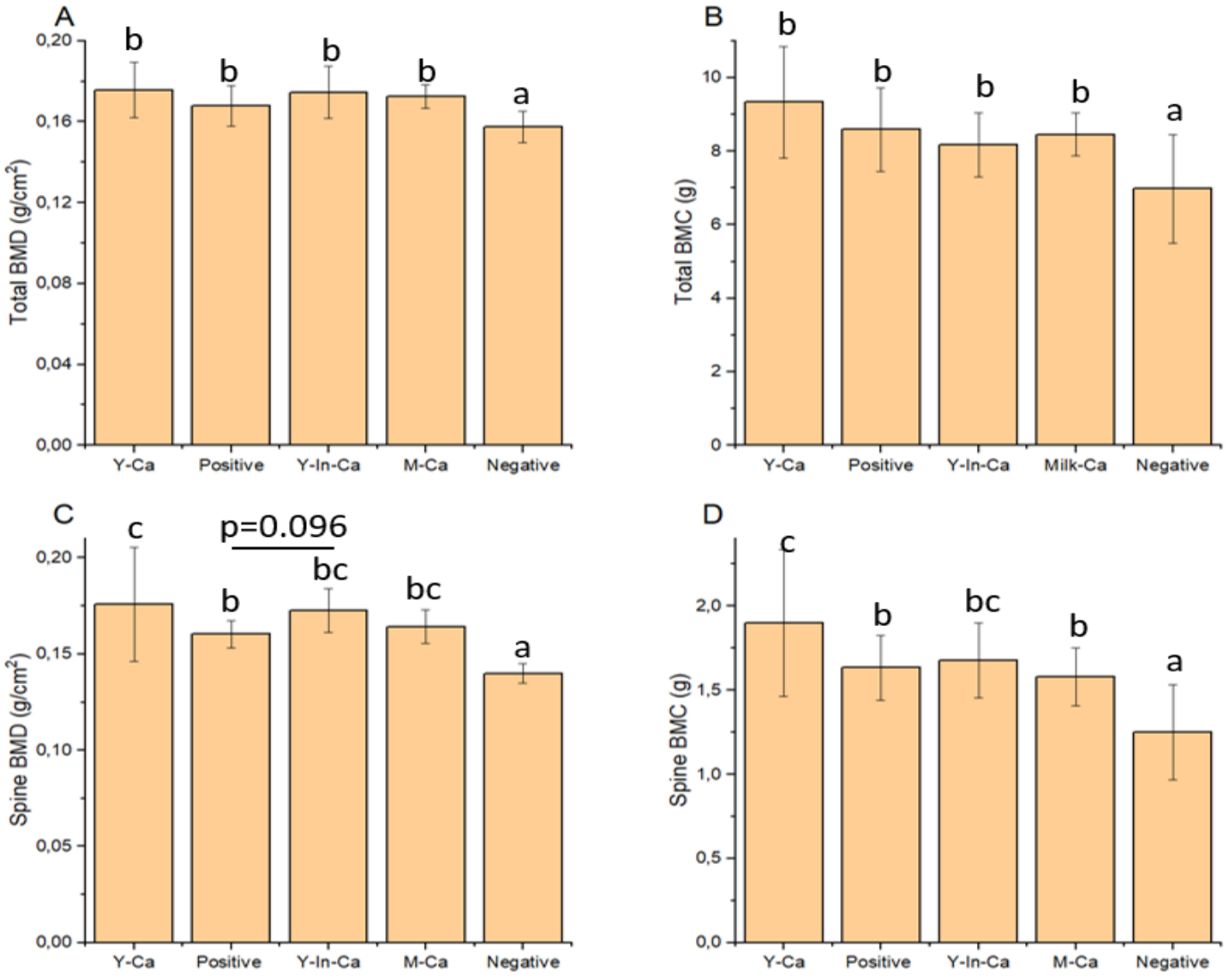
Blood:

- Metabolomics

INCLUSION OF INULIN IN THE FOOD MATRIX:

- Prebiotic fiber
- Stimulates fermentation in the gut
- Lowers gut pH
- Enhancing calcium absorption?

