

**THE PROFILE OF PAIN
IN OLDER WOMEN WITH ARTHRITIS**

A thesis presented by
Katie Elizabeth de Luca
B App Sci (Ex & Sp Sci), M Chiro

To the
School of Medicine & Public Health,
Faculty of Health & Medicine

**Submitted for the degree of
Doctor of Philosophy**

University of Newcastle
Newcastle, NSW, Australia

March 2016

PREFACE

DECLARATIONS

Statement of Originality

*The 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 the final version of my thesis being made available worldwide when deposited in the University's Digital Repository**, subject to the provisions of the Copyright Act 1968.*

***Unless an Embargo has been approved for a determined period.*

10th March 2016

Katie de Luca

Date

Statement 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 the thesis a statement clearly outlining the extent of collaboration, with whom and under what auspices.

10th March 2016

Katie de Luca

Date

Statement of Authorship

I hereby certify that the work embodied in this thesis contains published papers 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 work.

10th March 2016

Katie de Luca

Date

Thesis by Publication

I hereby certify that this thesis is in the form of a series of published papers of which I am a 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.

10th March 2016

Katie de Luca

Date

ACKNOWLEDGEMENTS

I acknowledge the guidance provided by my panel of supervisors - Professor Lynne Parkinson, Professor Fiona Blyth, Professor Julie Byles and Associate Professor Henry Pollard. I am grateful for your time, energy, perspective, enthusiasm & support. Lynne, I am so very thankful for your guidance during times of digression and support during times of uncertainty. However I am most thankful for your friendship, belief and generosity as a person. It is an honor to have been supervised by you and I will be forever grateful, as an academic and mother, from the compassion you have shown throughout the course of my thesis.

I am grateful to fellow PhD students Thomas Lo and Aron Downie for the collaboration and support during my doctorate. I wish to acknowledge Professor Gillian Hawker for her contribution to the design of the *Profile of Pain in Older Women with Arthritis Study* survey and Dr. Lynn Francis for her assistance in the statistical analysis of data.

I wish to acknowledge the Australian Longitudinal Study on Womens Health (ALSWH). ALSWH is conducted by the University of Newcastle and the University of Queensland, and supported by infrastructure and staff of the Research Centre for Gender, Health and Ageing. I wish to acknowledge the Hunter Medical Research Institute for funding of the *Profile of Pain in Older Women with Arthritis Study*, supported by the Lions Club of Adamstown Research Project Grant. Without this grant we would not have been able to conduct this project. I wish to acknowledge receipt of the Australian Postgraduate Award Scholarship and COCA Research Limited Top up Scholarship. For many years, the Chiropractic and Osteopathic College of Australasia have supported my desire to pursue Higher Degree Research, and their continued support for fostering research capacity and building an evidence base for chiropractic is exceptionally valuable to the progression of the profession.

I am thankful to the women who provided detailed information on their experiences of health, pain and arthritis in the *Profile of Pain in Older Women with Arthritis Study*. This research would not have been possible without them, and their commitment to participate in ALSWH to aid in the investigations of women's health and wellbeing is invaluable.

DEDICATIONS

This thesis is dedicated to my husband Troy de Luca, and our family. Troy, without your unwavering support for me to pursue my “nerdiness” or thirst for learning, this thesis would never have been possible. You are my rock. Thank you. To my beautiful three children - Marcus (4), Alexander (2) and Ivy (0) – you are the loves of my life. I hope to inspire you to explore your world and believe in yourself and seek beauty, charm and adventure as you grow. You guys have provided me with the laughs and distractions to remain focused and determined during this time. Finally, to my parents Phil and Jenny Hardy, thank you. You have always been my staunchest supporters and have provided me with unconditional love and direction throughout my life. This thesis would not have been possible without your understanding and many hours of babysitting.

LIST OF PAPERS INCLUDED AS PART OF THE THESIS

Paper 1

de Luca K, Parkinson L, Pollard H, Byles J, Blyth F. How is the experience of pain measured in older, community-dwelling people with osteoarthritis? A systematic review of the literature. *Rheumatology International* 2015;35:1461-1472. IF:1.516
DOI: 10.1007/s00296-015-3268-3

Paper 2

de Luca K, Parkinson L, Byles J. A study protocol for the profile of pain in older women: assessing the multi-dimensional nature of the experience of pain in arthritis. *Chiropractic & Manual Therapies* 2014;22:28.
DOI:10.1186/s12998-014-0028-5

