High Rates of Imminent Subsequent Fracture After Femoral Neck Fracture in the Elderly

Earl Bogoch, MD, FRCSC, Francesc A. Marcano-Fernández, MD, PhD, Emil H. Schemitsch, MD, FRCSC, Qi Zhou, PhD, Sofia Bzovsky, MSc, Mohit Bhandari, MD, PhD, FRCSC, Prism S. Schneider, MD, FRCSC, PhD, Marc Swiontkowski, MD, Sheila Sprague, PhD, the FAITH Investigators*, and the HEALTH Investigators*

Background: Fragility fractures of the hip are known to be followed frequently by subsequent fragility fractures, including second hip fractures. Data on subsequent fractures are available for aggregated index femoral neck and intertrochanteric femoral fractures, grouped generically as hip fractures, but not specifically for femoral neck fractures. There is increasing recognition that a subsequent fracture often occurs early after a hip fracture in the elderly, creating an emphasis on the concept of "imminent fracture risk." Since 2000, there have been many reports on the care gap in interventions after a fragility fracture, with concern regarding the slow uptake of appropriate systemic treatments designed to prevent a subsequent fracture in high-risk patients.

Methods: As planned a priori, we performed an analysis of subsequent fractures after an index femoral neck fracture in 2 prospective clinical trials involving 2,520 patients from 90 sites on 5 continents. We recorded the incidence and time of occurrence of all secondary fragility fractures as well as the reported use of bone-protective medication in all subjects.

Results: In the 24 months following the index femoral neck fracture, 226 (9.0%) of 2,520 patients sustained at least 1 subsequent fragility fracture, including 113 hip fractures (4.5%). The median interval from the index fracture to a subsequent fracture was approximately 9.0 months. Only 25.2% (634) of the 2,520 patients reported using bone-protective medications at any time during follow-up. Female patients, those with nondisplaced index fractures, and those treated with arthroplasty, were more likely to have received protective medication.

Conclusions: Subsequent fractures, including second hip fractures, occurred frequently and early following an index femoral neck fracture in 2 large global cohorts. Interventions to prevent a subsequent fracture were instituted in only 1 of 4 patients, even though a focused directive was included in both study protocols.

Level of Evidence: Prognostic Level II. See Instructions for Authors for a complete description of levels of evidence.

Approximately 9 million low-energy fractures occur each year worldwide, including 1.6 million proximal femoral fractures[1]. A recent fragility fracture is an important predictive factor for subsequent fracture[2]. A hip fracture occurring with minimal trauma is reported as the clinical risk factor that confers the highest risk of future fracture[3] and is included in multiple international guidelines as an indication for the administration of bone-protective medication[4-8]. Several medications are available internationally and have proven efficacy in preventing major fragility fractures[9].

Recent reports have emphasized the risk of a subsequent fracture occurring relatively soon (within 1 year) after a fragility fracture (an imminent fracture risk), highlighting the importance of initiating preventive measures early after hip and other fragility fractures[10,11]. Several medical societies have advocated for the establishment of systematic jurisdiction-wide fracture prevention programs, including the American Orthopaedic Association's "Own the Bone" initiative[12] and the Fracture Clinic Screening Program in Ontario, Canada[13,14]. Multiple studies have demonstrated that bone-protective medications can improve bone architecture and density, and they confer a degree of fracture protection within 6 months after initiation[15-17].

Patients with hip fractures are routinely treated as a single risk group. To our knowledge, no published studies have documented subsequent fracture risk levels specific to different proximal femoral fracture sites (femoral neck versus intertrochanteric).

*A list of the FAITH Investigators and a list of the HEALTH Investigators are included in a note at the end of the article.

Disclosure: The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (http://links.lww.com/JBJS/H218).

A **data-sharing statement** is provided with the online version of the article (http://links.lww.com/JBJS/H219).

We investigated the incidence and time of occurrence of subsequent fractures within 24 months of an index fracture of the femoral neck (and not other proximal femoral sites) in patients enrolled in 2 large international prospective trials, the FAITH (Fixation using Alternative Implants for the Treatment of Hip fractures) and HEALTH (Hip fracture Evaluation with ALternatives of Total hip arthroplasty versus Hemiarthroplasty) trials[18,19]. Disaggregating data on subsequent fracture risk for an index femoral neck fracture, as distinct from other anatomic sites of hip fracture, could result in an increased understanding of fracture risk in clinical practice, improved randomization protocols for pharmacotherapy trials, and optimized designs of secondary fracture prevention programs and the evaluation of their cost-effectiveness. We also sought to determine the status of current global fracture prevention practices for this high-risk group, after 20 years of widespread education and promotion by clinicians and societies regarding the need for interventions to prevent a subsequent fracture in high-risk patients with a fragility fracture[20].

Materials and Methods

FAITH Study Overview

The FAITH trial[18,21] (ClinicalTrials.gov NCT00761813) enrolled 1,079 patients who were at least 50 years old with a low-energy femoral neck fracture treated by fracture fixation with a sliding hip screw or cancellous screws and were from 81 clinical sites in 8 countries. Approximately one-third (350) of these fractures were displaced. The primary outcome was unplanned revision surgery to promote healing, relieve pain, treat infection, or improve function within 24 months of fracture fixation.

HEALTH Study Overview

The HEALTH trial[19,22] (ClinicalTrials.gov NCT00556842) compared total hip arthroplasty and hemiarthroplasty in 1,441 patients who were at least 50 years old with a displaced femoral neck fracture and were from 80 clinical sites in 10 countries. The primary outcome was unplanned revision surgery within 24 months of the femoral neck fracture.

Bone Health

Oral administration of calcium (600 mg per day) and vitamin D (1,000 IU per day) to all participants was required in the trial protocols. The study steering committee intended to include bone-protective medications in the protocol to reduce subsequent fracture risk. However, because of differences in national guidelines, practice patterns, and resources across sites worldwide, we were unable to make administration of bone-protective medications obligatory. The study protocols, therefore, included a requirement for study sites to manage fracture risk and osteoporosis according to practices of local bone health experts. The protocols further required fracture prevention to be addressed at each site by documenting the patient's medication use at each follow-up visit through self-reporting. The goal was to track the frequency with which bone health interventions were performed to lower subsequent fracture risk.

Analysis Plan

This secondary analysis, which had been planned a priori, addressed the following questions: (1) How many patients experienced a subsequent fracture at any skeletal site within 24 months following their index hip fracture, and after what time interval? (2) How many patients were taking bone-protective medication (bisphosphonates, calcitonin, teriparatide [Forteo], denosumab [Prolia], or zoledronic acid [Aclasta]) at the time of follow-up after the index femoral neck fracture? (3) What prognostic factors were associated with the use of bone-protective osteoporosis medications (not including vitamin D and calcium) during follow-up after the index femoral neck fracture?

Data Analysis

We used descriptive statistics to report the characteristics of patients with secondary fractures and osteoporosis medication use. We performed a logistic regression analysis, adjusted for 30-day mortality, to compare secondary fracture rates among participants from the trials and a multivariable logistic regression analysis to investigate the association between prognostic variables and osteoporosis medication use following the index femoral neck fracture. The dependent variable was osteoporosis medication use, and we included 7 independent variables, selected on the basis of the previous literature[23] and expert opinions, which were age, sex, type of surgical method, fracture displacement, American Society of Anesthesiologists (ASA) physical status, prefracture living setting, and prefracture functional status. The results are reported as odds ratios (ORs), with corresponding 95% confidence intervals (CIs), and p values. Analyses were conducted using R software (version 4.0.2; R Foundation for Statistical Computing).

Source of Funding

The HEALTH trial was supported by research grants from the Canadian Institutes of Health Research (CIHR), National Institutes of Health (NIH), ZorgOnderzoek Nederland-medische wetensehappen, Sophies Minde Foundation for Orthopaedic Research, McMaster Surgical Associates, and Stryker Orthopaedics. The FAITH trial was supported by research grants from CIHR, NIH, Stichting Nuts Ohra, the Netherlands Organisation for Health Research and Development, and Physicians' Services Incorporated. Dr. Bhandari was funded, in part, through the Early Research Award Program (McMaster University, Canada).

The FAITH trial was supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the NIH and by The County Durham & Tees Valley Comprehensive Local Research Network.

Results

Participant Characteristics

The combined cohort included 1,791 patients with a displaced femoral neck fracture, with 1,441 from the HEALTH trial and 350 from the FAITH trial. A detailed comparison of these cohorts has been described[24]. There were a total of 729 nondisplaced femoral neck fractures, which were all from the FAITH trial. Fracture displacement could not be confirmed for 8 FAITH participants because of poor radiographic image quality. There was

no significant difference in 30-day mortality between the HEALTH (n = 35; 2.4%) and FAITH trials (n = 18; 1.7%; p = 0.19).

