Osteoporos Int
DOI 10.1007/s00198-017-4049-5

ORIGINAL ARTICLE

Greater yogurt consumption is associated with increased bone mineral density and physical function in older adults

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Received: 8 November 2016 / Accepted: 10 April 2017

Abstract
Summary In this cohort of community dwelling older adults (>60 years), we observed significant positive associations between the frequencies of yogurt intake with measures of bone density, bone biomarkers, and indicators of physical function. Improving yogurt intakes could be a valuable health strategy for maintaining bone health in older adults.
Introduction The associations of yogurt intakes with bone health and frailty in older adults are not well documented. The aim was to investigate the association of yogurt intakes with bone mineral density (BMD), bone biomarkers, and physical function in 4310 Irish adults from the Trinity, Ulster, Department of Agriculture aging cohort study (TUDA).
Methods Bone measures included total hip, femoral neck, and vertebral BMD with bone biochemical markers. Physical function measures included Timed Up and Go (TUG), Instrumental Activities of Daily Living Scale, and Physical Self-Maintenance Scale.
Results Total hip and femoral neck BMD in females were 3.1–3.9% higher among those with the highest yogurt intakes ($n = 970$) compared to the lowest ($n = 1109$; $P < 0.05$) as were the TUG scores (−6.7%; $P = 0.013$). In males, tartrate-resistant acid phosphatase (TRAP 5b) concentrations were significantly lower in those with the highest yogurt intakes (−9.5%; $P < 0.0001$). In females, yogurt intake was a significant positive predictor of BMD at all regions. Each unit increase in yogurt intake in females was associated with a 31% lower risk of osteopenia (OR 0.69; 95% CI 0.49–0.96; $P = 0.032$) and a 39% lower risk of osteoporosis (OR 0.61; 95% CI 0.42–0.89; $P = 0.012$) and in males, a 52% lower risk of osteoporosis (OR 0.48; 95% CI 0.24–0.96; $P = 0.038$).
Conclusion In this cohort, higher yogurt intake was associated with increased BMD and physical function scores. These results suggest that improving yogurt intakes could be a valuable public health strategy for maintaining bone health in older adults.

Keywords Aging · BMD · Frailty · Physical function · Yogurt

Introduction

Osteoporosis is an increasingly common, chronic condition estimated to affect over 200 million individuals worldwide [1] with 6% of men and 21% of women aged 50–84 years affected in the EU alone [2]. It is characterized by decreased bone mineral density (BMD) with a significantly increased risk of fracture and, subsequently, morbidity and mortality [3]. The condition has been estimated to cause over 8.9 million fractures annually, with osteoporotic fractures accounting for 0.8% of the global burden of non-communicable disease and the loss of over 5.8 million disability-adjusted life years (DALYs) [4–6].

The development of osteoporosis can be influenced by a range of both demographic and lifestyle factors [1, 7, 8]. However, maintaining an optimal nutritional status is also a

Electronic supplementary material The online version of this article (doi:10.1007/s00198-017-4049-5) contains supplementary material, which is available to authorized users.

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Published online: 01 May 2017

key preventative measure, particularly for older adults (>50 years) [9]. Of the major food groups, dairy foods are one of the richest sources of the macro and micro nutrients that contribute to bone health such as protein, calcium, magnesium, and the B vitamins [10–14]. For example, dairy products are the primary source of calcium across most industrialized countries in Europe and the USA [11, 12]. Previous data from observational studies and randomized controlled trials (RCTs) have reported significant positive associations between dairy intakes and bone health as reviewed in recent commentaries and government reports [15, 16]. In one 12-year follow-up analysis of the Framingham Offspring Study (n = 2506; mean age 55 years), yogurt intake alone was positively associated with hip trochanter BMD and had a weak protective trend with hip fracture reduction [17]. Furthermore, fermented milk products have been associated with a lower fracture incidence and mortality [18]. There is, however, little information on the associations of yogurt intake with bone health biomarkers and with measures of functionality. In the current study, we examined the association of yogurt intakes with BMD, biochemical markers of bone health, and physical function measures in a large cohort of free-living older adults (n = 4310, age range 60–102 years).

Subjects and methods

Data analyzed for the current study originated from the Trinity Ulster Department of Agriculture (TUDA) aging cohort study, a large study of older Irish adults (>60 years) designed to investigate nutritional factors, related gene-nutrient interactions and a range of health and lifestyle factors in the development of chronic diseases of aging. Further details of sampling and recruitment have been described previously [18–21]. Of the 5186 participants recruited, 3 with severe frailty (replied no or had a missing answer to the self-feeding question in the Physical Self-Maintenance questionnaire (PSM)), 866 with cognitive impairment (Mini-Mental State Examination (MMSE) score <25), and those with a missing response to the yogurt intake question (n = 7) were excluded from the physical function analysis leaving a total of 4310 participants (Supplemental Fig. 1). Approximately 1699 participants did not have BMD measures taken. In addition to these exclusions, participants who reported receiving medications that could affect bone mineral metabolism (bisphosphonates; aromatase inhibitors; gonadotropin releasing hormone analogues or luteinizing hormone releasing agonists; anti-androgen medication; parathyroid hormone (PTH) treatment; strontium treatment; anti-epileptic medications; Paget's disease treatment) were also excluded from the BMD and bone biomarker analysis (Supplemental Fig. 1). Ethical approval was granted by the relevant authorities in each jurisdiction: the Research Ethics Committee of St. James's Hospital and The Adelaide and Meath Hospital, Dublin, and the Office for Research Ethics Committees Northern Ireland (ORECNI; reference 08/NI/RO3113) with corresponding approvals from the Northern and Western Health and Social Care Trusts, Northern Ireland.

