

# Increasing fish consumption in women of child-bearing age: an evaluation of risks and benefits

Lily Lai Hang Chan Bachelor of Nutrition and Dietetics Bachelor of Science (Honours) Bachelor of Pharmacy

Nutrition and Dietetics School of Health Sciences Faculty of Medicine, Nursing and Health Sciences Flinders University

> A thesis submitted for the degree of Doctor of Philosophy 2015

# **Table of Contents**

List of Figuresv		
List of Tablesvi		
List of Abbreviationsx		
Summary	xiii	
Declarationxv		
Presentationsxvi		
Acknowledgmentsxvii		
Overview and thesis structure1		
Chapter 1 Project rationale, aims and objectives	4	
1.1 Rationale	4	
1.2 Aims and objectives	5	
Chapter 2 Literature review — Long chain n-3 polyunsaturate	d fatty acids and	
fish intakes on maternal and infant outcomes	7	
2.1 Long chain n-3 polyunsaturated fatty acids (LCn3PUFA) and n	naternal & infant	
outcomes	7	
2.1.1 Pregnancy outcome and maternal health	9	
2.1.2 Child health and development		
2.1.3 Conclusion	68	
2.2 Fish intakes and maternal & infant outcomes	69	
2.2.1 Evidence based on randomised controlled trials	69	
2.2.2 Evidence based on seminal and/or large scale observation	1al studies 70	
2.2.3 Considerations by Australian and overseas health organis	ations77	
2.2.4 Conclusion		
2.3 Final conclusion	79	
Chapter 3 Fish consumption in Australian women of child-bea	ring age 80	
3.1 Data from 1995 National Nutrition Survey (NNS)	82	
3.1.1 1995 NNS Survey and analysis methods	82	
3.1.2 1995 NNS Survey results		
3.2 Data from the Australian Longitudinal Study on Women's Hea	lth (ALSWH)85	
3.2.1 ALSWH Survey and analyses methods		
3.2.2 ALSWH Survey results		

3.3	Discussion	
Chapte	er 4 Dietary Modelling—Comparing nutrient profiles of diet	s of differing
fish ar	d seafood contents	94
4.1	Background	94
4.2	Method	95
4.3	Statistical analysis	
4.4	Results and discussion	
Chapt	er 5 Compositional data of selected fish and fish products	113
5.1	Background	
5.2	Purpose of analysis	
5.3	Process	
5.3.1	Fish and fish products included for analysis	
5.3.2	Selection of suitable laboratory to conduct the analysis	
5.3.3	Analytes included and method of analysis	
5.3.4	Preparation of samples	
5.3.5	Quality assurance and quality control	
5.3.6	Calculated versus analysed results for cooked products	
5.4	Results and discussion	
5.4.1	Proximates	
5.4.2	Long chain n-3 polyunsaturated fatty acids (LCn3PUFA)	
5.4.3	Mercury and other metals	
5.4.4	Vitamins A, D and E	
5.4.5	Raw and cooked products	
Chapt	er 6 Acceptability and effects of a higher fish diet — a rando	mised
contro	lled trial	153
6.1	Methods	
6.1.1	Study design	
6.1.2	Study population	
6.1.3	Study intervention	
6.2	Study outcomes – methods of assessment	
6.2.1	Single nucleotide polymorphisms (SNPs) analysis	
6.2.2	Dietary assessment	
6.2.3	Fatty acids analysis	
6.2.4	Lipids study	
6.2.5	Iron study and haemoglobin	

6.2.6	Mercury analysis	
6.2.7	Selenium analysis	
6.2.8	Inflammatory marker analysis (C-reactive protein)	
6.2.9	Anthropometric and other assessments	
6.3	Sample size and statistical analyses	
6.4	Results	
6.4.1	Single Nucleotide Polymorphisms (SNPs)	
6.4.2	Dietary assessment	175
6.4.3	Fatty acids	
6.4.4	Lipids study	
6.4.5	Iron status and haemoglobin level	
6.4.6	Mercury	
6.4.7	Selenium	195
6.4.8	Inflammatory marker (C-Reactive Protein)	
6.4.9	Anthropometric and other assessments	
6.5	Discussion	
6.6	Conclusions	
Chapte	r 7 Cost-effective analysis of a higher fish diet	205
7.1	Introduction	205
7.2	Methods	205
7.3	Results	209
7.4	Discussion	
Chapte	r 8 Conclusion, implications for future practice and research	212
-		
Refere	nces	217
Appen	dices	234
Append	lix 1 Search Strategy for the literature review	
Append	lix 2 Description of studies included in the literature review	
Append	lix 3 Summary of risk of bias assessment for each included study	
Append	lix 4 Foods included in the dietary modelling	
Append	lix 5 List of omega-3 rich food or drinks to avoid or limit to small amo	ounts
during	the trial period	
Append	lix 6 Diet acceptability questionnaire	
Annend	lix 7 Center for Epidemiologic Studies Depression Scale (CES-D)	

