

# Change in Quantitative Ultrasound-assessed Speed of Sound as a Function of Age in Women and Men and Association With the Use of Antiresorptive Agents: The Canadian Multicentre Osteoporosis Study

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## Abstract

**Introduction:** Five-year changes in multisite quantitative ultrasound-assessed speed of sound (SOS in m/s) were studied in a cohort of women and men. The impacts of antiresorptive therapies and menopausal status on SOS were also assessed. **Methodology:** Two SOS assessments, clinical assessments, and comprehensive questionnaires were completed 5 years apart on 509 women and 211 men. Age at first assessment was grouped into: <40 yr, 40–49 yr, 50–59 yr, 60–69 yr, 70–79 yr and 80+ yr. Mean rate of change in SOS at the distal radius and tibia were calculated for each age grouping by sex. SOS changes were stratified by antiresorptive use (yes, no) or menopausal status (premenopausal, postmenopausal, or bilateral oophorectomy). **Results:** Mean losses in SOS occurred over the 5 years in almost all age groupings. In women, mean losses in SOS for the <40 yr, 40–49 yr, 50–59 yr, 60–69 yr, 70–79 yr, and 80+ yr age groupings were –59, –83, –107, –92, –80 and –66 ( $p = 0.30$ ; differences among age groupings) at the radius and –18, –16, –54, –1, –9 and 31 at the tibia ( $p < 0.05$ ), respectively. In men, mean SOS losses were –101, –56, –69, –67, –83 and –127 at the radius ( $p = 0.61$ ) and –46, –61, 0, –35, –29, and –26 at the tibia ( $p = 0.23$ ). At the tibia, women prescribed antiresorptives had a mean increase in SOS (8.6 m/s) whereas untreated participants had a mean loss (–23.0;  $p < 0.001$ ); there was no significant impact at the distal radius. There were no significant differences in change in SOS among menopausal groups ( $p > 0.26$ ). **Conclusions:** Mean SOS generally declined over 5 years in all age groupings of both sexes. The consistent mean losses in SOS over the age spans investigated are coincident with increasing fracture risk. Women on antiresorptive therapy had increased mean SOS over the 5-year assessment period at the tibia, whereas untreated women had mean losses in SOS.

**Key Words:** Quantitative ultrasound; osteoporosis; antiresorptives; menopause; fracture.

## Introduction

Low bone mineral density (BMD), assessed by dual-energy absorptiometry (DXA), is one of the strongest predictors of future fracture.<sup>1,2</sup> However, despite this, most women who experience a fragility fracture have BMD

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levels above the commonly-used osteoporosis threshold, a T-score of  $-2.5$ .<sup>3,4</sup> In attempts to better identify individuals at a heightened risk for fracture, researchers have developed 10-year risk fracture assessment tools by modeling data from numerous large epidemiologic investigations. These tools combine the information gathered from BMD assessment with easily-obtained clinical risk factors (e.g., FRAX or Canadian Association of Radiologists and Osteoporosis Canada 10-year fracture risk assessment tools).<sup>5,6</sup> Fracture risk assessment tools are an improvement from the use of BMD alone, but their prognostic ability could be improved. Further, DXA availability or access is limited or unavailable in some regions and low-dose radiation exposure is concerning for some.

Quantitative ultrasound (QUS) can identify individuals with increased fracture risk. QUS devices are attractive as they are portable, comparatively inexpensive, require minimal training, and free of ionizing radiation.

The BeamMed Omnisense multisite QUS (mQUS) has been shown to prospectively predict fracture risk in women over a 5-year follow-up, independent of DXA BMD, and clinical risk factors.<sup>7</sup> The mQUS device assesses bone at distal radius (DR), tibia (TIB), metatarsal and phalanx sites and provides an estimate of bone stiffness, expressed as speed of sound (SOS; in m/s). SOS values can be compared to normative mQUS values for both women and men,<sup>8</sup> allowing for the identification of individuals at an increased risk for future fracture. It is possible the fracture risk estimate provided from QUS could be used as a surrogate for BMD, or that that information offered through QUS could be combined with BMD assessments and other clinical risk factors to provide a better estimate of future fracture risk.

To date, mQUS data have been cross-sectional and has not investigated how SOS changes with administration of antiresorptive therapy in a population-based sample. Longitudinal data would provide a more accurate representation of the changes observed in patients over time and the ability to study the impact of antiresorptives on mQUS over time will provide valuable information about the utility of using mQUS for monitoring treatment in patients.

The objective of this investigation was to study the 5-year changes in SOS at the DR and TIB sites and to assess the impact of antiresorptives and menopausal status over this period in a large sample of randomly-selected, community-based individuals from the Canadian Multicentre Osteoporosis Study (CaMOS).

## Methods

### Participants

This investigation utilized a subset of participants from the CaMOS cohort. CaMOS is a prospective study that has the goal to better understand the factors that lead to osteoporosis and fractures in Canadians. The methods and objectives of the CaMOS study have been previously published.<sup>9</sup> Briefly, CaMOS is a prospective cohort study

involving 9423 randomly-selected community-dwelling women ( $n = 6539$ ) and men ( $n = 2884$ ) aged 25 years and older at baseline, living within 50 km of 9 major Canadian cities (St. John's, Newfoundland and Labrador; Halifax, Nova Scotia; Quebec City, Quebec; Toronto, Hamilton and Kingston, Ontario; Saskatoon, Saskatchewan; Calgary, Alberta; and Vancouver, British Columbia). Households were randomly selected from a list of residential phone numbers, and participants were randomly selected from eligible household members using a standard protocol. Of those selected, 42% agreed to participate and had a baseline interview. All research carried out in the CaMOS has been approved by local University ethics boards in each of the cities the study had centers in and have satisfied the criteria of the World Medical Association Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. All participants provided informed consent.

### Clinical Assessments

Data collection at baseline and each follow-up visit included an extensive, standardized interviewer-administered questionnaire and a clinical assessment. Full assessments (clinical measures and questionnaires) occurred at baseline, after 3 years (only for participants aged 40–60 years at baseline), after 5, 10, 15, and 20 years. Clinical assessment measures included height, weight and DXA BMD. Areal BMD ( $\text{g}/\text{cm}^2$ ) was assessed at the lumbar spine (L1-4; LS), femoral neck (FN) and total hip (TH) by DXA. DXA machines were cross-calibrated among centers using a common phantom.