Lifestyle and medications

Data associated with lifestyle factors were obtained by questionnaire. Information included gender, age, ethnicity, physical activity (reported as yes/no in the last two weeks), smoking status, and alcohol intake. Full details of dietary supplement and vitamin use including dose, frequency, and duration were confirmed from packaging or prescription information. A small number of supplements listed were unidentifiable or contained unidentifiable ingredients; individuals consuming such supplements were excluded from analysis.

Dietary dairy intake servings

Participants were given a modified food frequency questionnaire (FFQ) which asked if the participant consumed yogurt, milk (approximated as glasses of milk per day), and/or cheese and if yes, how often for each dairy type. The total frequency of the daily intake serving for yogurt, milk, and cheese was calculated from the FFQ responses (Supplemental Table 1). These values were then separated into tertiles of non-consumers, low consumers, and high consumers for each dairy type. Information was also recorded for the frequency of consumption of red meat and poultry (total meat), oily and white fish (total fish), and egg intakes. No product brand name or serving size information was available for the dairy intakes; however, the average serving intake size in a representative study of older Irish adults (>65 years) recruited at the same time period (as part of the National Adult Nutrition Study (NANS)) was 114 g (g) for yogurt, 123 g for milk, and 35 g for cheese [22].

Biochemical analysis

A non-fasting blood sample (50 ml) was collected by venipuncture into an evacuated clotting tube (Sarstedt; Numbrecht, Germany) by a trained phlebotomist. Samples were kept chilled and centrifuged (3000 rpm for 15 min) within 3 h of collection, and serum aliquots were labeled and stored at −80 °C until required for analysis. Serum bone biomarkers were measured in duplicate using an automated enzyme immunoassay method (EIA) following the manufacturer's instructions (Triturus®, Immunodiagnostics (IDS) limited, Boldon, Tyne & Wear, UK). Inter-assay CVs were as

follows: serum osteocalcin (OC) <4.5% (reference range for males of 9.6–40.8 ng/ml and for postmenopausal women 12.8–55.0 ng/ml), C-terminal telopeptides of type I collagen (CTX) <3.1% (reference range is 0.020 ng/ml to 3.380 ng/ml), bone-specific alkaline phosphatase (BAP) <1.5% (reference range for males of 5.7–32.9 μg/ml and for postmenopausal women 5.5–27.1 μg/ml), and tartrate-resistant acid phosphatase (TRAP 5b) <1.6% (reference range for males of 55–79 ng/ml and for postmenopausal women 41–81 ng/ml). Intact PTH was measured at St. James's Hospital, Dublin using an electrochemiluminescence immunoassay (ECLIA) (Modular E170, Roche Diagnostics, Dublin, Ireland) with an inter-assay CV of <2.9% and an assay measurement range of 1.2–5000 pg/ml. Vitamin D (25-hydroxyvitamin D (25(OH)D)) concentrations were quantified using LC-MS/MS (API 4000; AB SCIEX; Chromsystems GmbH) with an inter-assay CV of <5.7% (detection range 7.5–624 nmol/l) [18, 19]. Renal function tests (creatinine) were analyzed using a Roche Cobas c701 (Roche 8000 modular system) with an inter-assay CV <5%. Glomerular filtration rate (GFR) was estimated by use of the Cockcroft-Gault equation.

BMD and physical function measures

BMD was measured by dual energy X-ray absorptiometry (DXA) (Lunar iDXA™, UK) performed at the hip, the femoral neck, and the vertebral column by a fully trained operator according to ionizing radiation medical exposure regulations (IRMER), and scans were subsequently interpreted with the assistance of a radiographer. Results were expressed as grams of BMD per square centimeter (g/cm^2) and as T-scores using the manufacturer's reference database. Osteopenia was defined as a BMD T-score between −1.0 and −2.5 at any site and osteoporosis defined as a BMD T-score >−2.5 at any site (below the young adult mean) [23]. Physical function was primarily assessed by use of the Timed Up and Go (TUG) test which measured the time it took a participant to rise from a chair, walk three meters, turn around, walk back to the chair, and sit down again. A score of 12 s or more has been reported as an indication of reduced mobility [24]. Additional functionality measures included the PSM and the Instrumental Activities of Daily Living Scale (IADL) [25].

