A SELECTION OF TEN READINGS ON TOPICS RELATED TO "OSTEOPOROSIS: A GROWING PRIMARY CARE CONCERN"

Date: 13 March 2021; Time: 2.00 – 5.30pm, Via ZOOM
Some available as free full text and some requiring payment

Selection of readings made by A/Prof Goh Lee Gan

READING 1 – SITUATIONAL RISK FACTORS FOR FALL-RELATED FRACTURES

Yu WY(1)(2), Hwang HF(3), Chen CY(2), Lin MR(4). Situational risk factors for fall-related vertebral fractures in older men and women. Osteoporosis Int. 2021 Jan 7. doi: 10.1007/s00198-020-05799-x. PMID: 33415375.

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ABSTRACT

Situational factors might help explain why most vertebral fractures occur in older people without a previous osteoporosis diagnosis. After adjusting for predisposing risk factors, the activity before the fall, type of fall, and falling direction remained as strong determinants of fall-related vertebral fractures in older men and women.

INTRODUCTION: A matched case-control study was conducted to investigate the effects of situational factors, in addition to predisposing factors, on clinical vertebral fractures in older men and women in Taiwan.

METHODS: Cases were community-dwelling individuals aged ≥ 65 years who visited emergency departments (EDs) of two university-affiliated hospitals due to a fall and had a primary diagnosis of a vertebral fracture during a one-year period in 2017. Five control patients per case, matched by the time of falling, gender, and age, who sought care in the same ED due to a fall resulting in a soft tissue injury were selected. A total of 64 men (age range: 65 ~ 99 years) and 194 women (age range: 65 ~ 100 years), diagnosed with a vertebral fracture, participated in the study.

RESULTS: Multivariable logistic models were conducted separately for men and women. Results suggested that the following factors were significantly associated with an increased risk of vertebral fractures in men: a low educational level (adjusted odds ratio [OR] = 1.95; 95 percent confidence interval (CI), 1.02 ~ 3.71), asthma (OR = 2.96; 95 percent CI, 1.35 ~ 6.92), depression (OR = 4.31; 95 percent CI, 1.03 ~ 17.5), toileting (OR = 2.30; 95 percent CI, 1.04 ~ 4.94), slipping (OR = 5.27; 95 percent CI, 1.80 ~ 15.4), stepping down (OR = 3.99; 95 percent CI, 1.40 ~ 11.4), sudden leg weakness (OR = 3.73; 95 percent CI, 1.13 ~ 12.4), and falling backwards (OR = 3.78; 95 percent CI, 1.83 ~ 7.80); and in women: a fracture history (OR = 2.00; 95 percent CI, 1.07 ~ 3.76), osteoporosis (OR = 1.94; 95 percent CI, 1.15 ~ 3.49), getting in/out of the bed/chair (OR = 1.90; 95 percent CI, 1.07 ~ 3.39), stepping down (OR = 2.10; 95 percent CI, 1.17 ~ 3.77), and falling backwards (OR = 4.00; 95 percent CI, 2.39 ~ 6.68) and sideways (OR = 2.61; 95 percent CI, 1.38 ~ 4.96).

CONCLUSIONS: The combination of predisposing and situational risk factors may display a more comprehensive risk profile for the occurrence of VFs, and thus, interventions that add both types of risk factors may result in greater risk reduction of VFs, although those specifically targeted at situational risk factors during falls are limited and their effectiveness and efficiency remained to be explored.

READING 2 – OPTIMISING DXA TO ASSESS SKELETAL HEALTH

Kennel KA(1), Sfeir JG(1)(2)(3), Drake MT(1)(3)(4). Optimizing DXA to Assess Skeletal Health: Key Concepts for Clinicians. J Clin Endocrinol Metab. 2020 Dec 1;105(12):dgaa632. PMID: 32894765.

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ABSTRACT
CONTEXT: The diagnosis of osteoporosis and assessment of fracture risk prior to a sentinel fracture was transformed by the widespread clinical use of dual-energy X-ray absorptiometry (DXA) for the assessment of bone mineral density (BMD).