Antiresorptive users were defined as anyone that used hormone replacement therapy, bisphosphonates, calcitonin or raloxifene during the 5 years of follow-up. Menopausal status was only assessed in women who did not take antiresorptive therapy during the 5-year observation period and was categorized as premenopausal, menopausal or as having had a bilateral oophorectomy.

### mQUS

At the CaMOS 5-year follow-up investigation, 6 of the clinical sites (Calgary, Halifax, Hamilton, Saskatoon, Quebec City, and St. John's) expanded their protocol by assessing participants with a mQUS (BeamMed MultiSite Quantitative Ultrasound 7000S, Israel), in addition to the normal CaMOS assessments. These mQUS measures were repeated at the 10-year follow-up, but only by the Calgary, Saskatoon, Hamilton and Quebec City sites. Thus, a cohort of participants was prospectively followed by mQUS for a period of approximately 5 years.

At CaMOS baseline all participants were at least 25 years of age; consequently, all participants in this analysis were at least 30 years of age at the first mQUS measurement. The DR and TIB on the nondominant side of the participant were assessed and recorded as SOS (m/s). The metatarsal and phalanx sites were not assessed in

this investigation owing to low collection rates in the follow-up. Details regarding the standard manufacturer-suggested techniques with the mQUS have been described previously and were employed in this investigation.<sup>10-14</sup> Briefly, the mQUS emits and detects acoustic waves at a frequency of 1.25 MHz with the SOS measure defined as the time from sound wave emission to its detection. Daily quality control measurements were employed as recommended by the manufacturer. Intra-observer in-vivo short-term precision has been reported as 0.76% for the DR, 0.47% for the TIB and interobserver precision from 0.77% to 2.39%.<sup>15</sup> mQUS assessments were conducted by one technologist at each of the 6 study centers.

### Statistical Analyses

The rate of change in SOS for each individual was computed based on the number of days between assessments, and then proportionally adjusted to provide a 5-year estimate of the SOS change. Age at first assessment was used as a categorical variable and divided into 10-year age groupings, to <40 yr, 40–49 yr, 50–59 yr, 60–69 yr, 70–79 yr, and 80+ yr. The mean rate of change was calculated for each age grouping, with separate calculations by sex. Standard descriptive statistics were employed to present demographic and clinical data at baseline.

Statistically significant differences among age groups were established with the use of analysis of variance (ANOVA) models. When statistically significant differences were found among groups, Tukey post-hoc analyses were conducted to ascertain statistically significant differences between groups.

For analyses of the impact of age group on change in SOS, an ANOVA was employed with age grouping as the main effect tested.

For the analyses where antiresorptive use or menopausal status were tested with respect to age grouping, a factorial ANOVA model was employed to investigate main effects (antiresorptive use; menopausal status) and interactions (age group x antiresorptive use; age group x menopausal status).

Since there were few men prescribed antiresorptives ( $n = 10$ ) and few women prescribed raloxifene ( $n = 13$ ) or calcitonin ( $n = 3$ ), they were excluded from analyses that compared use and nonuse of antiresorptive therapies. Further, since only one woman under the age of 50 years was prescribed an antiresorptive (HRT), the analyses for this factor were limited to women 50 years of age and older.

All analyses were completed on a Windows-based workstation with Statistica, Version 12 (TIBCO, Palo Alto, USA). Statistical significance was considered to have occurred at an alpha of 0.05.

### Results

In this subset analysis of the CaMOS cohort, there were 509 women and 211 men who received an mQUS

assessment at both years 5 and 10 of follow-up allowing for 5 years of longitudinal data per participant.

The demographics and basic clinical characteristics of the cohort at the first mQUS assessment are provided in Table 1. Approximately a third of the women had received antiresorptive therapy sometime between year 5 and year 10 of CaMos, whereas only 4.7% of the men did. Only 11% of women were premenopausal at baseline. Not surprisingly, the prevalence of self-reported osteoporosis and previous low trauma fracture was higher in the women who were on antiresorptives than those who were not. Measures of SOS at the DR and TIB were similar for treated and untreated women. BMD was lower in all 3 sites in the treated as compared to the untreated women, also as expected since these therapies are often prescribed because of low BMD.

### Changes in SOS at the DR and TIB Sites Over the 5-Year Observation Period Among Age Groups ( $n = 720$ Participants)

At the DR site, the greatest mean SOS losses occurred in the women's 50–59 yr age group, an age generally associated with the onset of menopause (Fig. 1A;  $p = 0.30$ ). For men, the largest mean losses in SOS over 5 years were observed in later life in general – however, with the smaller sample sizes at extremes of the age span ( $n = 16$  and 8), caution is warranted in interpretation (Fig. 1B;  $p = 0.61$ ). At the TIB site, there was a similar pattern as at the DR site with the women, but there were statistically significant mean SOS differences observed between the 50–59 yr group and the 60–69 yr, and 80+ yr age groups (Fig. 1C;  $p < 0.05$ ). For the men, there was no statistically significant difference in the mean change of SOS over 5 years among the age groups (Fig. 1D;  $p = 0.23$ ).

### Changes in SOS at the DR and TIB Sites Over the 5-Year Observation Period Among Age Groups, Stratified by Antiresorptive Use ( $n = 468$ women)

A comparison of women treated with hormone replacement therapy, bisphosphonates, a combination of hormone replacement therapy and bisphosphonates or no treatment demonstrated that there was no overall treatment effect at either the DR or TIB sites ( $p = 0.27$  and 0.35, respectively), nor were there any significant interactions among the 4 groups at any of the age groupings (Fig. 2A and 2B;  $p = 0.83$  and 0.83, respectively). Accordingly, the antiresorptives were collapsed for further analyses.

