

## A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO MANAGEMENT OF FUNCTIONAL DECLINE IN OLDER ADULTS –

available as free full-text and some requiring payment

Selection of readings made by A/Prof Goh Lee Gan

### READING 1 – Vascular basis for brain degeneration

**Kalaria RN. Vascular basis for brain degeneration: faltering controls and risk factors for dementia. Nutr Rev. 2010 Dec;68 Suppl 2:S74-87. doi: 10.1111/j.1753-4887.2010.00352.x. Review. PubMed PMID: 21091952.**

URL: <http://onlinelibrary.wiley.com/doi/10.1111/j.1753-4887.2010.00352.x/pdf> (payment required)

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#### SUMMARY

The integrity of the vascular system is essential for the efficient functioning of the brain. Aging-related structural and functional disturbances in the macro- or microcirculation of the brain make it vulnerable to cognitive dysfunction, leading to brain degeneration and dementing illness. Several faltering controls, including impairment in autoregulation, neurovascular coupling, blood-brain barrier leakage, decreased cerebrospinal fluid, and reduced vascular tone, appear to be responsible for varying degrees of neurodegeneration in old age. There is ample evidence to indicate vascular risk factors are also linked to neurodegenerative processes preceding cognitive decline and dementia. The strongest risk factor for brain degeneration, whether it results from vascular or neurodegenerative mechanisms or both, is age. However, several modifiable risks such as cardiovascular disease, hypertension, dyslipidemia, diabetes, and obesity enhance the rate of cognitive decline and increase the risk of Alzheimer's disease in particular. The ultimate accumulation of brain pathological lesions may be modified by genetic influences, such as the apolipoprotein E ε4 allele and the environment. Lifestyle measures that maintain or improve cardiovascular health, including consumption of healthy diets, moderate use of alcohol, and implementation of regular physical exercise are important factors for brain protection. PMID: 21091952 [PubMed - indexed for MEDLINE]

### READING 2 – Moving against frailty – physical activity protects

**Landi F, Abbatecola AM, Provinciali M, Corsonello A, Bustacchini S, Manigrasso L, Cherubini A, Bernabei R, Lattanzio F. Moving against frailty: does physical activity matter? Biogerontology. 2010 Oct;11(5):537-45. Epub 2010 Aug 10. Review. PubMed PMID: 20697813.**

URL: <http://www.springerlink.com/content/2248332292413127/fulltext.pdf> (payment required)

Department of Gerontology and Geriatrics, Catholic University of Sacred Heart, Rome, Italy.

#### SUMMARY

Frailty is a common condition in older persons and has been described as a geriatric syndrome resulting from age-related cumulative declines across multiple physiologic systems, with impaired homeostatic reserve and a reduced capacity of the organism to resist stress. Therefore, frailty is considered as a state of high vulnerability for adverse health outcomes, such as disability, falls, hospitalization, institutionalization, and mortality. Regular physical activity has been shown to protect against diverse components of the frailty syndrome in men and women of all ages and frailty is not a contra-indication to physical activity, rather it may be one of the most important reasons to prescribe physical exercise. It has been recognized that physical activity can have an impact on different components of the frailty syndrome. This review will address the role of physical activity on the most relevant components of frailty syndrome, with specific reference to: (i) sarcopenia, as a condition which frequently overlaps with frailty;

(ii) functional impairment, considering the role of physical inactivity as one of the strongest predictors of physical disability in elders; (iii) cognitive performance, including evidence on how exercise and physical activity decrease the risk of early cognitive decline and poor cognition in late life; and (iv) depression by reviewing the effect of exercise on improving mood and increasing positive well-being. PMID: 20697813 [PubMed - indexed for MEDLINE]

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### READING 3 – Aging, frailty and age-related diseases

**Fulop T, Larbi A, Witkowski JM, McElhaney J, Loeb M, Mitnitski A, Pawelec G. Aging, frailty and age-related diseases. *Biogerontology*. 2010 Oct;11(5):547-63. Epub 2010 Jun 18. Review. PubMed PMID: 20559726.**

URL: <http://www.springerlink.com/content/2248332292413127/fulltext.pdf> (payment required)

