Copyright Statement

The digital copy of this thesis is protected by the Copyright Act 1994 (New Zealand).

This thesis may be consulted by you, provided you comply with the provisions of the Act and the following conditions of use:

- Any use you make of these documents or images must be for research or private study purposes only, and you may not make them available to any other person.
- Authors control the copyright of their thesis. You will recognise the author’s right to be identified as the author of this thesis, and due acknowledgement will be made to the author where appropriate.
- You will obtain the author's permission before publishing any material from their thesis.

To request permissions please use the Feedback form on our webpage. http://researchspace.auckland.ac.nz/feedback

General copyright and disclaimer

In addition to the above conditions, authors give their consent for the digital copy of their work to be used subject to the conditions specified on the Library Thesis Consent Form.
Epidemiological studies of leg ulcers in Auckland, New Zealand

Natalie K. Walker

Clinical Trials Research Unit
Department of Medicine
University of Auckland
Auckland
New Zealand

A thesis submitted for the degree of Doctor of Philosophy, University of Auckland, 2000
Abstract

A leg ulcer is generally considered to be any break in the skin on the lower leg (below the knee) or on the foot, which has been present for more than six weeks. Typically the condition is a consequence of disease of the circulatory system, and can cause considerable disability. The Auckland leg ulcer study is a community-based study of leg ulceration conducted in the North Auckland and Central Auckland health districts of New Zealand. The study aimed to determine the prevalence and incidence of leg ulcers in the community and investigate several possible risk factors for the condition. Cases were identified through notifications from health professionals and by self-notification. Cases aged between 40 and 99 years and on the electoral roll for the study region were invited to participate in a case-control study. Controls were individuals without leg ulcers and were selected from the electoral roll using a stratified random sampling process. Controls were also aged between 40 and 99 years and had to be resident within the study region to be eligible. Four hundred and twenty-six cases with current leg ulcers were identified during the 12-month study period, with 241 cases and 224 controls interviewed for the case-control study. Overall, the occurrence of leg ulcers in the general population was low, however, the prevalence and cumulative incidence increased dramatically with age, and changed according to gender and region. The average age at ulcer onset in interviewed cases was 65 years. Leg ulcers took approximately 12 months on average to heal, and recurrence occurred in 59% of cases. Treatment strategies were variable, and almost a quarter of all cases had been admitted to hospital within the last five years because of their ulcers. The average length of hospital stay was 34 days. Results from the case-control study indicated that deep vein thrombosis, lower limb surgery, leg fracture, and varicose veins were strong risk factors for the development of leg ulcers. Furthermore, nulligravida increased the risk of ulcer development while prolonged breast-feeding decreased risk, suggesting a hormonal component to the development of leg ulcers in women. These data have important implications for the prevention of this chronic condition.
The work presented in this thesis was undertaken during the tenure of a Training Fellowship from the Health Research Council of New Zealand, and was conducted at the Clinical Trials Research Unit, Department of Medicine, University of Auckland, Auckland, New Zealand. I am grateful to my colleagues at this unit for supporting me in my research over the last four years. In particular, I am indebted to Stephen MacMahon and Anthony Rodgers for providing me with the opportunity to undertake this study, and believing that I would succeed. As my supervisors, they were always encouraging, even when I wandered down the wrong path every now and again. Stephen “fine apart from the English” MacMahon – I hope you feel that my writing has finally improved! Anthony - I appreciate your support and thank you for providing the idea of a thesis topic. Thanks also to Gary Whitlock (my covert supervisor) for his endless patience while I asked inane questions about the most basic of epidemiological concepts, for cheering me up when it all seemed too hard, for the endless stream of coffee, and for the constant interruptions – it made sure I stopped and had a break!

Particular thanks should be given to all staff at the unit that worked on this study. To Susan McAuley, Faith Mahony, Fiona Mackay, and Cherie Mulholland who were the study nurses involved in data collection. Without their support, suggestions, and endless enthusiasm throughout the study, this project would never have been as successful as it was. Thanks also to Cosima Rickerby, Debbie Beaumont, and Colleen Ciobo. My thanks also to the statisticians at the unit: Joanna Broad, Alain Vandal, Stephen Vander Hoorn, Megan Pledger, and Michelle Woods who very patiently led me through the intricacies of SAS programming, and to Derrick Bennett for translating the statistical “Greek” into plain English. Thanks also to Deanne Douglas for all the desk-top publishing work and for making me laugh when I didn’t feel like it. Thanks to Jaco Van Rooyen and Alan McCulloch for their expert programming abilities in creating some seriously impressive data entry programmes, and to all data management staff involved in the study, in particular Amanda Milne, Claudia Retegan, Robert Dragnoi, and Kylie Yin.
Thanks also to Yvonne Cleverley, Kylie Yin, and Mike Yin for assisting with the storage of the blood samples.