# **List of Figures**

Figure 2.1 Essential fatty acid production and metabolism to form eicosanoids ......10

Figure 3.1 Per capita consumption of fish and seafood in Australia 1970–2009 according to the Food and Agriculture Organization of the United Nations (FAO) <i>Source: FAOSTAT</i>
Figure 3.2 Per capita consumption of fish and seafood of developed countries within the North American, Asian and Oceanic and the European Union regions in 2009 according to the Food and Agriculture Organization of the United Nations (FAO) <i>Source: FAOSTAT</i>
Figure 3.3 Mean fish daily intake in 2003 and 2009 by pregnancy status in the young cohort of the Australian Longitudinal Study on Women's Health as estimated by the Dietary Questionnaire for Epidemiological Studies (Version 2)
Figure 5.1 Illustration of the draining process for canned fish123
Figure 5.2 Equipment used to homogenise samples
Figure 6.1 A graphical representation of study protocol for the randomised controlled trial examining the acceptability and effects of a higher fish diet156
Figure 6.2:Intervention group study food157
Figure 6.3: Control group study food158
Figure 6.3: Control group study food
Figure 6.4 Flow diagram of the progress through phases of the randomised control trial
<ul> <li>Figure 6.4 Flow diagram of the progress through phases of the randomised control trial aimed at examining the acceptability and effects of a higher fish diet</li></ul>
<ul> <li>Figure 6.4 Flow diagram of the progress through phases of the randomised control trial aimed at examining the acceptability and effects of a higher fish diet</li></ul>
<ul> <li>Figure 6.4 Flow diagram of the progress through phases of the randomised control trial aimed at examining the acceptability and effects of a higher fish diet</li></ul>
<ul> <li>Figure 6.4 Flow diagram of the progress through phases of the randomised control trial aimed at examining the acceptability and effects of a higher fish diet</li></ul>

# **List of Tables**

Table 1. Project tasks
Table 2.1 RCTs with pregnancy outcomes (length of gestation, pre-term and post-term
delivery rates)
Table 2.2 RCTs with pregnancy outcomes (pregnancy-induced hypertension, pre- eclampsia, eclampsia)    25
Table 2.3 RCTs with maternal health as outcome (perinatal depression)
Table 2.4 RCTs with child health at birth as outcomes (Birth weight, birth length, headcircumference, low birth weight, IUGR)38
Table 2.5 RCTs with child health as outcomes (physical growth pattern)
Table 2.6 RCTs with child health as outcomes (neurological development)
Table 2.7 RCTs with child health as outcomes (visual function)
Table 2.8 RCTs with child health as outcomes (atopic disease)
Table 3.1 Proportion of women (18–49 years) consuming fish and seafood products and dishes on the day of the 1995 National Nutrition Survey by 24-hour recall (n=3576)83
Table 3.2 Mean daily intake of fish and seafood products and dishes on the day of the1995 National Nutrition Survey by 24-hour recall (n=3576)84
Table 3.3 Median daily intake of fish and seafood products and dishes amongst consumers on the day of the 1995 National Nutrition Survey by 24 hour recall
Table 3.4 Proportion of women (18–49 years) who consumed fish twice a week or more as reported in the 1995 National Nutrition Survey Food Frequency Questionnaire (n=2649)
Table 3.5 The number of women included and excluded from analysis
Table 3.6 Mean weekly intake frequency scores of fish in the young cohort of the Australian Longitudinal Study on Women's Health who consumed fish twice a week or more in 2003 and 2009 as estimated by the Dietary Questionnaire for Epidemiological Studies (Version 2)
Table 3.7 Median weekly intake frequency scores of fish in the young cohort of the Australian Longitudinal Study on Women's Health who consumed fish twice a week or more in 2003 and 2009 as estimated by the Dietary Questionnaire for Epidemiological Studies (Version 2)
Table 3.8 Mean daily intake of fish products in the young cohort of the Australian Longitudinal Study on Women's Health in 2003 and 2009 as estimated by the Dietary Questionnaire for Epidemiological Studies (Version 2)
Table 3.9 Median daily intake of fish products in the young cohort of the Australian Longitudinal Study on Women's Health in 2003 and 2009 as estimated by the Dietary Questionnaire for Epidemiological Studies (Version 2)

