

This is not the version on record. Published version - Harper, Lynette (2017) Optimal nutrition for bone health in people with a learning disability. Learning Disability Practice, 20(1), pp. 31-35 available here: <http://dx.doi.org/10.7748/ldp.2017.e1783>

Families, carers and service users are increasingly seeking advice on supplement use and dietary changes that can improve health. The NHS reported that supplement use is a growing market with an estimated £60.7 million being spent in the UK on supplements that target bone health in 2010 alone (NHS, 2011). This paper aims to review the evidence on bone health in people with learning disabilities, the benefit of vitamin supplementation and dietary approaches to support bone health before drawing together recommendations for practice.

Bone health in people with a learning disability.

People with learning disabilities are now living longer and thus susceptible to the degenerative conditions associated with aging (Emerson and Baines, 2012). Low bone mineral density, osteoporosis, osteopenia and fractures have all been found at higher prevalence rates in people with learning disabilities as compared to the general population (Srikanth et al, 2011). Lin et al (2014) reported that in a sample of individuals with learning disability over the age of 40 more than half had either osteoporosis or osteopenia. This is supported by evidence that rates of hip fractures are three times higher in people with learning disabilities compared to the general population (Burke et al, 2016).

Cheema et al's (2016) study reported that 28% of children with learning disabilities had bone mineral density profiles below the norm. This may be grossly under-reporting the true extent of the problem due to the exclusion criteria included taking steroid or antiepileptic medication, a diagnosis of diabetes mellitus, hypogonadism or hyperthyroidism which are all known to impact on bone density (Wang et al, 2015).

This is supported by evidence from other countries that show over half of adults with

a learning disability aged between 20 and 64 have abnormal bone mineral density with the majority of individuals or their carers being unaware of this (Chen et al, 2015). Bone mass accrual peaks around 20 years of age following this the speed of degeneration is impacted by both physiological and lifestyle factors so good dietary and lifestyle practices are best started during childhood and maintained throughout life. Thus it is vital to consider bone health across the lifespan, given that evidence has shown increasing weight-bearing activities and improving dietary regimes in childhood, adolescence or older age can improve bone health later in life.

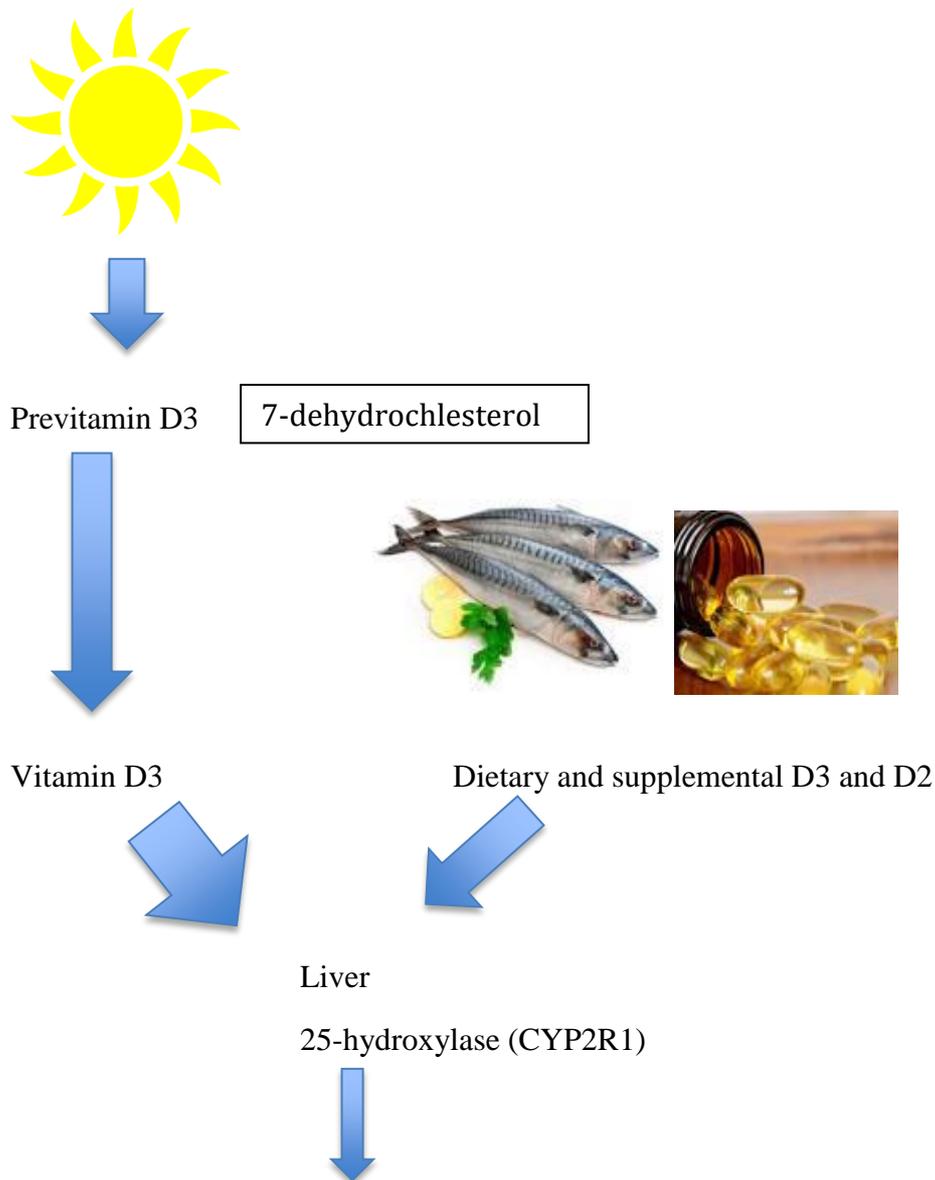
People with a learning disability have increased susceptibility of developing osteoporosis due to comorbid health complications such as hypothyroidism, side-effects from an increased use of polypharmacy including anti-epileptic and anti-psychotic medications, sedentary lifestyles and lack of weight-bearing exercise, poor diet, difficulties in accessing and complying with screening for BMD, bone health typically being omitted from annual health checks and a lack of screening for vitamin and mineral deficiencies (Emerson and Baines, 2010; Frighi et al, 2014; Burke et al, 2016).