BONE MINERAL DENSITY (BMD) AND CONTENT (BMC)



He et al. (2022). Mol Nutr Food Res.

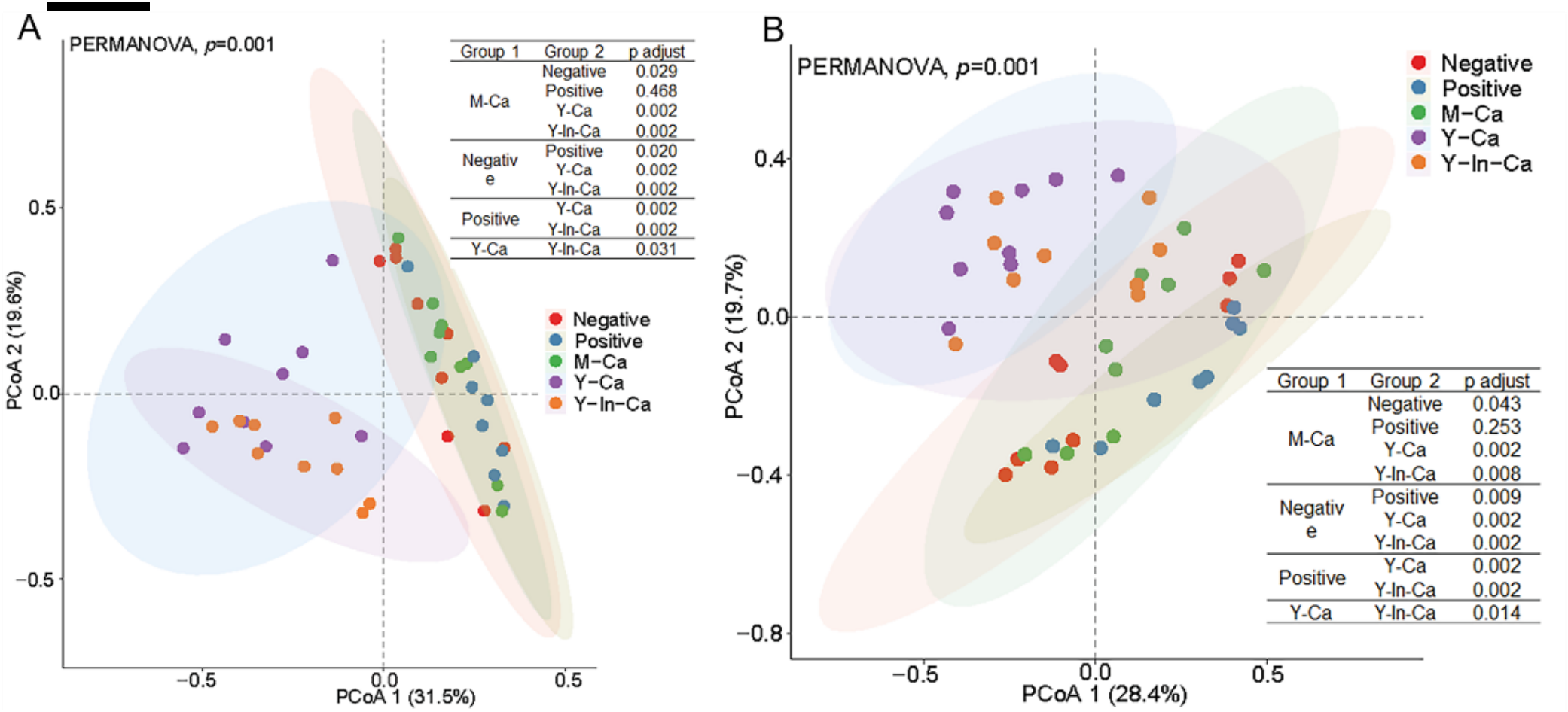
BONE PARAMETERS:

Bone parameters	Negative	Positive	M-Ca	Y-Ca	Y-In-Ca	*p* value
BMD and BMC (*n*=44)						
Total BMD (g/cm^2)	0.157±0.008^a	0.168±0.010^b	0.173±0.006^b	0.176±0.014^b	0.175±0.013^b	0.006
Spine BMD (g/cm^2)	0.140±0.005^a	0.160±0.007^b	0.164±0.009^{bc}	0.176±0.029^c	0.173±0.007^{bc}	<0.001
Total BMC (g)	6.97±1.48^a	8.59±1.14^b	8.46±0.58^b	9.33±1.52^b	8.18±0.87^b	0.004
Spine BMC (g)	1.25±0.28^a	1.63±0.19^b	1.56±0.17^b	1.90±0.44^c	1.68±0.22^{bc}	<0.001
Relative total BMC (g/kg)	20.9±3.2^a	25.2±3.1^b	24.3±1.8^b	24.5±2.3^b	24.2±2.4^b	0.018
Relative spine BMC (g/kg)	3.76±0.79^a	4.78±0.55^b	4.54±0.55^{ab}	5.02±1.12^b	4.99±0.90^b	0.019
Mechanical bone strength (*n*=44)						
Max. load (N)	93.9±5.5^a	109.7±6.5^b	105.7±9.7^b	109.1±11.2^b	108.3±14.8^b	0.017
Femur structure (*n*=25)*						
Tb.BV (mm^3)	1.91±0.37	2.59±0.50	2.51±1.30	3.36±1.82	3.39±1.40	0.14
Tb.BV/TV	0.081±0.022	0.125±0.021	0.130±0.086	0.145±0.053	0.145±0.040	0.078
Tb.Th (µm)	72.7±1.9^a	81.5±2.8^b	80.1±2.6^b	83.5±3.7^b	84.2±5.9^b	<0.001
Tb.Sp (mm)	1.14±0.31	0.90±0.21	0.91±0.40	0.80±0.21	0.82±0.29	0.41
Ct.BV (mm^3)	5.25±0.24	5.90±0.36	5.92±0.53	5.69±0.20	6.09±0.49	0.052
Ct.BV/TV	0.39±0.06	0.46±0.03	0.46±0.04	0.44±0.07	0.45±0.05	0.59
Ct.Th (µm)	157±26	159±6	171±21	161±16	169±5	0.22

X-ray tomography. Tb: Trabecular; BV: bone volume; Th: thickness; TV: tissue volume; Sp: separation; Ct: cortical.

He et al. (2022). Mol Nutr Food Res.

GUT MICROBIOME:

