Unlocking the Secrets of Stronger Bones: The Future of Personalized Recommendations for Bone Health

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Presentation sponsored by:
New England Dairy
NIAMS
UMASS LOWELL
HEROES
USDA
NIFA

Disclosures

- Current funding support:
  - USDA, NIFA 2021-67017-33936
  - HEROES Program, DOD
  - Toxic Exposures Research Program, DOD
- Related previous funding support:
  - NIH NIAMS 1R01AR072741-01A1
  - National Dairy Council Grant Award, 2021
  - Yogurt in Nutrition Initiative Grant Award, 2017

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Objectives

Outline	Nutrients, food groups and dietary patterns related to bone health
Describe	Mechanisms underlying associations between lifestyle choices and bone health
Discuss	How growing knowledge of the relationship between diet and bone health may shape personalized recommendations

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Osteoporosis is a Public Health Crisis

https://www.bonehealthpolicyinstitute.org/bone-facts

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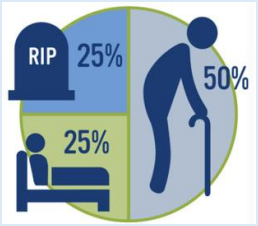
Burden of Osteoporotic Fractures

EACH YEAR IN THE U.S., APPROXIMATELY 300,000 HIP FRACTURES OCCUR



https://www.bonehealthpolicyinstitute.org/bone-facts

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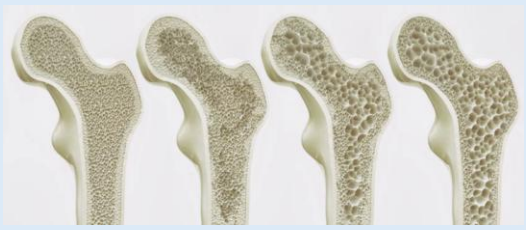
Osteoporosis (OP)

Decreased bone mass and alteration of microarchitecture which results in increased bone fragility and risk of fracture



Healthy Diseased

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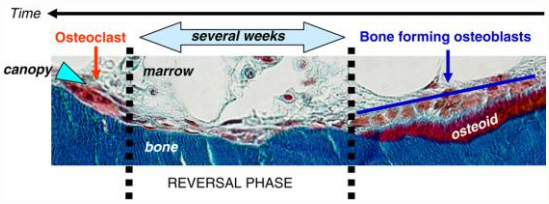
The skeleton is an active organ



Delaisse, 2014

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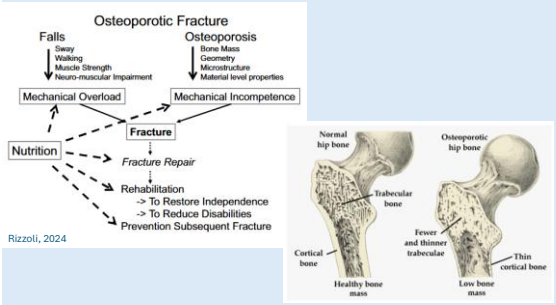
Determinants of Fracture Risk



Rizzoli, 2024

https://www.arthritiswa.org.au/condition/osteoporosis/

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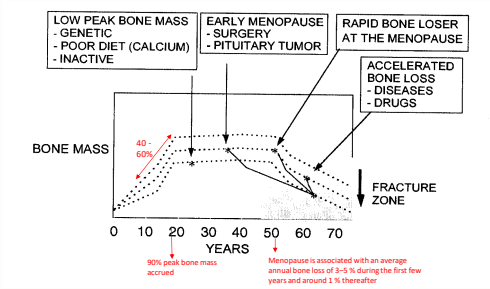
Osteoporosis: a pediatric disease with geriatric consequences



American Society for Bone and Mineral Research, 2003
Golden NH; 2014

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Modifiable Risk Factors As Points of Intervention

Sahni, Mangano, 2015
Fabiani, R., 2019
Friedman, M.A., 2022
Smith, K., 2021

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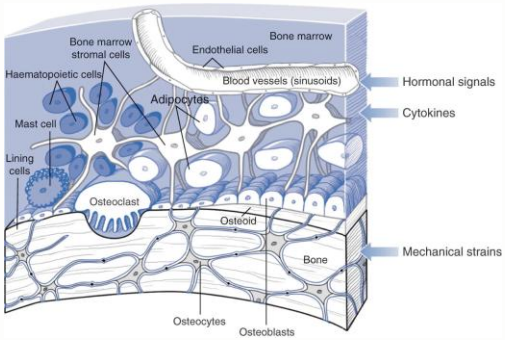
Nutrients influence bone via multiple pathways



Bartl, 2019

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What is a "bone healthy" diet?