Research Center on Aging, Immunology Program, Geriatric Division, Faculty of Medicine, University of Sherbrooke, Sherbrooke, QC, Canada. [tamas.fulop@usherbrooke.ca](mailto:tamas.fulop@usherbrooke.ca)

#### SUMMARY

The concept of frailty as a medically distinct syndrome has evolved based on the clinical experience of geriatricians and is clinically well recognizable. Frailty is a nonspecific state of vulnerability, which reflects multisystem physiological change. These changes underlying frailty do not always achieve disease status, so some people, usually very elderly, are frail without a specific life threatening illness. Current thinking is that not only physical but also psychological, cognitive and social factors contribute to this syndrome and need to be taken into account in its definition and treatment. Together, these signs and symptoms seem to reflect a reduced functional reserve and consequent decrease in adaptation (resilience) to any sort of stressor and perhaps even in the absence of extrinsic stressors. The overall consequence is that frail elderly are at higher risk for accelerated physical and cognitive decline, disability and death. All these characteristics associated with frailty can easily be applied to the definition and characterization of the aging process per se and there is little consensus in the literature concerning the physiological/biological pathways associated with or determining frailty. It is probably true to say that a consensus view would implicate heightened chronic systemic inflammation as a major contributor to frailty. This review will focus on the relationship between aging, frailty and age-related diseases, and will highlight possible interventions to reduce the occurrence and effects of frailty in elderly people. PMID: 20559726 [PubMed - indexed for MEDLINE]

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### READING 4 – Walking speed is a reliable barometer of functional decline

**Schrack JA, Simonsick EM, Ferrucci L. The energetic pathway to mobility loss: an emerging new framework for longitudinal studies on aging. *J Am Geriatr Soc*. 2010 Oct;58 Suppl 2:S329-36. doi: 10.1111/j.1532-5415.2010.02913.x. Review. PubMed PMID: 21029063.**

URL: <http://onlinelibrary.wiley.com/doi/10.1111/j.1532-5415.2010.02913.x/pdf> (payment required)

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#### SUMMARY

The capacity to walk independently is a central component of independent living. Numerous large and well-designed longitudinal studies have shown that gait speed, a reliable marker of mobility, tends to decline with age and as a consequence of chronic disease. This decline in performance is of utmost importance because slow walking speed is a strong, independent predictor of disability, healthcare utilization, nursing home admission, and mortality. Based on these robust findings, it has been postulated that age-associated decline in walking speed is a reliable barometer of the effect of biological aging on health and functional status. Despite the extraordinary prognostic information that walking speed provides, which is often superior to traditional medical information, there is a limited understanding of the mechanisms that underlie age- and disease-related gait speed decline. Identifying the mechanisms that underlie

the prognostic value of walking speed should be a central theme in the design of the next generation of longitudinal studies of aging, with appropriate measures introduced and analytical approaches incorporated. This study hypothesized that a scarcity of available energy induces the decline in customary walking speed with aging and disease. Based on work in the Baltimore Longitudinal Study of Aging, examples of measures, operationalized dimensions, and analytical models that may be implemented to address this are provided. The main premise is simple: the biochemical processes that maintain life, secure homeostatic equilibrium, and prevent the collapse of health require energy. If energy becomes deficient, adaptive behaviors develop to conserve energy. PMID: 21029063 [PubMed - indexed for MEDLINE]

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### READING 5 – Nutritional assessment is important to identify and treat patients at risk

**Ahmed T, Haboubi N. Assessment and management of nutrition in older people and its importance to health. Clin Interv Aging. 2010 Aug 9;5:207-16. Review. PubMed PMID: 20711440; PubMed Central PMCID: PMC2920201.**

URL: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2920201/pdf/cia-5-207.pdf> (free full text)

Adult and Elderly Medicine, Nevill Hall Hospital, Abergavenny, Wales, UK.

