Exploring the impact of global agricultural production and trade on infectious disease risks.

Department of Infectious Disease Epidemiology

Imperial College London

Thesis submitted for PhD examination

Hiral Anil Shah

August 2020

Abstract

Agriculture is considered a nexus issue on which the future of global sustainability, health and the environment depend. Although, the environmental impact of agriculture is well established, the potential human health impacts of agriculture are less well understood and quantified, despite their potential to hinder or undermine global health and development efforts.

In this thesis, using gold standard methods from the medical sciences, epidemiology, and industrial ecology, I explore the impacts of agricultural land use and trade on infectious diseases risks. Through conducting a systematic review and meta-analysis, I quantify the association between occupational or residential exposure to agricultural land uses and being infected with a pathogen using Southeast Asia as a focal model system (Chapter 2). I further extend these evidence synthesis methods to other geographical regions and integrate meta-analytic estimates with burden estimation methods and input-output analysis to calculate the global human infectious disease impacts of agricultural production and trade (Chapter 3). To address the possibility of spatial autocorrelation and confounding within agriculture-disease relationships, I focus on childhood malaria in sub-Saharan Africa as a case study. Here, I assess the relationships between agricultural land use and malaria whilst controlling for socio-economic and environmental confounders using hierarchical modelling (Chapter 4). Finally, I summarise the main findings of my research, synthesise the added value of the research conducted and highlight future research opportunities (Chapter 5).

To combat agricultural land use and trade induced infectious disease risks, governments must acknowledge and address the human health impacts involved with the production of agricultural commodities. The findings from this thesis provide decision makers with a number of impactful recommendations on how public health, development, economic and environmental practitioners can jointly respond to mitigate the negative health impacts of agricultural production and trade. This can aid governments in securing co-benefits and mitigating trade-offs when trying to achieve multiple sustainable development goals simultaneously.

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Declaration

I declare that the work contained in this thesis is my own. All secondary sources have been appropriately cited. This work has benefited from the guidance and help of my exceptional supervisors. Any participants involved in collaborative work have been stated in the Publications, Presentation and Posters section of this thesis.

Copyright

Acknowledgements

First and foremost, thank you to my primary supervisor, Dr Kris A Murray. Your unwavering support, constant availability and continuous encouragement has resulted in the last four years being a wonderful, exciting and interesting experience. Your mentorship and enthusiasm has really helped broaden my horizon, developed my quantitative skill set and led to many interesting and exciting interdisciplinary opportunities that would not have been possible otherwise. Thank you for being a great supervisor, mentor, colleague and friend.

I also owe much thanks to my secondary supervisor, Dr Luis Roman Carrasco. Thank you for being a great sounding board, providing important feedback and perspectives and always being available for discussions which has helped shape this PhD. Thank you for providing me the opportunity to work with you in Singapore, which was an unforgettable experience.

I have benefited substantially from being a part of one of the best epidemiology departments in the world. Within the Department of Infectious Disease Epidemiology (DIDE), I have had countless engaging conversations with colleagues. The rigorous scientific and quantitative mindset within the department has substantially improved the quality of this research. To my colleagues within DIDE, especially Bae 1 and the Murray Lab. I thank you for all the laughter, camaraderie and support over the last four years.

I gratefully acknowledge the funding received from the Grantham Institute – Climate Change and the Environment and the Commonwealth Scientific and Industrial Research Organisation (CSIRO) which has enabled me to conduct robust and novel scientific research. Here, both institutes have played an important role in shaping the interdisciplinary nature of this thesis.

Finally, and most importantly, I would like to thank my amazing family. Mum, Dad and Neha, the last four years have been a solitary road and I would never have finished without you. Thank you for putting up with my mood swings, keeping me grounded and providing me with constant support and space to pursue my work. It's taken a while, but we finally got there in the end. Thank you!

Publications

Shah HA, Carrasco LR, Hamlet A, Murray KA. Agricultural expansion increases childhood malaria risk across Sub-Saharan Africa. (In Preparation).

Shah HA, Moran D, Hamlet A, Luck A, Maynard E, Bajaj S, Carrasco LR, Murray KA. Global human infectious disease impacts of agricultural production and trade. (In Submission).

Shah HA, Huxley P, Elmes J, Murray KA. Agricultural land-uses consistently exacerbate infectious disease risks in Southeast Asia. Nature Communications. 2019. `https://www.nature.com/articles/s41467-019-12333-z`

Oral Presentations

Global agricultural production and trade drives infectious disease threats in developing nations. MRC Centre for Global Infectious Disease Analysis. Imperial College London. March 2020.

Historical deforestation for shifting agriculture predicts malaria in children in sub-Saharan Africa. National University of Singapore. March 2019.

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Agricultural land-uses consistently exacerbate infectious disease risks in South East Asia: a systematic review and meta-analysis. Planetary Health Alliance Annual General Meeting, Edinburgh, UK. May 2018.

Poster Presentations

Agricultural land-uses consistently exacerbate infectious disease risks in Southeast Asia. EPIDEMICS conference. Charleston, USA. December 2019.

Agricultural land-uses consistently exacerbate infectious disease risks in Southeast Asia. International Conference on One Medicine One Science, Minneapolis, USA. May 2018.

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Chapter 1

Introduction

1.1 Global Change, Global Goals

1.1.1 Impacts of the Anthropocene

Ecosystems around the world face degradation and collapse as a result of global environmental and social changes [1]. These global changes have been a direct result of human-induced activities and pressures which has led to the proposal of a new human-dominated geological epoch titled 'The Anthropocene' [2, 3]. Although various start dates have been proposed for 'The Anthropocene', anthropogenic pressures on the natural environment have been well documented over time and consistently highlight the correlation between human-driven socio-economic impacts and the changes to components of the global environment such as the oceans, coastal zones, atmosphere and land [2, 3, 4, 5, 6].

The industrial revolution, which began from about 1760 to 1840 and involved the transitioning from hand production methods to automated machines is widely considered an anthropogenic pressure [3, 7]. This is known to have resulted in greenhouse gases being emitted into the atmosphere resulting in global warming [7, 8]. The green agricultural revolution is also described as another anthropogenic pressure, which occurred between 1940 and 1970 [9]. Here, global grain production doubled thereby improving agricultural productivity and food security which contributed to the global population increasing 3.7-fold during the 20th century [9, 10]. In addition to these impacts, the green agricultural revolution is also known to have resulted in widespread environmental impacts such as biodiversity loss, deforestation, greenhouse gas emissions, air and water pollution [9, 11].

1.1.2 Globalisation

Globalisation, which has rapidly increased in the last century and is a significant component of The Anthropocene. It is considered the incorporation of national economies and societies into a world system through the movement of goods and services, capital, technology and labour [6, 12, 13]. This process has resulted in many positive impacts such as free trade and the reduction of barriers such as tariffs, taxes and subsidies, the creation of jobs, competition between companies and countries, lower prices for consumers and introduction of foreign capital and technology [14]. However, rapid increases in population size and per capita consumption alongside increases in globalisation has further intensified the destruction and degradation of ecosystems to meet economic demand over the last century. This has led to global challenges such as climate change, large scale conflict, biodiversity loss, degradation of ecosystems, inequality, corruption and a lack of education, food, safety, health and sanitation [4, 15, 16, 17].

1.1.3 Millenium Development Goals

To combat these global issues which have arisen from anthropogenic pressures and globalisation, the Millennium Development Goals (MDGs) were initially created by the United Nations (UN). Here, 147 heads of state adopted the MDGs to address income poverty, hunger, disease, lack of adequate shelter, and exclusion, whilst promoting education, gender equality, and environmental sustainability, with quantitative targets set for 2015 [18].

Many developing countries made substantial progress towards achieving the MDGs, especially in domains such as public health, for example there has been considerable progress in reductions in child and maternal mortality across Africa alongside other public health indicators (e.g. smoking rate reductions) [19, 20, 21, 22]. However, progress was highly variable across goals, countries and regions [18]. For example, the reduction in global income poverty is mainly due to the rapid growth of a select few countries in Asia, such as China, India, Indonesia and Vietnam. In many other countries, poverty reduction has been quite slow, or poverty has even increased. In addition, environmental sustainability remains a global challenge due to a fast decline of biodiversity and an increase in gas emissions. Primary education and gender equality remained unfulfilled, and there are severe inequalities that exist among populations, especially between rural and urban areas [23].

The lack of progress in achieving the MDGs in some countries was considered due to issues such as unmet commitment, inadequate resources, lack of focus and accountability and insufficient interest in sustainable development and its links to the environment [24].

Many stakeholders also considered the MDGs flawed in conception as the overall creation process was driven and spearheaded by high income countries and institutions such as the United States of America (USA), Europe and Japan, World Bank, International Monetary Fund (IMF) and Organisation for Economic Co-operation and Development (OECD) [18].

1.1.4 Sustainable Development Goals and Planetary Health

Following the shortcomings of the MDGs, the global community has now acknowledged the inter-connectedness of human and environmental systems and the need for sustainable development to achieve a better and more sustainable future for all [25]. This has resulted in the development of the Sustainable Development Goals (SDGs) and a new and important concept called “Planetary Health” [26, 27].

The SDGs otherwise known as the “global goals” are a universal call to action to end poverty, protect the planet and ensure that all people enjoy peace and prosperity [28]. They consist of 17 universal goals and 169 targets which are to be achieved by 2030 and were developed by the UN in 2015 [25, 29]. A central feature of the SDGs is that they are “integrated and indivisible, hence, synergies and trade-offs between individual SDGs require a systematic analysis [30]. Previous research, however, suggests that insufficient understanding and accounting of trade-offs, externalities and synergies across sectors or global goals have resulted in incoherent policies and adverse impacts in sustainable development [31, 32]. For example, continued deforestation of primary forests for shifting agriculture in sub-Saharan Africa can reduce poverty and improve livelihoods (SDG1) and provide food security (SDG2) and nutrition (SDG3) to marginal or smallholder farmers. However, this deforestation could also increase the unsustainable use and management of agrochemicals (SDG12) which can pollute drinking water (SDG6), increase biodiversity loss (SDG15), desertification (SDG15), soil erosion (SDG15), flooding (SDG15), and also potentially increase illnesses such as diarrheal diseases or malaria (SDG3). Failing to account for these trade-offs, externalities or synergies could result in poor cost-effectiveness, failure to meet the global goals or the creation of dis-benefits. Establishing evidence between the synergies and trade-offs will be an important component of simultaneously achieving multiple SDGs [32, 33, 34, 35, 36, 37, 38].

Achievement of such goals is largely dependent on national level factors such as countries formalising commitments and integrating policies across sectors [39]. However, the research community also has a vital commitment with regards to the measurement of progress towards these global goals, identifying and assessing externalities and co-benefit opportunities and integrating economic, social and environmental perspectives whilst shaping global governance [27, 39, 40]. This has resulted in global tracking of key sustainable development indicators such as The Lancet Countdown on Climate Change and Health, measurement of the health and environment related SDGs and The Planetary Health Watch [29, 41, 42]. The outputs and outcomes of monitoring progress on these key sustainable development indicators can help ensure the design of effective policy, targets, and actions and inform interventions that can simultaneously provide benefits across sectors at reduced monetary and non-monetary costs [27].

The concept of Planetary Health, which is embedded within the SDGs, refers to "the health of human civilization and the state of the natural systems on which it depends”. It provides a useful perspective for the identification and quantification of connections between sectors such as human health and environmental change. For example, conservation of ecosystems and species directly supports human health and wellbeing by providing goods like food, water and fibre, and global public goods like habitat for species and mitigation of climate change [43]. Planetary health also builds upon previous fields such as ecological public health, One Health, Eco Health and environmental health [44, 45] and yet focuses on the understanding that human civilisation and health depend on the sustainable management of natural systems [46].

The links between environmental change and human health can involve complex and dynamic interactions at multiple levels in the biological world that can lead to health outcomes that are hard to predict and result in unintended consequences [27]. The planetary health concept provides a lens to investigate these complex systems to identify, quantify and measure such interactions and decompose potential areas of success for sustainable development.

Planetary Health has gained more traction over time with key institutions such as the World Health Organisation (WHO), The Rockefeller Foundation, The Lancet and the Royal Society for Tropical Medicine and Health adopting planetary health within their core principles. For example, in 2017, The Lancet launched a new journal titled The Lancet Planetary Health with the aim of publishing research that broadly encompassed sustainable development and global environmental change, including the drivers of change, the implications of those changes for people and society, and practical policies and interventions for a healthier planetary future [47]. In addition, entire departments and academic collaborations that focus on planetary health are now formulating in universities globally, encouraging action within the research community and stimulating future generations [48].

1.2 Sustainability in Agriculture

1.2.1 Health and Environmental Impacts of Agricultural Land Use

One area where the possibility of large-scale co-benefits is in land-use management. Land use and land-use change are considered the alteration of land for domestic, residential, occupational or economic purposes [49, 50]. Land use is primarily described as an alteration in the use of land and can include deforestation, rangeland expansion, urbanisation and infrastructure development (railways, roads or powerlines), hydrological alteration (dams or irrigation), agricultural land use (crops or livestock) or natural resource extraction (mining, logging or hunting) [50, 51]. Such alterations are largely driven by social (e.g. urban infrastructure) and economic (e.g. trade in resources) considerations, but pursuit of these objectives often also creates dis-benefits (negative externalities/costs) in other sectors that are rarely considered in decision making. Hence, identification and quantification of connections and the dissemination of potential co-benefits or disbenefits across sectors will be a useful strategy for joint decision making for sustainable development.

Agricultural land use and land use change, including agricultural intensification is defined as land suitable for agricultural production, both crops and livestock in the form of arable land or pastureland. It is a common land use and has led to major increases in the production of food, timber, housing and other commodities [52, 53, 54]. Although delivering economic and social benefits, these activities have also resulted in substantial negative socio-ecological consequences, such as increased CO_2 [55, 56], air pollutant emissions [56], loss of biodiversity [57, 58, 59, 60, 61, 62], modifications in surface fluxes of heat and water vapour resulting in changing regional weather patterns [63, 64, 65], degradation of air and water quality [66, 67, 68], and a decrease in the supply of renewable fresh water [69]. While the impacts of agricultural land-use activities is relatively well characterised in some sectors (e.g. carbon emissions accounting frameworks [70], biodiversity loss [60, 71, 72], less well established are the potential impacts on human health. Here, the majority of existing research signposts towards the health impacts of occupational pesticide, chemical and heavy metal exposure [73, 74]. Previous research by the WHO estimates that 24% of the disease burden (estimated using disability adjusted life years (DALYs)) and an estimated 23% of all deaths (premature mortality) are attributable to a group of environmental factors such as agriculture and land use change, water and sanitation, pollution and infectious disease [75]. However, specific burdens attributable just to agricultural land use are not derived.

Evidence linking agricultural land use and infectious disease risk outcomes in humans, many of which are related to agriculture, is even more fragmented and geographically restricted; nor has it been systematically synthesised or assessed previously [50, 76, 77, 78, 79, 80, 81, 82, 83]. For example, there is a growing body of evidence that suggests that human-induced land-use changes such as deforestation for agriculture are the primary drivers or contributing factors of a range of infectious disease outbreaks and emergence events [50, 76, 77, 78, 80, 83]. These changes may also serve as modifiers of the transmission processes of endemic infections, in some cases resulting in increases in the number of cases and burden [76]. Forest loss has also been linked with increased malaria in Africa and South America [84] and Ebola Virus outbreaks in Africa [85]. Specific case studies include deforestation and associated environmental changes for palm oil production being a key drivers in *Plasmodium knowlesi* (cause of zoonotic malaria) transmission to humans in Malaysian Borneo [86]. Expansion and changes in agricultural practices are associated with the emergence of Nipah Virus in Malaysia [87, 88]. Malaria in children in Democratic Republic of Congo has also been associated with agricultural land use change [89]. Deforestation of dense forest for agricultural expansion, large-scale development projects and illegal timber harvesting has also been associated with an increased incidence of diarrhoea, fever and acute respiratory infection in children in Cambodia [90]. Finally, livestock farming and contact with pigs was associated with Hepatitis E and Japanese Encephalitis prevalence in Lao PDR [91].

1.2.2 Agriculture-Disease Mechanisms

Common mechanisms by which agricultural land use alters the transmission of infectious disease include vector, host, and pathogen niche alterations, changes in host and vector community composition, behaviour or movement change of vectors and/or hosts, altered spatial distribution of hosts and/or vectors, socioeconomic factors, and environmental contamination [50].

Many studies also look at the links between land use change, species diversity and infectious disease transmission otherwise known as biodiversity-disease relationships [50, 92]. Over time, there has been much debate regarding biodiversity-disease relationships where the majority of scholars suggest that decreased species diversity leads to an increase or decrease in infectious disease risk, otherwise known as the amplification or dilution effect, respectively [93, 94, 95, 96, 97, 98, 99, 100, 101].

There have also been some critics with regards to this mechanism. For example, Randolph and Dobson (2012) propose that the dilution effect only applies in certain circumstances and depends more on specific community composition rather than biodiversity [102]. In addition, Dobson et al (2006) also suggests that evaluation of the dilution or amplification effect can be biased and involve personal value as most people would prefer biodiversity to be good for their own health [50, 103]. Halliday and Rohr (2019) find that biodiversity generally inhibits disease at local scales, but this effect weakens as spatial scale increases [104]. To make generalisable predictions on biodiversity-disease relationships, more focus needs to be given to how species diversity impacts specific individual disease mechanisms such as host density, contact rates and transmissibility which can lead to increases and decreases in transmission [105, 106].

Another mechanism can be a change in exposure pathway with increased human-animal contact. The emergence of novel diseases from forests and the increase of endemic disease impacts in forested landscapes are thought to be related to encroachment and degradation arising from increasing human presence in these habitats [43]. For example, evidence suggests that deforestation has increased exposure to malaria in Africa and South America and subsequent hunting and wild-meat butchering was a key factor in initial outbreaks of HIV and Ebola virus in Africa [84, 107]. Land use and land use change alongside agricultural drivers have also been identified as a leading pathway for emerging infectious diseases (EIDs), however, there is considerable uncertainty surrounding this topic [108, 109, 110]. Evidence linking agricultural drivers to EIDS has always opted to use data drawn from a review of published literature. Here, individual studies carry their own biases, inaccuracies, and different approaches to collecting and documenting data, which are not investigated and could lead to spurious associations [109].

Agricultural land use and land use change can potentially create new suitable habitats that reservoirs or vectors can adapt too. For example, research in Malaysian Borneo suggests that variation in temperatures due to forest conversion dramatically increases development rates in *Aedes albopictus* mosquitoes [111]. In parts of Africa, forest cutting alongside the use of agrochemicals also alters the composition and density of aquatic snail species thereby increasing transmission of schistosomiasis [107, 112]. Research in Kenya also shows that vectoral capacity of *Anopheles gambiae* was at least 106% and 29% higher in the deforested area due to increases in temperature than in the forested area in dry and rainy seasons, respectively [113]. Guo et al. (2018) also find a general increase in host or vector community competence associated with land-use changes [114]. Research by Morris et al (2016) also suggests that deforestation driven food-web collapse has led to an increase in preferred hosts and thereby increased the potential abundance of *Mycobacterium ulcerans* [115].

Finally, rapid changes due to agricultural land use or land use change can impact host or vector communities through genetic modification which can impact disease transmission. For example, mass scale livestock farming where animals are in close confinement or within proximity to different species can increase genetic pathogen exchange resulting in pandemic infectious diseases such as H5N1 or Severe Acute Respiratory Syndrome (SARS) [116, 117, 118, 119].

Although many studies provide compelling evidence of a common link between agricultural land-use and infectious disease risk in specific countries or contexts, no previous research has been able to establish a generalisable agriculture-disease relationship.

1.2.3 Health and Environmental Impacts of Agricultural Trade

Agricultural land use can have multiple negative ecological impacts which are due to drivers (e.g. population growth, per capita income, new technologies, economic policies) that unsustainably expand or intensify agricultural land use. One of the key drivers is global demand and trade for commodities [16]. Here, it has been found that changing diets alongside increased consumer demand has resulted in substantial agricultural land use and subsequent ecological impacts [120]. For example, 10% - 70% of local environmental and social impacts are associated with (embodied in) the international trade of goods [16]. Within this body of research, authors find that approximately one third of global biodiversity loss can be attributed to the land-use impacts of international trade, with the remainder caused by domestic trade threats [121, 122]. Such approaches have also been used to assess other dis-benefits, such as pollution, energy supply chains, water footprints and carbon emissions [121, 122, 123, 124, 125, 126, 127].

There is also a growing body of research that focusses on linking international trade with social issues such as gender equality, mother and child health, governance and access to clean water or corruption [16, 128, 129]. Studies have also linked international trade with human health impacts associated with production-based environmental emissions, where 26% of global human health impacts and 22% of global premature deaths are related to PM2.5 pollution embodied in trade [16, 130]. However, previous research on the specific links between global agricultural trade and health impacts in producing countries is even more sparse. Here, the majority of research focusses on how certain agricultural policies may impact global food security, poverty reduction or nutrition and diet related chronic health impacts [131, 132, 133, 134, 135, 136].

At the same time, infectious diseases are emerging globally at an unprecedented rate while population and consumption growth will lead to an increasing global demand for commodities [110, 137]. Research that does link agricultural production or trade with infectious diseases suggests that >25% of all EID events and >50% of zoonotic EID events since the 1940s are linked specifically to agricultural drivers [110]. Chaves et al (2020) also find that about 20% of the malaria risk in deforestation hotspots is driven by the international trade of deforestation-implicated export commodities, such as timber, wood products, tobacco, cocoa, coffee and cotton [138]. Other studies linking agriculture to infectious disease risks more specifically have centred on the spread and control of emerging infectious diseases (EIDs), particularly as a biosecurity threat that could impact or halt global trade [139] (e.g. pandemic swine or bird flu [117, 140, 141, 142, 143, 144], bovine spongiform encephalopathy (BSE) [145, 146, 147, 148] and acute respiratory syndromes (e.g., SARS or MERS) [149].

Hence, ensuring sustainability in agricultural land use and its globalised supply chains is vital to achieving the global goals [150]. Especially if international demand and trade for products drives significant impacts (e.g. biodiversity loss, pollution) linked to agricultural activities in supplier countries. This is certainly exemplified by research that suggests that suggests exports from developing nations are more ecologically intensive than those from developed nations [151].

1.2.4 Agriculture-Disease Poverty Traps

The globalisation of agriculture and its supply chains has provided many families and individuals the opportunity to escape poverty by generating income through the growing, selling and exportation of cash crop. However, escaping poverty is a multi-dimensional complex phenomenon that not only includes improvements in income, but also includes improvements in wealth, education, health and socio-economic and ecological factors [152].

A poverty trap is a mechanism that makes it very difficult for people to escape poverty and is created when an economic system requires a significant amount of capital in order to earn enough to escape poverty. When individuals lack this capital, they may also find it difficult to acquire it, creating a self-reinforcing cycle of poverty [153, 154, 155, 156]. For example, Sachs et al (2004) suggest that people in sub-Saharan Africa are consistently prone to getting stuck in poverty traps due to very high transport costs, small market size, low-productivity agriculture, a high disease burden, adverse geopolitics and a slow diffusion of technology from abroad [157].

Research suggests many factors contribute to creating a poverty trap, including limited access to credit and capital markets, extreme environmental degradation (which depletes agricultural production potential), corrupt governance, capital flight, poor education systems, disease ecology, lack of public health care, war, and poor infrastructure [158].

The role of health conditions (infectious disease and malnutrition) as a driver of poverty traps has been attracting increasing attention [156, 157, 159, 160]. Here agricultural production can improve human health by reducing food prices, enhancing nutrition, improving agricultural livelihoods through cash crops which can all result in a decrease in susceptibility to infectious diseases due to improved wealth, education, access to care, food and nutrition [155, 156, 161]. However, this relationship is bidirectional where poverty can also be an important risk factor for developing or being infected with a disease [110, 155, 156, 162]. For example, freshwater habitats established for irrigation often increase the risk of parasitic and vector-borne diseases such as malaria and schistosomiasis [110, 112]. This is particularly important as people who are stuck in these poverty traps tend to live in rural areas that have very little access to healthcare or sanitation, heavily rely on subsistence agriculture, have low levels of education and are highly susceptible to infectious disease [110, 156].

Analysis of the links between agriculture, infectious disease and the poverty traps they form are limited [153, 155, 156, 160]. In essence, previous research argues that escaping such poverty traps are extremely difficult for the rural poor as agricultural land use alongside infectious diseases are governed by biological, epidemiological and ecological factors and processes, which are uncontrollable [155, 156, 161]. Understanding whether agriculture-disease associations remain significant when controlling for poverty trap socio-economic factors such as wealth, education and sanitation in addition to assessing whether these associations remain strong when accounting for spatial-temporal processes can provide further evidence on where resources need to be allocated to reduce disease burdens, maintain agricultural productivity and simultaneously lift those out of poverty.

1.3 Research Gap

The sustainability of agriculture is a key priority for many governments as it may positively impact ecological factors including biodiversity, climate change, water and air pollution. However, a key gap in the in the evidence base, is the relationship between agriculture and human health (specifically infectious diseases). There is now a window of opportunity to consolidate the impact of agriculture on infectious diseases which can aid in joint decision making across sectors to ensure achievement of multiple sustainable development goals and indicators.

A key challenge is that the relationship between upstream drivers such as exposure to agricultural land use and downstream impacts such as infectious diseases in humans has not been systematically assessed or quantified whilst taking into account the biases, inaccuracies, and different approaches used in the collection of primary data. Hence, exploration of heterogeneity, confounding and publication bias through a gold standard systematic review and meta-analysis methodology is critical to minimise the likelihood of spurious associations (Chapter 2).

In addition, no attempt has previously been made to quantify the current burden of disease linked to agricultural land use and no assessment has been made on whether the international trade of agriculture is a small or large driver of this agriculture induced burden (Chapter 3). Further compounding this is that agriculture-disease associations may be spurious when controlling for poverty trap socio-economic factors such as wealth, education, sanitation or potential processes such as spatial autocorrelation between deforestation for agriculture and disease incidence (Chapter 4).

Robust understanding of the agriculture-disease paradigm can identify mutual interests and facilitate joint decision making. This can lead to the deployment of specific land use, public health or economic interventions that may simultaneously improve health related quality of life, maintain agricultural productivity and improve livelihoods in a sustainable manner that is not detrimental to the environment. Cross sectoral policies that focus on the sustainability of agriculture can reduce economic costs, or increase effectiveness of actions designed to progress towards agreed health, environment and development targets in each of these domains, as compared to pursuing domain-specific goals in isolation (Chapter 5).

1.4 Aims and Objectives

The aim of this PhD is to quantify the relationships between agricultural land use and infectious diseases in humans to improve agricultural sustainability through using the SDG framework. In meeting this aim, the following research questions have been generated:

1. Is there an association between occupational or residential exposure to agricultural land uses and being infected with a pathogen in SE Asia?

2. What impact does agricultural land use and trade have on the global burden of infectious diseases?

3. What impact does exposure to differing agricultural land uses have on childhood malaria risk in sub-Saharan Africa when controlling for socio-economics and environmental factors?

1.5 Thesis Structure

This thesis is structured into three main studies which align with the research gap and questions stated above in the aims and objectives.

In Chapter 2, I test for a generalisable or net impact of occupational or residential exposure to agricultural land use on the risk of infectious disease in humans via a systematic review and meta-analysis approach, following PRISMA reporting standards for medical and epidemiological evidence syntheses. Here, I use Southeast Asia as an appropriate model system to test this association given its combination of biologically diverse landscapes [57], differing land uses [163] and because it is considered a zoonotic, parasitic and emerging disease hotspot area [164, 165].

Chapter 3 presents the integration of meta-analytic methods from Chapter 2, epidemiological methods such as population attributable fractions and the use of input output analysis to quantify the impact that agricultural land use has on global infectious disease mortality and morbidity in humans. I further explore the magnitude of the burden that is linked to international trade and provide insights into the links between importers and exporters of disease-implicated agricultural commodities.

Chapter 4 seeks to investigate the consistency of the agricultural exposure and infectious disease association when looking at a specific case study of malaria in children in Africa. Specifically, I aim to assess what effect exposure to differing agricultural land uses have on the probability of childhood malaria risk in Africa, whilst controlling for numerous socioeconomic and environmental confounders alongside spatial autocorrelation.

Chapter 5 presents a discussion where I summarise the main findings of my research, synthesise the added value of the research conducted and highlight future research opportunities. I also reflect upon my research and put it into the context of current understanding, practices and interventions that seek to reduce infectious disease transmission, improve agricultural productivity and improve livelihoods through agricultural sustainability through the SDG framework. Finally, I pinpoint the contributions I have made to specific global health, development and economic policies and provide potential linkages to the SDGs furthering the dialogue of mutual interests and co-benefits. I conclude the discussion, by dissecting the growing relative importance of infectious disease as a negative impact of agricultural land use and the rapid need for sustainability in agriculture to feed 10 billion by 2050 whilst controlling potential large-scale socio-ecological disbenefits.

1.6 Ethics and Funding

For this research no ethical clearance was needed as all analysis was conducted using secondary literature sources and open access data. Funding for this studentship was received from the Grantham Institute and Commonwealth Scientific and Industrial Research Organisation (CSIRO) and embedded within the Science and Solutions for a Changing Planet Doctoral Training Partnership at the Grantham Institute, Imperial College London. I also acknowledge joint centre funding by the UK Medical Research Council (MRC) and the UK Department for International Development (DFID) under the MRC/DFID Concordat agreement which is also part of the EDCTP2 programme supported by the European Union. Grant reference and affiliation: MR/R015600/1; MRC Centre for Global Infectious Disease Analysis, School of Public Health, Imperial College London.

Chapter 2

Agricultural land-uses consistently exacerbate infectious disease risks in Southeast Asia

2.1 Abstract

Background

Agriculture has been implicated as a potential driver of several human infectious diseases. However, the generality of disease-agriculture relationships has not been systematically assessed, hindering efforts to incorporate human health considerations into land-use and development policies.

Methods

Here, I conducted a systematic review and meta-analysis to test and quantify the associations between agricultural land-use and human infectious disease in SE Asia. Crude odds ratios were extracted, and a meta-analysis using a random effects logistic regression model was conducted to test *a priori* hypotheses. Further tests for heterogeneity, publication bias and confounding were calculated.

Results

Pooled results from 34 eligible studies show that people who exposed to agricultural land are on average 1.74 times more likely to be infected with a pathogen than controls (OR 1.74, CI 1.47 - 2.07, $p < 0.001$). This effect rose to a 2-4-fold increase in the odds observed for forest monocultures (palm oil OR 3.25, CI 2.29 - 4.61; rubber OR 2.27, CI 1.82 - 2.82) and was most pronounced for hookworm (OR 2.42, CI 1.56 - 3.75), malaria (OR 2.00, CI 1.46 - 2.73), Scrub typhus (OR 2.37, CI 1.41 - 3.96) *Schistosoma japonicum* (OR 1.71, CI 1.18 - 2.48), Spotted fever group (OR 3.91, CI 2.61 - 5.85) and *Trichuris trichiura* (OR 1.40, CI 1.27 - 1.53). In other subgroups, no change in infection risk was detected (e.g. livestock farming). No evidence of publication bias or confounding was detected.

Conclusion

Evidence thus suggests that agricultural land uses consistently exacerbate human infectious diseases in Southeast Asia. Although responses clearly vary by land-use and disease types, generalizable results from this and further studies will help identify co-management opportunities for health and the environment.

2.2 Introduction

Agricultural land use and land use change, including agricultural intensification and the conversion of forests, wetlands and grasslands into forest monocultures, crops and pasture has led to major increases in the production of food, timber, housing and other commodities [52, 53, 54]. Although delivering economic and social benefits, these human activities have also resulted in substantial negative socio-ecological consequences, such as increased CO2 [55, 56], air pollutant emissions [56], loss of biodiversity [57, 58, 59, 60, 61, 62], modifications in surface fluxes of heat and water vapour resulting in changing regional weather patterns [63, 64, 65], degradation of air and water quality [66, 67, 68], and a decrease in the supply of renewable fresh water [69].

This trade-off between the considerable costs and benefits at stake places the agricultural sector at the heart of global sustainability, health and environmental frameworks (e.g. Sustainable Development Goals (SDGs), Paris Agreement, Aichi Biodiversity Targets), and makes simultaneous achievement of key targets a formidable challenge [150].

While the impacts of agricultural land-use activities is relatively well characterised in some sectors (e.g. carbon emissions accounting frameworks [70], biodiversity loss [60, 71, 72], less well established are the potential impacts on human health, where the majority of existing research signposts towards the health impacts of occupational pesticide, chemical and heavy metal exposure [73, 74]. In particular, the evidence linking human-induced land-use changes and infectious disease risk outcomes in humans, many of which are related to agriculture [50, 76, 77, 78, 79, 80, 81, 83], has not been systematically evaluated or quantified.

Numerous case studies support a link between agricultural land-use or land-use change and infectious disease risks [166]. For example, irrigation-based agriculture and rural development can expand breeding habitats of Culex vectors and has led to Japanese encephalitis virus establishing a secondary cycle in domestic pig populations where it amplifies and spills over into human populations [166, 167, 168, 169]. Deforestation and associated environmental changes may facilitate the transmission of *Plasmodium knowlesi* (cause of zoonotic malaria) to humans in Malaysian Borneo [86]; expansion and changes in agricultural practices are associated with the emergence of Nipah Virus in Malaysia [88] and increased Leptospira infections and fatalities in Thailand have been observed in open habitats such as rice fields that are prone to flooding [170].

In addition, a number of theoretical modelling studies and meta-analyses suggest potentially generalisable links between land-use or land-use change and biodiversity loss (a key outcome of land-use change, albeit not necessarily specific to agricultural activities, some of which may be linked to increases in disease risk. For example, Guo et al. (2018) find a general increase in host or vector community competence associated with land-use changes [114]. Rohr et al. (2019) report that agricultural drivers are associated with more than 25% of emerging infectious diseases and more than 50% of emerging zoonotic infectious diseases in humans [110]. Faust et al. (2018) highlight changing host population densities and edge effects as mechanisms that could drive disease emergence in converted landscapes [81]. Civitello et al. (2015) show that host diversity inhibits parasite abundance (e.g. infection prevalence for microparasites, mean parasite load for macroparasites, density of infected vectors for vector-borne parasites, or percent diseased tissue for plant parasites) and therefore suggest that a generalizable 'dilution effect' may modulate disease risk across a number of disease systems [98]. However, the extent to which these effects extend to human infectious diseases remain highly contentious [105], and few studies focus on specific land-use types.

Here, I test for a generalisable or net impact of occupational or residential exposure to agricultural land use on the risk of infectious disease in humans in Southeast Asia (SE Asia) via a systematic review and meta-analysis approach, following PRISMA reporting standards for medical and epidemiological evidence syntheses.

A global review was deemed infeasible due to the vast collection of citations that would require double review to achieve PRISMA standards (50,000 citations). A narrower focus on SE Asia (defined here as the Association of Southeast Asian Nations (ASEAN) region, including, Vietnam, Cambodia, Laos PDR, Thailand, Myanmar, Malaysia, Indonesia, Singapore, Philippines, East Timor and Brunei) was considered as an appropriate model system given its combination of biologically diverse landscapes [57], differing land uses [163] and because it is considered a zoonotic, parasitic and emerging disease hotspot area [164, 165]. Specifically, I quantified an overall association between where people live or work in SE Asia and disease risk, finding that those in agricultural land are on average almost twice as likely to be infected with a pathogen than controls (OR 1.74, CI 1.47 – 2.07, $p < 0.001$). Consistent associations are also reported between forest mono-culture agriculture (oil palm and rubber) and a number of specific diseases of differing ecologies and epidemiologies, while accounting for potential effects of publication bias and both within and between study confounding. Although responses clearly vary by land-use and disease types, generalizable results from this and further studies will help identify co-management opportunities for health and the environment.

2.3 Methods

2.3.1 Search Strategy and Selection Process

Following PRISMA protocol and reporting standards for systematic reviews, I systematically screened articles in April 2017 using five academic literature databases: Medline, PubMed, Global Health, Web of Science and EMBASE alongside Google Scholar. Another collaborator also independently screened articles to ensure the review was systematic.

Search strings were created through a PECOS statement using three categories (exposure, location and outcome) with Boolean operators AND between categories and OR within categories. Where applicable, MeSH terms for communicable disease, SE Asia, land use and agriculture were also used. Differing land use types were incorporated into the search strategy to improve the sensitivity of the search. To improve the specificity of the search strategy, the location category was only applied for title and abstracts, to capture all publications that had a study context within SE Asia. No language restrictions were placed within the search strategy. An example of the search strategy used for EMBASE can be found below:

1. zoonoses or zoonosis or infectio* or communicab* or emerg* or disease*
2. exp Communicable Diseases
3. South east Asia or SE Asia or Southeast Asia or Brunei or Cambodia or Indonesia or Laos or Malaysia or Myanmar or Philippines or Singapore or Thailand or Timor or Vietnam – TITLE AND ABSTRACT ONLY
4. exp Asia, Southeastern
5. 1 or 2
6. 3 or 4
7. land use* or land cover* or landscape* or habitat* or deforest* or agricultur* or farm* or urbani* or suburbani* or fragment*
8. 5 and 6 and 7

Articles were initially assessed by myself and another independent reviewer for relevance first by title, as well as keywords if these were available, then by abstract and finally by full text. I then simultaneously assessed the suitability of the studies retained after screening for full text analysis for their potential inclusion in meta-analyses, rejecting studies for which risk or odds estimates could not be calculated. Disagreements were resolved by consensus, and where no consensus was achieved a third investigator was consulted. One reviewer (Hiral Shah) then extracted outcome and exposure data as well as data on population and study characteristics into a bespoke data extraction framework, which was then validated by a second reviewer [171].

2.3.2 Eligibility

Following PRISMA guidelines and the PICOS framework, I considered the following factors to determine eligibility criteria: 'study question', 'populations', 'exposure', 'comparators', and 'outcome'. A description of each follows.

Study Question - Is there an association between occupational or residential exposure to agricultural land uses and being infected with a pathogen for adults aged 18 and above in SE Asia?

Study Design – Empirical observational studies (longitudinal cohorts, case control or cross sectional) studies conducted in the ASEAN region and reported in English were considered eligible. I anticipated that the extent and effects of language bias may have diminished recently because of the shift towards publication of studies in English [172]; however, I reserved the option to have non-English articles translated to bolster sample sizes if a reasonable number of non-English studies were found.

