Community perspectives on vitamin D and bone health in three at-risk populations

_Dr Simon Vanlint_
_Discipline of General Practice_
_School of Population Health_
_University of Adelaide_

Submitted for the degree of Doctor of Philosophy
_October 18, 2012_
# Contents

Abstract............................................................................................................................................. 4

Declaration........................................................................................................................................ 6

Statement regarding contributions to jointly authored papers ...................................................... 7

Introduction ........................................................................................................................................ 10

Literature Review ............................................................................................................................. 12

Vitamin D: Physiology & Metabolism .............................................................................................. 12

Insufficiency & Deficiency .............................................................................................................. 17

Bone and muscle............................................................................................................................. 17

Neoplasia ........................................................................................................................................ 23

Cardiovascular disease ................................................................................................................ 25

Diabetes ........................................................................................................................................ 28

Respiratory disorders ..................................................................................................................... 32

Appropriate intake and target levels of vitamin D ..................................................................... 34

Drugs and vitamin D ...................................................................................................................... 38

Intellectual disability and bone health ........................................................................................ 43

Bone Structure & Function ........................................................................................................... 45

Anatomy & Structural Organisation .............................................................................................. 45

Bone modelling and remodelling .................................................................................................. 51

Growth and Ageing ....................................................................................................................... 52

Genetic determinants of bone health ............................................................................................ 54

Polyunsaturated fatty acids and bone .......................................................................................... 56

Vitamin D and Aboriginal Australians .......................................................................................... 58

Paper 1: “Vitamin D and fractures in people with intellectual disability” ................................ 60

Paper 2: “Vitamin D insufficiency in Aboriginal Australians” .................................................. 70

Paper 3: “Efficacy and tolerability of calcium, vitamin D and a plant-based omega-3 oil for osteopenia: A pilot RCT” .................................................................................. 78
Conclusion .................................................................................................................. 86
Bibliography .............................................................................................................. 89
Abstract

Background:
Disorders affecting bone health, including osteoporosis and fractures, cause significant morbidity and mortality in Australia. Specific sub-groups within the general population are at increased risk of poor bone health and fracture. Such groups include people with intellectual disability, Aboriginal Australians and people known to have osteopenia. These studies aim to document the extent of this increase in risk, examine the underlying reasons and evaluate possible treatment options.

Methods:
Three studies are described:

a) A 5 year retrospective audit of 280 individuals with intellectual disability examined data including age, gender, mobility, dietary status, incident fractures, medications and 25-hydroxyvitamin D (25D) levels, as well as response to vitamin D supplementation.

b) A cross-sectional study of 58 South Australian Aboriginal people investigating the adequacy of vitamin D status and the relationship between serum 25D levels and biochemical variables of calcium and bone mineral homeostasis.

c) A prospective, randomised, placebo-controlled pilot study of the efficacy, acceptability and tolerability of docosahexanoic acid (DHA) supplementation in addition to calcium and vitamin D₃ in 40 individuals with osteopenia.

Results:

a) 57% of intellectually disabled individuals tested were vitamin D insufficient. Vitamin D insufficiency was strongly correlated with reduced mobility (p<0.001) and difficulty consuming solids (p<0.001). The correlation between 25D levels and fractures was not significant (p = 0.3). Oral supplementation using vitamin D₃ 100,000 IU every 4 months was effective in correcting vitamin D insufficiency. 68 fractures occurred over the audit period in 52 individuals, a rate of 1 fracture every 23.8 person years. Peripheral fractures accounted for 54% of all fractures, being particularly prevalent in the most mobile individuals.

b) Serum 25D levels varied seasonally in South Australian Aboriginal people, being higher in summer (P < 0.001). The overall mean of 56.8 nmol/L (SD, 22.1) is below the
recommended target level of 60 nmol/L. Serum 25D levels correlated significantly with c-terminal telopeptide (CTx) \( (P = 0.03) \), but not with age, body mass index, levels of fasting glucose or PTH. BMI and PTH levels were significantly correlated with each other \( (P = 0.001) \).

c) CTx was suppressed after 12 months for all osteopenic participants \( (p=0.04) \) with no difference in effect size between DHA and control groups \( (p=0.53) \). Changes in CTx at 12 months were significantly correlated with changes in bone density at the lumbar spine \( (p=0.01) \) and total proximal femur (TPF) \( (p=0.03) \). Participants rated the supplements as tolerable and acceptable, with few adverse events.