After combining the antiresorptives, there was no significant main effect of antiresorptives on change in DR SOS ( $p = 0.237$ ), but there was a significant main effect for the change in TIB SOS ( $p < 0.001$ ). Women taking antiresorptives had an overall mean change in TIB SOS of 8.60 (95% confidence interval [CI] –14.49, 29.69) as compared to a mean change of –22.96 (95% CI –41.60, –4.33) in the untreated group. In terms of interactions,

**Table 1**  
 Characteristics at Baseline of 509 Women and 211 Men Aged 39–86 Years of Age Who Participated in the Canadian Multicentre Osteoporosis Study and Who had Quantitative Ultrasound Measures Performed at Years 5 and 10 of the Study

Characteristic at baseline	Women, no (%) <sup>*</sup>			Men, no (%) <sup>*</sup>		
	Users (n = 187) <sup>†</sup>	Nonusers (n = 322) <sup>‡</sup>	All included (n = 509)	Users (n = 10) <sup>†</sup>	Nonusers (n = 201) <sup>‡</sup>	All included (n = 211)
Age, yr (95% CI)	68.0 (66.8–69.3)	65.0 (63.6–66.3)		64.0 (55.8–72.2)	61.7 (59.8–63.5)	
Antiresorptive agent use						
Hormone replacement therapy	85 (45.5)	-	85 (16.7)	0 (0)	-	0 (0)
Bisphosphonates	107 (57.2)	-	107 (21)	10 (100)	-	0 (0)
Raloxifene	13 (7.0)	-	13 (2.6)	0 (0)	-	0 (0)
Calcitonin	3 (1.6)	-	3 (0.6)	0 (0)	-	0 (0)
Total <sup>§</sup>	187 (100)	-	187 (36.7)	10 (100)	-	10 (4.7)
Menopausal status						
Premenopausal	8 (4.3)	49 (15.2)	57 (11.2)	-	-	-
Postmenopausal	107 (57.2)	182 (56.5)	289 (56.8)	-	-	-
Bilateral oophorectomy	68 (36.4)	89 (27.6)	157 (30.8)	-	-	-
Falls in the last month	44 (23.5)	86 (26.7)	130 (25.5)	4 (40)	53 (26.4)	57 (27.0)
Self-reported osteoporosis	79 (42.2)	47 (14.6)	126 (24.8)	7 (70)	7 (3.5)	14 (6.6)
Osteoarthritis	77 (41.2)	120 (37.3)	197 (38.7)	4 (40)	42 (20.9)	46 (21.8)
Rheumatoid arthritis	7 (3.7)	12 (3.7)	19 (3.7)	0 (0)	5 (2.5)	5 (2.4)
Family history of fracture	85 (45.5)	133 (41.3)	218 (42.8)	3 (30)	63 (31.3)	66 (31.3)
Smokers <sup>¶</sup>	80 (42.8)	136 (42.2)	216 (42.4)	5 (50)	117 (58.2)	122 (57.8)
Previous low trauma fracture	63 (33.7)	74 (23.0)	137 (26.9)	4 (40)	41 (20.4)	45 (21.3)
Distal radius SOS, m/s (95% CI)	3951 (3930–3972)	3936 (3920–3952)	3942 (3929–3954)	3921 (3865–3978)	3988 (3971–4006)	3985 (3969–4002)
Tibial SOS, m/s (95% CI)	3813 (3795–3831)	3812 (3796–3827)	3812 (3800–3824)	3828 (3715–3940)	3904 (3888–3920)	3900 (3884–3916)
Bone mineral density, g/cm <sup>2</sup> , mean (95% CI)						
Lumbar spine, L1-L4 vertebrae	0.923 (0.899–0.946)	0.979 (0.960–0.998)	0.958 (0.943–0.973)	0.936 (0.817–1.056)	1.073 (1.050–1.097)	1.067 (1.044–1.090)
Femoral neck	0.682 (0.666–0.699)	0.735 (0.721–0.749)	0.716 (0.705–0.726)	0.702 (0.658–0.747)	0.829 (0.812–0.845)	0.823 (0.807–0.839)
Total hip	0.835 (0.816–0.854)	0.894 (0.878–0.909)	0.872 (0.860–0.884)	0.902 (0.829–0.976)	1.043 (1.024–1.061)	1.036 (1.017–1.054)
Height, cm, mean (95% CI)	159.3 (158.3–160.2)	161.1 (160.4–161.8)	160.4 (159.8–161.0)	175.4 (170.0–181.0)	175.9 (175.0–176.7)	175.8 (175–176.7)
Body mass index, mean (95% CI)	26.5 (25.9–27.1)	27.9 (27.3–28.5)	27.4 (26.9–27.8)	28.0 (25.9–30.1)	27.5 (26.9–28.0)	27.5 (27.0–28.0)

Abbr: CI, confidence interval.

