Iron deficiency in young Australian women: Role of iron knowledge, dietary intake and supplementation, and the effects on cognition

Alecia Jayne Leonard, BHSc. M.NutDiet, APD, AN

A thesis submitted for the degree of PhD (Nutrition and Dietetics)

University of Newcastle, NSW, Australia

July 2014
Statement of Originality

This thesis contains no material which has been accepted for the award of any other degree or diploma 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. I give consent to this copy of my thesis, when deposited in the University Library, being made available for loan and photocopying subject to the provisions of the Copyright Act 1968.

Alecia J Leonard
Copyright permission

I warrant that I have obtained, where necessary, permission from the copyright owners to use any of my own published work (i.e. journal publications) in which the copyright is held by another party.

Alecia J Leonard
Acknowledgement of collaboration

I hereby certify that the work embodied in this thesis has been done in collaboration with other researchers. I have included as part of my thesis a statement clearly outlining the extent of the collaboration, with whom and under what auspices.

Alecia J Leonard
Acknowledgement of authorship

I hereby certify that the work embodied in this thesis contains published papers/scholarly work of which I am a joint author. I have included as part of the thesis a written statement, endorsed by my supervisor, attesting to my contribution to the joint publications/scholarly work.

..............................................

Alecia J Leonard
Statement of contribution of others

I hereby certify that this thesis is in the form of a series of published papers of which I am joint author. I have included as part of the thesis a written statement from each co-author, endorsed by the Faculty Assistant Dean (Research Training), attesting to my contribution to the joint publications.

………………………………………………

Alecia J Leonard
Acknowledgements

I would like to express my gratitude to the following people for their contribution to my thesis.

First and foremost I sincerely thank my three supervisors and mentors, Dr. Amanda Patterson, Dr. Kerry Chalmers and Professor Clare Collins. I am so fortunate to have been supervised by such highly regarded researchers. Without your continuing advice, support and guidance this thesis would not have been possible. Your passions, skills and commitment to research have been an inspiration to me. I am indebted to you all for the immeasurable part you have played in my experience as a researcher.

I thank my fellow Nutrition and Dietetics RHD students with whom I shared many research frustrations as well as countless fun times both in and out of the office. Great friendships evolved in HA06 that will continue into the future. A special mention goes to Tracy for sharing your statistical knowledge on many an occasion.

To my incredibly supportive husband (Steve), thank you for being there for me every day, making me laugh, supporting me during the stressful times and reminding me that everything will be even better than OK. Thanks to my Mum (Karen), Dad (Tony) and Sister (Lauren), you have provided me with endless and unconditional love and support and are only ever a phone call away. I would like to thank my good friends who bring so much to my life and have been integral of my PhD journey by providing me with much needed downtime along the way.

I was fortunate to receive an Australian Post-Graduate Award for this PhD and additional financial support from Meat and Livestock Australia and the School of Health Sciences at the University of Newcastle.

Finally, but so importantly, thank you to the young women who participated in my research studies. I appreciate your interest in research, your time and your commitment as participants.
Conflict of Interest

Alecia Leonard received a postgraduate scholarship top-up from Meat and Livestock Australia Pty Ltd. Meat and Livestock had no role in the: design on the studies; analysis of data; writing of this thesis or the manuscripts it contains; or decision to submit the manuscripts for publication.
Publications and presentations arising from this thesis

Manuscripts in peer-reviewed journals: Published


Conference abstracts: Published in conference proceedings or peer-reviewed journals