EVIDENCE ACQUISITION**:** This review is based on a collection of primary and review literature gathered from a PubMed search of "dual energy X-ray absorptiometry," "trabecular bone score," and "atypical femur fracture" among other keywords. PubMed searches were supplemented by the authors' prior knowledge of the subject.

EVIDENCE SYNTHESIS: While uncertainty exists for some aspects of osteoporosis care, patient and clinician familiarity with BMD assessment for screening and monitoring is firmly established. Beyond BMD, lateral spine images obtained with DXA can diagnose osteoporosis and refine fracture risk through the detection of unrecognised vertebral fractures. In addition, analysis of DXA lumbar spine images can reflect changes in trabecular bone microarchitecture, a component of bone "quality" that predicts risk of fracture independent of BMD. Finally, monitoring of bone health by DXA may be extended to include assessment of the femoral cortices for rare but serious adverse effects associated with antiresorptive therapies.

CONCLUSIONS: Increasing technologic sophistication requires additional consideration for how DXA imaging is performed, interpreted and applied to patient care. As with any test, clinicians must be familiar with DXA performance, pitfalls in analysis, and interpretation within each clinical context in which DXA is applied. With this perspective, care providers will be well positioned to contribute to continuous improvement of DXA performance and, in turn, quality of osteoporosis care.

READING 3 – SCREENING FOR OSTEOPOROSIS IN OLDER MEN WITH HISTORY OF FALLS

Ito K (1) (2). Cost-effectiveness of Screening for Osteoporosis in Older Men With a History of Falls. JAMA Netw Open. 2020 Dec 1; 3(12):e2027584. PMID: 33258906.

URL: doi: 10.1001/jamanetworkopen.2020.27584. PMID: 33258906 (Free full text).

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ABSTRACT
IMPORTANCE: Falls and osteoporosis share the potential clinical end point of fractures among older patients. To date, few fall prevention guidelines incorporate screening for osteoporosis to reduce fall-related fractures. OBJECTIVE: To assess the cost-effectiveness of screening for osteoporosis using dual-energy x-ray absorptiometry (DXA) followed by osteoporosis treatment in older men with a history of falls.

DESIGN, SETTING, AND PARTICIPANTS: In this economic evaluation, a Markov model was developed to simulate the incidence of major osteoporotic fractures in a hypothetical cohort of community-dwelling men aged 65 years who had fallen at least once in the past year. Data sources included literature published from January 1, 1946, to July 31, 2020. The model adopted a societal perspective, a lifetime horizon, a one-year cycle length, and a discount rate of three percent per year for both health benefits and costs. The analysis was designed and conducted from October 1, 2019, to September 30, 2020. INTERVENTIONS: Screening with DXA followed by treatment for men diagnosed with osteoporosis compared with usual care.

MAIN OUTCOMES AND MEASURES: Incremental cost-effectiveness ratio (ICER), measured by cost per quality-adjusted life-year (QALY) gained. RESULTS: Among the hypothetical cohort of men aged 65 years, the screening strategy had an ICER of $33,169/QALY gained and was preferred over usual care at the willingness-to-pay threshold of $100,000/QALY gained. The number needed to screen to prevent one hip fracture was 1876; to prevent one major osteoporotic fracture, 746. The screening strategy would become more effective and less costly than usual care for men 77 years and older. The ICER for the screening strategy did not substantially change across a wide range of assumptions tested in all other deterministic sensitivity analyses. At a willingness-to-pay threshold of $50,000/QALY gained, screening was cost-effective in 56.0 percent of simulations; at $100,000/QALY gained, 90.8 percent of simulations; and at $200,000/QALY gained, 99.6 percent of simulations.

CONCLUSIONS AND RELEVANCE: These findings suggest that for older men who have fallen at least once in the past year, screening with DXA followed by treatment for those diagnosed with osteoporosis is a cost-effective use of resources. Fall history could be a useful cue to trigger assessment for osteoporosis in men.