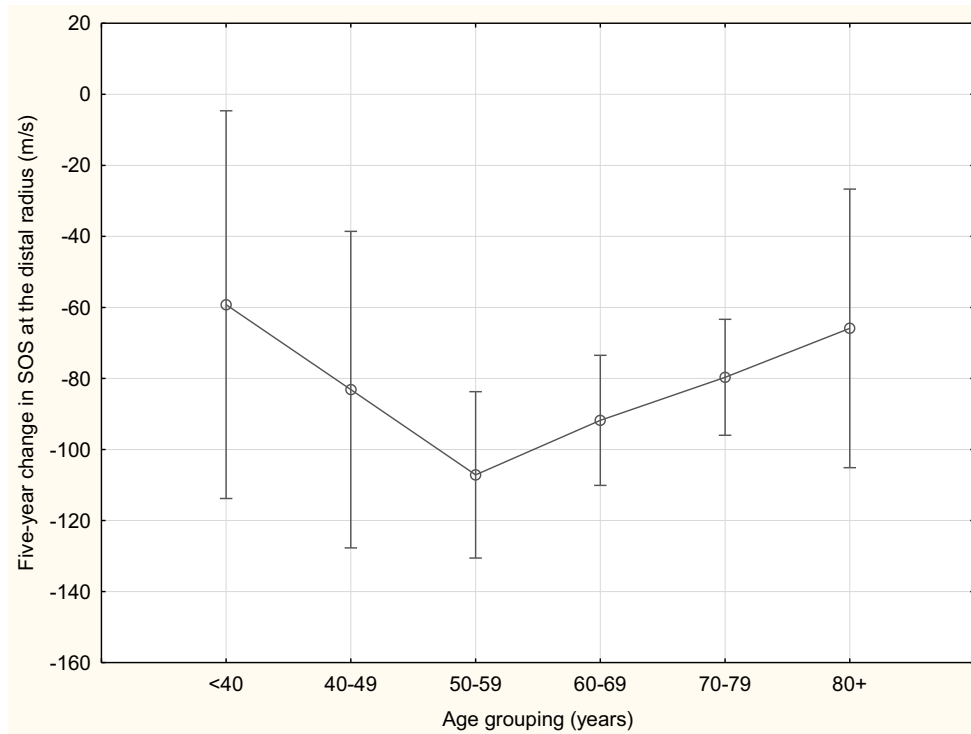
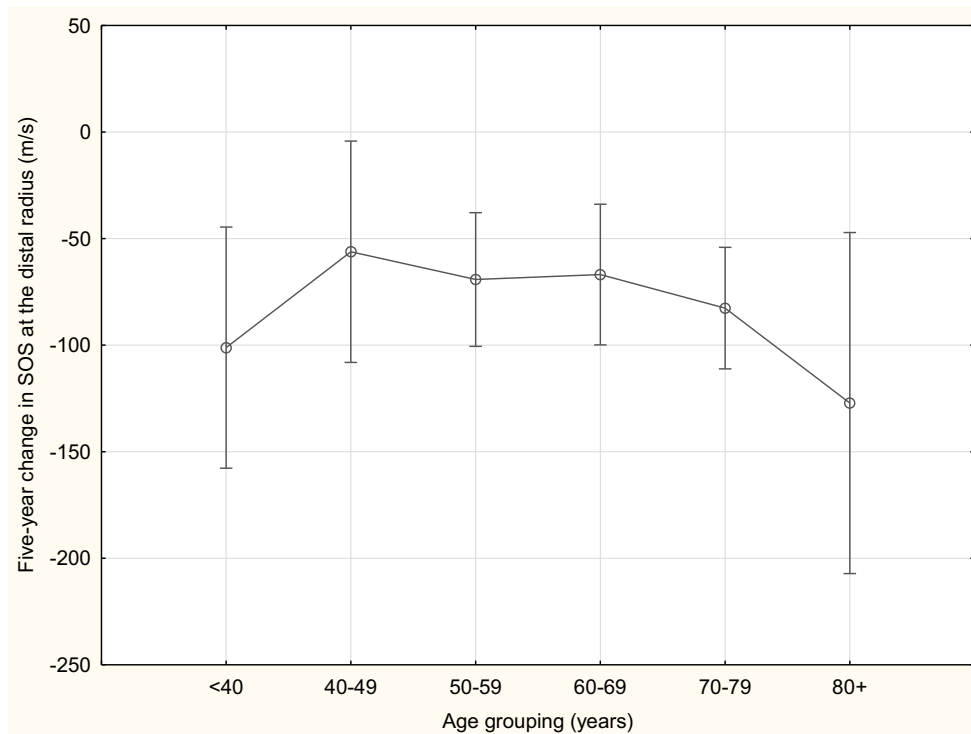
<sup>\*</sup>Unless otherwise indicated.

<sup>†</sup>Users of antiresorptive agents at baseline or during 5-year follow-up.

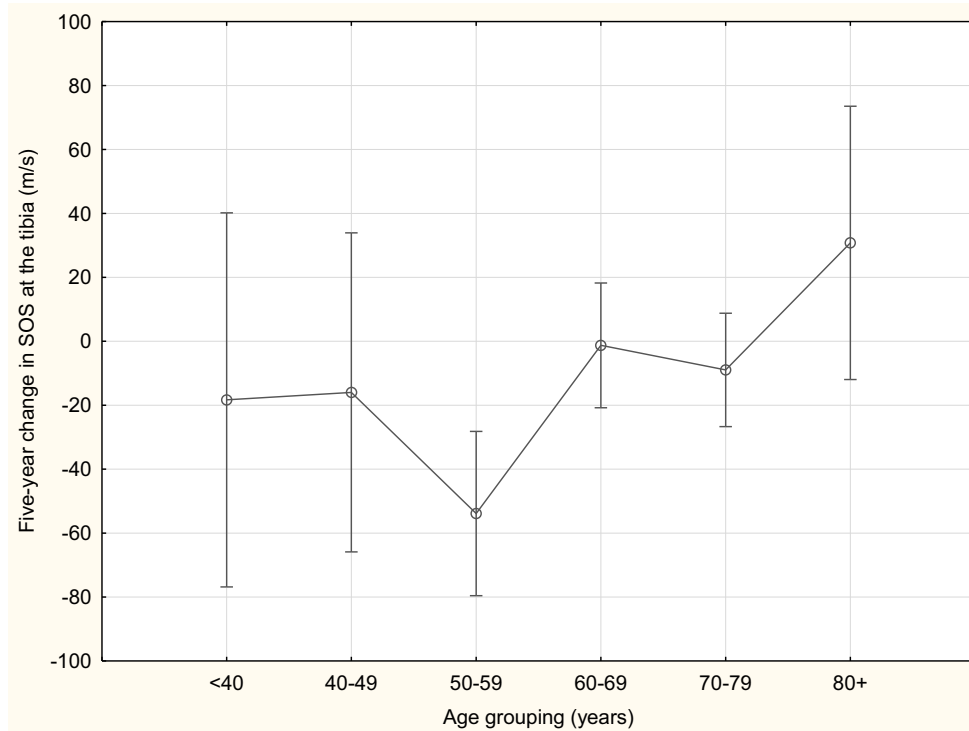
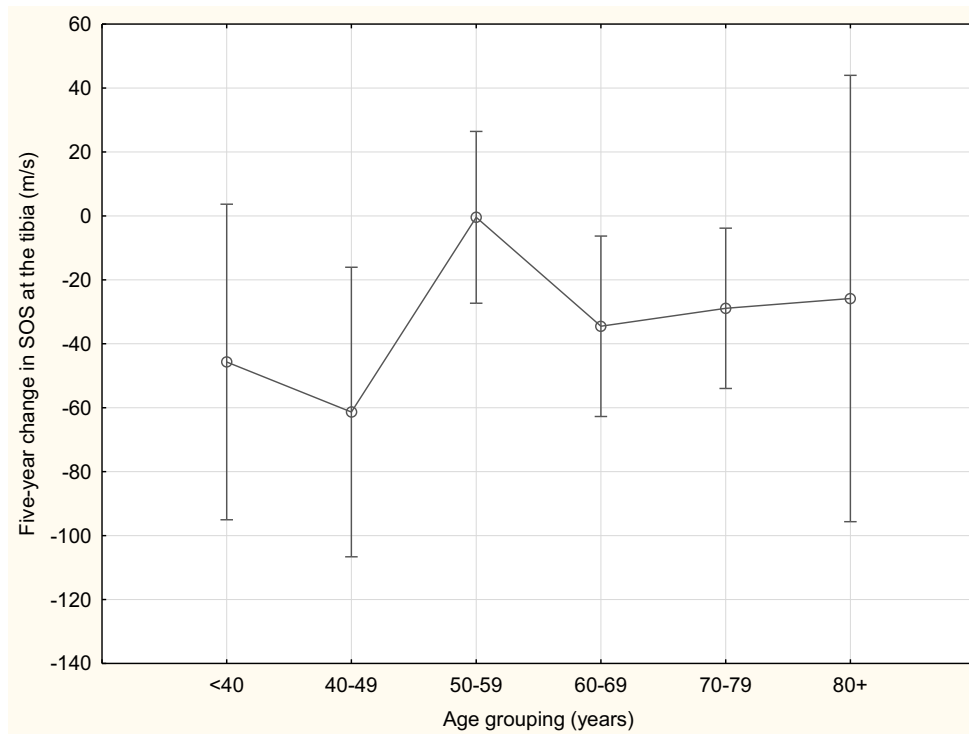
<sup>‡</sup>Nonusers of antiresorptive agents at baseline or during 5-year follow-up.