Populations – This study drew participants from the general adult population aged 18 and above in SE Asia. Studies that recruited participants of all ages (including children) were also included. Studies that focused exclusively on the child population were excluded. Exposure – The primary exposure of interest was defined as occupational or residential exposure to agriculture or agricultural land use. This was defined as whether study participants would be working or living in or near agricultural land. Specifically, agricultural exposure was defined as any person who partakes in the cultivation of land and breeding of animals and plants to provide food, fibre, medicinal plants and other products either for domestic, residential, occupational or economic purposes [49].

Comparators – Studies were included if they compared outcomes in the exposed group with those in a group of unexposed people (people who are not occupationally or residentially exposed to agriculture or agricultural land use).

Outcome – Studies were included if one of the primary outcomes include prevalence, seroprevalence or incidence for all infectious diseases that have a biologically plausible link to agriculture or agricultural land use.

Studies that investigated non-communicable disease or infectious diseases of plants, invertebrates or fish were excluded. I also excluded studies that were not based on SE Asia, did not include some form of land use as an exposure or study focus, were theoretical research papers, reviews, commentaries or letters, or were not published in English (following determining that few non-English studies meeting all other criteria were available, see above). Studies that presented odds ratios based on the co-infection of more than 1 disease were excluded as co-infection could increase susceptibility to other infectious diseases [173]. Studies that assessed the impact of using human faeces (night soil) as fertiliser in agriculture were also excluded [174, 175, 176]. This is because using human faeces as fertiliser was not considered a land use but rather a confounding behavioural activity. Studies that assessed risk factors of disease in children were also excluded [177, 178] as children may be exposed to agricultural work but may also be more susceptible to certain diseases . An explicit bulleted inclusion and exclusion criteria can be found below:

- Inclusion Criteria
  - Geographical Location – Southeast Asia defined as Vietnam, Cambodia, Laos PDR, Thailand, Myanmar, Malaysia, Indonesia, Singapore, Philippines, East Timor and Brunei as part of the ASEAN region.
  - Population – Adults in Southeast Asia aged 18 and above that work or live in or near agricultural land (NB – studies that assess total populations including both adult and children will be included).
  - Type of exposure - Agricultural land use exposure was defined as any person who partakes in the cultivation of land and breeding of animals and plants to provide food, fibre, medicinal plants and other products to sustain and enhance either for domestic, residential, occupational or economic purposes.
  - Type of comparator - No exposure to agricultural land use.
  - Types of outcome: Change in prevalence or incidence of infectious disease as a function of land use or land use change.
  - Type of disease: All infectious diseases that are prevalent in humans in Southeast Asia with a biologically plausible link to land-use change including emerging, zoonotic, bacterial, viral, parasitic and vector-borne infections.
  - Types of study – Peer reviewed empirical observational studies.
- Exclusion Criteria

- Articles based on non-communicable disease.
- Articles based on infectious diseases of plants, invertebrates or fish.
- Articles that do not study the impact of land use or land use change.
- Articles that do not have a study context in SE Asia.
- Articles not in English.
- Theoretical research, reviews, commentaries or letters.
- Studies that presented odds ratios based on the co-infection of more than 1 disease.
- Studies that assessed the impact of using human faeces (night soil) as fertiliser in agriculture.
- Studies that assessed risk factors of disease in children.

Duplicates were removed using reference management software (Endnote and Mendeley). If the inclusion of an article was in doubt in either the first two stages, the article was included, and the suitability determined at a later stage.

2.3.3 Study Quality

A methodological study quality assessment was conducted using two quality appraisal tools sourced from the Office of Health Assessment and Translation (OHAT) and the National Heart, Lung and Blood Institute's (NHLBI) Quality Assessment website.

The first tool was the OHAT Risk of Bias Rating Tool for Human and Animal Studies which evaluates the assessment of whether the design and conduct of the study compromised the credibility of the link between exposure and outcome. The OHAT for human studies contains 11 risk-of-bias questions that cover six different domains including selection, confounding, performance, attrition/exclusion, detection, and selective reporting bias. Six of the eleven questions are applicable for cross sectional and case control studies and are answered using one of four predefined answer choices (1) definitely low risk of bias; (2) probably low risk of bias; (3) probably high risk of bias; and (4) definitely high risk of bias. Studies were excluded from this review if they had an average rating of definitely high risk of bias and/or if there was substantial evidence that the studies showed threats to internal validity.

The second set of tools were for Observational Cohort and Cross-Sectional Studies (QAT – OCCSS), and for case control studies (QAT – CCS). Both tools had 14 and 9 items, respectively, that classified study quality using specific epidemiological parameters such as transparency of research question, sources of potential bias (e.g. selection or measurement), study power, confounding and other items that inferred internal validity of each study [179, 180]. A greater number of Yes responses indicated a higher study quality for both study quality tools. Studies were classed as good if they presented information on all key criteria within the tools such as: research question, study population, sample size justification, exposure measurement and outcome measurement. Studies were classed as fair if they presented some information on the key criteria. Poor studies were classed as studies that could not satisfy the majority of key criteria.

2.3.4 Data Synthesis and Statistical Analysis

Data were summarised as the number of individuals with and without infection stratified by whether they were exposed to agricultural land use or not. Associations were quantified using the odds ratio (OR) with a 95% confidence interval. This was extracted where possible from the studies or self-calculated using relevant data where possible. Where ORs could not be extracted or calculated due to poor or non-reported data, studies were excluded from the meta-analysis [171].

A regional meta-analysis was conducted with a random effects model [181, 182] to calculate a pooled estimate that quantifies the overall impact of how any occupational or residential exposure to agricultural land use impacts the odds of infectious disease prevalence. For this, I selected mutually exclusive studies and odds estimates to be incorporated into the regional meta-analysis. This was to avoid any double counting of estimates, which could otherwise bias pooled estimates. Only one estimate was used per study and other estimates from the same study population were excluded. This was achieved by systematically selecting risk/odds estimates based on agriculture as a general occupational exposure. However, in some cases, studies provided multiple agricultural exposures or multiple disease outcomes in the same study (e.g. oil palm, rice, rubber as an exposure type or hookworm, *Trichuris trichuria* and *Ascaris lumbrocoides* infection as the outcome). In these types of studies, I selected the exposure and outcome that had the largest number of cases to maximise study power. In some instances, there were multiple publications by the same author analysing the same study population [183, 184, 185]. In these cases, only the most recent publication was selected for incorporation into the overall analysis.

Random effects meta-analyses assume that a distribution of effects exists across all studies included in the analyses, resulting in heterogeneity among study results. The use of a random effects model was considered appropriate here because I assume that the associations between occupational or residential exposure to agricultural land use or land use change and infectious disease risks are likely to be inconsistent and idiosyncratic, which might otherwise bias the results. Therefore, I considered a random effects meta-analysis to be a more conservative approach than fixed effects analysis [181, 182].

All analyses were conducted in R version 3.2.5 [186] with the metafor package [187].

2.3.5 Heterogeneity and Subgroup Analysis

Heterogeneity of effect sizes was first tested among studies included in the overall analysis using the I^2 statistic and the Cochranes Q test. A value of >75% for the I^2 statistic is generally considered to suggest substantial heterogeneity [188, 189].

A subgroup analysis was performed to determine how robust the regional meta-analysis result would be to certain study characteristics using the estimates from the regional meta-analysis. Here I created *a priori* subgroups on study type, sampling strategy, study setting, outcome measurement, study quality, study country and the characteristics of the study population.

Subgroup analyses were also conducted on common exposures stratified by aetiological agent (parasitic, viral, bacterial) and transmission mode (vector-borne, zoonotic) or specific disease or disease complex subgroups that had more than two mutually exclusive estimates available. In order to preserve sample sizes and remain epidemiologically realistic, aetiological agent and transmission mode subgroups were not constrained to be mutually exclusive (e.g., a disease can be both vector-borne and zoonotic, such as zoonotic malaria).

Common exposures that had more than two estimates included non-specific agriculture (defined as a category where a person indicates they work in agriculture regardless of the type of agriculture), livestock farming, oil palm plantation work, rice paddy farming and rubber plantation work. Livestock farming was further stratified into common livestock groups including porcine, bovine and poultry related exposure. Common diseases that had more than two risk estimates included *Ascaris lumbrocoides*, *Entamoeba histolytica*, *Giardia intestinalis*, hookworm, leptospirosis, malaria, *Opisthorchis viverrini*, scrub typhus (*Orientia tsutsugamushi*), *Rickettsia typhi*, *Schistosoma japonicum*, spotted fever group and *Trichuris trichiura*.

2.3.6 Confounding

It was not possible to adjust pooled regional meta-analysis estimates for known confounders and effect modifiers due to lack of individual participant level data. However, I conducted a meta-analysis of adjusted odds ratios extracted from each study to assess the potential impact of within study confounding.

In addition, considering that the association between land use and infectious disease may be impacted by many variables that are unmeasured or unreported in published articles (e.g. temperature, rainfall, climate, soil type, topography, socio-economic status), I conducted a sensitivity analysis using an E-value to test for between study unmeasured confounding. The E-value represents the strength of association an unmeasured confounder would need to have with both the treatment and outcome to fully explain away a specific risk factor-outcome association [190]. The E-value is calculated using the following equation:

$$E - Value = OR + \sqrt{OR \times (OR - 1)} \tag{2.1}$$

When calculating the E-value, unmeasured confounders are not listed and tested explicitly. Additionally, the E-value, does not assess measurement or selection bias. The E-value results also do not guarantee that if a confounder with parameters of a particular strength exists, then it necessarily explains away the effect. Rather, it is, only possible to construct scenarios in which it could. Readers and other researchers may then assess whether any confounding associations of that magnitude are biologically plausible [190].

2.3.7 Publication Bias

Publication bias was assessed in three ways. First, I plotted individual study effect sizes against the standard error of each study as a measure of the study size in funnel plots to visually assess asymmetry [191]. Second, I tested this asymmetry using Egger's linear regression test, in which significant asymmetry would suggest bias or heterogeneity [192]. Finally, I used a trim and fill method to further assess if there was a likelihood of missing studies that might exist and whether this would impact the pooled estimate. This method imputes hypothetical negative unpublished studies to mirror the positive studies, and recalculates a pooled estimate to assess the impact these hypothetical studies have on the pooled effect size [193, 194].

2.3.8 Data Availability

The final data set used that support the findings of this study can be made available upon request.

2.4 Results

2.4.1 Narrative Synthesis

The search strategy returned 15,426 potentially relevant publications in total, 58 of which met the inclusion criteria for full text analysis (see Figure 2.1). Of these, 34 mutually exclusive studies were included in the regional meta-analysis and a total of 37 mutually exclusive studies were included in the multiple subgroup analyses. Studies spanned five countries (Thailand = 11, Malaysia = 10, Vietnam = 9, Philippines = 2, Lao PDR = 2), two designs (cross-sectional = 27, case-control = 7) and were assessed as being of varying quality using two study quality tools (OHAT – definitely low risk of bias = 2, probably low risk of bias = 25, probably high risk of bias = 10 and NHLBI – good = 7, fair = 23, poor = 4). A total of 80 effect estimates were extracted consisting of 26 infectious diseases and 12 different exposures. All included studies were in English and no studies were found to be in any other language.

2.4.2 Regional Meta-Analysis

Overall, occupational or residential exposure to agricultural land use was consistently associated with increased infectious disease risks, but effects varied widely among studies, differing disease groups and agricultural types. A regional analysis of 34 mutually exclusive crude odds ratios from 34 studies demonstrated that people exposed to agricultural land either occupationally or residentially were at a 74% increased risk of being infected with a pathogen than those unexposed (OR 1.74, CI 1.45 – 2.05, $p < 0.001$, E = 2.01, (see Figure 2.2). Although a larger number of positive studies were included within the sample dataset, as shown in the funnel plot (see Figure 2.3), linear regression tests and the trim and fill analyses (see Figure 2.2) highlighted no evidence of publication bias on the overall effect size. High between-study heterogeneity (I^2 = 83.5%) was nevertheless observed, indicating considerable variability in effects among studies.

To assess the impact for within study confounding, a meta-analysis of 17 mutually exclusive adjusted odds ratios from 17 studies was conducted suggesting that people exposed to agricultural land either occupationally or residentially were similarly at significantly increased risk of being infected with a pathogen than those unexposed (OR 1.46, CI 1.11 – 1.92, $p < 0.001$, (see Figure 2.4). Tests of the potential effect of unmeasured confounders suggested that an excluded variable(s) would have to have a minimum odds ratio of 2.03 with both the exposure and outcome to fully explain away the pooled result (E=2.03).

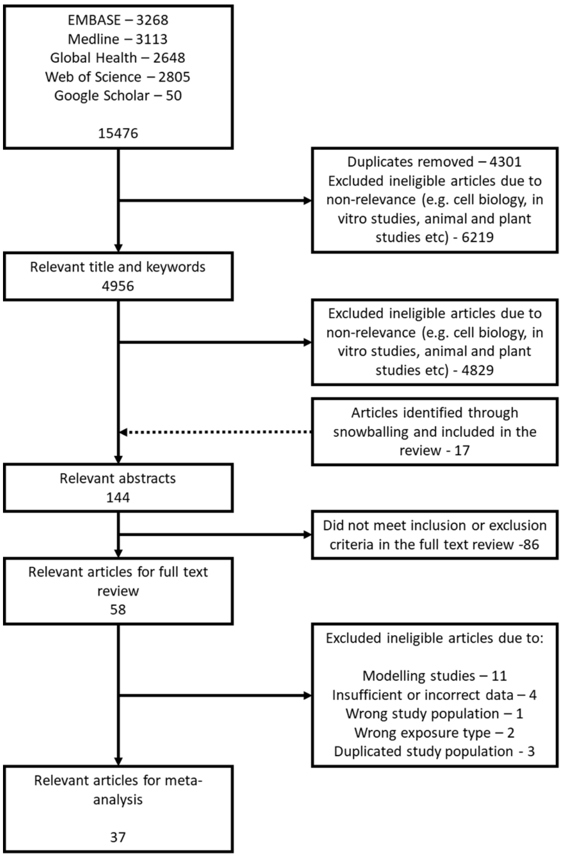
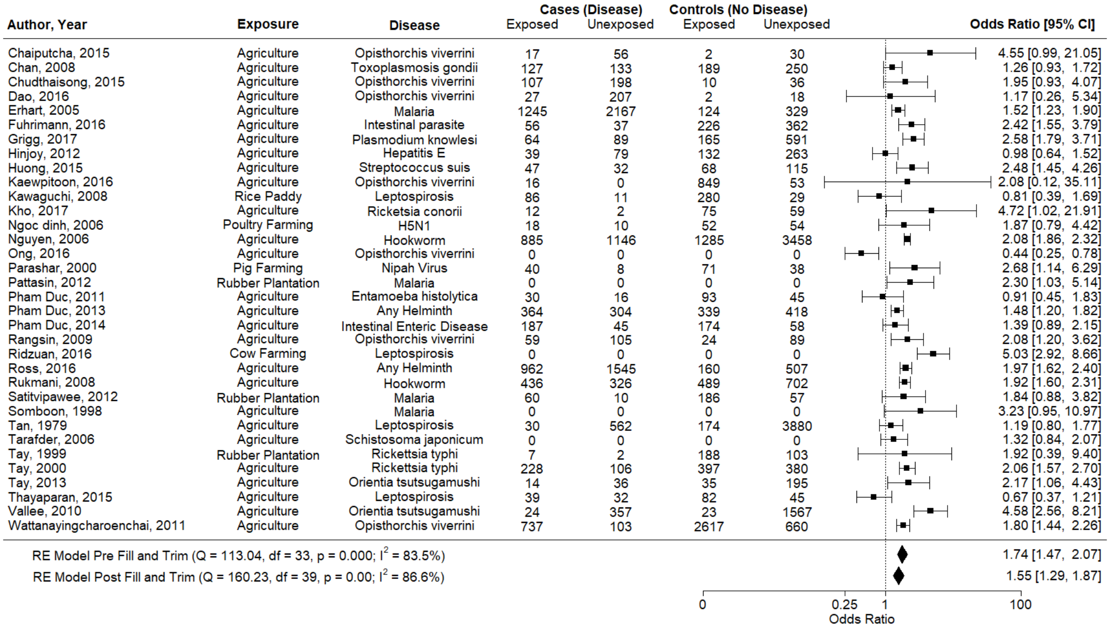


Figure 2.1: PRISMA diagram.

A flow chart of the study selection process



			Cases (Disease)		Controls (No Disease)		
Author, Year	**Exposure**	**Disease**	Exposed	Unexposed	Exposed	Unexposed	**Odds Ratio [95% CI]**
Chaiputcha, 2015	Agriculture	Opisthorchis viverrini	17	56	2	30	4.55 [0.99, 21.05]
Chan, 2008	Agriculture	Toxoplasmosis gondii	127	133	189	250	1.26 [0.93, 1.72]
Chudthaisong, 2015	Agriculture	Opisthorchis viverrini	107	198	10	36	1.95 [0.93, 4.07]
Dao, 2016	Agriculture	Opisthorchis viverrini	27	207	2	18	1.17 [0.26, 5.34]
Erhart, 2005	Agriculture	Malaria	1245	2167	124	329	1.52 [1.23, 1.90]
Fuhrimann, 2016	Agriculture	Intestinal parasite	56	37	226	362	2.42 [1.55, 3.79]
Grigg, 2017	Agriculture	Plasmodium knowlesi	64	89	165	591	2.58 [1.79, 3.71]
Hinjoy, 2012	Agriculture	Hepatitis E	39	79	132	263	0.98 [0.64, 1.52]
Huong, 2015	Agriculture	Streptococcus suis	47	32	68	115	2.48 [1.45, 4.26]
Kaewpitoon, 2016	Agriculture	Opisthorchis viverrini	16	0	849	53	2.08 [0.12, 35.11]
Kawaguchi, 2008	Rice Paddy	Leptospirosis	86	11	280	29	0.81 [0.39, 1.69]
Kho, 2017	Agriculture	Ricketsia conorii	12	2	75	59	4.72 [1.02, 21.91]
Ngoc dinh, 2006	Poultry Farming	H5N1	18	10	52	54	1.87 [0.79, 4.42]
Nguyen, 2006	Agriculture	Hookworm	885	1146	1285	3458	2.08 [1.86, 2.32]
Ong, 2016	Agriculture	Opisthorchis viverrini	0	0	0	0	0.44 [0.25, 0.78]
Parashar, 2000	Pig Farming	Nipah Virus	40	8	71	38	2.68 [1.14, 6.29]
Pattasin, 2012	Rubber Plantation	Malaria	0	0	0	0	2.30 [1.03, 5.14]
Pham Duc, 2011	Agriculture	Entamoeba histolytica	30	16	93	45	0.91 [0.45, 1.83]
Pham Duc, 2013	Agriculture	Any Helminth	364	304	339	418	1.48 [1.20, 1.82]
Pham Duc, 2014	Agriculture	Intestinal Enteric Disease	187	45	174	58	1.39 [0.89, 2.15]
Rangsin, 2009	Agriculture	Opisthorchis viverrini	59	105	24	89	2.08 [1.20, 3.62]
Ridzuan, 2016	Cow Farming	Leptospirosis	0	0	0	0	5.03 [2.92, 8.66]
Ross, 2016	Agriculture	Any Helminth	962	1545	160	507	1.97 [1.62, 2.40]
Rukmani, 2008	Agriculture	Hookworm	436	326	489	702	1.92 [1.60, 2.31]
Satitvipawee, 2012	Rubber Plantation	Malaria	60	10	186	57	1.84 [0.88, 3.82]
Somboon, 1998	Agriculture	Malaria	0	0	0	0	3.23 [0.95, 10.97]
Tan, 1979	Agriculture	Leptospirosis	30	562	174	3880	1.19 [0.80, 1.77]
Tarafder, 2006	Agriculture	Schistosoma japonicum	0	0	0	0	1.32 [0.84, 2.07]
Tay, 1999	Rubber Plantation	Rickettsia typhi	7	2	188	103	1.92 [0.39, 9.40]
Tay, 2000	Agriculture	Rickettsia typhi	228	106	397	380	2.06 [1.57, 2.70]
Tay, 2013	Agriculture	Orientia tsutsugamushi	14	36	35	195	2.17 [1.06, 4.43]
Thayaparan, 2015	Agriculture	Leptospirosis	39	32	82	45	0.67 [0.37, 1.21]
Vallee, 2010	Agriculture	Orientia tsutsugamushi	24	357	23	1567	4.58 [2.56, 8.21]
Wattanayingcharoenchai, 2011	Agriculture	Opisthorchis viverrini	737	103	2617	660	1.80 [1.44, 2.26]
RE Model Pre Fill and Trim (Q = 113.04, df = 33, p = 0.000; I^2 = 83.5%)							1.74 [1.47, 2.07]
RE Model Post Fill and Trim (Q = 160.23, df = 39, p = 0.00; I^2 = 86.6%)							1.55 [1.29, 1.87]

Figure 2.2: Regional meta-analysis.

Regional meta-analysis of mutually exclusive risk estimates to determine the association between occupational or residential exposure to agricultural land-use and infectious disease prevalence. Exposure to 'agriculture' is defined as a category where a person indicates they work or live in or near agriculture regardless of the type of agriculture. Square points show the crude odds ratio for each study, solid diamonds show the pooled meta-analysis estimates and error bars are defined as the 95% confidence interval. Note: Q, the Cochrane Q-test. Df, degrees of freedom. p, p-value. I^2, test for heterogeneity. RE, random effects

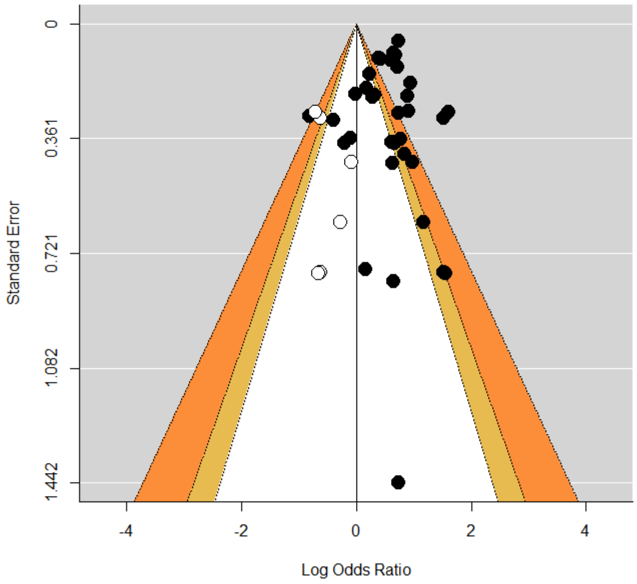


Figure 2.3: Funnel plot for the regional meta-analysis.

A plot of the logarithmic risk estimates vs. the precision (standard error) for each study, with adjustment using the trim and fill method. Closed circles denote identified studies and their summary measures, respectively. Open circles represent missing studies after adjustment for funnel plot asymmetry and the summary measure incorporating hypothetical studies, respectively. Key areas of statistical significance have been superimposed on the funnel, and the plot is now centred at zero. The yellow zones show effects between p=0.10 and p=0.05, and the orange zones show effects between p=0.05 and p=0.01. Effects in the white zone are greater than p=0.10 and effects in the grey zones are smaller than p=0.01. A Z-test was conducted to calculate p-values.

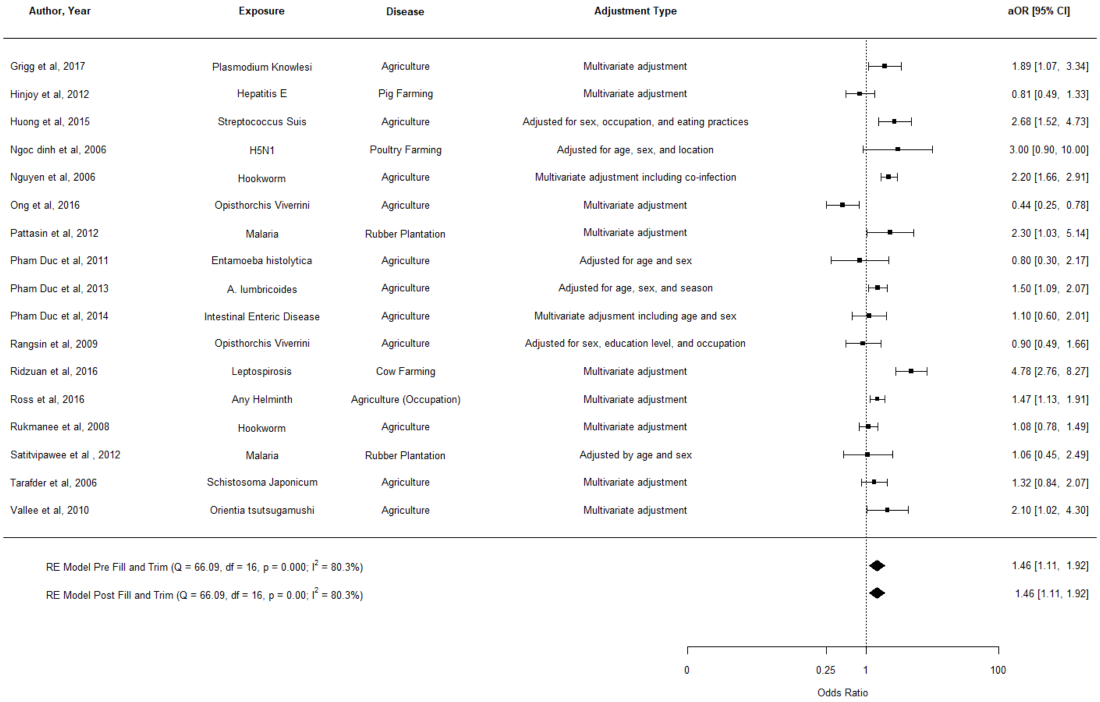


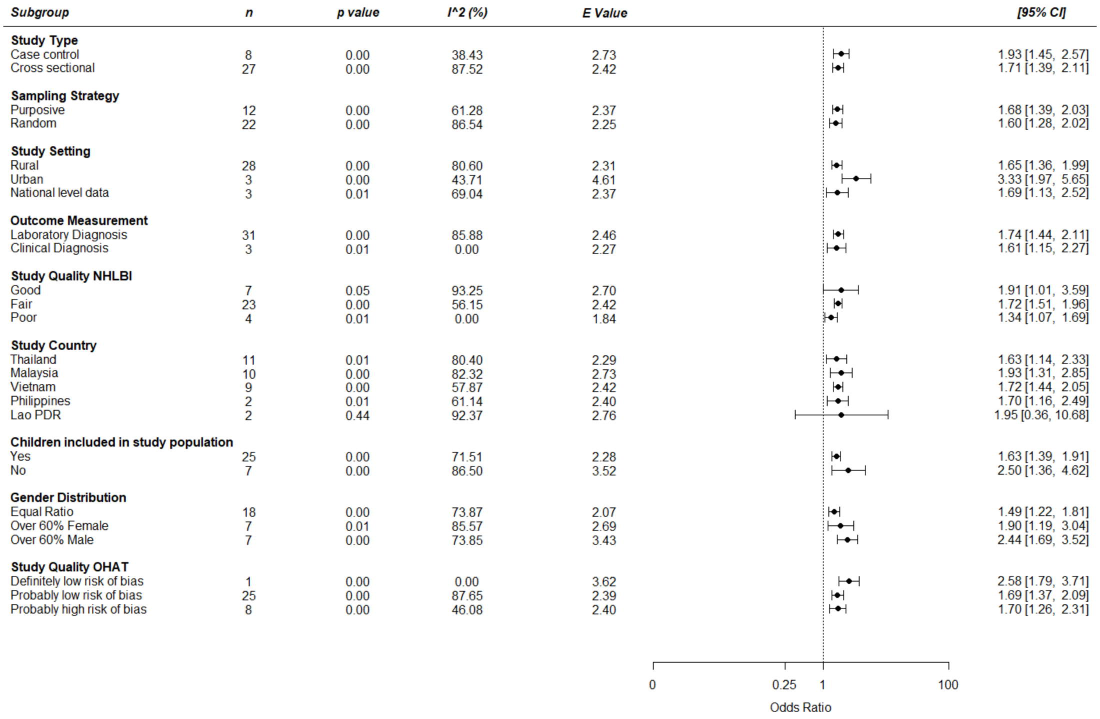
Figure 2.4: Adjusted odds meta-analysis.

Adjusted meta-analysis of mutually exclusive risk estimates to determine the impact of within study confounding on the association between occupational or residential exposure to agricultural land use and infectious disease prevalence. Agriculture (Non-specific) is defined as a category where a person indicates they work or live in or near agriculture regardless of the type of agriculture. Multivariate adjustment is defined as adjustment for multiple factors which are not listed in the original study. A Z test was conducted to calculate p values. Square points show the crude odds ratio for each study, solid diamonds show the pooled meta-analysis estimate and error bars are defined as the 95% confidence interval. Note: Q, the Cochrane Q test. Df, degrees of freedom. p, p value. I^2, test for heterogeneity. RE, random effects.

2.4.3 Study Characteristics Sensitivity Analysis

To evaluate the impact of between study confounding, I examined the influence of a range of additional study and sample characteristics on effect size and direction, including study type and methodology, socio-demographic characteristics (gender, whether children were included in the sample population, and rural vs urban), both study quality assessments and study location. In this test, associations consistent with the overall positive effect were observed irrespective of study and sample characteristics (see Figure 2.5), strengthening confidence that the pooled result is robust to a range of measured and, by extension, unmeasured confounders. In addition, the significant heterogeneity observed amongst studies in the regional pooled analysis (see Figure 2.2) does not suggest the presence of systematic bias from unmeasured confounders.

Nevertheless, one effect modifier/confounder variable (study setting) exhibited a divergence in effect sizes between groups, suggesting a possible interaction with the main effect of agricultural exposure. Here, the effect of agricultural exposure on infection was more than twice as strong in studies in urban than in rural settings, preserving the possibility that the pooled effect is vulnerable to the effect of unmeasured confounders, albeit here insufficient to explain away the pooled result. In addition, a single subgroup indicated a lack of significant association (studies based in Lao PDR). However, given the effect sizes and direction for these groups did not deviate considerably from the pooled effect, I considered this more likely due to small sample size than evidence of potential confounding. Finally, low heterogeneity for some stratum specific covariates alongside consistent effect sizes indicates that the source of heterogeneity is likely coming from elsewhere, warranting the use of further subgroup analyses to scrutinize the pooled result and to test hypotheses on differences in effect between agricultural types and disease groups.



Subgroup	*n*	*p value*	*I^2 (%)*	*E Value*	*[95% CI]*
Study Type					
Case control	8	0.00	38.43	2.73	1.93 [1.45, 2.57]
Cross sectional	27	0.00	87.52	2.42	1.71 [1.39, 2.11]
Sampling Strategy					
Purposive	12	0.00	61.28	2.37	1.68 [1.39, 2.03]
Random	22	0.00	86.54	2.25	1.60 [1.28, 2.02]
Study Setting					
Rural	28	0.00	80.60	2.31	1.65 [1.36, 1.99]
Urban	3	0.00	43.71	4.61	3.33 [1.97, 5.65]
National level data	3	0.01	69.04	2.37	1.69 [1.13, 2.52]
Outcome Measurement					
Laboratory Diagnosis	31	0.00	85.88	2.46	1.74 [1.44, 2.11]
Clinical Diagnosis	3	0.01	0.00	2.27	1.61 [1.15, 2.27]
Study Quality NHLBI					
Good	7	0.05	93.25	2.70	1.91 [1.01, 3.59]
Fair	23	0.00	56.15	2.42	1.72 [1.51, 1.96]
Poor	4	0.01	0.00	1.84	1.34 [1.07, 1.69]
Study Country					
Thailand	11	0.01	80.40	2.29	1.63 [1.14, 2.33]
Malaysia	10	0.00	82.32	2.73	1.93 [1.31, 2.85]
Vietnam	9	0.00	57.87	2.42	1.72 [1.44, 2.05]
Philippines	2	0.01	61.14	2.40	1.70 [1.16, 2.49]
Lao PDR	2	0.44	92.37	2.76	1.95 [0.36, 10.68]
Children included in study population					
Yes	25	0.00	71.51	2.28	1.63 [1.39, 1.91]
No	7	0.00	86.50	3.52	2.50 [1.36, 4.62]
Gender Distribution					
Equal Ratio	18	0.00	73.87	2.07	1.49 [1.22, 1.81]
Over 60% Female	7	0.01	85.57	2.69	1.90 [1.19, 3.04]
Over 60% Male	7	0.00	73.85	3.43	2.44 [1.69, 3.52]
Study Quality OHAT					
Definitely low risk of bias	1	0.00	0.00	3.62	2.58 [1.79, 3.71]
Probably low risk of bias	25	0.00	87.65	2.39	1.69 [1.37, 2.09]
Probably high risk of bias	8	0.00	46.08	2.40	1.70 [1.26, 2.31]

Figure 2.5: Sensitivity analysis of the regional meta-analysis.

A priori subgroups based on study characteristics to test the sensitivity of the regional meta-analysis. Results suggest that subgroups based on study characteristics do not significantly alter the direction of the association between occupational or residential exposure to agricultural land-use and infectious disease prevalence. Circle points show the pooled subgroup estimates and error bars are defined as the 95% confidence interval. Note: n, number of studies included in each pooled estimate. CI, confidence intervals. OHAT, Office of Health Assessment and Translation. NHLBI, National Heart, Lung and Blood Institute

2.4.4 Exposure-based Subgroup Analysis

Further subgroup analysis was performed using mutually exclusive estimates based on common exposure types (see Figure 2.6, 2.7) and for specific disease classes (see Figure 2.8). Consistent associations between agricultural exposure and infection were again evident. For the non-specific agricultural group, a similar effect was observed with all infectious diseases (OR 1.71, CI 1.38 – 2.13). When stratifying the non-specific agricultural group by disease class, significant effects were observed for parasitic (OR 1.74, CI 1.41 – 2.13), vector-borne (OR 1.85, CI 1.18 – 2.90) and zoonotic diseases (OR 1.63, CI 1.19 – 2.24). A marginal non-significant effect was found for bacterial diseases (OR 1.79, CI 0.97 – 3.31, I2 = 89.4%) (see Figure 2.6).

Among the specific agricultural subgroups, the effect was higher in populations working or living in or near oil palm and being infected with vector-borne zoonotic diseases (leptospirosis and P. falciparum) compared to those unexposed (OR 3.25, CI 2.29 – 4.61). Similarly, exposure to rubber plantations increased the risk of being infected with all types of pathogens (OR 2.27, CI 1.82 – 2.82). This effect was also consistent when stratified by disease class where significant associations were found for bacterial (OR 2.27, CI 1.79 – 2.89), parasitic (OR 2.24, CI 1.35 – 3.74), vector-borne (OR 2.27, CI 1.82 – 2.82) and zoonotic (OR 2.31, CI 1.83 – 2.94) disease class subgroups (see Figure 2.7).

Significant associations were observed for general livestock farming (see Figure 2.7) and all diseases (OR 2.54, CI 1.37 – 4.72), zoonotic (OR 2.46, CI 1.35 – 4.48), vector-borne (OR 2.52, CI 1.48 – 4.28) and bacterial (OR 4.47, CI 1.30 – 15.39) diseases. A marginal non-significant positive association was also established between livestock farming and viral diseases (OR 1.55, CI 0.83 – 2.81). Further subgrouping by livestock type showed consistent marginal non-significant positive effects. Specifically, marginal associations were observed between porcine animals and all diseases (OR 3.57, CI 0.84 – 15.23), vector-borne (OR 3.09, CI 0.58 – 16.46), zoonotic (OR 3.57, CI 0.84 – 15.23) and viral (OR 4.31, CI 0.49 – 37.81) diseases. Effect sizes found for bovine animals were consistent for all, vector-borne or zoonotic diseases (OR 2.09, CI 0.80 – 5.49) and bacterial diseases (OR 2.40, CI 0.57 – 10.12). No associations were found for exposure to poultry and all, vector-borne or zoonotic diseases (OR 0.91, CI 0.24 – 3.45). There was no evidence of publication bias for any other exposure-based subgroups.