Statistical analysis

The statistical analysis was performed using the Statistical Package for Social Sciences (version 23.0; SPSS UK Ltd.; Chersey, UK). Data were assessed for normality and where necessary, data were log-transformed for normalization purposes. Data within tables are primarily expressed as adjusted means with 95% confidence intervals. Estimated marginal means were adjusted for age, gender, BMI, GFR, calcium, and vitamin D supplement usage (yes/no). Where appropriate, an independent Student's t test, one-way ANOVA, or ANCOVA with pairwise comparisons was applied to determine statistical differences between groups ($P < 0.05$). Data were corrected for multiple comparisons using the Bonferroni correction. Categorical variables were assessed by chi-square analysis. Hierarchical multiple regression models with adjustment for age, gender, education, BMI, smoking status, alcohol consumption, physical activity (in past two weeks), vitamin D and calcium supplement usage, 25(OH) D concentration, daily milk, yogurt, cheese, total meat (red meat and poultry), total fish (oily and white), and daily egg servings were applied to determine significant predictors of BMD concentrations and physical function measure scores. To determine the predictors of bone health (osteopenia or osteoporosis), a multinomial logistic regression model was used (with normal bone health as the reference category) with relevant copredictors including the nominal variables age, BMI, education, 25(OH) D concentration, PTH concentration, GFR, frequency of daily servings of milk, yogurt, cheese, total meat, and total fish and eggs and the categorical variables gender (reference male), vitamin D supplement user (reference non-vitamin D supplement user), non-smoker (reference smoker), non-alcohol consumer (reference alcohol consumer), and physical activity: yes (reference physical activity: no).

Results

General characteristics of participants in the TUDA cohort as defined by gender are shown in Table 1. The majority of participants were female (67.4%), who were significantly older ($P = 0.004$), lighter ($P < 0.0001$), and contained a higher proportion of individuals receiving vitamin D or calcium supplements ($P < 0.0001$) in comparison with males. A higher percentage of females were yogurt consumers with mean daily yogurt servings significantly higher than males (0.42 vs 0.32/day, respectively) ($P < 0.0001$). In yogurt consumers, the proportion who answered yes to physical activity was 80.9% while in non-consumers, it was 74.7%. In participants who had measures of BMD performed, 41.3% had osteopenia while 27% had osteoporosis which was more common in females than males (35.6 vs 14.8% respectively; $P < 0.0001$). Data for the BMD, the bone biomarker concentrations, and the physical function measures across the frequency of daily yogurt intakes (split by gender) are presented in Tables 2 and 3. In females, after adjustment for covariates (and exclusion of those receiving medications that may affect BMD), total hip BMD was 3.1% higher ($P = 0.005$) and femoral neck BMD was 3.9% higher ($P < 0.0001$) in the high yogurt consumers (>once per day serving) compared to the non-consumers (<once per week serving/never). In males,

Table 1 Demographic and health characteristics of the TUDA cohort study by gender

Variable	Total (n = 4310)	Male (n = 1405)	Female (n = 2905)	P value
Age[a] (years)	73.1 (7.9)	72.6 (7.8)	73.3 (8.0)	0.004
60–69[b] (years), n (%)	1690 (39.2)	567 (40.4)	1123 (38.7)	0.284
70–79[b] (years), n (%)	1697 (39.4)	568 (40.4)	1129 (38.9)	0.325
>80,[b] n (%)	923 (21.4)	270 (19.2)	653 (22.5)	0.014
Age finished education[a] (years)	16.2 (3.0)	16.2 (3.2)	16.2 (2.9)	0.564
Health and lifestyle				
BMI[a] (kg/m^2)	28.0 (5.3)	28.6 (4.4)	27.7 (5.7)	<0.0001
GFR[a] (ml/min)	69.4 (24.4)	77.1 (25.4)	65.6 (22.9)	<0.0001
Current smoker,[b] n (%)	515 (12.0)	156 (11.1)	359 (12.4)	0.231
Current alcohol consumer,[b] n (%)	2551 (59.2)	919 (65.5)	1632 (56.2)	<0.0001
Physical activity in last two weeks,[b] n (%)	3403 (79.0)	1094 (77.9)	2309 (79.5)	0.214
Receives Bone medications,[b] n (%)	1484 (34.4)	244 (17.4)	1240 (42.7)	<0.0001
Yogurt consumer,[b] n (%)	2658 (61.7)	725 (51.6)	1933 (66.5)	<0.0001
Milk (as a drink) consumer,[b] n (%)	1806 (42.9)	640 (46.4)	1166 (41.1)	0.001
Cheese consumer,[b] n (%)	3651 (84.7)	1209 (86.0)	2442 (84.1)	0.089
Supplement use,[b] n (%)				
Vitamin D supplement user	2042 (47.8)	447 (33.2)	1595 (58.4)	<0.0001
Calcium supplement user	1742 (40.4)	308 (21.9)	434 (49.4)	<0.0001
Phosphate supplement user	262 (6.1)	82 (5.8)	180 (6.2)	0.643

Values are means (±SD) for continuous variables

[a] Student's independent t test was used to test differences between log-transformed continuous variables

[b] Chi-square tests were used to test differences between categorical variables

vertebral BMD was 4.1% higher in low yogurt consumers compared with non-consumers (P = 0.028). Similarly, mean vitamin D concentrations (after exclusion of those receiving vitamin D supplements) were 12.9% higher (P = 0.006) and mean TRAP 5b concentrations were 9.5% lower (P = 0.003) in the male high yogurt consumers compared to the non-consumers. No significant change in concentration across yogurt consumption was observed for PTH or the remaining bone biomarkers in either gender (Tables 2 and 3).