The science behind Vitamin D being needed for bone health.

Ultraviolet B from sunshine induces vitamin D₃ production in the skin which can also be ingested from natural dietary sources such as fish including salmon, mackerel and herring, this can then be hydroxylated by the liver and kidneys to produce 1,25(OH)₂D the active form of vitamin D. Vitamin D has a vital role in the regulation of calcium through binding 1,25(OH)₂D to receptors in the bones, increasing absorption of calcium and phosphorous in the gastro-intestinal tract and

lowering parathyroid hormone (Liao et al, 2014). Vitamin D also indirectly effects bone health and healing via its influence on inflammatory markers, cytokines, growth factors and proliferation of cells thus improving consolidation and mineralisation of bone (Gorter et al, 2014). Deficiency in synthesis of vitamin D in the bone and kidneys as well as deficiencies in growth hormones (which reduces synthesis of bone matrix proteins) are found in the aging population and thus have a double assault on bone regulation (Liao et al, 2014).

Figure 1: Vitamin D metabolism pathway (Modified from SACN (2015)).



25(OH)D



Kidneys

1 α -hydroxylase (CYP27B1)



1,25(OH)2D

Vitamin D levels in individuals with a Learning Disability.

Cheema et al (2016) found that 85% of their sample of children with learning disabilities had low levels of vitamin D. In addition evidence finding that the increase in prevalence of osteoporosis and fractures in people with a learning disability is linked to vitamin D deficiency (Frighi et al, 2014). People with learning disabilities living in England were shown to be nearly twice as likely to be either vitamin D insufficient or vitamin D deficient compared to the general population.

Contributing factors for reduced levels of vitamin D in people with learning disabilities include:

- Reduced exposure to sunlight particularly in those living in institutions or secure services.
- An increased prevalence of hypogonadism has been reported in people with learning disabilities, which has been linked to vitamin D status.
- Increased levels of obesity in people with a learning disability which reduces bioavailability of vitamin D.
- Increased levels of being underweight and lacking in adequate dietary intake of both micro and macro-nutrients.
- Increased use of high factor sunblock, sun avoidance and smaller skin exposed surface areas especially in those prescribed medications that are known to be photosensitive.
- Use of anti-epileptic medications, anti-psychotic medications or levothyroxine which increase 25-hydroxyvitamin D metabolism thus reduce vitamin D levels available (He et al, 2016).

