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Occupational leptospirosis in New Zealand

A thesis presented
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Abstract

Although a decreasing trend of human notifications was observed from 2001 to 2014 (Chapter 1), the incidence of human leptospirosis in New Zealand continues to be higher than in other high-income countries and affecting predominately people occupationally exposed to livestock (i.e. abattoir workers and farmers). Additionally, evidence suggests that leptospirosis may have a higher detrimental effect on production in deer compared with beef cattle or sheep. It was also observed that vaccination against *Leptospira* of not previously infected animals reduce the risk of urinary shedding of leptospires after challenge, and that there is limited evidence supporting or disproving that maternally derived antibodies interfere with the effect of vaccination when animals are vaccinated at a young age.

When sero-positivity was defined as a serum microscopic agglutination test (MAT) titre of ≥ 48 , 6.6% of farmers (Chapter 2) and 5.1% of veterinarians (Chapter 3) were sero-positive to at least one of five *Leptospira* serovars (Hardjo-bovis, Pomona, Copenhageni, Ballum, Tarassovi). Veterinarians had a higher risk of being sero-positive when they slaughtered cattle or pigs at home or worked in a mixed animal practice. Assisting calving of cattle or deer, farming deer alone or in combination with cattle and/or sheep, flat terrain on farm, and abundance of wild deer on farm, increased *Leptospira* sero-positivity of farmers. Apart from vaccinating farmed livestock, increased awareness of such risk factors and the use of protective equipment may reduce the human leptospirosis incidence in these occupational groups.

Similar to earlier observations in abattoir workers, *Leptospira* sero-prevalence of farmers and veterinarians was associated with the recall of influenza-like illness of sampled individuals. Using the estimated incidence of influenza-like illness attributable to *Leptospira* infection (population attributable risk) of veterinarians (0.05%), farmers (1.3%) and abattoir workers (2.7%), we quantified the burden of human leptospirosis in terms of disability-adjusted life years (DALYs) and economic

cost of infection; the latter including the cost of vaccination, which is primarily used in dairy cattle (Chapter 4). Annual DALYs were estimated to be 0.43 per 100,000 people in New Zealand, and 16.76 per 100,000 people when only considering the occupationally-exposed population (abattoir workers, farmers, veterinarians). This ranks leptospirosis in New Zealand's high-risk population similar to worldwide estimates of DALYs for rabies and dengue. The total annual cost of leptospirosis due to human disease (i.e. treatment and absence from work); production loss in deer, beef cattle, and sheep; and the cost for vaccinating them was estimated to be NZ\$25.36 million. One third of this total was attributed to vaccination of dairy cattle. The annual cost of human treatment and workplace absence due to severe and mild leptospirosis was NZ\$4.49 million. Total lost production cost was NZ\$11.31 million, half of which was attributable to reproductive and growth reduction in deer. No estimates are currently available from any other country for the public health burden and the overall economic loss including farmed livestock for this disease.

Since vaccination of livestock is currently regarded as the most effective means of preventing human exposure, the literature on the efficacy of *Leptospira* vaccines for preventing urinary shedding was systematically reviewed (Chapter 5). The meta-analysis of vaccination trial results, using articles with sufficiently detailed data, resulted in a pooled vaccine efficacy estimate of 82% when shedding was assessed by culture.

The findings of this thesis contribute towards a better understanding of the public health burden, economic cost, infection sources for humans, and the efficacy of vaccination for reducing the risk of *Leptospira* urinary shedding in domestic livestock.

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Declaration

This thesis was formatted as five independent research chapters suitable for journal publication. Therefore, concepts and/or methodology described in a chapter may be repeated in another chapter. My input as main author of this research was to plan and coordinate sampling of veterinarians and farmers, develop questionnaires to record relevant information, process samples in the laboratory and test them for antibodies against *Leptospira*, conduct systematic literature search, select studies for meta-analysis, analyse data, and draft manuscripts reporting findings. People that contributed substantially to the research were made co-authors as listed at the beginning of each chapter.

List of abbreviations

MUHEC:	Massey University Human Ethics Committee
MAT:	Microscopic Agglutination Test
OR:	Odds Ratio
RR:	Relative Risk
PR:	Prevalence Ratio
CI:	Confidence Interval
PI:	Probability Interval
PAR:	Population Attributable Risk
PAF:	Population Attributable Fraction
LRT:	Likelihood Ratio Test
REML:	Restricted Maximum Likelihood
MCMC:	Markov Chain Monte Carlo
DALYs:	Disability-Adjusted Life Years
YLL:	Years of Life Lost
YLD:	Years Lost due to Disability
MDA:	Maternally Derived Antibodies
IgM:	Immune Globulin of class M
IgG:	Immune Globulin of class G
PBMC:	Proliferation of peripheral Blood Mononuclear Cells
PCR:	Polymerase Chain Reaction
FA:	Fluorescent Antibody
DFM:	Dark Field Microscopy
ACC:	Accident Compensation Corporation

List of publications

- Benschop, J., C. Heuer, J. Collins-Emerson, L. Stringer, J. Sanhueza, and P. Wilson (2012). “An independent review of leptospirosis vaccination guidelines”. In: *Proceedings of the Society of Dairy Cattle Veterinarians of the New Zealand Veterinary Association*. Vol. 66, pp. 2.13.1–2.13.5.
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- Sanhueza, J., C. Heuer, P. Wilson, J. Benschop, and J. Collins-Emerson (2013). “*Leptospira spp.* seroprevalence in veterinarians: preliminary results and challenges in quantifying exposure”. In: *Proceedings of the Food Safety, Animal Welfare & Biosecurity, Epidemiology & Animal Health Management, and Industry Branches of the New Zealand Veterinary Association*. Vol. 66, pp. 141–146.