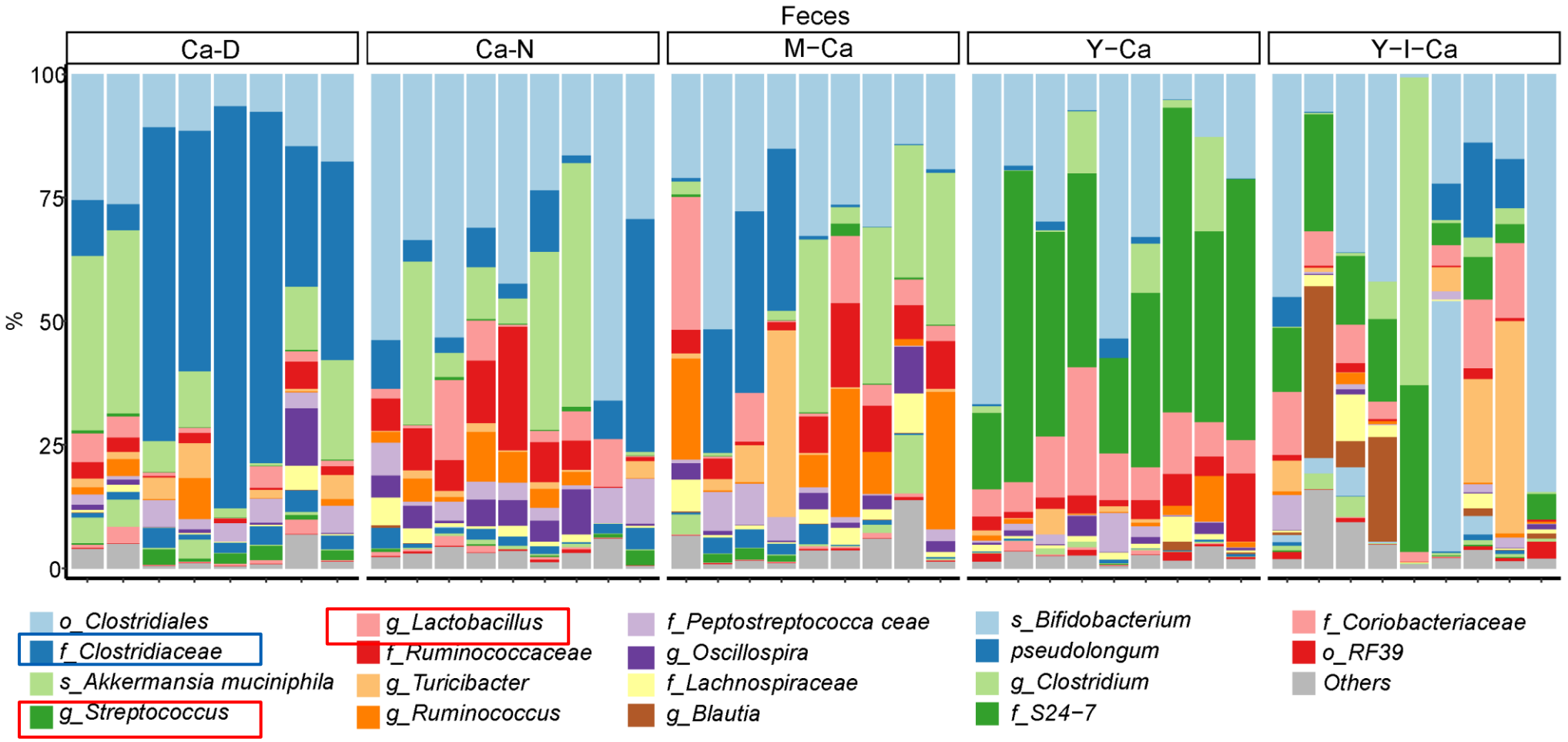


Group 1	Group 2	p adjust
M-Ca	Negative	0.029
	Positive	0.468
	Y-Ca	0.002
	Y-In-Ca	0.002
Negative	Positive	0.020
	Y-Ca	0.002
	Y-In-Ca	0.002
Positive	Y-Ca	0.002
	Y-In-Ca	0.002
Y-Ca	Y-In-Ca	0.031

Group 1	Group 2	p adjust
M-Ca	Negative	0.043
	Positive	0.253
	Y-Ca	0.002
	Y-In-Ca	0.008
Negative	Positive	0.009
	Y-Ca	0.002
	Y-In-Ca	0.002
Positive	Y-Ca	0.002
	Y-In-Ca	0.002
Y-Ca	Y-In-Ca	0.014

He et al. (2022). Mol Nutr Food Res.

