

***Healthy Ageing, Appetite, Frailty and Sarcopenia: a brief overview***  
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Word count 2923

***Old age is not a disease - it is strength and survivorship, triumph over all kinds of vicissitudes and disappointments, trials and illnesses.***

***Maggie Kuhn (1905-1995)***

1. Frailty; 2. Ageing; 3. Nutrition; 4. Inflammation; 5. Exercise

## **Introduction**

In many societies the population is getting older, such that in some western countries it is expected that those over 80 years of age will make up 30% of the population (1-2). In the modern era, due to improved health and better medical support/treatment, many people may spend as many years retired as they did working. Unfortunately, as one ages, the burden of disease increases (2.9 million people in England have >1 long-term condition), longevity is compromised by disability; therefore the drive must be to add life to years rather than just years to life. When people live long, the media often asks “what is the success associated with longevity or successful (healthy) ageing?” Is it a success to live a long life, or is successful ageing the key? Healthy ageing, is defined as a state, where the effect of frailty, sarcopenia, disease and disability have been minimised. Farpour et al (3) discuss the effect that aging has on Iranian people, and Liang et al discuss the findings of a systematic review looking at traditional Chinese’ medicine and subhealth (4), which could be aligned to prefrailty.

In 2015 the WHO defined Health as “a state of complex physical, mental and social well-being and not merely absence of disease” (5). Healthy ageing was also defined as “the process of developing and maintaining the functional ability that enables well-being in older age”. Rowe and Khan (1987) commented that to age successfully one must avoid disease, remain engaged with life and maintain a high level of physical and cognitive function (6). Healthy ageing is, therefore, a complex interplay between physical, cognitive and social factors, and perhaps is dependent on how we individually respond to the internal and external forces at play (table 1).

The definition of what is normal and what is abnormal is fraught with difficulty; what is acceptable and what is not? There is a risk that where normative parameters (for younger adults) are exceeded there will be a medicalisation of “older age”!

What ultimately matters is the preservation of functional ability, which the majority (75%) of very old people are able to do and live relatively independent lives (6). This paper will discuss the interdependency between healthy ageing, appetite, frailty and sarcopenia and their impact on functional ability.

## **Ageing**

Ageing is a life-long process and not a disease. In western countries the onset of old age has been the age of retirement and access to a pension. If the onset of old age is taken at the age of 65 years, then this third age can be divided into the young (65-74), old (75-85) and very old (‘old-old’; 85+). It is projected that, by 2041, two thirds of the population will be older than 70 years (1, 2) and by 2050, 20% of the world’s population of 2 billion will be >65 years ( $1.2 \times 10^{11}$ ). Those > 80 years are set to increase by 300% and centenarians 15 fold (3). Generally, within these age groups women are predominant, particularly in the old-old. Chronological age marches relentlessly onward unless interrupted by sudden death (eg trauma or cancer). The velocity of biological ageing is influenced by both internal (genetics) and external factors (smoking, poor diet, pollution, illicit drugs, alcohol; see Table 1).

However, one must ask; when does one become ‘old’? Today, who is old and what determines old age depends on the society and culture in which we live. Old, on the whole, is often simply older than oneself! Age is a number determined from the year

of birth, and at birth age is either one or zero depending on Eastern or Western culture. In other cultures, age may be determined by significant events in the calendar, such as seasons or momentous events.

As society and its members age, Society is engrossed with age, or rather with delaying the inevitable. Money and time are spent undergoing surgery or buying creams to hide the appearance of wrinkles (7), tell-tale signs of getting older.

### **Energy requirement, appetite and efficiency**

With increasing age, there is a reduction in physical activity, energy requirement, appetite regulation and energy efficiency. As age increases people eat and drink less and what they do eat is not efficiently converted to energy and utilised. Frailty intervenes when there is a decline in physical function due to changes at the molecular and cellular level, particularly in the musculoskeletal system.