List of conference presentations

- Benschop, J., C. Heuer, J. Collins-Emerson, L. Stringer, J. Sanhueza, and P. Wilson (2012). “An independent review of leptospirosis vaccination guidelines”. In: *Proceedings of the Society of Dairy Cattle Veterinarians of the New Zealand Veterinary Association*. Vol. 66, pp. 2.13.1–2.13.5.
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- Heuer, C., J. Sanhueza, E. Vallee, P. Wilson, J. Benschop, and J. Collins-Emerson (2015c). “Hardjo and Pomona - Two pathogens with different ecological risk”. In: *9th Scientific Meeting of International Leptospirosis Society (ILS)*.
- Heuer, C., J. Sanhueza, E. Vallee, P. Wilson, J. Benschop, and J. Collins-Emerson (2015d). “Hardjo and Pomona - Two pathogens with different ecological risk”. In: *9th Scientific Meeting of International Leptospirosis Society (ILS)*.
- Sanhueza, J., C. Heuer, P. Wilson, J. Benschop, and J. Collins-Emerson (2013a). “*Leptospira* spp. seroprevalence in veterinarians: preliminary results and challenges in quantifying exposure”. In: *Proceedings of the Food Safety, Animal Welfare & Biosecurity, Epidemiology & Animal Health Management, and Industry Branches of the New Zealand Veterinary Association*. Vol. 66, pp. 141–146.
- Sanhueza, J., C. Heuer, P. Wilson, J. Benschop, and J. Collins-Emerson (2013b). “Occupational exposure and risk factors for *Leptospira* in New Zealand workers”. In: *8th Scientific Meeting of International Leptospirosis Society (ILS)*.
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- Sanhueza, J., C. Heuer, E. Vallee, P. Wilson, J. Benschop, and J. Collins-Emerson (2015c). “Population impact of leptospirosis on public health and livestock production”. In: *14th International Symposium on Veterinary Epidemiology & Economics (ISVEE)*.

Contents

Abstract	iii
Acknowledgement	v
Declaration	vii
List of abbreviations	ix
List of publications	xi
List of conference presentations	xiii
List of figures	xxi
List of tables	xxiii
Introduction	xxv
1 Literature review	1
1.1 Summary	2
1.2 Introduction	4
1.3 Materials and Methods	5
1.4 Human leptospirosis	5
1.5 <i>Leptospira</i> in domestic animals and wildlife	8
1.6 Production effects	14
1.6.1 Cattle	14
1.6.2 Sheep	15
1.6.3 Deer	16
1.7 Registered vaccines	17
1.8 Vaccine coverage	17
1.9 Immunity against <i>Leptospira</i>	24

1.9.1	Humoral immune response	24
1.9.2	Cell-mediated immunity	26
1.10	Maternally derived antibodies (MDA) and vaccination	27
1.11	Vaccine efficacy	29
1.11.1	Cattle	30
1.11.2	Deer and sheep	31
1.12	Multivalent and monovalent vaccines	33
1.13	Long term vaccine efficacy	34
1.14	Conclusion	36
1.15	Acknowledgement	38
	References	39
2	<i>Leptospira</i> sero-positivity in farmers	51
2.1	Summary	52
2.2	Introduction	53
2.3	Material and Methods	55
2.3.1	Sampling frame	55
2.3.2	Sample collection	55
2.3.3	Serological testing	55
2.3.4	Questionnaire	56
2.3.5	Data description	56
2.3.6	Sero-prevalence in farmers and animals	56
2.3.7	Multivariable model building	57
2.3.8	Multivariable model specification and convergence diagnostics	57
2.3.9	Leptospirosis in farmers pre-sampling	57
2.3.10	Influenza-like illness	58
2.3.11	Statistical software	58
2.3.12	Human ethics application	58
2.4	Results	59
2.4.1	Serology in farmers	59
2.4.2	Animal contact, vaccination and previous animal serological status	61
2.4.3	Association between previous animal sero-prevalence and farmer sero-status	61
2.4.4	Risk factors for <i>Leptospira</i> sero-positivity in farmers	63

