



Dr. David Goltzman

## Our 20th Anniversary

**DR DAVID GOLTZMAN, CO-PRINCIPAL INVESTIGATOR, MONTREAL**

We are now celebrating the 20th anniversary of the beginning of CaMos and are especially thankful for all participants who have kept with this study over this period. CaMos has truly been an exceptional Canadian resource and continues to be a vital part of learning about health and aging in Canada. There are now well over 100 published research articles based on the CaMos dataset, with topics ranging from osteoporosis to genetics to quality of life. We are continuing follow-up and data collection for the main study and will continue to analyze the blood and urine samples, and questionnaires to provide new insights into the health of people across Canada. ♦

## Question from the participants

*How long should I take my treatment for osteoporosis?*

**Answer by DR SUZANNE MORIN, INVESTIGATOR, MONTREAL**



Dr. Suzanne Morin

Your physician will have recommended that you take anti-osteoporosis medication because your risk for having a fragility fracture is high. In addition to adequate daily intake of calcium and vitamin D and an individualized exercise program, physicians recommend the use of bisphosphonates such as etidronate (Didrocal), alendronate (Fosamax), rise-

dronate (Actonel) or zoledronic acid (Aclasta), denosumab (Prolia), raloxifene (Evista) or teriparatide (Forteo) for the treatment of osteoporosis and to reduce the risk for fractures. All of these medications have been studied rigorously and clinical trials support their use for prevention of fractures in patients at high risk.

Bisphosphonates have been available in Canada since the 1990s and are the most frequently prescribed medications for osteoporosis. They are usually well tolerated and very efficacious in lowering fracture risk. However, in recent years, there have been reports of rare adverse events in patients who have used bisphosphonates for prolonged periods of time (usually longer than 10 years). Osteonecrosis of the jaw and atypical femur fractures are such adverse events that have been described in selected patients. Although rare, the occurrence of these serious side effects has caused much concern to patients and clinicians. Though still incompletely understood, the cause of these adverse events seems to be related to long-term use of bisphosphonates in addition to other risk factors. For example, osteonecrosis of the jaw is more likely to arise in patients who also take other medications such as glucocorticoids (prednisone) for medical conditions, who have diabetes or cancer in addition to the use of a bisphosphonate for the treatment of osteoporosis. Similarly patients who develop an atypical femur fracture, a stress-like fracture that occurs in the upper leg (thigh), have demonstrated other risk factors in addition to the use of bisphosphonates.

Because of the occurrence of these adverse events, experts in the field of bone health now recommend that bisphosphonate therapy be re-evaluated after 5 years of continuous therapy. Depending on each individual's



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► (Question from page 1)

risk for future fragility fracture, bisphosphonate treatment can be interrupted (drug holiday), continued (up to 10 years) or switched to another type of medication depending on each individual's risk. Treatment interruptions (drug holiday) are usually not recommended with other types of medications (denosumab or raloxifene). Teriparatide (Forteo) can only be used for up to 2 years as mandated by Health Canada and must be discontinued after that time; such discontinuation is not considered a drug holiday.

Your primary care physician, pharmacist or other health-care professional can provide guidance and participate in discussion with you on this topic. You can also find additional information on the Osteoporosis Canada website ([www.osteoporosis.ca](http://www.osteoporosis.ca)).

Adherence to your osteoporosis treatment program is crucial in reducing your risk for fractures; it is important to discuss any concerns you may have with your primary care professional. ♦

## The CaMos Bone Quality Study (BQS)

**DR JONATHAN D. ADACHI**, INVESTIGATEUR PRINCIPAL FOR THE BQS AND DIRECTOR FOR THE HAMILTON CAMOS CENTRE

**DR ANDY KIN ON WONG**, DIRECTOR FOR THE BQS

The CaMos Bone Quality Study (BQS) has completed its baseline enrolment of over 600 participants. Total hip and lumbar spine bone density scans were performed as well as high- and low-resolution CT scans. The last set of these medical images are currently being analyzed to generate useful information regarding our participants' bone quality. We expect to complete these analytical procedures by March of 2015.

Based on our first set of data, we discovered that lower volumetric bone density measured using either high- or low-resolution CT scans both related to higher odds for fractures to a similar extent. If our initial findings are confirmed with the complete dataset, it is possible that we could obtain information about bone quality from the less expensive, albeit, less detailed, low-resolution CT scanner in the future. We will continue to follow our participants in the coming years to see how both these measures can predict future fractures.