Glossary of common abbreviations

WHO  World Health Organization
RCT  Randomised controlled trial
DQES  Dietary Questionnaire of Epidemiological Studies
HMRI  Hunter Medical Research Institute
JBI  Joanna-Briggs Institute
JBI-MAStARI  Joanna Briggs Institute-Meta Analysis of Statistics Assessment and Review Instrument
NUTTAB  Nutrient Data Tables for use in Australia
ADP  Australian Digital Theses
HAPS  Hunter Area Pathology Service
Fe$^{3+}$  Ferric iron
Fe$^{2+}$  Ferrous iron
sTfR  Soluble transferrin receptor
sTfR-ferritin index  Soluble transferrin receptor/Log ferritin
Ft  Serum ferritin
Hb  Haemoglobin
AAG  Alpha-1-glycoprotein
CRP  C-reactive protein
DMT1  Divalent metal transporter
ALSWH  Australian Longitudinal Study of Women’s Health
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AusDiab</td>
<td>Australian Diabetes, Obesity and Lifestyle Study</td>
</tr>
<tr>
<td>CCV</td>
<td>Cancer Council of Victoria</td>
</tr>
<tr>
<td>SF-36</td>
<td>Short-form 36 Health Survey</td>
</tr>
<tr>
<td>FFQ</td>
<td>Food Frequency Questionnaire</td>
</tr>
<tr>
<td>NKQ</td>
<td>Nutrition Knowledge Questionnaire</td>
</tr>
<tr>
<td>NSW</td>
<td>New South Wales</td>
</tr>
<tr>
<td>US</td>
<td>United States</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>WMS-R</td>
<td>Wechsler Memory Scale revised</td>
</tr>
<tr>
<td>WAIS</td>
<td>Welscher Adult Intelligence Scale</td>
</tr>
<tr>
<td>WAIS-R</td>
<td>Revised Welscher Adult Intelligence Scale</td>
</tr>
<tr>
<td>CANTAB</td>
<td>Cambridge Neuropsychological Test Automated Battery</td>
</tr>
<tr>
<td>N/A</td>
<td>Not applicable</td>
</tr>
<tr>
<td>NRV's</td>
<td>Nutrient Reference Values</td>
</tr>
<tr>
<td>RDI</td>
<td>Recommended Dietary Intake</td>
</tr>
<tr>
<td>EAR</td>
<td>Estimated Average Requirement</td>
</tr>
<tr>
<td>NNS</td>
<td>National nutrition survey</td>
</tr>
<tr>
<td>NHMRC</td>
<td>National Health and Medical Research Council</td>
</tr>
<tr>
<td>kg</td>
<td>Kilograms</td>
</tr>
<tr>
<td>m</td>
<td>Metres</td>
</tr>
<tr>
<td>mg</td>
<td>Milligrams</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>g</td>
<td>Grams</td>
</tr>
<tr>
<td>µg</td>
<td>Micrograms</td>
</tr>
<tr>
<td>L</td>
<td>Litre</td>
</tr>
<tr>
<td>SMD</td>
<td>Standardised Mean Difference</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>TAFE</td>
<td>Technical Education College</td>
</tr>
<tr>
<td>ANOVA</td>
<td>One-way analysis of variance</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SEM</td>
<td>Standard error of mean</td>
</tr>
<tr>
<td>n</td>
<td>Numbers (sample)</td>
</tr>
<tr>
<td>OCP</td>
<td>Oral contraceptive pill</td>
</tr>
<tr>
<td>EIA</td>
<td>Enzyme immunoassay</td>
</tr>
<tr>
<td>IEMA</td>
<td>Immunoenzymometric assay</td>
</tr>
<tr>
<td>ELISA</td>
<td>Enzyme linked immunosorbent assay</td>
</tr>
</tbody>
</table>
Contents

Abstract ........................................................................................................................................... 1

Chapter 1. Introduction ..................................................................................................................... 3

1.1 Overview .................................................................................................................................... 4

1.2 Iron deficiency: A nutritional crisis ............................................................................................ 4

1.2.1 Factors contributing to iron deficiency in young women .................................................. 6

1.2.2 The consequences of iron deficiency .................................................................................. 6

1.3 Iron deficiency research in women of childbearing age ............................................................ 7

1.3.1 The impact of knowledge on dietary iron intake, and dietary iron intake on iron status .......................................................... 7

1.3.2 The effect of iron deficiency on cognitive function ........................................................... 8

1.3.3 Appropriate iron dosage for use in a blinded trial ............................................................ 8

1.3.4 Markers used to measure iron status .................................................................................. 9

1.3.5 Strategies to recruit and retain women of childbearing age in health research studies ....... 9

1.4 Research aims and hypotheses .................................................................................................. 10

1.5 Thesis structure and study design ............................................................................................. 11

1.5.1 Overview .......................................................................................................................... 11

1.5.2 Systematic review – Chapter 3 .......................................................................................... 13

1.5.3 Relationships between knowledge of dietary iron and iron status - Chapter 4 ................. 13

1.5.4 Pilot randomised controlled trial – Chapters 5 & 6 ............................................................ 13

1.5.5 Comparison of two doses of elemental iron in the treatment of latent iron deficiency – Chapter 7 .......................................................................................... 15

1.5.6 The use of soluble transferrin receptor as a marker in early stage iron deficiency – Chapter 8 .......................................................................................... 16