Recent reports highlighting medication regimes of cohorts of individuals with learning disabilities found that 39% of people in the learning disability were prescribed anti-epileptic medication (Heslop et al, 2013), and between 9 -44% are prescribed anti-psychotic medication (Emerson and Baines, 2012) which are associated with risk of bone fractures. In addition to this up to 50% of adults with Down Syndrome have hypothyroidism which is typically treated with levothyroxine, too high a dose of this replacement therapy has been linked to osteoporosis (National Osteoporosis Society, 2014). Thus available evidence indicates the importance of

considering vitamin D status as well as monitoring for correct therapeutic thresholds of prescribed medications in this peer group.

Advice on supplementation.

A dearth of research is available on the recommended daily amounts and supplementation of vitamins in people with learning disabilities. It is reasonable to assume that the national recommendations for children and adults remain applicable which will be reported on here.

Supplementary or dietary intake of calcium alone or in combination with vitamin D have been shown to improve the bone mineral density of adults from the general population in systematic reviews and meta-analyses (Van der Velde et al, 2014). This has recently been supported by the Scientific Advisory Committee on Nutrition (2015) concluding sufficient levels of vitamin D are needed for musculoskeletal health.

Some researchers argue that bone health should not be separated from musculoskeletal health with vitamin D being shown to improve muscle mass, muscle strength, bone mineral density loss and decreased bone turnover markers concomitantly reducing risk of falls and fractures in meta-analyses (Murad et al, 2011). Data from the National Diet and Nutrition Survey indicate that vitamin D deficiency is highly prevalent in the aging population requiring supplementation of above 800IU/daily (Van der Velde et al, 2014). Improved outcomes are more consistently found when vitamin D is combined with calcium (Stubbs et al, 2014). In agreement NICE (2015) advocate that vitamin D levels should be assessed and treated

accordingly in combination with calcium in order to improve bone health as well as overall morbidity and mortality.

Monotherapy with vitamin D is less effective to reduce the risk of overall mortality and calcium increases risk of myocardial infarct when used as singular supplement, combinations of these micro-nutrients are advised to improve morbidity, musculoskeletal and bone health. Excessive vitamin D from supplements may increase bone turnover via increasing osteoclast activity and decreasing osteoblast activity (Rossini et al, 2012). Thus the Scientific advisory committee on nutrition (SACN) and NICE guidelines (2015) endorse combinations of calcium and vitamin D within safe upper tolerable limits to improve the safety of supplement use.

Evidence supports the need to frequent monitoring and to adjust supplementation according to season and individual differences in order to treat deficiencies and maintain stability once adequate vitamin D levels are achieved due to greater seasonal cycling increasing PTH and thus bone resorption (Darling et al, 2014).

Optimal vitamin D status has also been linked to reduced odds ratios of cardiovascular disease, type 2 diabetes, certain cancers including bowel and breast cancer and aids immunity (Pearce and Cheetham, 2010). This is significant given the increased prevalence rates of metabolic and cardiovascular disease and weakened immune systems in individuals with learning disabilities.

Dietary interventions; beyond the vitamin D debate.

The clinical significance of improvements following vitamin D supplementation has been questioned with additional dietary factors having an accumulative effect on bone health to reduce risk and progression of osteoporosis. No studies specifically concerning the target population of people who have a learning disability emerged in a literature search, results applied from the general population will thus be reported here to show the need for further research in this area.

Protein, vitamin D and an acid base balance have all gained some support in the literature for their link with the pathogenesis of osteoporosis, with these factors appearing to some extent to be inter-related. Healthy bone undergoes continuous remodelling that requires adequate supplies of protein (which makes up to 50% of its volume) and micronutrients such as calcium, potassium and phosphate. Excess or deficiency of one or more of these nutrients may disturb the acid-alkaline homeostasis and thus increase bone resorption and decrease bone formation.

Protein for bone formation.

The Recommended Daily Intake of protein is 0.8g/kg body weight though the elderly are expected to require higher amounts of up to 1.5g/kg day (Okreglicka, 2015).