READING 4 – HEALTHCARE UTILISATION IN WOMEN WITH MENOPAUSE

Sharman Moser S(1), Chodick G(1)(2), Bar-On S(3), Shalev V(1)(2). Healthcare Utilization and Prevalence of Symptoms in Women with Menopause: A Real-World Analysis. Int J Womens Health. 2020 Jun 3;12:445-454. doi: 10.2147/IJWH.S246113. PMID: 32606996

URL: doi: 10.2147/IJWH.S246113. PMID: 32606996 (Free full text).

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ABSTRACT
OBJECTIVE: Self-reported studies estimated that as many as 50-75 percent of women experience symptoms during menopause; however, limited real-world clinical data are available to support this observation. The electronic databases of Maccabi Healthcare Services were used to describe the prevalence of menopause symptoms in Israel and to characterise patients with regard to socioeconomic status, comorbidities and use of healthcare services.

METHODS: Females aged 45-54 years diagnosed with menopausal symptoms (N=17,046, cumulative incidence of eight percent during the study period) were identified from the Maccabi Healthcare Services electronic database and matched to female members without menopause symptoms, one-to-one on birth year and enumeration area.

RESULTS: Symptomatic peri- and post-menopausal women, and particularly those under 52 years, were more likely to have a higher prevalence of comorbid conditions such as depression, anxiety, osteoporosis and insomnia in the year following index. Correspondingly, selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors and hypnotic drug use were significantly higher in symptomatic women as was healthcare utilisation including hospitalisation (OR=1.10; 95 percent CI=1.00-1.20), primary care visits (1.90; 1.73-2.08), gynaecologist visits (24.84; 22.36-27.59) and hysterectomy procedures (2.26; 1.63-3.14).

CONCLUSION: Medically documented menopausal symptoms are associated with increased burden of disease (particularly among women diagnosed with menopausal symptoms prior to age 52 years), healthcare utilisation and greater likelihood of undergoing hysterectomy within one year of diagnosis. This burden is expected to rise further as awareness and social acceptance of peri- and post-menopausal symptoms increase.

READING 5 – AN AUDIT CYCLE OF MANAGEMENT OF OSTEOPOROSIS IN PRIMARY CARE

Jothimurugan S(1), Jothimurugan S(2), Sanganee D(2), Wickramaratne T(3), Lynn M(3). A pilot project on the management of osteoporosis in primary care: results of the audit cycle. Br J Gen Pract. 2020 Jun;70(suppl 1):bjgp20X711653. PMID:32554686

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ABSTRACT
BACKGROUND: Osteoporosis is a major public health problem with the ageing population in the UK. However, there is no known national algorithm for the management of osteoporosis in primary care. Therefore, a treatment pathway was developed in secondary care for patients in the community.

AIM: This audit cycle investigates whether patients at a GP practice with a population of 14 000 have been appropriately identified, coded as osteoporosis, treated, and have followed the recommended pathway.

METHOD: A search of the practice clinical system was undertaken for three groups of patients coded as: patients currently on the existing osteoporosis register; patients with a code of 'osteoporosis' or 'fragility fracture' but not prescribed an osteoporosis treatment; and patients currently prescribed an osteoporosis treatment with no coding for 'osteoporosis' or 'fragility fracture'. The words 'osteoporosis', 'fragility fracture', 'QOF', and all individual drug names were used in the search engine. RESULTS: The completed audit cycle shows an increase in the proportion of patients following the local guidelines pathway, from 75 percent in 2018 to 81 percent in 2019, emphasising the importance of having a guideline for GPs to follow in order to optimise treatment and prevent future fragility fractures.

CONCLUSION: This is a pilot project to assess the ability to identify patients who have osteoporosis and review their treatment pathway. The results are promising as the analysed data indicate that GP practice lists can be used to identify and treat high-risk patients for osteoporosis and assess the adherence to the pathway. Using the pathway, GPs can more efficiently diagnose and manage patients.