Incidence of Subsequent Fractures Following a Hip Fracture and the Interval to Subsequent Fracture

In the 24 months following a femoral neck fracture, 226 (9.0%) of the 2,520 patients enrolled in the 2 trials sustained a subsequent fracture, resulting in a total of 282 fractures (Table I). Females accounted for 77.0% (174) of the 226 patients who had a subsequent fracture and 65.7% (1,657) of all 2,520 patients. The average age of those with a subsequent fracture was 76.9 years in the FAITH cohort and 79.5 years in the HEALTH cohort (Table II). The median interval from index fracture to secondary fracture occurrence was 9.0 months for FAITH trial patients and 9.6 months for HEALTH trial patients.

A significantly higher proportion of patients sustained subsequent fractures in the HEALTH (arthroplasty) cohort (164 [11.4%] of 1,441) than in the FAITH (internal fixation) cohort (62 [5.7%] of 1,079) ($p < 0.001$) (Table I). However, the patients in the HEALTH trial were considered to be at higher risk for subsequent fracture because they were significantly more likely to be female; have an ASA classification of III, IV, or V; and have a diagnosis of osteoporosis compared with the patients in the FAITH cohort with displaced femoral neck fractures ($p < 0.001$) (Table II)[24]. Adjusting our logistic regression analysis for 2-year mortality when comparing secondary fracture rates among participants from the trials did not alter the results of the original analysis, which adjusted for 30-day mortality.

There were 282 secondary fractures reported in 226 patients. The most common location for a subsequent fracture was the contralateral hip (113 fractures; 40.1%), followed by the proximal humerus (33 fractures; 11.7%), a vertebra (29 fractures; 10.3%), the pelvis (25 fractures; 8.9%), and a rib (20 fractures; 7.1%). The incidence of secondary fractures over the 24-month follow-up period is displayed in Figure 1.

Osteoporosis Medication Use

Bone-protective or osteoporosis medication use following the index hip fracture was recorded, per the protocol, during all follow-up visits for all patients (Table III). Participants indicated whether they used 1 type or a combination of different medications. The proportion of participants using bone-protective medications was low and relatively constant throughout the follow-up period. Overall, only 25.2% (634) of the 2,520 patients in both cohorts reported taking bone-protective medications at any time between the index fracture and final follow-up at 2 years.

Females (OR, 1.75 [95% CI, 1.41 to 2.17]; $p < 0.001$), those with nondisplaced fractures (OR, 1.81 [95% CI, 1.23 to 2.78]; $p = 0.003$), and those treated with arthroplasty (OR, 3.48 [95% CI, 2.39 to 5.20]; $p < 0.001$) had significantly higher odds of medication administration (Table IV).

Discussion

Using data from the FAITH and HEALTH trials, we investigated the incidence and pattern of secondary fractures during the first 24 months after a low-energy femoral neck fracture in patients over the age of 50 years who were managed with internal fixation or arthroplasty.

The incidence of a secondary fracture (following the index hip fracture) in our combined cohorts at 2 years was 9.0% (226) of 2,520 patients, including a second hip fracture in 4.5% (113) of all 2,520 patients. In a jurisdiction-wide study following patients who sustained hip fractures in the province of Ontario, Canada, 3.0% of patients sustained a subsequent fracture within 1 year, 6.7% within 2 years, and 13.3% within 5 years, providing an indication of the burden of expected secondary fractures[10,25,26].

HEALTH trial patients who underwent joint replacement procedures after a femoral neck fracture had a significantly higher rate of all subsequent secondary fragility fractures (11.4% [164 of 1,441]) than patients in the FAITH trial who were treated with internal fixation of the fracture (5.7% [62 of 1,079]; $p < 0.001$). The significance of this finding is unclear because of probable selection bias in the treatment of patients. Surgeons may have had individual or regional preferences or bias for selection of internal fixation versus prosthetic arthroplasty, and for subtypes of both internal fixation and prosthetic arthroplasty, depending on patient age, bone quality, fracture displacement, local resources, and personal operative experience. Therefore, we cannot conclude that the difference in subsequent fracture rates between treatment groups in the 2 trials has predictive value.

It is widely assumed that "hip fractures," i.e., fractures of the proximal part of the femur, are a single group with respect to future (secondary) major fragility fracture risk, including a future (second) hip fracture. For example, the inclusion criteria for the HORIZON (Health Outcomes and Reduced Incidence with Zoledronic Acid Once Yearly) prospective randomized clinical trial of zoledronic acid (Aclasta) versus placebo included all patients with a recent hip fracture, without reference to fracture location in the femoral neck or intertrochanteric

TABLE I Secondary Fracture Rates After Index Femoral Neck Fracture in FAITH and HEALTH Studies

	FAITH Patients (N = 1,079)	HEALTH Patients (N = 1,441)	Total (N = 2,520)	P Value*
No. (%) of secondary fractures	88 (8.2)	194 (13.5)	282 (11.2)	<0.001
No. (%) of patients with a secondary fracture	62 (5.7)	164 (11.4)	226 (9.0)	<0.001

*Regression adjusted for 30-day mortality.

TABLE II Characteristics of Patients Who Experienced Secondary Fractures in FAITH and HEALTH Studies

Variable	FAITH Patients (N = 62) with Secondary Fractures (N = 88)	HEALTH Patients (N = 164) with Secondary Fractures (N = 194)
Secondary fractures *(no. [%] of patients)*		
1	43 (69.4)	137 (83.5)
2	13 (20.9)	24 (14.6)
3	5 (8.1)	3 (1.8)
4	1 (1.6)	0 (0.0)
Location of fracture *(no. [%] of fractures)*		
Hip	24 (27.3)	89 (45.9)
Pelvis	12 (13.6)	13 (6.7)
Vertebra	9 (10.2)	20 (10.3)
Humerus	9 (10.2)	24 (12.4)
Rib	9 (10.2)	11 (5.7)
Femur	7 (8.0)	4 (2.1)
Ankle	5 (5.7)	0 (0.0)
Tibia	4 (4.5)	7 (3.6)
Radius	3 (3.4)	11 (5.7)
Wrist	2 (2.3)	4 (2.1)
Sacrum	2 (2.3)	0 (0.0)
Ulna	1 (1.1)	1 (0.5)
Fibula	1 (1.1)	1 (0.5)
Patella	0 (0.0)	5 (2.6)
Clavicle	0 (0.0)	4 (2.1)
Taking osteoporosis medication at time of secondary fracture *(no. [%] of patients)*		
Yes	6 (9.7)	37 (22.6)
No	56 (90.3)	127 (77.4)
Time to fracture occurrence* *(mo)*	9.0 (11.3)	9.6 (14.1)
Mean age (stand. dev.) *(yr)*	76.9 (10.7)	79.5 (8.1)
Sex *(no. [% of patients])*		
Male	16 (25.8)	36 (22.0)
Female	46 (74.2)	128 (78.0)
Ethnicity *(no. [%] of patients)*		
South Asian	2 (3.2)	1 (0.6)
East Asian	0 (0.0)	1 (0.6)
Black	3 (4.8)	2 (1.2)
Hispanic or Latino	1 (1.6)	2 (1.2)
White	56 (90.3)	158 (96.3)
Country *(no. [%] of patients)*		
Canada	18 (29.0)	39 (23.8)
U.S.	35 (56.5)	22 (13.4)
Finland	0 (0.0)	7 (4.3)
Netherlands	0 (0.0)	20 (12.2)
Norway	3 (4.8)	26 (15.9)
Spain	0 (0.0)	28 (17.1)
U.K.	0 (0.0)	11 (6.7)
Australia	3 (4.8)	9 (5.5)
New Zealand	0 (0.0)	2 (1.2)
India	3 (4.8)	0 (0.0)
Continent *(no. [%] of patients)*		
Europe	3 (4.8)	92 (56.1)
North America	53 (85.5)	61 (37.2)
Oceania	3 (4.8)	11 (6.7)
Asia	3 (4.8)	0 (0.0)
Comorbidities *(no. [%] of patients)*		
Heart disease	25 (40.3)	67 (40.9)
High blood pressure	42 (67.7)	95 (57.9)
Lung disease	14 (22.6)	31 (18.9)
Diabetes	16 (25.8)	30 (18.3)
Ulcers or stomach disease	17 (27.4)	12 (7.3)
Kidney disease	6 (9.7)	15 (9.1)
Anemia or other blood disease	10 (16.1)	11 (6.7)
Depression	15 (24.2)	23 (14.0)
Cancer	9 (14.5)	17 (10.4)
Osteoarthritis or degenerative arthritis	20 (32.3)	26 (15.9)
Back pain	20 (32.3)	18 (11.0)
Rheumatoid arthritis	3 (4.8)	5 (3.0)

*The values are given as the median, with the width of the interquartile range in parentheses.

region[27]. Secondary fractures and subsequent fracture risk were reported without reference to the anatomical location of the index hip fracture. Large jurisdiction-wide fracture liaison services, such as the Ontario, Canada, system, have reported a subsequent fracture after an index hip fracture without reference to the specific site of the index fracture, and therefore without defining any potential differential in subsequent fracture risk for the 2 major anatomic sites of hip fracture[10,28]. The data we present provide information on subsequent fracture rates (at all sites) solely after an index femoral neck fracture in 2 patient cohorts. If similar data become available for a subsequent fracture after an intertrochanteric fracture of the femur (the other