1.5.7 Recruitment and retention of young women – Chapter 9 .................................................. 16

Chapter 2. Background Literature ................................................................................................ 17

2.1 Overview .................................................................................................................................... 18

2.2 Iron in the body ........................................................................................................................ 18

2.2.1 Function of iron .................................................................................................................. 18

2.2.2 Iron distribution and homeostasis ....................................................................................... 18

2.3 Stages of iron deficiency ........................................................................................................... 20

2.3.1 Iron depletion ...................................................................................................................... 20

2.3.2 Latent iron deficiency ....................................................................................................... 20

2.3.3 Iron deficiency anaemia .................................................................................................... 20
3.5.3 Terms .................................................................................................................. 46
3.5.4 Types of outcome measures ............................................................................... 47
3.5.5 Keywords used in search .................................................................................. 47
3.5.6 Search strategy .................................................................................................. 47
3.5.7 Study selection .................................................................................................. 48
3.5.8 Data extraction process ..................................................................................... 48
3.5.9 Analysis .............................................................................................................. 49
3.6 Results .................................................................................................................. 49
3.6.1 Study characteristics ....................................................................................... 49
3.6.2 Study aims ......................................................................................................... 52
3.6.3 Sample demographic information .................................................................... 52
3.6.4 Iron status at baseline ...................................................................................... 52
3.6.5 The markers used to assess iron status ......................................................... 52
3.6.6 Iron supplement interventions ......................................................................... 53
3.6.7 The effect of iron deficiency on cognitive functioning ................................... 59
3.6.8 Meta-analysis of the effects of iron supplement intervention on cognition .... 62
3.6.9 The effect of iron deficiency on Mental Health and Fatigue ......................... 65
3.6.10 Overall study quality ...................................................................................... 66
3.7 Discussion ............................................................................................................ 67
3.7.1 Variation in the measurement and diagnosis of iron deficiency ...................... 67
3.7.2 Relationship between iron status and cognitive function, mental health and fatigue ................................................................. 68
3.7.3 Effect of iron treatment on iron status in women of childbearing age ....... 70
3.7.4 Limitations ....................................................................................................... 70
3.7.5 Implications for practice ................................................................................ 71
3.7.6 Implications for research ............................................................................... 71
3.8 Conclusion ............................................................................................................ 72
3.9 Acknowledgements .............................................................................................. 72
3.10 Author contributions .......................................................................................... 73
3.11 Conflicts of interest ............................................................................................. 73

Chapter 4. The effect of nutrition knowledge and dietary iron intake on iron status in young women ........................................................................ 74
4.1 Overview ............................................................................................................... 75
4.2 Abstract ............................................................................................................... 75
4.3 Introduction ......................................................................................................... 76
4.4 Methods .............................................................................................................. 78
4.4.1 Design and participants ................................................................................. 78
4.4.2 Materials ............................................................................................................ 79
4.4.3 Procedure .......................................................................................................... 81
4.4.4 Statistical analysis ............................................................................................ 82

4.5 Results ....................................................................................................................... 82
4.5.1 Sample information ......................................................................................... 82
4.5.2 Nutrition knowledge of dietary iron ............................................................. 83
4.5.3 Relationship between nutrition knowledge of dietary iron and dietary iron intake ............................................................. 83
4.5.4 Relationship between dietary intake and iron status.................................. 84
4.5.5 Relationship between nutrition knowledge of dietary iron and iron status ............................................................................................................................. 86

4.6 Discussion ................................................................................................................ 86
4.7 Conclusion ................................................................................................................ 90

Chapter 5. A study of the effects of latent iron deficiency on measures of cognition: A pilot randomised controlled trial of iron supplementation in young women - Baseline analysis .................................................................................................... 91
5.1 Overview ................................................................................................................... 92
5.2 Introduction ............................................................................................................. 92
5.3 Methods .................................................................................................................... 93
5.3.1 Participants and recruitment .......................................................................... 93
5.3.2 Cognitive testing ............................................................................................ 94
5.3.3 Haematological testing.................................................................................... 95
5.4 Statistical analysis ................................................................................................... 95
5.5 Results ....................................................................................................................... 96
5.5.1 Relationship between iron status and cognitive function .......................... 96
5.6 Discussion .............................................................................................................. 103