READING 6 – PUBLIC PRIORITIES FOR OSTEOPOROSIS AND FRACTURE RESEARCH

Hawarden A(1)(2), Jinks C(3), Mahmood W(3), Bullock L(3), Blackburn S(3), Gwilym S(4), Paskins Z(3)(5). Public priorities for osteoporosis and fracture research: results from a focus group study. Arch Osteoporosis. 2020 Jun 16;15(1):89. PMID: 32548718.

URL: doi: 10.1007/s11657-020-00766-9. PMID: 32548718 (Full free text).

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ABSTRACT
Four focus groups were conducted with members of the public to identify important areas for future osteoporosis research. Participants identified priorities to increase public awareness of osteoporosis, reduce delays in diagnosis, and improve communication between healthcare providers and to improve follow-up and information provision about causes of osteoporosis, medication harms and prognosis.

PURPOSE: Patients and the public must be involved in setting research agendas to ensure relevant and impactful questions are prioritised. This study aimed to understand what people living with osteoporosis and fragility fractures felt was important to research, to inform the content of a national survey on research priorities in this area.

METHODS: Focus groups were conducted with members of the public with experience of osteoporosis or fragility fractures. The topic guide was co-developed with a patient and public involvement research user group, and explored participants' experiences of osteoporosis including diagnosis, management and effect upon their lives, what aspects of their ongoing care was most important to them and what about their care or condition could be improved. Focus groups were audio-recorded, transcribed and analysed thematically.

RESULTS: A total of twenty-three participants were recruited to four focus groups. Analysis identified two main themes: challenges in living with osteoporosis and healthcare services for osteoporosis. Information needs was a further cross-cutting theme. Participants called for increased public awareness of osteoporosis and wanted healthcare services to address conflicting messages about diet, exercise and medication. Participants described long delays in diagnosis, poor communication between primary and secondary care and the need for structured follow-up as important areas for future research to address.

CONCLUSION: The findings from this study provide an understanding of research priorities from the perspective of patients and the public, have informed the content of a national survey and have implications for patient education, health services research and policy.

READING 7 – ANTICOAGULANT THERAPY AND RISK OF OSTEOPOROTIC FRACTURES IN PATIENTS WITH ATRIAL FIBRILLATION: A POPULATION BASED COHORT STUDY

Lau WCY(1), Cheung CL(2), Man KKC(1), Chan EW(2), Sing CW(2), Lip GYH(3), Siu CW(4), Lam JKY(5), Lee ACH(5), Wong ICK(6). Association Between Treatment With Apixaban, Dabigatran, Rivaroxaban, or Warfarin and Risk for Osteoporotic Fractures Among Patients With Atrial Fibrillation: A Population-Based Cohort Study. Ann Intern Med. 2020 Jul 7;173(1):1-9. PMID: 32423351.

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ABSTRACT
BACKGROUND: It is unclear whether anticoagulant type is associated with the risk for osteoporotic fracture, a deleterious complication of anticoagulants among patients with atrial fibrillation (AF).

OBJECTIVE: To compare the risk for osteoporotic fracture between anticoagulants. DESIGN: Population-based cohort study. SETTING: Territory-wide electronic health record database of the Hong Kong Hospital Authority. PARTICIPANTS: Patients newly diagnosed with AF between 2010 and 2017 who received a new prescription for warfarin or a direct oral anticoagulant (DOAC) (apixaban, dabigatran, or rivaroxaban). Follow-up ended on 31 December 2018.

MEASUREMENTS: Osteoporotic hip and vertebral fractures in anticoagulant users were compared using propensity score-weighted cumulative incidence differences (CIDs). RESULTS: There were 23 515 patients identified (3241 apixaban users, 6867 dabigatran users, 3866 rivaroxaban users, and 9541 warfarin users). Overall mean age was 74.4 years (SD, 10.8), ranging from 73.1 years (warfarin) to 77.9 years (apixaban). Over a median follow-up of 423 days, 401 fractures were identified (crude event number [weighted rate per 100 patient-years]: apixaban, 53 [0.82]; dabigatran, 95 [0.76]; rivaroxaban, 57 [0.67]; and warfarin, 196 [1.11]). After 24-month follow-up, DOAC use was associated with a lower risk