Conclusions:

a) Fractures are common in people with intellectual disability. Vitamin D insufficiency may contribute to this increased risk, although this study did not conclusively establish this. Oral vitamin D\(_3\) supplementation is effective in restoring normal vitamin D levels.

b) Vitamin D insufficiency is highly prevalent in adult Aboriginal Australians, with low mean values found in all seasons other than summer.

c) The combination of oral calcium, vitamin D\(_3\) and DHA was safe, tolerable and acceptable when used for 12 months by osteopenic individuals. Both combinations (i.e. calcium, vitamin D\(_3\) and DHA; and calcium, vitamin D\(_3\) and placebo) had a positive effect on bone health, with no significant effect from the addition of DHA.
Declaration

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university, and, to the best of my knowledge and belief, the thesis contains no material previously published or written by another person, except where due reference is made in the text.

I give consent to the thesis, when deposited in the University library, being made available for loan and photocopying, subject to the provisions of the Copyright Act 1968.

The author acknowledges that copyright of published works contained within this thesis (as listed below) resides with the copyright holder(s) of those works. I also give permission for the digital version of my thesis to be made available on the web, via the University’s digital research repository, the Library catalogue, the Australian Digital Thesis Program (ADTP) and also through web search engines, unless permission has been granted by the University to restrict access for a period of time. The publications contained within this thesis are as follows:


Signature: ________________________________________________

Date: 01 October 2012
Statement regarding contributions to jointly authored papers

Vitamin D & fractures in people with intellectual disability

Co-author: Dr Michael Nugent
Contribution: Dr Nugent was employed as a medical officer at the Strathmont Centre, a residential facility caring for adults with intellectual disability. I approached Dr Nugent to initiate this study, having worked as a locum tenens at the Centre. I planned the study and took the lead role in obtaining ethical approval, followed by data transcription, analysis and manuscript preparation/submission. Dr Nugent provided comments regarding study design, assisted with recruitment, data collection and analysis, and suggested modifications to the manuscript prior to publication. Without his active participation this study would not have been possible.

I give my permission for the inclusion of the above-named paper in this doctoral thesis.

Signature of co-author:___________________  ____ (M. Nugent)
Vitamin D insufficiency in Australian Aboriginals

Co-authors: Prof. Jonathan Newbury, Prof. Howard Morris, Assoc. Prof. Alan Crockett
Contributions: these co-authors are also my PhD supervisors. All have extensive experience in the design, running and reporting of clinical trials. In addition, Prof. Morris is recognised internationally as an expert in the vitamin D field. I initiated this study and proposed the study design, upon which they provided comment. I was responsible for obtaining ethics approval (which included community consultation & engagement), participant recruitment and data collection. I took the lead role in data analysis and manuscript preparation/submission, but received significant support and advice from all three supervisors, particularly Prof. Morris, as this topic fell within his area of specific expertise.

We give our permission for the inclusion of the above-named paper in this doctorial thesis.

Signature of co-author: __________________ (J. Newbury)

Signature of co-author: __________ (H. Morris)

Signature of co-author: __________ (A. Crockett)
Efficacy & tolerability of calcium, vitamin D and a plant-based omega – 3 oil for osteopenia: a pilot RCT

Co-author: Dr Karin Ried
Contributions: Dr Ried has a major interest in nutritional and complementary therapies, and I approached her to be my co-investigator because of this expertise. I proposed the study design, upon which she provided comment. I was primarily responsible for obtaining ethics approval and negotiating practical matters such as supply of investigational agents and participant recruitment. Participant research visits, data collection and data analysis were shared. I took the lead role in manuscript preparation/submission, with significant comments, suggestions and revisions being made by Dr Ried.

I give my permission for the inclusion of the above-named paper in this doctoral thesis.

Signature of co-author: _____________________________ (K. Ried)