Exposure to rice paddy farming (see Figure 2.6) resulted in a non-significant association for all diseases (OR 1.34, CI 0.81 – 2.23), bacterial (OR 1.40, CI 0.71 – 2.77), zoonotic or vector-borne (OR 1.17, CI 0.62 – 2.21) disease class subgroups. However, trim and fill tests indicated the presence of publication bias in which positive associations between agricultural exposure and general infection were under-reported among studies on rice paddy

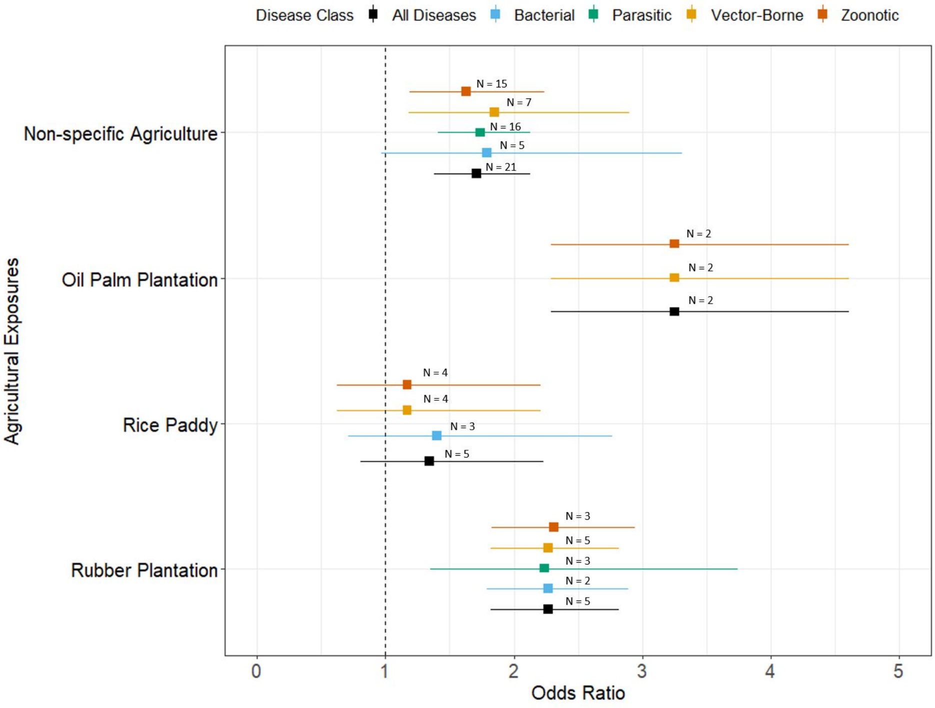


Figure 2.6: Agricultural exposure based subgroup analysis

Subgroups were created *a priori* based on exposures that had two or more mutually exclusive estimates. Agriculture (non-specific) is defined as a category where a person indicates they work in agriculture regardless of the type of agriculture. Square points show the pooled subgroup estimates and error bars are defined as the 95% confidence interval

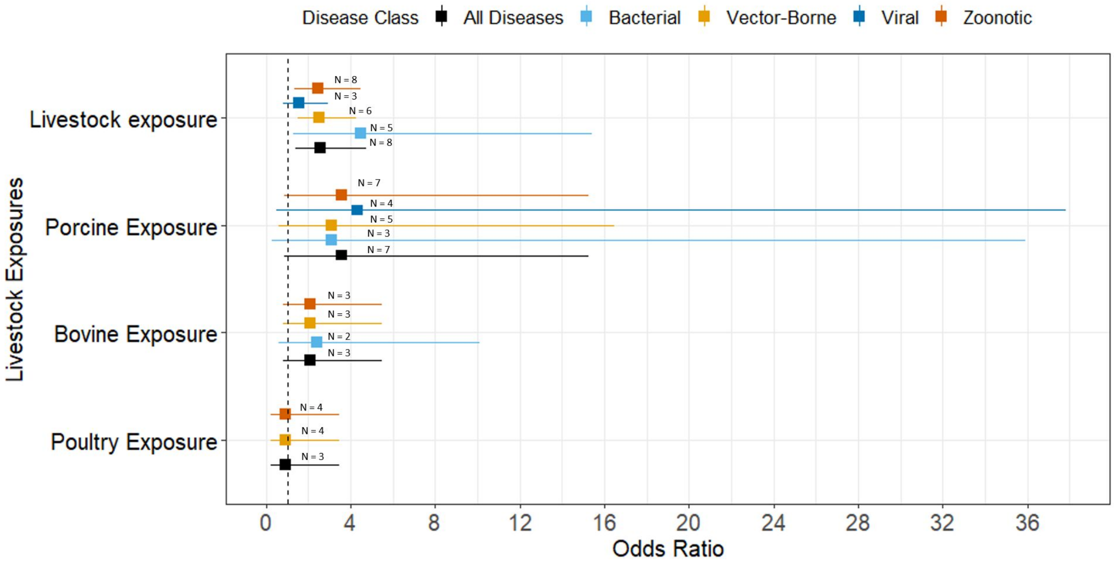


Figure 2.7: Livestock exposure based subgroup analysis

Livestock farming is defined as a category where a person indicates they are exposed to livestock generally regardless of the specific type of livestock (e.g., chickens). Porcine, Bovine or Poultry exposure is defined as a person being exposed to each of these respective animal types. Square points show the pooled subgroup estimates and error bars are defined as the 95% confidence interval farming. When accounted for, the effect of agricultural exposure on infection risk within the rice paddy farming subgroup became significant (OR 1.81, CI 1.04 – 3.17, p = 0.037, E = 1.47), suggesting that the overall effect is likely conservative.

2.4.5 Disease-based subgroup analysis

A final subgroup analysis based on specific diseases or disease complexes again showed consistent associations between infection and agricultural exposure (see Figure 2.8), notably for spotted fever group rickettsioses (OR 3.91, CI 2.61 – 5.85), hookworm (OR 2.42, CI 1.56 – 3.75), scrub typhus (OR 2.37, CI 1.41 – 3.96), malaria (OR 2.00, CI 1.46 – 2.73), *S. japonicum* (OR 1.71, CI 1.18 – 2.48) and *T. trichuria* (OR 1.40, CI 1.27 – 1.53). In contrast, no significant association was observed for the *A. lumbrocoides*, *O. viverrini*, *E. histolytica*, *G. intestinalis*, Leptospirosis and *R. typhi* subgroups. Again, there was little evidence of publication bias or unmeasured confounding for significant effect sizes, although heterogeneity remained present in many groups (see A.1, A.2, A.3)

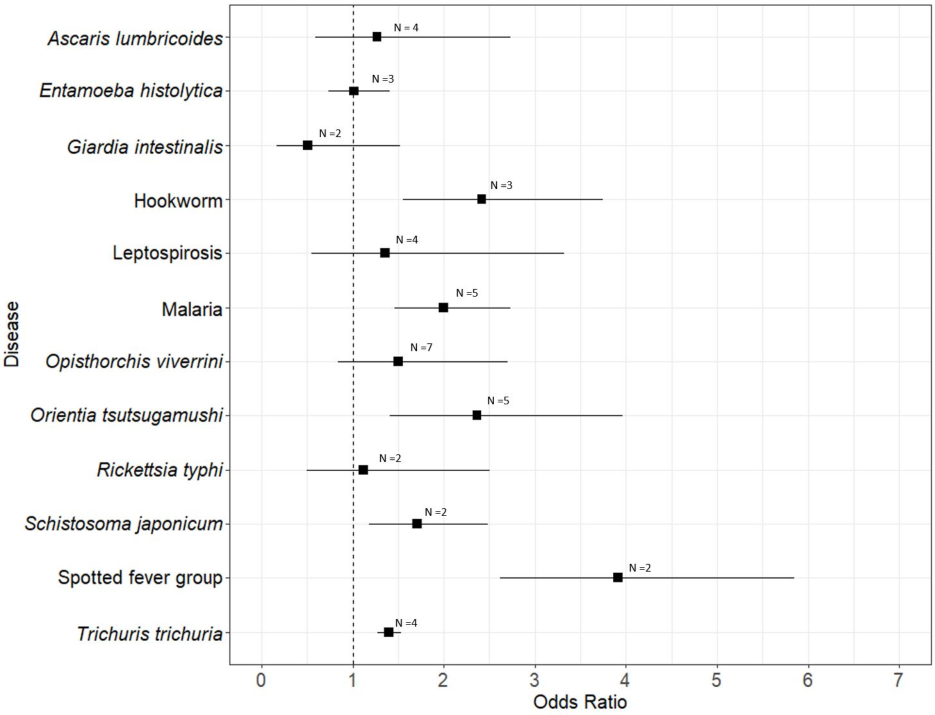


Figure 2.8: Disease Based Subgroup Analysis

Subgroups were created *a priori* based on diseases that had two or more mutually exclusive estimates. *Orientia tsutsugamushi* is also known as Scrub typhus. *Rickettsia typhi* is otherwise known as murine typhus. *Opisthorchis viverrini* is also known as Opisthorchiasis. Square points show the pooled subgroup estimates and error bars are defined as the 95% confidence interval

2.5 Discussion

2.5.1 Overview

Agricultural land use or land-use change has been repeatedly linked to infectious disease risks in humans [50, 77, 78, 81, 83, 85, 86, 90, 110, 114, 195, 196, 197, 198]; however, no study has systematically assessed or quantified this association. Based on currently available evidence from 37 eligible studies drawn from a corpus of over 15,000 peer-reviewed publications, results strongly suggest that exposure to agricultural land use either occupationally or residentially is consistently associated with increased infectious disease risk (average 74% increase), an effect evident across a wide range of agricultural types and disease groups. After pooling adjusted risk estimates from 17 eligible studies, a similar significant association was still evident, suggesting that there was little within study confounding.

Effects were most pronounced for oil palm monoculture (>3 times the risk) and rubber (>2 times the risk) forest monocultures and a strong association was also found for livestock farming. Associations for specific diseases or disease complexes were present for spotted fever group rickettsioses, hookworm, scrub typhus, malaria, *S. japonicum* and *T. trichuria*, but absent for other groups (*A. lumbrocoides*, *G. intestinalis*, *E. histolytica*, leptospirosis, opisthorchiasis and *R. typhi*). No evidence of publication bias was detected in the regional meta-analysis, but evidence of bias was present in the rice paddy farming subgroup analysis, whereby studies documenting positive associations between agriculture and all types of infection were under-represented, suggesting the overall effect is conservative. Considerable heterogeneity among studies and subgroups alongside negative tests for potential confounding from both measured and unmeasured effect modifiers further suggest that the results are robust to a range of possible sources of bias.

2.5.2 Exposure-based Subgroups

Sub-group analysis, in which data were grouped by common exposures and then stratified by aetiological agent (parasitic, viral, bacterial), transmission mode (vector-borne, zoonotic) or specific disease types or disease complexes, nevertheless highlight the potential complexity and variability of agriculture-infectious disease associations. The particularly strong effects that were observed for the two-forest monoculture-based agricultural types (oil palm and rubber) are key findings. All these crops have been planted extensively in recent decades and been major contributors to land-use changes in this region. For example, between 2005 and 2010, almost 250,000 hectares of natural vegetation with tree cover was converted to rubber plantations in SE Asia [199, 200], and the loss of primary forests for the cultivation of oil palm in Indonesia (especially on Sumatra and Borneo islands) quadrupled between 2000 and 2012 to 800,000 hectares a year [201]. In 2010, with an estimated 122 million people working in agriculture in SE Asia, approximately 115 million hectares (approx. 28% of the total area) were harvested for rice, maize, oil palm, natural rubber and coconut [202, 203]. These results thus have far reaching implications for a large fraction of SE Asia currently under cultivation or planned for agricultural conversion; that agricultural land-uses and even differing agricultural types appear to exacerbate infectious disease risks more than others raises the possibility that land-use decisions could be tailored to minimise human health impacts.

Mechanisms by which crop monocultures impact the risk of infectious diseases are difficult to untangle and likely idiosyncratic. Deforestation or different agricultural land-uses may favour some disease hosts or vectors (influencing e.g., abundance, distributions or transmission dynamics), while the loss of biodiversity has also been linked to increases in disease risk in some cases [197]. For example, a decrease in wild mammal species richness in fragmented habitats was associated with a higher seroprevalence of Chagas disease in small mammal reservoir hosts [50, 204]. In other cases, different agricultural land-use types could be frequented by people, modifying contact rates with animal hosts or vectors, and combinations of these effects are also probable. Fornace et al. (2016), for example, show that a higher incidence of *P. knowlesi* is associated with larger amounts of forest loss surrounding villages, which may have caused changes in macaque or mosquito habitats in addition to increased levels of human activity, thereby increasing the risk of infection in humans [86].

Landscape factors such as distribution, density, behaviour and population dynamics of vectors and their hosts are partially controlled by landscape features such as vegetation cover, surface moisture, topography or soil type; which in turn may also influence the level of transmission of an infection [78]. Oil palm, rubber plantation and rice paddy monocultures have reduced species richness compared with primary and secondary forests [205, 206], and these monocultures are structurally less complex than natural forests typically exhibiting a more uniform age structure, lower or no canopy, sparse undergrowth, less stable and more extreme microclimates, and greater levels of human disturbance and presence [206, 207]. Evidence suggests that such changes related to physical characteristics of the landscape or biodiversity loss itself could favour disease carrying hosts or vectors or increase the efficacy of disease transmission to remaining hosts (in this case people). For example, Burkett-Cadena et al (2018) suggest that an increased mosquito vector abundance was positively associated with deforestation. Of the mosquito species that were favoured by deforestation, 56.5% were confirmed vectors of human pathogens, compared to 27.5%

of species that were negatively impacted by deforestation [208]. Faust et al (2018) also suggest that the greatest risk of spillover events occur at intermediate levels of habitat loss, whereas the largest, but rarest, epidemics occur at extremes of land conversion [81]. These results are thus consistent with these previous empirical [89, 209] and modelling studies [81, 85, 86, 90, 198] and further support suggestions that deforestation resulting in crop monocultures is particularly problematic for elevating infection risks in susceptible nearby populations.

Whereas many previous studies have focussed on land-use change and deforestation explicitly, my analysis is largely blind to prior land-cover history. I nevertheless find variation in disease risk among specific agricultural land-use types, suggesting that an effect on disease risk likely goes beyond simply a change in land cover (e.g., from forest to crop monoculture) to include the final characteristics of modified agricultural landscapes. To further untangle mechanisms here would require a more detailed dataset on land-cover history (e.g., class transitions), scale and context.

Previous research on the association between livestock farming and infectious disease risk has been inconsistent [170, 210, 211, 212, 213, 214, 215, 216], whereas here I find consistent associations between infectious disease risks and exposure to livestock farming. The subgroup analysis for separate livestock categories (see Figure 2.7) suggests that infection risk may vary according to exposure to the type of animals farmed, with pigs and cattle exposure being positively associated with infection while poultry exposure having no association. Results further show consistent positive associations between livestock farming and differing disease classes, whereby exposure to livestock can result in 2 to 4 times the risk of being infected with vector-borne, bacterial or zoonotic diseases. I also find a marginal association with livestock farming and viral diseases, albeit with small sample sizes likely limiting power to confirm the positive effect. Livestock disease transmission can occur through multiple routes including airborne, direct faecal-oral, animal bites and scratches, contaminated animal products and consumption of uncooked meat [215, 217]. Alternatively, the impact of livestock may be to act as amplifier hosts [218, 219], while livestock housing studies show that keeping livestock such as cattle in the house as opposed to shelters outside the house contributes to increased disease risk rather than zoo-prophylaxis [220, 221]. In addition, global changes in climate, agricultural intensification and expansion for livestock, trade, travel, and closer interactions with livestock has facilitated infectious disease transmission [222]. Further empirical data from appropriately powered epidemiological studies are required to confirm my results and better identify mechanisms.

2.5.3 Disease-based Subgroups

Effect variability was also observed among specific disease or disease complex subgroups. Significant associations ranging between 1.4 to 2.9 times the risk of infection when exposed to agricultural land-use were identified for hookworm, malaria, scrub typhus, *S. japonicum*, spotted fever group rickettsioses and *Trichuris trichiura*. In contrast, no effect was seen for *A. lumbrocoides*, *E. histolytica*, *G. intestinalis*, *O. viverrini*, Leptospirosis and *R. typhi*. These results again illustrate the potential complexity of agriculture-disease associations, whereby agricultural land use could be impacting the transmission cycles of these disease groups in different ways or otherwise unmeasured effect modifiers could be at play.

Specific disease traits or epidemiological characteristics likely explain these differences, at least in part. For example, previous research suggests that arthropod vectors, such as mosquitoes and ticks, and helminths may be more vulnerable to environmental changes such as agricultural land uses than other taxa [214]. Since I find significant associations only for parasitic or vector-borne diseases (and no association for directly transmitted zoonotic or faecal-oral route diseases), my results broadly support this suggestion. Mechanistically, this may be linked to the modification of environmental niches, changes in the community composition, or alterations in the behaviour or movement of vector species [50, 76, 196, 207, 223]. For example, malaria in the Mekong region has been associated with dense forest cover and also with cultivated areas [84, 224]. Forest-fringe and deforested regions can also create suitable habitats for malaria vectors (e.g. *Anopheles minimus*)[225]. Therefore, the wide mosquito vector diversity and the potential for mosquito vectors to adapt in deep-forests and forest-fringes, in addition to the movement of susceptible humans to and from the forest, provide ideal conditions for sustained and novel transmission [84].

Despite this trend, some diseases for which no effect was observed were helminths, and in this case variation in effect may be related to subtler transmission characteristics or other unmeasured confounders. *A. lumbrocoides* or *O. viverrini*, for example, are transmitted via the faecal-oral route whereas *T. trichuria*, *S. japonicum* and hookworm are transmitted through skin penetration. Although both cases and controls will be infected via the same transmission mechanism, people exposed to agriculture may be more susceptible to infection with faecal-oral route transmitted diseases due to the use of night soil (human faeces) as fertiliser to improve crop yield. Using nightsoil as fertiliser is prevalent in SE Asia, although there are no estimates on how widespread it may be [174, 175, 176], making it difficult to include explicitly as a potential confounding factor. Similarly, variation in effects between diseases could be a result of differential responses to public health interventions. For example, the efficacy of praziquantel mass drug administration is higher for *A. lumbrocoides* compared to *T. trichuria* or hookworm [226], but again incorporating treatment history as a potential effect modifier was not possible here.

Results show significant associations between exposure to agriculture and spotted fever group rickettsioses or scrub typhus but not *R. typhi*. This difference could again be linked to transmission characteristics. Although all are vector-borne, spotted fever rickettsioses is tick borne, scrub typhus is transmitted by larval mites, while *R. typhi* is transmitted by both fleas and lice. This is in line with current research that suggests ticks and mites are highly susceptible to environmental change [49, 227, 228]. For example, Lyme disease (a tick borne disease) has increased with forest fragmentation in North America [229, 230, 231]. Ostfeld et al (2018) also find that tick-borne infection prevalence was lowest when forest cover within a 1 km radius was high [232]. I found very little research to suggest environmental change was having large impacts on flea borne diseases [49, 227]. Previous research does suggest that *R. typhi* is largely an urban disease where overcrowding, poor public health and sanitation measures are considered key risk factors for transmission [233]. Specifically, *R. typhi* typically thrives in markets, grain stores, breweries, and garbage depots where rats serve as the main reservoir, which may explain the lack of association with agriculture reported here [233].

Results also contrast with previous studies in the case of agriculture and leptospirosis. Whereas I found no overall effect for leptospirosis, previous studies have yielded mixed results [234, 235, 236]. Research conducted in Thailand suggests that the sources of human and rodent infections are different, where humans are infected in villages in non-forested areas located near rivers while rats are infected in forest patches situated in the hilly areas [170]. In Asia, humans are known to be infected through prolonged contact with water that may be contaminated by infected animal hosts [237, 238]. Such environmental transmission is directly linked to frequent occupational exposure to agricultural land use and establishing causal pathways between the environment, animal hosts and human risk is therefore required for such complex eco-epidemiologies.

2.5.4 Limitations

Although consistent associations were found between agricultural land-use and infectious disease risk in humans, there are several inherent challenges in resolving agriculture-disease associations and some limitations in this study that could be improved upon or resolved in future studies.

First, despite the diverse range of generally robust results reported in this study, the systematic assessment of study quality in this analysis does highlight an apparent lack of robust and high-quality studies that assess the impact of differing agriculture types, the degree of exposure to agriculture (e.g. more or less) and land use change on infectious disease risks in SE Asia. Considering an initial 15,476 articles were generated from a sensitive and specific search strategy, just 34 (0.2%) met the inclusion and exclusion criteria and were included in the regional meta-analysis. All retained articles focus on agriculture as the main land use types, as opposed to other conventional land use practices, such as road building, dam building, mining and urbanisation. Only a small number of studies focus on the final human health outcome, while in contrast many studies focus on infectious diseases in plants or animals [118, 196, 239, 240]. Similar research aiming to evaluate the impacts of agricultural land-use on biodiversity appears far more prevalent and incorporates a wider range of land use types [58, 71, 241, 242]. Caution is therefore advised in interpreting results so as to avoid generalisations not supported by the data.

In addition, studies in the meta-analysis were all either case control or cross-sectional studies, which, in the hierarchy of evidence within the medical sciences, are considered more prone to bias and confounding than some other study designs (i.e., cohort studies or randomised controlled trials) [243]. Nevertheless, most of the studies were evaluated to have probably low risk of bias or be of fair quality, indicating that there is only a small chance that a fatal flaw would invalidate an individual study's findings. Despite this, I identify a general paucity of the highest quality studies on the human health implications of land-use decision making and policy, and its impacts on infectious diseases. Further studies that capture bias, confounding and effect modification would be particularly valuable.

Second, understanding whether the associations are significant spatially and temporally or if the associations are transient was not possible. Understanding whether the association between land use and infectious disease is consistent both spatially and temporally is an important avenue for future research. Specifically, understanding the causal relationships, leading from distal environmental changes to alterations in more proximal environmental characteristics and disease transmission cycles, which eventually lead to a shift in the risk of infectious diseases at the landscape level should be prioritised for future research [195].

Third, although extensive efforts to control (through the inclusion/exclusion criteria and the subgroup analysis) or at least detect (through tests of heterogeneity, the meta-analysis of adjusted odds ratios and E score tests) the potential effect of confounders and effect modifiers were made, there are likely to be environmental, social, demographic or even economic factors that could impact the association between land use and infectious disease risks. Participatory epidemiology offers the opportunity to conduct bottom up agro-system analytical research on the patterns of diseases in animal and human populations [244, 245, 246]. Participatory epidemiological research has previously provided insights into how social factors (which can be potential confounders or effect modifiers) can impact ecological processes. For example, the involvement of women in the care and preparation of poultry carcasses in Egypt could contribute to higher incidence of highly pathogenic avian influenza in women [244, 247]. Similarly, understanding how local indigenous herder knowledge on the clinical signs of classical acute and milder rinderpest has previously aided in the control and eradication of rinderpest [244, 248] . Hence, participatory mixed methods research is an ideal platform to assess effect modification and confounding and their potential impact on disease-agriculture relationships.

Finally, substantial heterogeneity was also observed in the regional meta-analyses, where I^2 values were higher than 80%. The substantial heterogeneity may be due to clinical heterogeneity or statistical heterogeneity. Clinical heterogeneity occurs where the exposure is modified by factors that vary across studies, the type of exposure (e.g. different agricultural types – rice vs rubber) or study participant characteristics [182]. Differences between studies in the definition or the measurement of exposure or outcome, may all lead to a difference in effects. In contrast, statistical heterogeneity exists when the true effects being evaluated differ between studies and may be detectable if the variation between the results of the studies is above that expected by chance [188]. Further sub-group and sensitivity analysis showed that heterogeneity decreased to a moderate level ($I^2 < 60\%$) only for certain subgroups [171, 188]. This suggests that some of the observed heterogeneity is attributable to epidemiological and environmental differences within this subgroup [188, 189]. Within our analysis, we did not plan for or conduct multiple comparison tests. Specifically, multiple testing was considering difficult to plan for as it might not be known, at the outset, which outcomes and which effect measures will be available from the included studies. However, further research is required to develop adequate multiple comparison procedures for use in systematic reviews [172]. There was little evidence of significant publication bias in my analyses (except for rice paddy farming), and any publication bias that was present had very little impact on the pooled association.

2.6 Conclusion

This meta-analysis provides broad evidence that occupational or residential exposure to differing types of agriculture can consistently exacerbate infectious disease risks in humans in SE Asia. These trends suggest that further expansion or intensification of land use for agricultural purposes may result in the novel emergence of pathogens as observed elsewhere (e.g., [83, 85, 88, 109, 249] or increased transmission of zoonotic, parasitic or vector-borne diseases (e.g., [84, 86, 90]. However, the results presented in this study also provide an opportunity for land use decision makers, governments, companies and agriculturalists to recognise the impact that agricultural land use or land use change may have on susceptible populations and proactively identify measures to mitigate these risks.

Given a range of other negative externalities of agriculture identified in other fields (e.g. carbon emissions, air pollution, biodiversity loss), the potential for better land-use decisions to collectively minimise infectious disease impacts alongside these other impacts is large. Enhancing the sustainability of agriculture has already been identified as a nexus issue that is central to meeting a diverse range of development and environmental targets, such as the SDGs, the Aichi biodiversity targets, and the Paris agreement [150]. Key measures are already being proposed to sustainably meet this multiplicity of demands through policy changes, such as reducing food wastage throughout the food supply chain [250, 251], advocation of reduced emissions and more sustainable diets [252, 253], efforts in soil management techniques [254], responsible consumption of animal products [254], and biodiversity-friendly farming practices [255]. This study provides critical additional evidence to propel human health impacts from infectious diseases into this mix to further advance health targets (e.g., SDG3, Target 3.3) [256] as a central component of improving the sustainability of agricultural development more broadly.

Chapter 3

Global human infectious disease impacts of agricultural production and trade

3.1 Abstract

Background

Infectious disease has typically been understood as a domestic burden, influenced primarily by in-country factors. The existence of a link between public health and agriculture trade has been a 'known unknown'. This study provides evidence establishing such a link where global agricultural production and trade, which is known to be associated with a range of environmental impacts, is also a substantial driver of the infectious disease burden in many countries.

Objectives/Methods

A literature review and meta-analysis was conducted to test for country-specific associations between exposure to agriculture and human infectious diseases. Country-specific meta-analytic effect sizes were then integrated with spatial averaging methods and population attributable fraction calculations to quantify the country-specific burden of infectious disease associated with agriculture. These country-specific burdens were then combined with a global input-output model to estimate what proportion of the burden of infectious diseases associated with agricultural is linked due to international trade.

Results

People who are exposed to agriculture are at more than double (107%) the risk of being infected with any pathogen compared to those unexposed, with agriculture being associate with approximately 13.1% (CI 7.9% - 18.4%) of the global burden of communicable diseases. Around one third (34.6%, CI 24.8% - 57.6%)) of this burden is linked to the international trade of agricultural commodities, with demand from high-income countries and regional powerhouses (USA, UK, EU, India, China and Japan) contributing the most to disease risks in primarily developing countries. The highest burden of trade related infectious disease occurs in Sub-Saharan Africa, particularly West Africa.

Interpretation

For burdened countries where both infectious disease and agricultural exports are prevalent, multinationals, multilaterals, governments, and public health funding bodies should

aim to ease these burdens through public health, environmental and sustainable development interventions. For consumer nations, SDG-aligned policies promoting sustainable consumption and diets must be extended to consider the eco-epidemiological costs of international food production and trade.

3.2 Introduction

The globalisation of agriculture has led to increases in production and trade and has reduced hunger, expanded consumer choice, enriched diets, improved efficiencies, and fuelled economic growth [14, 257]. However, these benefits have come at some cost: agriculture is also substantially responsible for greenhouse gas emissions, water and air pollution, and biodiversity loss [57, 71, 72, 258]. The impacts of agriculture are likely to increase as population growth continues. Sustainably feeding a global population of 10 billion by 2050 is one of the grand challenges recognized by the UN Sustainable Development Goals (SDGs) [150].

The direct environmental and social impacts of agriculture are well described. For example, over 50% of new agricultural land recruited during the 1980s and 1990s in the tropics was converted from previously intact forests, endangering essential environmental services and driving biodiversity loss globally [57, 71, 72, 258]. Similarly, studies assessing the links between human health and agriculture show impacts of agriculture on increasing the prevalence of both non-communicable (e.g. asthma) and infectious diseases (e.g. malaria or emerging infectious disease) [110, 259]. However, evidence on how demand for agriculture can drive these negative health impacts is limited or geographically restricted [138].

In current evaluations of sustainable agriculture, the health impacts of agricultural production and food imports are largely unknown. While bad labour footprints [260, 261] and the environmental footprint of foods and diets has been well studied [262, 263, 264, 265, 266, 267], the links between agricultural trade and public health have remained an unquantified ‘known unknown’.

The World Health Organisation has estimated the burden of disease broadly linked to environmental determinants but this currently excludes explicit agriculture-disease associations [268, 269]. Only partially filling this gap, the majority of studies that assess the association between agriculture and/or agricultural trade and infectious disease outcomes are geographically restricted empirical [138, 270] or modelling studies focussed on single infectious diseases [259, 271] or specific disease subsets (e.g. emerging infectious diseases, EIDs) [110]. Rohr et al., (2019) estimated that >25% of emerging infectious disease (EID) ‘events’ and >50% of zoonotic EID ‘events’ globally in the period 1940-2004 were linked to agricultural drivers; however, EIDs represent just a subset of the global burden of infectious diseases with a relatively small burden and trade routes were not assessed. Chaves et al., (2020) also find that 20% of the malaria risk in deforestation hotspots is driven by the international trade of deforestation-implicated export commodities, such as timber, wood products, tobacco, cocoa, coffee and cotton [138].

As agriculture continues to expand and intensify to meet the demands of a growing global population, monitoring and evaluating agriculture-based infectious disease threats will be of global importance and require quantification. I aimed to fill these gaps by developing a framework to explicitly estimate the agriculture-related burden of human infectious diseases at a global scale and map its trade-related demand network with input-output analysis. These results will be of value to land use decision makers, economists, governments, companies and agriculturalists seeking to recognise the impact that agricultural land use and trade can have on susceptible populations, alongside various other negative externalities, and to proactively identify measures that seek to achieve multiple global targets and indicators.

3.2.1 Agriculture-Disease Mechanisms

Common mechanisms by which agricultural land use alters the transmission of infectious disease include vector, host, and pathogen niche alterations, changes in host and vector community composition, behaviour or movement change of vectors and/or hosts, altered spatial distribution of hosts and/or vectors, socioeconomic factors, and environmental contamination [50]. Within this analysis, I only included specific diseases and disease categories that had a biologically plausible link on the basis of relevant literature which can be found in Table 2. Here I provide a narrative description of some the potential ecological mechanisms between agriculture and various diseases included within our analysis.

Diarrheal Diseases

Diarrheal diseases are most commonly caused by the transmission of bacterial, parasitic, or viral enteric organisms to humans through the contamination of water or food sources by faeces [272]. For example, recent studies have found that the local loss of dense forests, largely from agricultural expansion, affected diarrheal diseases in Cambodian children. Here, the authors suggest that deforestation due to agricultural expansion can impact hydrological cycles by increasing peak flows or soil erosion or reducing groundwater recharge or flow, which thereby increases microbial load and exposure, potentially raising the risk of diarrhoea in susceptible communities that use water resources [90].

Studies conducted in Vietnam also found that exposure to wastewater and excreta, which is typically used in Southeast Asia as fertiliser during agricultural activities, are significantly contributing to the risk of diarrhoea in adults [174, 175, 176, 273]. One study conducted in Wisconsin, USA found that living on a farm increased the risk of diarrheal diseases such as *Campylobacter jejuni* and *Escherichia coli*. Here, authors hypothesised that livestock exposure and consumption of unpasteurised (e.g. milk) or contaminated livestock or food products resulted in a higher risk for children living on a farm compared to those not living on a farm [274].

Viral Infections

A majority of emerging infectious viruses have origins in zoonotic animal reservoirs and are often transmitted to humans via intermediate hosts, such as domestic animals and livestock or wildlife species. Specifically, modern agricultural practices that can concentrate livestock and bring them into contact with wild animals can lead to increased disease risk amongst humans [275]. Examples of viruses that have emerged in this manner include influenza, coronaviruses such as the ones causing severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), and Nipah virus [88, 116, 149]. Viruses can also be foodborne, such as hepatitis E virus, tick-borne encephalitis virus in addition to numerous species of the enterovirus, adenovirus, and astrovirus viral families, among others [276].

Arboviruses such as rift valley fever, yellow fever, dengue, Japanese Encephalitis, and Crimean-Congo haemorrhagic fever virus (CCHFV) have also been known to be associated with agricultural practices. For example, in a recent study by [277], specific types of vegetation or land use were often found to be associated with increased disease risk through their impacts on suitable habitat for vectors and reservoir (or intermediate) hosts. Agricultural practices such as the creation of rice paddies, abandonment of farmlands, and a high rate of habitat fragmentation is hypothesised to have led to enhancing breeding sites for arbovirus vectors, increase host and vector densities and contact rates, and stimulate host and vector movement between habitat patches [277]

Respiratory Infections

Respiratory infections have long been recognized in association with work in farming. For example, inhalation of fungal spores from mouldy hay, straw, or grain can result in increased morbidity and mortality in farmers [278]. The incidence of pulmonary tuberculosis caused by Mycobacterium bovis is also higher in occupationally exposed individuals such as farm and slaughterhouse workers than in urban inhabitants in India. Here, little is known about disease transmission from human to cattle and vice-versa; however, researchers hypothesise that the consumption of unpasteurised bovine products can be a risk factor [279]. Other agricultural zoonoses that can lead to respiratory infections include psittacosis and Q fever. Psittacosis follows inhalation of desiccated droppings or secretions of poultry infected with Chlamydia psittaci and Q fever, is caused by inhalation of Coxiella burnetii from infected cattle, goats, and sheep [280]. In Cambodia, deforestation for agricultural expansion has also been associated with respiratory illnesses through various mechanisms. For example, fire is often used to clear tropical forests, and fine particulate matter from biomass smoke can penetrate deep into the lungs, thereby increasing the risk of respiratory infection (including pneumonia) [90]. Finally, in sub-Saharan Africa, biomass burning which typically occurs in poverty stricken agricultural landscapes is also associated with an increased risk of acute respiratory infection [281]

Helminth Infections

In general, human helminth infections (e.g., tapeworms, flukes, and roundworms) can occur in areas where the reuse of wastewater and sludge for agriculture is common. Specifically, the unrestricted use of wastewater for irrigation presents a serious health risk to farmers due to the dissemination of pathogens, particularly helminth eggs. Helminth eggs survive in water, soil, and crops for several months and over much longer periods than other microorganisms [282, 283]. Furthermore, some helminth infections, can even cause eating disorders, such as geophagy (desire to eat soil), bulimia and anorexia [110].

A key driver of increased helminth infection is agricultural irrigation and freshwater redistribution. For example, in a large meta-analysis, results showed that humans living near irrigation schemes or in close proximity to large dam reservoirs had significantly higher risk of schistosome infections than humans that did not live near these water resources [284]. Similarly, a more recent analysis of schistosomiasis case data from the past 70 years across sub-Saharan Africa showed that creating dams caused an ecosystem shock and blocked the migration of snail-eating river prawns, resulting in an increased risk of schistosomiasis for almost 400 million people [285].

The use of agrochemicals is also considered a risk factor for helminth infections by altering the densities of hosts or parasites or their natural enemies or mutualists [110]. Several pesticides can alter host behaviours or be directly toxic to hosts and parasites, which in turn can modify contact rates between parasites and human hosts. In addition, pesticides can alter community composition, which can indirectly affect behaviours or densities of intermediate and zoonotic hosts and parasites. For example, nitrogen- and phosphorous-based fertilizer use can increase the number of snails that transmit flatworms that cause human schistosomiasis [112]

Malaria

Agriculture is often cited as playing an important part in malaria ecology. For example, pre-production environmental changes, such as forest loss for agricultural expansion or intensification, can impact malaria transmission through changing habitat suitability. For example, forest loss leads to a decreased forest canopy thereby increasing sunlight and standing water creating optimum habitats for certain malaria transmitting mosquitoes [208]. In addition, frontier malaria can also occur due to unstable socio-economic conditions linked to deforestation such as increased migration, novel human exposure and low immunity, poor housing quality, and a lack of health services [76, 84, 161, 208, 240, 286, 287]. Crop production also plays an important role in malaria ecology and epidemiology across sub-Saharan Africa, yet only a few studies assess the relationship between differing crop types and malaria outcomes in humans [89, 288, 289, 290].

3.3 Methods

3.3.1 Methodological Overview

I integrated methods from epidemiology (literature review and meta-analysis), statistics (spatial averaging, population attributable fractions) and industrial ecology (input-output analysis) to quantify the burden of infectious disease associated with agriculture and further assess which countries ultimately drive these agriculture-associated disease burdens through their importation of agricultural commodities. In specific, I aimed to develop a 'framework' for the estimation of the burden of disease linked to agricultural production and trade. This framework can be applied at the global or regional level given available data, but importantly it can incorporate new information or data as it becomes available.

Within the systematic review, I focussed on searching and screening literature from 29 countries in Southeast Asia, South America and sub-Saharan Africa. However, through the screening process and data extraction, I only found 82 mutually exclusive studies that were from 14 of the 29 countries and which met my inclusion and exclusion criteria. Therefore, I calculated 14 country-specific pooled meta-analytic odds ratio estimates from empirical data extracted from a comprehensive literature review and meta-analysis to quantify the risk of being infected when exposed to agriculture compared to those unexposed. Using nearest neighbour weighted spatial averaging on the meta-analytic pooled odds ratios, I imputed and extrapolated associations for 135 countries (excluding island nations). I then calculated the burden of disease associated with agriculture and link these burdens to a global input output table to determine the total infectious disease footprint of agricultural trade across all countries, map the location of the likely impacts according to agricultural land-use extent, and detail the most impactful and impacted country connections.

3.3.2 Literature Review and Meta-Analysis

Overview

The systematic review methodology from Chapter 2 which focused on Southeast Asia was extended to then include 10 additional countries from sub-Saharan Africa and 10 countries from South America. With the aid of two MSc students, I reviewed articles that assessed the association between occupational or residential exposure to agriculture and the prevalence or incidence of infectious disease compared to the counterfactual of no exposure [270].

Here, studies between 1970 and 2017 from 29 countries across Southeast Asia, Africa and South America that provided data on the prevalence of infectious disease in people either occupationally or residentially exposed and unexposed to agricultural land use were reviewed. A random effects meta-analysis was subsequently performed to calculate global, regional and country-specific infectious disease risks of occupational or residential exposure to agricultural land use. Fixed effect models were only used in an instance where pooled estimates were calculated from a sample size of 2 studies.

Global and WHO regional effect estimates were initially calculated and data were then stratified by disease category subgroups defined as "all infectious diseases", "diarrheal disease", "parasitic and vector borne diseases", "intestinal nematodes" and "all other diseases"; which are based on specific categories stated within the Global Burden of Disease Project [291]. To assess country-level effects, I further stratified the global data set by country and quantified pooled odds ratios using two or more mutually exclusive crude estimates per country. Exposure based and disease based subgroup analysis was also conducted to assess whether associations were robust at the global level in relation to exposure type or disease type. Finally, I performed a covariate sensitivity analysis to determine how robust the global meta-analysis results would be to certain study, socioeconomic and environmental characteristics using the estimates from the global meta-analysis.

Eligibility Criteria

The following eligibility criteria were adhered to:

Study Question - “Is there an association between occupational or residential exposure to agricultural land uses and being infected with a pathogen for adults aged 18 and above in the 29 countries being investigated?”

Study Design – Empirical observational studies (longitudinal cohorts, case control or cross sectional) studies conducted within the last century in the 29 countries being investigated and reported in English were considered eligible.

Populations – This study ideally drew participants from the general adult population aged 18 and above. Studies that recruited participants of all ages (including children) were also included. Studies that focused exclusively on the child population were excluded.

Exposure – The primary exposure of interest is occupational or residential exposure to agriculture or agricultural land use. This is defined as whether study participants would be working or living in or near agricultural land. Specifically, agricultural exposure was defined as any person who partakes in the cultivation of land and breeding of animals and plants to provide food, fibre, medicinal plants and other products to sustain and enhance either for domestic, residential, occupational or economic purposes [49].