For physical function measures in females, non-consumers of yogurt were 0.9 s (6.7%) slower than the high consumers (13.8 vs 12.9 s; P = 0.020). Similarly, PSM and IADL scores were significantly higher in the yogurt high consumers compared to the non-consumers (P = 0.010 and P = 0.003, respectively). No significant difference was observed for males. This analysis was then repeated to examine BMD, bone biomarker, and physical function measures across frequency of milk and cheese intakes (Supplemental Tables 2–5). No significant difference was observed across milk intake frequencies for BMD or bone biomarker concentrations. However, TUG scores were significantly lower in the non-milk consumers compared to the high milk consumers in both men and women (P < 0.05). In addition, there were slight increases in PSM and IADL scores across milk intakes in both genders while no significant difference was observed across cheese intake frequencies for any of the measures.

In a hierarchical multiple regression model (Table 4) examining predictors of BMD, bone markers, and physical function measures, increasing yogurt intake was a significant positive predictor for BMD in females at all three sites after adjustment for relevant covariates. For instance, with each unit increase in yogurt intake (i.e., an increase of one serving per week), total hip BMD increased by 0.015 g/cm^2 (P = 0.002), vertebral BMD by 0.026 g/cm^2 (P = 0.005), and femoral neck BMD increased by 0.023 g/cm^2 (P < 0.0001). Furthermore, with each yogurt unit increase, TUG scores decreased by 0.59 s (P = 0.021). In men only, with each unit increase in yogurt intake, concentrations of TRAP 5b decreased by 0.118 μg/l (P < 0.0001). Significant predictors of bone health status are outlined in Tables 5 and 6. Daily yogurt intake was a significant predictor of bone health with each unit increase in yogurt intake associated with a 31% lower risk of having osteopenia (OR 0.69; 95% CI 0.49–0.96; P = 0.032) and a 39% lower risk of being characterized as osteoporotic (OR 0.61; 95% CI 0.42–0.89; P = 0.012) in females and in males a 52% lower risk of osteoporosis (OR 0.48; 95% CI 0.24–0.96; P = 0.038). For females, those on vitamin D supplements had a significantly reduced risk of osteopenia (OR 0.51; 95% CI 0.34–

Table 2 Comparison of bone mineral density (BMD), biomarkers of bone health, and mean frailty measures across frequencies of daily yogurt intake in females in the TUDA cohort study

	Tertile of daily yogurt intakes								
	Non-consumer			Low consumer			High consumer		
	Mean yogurt frequency (0.0 daily/<once per week/never)			Mean yogurt frequency (0.34 daily/2–3 times per week)			Mean yogurt frequency (1.03 daily/ >once per day)		
	n = 970			*n* = 826			*n* = 1109		
Variable	*n*	Mean	95% CI	*n*	Mean	95% CI	*n*	Mean	95% CI
BMD region[a] (g/cm^2)									
Total hip	320	0.890	0.877–0.903	331	0.904	0.891–0.917	406	0.918*	0.907–0.930
Femoral neck	319	0.824	0.812–0.836	331	0.843	0.831–0.855	405	0.857**	0.846–0.867
Vertebral	260	1.005	0.984–1.025	251	1.027	1.006–1.047	330	1.036	1.018–1.054
Bone health biomarkers									
CTX[a] (ng/ml)	226	0.34	0.32–0.36	258	0.33	0.31–0.35	278	0.32	0.30–0.34
OC[a] (ng/ml)	225	19.2	18.0–20.5	252	18.7	17.5–19.8	278	18.8	17.7–19.9
BAP[a] (μg/l)	226	17.8	16.9–18.7	252	18.0	17.1–18.8	278	17.7	16.9–18.5
TRAP 5b[a] (μg/l)	226	3.30	3.17–3.43	252	3.29	3.17–3.41	279	3.24	3.12–3.35
25(OH)D[b] (nmol/l)	412	41.0	38.9–43.2	347	43.4	41.1–45.7	361	43.5	41.2–45.8
PTH[a] (pg/ml)	505	50.0	47.5–52.5	446	47.0	44.4–49.7	578	46.3	43.9–48.6
Physical function measures[b]									
Timed Up and Go (s)	868	13.8	13.3–14.2	740	13.0	12.5–13.5	1016	12.9*	12.5–13.3
IADL	906	24.4	24.2–24.6	751	24.5	24.3–24.8	1014	24.8*	24.6–25.0
PSM	913	22.9	22.8–23.0	767	22.9	22.8–23.0	1035	23.1*	23.0–23.2

Values are estimated marginal means (95% CI) adjusted for multiple covariates. Differences in means were assessed by pairwise comparisons and adjusted for multiple comparisons: Bonferroni correction. Non-consumer frequency range (0–0.07 U/<once per week/never); low consumer frequency range (>0.07–0.50 U/>once per week to 3–4 times per week); high consumer frequency range (>0.50–2.00 U/>3–4 times per week to twice per day). OC reference range for males of 9.6–40.8 ng/ml and for postmenopausal women 12.8–55.0 ng/ml; CTX reference range is 0.020 ng/ml to 3.380 ng/ml; BAP reference range for males of 5.7–32.9 μg/ml and for postmenopausal women 5.5–27.1 μg/ml; TRAP 5b reference range for males of 55–79 ng/ml and for postmenopausal women 41–81 ng/ml; intact PTH measurement range of 1.2–5000 pg/ml and 25(OH) D detection range 7.5–624 nmol/l