- Optimal dietary protein intake of 1.0–1.2 g/kg body weight/d with at least 20–25 g of high-quality protein at each main meal
- Adequate vitamin D intake at 800 IU/d to maintain serum 25-hydroxyvitamin D levels >50 nmol/L
- Calcium intake of 1000 mg/d, alongside regular physical activity/exercise 3–5 times/week combined with protein intake near exercise
- Variety of nutrient dense, bioavailable sources

A consensus statement from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (2014)

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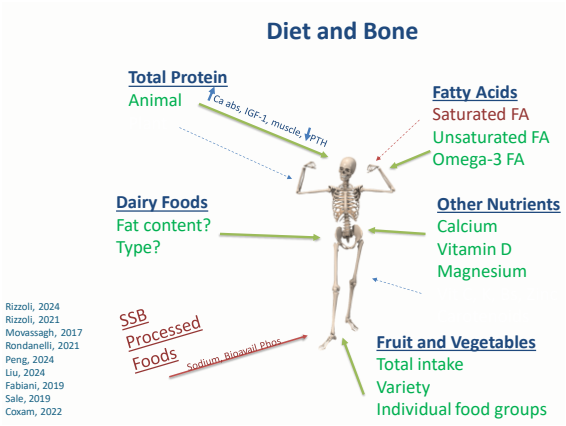

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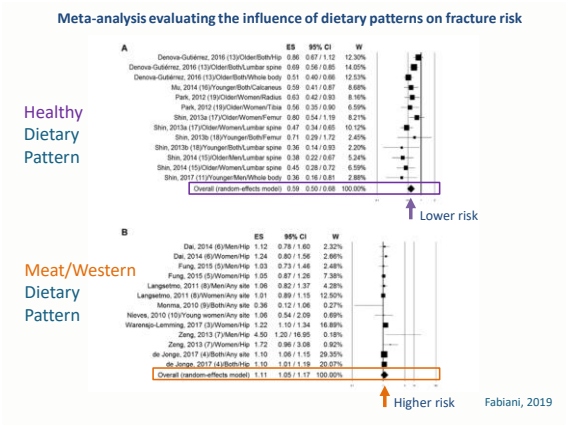

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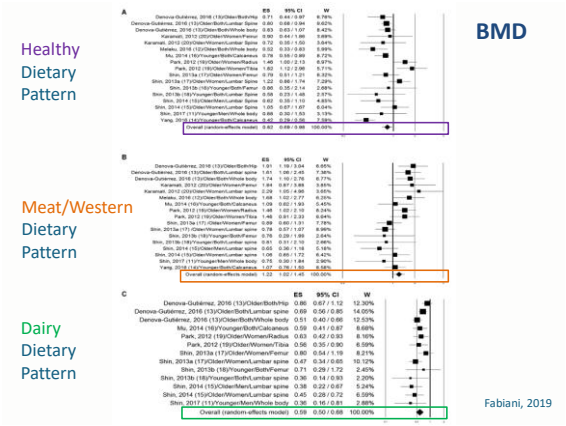

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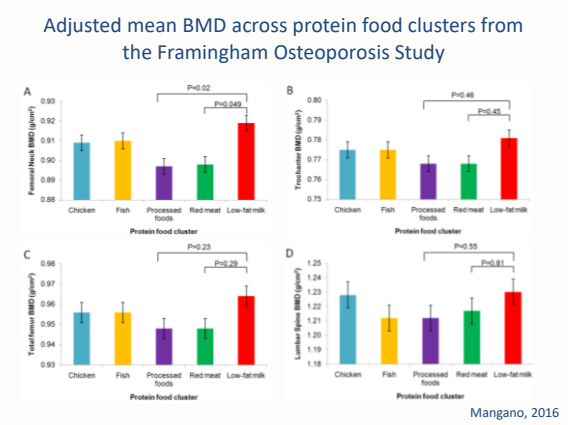

