Geriatrics & Bone Health
RESEARCH REVIEW™

Making Education Easy | Issue 1 – 2015

In this issue:

Abbreviations used in this issue
BMD = bone mineral density
HF = heart failure
MI = myocardial infarction
WBVT = whole-body vibration training

Welcome to the latest issue of Geriatrics and Bone Health Research Review.

Highlights include a report of the risk of death or readmission to hospital in the year following hospitalisation for HF, acute MI, or pneumonia in older people. This is followed by a useful epidemiological study of the impact of heat waves in the aged, and promising findings for an enriched nutritional formula in patients with pressure ulcers. We also report a NZ study of the benefits of home safety modifications. On the downside, whole-body vibration training does not improve bone quality in osteopenic postmenopausal women, and the orally active calcium-sensing receptor antagonist MK-5442 does not improve BMD.

We hope you find the selected studies interesting and look forward to receiving any feedback you may have.

Kind regards

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Trajectories of risk after hospitalization for heart failure, acute myocardial infarction, or pneumonia

Authors: Dharmarajan K et al.

Summary: This retrospective cohort study examined the risk for older patients of death or readmission to hospital in the year after hospitalisation for HF, acute MI, or pneumonia. Outcomes for >3 million Medicare beneficiaries aged ≥65 years who had survived hospitalisation for HF, acute MI, or pneumonia were reviewed. Within 1 year of hospital discharge, readmission to hospital and death, respectively, occurred after 67.4% and 35.8% of hospitalisations for HF, 49.9% and 25.1% for acute MI, and 55.6% and 31.1% for pneumonia. After hospitalisation for HF, acute MI, or pneumonia, the relative risk of hospital admission over the first 90 days was 8, 6, and 6 times greater than that of the general older population; the corresponding risk of death was 11, 8, and 10 times greater.

Comment (MC): We all recognise intellectually that blue whales are very large. However, when I saw one close-up for the first time my reaction was "Wow, they're enormous!" This paper falls into my personal "aren't blue whales enormous!?" categorisation of research outputs, both in terms of the absolute risk and relative risks of hospital readmission and of death following the defined diagnoses, and in terms of the decline in those rates over a relatively short period of time. This is a well-conducted and very large study (across nearly 5000 hospitals), from a highly respected group. It includes the 'young old' and the 'old old'. It can thus be reliably described as being representative and generalisable. Its greatest value (as the authors point out) is that it informs physicians and service planners in their efforts to avoid or ameliorate adverse outcomes in this highly vulnerable patient group.

Reference: BMJ 2015;350:h411
Abstract

Cause-specific risk of hospital admission related to extreme heat in older adults

Authors: Bobb J et al.

Summary: This study investigated the causes of hospital admissions in older adults during extreme heat events. Hospital admissions data for 23.7 million Medicare enrollees aged ≥65 years were reviewed for the period 1999–2010. Risks of hospitalisation for fluid and electrolyte disorders, renal failure, urinary tract infection, septicaemia, and heat stroke were significantly higher on heat wave days than non-heat wave days, but the risk of hospitalisation for congestive heart failure was lower ($p<0.05$). For fluid and electrolyte disorders and heat stroke, the risk of hospitalisation increased during more intense and longer-lasting heat-waves. Risks were generally highest on the heat-wave day but remained elevated for up to 5 days.

Comment (MC): This is a very useful epidemiological study from a highly respected team. Given its size (24 million older people), its inclusiveness (85% of all US Medicare enrollees) and its excellent methodology and long duration, it would not be unreasonable to describe this as a definitive study in its field. Its finding are, qualitatively, unsurprising (indeed with the possible exception of the findings for septicaemia they may be described as intuitive), but the relatively small increases in absolute risks found, though perhaps less intuitively 'apparent', are reassuring. In this regard at least, older people are perhaps more robust (and/or they take more care) than we previously thought.