### **Energy Requirements**

Physical activity decreases between the ages of 20 and 80 years. At the same time, there is an increase in coexistent chronic disease, a reduction in basal metabolic rate (BMR; 2% each decade, from the age of 20 years) and a dysregulation of appetite (8,9). As a consequence, there is a linear decline in energy requirements of 165 kcal/decade in men and 103 kcal/decade in women to approximately 2000 kcal/day or less (10,11). Energy intake is markedly variable (20-25% variability) coupled with only a 10% variability in energy expenditure (12). This imbalance, results in a general weight loss of up to 0.65kg/year. Weight regulation is further affected in that the ability to return to the previous body weight following gain (or loss) is markedly impaired (13). When the body is under extra stress, and extra energy is required, the body may be unable to utilise the body's energy sources efficiently (eg through mitochondrial down-regulation). The imbalance between energy intake and expenditure, coupled with inefficient energy use, results in fatigue and tiredness.

### **Nutrition and hydration**

With frailty, not only is there a reduction in food and fluid intake and energy efficiency, but additionally the type of food eaten by frail older people may be different to that of younger people. Changes to diet are often driven, in part by food cost, availability and accessibility in older age. Declining numbers of teeth, use (or not) of dentures, age-related changes to taste and smell, a reduction in the number of taste buds/ papillae in the tongue (which leads to a relative preponderance of bitter and sweet receptors) all contribute to changes in diet. In many instances food can taste bland, such that strong flavours (14) are preferred.

Societies, particularly in the west are besotted with diets both to lose weight and prolong age. A healthy well balanced diet with adequate protein (15) will enhance well-being and reduce morbidity. Yet, many older people in poverty frequently eat food that is energy rich and nutrient poor or energy and nutrient poor. There have been several recent reviews of the nutritional needs of the older person (13, 16-19).

In many frail older people, dehydration is a real issue that can cost lives. Thirst may decline with age, and this may be related to decline in endocrine and renal function (20). Medication (diuretics), which in adverse circumstances (hot weather, excessive

fluid loss [diarrhoea]), may result in a shift of fluid balance and an increase in osmolality (21), resulting in delirium, falls and cardiac arrhythmias which could be fatal for frail older people.

### **Appetite**

Appetite is complex and will be influenced by endogenous (hormonal and neurological pathways), disease (eg cancer, infection and cardiorespiratory disease), mood (eg depression or phobias) and medication (eg metformin and cytotoxins; (22). Many frail old people will be on a multitude of medicines and may have several medical conditions. Untangling the contributory effects can therefore be difficult. Frail older people have a greater degree of non-specific satiation with food (23) and a reduction in hunger drive (24). The exact mechanism is uncertain but is a combination between the feedback from stomach stretch receptors and changes to gut hormone levels delaying gastric emptying (14) particularly neuropeptide Y (response to fasting attenuated), cholecystokinin (raised fivefold) and leptin (raised) (25). Studies have noted a reduction in taste and olfactory function with many foods tasting bland, resulting in a tendency for strong/pungent flavours with a high fat content (14). Loss of fine-tuning of the appetite-energy balance loop has one benefit (24); when food supplements (eg drinks and snacks) are provided in order to boost energy intake (26) and given 90 minutes before a main meal, there is no diminution of energy intake from that meal. The net result is an increase in the daily energy intake. Constipation may also be an aetiological factor leading to loss of appetite and can be difficult to treat Yue et al suggest a herbal formula that may be of use where all else may not be effective (27).

### **Energy efficiency**

Between the ages of 40-75 years there is a 25% reduction in food and energy intake (28). Not only is intake reduced, utilisation is inefficient. The body is unable to respond to increased energy input after a period of illness and or starvation (14,29). Amino acid availability from a protein load is blunted, resulting in a 2% deficit in muscle synthesis from a 20g protein meal (30,31). This is exacerbated by many meals being protein poor.

Any stored energy is not utilised efficiently, and given that physical activity may use up to 35% of energy expenditure (32), the inefficient use of energy may contribute to the slowing of the pace at which physical tasks are completed. Thus healthy women of 70 years of age will expend 20% more energy than younger women, when walking at the same standard speed (and even more energy if requiring aids, eg Zimmer Frame).