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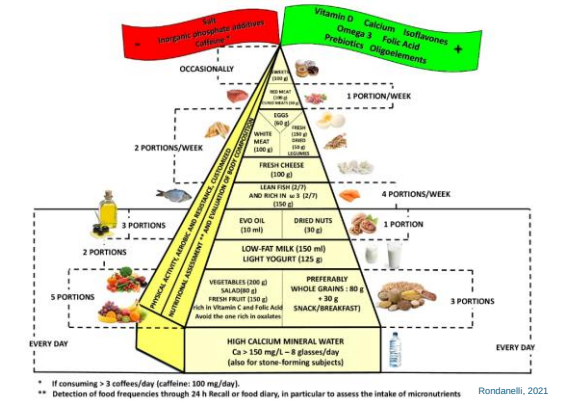

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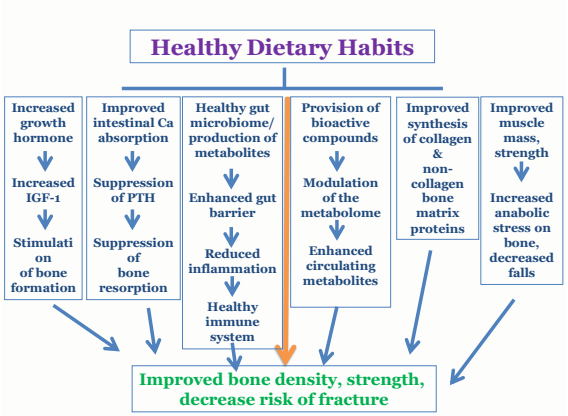

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Does one dietary pattern or a bone specific diet meet the needs of all persons?

Would personalized data support the adaption of these diets for all people?

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What should be considered when personalizing recommendations

1. Genetic ancestry
2. Dietary habits (cultural, religious, allergies)
3. Sex
4. Gut Microbiome
5. Metabolome
6. Underlying health parameters/conditions

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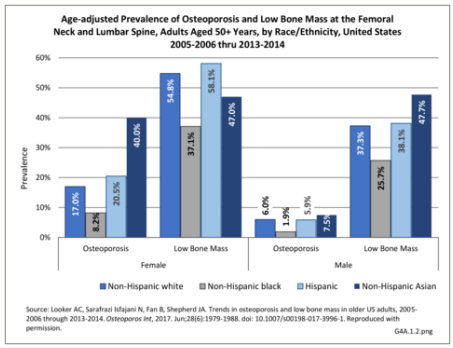
Health Disparities and Bone



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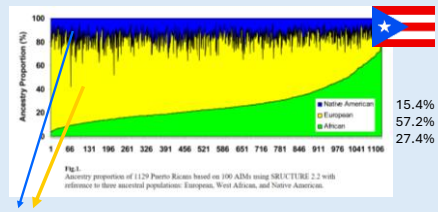
Genetic ancestry among Puerto Rican adults



15.4%
57.2%
27.4%

Inversely associated with lower BMD at the femoral neck and/or greater trochanter.

Lai, Hum Genet., 2009
Noel, J Bone Miner Metab., 2017

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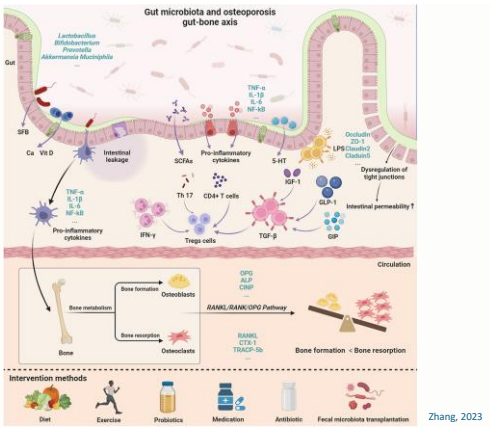

Zhang, 2023

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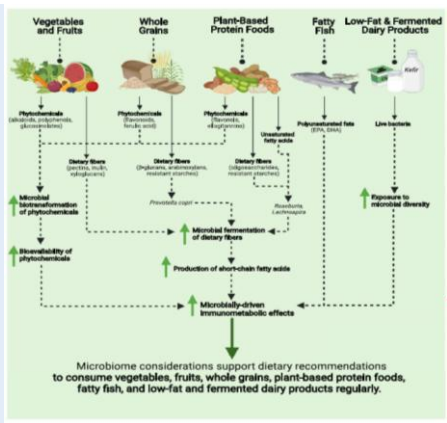