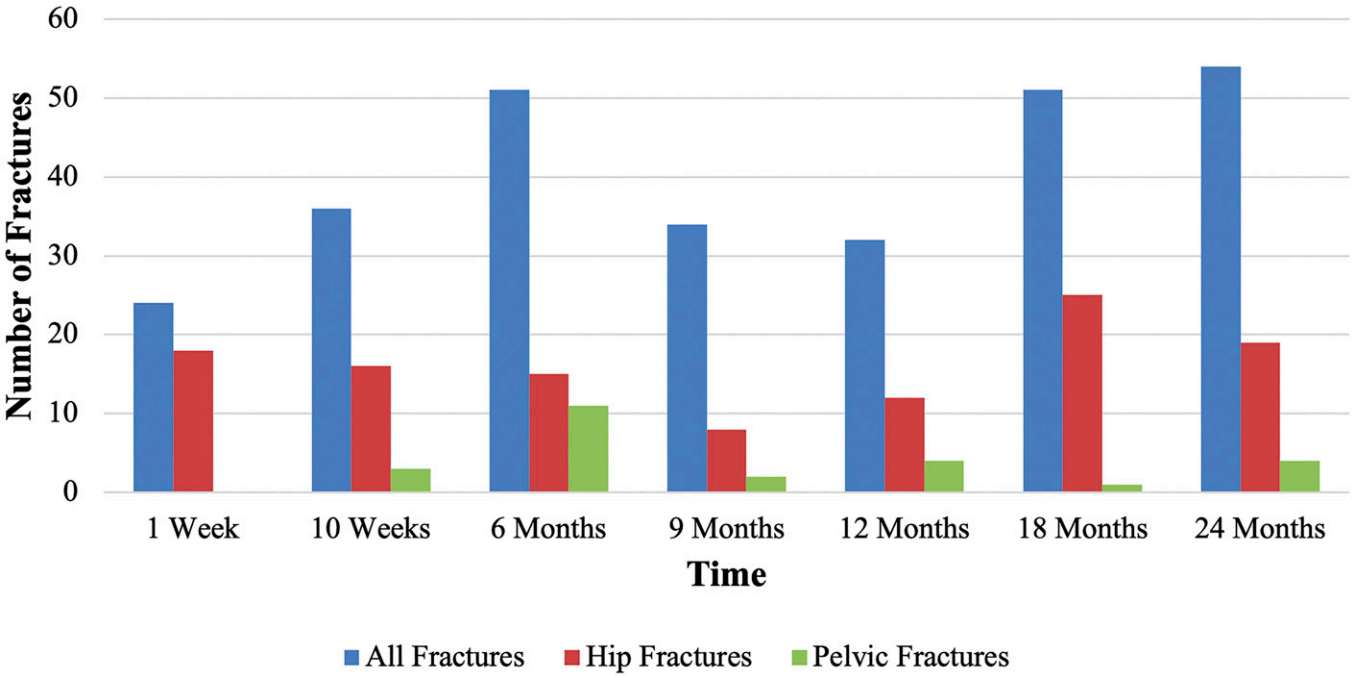

Fig. 1

Distribution of secondary fractures over 24 months in the FAITH and HEALTH trials.

frequent site of hip fracture), a differential in subsequent fracture risk may become apparent. It would then be possible to determine whether aggregation of all hip fractures into a single risk group is valid, or conversely whether disaggregation has value. We speculate that this could improve randomization in drug trials and performance audits of fracture prevention programs.

The standardized protocol in the HEALTH and FAITH trials for postoperative care for all enrolled patients included the initiation of treatment with 600 mg of calcium by mouth daily and 1,000 IU of vitamin D per day (in the absence of contraindications). Because of widely varying practices and resources in the numerous sites in 12 countries, we were unable to mandate prescription of bone-protective medications after the index hip fracture as a condition of participation. The protocol, therefore, required further investigation and treatment of osteoporosis (or intervention for fracture risk reduction) by local experts to be carried out at the study sites[21], since all included patients were considered at high risk for future fracture according to current guidelines[4]. Despite the fact that the study protocols directed the attention of participating surgeons and other study personnel to the importance of fracture prevention, only 25.2% of patients reported taking bone-protective medications at any time during the study. Unfortunately, we are unable to distinguish patients who did not fill prescriptions from those for whom no prescription was ordered. This distinction is important to the procedures of fracture liaison services in correcting undertreatment of patients at high risk for future major osteoporotic fractures. High-functioning fracture liaison services have reported medication prescription rates for older patients with a fragility fracture to be in the range of 66.2% to 90.5%[29-31].

The significantly higher number of females than males who have reported taking bone-protective medication is consistent with the widespread perception associating osteoporosis with female sex, although men who sustain hip fractures have equally high subsequent fracture rates and greater mortality risk[2]. The higher rates of treatment in patients who had nondisplaced rather than displaced fractures and in patients treated with arthroplasty rather than internal fixation may reflect surgeon perceptions and bias and are otherwise unexplained. Resource availability for surgical procedures and osteoporosis treatment may affect treatment rates. Medication costs may represent a barrier to prescriptions for reduction of fracture risk, although low-cost generic bisphosphonates are available in numerous countries.

As the 90 sites on 5 continents participated at least in part on the basis of the interest of a leading local surgeon investigator,

TABLE III Use of Osteoporosis Medications During at Least 1 Follow-up Visit in FAITH and HEALTH Studies

	FAITH (N = 1,079) *(no. [%])*	HEALTH (N = 1,441) *(no. [%])*
Osteoporosis medication		
Yes	177 (16.4)	457 (31.7)
Type of medication		
Bisphosphonates	149 (13.8)	322 (22.3)
Calcitonin	18 (1.7)	10 (0.7)
Other osteoporosis medications	15 (1.4)	148 (10.3)

TABLE IV Prognostic Variables Associated with Osteoporosis Medication Use (N = 2,457*; 634 Events with Use)

Variable†	Odds Ratio (95% CI)	P Value
Surgical method		
Arthroplasty versus internal fixation	3.48 (2.39, 5.20)	<0.001
Fracture displacement		
Nondisplaced versus displaced	1.81 (1.23, 2.78)	0.003
Sex		
Female versus male	1.75 (1.41, 2.17)	<0.001
Age (per 10-year increase)	0.96 (0.87, 1.06)	0.40
ASA physical status		
Class III, IV, and V versus class I and II	1.19 (0.97, 1.44)	0.09
Prefracture living setting		
Institutionalized versus not institutionalized	0.71 (0.42, 1.13)	0.20
Prefracture functional status		
Use of aid versus independent ambulator	1.02 (0.81, 1.29)	0.80

*Participants with complete data for this analysis. †The reference group is the second group listed. ASA = American Society of Anesthesiologists.

we considered that the sites were not necessarily fully representative of their country or continent. This selection bias discouraged us from comparing the data across regions. However, this did not, in our opinion, weaken our principal findings about the frequency of subsequent fractures and the low rate of secondary prevention through the use of bone-protective medications, which were consistent across all study sites.

The low rate of preventive intervention in these studies is consistent with the widely documented so-called care gap in clinical practice[32], i.e., the gap between evidence-based guideline recommendations for provision of preventive care and the widespread lack of treatment after hip fracture[33]. The failure, over the past 20 years, of individual practitioners and health systems to correct the well-documented lack of preventive treatment for high-risk patients who have sustained a hip fracture is a perplexing problem that has resisted correction[34,35]. In recent years, intensive focus has been placed on developing and implementing systematic fracture prevention programs in numerous countries[36-39]. This study demonstrates that the goal of systematically initiating preventive interventions following hip fracture has not been accomplished in most jurisdictions. The findings highlight the need for more effective methods to reverse the global shortfall in fracture liaison services or other effective systematic preventive programs.

The occurrence of a second fragility fracture in 9.0% of subjects, including a second hip fracture in 4.5%, within 24 months after the index femoral neck fracture in these 2 global cohorts supports the concept of an "imminent risk" of a subsequent fracture[25,26,40]. The median intervals from index fracture to secondary fracture in the 2 trials were 9.0 and 9.5 months. The short interval to a secondary fracture highlights the urgency of rapidly initiating preventive treatment after a fragility fracture as there is evidence of early improvement of bone architecture and bone density and early diminution of fracture risk within 6 months after initiating bone-protective medication[15-17]. We acknowledge that even prompt administration of medication might not provide protection from subsequent fractures that occur within the first few months following the index fracture.

This secondary analysis is strengthened by including >2,500 patients from 90 sites on 5 continents. The large sample size increases the external validity and generalizability of the outcomes. The frequent follow-up visits over 2 years allowed for a thorough assessment of study participants and detection of secondary fragility fractures, and for close monitoring of bone-protective medication use. We acknowledge that although data on medication use was collected as per the protocol by the study coordinators at each of the 7 follow-up visits, the data are weakened by being self-reported by participants.