Paper 3

de Luca K, Parkinson L, Byles J, Lo TKT, Pollard H, Blyth F. The prevalence and cross-sectional associations of neuropathic-like pain among older, community-dwelling women with arthritis. *Pain Medicine* 2016;0:1–9. IF:2.243

Paper 4

de Luca K, Parkinson L, Downie A, Byles J, Blyth F. Identification of three subgroups of pain profiles in 227 older, community-dwelling women with arthritis via latent class analysis: results from a cross-sectional study. *Submitted for peer-review, Arthritis Research & Therapy*. IF:3.75

LIST OF ADDITIONAL PAPERS RELEVANT TO, BUT NOT INCLUDED IN, THE THESIS

Additional Paper 1

de Luca K, Parkinson L, Haldeman S, Byles J, Blyth F. How is spinal pain associated with comorbidity? A cross-sectional analysis of the relationship between spinal pain and chronic diseases. *Manuscript in preparation*.

LIST OF CONFERENCE PRESENTATIONS RELEVANT TO THE THESIS

Conference Podium Presentations

1. **de Luca K**, Parkinson L, Downie A, Byles J, Blyth F. Three subgroups of pain phenotypes in 227 older, women with arthritis. CAA National Research Symposium, Melbourne, Australia, October 2015.
 - **Chiropractors Association of Australia National award winning podium: Grand Prize for Research Excellence**
2. **de Luca K**, Parkinson L, Byles J, Blyth F, Pollard H. How catastrophic are different types of pain in women with arthritis. 142nd APHA Annual Meeting and Exposition, New Orleans, USA. November 15-19 2014.
3. **de Luca K**, Parkinson L, Byles J, Blyth F, Pollard H. How does neuropathic pain affect quality of life in women with arthritis. 142nd APHA Annual Meeting and Exposition, New Orleans, USA. November 15-19 2014.
4. **de Luca K**, Parkinson L, Byles J, Blyth F, Pollard H. How does neuropathic pain affect quality of life in women with arthritis. COCA Biennial Conference. Sydney, Australia, October 2014.
5. **de Luca K**, Parkinson L, Byles J, Blyth F, Pollard H. How does neuropathic pain affect quality of life in women with arthritis. CAANSW Inaugural Research symposium. Sydney, Australia, September 2014.
6. **de Luca K**, Parkinson L, Byles J, Blyth F, Pollard H. Pain and the older woman: results from a cross-sectional survey. AAG & ACS Regional Conference. Port Macquarie, Australia. March 5-7, 2014.
7. **de Luca K**, Parkinson L, Byles J, Blyth F, Pollard H. A Cross sectional survey of pain in older women with arthritis: Study protocol. Emerging Researchers In Ageing National Conference, Brisbane, Australia, November 2012.

Conference Poster presentation

1. **de Luca K**, Parkinson L, Haldeman S, Byles J. Is spinal pain associated with comorbidity? A cross-sectional analysis of the relationship between spinal pain and lifestyle diseases. CAA National Research Symposium, Melbourne, Australia, October 2015.

- **Chiropractors Association of Australia National award winning poster: Best Post Graduate Student (Masters of Research or PhD student) and Prize for Research Excellence**
- 2. **de Luca K**, Parkinson L, Downie A, Byles J, Blyth F. Mild, moderate or severe pain? How 227 older women living with arthritis have different profiles of the multi-dimensional experience of pain and the impact of profile membership on their health. 2nd CAANSW Research Symposium. Sydney, September, 2015.
- 3. **de Luca K**, Parkinson L, Byles J, Lo TKT, Blyth F, Pollard H. The prevalence and impact of neuropathic like pain in older women with arthritis. 2nd CAANSW Research Symposium. Sydney, September, 2015.
- 4. **de Luca K**, Parkinson L, Byles J, Blyth F, Downie A. Discovering three distinct profiles of pain in 227 older women with arthritis. World Federation of Chiropractic, 12th Biennial Conference. Greece, May 2015.
- 5. **de Luca K**, Parkinson L, Byles J, Lo TKT, Blyth F, Pollard H. The prevalence and impact of neuropathic pain in older women with arthritis. World Federation of Chiropractic 12th Biennial Conference. Greece, May 2015.
- **World Federation of Chiropractic award winning poster: Best regional poster award.**
- 6. **de Luca K**, Parkinson L, Byles J, Blyth F, Downie A. How catastrophic are different types of pain in women with arthritis. 7th World Congress, World Institute of Pain. Maastricht, Netherlands. May 7-10 2014.
- 7. **de Luca K**, Parkinson L, Byles J, Blyth F, Pollard H. How is the experience of pain measured in older, community dwelling women with osteoarthritis – A systematic review of the literature. 7th World Congress, World Institute of Pain. Maastricht, Netherlands. May 7-10 2014.
- 8. **de Luca K**, Parkinson L, Byles J, Blyth F, Pollard H. How does neuropathic pain affect quality of life in women with arthritis. 7th World Congress, World Institute of Pain. Maastricht, Netherlands. May 7-10 2014.
- 9. **de Luca K**, Parkinson L, Byles J, Blyth F, Pollard H. How is the experience of pain measured in older, community dwelling people with osteoarthritis – A systematic review of the literature. Emerging Researchers In Ageing National Conference, Brisbane, November 2012.