Armet, 2022

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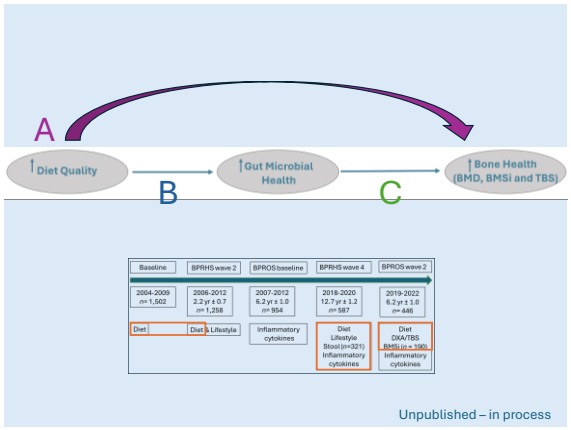

Unpublished – in process

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Dietary Approaches to Stop Hypertension (DASH) Predicts Bone Quantity in Puerto Rican Women

	DASH Postmenopausal women (n = 507)	
	Q1 (12–19)	Q5 (28–38)
Bone mineral density, g/cm^2		
Trochanter	0.752 ± 0.015	0.814 ± 0.011**
Femoral neck	0.868 ± 0.015	0.911 ± 0.011
Total hip	0.951 ± 0.017	1.01 ± 0.012*
Lumbar spine	1.09 ± 0.019	1.14 ± 0.015
Osteoporosis; femoral neck or lumbar spine, %	17.6	5.3*

* P value of <0.05, ** P <0.01

Diet Quality → ? → Bone Quality

Noel, Mangano, 2020

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DASH Score to Assess Overall Diet Quality

Adherence to diet score (8-40)*:

Fruits
Vegetables
Whole Grains
Low-fat Dairy
Nuts, Seeds, Legumes
} 1 (lowest) to 5 (highest)

Sodium
SSBs
(lowest)
Red & Processed Meat
} 1 (highest) to 5

*Mean of Baseline, wave 2, wave 4

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A DASH is related to BMD; not with Bone Quality

	Bone quality				Bone quantity - BMD			
	BMSi (*n* = 132)		TBS (*n* = 412)		Femoral Neck (*n* = 414)		Total Hip (n = 410)	
Diet quality	β ± SE	*P*	β ± SE	*P*	β ± SE	*P*	β ± SE	*P*
Model 2 (fully adjusted)*								
DASH score	-0.16 ± 0.16	0.32	0.002 ± 0.001	0.86	0.0032 ± 0.0016	0.05	0.0045 ± 0.0018	0.01

All models adjusted for sex, age, BMI
BMSi, model 1 + serum pentosidine and 25(OH)D, inflammation BMS
TBS, model 1 + smoking status
BMD, model 1 + height, diagnosis of diabetes, inflammation BMS

Unpublished – in process

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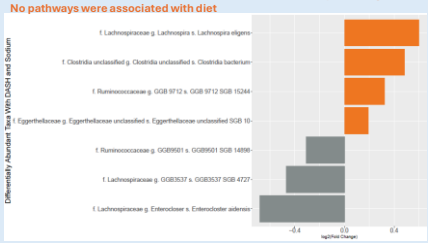
B 7 Taxa Associated With Diet

7 taxa were associated with diet and included in ML models predicting BMD; No pathways were associated with diet



sex, age, total energy, alcohol intake, and frequency of laxative use; FDR q-value ≤ 0.25

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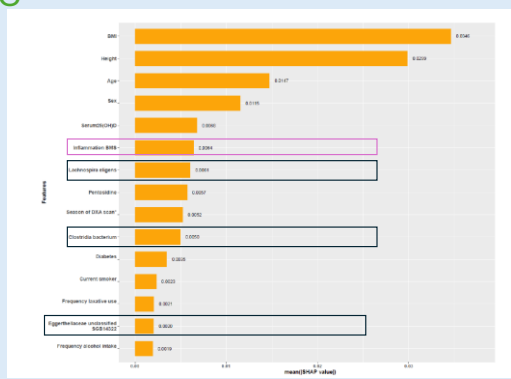
C SHAPley Global Effects Depict Feature Importance for BMD



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From: Are Probiotics the New Calcium and Vitamin D for Bone Health?