Comparators – Studies were included if they compared outcomes in the exposed group with those in a group of “unexposed” people (people who are not occupationally or residentially exposed to agriculture or agricultural land use).

Outcome – Studies were included if one of the primary outcomes include prevalence, sero-prevalence and incidence for all parasitic or vector-borne diseases that have a biologically plausible link to agriculture or agricultural land use.

Studies that investigated non-communicable disease or infectious diseases of plants, invertebrates or fish were excluded. I also excluded studies that were not conducted in the 29 listed countries, did not include some form of land use as an exposure or study focus, were theoretical research papers, reviews, commentaries or letters, or were not published in English. Studies that presented odds ratios based on the co-infection of more than 1 disease were excluded as co-infection could increase susceptibility to other infectious diseases [173]. Studies that assessed the impact of using human faeces (night soil) as fertiliser in agriculture were also excluded [174, 175, 176]. This is because using human faeces as fertiliser was not considered a land use but rather a confounding behavioural activity. Studies that assessed risk factors of disease in children were also excluded as children may be exposed to agricultural work but may also be more susceptible to certain diseases.

Countries that are members of ASEAN were selected as a culturally, environmentally and geographically rich, diverse and dynamic region of the world where significant natural resources including globally important stocks of biological diversity can be found. SE Asia also contributes 27% of the global burden of infectious and parasitic diseases, 30% of respiratory infections, 33% of maternal conditions, 37% of perinatal conditions and 35% of nutritional deficiencies [164]. All countries from South America were included as commercial agriculture is the biggest driver of deforestation in Latin America, with around 2/3 of deforested areas are for this purpose and the region is increasingly producing for international markets for example palm oil and soybean in particular in the Amazon region [292, 293]. At the same time, neglected tropical diseases disproportionally affect poorer communities in Latin America with the region experiencing some of the highest levels of inequality [154]. Finally, 10 countries were selected from Africa as these countries were considered to have high disease burdens, yet at the same time have high levels of agricultural land use.

- Inclusion Criteria

  - Geographical Location – The 29 selected countries included Argentina, Bolivarian Republic of Venezuela, Bolivia, Brazil, Brunei, Burundi, Cambodia, Chile, Colombia, Cote D'Ivoire, East Timor, Ecuador, Ghana, Indonesia, Laos PDR, Malawi, Malaysia, Myanmar, Nigeria, Paraguay, Peru, Philippines, Rwanda, Sierra Leone, Singapore, Tanzania, Thailand, Uganda, Uruguay, Vietnam and Zimbabwe.
  - Population – Adults aged 18 and above that work or live in or near agricultural land (NB – studies that assess total populations including both adult and children will be included).
  - Type of exposure - Agricultural land use exposure was defined as any person who partakes in the cultivation of land and breeding of animals and plants to provide food, fiber, medicinal plants and other products to sustain and enhance either for domestic, residential, occupational or economic purposes.
  - Type of comparator - No exposure to agricultural land use.
  - Types of outcome: Change in prevalence or incidence of infectious disease as a function of land use or land use change.
  - Type of disease: All infectious diseases that are prevalent in humans with a biologically plausible link to land-use change including emerging, zoonotic, bacterial, viral, parasitic and vector-borne infections.
  - Types of study – Peer reviewed empirical observational studies.

- Exclusion Criteria
  - Articles based on non-communicable disease.
  - Articles based on infectious diseases of plants, invertebrates or fish.
  - Articles that do not study the impact of land use or land use change.
  - Articles not in English.
  - Theoretical research, reviews, commentaries or letters.
  - Studies that presented odds ratios based on the co-infection of more than 1 disease.
  - Studies that assessed the impact of using human faeces (night soil) as fertiliser in agriculture.
  - Studies that assessed risk factors of disease in children.

Statistical Analysis

Associations were quantified using the odds ratio (OR) with a 95% confidence interval. This was extracted where possible from the studies or self-calculated using relevant data where possible. Where ORs could not be extracted or calculated due to poor or non-reported data, studies were excluded from the meta-analysis [171]. Crude odds ratios were then analysed using a random effects model. Random effects meta-analyses assume that a distribution of effects exists across all studies included in the analyses, resulting in heterogeneity among study results. The use of a random effects model was considered appropriate here because I assume that the associations between occupational or residential exposure to agricultural land use or land use change and infectious disease risks are likely to be inconsistent and idiosyncratic, which might otherwise bias the results. Therefore, I considered a random effects meta-analysis to be a more conservative approach than fixed effects analysis [181, 182].

As specified in Chapter 2, a study quality assessment was also conducted for all studies using the using a quality appraisal tools sourced from the National Heart, Lung and Blood Institute's (NHLBI) [179, 180]. Heterogeneity was quantified using the I^2 statistic and the Cochranes Q test. A value of $>$75% for the I^2 statistic is generally considered to suggest substantial heterogeneity [188, 189]. I also conducted a sensitivity analysis using an E-value to test for between study unmeasured confounding. The E-value represents the strength of association an unmeasured confounder would need to have with both the treatment and outcome to fully explain away a specific risk factor-outcome association [190]. Finally, publication bias was also assessed using three separate methods which have been described in Chapter 2: funnel plots, Egger's linear regression test and the trim and fill method [191, 192, 193, 194].

Subgroup and Sensitivity Analysis

Agriculture-disease relationships may be moderated by many confounders or effect modifiers. Exposure based and disease based subgroup analysis was also conducted to assess whether associations were robust at the global level in relation to exposure type or disease type (as specified earlier in Chapter 2). In addition, I performed a sensitivity analysis using the data extracted from the systematic review to determine how robust the regional meta-analysis result would be to certain study characteristics, environmental and socio-economic study level confounders [270]. I endeavoured to create subgroups by study location specific or subnational data; however, where no such granularity in data was found, I opted to use country-level data to formulate subgroups.

Here, I created a priori subgroups on i) study type, ii) sampling strategy, iii) study setting, iv) outcome measurement, v) study quality and iv) various characteristics of the study population. I also performed a sensitivity analysis with environmental covariates including i) mean annual temperature, ii) precipitation, iii) humidity, iv) climate zones and v) latitude [294, 295, 296]. Finally, a socioeconomic sensitivity analysis was also performed where a priori subgroups were created using the i) human development index (HDI), ii) gross domestic product per capita, iii) percentages of the population that have improved water and improved sanitation, respectively, and iv) country-specific overseas development assistance stratification. I could not use the income adjusted human development index to account for household consumption as these indicators are not available at the subnational level [297].

Although there was some variation amongst countries, the effect of agricultural exposure on infectious disease risk was relatively consistent, with minor variation being observed across countries and through the subgroup and sensitivity analyses (see Figures 3.1, 3.2, 3.3). In addition, although I find considerable heterogeneity at the global, regional, and country-specific level thereby justifying the use of subgroup analysis, I find no strong evidence of consistent covariate driven bias impacting our overall direction of association. This consistency supports the generality of an effect across diverse social and environmental settings and presents the possibility of using the estimates obtained to impute values for countries with no estimates (within reason) in order to increase the size of the trade network component of the analysis. This presents the two issues of 1) valid interpolation and 2) extrapolation beyond the range of the available data, when aiming to achieve wider and ultimately global agriculture-disease risk coverage.

3.3.3 Spatial Averaging

Interpolation

There are many methods of interpolation that can be used to assign missing values for countries with no estimates, all of which require certain assumptions to be made. Here countries without estimates are those for which no studies were identified in the literature review yielding the required data to calculate an odds ratio (i.e., no eligible studies retrieved). In these cases, the challenge is to determine whether a valid estimate can be assigned to it from what is known or can be learnt about the estimates derived from the sampled countries, since not having an estimate of its own is likely to reflect an unmeasured rather than an absence of an effect. For example, I could first apply the ‘global’ pooled meta-analytic effect size calculated using all data from sampled countries in the literature review to unsampled countries within the same study region (i.e., South and Southeast Asia, Africa and

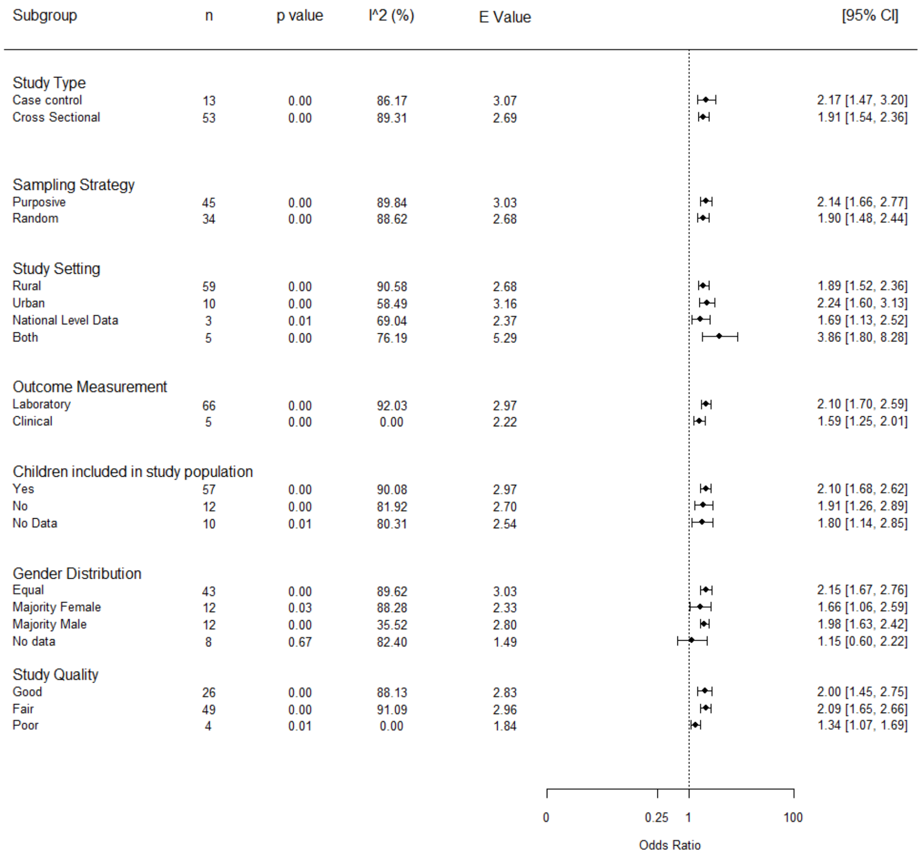
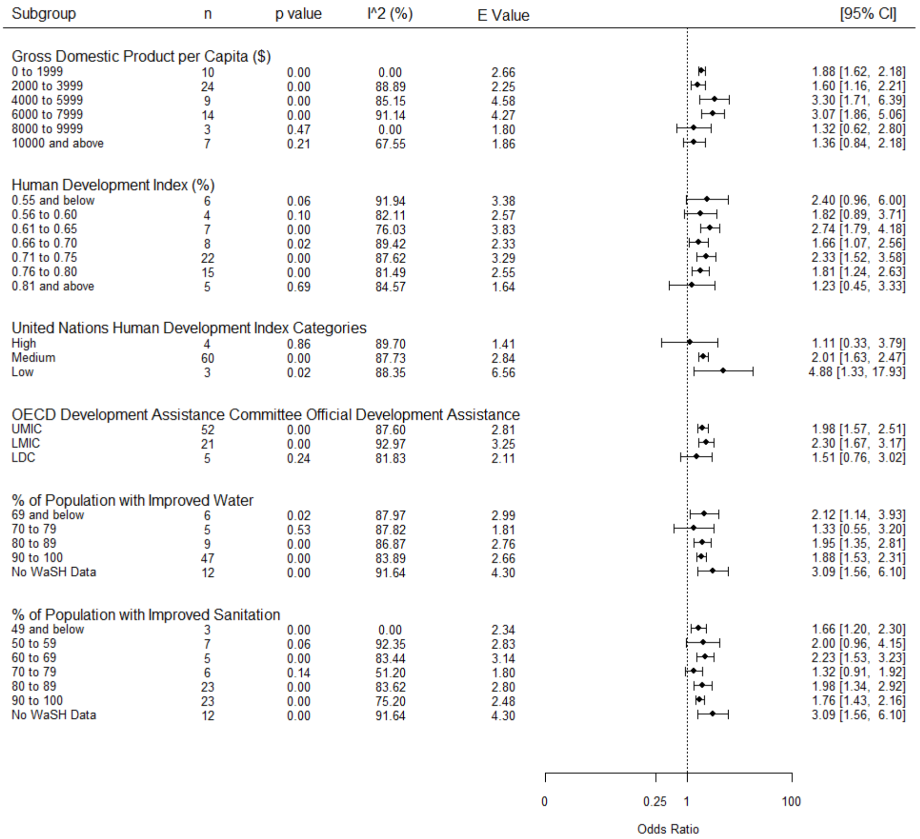


Figure 3.1: Study Characteristics Sensitivity Analysis

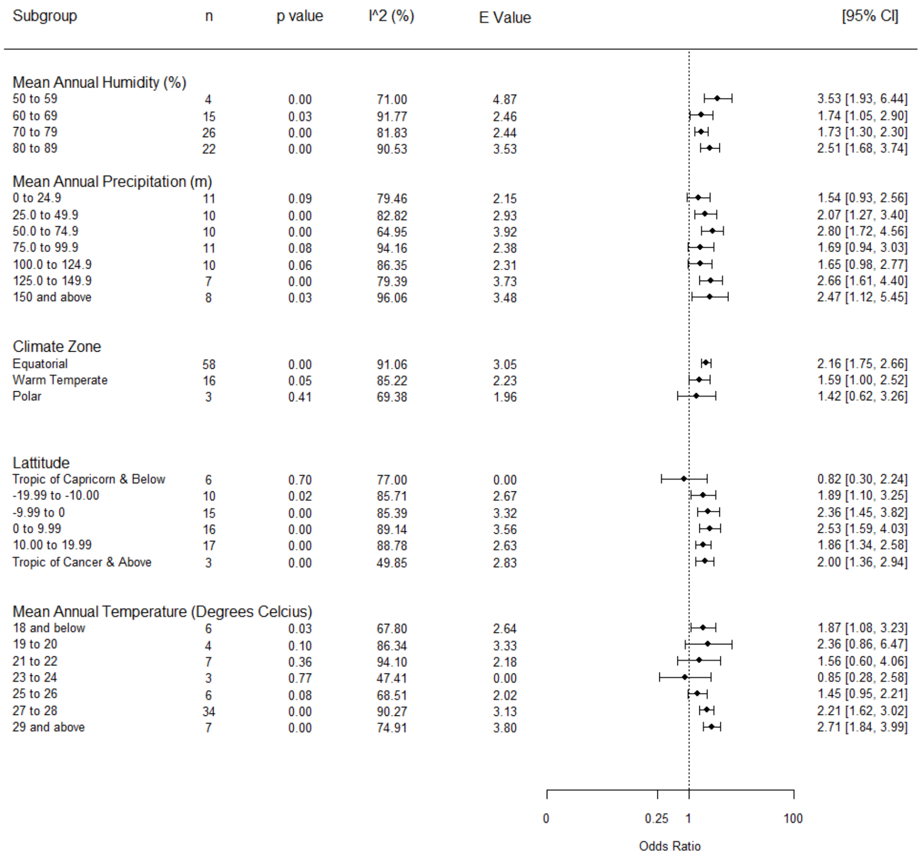
Sensitivity analysis of the global meta-analysis. A priori subgroups based on study characteristics to test the sensitivity of the global meta-analysis. Results suggest that subgroups based on study characteristics do not significantly alter the direction of the association between occupational or residential exposure to agricultural land-use and infectious disease prevalence. Circle points show the pooled subgroup estimates and error bars are defined as the 95% confidence interval. Note: n, number of studies included in each pooled estimate. CI, confidence intervals.



Subgroup	n	p value	I^2 (%)	E Value	[95% CI]
Gross Domestic Product per Capita ($)					
0 to 1999	10	0.00	0.00	2.66	1.88 [1.62, 2.18]
2000 to 3999	24	0.00	88.89	2.25	1.60 [1.16, 2.21]
4000 to 5999	9	0.00	85.15	4.58	3.30 [1.71, 6.39]
6000 to 7999	14	0.00	91.14	4.27	3.07 [1.86, 5.06]
8000 to 9999	3	0.47	0.00	1.80	1.32 [0.62, 2.80]
10000 and above	7	0.21	67.55	1.86	1.36 [0.84, 2.18]
Human Development Index (%)					
0.55 and below	6	0.06	91.94	3.38	2.40 [0.96, 6.00]
0.56 to 0.60	4	0.10	82.11	2.57	1.82 [0.89, 3.71]
0.61 to 0.65	7	0.00	76.03	3.83	2.74 [1.79, 4.18]
0.66 to 0.70	8	0.02	89.42	2.33	1.66 [1.07, 2.56]
0.71 to 0.75	22	0.00	87.62	3.29	2.33 [1.52, 3.58]
0.76 to 0.80	15	0.00	81.49	2.55	1.81 [1.24, 2.63]
0.81 and above	5	0.69	84.57	1.64	1.23 [0.45, 3.33]
United Nations Human Development Index Categories					
High	4	0.86	89.70	1.41	1.11 [0.33, 3.79]
Medium	60	0.00	87.73	2.84	2.01 [1.63, 2.47]
Low	3	0.02	88.35	6.56	4.88 [1.33, 17.93]
OECD Development Assistance Committee Official Development Assistance					
UMIC	52	0.00	87.60	2.81	1.98 [1.57, 2.51]
LMIC	21	0.00	92.97	3.25	2.30 [1.67, 3.17]
LDC	5	0.24	81.83	2.11	1.51 [0.76, 3.02]
% of Population with Improved Water					
69 and below	6	0.02	87.97	2.99	2.12 [1.14, 3.93]
70 to 79	5	0.53	87.82	1.81	1.33 [0.55, 3.20]
80 to 89	9	0.00	86.87	2.76	1.95 [1.35, 2.81]
90 to 100	47	0.00	83.89	2.66	1.88 [1.53, 2.31]
No WaSH Data	12	0.00	91.64	4.30	3.09 [1.56, 6.10]
% of Population with Improved Sanitation					
49 and below	3	0.00	0.00	2.34	1.66 [1.20, 2.30]
50 to 59	7	0.06	92.35	2.83	2.00 [0.96, 4.15]
60 to 69	5	0.00	83.44	3.14	2.23 [1.53, 3.23]
70 to 79	6	0.14	51.20	1.80	1.32 [0.91, 1.92]
80 to 89	23	0.00	83.62	2.80	1.98 [1.34, 2.92]
90 to 100	23	0.00	75.20	2.48	1.76 [1.43, 2.16]
No WaSH Data	12	0.00	91.64	4.30	3.09 [1.56, 6.10]

Figure 3.2: Socio-economics Sensitivity Analysis

Socioeconomic Sensitivity analysis of the regional meta-analysis. A priori subgroups based on open access socioeconomic data to test the sensitivity of the global meta-analysis. Results suggest that subgroups based on socioeconomic determinants do not significantly alter the direction of the association between occupational or residential exposure to agricultural land-use and infectious disease prevalence. Circle points show the pooled subgroup estimates and error bars are defined as the 95% confidence interval. Note: n, number of studies included in each pooled estimate. CI, confidence intervals.



Subgroup	n	p value	I^2 (%)	E Value	[95% CI]
Mean Annual Humidity (%)					
50 to 59	4	0.00	71.00	4.87	3.53 [1.93, 6.44]
60 to 69	15	0.03	91.77	2.46	1.74 [1.05, 2.90]
70 to 79	26	0.00	81.83	2.44	1.73 [1.30, 2.30]
80 to 89	22	0.00	90.53	3.53	2.51 [1.68, 3.74]
Mean Annual Precipitation (m)					
0 to 24.9	11	0.09	79.46	2.15	1.54 [0.93, 2.56]
25.0 to 49.9	10	0.00	82.82	2.93	2.07 [1.27, 3.40]
50.0 to 74.9	10	0.00	64.95	3.92	2.80 [1.72, 4.56]
75.0 to 99.9	11	0.08	94.16	2.38	1.69 [0.94, 3.03]
100.0 to 124.9	10	0.06	86.35	2.31	1.65 [0.98, 2.77]
125.0 to 149.9	7	0.00	79.39	3.73	2.66 [1.61, 4.40]
150 and above	8	0.03	96.06	3.48	2.47 [1.12, 5.45]
Climate Zone					
Equatorial	58	0.00	91.06	3.05	2.16 [1.75, 2.66]
Warm Temperate	16	0.05	85.22	2.23	1.59 [1.00, 2.52]
Polar	3	0.41	69.38	1.96	1.42 [0.62, 3.26]
Lattitude					
Tropic of Capricorn & Below	6	0.70	77.00	0.00	0.82 [0.30, 2.24]
-19.99 to -10.00	10	0.02	85.71	2.67	1.89 [1.10, 3.25]
-9.99 to 0	15	0.00	85.39	3.32	2.36 [1.45, 3.82]
0 to 9.99	16	0.00	89.14	3.56	2.53 [1.59, 4.03]
10.00 to 19.99	17	0.00	88.78	2.63	1.86 [1.34, 2.58]
Tropic of Cancer & Above	3	0.00	49.85	2.83	2.00 [1.36, 2.94]
Mean Annual Temperature (Degrees Celcius)					
18 and below	6	0.03	67.80	2.64	1.87 [1.08, 3.23]
19 to 20	4	0.10	86.34	3.33	2.36 [0.86, 6.47]
21 to 22	7	0.36	94.10	2.18	1.56 [0.60, 4.06]
23 to 24	3	0.77	47.41	0.00	0.85 [0.28, 2.58]
25 to 26	6	0.08	68.51	2.02	1.45 [0.95, 2.21]
27 to 28	34	0.00	90.27	3.13	2.21 [1.62, 3.02]
29 and above	7	0.00	74.91	3.80	2.71 [1.84, 3.99]

Figure 3.3: Environmental Sensitivity Analysis

Environmental Sensitivity analysis of the regional meta-analysis. A priori subgroups based on open access environmental data to test the sensitivity of the global meta-analysis. Results suggest that subgroups based on environmental determinants do not significantly alter the direction of the association between occupational or residential exposure to agricultural land-use and infectious disease prevalence. Circle points show the pooled subgroup estimates and error bars are defined as the 95% confidence interval. Note: n, number of studies included in each pooled estimate. CI, confidence intervals.

South and Central America). This method assumes a general average effect size linking agriculture exposure to disease risk that is interpolated from sampled to unsampled countries along with the respective uncertainty, reflecting the various potential sources of error in estimating this value from the variation among sampled country estimates (e.g., number of studies, sample sizes or methodological differences, different disease compositions, socio-ecological differences) [298].

Secondly, I could use a more nuanced interpolation approach to try to leverage heterogeneity among sampled country estimates to arrive at interpolated values closer to the real (unobserved) value for countries with missing data. One of the simplest approaches for this purpose is to use a “nearest neighbour” as a proxy, which for geographic studies can literally mean using the values of neighbouring countries (e.g., longest shared border, closest capital city) or an average from all neighbouring countries with values. Without additional analysis, this approach invokes the assumption that points closer together will be, on average, more similar in their characteristics than points further apart. This is a robust assumption that is the basis of some routines in the analysis of spatial data, such as in the field of model based geostatistics [299, 300]. It is a method often used where the analysis of variation in estimates is not an explicit objective (e.g., where no covariates have been hypothesised or collated).

Interpolation approaches can also identify “nearest neighbours” in covariate space rather than geographic space. Here, covariates could be selected on the basis of a priori hypotheses about their effects on the outcome of interest. For instance, for strongly age-related diseases, it may be more appropriate to impute missing values for countries with no data from countries with data which also have the most similar age structure irrespective of whether they are geographic neighbours or not [301].

Extending this method, nearest neighbours can also be identified in multivariate space, which estimates distance according to numerous covariates. This could be preferable where fewer assumptions about the dependence of the outcome on its covariates are made. For instance, I can hypothesise that some outcome is in some way related to socio-economic development, but there may be limited grounds to favour the influence of one development-related covariate over another similar one, particularly where these are inter-correlated (e.g., GDP per capita vs HDI). In these cases, multivariate methods (e.g., hierarchical clustering) can be used to calculate distances between countries for interpolation [302].

Finally, statistical models can also be used directly for the estimation of missing values on the basis of identifiable associations within the data. This is the basis of methods such as regression imputation (and its extensions, such as multiple imputation) or machine learning methods (e.g., random forest-based imputation). Such methods rely, however, on the presence of meaningful associations between covariates and the outcome [303].

To assess which of the above methods may be the most appropriate here, I first visually inspected the variation in estimates across countries and within the subgroup analyses. The results of the sensitivity analyses did not show clear evidence of significant covariate effects on the meta-analytic odds ratios, suggesting statistical model-based imputations or interpolations for countries with no data would be of limited value (see Figures 3.1, 3.2, 3.3). This is based on the evaluation of the mean effect sizes and their associated variation, where significant effects should manifest themselves as changes in the direction of effect (i.e., moving from positive to negative), non-overlapping confidence intervals among levels or clear trends in effect size across different levels of a factor (indicating possible interaction effects).

Next, in order to evaluate the plausibility of using nearest neighbour interpolation (both geographic and covariate based), I considered the differences in covariate and outcome values between neighbouring and non-neighbouring country pairs. Using the 14 meta-analytic estimates, I plotted neighbouring vs non-neighbouring countries to compare the pair-wise differences in a) effect size (log odds ratios), b) geographic distance (based on distance between capital cities) and c) SDG distance (see Figures 3.4). With this, I test whether neighbouring countries had more similar effect sizes than non-neighbours and find that while overall there was some evidence for this (lower median difference among neighbours; smaller range of difference values among neighbours), the mean difference values and overall distribution of values were similar whether neighbour or non-neighbour (see Figures 3.4). This prevents us from categorically rejecting the validity of nearest neighbour interpolation as an improvement over simple averaging, but also cautions against its blind adoption.

Next, I confirmed the geographic proximity of neighbours as well as show that neighbouring countries are also more similar in multivariate covariate (i.e. Moritisita-Horn Dissimilarity Index)) space than non-neighbours (see Figures 3.4). Here, I used the difference in SDG attainment scores to assess this, which was quantified using data on all available SDG indicators for each country. Specifically, I applied the Morisita-Horn index to quantify pairwise dissimilarity in country progress towards all SDG indicators. The value of the Morisita-Horn index ranges from 0, indicating complete similarity between two countries (all SDG indicators are equal), to 1, when the two countries are completely dissimilar [304]. This confirms the basis for an ‘isolation by distance’ effect on measured (and by extension) unmeasured social and ecological confounders and presents itself as alternative approach to valid interpolation.

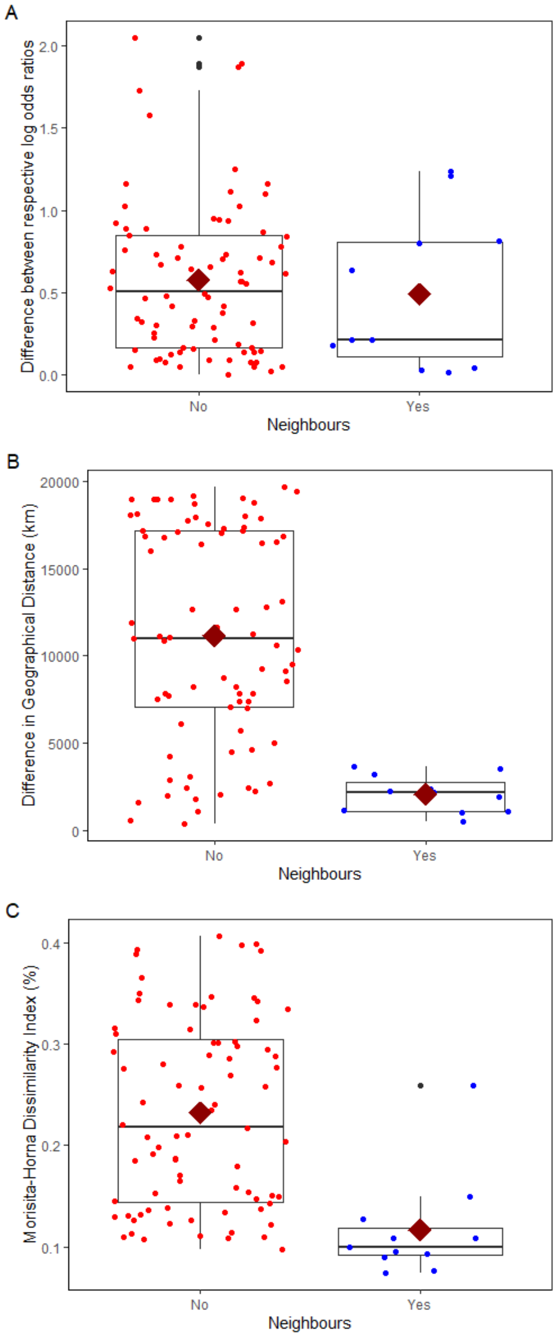


Figure 3.4: Boxplots of Neighbouring vs Non-Neighbouring countries

Boxplots of neighbouring vs non-neighbouring countries by their pair-wise difference in the A) log odds ratios, B) standard errors, C) geographic distance (based on distance between capital cities) and D) SDG distance. Diamond points indicate mean values.

On the basis of these preliminary investigations, I therefore implemented a hybrid approach to interpolation that I believe to be a superior and more conservative alternative to taking a simple average of effect sizes for interpolation. The method chosen is based on geographic neighbour interpolation weighted by distance in covariate space, where covariates were selected to capture the similarity of countries in their progress towards the SDGs. I constrained interpolation to neighbouring countries to account for the weak indication that effect sizes among neighbours are indeed more likely to be similar than more distant countries but more importantly to minimise the risk of inadvertently introducing additional sources of bias related to 'isolation by distance' spatial effects (see Figures 3.4). I then reasoned that neighbouring countries that also have more similar SDG performance should have more similar agriculture disease outcomes than countries that are less similar in this respect, reflecting the fact that I hypothesise that both social and environmental development factors combine to mediate all cause infectious disease risk.

Extrapolation

In this analysis, the literature review yielding meta-analytic odds ratios were a non-random subset of all countries globally. Yet global trade with these countries is much more expansive, so it was desirable to increase the number of countries included in the study as far as possible to try to capture as many global connections as possible and gain a preliminary estimate of the global burden of infectious disease linked to agriculture and its trade. As discussed above, I commenced this by interpolating effect sizes from sampled countries to non-sampled countries. However, this then raises an additional issue of extrapolation, i.e., to what extent is interpolation to countries with no data a reasonable methodological approach.

Extrapolation refers to the application of a statistical model beyond the range of data used to develop it, and is a common problem to address in spatial analyses [305]. In ecological studies, extrapolation is usually assessed by examining the range of environmental conditions used to 'train' a model (e.g., at the locations in which a species is observed) and comparing it to the range of environmental conditions in which it is applied (e.g., in a new geographic range, or under future climates). Where there is a mismatch (e.g., novel environments on a different continent), results must be interpreted with additional caution. In cases where model inputs include socio-economic factors that may also be spatially heterogeneous, a similar level of caution must be used to safeguard against spurious interpretation related to extrapolation [306].

I therefore examined the degree to which various decisions regarding which countries to include in the analysis were likely to be vulnerable to extrapolation following the interpolation

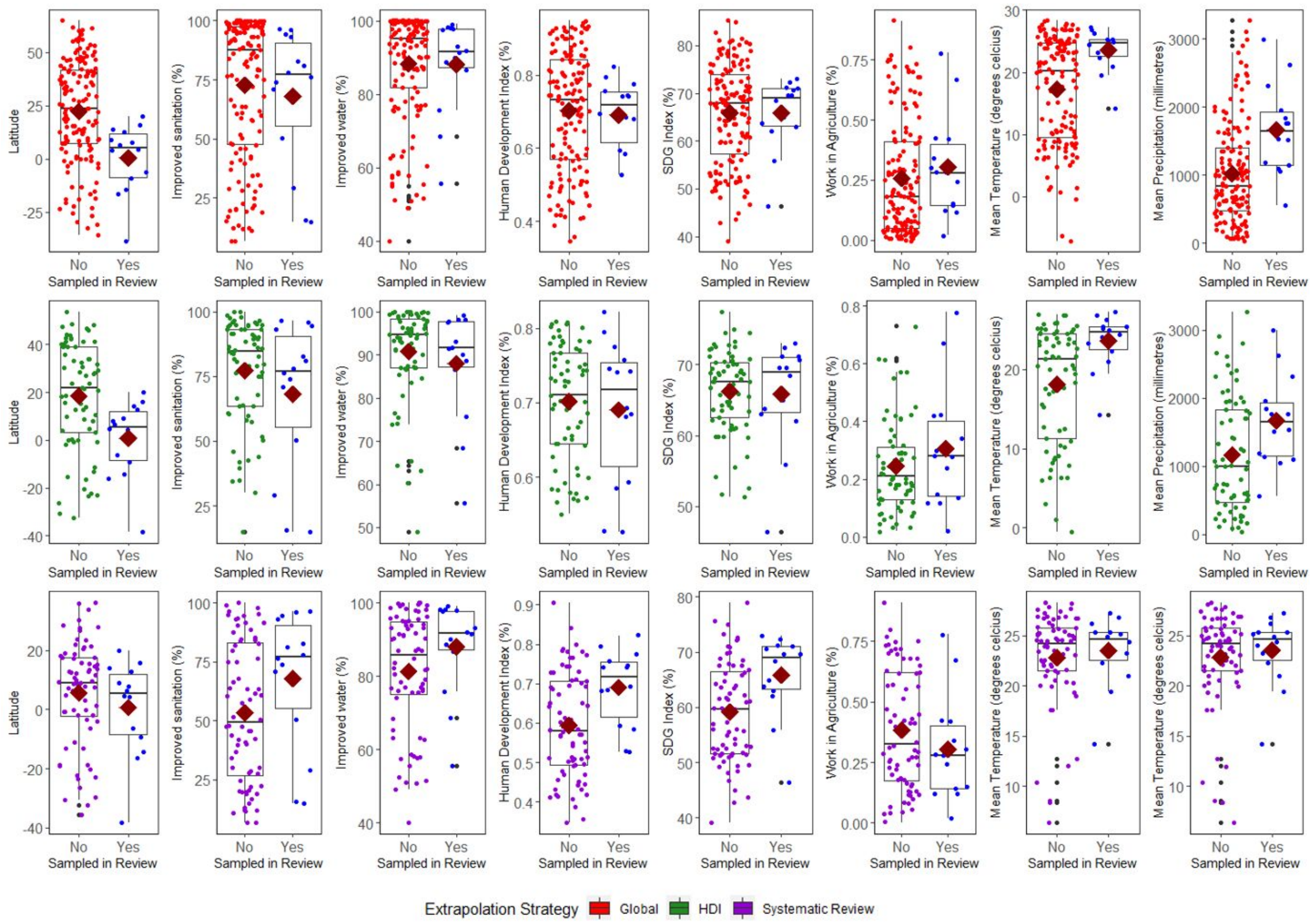


Figure 3.5: Boxplots of Covariates across Sampled and Non-Sampled Countries

Boxplots showing difference in latitude, HDI, SDG Index, proportion of population that has access to improved sanitation and improved water and the proportion of the population that works in agriculture between sampled and non-sampled countries across three extrapolation strategies. Point values are jittered.

step. To do this, I visually inspected the differences in latitude, HDI, SDG Index, proportion of population that has access to improved sanitation and improved water, mean annual temperature and precipitation and the proportion of the population that works in agriculture between sampled and non-sampled countries (see Figure 3.5). Boxplots were generated for three 'interpolation strategies' including: i) global (interpolate to all countries) ii) HDI-restricted (interpolate only to countries that fall within the range of HDI values represented by sampled countries, here $0.5 < \text{HDI} > 0.8$), iii) systematic review restricted (interpolate only to countries that fall within the geographic scope of the initial review protocol i.e., South and Central America, South and Southeast Asia and Africa). Boxplot summaries showing the distributions of data for the above covariates for sampled vs unsampled countries are shown in (see Figure 3.5).

Here, the 'global' strategy shows considerable potential for extrapolation beyond the range of data from sampled countries for most key covariates and therefore opted to use a global spatial interpolation approach as a base case analysis. On the other hand, the 'HDI-restricted' strategy suggests limited evidence of considerable extrapolation for most co-variates. The 'systematic review restricted' strategy falls in between these two extremes.

Spatial Averaging

Based on the exploration of interpolation and extrapolation methods, I opted to use the 'global spatial interpolation' approach which I describe below.

Using the country-specific pooled subgroup estimates from the meta-analysis (see Table 3.1), nearest-neighbour weighted spatial averaging was performed to estimate the mean infectious disease subgroup risk and its corresponding standard error when exposed to agricultural land use compared to those unexposed for all countries (excluding islands) [307]. Due to no agriculture related risk estimates being generated for the "All Other Diseases" category and due to no data being found in the literature review on association between agriculture and intestinal nematodes in the African and Americas contexts for intestinal nematodes which include *Ascaris lumbrocoides, Trichuris Trichura and Hookworm* and food-borne trematodes such as *Opisthorchis viverrini*, three assumptions were made.

The first assumption was the "All Other Diseases" category would have the same risk as "All Diseases". The second assumption was that spatial averaging for the African context could be conducted using a single odds ratio taken from a specific study from Nigeria which shows that people who work or live in agriculture in Nigeria are 168% as likely to be infected with Hookworm [308]. As no studies were found that estimated the risk of agricultural land use on intestinal nematode risk in any in South America, the third assumption I made was that people who live or work in agriculture in Brazil would be at a similar risk of being infected with intestinal nematodes as they would be at a risk of parasitic and vector borne diseases at the Americas regional level. Hence, I used the regional Americas parasitic and vector borne diseases pooled risk estimate to spatially average (see Table 3.1) which is similar to global risk of working in agriculture and being infected with an intestinal nematodes.

Hence, using the risk estimates from Table 3.1, I aimed to compute the estimated odds ratio for an unsampled country, denoted by $\mathrm{Z_0}$, given a set of neighbouring geographical neighbours that share any land border sampled values $\mathrm{Z_i}$, sampled for countries $\mathrm{X_i}$. Here log refers to the natural logarithm. The odds ratio interpolating relationship is:

$$Z_0 = \exp(\sum_{i=0}^{n} \gamma_\mathrm{i} \times \log(Z(X_\mathrm{i}))0)); \sum_{i=1}^{n} \gamma_\mathrm{i} = 1 \tag{3.1}$$

where γ_i represents the weights assigned to each of the respective i neighbouring values, and the sum of the weights is one [307].