Reference: JAMA 2014;312(24):2659-2667
Abstract

Independent commentary by Professor Martin Connolly

Martin Connolly trained in the UK and since 2006 has been Freemasons' Professor of Geriatric Medicine at the University of Auckland, New Zealand. He has published extensively in many areas including COPD, depression, chronic conditions management, frailty, residential aged care and healthy aging. He directs a multidisciplinary research group composed of members with medical, nursing, epidemiological and statistical expertise.

The burden of disease in older people and implications for health policy and practice

Authors: Prince M et al.

Summary: Nearly one-quarter of the total global burden of disease is due to disorders in people aged 60 years and older. The leading contributors to this disease burden are cardiovascular diseases (30.3%), malignant neoplasms (15.1%), chronic respiratory diseases (9.5%), musculoskeletal diseases (7.5%), and neurological and mental disorders (6.6%). Primary prevention in younger adults will improve health in successive cohorts of older people, but more effective primary, secondary, and tertiary prevention targeting older people also has great potential to reduce the disease burden. Obstacles include ageism, misplaced global health priorities, the poor preparedness of health systems to deliver age-appropriate care, and the complexity of integrating care for patients with multimorbidities.

Comment (MC): A breath of fresh air! This paper helps set an important tone for both future research and for policy development in terms of the prevention of disease and disability in older people. It (rightly) does not pull its punches. It correctly stresses the need for not only increased primary prevention in older people (as opposed to just in younger people) but also the need for secondary and even tertiary prevention, as opposed to the all too often nihilistic attitudes seen in this area. The emphasis on the burden of disease (and thus quality of life and wellness) and on disability is appropriate, timely, and welcome. In direct contrast to doom-mongering concerns ("the demographic time-bomb"; the "tsunami" of older people) the authors are positive and emphasise potential. This paper is a pleasure to read and I encourage everyone to do so.

Reference: Lancet 2015;385(9967):549-562
Abstract

A nutritional formula enriched with arginine, zinc, and antioxidants for the healing of pressure ulcers

Authors: Cereda E et al., for the OligoElement Sore Trial Study Group

Summary: This study investigated the effects of supplementation with arginine, zinc, and antioxidants within a high-calorie, high-protein formula on pressure ulcer healing. 200 malnourished adults with stage II–IV pressure ulcers were randomised to receive the enriched nutritional formula or an equal volume of an isocaloric, isonitrogenous formula (400 ml/day) for 8 weeks. Supplementation with the enriched formula resulted in a greater reduction in pressure ulcer area than the control formula (mean 60.9% vs 45.2% reduction; $p=0.017$). A more frequent reduction in area of 40% or greater at 8 weeks was also seen with the enriched formula ($p=0.018$).

Comment (MC): The title of this paper did not enthuse me – but I was wrong in my first impression. This is an independent, multicentre, adequately powered, well-conducted, randomised, blinded, controlled trial. Inclusion criteria were appropriate (and, although the study included younger subjects, the mean age of participants was 81 years) and end-points were clinically relevant and quantifiable. The results, in terms of wound healing, were statistically significant for both primary and secondary end-points, and although in clinical terms they cannot be described as 'stunning' (in the area of pressure ulcer healing we would be naive to expect this) they are certainly clinically useful. Side effects, particularly gastrointestinal, were reassuringly uncommon. The authors are to be congratulated, as this is a difficult field in which to accrue good data.

Reference: Ann Intern Med 2015;162(3):167-174
Abstract

Home modifications to reduce injuries from falls in the Home Injury Prevention Intervention (HIPI) study

Authors: Keall M et al.

Summary: This NZ study examined the impact of home safety modifications on injuries from falls. 842 households in the Taranaki region were randomised to either immediate home modifications (treatment group) or a 3-year wait before modifications (control group). Home modifications included handrails for outside steps and internal stairs, grab rails for bathrooms, outside lighting, edging for outside steps, and slip-resistant surfacing for outside areas such as decks and porches. After a median observation period of 1148 days, the crude rate of fall injuries per person per year was 0.061 in the treatment group and 0.072 in the control group (relative rate 0.86, 95% CI 0.66–1.12). After adjustment for confounding factors, there was a 26% reduction in the rate of injuries caused by falls at home per year in the treatment group compared with the control group.