Outside of the unit, a great number of people have been involved in the study, providing invaluable advice and support. Firstly, my thanks to Robyn Norton, Sue Sharpe, Nicholas Birchall, Helen Francis, Anita Latta, Jill Waters, and Sue Thomas, who were involved in the steering committee for the study. Thanks also to Peter Charlesworth, André van Rij, and Nicholas Birchall for the endless amount of time they gave freely to the study to grade the cases according to ulcer type. Extra special thanks should be given to Peter for his time and patience in training the study nurses in the use of the Doppler. Staff at the vascular unit at Auckland hospital also provided additional help with this process. Thanks to Jennifer Holden for undertaking the capture-recapture analysis as part of her PhD in statistics, and to Christopher Triggs for finding Jennifer for me. Thanks also to Andrew Jull, Tom Morris, Robert Frith, Murray Tilyard, and staff at the Dunedin vascular clinic for providing advice when I sought it. Thanks also to Carolyn Coggin for her assistance with running the focus groups conducted in the pilot study. It was nice to be able to combine some qualitative research with quantitative research for a change. My thanks also to Binky Taua for advice and assistance with Maori and Pacific Island consultation. Thanks finally to the authors of the Lothian and Forth Valley cross-sectional study, the 1989 Gothenburg prevalence study, the 1988 Skaraborg prevalence study, and the Perth cross-sectional study for providing copies of the questionnaires used in their research.

Financial support for the pilot phase of this study was provided by the Health Research Council of New Zealand. Financial support for the main study was provided, in part, by ConvaTec. Dressings were supplied by ConvaTec and Smith and Nephew, while Fisher and Paykel Healthcare Ltd and Huntleigh Healthcare Pty Ltd provided Doppler’s. My thanks to all of these groups for your support, particularly given that this project fell outside the more “sexy” research areas normally funded. It should be noted that this study was designed, conducted, analysed, and interpreted independently of all sponsors.
Special thanks should be given to the 398 health professionals that agreed to be involved in this study. Without their support this research project would never have been successful. Thanks also to the 241 cases and 224 controls who welcomed us into your homes and freely gave a considerable amount of their time to this study. I hope that the results obtained from this study will benefit them in the years to come.

My greatest thanks should go to my husband, my friends, and my family. First, to my husband Don, for his fantastic support and endless patience throughout this journey. I know at times it seemed so endless and you didn’t always understand why there were tears, but the flowers, the dinners, and the oysters and champagne when it was all too hard will always be appreciated. Words can not express how much you mean to me. Specials thanks also to Sue and Peter Greenaway for putting up with the sprawl of papers all over your floor when I was writing, and for giving me a break away from the city. Your hospitality was endless and your house a sanctuary from the stress. Finally, thanks to my family and friends who I have largely ignored over the past few years. Thanks for your support and understanding while I have withdrawn from your company to complete this project and for letting me know that you will be there when I return. Special thanks to Inawa for ensuring I did something other than work all the time, and to Mel who has been through all this before and is the only one I feel truly understands the stress involved – thanks for being such an old friend and for grammar-checking this huge tome!

This thesis was submitted on 20\textsuperscript{th} September 2000. At that time, I was 33 weeks pregnant. Nothing like leaving things to the last moment!
Contribution of Study Investigators

The research presented in this thesis is based on data obtained from the Auckland Leg Ulcer Study - a study conducted at the Clinical Trials Research Unit, Department of Medicine, University of Auckland, Auckland, New Zealand. Professor Stephen MacMahon¹ and Dr Anthony Rodgers² acted as my supervisors for this thesis.

Both the pilot phase of this study and the main study were conceived and designed by myself and Dr Anthony Rodgers² in 1996, with advice provided by Professor Stephen MacMahon¹, Professor Robyn Norton³, and Dr Nicholas Birchall⁴. In 1997, I coordinated the pilot phase of the study in the Whangapapaora region of Auckland. Susan McAuley⁵ was responsible for all data collection in the pilot study and Dr Carolyn Coggan⁶ was responsible for facilitating the focus groups. Between 1997 and 1998, I was principally responsible for the co-ordination of the main study in the North Auckland and Central Auckland health districts. Susan McAuley⁵, Faith Mahoney⁵, Fiona MacKay⁵, and Cherie Mulholland⁵ undertook all data collection for the main study. Dr Peter Charlesworth⁷, Professor André van Rij⁸ and Dr Nicholas Birchall⁴ were responsible for grading all interviewed leg ulcer cases according to ulcer type.