<sup>§</sup>Total may not equal sum of values because some patients used more than 1 antiresorptive agent.

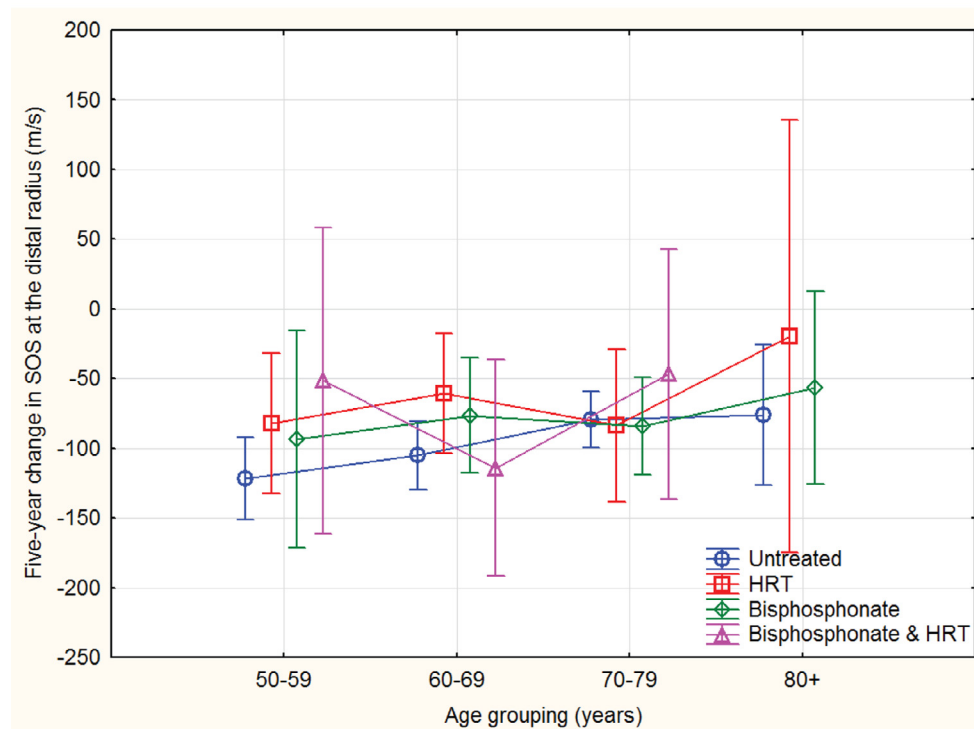
<sup>¶</sup>Ever smoked for at least 6 months.

**A. Distal radius in women.****B. Distal radius in men.**

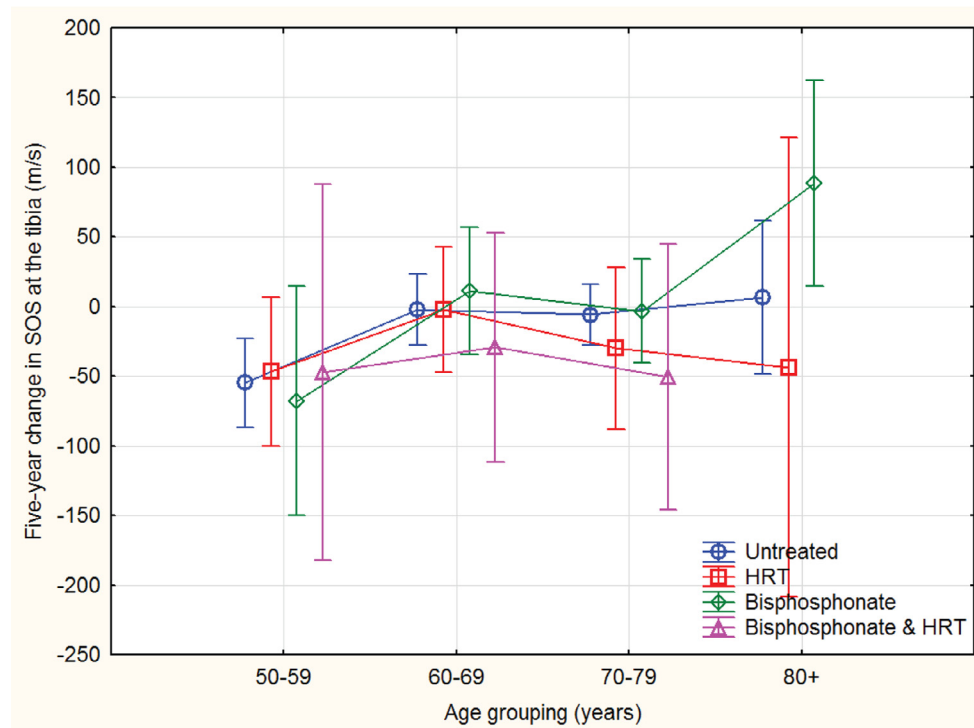
**Fig. 1.** Mean (95% confidence interval) 5-year change of SOS at the DR and TIB among the age groupings in women and men. A. Distal radius in women. *Abbr:* DR, distal radius; SOS, speed of sound; TIB, tibia.