Reference: Lancet 2015;385(9964):231-238
Abstract

Comment (MC): This paper falls into a relatively small and select group of important studies – it describes one of the very few initiatives (of an enormous number attempted) that have been successful in reducing injurious falls in older people. The study protocol is straightforward and the analysis appropriate. Though it appears that the study may have been underpowered to detect a significant reduction in crude rate of falls, it did demonstrate a significant (and clinically large and important) reduction in rate of injurious falls. The inclusion criteria for the study would give one pause to question the generalisability of its findings, but it is intuitively difficult to do so. The paper may represent an important advance that should stimulate both more research (including in other jurisdictions with different housing stock) and translation into practice in NZ and elsewhere.

Comment (MB): In this NZ study, 842 households were randomly assigned to a home modification programme immediately or deferred for 3 years. The modifications cost on average $NZ560 and were capped at a maximum of $NZ3000. The average age of householders was about 45 years. The modifications did not affect the rate of fall injuries or of fall injuries specific to the interventions, but the confidence intervals around the effect sizes were fairly wide. Individuals living in modified houses had a higher rate of fall injuries prior to the house modifications, and when this was taken into account the modifications did reduce injuries from falls. Although the authors suggest this programme could be rolled out nationwide, questions remain. The majority of benefits seemed to arise in younger people, with few benefits in the 40% of people aged >60 years. In an ideal world, a larger trial in older individuals at higher risk of falls is needed, particularly when the conclusions that the modifications are effective are based on adjusted analyses.

Comparison of fracture risk prediction by the US Preventive Services Task Force strategy and two alternative strategies in women 50-64 years old in the Women's Health Initiative

Author: Crandall C et al.

Summary: This study compared fracture risk prediction by the US Preventive Services Task Force (USPSTF) screening strategy, the Osteoporosis Self-Assessment Tool, and the Simple Calculated Osteoporosis Risk Estimate (SCORE) in postmenopausal women. 62,492 women aged 50–64 years who were participating in the Women's Health Initiative who were not taking osteoporosis medication were assessed for incident major osteoporotic fracture (MOF) over a 10-year follow-up period. For identifying women with incident MOF, sensitivity of the strategies ranged from 25.8–39.8%, specificity ranged from 60.7–65.8%, and area under the receiver operating characteristic curve (AUC) values ranged from 0.52–0.56. The sensitivity of the USPSTF strategy for identifying incident MOF ranged from 4.7% in women aged 50–54 years to 37.3% in women aged 60–64 years. These findings do not support use of the USPSTF strategy, Osteoporosis Self-Assessment Tool, or SCORE to identify younger postmenopausal women at higher risk of fracture.

Comment (MB): Predicting future events is difficult, and predicting fractures is no exception. Early postmenopausal women are often concerned about their risk of osteoporosis. This study assessed how well 3 different prediction models could predict the chance of a major osteoporosis fracture in the next 10 years in women aged <65 years. The answer? Slightly better than tossing a coin. Notably, the Fracture Risk Assessment Tool (FRAX) was one of the models assessed (used by the USPSTF). It continues to perform poorly when independent investigators assess its utility in a variety of population groups.

Reference: J Clin Endocrinol Metab 2014;99(12):4514-22
Abstract

Changes in bone mineral density at 3 years in postmenopausal women receiving anastrozole and risedronate in the IBIS-II bone substudy

Authors: Sestak I et al.