I conducted all analyses presented in this thesis, with the exception of the capture-recapture analyses and the production of the regression spline graphs. Capture-recapture analysis was undertaken by Ms Jennifer Holden⁹ as part of her PhD dissertation in

¹ Currently: Director, Institute for International Health, University of Sydney, Australia. Formally: Associate Professor of Medicine and Director, Clinical Trials Research Unit, University of Auckland
² Co-Director, Clinical Trials Research Unit, University of Auckland
³ Currently: Director, Institute for International Health, University of Sydney, Australia. Formally: Director, Injury Prevention Research Centre, University of Auckland
⁴ Consultant Dermatologist, Auckland Dermatology, 17 Gilgit Road, Epsom, Auckland
⁵ Study Nurse, Clinical Trials Research Unit, University of Auckland
⁶ Associate Director, Injury Prevention Research Centre, University of Auckland
⁷ Consultant General and Vascular Surgeon, 9 St Marks Road, Remuera, Auckland
⁸ Professor of Surgery, Department of Surgery, Otago University, Dunedin
⁹ PhD student, Department of Statistics, University of Auckland
statistics, under the supervision of Professor Christopher Triggs\textsuperscript{10}. Ms Holden's research was supported by a grant from the Marsden Fund. Regression spline graphs were produced by Stephen Vander Hoorn\textsuperscript{11} and Michelle Wood\textsuperscript{11}.

\textsuperscript{10} Professor of Statistics, Department of Statistics, University of Auckland
\textsuperscript{11} Statistician, Clinical Trials Research Unit, University of Auckland
# Table of contents

ABSTRACT ............................................................................................................. I

ACKNOWLEDGEMENTS .................................................................................. II

CONTRIBUTION OF STUDY INVESTIGATORS ............................................. V

TABLE OF CONTENTS ....................................................................................... VII

LIST OF TABLES ................................................................................................. XIV

LIST OF FIGURES .............................................................................................. XXIV

SUMMARY ........................................................................................................... XXVII

SECTION 1 ........................................................................................................... 1

1. THE PATHOPHYSIOLOGY, TREATMENT, AND PUBLIC HEALTH IMPORTANCE OF
   LEG ULCERS ............................................................................................... 1
   1.1 DEFINITION OF A LEG ULCER ................................................................ 2
   1.2 THE PATHOPHYSIOLOGY OF LEG ULCERS ........................................ 3
       1.2.1 Historical views on the pathophysiology of leg ulcers ................. 3
       1.2.2 Current views on the pathophysiology of leg ulcers .................. 4
       1.2.2.1 Circulation of the lower leg .................................................. 5
       1.2.2.2 Types of leg ulcers .............................................................. 7
   1.3 THE MANAGEMENT OF LEG ULCERS .............................................. 14
       1.3.1 Historical approach to the management of leg ulcers ............... 14
       1.3.2 Current approach to the management of leg ulcers .................... 15
           1.3.2.1 Dressings ........................................................................... 16
           1.3.2.2 Topical applications ......................................................... 17
           1.3.2.3 Compression therapy ....................................................... 17
           1.3.2.4 Surgery ............................................................................ 18
           1.3.2.5 Pharmacological agents ................................................... 19
           1.3.2.6 Ultrasound, electrical stimulation, and laser therapy .......... 20
           1.3.2.7 Leg elevation and exercise ................................................ 21
           1.3.2.8 Zinc .................................................................................. 21
           1.3.2.9 Naturopathic medications ................................................ 22
           1.3.2.10 Other therapeutic options .............................................. 23
   1.4 THE PUBLIC HEALTH IMPORTANCE OF LEG ULCERS .................. 23
       1.4.1 Health problems caused by leg ulcers ...................................... 23
           1.4.1.1 The natural history of leg ulcers ....................................... 24
           1.4.1.2 The impact of leg ulcers on quality of life ......................... 25
           1.4.1.3 Morbidity and mortality in individuals with leg ulcers ....... 27
       1.4.2 Health care resources consumed in the care of leg ulcers ............ 28
       1.4.3 Disease prevention and the need for further research ............... 31
6.5.2.3 Overall quality of the evidence................................................. 104
6.5.3 Venous thrombosis and related risk factors for leg ulcers................... 105
6.5.3.1 History of venous thrombosis.............................................. 105
6.5.3.2 Surgical interventions...................................................... 107
6.5.3.3 Reproductive health....................................................... 112
6.5.3.4 Immobility................................................................. 115
6.5.3.5 Other risk factors for venous thrombosis............................... 116
6.5.3.4 Established cardiovascular risk factors in relation to leg ulcers........ 116
6.5.4.1 Obesity............................................................................ 117
6.5.4.2 Alcohol consumption...................................................... 118
6.5.4.3 Tobacco use................................................................. 119
6.5.4.4 Nutrition and blood factors.............................................. 121
6.5.4.5 Prior vascular disease.................................................... 124
6.5.4.6 Diabetes........................................................................ 126
6.5.5 Other putative risk factors for the development of leg ulcers............. 129
6.5.5.1 Demographic risk factors................................................. 129
6.5.5.2 Socio-economic status.................................................... 131
6.5.5.3 Arthritis.......................................................................... 132
6.5.5.4 Other possible risk factors............................................... 133
6.6. CONCLUSIONS.......................................................................... 134