**C. Tibia in women.****D. Tibia in men.****Fig. 1** Continued.

## A. Distal radius in women.

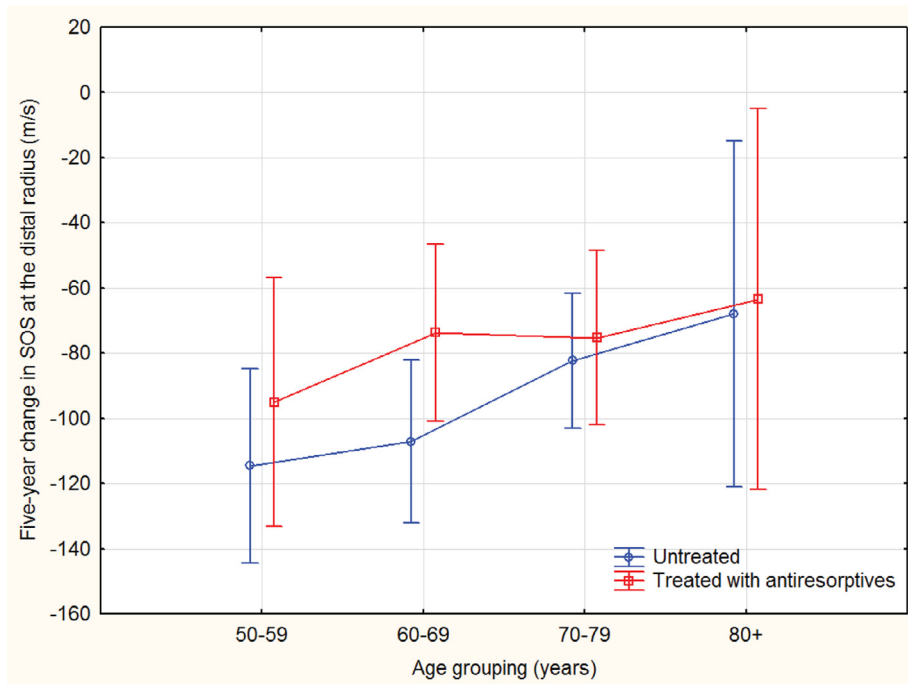


## B. Tibia in women.

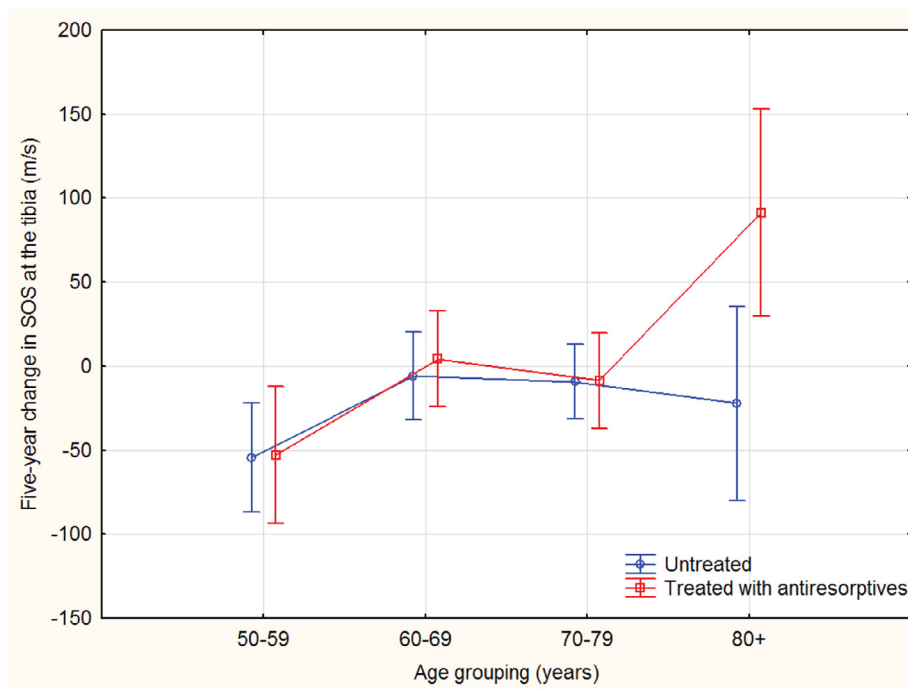


**Fig. 2.** The impact of antiresorptive therapy on mean (95% confidence interval) 5-year change in SOS in women among age groupings. SOS, speed of sound.

**C. Distal radius in women.**



**D. Tibia in women.**



**Fig. 2 Continued.**



there were no statistically significant differences in the change in DR SOS between those women who took an antiresorptive during the 5-year observation period by age grouping (Fig 2C;  $p = 0.75$ ) and no significant interaction between antiresorptive use and age grouping for TIB SOS (Fig 2D;  $p = 0.11$ ).

### **Changes in SOS at the DR and TIB Sites Over the 5-Year Observation Period Among Age Groups, Stratified by Menopausal Status ( $n = 322$ women)**

There were no statistically significant differences among menopausal groups for either change in DR or TIB SOS ( $p = 0.26$  and  $0.48$ , respectively). There were no statistically significant interactions of age grouping by menopausal group in the change in SOS over 5 years (Figures 3A and 3B;  $p = 0.79$  and  $p = 0.56$ , respectively).

## **Discussion**

In this longitudinal investigation, the clear majority of participants had losses in SOS at the DR and TIB sites over the 5 years of observation, regardless of age. The youngest participants were 30 years of age, which is after the time of peak bone mass in men and women, so the observed losses in bone strength, as assessed by SOS, are logical. A large cross-sectional study of Mexican people (1–75 years of age) that utilized the same mQUS as this study, reported that SOS values increased until about 30 years of age in men and women and then declined with age thereafter,<sup>16</sup> similar to what was observed in this study. A study by de Moraes et al<sup>17</sup> with children aged 9–16 years found that QUS-assessed SOS at the phalanges (DMB Sonic Bone Profile; Agea, Carpi, Italy) increased significantly over the pubertal growth period, demonstrating that there is a period of time in the age span where there are substantial increases in QUS-assessed SOS. It bears noting, however, that the study by de Moraes et al<sup>17</sup> used a different machine and assessed a different site than the current investigation.