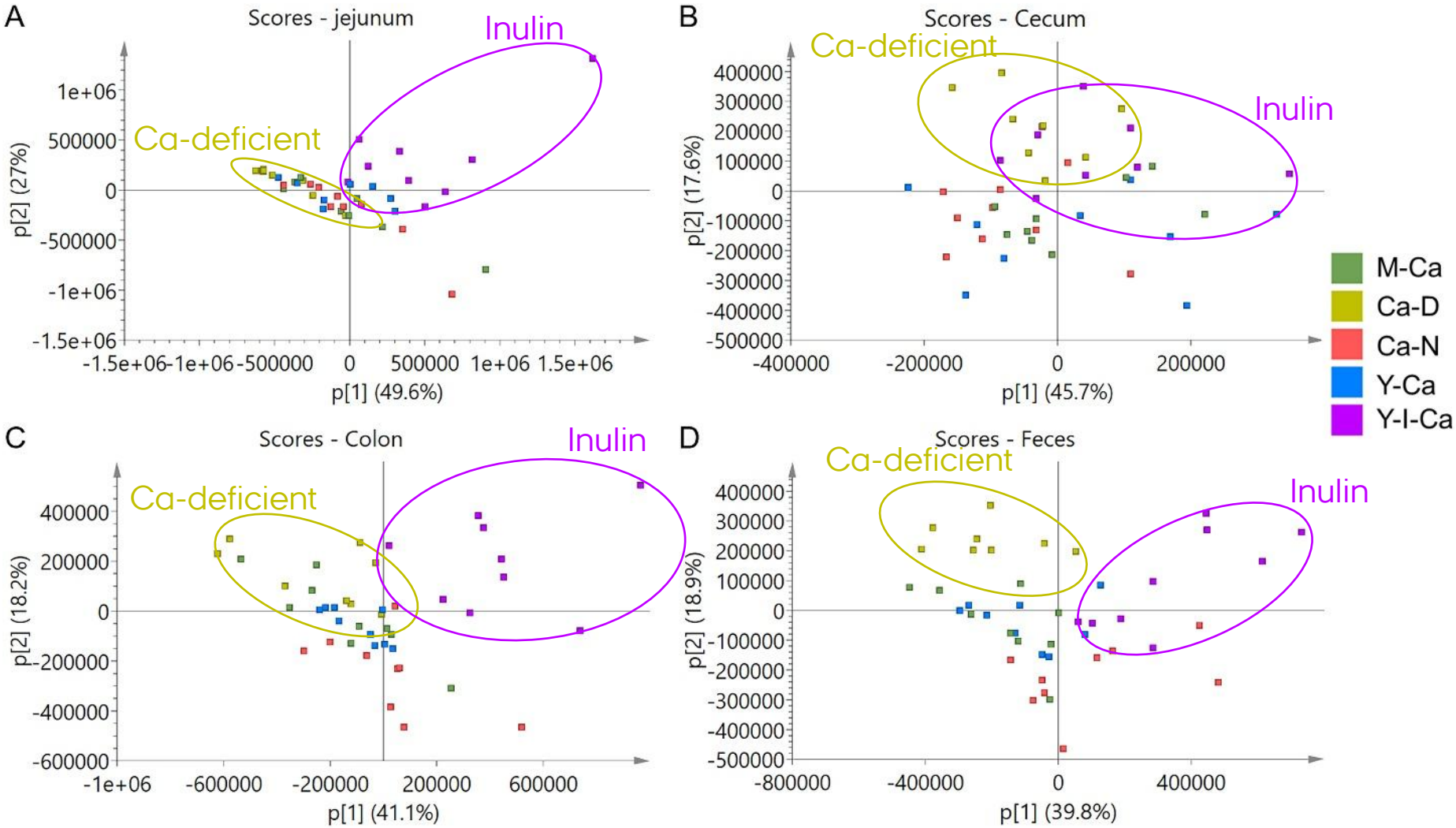
GUT MICROBIOME:



Yogurt intake enhanced *Lactobacillus* and *Streptococcus* and decreased *Clostridiaceae* and *Clostridium.*