10. **de Luca K**, Parkinson L, Byles J, Blyth F, Pollard H. Development and pilot of a survey instrument for measuring pain in older women with arthritis. Emerging Researchers In Ageing National Conference, Brisbane, November 2012.
11. **de Luca K**, Parkinson L, Byles J, Blyth F, Pollard H. How is the experience of pain measured in older, community dwelling people with osteoarthritis – A systematic review of the literature. COCA National Conference, Sydney, October 2012.
12. **de Luca K**, Parkinson L, Byles J, Blyth F, Pollard H. Development and pilot of a survey instrument for measuring pain in older women with arthritis. COCA National Conference, Sydney, October 2012.
13. **de Luca K**, Parkinson L, Byles J, Blyth F, Pollard H. A cross sectional survey of pain in older women with arthritis: A study protocol. COCA National Conference, Sydney, October 2012.

CONTENTS

PREFACE	i
Declarations	i
Acknowledgements	iii
List of papers included as part of the thesis	v
List of additional papers relevant to, but not included in, the thesis	v
List of conference presentations relevant to the thesis	vi
Conference podium presentations	vi
Conference poster presentation	vi
CONTENTS	ix
List of tables	xiii
List of figures	xv
List of appendices	xvi
SYNOPSIS	xvii
INTRODUCTION.....	1
Arthritis	1
Pain in arthritis.....	3
Mechanisms of pain in arthritis	5
Neuropathic pain	8
Arthritis and neuropathic pain.....	10
Epidemiological studies of arthritis	11
Studies of pain in arthritis.....	12
Management of pain in arthritis.....	14
Management of neuropathic pain	17
Future directions.....	21
Conclusions	21
STRUCTURE OF THESIS.....	22
THE PROFILE OF PAIN IN OLDER WOMEN WITH ARTHRITIS STUDY.....	23
Rationale	23
Design.....	23
AIMS OF THE THESIS.....	24
References	25

PAPER 1	43
How is the experience of pain measured in older, community dwelling people with osteoarthritis? A systematic review of the literature.	43
SYNOPSIS	43
Abstract	44
Introduction.....	45
Methods	47
Results	48
Discussion.....	52
Conclusions.....	56
References.....	56
PAPER 2	72
A study protocol for the profile of pain in older women: Assessing the multi-dimensional nature of the experience of pain in arthritis	72
SYNOPSIS	72
Abstract	73
Background.....	73
Methods	75
Discussion.....	78
Conclusion	79
References.....	80
PAPER 3	88
The prevalence and cross-sectional associations of neuropathic-like pain among older, community-dwelling women with arthritis.	88
SYNOPSIS	88
Abstract	89
Introduction.....	90
Methods	91
Results	93
Discussion.....	95
Conclusion	100
References.....	100

PAPER 4	105
Identification of three subgroups of pain profiles in 227 older, community-dwelling women with arthritis via latent class analysis: results from a cross-sectional study.....	105
SYNOPSIS.....	105
Abstract.....	106
Introduction	107
Methods.....	108
posterior probabilities across one to ten cluster models.Results	113
Discussion.....	117
References	123
DISCUSSION	128
SYNOPSIS.....	128
Paper 1	129
Paper 2	132
Paper 3	133
Paper 4	135
STRENGTHS AND LIMITATIONS OF THE THESIS	137
Representativeness of the study sample.....	137
Response rate of the study sample.....	138
Appropriateness of the measures used	138
Data entry and missing data	139
Cross-sectional study design limitations.....	142
Profile of Pain in Older Women with Arthritis Study arthritis definition.....	143
IMPLICATIONS OF FINDINGS AND RECOMMENDATIONS FOR FUTURE RESEARCH.....	144
CONCLUSION	145
References	146
APPENDICES.....	156
Appendix 1: Paper 1	156
<i>Appendix 1.1: Statements of contribution from co-authors</i>	<i>156</i>
<i>Appendix 1.2: The Effective Public Health Practice Project (EPHPP) quality assessment tool for quantitative studies.</i>	<i>159</i>
<i>Appendix 1.3: Data Extraction Tool</i>	<i>163</i>