2.4.5	Previous leptospirosis	64
2.4.6	Association between serology and influenza-like illness	65
2.5	Discussion	67
2.6	Conclusion	72
2.7	Acknowledgement	73
References		75
3	<i>Leptospira</i> sero-positivity in veterinarians	81
3.1	Summary	82
3.2	Introduction	83
3.3	Materials and Methods	85
3.3.1	Study Design	85
3.3.2	Recording of risk factors	85
3.3.3	Statistical analysis	86
3.3.4	Human ethics application	87
3.4	Results	88
3.4.1	Titre distribution	88
3.4.2	Sero-prevalence	88
3.4.3	Age and gender	89
3.4.4	Occupational exposure to animals	89
3.4.5	History of previous leptospirosis episodes	90
3.4.6	Influenza-like illness in the last 18 months	91
3.4.7	Unadjusted associations	91
3.4.8	Multivariable analysis	92
3.5	Discussion	94
3.6	Conclusion	98
3.7	Acknowledgement	99
References		101
4	Burden of leptospirosis in New Zealand	105
4.1	Summary	106
4.2	Introduction	107
4.3	Materials and Methods	109
4.3.1	Simulation model	109
4.3.2	Burden of leptospirosis	109

4.3.3	Cost of leptospirosis	112
4.4	Results	118
4.4.1	Annual number of human leptospirosis cases	118
4.4.2	DALYs	118
4.4.3	Human and animal cost of leptospirosis	119
4.5	Discussion	123
4.6	Conclusion	128
4.7	Acknowledgement	129
References		131
5	Meta-analysis of vaccine efficacy	137
5.1	Summary	138
5.2	Introduction	140
5.3	Materials and Methods	143
5.3.1	Research question	143
5.3.2	Literature search strategy	143
5.3.3	Screening of records	143
5.3.4	Eligibility criteria	144
5.3.5	Data extraction	144
5.3.6	Bias assessment for individual studies	144
5.3.7	Methods for measuring shedding of leptospire in urine	145
5.3.8	Meta-analysis	145
5.3.9	Software	146
5.4	Results	147
5.4.1	Selection of articles	147
5.4.2	Data extraction and bias assessment	148
5.4.3	Meta-analysis exclusions	148
5.4.4	Articles included in meta-analyses	150
5.4.5	Meta-analysis of vaccine efficacy assessed by culture	150
5.4.6	Meta-analysis of vaccine efficacy assessed by PCR	152
5.4.7	Meta-analysis of vaccine efficacy assessed by FA	153
5.4.8	Urinary shedding assessed by DFM	154
5.5	Discussion	155
5.6	Conclusion	160
5.7	Acknowledgement	161

References **163**

6 General discussion **171**

6.1	Introduction	172
6.2	Under-ascertainment of human leptospirosis	172
6.3	Occupational exposure	174
6.4	<i>Leptospira</i> sero-positivity and influenza-like illness	176
6.5	Burden of leptospirosis in New Zealand	177
6.6	Control of leptospirosis	178
6.7	Methodology critiques	181
6.7.1	Microscopic agglutination test	181
6.7.2	Antibody titre duration	181
6.7.3	Recalling influenza-like illness	182
6.8	Future research	183
6.8.1	Leptospirosis in dairy cattle	183
6.8.2	Leptospirosis in wildlife	183
6.8.3	Sero-prevalence to serovars other than Hardjo-bovis and Pomona in livestock	184
6.8.4	Spatial analysis of animal's serology data	184
6.8.5	Post-acute leptospirosis sequelae	185
6.8.6	Serological surveys in other at risk occupations	185
6.8.7	Analysis of human notified cases	185

References **187**

Appendices **195**

.1	Appendix I: Farmer questionnaire	196
.2	Appendix II: Prevalence model	208
.3	Appendix III: Prevalence model clustering	209
.4	Appendix IV: Multivariable model	210
.5	Appendix V: Veterinarian questionnaire	215
.6	Appendix VI: Burden and cost Code	222
.7	Appendix VII: Burden and cost assumptions	240
.8	Appendix VIII: Summary of trials for meta-analysis	245

List of figures

1.1	Number of notified cases 2001-2014	7
1.2	Number of notified cases by serovar 2001-2014	8
1.3	Percentage of notified cases by occupation 2001-2014	9
2.1	Spatial distribution of farms	59
2.2	MAT titre distribution	60
3.1	MAT titre distribution by serovar	88
3.2	Percentage of time spent in contact with different animal species . . .	90
4.1	Density distribution of annual cost per 100,000 people by species . . .	121
5.1	Systematic selection of studies	147
5.2	Forest plot culture	151
5.3	Funnel plot culture	152
5.4	Forest plot PCR	153
5.5	Forest plot FA	154

List of tables

1.1	Sero-prevalence in beef cattle, sheep, and deer	11
1.2	Registered vaccines	19
2.1	<i>Leptospira</i> sero-prevalence	60
2.2	<i>Leptospira</i> animal sero-prevalence	62
2.3	Unconditional associations	63
2.4	Multivariable model	65
2.5	<i>Leptospira</i> sero-status and influenza-like illness	66
3.1	Sero-prevalence in veterinarians	89
3.2	<i>Leptospira</i> sero-positivity and influenza-like illness	91
3.3	Unadjusted associations	92
3.4	Multivariable model	93
4.1	Expected annual incidence	118
4.2	DALYs	119
4.3	Cost of leptospirosis	120
5.1	Systematic bias assessment	149