6.1 Overview .................................................................................................................. 107
6.2 Abstract ................................................................................................................... 107
6.3 Introduction ........................................................................................................... 108
6.4 Methods .................................................................................................................. 111
6.4.1 Haematological testing.................................................................................. 112
6.4.2 Cognitive testing ............................................................................................ 113
6.4.3 Treatment blinding ........................................................................................ 114
6.4.4 Required Sample Size for An Adequately Powered RCT ........................ 115
6.4.5 Statistical Analysis ......................................................................................... 115
Chapter 9. Recruitment and retention of young women into nutrition research studies: practical considerations ................................................................. 151
  9.1 Overview ................................................................................................. 152
  9.2 Abstract .................................................................................................. 152
  9.3 Introduction ............................................................................................. 153
  9.4 Methods .................................................................................................. 155
    9.4.1 Study descriptions ............................................................................... 155
  9.5 Results ..................................................................................................... 159
    9.5.1 Comparing the effectiveness of recruitment ...................................... 159
    9.5.2 Reasons for ineligibility ..................................................................... 160
    9.5.3 Retention strategy effectiveness ......................................................... 160
  9.6 Discussion ............................................................................................... 161
    9.6.1 Recommendations for researchers .................................................. 164
  9.7 Conclusion ............................................................................................... 165

Chapter 10. Final discussion and recommendations for research and practice .. 166
  10.1 Overview ............................................................................................... 167
  10.2 Introduction ............................................................................................ 167
    10.2.1 The relationship between nutrition knowledge and dietary iron intake on iron status in young women ............................................. 167
    10.2.2 Systematic review on the effect of iron deficiency on cognition, mental health and fatigue in young women ........................................... 169
    10.2.3 Pilot randomised controlled trial ....................................................... 170
    10.2.4 The efficacy of elemental iron dosage in the treatment of iron deficiency in young women ............................................................... 172
    10.2.5 The usefulness of soluble transferrin receptor in the diagnosis of latent iron deficiency ................................................................. 173
    10.2.6 Recruitment and retention of young women in heath research ......... 174
<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.3</td>
<td>Implications of the body of research</td>
<td>176</td>
</tr>
<tr>
<td>10.3.1</td>
<td>For practice</td>
<td>176</td>
</tr>
<tr>
<td>10.3.2</td>
<td>Future research</td>
<td>177</td>
</tr>
<tr>
<td>10.4</td>
<td>Concluding remarks</td>
<td>178</td>
</tr>
<tr>
<td>References</td>
<td></td>
<td>180</td>
</tr>
<tr>
<td>Appendices</td>
<td></td>
<td>197</td>
</tr>
<tr>
<td>Appendix 1: Ethics approval</td>
<td></td>
<td>197</td>
</tr>
<tr>
<td>Appendix 2: Study flyer</td>
<td></td>
<td>202</td>
</tr>
<tr>
<td>Appendix 3: Screening form</td>
<td></td>
<td>204</td>
</tr>
<tr>
<td>Appendix 4: Information statement</td>
<td></td>
<td>209</td>
</tr>
<tr>
<td>Appendix 5: Consent form</td>
<td></td>
<td>214</td>
</tr>
<tr>
<td>Appendix 6: Food frequency questionnaire</td>
<td></td>
<td>216</td>
</tr>
<tr>
<td>Appendix 7: Nutrition knowledge of iron questionnaire</td>
<td></td>
<td>221</td>
</tr>
<tr>
<td>Appendix 8: Tips and reminders for taking capsules</td>
<td></td>
<td>229</td>
</tr>
<tr>
<td>Appendix 9: Tips to assist with nausea and constipation</td>
<td></td>
<td>231</td>
</tr>
<tr>
<td>Appendix 10: Symptom pro forma</td>
<td></td>
<td>233</td>
</tr>
<tr>
<td>Appendix 11: End of intervention letter</td>
<td></td>
<td>235</td>
</tr>
<tr>
<td>Appendix 12: IntegNeuro test description</td>
<td></td>
<td>237</td>
</tr>
<tr>
<td>Appendix 13: IntegNeuro scoring system</td>
<td></td>
<td>242</td>
</tr>
<tr>
<td>Appendix 14: Statement of contribution and collaboration for Chapter Three</td>
<td></td>
<td>246</td>
</tr>
<tr>
<td>Appendix 15: Statement of contribution and collaboration for Chapter Four</td>
<td></td>
<td>248</td>
</tr>
<tr>
<td>Appendix 16: Statement of contribution and collaboration for Chapter Six</td>
<td></td>
<td>250</td>
</tr>
<tr>
<td>Appendix 17: Statement of contribution and collaboration for Chapter Seven</td>
<td></td>
<td>252</td>
</tr>
<tr>
<td>Appendix 18: Statement of contribution and collaboration for Chapter Eight</td>
<td></td>
<td>254</td>
</tr>
<tr>
<td>Appendix 19: Statement of contribution and collaboration for Chapter Nine</td>
<td></td>
<td>256</td>
</tr>
</tbody>
</table>
List of tables
Table 2.1 Recent data on prevalence of iron deficiency among Australia females........ 25
Table 2.2 Annual blood and iron losses in reproductive aged females
Lifestyle/Physiology ........................................................................................................... 25
Table 2.3 Assessment tools used by studies to measure cognitive function............ 38
Table 3.1. Characteristics of included studies ............................................................. 51
Table 3.2. Iron status measures and results ................................................................. 54
Table 3.3. Cognitive tests used in the studies included in the meta-analysis .......... 62
Table 3.4. Study quality ............................................................................................... 67
Table 4.1: Questions, correct answers and maximum possible scores for the Food
Knowledge and Iron Physiology subscales from Part B of the Nutrition Knowledge
Questionnaire .................................................................................................................... 80
Table 4.2 Correlation coefficients for the relationship between dietary intake of iron,
calcium, fibre, vitamin C and zinc per day and haematological markers of iron status 84
Table 4.3 Spearman’s correlation coefficients (p value) for the relationship between
haematological markers of iron status and daily equivalent frequencies of iron
containing foods ................................................................................................................... 85
Table 5.1. Differences in cognitive domain scores between ferritin categories at baseline ............................................................ 97
Table 5.2. Differences in cognitive domain scores between iron-deficient and iron-
sufficient participants at baseline (based on ferritin cut offs used in published
literature) ........................................................................................................................... 98
Table 5.3 Factor loadings based on a principle components analysis with varimax
rotation for the 34 items from the IntegNeuro battery of cognitive tests (n=112)...... 100
Table 6.1 Median (and interquartile range) for each cognitive domain score from a pilot
double-blinded, placebo-controlled randomised control trial of the effects of iron
supplementation (60 or 80mg iron or placebo for 16 weeks) on the cognitive function of
iron-deficient (Ferritin <20ug/L, Haemoglobin ≥120g/L) and iron-sufficient (ferritin
≥20ug/L, haemoglobin ≥120g/L) women (18-35 years), at baseline and follow-up by
group (60 or 80mg iron, iron-deficient placebo or iron-sufficient control) ............... 118
Table 6.2 Cognitive domain change scores for iron treatment and no treatment groups
............................................................................................................................................... 120
Table 6.3 Cognitive domain change scores for ferritin improvers and non-improvers 120
Table 6.4 Cognitive domain change scores for haemoglobin improvers and non-
improvers ............................................................................................................................. 121
Table 7.1. Participant demographics (n = 24) ............................................................. 135
Table 7.2. Mean (±SEM) haematological markers of iron status at baseline, follow-up
and change scores by treatment group ............................................................................ 135
Table 7.3. Comparison of haematological markers at baseline, follow-up and change scores.......................................................................................................................................................................................... 136