To calculate the confidence intervals for the odds ratio of the unsampled country $\mathrm{Z_0}$, I first calculated the confidence interval on the log odds scale by interpolation using the given standard errors for the neighbouring countries $\mathrm{Z_i}$ denoted as SE $\log_{\mathrm{Zi}}$:

$$SE \log_{\mathrm{Zi}} = \sqrt{(\sum_{i=1}^{n} \gamma_\mathrm{i}{}^2 \times SE^2 \log(Z_\mathrm{i}))} \tag{3.2}$$

$$CI \log_{\mathrm{Z0}} = \log_{\mathrm{Z0}} \pm 1.96 \times SE \log_{\mathrm{Z0}} \tag{3.3}$$

$$CI_{\mathrm{Z0}} = \exp(\log_{\mathrm{Z0}} \pm 1.96 \times SE \log_{\mathrm{Z0}}) \tag{3.4}$$

Considering the majority of odds ratios found through the systematic review were considered relatively low, I assumed that odds ratios were equivalent to risk ratios [309].

Country weights were calculated based on the disease burden and sustainability footprint of each country relative to all other countries. Here I extracted data on 41 health-related SDG indicators for the year 2015 for all countries [310]. Using all extracted SDG indicators, pairwise distance values were calculated between every pair of countries given their values for each indicator, indicating their overall similarity of progress towards all SDG goals using the Morisita-Horn similarity index. The value of the Morisita-Horn similarity index ranges

Table 3.1: Odds ratios used for spatial averaging

Study Context	Category	n	Odds Ratio	Standard Error
Argentina	All Diseases	2	0.61	1.34
Bolivia	All Diseases	2	2.04	0.23
Brazil	All Diseases	18	2.10	0.22
Colombia	All Diseases	2	4.74	0.77
Ghana	All Diseases	2	4.05	0.24
Lao PDR	All Diseases	2	1.95	0.87
Malaysia	All Diseases	10	1.95	0.22
Nigeria	All Diseases	7	2.96	0.44
Peru	All Diseases	7	2.13	0.44
Philippines	All Diseases	2	1.70	0.19
Tanzania	All Diseases	2	3.44	1.06
Thailand	All Diseases	11	1.58	0.18
Venezuela	All Diseases	2	3.97	0.72
Vietnam	All Diseases	8	1.86	0.18
Brazil	Diarrheal	7	1.65	0.33
Malaysia	Diarrheal	4	1.80	0.43
Nigeria	Diarrheal	2	1.41	1.15
Peru	Diarrheal	2	2.10	0.56
Philippines	Diarrheal	2	1.70	0.19
Thailand	Diarrheal	3	2.20	0.25
Vietnam	Diarrheal	4	1.86	0.34
Thailand	Nematodes	7	1.58	0.18
Vietnam	Nematodes	3	1.55	0.38
Argentina	Parasitic & Vector Borne	2	0.61	1.34
Brazil	Parasitic & Vector Borne	17	2.07	0.23
Lao PDR	Parasitic & Vector Borne	2	1.95	0.87
Malaysia	Parasitic & Vector Borne	10	1.95	0.22
Nigeria	Parasitic & Vector Borne	6	3.12	0.51
Peru	Parasitic & Vector Borne	6	2.16	0.56
Philippines	Parasitic & Vector Borne	2	1.70	0.19
Thailand	Parasitic & Vector Borne	10	1.69	0.20
Vietnam	Parasitic & Vector Borne	7	1.78	0.20
Argentina	All Other Diseases	2	0.61	1.34
Bolivia	All Other Diseases	2	2.04	0.23
Brazil	All Other Diseases	18	2.10	0.22
Colombia	All Other Diseases	2	4.74	0.77
Ghana	All Other Diseases	2	4.05	0.24
Lao PDR	All Other Diseases	2	1.95	0.87
Malaysia	All Other Diseases	10	1.95	0.22
Nigeria	All Other Diseases	7	2.96	0.44
Peru	All Other Diseases	7	2.13	0.44
Philippines	All Other Diseases	2	1.70	0.19
Tanzania	All Other Diseases	2	3.44	1.06
Thailand	All Other Diseases	11	1.58	0.18
Venezuela	All Other Diseases	2	3.97	0.72
Vietnam	All Other Diseases	8	1.86	0.18
Americas	Parasitic & Vector Borne	27	1.99	0.21
Nigeria	Hookworm	1	2.67	0.04

from 0, indicating no similarity between two countries, to 1, when the two countries are the same (all SDG indicators are equal) [304].

To assess the sensitivity of weighting indicators, I also used the income adjusted human development index as an alternative indicator. I found a 99% correlation between the SDG index and the human development index (iHDI) and therefore opted to use the SDG index due to its holistic amalgation of indicators (see Figure 3.6).

3.3.4 Impact Fractions and Population Attributable Fractions

Using the weighted risk ratios that were calculated from spatial averaging, I calculated country-specific impact fractions (IF). Impact fractions describe the percentage of the risk that can be attributed to hazardous exposures or risky behaviours, multiple levels of exposure, or to incomplete elimination of exposure [75, 269, 311]. To calculate country-specific impact fractions, the following formula was implemented:

$$IF = \frac{\sum P_i \times RR_i - 1}{\sum RR_i} \tag{3.5}$$

Where P_i represents the proportion of population that are exposed to agriculture. In this instance, I used occupational data from the World Bank that shows the proportion of people that work in agriculture out of the entire labour force population where the labour force is defined as the sum of person in employment plus persons in unemployment [203]. In this analysis, I could not account for informal employment due to lack of data. RR_i denotes the relative risk of exposure compared to the counter factual risk which were obtained from the process of meta-analysis and spatial interpolation. Specifying normal distributions using the country-specific weighted interpolated means and standard deviations, I randomly sampled 1000 times and recalculated the impact factor for each sample for each country. The average impact factor alongside the upper and lower confidence interval was then calculated for each country and could then be used to calculate the population attributable fraction.

The population attributable fraction (PAF) of a risk factor is the proportional reduction in population death or disease that would occur if exposure to this factor was removed or reduced to an achievable, alternative (or counterfactual) exposure distribution. That is, I aimed to calculate the attributable fraction, PAF, for each country (i) [75, 269].

$$PAF_i = IF_i \times TotalBurden_i \tag{3.6}$$

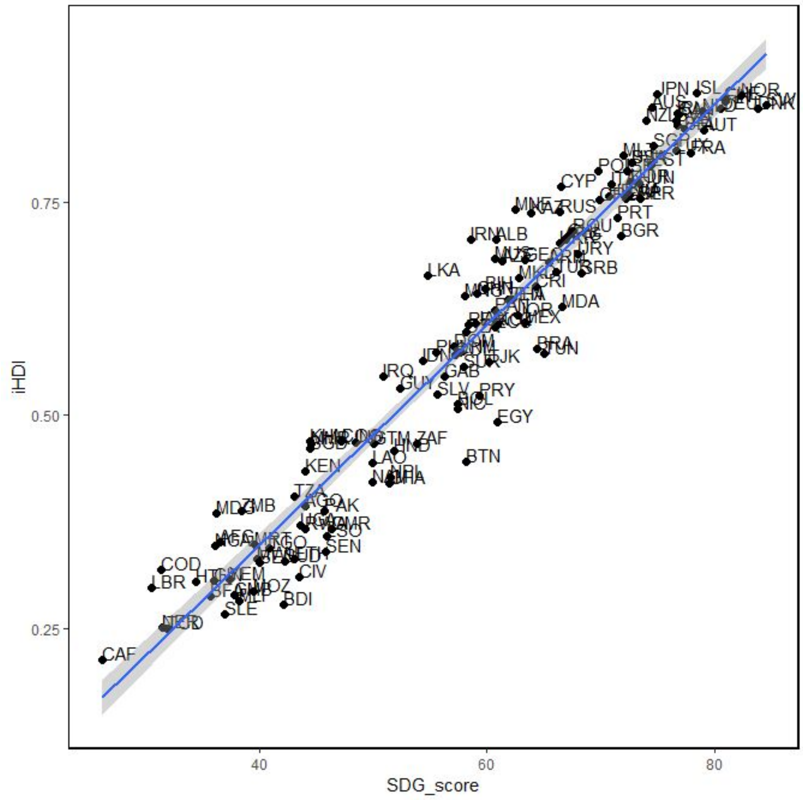


Figure 3.6: Correlation between the SDG Index and the iHDI.

Scatter plot between the SDG index and the income adjusted human development index thereby suggesting the use of either of these measures in the spatial interpolation of risk ratio’s would result in very little change to the spatially interpolated risk ratio map.

where IF represents the mean country level impact fraction and total burden denotes the total country level burden lost due to infectious disease that are linked to agriculture through a biologically plausible mechanism. Here, a biologically plausible mechanism is defined as a hypothesised causal pathway by which agriculture can increase infectious disease risk which has been highlighted in previous research (see Appendix A.4). I calculated PAFs for both deaths and DALYs by multiplying the calculated impact fractions by the mortality and burdens of infectious disease linked to agricultural land use using World Health Orgnisation data that is already categorised into All Diseases, Diarrheal Diseases, Parasitic and Vector-Borne Diseases and Other Diseases [291]. I only included specific diseases and disease categories that had a biological plausible link on the basis of relevant literature (see Appendix A.4).

3.3.5 Input Output Analysis

To calculate the burden of disease associated with the international trade of agriculture and identify the top importers of disease implicated agricultural commodities, I linked country level agriculture associated infectious disease burdens to environmentally extended input output (EEIO) analysis.

Input output tables provide a database of global trade flows, alongside production and consumption recipes involved in the supply and distribution of each commodity or sector. Hence, input output analysis is a form of macroeconomic analysis based on the interdependencies between different economic sectors or industries. It is a well-known and widely used method amongst macro-economists for estimating the impacts of positive or negative economic shocks and analysing the ripple effects of trade or implicated commodities throughout an economy [312].

EEIO analysis, an extension to input output analysis, provides a simple and robust method for evaluating the linkages between economic consumption activities and its downstream environmental impacts, including the harvest and degradation of natural resources [313]. EEIO is commonly used by macroeconomists, industrial ecologists, and many other researchers within the sustainability community to quantify the environmental impact of producing and distributing a specific commodity [121, 314, 315]. However, to date, application of EEIO to human health has been limited [138, 315]. In one example, Chaves et al (2020) use input output analysis to quantify the proportion of malaria risk held in deforestation hotspots that is driven due to international trade [138]. Using a similar methodology, I adapt EEIO to quantify the relationships between international agricultural consumption activities and how they link to agricultural production associated infectious disease impacts.

To do this, I use the Eora global input output table, which documents the domestic and international monetary transactions between 15,909 industry sectors across 187 countries [121, 122, 316]. By combining the Eora database with input output analysis and structural path analysis, I am able to identify supply chains and production or consumption "recipes". For example, "A typical $10,000 automobile purchased in the US requires $1200 worth of Japanese steel parts, the production of which in turn requires $600 worth of Chinese rolled steel, the production of which in turn requires $200 worth of Australian iron ore". In essence, I am able to link countries who import commodities (e.g. $10,000 automobile purchased in the US) to a supplier (e.g. Australian Iron Ore) [317], where the extraction of Australian Iron Ore at its source may then be linked to an environmental impact (e.g. carbon emissions, biodiversity impacts, infectious disease risks).

To conduct such an EEIO analysis on infectious disease impacts, I connected an infectious disease "environmental satellite account", which contains estimates of agriculture-associated infectious disease burdens (and relative standard deviations) from a robust meta-analysis to all agricultural sectors in the input output table. In cases where a country's input output table describes multiple agricultural goods sectors, the burden was allocated amongst them based on the sectors' proportional contribution to total agricultural output in the country. Therefore, to construct the agriculture-associated infectious disease satellite account for the EEIO analysis, all sectors are given 0 disease impact, except the agriculture sector(s) which are given a value of 1.

After making the link between infectious disease risk and the agricultural sectors, I then determined infectious disease 'footprints' using the standard Leontief input output calculus [312]. Specifically, the infectious disease footprint induced through agricultural consumption of each country s, comprising the sum of the deaths or DALYs due to infectious disease associated with agricultural land use in each country r exerted directly by the agricultural industry (consisting of agriculture) due to consumption in country s of the good j, inclusive of the upstream and indirect impacts involved in provisioning j, can be expressed as:

$$F_{\mathrm{j}}^{\mathrm{(c)s}} = \sum_{i,r} q_{\mathrm{i}}^{\mathrm{r}} \sum_{t} L_{\mathrm{ij}}^{\mathrm{rt}} \times y_{\mathrm{j}}^{\mathrm{ts}} \tag{3.7}$$

where q is an infectious disease coefficient, L is the Leontief inverse and y is the final demand [122].

The Leontief method has been well explained previously and many publications describe the method in addition to how it can be applied to different case studies [121, 122, 138, 313, 317]. Within this analysis, I collaborated with industrial ecologists at the Norwegian University of Science and Technology who have developed existing and currently best-practice models for EEIO and which can be adapted for other environmental or health impacts [122, 317]. Through such an analysis, I then estimate what proportion of the burden of infectious disease associated with agriculture is related to agricultural exports and thereby assess which countries are the largest consumers of agricultural commodities that have an associated infectious disease impact. I refer to this as disease implicated commodities, following the terminology used when this method has been applied to other impact endpoints [121].

3.3.6 Interpolation and Extrapolation Sensitivity Analysis

Within this analysis, I consider the spatial averaging, interpolation and extrapolation of agriculture-disease risk a rate determining step to quantifying the burden of infectious disease associated with agriculture. Hence, I finally performed a sensitivity analysis to assess the impact of various interpolation (and by extension extrapolation) strategies on the burden of infectious disease associated with agriculture. Here, interpolation strategies included:

1) A “global average risk” strategy where no spatial interpolation was conducted, and global risk was assumed to be equivalent to country-specific risk. Hence, all countries (excluding island nations) were included within this strategy.

2) A “global spatial interpolation” which used a nearest neighbour weighted spatial interpolation approach where neighbouring countries that also have more similar SDG performance should have more similar agriculture-disease outcomes than countries that are less similar in this respect. Hence, I interpolate country-specific meta-analytic odds ratios and their respective standard errors to all other countries that share a land border including all countries in Africa, the Americas, Asia, Europe, and the Middle East.

3) A “HDI limited interpolation” strategy which restricts spatial interpolation using the nearest neighbour weighted interpolation approach to only those countries that have a HDI above 0.51 or below 0.81, representing the range of values in sampled countries from the literature review.

4) A ‘systematic review limited interpolation’ strategy, that restricts interpolation using the nearest neighbour weighted interpolation approach to only those countries within the geographic scope of the original literature review, including Africa, South and Central America and South and Southeast Asia.

3.3.7 Assumptions

Here I provide an explicit description of assumptions to ensure transparency in our methodological approach. As stated earlier, I assume that the associations between occupational or residential exposure to agricultural land use or land use change and infectious disease risks are likely to be inconsistent and idiosyncratic, which might otherwise bias the results. I also assume that meta-analytic odds ratios are considered equivalent to risk ratios [309]. I further assume that countries who share a land border and are on a similar track to achieve the SDG indicators will have a similar agriculture-infectious disease risk compared to countries who do not share a land border or who are not similar in achieving the SDG indicators. Finally, I assume that international imports of agricultural commodities are linked to local agricultural land use associated infectious disease risks and burdens.

3.4 Results

3.4.1 Narrative Synthesis

From the global systematic literature review, 83 out of 43,095 potentially relevant publications met the eligibility criteria for full text analysis and data extraction. Although the initial search strategy specified 29 countries, included studies only spanned 18 countries and were assessed as being of varying quality. Of the 18 countries, only 14 countries had more than two mutually exclusive effect estimates that could be used to generate pooled effect sizes. Of the 83 studies, 34, 36 and 13 studies were located in Southeast Asia, South America and Africa, respectively (see Figure 3.7, 3.8, 3.9). A total of 148 effect estimates were extracted consisting of 31 differing infectious diseases and 12 different exposures.

3.4.2 Infectious Disease Risk due to Agricultural Land Use Exposure

Globally, people who live or work in agriculture are at an 107% increased risk of being infected with any pathogen compared to those unexposed (OR 2.07, CI 1.72 – 2.38, $p < 0.001$, I2 = 90.47%, (see Figure 3.10). Consistent associations were also found at the regional level, where being exposed to agricultural land use increased the risk of being infected with any pathogen compared to those unexposed in Southeast Asia (OR 1.58, CI 1.10 – 2.24), Western Pacific (OR 1.88, CI 1.46 – 2.41), South America (OR 2.13 , CI 1.54 – 2.95) and Africa (OR 2.68, CI 1.50 – 4.79) (see Figure 3.10).

Similar results were observed when stratifying the global data by disease class, with significant effects for diarrheal disease (OR 1.63, CI 1.32 – 2.17), parasitic and vector borne diseases (OR 1.98, CI 1.60 – 2.44) and intestinal nematodes (OR 1.98, CI 1.17 – 3.35) overall but with some variation among regions (see Figure 3.10). Further regional stratification by disease type revealed strong positive associations between exposure to agricultural land use and parasitic and vector borne diseases in South America (OR 1.99, CI 1.32 – 2.98), Africa (OR 2.43, CI 1.13 – 5.25), Southeast Asia (OR 1.69, CI 1.15 – 2.48) and the Western Pacific (OR 1.85, CI 1.43 – 2.40); intestinal nematodes in the Western Pacific (OR 1.78, CI 1.14 – 2.79); and diarrheal disease in Southeast Asia (OR 2.20, CI 1.34 – 3.60) and the Western Pacific (OR 1.68, CI 1.15 – 2.44). Positive but marginally non-significant associations where also found for intestinal nematodes in Southeast Asia (OR 1.53, CI 0.92 – 2.55) and diarrheal disease in Africa (OR 1.39, CI 0.54 – 3.54) and South America (OR 1.55, CI 0.88 – 2.76). No pooled risk estimates were calculated for exposure to agricultural land use and the risk of being infected with intestinal nematodes in Africa or South America

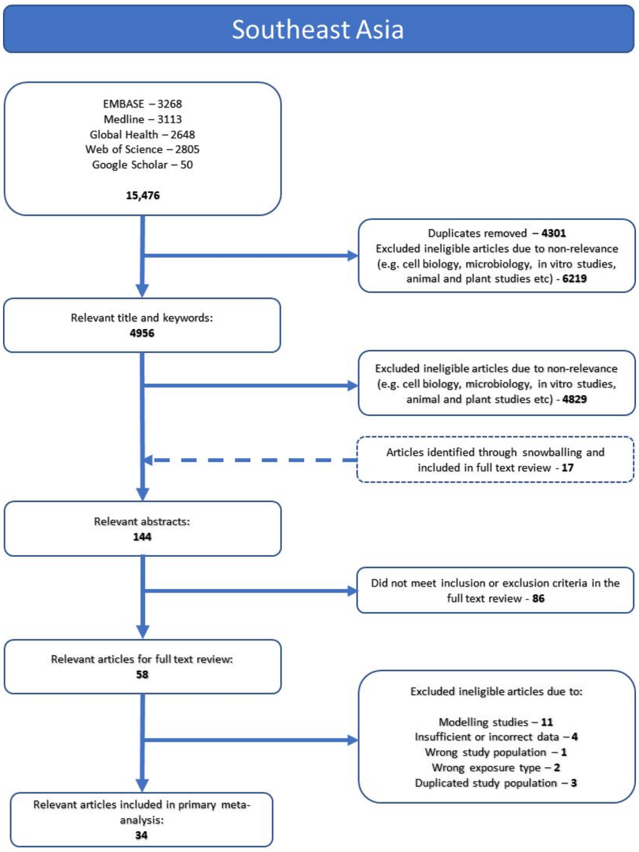


Figure 3.7: Southeast Asia PRISMA Diagram

A flow chart of the study selection process

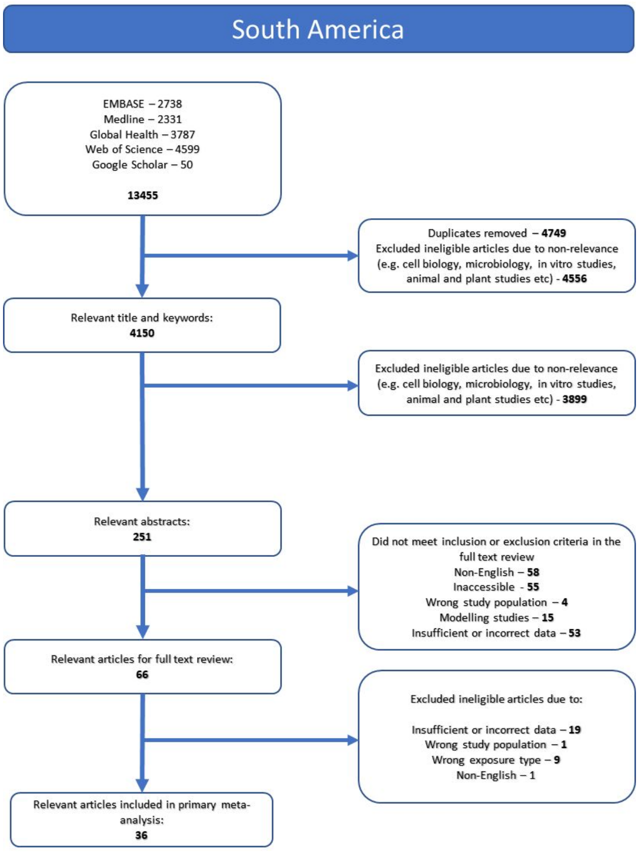


Figure 3.8: South America PRISMA diagram

A flow chart of the study selection process

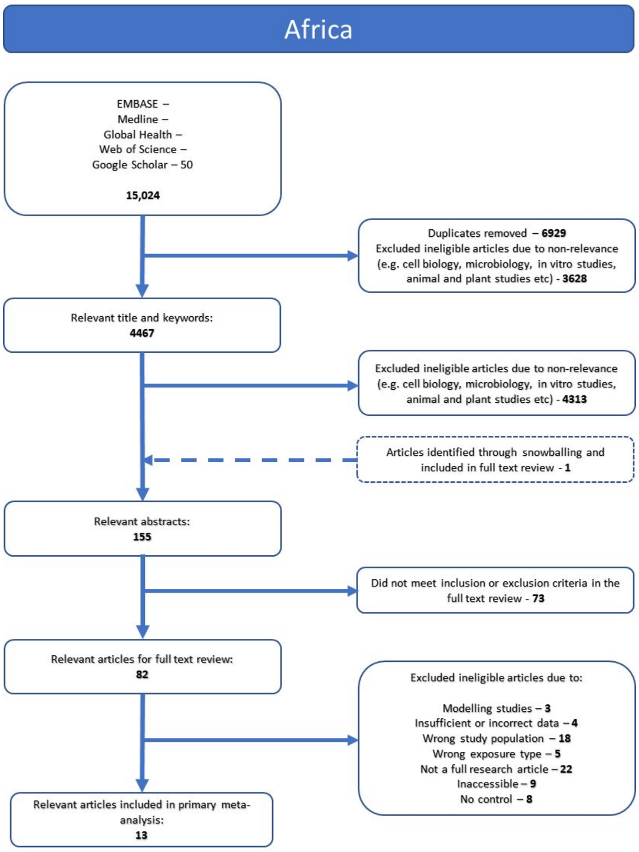


Figure 3.9: Africa PRISMA diagram

A flow chart of the study selection process

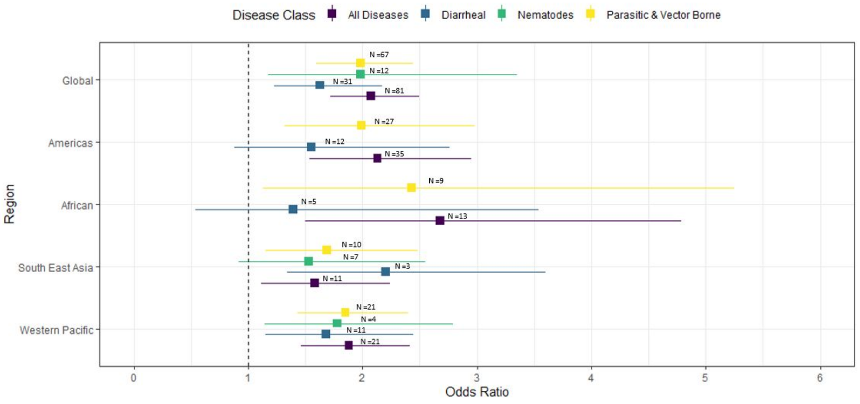


Figure 3.10: Global and regional meta-analysis

The global meta-analytic estimate consists of mutually exclusive risk estimates to determine the overall global association between occupational or residential exposure to agricultural land use and infectious disease prevalence. Regional subgroups were created *a priori* based on World Health Organisation regions that had two or more mutually exclusive estimates. Square points show the pooled subgroup estimates and error bars are defined as the 95% confidence interval.

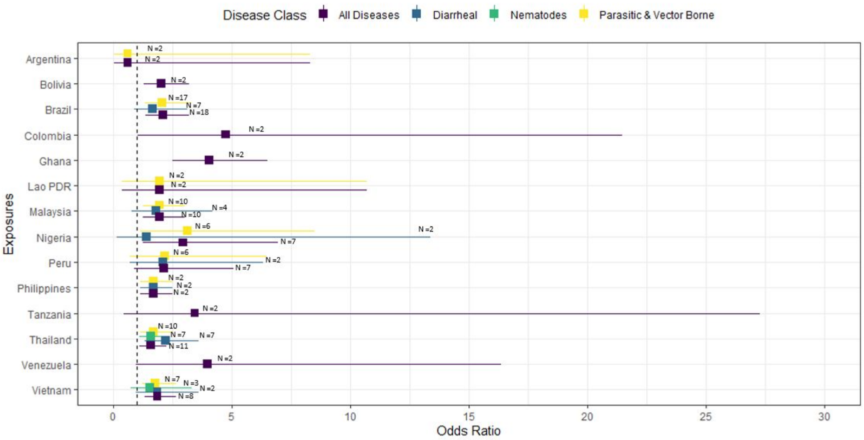


Figure 3.11: Country-based subgroup analysis

Subgroups were created *a priori* based on countries that had two or more mutually exclusive estimates. Square points show the pooled subgroup estimates and error bars are defined as the 95% confidence interval

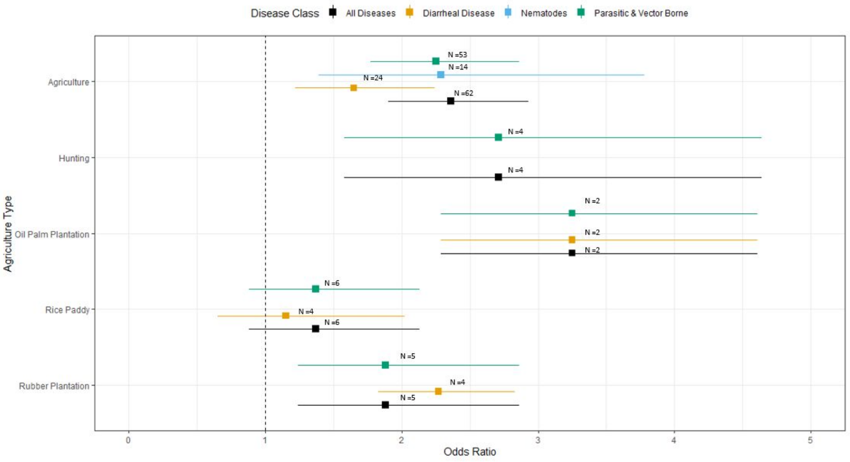


Figure 3.12: Agricultural exposure-based subgroup analysis

Subgroups were created *a priori* based on exposures that had two or more mutually exclusive estimates. Agriculture (non-specific) is defined as a category where a person indicates they work in agriculture regardless of the type of agriculture. Square points show the pooled subgroup estimates and error bars are defined as the 95% confidence interval

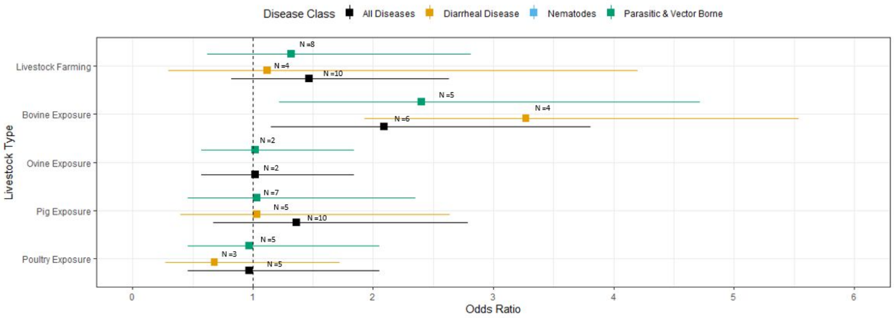


Figure 3.13: Livestock exposure-based subgroup analysis

Livestock farming is defined as a category where a person indicates they are exposed to livestock generally regardless of the specific type of livestock (e.g., chickens). Porcine, Bovine or Poultry exposure is defined as a person being exposed to each of these respective animal types. Square points show the pooled subgroup estimates and error bars are defined as the 95% confidence interval

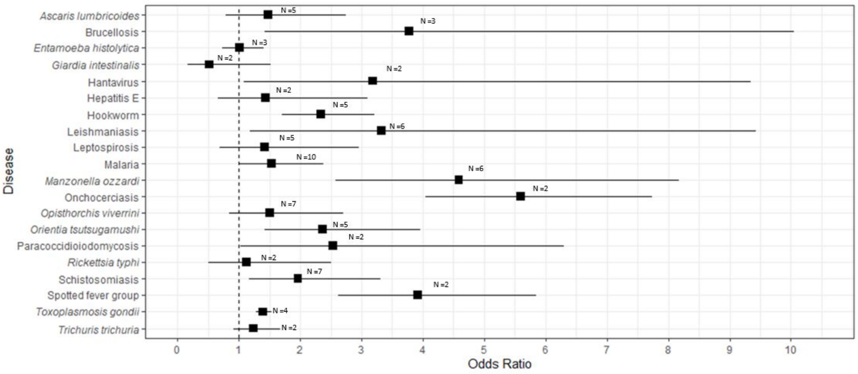


Figure 3.14: Disease-based subgroup analysis

Disease-based subgroup analysis. Subgroups were created *a priori* based on diseases that had two or more mutually exclusive estimates. *Orientia tsutsugamushi* is also known as Scrub typhus. *Rickettsia typhi* is otherwise known as murine typhus. *Opisthorchis viverrini* is also known as Opisthorchiasis. Square points show the pooled subgroup estimates and error bars are defined as the 95% confidence interval due to a lack of published peer reviewed studies that met the eligibility criteria.

When conducting a stratified country-specific subgroup meta-analysis, national level pooled estimates for 13 countries similarly showed positive associations between agricultural land use exposure and differing infectious disease risks (see Figure 3.11). Stronger positive associations were generally found for equatorial countries, while five country level estimates had confidence intervals that cross the line of no association. A single country subgroup (Argentina) indicated a negative albeit non-significant association (OR 0.61, CI 0.04 – 8.31). There was again some variation with disease class at country level (see Figure 3.11).

Non-specific agricultural exposure (OR 2.36, CI 1.90 – 2.93), oil palm plantation (OR 3.25, CI 2.29 – 4.61), rubber plantation (OR 1.88, CI 1.24 – 2.86), bovine farming (OR 2.09, CI 1.15 – 3.81) and hunting (OR 2.71, CI 1.58 – 4.64) were all associated with elevated all infectious disease risks overall, while a marginal but non-significant effect was identified for rice (OR 1.37, CI 0.88 – 2.13) (see Figure 3.12).

Subgroup Analysis

Consistent positive associations were again identified when stratifying by disease class within each agricultural land use type (see Figure 3.12). Specifically, exposure to general agricultural land use consistently increased the risk of being infected with parasitic and vector-borne diseases (OR 2.25, CI 1.77 – 2.86), intestinal nematodes (OR 2.29, CI 1.39 – 3.78) and diarrheal diseases (OR 1.65, CI 1.22 – 2.24). People exposed to hunting as a land use were at an increased risk of parasitic and vector-borne diseases (OR 2.71, CI 1.58 – 4.64). The effect was higher in populations working or living in or near oil palm and being infected with vector-borne zoonotic diseases (leptospirosis and *Plasmodium falciparum*) compared to those unexposed (OR 3.25, CI 2.29 – 4.61) [270]. Weak positive associations were found between exposure to rice paddy and parasitic and vector borne diseases (OR 1.37, CI 0.88 – 2.13) and diarrheal diseases (OR 1.15, CI 0.65 – 2.02), where the confidence intervals for both subgroups crossed the line of no association. Exposure to rubber plantations consistently increased the risk of parasitic and vector-borne diseases (OR 1.88, CI 1.24 – 2.86) in addition to an increased risk for diarrheal diseases (OR 2.27, CI 1.83 – 2.83). Consistent marginal positive associations for exposure to rice paddy and diarrheal disease (OR 1.15, CI 0.65 – 2.02), parasitic and vector-borne diseases (OR 1.37, CI 0.88 – 2.13). Hunting was also strongly positively associated with parasitic and vector-borne diseases (OR 2.71, CI 1.58 – 4.64).

Considerable variability in effects was found for differing livestock exposure and disease classes (see Figure 2.7). Significant positive associations were only found for bovine exposure and all diseases (OR 2.09, CI 1.15 – 3.81), diarrheal diseases (OR 3.27, CI 1.93 – 5.54) or parasitic and vector-borne diseases (OR 2.40, CI 1.22 – 4.72). Weak positive associations were found between general livestock farming and all diseases (OR 1.47, CI 0.82 – 2.63), diarrheal diseases (OR 1.12, CI 0.30 – 4.20) and parasitic and vector-borne diseases (OR 1.32, CI 0.62 – 2.81), although confidence intervals crossed the line of no association. A weak negative association was also found for poultry exposure and diarrheal disease (OR 0.68, CI 0.27 – 1.72). However, no association was found for exposures such as ovine, porcine and poultry exposure with differing disease categories.

Disease based subgroups showed consistent significant associations for Brucellosis (OR 3.78, CI 1.42 – 10.05), Hantavirus (OR 3.18, CI 1.08 – 9.34), Hookworm (OR 2.34, CI 1.70 – 3.20), Leishmaniasis (OR 3.33, CI 1.18 – 9.43), Malaria (OR 1.54, CI 1.00 – 2.38), *Manzonella ozzardi* (OR 4.59, CI 2.57 – 8.18), Onchocerciasis (OR 5.59, CI 4.0.4 – 7.74), Scrub typhus (OR 2.37, CI 1.41 – 3.96), Paracoccidiodomycosis (OR 2.54, CI 1.02 – 6.30), Schistosomiasis (OR 1.96, CI 1.17 – 3.30), Spotted fever group diseases (OR 3.91, CI 2.61 – 5.85) and *Trichuris trichuria* (OR 1.40, CI 1.27 – 1.53) (see Figure 2.8).

Within the geographic subgroup analysis that assessed global, regional and national associations, publication bias was found for nematode subgroups in which positive associations between agricultural exposure and nematode infection were under-reported at the global level and at the western pacific regional level (see Table A.4). There was no evidence of publication bias or unmeasured confounding for any other exposure-based subgroups (see Tables A.5, A.6 and A.7). Full details of sample characteristics for each study including analysis groups are presented in Table A.8.

Sensitivity Analysis

To evaluate the influence of between-study confounding, I examined the impact of a range of additional study and sample characteristics on effect size and direction, including study type and methodology, socio-demographic characteristics (gender, whether children were included in the sample population, and rural vs. urban), study quality assessments and study location. I further extended this analysis to assess the impact of environmental and socio-economic confounders on the size and direction of effects.

Within this study characteristics sensitivity analysis, associations consistent with the overall positive effect were observed irrespective of study and sample characteristics (see Figure 3.1), strengthening confidence that the pooled result is robust to a range of measured and, by extension, unmeasured confounders. When conducting the same analysis using environmental covariates, there was some evidence of degraded effect sizes in sites with intermediate mean temperatures, and study locations situated below the Tropic of Capricorn or in Polar regions (see Figure 3.3). Similarly, in a socio-economic sensitivity analysis, there was evidence of degraded effect sizes in places with the highest human development index scores ($>$ 0.81 or classified as ‘high’ by UN) (see Figure 3.2).

However, these results must be interpreted in light of the effect size trends across the other levels of each factor tested as well as the reduced sample sizes at this more granular level of analysis. Overall, I conclude weak potential confounding effects of very high HDI and in high/low latitude settings. Hence, the results of this analysis warrant further investigation of how spatially interpolating from sampled countries to unsampled countries impacts the estimated burden of infectious disease associated with agriculture.

3.4.3 Global Burden of Disease Linked to Agricultural Land Use

Overall, 10.33% (CI 5.94% - 14.71%) of global deaths and 13.12% (CI 7.86% - 18.37%) of global disability adjusted life years (DALYs) lost due to communicable diseases in the reference year (2015) were associated with exposure to agricultural land use in the reference year (2015) (see Tables 3.2 and 3.3). This is equivalent to 886,355 (CI 510,217 - 1,262,585) deaths and 63,627,960 (CI 38,146,978 – 89,112,345) DALYs.

Agriculture was further associated with 4.49% (CI 1.72% - 7.34%), 0.04% (CI 0.03% - 0.06%), 3.02% (CI 2.15% - 3.89%) and 1.11% (CI 0.61% - 1.61%) of communicable disease deaths in 2015 due to diarrheal diseases, intestinal nematodes, parasitic and vector-borne diseases and other types of infectious diseases, respectively (see Tables 3.2 and 3.3). When accounting for morbidity, agriculture was associated with 4.73% (CI 1.60% - 7.96%), 0.22% (CI 0.12% - 0.31%), 4.56% (CI 3.28% - 5.84%) and 1.52% (CI 0.85% - 2.18%) of all communicable disease DALYs lost in 2015 due to diarrheal diseases, intestinal nematodes, parasitic and vector-borne diseases and other types of infectious diseases, respectively. Detailed lists of the country-specific deaths and DALYs linked to agricultural land use are presented in Tables A.9 and A.10.