7. THE AUCKLAND LEG ULCER CASE-CONTROL STUDY – STUDY RATIONALE AND
   DESIGN......................................................................................... 136

7.1 STUDY RATIONALE......................................................................... 136
7.1.1 Study goals and objectives.................................................... 136
7.1.2 Choice of study design......................................................... 137
7.1.3 Study hypotheses.................................................................. 138
7.2 GENERAL DESIGN CONSIDERATIONS........................................ 138
7.2.1 Study base........................................................................... 138
7.2.2 Definition of a leg ulcer....................................................... 139
7.2.3 Case definition..................................................................... 139
7.2.4 Control definition.............................................................. 139
7.2.5 Inclusion and exclusion criteria............................................ 140
7.3 RECRUITMENT OF STUDY PARTICIPANTS.................................... 140
7.3.1 Identification and recruitment of cases................................. 140
7.3.2 Identification and recruitment of controls.............................. 141
7.3.2.1 Selection of controls from the electoral roll....................... 141
7.3.2.2 Strategies for improving control recruitment.................... 142
7.3.3 Cultural issues..................................................................... 143
7.3.4 Ethics and privacy issues.................................................... 144
7.4 SAMPLE SIZE............................................................................. 144
7.4.1 Estimated sample size and study power for all leg ulcer cases........ 144
7.4.2 Estimated sample size and study power for subgroup analyses....... 146
7.5 STUDY INTERVIEW...................................................................... 147
7.5.1 Obtaining consent................................................................ 147
7.5.2 Assessment of cognitive status.......................................... 148
7.5.3 Collection of health status information................................. 149
7.5.4 Collection of descriptive case information............................ 150
7.5.5 Collection of exposure information.................................... 150
7.5.5.1 Demographic risk factors............................................... 151
7.5.5.2 Modifiable risk factors.................................................... 151
7.5.5.3 Non-modifiable risk factors.............................................. 152
7.5.5.4 Haematological risk factors............................................ 153
7.5.6 Collection of outcome information..................................... 155
7.5.6.1 Lower leg signs and symptoms....................................... 155
7.5.6.2 Assessment of intermittent claudication........................... 155
8. THE AUCKLAND LEG ULCER CASE-CONTROL STUDY – RESULTS

8.1 RECRUITMENT SUMMARY

8.1.1 Study participants

8.1.2 Demographic characteristics

8.1.3 Cognitive status of participants

8.2 DESCRIPTIVE CASE INFORMATION

8.2.1 Number and location of current leg ulcers

8.2.2 Number and location of previous leg ulcers

8.2.3 Age at onset

8.2.4 Ulcer recurrence and duration

8.2.5 Treatment

8.2.5.1 Current caregivers

8.2.5.2 Current treatment

8.2.5.3 Hospitalisation

8.2.6 Patients’ perceptions

8.3 ULCER TYPE

8.3.1 Classification of ulcer type

8.3.2 Validation of grading process

8.4 STUDY POWER

8.5 DETERMINANTS OF ULCER OCCURRENCE AND RECURRENCE

8.5.1 History of venous thrombosis

8.5.2 Surgical interventions

8.5.2.1 Previous surgery

8.5.2.2 Anaesthesia type

8.5.2.3 Prolonged immobility due to surgery

8.5.2.4 Leg fracture or injury

8.5.3 Varicose veins

8.5.4 Reproductive health

8.6 RISK FACTOR ASSESSMENT BY SUBGROUPS

8.6.1 Analysis by ulcer type

8.6.2 Analysis by first-ever ulcer cases versus recurrent ulcer cases
9. **THE AUCKLAND LEG ULCER CASE-CONTROL STUDY – DISCUSSION**...195

