

# Contents

<b>1</b>	<b>Introduction .....</b>	<b>1</b>
1.1	The threadworm <i>Strongyloides stercoralis</i> , an overlooked soil-transmitted helminth .....	2
1.1.1	<i>Strongyloides stercoralis</i> biology & life cycle .....	2
1.1.2	Strongyloidiasis.....	4
1.1.3	Hyperinfection.....	6
1.1.4	Diagnosis.....	9
1.1.5	Treatment.....	11
1.1.6	Epidemiology .....	12
1.1.7	Risk factors for <i>S. stercoralis</i> and hookworm infection.....	14
1.2	The three “major soil-transmitted helminths” .....	17
1.3	Preventive chemotherapy to control soil-transmitted helminths .....	19
1.4	Identification of parasite geographical distribution and high risk areas.....	22
1.5	Knowledge gaps for <i>S. stercoralis</i> control .....	23
<b>2</b>	<b>Aims of the thesis, study objectives and research questions .....</b>	<b>27</b>
2.1	Aims of the thesis .....	28
2.2	Main objectives .....	28
2.3	Research questions .....	29
<b>3</b>	<b>Material and methods .....</b>	<b>31</b>
3.1	Ethical considerations .....	32
3.2	Study area.....	32
3.2.1	Study countries.....	32
3.2.2	Study sites.....	35
3.3	Diagnosis and treatment .....	36
3.4	Research approach and study design .....	38
3.4.1	Community-effectiveness of annual targeted ivermectin treatment against <i>S. stercoralis</i> .....	38
3.4.2	Cost-effectiveness of control options .....	40
3.4.3	National <i>S. stercoralis</i> distribution and case number in Cambodia .....	42
3.4.4	Distribution of hookworm - <i>S. stercoralis</i> co-infection in North Cambodia .....	42
3.4.5	Distribution of, and risk factors for, hookworm infection risk and intensity, Southern Lao PDR .....	44

<b>4</b>	<b>Ivermectin and sanitation can control <i>S. stercoralis</i></b>	<b>47</b>
4.1	Introduction	49
4.3	Methods	51
4.3.1	Ethics statement	51
4.3.2	Study setting and population	51
4.3.3	Study design and participants	51
4.3.4	Demographic, socioeconomic, knowledge and behavioural data	52
4.3.5	Parasitological data	52
4.3.6	Quality control	54
4.3.7	Statistical analysis	54
4.4	Results	57
4.4.1	Study population and compliance	57
4.4.2	<i>S. stercoralis</i> infection risk at baseline and at follow-up	58
4.4.3	Cure rate of ivermectin	59
4.4.4	Risk factors for <i>S. stercoralis</i> infection at baseline and at follow-up	60
4.5	Discussion	63
4.6	Acknowledgments	69
4.7	Appendix	69
4.7.1	Baseline characteristics of participants included in the analysis of <i>S. stercoralis</i> infection at baseline and at follow-up	69
4.7.2	Bivariate associations between explanatory variables submitted for variable selection and <i>S. stercoralis</i> infection risk at baseline and at follow-up	71
4.7.3	Incidence rate ratios for risk factors of <i>S. stercoralis</i> infection risk at follow-up	73
4.7.4	Results of the multivariate model for <i>S. stercoralis</i> infection risk at follow-up, excluding the village with 4% sanitation coverage	74
<b>5</b>	<b>Morbidity associated with <i>S. stercoralis</i></b>	<b>75</b>
5.1	Introduction	77
5.2	Methods	79
5.2.1	Ethics statement	79
5.2.2	Study area, design and population	80
5.2.3	Clinical assessment	81
5.2.4	Assessment of parasitological infection	81
5.2.5	Data management and statistical analysis	82
5.3	Results	83
5.3.1	Study population	83

5.3.2	Symptoms associated with <i>S. stercoralis</i> infection	87
5.3.3	Symptom resolution after treatment	87
5.3.4	Growth retardation in children and <i>S. stercoralis</i> infection	88
5.4	Discussion	92
5.5	Acknowledgements	98
5.6	Appendix	99
5.6.1	Prevalences and number of cases of all diagnosed helminths and protozoa	99
5.6.2	Association between symptoms and <i>S. stercoralis</i> parasite load	100
5.6.3	Complete results of multivariate logistic regressions assessing the association between each reported symptom and <i>S. stercoralis</i>	101
5.6.4	Symptoms reported before and after ivermectin treatment by <i>S. stercoralis</i> infected patients including co-infection with other parasites (208 patients)	106
<b>6</b>	<b>Cost-effectiveness of control strategies for <i>S. stercoralis</i></b>	<b>109</b>
6.1	Introduction	111
6.2	Methods	113
6.2.1	Study setting & population	113
6.2.2	Study perspective and outcomes	114
6.2.3	Modelling	114
6.2.4	Interventions	116
6.2.5	Clinical	117
6.2.6	Costs	118
6.2.7	Uncertainty	123
6.3	Results	123
6.4	Discussion	130
6.5	Acknowledgements	137
<b>7</b>	<b><i>S. stercoralis</i> mapping in Cambodia</b>	<b>139</b>
7.1	Introduction	142
7.2	Methods	144
7.2.1	Ethics statement	144
7.2.2	Study setting	144
7.2.3	Study population and design	145
7.2.4	Assessment of <i>Strongyloides stercoralis</i> infection	145
7.2.5	Individual risk factor data	146
7.2.6	Environmental data	146
7.2.7	Data management	147