We continue to seek funding for our sister study, the CaMos Muscle Quality Study (MQS), where we hope



Dr. Jonathan Adachi

to examine muscle composition measures using the low-resolution CT, as well as strength and balance changes using simple function tests, investigated over 6 years. We believe that various aspects of muscle may be related to frailty and to an increased risk of falling and therefore more fractures.

In our preliminary analyses of muscle measurements, we revealed that, among individuals who were less frail, having more fat within muscles had a direct effect on loss of bone strength and fractures. In frailer individuals, muscle may be precipitating the symptoms of frailty, leading to more frequent falls and fracturing. These different pathways towards a fracture depend on the frailty status of individuals and can shed light on how we should treat these people differently. Certainly, we will need to extend this study to draw associations with changes in the future in order to generate more conclusive evidence.

In the coming months, we will be submitting a new application to fundraise over \$5 million to enable analyses of muscle and frailty changes over time. This project application for the CaMos MQS will help establish benchmarks in muscle changes with healthy aging. It will also inform us on how to address patients who experience repeat fractures. ♦

## Selected CaMos publications

*The following are excerpts from some of the articles, published in the past year, which use data collected during CaMos interviews and follow-up questionnaires.*

**A Frailty Index predicts 10-year fracture risk in adults age 25 years and older: results from the Canadian Multicentre Osteoporosis Study (CaMos)** Osteoporosis International 2014 Dec;25(12):2825-3 *by Courtney Kennedy*



Dr. Courtney Kennedy

Older people can be vulnerable to having very serious adverse events and poor subsequent recovery. A major risk factor for these poor outcomes is frailty, a concept that is often used but poorly understood. Frailty can be defined by combining multiple health related assessments into a single index. We used the CaMos cohort to define a frailty index based on 30 key indicators. We found that this frailty index was associated with increased risk of fracture (and in particular, hip fractures and vertebral fractures) independent of age and bone mineral density. This suggests that overall health status, not just bone strength, plays a role in fracture outcomes.

(see Publications, page 3) ►

**The causal effect of vitamin D binding protein (DBP) levels on calcemic and cardiometabolic diseases: a Mendelian randomization study** *PLoS Medicine*, 2014 Oct 28;11(10):e1001751  
by Aaron Leong

Vitamin D has long been known to be necessary for bone health since vitamin D deficiency can lead to rickets, osteomalacia, and osteoporosis. Vitamin D is also unique in that the necessary vitamin D can be obtained from the combination of skin exposed to sunlight or from dietary sources. Vitamin D may also play a role in health outcomes other than bone health. We know from previous studies that low vitamin D in the blood is associated with heart disease and some cancers, but since these studies were not randomized trials we don't know if the vitamin D itself is preventing the outcomes or whether vitamin D is just associated with the real underlying cause. Mendelian randomization is an efficient alternative to conducting randomized trials. The idea is that genetic variants appear randomly in the population, and if a genetic variant is related to both an exposure and an outcome as hypothesized then there is mechanism connecting the two. In this study we looked at genetic variants associated with the vitamin D binding protein, and found they were also associated with level of vitamin D in the blood. However these same genetic variants were not linked causally to other outcomes such as diabetes, hypertension, and heart disease. Thus if vitamin D levels in the blood are linked by some mechanism to these outcomes, then the mechanism is independent of component related to the vitamin D binding protein.

**Ten-year incident osteoporosis-related fractures in the population-based Canadian Multicentre Osteoporosis Study – Comparing sites and age-specific risks in women and men.** *Bone*, 2015 Feb;71:237-243 by Jerilynn Prior



Dr. Jerilynn Prior

We found in this study that fractures in women were most likely to be of wrists/forearm but that men were more likely to break ribs. Another new finding—older men and women who were 75-84 years at baseline and living in the community—not in assisted living or extended care homes—were equally likely to break a hip for the next ten years.

**Glucocorticoids predict 10-year fragility fracture risk in a population-based ambulatory cohort of men and women: Canadian Multicentre Osteoporosis Study (CaMos).** *Arch Osteoporosis*, 2014 Feb; 9(1):169.  
by George Ioannidis



Dr. George Ioannidis

Glucocorticoids are not as widely used, however there has been even greater concern that their use might be associated with bone fragility. Using the CaMos cohort database, we showed that glucocorticoid use is associated with increased fracture risk in ambulatory men and women across Canada.