Appendix 2: Paper 2	164
<i>Appendix 2.1: Published Paper</i>	164
<i>Appendix 2.2: Statements of contribution from co-authors</i>	171
Appendix 3: Paper 3	174
<i>Appendix 3.1: Statements of contribution from co-authors</i>	174
Appendix 4: Paper 4	177
<i>Appendix 4.1: Statements of contribution from co-authors</i>	177
Appendix 5: Additional Paper 1	180
<i>Appendix 5.1: How is spinal pain associated with comorbidity? A cross-sectional analysis of the relationship between spinal pain and chronic diseases</i>	180
<i>Appendix 5.2: Statements of contributions from co-authors</i>	196
Appendix 6: Study information packages	199
<i>Appendix 6.1: Certificates of ethics approvals</i>	199
<i>Appendix 6.2: WHA Profile of Pain in Older Women with Arthritis Study – Information for participants</i>	202
<i>Appendix 6.3: WHO Profile of Pain in Older Women with Arthritis Study – Participant consent form</i>	204
<i>Appendix 6.4: WHA Profile of Pain in Older Women with Arthritis Study – Survey</i>	205
<i>Appendix 6.5: WHA Profile of Pain in Older Women with Arthritis Study: Reminder leaflet</i>	225
<i>Appendix 6.6: WHO Profile of Pain in Older Women with Arthritis Study – Thank you leaflet</i>	226

LIST OF TABLES

Paper 1

Table 1.1:	Characteristics and methodological quality grade of the 11 included studies, ordered by publication date	65
Table 1.2:	Dimensions of the osteoarthritis pain experience measured by eleven studies included in this review	70

Paper 2

Table 2.1:	Health, arthritis and pain measures used to assess multiple dimensions of pain in arthritis in this study	80
------------	---	----

Paper 3

Table 3.1:	Socio-demographic characteristics of older women with arthritis, with nociceptive or neuropathic-like pain	94
Table 3.2:	Health and pain characteristics of older women with arthritis, with nociceptive or neuropathic-like pain	95
Table 3.3:	Univariable logistic regression analysis of neuropathic-like pain in older women with arthritis (n=147)	96
Table 3.4:	Multiple variable logistic regression analysis of variables associated with neuropathic-like pain in older women with arthritis (n=147)	99

Paper 4

Table 4.1:	Ordinal categories of the Graded Chronic Pain Scale and the McGill Pain Questionnaire (Short Form) present pain intensity subscale	108
Table 4.2:	Socio-demographic characteristics of the total sample and socio-demographic characteristics by cluster	110
Table 4.3:	Latent class analysis goodness of fit indices and posterior probabilities across one to ten cluster models	113
Table 4.4:	The overall proportions of each variable count per cluster	115
Table 4.4:	Difference in proportions of women classified in the 3-cluster latent class analysis model, between women with arthritis as compared to women with osteoarthritis	117

Discussion

Table 5.1:	Missing data for measures of health, pain and arthritis for the sample and for women with arthritis	140
Table 5.2:	Descriptive statistics of the sample	141
Table 5.3:	Descriptive statistics of women with arthritis	142

Appendices - Additional Paper 1

Table 6.1:	Sample characteristics of 579 community-dwelling older women, and the proportion of comorbidities between women with and without self-reported spinal pain	200
Table 6.2:	Association between type and number of comorbidity for women with self-report spinal pain compared with women without spinal pain	201

LIST OF FIGURES

Paper 1

Figure 1.1:	A flow chart of the PRISMA screening and selection process	50
-------------	--	----

Paper 4

Figure 4.1:	Response probabilities of each pain dimension variable, per cluster: cluster one (n=95), cluster two (n=83) and cluster three (n=49)	118
Figure 4.2:	Risk profile for cluster two and cluster three, compared to cluster one ..	120

LIST OF APPENDICES

Appendix 1: Paper 1

Appendix 1.1: Statements of contribution from co-authors.....	156
Appendix 1.2: The Effective Public Health Practice Project (EPHPP) quality assessment tool for quantitative studies.	159
Appendix 1.3: Data Extraction Tool.....	163

