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CaMos

Canadian Multicentre Osteoporosis Study
Étude Canadienne multicentrique sur l'ostéoporose

BONE HEALTH *for life*

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Dr. David Goltzman

CaMos Update

DR. DAVID GOLTZMAN, CO-PRINCIPAL INVESTIGATOR, MONTREAL

CaMos would like to thank each and every participant for continuing to support our study over the years.

Because of your commitment, the Year 16 follow-up, which ended at the beginning of 2014, has been an unqualified success. We are currently continuing with the yearly postal questionnaire for all CaMos participants for our Year 17 follow-up, which should end later in 2014. Due to the enthusiastic support of participants and CaMos regional centers, we will also continue with our Year 18 follow-up in 2014-2015, again with postal questionnaires for all participants. Rest assured that your involvement has been and continues to be essential to shaping our understanding of osteoporosis, both in Canada and internationally. ◆

Question from the participants

Should I quit taking my calcium supplements?

Answer by DR. DAVID GOLTZMAN CO-PRINCIPAL INVESTIGATOR, MONTREAL

Many individuals are concerned about taking calcium supplements in view of widely publicized reports that claim that calcium supplements may increase heart disease and strokes. Adequate calcium and vitamin D intake is necessary for the maintenance of bone for everyone, and this is especially true for those with osteoporosis. In 2010, the Institute of Medicine reviewed the literature and updated the dietary reference intakes. The recommended dietary allowance for calcium in the general population was set at 1000 mg per day for men ages 50-70 years and 1200 mg per day for women 50 and older and men ages 70 and older.

The first suggestion that calcium supplement intake posed a possible health risk came from a scientific paper by Bolland and colleagues published in the British Medical Journal (BMJ) in 2008, reporting an increased risk of heart attacks in the calcium supplement group of a New Zealand clinical trial. The data from this study was then combined with other calcium supplement trials (BMJ 2010), further suggesting that calcium supplements might increase the risk of heart attacks and strokes. Lewis and colleagues, in a more recent article, sought to verify the proposed way that calcium could be harmful in an Australian study that used ultrasound measurement of blood vessel walls to measure damage to blood vessels. Among participants who regularly took their study medication, they found less damage of the blood vessels in the calcium group compared to the placebo group.

There have been two reports on this topic from the Women's Health Initiative study in the United States, the largest trial of calcium and vitamin D supplements worldwide. Reid and colleagues claimed that in their analysis of the results, women who did not already use supplements had increased heart risk if they were assigned to take calcium and vitamin D rather than a placebo. This analysis completely ignored women in the trial who were already taking their own supplements. Prince and colleagues countered that there was no increased heart risk in the entire calcium and vitamin D group compared with the entire placebo group as they

(see **Question**, page 2) ➤

➤ (**Question** from page 1)

had initially reported. Furthermore, those assigned to the calcium and vitamin D group rather than the placebo group had an overall lower risk of death.

CaMos investigators have examined calcium and vitamin D and their association with deaths due to all causes in the CaMos cohort. Our results, reported in the Journal of Clinical Endocrinology and Metabolism in 2013, were concurrent with the results from the Women's Health Initiative from Prince and colleagues. Specifically, we showed that women taking up to 1000 mg per day of calcium supplements had a lower risk of death than those taking no calcium supplements (irrespective of vitamin D use). We also showed that higher dietary calcium was also associated with reduced risk of death.

A diet high in calcium rich foods may be all that is needed to reach the recommended daily intake. Dairy products (milk, yogurt, and cheese) are the main sources of calcium in the diet, but other sources include salmon, legumes, greens, tofu, almonds, and fortified beverages. Therefore, the first thing to do is to determine whether your diet provides enough calcium. Osteoporosis Canada (www.osteoporosis.ca) has developed a tool to calculate your calcium intake. If you cannot meet the guidelines based on diet alone, then you can consider taking calcium supplements. It would be prudent to take the lowest supplement dose necessary to meet your recommended intake but to date the evidence that the supplements are harmful remains highly controversial. ◆

Selected CaMos publications

25-hydroxyvitamin D in Canadian adults: biological, environmental and behavioural correlates. OI, 2011; 22(5): 1389-99. ***by Linda Greene-Finestone et al.***