BAP bone-specific alkaline phosphatase, *CTX* C-terminal telopeptides of type I collagen, *IADL* Instrumental Activities of Daily Living Scale, *OC* osteocalcin, *PSM* Physical Self-Maintenance Scale, *PTH* parathyroid hormone, *TRAP 5b* tartrate-resistant acid phosphatase 5b, *25(OH) D* 25-hydroxyvitamin D

*$P < 0.05$; **$P < 0.0001$ different from the lowest yogurt intake tertile

[a] Adjusted for age, education, BMI, GFR, physical activity, total daily serving milk (glass only), total daily serving of cheese, and calcium or vitamin D supplements (participants receiving medications that could affect bone metabolism were removed from the analysis)

[b] Adjusted for age, BMI, total daily serving milk (glass only), and total daily serving of cheese (participants receiving vitamin D supplements were removed from the 25(OH)D analysis)

0.76; $P = 0.001$) and a significantly reduced risk of osteoporosis (OR 0.41; 95% CI 0.26–0.64; $P < 0.0001$). For males, those on vitamin D supplements also had a significantly reduced risk of osteoporosis (OR 0.40; 95% CI 0.22–0.72; $P = 0.003$).

Discussion

In this study, we observed significant positive associations of increased frequency of yogurt intakes with bone health and measures of physical function in a cohort of older adults. Females with the highest yogurt intakes had significantly higher BMD and better physical function scores compared to individuals with the lowest intakes. Furthermore, we show for the first time that, after adjustment for covariate predictors, each unit increase in yogurt intake significantly decreased the odds of being characterized as osteopenic or osteoporotic in women and as osteoporotic in men.

The significant positive associations of yogurt with BMD within this large study are consistent with previous observations from the Framingham Offspring observational study [17]. In 2733 adults (26–85 years), higher yogurt intake was positively associated with trochanteric BMD over a 12-year

Table 3 Comparison of bone mineral density (BMD), biomarkers of bone health, and mean frailty measures across frequencies of daily yogurt intake in males in the TUDA cohort study

	Tertile of daily yogurt intakes								
	Non-consumer			Low consumer			High consumer		
	Mean yogurt frequency (0.0 daily/<once per week/never)			Mean yogurt frequency (0.29 daily/2–3 times per week)			Mean yogurt frequency (1.00 daily/ >once per day)		
	n = 680			*n* = 392			*n* = 333		
Variable	*n*	Mean	95% CI	*n*	Mean	95% CI	*n*	Mean	95% CI
BMD region[a] (g/cm^2)									
Total hip	339	1.041	1.026–1.056	239	1.057	1.039–1.075	185	1.058	1.038–1.079
Femoral neck	339	0.925	0.911–0.939	239	0.945	0.928–0.962	185	0.947	0.928–0.966
Vertebral	271	1.207	1.183–1.231	180	1.258*	1.229–1.287	134	1.235	1.201–1.269
Bone health biomarkers									
CTX[a] (ng/ml)	306	0.27	0.25–0.29	231	0.27	0.25–0.29	169	0.27	0.25–0.29
OC[a] (ng/ml)	305	14.7	13.9–15.7	231	14.9	13.9–15.8	169	15.0	13.8–16.2
BAP[a] (μg/l)	305	16.2	15.3–17.1	231	15.7	14.6–16.7	168	16.2	15.0–17.5
TRAP 5b[a] (μg/l)	306	2.96	2.87–3.06	231	2.89	2.78–3.00	169	2.69**	2.56–2.82
25(OH)D[b] (nmol/l)	443	41.8	39.7–44.0	243	49.3**	46.3–52.2	205	47.6*	44.4–50.8
PTH[a] (pg/ml)	527	45.2	42.7–47.8	310	43.7	40.4–47.0	258	47.9	44.3–51.5
Physical function measures[b]									
Timed Up and Go (s)	627	13.3	12.6–13.9	361	12.0*	11.1–12.8	302	12.7	11.8–13.6
IADL	636	24.6	24.3–24.9	372	25.4*	25.0–25.8	309	24.7	24.4–25.2
PSM	647	23.2	23.1–23.4	374	23.4	23.2–23.5	315	23.2	23.0–23.4

Values are estimated marginal means (95% CI) adjusted for multiple covariates. Differences in means were assessed by pairwise comparisons and adjusted for multiple comparisons: Bonferroni correction. Non-consumer frequency range (0–0.07 U/<once per week/never); low consumer frequency range (>0.07–0.50 U/>once per week to 3–4 times per week); high consumer frequency range (>0.50–2.00 U/>3–4 times per week to twice per day). OC reference range for males of 9.6–40.8 ng/ml and for postmenopausal women 12.8–55.0 ng/ml; CTX reference range is 0.020 ng/ml to 3.380 ng/ml; BAP reference range for males of 5.7–32.9 μg/ml and for postmenopausal women 5.5–27.1 μg/ml; TRAP 5b reference range for males of 55–79 ng/ml and for postmenopausal women 41–81 ng/ml; intact PTH measurement range of 1.2–5000 pg/ml and 25(OH)D detection range 7.5–624 nmol/l

BAP bone-specific alkaline phosphatase, *CTX* C-terminal telopeptides of type I collagen, *IADL* Instrumental Activities of Daily Living Scale, *OC* osteocalcin, *PSM* Physical Self-Maintenance Scale, *PTH* parathyroid hormone, *TRAP 5b* tartrate-resistant acid phosphatase 5b, *25(OH) D* 25-hydroxyvitamin D