7.2.8	Statistical Analysis .....	147
7.2.9	Prediction of <i>S. stercoralis</i> at non-surveyed locations.....	149
7.3	Results .....	149
7.3.1	Study population .....	149
7.3.2	<i>Strongyloides stercoralis</i> prevalence.....	151
7.3.3	Spatial correlation .....	153
7.3.4	Result of the model validation and predictive model .....	154
7.3.5	Risk factors for <i>S. stercoralis</i> infection .....	155
7.3.6	Spatial prediction of <i>S. stercoralis</i> infection risk .....	158
7.4	Discussion .....	160
7.5	Acknowledgements .....	166
7.6	Appendix.....	166
7.6.1	Bayesian Model Formulation .....	166
7.6.2	Maps of environmental predictors.....	169
7.6.3	Results of the bivariate non-spatial regressions for individual-level risk factors.....	170
8	<b><i>S. stercoralis</i>-hookworm co-infection in Cambodia .....</b>	<b>172</b>
8.1	Introduction.....	175
8.2	Methods .....	177
8.2.1	Study setting and design .....	177
8.2.2	Parasitological data and case definition.....	177
8.2.3	Demographic, socioeconomic, knowledge and hygiene practices data .....	178
8.2.4	Environmental data .....	179
8.2.5	Statistical analysis.....	180
8.3	Results .....	182
8.3.1	Study population and size .....	182
8.3.2	<i>S. stercoralis</i> and hookworm prevalence .....	185
8.3.3	Determinants of <i>S. stercoralis</i> and hookworm mono- and co-infection risks.....	185
8.3.4	Clustering tendency of <i>S. stercoralis</i> and hookworm mono- and co-infection.....	186
8.3.5	Prediction of <i>S. stercoralis</i> and hookworm mono- and co-infection risks .....	191
8.4	Discussion .....	193
8.5	Conclusion .....	199
8.6	Ethics approval and consent to participate.....	199
8.7	Acknowledgements .....	200
8.8	Appendix.....	200
8.8.1	Formulation of the multinomial model .....	200

8.8.2	Results of the variable selection using bivariate multinomial regressions .....	202
8.8.3	Results of model validation for predictive models.....	205
9	<b>Hookworm risk profiling in Southern Lao PDR .....</b>	<b>206</b>
9.1	Introduction.....	208
9.2	Methods .....	209
9.2.1	Ethics Statement .....	209
9.2.2	Study Area .....	209
9.2.3	Parasitological, Demographic, Socioeconomic, and Behavioural Data .....	210
9.2.4	Environmental Data.....	210
9.2.5	Statistical Analysis .....	212
9.2.6	Model Selection for Hookworm Infection Risk .....	213
9.2.7	Model Selection for Hookworm Infection Intensity.....	214
9.2.8	Bayesian Models of Hookworm Prevalence and Intensity of Infection .....	215
9.2.9	Risk Factor Analysis of Hookworm Infection Risk and Intensity .....	215
9.2.10	Prediction of Hookworm Infection Risk and Intensity.....	216
9.2.11	Parameter Estimation.....	216
9.3	Results .....	217
9.3.1	Study Population .....	217
9.3.2	Hookworm Infection Prevalence and Intensity.....	219
9.3.3	Spatial Correlation of Hookworm Infection Risk and Intensity .....	219
9.3.4	Results of Model Validation .....	221
9.3.5	Risk Factors for Hookworm Infection Risk and Intensity.....	222
9.3.6	Prediction of Hookworm Infection Risk.....	226
9.3.7	Prediction of Hookworm Infection Intensity .....	228
9.4	Discussion .....	229
9.6	Acknowledgments .....	235
9.7	Appendix.....	235
9.7.1	Formulation of logistic, NB, ZIP and ZINB models.....	235
9.7.2	Results of the model validation for hookworm prevalence and intensity risk profiling. 238	
9.7.3	Distribution of environmental factors in Champasack province, southern Lao PDR..	239
9.7.4	Odds ratios (ORs) and incidence rate ratios (IRRs) of environmental covariates in the predictive models .....	240
10	<b>Discussion .....</b>	<b>242</b>
10.1	Major findings on <i>Strongyloides stercoralis</i> infection and control in Cambodia .....	243

10.1.1	Community-effectiveness of ivermectin treatment.....	244
10.1.2	Cost effectiveness of potential control approaches for <i>Strongyloides stercoralis</i> .....	247
10.2	STH infections in Cambodia.....	249
10.3	Limitations.....	250
10.4	STH control effectiveness and underlying factors.....	252
10.4.1	Drug efficacy.....	254
10.4.2	Reinfection.....	256
10.4.3	Coverage and compliance.....	257
10.4.4	Sanitation.....	259
10.5	Control impact assessment, programme monitoring and evaluation.....	260
10.6	Challenges in measuring STH control impact on morbidity.....	263
10.7	Sanitation improvement for sustainable control.....	264
10.8	Integration of <i>Strongyloides stercoralis</i> into STH control in Cambodia.....	268
10.9	Next steps to have <i>Strongyloides stercoralis</i> recognized as a major STH.....	272
<b>11</b>	<b>Further research needs and recommendations.....</b>	<b>277</b>
11.1	Global needs for <i>S. stercoralis</i> research.....	278
11.2	Research needs in Cambodia.....	279
<b>12</b>	<b>Conclusion.....</b>	<b>281</b>
<b>13</b>	<b>Bibliography.....</b>	<b>283</b>
	<b>Curriculum vitae.....</b>	<b>308</b>