for fracture than warfarin use (apixaban CID, -0.88 percent [95 percent CI, -1.66 percent to -0.21 percent]; dabigatran CID, -0.81 percent [CI, -1.34 percent to -0.23 percent]; and rivaroxaban CID, -1.13 percent [CI, -1.67 percent to -0.53 percent]). No differences were seen in all head-to-head comparisons between DOACs at 24 months (apixaban vs. dabigatran CID, -0.06 percent [CI, -0.69 percent to 0.49 percent]; rivaroxaban vs. dabigatran CID, -0.32 percent [CI, -0.84 percent to 0.18 percent]; and rivaroxaban vs. apixaban CID, -0.25 percent [CI, -0.86 percent to 0.40 percent]).

LIMITATION: Residual confounding is possible.

CONCLUSION: Among patients with AF, DOAC use may result in a lower risk for osteoporotic fracture compared with warfarin use. Fracture risk does not seem to be altered by the choice of DOAC. These findings may help inform the benefit-risk assessment when choosing between anticoagulants.

READING 8 – LONG-TERM DRUG THERAPY, DRUG DISCONTINUATIONS AND DRUG HOLIDAYS FOR OSTEOPOROSIS FRACTURE PREVENTION

Fink HA(1), MacDonald R(1), Forte ML(2), Rosebush CE(2), Ensrud KE(1), Schousboe JT(3), Nelson VA(2), Ullman K(1), Butler M(2), Olson CM(2), Taylor BC(1), Brasure M(2), Wilt TJ(1). Long-Term Drug Therapy and Drug Discontinuations and Holidays for Osteoporosis Fracture Prevention: A Systematic Review. Ann Intern Med. 2019 Jul 2; 171(1):37-50. PMID: 31009947.

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Comment in
- Ann Intern Med. 2019 Jul 2; 171(1):62-63.
- Ann Intern Med. 2019 Aug 20; 171(4):JC22.

ABSTRACT
BACKGROUND: Optimal long-term osteoporosis drug treatment (ODT) is uncertain. PURPOSE: To summarise the effects of long-term ODT and ODT discontinuation and holidays. DATA SOURCES: Electronic bibliographic databases (January 1995 to October 2018) and systematic review bibliographies.

STUDY SELECTION: 48 studies that enrolled men or postmenopausal women aged 50 years or older who were being investigated or treated for fracture prevention, compared long-term ODT (>3 years) versus control or ODT continuation versus discontinuation, reported incident fractures (for trials) or harms (for trials and observational studies), and had low or medium risk of bias (ROB).

DATA EXTRACTION: Two reviewers independently rated ROB and strength of evidence (SOE). One extracted data; another verified accuracy.

DATA SYNTHESIS: Thirty-five trials (nine unique studies) and 13 observational studies (11 unique studies) had low or medium ROB. In women with osteoporosis, four years of alendronate reduced clinical fractures (hazard ratio [HR], 0.64 [95 percent CI, 0.50 to 0.82]) and radiographic vertebral fractures (both moderate SOE), whereas four years of raloxifene reduced vertebral but not nonvertebral fractures. In women with osteopenia or osteoporosis, six years of zoledronic acid reduced clinical fractures (HR, 0.73 [CI, 0.60 to 0.90]), including nonvertebral fractures (high SOE) and clinical vertebral fractures (moderate SOE). Long-term bisphosphonates increased risk for two rare harms: atypical femoral fractures (low SOE) and osteonecrosis of the jaw (mostly low SOE). In women with unspecified osteoporosis status, 5 to 7 years of hormone therapy reduced clinical fractures (high SOE), including hip fractures (moderate SOE), but increased serious harms. After 3 to 5 years of treatment, bisphosphonate continuation versus discontinuation reduced radiographic vertebral fractures (zoledronic acid; low SOE) and clinical vertebral fractures (alendronate; moderate SOE) but not nonvertebral fractures (low SOE). LIMITATION: No trials studied men, clinical fracture data were sparse, methods for estimating harms were heterogeneous, and no trials compared sequential treatments or different durations of drug holidays.