Appendix 2: Paper 2

Appendix 2.1: Published paper.....	164
Appendix 2.1: Statements of contribution from co-authors.....	171

Appendix 3: Paper 3

Appendix 3.1: Statements of contribution from co-authors.....	174
---	-----

Appendix 4: Paper 4

Appendix 4.1: Statements of contribution from co-authors.....	177
---	-----

Appendix 5: Additional Paper 1

Appendix 5.1: Manuscript in preparation	180
Appendix 5.2: Statements of contribution from co-authors.....	196

Appendix 6: Study information packages

Appendix 6.1: Certificates of ethics approvals	199
Appendix 6.2: Profile of Pain in Older Women with Arthritis Study - Information for participants.....	202
Appendix 6.3: Profile of Pain in Older Women with Arthritis Study – Participant consent form	204
Appendix 6.4: Profile of Pain in Older Women with Arthritis Study – Survey	205
Appendix 6.5: Profile of Pain in Older Women with Arthritis Study – Reminder leaflet ..	225
Appendix 6.6: Profile of Pain in Older Women with Arthritis Study – Thank you leaflet .	226

SYNOPSIS

Arthritis covers a diverse group of diseases commonly involving degeneration and inflammation of the joints. It is very common, estimated to affect 18.5% of the Australian population, or approximately 3.9 million people. Although pain is the most prevalent presenting symptom in the very debilitating condition of arthritis, it has been insufficiently researched and therefore is not well understood, nor well managed in clinical practice. Traditionally, pain in arthritis has been attributed to peripheral, local tissue injury and the mechanism of nociceptive pain. However, the understanding of the experience of pain in arthritis is being increasingly broadened to include the complex interactions between nociceptive and neuropathic mechanisms. Recently, the Osteoarthritis Research Society International (OARSI) and the US Food and Drug Administration (FDA) have called for research to define the disease state of arthritis, and this includes the identification and evaluation of different types of pain in arthritis.

The aim of this thesis was to explore the experience and impact of pain in arthritis. Specifically, this thesis focuses on the multi-dimensional nature of the experience of pain in older women with arthritis. This thesis by publication comprises a series of four papers, constituting elements of an integrated project. The flow of the thesis includes an introduction, chapters consisting of four inter-related papers, a discussion and a conclusion.

Paper 1 is a systematic review of the literature on how the experience of pain is measured in older, community dwelling people with osteoarthritis. This paper concluded that the most commonly used measures of pain do not effectively assess the multi-dimensional nature of the experience of pain in osteoarthritis, nor have the majority of epidemiological studies in arthritis captured the multi-dimensional nature of the experience of pain in osteoarthritis.

In acknowledging the findings from Paper 1, the *Profile of Pain in Older Women with Arthritis Study* was undertaken to better assess the multi-dimensional nature of the experience of pain in arthritis. **Paper 2** outlines the study protocol for the *Profile of Pain in Older Women with Arthritis Study* and discusses the appropriateness of eleven measures of health, pain and arthritis used to explore the experience and impact of pain in arthritis.

Paper 3 used data generated from the *Profile of Pain in Older Women with Arthritis Study* (Paper 2). Paper 3 reports that neuropathic-like pain in arthritis is common and is associated with greater disability and poorer quality of life. Furthermore, women who have arthritis and neuropathic-like pain have significantly more severe pain, a heightened pain experience and more fatigue. Abnormal sensory changes, higher pain catastrophizing and using more medications are significantly associated with neuropathic-like pain.

OARSI and FDA have called for research to define the disease state of arthritis, and this includes the identification and evaluation of different types of pain in arthritis. **Paper 4** identified three subgroups of older, community dwelling women with arthritis with very different, very distinct profiles of pain. Profiles consisted of 39.5% of women having uni-dimensional pain, 38.6% of women having moderate multi-dimensional pain and 21.9% of women having severe multi-dimensional pain. Once profiles were identified, women with moderate and severe multi-dimensional pain profiles were at a significantly greater risk of poorer physical and mental health related quality of life.

This thesis has explored the experience and impact of pain in arthritis. The papers presented provide a significant and important contribution to the field of arthritis and pain, by providing preliminary evidence on the identification and evaluation of different types of pain in arthritis. The next challenge is in the study of the treatment of pain mechanisms in arthritis. This area of research has great promise to improve pain management and decrease the significant socio-economic burden associated with arthritis.