Institution: University of Ulster

Unit of Assessment: 3B Allied Health Professions, Dentistry, Nursing and Pharmacy – Biomedical Sciences

Title of case study: Vitamin D and Health

1. Summary of the impact (indicative maximum 100 words)

The University has been at the forefront of Vitamin D research over the past decade, with the findings of the work used to change the dietary intake guidelines on the international stage, most notably in the U.S by the Institute of Medicine, the international body responsible for agenda setting of dietary recommendations worldwide. The extensive research has also been crucial in informing UK and Irish Health Service reports on vitamin D assessment and use during pregnancy and in infants and has provided robust scientific evidence to the food industry for fortification strategies. In addition to establishing the vitamin D requirements of population sub-groups, the research at Ulster has also focused on investigating the relationship between vitamin D status and skeletal & cardiovascular health and immune function.

2. Underpinning research (indicative maximum 500 words)

As the UK lies at a high latitude, thereby reducing the opportunity for vitamin D synthesis, it is not surprising that low vitamin D status is common not only among recognised at risk groups, such as pregnant women and elderly or institutionalised adults, but also in the general population. Recent global estimates suggest that up to one billion people worldwide are vitamin D insufficient.

A number of key studies have underpinned the vitamin D research carried out over the last decade at the Northern Ireland Centre for Food and Health (NICHE), which is based in Ulster's Biomedical Sciences Research Institute.

Work undertaken as part of the Northern Ireland Young Hearts Project investigated dietary vitamin D intake and bone health. This work was led by Professor Sean Strain at Ulster (employed at Ulster since 1981) and a paper which reported that vitamin D intake in adolescents and young adults was associated with bone mineral density (BMD) was published in 2002 (Neville *et al.,* 2002, *Calcified Tissue International*). This finding led to a successful application for funding to The Higher Education Authority in 2003 to examine vitamin D status in adolescents and to investigate possible relationships with bone health. This was a collaborative project, led by Professor Julie Wallace (deceased) and Professor Sean Strain, with the Vitamin D Research Group at University College Cork; a collaboration which was to produce a number of subsequent applications for research funding and a number of high impact papers in the area of vitamin D. Results from this first investigation highlighted low vitamin D status among 12 and 15 year olds and which was most evident in girls (Cashman *et al.,* 2008; Hill *et al.,* 2010). This finding was of concern, as it was also noted that vitamin D status was associated with BMD in these adolescents. In addition, our work also highlighted that low vitamin D status was evident among young adults in wintertime and 8 weeks supplementation was effective at improving status (Barnes *et al.,* 2006).

In 2006, the Centre secured funding from the UK Food Standards Agency to undertake research to investigate the relative contribution of dietary intake and sunlight to vitamin D status in young adults and in older individuals. This grant was followed in 2008 by additional funding from the UK Food Standards Agency to assess potential benefits of vitamin D supplementation on bone health, immune function and cardiovascular risk markers. The outputs from this research (Cashman *et al.,* 2008, 2009) have had considerable impact in terms of informing regulators preparing dietary guidelines for vitamin D (see section 4).

In 2008, research investigating vitamin D status during pregnancy was conducted by Dr Maria Mulhern (née Barnes) at Ulster (employed at Ulster since 2007) and published in the British Journal of Nutrition (Holmes *et al.,* 2009). This work highlighted that not only was status low, with deficiency evident and insufficiency highly prevalent, but also importantly that status remained low even among women who reported taking pregnancy targeted supplements during their pregnancy; suggesting that such supplements may provide insufficient vitamin D.

Key Researchers at Ulster:
Key staff: Professor JJ (Sean) Strain (Professor of Human Nutrition and Director of NICHE; 1981-present); Dr Maria Mulhern (née Barnes) (Lecturer; 2007-present); Dr Emeir McSorley (née Duffy) (Senior Lecturer; 2002-present); Professor Julie Wallace (Professor; deceased)

3. References to the research (indicative maximum of six references)

Hill, T. R., Cotter, A. A., Mitchell, S., Boreham, C. A., Dubitzky, W., Murray, L., Strain, J. J., Flynn, A., Robson, P. J., Wallace, J. M. W., Kiely, M. and Cashman, K. D. (2010). Vitamin D status and parathyroid hormone relationship in adolescents and its association with bone health parameters: analysis of the Northern Ireland Young Heart's Project. *Osteoporosis International,* 21(4): 695-700.
DOI: 10.1007/s00198-009-0959-1
Times Cited: 12 SJR: 1.636 SNIP: 1.821 Impact Factor: 4.580

Holmes, V. A., Barnes, M. S., Alexander, H. D., McFaul, P. and Wallace, J. M. W. (2009). Vitamin D deficiency and insufficiency in pregnant women: a longitudinal study. *British Journal of Nutrition,* 102(6): 876-881.
DOI: 10.1017/s0007114509297236
Times Cited: 66 SJR: 1.052 SNIP: 1.176 Impact Factor: 3.013