Author	Year	Population	No	Age (years)	Duration (months)	Probiotics dose	Control	BMD	BTM
Jafarnejad [42]	2017	Postmenopausal women with osteopenia	50	58	6	7 probiotic bacteria species 1 caps/day + Ca 500 mg + vitamin D 200UI/day	Placebo + Ca 500 mg + vitamin D 200UI/day	NS	Lower sCTX, BAP, PTH and TNFα
Lambert [43]	2017	Postmenopausal women with osteopenia	78	61.8	12	60 mg isoflavone aglycones/day and probiotic lactic acid bacteria + calcium 1200 mg/day, magnesium 550 mg/day, calcitriol 0.25 μg/day)	Placebo + calcium 1200 mg/day, magnesium 550 mg/day, calcitriol 0.25 μg/day)	Attenuated BMD loss (Δ%points: LS, 1.2; FN, 2.0; Tr, 2.1)	Lower sCTX
Nilsson [44]	2018	Postmenopausal women with osteopenia	90	76.3	12	*L. reuteri* 2 × 5 × 10e9 CFU/day	Placebo	Lower reduction (mean difference 95% CI) in: – tibia total vBMD: ITT 1.02% (0.02–2.03), PP 0.93% (0.21–1.65). – trabecular bone volume fraction: PP 0.80% (0.13–1.46)	NS
Takimoto [45]	2018	Non-osteoporotic postmenopausal women	61	57.6	6	*B. subtilis* 3.4 × 10e9 CFU/day	3.4 × 10e9 CFU/day	Increased hip BMD: Δ%points: Hip, 1.7; LS, 0.9 (NS)	Lower uNTX
Jansson [46]	2019	Early postmenopausal women	249	58.6	12	Three *Lactobacillus* strains (*Lactobacillus paracasei* DSM 13434, *Lactobacillus plantarum* DSM 15312, and *Lactobacillus plantarum* DSM 15313) 1 × 10e10 CFU/day	Placebo	Attenuated BMD loss LS: mean difference 95% CI: 0.71%, (0.06–1.35)	NS

Rizzoli, 2020

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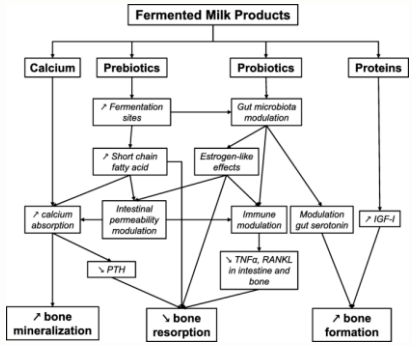

Rizzoli, 2020

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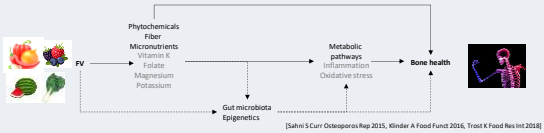
Diet-derived fruit and vegetable metabolites show sex-specific inverse relationships to osteoporosis status[a]

Kelsey M. Mangano[a,*], Sabrina E. Noel[b], Chao-Qiang Lai[c], Jacob J. Christensen[a,d], Jose M. Ordovas[e], Ben Dawson-Hughes[f], Katherine L. Tucker[g], Laurence D. Parnell[h]

Fruit & vegetable intake may protect against low BMD, OS and fractures



[Sahni S Curr Osteoporos Rep 2015, Klinder A Food Funct 2016, Trost K Food Res Int 2018]

- Boston Puerto Rican Health Study
- n=600
  - Dietary intake (FFQ)
  - Sociodemographic (Q)
  - Health (Blood, Mx Diagnoses)
  - Bone health (DXA)
  - Metabolomics (Plasma)
- 525 plasma metabolites passed quality control

Mangano, 2021

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FV intake and variety are significantly related to lower odds of osteoporosis

	OR (95 % CI)	*P*
FV intake (s/d)	0.73 (0.57-0.94)	0.013
FV variety	0.72 (0.56-0.93)	0.012

Mangano, 2021

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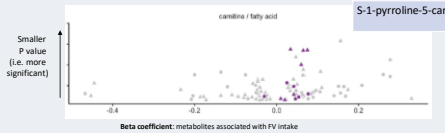
Metabolites significantly related to *FV intake* differ by sex