9.1 **SUMMARY OF KEY FINDINGS**.................................195
  9.1.1 Recruitment summary........................................195
  9.1.2 Summary of case information................................195
  9.1.3 Summary of ulcer type........................................197
  9.1.4 Summary of main risk factors.................................197
  9.1.5 Summary of subgroup analyses..............................199
  9.1.6 Other measures of association...............................199

9.2 **STUDY STRENGTHS AND LIMITATIONS**.......................200
  9.2.1 Precision....................................................200
  9.2.2 Validity.......................................................201
    9.2.2.1 Selection bias...........................................202
    9.2.2.2 Information bias........................................207
    9.2.2.3 Confounding..............................................213
  9.2.3 Overall quality of the study................................214

9.3 **CONSISTENCY WITH PREVIOUSLY PUBLISHED FINDINGS**....215
  9.3.1 Descriptive case information................................216
  9.3.2 Ulcer type....................................................218
  9.3.3 Risk factor information......................................220
    9.3.3.1 Deep vein thrombosis as a risk factor....................220
    9.3.3.2 Surgery as a risk factor................................221
    9.3.3.3 Anaesthesia type as a risk factor........................224
    9.3.3.4 Prolonged immobility due to surgery as a risk factor..225
    9.3.3.5 Leg fracture or injury as a risk factor..................225
    9.3.3.6 Varicose veins as a risk factor..........................226
    9.3.3.7 Reproductive risk factors in women.......................227

9.4 **IMPLICATIONS**..................................................233
  9.4.1 Prevention of leg ulcers.....................................233
    9.4.1.1 Prevention of leg ulceration via the prevention of venous thromboses..............................................234
    9.4.1.2 Prevention of leg ulceration via the prevention of risk factors related to venous thromboses........235
  9.4.2 Diagnosis of leg ulcers.......................................237
  9.4.3 Other implications............................................237

SECTION 4........................................................................239

10. **OVERALL CONCLUSIONS**..........................................239
  10.1 The occurrence of leg ulcers...................................239
  10.2 The burden associated with leg ulcers.......................240
  10.3 Risk factors for the development of leg ulcers............240

TABLES............................................................................242

FIGURES............................................................................243
APPENDIX A .......................................................................................................................... 244

1. PILOT PHASE OF THE AUCKLAND LEG ULCER STUDY ............................................. 244
   1.1 STUDY GOALS AND OBJECTIVES ................................................................. 244
   1.2 GENERAL DESIGN CONSIDERATIONS ...................................................... 244
      1.2.1 Study design ...................................................................................... 244
      1.2.2 Study base ...................................................................................... 245
      1.2.3 Case and control definitions ............................................................. 245
   1.3 RECRUITMENT OF STUDY PARTICIPANTS ............................................. 245
      1.3.1 Identification and recruitment of health professionals................ 246
      1.3.2 Identification and recruitment of cases ............................................ 246
      1.3.3 Identification and recruitment of controls ....................................... 247
   1.4 COLLECTION OF EXPOSURE INFORMATION ........................................... 248
      1.4.1 Questionnaire design ...................................................................... 248
      1.4.2 Focus group assessment of the study questionnaire .................... 248
      1.4.3 Case and control assessment of the study questionnaire .............. 249
   1.5 STUDY RESULTS .......................................................................................... 250
      1.5.1 Practicalities and appropriateness of case identification .............. 250
      1.5.2 Practicalities and appropriateness of control identification ......... 251
      1.5.3 Development and testing of the study questionnaire ..................... 252
      1.5.4 Assessment of the need for matching .............................................. 253
      1.5.5 Assessment of time and resources .................................................. 253
   1.6 CONCLUSIONS .............................................................................................. 254

APPENDIX B: STUDY MATERIALS USED IN THE AUCKLAND LEG ULCER STUDY ...... 257

APPENDIX C ..................................................................................................................... 258

1. GUIDELINES USED BY THE ASSESSMENT COMMITTEE TO GRADE LEG ULCER CASES ................................................................. 258
   1.1 VENOUS LEG ULCER CASES .................................................................. 258
   1.2 ARTERIAL LEG ULCER CASES ................................................................. 258
   1.3 MIXED LEG ULCER CASES .................................................................... 259
   1.4 OTHER TYPES OF LEG ULCER CASES .................................................. 259