The losses in SOS were accelerated in the 50–59 year old group of women, significantly so at the TIB, a period coincident with the onset of menopause in the majority of women. DXA BMD and bone turnover marker studies have also reported accelerated bone loss in the perimenopause.<sup>18,19</sup> Estrogen helps modulate bone's response to mechanical loading.<sup>20</sup> While there were losses in SOS at both the radius and tibia during the age group most women are transitioning through menopause, the losses were only significant at the tibia – a weight-bearing site that is generally mechanically loaded to a greater extent than the radius. Since the tibia is a site that is more normally loaded in everyday activity as compared to the radius, the overall decrement in bone mass around the menopause may be relatively more pronounced in the tibia than the radius. At all age groups in the women, there was a greater loss on SOS at the radius than the

tibia, perhaps further highlighting the importance of loading in the preservation of bone mass.

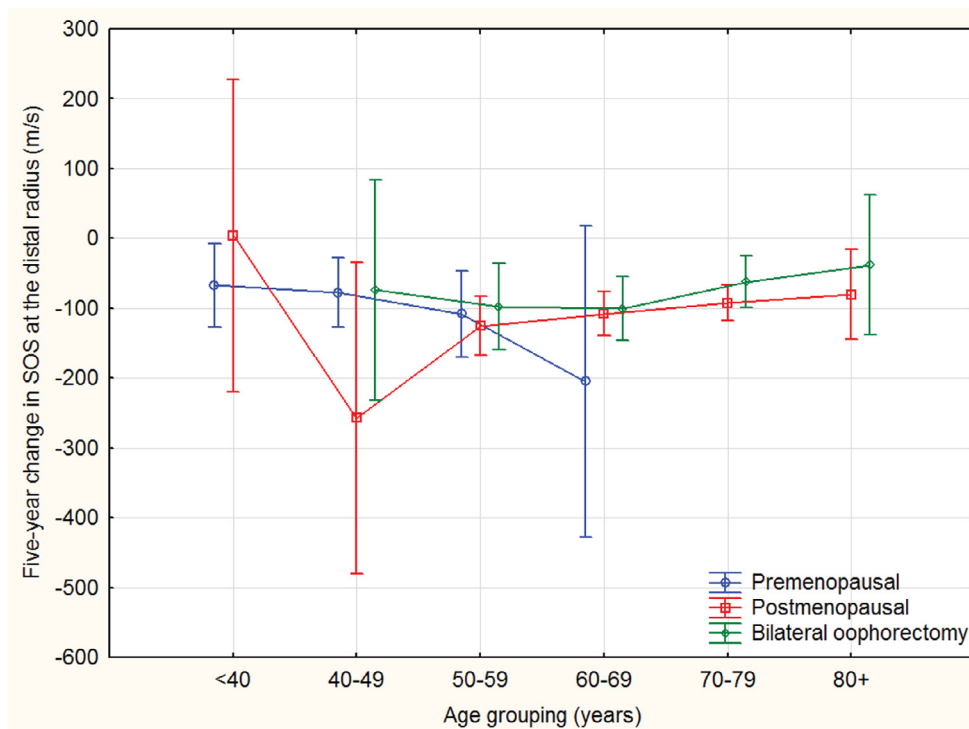
For the men, losses in SOS over the age groups were relatively consistent, with the highest rates observed in the youngest and oldest groups at the DR site (not statistically significant); however, the small sample sizes in these 2 groups preclude meaningful interpretation.

In this investigation, there was a significant difference in the change in SOS at the tibia over 5 years with the women given antiresorptives having a mean gain in SOS as compared to a mean loss in women not taking antiresorptives; this association was not significant at the distal radius. At baseline, there were no significant mean differences in SOS between the group using antiresorptives and the group not using them at either site. These findings suggest that the mQUS may be able to monitor women on antiresorptives, at least at the tibia site. A recent small study of women with breast cancer provided denosumab to prevent bone loss associated with aromatase inhibitor treatment found that QUS-assessed SOS at the proximal phalangeal metaphysis of the last 4 digits (DBM Sonic Bone Profiler; Igea, Carpi, Italy) increased (3.8%) over a 2-year follow-up while the same measure in the control group decreased (–3.0%) over the same period.<sup>21</sup> The current trial did not investigate the impact of denosumab on mQUS as denosumab was not marketed at the time, but in general the trend for antiresorptive use was comparable.

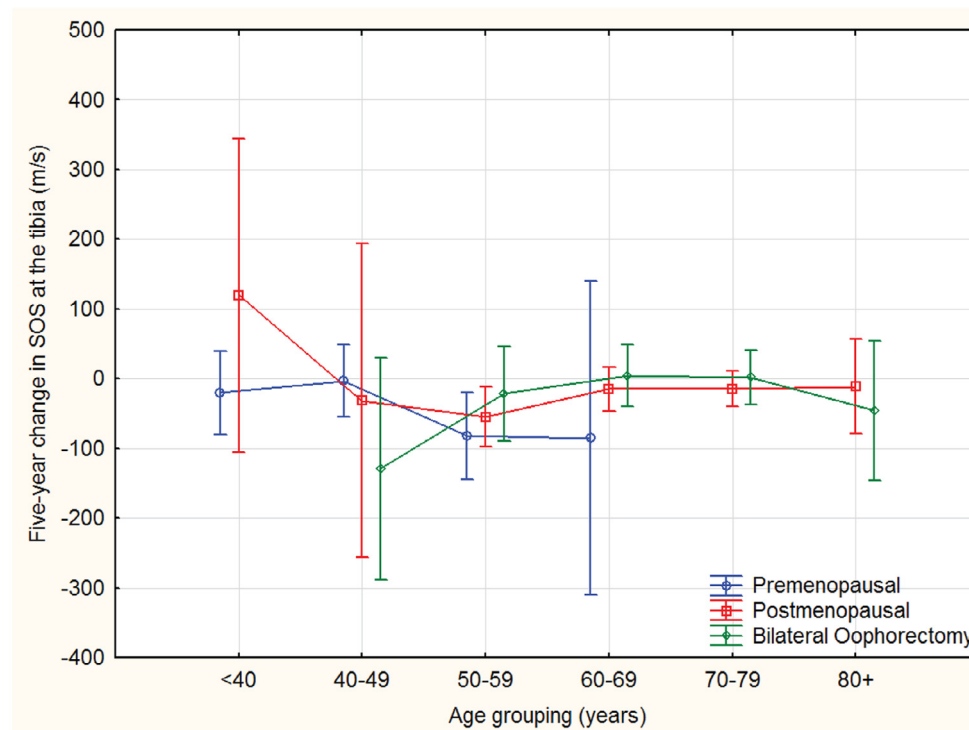
When menopausal status is considered, there were no significant differences in mean SOS loss among those who were premenopausal, menopausal or who had received a bilateral oophorectomy in either of the investigated sites. The lack of statistical difference between the SOS between premenopausal and menopausal women was surprising, particularly given the observed decrease in the mean SOS of women in the 50–59 yr age group. It needs note, however, that in this analysis menopausal women included all women of any age who were naturally menopausal. It is possible that in our analysis the merging of all menopausal women together, regardless of the time since the onset of menopause, may have attenuated the rapid loss observed in the relatively short time surrounding the onset of menopause with the long span of time thereafter in which the women were categorized as menopausal, but had slower bone loss.