Protein not only affords bones structural matrix but also stimulates IGF-1 to increase osteoblast activity and increases calcium absorption in the intestine (Heaney and Layman, 2008). Low protein diets have a negative additive effect with low calcium or

low vitamin D status on skeletal integrity especially in postmenopausal women (Marotte et al, 2013).

Protein insufficiency reduces calcium absorption in the intestine and thus PTH levels increase to signal calcium to be released from bone (Kerstetter et al, 2013). However chronic excess of protein in individuals with low serum calcium can be detrimental especially in postmenopausal women (Nascimento da Silva et al, 2014) thus an inverted 'U' on the beneficence of protein has been hypothesised. Bone mass, microstructure (including material properties) and strength have all been found to be negatively impacted in isocaloric low protein diets in animal studies (Hengsberger et al, 2005; Ammann et al, 2015). Results from human trials have been more inconsistent due to heterogeneity in outcome measures (e.g. site of bone), source of protein and baseline levels of micronutrients (Darling et al, 2009; Jesudason et al (2013). However many studies report marginal beneficial effects at least at one site and reductions in fractures possibly due to improved balance and muscle with high protein diets. A meta-analysis found protein intake improved markers of bone resorption, BMD and Bone Mineral Content (Darling et al, 2009). With evidence that protein and vitamin D supplements used in conjunction reduce skeletal-muscle loss and thus protecting bone health through reducing risk of fractures and falls (Verreijen et al, 2015).

The source of the protein has been argued as salient due to animal protein effecting physiological pH (excess of H⁺ ions) to a greater extent than vegetable based proteins and soy. The latter contain sources of alkali minerals and protect against bone wastage (Lanham-New et al, 2012). Data from studies specifically focussing on people with learning disabilities have found that the consumption of fruit and

vegetables is generally below that found in the general population (Adolfsson et al, 2008) adding further insult to bone integrity.

The acid-ash hypothesis and getting the recommended 5 a day.

Partial support for increased vegetable based proteins comes from the DASH diet that is high in vegetables, calcium and potassium reducing calcium excretions and markers of bone resorption. However the DASH diet is low in salt despite the acid-ash hypothesis considering salt as protective of bone integrity thus reductionist robust, long-term studies are needed (Lin et al, 2003).

In order to sustain pH homeostasis in a deplete calcium state the body releases phosphate that is bound to calcium from bone tissue into the blood (Nicoll et al (2014). In addition in vitro studies have also found that increased acidity in the intracellular environment decreases osteoblast mineralisations and the loss of potassium, sodium and bicarbonate from bone surfaces via osteoclastic action (Bushinsky and Frick, 2000; Brandao-Burch et al, 2005), whereas metabolic alkalosis has the opposite effect. This is supported by human trials using urinary excretions as markers of bone mineral losses (New et al, 2004), critique of these studies are due to a lack of evidence to support a direct correlation with bone accrual, fractures or bone integrity (McLean et al, 2011; Fenton et al, 2009,2010). Additional criticism comes from reports that a healthy body is able to neutralise excess of H⁺ without detrimental effects to the musculoskeletal system (Bonjour, 2013). Thus alkalinising salts had no effect on BMD when taken over 2 years in a randomised controlled trial (Macdonald

et al, 2008), However chronic acidosis in calcium and potassium deficient subjects increases risk of osteopenia and bone disturbances in studies over longer durations and thus further research is required. However caution should be taken when advocating for a diet low in meat protein due to these sources being high in zinc, calcium, B-vitamins and amino acids that are required for bone health (Paknahad et al, 2014).

Conclusion.

In conclusion people with a learning disability across the lifespan are at an increased risk of poor bone health. Practitioners supporting this client group are recommended to ensure that annual health checks are completed and ensure that this includes monitoring and review of bone mineral density, prescribed medication and vitamin D levels. This assessment will guide practitioners in clinical decision making and determine if supplementation to support optimum vitamin D and calcium levels is required. This should be done in conjunction with promoting a lifestyle that