### **Frailty**

Frailty is the result of a decline in molecular, cellular and physiological systems (33,34), resulting in an impaired homeostatic reserve and reduced capacity to withstand physiological stress. The final underlying pathway is uncertain, but the inflammatory system is thought to be the common pathway (35,36) supported by the fact that both turmeric and melatonin (37,38) are reported to affect ageing/frailty via the immunoglobulin and cytokine systems.

The clinical effects are demonstrated as an age-related cumulative physical decline, typified by weight loss (significant un-intentional weight loss with age often precedes significant disease; (39,40)). Also, weakness, exhaustion, reduced energy expenditure, slow gait speed and low physical activity are contributors (33,41,-43); Frailty describes the vulnerability of older people regarding health-related disability, dependency and the need for long-term care. Pre-frailty is typically defined as the transitional stage between the non-frail and frail state (44), where only one or two factors of frailty are present. Frailty and sarcopenia frequently occur together (33,41). There are several tools to grade the severity of frailty. In the UK, the most common are the Clinical Frailty Scale, used in secondary care (45) and the EFI, commonly used in primary care (46).

### **Sarcopenia**

Sarcopenia has been defined as the age-related changes that occur in skeletal muscle influenced by hormonal, neurological, inflammatory, and dietary factors (25). Sarcopenia has been shown to have a negative impact on other systems increasing the risk of and associated with increased fragility fractures and lower bone density (47) and increased cognitive impairment (48). Neuromuscular activation is reduced in sarcopenia (49) and muscle tissue is replaced with fat and connective tissue (50). One key aspect of sarcopenia relates to the specific atrophy of type II muscle fibres during ageing - muscle fibres which are associated with strength, power and muscle mass (greater cross sectional area) (50,51), which is disproportionately greater than the loss of muscle mass (i.e. rate of loss with age) indicating involvement of other factors. Manini and Clark have termed this loss in strength and power with ageing 'dynapenia' (49).

The scale of muscle loss and strength, ranges from 15%, (50-60 years) to 30% (70-80 years) and >50% in those >80 years (more so in males). However, this is not inevitable and can be reversed by an exercise programme and increased protein intake (25,52,53). Sarcopenia is typified by a decrease in muscle mass, strength and function (16).

### **Geriatric Syndrome**

At the inception of Geriatric Medicine, the 'giants' or 'syndromes' identified were few (continence, cognitive decline, acute confusion, falls). In later years many more areas have been put forward, including frailty (54). All geriatric syndromes are associated with multiple aetiological factors and general decline with an increased risk of death. Frailty is no exception.

### **Functional fitness**

Functional fitness represents the physical capacity that is needed to undertake normal everyday activities, independently and without the early onset of fatigue (55). Functional fitness is a composite of physical and mental health (56); death was associated with being less physically active (RR = 2.69) and self-rating of fair/poor on the global health score (RR = 2.13; 51). Milanovic et al, compared young elderly (60-69years of age) and old elderly (70-80years of age) in a total of 1288 study participants (57). They found that physical activity (assessed using the International

Physical Activity Questionnaire) and functional fitness (assessed using a 'Seniors Fitness test' back scratch, chair sit and reach, 8-foot up and go, chair stand up for 30 seconds, arm curl, and 2-minute step test) was lower in the old frail group.

Frailty and sarcopenia contribute to a decline in functional fitness (and an increase in all-cause mortality; (58)) and is a consequence of loss in strength, proprioception and power (59). This decline is exacerbated by the intervention of stressors (falls/trauma, infection, medication, infection) due to the precarious homeostatic state that frail patients seem to be in.

Recovery from the stressor insult is frequently slow and incomplete, resulting in a lower functional fitness. Immobility (often enforced) is a great threat to functional fitness. In 1960, the US Public Health Service reported that disability from immobilization was one of 10 preventable health problems and argued that, with existing knowledge, such disability could be reduced by 50-75% (60). Illness, admission to hospital and bedrest will result in the beginning of functional decline by the second day and 16% of patients who experienced functional decline during hospitalization died within three months of discharge (60).

### **Intervention (Fig 1)**

Can the inevitable decline be prevented or reversed? Prevention is better than cure and one approach is to identify 'at-risk' people at the pre-frail stage. Then, a multimodal intervention is needed. A single approach, i.e. muscle training will probably improve strength but this may not improve functional ability.

