

**LACK OF DEMONSTRABLE HARMFUL EFFECT OF  
HIGHER PROTEIN WEIGHT LOSS DIETS  
ON BONE HEALTH AND NEPHROPATHY  
IN TYPE 2 DIABETES**

**Dr David Jesudason, MBBS, FRACP**

**Food and Nutritional Sciences,**

**Commonwealth Scientific and Industrial Research Organisation**

**Centre of Clinical Research Excellence in Human Nutrition,**

**School of Medicine, University of Adelaide**

**Submitted in fulfilment of the**

**Degree of Doctor of Philosophy,**

**University of Adelaide,**

**July 2014**

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# THESIS ABSTRACT

The optimal macronutrient composition of diets to maximize weight loss has been a subject of great interest in obesity research. High protein weight loss diets have gained widespread popularity. However their safety regarding osteoporosis risk and progression of diabetic nephropathy has been questioned.

With regard to bone, higher dietary protein could cause a low grade metabolic acidosis, leading to hypercalciuria with loss of calcium from bone, causing osteoporosis. Recent studies suggest the situation is more complicated. The interaction with other dietary components such as calcium, fruit and vegetables is important. Historically, nephrologists have advocated lower protein diets in subjects with renal impairment to slow the decline in glomerular filtration rate. Whether this could be extrapolated to subjects with nephropathy from type 2 diabetes remains unclear. These subjects are often obese and potential candidates for high protein diets. If weight loss was achieved, this should slow the deterioration in renal function both directly as well as by improving lipid, blood pressure and glycaemic control which are risk factors for diabetic nephropathy. This thesis aims to test the hypothesis that higher protein diets are harmful to bone and renal health.

We designed two clinical trials to test the effect of higher protein weight loss diets compared to lower protein weight loss diets on bone health, in overweight but otherwise healthy post-menopausal women over 2 years and on decline in glomerular filtration rate

over 1 year in subjects with early nephropathy from type 2 diabetes. These two trials were conducted at the Commonwealth Scientific and Industrial Research Organisation in collaboration with the Centre of Clinical Research Excellence in Human Nutrition at the University of Adelaide. As a separate sub-study, I analysed the accuracies of the three Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations using creatinine, cystatin C and both, compared to radioisotope methods in our obese subjects from the renal study. These results and accompanying discussion are presented in a combined narrative and publication format as per University of Adelaide guidelines.

The results of my studies did not demonstrate any signal of increased bone loss from higher protein diets; our results are consistent with a modest beneficial effect based on lower bone turnover with higher dietary protein. With the renal study, there was no evidence that the higher protein diet accelerated decline in GFR in type 2 diabetes. The main benefit came from weight loss; subjects who hyperfiltered (estimated GFR greater than 120 ml/min/1.73m<sup>2</sup>) had a decrease in eGFR. Subjects with a baseline eGFR between 40-120 ml/min/1.73m<sup>2</sup> had an increase in GFR with weight loss. I also demonstrated that after weight loss, the CKD-EPI equations using cystatin C or both cystatin C and creatinine had higher precision compared to the equation using creatinine alone. This reflected the loss of lean mass with weight loss, which has a bigger influence on serum creatinine than cystatin C.

Therefore, in post-menopausal women and subjects with early type 2 diabetic nephropathy, higher protein weight loss diets are not harmful to bone and renal health.

# THESIS DECLARATION

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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# ACKNOWLEDGEMENTS

There are many people who have been of great assistance to me over the course of my PhD. Firstly I am very grateful for the mentorship and guidance of my principal supervisor, Professor Peter Clifton throughout my PhD. Peter conceived the idea of studying the areas of bone and renal health and the link with dietary protein. He was instrumental in conducting the two major clinical trials at the CSIRO from design to completion. I have learnt a lot from him about forward planning and attention to detail which is required for such an enterprise. I am also appreciative of his insightful comments and analysis as we have translated the results from the trials into manuscripts and this PhD. I also would like to acknowledge the support of my co-supervisors, Professors Michael Horowitz and Professor Gary Wittert firstly in pointing out the benefits of undertaking a PhD and for their support for my career in Endocrinology over the last 15 years. With Professor Clifton, they were able to facilitate the financial and intellectual collaboration between the CSIRO and the Centre of Clinical Research Excellence in Human Nutrition at the University of Adelaide which has supported this research.

I also would like to acknowledge the expertise of my other co-authors on the manuscripts presented here. Our renal trial would not have been possible without the expertise of Dr Eva Pedersen our lead dietician who worked tirelessly with subjects to encourage dietary compliance and weight loss of our subjects as well as intellectual input into the manuscripts as acknowledged on the “statements of authorship”. A/Prof Jennifer Keogh was instrumental in designing and monitoring trial diets for our bone study and also

critically reviewed and advised on the manuscript. We were also able to draw on the vast experience and insight of Professor B E Christopher Nordin as we designed our bone trial.

We would not have been able to undertake the trials without the generosity and goodwill of our many subjects who volunteered their time and effort for the sake of science. We are very much indebted to them. Many clinic staff at the CSIRO played important roles in the conduct of this trial such as organising appointments for subjects, venepuncture and specimen processing, assisting with adherence to diets and storing of data. Special thanks to Julia Weaver, Lindy Lawson, Kathryn Bastiaans, Rosemary McArthur, Anne McGuffin and Pennie Taylor. I have also benefitted from the statistical advice provided by Ms Kylie Lange from Adelaide University and Mr. Jim Wang from the Queen Elizabeth Hospital.

Finally it is always a challenge to strike the right balance between time spent on my clinical work as an Endocrinologist, the time required to undertake a PhD and home life. I have always been grateful for the love and support of my parents Joyce and Cyril. However it has been the presence of my two children Daniel (who was 3 years old when I started this PhD) and Sonali who was born during my PhD who have kept me grounded and provided me with much joy and delight during this time. However most important of all, I must acknowledge the love, support and constant encouragement of my wife Shilpa as I attempted to balance my PhD with all the competing priorities in my life. She has been the bedrock of our family and I dedicate this thesis to her.



# RESEARCH PRESENTATIONS

2010: CSIRO Research meeting (oral)

2011: Endocrine Grand Round, Royal Adelaide Hospital – Oral Presentation

2012: International Congress of Endocrinology/European College of Endocrinology  
Combined

Meeting, Florence, Italy – Oral Presentation

2012: European Congress of Obesity, Lyon France – Poster Presentation

2012: Endocrine Grand Round, Royal Adelaide Hospital – Oral Presentation

2013: School of Medicine, Seminar Program, Adelaide University

2013: International Diabetes Federation, Melbourne, Australia –Poster Presentation