*$P < 0.05$; **$P < 0.0001$ different from the lowest yogurt intake tertile

[a] Adjusted for age, education, BMI, GFR, physical activity, total daily serving milk (glass only), total daily serving of cheese, and calcium or vitamin D supplements (participants receiving medications that could affect bone metabolism were removed from the analysis)

[b] Adjusted for age, BMI, total daily serving milk (glass only), and total daily serving of cheese (participants receiving vitamin D supplements were removed from the 25(OH)D analysis)

follow-up with a weak protective trend of yogurt (but not other dairies) on the risk of hip fracture. In a cohort of 61,000 Swedish women (aged 39–74 years), fermented milk products (yogurt) were associated with a significant decrease in fracture incidence and mortality over a mean follow-up of 20 years. With each increase in fermented dairy intakes, hip fractures were reduced by 10–15% [18]. Although the current dataset did not have data on fracture incidence, the effect of increased yogurt intake seen in this cohort has the potential to reduce non-vertebral fractures by up to 46% in women, as fracture risk reduction has been modeled as 46% decrease for 3% hip BMD increase [26]. However, it is important to note that the meta-analysis [26] was conducted in women all diagnosed with osteoporosis whereas in the current study, only 60% of the women were osteoporotic and thus the potential for yogurt to reduce fractures at the same rate should be viewed with caution. The potential protective effects of yogurt on bone health are also supported by the positive associations of yogurt with the bone biomarker Trap 5b, the concentrations of which were 9.5% lower in those with the highest yogurt intake compared to the lowest, though only in men. Trap 5b is a direct marker of osteoclast number and bone resorption (indicating positive bone balance), with better sensitivity than CTX (a by-product of collagen breakdown) [27] and has been

Table 4 Yogurt consumption as a predictor of markers of bone health and physical function in the TUDA cohort study

Variable	Total hip BMD[a] (g/cm^2) β	Femoral neck BMD[a] (g/cm^2) β	Vertebral BMD[a] (g/cm^2) β	TRAP 5b[a] (μg/l) *B*	Timed Up and Go[b] (s) β	IADL[b] β	PSM[b] β
Total sample	0.015 (0.007)	0.023 (0.006)	0.026 (0.011)	−0.118 (0.055)	−0.599 (0.252)	0.220 (0.115)	0.084 (0.054)
P value	0.015	<0.0001	0.016	0.032	0.018	0.056	0.121
Female only	0.024 (−0.008)	0.031 (0.007)	0.034 (0.012)	0.015 (−0.077)	−0.641 (0.277)	0.272 (0.126)	0.157 (0.065)
P value	0.002	<0.0001	0.005	0.847	0.021	0.031	0.016
Male only	0.004 (−0.013)	0.009 (−0.012)	0.012 (−0.021)	−0.292 (0.080)	−0.496 (−0.543)	0.06 (−0.248)	−0.141 (−0.096)
P value	0.761	0.431	0.557	<0.0001	0.361	0.809	0.144

Values are unstandardized beta (β) coefficients (standard error) derived from a hierarchical multiple regression analysis

IADL Instrumental Activities of Daily Living Scale, *PSM* Physical Self-Maintenance Scale, *TRAP 5b* tartrate-resistant acid phosphatase 5b, *25(OH)D* 25-hydroxyvitamin D

[a] Adjustment for age, gender (total sample only), education, BMI, smoking status, alcohol consumption, vitamin D or calcium supplement use, 25(OH)D, GFR, physical activity, total daily serving milk (glass only), total daily serving of cheese, total daily serving of meat (red meat and poultry), total daily serving of fish (white and oily), and total daily serving of eggs (participants receiving medications that could affect bone metabolism were removed from the analysis)

[b] Adjustment for age, gender (total sample only), BMI, total daily serving milk (glass only), total daily serving of cheese, total daily serving of meat (red meat and poultry), total daily serving of fish (white and oily), and total daily serving of eggs

Table 5 The predictors of bone health status of females within the TUDA cohort study

Variable	Odds ratio [95% CI] Osteopenia vs normal (*n* = 411 vs 266)	*P* value	Odds ratio [95% CI] Osteoporosis vs normal (*n* = 360 vs 266)	*P* value
Age (years)	1.02 [0.99–1.06]	0.073	1.04 [1.00–1.08]	0.018
BMI (kg/m^2)	0.93 [0.89–0.96]	<0.0001	0.79 [0.76–0.83]	<0.0001
25(OH)D (nmol/l)	0.99 [0.99–1.00]	0.869	1.00 [0.99–1.01]	0.148
Vitamin D supplement user	0.51 [0.34–0.76]	0.001	0.41 [0.26–0.64]	<0.0001
PTH (pg/ml)	1.00 [0.99–1.01]	0.322	1.00 [0.99–1.01]	0.068
Education (years)	0.97 [0.91–1.03]	0.360	0.95 [0.88–1.02]	0.181
Non-smoker[a]	0.89 [0.50–1.58]	0.710	0.61 [0.34–1.12]	0.116
Non-alcohol user[b]	0.85 [0.60–1.20]	0.372	1.06 [0.72–1.57]	0.740
Physical activity: yes[c]	0.89 [0.56–1.43]	0.645	0.61 [0.35–1.56]	0.078
GFR (ml/min)	0.99 [0.98–1.00]	0.810	1.00 [0.99–1.01]	0.601
Daily yogurt serving	0.69 [0.49–0.96]	0.032	0.61 [0.42–0.89]	0.012
Daily milk serving	0.77 [0.53–1.11]	0.167	0.75 [0.49–1.13]	0.175
Daily cheese serving	1.05 [0.65–1.69]	0.831	1.18 [0.70–2.00]	0.516
Daily meat serving	0.91 [0.58–1.41]	0.676	1.16 [0.70–1.92]	0.546
Daily fish serving	0.94 [0.39–2.26]	0.892	0.48 [0.17–1.35]	0.168
Daily egg serving	1.24 [0.63–2.46]	0.528	1.66 [0.76–3.61]	0.201