Take Home messages

- *Check vitamin D status bi-annually and treat deficiencies.*
- *Encourage daily intake of green vegetables, and a variety of fruit and vegetables.*
- *Offer fatty fish on menus at least twice a week.*
- *Support individuals to be of a healthy weight.*
- *Speak to a physiotherapist or G.P. about how you can use weight bearing exercises.*
- *Ensure that all medication is regularly reviewed and a plan to reduce unnecessary high dosage regimes is put in place.*
- *Review bone density as part of the annual health check.*

encompasses outdoor activity and weight bearing activities if able. Practitioners should encourage a varied and balanced diet that includes adequate protein particularly from vitamin D fortified /calcium rich dairy and from vegetables. Finally the evidence available supports a diet rich in alkalinising fruits which will work synergistically to promote musculoskeletal health and can be pureed or used as a healthy snack between meals. A deficiency in any of these lifestyle factors has an accumulative deficit on bone integrity and general well-being which may in part explain some of the health inequalities faced by people with a learning disability.

References.

- Adolfsson P, Sydner YM, Fjellstrom C, Lewin B, and Andersson A. (2008). Observed dietary intake in adults with intellectual disability living in the community. *Food Nutrition Research*. 2008;52.
- Ammann P, Zacchetti G, Gasser JA, Lavet C, Rizzoli R. (2015). Protein malnutrition attenuates bone anabolic response to PTH in female rats. *Endocrinology*. 2015 Feb;156(2):419-28.
- Bonjour JP.(2013). Nutritional disturbance in acid-base balance and osteoporosis: a hypothesis that disregards the essential homeostatic role of the kidney. *British Journal of Nutrition*. 2013 Oct;110(7):1168-77.
- Brandao-Burch A, Utting JC, Orriss IR, Arnett TR. (2005). Acidosis inhibits bone formation by osteoblasts in vitro by preventing mineralization. *Calcified Tissue International*. 2005 Sep;77(3):167-74.
- Burke E, McCallion P, Carroll R, Walsh J, and McCarron M. (2016). An exploration of the bone health of older adults with an intellectual disability in Ireland. *Journal of Intellectual Disability Research*. 2016 Apr 21.
- Bushinsky D. and Frick K. (2000). The effects of acid on bone. *Current Opinion in Nephrology and Hypertension* Jul;9(4):369-79.
- Cheema M, Lone K, and Razi F. (2016). Quantitative ultrasound bone profile and vitamin D status in 5-11 years old children with intellectual disability. *Journal of Pakistan Medical Association*. 2016 Jun;66(6):694-8.

- Chen P, Chen C, Lin Y, and Chen M. (2015). Low bone mineral density among adults with disabilities in Taiwan: A cross-sectional descriptive study. *Disability and Health Journal*. 2015 Oct;8(4):635-41.
- Darling AL, Hart KH, Gibbs MA, Gossiel F, Kantermann T, Horton K, Johnsen S, Berry JL, Skene DJ, Eastell R, Vieth R, Lanham-New SA. (2014). Greater seasonal cycling of 25-hydroxyvitamin D is associated with increased parathyroid hormone and bone resorption. *Osteoporosis International*. 2014 Mar;25(3):933-41.
- Darling AL, Millward DJ, Torgerson DJ, Hewitt CE, Lanham-New SA. (2009). Dietary protein and bone health: a systematic review and meta-analysis. *American Journal of Clinical Nutrition*. 2009 Dec;90(6):1674-92.
- Emerson E., Baines S., Allerton L. and Welch V. (2012). *Health Inequalities and people with learning disabilities in the UK: 2012. Improving health and lives; Learning disability observatory. UK.*
- Fenton TR, Lyon AW. (2011). Milk and acid-base balance: proposed hypothesis versus scientific evidence. *Journal of American College of Nutrition*. 2011 Oct;30(5 Suppl 1):471S-5S. Review.
- Fenton TR, Eliasziw M, Tough SC, Lyon AW, Brown JP, Hanley DA. (2010). Low urine pH and acid excretion do not predict bone fractures or the loss of bone mineral density: a prospective cohort study. *BMC Musculoskeletal Disorders*. 2010 May 10;11:88.
- Frighi, V., Morovat, A., Stephenson, M., White, S., Hammond, C., Goodwin G. (2014). Vitamin D deficiency in patients with intellectual disabilities: prevalence, risk factors and management strategies. *The British Journal of Psychiatry* Dec 2014, 205 (6) 458-464.
- Gorter EA, Hamdy NA, Appelman-Dijkstra NM, Schipper IB. (2014). The role of vitamin D in human fracture healing: a systematic review of the literature. *Bone*. 2014 Jul;64:288-97.
- He X., Jiang P, Zhu W, Xue Y, Li H, Dang R, Cai H, Tang M, Zhang L, Wu Y. (2016). Effect of Antiepileptic Therapy on Serum 25(OH)D3 and 24,25(OH)2D3 Levels in Epileptic Children. *Annals of nutrition and metabolism*. 2016;68(2):119-27.
- Heaney RP, Layman DK. (2008). Amount and type of protein influences bone health. *American Journal of Clinical Nutrition*. 2008 May;87(5):1567S-1570S. Review.
- Hengsberger S, Ammann P, Legros B, Rizzoli R, Zysset P. (2005). Intrinsic bone tissue properties in adult rat vertebrae: modulation by dietary protein. *Bone*. 2005 Jan;36(1):134-41. Epub 2004 Nov 24.
- Heslop P., Blair P., Fleming P., Hoghton M., Marriott A. and Russ L. (2013). *Confidential enquiry into the premature deaths of people with learning disabilities: Final report. Norah Fry Research Centre: Bristol.*