3.4.4 Global Burden of Disease Linked to International Agricultural Trade

Globally, 3.52% (CI 3.48% - 3.57%) of deaths and 4.54% (CI 4.53% - 4.55%) of DALYs lost due to communicable disease were linked to international agricultural trade in 2015, equivalent to 302,367 (CI 298,546 – 306,189) deaths and 22,037,894 (CI 22,005,135 – 22,070,652) DALYs. This equates to 34.11% (CI 24.25% - 58.52%) and 34.64% (CI 24.77%

- 57.6%) of all agricultural land use related infectious disease deaths and DALYs being linked to international trade, respectively, with the remainder linked to domestic trade and consumption (see Tables 3.2 and 3.3).

When stratifying by disease categories, the international trade of agriculture was linked to 1.38% (CI 1.34% - 1.41%), 0.01% (CI 0.01% - 0.02%), 1.03% (CI 1.01% - 1.05%) and 0.37% (CI 0.35% - 0.38%) of the global communicable disease deaths in 2015 due to diarrheal diseases, intestinal nematodes, parasitic and vector-borne diseases and other types of infectious diseases, respectively (see Tables 3.4 and 3.5). When accounting for morbidity, international agricultural trade was linked to 1.51% (CI 1.51% - 1.52%), 0.07% (CI 0.07% - 0.07%), 1.55% (CI 1.55% - 1.55%) and 0.52% (CI 0.52% - 0.52%) of the global communicable disease DALYs lost in 2015 due to diarrheal diseases, intestinal nematodes, parasitic and vector-borne diseases and other types of infectious diseases, respectively.

Therefore, the international trade of agricultural commodities contributed 30.6%, 32.6%, 34.1% and 33.1% of all agricultural land use related deaths and 32.0%, 32.4%, 33.9% and 34.5% of all agricultural land use related DALYs due to diarrheal diseases, intestinal nematodes, parasitic and vector-borne and other infectious disease deaths, respectively. The remainder is linked to domestic trade and consumption. Detailed lists of the country-specific deaths and DALYs linked to agricultural trade are presented in Tables A.11 and A.12.

Table 3.2: Global deaths linked to agricultural land use

	Global Deaths linked to Agricultural Land Use					
	Mean	%	CI Low	%	CI High	%
All Disease	886,355	10.325	510,217	5.943	1,262,585	14.707
All Other Diseases	95,430	1.112	52,586	0.613	138,343	1.611
Diarrheal Disease	385,256	4.488	147,758	1.721	630,193	7.341
Intestinal Nematodes	3,475	0.040	2,234	0.026	4,718	0.055
Parasitic & Vector Borne Diseases	259,369	3.021	184,589	2.150	334,165	3.892

Table 3.3: Global DALYs linked to agricultural land use

	Global DALYs linked to Agricultural Land Use					
	Mean	%	CI Low	%	CI High	%
All Disease	63,627,960	13.116	38,146,978	7.864	89,112,345	18.370
All Other Diseases	7,352,677	1.516	4,130,841	0.852	10,576,121	2.180
Diarrheal Disease	22,958,902	4.733	7,780,461	1.604	38,628,316	7.963
Intestinal Nematodes	1,055,227	0.218	589,832	0.122	1,520,736	0.313
Parasitic & Vector Borne Diseases	22,140,126	4.564	15,949,255	3.288	28,331,754	5.840

Table 3.4: Global deaths linked to international agricultural trade

	Global Deaths linked to International Agricultural Trade					
	Mean	%	CI Low	%	CI High	%
All Disease	302,367	3.522	298,546	3.478	306,189	3.567
All Other Diseases	31,453	0.366	30,049	0.350	32,857	0.383
Diarrheal Disease	118,056	1.375	114,848	1.338	121,264	1.413
Intestinal Nematodes	1,135	0.013	998	0.012	1,272	0.015
Parasitic & Vector Borne Diseases	88,309	1.029	86,655	1.009	89,964	1.048

Table 3.5: Global DALYs linked to international agricultural trade

	Global DALYs linked to International Agricultural Trade					
	Mean	%	CI Low	%	CI High	%
All Disease	22,037,894	4.543	22,005,135	4.536	22,070,652	4.550
All Other Diseases	2,528,168	0.521	2,516,042	0.519	2,540,294	0.524
Diarrheal Disease	7,338,390	1.513	7,312,648	1.507	7,364,132	1.518
Intestinal Nematodes	339,334	0.070	336,610	0.069	342,059	0.071
Parasitic & Vector Borne Diseases	7,511,490	1.548	7,496,583	1.545	7,526,397	1.551

3.4.5 Infectious Disease Footprints

European countries drive approximately 42.52% (CI 33.17% - 59.20%) of the burden of infectious disease through their agricultural imports (Figure 2). The Western Pacific region drives approximately 18.59% (CI 14.51% - 25.89%) and the Americas drive an estimated 14.47% (CI 11.29% - 20.14%). 8.30% (CI 6.48% - 11.57%) is also driven by the Southeast Asia region, 4.74% (CI 3.70% - 6.60%) is driven by the African region and 3.23% (CI 2.52% - 4.50%) is driven by the Eastern Mediterranean region (Figure 2). On the other hand, 84.33% (CI 82.60% - 84.32%) of the burden of communicable disease linked to agricultural trade is being suffered in Africa, with Europe (37.94%, CI 29.60% - 52.82%), the Americas (11.61%, CI 9.05% - 16.15%) and the Western Pacific (15.02%, CI 11.72% - 20.91%) driving an aggregated 65% of this burden in Africa (see Figures 3.15).

Country-specific regional footprints (i.e., the infectious disease impacts in producing countries that can be traced back to consuming countries through trade networks), show that the USA, five European countries (Germany, France, UK, Spain, and Italy) and Asia's three largest superpowers (Japan, China, and India) are the largest importers of disease implicated commodities (see Figures 3.16). Together they drive 57.51% of the total infectious disease burden induced through agricultural trade. These 9 countries combined infectious disease footprints were mostly located in sub-Saharan Africa (see Figure 3.17).

Here, the USA has the largest footprint (DALYs), totalling approximately 2.1 million DALYs (CI 1.78 million – 2.36 million) which is equivalent to 9.38% (CI 8.04% - 10.71%) of global DALYs lost due to agricultural trade. Approximately 41.70% of the USA's footprint occurs in only 5 countries: Ethiopia (10.80%), Chad (9.40%), Cote d'Ivoire (7.70%), India (7.50%) and Liberia (6.30%).

Japan (9.08%), China (7.21%) and India (6.22%) drive a combined 4.96 million DALYs through the importation of disease implicated commodities, equivalent to a total 22.51% of global DALYs lost due to agricultural trade. The top countries that suffered this absolute burden driven by the Asian powerhouses included Ethiopia (28.29%), Nigeria (13.98%), Tanzania (6.37%), Pakistan (3.93%), Cameroon (3.14%), India (2.59%), Afghanistan (2.21%), Cote d'Ivoire (2.10%), Mozambique (1.96%) and Burkina Faso (1.17%). India was found to be both a large driver and sufferer of global agricultural trade related infectious disease.

The five European countries (Germany (8.00%), France (6.11%), UK (4.63%), Italy (3.88%) and Spain (3.00%)) drove approximately 5.65 million DALYs, equivalent to 25.52% of the disease burden through importing implicated commodities. These infectious disease footprints were all located in sub-Saharan Africa and included Cote d'Ivoire (11.18%), Nigeria (9.93%), Ethiopia (6.74%), Chad (4.13%), Tanzania (3.18%), Burkina Faso (3.21%), Ghana

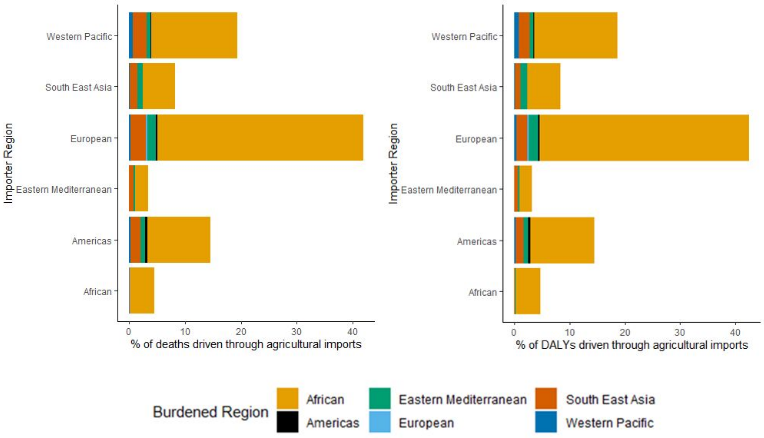


Figure 3.15: Regional importers and burdens

The absolute deaths (left pane) and DALYs (right pane) of all infectious diseases associated with international agricultural trade that is driven at a regional level. Regions are as defined by the World Health Organisation Regions.

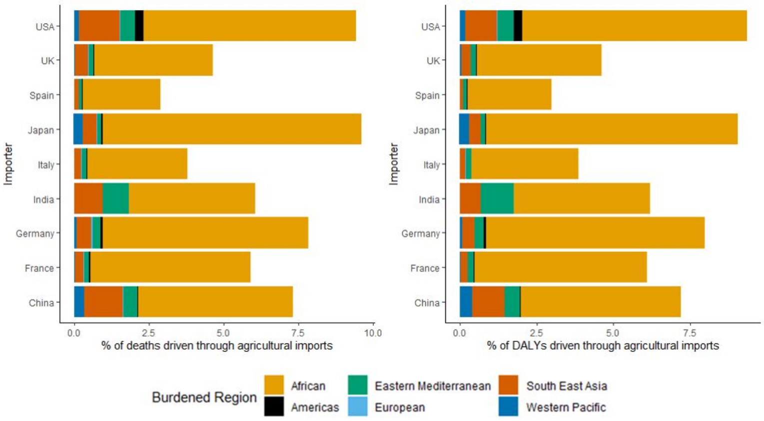


Figure 3.16: Top 9 importers and regional impacts

The absolute deaths (left pane) and DALYs (right pane) of all infectious diseases associated with international agricultural trade that is driven by the top 9 importers of disease implicated commodities. Regions are as defined by the World Health Organisation Regions.

(2.95%), Mali (1.83%), DR Congo (1.29%), Cameroon (1.00%), Kenya (0.91%) and Guinea (0.86%).

Further details on the regional and country-specific footprint of diarrheal, intestinal nematodes, parasitic and vector-borne and other infectious diseases can be found in Figures 3.18 and 3.19. Further details on the flow of diarrheal, intestinal nematodes, parasitic and vector-borne and other infectious diseases implicated commodities can be found in Figure 3.20.

3.4.6 Interpolation & Extrapolation Sensitivity Analysis

To ascertain how sensitive the burden of infectious disease associated with agriculture is to spatial interpolation and by extension extrapolation, I performed a sensitivity analysis using different interpolation strategies.

Here, I find that although mean effect sizes are non-sensitive, uncertainty in the burden of infectious disease associated with agriculture is somewhat sensitive to a global average risk approach (see Figure 3.21). Specifically, uncertainty was greater when estimated through spatial interpolation approaches. However, confidence intervals overlapped across all outcomes suggesting that our overall analysis is stable and insensitive to large scale methodological changes. Therefore, our results at the global level can be considered relatively insensitive to the interpolation assumptions.

In sensitivity analyses on the interpolation strategy (i.e., global average risk, global spatial interpolation, HDI focussed and systematic review focussed) on the burden of disease associated with agriculture. Here, I find consistency between global extrapolation and a limited systematic review-based extrapolation thereby suggesting that extrapolations can be made to Africa, South and Central America, South and Southeast Asia (see Figure 3.21). However, when limiting extrapolations to countries that have a HDI score between 0.51 and 0.81, I find that the burden of disease associated with the production of agricultural commodities is reduced for all diseases and especially for parasitic and vector-borne diseases. This is likely due to the exclusion of countries with a low HDI score (< 0.51) that may typically have a larger burden of infectious disease and a higher proportion of the population working in agriculture.

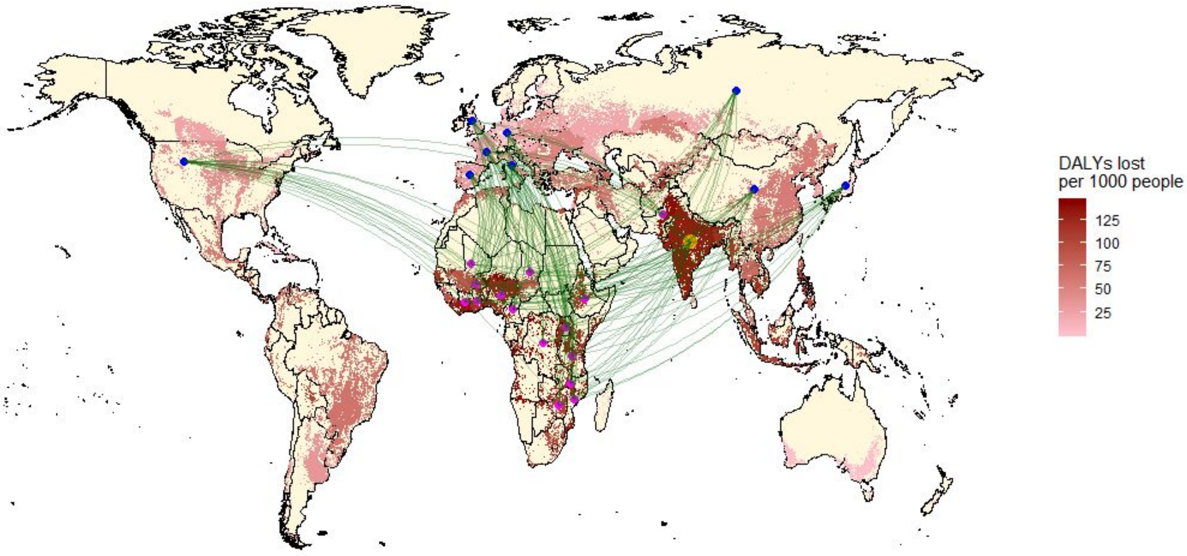


Figure 3.17: Flow map of the top trade routes of disease implicated commodities

Note that the green lines directly link the agriculture producing countries, where agriculture associated disease burdens are incurred (magenta circles), and the top nine final consumer countries that drive these burdens through their import (blue circles). India is both an importer and sufferer. Supply-chain links in intermediate countries are accounted for but not explicitly visualized.

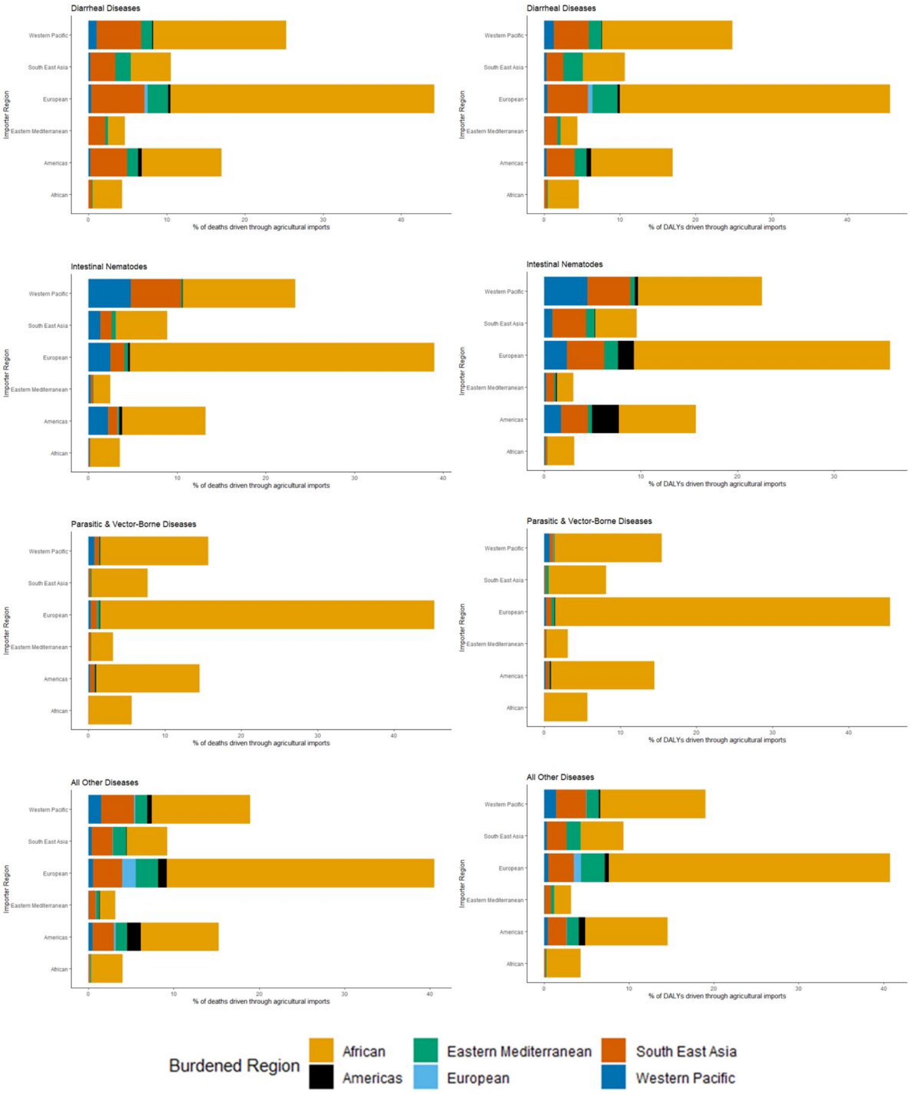


Figure 3.18: Regional importers and mortality

The absolute deaths (left pane) and DALYs (right pane) of diarrheal, intestinal nematodes, parasitic and vector-borne and other infectious diseases associated with international agricultural trade that is driven at a regional level. Regions are as defined by the World Health Organisation Regions.

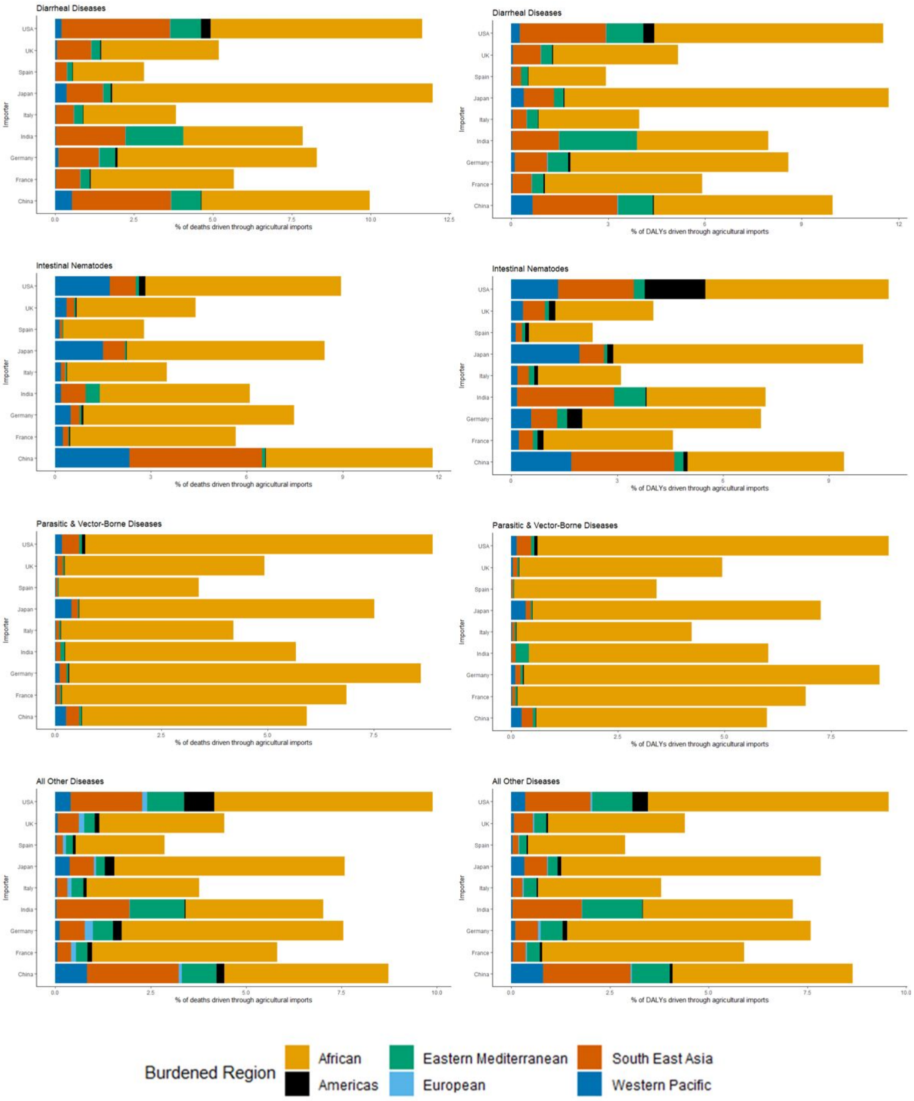


Figure 3.19: Top 9 importers and regional impacts

The absolute deaths (left pane) and DALYs (right pane) of diarrheal, intestinal nematodes, parasitic and vector-borne and other infectious diseases associated with international agricultural trade that is driven by the top 9 importers of disease implicated commodities. Regions are as defined by the World Health Organisation Regions.

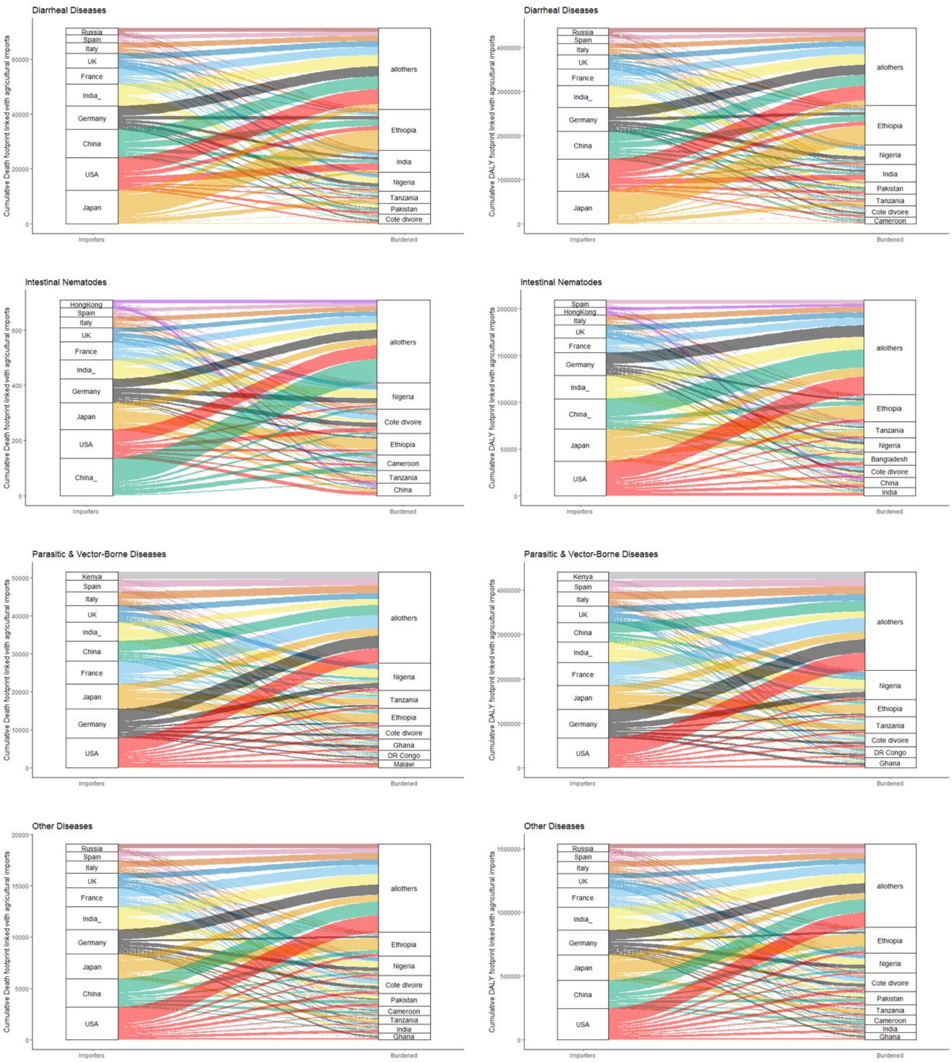


Figure 3.20: Flow of the top trade routes of disease implicated commodities

The flow of absolute deaths (left pane) and DALYs (right pane) of diarrheal, intestinal nematodes, parasitic and vector-borne and other infectious diseases associated with international agricultural trade that is driven by the top 9 importers of disease implicated commodities.

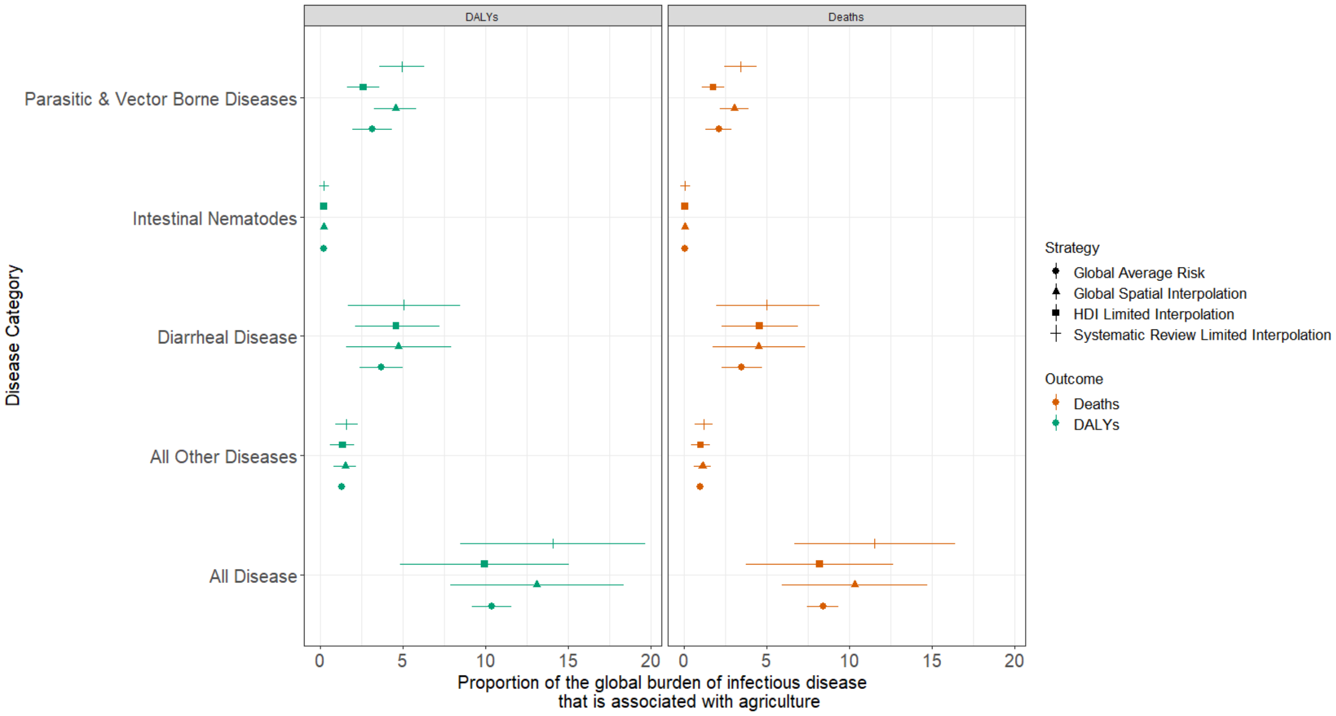


Figure 3.21: Interpolation & Extrapolation Sensitivity Analysis

Sensitivity analysis showing the impact of three different interpolation strategies.

3.5 Discussion

3.5.1 Overview

Globally, people who work or live in agriculture are more than twice (107%) as likely to be infected with a pathogen than those unexposed. This effect is robust across continents, countries, exposure categories and disease types. Due to this elevated risk of infection among people exposed to agriculture, around 10.33% of deaths and 13.12% of global DALYs lost due to communicable diseases are directly associated with agricultural exposure. This burden is roughly twice that of the global burden of malaria [291]. Of this, around one third was linked to international agricultural trade, which I traced back through input-output analyses to wealthy high-income consumer countries as well as the biggest economies in Asia. This international trade impact on human health is itself equivalent to more than half (58%) the global malaria burden [291].

This analysis quantifies a relatively small yet likely significant fraction of the full infectious disease burden that agricultural land use (~13.12%) and trade (~4.54%) is likely to be incurring. The novel framework employed in this study can also be readily applied to other health areas to deliver a more complete picture of the true health footprint of agricultural land use and trade. Future assessments could include other similarly fragmented areas such as animal bites and stings [318], allergic reactions [319, 320], respiratory issues due to dust, smoke from burning and air pollution [321, 322, 323] and toxic carcinogens [323, 324, 325, 326]. Such estimates following the methodology used in this study could be used to incorporate potential social and health impacts of agricultural land-use or production into environmental, development and trade policies, which could aid in better uptake of sustainable products that are not sourced at the expense of the health of local populations.

3.5.2 Burdened Countries

The majority of the infectious disease burden associated with agricultural land use and trade accrues in sub-Saharan Africa, and west Africa in particular, which is in line with previous research [138]. This may be partly explained by the fact that West Africa has some of the worst contemporary rates of deforestation and a rapidly increasing area under agricultural cultivation, largely due to cash crop exports such as cocoa and palm oil [327]. In addition, deforestation (often related to timber harvesting and charcoal production for use as fuel for heating and cooking [328] and consequent biodiversity loss are common precursors to agricultural expansion, and both have been linked to increases in disease risk via various mechanisms in other contexts; for example, by favouring certain disease hosts or vectors [84, 270]. At the same time, Sub-Saharan countries also have some of the largest proportions of people working in agriculture who predominantly live in rural settings with little access to education or health care [203].

More broadly, given that the majority of land-use change resulting in loss of tree cover is related to agricultural expansion, results appears broadly consistent with previous studies that have shown significant positive associations between tree cover and diarrheal disease, deforestation and disease carrying mosquito vectors and general theoretical associations between deforestation, certain tree covers and infectious disease risk [81, 161, 198, 208, 270, 329]

3.5.3 Importing Countries

High income western territories such as the USA, UK, and European Union alongside Asian powerhouses such as India, China and Japan drive approximately 57.54% of the total burden of agricultural trade induced infectious diseases. This analysis suggests that trade routes of disease implicated commodities follow some historical trade pathways, while also reflecting new or evolving trade relationships. For example, the USA and Europe have previously been established as substantial importers from sub-Saharan Africa, while China has emerged more recently as Africa's largest trading partner [330, 331, 332, 333, 334, 335]. Analysis of infectious disease footprints is thereby consistent with previous research and suggests exports from developing nations are more ecologically and now epidemiologically intensive than those from developed nations [151].

3.5.4 Accounting and Accountability

To date, no clear global trade policy has been established that focusses on aiding exporting nations in minimising local health threats induced through agricultural production. The World Trade Agreement on the Application of Sanitary and Phytosanitary Measures Agreement (1995) does specify a need to "take into account . . . [the] prevalence of specific diseases or pests". However, this focusses on potential trade restrictions due to infectious diseases being a biosecurity threat through the movement of trade [139, 336].

Accountability and responsibility of negative impacts of production and trade is highly debated issue [121]. For example, when looking at carbon accounting, China's official stance is that final consumers of implicated products should be held accountable and responsible for the greenhouse gases emitted during the production of China's export goods [121, 337]. This, however, is in contrast to most methods of carbon accounting (e.g. the Paris Agreement) which is more typically seen for traded commodities [338].

Complicating matters, and within the context of agricultural land use or trade induced disease risks, appetite for claiming responsibility may be low amongst high income importing countries considering these countries already fund public health programmes in low and middle income countries through international development aid [339]. However, if international development aid is increased to allow for the impact of agricultural production and trade, supplier country governments could improve or change land use and health policy to ensure agricultural workers are less impacted by agricultural land use and trade induced infectious disease risks. Key measures that may mitigate agriculture induced burdens of disease could include Universal Health Coverage (UHC), Vaccines and Immunisation for all or Water Sanitation and Hygiene (WaSH) interventions [340, 341, 342, 343, 344, 345, 346]. Improving the funding streams of such programmes is essential and if consumer countries wish to accept responsibility of the impact their consumption is having on agricultural workers, then increasing funding through multilateral organisations that implement these environmental measures may be a starting point [340, 341, 343, 344, 345, 346].

Other accountability measures also exist to help limit the impact that international demand will have locally. For example, sustainable certification schemes have been applied for commodities such as coffee or palm oil (with a focus on biodiversity and livelihoods) with varying success [347, 348]. Here, the inclusion of agriculture-disease indicators within sustainability certification is a goal that could be easily implemented in the short term if human health is incorporated more effectively into sustainable development and land use policy making.

In addition to these relatively lower hanging fruits, environmental interventions and nature-based solutions are being increasingly highlighted as essential to meet a range of interconnected global targets within and across different sectors [338, 349]. For example, changing from current agricultural practice to sustainable agriculture which integrates three main goals: environmental health, economic profitability, and social equity, could help to prevent climate change, improve livelihoods, reduce pollution and simultaneously provide ancillary benefits in reducing biodiversity loss or mitigating disease risk [350]. Economic mechanisms such as Pigouvian taxes, trade tariffs or market based systems such as Cap-and-trade measures may be also on the horizon if global consensus can be achieved and robust agriculture-health based accounting frameworks can be created [351, 352].

3.5.5 Limitations

There are a number of limitations in this first study of the links between infectious disease burden and global agricultural trade. My macroeconomic assessment is a cross sectional snapshot (data compiled for the year 2015) which focusses on associations at the ecological (aggregated) level rather than at the individual level. Hence, I have limited ability to assess the causal relationship between agriculture, trade and infectious disease risks [353].

I did make extensive efforts to control (through our inclusion/exclusion criteria, sensitivity and the subgroup analysis) or at least detect (through tests of heterogeneity and E-score tests) the potential effect of confounders and effect modifiers. In specific, through our study characteristics, environmental and socio-economic sensitivity analysis, I found very little evidence of confounding. Here, only four confounders showed no association between agricultural exposure and infection (i.e. study locations conducted below the Tropic of Capricorn and study locations that had a human development index higher than 0.80 or deemed of high human development by the United Nations). However, as stated earlier, the entirety of this analysis was conducted at the ecological (aggregated) level rather than at the individual level whereas there may be additional individual level confounders such as education, socio-economic status, household income, geographical accessibility to healthcare services or a variety of environmental factors such as seasonality of crops at the individual level which requires more granular data to assess the impact of confounding [109, 270, 354, 355]. In addition, through further subgroup analysis and testing that countries that are closer have similar risk estimates, I find that the global burden of infectious disease associated with agriculture is not sensitive to these assumptions.

One method to address issues surrounding confounding and effect modification would be to conduct large-scale field experiments to quantify the impact of land-use, land-use change and forestry activities on multiple health, environment and development outcomes, which could provide primary data, better address causality, confounding and effect modification and give greater insights on the sustainability of agricultural production activities [356].

Within our analysis, we also did not plan for or conduct multiple comparison tests. Specifically, multiple testing was considering difficult to plan for as it might not be known, at the outset, which outcomes and which effect measures will be available from the included studies. However, further research is required to develop adequate multiple comparison procedures for use in systematic reviews [172].

There was also a lack of studies that assess the impact of differing agriculture types, the degree of exposure to agriculture (e.g. more or less) and land use change on infectious disease risks globally. Such a paucity in data has led to further limitations. For example, risk estimates from 14 tropical or subtropical countries calculated from the literature review and meta-analysis were extrapolated through spatial averaging to infer the risk of infection for all countries (excluding island nations) whilst accounting for similarity between country demographics and progress towards the SDG goals. While the methods used in this study maximises available data in neighbouring countries to impute missing data for countries with no meta-analytic results, it would plainly be better to derive estimates for individual countries directly from existing data. Nevertheless, this analysis improves upon other methods of data imputation for countries with missing data (e.g., nearest neighbour within WHO epidemiological regions) [357], and provides a robust and reproducible framework which can be used for multiple agricultural impacts on health and can be updated with new evidence as it accrues.

Through using Eora, I am able to link country-specific agriculture-disease burdens to a general agriculture sector and perform a macroeconomic assessment which is likely to include aggregation errors [358]. For example, certain countries may report a single “Agriculture” sector that could contain commodities and services such as palm oil, maize, beef products or timber, each with differing environmental and epidemiological risks [270]. This can mean that the whole agricultural sector in the input output table is a poor approximation of its constituent flows. This can be rectified through hybrid life cycle-analysis [317, 359, 360, 361, 362]. In addition, I do not estimate the reductions of disease from agriculture, where this would be mostly on non-communicable diseases, nor do I examine the bidirectionality where agricultural land use and trade driven disease risks impact agricultural productivity. Further research in the form of a cost-benefit analysis of agricultural production should aim to disentangle the overall net gain or loss in economic and development indicators from agricultural production [110, 267].

3.6 Conclusion

Global agricultural trade has had many positive economic and social benefits. However, the growing demand for agricultural products has led to high-income countries disproportionately exerting pressure that drives infectious disease risks in lower income nations. To combat this, governments must acknowledge and address the human health cost involved in land use and ag-trade decisions.

Chapter 4

Agricultural expansion increases childhood malaria risk across sub-Saharan Africa

4.1 Abstract

Background

Agricultural expansion in Africa is amongst the most rapid in the world due to a growing population and increased food demand. However, expansion of agriculture can have a number of disbenefits for the environment and human health. Here, we assess the effect of differing agricultural land uses on childhood malaria risk while controlling for socio-economic and environmental confounders across 12 countries in sub-Saharan Africa.

Methods

Here, I compiled a geo-referenced dataset of 24,034 children with information on childhood malaria incidence, agricultural land cover classes (rainfed, irrigated or post-flooding, crop-dominant mosaic, and veg-dominant mosaic), forest cover, socioeconomic and environmental confounding factors. Using a multi-model inference hierarchical modelling framework, I tested a number of *a priori* hypotheses on the relationships between agricultural land use and malaria whilst controlling for confounders.