Values are odds ratios (95% CI lower and upper) derived from a multinomial logistic regression analysis. Overall reference category is normal bone health based on the WHO definition of osteopenia and osteoporosis [23] using the combination of total hip, femoral neck, or vertebral BMD where available. Participants receiving medications that could affect bone metabolism were removed from the analysis

[a] Reference is smoker

[b] Reference is user

[c] Reference is physical activity: no in the last 2 weeks

Table 6 The predictors of bone health status of males within the TUDA cohort study

Variable	Odds ratio [95% CI] Osteopenia vs normal (n = 332 vs 315)	P value	Odds ratio [95% CI] Osteoporosis vs normal (n = 104 vs 315)	P value
Age (years)	0.98 [0.95–1.01]	0.318	1.01 [0.96–1.06]	0.643
BMI (kg/m[a])	0.96 [0.91–1.01]	0.128	0.80 [0.73–0.87]	<0.0001
25(OH)D (nmol/l)	1.00 [0.99–1.00]	0.703	0.99 [0.98–1.00]	0.213
Vitamin D supplement user	0.79 [0.52–1.21]	0.286	0.40 [0.22–0.72]	0.003
PTH (pg/ml)	1.00 [0.99–1.01]	0.238	1.01 [1.00–1.01]	0.026
Education (years)	0.95 [0.91–1.00]	0.106	0.96 [0.88–1.04]	0.389
Non-smoker[b]	0.58 [0.32–1.07]	0.085	0.39 [0.18–0.85]	0.019
Non-alcohol user[a]	0.77 [0.53–1.11]	0.170	0.94 [0.54–1.64]	0.846
Physical activity: yes[c]	0.59 [0.37–0.92]	0.022	1.09 [0.51–2.35]	0.812
GFR (ml/min)	0.98 [0.97–0.99]	0.016	0.98 [0.97–1.00]	0.128
Daily yogurt serving	0.88 [0.59–1.30]	0.537	0.48 [0.24–0.96]	0.038
Daily milk serving	0.84 [0.58–1.19]	0.338	1.58 [0.99–2.52]	0.055
Daily cheese serving	1.79 [1.11–2.88]	0.016	2.36 [1.16–4.82]	0.018
Daily meat serving	0.64 [0.42–0.99]	0.045	1.10 [0.58–2.07]	0.756
Daily fish serving	0.74 [0.30–1.81]	0.522	0.69 [0.17–2.85]	0.617
Daily egg serving	1.27 [0.69–2.32]	0.439	1.16 [0.47–2.86]	0.740

Values are odds ratios (95% CI lower and upper) derived from a multinomial logistic regression analysis. Overall reference category is normal bone health based on the WHO definition of osteopenia and osteoporosis [23] using the combination of total hip, femoral neck, or vertebral BMD where available. Participants receiving medications that could affect bone metabolism were removed from the analysis

[a] Reference is user

[b] Reference is smoker

[c] Reference is physical activity: no in the last 2 weeks

described as one of the most sensitive markers to monitor the response of diet intervention on bone resorption [28]. Significantly fewer men than women were high yogurt consumers, and it is possible that this marker was detecting subtle bone turnover changes in men only as not enough yogurt was being consumed to affect BMD but enough to affect bone turnover, though this hypothesis needs to be tested. If the results from the current study are confirmed, there is the potential that increased yogurt intakes may add an inexpensive and relatively low-risk strategy to improve bone health in conjunction with bone treatment. However, future research and randomized controlled trials are needed to explore this approach.

Notably, this study also observed that greater consumption of yogurt was associated with a significantly lower TUG score (6.7% difference lowest vs highest yogurt intakes) in women only. TUG has been described as a composite measure of functional mobility with worse scores associated with poorer muscle strength and balance, both of which are risk factors for falling in older adults [29]. Our results are in agreement with Lana et al. who observed that higher consumption of yogurt (and milk) was associated with a lower risk of frailty and a lower risk of a slow walking speed in 1871 community dwelling older adults [30]. Furthermore, in a cross-sectional study of elderly Australian women (no. 1456), higher dairy intake was associated with increased grip strength and decreased likelihood of a lower TUG score [31].