Cashman, K. D., Wallace, J. M. W., Horigan, G., Hill, T. R., Barnes, M. S., Lucey, A. J., Bonham, M. P., Taylor, N., Duffy, E. M., Seamans, K., Muldowney, S., FitzGerald, A. P., Flynn, A., Strain, J. J. and Kiely, M. (2009). Estimation of the dietary requirement for vitamin D in free-living adults ≥64 y of age. *American Journal of Clinical Nutrition,* 89(5): 1366-1374.
DOI: 10.3945/ajcn.2008.27334
Times Cited: 52 SJR: 2.816 SNIP: 2.404 Impact Factor: 6.669

Cashman, K. D., Hill, T. R., Lucey, A. J., Taylor, N., Seamans, K. M., Muldowney, S., FitzGerald, A. P., Flynn, A., Barnes, M. S., Horigan, G., Bonham, M. P., Duffy, E. M., Strain, J. J., Wallace, J. M. W. and Kiely, M (2008). Estimation of the dietary requirement for vitamin D in healthy adults. *American Journal of Clinical Nutrition,* 88(6): 1535-1542.
DOI: 10.3945/ajcn.2008.26594
Times Cited: 92 SJR: 2.816 SNIP: 2.404 Impact Factor: 6.669

Cashman, K. D., Hill, T. R., Cotter, A. A., Boreham, C. A., Dubitzky, W., Murray, L., Strain, J. J., Flynn, A., Robson, P. J., Wallace, J. M. W. and Kiely, M. (2008). Low vitamin D status adversely affects bone health parameters in adolescents. *American Journal of Clinical Nutrition,* 87(4): 1039-1044.
Times Cited: 48 SJR: 2.816 SNIP: 2.404 Impact Factor: 6.669

Barnes, M. S., Robson, P. J., Bonham, M. P., Strain, J. J., and Wallace, J. M. (2006). Effect of vitamin D supplementation on vitamin D status and bone turnover markers in young adults. *European Journal of Clinical Nutrition,* 60(6): 727-33.
DOI: 10.1038/sj.ejcn.1602374
Times Cited: 19 SJR: 1.001 SNIP: 1.106 Impact Factor: 2.462

Grant income obtained to undertake the studies were from:
McNulty, H., Strain, J. J., Ward, M. and Wallace, J. M. W. Irish Universities Nutrition Alliance Project: Building additional and sustainable research capacity in nutrition and bone health at the University of Ulster. Funded by the Department for Employment and Learning, 2009-2011; £1.24m.

Wallace, J. M. W., Bonham, M. P., Duffy, E. M., Magee, P. J., Campbell, D. J. and Strain, J. J. Vitamin D status and associated health outcomes: Towards an evidence basis for defining vitamin D status sufficient to reduce risk of chronic disease. Funded by Food Standards Agency, 2008-2010; £162,000.

Wallace, J. M. W., Bonham, M. P., Duffy, E. M. and Strain, J. J. Dietary requirements for vitamin D:

An investigation of the relative significance of dietary intake and sunlight on vitamin D status in adolescents and adults. Funded by the Food Standards Agency, 2006 -2009; £330,000.

Wallace, J. M. W., Robson, P. J., Boreham, C. and Dubitsky, W. Evaluation of the prevalence of vitamin D deficiency in a representative sample of adolescents from Northern Ireland and its implications for bone health (in collaboration with University College Cork). Funded by the Higher Education Authority of Ireland, 2003-2006; £84,000.

4. Details of the impact (indicative maximum 750 words)

Research undertaken within NICHE in collaboration with others has highlighted the prevalence of low vitamin D status, not just among the 'at risk' groups, but throughout a large proportion of the general population. This work has had a major global impact in setting dietary reference intake (DRI) values for vitamin D, which are dietary recommendations specifying the average daily requirements for nutrients for the general public.

Most notably, the data emanating from the work at Ulster, in collaboration with University College Cork (Cashman *et al.,* 2008, 2009), were vital in establishing a scientific opinion to set the new DRI for vitamin D produced by the Institute of Medicine (IOM) of the National Academies in the U.S **[1]**. The IOM, which is the international body responsible for agenda setting of dietary recommendations, is the most influential committee for other organisations such as the European Food Safety Authority (EFSA) and the UK Scientific Advisory Committee on Nutrition (SACN) to follow regarding change in policies. The IOM recognised that sufficient scientific evidence of high quality was available to warrant a review of the 2007 DRI for vitamin D, and subsequently published a re-evaluation in 2011, following a comprehensive assessment of more than 1000 studies and reports on potential health outcomes. On the back of this significant research, the IOM deemed it necessary to raise the DRI for vitamin D for younger adults (19-50 years) from 200 IU/day to 600 IU/day and older adults (51-70 years) from 400 IU/day to 600 IU/day. These revisions represent recommendations for a significant increase on current population intakes and highlight the need for food-based vitamin D deficiency prevention strategies.