If the primary aetiology is the inflammatory pathway, then the use of antioxidants and anti-inflammatory agents (Turmeric, Melatonin, Ibuprofen) may be appropriate. Improving nutrition with fresh fruit (eg blueberries), vegetables and spices (eg turmeric; (37,38,61) may prevent the damage brought about by reactive oxygen species (free radicals).

Environmental changes that are more conducive to socialisation and eating will improve calorie intake. Improving dairy intake will support improved muscle function, increased skeletal mass and increased grip strength (62). A balanced diet (eg 'mediterranean diet' (63)) has been shown to improve physical and cognitive function, though the consensus would be that whole food is more beneficial and less harmful than individual components, even if they are reported as having anti-oxidant potential (35).

Weight-bearing physical activity (e.g. walking and dance; (64,65) has been shown to improve outcome. The role of growth hormone, insulin and non-steroidal anti-inflammatory (ibuprofen) medication is less certain and, although muscle mass may reduce falls, strength increases may not. There is a suggestion that proprioception may be a better approach than solely increased muscle strength and mass, which may be why dance has been shown to be effective in a number of studies. Also, some research suggests that resistance training needs to be incorporated into a programme of exercises that include flexibility and balance (see [www.nhs.uk/exercises-for-older-people](http://www.nhs.uk/exercises-for-older-people)).

However, there is uncertainty as to which form of resistance training is beneficial in curtailing sarcopenia and frailty. Different approaches have included conventional strength training, maximal strength training and high velocity training (51,66-68). The essential outcome of any exercise programme is a positive outcome on functional activities of daily living (walking, climbing stairs). Recent reviews appear to suggest that higher velocity training (68) may be more beneficial than high resistance (67) even in older people living in care homes (68).

A systematic review of 62 studies involving progressive resistance training for older adults (n = 3674; 64) showed that, despite many trials being of poor quality, the overall trend was for a positive effect of progressive resistance training on strength and function (eg gait speed) (69). Indeed, in 2009, the Cochrane Database systematic review of 121 trials (n=6700) on the effects of progressive resistance training on physical function (70,71) found that it was associated with a small but significant improvement in physical ability and function, e.g. gait speed and sit-to-stand, alongside significant improvements in strength, with no adverse effects.

If the progress to frailty is not arrested, society (health and social) will be required to treat and support an ever increasing burden. Western medicine may have its limits and several articles published in this edition look at osteoporosis (72), osteoarthritis (73) and stroke treatment (74-77).

## **Conclusion**

We all get older; we eat less and exercise less. Many of these changes are physiological and can result in ill-health. This seems to be because a decline in cellular systems results in a compromise in homeostasis and an inability of the individual to cope with external stress (trauma, infection, constipation, medication change). Frailty is the Geriatric Syndrome that encompasses this and is associated with high levels of morbidity and mortality. However, it may be possible to delay this decline. It may be possible to avoid repeated hospitalisation, by suitable intervention, involving multi-modal programmes that include modification and monitoring of diet, exercise and medication.

Questions to be answered with respect to frailty include; What is the best pathway to healthy ageing such that frailty be prevented? Can frailty be reversed, especially to reduce hospitalisation rates? Certainly, growing evidence is suggesting that nutrition and exercise, often together, can improve outcome (66) and maintain independence.

## **Contribution**

Both authors contributed equally to the writing of the paper

## **Funding**

There is no Financial support



**Conflict of Interest**

The authors declare that there is no conflict of interest.