Results

After controlling for socio-economic and environmental factors, rainfed cropland (OR 1.19, CI 1.10 – 1.28), irrigated or post-flooding cropland (OR 1.05, CI 1.00 – 1.11) and veg-dominant mosaic (OR 1.04, CI 0.99 – 1.10) were all associated with an overall increase in childhood malaria risk. However, exposure to crop-dominant mosaic was not associated with childhood malaria and may be mildly protective (OR 0.97, 0.91 – 1.02). Effects further varied across rural and urban settings, with the overall effects all pronounced in rural settings, except for the irrigated or post flooding cropland effect which was more pronounced in urban settings.

Interpretation

Expansion of agriculture will likely increase childhood malaria in Sub-Saharan Africa, which is detrimental to malaria eradication efforts and the achievement of sustainable development targets. Environmental interventions such as creating mosaics of natural vegetation within existing or newly developed cropland systems may help reduce or neutralise malaria

risk compared to more intensive agriculture, particularly in rural settings, and hold promise for decision makers that need to balance the future sustainability of agriculture and health.

4.2 Introduction

Although sub-Saharan Africa has made remarkable gains in many areas of health, such as reduced smoking rates and reductions in maternal mortality, the region has many continuing health challenges to resolve, particularly at the interface of the environment and health [20, 310, 363]. Foremost among them is the elimination and eradication of malaria, where the Africa region accounts for 93% of all malaria cases worldwide and in which children aged under 5 years are the most vulnerable group [364].

At the same time, the current population across sub-Saharan Africa is projected to rise from approximately 1.03 billion in 2020 to 4.2 billion by 2100, with much of this growth occurring in rural areas [89, 365, 366]. Such growth places considerable demand on the region's food supply and governments are now considering or implementing large-scale agricultural projects to meet this increased need. However, increasing agricultural expansion or intensification in an unsustainable manner may be detrimental to eliminating or eradicating malaria; for example, by bolstering mosquito populations or accelerating chemical use and resistance [89, 288, 367, 368]. Projections also show that many African workers and their families will remain engaged in agricultural work in rural areas; hence, agriculture may continue to influence malaria risk in future [89, 366].

Better resolving the links between differing agricultural land-uses and malaria risk could help policy makers identify to what extent expansion of specific agricultural land uses may impact malaria risk in the region, thereby improving agricultural productivity and sustainability. For instance, expansion of differing agricultural land uses may have varied impacts on habitat suitability of specific malaria transmitting mosquitoes and subsequent malaria transmission [208]. Frontier malaria may also occur, where a change in spatial or temporal malaria risk of previously undeveloped areas occurs as a result of large-scale land-use transformations due to agriculture [76, 84, 161, 208, 240, 286, 287].

So far, few studies have assessed the relationships between agriculture and malaria outcomes in humans [89, 289, 290]. For example, Ijumba et al (2002) found that the incidence of clinical episodes of malaria was significantly less in children living close to a large area of irrigated rice production than in other communities without rice [290]. However, the study failed to control for important confounders, such as socio-economic, demographic (e.g., urban vs rural) or climatic factors. On the other hand, previous research has found that increased exposure to agriculture increased malaria risk in children younger than 5 years across rural and ecologically diverse settings. However, here the authors were not able to assess the relationship between childhood malaria and specific agricultural land use types (e.g. irrigated vs rainfed croplands) [89].

Here, I aimed to resolve the linkages between agriculture and childhood malaria risk in Sub-Saharan Africa. Specifically, I combined remotely-sensed land cover and land use data with a large geo-referenced malaria dataset from the Demographic and Health Surveys (DHS), comprising 24,034 children across 12 countries, to ask: what impact does increasing exposure to differing agricultural land cover types (including rainfed, irrigated, post flooding and cropland-natural vegetation mosaics with varying levels of coverage (i.e., dominated by either cropland, hereafter crop-dominant mosaics, or natural vegetation, hereafter veg-dominated mosaics)) have on childhood malaria risk in rural and urban households across sub-Saharan Africa?

I use a multi-model inference hierarchical modelling framework to assess relationships between malaria infection status and the agricultural covariates while controlling for a number of important individual (age and sex of child), household (education level of the mother, wealth of household, access to improved sanitation and water sources, whether the household had a bed-net and whether the dwelling was sprayed with insecticide within the last 12 months) [369] and extrinsic or environmental confounders (population density, forest cover, forest loss, temperature, precipitation and elevation) [84, 370, 371, 372, 373, 374, 375, 376, 377].

Here, I find that malaria risk differs considerably among these agricultural land cover classes, with rainfed cropland generally associated with the largest overall increase in malaria risk and irrigated or post-flooding cropland also associated with an elevated risk. In contrast, crop-dominant mosaics marginally decreased childhood malaria risk. Identifying generalisable associations using multi-country data between differing agricultural land uses (irrigated, rainfed, mosaics) and childhood malaria risk raises the possibility that land-use policies (e.g. increasing irrigation schemes, mosaic landscape design) could both positively and negatively impact malaria risk. Better understanding the potential for adaptive vs maladaptive agricultural development strategies could aid in reducing or eliminating malaria and also intersect with other sustainability issues and priorities, such as education, poverty reduction, income growth, food or water security, biodiversity or climate change [367].

4.3 Methods

4.3.1 Data Integration

I used the Demographic and Health Surveillance Data (DHS) and Malaria Indicator Surveys (MIS) to compile datasets for analysis. These are nationally-representative household surveys that provide data for a wide range of monitoring and impact evaluation indicators in the areas of population, health, socio-economics and nutrition [90, 198, 363, 371, 378]. Here, I analysed data for 12 sub-Saharan countries (consisting of 12 mutually exclusive DHS datasets) from the years 2010 to 2015 with all variables that were hypothesised (see below) to be important risk factors for the probability of malaria whilst controlling for potential confounders. More countries are included in these datasets, but I restricted our analyses to those for which covariate data were the most complete.

The final dataset included 24,034 cases from respondents of households within clusters within each country between 2010 – 2015. For analysis, 21 socio-economic, environmental, and agricultural land use variables were compiled into a single dataset on the basis of their hypothesised or known links to malaria from previous studies. Socio-economic variables included age, sex, education, whether a bed-net was used, whether the dwelling was sprayed with insecticide, wealth index, urban/rural, water source, sanitation type and population density (extracted from the Gridded Population of the World, Version 4 (GPWv4)) [379]. Environmental variables included forest cover, forest loss, temperature, precipitation, elevation extracted from the Global Forest Change and WorldClim datasets [380, 381, 382]. Agricultural land use variables included rainfed cropland, irrigated or post flooding cropland and crop-dominated or veg-dominated mosaics (see below) from the European Space Agency (ESA) Climate Change Initiative Land Cover (CCI-LC) dataset [294].

The DHS program does not report exact coordinates for the clusters included in the survey, but randomly displaces the cluster coordinates up to 2km for urban clusters and up to 5km for rural clusters, with a further 1% of rural clusters displaced up to 10km. This is done to ensure privacy protections of survey participants [90, 198]. Hence, to address the possible displacement of the exact locations, all environmental data were resampled to a resolution of 10 km to approximate the environmental conditions for each household in the year of sampling. A 10-km radius also corresponds to the maximum flight distance of a female, human blood-fed *Anopheles gambiae* mosquito, representing the maximum extent at which human and specific mosquito populations can be expected to interact [89].

4.3.2 Variables

Biology and Ecology of Malaria

A key factor within the agriculture-malaria relationship is the water-dependent life cycle of anopheles mosquitoes that transmit human Plasmodium and the types of water they prefer. Specifically, the life cycle of an anopheles individual proceeds through four stages: three immature stages, which occur in a water body – egg, larva, pupa – and then the mature stage, a flying adult [383]. Research suggests that anopheles larvae occur in a wide range of habitats, but most species prefer clean, unpolluted water. Larvae of Anopheles mosquitoes have been found in freshwater or saltwater marshes, mangrove swamps, rice fields, grassy ditches, the edges of streams and rivers, and small, temporary rain pools. Many species prefer habitats with vegetation such as forest edges. Others prefer habitats with none. Some breed in open, sun-lit pools, while others are found only in shaded breeding sites in forests [384]. Hence, any land use or land use change such as agriculture that can impact habitat suitability for the Anopheles mosquito has the potential to incur a change in human risk.

Malaria Outcome Variable

The DHS and MIS survey explicitly test for the presence or absence of malaria in children under 5 years using blood smear tests or rapid diagnostic tests [385, 386, 387]. Although rapid diagnostic tests have been found to be superior in detecting the presence of *P. falciparum*, research suggests that the two outcome variables are well correlated (r = 0.58) [371]. Using this information, a binary outcome variable was constructed that is equal to 1 if the child had malaria either diagnosed by BSTs or RDTs and 0 otherwise.

Agricultural Exposure

Agriculture has consistently been considered a risk factor for malaria infection in multiple geographical contexts [89, 161, 259, 270, 286]. However, research that investigates specific agricultural land uses (rainfed, irrigated or post-flooding and mosaic systems) and malaria infection is sparse and heterogeneous. To test the associations between differing agricultural land uses, I extracted data for each cluster in the survey year on rainfed, post flooding or irrigated and mosaic croplands using the European Space Agency (ESA) Climate Change Initiative Land Cover (CCI-LC) dataset [294]. Within this analysis, I focus on three agricultural production methods (rainfed and irrigated or post-flooding and mosaic systems) as potential risk factors of malaria and therefore exclude all other covariates (e.g., mosaic natural vegetation, shrubland, grasslands). Mosaic systems are further stratified into mosaic cropland and mosaic natural vegetation, with mosaic cropland constituting more than 50% of the allocated pixel and mosaic natural vegetation constituting more than 50% of the pixel [294].

Forest Cover Change

Forest loss and forest cover have similarly been considered important factors in malaria ecology across sub-Saharan Africa [84, 208, 259, 371]. In addition, agriculture is considered the leading driver of forest loss in sub-Saharan Africa [388]. Here, I extracted forest loss and forest cover data from the Global Forest Change Dataset for each cluster in the survey year to capture forest cover change for pre-production agriculture [380]. This dataset is a published high resolution spatially explicit global raster of 21st century forest cover change at a 30-meter resolution from 2001 to 2017. I do not include forest gain due to concerns on the reliability of these data, following previous studies [389].

Socio-economics

Age and sex: Our dataset specifies the age (years) and sex of each child, allowing me to control for their commonly reported effects on malaria [390].

Education and wealth: Education and wealth have previously been found to be important variables in malaria epidemiology and ecology across sub-Saharan Africa [391]. Therefore, maternal education and wealth were included as potential confounders. Maternal education is defined as the level of education of the mother of each child and was classified into three categories: No education, Primary, and Secondary. Wealth within the DHS data is a composite measure of a household's living standard and is considered to be a surrogate of a household's economic status [198, 392]. The index places households into categories representing wealth quintiles, where the higher the wealth quintile, the higher the economic status of the household.

Rural/Urban: Within the integrated dataset, children are classified as either living in rural or urban clusters. The rural-urban context has also previously been shown to be a major determinant of malaria risk where the risk of malaria infection was shown to decline from rural areas through peri-urban settlements to urban central areas [372]. In addition, the majority of global population growth this century is predicted to occur in Africa with dramatic changes to population densities in both rural and urban landscapes expected. Given the importance of the rural-urban context, in addition to the primary analyses, an additional subgroup analysis was performed to determine how the agriculture-malaria relationship may differ across rural or urban landscapes (see ‘Statistical analysis’ section below for further details).

Water source and sanitation: Drinking water and poor sanitation have previously been found to be risk factors of malaria infection in sub-Saharan Africa [393]. DHS identifies the main source of drinking water used by the household, and the type of sanitary facility primarily used by each household. Here, I grouped the type of water and sanitation used by the household into dichotomous measures reflecting improved or unimproved sanitation and water source based on existing peer-reviewed literature [198].

Bed-net ownership and spraying of dwellings: Insecticide-treated mosquito nets (ITNs) and indoor residual spraying (IRS) are the two most frequent interventions used to combat malaria in Africa [394, 395]. Such interventions may confound the agriculture-malaria relationship and therefore have been included as potential confounding variables. The DHS and MIS datasets provide binary variables for whether the household has a bed-net for sleeping and whether the dwelling has been sprayed against mosquitoes in the last 12 months (0 = no, 1 = yes).

Population density: Population density is another important factor in malaria epidemiology and the process of urbanization and accompanying demographic change is associated with decreased risks of infection due to reduction of suitable breeding grounds for malaria vectors through reduction of vegetative cover, water surfaces and other natural surfaces with building structures and other paved surfaces as well as through pollution of available breeding sites [372, 396]. To control for potential confounding, population density data were extracted from the Gridded Population of the World, Version 4 (GPWv4)) and included for each cluster using 2010 as an average year [379].

Climatic Factors

Mean temperature and precipitation have been shown to be significant predictors of malaria in sub-Saharan Africa [286, 374, 397, 398, 399]. The temperature and precipitation variables in our dataset are the long-term (1950-2000) mean temperature (degrees Celsius) and precipitation (millimetres) in the cluster during the survey month. Both variables were sourced from the WorldClim v1 dataset, which provides monthly mean precipitation from interpolated station data over the period 1950–2000 [381].

Elevation is an appealing environmental proxy for a variety of fundamental dynamic ecological factors (e.g. temperature, humidity, precipitation, air pressure, sunshine, wind velocity, altitudinal farming) critical for mosquito development [41, 400]. For these reasons, elevation also relates to both where certain crops are grown (e.g., in highland vs lowland regions) as well as suitability for malaria transmission. Although I aimed to include some of the proximal factors proxied by elevation directly into the analyses, I retained elevation as a covariate in analyses to control for these other elevation-related potential confounders. Elevation measurements were extracted from the Amazon Web Services Terrain Tiles dataset using the 'elevatr' package within R [382].

4.3.3 Statistical Analysis

Descriptive Analysis

Our initial dataset consisted of approximately 2.3 million respondents based on all DHS and MIS surveys extracted in 2018. Here I excluded surveys that had no geo-referenced presence/absence of malaria tested through BSTs or RDTs alongside socio-economic variables. Variables (e.g. presence of specific malaria species, presence of soap/detergent, main housing material used, and type of bed net used) that were correlated with existing socio-economic variables such as sanitation, water sources, bed-net ownership were also excluded. Variables describing livestock ownership type (e.g. cows, chickens, goats etc) were also excluded due to a high level of missingness (>95%) which was not random. Finally, I removed duplicate records and performed a complete case analysis that only included participants for which we had no missing data on the variables of interest. Baseline characteristics and descriptive characteristics were computed and are presented in the results [401].

Missing Data, Pairwise Correlation & Multicollinearity

When first cleaning the dataset, I removed variables that had 95% or more missing data. I then tested for pairwise correlations and removed one of the two variables that had more than a 70% correlation with another variables. As a final step, I tested for multicollinearity.

Multicollinearity arises in statistical models when two or more covariates are not statistically independent (i.e., correlated), leading to unstable estimates of variances of regression coefficients. To control for multicollinearity, the variance inflation factor (VIF) was calculated, which represents the amount of variability of a covariate which is explained by other covariates [402]. Here, I calculated the VIF for the candidate set of environmental, agricultural, and socio-economic variables. Methods state that variables that have a VIF greater than

10 should be excluded [403]. No variables met this threshold for exclusion and VIF scores are presented alongside the results.

Hierarchical Modelling

Data were analysed within a multi-model inference framework [90, 198, 404], chosen to reduce the risk of overfitting, avoid the arbitrary stepwise approach to model selection and allow for the simultaneous assessment of different models and their associated hypotheses [405]. Within this framework, hierarchical models were used as they can control for covariates measured at different levels within the hierarchical dataset, thereby allowing the correction of biases in parameter estimates due to clustering of observations [198, 406].

The dataset is structured as individuals (level 1) that reside in households (level 2) that are in clusters (level 3) located within countries (level 4). Hence, I fitted a four-level hierarchical model using a binomial distribution for malaria presence/absence with a logit link function. Here, I assume that there may be random variability across households, clusters and countries and therefore added a random effect at each of the four levels [198, 407].

I specified 81 candidate models using *a priori* hypotheses. These models included various combinations of socio-economic, agricultural land use, forest cover, forest loss, and climate explanatory variables. To assess predictive accuracy, model averaging was conducted based on Akaike's Information Criterion (AIC), where predictions were combined using Akaike weights based on the inclusion of all candidate models with an AIC less than 5 compared to the best performing model (defined as the model with the lowest AIC value) [408, 409, 410, 411].

As with demographic and economic transitions, landscapes often also follow a sequence of different land-use regimes: from pre-settlement natural vegetation to frontier clearing, then to subsistence agriculture and small-scale farms, and finally to intensive agriculture, urban areas, and protected recreational lands [51]. Hence, initial results at the regional level are thus expressed in odds ratios across differing land use segments reflecting this successional transition process, starting with natural vegetation, through to the mosaic (crop-dominated or veg-dominated) systems and finally intensive agricultural land use systems (rainfed, irrigated or post-flooding).

Appendix A.17) provides a description of the variables included within each of the 81 *a priori* models. Appendix A.16) shows the AIC for each model.

Rural Urban Subgroup Analysis

Further subgroup analysis was performed by stratifying rural and urban clusters to assess whether geographical heterogeneity may influence or explain the association between differing agricultural land uses and childhood malaria risk. Specifically, I hypothesise that socio-economic and environmental factors will likely be different across rural and urban gradients. For example, urban areas are likely to have improved education, wealth, improved housing, sanitation, and water sources which are all considered potential confounders in the agriculture-malaria relationship [84, 363, 377, 412, 413, 414]. Hence, I aimed to capture variation in the key socio-economic and environmental variables across an urban and rural stratification and hypothesise that urban or rural clusters can provide a proxy for such confounding socio-economic or environmental factors that may be related to disease risk.

Marginal Effects Analysis

Marginal effects measure the instantaneous effect that a change in a particular explanatory variable has on the predicted probability of the outcome (here malaria occurrence), when the other covariates are kept fixed [415]. In nonlinear models the marginal effects differ from the estimated coefficient as these depend on the values of the other explanatory variables, and in this analysis, also depend on the estimated random effects of the hierarchical model [198]. Here, marginal effects were calculated using a global model to estimate the impact on the probability of childhood malaria of increasing exposure to each of the agricultural, environmental, forest cover change and socioeconomic variables.

The interpretation of marginal effects differs for discrete and continuous variables. For discrete variables, the marginal effect corresponds to changes in each of these variables from 0 to 1 (e.g. no to yes responses or unimproved to improved states). The marginal effect of a continuous independent variable such as rainfed cropland is the instantaneous rate of change (e.g. the change in the probability of malaria given very small changes (close to zero) in the independent variable (e.g. rainfed cropland) [198].

To specify the global model (with all covariates) used for the marginal effect's analysis, I observe M_{ijkl}, a binary variable for malaria presence or absence for child "i" in household "j" in cluster "k" in country "l". I define the probability of malaria equal to 1 as $P_{ijkl} = Pr(M_{ijkl} = 1)$ and let P_{ijkl} be modelled using a logit link function. The four-level global model can be written as:

$$\begin{aligned}
\log[P_{ijkl}/(1-P_{ijkl})] = \beta_0 + \beta_1 Age_{ijkl} + \beta_2 Sex_{ijkl} \\
+\beta_3 Wealth_{jkl} \\
+\beta_4 Education_{jkl} \\
+\beta_5 RuralUrban_{jkl} \\
+\beta_6 Year_{jkl} \\
+\beta_7 ImprovedSanitation_{jkl} \\
+\beta_8 ImprovedWaterSources_{jkl} \\
+\beta_9 HasABednet_{jkl} \\
+\beta_{10} DwellingSprayed_{jkl} \\
+\beta_{11} PopulationDensity_{kl} \\
+\beta_{12} Temperature_{kl} \\
+\beta_{13} Precipitation_{kl} \\
+\beta_{14} Elevation_{kl} \\
+\beta_{15} ForestLoss_{kl} \\
+\beta_{16} ForestCover_{kl} \\
+\beta_{17} RainfedCropland_{kl} \\
+\beta_{18} IrrigatedPostFloodingCropland_{kl} \\
+\beta_{19} MosaicCropland_{kl} \\
+\beta_{21} MosaicNaturalVegetaion_{kl} \\
+\beta_{22} PopulationDensity_{kl} \\
+\epsilon_{jkl} + \epsilon_{kl} + \epsilon_{l}
\end{aligned}$$

where

ϵ_{jkl} = household-level random intercept, independent across households, within clusters, within countries

ϵ_{kl} = cluster-level random intercept, independent across clusters, within countries

ϵ_{l} = country-level random intercept, independent across countries

4.3.4 Assumptions

Here I provide an explicit description of assumptions to ensure transparency in our methodological approach. As stated earlier, I assume assume that there may be random variability across households, clusters and countries and therefore added a random effect at each of the four levels. I further assume that that between the 2010–2015 time period, climatic environments do not vary from long-term climate trends already found in a given region.

4.4 Results

4.4.1 Descriptive Analysis and Multicollinearity

Our final data set sourced from the DHS consisted of 24,034 individuals in 14,281 households in 4028 clusters located in 12 countries (see Figure 4.1). Of these individuals, 22.1% were tested positive for malaria using either a blood smear test (BST) or rapid diagnostic test (RDT) (Table 1). Data were collected between the years of 2010 until 2015, with 12.42% samples collected in 2010, 11.53% in 2011, 24.89% in 2012, 7.42% in 2013, 9.08% in 2014 and 34.42% in 2015.

Countries included Angola (5.66%), Burkina Faso (5.24%), Benin (5.07%), Burundi (8.43%), Cote D'Ivoire (4.34%), Ghana (2.57%), Guinea (2.32%), Mali (5.68%), Mozambique (7.88%), Nigeria (13.93%), Senegal (25.11%) and Tanzania (13.75%). No variables within this dataset had a Variance Inflation Factor (VIF) greater than two and therefore all variables were included for analysis (see Table 4.1). A correlation matrix of all variables can also be found in Appendix A.17). Further descriptive statistics stratified by urban and rural clusters can be found in Appendix A.18

Table 4.1: Descriptive statistics

	Malaria (-ve)	Malaria (+ve)
Total Sample	18712 (77.86%)	5322 (22.14%)
Age (VIF = 1.03)		
Mean	2.348	2.520
SD	1.486	1.395
Sex (VIF = 1.00)		
Female	9251 (49.44%)	2743 (51.54%)
Male	9461 (50.66%)	2579 (48.56%)
Country		
Angola	1176 (86.47%)	184 (13.53%)
Burkina Faso	417 (33.10%)	843 (66.90%)
Benin	958 (78.65%)	260 (21.35%)
Burundi	1800 (88.80%)	227 (11.20%)
Cote D'Ivoire	637 (61.02%)	407 (38.98%)
Ghana	344 (55.75%)	273 (44.25%)
Guinea	391 (70.07%)	167 (29.92%)
Mali	900 (65.89%)	466 (34.11%)
Mozambique	1261 (66.54%)	634 (33.46%)

Nigeria	1901 (56.76%)	1448 (43.24%)
Senegal	5906 (97.86%)	129 (2.14%)
Tanzania	3021 (91.41%)	284 (8.59%)
Mothers Education (VIF = 1.02)		
No Education	18514 (98.94%)	5283 (99.27%)
Primary	196 (1.05%)	38 (0.71%)
Secondary and Higher	2 (0.01%)	1 (0.02%)
Household has a bed-net for sleeping (VIF = 1.04)		
Yes	14497 (77.47%)	3913 (73.52%)
No	4215 (22.52%)	1409 (26.48%)
Dwelling sprayed against mosquitoes (VIF = 1.02)		
Yes	5034 (26.90%)	288 (5.41%)
No	16980 (90.74%)	1732 (32.54%)
Wealth Index (VIF = 1.45)		
1 = Poorest	3390 (18.12%)	1386 (26.04%)
2 = Poorer	3519 (18.81%)	1309 (24.60%)
3 = Middle	3739 (19.98%)	1244 (23.37%)
4 = Richer	4097 (21.90%)	903 (16.97%)
5 = Richest	3967 (21.20%)	480 (9.02%)
Water Source (VIF = 1.91)		
Improved	9359 (50.02%)	1063 (19.97%)
Unimproved	9353 (49.98%)	4259 (80.03%)
Year (VIF = 1.11)		
2010	1578 (8.43%)	1407 (26.44%)
2011	2087 (11.15%)	683 (12.83%)
2012	4641 (24.80%)	1340 (25.18%)
2013	1549 (8.28%)	215 (4.04%)
2014	1966 (10.51%)	296 (5.56%)
2015	6891 (36.83%)	1381 (25.95%)
Sanitation (VIF = 1.79)		
Improved	11355 (60.68%)	2417 (45.42%)
Unimproved	7357 (39.31%)	2905 (54.58%)
Cluster Type (VIF = 1.44)		
Urban	7500 (40.08%)	1126 (21.16%)
Rural	11212 (59.92%)	4196 (78.84%)
Population Density (VIF = 1.41)		

Mean	179.11	103.79
SD	5.47	3.83
Rainfed Cropland (%) (VIF = 1.11)		
Mean	26.285	35.172
SD	27.838	30.525
Irrigated/Post-Flooding Cropland (%) (VIF = 1.09)		
Mean	2.529	2.769
SD	9.375	11.457
Mosaic cropland (%) (VIF = 1.14)		
Mean	5.963	7.306
SD	9.218	9.192
Mosaic natural vegetation (%) (VIF = 1.22)		
Mean	3.568	5.932
SD	6.516	9.491
Forest Loss (VIF = 1.15)		
Mean	0.147	0.179
SD	0.356	0.434
Forest Cover (%) (VIF = 1.35)		
Mean	12.84	16.41
SD	13.47	16.25
Mean Temperature (°C) (VIF = 1.48)		
Mean	24.926	25.330
SD	3.467	2.589
Precipitation (mm) (VIF = 1.13)		
Mean	77.566	86.092
SD	91.771	98.477
Elevation (m) (VIF = 1.59)		
Mean	453.03	391.87
SD	593.96	367.22

4.4.2 Sub-Saharan Africa Analysis

At the regional level, a non-linear “U-Shaped” relationship was found across land use classes and childhood malaria, reflecting the transitions from forest cover (highest risk)

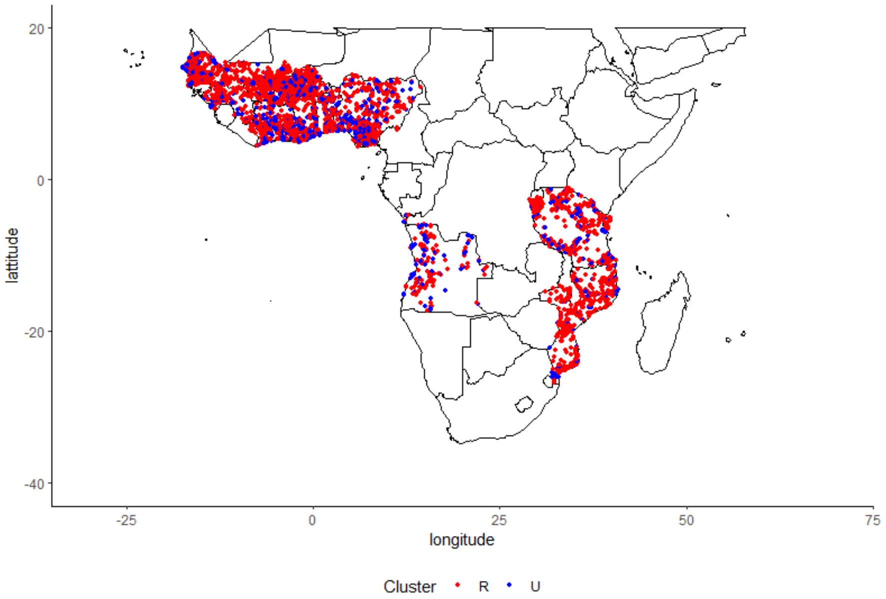


Figure 4.1: Location of household clusters

The georeferenced dataset includes 24,034 children in 14,281 households in 4028 clusters located in 12 countries between 2010 and 2015. The dataset links geo-referenced Demographic and Health Surveys (DHS) individual and household information with data on agricultural land uses, forest cover change and climate. "R" denotes rural clusters and "U" denotes urban clusters.

to mosaics (lower risk) and intensive agriculture (intermediate risk) (see Figure 4.2). Here, the greatest risk was observed for exposure to complete forest cover, which increased the probability of childhood malaria risk by 34% (OR 1.34, CI 1.23 – 1.46). This risk diminishes when mosaics include cropland but remain dominated by natural vegetation (veg-dominated mosaics; OR 1.04, CI 0.99 – 1.10). Risk reduced further in mosaics that are dominated by crops but also include natural vegetation, and this represents the only land use class that potentially neutralises or even reduces the risk of childhood malaria (OR 0.97, 0.91 – 1.02) overall. Exposure to intensive agricultural land-classes sees this risk increase once again; exposure to irrigated or post-flooding cropland resulted in a 5% increase in malaria risk (OR 1.05, CI 1.00 – 1.10), while exposure to rainfed cropland was associated with a larger overall 19% increase in the probability of childhood malaria risk (OR 1.19, CI 1.10 – 1.28).

When controlling for environmental confounders, no associations were found between malaria infection and forest loss (OR 0.98, CI 0.96 – 1.01), mean temperature (OR 1.00, CI 1.00 – 1.01), precipitation (OR 1.00, CI 1.00 – 1.00), or elevation (OR 0.97, CI 0.84 – 1.13) (see Figure 4.2).

With respect to potential socio-economic and other confounders, unimproved water sources and unimproved sanitation resulted in a 31% (OR 1.31, CI 1.10 – 1.56) and 15% (OR 1.15, CI 0.99 – 1.34) increase in the probability of childhood malaria when compared to improved water sources or sanitation, respectively. A child's age (OR 1.28, CI 1.24 – 1.32) was positively associated with a higher probability of malaria. Higher maternal education levels were correlated with lower levels of malaria infection (OR 0.42, CI 0.27 – 0.66). Increased population density reduced the risk of childhood malaria (OR 0.77, CI 0.73 – 0.82). Higher wealth was found to reduce the probability of childhood malaria (OR 0.69, CI 0.66 – 0.73), while spraying the dwelling with insecticide was marginally negatively associated with the probability of childhood malaria risk (OR 0.91, CI 0.73 – 1.13). No association was found between childhood malaria risk and a child's sex (OR 1.00, OR 0.91 – 1.09) or for bed-net ownership (OR 1.02, CI 0.90 – 1.14) (Figure 2). Finally, there was a temporal trend showing that childhood malaria decreased between 2010 and 2015 (OR 0.95, CI 0.91 – 0.99) (See Figure 4.2). Full details of these results are summarised in Supplementary Information Table A.13.

4.4.3 Analysis of Urban and Rural Households

The overall effects of differing agricultural land uses did in some cases vary considerably between rural and urban clusters, as shown by the subgroup analysis (see Figure 4.3). Specifically, a positive association was found for rainfed cropland in rural clusters (OR 1.19,

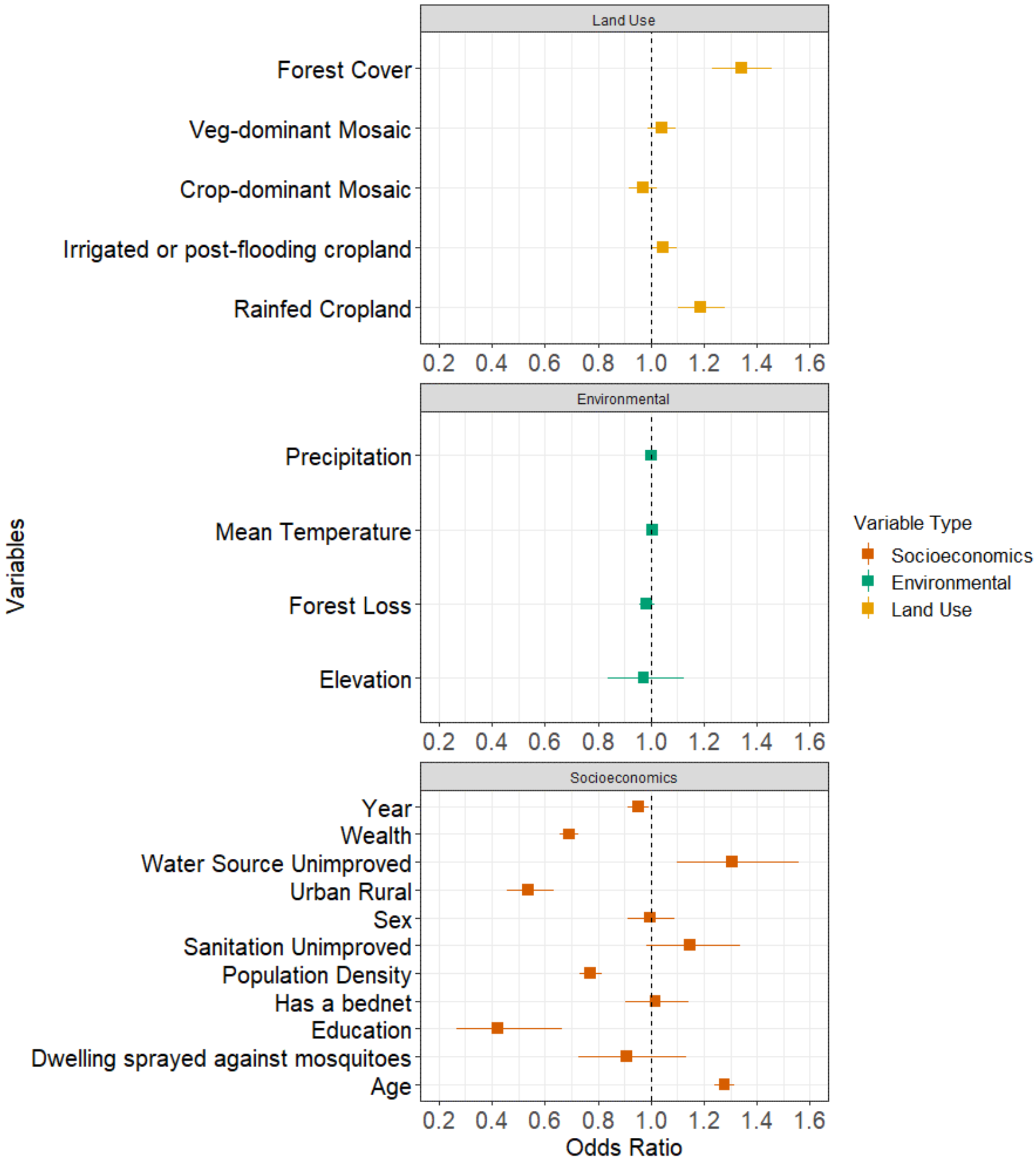


Figure 4.2: Sub-Saharan regional analysis

Factors associated with the probability of childhood malaria. Error bars are defined as the 95% confidence interval. Variables increasing the probability of childhood malaria have odds ratios greater than 1 to the right of the vertical line. Crop-dominated mosaic denotes mosaic cropland and veg-dominated mosaic denotes mosaic natural vegetation within the European Space Agency (ESA) Climate Change Initiative Land Cover (CCI-LC) dataset.

CI 1.09 – 1.31), but not in urban areas (OR 0.99, CI 0.97 – 1.02). On the other hand, irrigation or post-flooding cropland was marginally associated with childhood malaria risk in urban clusters (OR 1.05, CI 0.99 – 1.12), but not in rural areas (OR 1.02, CI 0.98 – 1.06). In rural clusters, crop-dominant mosaics (OR 0.94, CI 0.90 – 1.00) and veg-dominant mosaics (OR 1.04, CI 1.00 – 1.08) were negatively and positively associated with childhood malaria, respectively. However, no effect was found for either mosaic classes in urban clusters.

The overall effect of forest cover was emphasised in urban vs rural clusters (urban: OR 1.55, CI 1.34 – 1.79; rural: OR 1.24, CI 1.11 – 1.38) (see Figure 4.3); however, no association was found between exposure to forest loss and childhood malaria risk across urban or rural clusters. When assessing climatic factors, a marginal negative association was found for elevation in rural clusters (OR 0.87, CI 0.72 – 1.06) yet confidence intervals cross the line of no association.

The association between childhood malaria and water, sanitation, and hygiene (WaSH) related socio-economic variables varied across rural and urban households (see Figure 4.3). Unimproved sanitation in urban households was associated with a higher probability of childhood malaria (OR 1.63, CI 1.17 – 2.26) compared to improved sanitation, whilst no association was found for unimproved sanitation in rural areas (OR 1.04, CI 0.87 – 1.24). On the other hand, unimproved water sources in rural areas had a higher probability of childhood malaria risk compared to improved water sources (OR 1.37, CI 1.10 – 1.71), where no association was found in urban areas (OR 0.99, CI 0.72 – 1.38).

A consistent pattern was found for maternal education (urban OR 0.28, CI 0.11 – 0.69; rural OR 0.49, CI 0.29 – 0.83), wealth (urban OR 0.54, CI 0.49 – 0.61; rural OR 0.76, CI 0.72 – 0.81) and population density (urban OR 0.78, CI 0.72 – 0.85; rural OR 0.81, CI 0.75 – 0.88), all of which reduced the risk of childhood malaria in both rural and urban clusters (although the largest protective effect sizes were observed in urban clusters) (see Figure 4.3). On the other hand, we found that between 2010 and 2015 (equivalent to year of survey), childhood malaria decreased more for urban clusters (OR 0.76, CI 0.66 – 0.89) but not for rural clusters (OR 1.01, CI 0.95 - 1.06) (see Figure 4.3). We also found consistent and expected positive associations between a child's age and childhood malaria in both rural (OR 1.28, CI 1.24 – 1.33) and urban clusters (OR 1.26, CI 1.19 – 1.34).

Spraying the dwelling with insecticide was marginally negatively associated with the probability of childhood malaria risk in rural clusters (OR 0.83 CI 0.64 – 1.07), however, confidence intervals cross the line of no association. On the other hand, spraying the dwelling with insecticide in urban clusters, a child's sex, or bed-net ownership (in either cluster type) was not associated with childhood malaria (see Figure 4.3). Full results are presented in tabular format in Supplementary Information Tables A.14, A.15.