Vitamin D, either from sunlight or from food and supplement intake, is essential for bone health. It is converted into a form of vitamin D which circulates in blood named 25-hydroxyvitamin D [25(OH)D]. Since one source of vitamin D is sunlight, the northern latitude and long winter leads to concerns regarding the potential for vitamin D insufficiency in Canadians. Using CaMos, we found that 20% of the CaMos participants had low levels of 25(OH)D (< 50 nmol/L), varying from 1% in August to 45% in December. However, among users of at least 400 IU of vitamin D supplements daily, the percentage was < 10% year round. We also found that maintenance of normal weight is an important modifiable factor for enhancing vitamin D status.

Physical Activity, Body Mass Index and Bone Mineral Density - Associations in a Prospective Population-based Cohort of Women and Men. Bone, 2012; 50(1): 401-8. ***by Lisa Langsetmo et al.***

Dr. Lisa Langsetmo

This study examined physical activity over time and its association with body mass index (weight/height^2) and bone mineral density. The amount of daily strenuous exercise (e.g. jogging) or vigorous work (e.g. shovelling) was strongly related to age, with average time in men decreasing from an hour and a half among those 25-29 years old to under 10 minutes among those 70 years and older, whereas in women the average time decreased from 30 minutes among those 25-29 to less than 5 minutes among those 70 years and older. The amount of walking and moderate activity (e.g. housework) also varied with age. Those who had reduced levels of total physical activity over time gained weight (hence increased body mass index) and lost bone mineral density.

WNT16 influences bone mineral density, cortical bone thickness, bone strength, and osteoporotic fracture risk. PLoS Genet., 2012; 8(7) ***by Hou-Feng Zheng et al.***

The development of low bone mineral density (BMD) and osteoporotic fracture depends in part on genetic factors. The present study compared common genetic variants among two cohorts to determine variants that were associated with cortical thickness of the tibia (lower leg bone) or forearm BMD. The authors identified a gene (WNT16) associated with cortical bone thickness and BMD and tested four variants in 2,023 osteoporotic forearm fracture cases and 3,740 controls including those in CaMos. In a separate study, laboratory mice with targeted disruption of the WNT16 gene were found to have thinner bone cortices and weaker bones than litter mates without the disruption. These findings help understand the biologic pathways associated with the WNT16 gene and clarify the development of low BMD, and possibly suggest relevant targets for osteoporosis treatment.

The burden of osteoporotic fractures beyond acute care. Age and Ageing, 2011; 40(5): 602-7 ***by Sarah Kaffashian et al.***

The burden of fractures on individuals and their caregivers go beyond the immediate treatment and have long-term impacts on quality of life. This study analyzed the use of formal and informal care necessary after the initial treat-

(see **Publications**, page 3) ➤

➤ (**Publications** from page 2)

ment period. Among CaMos participants with a major fracture who returned home after initial treatment, 37% used rehabilitation services and 18% reported receiving home care (nurse visits or homemaker services). Those with hip fracture used more services than those with fractures at other sites. An important new finding of this study was that nearly half reported receiving care from informal caregivers (i.e. relatives and friends), 36% of these caregivers had paid jobs and worked outside the home.

Multisite quantitative ultrasound for the prediction of fractures over five years of follow-up. J Bone Miner Res., 2013; 28(9): 2027-34 ***by Wojciech P. Olszynski et al.***

Dr. W.P. Olszynski

Ultrasound machines are attractive tools for assessing fragility fracture risk as they are often portable, comparatively inexpensive, require little training for their use, and emit no radiation (unlike X-rays and DXAs). This study used ultrasound measures at Year 5 follow-up on a total of 3741 women and men to assess fracture risk over 5 years. We found that ultrasound measures at the wrist and lower leg did not add to the factors included in the FRAX tool in predicting hip fracture risk. However, they could significantly predict all clinical fractures and non-vertebral fractures within the next 5 years in women, but not in men.