## References

1. United Nations, Department of Economic and Social Affairs, Population Division (2015). *World Population Ageing 2015* (ST/ESA/SER.A/390).
2. Zaidi A. Features and challenges of population ageing: the European Perspective. Policy Brief March (1) 2008 (Internet) 2008. Available at [http://www.euro.centre.org/data/1204800003\\_27721.pdf](http://www.euro.centre.org/data/1204800003_27721.pdf) (accessed 21 August 2018).
3. Farpour S, Farpour HZ, Smithard DG. Oropharyngeal dysphagia and its related health problems in Iranian Elderly. A scope of work for the future. *EuJIM* 2018;21:94-100
4. Ning Liang, XueFeng, Jianping Liu, HuijuanCao. The effect of traditional Chinese medicine education program on people's subhealth status: A systematic review of clinical studies *EuJIM* 2018;22: 69-75  
<https://doi.org/10.1016/j.eujim.2018.07.009>
5. World report on Ageing and Health. WHO 2015
6. Rowe JW, Kahn RL. Human aging: usual and successful. *Science* 1987;237:143-149
7. Im AR, Nam J, Cha S, Seo YK, Chae S, Kim JY. Wrinkle reduction using a topical herbal cream in subjects with greater yin (Tae- eumin) type: A randomized double-blind placebo-controlled study. *EuJIM* 2018;20:173-181.
8. Elia M. Obesity in the elderly. *Obesity Research* 2001;244S-248S.
9. Sinclair AJ. Anorexia of ageing as a risk factor for weight loss in older humans. *Rev Clin Gerontol* 2000;10:97-98.
10. McGandy RB, Barrows CH, Spanias A. Nutrient intakes and energy expenditure in men of different ages. *J Gerontol* 1966;21:581-587.
11. NHANES 3<sup>rd</sup> National and Nutrition Examination Survey, phase III 1988-1991. Daily dietary fat and total food energy intakes. *MMWR Morb Mortal Weekly Rep* 1994;43:116-125.
12. Roberts SB; Rosenberg I. Nutrition and Aging: Changes in the regulation of energy metabolism with aging. *Physiol Rev* 2006;86: 651-667.
13. Morley JE. Anorexia of aging: physiologic and pathologic. *Am J Clin Nutr* 1997;66:760-773.
14. Van Staveren WA, de Graaf C, de Groot LCPGM. Regulation of appetite in frail persons. *Clinics in Geriatric Medicine*. 2002;18:675-684.

15. Donaldson AIC, Johnstone AM, Roos B, Myint PK Protein intake and healthy ageing *EuJIM* 2018;23:32-36  
<https://www.sciencedirect.com/science/journal/18763820/23/supp/C>
16. Thomas N. Nutrition in practice: nutrition in the elderly. *Nursing Times* 1998;94:suppl 1-6.
17. Hudson HM, Daubert CR, Mills RH. The interdependency of protein energy malnutrition, aging and dysphagia. *Dysphagia* 2000;15:31-38.
18. Suominen MH, Jyvakorpi SK, Pitkala KH, Finne-Soveri H, Hakala P, Soimi H, Sarlio-Lahteenkorva S. Nutritional guidelines for older people in Finland. *J Nutr Health Aging* 2014;18:861-867.
19. Soini H, Suominen MH, Muurinen S, Strandberg TE, Pitkala KH. Malnutrition according to the mini nutritional assessment in older adults in different settings. *JAGS* 2011;59:
20. Philips PA, Rolls BJ, Ledingham JGG et al. reduced thirst after water deprivation in healthy elderly men. *N Engl J Med* 1984;311:753-759.
21. Luckey AE, Parsa CJ. Fluid and electrolytes in the Aged. *Archives of Surgery* 2003;138:1055-1060.
22. Kelly J, D'Cruz G, Wright D. Patients with dysphagia: experiences of taking medication. *J Adv Nurs* 2010;66:82-91
23. Blundell JE, Stubbs RJ. High and low carbohydrate and fat intakes: limits imposed by appetite and palatability and their implications for energy balance. *Eur J Clin Nutr* 1999;53(S1):S148-S165.
24. Adams KF, Schatzkin A, Harris TA, Kipnis V. et al. Overweight, obesity and mortality in a large prospective cohort of person 50-71 years old. *NEJM* 2006;355:763-78.
25. Doherty T. Aging and sarcopenia. *J Appl Physiol.* 2003;95:1717-1727.
26. Gall MJ, Grimble GK, Reeves NJ, Thomas SJ. The effects of providing fortified meals and between meal snacks on energy and protein intake of hospital patients. *Clin Nutr* 1998;17:259-264.
27. Yue Y, Wang X, Yang H, Sun M, Chen S, Qian H, Xu T, Yan S. Clinical Efficacy of the Traditional Chinese Herbal Formula, (Tong Bian Decoction) on Laxative Dependence Constipation in Elderly Persons: A Randomized, Multicenter, Controlled Trial. *EuJIM* 2018;24:23-29  
<https://www.sciencedirect.com/science/journal/18763820/24/supp/C>
28. Otsuka R, Matsui C, Tange C, Nishita Tomida M, Fujiko A, Shimokata H, Arai H. What is the best adjustment of appendicular mass for predicting mortality