DRI recommendations are utilised by various stakeholders, including national nutrition and healthcare policy makers and public health officials and practitioners to counsel individuals about dietary intakes for health benefits; the food industry for food product development and nutrition labelling; and the catering industry for dietary composition of meals provided to schools, hospitals, nursing homes and prisons. This newly revised DRI will provide the food industry with an opportunity to develop fortified foods/beverages that can help to improve vitamin D status in the general population.

The AHRQ-Ottawa Evidence-Based Report on Effectiveness and Safety of Vitamin D in Relation to Bone Health, requested by the National Institutes of Health, formed a large part of the evidence utilised by the IOM in the recent DRI review. The aim of this report was to review the published literature to identify the potential indicators of health outcomes, specifically bone health, to provide evidence in the determination of nutrient requirements for vitamin D. Data from Ulster (Barnes *et al.*, 2006) were included in this review and the data were assigned a Jadad score of 3/5, consistent with high quality **[2]**.

Within the UK, dietary recommendations on vitamin D were last reviewed in 2007. However, SACN will meet again in 2014 to inform the Dietary Reference Values (DRV) for vitamin D intake and are anticipated to make similar recommendations to those by the IOM. A risk assessment of the vitamin D status of the UK population is currently being conducted and includes an assessment of the relative contributions of diet and cutaneous vitamin D synthesis to vitamin D status and a review of the associations between vitamin D status and various health outcomes. It is indicated in SACN minutes **[3]** that the high quality research from Ulster will form a large part of this review. In addition, these data have also been used by the Health Council of the Netherlands, an independent scientific advisory board which advises the government, to update the vitamin D DRV in the Netherlands **[4]** and by the European Food Safety Authority (EFSA) **[5]** to endorse health

claims on the role of vitamin D for the reduction of osteoporotic fracture risk.

Ulster's research investigating vitamin D status during pregnancy, including an assessment of the effects of supplement use, has been crucial in evolving stakeholder opinion on the importance of the vitamin and how best to optimise status for both the mother and child at this critical developmental time period. This work was of particular interest to the media (scientific and general) and has been used by food companies such as Avonmore Dairy to promote and market their products enriched with vitamin D to pregnant women and their children as a means of improving status **[6-7]**. Furthermore, this work has been and continues to be used as evidence to assess and influence health service policies and practices related to the promotion and prescription of vitamin D to pregnant women, infants and premature babies across the UK and Ireland **[8-10]**.

5. Sources to corroborate the impact (indicative maximum of 10 references)

1. Institute of Medicine (IOM) of the National Academies. Dietary References Intakes (DRI) for Calcium and Vitamin D. (30 November 2010) http://www.iom.edu/Reports/2010/Dietary-Reference-Intakes-for-Calcium-and-Vitamin-D.aspx
2. AHRQ-Ottawa Evidence-Based Report on Effectiveness and Safety of Vitamin D in Relation to Bone Health (August 2007) http://archive.ahrq.gov/downloads/pub/evidence/pdf/vitamind/vitad.pdf
3. Scientific Advisory Committee on Nutrition (SACN) Minutes, 4th Meeting of Vitamin D Working Group. (28 June 2012) http://www.sacn.gov.uk/pdfs/sacn_vitamin_d_28_june_2012_final_minutes.pdf SACN Minutes, 32nd Main SACN Meeting (15 October 2010) http://www.sacn.gov.uk/pdfs/SACN1017%20-%20Draft%20Scope%20for%20Vitamin%20D%20review.pdf
4. Health Council of the Netherlands Evaluation of dietary reference values for vitamin D. The Hague: Health Council of the Netherlands, publication no. 2012/15E. (2012) http://www.gezondheidsraad.nl/sites/default/files/201215EEvaluationDietaryReferenceVitaminD.pdf
5. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) (2010) Scientific Opinion in relation to the authorisation procedure for health claims on calcium and vitamin D and the reduction of the risk of osteoporotic fractures by reducing bone loss pursuant to Article 14 of Regulation (EC) No 1924/20061. EFSA Journal, 8(5):1609 DOI 10.2903/j.efsa.2010.1609 http://www.efsa.europa.eu/en/efsajournal/pub/2813.htm
6. Nutraingredients: 'Current vitamin D doses insufficient for mothers-to-be' (16 September 2009) http://www.nutraingredients.com/Research/Current-vitamin-D-doses-insufficient-for-mothers-to-be
7. Avonmore Supermilk range: 'Super mums' http://www.avonmore.ie/our-range/super-milk/super-mums
8. Stockport NHS Foundation Stockport NHS Foundation Trust (June 2011) Measuring and Improving Vitamin D: Promotion and Prescribing to Prenatal and Postnatal Women within the North West. http://www.vitamindwiki.com/tiki-download_wiki_attachment.php?attId=662
9. East of England Perinatal Network (May 2011) Clinical Guideline: Enteral Feeding – Vitamin supplementation http://www.neonatal.org.uk/documents/5549.pdf
10. Health Service Executive (May 2010) Vitamin D supplementation for Infants – Information for Health Professionals. http://www.hse.ie/eng/services/healthpromotion/Vitamin_D_and_your_baby/Vitamin%20D%20Information%20for%20professionals.pdf