This study also exposes the persistence of the infamous care gap—the failure of most centers to initiate a systematic preventive intervention after hip fracture, even when recommended by the protocol within the context of 2 large clinical trials. This highlights the global need to incorporate reliable systems for secondary prevention of future fractures into the management protocols of patients who sustain hip fractures.

In conclusion, subsequent fractures, including second hip fractures, occurred frequently and early following an index femoral neck fracture in 2 large prospectively followed global cohorts. Preventive interventions to reduce a subsequent fracture were instituted in only 1 of 4 patients even though a directive was included in each study protocol. ■

NOTE: The FAITH Investigators include Arvind Jain, Ash Moaveni, David Stephen, Davy J. Olakkengil, Deanna Lawson, Gillian Horner, Glynis Rose, Greg Etherington, Hamish Curry, Jules Dumais, Kate Eke, Rajanikanth Logishetty, Simone Evans, Sophie Lewis, Stephanie Shepard, Aaron Nauth, Aaron T. Creek, Abby Zellar, Abdel-Rahman Lawendy, Adam Dowrick, Ajay Gupta, Akhil Dadi, Albert van Kampen, Albert Yee, Alexander C. de Vries, Alexander de Mol van Otterloo, Alisha Garibaldi, Allen Liew, Allison W. McIntyre, Amal Shankar Prasad, Amanda W. Romero, Amar Rangan, Amber Oatt, Amir Sanghavi, Amy L. Foley, Anders Karlsten, Andrea Dolenc, Andrew Bucknill, Andrew Chia, Andrew Evans, Andrew Gong, Andrew H. Schmidt, Andrew J. Marcantonio, Andrew Jennings, Angela Ward, Angshuman Khanna, Anil Rai, Anke B. Smits, Annamarie D. Horan, Anne Christine Brekke, Annette Flynn, Aravin Duraikannan, Are Stødle, Arie B. van Vugt, Arlene Luther, Arthur W. Zurcher, Asgeir Amundsen, Ashley Carr, Ateet Sharma, Austin D. Hill, Axel Trommer, B. Sachidananda Rai, Barbara Hileman, Bart Schreurs, Bart Verhoeven, Benjamin B. Barden, Bernhard Flatøy, Berry I. Cleffken, Berthe Bøe, Bertrand Perey, Birgit C. Hanusch, Brad Weening, Bram Fioole, Bram Rijbroek, Brett D. Crist, Brett Halliday, Brett Peterson, Brian Mullis, C. Glen Richardson, Callum Clark, Carlos A. Sagebien, Carmen C. van der Pol, Carol Bowler, Catherine A. Humphrey, Catherine Coady, Cees L. Koppert, Chad Coles, Chadi Tannoury, Charles J. DePaolo, Chris Gayton, Chris Herriott, Christina Reeves, Christina Tieszer, Christine Dobb, Christopher G. Anderson, Claire Sage, Claudine Cuento, Clifford B. Jones, Coks H.R. Bosman, Colleen Linehan, Cor P. van der Hart, Corey Henderson, Courtland G. Lewis, Craig A. Davis, Craig Donohue, Cyril Mauffrey, D.C. Sundaresh, Dana J. Farrell, Daniel B. Whelan, Daniel Horwitz, Daniel Stinner, Darius Viskontas, Darren M. Roffey, David Alexander, David E. Karges, David Hak, David Johnston, David Love, David M. Wright, David P. Zamorano, David R. Goetz, David Sanders, David Yen, Davide Bardana, Deborah Maddock, Debra L. Sietsema, Deeba Pourmand, Dennis Den Hartog, Derek Donegan, Diane Heels-Ansdell, Diane Nam, Dominic Inman, Dory Boyer, Doug Li, Douglas Gibula, Dustin M. Price, Dylan J. Watson, E. Mark Hammerberg, Edward C.T.H. Tan, Eelco J.R. de Graaf, Elise Berg Vesterhus, Elizabeth Roper, Elton Edwards, Emil H. Schemitsch, Eric R. Hammacher, Eric R. Henderson, Erica Whatley, Erick T. Torres, Erik G.J. Vermeulen, Erin Finn, Esther M.M. Van Lieshout, Eugene K. Wai, Evan R. Bannister, Evelyn Kile, Evert B.M. Theunissen, Ewan D. Ritchie, Farah Khan, Farhad Moola, Fiona Howells, Frank de Nies, Frank H.W.M. van der Heijden, Frank R.A.J. de Meulemeester, Frede Frihagen, Fredrik Nilsen, G. Ben Schmidt, G.H. Robert Albers, Garland K. Gudger Jr., Garth Johnson, Gary Gruen, Gary Zohman, Gaurav Sharma, Gavin Wood, Geert W.M. Tetteroo, Geir Hjorthaug, Geir Jomaas, Geoff Donald, Geoffrey Ryan Rieser, Gerald Reardon, Gerard P. Slobogean, Gert R Roukema, Gijs A. Visser, Gilbert Moatshe, Gordon Guyatt, Graham Chuter, Gregory J. Della Rocca, Guri Ekås, Gwendolyn Dobbin, H. Michael Lemke, Han Boxma, Hannah Gissel, Hans Kreder, Hans Kuiken, Hans L.F. Brom, Hans-Christoph Pape, Harm M. van der Vis, Harvinder Bedi, Heather A. Vallier, Heather Brien, Heather Silva, Heike Newman, Helena Viveiros, Henk van der Hoeven, Henry Ahn, Herman Johal, Herman Rijna, Heyn Stockmann, Hong A. Josaputra, Hope Carlisle, Igor van der Brand III, Imro Dawson, Ivan Tarkin, Ivan Wong, J. Andrew Parr, J. Andrew Trenholm, J. Carel Goslings, J. David Amirault, J. Scott Broderick, Jaap P. Snellen, Jacco A.C. Zijl, Jaimo Ahn, James Ficke, James Irrgang, James Powell, James R. Ringler, James Shaer, James T. Monica, Jan Biert, Jan Bosma, Jan Egil Brattgjerd, Jan Paul M. Frölke, Jan Wille, Janakiraman Rajakumar, Jane E. Walker, Janell K. Baker, Janos P. Ertl, Jean Paul P.M. de Vries, Jean W.M. Gardeniers, Jedediah May, Jeff Yach, Jennifer T. Hidy, Jerald R. Westberg, Jeremy A. Hall, Jeroen van Mulken, Jessica Cooper McBeth, Jochem