A number of potential mechanisms may explain the observed positive associations. Yogurt naturally contains significant concentrations of bone promoting minerals and vitamins [10–14] which have also been associated with improved frailty measures [32, 33]. In data from the Framingham Heart Study offspring cohort, yogurt consumers were 47 and 55% less likely to have inadequate intakes of vitamins B2 and B12, respectively [34], while in 2797 Italian adults (aged 18–97 years), yogurt consumers were more likely to have adequate intakes of vitamins and minerals compared to non-consumers [35]. Yogurt also contains significant quantities of protein, bioactive peptides, and biocultures which have been associated with bone health and immunological benefits [36–42]. For example, yogurt (and other dairy products) contains branched chain amino acids (BCAAs) which are potent stimulators of muscle protein synthesis [43, 44]. Furthermore, in a recent review, it was suggested that the modifiable nature of the gut microbiome could provide a potential therapeutic target to intervene in musculoskeletal conditions of aging [45]. It is perhaps this unique combination of macro- and micronutrients with bioactive compounds within yogurt that

confers bone promotion and improved physical function. It is also possible that increased yogurt intakes could also be a reflection of a long-term dietary habit of an overall healthy eating pattern and lifestyle [35], though diet quality (including vitamin D and calcium) was adjusted for in the current analysis. Yogurt has been the target of some criticism, especially with the renewed concerns regarding excess sugar intakes and associations with obesity [46] given that some processed "sweetened" yogurts can contain substantial quantities of sugar [47]. Yet not all yogurts have a high sugar content [48], and further exploration is required to identify the types of yogurts and the individual components within that may exhibit health benefits.

We also examined the associations of the other dairy products (milk and cheese) with BMD and functionality. We observed no significant difference in BMD across milk intakes, in line with inconsistent data from previous observational studies. For example, some studies have observed strong associations between childhood and adolescent milk consumption with BMD [49]. For older adults (>60 years), studies have observed no associations or a negative association of milk intakes with fracture risk [49]. The majority of positive randomized trials with milk which have observed significant decreases in the concentrations of bone biomarkers and improvements in bone metabolism have all utilized fortified milk [50]. The milk intakes in the current study were not heavily fortified at this time period (2008–2012) and could account for the lack of any such association. Furthermore, we have previously reported that in this population, with increasing age, milk intakes increased while yogurt intakes significantly decreased [21]. This could help explain why some of the physical function measures became poorer with increased milk intakes. As milk intakes increased, we suggest that there was a loss of a particular protective component within the yogurt that enhanced bone health/improved physical function, though this hypothesis requires verification. Interestingly, we observed no significant associations of cheese intakes with BMD though male participants with osteoporosis were more likely to have a higher frequency of cheese consumption. Cheese products generally have a different nutritional profile in comparison with yogurts and we previously observed in TUDA that cheese intakes had no significant effect on the concentrations of vitamin D, folate, and vitamins B12, B6, or B2 [21]. Furthermore, it has been suggested that the high sodium content of certain cheeses could be less beneficial for bone health by negatively altering calcium metabolism, though few studies have examined this issue [51] and the sodium-induced calciuria hypothesis has not been supported by any long-term observations. Moreover, fortified cheese products have been positively associated with bone metabolism [52]. Further research is needed to identify the relationship between cheese intakes and BMD in men.

Our study has several limitations. The data are observational and cross-sectional, and such observed associations between yogurt intakes and bone health do not necessarily indicate a causal relationship. However, one of the major strengths of this study was the size, as to the best of our knowledge, it is the largest observational study conducted to date investigating such associations. Potential weaknesses of this study also include our reliance on self-reported intakes, and we were unable to quantify the dairy or yogurt intakes through food dairies or other more quantitative dietary collection (and thus did not have information on serving sizes or product types). However, although we could not adjust for total energy intake, we did adjust for frequency of intake of other important dietary components including meat, fish, egg, and other dairy constituents which can give a proxy measure of diet quality. Furthermore, those with severe cognitive impairment or frailty were removed from the analysis to increase recall accuracy.

In conclusion, to our knowledge, this is the largest study to demonstrate an association between the frequency of yogurt intakes, BMD, bone biomarkers, and measures of physical function exclusively within free-living, older adults (>60 years). The findings provide evidence that lower frequency of yogurt intake is significantly associated with a lower BMD and that improving yogurt intakes could be a valuable and cost-effective health measure for maintaining bone health and in reducing frailty in older adults. Future RCT trials are required to assess and investigate the efficacy of such approaches.

Acknowledgements The TUDA study was funded by the Irish Department of Agriculture, Food, and the Marine through the grants 07FHRIUCD1 ("JINGO" 2007–2013) and 13F407 ("JINGO–JPI"/"ENPADASI" 2014–2016) and from the Northern Ireland Department for Employment and Learning under its "Strengthening the all-Ireland Research Base" initiative. Funding for this study was also provided from The National Dairy Council Ireland. The funding organizations had no role in the design and conduct, collection, management, analysis, and interpretation of the data or in the preparation, review, or approval of this manuscript. The authors also acknowledge Drs Martin Healy, Adrian McCann, and Liadhan McAnena for bone biochemical analysis.

Compliance with ethical standards Ethical approval was granted by the relevant authorities in each jurisdiction: the Research Ethics Committee of St. James's Hospital and The Adelaide and Meath Hospital, Dublin, and the Office for Research Ethics Committees Northern Ireland (ORECNI; reference 08/NI/RO3113) with corresponding approvals from the Northern and Western Health and Social Care Trusts, Northern Ireland.

Conflict of interest None.

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