or disability among Japanese community dwellers? BMC Geriatrics 2018;18:8  
<https://doi.org/10.1186/s12877-017-0699-6>

29. Russell RM. The aging process as a modifier of metabolism. *Am J Clin Nutr* 2000;72(suppl):529S–32S.
30. Cramer JT, Cruz-jentoft AJ, Landi F, Hickson M, Zamboni M, Pereira SL, Hustead DS, Mustard VA. Impacts of high-protein oral nutritional supplements among malnourished men and women with sarcopenia: a multicentre, randomized, double blinded, control trial. *J Am Dir Ass* 2016;17:1044-1055.
31. Robinson SM, Reginster JY, Rizzoli R, Shaw SC, Kanis JA, Bautmans I, Bischoff-Ferrari H, Bruyere O, Cesari M, Dawson-Hughes B, Fielding RA, Kaufman JM, Landin F, Malafarina V, Rolland Y, van Loon LJ, Vellas B, Visser M, Cooper C. Does nutrition play a role in the prevention and management of sarcopenia. *Clin Nutr* 2018;37:1121-1132
32. Elia M. Energy expenditure in the whole body. In Kinney JM, Tucker HN (eds) *Energy metabolism: Tissue determinates and cellular corollaries*. Raven Press, New York 1992: 19-59.
33. Fried LP, Tangen CM, Walsten J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA. Frailty in older adults; Evidence for a phenotype. *J Gerontol* 2001;56A:M146-M156
34. *Strandberg TE, Pitkälä KH: Frailty in elderly people. Lancet. 2007, 369: 1328-1329. 10.1016/S0140-6736(07)60613-8.*
35. *Brown-Borg H, Anderson R, McCarter R, Morley J, Musi N, Olshansky SJ, Shukitt-Hale B, Jacques P St., Walston J, Willcox B. Nutrition in aging and disease: update on biological sciences. Aging Health 2012;8:13-16.*
36. Shivappa N, Stubbs B, Hebert JR, Cesari M, Schofield P, Soysal P, Maggi S, Veronese N. The relationship between the dietary inflammatory index and incident frailty: a longitudinal cohort study. *J Am Med Dir Ass.* 2018;19:77-82.
37. Bhardwaj RL, Nandal U, Pal A, Jain S. Bioactive compounds and medicinal properties of fruit juices. *Fruits* 214;69:391-412
38. Ishmail IA, El-BAkry HA, Soliman SS. Melatonin and turmeric ameliorate aging-induced changes: implication of immunoglobulins, cytokines, DJ-1/NRF2 and apoptosis regulation. *Int J Physiol Pathophysiol Pharmacol* 2018;10:70-82
39. Morley JE. Anorexia in older persons: epidemiology and optimal treatment. *Drugs Aging* 1996;8:134-155.
40. Morley JE, Thomas DR. Anorexia and aging: pathophysiology. *Nutrition* 1999;15:499-506.