APPENDIX D: EXPLORATORY ANALYSIS OF CONTINUOUS EXPOSURE AND CONFOUNDING VARIABLES ................................................................. 261

REFERENCES .................................................................................................................. 262
# List of tables

Table

1. Summary of population-based leg ulcer prevalence studies, sorted by ulcer type then ulcer status (study design and results)

2. Summary of health professional-based leg ulcer prevalence studies, sorted by ulcer type then ulcer status (study design and results)

3. Previous studies indicating the principal sources of care for individuals with leg ulcers

4. Summary of the prevalence of leg ulcers: all studies combined

5. Summary of the point prevalence of leg ulcers: all studies combined

6. Hospitalisation rates based on the number of people discharged from public hospitals in 1996/1997 with “chronic ulcers of the skin”

7. Hospitalisation rates for Maori and non-Maori, based on the number of people discharged from public hospitals in 1996/1997 with “chronic ulcers of the skin”

8. Number and type of health professional groups involved in the Auckland leg ulcer study, according to study region

9. Number and source of case notifications

10. Age and region-specific point prevalence (current leg ulcer cases only)
<table>
<thead>
<tr>
<th>Table</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.</td>
</tr>
<tr>
<td>12.</td>
</tr>
<tr>
<td>13.</td>
</tr>
<tr>
<td>14.</td>
</tr>
<tr>
<td>15.</td>
</tr>
<tr>
<td>16.</td>
</tr>
<tr>
<td>17.</td>
</tr>
<tr>
<td>18.</td>
</tr>
<tr>
<td>19.</td>
</tr>
<tr>
<td>20.</td>
</tr>
<tr>
<td>21.</td>
</tr>
</tbody>
</table>
Table

22. Comparison between cases notified with healed leg ulcers only and cases notified with current leg ulcers

23. Comparison between self-notified cases and cases notified by health professionals

24. Age and region-specific cumulative incidence rates (current leg ulcer cases only)

25. Age-adjusted cumulative incidence according to study region (current leg ulcer cases only), using the 1996 New Zealand population as the standard population

26. Age and gender-specific cumulative incidence rates (current leg ulcer cases only)

27. Age-adjusted cumulative incidence according to gender (current leg ulcer cases only), using the 1996 New Zealand population as the standard population

28. Comparison of demographic characteristics of current leg ulcer cases, by source of notification

29. Number of notified current leg ulcer cases in Central and North Auckland, according to source of ascertainment (subgroup information)

30. Capture-recapture data for all current leg ulcer cases. Fitted estimates and coefficients from all models involving up to three 2-way interaction terms, ordered by AIC (lowest to highest)
Table

31. Capture-recapture data for all current leg ulcer cases (incident cases only). Fitted estimates and coefficients from all models involving up to three 2-way interaction terms, ordered by AIC (lowest to highest)

32. Capture-recapture data for all current leg ulcer cases (prevalent cases only). Fitted estimates and coefficients from all models involving up to three 2-way interaction terms, ordered by AIC (lowest to highest)

33. Capture-recapture data for all current leg ulcer cases (males only). Fitted estimates and coefficients from all models involving up to three 2-way interaction terms, ordered by AIC (lowest to highest)

34. Capture-recapture data for all current leg ulcer cases (females only). Fitted estimates and coefficients from all models involving up to three 2-way interaction terms, ordered by AIC (lowest to highest)

35. Capture-recapture data for all current leg ulcer cases (0 to 69 year old cases only). Fitted estimates and coefficients from all models involving up to three 2-way interaction terms, ordered by AIC (lowest to highest)

36. Capture-recapture data for all current leg ulcer cases (70 to 79 year old cases only). Fitted estimates and coefficients from all models involving up to three 2-way interaction terms, ordered by AIC (lowest to highest)

37. Capture-recapture data for all current leg ulcer cases (80 years plus cases only). Fitted estimates and coefficients from all models involving up to three 2-way interaction terms, ordered by AIC (lowest to highest)
Table

38. Adjusted rates for all cases with current leg ulcers in Auckland, using capture-recapture analysis

39. Comparison of age-adjusted point prevalence and period prevalence data for leg ulcers from five countries, using the Segi world population as the standard population

40. Demographic profile of the Auckland leg ulcer study region compared to the New Zealand population as a whole, based on 1996 census data