Hoogendoorn, Jodi M. Hoffman, Joe Joseph Cherian, John A. Tanksley, John Clarke-Jenssen, John D. Adams, John Esterhai, John F. Tilzey, John Murnaghan, John P. Ketz, John S. Garfi, John Schwappach, John T. Gorczyca, John Wyrick, Jonas Rydinge, Jonathan L. Foret, Jonathan M. Gross, Jonathan P. Keeve, Joost Meijer, Joris J.G. Scheepers, Joseph Baele, Joseph O'Neil, Joseph R. Cass, Joseph R. Hsu, Julia Lee, Julie A. Switzer, Julie Agel, Justin E. Richards, Justin W. Langan, Kahn Turckan, Kaili Pecorella, Kamal Rai, Kamran Aurang, Karl Shively, Karlijn van Wessem, Karyn Moon, Katie Erwin, Katrine Milner, Kees Jan Ponsen, Kelli Mills, Kelly Apostle, Kelly Johnston, Kelly Trask, Kent Strohecker, Kenya Stringfellow, Kevin K. Kruse, Kevin Tetsworth, Khalis Mitchell, Kieran Browner, Kim Hemlock, Kimberly Carcary, Knut Jørgen Haug, Krista Noble, Kristin Robbins, Krystal Payton, Kyle J. Jeray, L. Joseph Rubino, Lauren A. Nastoff, Lauren C. Leffler, Lawrence K. O'Malley II, Lawrence M. Specht, Lehana Thabane, Leo M.G. Geeraedts, Leslie E. Shell, Linda K. Anderson, Linda S. Eickhoff, Lindsey Lyle, Lindsey Pilling, Lisa Buckingham, Lisa K. Cannada, Lisa M. Wild, Liz Dulaney-Cripe, Lodewijk M.S.J. Poelhekke, Lonneke Govaert, Lu Ton, Lucksy Kottam, Luke P.H. Leenen, Lydia Clipper, Lyle T. Jackson, Lynne Hampton, Maarten C. de Waal Malefijt, Maarten P. Simons, Maarten van der Elst, Maarten W.G.A. Bronkhorst, Mahesh Bhatia, Marc Swiontkowski, Margaret J. Lobo, Marilyn Swinton, Marinis Pirpiris, Marius Molund, Mark Gichuru, Mark Glazebrook, Mark Harrison, Mark Jenkins, Mark MacLeod, Mark R. de Vries, Mark S. Butler, Markku Nousiainen, Martijne van 't Riet, Martin C. Tynan, Martin Campo, Martin G. Eversdijk, Martin J. Heetveld, Martin Richardson, Mary Breslin, Mary Fan, Matt Edison, Matthew Napierala, Matthias Knobe, Matthias Russ, Mauri Zomar, Maurits de Brauw, Max Esser, Meghan Hurley, Melissa E. Peters, Melissa Lorenzo, Mengnai Li, Michael Archdeacon, Michael Biddulph, Michael Charlton, Michael D. McDonald, Michael D. McKee, Michael Dunbar, Michael E. Torchia, Michael Gross, Michael Hewitt, Michael Holt, Michael J. Prayson, Michael J.R. Edwards, Michael L. Beckish, Michael L. Brennan, Michael P. Dohm, Michael S.H. Kain, Michelle Vogt, Michelle Yu, Michiel H.J. Verhofstad, Michiel J.M. Segers, Michiel P.C. Siroen, Mike Reed, Milena R. Vicente, Milko M.M. Bruijninckx, Mittal Trivedi, Mohit Bhandari, Molly M. Moore, Monica Kunz, Morten Smedsrud, Naveen Palla, Neeraj Jain, Nico J.M. Out, Nicole Simunovic, Niels W.L. Schep, Oliver Müller, Onno R. Guicherit, Oscar J.F. Van Waes, Otis Wang, Pascal G. Doornebosch, Patricia Seuffert, Patrick J. Hesketh, Patrick Weinrauch, Paul Duffy, Paul Keller, Paul M. Lafferty, Paul Pincus, Paul Tornetta III, Paul Zalzal, Paula McKay, Peter A. Cole, Peter D. de Rooij, Peter Hull, Peter M.N.Y.M. Go, Peter Patka, Peter Siska, Peter Weingarten, Philip Kregor, Philip Stahel, Philip Stull, Philippe Wittich, Piet A.R. de Rijcke, Pim Oprel, P.J. Devereaux, Qi Zhou, R. Lee Murphy, Rachel Alosky, Rachel Clarkson, Raely Moon, Rajesh Nanda, Raymond J. Sullivan, Rebecca G. Snider, Richard E. Buckley, Richard Iorio, Richard J. Farrugia, Richard Jenkinson, Richard Laughlin, Richard P.R. Groenendijk, Richard W. Gurich Jr., Ripley Worman, Rob Silvis, Robert Haverlag, Robert J. Teasdall, Robert Korley, Robert McCormack, Robert Probe, Robert V. Cantu, Roger B. Huff, Rogier K.J. Simmermacher, Rolf Peters, Roman Pfeifer, Ronald Liem, Ronald N. Wessel, Ronald Verhagen, Ronald Vuylsteke, Ross Leighton, Ross McKercher, Rudolf W. Poolman, Russell Miller, Ryan Bicknell, Ryan Finnan, Ryan M. Khan, Samir Mehta, Sandy Vang, Sanjay Singh, Sanjeev Anand, Sarah A. Anderson, Sarah A. Dawson, Scott B. Marston, Scott E. Porter, Scott T. Watson, Sebastiaan Festen, Shane Lieberman, Shannon Puloski, Shea A. Bielby, Sheila Sprague, Shelley Hess, Shelley MacDonald, Sofia Bzovsky, Sondre Hasselund, Stein Ugland, Stephanie Caminiti, Stephanie L. Tanner, Stephanie M. Zielinski, Stephen A. Sems, Stephen D. Walter, Stephen Doig, Stephen H. Finley, Stephen Kates, Stephen Lindenbaum, Stephen P. Kingwell, Steve Csongvay, Steve Papp, Steven E. Buijk, Steven J. Rhemrev, Steven M. Hollenbeck, Steven M. van Gaalen, Steven Yang, Stuart Weinerman, Subash, Sue Lambert, Susan Liew, Sven A.G. Meylaerts, Taco J. Blokhuis, Tammo S. de Vries Reilingh, Tarjei Lona, Taryn Scott, Teresa K. Swenson, Terrence J. Endres, Terry Axelrod, Teun van Egmond, Thomas B. Pace, Thomas Kibsgård, Thomas M. Schaller, Thuan V. Ly, Timothy J. Miller, Timothy Weber, Toan Le, Todd M. Oliver, Tom M. Karsten, Tor Borch, Tor Magne Hoseth, Tor Nicolaisen, Torben Ianssen, Tori Rutherford, Tracy Nanney, Trevor Gervais, Trevor Stone, Tyson Schrickel, Tyson Scrabeck, Utsav Ganguly, V. Naumetz, Valda Frizzell, Veronica Wadey, Vicki Jones, Victoria Avram, Vimlesh Mishra, Vineet Yadav, Vinod Arora, Vivek Tyagi, Vivian Borsella, W. Jaap Willems, W.H. Hoffman, Wade T. Gofton, Wesley G. Lackey, Wesley Ghent, William Obremskey, William Oxner, William W. Cross III, Yvonne M. Murtha, and Zoe Murdoch.