- Table 4.2 Nutrient reference values (NRVs) for Australia and New Zealand<sup>a</sup> on selected nutrients for non-pregnant, non-lactating women aged 19–50 years...........100

- Table 4.5 Number of serves of fish and seafood required per week to achieve recommendations as per Model 2 (i.e. high LCn3PUFA fish must be included)

- Table 4.8 Theoretical mean daily nutrient intake profile in women aged 19–50 years as estimated by the simulation of 1000 diets that followed the recommendations of the Australian Dietary Guidelines but with a higher fish content (around three serves of oily fish and seafood per week)......109
- Table 4.9 Proportion of 1000 simulated diets meeting Suggested Dietary Targets (SDT)and FAO/WHO recommended daily intake of 250 mg of EPA+DHA111
- Table 5.1 Proximates selected for analysis and analytical method details
   119

   Table 5.2 Fatty acids selected for analysis and analytical method details
   120

   Table 5.3 Minerals and heavy metals selected for analysis and analytical method details
   121

   Table 5.4 Vitamins selected for analysis and analytical method details
   121

   Table 5.5 Compositional profile for John West Atlantic Salmon (Skin Off)
   131

   Table 5.6 Compositional profile for John West Yellowtail Kingfish
   134

   Table 5.7 Compositional profile for John West Sardines in Tomato Sauce and Pink Salmon
   137

   Table 5.8 Compositional profile for John West Red Salmon and Salmon Tempters
   139

Table 5.9 Compositional profile for John West Tuna Tempters and Tuna in Springwater
Table 5.10 Compositional profile for Birds Eye Atlantic Salmon Lemon Pepper143
Table 5.11 Compositional profile for Birds Eye Lightly Seasoned Fish Fillets (Hoki) – Lemon & Cracked Pepper
Table 5.12 Compositional profile for Birds Eye Fish Fingers 1 kg (Hoki/Hake)147
Table 5.13 Compositional profile for Birds Eye Oven Bake Fish Fillets (Hoki/Hake)Original Crumb 425 g149
Table 5.14 Compositional profile for Birds Eye Deep Sea Dory Fish Portions Original Crumb 425 g151
Table 6.1 Forward primers, reverse primers and probes used in the polymerase chain reaction
Table 6.2 Characteristics of study participants at baseline    171
Table 6.3 Minor allele frequencies and testing for Hardy-Weinberg equilibrium172
Table 6.4 Mean (standard deviation) fatty acids levels by genotypes (count, %) at baseline
Table 6.5 Mean (standard deviation) total mercury and methyl mercury levels by genotypes (count, %) at baseline       174
Table 6.6 Estimated key nutrients intake (per day) prior to (Run-in^) and during the study period (Trial^) as obtained from the averages of 3-day weighed-food record
Table 6.7 Estimated intakes (per day) of selected vitamins prior to (Run-in^) and during the study period (Trial^) as obtained from the averages of 3-day weighed-food record
Table 6.8 Estimated intakes (per day) of selected minerals prior to (Run-in^) and during the study period (Trial^) as obtained from the averages of 3-day weighed-food record
Table 6.9 Acceptability of a diet higher in fish (intervention) versus a low fish diet (control) rated on a 1 to 7 scale
Table 6.10 Effects of a diet higher in fish (intervention) versus a low fish diet (control) on erythrocyte EPA, DPA, DHA and AA as a proportion of total fatty acids .188
Table 6.11 Effects of a diet higher in fish (intervention) versus a low fish diet (control)on plasma phospholipids EPA, DPA, DHA and AA as a proportion of total fattyacids
Table 6.12 Effects of a diet higher in fish (intervention) versus a low fish diet (control)on serum lipid and lipoproteins
Table 6.13 Effects of a diet higher in fish (intervention) versus a low fish diet (control)on serum iron and haemoglobin levels
Table 6.14 Effects of a diet higher in fish (intervention) versus a low fish diet (control) on total mercury and methyl mercury levels
Table 6.15 Effects of a diet higher in fish (intervention) versus a low fish diet (control)on plasma and whole blood selenium levels195