#### SUMMARY

Nutrition is an important element of health in the older population and affects the aging process. The prevalence of malnutrition is increasing in this population and is associated with a decline in: functional status, impaired muscle function, decreased bone mass, immune dysfunction, anemia, reduced cognitive function, poor wound healing, delayed recovery from surgery, higher hospital readmission rates, and mortality. Older people often have reduced appetite and energy expenditure, which, coupled with a decline in biological and physiological functions such as reduced lean body mass, changes in cytokine and hormonal level, and changes in fluid electrolyte regulation, delay gastric emptying and diminish senses of smell and taste. In addition pathologic changes of aging such as chronic diseases and psychological illness all play a role in the complex etiology of malnutrition in older people. Nutritional assessment is important to identify and treat patients at risk, the Malnutrition Universal Screening Tool being commonly used in clinical practice. Management requires a holistic approach, and underlying causes such as chronic illness, depression, medication and social isolation must be treated. Patients with physical or cognitive impairment require special care and attention. Oral supplements or enteral feeding should be considered in patients at high risk or in patients unable to meet daily requirements. PMCID: PMC2920201 PMID: 20711440 [PubMed - indexed for MEDLINE]

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### READING 6 – Sarcopenia and significance

**Narici MV, Maffulli N. Sarcopenia: characteristics, mechanisms and functional significance. Br Med Bull. 2010;95:139-59. Epub 2010 Mar 2. Review. PubMed PMID: 20200012.**

URL: <http://bmb.oxfordjournals.org/content/95/1/139.full.pdf+html> (payment required)

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#### SUMMARY

Sarcopenia reflects a progressive withdrawal of anabolism and an increased catabolism, along with a reduced muscle regeneration capacity. Muscle force and power decline more than muscle dimensions: older muscle is intrinsically weak. Sarcopenic obesity (SO) among the elderly corroborates to the loss of muscle mass increasing the risk of metabolic syndrome development. Recent studies on the musculoskeletal adaptations with ageing and key papers on the mechanisms of muscle wasting, its functional repercussions and on SO are included. Neuropathic, hormonal, immunological, nutritional and physical activity factors contribute to sarcopenia. Selective fast fibre atrophy, loss of motor units and an increase in hybrid fibres are typical findings of ageing. Satellite cell number decreases reducing muscle regeneration capacity. SO promotes further muscle wasting and increases risk of metabolic syndrome development.

The proportion of fast to slow fibres seems maintained in old age. In elderly humans, nuclear domain is maintained constant. Basal protein synthesis and breakdown show little changes in old age. Instead, blunting of the anabolic response to feeding and exercise and of the antiproteolytic effect of insulin is observed. Further understanding of the mechanisms of sarcopenia requires disentangling of the effects of ageing alone from those of disuse and disease. The causes of the greater anabolic resistance to feeding and exercise of elderly women need elucidating. The enhancement of muscle regeneration via satellite cell activation via the MAPK/notch molecular pathways seems particularly promising. PMID: 20200012 [PubMed - indexed for MEDLINE]

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## READING 7 – Health and disease in 85 year olds

**Collerton J, Davies K, Jagger C, Kingston A, Bond J, Eccles MP, Robinson LA, Martin-Ruiz C, von Zglinicki T, James OF, Kirkwood TB. Health and disease in 85 year olds: baseline findings from the Newcastle 85+ cohort study. BMJ. 2009 Dec 22;339:b4904. doi: 10.1136/bmj.b4904. PubMed PMID: 20028777; PubMed Central PMCID: PMC2797051.**

URL: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2797051/pdf/bmj.b4904.pdf> (free full text)

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### SUMMARY

Comment in:

BMJ. 2009;339:b4715.

**OBJECTIVES:** The Newcastle 85+ Study aims to systematically study the clinical, biological, and psychosocial attributes of an unselected cohort of 85 year olds and to examine subsequent health trajectories as the cohort ages; health at baseline is reported.

**DESIGN:** Cross sectional analysis of baseline data from a cohort study.

**SETTING:** Newcastle upon Tyne and North Tyneside primary care trusts, United Kingdom.

**PARTICIPANTS:** 1042 people born in 1921 and registered with the participating general practices.

**MAIN OUTCOME MEASURES:** Detailed health assessment and review of general practice records (disease, medication, and use of general practice services); participants could decline elements of the protocol.