The HEALTH Investigators include Aaron Nauth, Abdullah Mamun, Abdulmajid Ibrahim, Abigail Weeks, Ad F.A. van Beurden, Adam Dowrick, Adam Watson, Adolfo Galán, Adriaan Mostert, Adrian Butler-Manuel, Adrianus C.H. Slingerland, Adrianus F.C.M. Moonen, Adrianus J.P. Joosten, Aftab Akbari, Agustí Bartra, Aileen Manganaro, Aimee Theriault, Ajay Malviya, Ajay Manjoo, Alanna Milne, Alberto Carli, Alex Vris, Alexander F.W. Barnaart, Alexandre Leclerc, Ali Oliashirazi, Alison Lewis, Alonso Zumbado, Alyson Andrew, Amanda Cowland, Amanda D. Klaassen, Amar Rangan, Ami R. Stuart, Amit W. Bidwai, Amr Abdelgawad, An Murty, Andrea Gurule, Andrew Armitage, Andrew Brown, Andrew Chia, Andrew Furey, Andrew Gong, Andrew Marcantonio, Andrew Parr, Andrew Patten, Andrew Sems, Andrew Thomson, Andrew Trenholm, Angela Bradbury, Anna Berridge, Anna Fouracres, Anna Rose Soliman, Annamarie Horan, Anne Christine Brekke, Annie Arteau, Anthony Hui, Antoni Fraguas Castany, Antoni Nargol, Antonio Royo, Araby Sivananthan, Arantxa Capel-Agundez, Aravin Duraikannan, Arnard van der Zwan, Arthur E.B. Kleipool, Arthur van Noort, Arthur W. Zurcher, Arvind Jain, Ash Moaveni, Ashley Carr, Ashley Neese, Atul Kamath, Aujlia Randeep, Barbara Foreman, Barbara M. Hileman, Bastiaan Boetes, Bauke W. Kooistra, Ben Miller, Benedict Lankester, Benita Adams, Benita Okocha, Benjamin K. Potter, Benjamin M. Stronach, Benoit Benoit, Bernard G. Schutte, Bernard Laliberté, Bernhard Flatøy Stian Svenøy, Bertrand Perey, Bhaveen Kapadia, Bindu Mohan, Birgit Hanusch, Bregje J.W. Thomassen, Brenda Chen Fan, Brian Mullis, C. Glen Richardson, Cameron Howes, Carl Erik Alm, Carl Moores, Carla Carbonell Rosell, Carlos Sagebien, Carly St. Germain, Carol Bowler, Catherine Coady, Catherine Hilton, Catherine McDougall, Chad Coles, Charles DePaolo, Chatar Goyal, Cheryl Kreviazuk, Chris Herriott, Christina Haines, Christina Riggsbee, Christine Dobb, Christopher Gooding, Christopher Kennedy, Christopher Martin, Christopher Mutty, Christopher Pelt, Christopher Peters, Christopher Tullock, Cindy Fastje, Claire Sage, Clay A. Spitler, Clifford B. Jones, Craig Davis, Craig Donohue, Craig Stone, Craig White, Cristina Martinez Merchan, Daniel Haverkamp, Daniel P. Waren, Daniel Squire, Daniel Whelan, Daniel Williams, Danielle D. Langeloo, Darius Viskontas, Daud Chou, David Alexander, David Bainbridge, David Bowyer, David Harwood, David Isaac, David Johnston, David Novikov, David Rothberg, David Stephen, David Townshend, David Walmsley, David Zamorano, Dean G. Malish, Debbie Lee, Debbie Read, Deborah Bunn, Debra L. Sietsema, Deeba Pourmand, Denise Eygendaal, Derek Donegan, Derek F.P. van Deurzen, Derek Kramer, Diana Noriego, Diane Heels-Ansdell, Diederik A. Vergroesen, Diederik H.R. Kempen, Diego Collado Gastalver, Dileep Kumar, Dinesh Sharma, Dirk Jan F. Moojen, Dominic Inman, Dory Boyer, Doug Li, Douglas Kiester, Earl R. Bogoch, Edgar J.T. ten Holder, Eduard L.A.R. Mutsaerts, Edward Westrick, Eldridge Batuyong, Elise Berg Vesterhus, Elisha A. Chance, Elizabeth Corbishley, Ellie B.M. Landman, Elton Edwards, Elvira R. Flikweert, Emil H. Schemitsch, Emilio Delgado-Diaz, Encarnación Cruz, Enes Kanlic, Engelke Randers, Enrike H.M.J. van der Linden-van der Zwaag, Enrique Guerado, Eric A. Hoebink, Eric E.J. Raven, Erik N. Kubiak, Erin Baker, Ernesto Guerra-Farfán, Esmat Dessouki, Esther M.M. Van Lieshout, Étienne Belzile, Farhad Moola, Fathima Adamsahib, Felipe Moreira Borim, Felix Cheung, Ferry Steenstra, Finnur Snorrason, Fiona Hammonds, Frances New, Francesc Anglés, François Marquis, Frank R.A.J. de Meulemeester, Frank van Bommel, Franklin D. Shuler, Frans J. Kurek, Frede Frihagen, G.-Yves Laflamme, G. Solinge, G.H. Rob Albers, Gail Waddell, Gavin Bartlett, Geir Hjorthaug, Geoff Dervin, Gerald Reardon, Gerard P. Slobogean, Glenn Boyce, Gordon H. Guyatt, Gordon Higgins, Graeme Brown, Grant Buchanan, Greg Erens, Gregg Strathy, Gregory Abelseth, Guy Selmon, Gythe H. Bulstra, H. Michael Lemke, Hannie H.F. Elskamp-Meijerman, Hans Kreder, Hans Schüller, Hans-Peter W. van Jonbergen, Harald I.H. Lampe, Harm M. van der Vis, Harvinder Bedi, Heather Cosgrove, Heather Silva, Helen Shirley, Hélène Côté, Henry Ahn, Henry M. Broekhuyse, Hesham Abdelbary, Hope Carlisle, Hugo W. Bolhuis, Huub J.L. van der Heide, Ian Carluke, Ian Wallace, Ian Young, Ibo van der Haven, Ihsan Amajjar, Iñaki Mimendia Sancho, Ingunn Skaugrud, Irene Leung, Iriss Mariano, Istvan Batta, Ivan Wong, J. Bernard Mullers, J. David Amirault, Jackie Dingle, Jaimo Ahn, James D. Slover, James Day, James MacKenzie, James P. Waddell, James R. Ringler, James Roberson, James Webb, Jamila Kassam, Jan P. van Dijk, Jan-Willem A. Swen, Janell Baker, Janet Austin, Janet Sinclair, Jani Knifsund, Janos Ertl, Jari Mokka, Jason Werle, Jasper de Vries, Jaume Mestre Torres, Javad Parvizi, Jean Lamontagne, Jenaro A. Fernandez-Valencia, Jennifer S. Barr, Jennifer T. Hidy, Jenny Nichols, Jeremy A. Hall, Jeremy Gililland, Jessica Peattie, Jessica Summers, Joan Minguell Monyart, Joaquin Sanchez-Sotelo, Jochem Nagels, Joel Werier, Johanna Dobransky, John S.J. Ham, John A. Scolaro, John Antoniou, John Cheung, John Clarke-Jenssen, John Davison, John Garfi, John L. Esterhai Jr., John Skelley, John Tilzey, John Townley, John V. Gentile, Joint Research Group, Jonas Rydinge, Jonathan M. Vigdorchik, Jonathon Coorsh, Jonathon Salava, Jonathon White, Joost A.A.M. van den Hout, Joost M. Reuver, Jordi Selga Marsà, Jordi Teixidor Serra, Jordi Tomás Hernández, Jorge Nuñez Camarena, José A. Moreno-Beamud, José Andrés Peiró, José Luis Camarena, Joseph Cass, Joseph Guth, Joseph Queally, Joshua Lee, Josie M. Hydrick, Juan Antonio Porcel Vázquez, Juan Ramon Cano, Juan Shunia, Judd Cummings, Judith Sánchez-Raya, Juhu Joseph, Julie Fournier, Juliet James, Julio Fernandes, Justin LeBlanc, K. van Egmond, Kaare Midtgaard, Kari Isotalo, Karin E. de Kroon, Karine Tardif, Karl Shively, Karyn Moon, Kate Weatherly, Kathleen Peter, Katie McIlquham, Katrine Milner, Keegan Au, Keemu Hannes, Keijo Mäkelä, Kelly A. Lefaivre, Kelly Apostle, Kelly Fusco, Kelly Johnston, Kelly Trask, Kendra Marr, Kenneth A. Egol, Kenneth J. Koval, Kerry Tai, Kerry Third, Kevin Emmerson, Kevin Eng, Kevin J. Bozic, Kevin Tetsworth, Kim Madden, Kim Miles, Kimberly Carcary, Kimona Issa, Kirby Corbey, Knut Erik Mjaaland, Kyle Webb, Kyrsten Payne, Lars Nordsletten, Laura Ramos, Lawrence Specht, Leah Schultz, Lehana Thabane, Lein Schuman, Lene B. Solberg, Leon H.G.J. Elmans, Leonard Marais, Leslie N. Johnson, Lijkele Beimers, Linda Morgan, Lisa Buckingham, Lisa Murphy, Loes W.A.H. van Beers, Lonneke Buitenhuis, Lu Ton, Luc Bedard, Luc Lemire, Luc Petitclerc, Lucksy Kottam, Lucy Pippard, Luke Brunton, Luken Zubizarreta Barrutia, M. Cristina García Martínez, Maarten P. Simons, Maarten Rademakers, Madhu Mazumdar, Manish Divekar, Manjit Attwal, Manjunathan Sivaprakasam, Manuel Godino, Marc Bouchard, Marcia Clark, Maria Gordon, Maria Jurado Ruiz, Maria Manson, Maria Villar Casares, Marianne Westberg, Marie-ève Roger, Mariëlla E.M. Volkers, Marilyn Swinton, Mark Anders, Mark C. Altena, Mark Glazebrook, Mark L.M. Falke, Mark Luborsky, Mark T. Russell, Mark Webster, Markku Nousiainen, Marla Ross, Marta Gutierrez, Martí Bernaus, Martí Plomer Sánchez, Martin Bédard, Martin J. Heetveld, Martin Lesieur, Martin M. Campo, Mary Bayers-Thering, Mary Beth Cordle, Mary June Francisco, Marylou Mullen, Mathijs P. Somford, Matthew Hall, Matthew Phillips, Matthias Russ, Matti Seppänen, Mauri Zomar, Max Esser, Meaghan Morton, Melanie MacNevin, Melanie T. MacNevin, Melissa Lorenzo, Michael Biddulph, Michael D. McKee, Michael Dohm, Michael Dunbar, Michael Gross, Michael H. Maher, Michael Hewitt, Michael Kain, Michael Mont, Michael Taunton, Michael Torchia, Michel Malo, Michel P.J. van den Bekerom, Michèle Angers, Michelle Arakgi, Michelle J. Lespasio, Miguel Angel Froufe Siota, Miguel Hirschfeld, Mika Junnila, Mike Hogervorst, Mike Reed, Mikko Karvonen, Milad Modarresi, Milena R. Vicente, Minnie Parsons, Miranda Champion, Míriam Garrido Clua, Mohit Bhandari, Molly Moore, Mona Mohamed, Monica Kunz, Nathan Donovan, Nathan N. O'Hara, Naveen Khan, Neil Sheth, Neil White, Nicki Devooght-Johnson, Nienke W. Willigenburg, Niko Strandberg, Nirmal C. Tejwani, Ole Christian Brun, Oliver Keast-Butler, Omar Dessouki, Osama Gharsaa, Oscar Ares, Otis Shirley, Otis Wang, P. Houben, P.J. Devereaux, Pablo Castillón, Palakkad Easwaran, Pankajkumar Patel, Paqui Fontalba, Paril Suthar, Patricia Seuffert, Patrick F. Bergin, Patrick Hesketh, Paul Baker, Paul Beaulé, Paul Cameron, Paul Duffy, Paul Johnson, Paul Kim, Paul Latimer, Paul Partington, Paul Porter, Paul T.P.W. Burgers, Paul Tornetta III, Paula McKay, Pauline Mercer, Pedro Caba-Dousseaux, Peter A. Nolte, Peter H.C. den Hollander, Peter Hull, Peter J. O'Brien, Peter Lapner, Peter Rockwood, Peter Weingarten, Philip Stull, Phumeena Balasuberamaniam, Pierre Guy, Pierre Ranger, Pieter H.J. Bullens, Pieter Jan Damen, Pilar Camacho-Carrasco, Pilar Gavira, Piotr A. Blachut, Prism Schneider, Quazi Ibrahim, R. Nijveldt, R.G. Zuurmond, Rachel Reilly, Raely Pritchard, Rafael Navarro-Arribas, Rafael Sierra, Rajesh Kakwani, Rajesh Nanda, Rajnikanth Logishetty, Raman Johal, Ran Schwarzkopf, Ravi Tuazon, Rebecca Boulton, Rebecca Danielwicz, Rebecca Ferrier, Reitze Rodseth, René J.T.M. Bleker, Ria De Gorter (Cagaanan), Rian Smit, Richard Angliss, Richard Buckley, Richard Freeman, Richard Jeavons, Richard Jenkinson, Richard Page, Rinco C.T. Koorevaar, Ripley Worman, Rob H. Jansen, Rob Kooijman, Rob Sharp, Robert D. Zura, Robert Haverlag, Robert J. Feibel, Robert Korley, Robert McCormack, Robert Wagenmakers, Robin Kincaid, Roelf R. Postema, Ronald E. Delanois, Rory Middleton, Roshan Raghavan, Ross Leighton, Ross McKercher, Rover Krips, Roy I. Davidovitch, Rudolf W. Poolman, Russell Meldrum, Russell Miller, Rutger C.I. van Geenen, S. Subramanian, Saara Meronen, Saboura Mahdavi, Sachin P. Badhe, Sagar Desai, Sally Beattie, Sameer Khan, Samer Al-dirra, Samir Chhabra, Samir Mehta, Sammy Hanna, Sandra Ponce Ruiz, Sanjit R. Konda, Sara A. Ruggiero, Sarah Anthony, Sarah Shelton, Sarah Ward, Sarim S. Ahmed, Saskia C. Wiersma, Satish Ganesan, Scott Crawford, Scott Muller, Sebastian Rodriguez-Elizalde, Sebastian Tomescu, Shanaz Ahmad, Shannon Puloski, Sharon Siddons, Shaun Sexton, Sheila Sprague, Shelley MacDonald, Sherina Holland, Shyam Maimen, Simon Hoskinson, Simon Jameson, Simon Pearce, Simon Williams, Simone Hargreaves, Simphiwe Gumede, Sissel Knuts, Siva Chandrasekaran, Sofia Bzovsky, Sreebala C.M. Srinivasan, Sridhar Rachala, Stefan B. Keizer, Stefan B.T. Bolder, Stefan Breugem, Stephan Röhrl, Stéphane Pelet, Stephanie Yee, Stephen D. Walter, Stephen Doig, Stephen Hunt, Stephen Kayiaros, Stephen Key, Stephen Lyman, Stephen McDonnell, Steve Blake, Steve Csongvay, Steve Millington, Steven Lindenbaum, Steven Olson, Stewart Weinerman, Stuart Goodman, Sue Grice, Susan Liew, Susan Muray, Sven H. van Helden, Sylvain Belzile, Sylvie Turmel, Tab Mabry, Tanja Harrison, Taryn Scott, Teresa Sanclemente Boli, Terry Axelrod, Theresa B. Pedutem, Thomas A. Einhorn, Thomas Bradbury, Thomas F. Higgins, Thomas Rose, Tiffany Morrison, Tigran Garabekyan, Tim Ramsay, Timothy J. Sauber, Timothy R. Daniels, Timothy Wilson-Byrne, Tina Samuel, Tjitte de Jong, Toni M. McLaurin, Torben Ianssen, Tracey Nanney, Trevor B. Stone, Tyson T. Schrickel, Valda Frizzell, Valisha Keough, Vanessa A.B. Scholtes, Veronica Conboy, Veronica Wadey, Vicente Molero García, Víctor Barro Ojeda, Victor Solis, Victoria Avram, W. Paul C.A. Winia, W. Peter J. Fontijne, W.R. Spanjersberg, Wasim Khan, Wesley Ghent, Willem H. Roerdink, Willem Jan Kleyn Molekamp, William Cross, William Eardley, William Farrington, William Moores, William Oxner, William R. Creevy, Wouter H. van Helden, Xavier Madirolas, Yaiza García Sánchez, Ydo V. Kleinlugtenbelt, Yousef El-Houdiri, Zaid Al-Wattar, and Zoe Murdoch.