CONCLUSION: Long-term alendronate and zoledronic acid therapies reduce fracture risk in women with osteoporosis. Long-term bisphosphonate treatment may increase risk for rare adverse events, and continuing treatment beyond 3 to 5 years may reduce risk for vertebral fractures. Long-term hormone therapy reduces hip fracture risks but has serious harms.

READING 9 – COMPARISON OF DENOSUMAB AND BISPHOSPHONATES IN IMPROVING BONE STRENGTH IN POST-MENOPAUSAL OSTEOPOROSIS

Chandran T(1), Venkatachalam I(2). Efficacy and safety of denosumab compared to bisphosphonates in improving bone strength in postmenopausal osteoporosis: a systematic review. Singapore Med J. 2019 Jul;60(7):364-378. PMID: 30854568.

URL: doi: 10.11622/smedj.2019028. PMID: 30854568 (Full free text).

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ABSTRACT

INTRODUCTION: Osteoporosis is the main cause of fractures among women after menopause. This study aimed to evaluate the efficacy and safety of denosumab compared to bisphosphonates in treating postmenopausal osteoporosis.

METHODS: Databases including PubMed and the Cochrane Central Register of Controlled Trials were systematically searched for randomised controlled trials (RCTs) that directly compared denosumab and bisphosphonates. RCTs that studied both denosumab and bisphosphonates in postmenopausal women with osteoporosis and had a Jadad score ≥ 3 were included.

RESULTS: Nine studies were eligible for inclusion. They were further categorised into six cohort groups. All studies had denosumab with oral bisphosphonates as the active comparator. Four out of six cohort studies showed significant improvements in bone strength ($p < 0.001$) at the distal radius, tibia, total hip, femoral neck, lumbar spine and trochanter at 12 months for patients on denosumab compared to the bisphosphonate group. Serum C-telopeptide of cross-linked collagen, a bone turnover marker, was consistently lower in the denosumab group in all studies. There were no significant differences in hypocalcaemia, atypical fractures, fragility fractures, and osteonecrosis of the jaw, all infections (including fever or influenza-like symptoms), gastrointestinal side effects or dermatological conditions in all studies, except for one that did not document side effects.

CONCLUSION: Denosumab can be used both as a first-line agent and an alternative to bisphosphonate in the treatment of postmenopausal osteoporosis. There is currently insufficient data to show that denosumab is not inferior to bisphosphonates in fracture prevention.

READING 10 – OSTEOPOSIS PATIENT MANAGEMENT

Burns RB(1), Rosen H(1), Berry S(1), Smetana GW(1). How Would You Manage This Patient With Osteoporosis?: Grand Rounds Discussion From Beth Israel Deaconess Medical Center. Ann Intern Med. 2018 Jun 5;168(11):801-808. PMID: 29868815.

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ABSTRACT

Osteoporosis is a skeletal disorder characterised by reduced bone strength that increases the risk for fracture. Approximately ten million men and women in the United States have osteoporosis, and more than two million osteoporosis-related fractures occur annually.

In 2016, the American Association of Clinical Endocrinologists issued the "Clinical Practice Guideline for the Diagnosis and Treatment of Postmenopausal Osteoporosis," and in 2017, the American College of Physicians issued the guideline "Treatment of Low Bone Density or Osteoporosis to Prevent Fracture in Men and Women."

Both guidelines agree that patients diagnosed with osteoporosis should be treated with an antiresorptive agent, such as alendronate, that has been shown to reduce hip and vertebral fractures. However, there is no consensus on how long patients with osteoporosis should be treated and whether bone density should be monitored during and after the treatment period.

In this Beyond the Guidelines, two experts discuss management of osteoporosis in general and for a specific patient, the role of bone density monitoring during and after a five-year course of alendronate, and treatment recommendations for a patient whose bone density decreases during or after a five-year course of alendronate.