41. Summary of case-control studies that have investigated risk factors for leg ulceration, sorted by ulcer type then year of publication (study design, risk factors, strengths and limitations)

42. Power calculations for case-control studies that have investigated risk factors for leg ulceration

43. Summary of findings from case-control studies that reported on venous thrombosis, leg fracture or injury, varicose veins, and reproductive health issues (women only), as risk factors for leg ulcers

44. Summary of findings from case-control studies that reported on surgical risk factors for leg ulcers

45. Summary of findings from case-control studies that reported on mobility, body mass index, alcohol use, and smoking as risk factors for leg ulcers

46. Mean body mass index results from four case-control studies that reported on obesity as a risk factor for foot ulcers
Table

<p>| 47. | Mean serum and plasma zinc levels from three case-control studies that reported on zinc status as a risk factors for leg ulcers |
| 48. | Iron metabolism and serum proteins as risk factors for leg ulcers, as reported by Schraibman et al. (1985) |
| 49. | Summary of findings from case-control studies that reported on gender, ethnicity, and other risk factors for leg ulcers |
| 50. | Mean serum selenium, iron, and copper levels, albumin levels, and the copper/zinc ratio as risk factors for leg ulcers, as reported by Agren et al. (1986) |
| 51. | Mean total cholesterol, HDL-cholesterol, and triglyceride levels as risk factors for diabetic foot ulcers, as reported by Sriussadaporn et al. (1997) |
| 52. | Summary of findings from case-control studies that reported on prior vascular disease as a risk factor for leg ulcers |
| 53. | Summary of findings from case-control studies that reported on diabetes and diabetes-related conditions as risk factors for leg ulcers |
| 54. | Serum creatinine, urea, haemoglobin A1c, plasma glucose, and serum glucose levels from two case-control studies that reported on biochemical risk factors for diabetic foot ulcers |
| 55. | Mean duration of diabetes (in years) from four case-control studies that reported on risk factors for foot ulcers |</p>
<table>
<thead>
<tr>
<th>Table</th>
</tr>
</thead>
<tbody>
<tr>
<td>56.</td>
</tr>
<tr>
<td>57.</td>
</tr>
<tr>
<td>58.</td>
</tr>
<tr>
<td>59.</td>
</tr>
<tr>
<td>60.</td>
</tr>
<tr>
<td>61.</td>
</tr>
<tr>
<td>62.</td>
</tr>
<tr>
<td>63.</td>
</tr>
<tr>
<td>64.</td>
</tr>
<tr>
<td>65.</td>
</tr>
</tbody>
</table>
Table

66. Summary of Mini-Mental State Examination scores for interviewed cases and controls

67. Reliability of data, based on Mini-Mental State Examination score and interviewer assessment

68. Number and location of current leg ulcers in interviewed cases

69. Number and location of previous leg ulcers in interviewed cases

70. Duration of leg ulcers in interviewed cases

71. Leg ulcer treatment in interviewed cases

72. Number of cases who were hospitalised within the last five years because of their leg ulcers

73. Ulcer aetiology according to assessment committee grading (based on ankle-brachial index and pre-determined clinical criteria)

74. Level of agreement in ulcer grading - comparison between first and second assessor (3 categories)

75. Level of agreement in ulcer grading - comparison between first and second assessor (5 categories)

76. Level of agreement in ulcer grading - comparison between first assessment (paper based) and second assessment (clinical examination) - 3 categories
Table

77. Level of agreement in ulcer grading - comparison between first assessment (paper based) and second assessment (clinical examination) - 5 categories

78. Ulcer aetiology based on ankle-brachial index only (using an index of 0.6 as the cut-off)

79. Study power for actual sample size (241 cases and 224 controls), based on a 95% level of confidence, a minimum detectable odds ratio of 2.5, and a minimum exposure on the control group of 15%