The CaMos Bone Quality Study (BQS) Progress and Developments

It has been a year since we first started recruitment for the CaMos BQS, a study focused on quantifying bone structure and density in three dimensions. To date, we have recruited over 500 women between 60-85 years of age; scanned them on a high- and/or lower-resolution CT scanners at their wrists and ankles, and obtained DXA scans to measure bone density of the hip and spine. We will follow these study participants for the next five years to draw associations between three-dimensional bone measurements and any fractures that may occur during this period. In addition to the bone outcomes, we also measured the quality of muscle at the largest section of the calf in a subset of these same women. We believe that fattier muscles are linked to a higher risk of falling and becoming frail.

The CaMos BQS has recently drawn international attention. We have been approached by International Innovation– a journal focused on highlighting global scientific achievements. In particular, our work on advancing a full musculoskeletal assessment was identified as an innovative strategy for tackling an aging population faced with the challenges of frailty and bone fragility. We have also entered into three major collaborations. Scientists from the United States will combine the CaMos BQS data with similar national multicentre bone structure imaging studies across the world to answer questions regarding genetics and the predictability of fractures. Other collaborators will relate our bone structure data to other tools based on modification of existing DXA scans.

We have seen innovative research from our CaMos BQS centres. The Calgary group assessed longitudinal changes in bone strength and architecture over time. They observed

(see **Bone Quality Study**, page 4) ➤

NEW CO-INVESTIGATORS

Dr. Angela M. Cheung

Dr. Angela Cheung is Professor of Medicine at the University of Toronto. She is Chair of the Scientific Advisory Council of Osteoporosis Canada. Her research interests are in the area of postmenopausal osteoporosis, especially in prevention and early diagnosis, and evaluation of new technologies and therapies.

Dr. Suzanne Morin

Dr. Suzanne Morin is Associate Professor in the Department of Medicine. She is Vice-Chair of the Scientific Advisory Council of Osteoporosis Canada. Her research interests include health-related outcomes of osteoporosis, particularly following hip fractures and, long-term safety of osteoporosis treatments.

➤ (**Bone Quality Study**, from page 3)

CaMos BQS Team

decreases in bone density of roughly 1% per year. In addition, they found that the outer shell or cortex of the bone becomes markedly weaker with age due to the larger numbers of holes (increasing by 7-11% per year) in the normally solid structure. The Saskatoon group has also been measuring annual rates of loss of bone, and was also able to quantify changes in muscle and its fattiness in older versus younger participants. In Hamilton, from just the baseline bone structure measurements alone, we were able to see that higher-resolution CT scanners yielded more reproducible measurements and saw associations that were stronger for the thickness of the cortex. Soon, we will be able to further support these findings and determine whether the striking changes in bone observed are actually related to an increased risk of fractures. ◆

Congratulations

2013 Osteoporosis Canada CaMos Fellowship Award Recipient – Kyla Naylor

Kyla Naylor

Kyla Naylor is working on a Ph.D. in Epidemiology and Biostatistics at Western University. Her research project on the evaluation of FRAX in chronic kidney disease patients using the CaMos data has won the 2013 Osteoporosis Canada-CaMos award in helping her to continue her project.

2013 ASBMR Young Investigator Award – Lauren Burt, Ph.D.

Lauren Burt

Lauren is a postdoctoral fellow working on the CaMos project in Calgary. At this year's American Society for Bone and Mineral Research Annual Meeting (ASBMR, October 2013), Lauren received a Young Investigator Award and distinguished oral presentation for her work on changes in bone quality over time. She was also a recipient of the Tim Murray Osteoporosis Canada award.

Lindy Fraser Memorial Award – David Goltzman

In April 2013, the 2012 Lindy Fraser Memorial Award was presented to Dr. David Goltzman at the annual CaMos meeting in Montreal. This prestigious award, established in 1993 by Osteoporosis Canada, recognizes individuals who have done exemplary research and have helped to increase the knowledge about osteoporosis.

Queen Elizabeth II Diamond Jubilee Medal

To celebrate the 60th anniversary of Her Majesty Queen Elizabeth II's accession to the throne as Queen of Canada, Osteoporosis Canada presented five CaMos directors (Dr J.D. Adachi-Hamilton, Dr J.P. Brown-Quebec City, Dr D.A. Hanley-Calgary, Dr R.G. Josse-Toronto, and Dr S.M. Kaiser-Halifax) with the Diamond Jubilee Medal because of their outstanding contributions to their community and country.

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