**RESULTS:** Of the 1453 eligible people, 851 (58.6%) were recruited to health assessment plus record review, 188 (12.9%) to record review only, and 3 (0.2%) to health assessment only. Data from record review are reported on a maximum of 1030 and from health assessment on a maximum of 853; individual denominators differ owing to withdrawal and missing values. Of the health assessment sample (n=853), 62.1% (n=530) were women and 10.4% (n=89) were in institutional care. The most prevalent diseases were hypertension (57.5%, 592/1030) and osteoarthritis (51.8%, 534/1030). Moderate or severe cognitive impairment was present in 11.7% (96/824) of participants, severe or profound urinary incontinence in 21.3% (173/813), hearing impairment in 59.6% (505/848), and visual impairment in 37.2% (309/831). Health assessment identified participants with possible disease but without a previous diagnosis in their medical record for hypertension (25.1%, 206/821), ischaemic heart disease (12.6%, 99/788), depression (6.9%, 53/772), dementia (6.7%, 56/840), and atrial fibrillation (3.8%, 30/788). Undiagnosed diabetes mellitus and thyroid disease were rare (1%, 7/717 and 6/762, respectively). A median of 3 (interquartile range 1-8) activities of daily living were undertaken with difficulty. Overall, 77.6% (646/832) of participants rated their health compared with others of the same age as good, very good, or excellent. High contact rates in the previous year with general practitioners (93.8%, 960/1024) were recorded. Women had significantly higher disease counts (medians: women 5, men 4; P=0.033) and disability scores (medians: women 4, men 2; P=0.0006) than men, but were less likely to have attended outpatient clinics in the previous three months (women 29% (150/524), men 37% (118/320), odds ratio 0.7, 95% confidence interval 0.5 to 0.9).

**CONCLUSIONS:** This large cohort of 85 year olds showed good levels of both self rated health and functional ability despite significant levels of disease and impairment. Hypertension, ischaemic heart disease, atrial fibrillation, depression, and dementia may be underdiagnosed. Notable differences were found between the sexes: women outnumbered men and had more disease and disability. PMCID: PMC2797051 PMID: 20028777 [PubMed - indexed for MEDLINE]

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**READING 8 – Approaches to characterize geriatric depression**

**Steffens DC. A multiplicity of approaches to characterize geriatric depression and its outcomes. Curr Opin Psychiatry. 2009 Nov;22(6):522-6. Review. PubMed PMID: 19625967; PubMed Central PMCID: PMC2833219.**

URL: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2833219/pdf/nihms-180955.pdf> (free full text)

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SUMMARY

**PURPOSE OF REVIEW:** Research in geriatric depression has always had a multidisciplinary bent, particularly in methods used to characterize depression. Understanding diagnosis, psychiatric comorbidities, and course continues to be a goal of clinical researchers. Those interested in cognitive neuroscience and basic neuroscience have more recently trained their sights on late-life depression. This review identifies recent progress in the characterization of geriatric depression using a variety of methodologies.

**RECENT FINDINGS:** Depression in the elderly remains underdetected and underdiagnosed, particularly in nonmental health settings. Studies of the impact of psychiatric comorbidities and of the negative outcomes of depression in older adults demonstrate that geriatric depression is a serious medical condition that not only affects mood but can also lead to functional and cognitive decline. Advances in neuroimaging technology have demonstrated structural and functional changes in the brains of older depressed patients. With the advent of brain banks in neuropsychiatry, we are now seeing postmortem neuroanatomical studies that seek to extend findings from clinical practice and from neuroimaging research.

**SUMMARY:** Clinicians should become more aware of advances in detection of depression, the effect of psychiatric comorbidities, the poor mood and cognitive outcomes associated with late-life depression and should keep abreast of recent neuroimaging and neuroanatomical findings. PMCID: PMC2833219 PMID: 19625967 [PubMed - indexed for MEDLINE]

**READING 9 – Progressive resistance strength training (PRT) exercises increase strength.**

**Liu CJ, Latham NK. Progressive resistance strength training for improving physical function in older adults. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD002759. Review. PubMed PMID: 19588334.**

URL: <http://onlinelibrary.wiley.com/o/cochrane/clsysrev/articles/CD002759/frame.html> (payment required)

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SUMMARY

Update of:

Cochrane Database Syst Rev. 2003;(2):CD002759.

**BACKGROUND:** Muscle weakness in old age is associated with physical function decline. Progressive resistance strength training (PRT) exercises are designed to increase strength.