- Jesudason D, Nordin BC, Keogh J, Clifton P. (2013). Comparison of 2 weight-loss diets of different protein content on bone health: a randomized trial. *American Journal of Clinical Nutrition*. 2013 Nov;98(5):1343-52.
- Kerstetter JE, Bihuniak JD, Brindisi J, Sullivan RR, Mangano KM, Larocque S, Kotler BM, Simpson CA, Cusano AM, Gaffney-Stomberg E, Kleppinger A, Reynolds J, Dziura J, Kenny AM, Insogna KL. (2015). The Effect of a Whey Protein Supplement on Bone Mass in Older Caucasian Adults. *Journal of Clinical Endocrinology and Metabolism*. 2015 Jun;100(6):2214-22.
- Lanham-New SA, Lambert H, Frassetto L. (2012). Potassium. *Advances in Nutrition*. 2012 Nov 1;3(6):820-1.
- Liao RX, Yu M, Jiang Y, Xia W. (2014). Management of osteoporosis with calcitriol in elderly Chinese patients: a systematic review. *Clinical Interventions in Aging*. 2014 Mar 28;9:515-26.
- Lin LP, Hsu SW, Yao CH, Lai WJ, Hsu PJ, Wu JL, Chu CM, Lin JD. (). Risk for osteopenia and osteoporosis in institution-dwelling individuals with intellectual and/or developmental disabilities. *Research in Developmental Disabilities*. 2014 Oct 16;36C:108-113.
- Lin PH, Ginty F, Appel LJ, Aickin M, Bohannon A, Garner P, Barclay D, Svetkey LP. The DASH diet and sodium reduction improve markers of bone turnover and calcium metabolism in adults. *Journal of Nutrition*. 2003 Oct;133(10):3130-6.
- Macdonald HM1, Black AJ, Aucott L, Duthie G, Duthie S, Sandison R, Hardcastle AC, Lanham New SA, Fraser WD, Reid DM. (2008). Effect of potassium citrate supplementation or increased fruit and vegetable intake on bone metabolism in healthy postmenopausal women: a randomized controlled trial. *American Journal of Clinical Nutrition*. 2008 Aug;88(2):465-74.
- Marotte C, Gonzales Chaves MM, Pellegrini GG, Friedman SM, Lifshitz F, Mandalunis P, Zeni SN. (2013). Low protein intake magnifies detrimental effects of ovariectomy and vitamin D on bone. *Calcified Tissue International*. 2013 Aug;93(2):184-92.
- McLean RR, Qiao N, Broe KE, Tucker KL, Casey V, Cupples LA, Kiel DP, Hannan MT. (2011). Dietary acid load is not associated with lower bone mineral density except in older men. *Journal of Nutrition*. 2011 Apr 1;141(4):588-94.
- Misra D, Berry SD, Broe KE, McLean RR, Cupples LA, Tucker KL, Kiel DP, Hannan MT. (2011). Does dietary protein reduce hip fracture risk in elders? The Framingham Osteoporosis Study. *Osteoporosis International*. 2011 Jan;22(1):345-9.
- Murad MH, Elamin KB, Abu Elnour NO, Elamin MB, Alkatib AA, Fatourehchi MM, Almandoz JP, Mullan RJ, Lane MA, Liu H, Erwin PJ, Hensrud DD, Montori VM. (2011). Clinical review: The effect of vitamin D on falls: a systematic

review and meta-analysis. *Journal of Clinical Endocrinology and Metabolism*. 2011 Oct;96(10):2997-3006.