Women (*P*<0.05): **66** / 525 (12.6 %) metabolites

Men (*P*<0.05): **38** / 525 (7.2 %) metabolites

7 shared metabolites	β
DHA 22:6n3	-
Iminodiacetate	-
Homoarginine	-
Theobromine	+
1-linoleoylglycerol 18:2	+
2-linoleoylglycerol 18:2	+
S-1-pyrroline-5-carboxylate	+



Beta coefficient: metabolites associated with FV intake

Mangano, 2021

Mangano, 2021

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Metabolites significantly related to *OS status* differ by sex

Women (*P*<0.05): **33** / 525 (6.3 %) metabolites → 10 STEROID HORMONE METABOLITES – LOWER with OS

Men (*P*<0.05): **40** / 525 (7.6 %) metabolites → 9 BRANCHED CHAIN AA METABOLITES – HIGHER with OS

2 overlapping metabolites	Women	Men
N-(2-furoyl)glycine	Higher with OS	Higher with OS
Androstenediol (3β,17β) monosulfate	Lower with OS	Higher with OS

Mangano, 2021

Mangano, 2021

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Replication of metabolites with other cohorts

Replication Chinese Pop - TwinsUK

Trait	Metabolite
Femoral neck BMD	4-androsten-3beta,17beta-diol disulfate 1
	Epiandrosterone sulfate
	Androsterone sulfate
	5alpha-androstan-3beta,17beta-diol disulfate
Total hip BMD	4-androsten-3beta,17beta-diol disulfate 1
	Epiandrosterone sulfate
	Androsterone sulfate
	5alpha-androstan-3beta,17beta-diol disulfate
Lumbar spine BMD	4-androsten-3beta,17beta-diol disulfate 1
	Epiandrosterone sulfate
	Androsterone sulfate
	5alpha-androstan-3beta,17beta-diol disulfate

Zhang JBMR Name – FN BMD
leucine
xanthurenate
aconitate
pyridoxate
SM C22:0
sucrose
PC C36:2
glycine
SM C16:1
LPE C18:2
hydroxyglutarate
pantothenate
dimethylglycine

Zhang JBMR Name – LS BMD
pyridoxate
fruc_gluc_galac
SM C18:1
TAG C50:1
serotonin
leucine
serine
xanthurenate
glycine
creatinine
hypoxanthine
ADP
TAG C54:4
creatine
LPC C18:1
PC C36:1
TAG C58:10
SM C22:0
TAG C48:0

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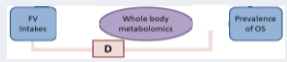
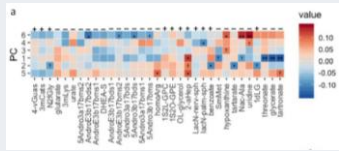
Greater intake of some FV groups associated with metabolites, linked to less likelihood of OS



Associations differ by sex:

FV groups

1 Traditional/sofrito
2 American vegetables
3 Tropical fruits
4 Other fruits
5 Berries and melons
6 Dark leafy greens



Mangano, 2021

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Take Home Messages

- Nutrition Plays a Key Role in Bone Health
  - A well-balanced diet rich in protein, calcium, vitamin D, and a variety of nutrient-dense foods (highlighting fruits and vegetables) supports bone density, strength, and overall skeletal health, due to their positive impact on the gut microbiome and their ability to alter the human metabolome.
- Dietary Patterns Influence Fracture Risk
  - Adopting a "bone-healthy" dietary pattern, such as the Mediterranean or DASH diet, is associated with improved bone mineral density (BMD) and a lower risk of osteoporosis-related fractures.
- Personalized Nutrition is the Future
  - Individual factors like genetics, gut microbiome, cultural dietary habits, and metabolic profiles should be considered when creating personalized dietary recommendations for optimal bone health.

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Acknowledgements

Lisa Merrill, ScD
Sabrina E. Noel, PhD, RDN
Bess Dawson-Hughes, MD
Katherine L. Tucker, PhD
Liam Fouhy, PhD
Mahdi Garelnahbi, PhD
Dhimiter Bello, PhD
Soumita Das, PhD
Pengyuan Liu, PhD
Larence Parnell, PHD
Gokalp Kurtoglu, MD

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