80. Minimum odds ratios detectable for each major subtype of leg ulcers, for a variety of possible risk factors

81. Association between potential confounding variables and the risk of developing leg ulcers

82. Association between deep vein thrombosis and the risk of developing leg ulcers

83. Relationship between leg ulcers and deep vein thrombosis – stratification by varicose veins

84. Association between surgery and surgical type, and the risk of developing leg ulcers

85. Association between anaesthesia and number of bed days, and the risk of developing leg ulcers

86. Association between leg fracture or injury and varicose veins, and the risk of developing leg ulcers
<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>87.</td>
<td>Relationship between leg ulcers and varicose veins – stratification by deep vein thrombosis</td>
</tr>
<tr>
<td>88.</td>
<td>Association between pregnancy and breast-feeding and subsequent risk of leg ulcers in women</td>
</tr>
<tr>
<td>89.</td>
<td>Association between exposure to oestrogen and subsequent risk of leg ulcers in women</td>
</tr>
<tr>
<td>90.</td>
<td>Relationship between leg ulcers and deep vein thrombosis – stratification by pregnancy</td>
</tr>
<tr>
<td>91.</td>
<td>Relationship between leg ulcers and varicose veins – stratification by pregnancy</td>
</tr>
<tr>
<td>92.</td>
<td>Characteristics of nulligravid women according to marital status</td>
</tr>
<tr>
<td>93.</td>
<td>Association between pregnancy and marital status, and subsequent risk of leg ulcers in women</td>
</tr>
<tr>
<td>94.</td>
<td>Subgroup analyses results for the seven main risk factors for leg ulcers identified in this thesis</td>
</tr>
<tr>
<td>95.</td>
<td>The attributable risk percent and population attributable risk percent for the seven main risk factors for leg ulcers identified in this thesis</td>
</tr>
<tr>
<td>96.</td>
<td>Comparison between interviewed cases who were self-notified and those cases who were notified by a health professional, according to the seven main risk factors identified in this thesis</td>
</tr>
</tbody>
</table>
List of figures

Figure

1. Discharges from public hospitals in 1996/1997 for “chronic ulcers of the skin”, according to age (day and inpatients combined)

2. Auckland leg ulcer study region

3. Methods used to estimate the prevalence and incidence of leg ulcers, showing the traditional method versus the capture-recapture method of estimation

4. Age and gender distribution of all notified leg ulcer cases (current and healed)

5. Age and gender-specific point prevalence for current leg ulcer cases

6. Age and gender-specific period prevalence for current and healed leg ulcer cases

7. Age and gender-specific period prevalence for current leg ulcer cases

8. Age distribution of leg ulcer cases (healed versus current leg ulcer cases)

9. Age distribution of leg ulcer cases (self-notified cases versus cases notified by a health professional)

10. Age and gender-specific cumulative incidence rates for current leg ulcer cases

11. Number of current leg ulcer case notifications received each month during the study period, according to prevalent and incident cases
Figure

12. Age distribution of interviewed cases and controls

13. Number of current leg ulcers per case, according to gender

14. Number of leg ulcers in a lifetime, according to gender

15. Number of episodes of leg ulcers in a lifetime, according to gender

16. Age first developed leg ulcers, according to gender

17. Number of years with leg ulcers (recurrent cases only), according to gender

18. Duration of last leg ulcer (recurrent cases only), according to gender

19. Duration of current leg ulcer, according to gender

20. Number of bed days for cases hospitalised for leg ulcers, according to gender

21. Age when first baby born, in female participants

22. Age when last baby born, in female participants

23. Number of births, in female participants

24. Age at menarche, in female participants

25. Total oestrogen years, in female participants

26. Age at last natural period, in female participants
<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>27.</td>
<td>Odds ratios and 95% confidence intervals for the seven main risk factors for leg ulcers</td>
</tr>
<tr>
<td>28.</td>
<td>Odds ratios and 95% confidence intervals for the seven main risk factors for leg ulcers, by ulcer type</td>
</tr>
<tr>
<td>29.</td>
<td>Odds ratios and 95% confidence intervals for the seven main risk factors for leg ulcers, by ulcer event</td>
</tr>
<tr>
<td>30.</td>
<td>Odds ratios and 95% confidence intervals for the seven main risk factors for leg ulcers, by case type</td>
</tr>
<tr>
<td>31.</td>
<td>Odds ratios and 95% confidence intervals for history of venous thrombosis as a risk factor for leg ulcers</td>
</tr>
<tr>
<td>32.</td>
<td>Odds ratios and 95% confidence intervals for leg surgery, abdominal surgery, and varicose vein surgery as risk factors for leg ulcers</td>
</tr>
<tr>
<td>33.</td>
<td>Odds ratios and 95% confidence intervals for history of leg fracture and major leg injury as risk factors for leg ulcers</td>
</tr>
<tr>
<td>34.</td>
<td>Odds ratios and 95% confidence intervals for history of varicose veins as a risk factor for leg ulcers</td>
</tr>
<tr>
<td>35.</td>
<td>Odds ratios and 95% confidence intervals for nulligravida and oral contraceptive use as risk factors for leg ulcers in women</td>
</tr>
</tbody>
</table>