Nascimento da Silva Z, Azevedo de Jesus V, De Salvo Castro E, Soares da Costa CA, Teles Boaventura G, Blondet de Azeredo V. (2014). Effect of the “protein diet” and bone tissue. *Nutricion Hospitalaria*. 2014 Jan 1;29(1):140-5.

National Institute of Clinical Excellence (2015). Found at <http://cks.nice.org.uk/osteoporosis-prevention-of-fragility-fractures> On the 05.9.2015

National Osteoporosis Society (2014). Thyroid disease and osteoporosis. Found at [https://www.nos.org.uk/healthy-bones-and-risks/~document.doc?id=1368](https://www.nos.org.uk/healthy-bones-and-risks/~/document.doc?id=1368) on 18.7.2016.

New SA, MacDonald HM, Campbell MK, Martin JC, Garton MJ, Robins SP, Reid DM. (2004). Lower estimates of net endogenous non-carbonic acid production are positively associated with indexes of bone health in premenopausal and perimenopausal women. *American Journal of Clinical Nutrition*. 2004 Jan;79(1):131-8.

Nicoll, R.; McLaren Howard, J. (2014). The acid–ash hypothesis revisited: a reassessment of the impact of dietary acidity on bone. *Journal of Bone and Mineral Metabolism* 2014, 32, 469.

Okreglicka K. (2015). Health effects of changes in the structure of dietary macronutrients intake in western societies. *Roczniki Panstwowego Zakladu Higieny*. 2015;66(2):97-105.

Paknahad Z, Mohammadifard N, Bonakdar Z, Hasanzadeh A. (2014). Nutritional status and its relationship with bone mass density in postmenopausal women admitted in osteodensitometry center, Isfahan-Iran. *Journal of Education and Health Promotion*. 2014 May 5;3:48.

Rossini M, Gatti D, Viapiana O, Fracassi E, Idolazzi L, Zanoni S, Adami S. (2012). Short-term effects on bone turnover markers of a single high dose of oral vitamin D₃. *Journal of Clinical Endocrinology and Metabolism*. 2012 Apr;97(4):E622-6.

Scientific Advisory Committee on Nutrition (2015). Draft Vitamin D and Health report. Accessed at [https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/447402/Draft SACN Vitamin D and Health Report.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/447402/Draft_SACN_Vitamin_D_and_Health_Report.pdf) on 18.7.2016.

Srikanth R., Cassidy G., Joiner C. and Teeluckdharry S. (2011). Osteoporosis in people with intellectual disabilities: a review and a brief study of risk factors for osteoporosis in a community sample of people with intellectual disabilities. *Journal of Intellectual Disability Research*. January 2011 Vol 55 (1), p53–62.

Stubbs B, Brefka S, Denkinger MD. (2015). What Works to Prevent Falls in Community-Dwelling Older Adults? Umbrella Review of Meta-analyses of Randomized Controlled Trials. *Physical Therapy*. 2015 Aug;95(8):1095-110.

van der Velde RY, Brouwers JR, Geusens PP, Lems WF, van den Bergh JP. (2014). Calcium and vitamin D supplementation: state of the art for daily practice. *Food and Nutrition Research*. 2014 Aug 7;58.

Verreijen AM, Verlaan S, Engberink MF, Swinkels S, de Vogel-van den Bosch J, Weijs PJ. (2015). A high whey protein-, leucine-, and vitamin D-enriched supplement preserves muscle mass during intentional weight loss in obese older adults: a double-blind randomized controlled trial. *American Journal of Clinical Nutrition*. 2015 Feb;101(2):279-86.

Wang N., Han B., Li Q., Chen Y., Chen Y., Xia F., Lin D., Jensen MD. and Lu Y. (2015). Vitamin D is associated with testosterone and hypogonadism in Chinese men. *Reproductive biology and endocrinology* 13(1):74.