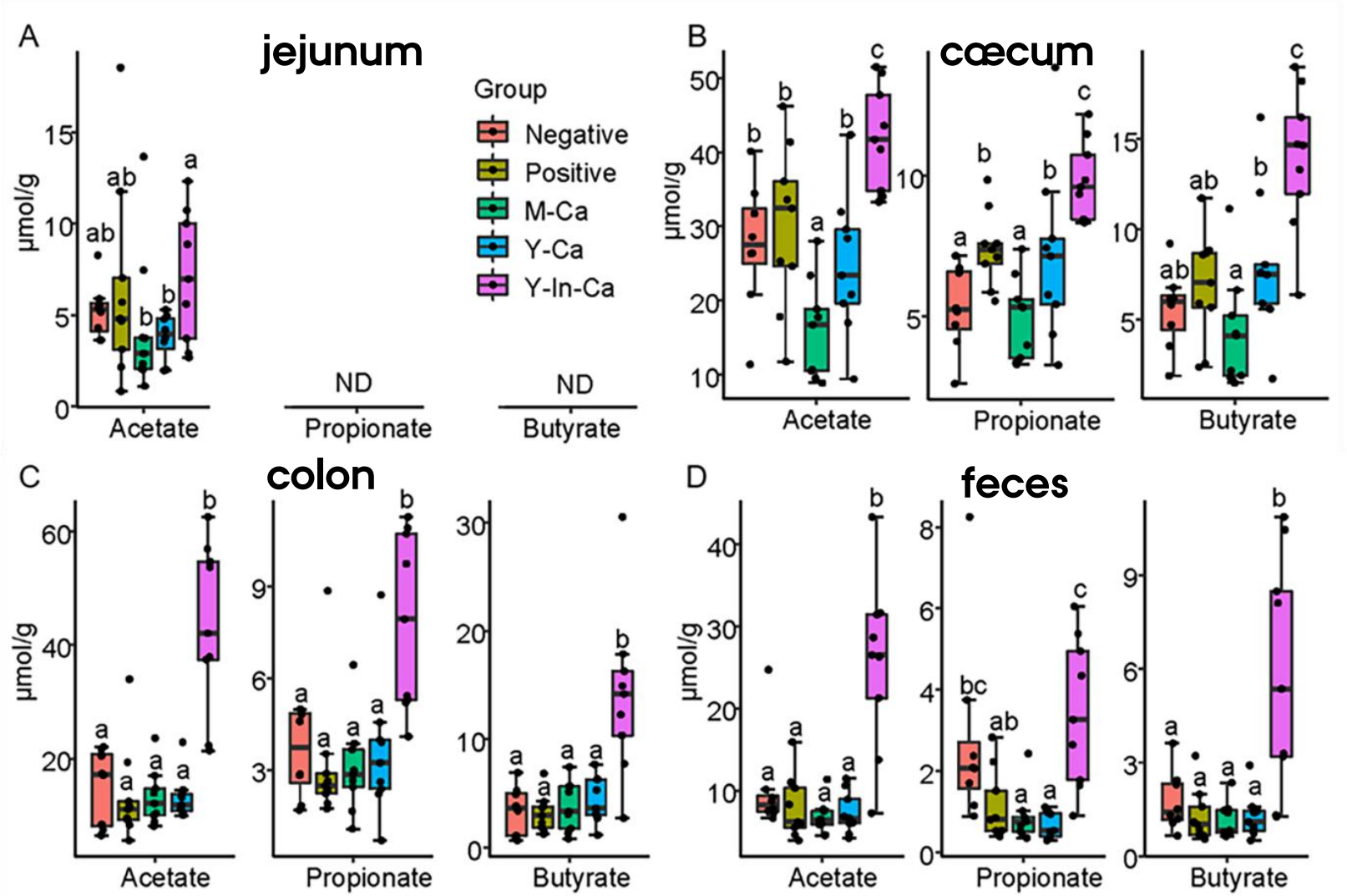
He et al. (2022). Mol Nutr Food Res.

GUT METABOLOME:



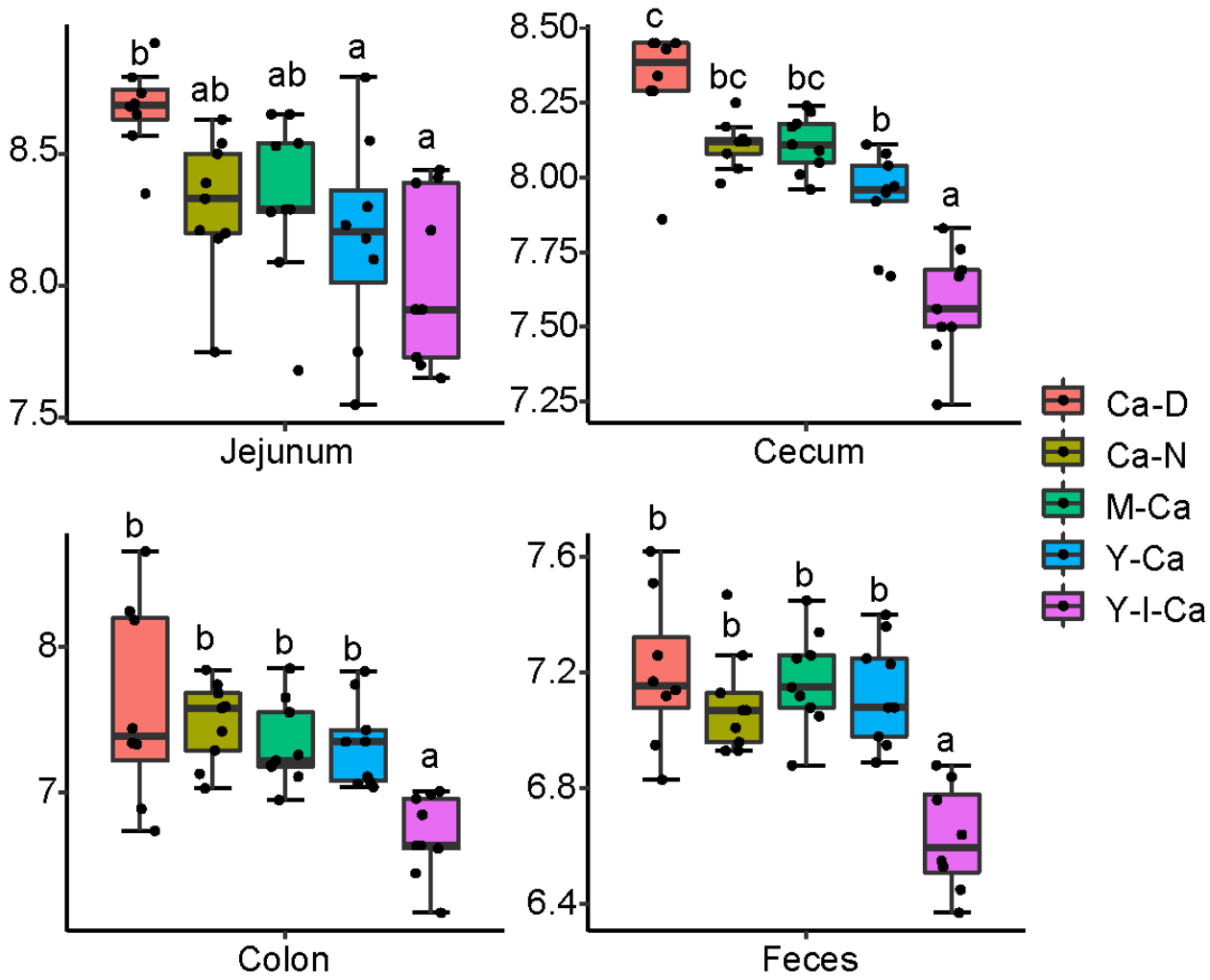
He et al. (2022). Mol Nutr Food Res.

SHORT-CHAIN FATTY ACIDS:



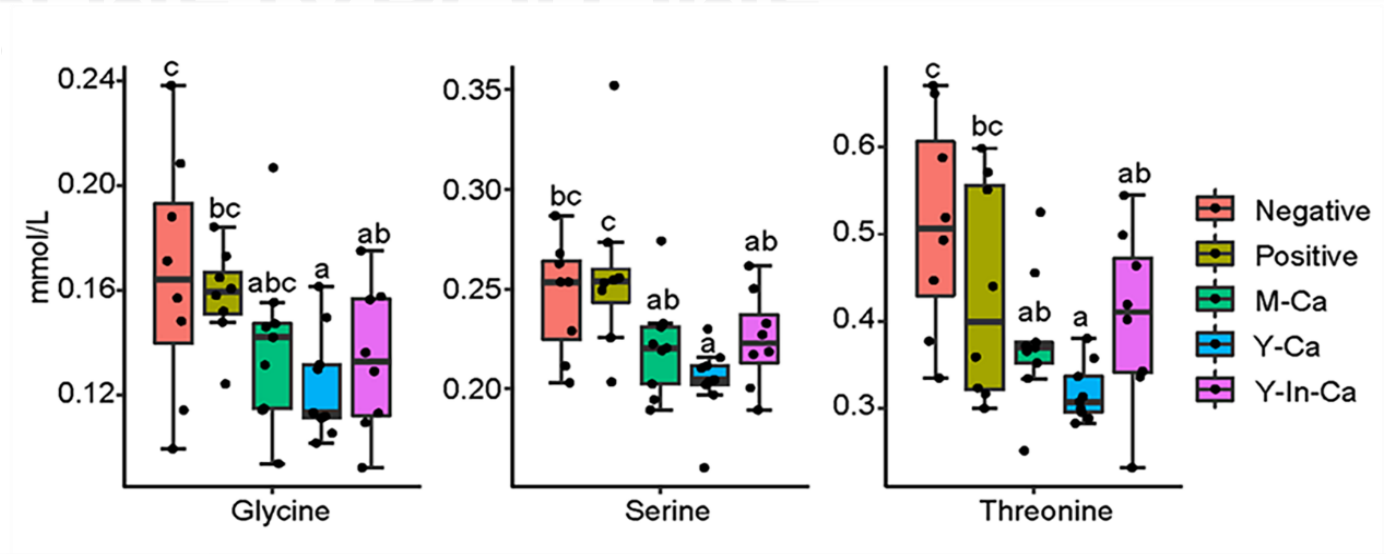
He et al. (2022). Mol Nutr Food Res.