Table 7.4. Iron status outcome, compliance, side effects and treatment guesses by treatment group.......................................................................................................................................................................................... 137

Table 8.1. Studies Examining Soluble Transferrin Receptor as a Marker of Early Stage Iron Deficiency .......................................................................................................................................................................................... 146

Table 8.2. Mean and standard deviation for each haematological marker of iron status in the Iron and Cognition Study at baseline.......................................................................................................................................................................................... 147

Table 9.1. Details of three studies that recruited young women, conducted at the University of Newcastle, Australia.......................................................................................................................................................................................... 157

Table 9.2. Length of recruitment and participant flow in each of the three included studies.......................................................................................................................................................................................... 160
List of figures

Figure 1.1. The prevalence of iron deficiency anaemia in non-pregnant women by country 1993-2005 (World Health Organization 2008) ........................................................ 5

Figure 1.2. Flow diagram of the six manuscripts that form this thesis ......................... 12

Figure 1.3. Flow chart describing the study design of a pilot double-blinded, placebo-controlled randomised controlled trial of the effects of iron supplementation (60 or 80mg iron or placebo for 16 weeks) on the cognitive function of iron-deficient (Ferritin <20ug/L, Haemoglobin ≥120g/L) and iron-sufficient (Ferritin ≥20ug/L, Haemoglobin ≥120g/L) women (18-35 years)................................................................................................ 15