**OBJECTIVES:** To assess the effects of PRT on older people and identify adverse events.

**SEARCH STRATEGY:** We searched the Cochrane Bone, Joint and Muscle Trauma Group Specialized Register (to March 2007), the Cochrane Central Register of Controlled Trials (The Cochrane Library 2007, Issue 2), MEDLINE (1966 to May 01, 2008), EMBASE (1980 to February 06 2007), CINAHL (1982 to July 01 2007) and two other electronic databases. We also searched reference lists of articles, reviewed conference abstracts and contacted authors.

**SELECTION CRITERIA:** Randomised controlled trials reporting physical outcomes of PRT for older people were included.

**DATA COLLECTION AND ANALYSIS:** Two review authors independently selected trials, assessed trial quality and extracted data. Data were pooled where appropriate.

**MAIN RESULTS:** One hundred and twenty one trials with 6700 participants were included. In most trials, PRT was performed two to three times per week and at a high intensity. PRT resulted in a small but significant improvement in physical ability (33 trials, 2172 participants; SMD 0.14, 95% CI 0.05 to 0.22). Functional limitation measures also showed improvements: e.g. there was a modest improvement in gait speed (24 trials, 1179 participants, MD 0.08 m/s, 95% CI 0.04 to 0.12); and a moderate to large effect for getting out of a chair (11 trials, 384 participants, SMD -0.94, 95% CI -1.49 to -0.38). PRT had a large positive effect on muscle strength (73 trials, 3059 participants, SMD 0.84, 95% CI 0.67 to 1.00). Participants with osteoarthritis reported a reduction in pain following PRT (6 trials, 503 participants, SMD -0.30, 95% CI -0.48 to -0.13). There was no evidence from 10 other trials (587 participants) that PRT had an effect on bodily pain. Adverse events were poorly recorded but adverse events related to musculoskeletal complaints, such as joint pain and muscle soreness, were reported in many of the studies that prospectively defined and monitored these events. Serious adverse events were rare, and no serious events were reported to be directly related to the exercise programme.

**AUTHORS' CONCLUSIONS:** This review provides evidence that PRT is an effective intervention for improving physical functioning in older people, including improving strength and the performance of some simple and complex activities. However, some caution is needed with transferring these exercises for use with clinical populations because adverse events are not adequately reported. PMID: 19588334 [PubMed - indexed for MEDLINE]

## **READING 10 – Aging, exercise, and muscle protein metabolism**

**Koopman R, van Loon LJ. Aging, exercise, and muscle protein metabolism. J Appl Physiol. 2009 Jun;106(6):2040-8. Epub 2009 Jan 8. Review. PubMed PMID: 19131471.**

URL: <http://jap.physiology.org/content/106/6/2040.long> (full free text)

Department of Human Movement Sciences, Maastricht University, 6200 MD Maastricht, The Netherlands.

### SUMMARY

Aging is accompanied by a progressive loss of skeletal muscle mass and strength, leading to the loss of functional capacity and an increased risk of developing chronic metabolic disease. The age-related loss of skeletal muscle mass is attributed to a disruption in the regulation of skeletal muscle protein turnover, resulting in an imbalance between muscle protein synthesis and degradation. As basal (fasting) muscle protein synthesis rates do not seem to differ substantially between the young and elderly, many research groups have started to focus on the muscle protein synthetic response to the main anabolic stimuli, i.e., food intake and physical activity. Recent studies suggest that the muscle protein synthetic response to food intake is blunted in the elderly. The latter is now believed to represent a key factor responsible for the age-related decline in skeletal muscle mass. Physical activity and/or exercise stimulate postexercise muscle protein accretion in both the young and elderly. However, the latter largely depends on the timed administration of amino acids and/or protein before, during, and/or after exercise. Prolonged resistance type exercise training represents an effective therapeutic strategy to augment skeletal muscle mass and improve functional performance in the elderly. The latter shows that the ability of the muscle protein synthetic machinery to respond to anabolic stimuli is preserved up to very old age. Research is warranted to elucidate the interaction between nutrition, exercise, and the skeletal muscle adaptive response. The latter is needed to define more effective strategies that will maximize the therapeutic benefits of lifestyle intervention in the elderly. PMID: 19131471 [PubMed - indexed for MEDLINE]

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Elder JT, Travakol A, Klein SB, et al. Protooncogene expression in normal and psoriatic skin. *J Invest Dermatol*, 1990;94:19-20.

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