Earl Bogoch, MD, FRCSC[1,2]
Francesc A. Marcano-Fernández, MD, PhD[3]
Emil H. Schemitsch, MD, FRCSC[4]
Qi Zhou, PhD[5]
Sofia Bzovsky, MSc[6]
Mohit Bhandari, MD, PhD, FRCSC[5,6]
Prism S. Schneider, MD, FRCSC, PhD[7]
Marc Swiontkowski, MD[8]
Sheila Sprague, PhD[5,6]

[1]Department of Surgery, University of Toronto, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Ontario, Canada

[2]University of Toronto, Toronto, Ontario, Canada

[3]Orthopaedic Department, Parc Taulí Hospital Universitari, Institut d'Investigació i Innovació Parc Taulí I3PT, Universitat Autònoma de Barcelona, Sabadell, Spain

[4]Department of Surgery, University of Western Ontario, London, Ontario, Canada

[5]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada

[6]Division of Orthopaedic Surgery, Department of Surgery, McMaster University, Hamilton, Ontario, Canada

[7]Division of Orthopaedic Trauma, Department of Surgery, University of Calgary, Calgary, Alberta, Canada

[8]Department of Orthopaedic Surgery, University of Minnesota, Minneapolis, Minnesota

Email for corresponding author: Earl.Bogoch@unityhealth.to

References

1. Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int. 2006 Dec;17(12):1726-33.

2. Leslie WD, Yan L, Lix LM, Morin SN. Time dependency in early major osteoporotic and hip re-fractures in women and men aged 50 years and older: a population-based observational study. Osteoporos Int. 2022 Jan;33(1):39-46.

3. Colón-Emeric C, Kuchibhatla M, Pieper C, Hawkes W, Fredman L, Magaziner J, Zimmerman S, Lyles KW. The contribution of hip fracture to risk of subsequent fractures: data from two longitudinal studies. Osteoporos Int. 2003 Nov;14(11):879-83.

4. Lentle B, Cheung AM, Hanley DA, Leslie WD, Lyons D, Papaioannou A, Atkinson S, Brown JP, Feldman S, Hodsman AB, Jamal AS, Josse RG, Kaiser SM, Kvern B, Morin S, Siminoski K; Scientific Advisory Council of Osteoporosis Canada. Osteoporosis Canada 2010 guidelines for the assessment of fracture risk. Can Assoc Radiol J. 2011 Nov;62(4):243-50.

5. Compston J, Cooper A, Cooper C, Gittoes N, Gregson C, Harvey N, Hope S, Kanis JA, McCloskey EV, Poole KES, Reid DM, Selby P, Thompson F, Thurston A, Vine N; National Osteoporosis Guideline Group (NOGG). UK clinical guideline for the prevention and treatment of osteoporosis. Arch Osteoporos. 2017 Dec;12(1):43.

6. Qaseem A, Forciea MA, McLean RM, Denberg TD, Barry MJ, Cooke M, Fitterman N, Harris RP, Humphrey LL, Kansagara D, McLean RM, Mir TP, Schünemann HJ; Clinical Guidelines Committee of the American College of Physicians. Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update from the American College of Physicians. Ann Intern Med. 2017 Jun 6;166(11):818-39.

7. Kanis JA, Delmas P, Burckhardt P, Cooper C, Torgerson D; The European Foundation for Osteoporosis and Bone Disease. Guidelines for diagnosis and management of osteoporosis. Osteoporos Int. 1997;7(4):390-406.

8. Kanis JA, McCloskey EV, Johansson H, Cooper C, Rizzoli R, Reginster JY; Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the Committee of Scientific Advisors of the International Osteoporosis Foundation (IOF). European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int. 2013 Jan;24(1):23-57.

9. Lin SY, Hung MC, Chang SF, Tsuang FY, Chang JZC, Sun JS. Efficacy and Safety of Postmenopausal Osteoporosis Treatments: A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials. J Clin Med. 2021 Jul 8;10(14):3043.

10. Sujic R, Beaton DE, Mamdani M, Cadarette SM, Luo J, Jaglal S, Sale JEM, Jain R, Bogoch E; Ontario Osteoporosis Strategy Fracture Screening and Prevention Program Evaluation Team. Five-year refracture rates of a province-wide fracture liaison service. Osteoporos Int. 2019 Aug;30(8):1671-7.

11. Sheikh HQ, Hossain FS, Khan S, Usman M, Kapoor H, Aqil A. Short-term risk factors for a second hip fracture in a UK population. Eur J Orthop Surg Traumatol. 2019 Jul;29(5):1055-60.

12. Bunta AD, Edwards BJ, Macaulay WB Jr, Jeray KJ, Tosi LL, Jones CB, Sietsema DL, Kaufman JD, Murphy SA, Song J, Goulet JA, Friedlaender GE, Swiontkowski MF, Dirschl DR. Own the Bone, a System-Based Intervention, Improves Osteoporosis Care After Fragility Fractures. J Bone Joint Surg Am. 2016 Dec 21;98(24):e109.

13. Jaglal SB, Hawker G, Cameron C, Canavan J, Beaton D, Bogoch E, Jain R, Papaioannou A; Osteoporosis Research, Monitoring and Evaluation Working Group. The Ontario Osteoporosis Strategy: implementation of a population-based osteoporosis action plan in Canada. Osteoporos Int. 2010 Jun;21(6):903-8.