Summary: This study assessed the effectiveness of oral risedronate for prevention of reduction in BMD after 3 years of follow-up in a subset of patients taking anastrozole in the IBIS-II trial. The IBIS-II trial recruited 3864 healthy, postmenopausal women at increased risk of breast cancer and randomised them to receive oral anastrozole or placebo in a double-blind design. 36% of them were then enrolled in a bone substudy and stratified into 3 groups according to baseline T score at spine or femoral neck (stratum I: T score at least –1.0; stratum II: T score at least –2.5 but less than –1.0; stratum III: T score less than –2.5 but greater than –4.0). Women in stratum I were monitored only; women in stratum II were randomised to risedronate (35 mg/week) or placebo; women in stratum III were all given risedronate. In stratum II, 3-year mean BMD change at the lumbar spine was 1.1% and –2.6% in the anastrozole/risedronate and anastrozole/placebo groups, respectively ($p<0.0001$). For the total hip, 3-year mean BMD change was –0.7% and –3.5% in the respective groups ($p=0.0001$).

Comment (MB): Concern has been raised that women treated with aromatase inhibitors as adjuvant treatment for breast cancer have accelerated bone loss from reductions in oestrogen levels. In this randomised controlled trial, the aromatase inhibitor anastrozole decreased bone density by about 1% per year compared with placebo in women with normal bone density or osteopenia. Risedronate largely prevented this bone loss, but the effects of risedronate were smaller in women taking anastrozole than in women taking placebo. The trial provides strong evidence that the effects of aromatase inhibitors on bone density are fairly small (and elsewhere have been reported to be reversible once the aromatase inhibitors are stopped). There seems little need to worry about the bone density of women without strong risk factors for low bone density or fracture who are taking a 5-year course of an aromatase inhibitor.

Reference: Lancet Oncol 2014;15(13):1460-68
Abstract

Independent commentary by Dr Mark Bolland

Dr Mark Bolland is an Endocrinologist at Counties Manukau DHB and a Senior Research Fellow in the Department of Medicine at The University of Auckland.

Bone quality in osteopenic postmenopausal women is not improved after 12 months of whole-body vibration training

Authors: Liphardt A et al.

Summary: This study investigated the effects of whole-body vibration training (WBVT) on bone structure in osteopenic postmenopausal women. 22 women received 2–3 sessions/week of WBVT for 12 months, and 20 women served as controls. During the 12-month period, total BMD, cortical area, cortical thickness, and cortical porosity all decreased significantly in both groups. WBVT had no effect on balance or muscle strength outcomes compared with controls.

Comment (MB): Didn't we know that vibration treatment has no effect on bone density? Yes, we did. But these authors wondered whether it might improve bone quality, muscle strength or balance. It doesn't.

Reference: Osteoporos Int 2015;26(3):911-920
Abstract

A phase 2, randomized, placebo-controlled, dose-ranging study of the calcium-sensing receptor antagonist MK-5442 in the treatment of postmenopausal women with osteoporosis

Authors: Halse J et al.

Summary: MK-5442 is an orally active calcium-sensing receptor antagonist that is hypothesised to stimulate bone formation. This dose-ranging study investigated the dose of MK-5442 required to produce osteoanabolic effects without excessive hypercalcaemia. 383 postmenopausal women with osteoporosis were randomised in a double-blind design to receive a daily oral dose of MK-5442 (2.5, 5, 7.5, 10, or 15mg) or placebo for 6 months. A dose-dependent transient increase in parathyroid hormone (PTH) occurred after each dose of MK-5442 that lasted >3.5 hours. Compared with placebo, significant increases in bone formation markers were observed by 6 months, whereas bone resorption markers initially decreased but were also significantly increased by 6 months. However, there were no significant differences between any of the MK-5442 doses and placebo in percent change in BMD from baseline to 6 months. The frequency of hypercalcaemia increased as MK-5442 dose increased.

Comment (MB): It seemed such a good idea that if exogenous PTH increases bone density, then calcium-sensing receptor antagonists that cause endogenous secretion of pulses of PTH should also. But the hypothesis turned out to be wrong. Calcium-sensing receptor antagonists affect bone turnover but have no effect on bone density. This raises interesting questions about why PTH and PTH analogues given exogenously are effective but endogenous pulsed PTH is not.

Reference: J Clin Endocrinol Metab 2014;99(11):E2207-15
Abstract