**The Effect of Anticholinergic Medications on Falls, Fracture Risk, and Bone Mineral Density Over a 10-Year Period.** *Ann Pharmacotherapy*, 2014 April;48(8):954-961 by Lisa-Ann Fraser

Many medications used in older adults have strong anticholinergic (ACH) properties, which may increase the risk of falls and fractures. While ACH medications were associated with increased fracture risk, this association risk was not attributable to the medication itself, but rather to other risk factors that were more common among users of these medications.

**Antidepressant use and 10-year incident fracture risk: the population-based Canadian Multicentre Osteoporosis Study (CaMos).** *Osteoporosis International*, 2014 May;25(5):1473-81  
by Cristiano Moura

There has been concern that antidepressants such as selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs) might be associated with increased risk of fracture. We found an increased risk of fractures in individuals who used SSRI or SNRI, even after controlling for multiple risk factors including the underlying depression. ♦





Dr Steven Boyd

## Co-Director of the Calgary Centre

Dr. Steven Boyd holds a PhD in Mechanical Engineering, specialized in Biomedical Engineering. Appointed as a faculty member at the University of Calgary in 2002, he is a Professor in the Cumming School of Medicine (Radiology), and jointly appointed at the Schulich School of Engineering (Mechanical Engineering) and Faculty of Kinesiology. He is a principal investigator at the McCaig Institute for Bone and Joint Health in medicine, and his research uses a multi-disciplinary biomedical engineering approach for development of early detection and monitoring of bone and joint health, with particular focus on osteoporosis and osteoarthritis. The Bone Imaging Laboratory he established in 2004 develops methods for bone quality detection using high-resolution computed tomography and computer methods such as the finite element analysis to investigate bone and joint diseases. ♦



Dr Robert Josse

## Regional News

### Toronto

The St. Michael's Hospital Osteoporosis and Metabolic Bone Disease Program held its 11th Annual Symposium on March 20, 2015 at the Park Hyatt in Toronto. This yearly event was hosted by Dr. Robert G. Josse, Toronto CaMos Director, and organized by Barbara J. Gardner-Bray, Toronto CaMos Coordinator. The objectives of this accredited program are to provide up-to-date, evidence-based, scientifically sound, useful and practical information for specialists on different aspects of metabolic bone disease, focusing on osteoporosis. The program has grown from strength to strength over the years and features international and Canadian speakers, all experts in the field of metabolic bone disease and osteoporosis.

### Vancouver

Dr. Jerilynn Prior has led new research focusing on oral contraceptives. In particular, using the CaMos cohort it was

shown that those who had ever used "The Pill" (combined hormonal contraceptives [CHC]) had lower spine and hip bone mineral density. Further assessment of change over time suggests that CHC prevents teenagers from achieving their optimal peak bone mass. ♦

## Celebrating excellence

### International Osteoporosis Foundation recognizes leading Canadian investigator for outstanding scientific contributions to the field of osteoporosis

Dr. Jonathan D. Adachi was awarded the prestigious International Osteoporosis Foundation's (IOF) 2014 Olof Johnell Science Award. Dr. Adachi is Professor and Alliance for Better Bone Health Chair in Rheumatology at the Department of Medicine of McMaster University, Director of the CaMos Hamilton Centre and Principal Investigator of the CaMos Bone Quality Study. ♦

## Congratulations

### 2014 Osteoporosis Canada CaMos Fellowship Award Recipient – Dr. Andy Kin On Wong



Dr Andy Kin On Wong

Dr. Andy Kin On Wong recently received a Doctor of Philosophy in Medical Sciences at McMaster University under the supervision of Dr. Jonathan Adachi. His thesis focused on bone quality quantification using peripheral quantitative computed tomography (pQCT) and magnetic resonance imaging (MRI) scanners. He is now completing his post-doctoral fellowship with Dr. Angela Cheung at the Osteoporosis Program of the University Health Network. With this OC-CaMos Fellowship, Andy will be dedicated to his project entitled "The CaMos Muscle Quality and Frailty Study", which will examine both bone and muscle in men and women across six cities in Canada to link these outcomes to the CaMos frailty index, through collaboration with Drs. Courtney Kennedy and Alexandra Papaioannou. ♦

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