Table 6.16 Effects of a diet higher in fish (intervention) versus a low fish diet (control)on serum C-reactive protein (CRP) levels
Table 6.17 Effects of a diet higher in fish (intervention) versus a low fish diet (control)on weight, BMI and body composition
Table 6.18 Effects of a diet higher in fish (intervention) versus a low fish diet (control) on blood pressure         198
Table 6.19 Effects of a diet higher in fish (intervention) versus a low fish diet (control)on depression mood indicator
Table 7.1 Food provided to participants during the 8-week intervention period207
Table 7.2 Unit costs of resources used
Table 7.3 Comparative costs of the study foods providing 200mg of DHA209
Table 7.4 Cost effectiveness of a higher fish diet to achieve higher DHA intake and DHA level in red blood cells         209

# List of Abbreviations

AA	Arachidonic acid
ABS	Australian Bureau of Statistics
AHP	Allied Health Professional
AHRQ	Agency for Healthcare Research and Quality
AI	Adequate intakes
ALA	Alpha-linolenic acid
ALSPAC	Avon Longitudinal Study of Parents and Children
ALSWH	Australian Longitudinal Study on Women's Health
AMDR	Acceptable macronutrient distribution ranges
AQ	AsureQuality Limited
BDI	Beck Depression Inventory
BMI	Body mass index
BSID	Bayley Scales of Infant Development-Mental Development
CLAMSDQ	Clinical Linguistic and Auditory Milestone Scale Developmental Quotients
CRP	C-reactive protein
CSIRO	Commonwealth Scientific and Industrial Research Organisation
CURF	Confidentialised Unit Record Files
CVFAS	Cold vapour atomic fluorescence spectroscopy
DHA	Docosahexaenoic acid
DOMInO	DHA to Optimize Mother Infant Outcome
DNBC	Danish National Birth Cohort
DPA	Docosapentaenoic acid
DQES	Dietary Questionnaire for Epidemiological Studies
EAR	Estimated average requirement
EEG	Electroencephalogram
EPA	Eicosapentaenoic acid
EPC	Evidence-based Practice Center

EPDS	Edinburgh Postnatal Depression Scale
ERG	Electroretinogram
FRDC	Fisheries Research & Development Corporation
FSANZ	Food Standards Australia New Zealand
GEE	Generalised estimating equations
HDL	High-density lipoprotein
HPLC	High-performance liquid chromatography
ICER	Incremental cost effectiveness ratio
IgE	Immunoglobulin E
IOM	The Institute of Medicine of the National Academies of Science
IUGR	Intrauterine growth retardation
LCn3PUFA	Long chain n-3 polyunsaturated fatty acids
LOR	Limit of Reporting
MADRS	Montgomery-Asberg Depression Rating Scale
MAR	Minimal angle of resolution
MDI	Mental Developmental Index
MeHg	Methyl mercury
NATA	National Association of Testing Authorities
NHANES	National Health and Nutrition Examination Survey
NHMRC	National Health and Medical Research Council
NMI	National Measurement Institute
NNS	National Nutrition Survey
NRV	Nutrient reference values
NUHEAL	Nutraceuticals for a Healthier Life
PAL	Physical activity level
PCR	Polymerase chain reaction
PDI	Psychomotor Development Index
PIH	Pregnancy-induced hypertension

- PUFA Polyunsaturated fatty acids RCT Randomised controlled trials RDI Recommended dietary intake RMIT Royal Melbourne Institute of Technology RPD Relative percentage difference South Australian Research and Development Institute SARDI SCORing Atopic Dermatitis SCORAD SDT Suggested dietary target SiPS Salmon in Pregnancy Study SLS Sodium lauryl sulphate SNP Single nucleotide polymorphisms Solid phase microextraction SPME Total mercury THg Upper level of intake UL VEP Visual evoked potential
- WHO World Health Organization

#### **Summary**

Epidemiological studies have consistently demonstrated positive association of infant neurodevelopment with maternal fish consumption, mostly attributed to the abundance of long chain n-3 polyunsaturated fatty acids (LCn3PUFA) in fish. However, fish consumption by Australian women is overall less than optimal. Secondary analysis of nationally conducted surveys [1995 National Nutrition Survey and the Australian Longitudinal Study on Women's Health (ALSWH) in 2003 and 2009] demonstrated that less than half of Australian women of child-bearing age would consume fish at least twice a week as recommended by the Australian Dietary Guidelines. Of concern was the even lower fish intake in women who were pregnant or had recently given birth when compared with other women in the ALSWH surveys. This observation suggests that women may consume less fish whilst pregnant for fear of potential contaminants that might be present in fish.

A dietary modelling exercise based on the food consumption pattern from the Australian Dietary Guidelines confirms that one would need to consume three serves of oily or high LCn3PUFA fish per week to meet the suggested dietary target of 430 mg of LCn3PUFA for women as recommended by the National Health and Medical Research Council.