Figure 2.1 Absorption of iron in an enterocyte (Schuster 2011) ................................. 19

Figure 3.1 Flow diagram of number of studies screened, assessed for eligibility, and included in the review with reasons for exclusion.............................................................. 50

Figure 3.2. Digit Symbol scores at baseline and after iron treatment intervention ...... 63

Figure 3.3. Total Digit Span scores before and after iron treatment intervention ........ 64

Figure 3.4. Arithmetic scores before and after iron treatment intervention ............... 64

Figure 3.5. Block Design scores before and after iron treatment intervention .......... 65

Figure 6.1 Study Recruitment and Randomisation Flow chart ................................. 112

Figure 7.1 Study recruitment and randomisation flow chart ..................................... 132
Abstract

Iron deficiency was labelled a major public health concern in the late 1980s due to its recognition as the most prevalent nutritional disorder in the world. According to the World Health Organization (2001), iron deficiency remains the most common nutritional deficiency worldwide. Within Australia, one in five young women are affected by iron deficiency. A strong link between iron deficiency anaemia and impaired cognitive function has been established in children. The effect of latent iron deficiency on cognition in young women has not been well investigated.

The aims of this research were to: 1) determine the level of nutrition knowledge of dietary iron in a subgroup of young women living in Newcastle, NSW and its relationship to their iron intake and iron status; 2) examine the suitability of a validated battery of tests (IntegNeuro) for assessing cognitive function in iron deficient and iron sufficient women; 3) determine an appropriate sample size for a future RCT on iron deficiency and cognition in young women; 4) determine an effective dose of elemental iron to treat iron deficiency in latent iron-deficient participants, while maintaining blinding to treatment.

A study on the effect of nutrition knowledge on dietary iron intake and iron status was conducted in young women. This involved the distribution of a Nutrition Knowledge Questionnaire and Food Frequency Questionnaire to females who were enrolled or interested in enrolling in the pilot RCT (described below). The results of this study showed a significant relationship between knowledge and total iron intake. However, better knowledge did not result in better iron status. Results also showed a positive relationship between the frequency of flesh food intake and iron status.

A pilot double-blinded, placebo-controlled intervention trial was conducted in iron-deficient and iron-sufficient young women (18-35 years). Cognitive function and haematological markers of iron status were measured at baseline and follow-up. Iron-deficient participants were randomised to receive placebo, 60mg or 80mg elemental iron daily for 16 weeks. A control group of iron-sufficient participants was allocated placebo capsules. Participants in the iron treatment groups had greater cognitive change scores
compared to no-treatment groups. Change scores for Impulsivity and Attention were significantly greater in plasma ferritin improvers than in non-improvers ($p=.004$, and $p=.026$, respectively). IntegNeuro was easy to administer and acceptable to young women. Based on differences in Memory and Attention scores between iron-sufficient and iron-deficient participants, further research with a sample size of 26 or 84 iron-deficient participants per group is required for an adequately powered trial.

In conclusion, this thesis contributes to various areas of iron deficiency research in young women. Nutrition knowledge regarding iron in young women is a novel area of research. Some positive associations between knowledge and intake were found. Results revealed that a validated questionnaire with a greater focus on dietary enhancers and inhibitors of iron is required to further this area of research. Dietary intake of flesh foods was positively related to serum ferritin. There is a need to establish strategies for increasing iron intake and absorption in young women. Such strategies may include educating non-vegetarians about the benefits of increased flesh food consumption and vegetarians about dietary iron enhancers and inhibitors.

Few significant differences in cognition scores between iron-deficient and iron-sufficient young women at baseline, and after the 16 week intervention were expected in an under-powered pilot study. It is important to consider that the detection of differences in cognition was not the primary aim of this pilot study. Future studies in this area should be well powered, multi-centred randomised-controlled trials using a cognitive battery that has been validated for use in this population.

The pilot RCT revealed some important information relating to methodological advancements in this area of research. These include: 1) the IntegNeuro battery of cognitive tests is a useful method for use in young women, which is important due to the diverse range of cognitive tests used in previous research; 2) a 60mg dose of elemental iron is as effective in treating iron deficiency and causes fewer side effects than an 80mg dose; and 3) sTfR alone does not enhance the ability to detect iron deficiency in its early stages, although the sTfR-ferritin index is more useful.