41. Cruz-Jentoft AJ, Baeyens JP, Bauer JM et al. Sarcopenia: European consensus on definition and diagnosis. *Age and Ageing* 2010;39:412-423.
42. Horan MA. Advances in understanding the concept of biological ageing. In Tallis RC (ed). *Increasing longevity*. Royal College of Physicians, London, 1998.
43. Stratton RJ, Hackston A, Longmore D, Dixon R, Price S, Stroud M, King C, Elia M. Malnutrition in hospital outpatients and inpatients: prevalence concurrent validity and ease of use of the 'malnutrition universal screening' ('MUST') for adults. *B J Nutr* 2004;92:799-808.
44. Lang PO, Michel JP, Zekry D: *Frailty syndrome: a transitional state in a dynamic process*. *Gerontology*. 2009, 55: 539-549. 10.1159/000211949
45. Rockwood K, Howlett SE, MacKnight C, Beattie BL, Bergman H, Hebert R, Hogan DB, Wolfson C, McDowell I. Prevalence, attributes, and outcomes of fitness and frailty in community-dwelling older adults: report from the Canadian study of health and aging. *J Gerontol: Medical sciences* 2004;59A:1310-1317.
46. Clegg A, Bates C, Young J, Ryan R, Nichols L, Teale EA, Mohammed MA, Parry J, Marshall T. Development and validation of an electronic frailty index using routine primary care electronic health record data. *Age and Ageing* 2018;45:353-360
47. Marty E, Liu Y, Samuel A, Or O and Lane J. A review of sarcopenia: enhancing awareness of an increasingly prevalent disease. *Bone* 2017; 105: 276-286.
48. Chang K-V, Tsu T-H, Wu W-T, Huang K-C and Han D-S. Association between sarcopenia and cognitive impairment: a systematic review and meta-analysis. *JAMDA* 2016; 17:1164e7-e15.
49. Manini TM and Clark BC. Dynapenia and aging: an update. *J Gerontol A Biol Sci Med Sci* 2012; 67(1): 28-40.
50. Lexell J. Human aging, muscle mass, and fiber type composition. *J Gerontol A Biol Sci Med Sci*. 1995; 50:11-6.
51. Nilwik R, Snijders T, Leenders M, Groen BB, van Kranenburg J, Verdijk LB, van Loon LJ. The decline in skeletal muscle mass with aging is mainly attributed to a reduction in type II muscle fiber size. *Exp Gerontol*. 2013; 48(5):492-8.
52. Evans WJ, Cyr-Campbell D. Nutrition, exercise and healthy aging. *J Am Diet Assoc* 1997;97:632-638.
53. Nijs KAND, de Graaf C, Siebelink E, Blauw YH, Vanneste V, Kok FJ, van Staveren WA. Effect of family-style meals on energy intake and risk of

malnutrition in Dutch nursing home residents: a randomized controlled trial. *Journals of Gerontology* 2006;61A:935-942.

54. Morely JE. Frailty and sarcopenia: the new geriatric giants. *Rev Inves Clin* 2016;68:59-67.
55. Kostić R, Pantelić S, Uzunović S, Djuraskovic R. A comparative analysis of the indicators of the functional fitness of the elderly. *Facta Univ Ser Phys Educ Sport*. 2011;9(2):161–171.
56. Lee Y. The predictive value of self assessed general, physical, and mental health on functional decline and mortality in older adults. *J Epidemiol Community Health* 2000;54:123-129
57. Milanović Z, Pantelić S, Trajković N, Sporiš G, Kostić R, James N. Age-related decrease in physical activity and functional fitness among elderly men and women. *Clin Interv Aging*. 2013;8:549-56.
58. Kelley GA and Kelley KS. Is sarcopenia associated with an increased risk of all-cause mortality and functional disability? *Exp Gerontol* 2017; 96:100-103.
59. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. *J Am Ger Soc* 2002;50:889-896.
60. Graf C. Functional decline in hospitalised patients. *AJN* 2006;106:58-67.
61. Chen X, Mao G, Leng SX. Frailty syndrome: an overview. *Clin Interv Aging* 2014;9:433-411
62. Radavelli-Bagatini S, Zhu K, Lewis JR, Dhaliwal SS, Prnice RL. Association of dairy intake with body composition and physical function in older community-dwelling women. *J Acadamey Nutrition and Dietetics* 2013;113:1669-1674.
63. Leon-Munoz LM, Guallar P, Lopex-Garcia E, Rodriguez-Artalejo F. Mediterranean diet and the risk of frailty in community dwelling older adults. *J Am Dir Ass*. 2014;15:889-903
64. Federici A, Bellagamba S, Rocchi MBL. Does dance-based training improve balance in adult and young old subjects? A pilot randomized controlled trial. *Aging Clin Exp Res* 2005;17:385-389.
65. Filar-Mierzwa K, Dtugsz M, Marchewka A, Dabrowski Z, Poznanska A. The effect of dance therapy on the balance of women over 60 years of age: the influence of dance therapy for the elderly. *J Women and Aging*  
<http://dx.doi.org/10.1080/08952841.2016.1194689>
66. Wang E, Nyberg SK, Hoff J, Zhao J, Leivseth G, Tørhaug T, Schnell Husby OS, Helgerud J, Richardson RS. Impact of maximal strength training on work