14. Beaton DE, Mamdani M, Zheng H, Jaglal S, Cadarette SM, Bogoch ER, Sale JEM, Sujic R, Jain R; Ontario Osteoporosis Strategy Fracture Clinic Screening Program Evaluation Team. Improvements in osteoporosis testing and care are found following the wide scale implementation of the Ontario Fracture Clinic Screening Program: An interrupted time series analysis. Medicine (Baltimore). 2017 Dec;96(48):e9012.

15. Lyles KW, Colón-Emeric CS, Magaziner JS, Adachi JD, Pieper CF, Mautalen C, Hyldstrup L, Recknor C, Nordsletten L, Moore KA, Lavecchia C, Zhang J, Mesenbrink P, Hodgson PK, Abrams K, Orloff JJ, Horowitz Z, Eriksen EF, Boonen S; HORIZON Recurrent Fracture Trial. Zoledronic acid and clinical fractures and mortality after hip fracture. N Engl J Med. 2007 Nov 1;357(18):1799-809.

16. Reginster J, Minne HW, Sorensen OH, Hooper M, Roux C, Brandi ML, Lund B, Ethgen D, Pack S, Roumagnac I, Eastell R; Vertebral Efficacy with Risedronate Therapy (VERT) Study Group. Randomized trial of the effects of risedronate on vertebral fractures in women with established postmenopausal osteoporosis. Osteoporos Int. 2000;11(1):83-91.

17. Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, Delmas P, Zoog HB, Austin M, Wang A, Kutilek S, Adami S, Zanchetta J, Libanati C, Siddhanti S, Christiansen C; FREEDOM Trial. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. N Engl J Med. 2009 Aug 20;361(8):756-65.

18. Fixation using Alternative Implants for the Treatment of Hip fractures (FAITH) Investigators. Fracture fixation in the operative management of hip fractures (FAITH): an international, multicentre, randomised controlled trial. Lancet. 2017 Apr 15;389(10078):1519-27.

19. Bhandari M, Einhorn TA, Guyatt G, Schemitsch EH, Zura RD, Sprague S, Frihagen F, Guerra-Farfán E, Kleinlugtenbelt YV, Poolman RW, Rangan A, Bzovsky S, Heels-Ansdell D, Thabane L, Walter SD, Devereaux PJ; HEALTH Investigators. Total Hip Arthroplasty or Hemiarthroplasty for Hip Fracture. N Engl J Med. 2019 Dec 5;381(23):2199-208.

20. Dreinhöfer KE, Mitchell PJ, Bégué T, Cooper C, Costa ML, Falaschi P, Hertz K, Marsh D, Maggi S, Nana A, Palm H, Speerin R, Magaziner J; on behalf of: the Fragility Fracture Network (FFN); European Geriatric Medicine Society (EuGMS); European Federation of National Associations of Orthopaedics and Traumatology (EFORT); International Collaboration of Orthopaedic Nursing (ICON); International Geriatric Fracture Society (IGFS); International Osteoporosis Foundation (IOF). A global call to action to improve the care of people with fragility fractures. Injury. 2018 Aug;49(8):1393-7.

21. FAITH Investigators. Fixation using alternative implants for the treatment of hip fractures (FAITH): design and rationale for a multi-centre randomized trial comparing sliding hip screws and cancellous screws on revision surgery rates and quality of life in the treatment of femoral neck fractures. BMC Musculoskelet Disord. 2014 Jun 26;15(1):219.

22. Bhandari M, Devereaux PJ, Einhorn TA, Thabane L, Schemitsch EH, Koval KJ, Frihagen F, Poolman RW, Tetsworth K, Guerra-Farfán E, Madden K, Sprague S, Guyatt G; HEALTH Investigators. Hip fracture evaluation with alternatives of total hip arthroplasty versus hemiarthroplasty (HEALTH): protocol for a multicentre randomised trial. BMJ Open. 2015 Feb 13;5(2):e006263-006263.

23. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol. 1996 Dec;49(12):1373-9.

24. Blankstein M, Schemitsch EH, Bzovsky S, Axelrod D, Poolman RW, Frihagen F, Bhandari M, Swiontkowski M, Sprague S, Schottel PC; FAITH Investigators; HEALTH Investigators. The FAITH and HEALTH Trials: Are We Studying Different Hip Fracture Patient Populations? J Orthop Trauma. 2020 Nov;34(Suppl 3):S1-8.

25. Johansson H, Siggeirsdóttir K, Harvey NC, Odén A, Gudnason V, McCloskey E, Sigurdsson G, Kanis JA. Imminent risk of fracture after fracture. Osteoporos Int. 2017 Mar;28(3):775-80.

26. Roux C, Briot K. Imminent fracture risk. Osteoporos Int. 2017 Jun;28(6):1765-9.

27. Black DM, Delmas PD, Eastell R, Reid IR, Boonen S, Cauley JA, Cosman F, Lakatos P, Leung PC, Man Z, Mautalen C, Mesenbrink P, Hu H, Caminis J, Tong K, Rosario-Jansen T, Krasnow J, Hue TF, Sellmeyer D, Eriksen EF, Cummings SR; HORIZON Pivotal Fracture Trial. Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis. N Engl J Med. 2007 May 3;356(18):1809-22.

28. Judge A, Javaid MK, Leal J, et al Models of Care for the Delivery of Secondary Fracture Prevention after Hip Fracture: A Health Service Cost, Clinical Outcomes and Cost-Effectiveness Study within a Region of England. NIHR Journals Library; 2016. Accessed August 27, 2021. http://www.ncbi.nlm.nih.gov/books/NBK385615/

29. Singh S, Whitehurst DG, Funnell L, Scott V, MacDonald V, Leung PM, Friesen K, Feldman F. Breaking the cycle of recurrent fracture: implementing the first fracture liaison service (FLS) in British Columbia, Canada. Arch Osteoporos. 2019 Nov 27;14(1):116.

30. Wallace I, Callachand F, Elliott J, Gardiner P. An evaluation of an enhanced fracture liaison service as the optimal model for secondary prevention of osteoporosis. JRSM Short Rep. 2011 Feb 10;2(2):8.

31. Ansari H, Beaton DE, Sujic R, Rotondi NK, Cullen JD, Slater M, Sale JEM, Jain R, Bogoch ER; Ontario Osteoporosis Strategy Fracture Screening and Prevention Program Evaluation Team. Equal treatment: no evidence of gender inequity in osteoporosis management in a coordinator-based fragility fracture screening program. Osteoporos Int. 2017 Dec;28(12):3401-6.

32. Ross BJ, Lee OC, Harris MB, Dowd TC, Savoie FH 3rd, Sherman WF. Rates of Osteoporosis Management and Secondary Preventative Treatment After Primary Fragility Fractures. JBJS Open Access. 2021 Jun 14;6(2):e20.00142.

33. Kristensen PK, Ehrenstein V, Shetty N, Pedersen AB. Use of anti-osteoporosis medication dispensing by patients with hip fracture: could we do better? Osteoporos Int. 2019 Sep;30(9):1817-25.

34. Switzer JA, Jaglal S, Bogoch ER. Overcoming barriers to osteoporosis care in vulnerable elderly patients with hip fractures. J Orthop Trauma. 2009 Jul;23(6):454-9.

35. Åkesson KE, Ganda K, Deignan C, Oates MK, Volpert A, Brooks K, Lee D, Dirschl DR, Singer AJ. Post-fracture care programs for prevention of subsequent fragility fractures: a literature assessment of current trends. Osteoporos Int. 2022 Mar 24.

36. Sale JEM, Beaton D, Posen J, Elliot-Gibson V, Bogoch E. Systematic review on interventions to improve osteoporosis investigation and treatment in fragility fracture patients. Osteoporos Int. 2011 Jul;22(7):2067-82.

37. Ganda K, Puech M, Chen JS, Speerin R, Bleasel J, Center JR, Eisman JA, March L, Seibel MJ. Models of care for the secondary prevention of osteoporotic fractures: a systematic review and meta-analysis. Osteoporos Int. 2013 Feb; 24(2):393-406.

38. Wu CH, Tu ST, Chang YF, Chan DC, Chien JT, Lin CH, Singh S, Dasari M, Chen JF, Tsai KS. Fracture liaison services improve outcomes of patients with osteoporosis-related fractures: A systematic literature review and meta-analysis. Bone. 2018 Jun;111:92-100.

39. Barton DW, Piple AS, Smith CT, Moskal SA, Carmouche JJ. The Clinical Impact of Fracture Liaison Services: A Systematic Review. Geriatr Orthop Surg Rehabil. 2021 Jan 11;12:2151459320979978.

40. Center JR, Bliuc D, Nguyen TV, Eisman JA. Risk of subsequent fracture after low-trauma fracture in men and women. JAMA. 2007 Jan 24;297(4):387-94.