In previous investigations with this mQUS device, we have shown that the measurement of SOS at the DR and TIB sites allows for the estimation of fracture risk in women over a 5-year follow-up.<sup>7</sup> On average, a one SD decrease in SOS was associated with an approximate 52%–130% higher fragility fracture risk over 5 years in women. Of note, the predictive ability of the mQUS for fracture remained even after controlling for FN BMD and all the clinical risk factors included in the FRAX 10-year fracture risk assessment tool. Another investigation from our group further demonstrated that BMD and SOS measures were independent from one another.<sup>22</sup> Therefore, the

## A. Distal radius.



## B. Tibia.



**Fig. 3.** Impact of menopausal status on mean (95% confidence interval) 5-year change in SOS change among age groupings. SOS, speed of sound.

combination of mQUS and DXA should be superior to either one alone in predicting fractures. These data suggest that the addition of SOS measures to 10-year fracture risk assessment tools would more accurately stratify fracture risk in patients. However, a study done on Sri Lanka with the same mQUS as used in this investigation found that the inclusion of the mQUS DR information did not improve the fracture risk stratification in a small ( $n = 207$ ) cohort of women.<sup>23</sup> Catalano et al<sup>24</sup> reported similar agreement between QUS-assessed SOS at the phalanges (DBM Sonic Bone Profiler; Igea, Carpi, Italy) and DXA-assessed BMD with FRAX 10-year fracture risk assessments (without BMD) in a group of women being treated with aromatase inhibitors for breast cancer management. Further, QUS measures and DXA measures were significantly lower in women treated with aromatase inhibitors as compared to health controls after 18 months of follow-up. A novel pulse-echo QUS device (Bindex; Bone Index Finland Ltd., Dallas), with measurements acquired at the radius and tibia, demonstrated that it could be used as an initial screening test for DXA-defined hip osteoporosis.<sup>25</sup> Hip osteoporosis was detected with 80%–82% sensitivity and 81% specificity from which it was estimated that follow-up DXA assessments would only be required in one-quarter to one-third of the women assessed, resulting in significant cost-savings.

Biver et al<sup>26</sup> performed a preliminary investigation that assessed the ability of a QUS measurement at the radius (OsCare, Sono; Vantaa, Finland) to screen for fracture risk in a group of men and women from the Geneva Retirees Cohort. There was a significant correlation between QUS low-frequency SOS and DXA-assessed distal-third radius BMD ( $r^2 = 0.52$ ;  $p < 0.001$ ) and was shown to be a significant ( $p = 0.024$ ) predictor of prevalent low-trauma fractures. Phalangeal QUS (DBM Sonic 1200; Igea, Carpi, Italy) found no difference between children with bronchial asthma as compared to health controls,<sup>27</sup> but was found to be of use in discerning skeletal disturbances in children with limited glomerular filtration rates and who were unexposed to glucocorticoids.<sup>28</sup>

New technologies, such as radiofrequency echographic multi-spectrometry (REMS) offer other nonionizing ultrasound techniques to assess bone strength.<sup>29,30</sup> One recent investigation utilizing REMS found that it provided convincing estimates of DXA-acquired BMD at the lumbar spine and femoral neck, 2 sites that are of clinical importance.<sup>29</sup>

We previously generated a robust normative database for mQUS using over 4000 participants from CaMos<sup>31</sup> to assist in the identification of those at heightened risk of fracture. The mean SOS values we calculated were generally in agreement with other smaller investigations with mQUS in North American populations.<sup>11,32,33</sup> These norms are particularly useful in areas where there is not wide availability to DXA. In these areas, the mQUS could be used in concert with the FRAX 10-year fracture assessment tool, without BMD input, to provide a better indicator of fracture risk in patients.

There were a few limitations to this study. One was the relatively small sample size, particularly for the youngest and oldest age groups, which warrants caution in the interpretation of trends for these 2 age groups. We did not assess adherence to antiresorptive therapy beyond a self-reported questionnaire. The mQUS assessments in this investigation only assessed peripheral skeletal sites (radius and tibia); measurements of femoral neck and lumbar spine strength via emerging QUS technologies, such as REMS,<sup>29</sup> would strengthen the investigation. This study had numerous strengths, including a randomly selected population from the general Canadian population, a large sample size and large span of included ages. Further, this investigation was longitudinal in nature, allowing the true assessment of loss of SOS over time as compared to estimates provided from cross-sectional assessments.

## Conclusions

In this cohort SOS declined at the DR and TIB sites over an observation period of 5 years, as would be expected for individuals who had attained their peak bone mass. In the women, there were trends for the most significant losses being at the age group usually associated with the onset of menopause and punctuated bone loss (50–59 yr), with losses at the TIB being statistically significant.

Antiresorptive therapy had a positive impact on the change in SOS at the tibia. These findings suggest that the mQUS device may be of use in monitoring women on antiresorptive therapy and deserves further study.

Lastly, SOS losses were similar for women who were premenopausal, menopausal or who had a bilateral oophorectomy.

These findings are encouraging as they show an overall consistent loss in SOS over the age spans investigated, which is coincident with increasing risk for fracture.

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