efficiency and muscle fiber type in the elderly: Implications for physical function and fall prevention. *Exp Gerontol* 2017; 91: 64-71

67. Guizelini PC, de Aguiar RA, Denadai BS, Caputo F and Greco CC. Effect of resistance training on muscle strength and rate of force development in healthy older adults: a systematic review and meta-analysis. *Exp Gerontol* 2018; 102: 51-58.
68. Cadore LE, Pinto SR, Reishak-Oliveira A and Izquierdo M. Explosive type of contractions should not be avoided during resistance training in elderly. *Exp Gerontol* 2018; 102: 81–83.
69. Latham NK, Bennett DA, Stretton CM, Anderson CS. Systematic review of progressive resistance strength training in older adults. *J Gerontol A Biol Sci Med Sci.* 2004; 59(1):48-61.
70. Liu CJ and Latham NK. Progressive resistance strength training for improving physical function in older adults. *Cochrane Database Syst Rev.* 2009; 8;(3):CD002759.
71. Artaza-Artabe I, Saez-Lopez P, Sanchez-Hernandez N, Fernandez-Gutierrez N, 93:89-99.Malafarina V. The relationship between nutrition and frailty: effects of protein intake, nutritional supplementation, vitamin D and exercise on muscle metabolism in the elderly. A systematic review. *Maturita* 2016;
72. Yun GW, Kang JH, Lee H.Effects of Korean herbal medicine (Cheong-A-Won) for treatment of bone mineral density in women with osteoporosis: A randomized, double blind, placebo controlled trial. *EuJIM* 2018;20:84-89
73. Luo Y-N, Zhou Y-M, Zhong X, Zhao L, Zheng Q-H, Zheng H, Tang L, Jia P-L, Wu Q, Huang C, Li Y, Liang F-R.Observation of Pain-Sensitive Points in Patients with Knee Osteoarthritis: A Pilot Study. *EuJIM* 2018;21:77-81  
"https://www.sciencedirect.com/science/journal/18763820/21/supp/C"Volume 21, August 2018, Pages 77-81 <https://doi.org/10.1016/j.eujim.2018.06.006>
74. Han CH, Ma JN, An N, Yoon SG, Kim M. Moxibustion for stroke: Systematic review, meta-analysis, and GRADE-based recommendations. *EuJIM* 2018;21:77-81 <https://doi.org/10.1016/j.eujim.2018.06.006>
75. Zheng C, Lee Y, Hu B, Wu J. A randomized controlled trial comparing electroacupuncture with manual acupuncture for motor function recovery after ischemic stroke *EuJIM* 2018;22:76-80  
<https://doi.org/10.1016/j.eujim.2018.08.005>
76. Luo Z-J, Guo T-M, Tua Q, Cheng X-L, Huang Y, Xiang MQ. Therapeutic Effect of Integrating Chinese patent medicine Xuesaitong Injection and Western Medicine in Treating Patients with Hypertensive Intracerebral Haemorrhage: a prospective randomized controlled trial *EuJIM* 2018;23:26-3  
<https://doi.org/10.1016/j.eujim.2018.09.005>

77. Zhang T, Wu X, Cao S, Park S. Efficacy of the Oriental herbal medicine, Jie Yu Dan, for alleviating post-stroke aphasia: A Systematic Review and meta-analysis of randomized clinical trials. *EuJIM* 2018;24:35-48  
<https://doi.org/10.1016/j.eujim.2018.1>