In order to ascertain the levels of LCn3PUFA and other nutrients present in Australian fish/fish products, several commonly consumed fish/fish products selected for use in the ensuing randomised trial were analysed following standardised procedure. Mercury contents of these fish study foods were also tested and found to be relatively low (range:  $1.1 \mu g$ – $7.0 \mu g$ /100 g).

To assess the acceptability of a diet that included more fish and its effects on biological parameters, a single-blinded randomised controlled eight-week trial was conducted in healthy women aged 18–50 years who normally consumed no more than one oily fish meal per week. The higher fish diet included four serves per week of a variety of fresh and convenience fish products (including canned and frozen, oily and non-oily) and were provided to the participants. The control group was asked to maintain their usual lower fish/higher meat diet and participants were provided with four serves of beef, chicken or deli-meat per week. After eight weeks,

significant increases in mean eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and methyl mercury levels were observed in the intervention group when compared to the control group. Although blood mercury level did rise with increased fish intake, it was still at a level accepted as safe. The median acceptability score for both diets was the same suggesting no difference in diet acceptance.

A cost-effectiveness study conducted post-trial demonstrated that including fish in a diet is an economical means to obtain LCn3PUFA. To obtain equal amount of DHA, it would have cost sixty times more if consuming the meat study food compared to the fish study food.

In conclusion, it has been demonstrated that consuming a variety of fish and fish products several times a week is an acceptable and cost-effective means of improving LCn3PUFA status without causing detrimental increases in mercury levels, provided low-mercury containing fish are consumed. Women of child-bearing age are advised to consume high-LCn3PUFA but low-mercury containing fish as part of a healthy diet.

## **Declaration**

I certify that this thesis does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university; and that to the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text.

Lily L H Chan

#### **Presentations**

#### **Poster presentation**

Chan, L, Grieger, JA, Miller, Cobiac, L 2010, 'Simulation of fish intake in women of child-bearing age', poster presented to the 2010 Annual Scientific Meeting of the Nutrition Society of Australia, Perth, Australia, 30 November–3 December.

#### **Oral presentation**

Chan, L, Grieger, JA, Cobiac, L 2010, 'Fish and seafood intake in Australian women of child-bearing age', abstract presented to the International Seafood & Health Conference, Melbourne, Australia, 8–10 November.

Chan, L, Miller, M, Thompson, C, Midgley, J, Cobiac, L 2011, 'Assessment of the effects and acceptability of a higher fish diet in women of child-bearing age' abstract presented to the 35th Annual Scientific Meeting of the Nutrition Society of Australia and New Zealand, Queenstown, New Zealand, 30 November–2 December.

Oral presentation at the Flinders Clinical and Molecular Medicine Cluster Seminar Series, Flinders University, 25 August 2010 and 3 August 2011.

### Acknowledgments

I would like to thank my supervisors Professor Lynne Cobiac, Associate Professor Michelle Miller and Professor Campbell Thompson for their support, both on an academic level and on a personal level. They provided continual guidance on my research and unlimited reassurance and encouragement throughout my candidature.

I would also like to thank the Australian Seafood Cooperative Research Centre (CRC) for funding the project. In addition, the CRC also provided opportunities and programmes to assist with the development of various skills and insight into the industry.

Many thanks also go to Simplot Australia, another sponsor of our project, and its staff. Dr Jocelyn Midgley, Ms Sasha King and Ms Crystal Yam have all been very helpful and provided valuable comments on the draft reports.

I would also like to thank Dr Susan Kim and Mr Pawel Skuza who have on many occasions enlightened me with their statistical expertise.

I am indebted to Dr Kathryn Burdon and her staff and students in the Department of Ophthalmology (Flinders University), and Professor Robert Gibson and his staff at the Fatty Acid Laboratory (Adelaide University) for allowing me to work in their laboratories and to learn from them. I also appreciate the help from Professor Julie Ratcliffe who guided me through the cost-effective analysis.

The Australian Bureau of Statistics and the PSA Committee of Australian Longitudinal Study on Women's health have both kindly provided survey data for the secondary analysis of fish consumption in Australian women.

Professional editor, Dr Gaye Wilson, provided copyediting and proofreading services, according to the guidelines laid out in the university-endorsed national guidelines, 'The editing of research theses by professional editors'. The integrity of the final submitted thesis remains my responsibility.

And last but not least, I would like to thank my family, in particular, my mother who has accompanied me all through this journey in search of knowledge and making sure that I have adequate rest and nutrition.