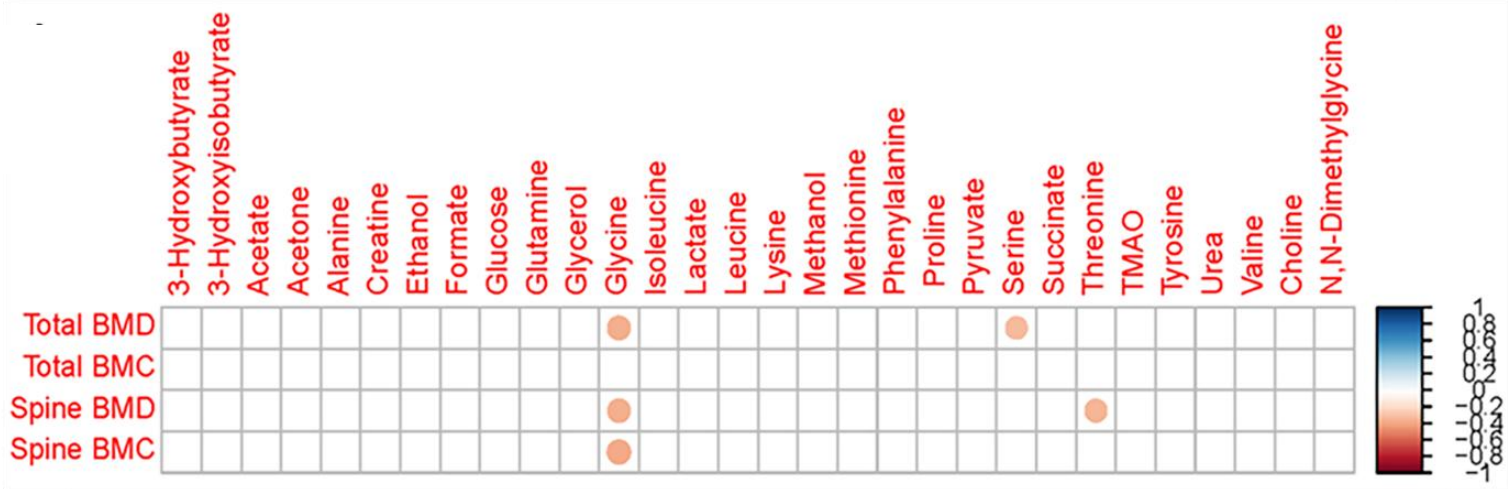
pH IN THE GI TRACT:



He et al. (2022). Mol Nutr Food Res.

SERUM METABOLOME:





*Negative association between plasma glycine and BMD also found in Hong Kong Osteoporosis Study (Zhang et al. *J. Bone Miner. Res.* **2021**, *36*, 729–738).

He et al. (2022). Mol Nutr Food Res.

CONCLUSIONS

- Yogurt as food matrix was superior to milk to enhance bone mineral density
- Increased SCFAs with inulin fortification of the food matrix was not associated with changes in bone mineralization
- Both yogurt and yogurt-inulin combination had a pronounced effect on the gut microbiome and stimulated Streptococcus and Lactobacillus on the expense of Clostridia
- The beneficial effects of yogurt on bone mineral density may involve glycine-related pathways (glycine, serine and threonine metabolism).
- Calcium supplementation changed the gut microbiota and its metabolic activity

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