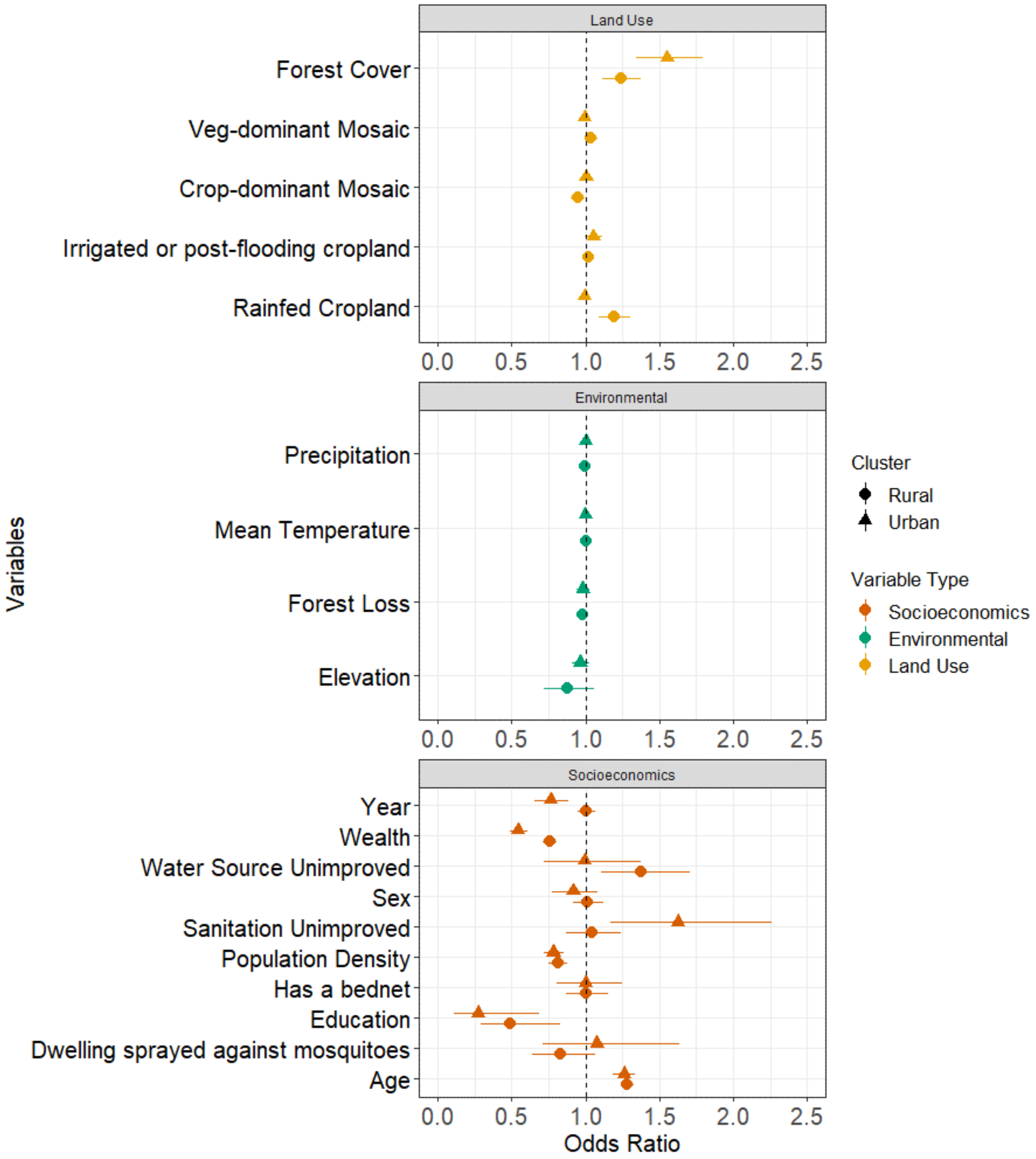


Figure 4.3: Analysis of rural and urban households

Factors associated with the probability of childhood malaria differ between rural and urban households. Error bars are defined as the 95% confidence interval. Variables increasing the probability of childhood malaria have odds ratios greater than 1 to the right of the vertical line. Crop-dominated mosaic denotes mosaic cropland and veg-dominated mosaic denotes mosaic natural vegetation within the European Space Agency (ESA) Climate Change Initiative Land Cover (CCI-LC) dataset.

4.4.4 Marginal Effects

For continuous predictors, the probability of childhood malaria at the sub-Saharan regional level was predicted to steadily increase with increasing rainfed and irrigated or post-flooding cropland (see Figure 4.4). Increasing crop-dominated mosaics steadily decreased childhood malaria risk, whereas increasing veg-dominated mosaics steadily increased childhood malaria risk. A rapid increase in childhood malaria risk was also predicted with increasing forest cover (note, however that this does not reflect reforestation but rather the static extent of forest cover in the dataset). However, as population density increased, we predicted a sharp decline in the probability of childhood malaria. When assessing increasing forest loss, the probability of childhood malaria at the regional level was predicted to decrease with increasing forest loss (see Figure 4.4).

When stratifying by cluster type, similar increases were found in childhood malaria risk when increasing irrigated or post-flooding cropland and mean temperature in both rural and urban clusters (see Figure 4.4). On the other hand, increasing rainfed cropland in rural clusters resulted in an increased childhood malaria risk, however, no effect was found in urban clusters. Increasing crop-dominated mosaics in rural clusters led to consistent decline in the probability of malaria whereas increasing veg-dominated mosaics in rural clusters steadily increased childhood malaria risk. No trend was found for either mosaic classes in urban clusters (see Figure 4.4). Increasing forest cover in either rural or urban clusters resulted in substantially increased probability of childhood malaria. Similar impacts were also found when increasing population density or forest loss in rural or urban clusters, which resulted in a decreased childhood malarial risk. Increasing precipitation in rural areas decreased the risk of childhood malaria; however, an inverse relationship was found for urban areas (see Figure 4.4). Marginal effects for socio-economic interventions were consistent and expected at the overall level and across rural and urban clusters (see Figure 4.5).

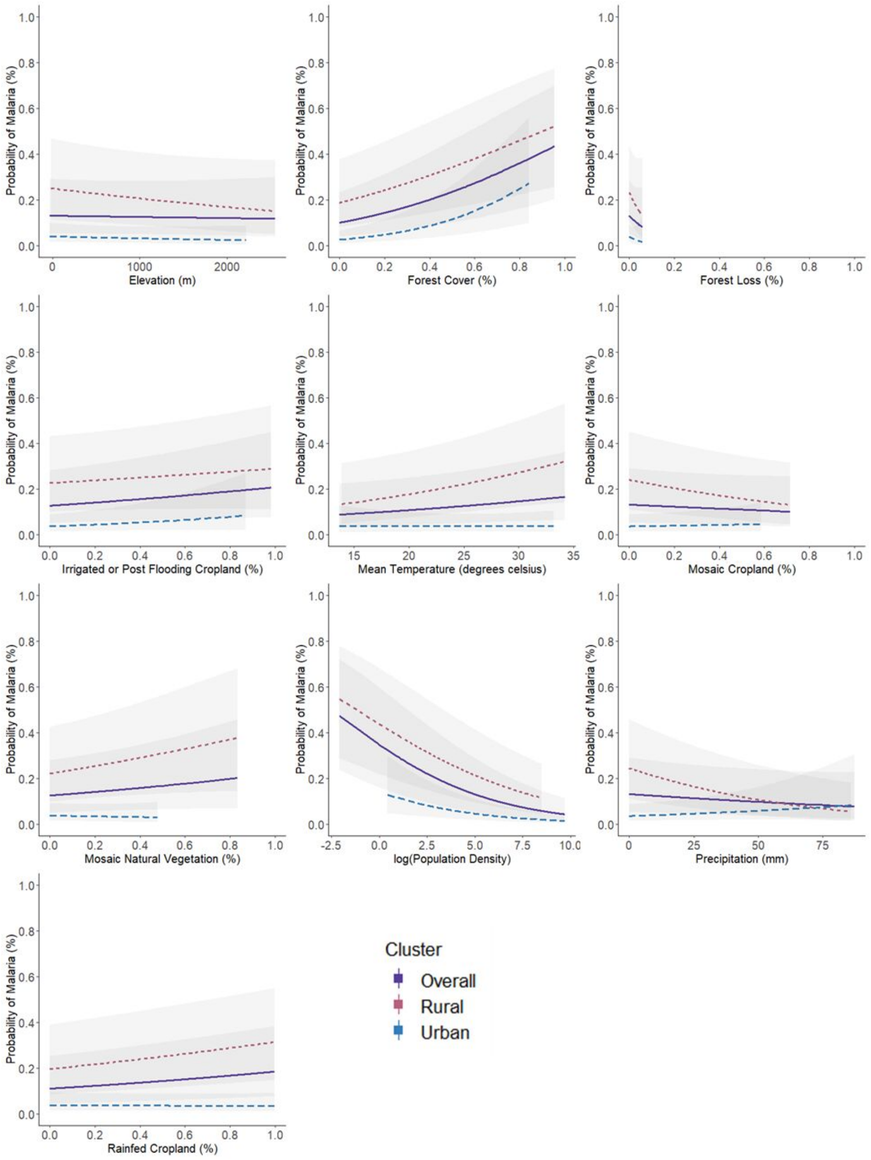


Figure 4.4: Marginal effects for continuous predictors

Marginal effects curves for continuous predictors included within the global model. The global model consists of all variables within the georeferenced dataset and represents the most complex model. Marginal effects measure the instantaneous effect that a change in a particular explanatory variable has on the predicted probability of malaria, when the other covariates are kept fixed.

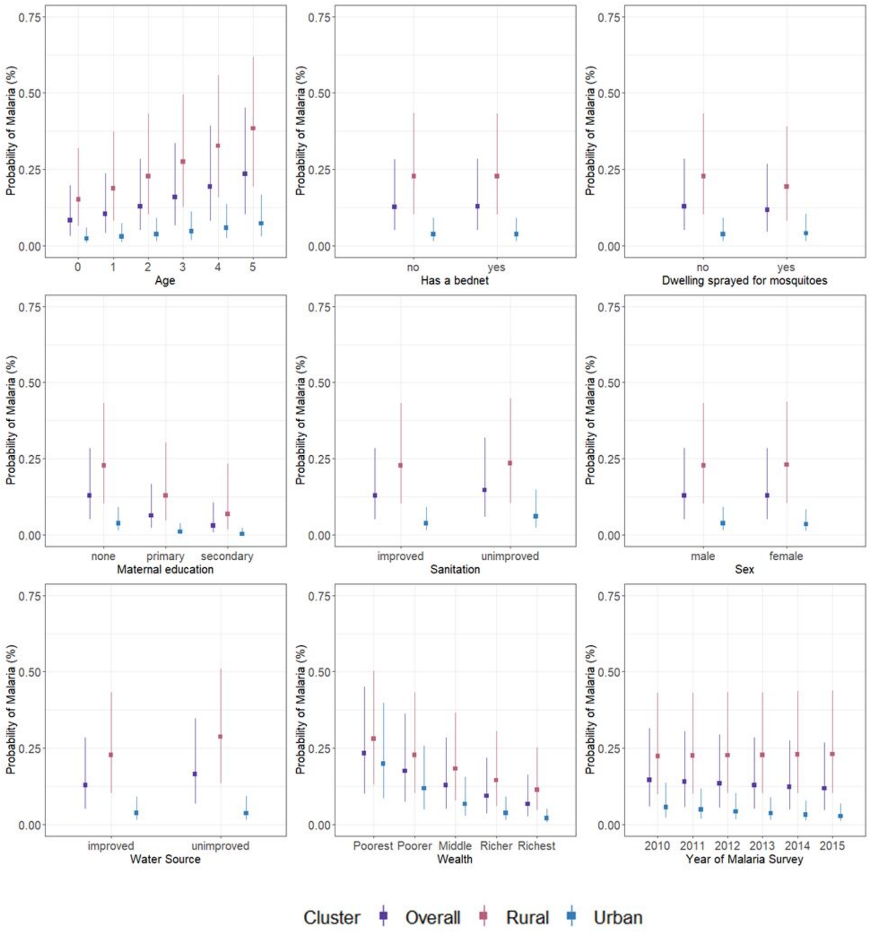


Figure 4.5: Marginal effects for discrete predictors

Marginal effects curves for discrete predictors included within the global model. The global model consists of all variables within the georeferenced dataset and represents the most complex model. Marginal effects measure the instantaneous effect that a change in a particular explanatory variable has on the predicted probability of malaria, when the other covariates are kept fixed.

4.5 Discussion

4.5.1 Overview

Land use change can involve many different transitions such as pre-settlement natural vegetation (highest risk) to frontier clearing, subsistence agriculture and small-scale farms (lower risk), and finally to intensive agriculture (intermediate risk) and urban areas. Here, the greatest risk was observed for exposure to complete forest cover (34%). However, this risk diminished when mosaics include cropland but remain dominated by vegetation (4%). The risk of childhood malaria was further refused or potentially neutralised in mosaics that are dominated by crops but also included some natural vegetation. Childhood malaria risk again increased for intensive agricultural land uses such as rainfed cropland (19%) or irrigated or post-flooding cropland (5%).

4.5.2 Mechanisms

Rainfed cropland is the most common agricultural method used by marginal or smallholder subsistence farmers across sub-Saharan Africa. With the sub-Saharan African population projected to further increase between 2050 and 2100 by a factor of 1.9, there is likely to be a vast expansion of rainfed cropland across the region [416, 417]. Here I find these activities are associated with the highest malaria risk generally outside forested areas, as well as primarily within rural clusters after controlling for other factors [417]. These results align with existing research that suggests, for example, that agriculture in the Democratic Republic of Congo is associated with an increased risk of childhood malaria risk in rural areas [89]. Mechanisms by which rainfed cropland could influence malaria transmission may include slash and burn practices for shifting agriculture, where an area of ground is cleared of vegetation and cultivated for a few years and then abandoned for a new area until its fertility has been naturally restored [418]. This process could influence malaria transmission through changing habitat suitability of mosquito vectors through increasing sunlight, standing water and high temperatures, which favour some types of malaria transmitting mosquitoes. In addition, rainfed landscapes may also have fewer insectivores, greater competition among remaining species for ecological niches and fewer dead-end hosts to dilute malaria ([371, 419].

Irrigated cropland, on the other hand, only accounts for approximately 6% of all agriculture across sub-Saharan Africa [366]. I found that irrigation or post-flooding cropland significantly increased the risk of childhood malaria across sub-Saharan Africa, and especially within urban clusters, albeit this increase is less than in rainfed systems. Previous research has generally been inconclusive, with some studies suggesting that irrigation can increase malaria transmission and other studies suggesting that crop irrigation has little impact on malaria transmission and is dependent on endemic or non-endemic setting status [288, 420]. Heterogeneity in effects is potentially explained by a number of factors which can be heterogenous on geography (e.g. urban, rural, highlands, desert fringes) such as improvements in wealth, housing, access to care, the widespread use of bed-nets and the antimalarials in villages [288, 363, 392, 421]. However, this analysis provides evidence when accounting for numerous environmental and socio-economic factors that irrigation could confer a somewhat reduced risk when compared to rainfed cropland in rural areas.

Mosaic landscapes, which consist of varying mixes and degrees of cropland or natural vegetation, may occur due to frontier clearing for agricultural, subsistence or smallholder farming, or associated with restoration efforts in previously degraded agricultural areas (e.g., agroforestry). My results show that in rural areas, veg-dominated mosaic systems increased the risk of childhood malaria. However, crop-dominated mosaics interspersed with natural vegetation had a neutralising or protective effect against childhood malaria risk. These results suggest a fine balance in mechanisms that may either increase or decrease disease risk in complex landscapes, depending on majority land-cover classes and their associated factors.

Identifying potential explanations for this intriguing result is a challenge given current knowledge on disease ecology in more complex, potentially fragmented but otherwise more biodiverse landscapes (i.e., compared to crop monocultures). Previous research suggests that species diversity within mosaic systems can act differently on competing drivers of disease transmission (host density, vector biting rates, vector habitat suitability and transmissibility) and may cause simultaneous increases (amplification) and decreases (dilution) in malaria transmission [106, 287, 422]. For example, increasing vegetation can lead to increases in humidity which favours mosquito survival and increases biting rates [423]. Specific crops may be linked to increased (e.g. sweet potatoes or yams) or decreased (e.g. millet) malaria transmission due to respective water requirements thereby impacting mosquito habitat suitability [424]. Subsistence or small-holder farming can also include the use of livestock which are known to be a zoo-prophylaxis for malaria [425]. More broadly, loss of dilution of disease transmission (which is itself related to higher biodiversity) may be broadly underpinned by biodiversity loss. These results are consistent with a growing body of literature suggesting that the role of biodiversity in regulating ecosystem processes depends on characteristics of species or individuals present in those ecosystems [426].

Forest conservation has often been suggested as a potential anti-malarial intervention. However, results from this study suggest that increasing forest cover (natural vegetation) substantially increases childhood malaria risk in both rural and urban clusters across the region. Our results also showed no association between forest loss and childhood malaria risk, which is in line with previous research [371]. Mechanisms by which forest cover may impact malaria transmission include changing habitat suitability due to clearing of forest frontiers in rural areas [419]. In urban areas, malaria is often linked to poor housing located at the periphery of cities and thus closer to forests [427]. Given the strong association between forest cover and childhood malaria risk, it would be more effective to prioritize proven anti-malarial interventions such as improvements in education and wealth, insecticide treated nets, spraying of dwellings, and housing improvements. Forest conservation efforts in Africa should instead focus on securing known and proven benefits such as carbon storage, clean water provision, biodiversity, food provision, and other aspects of human health (e.g. diarrheal disease) [90, 198, 371]. Nevertheless, given the heterogeneity we observed within mosaic systems, further research is required to assess whether such effects are true or spurious and further disentangle how ecological drivers of malaria transmission mechanistically relate to changes in disease risk across landscape types in agricultural systems.

4.5.3 Environmental and Socio-economic Confounding

The agricultural-malaria relationship can be influenced by many differing environmental and socio-economic factors [270]. Results suggest consistent and expected confounding effects at the general level and across rural and urban clusters. For example, no association was found between environmental confounders such as mean temperature, precipitation or elevation at the general level or across a rural urban stratification, which is consistent with previous research [371, 374, 400, 428, 429]. Socioeconomic confounding effects were also generally consistent with previous research, which has consistently shown that improvements in maternal education [430, 431, 432], wealth [391, 433], sanitation and water sources [393, 414] alongside increasing urbanisation or population density [434] all had protective effects. Increases in child age increased malaria risk whereas child sex had no association with malaria risk, results which follow previous research [19, 435, 436].

Results also suggest that spraying dwellings for mosquitoes decreased childhood malaria risk in rural areas; however, no association was found between bed-net ownership and malaria compared to no bed-net ownership. It is important to acknowledge that I assess the impact of bed-net “ownership” as opposed to “use” or “adherence” [437]. Previous research has shown that improving maternal education and wealth can improve adherence of malarial interventions such as bed-net usage [391, 430, 431, 432, 433]. Hence, our results do not suggest that bed-nets have no impact on childhood malaria risk, however, malaria policy should continue focussing on advocating for high adherence to malarial interventions such as spraying dwellings and bed-nets [373].

4.5.4 Policy Implications: Agricultural Sustainability and Health

Given the increase in demand for agricultural commodities within the region and the potential for malaria eradication, it is now essential to acknowledge and better assess the impact that differing agricultural land use methods have on childhood malaria [138, 438]. Rainfed cropland is often seen as a more sustainable method compared to irrigated agriculture as a result of its environmental friendliness and sustainability over long periods of time. However, rainfed cropland generally results in lower crop yield levels, increased water losses [5, 439] and, based on our analysis, increased childhood malaria risk. On the other hand, irrigated cropland which has known barriers to implementation (e.g. agronomic, hydrologic and economic) and is often seen as environmentally unsustainable can lead to improved yields, food security, water and sanitation infrastructure, environmental resilience and an increase in wealth and livelihoods thereby meeting many of the SDGs [440, 441]. Although, this analysis suggests irrigation increases the risk of childhood malaria and is known to increase the risk of other parasitic or vector-borne diseases such as schistosomiasis, irrigation could confer a somewhat reduced risk of malaria when compared to rainfed cropland especially in rural areas [110, 112, 442]. Careful consideration of both the pros and cons of irrigation is plainly critical for the sustainability of future agricultural development projects.

Environmental interventions that can be employed in rural areas also offer increased potential to reduce the risk of childhood malaria that is associated with agricultural land uses, thereby improving agricultural sustainability. By acting on elements of mosquito vector ecology or disease transmission processes, interventions such as creating mosaics of natural vegetation within intensive cropland systems may reduce or neutralise malaria risk compared to more intensive agriculture, particularly in rural settings, and hold promise for decision makers that need to balance the future sustainability of agriculture and health. Other environmental interventions can also include drainage of canals that are used for irrigation, site clearing, canal lining, water level or vegetation management or improvements in housing, sanitation or water sources have historically been shown to be effective at reducing malaria across sub-Saharan Africa [443, 444]. Wider deployment of these measures requires more empirical evidence on the cost-effectiveness of environment interventions in rural and urban areas to assess whether an overall net benefit is found.

4.5.5 Limitations

There are several limitations to this study. Firstly, this analysis is a cross-sectional analysis that is limited to the countries that have been included in recent DHS surveys between 2010 and 2015 that had no missing data on the variables incorporated within our analysis. Hence, I could not assess the temporal association between land use change and malaria incidence within countries. Future research must be focused on establishing whether such associations are consistent across time and whether health impacts accrue over time.

Although I aim to control for a large number of potential confounders due to socio-economic and environmental factors, this analysis is still correlational in its approach and should be interpreted as such, preventing us from firmly implying causal relationships [198]. Three particular confounders that were not controlled for was the type of crop, livestock, and humidity. Previous research suggests that mosquitoes readily feed on natural sources of plant sugars, hence crop type could be an important confounder as mosquitoes feeding on peri-domestic plant- and fruit-derived sugar sources can change malaria transmission dynamics [424, 445]. Livestock were not incorporated as a variable considering our analysis focusses on specific agricultural land uses (e.g. rainfed). However, it is important to note that livestock have been shown to be a zoo-prophylaxis for malaria in certain locations and livestock are also important as sources of income and nutrition that improve the well-being of the populations who have access to them [198, 446]. Humidity also could not be explicitly included as a variable due to substantial variability in humidity across a 10km resolution, however, increases in humidity favour mosquito survival and increases biting rates [423]. Finally, we opted to include DHS variables such as improved or unimproved water sources or sanitation, however, inclusion of additional variables such as the amount of freshwater within a cluster can be an alternative analysis considering the life-cycle of a mosquito is water-dependent [383].

Another significant limitation is the spatial resolution within this analysis and its impact on selecting explanatory variables. Deforestation across sub-Saharan Africa is largely due to shifting agriculture by marginal or smallholder farmers who employ agricultural methods on small (e.g., <1km squared) transects of land [388]. As stated in the methods, the displacement of rural clusters up to 10km and urban clusters up to 1km by the DHS is needed for confidentiality reasons. However, this displacement alongside the use of a 10km resolution within this analysis does not adequately capture the association between forest loss and malaria at finer spatial scales and could also artificially amplify the relationship between forest cover and malaria [447].

This analysis is also limited to childhood malaria risk considering the majority of the malaria burden occurs in children across sub-Saharan Africa; however, quantifying the association between agriculture and malaria in agricultural workers in terms of occupational hazards is a priority for sustainable development across Africa. Temperature and precipitation variables control for climatic conditions of survey month based on long-term monthly averages, but this assumption only holds if the 2010–2015 period does not depart from long-term climate in a given region [198].

4.6 Conclusion

Current expansion of intensive agricultural land uses will increase childhood malaria risk across sub-Saharan Africa, which is detrimental to achieving malaria eradication. Decreasing agricultural expansion may not be considered an appropriate blanket policy option due to unintended consequences such as increased poverty, hunger, or decreased wealth. Based on the results from this analysis, environmental interventions such as creating mosaics of natural vegetation within intensive cropland systems may reduce the burden of malaria that is associated with agricultural expansion, and such actions should be considered in tandem with other better studied socio-economic and demographic factors. However, decision makers require further evidence on the optimal design and cost-effectiveness of such environmental interventions in rural and urban systems and how these measures will impact all aspects of sustainability including but not limited to water availability, biodiversity loss, malaria eradication, carbon emissions and soil health.

Chapter 5

Discussion and Conclusion

5.1 Discussion and conclusion

5.1.1 Prior Evidence

Numerous case studies have supported a link between agricultural land-use or land-use change and infectious disease risks [80, 86, 89, 110, 166]. In addition, a number of theoretical modelling studies and meta-analyses suggest potentially generalisable links between land-use or land-use change and biodiversity loss (a key outcome of land-use change, albeit not necessarily specific to agricultural activities), some of which may be linked to increases in disease risk [92, 98, 105, 114]. However, the generality of disease-agriculture relationships had not been systematically assessed prior to the research conducted in this thesis.

Measuring progress toward the UN's Sustainable Development Goals (SDGs) has also been an important international priority since the SDGs were introduced in 2015. For example, the Global Burden of Disease Project published a comprehensive analysis of the progress from 1990 to 2017 in attaining the health-related Sustainable Development Goals for 195 countries and territories in 2017; however, that study did not attribute the disease burden to upstream drivers such as agricultural exposure [29].

In 2016, The World Health Organisation also estimated the burden of disease broadly linked to environmental determinants, where approximately 24% of the disease burden (disability adjusted life years (DALYs)) and an estimated 23% of all deaths (premature mortality) was attributed to environmental factors, such as proximity to agriculture and land use change, water and sanitation, pollution and infectious disease [269]. However, this study also did not explicitly link burdens to agricultural production and trade.

Although some studies have assessed the relationship between deforestation and infectious diseases (e.g. malaria) using multi-country data, these studies draw differing conclusions [84, 198, 370, 371]. No prior research has assessed differing agricultural land uses and infectious disease relationships with multi-country georeferenced data whilst controlling for socio-economic and environmental factors, and none have evaluated differential impacts across varied contexts (e.g. urban vs rural). Hence, when it comes to the impact of research on informing sustainability and agricultural policy, generalisability of agriculture-disease associations whilst controlling for important confounders has been lacking in particular.

5.1.2 Summary of Key Findings

The overall aim of my thesis was to quantify the relationships between agricultural land use and infectious diseases in humans to facilitate new approaches, data and policy suggestions that can enhance agricultural sustainability in meeting multiple health, environment and development-based SDG-related goals and indicators. Through a diversified methodological approach and through controlling for potential socio-economic and environmental confounders, I document across multiple studies that exposure to agriculture consistently increases the risk of infectious diseases in humans. This increased risk also results in a small yet sizeable burden of disease which is directly associated with agricultural land use and the international trade of agricultural commodities.

Using Southeast Asia as an initial model system (Chapter 2), I aimed to quantify the association between occupational or residential exposure to agricultural land uses and being infected with a pathogen. Through a systematic review and meta-analysis following PRISMA reporting procedures, I found that people who live or work in agricultural land in Southeast Asia are on average 1.74 (CI 1.47–2.07) times as likely to be infected with a pathogen than those unexposed. I also found that associations were greatest for exposure to oil palm, rubber, and non-poultry-based livestock farming. When looking at specific diseases I found that significant associations were found between exposure to agriculture and hookworm, malaria, scrub typhus and spotted fever group; however, no association was found for faecal-oral route diseases [270].

I then quantified what impact agricultural land use and trade have on the global burden of infectious diseases (Chapter 3). Through extension of the literature review methodology from Chapter 2 to sub-Saharan Africa and South America, and by combining meta analytic methods, population attributable fractions and input-output analysis, I show that globally, people exposed to agriculture are at more than double (107%) the risk of being infected with any pathogen compared to those unexposed. Furthermore, agriculture was associated with approximately 13.1% (CI 7.9% - 18.4%) of the global burden of communicable diseases. Around one third (34.6%, CI 24.8% - 57.6%)) of this burden is driven by the international trade of agricultural commodities, with demand from high-income countries and regional powerhouses (USA, UK, EU, India, China and Japan) contributing the most to disease risks in primarily developing countries. The highest burden of trade related infectious disease occurs in Sub-Saharan Africa, particularly West Africa.

Consistent positive associations at the global, regional, and country-level alongside positive associations in differing geographies, with multiple exposures and diseases are found with very little evidence of publication bias or general study-level confounding. However, there is also considerable heterogeneity among studies and subgroups within the meta-analyses conducted in Chapters 2 and 3. The agriculture-disease association can also be influenced by multiple confounders or effect modifiers at differing levels (i.e. individual, household, administrative), which could not be controlled for in the review and meta-analysis process. Understanding the complex agriculture-disease relationship whilst controlling for confounders and spatial autocorrelation was a logical step, explored in Chapter 4, in building generalisable evidence to further resolve whether such associations were likely to be robust or spurious.

Through creating a novel dataset that incorporates information on malaria, socioeconomics, agricultural land use, forest cover, forest loss and climatic factors, I aimed to understand what impact exposure to differing agricultural land uses have on the probability of childhood malaria risk across sub-Saharan Africa (Chapter 4). I find that the greatest risk for malaria occurs within land use regimes such as natural vegetation (34% increase in childhood malaria risk), veg-dominated mosaics (4% increase in childhood malaria risk) (which includes both frontier clearing, subsistence or small-holder farming) and full scale intensive agriculture (rainfed (19% increase in childhood malaria risk), irrigated or post-flooding (5% increase in childhood malaria risk)). On the other hand crop-dominated mosaic systems, which can include subsistence or small-holder farming or areas that have been partially restored (e.g., agroforestry projects), may neutralise or protect against childhood malaria, not only when compared to either complete forest cover or complete agricultural crop cover, but also reduce overall risk . These effects vary across rural and urban settings, with overall rainfed cropland effects more pronounced in rural settings whereas irrigated or post flooding cropland effects being more pronounced in urban settings. Hence, on the basis of these results, I predict that expansion of agriculture is likely to lead to continued increases in childhood malaria in sub-Saharan Africa, which will be detrimental to achieving malaria control or eradication and hinder achievement of sustainable development targets. Environmental interventions such as shifting from rainfed to irrigated cropland or creating mosaics of natural vegetation within cropland systems may reduce or neutralise malaria risk compared to more intensive agriculture, particularly in rural settings, and hold promise for decision makers that need to balance the future sustainability of agriculture and health

5.1.3 Implications of findings

Global, regional, national, and subnational data for population health indicators are needed to monitor health and to guide resource allocation. Such indicators are also used by government officials, non-governmental organisations, and funding agencies to make comparisons among populations, to track changes over time, and to monitor progress toward targets such as the Sustainable Development Goals—and to obtain a comprehensive picture of causes of death, burden of disease, or risks to health [29, 448].

The implications of the systematic review and meta-analysis conducted in Chapter 2 include and address the fundamental and novel question of whether exposure to agriculture changes human infectious disease risk using a gold-standard approach for evidence synthesis in the medical sciences. The study therefore has the potential to resonate with a more medically-oriented audience and other global health stakeholders. These results go beyond previous studies, as the first to quantify the risk of occupational or residential exposure to agriculture on infectious disease at a SE Asian regional scale. Additionally, ours is the first study to also quantify the risk of multiple infectious diseases associated with multiple agricultural land use types. Hence, these findings are of global relevance and significance as they have major implications for land use policy and infectious disease research that could help identify co-benefit opportunities for health and the environment across SE Asia. The results should also stimulate further similar studies in other regions to widen the evidence base, and broadly raise interest in the role of, and impacts to, health as it relates to agricultural development globally.

The added value of the macroeconomic assessment conducted in Chapter 3 is that infectious disease has typically been understood as only a domestic problem governed primarily by local factors. The existence of a link between public health and agriculture trade has been a ‘known unknown’. However, the study conducted in Chapter 3 reveals such a link and highlights that foreign demand and the global food trade is a major driver of infectious disease. Further quantification of how food and agriculture production, including the portion driven by foreign demand, contributes to the infectious disease burden in suffering supplier countries is of critical value to global audiences. This study provides readers with evidence on how international macro-economic production and consumption contribute to infectious disease burdens. It also provides several recommendations on how public health, development, economic and environmental practitioners might help mitigate the negative health impacts of agricultural production and trade.

To my knowledge, my highly interdisciplinary study is the first to quantify the human health cost in terms of infectious disease risk of agriculture inter-continentally, taking aim at a global scale. The approach presented here could be further applied in future to estimate a broader range of human health costs from a range of extractive industries (e.g. mining) and the trade of resulting products. Hence, this study can become a benchmark for other researchers to use systems approaches to explore connections between such distal exposures (agriculture and its supply chains) and downstream impacts (human health).

The added value of the hierarchical modelling study conducted in Chapter 4 is that even after controlling for socio-economic and environmental confounders at the individual, household, or cluster level, differing agricultural land uses increase childhood malaria risk across sub-Saharan Africa. Hence, I predict that expansion of agriculture will lead to continued increases in childhood malaria, especially in rural areas. This will be detrimental to achieving malaria eradication and hinder achievement of sustainable development targets.

Considering the robust and consistent agriculture-disease associations found in this body of work, environmental interventions such as shifting from rainfed to irrigated cropland in rural areas or creating mosaics of natural vegetation within cropland systems now hold promise for decision makers that need to balance the future sustainability of agriculture and health. For example, decreasing expansion of agriculture may not be a feasible solution or attractive politically, and may also have other unintended consequences such as increased poverty, hunger, or decreased wealth. However, through improving practices within the agricultural sector such as drainage of canals that are used for irrigation, site clearing, canal lining, water level or vegetation management or improvements in housing, sanitation or water sources may help harness co-benefits across sectors such as improving health, education, wealth and simultaneously reduce biodiversity loss, greenhouse gas emissions and water or air pollution.

5.1.4 Future work

The body of work presented in Chapters 2, 3 and 4 provide significant evidence on the impact that agriculture has on infectious diseases globally and have allowed me to identify and consider future research priorities.

Among the more direct opportunities for future work would be to further extend the systematic literature review and meta-analysis process to include countries in Europe, North America, Central America and the Caribbean, East Asia, and Oceania. This would generate a truly unique global dataset of crude odds ratios as a function of differing agricultural land uses, which could be used to further update the risk of disease linked to agricultural exposure and the burden of disease linked to agricultural land use and trade. The systematic review process could also be extended to include other extractive industries and land use types such as rangeland expansion, urbanisation and infrastructure development (railways, roads or powerlines), hydrological alteration (dams or irrigation) or natural resource extraction (mining, logging or hunting) [50].

Data extracted from the systematic review process can only generate ecological associations whereas there is a clear gap in the evidence regarding the causality of agriculture-disease relationships [353]. One method to address causality would be to conduct large-scale field experiments to address health outcomes, following similar methodologies in ecology that address similarly large-scale and complex phenomena related to land-use change and its impacts on biodiversity (e.g., the ecological impacts of tropical forest modification) [356]. A similar study design extending across multiple countries that also incorporates current best practices in epidemiological studies, such as cluster randomised controlled trials or cohort studies, that aim to quantify the impact of land-use, land-use change and forestry activities on multiple health, environment and development outcomes could provide unique data, better address causality and give greater insights on the sustainability of land use, land use change and forestry activities. In addition, such study designs could also incorporate smaller scale pilot studies which could be used to test the efficacy, effectiveness, and cost-effectiveness of specific environmental or other upstream interventions from a health, environment, and sustainable development perspective. Field based controlled trials can also generate data on epidemiological and ecological patterns that operate over a wide range of spatial scales [356].

This body of work also highlights that differing agricultural land uses have a varied impact on infectious disease risk. For example, rainfed cropland had a higher risk of childhood malaria risk whereas irrigated or post-flooding cropland had less of a risk. Understanding how landscapes can be tailored to maximise yield yet minimise negative externalities is an important avenue of future research, and mosaic systems may hold promise in a similar way that a similar land-sparing vs land-sharing debate has helped inform biodiversity conservation strategies at landscape scales [449]. Here, the use of large-scale field experiments could further explore the optimal landscape configuration that can generate win-wins across multiple environmental and health indices, which could be the subject of future primary research [450].

Although the entirety of this thesis focusses on exposure to agriculture and its association to infectious diseases in humans, such a relationship can be bidirectional. Research on the impacts of infectious diseases on worker health and subsequent agricultural productivity suggests that any source of ill health can significantly impact people's productivity, yields and agricultural output [110, 154, 155, 156]. However, this research is highly localised and based on specific case studies. For example, crop production in Kenya by rural subsistence-farming families dropped 57% after the death of a male head of household [451]. Agricultural workers with lymphatic filariasis, trachoma, schistosomiasis, hookworm or onchocerciasis had substantially lower agricultural productivity or were forced to stop working altogether in certain geographical contexts such as Nigeria or Southern India [154, 402, 452, 453, 454, 455]. Recent research shows that deforestation significantly increased malaria transmission in South America, while a high malaria burden simultaneously reduced forest clearing possibly mediated by human behaviour or economic development [271]. This suggests that there is a clear research gap to quantify the impact that agriculture-induced infectious disease risks can have on global agricultural productivity and yields [110].

Although this body of work assesses the complex spatial associations between childhood malaria risk and differing agricultural land uses, socioeconomic, and environmental factors, I was unable to assess whether such associations were consistent temporally. Specifically, whether increases in agricultural land use over time have increased the risk of infectious disease over time. In addition, previous research suggests that there could be temporal lags between initial land use events and future health impacts. For example, Ebola outbreaks in sub-Saharan Africa located along the limits of the rainforest biome were significantly associated with forest losses within the previous 2 years [85]. Assessing whether such temporal lags exist for other diseases (e.g. malaria or neglected tropical diseases) is an important avenue for future research and could influence decision making where this involves consideration of future health, environmental and economic impacts. Additionally, the majority of my analysis focused on assessing direct associations and main effects between agriculture and infectious disease whilst trying to control for confounders or effect modifiers. Further research should explore the impact of statistical interactions between agriculture, infectious disease and other independent variables such as rural/urban.

Finally, previous research has accounted for the total impact of sustainable diets on the environment [263, 264, 267]. However, the human health impacts induced from agricultural production and consumption have not been quantified. Future research should therefore aim to estimate the total health impact of producing each agricultural commodity (e.g. palm oil, beef, timber). By quantifying the total health impact, further analysis that aims to quantify the cost-benefit of the production of specific agricultural commodities can elucidate the overall net gain or loss in health, environment, and development indicators from its production. Hence, there is an opportunity to conduct future hybrid or social life cycle-analysis which can include health impacts, thereby aiding global behavioural change towards sustainable diets [267, 314].

5.1.5 Global Policy Implications

Even though the SDGs were established in 2015, until now global health governance processes and financing allocations have still largely focused on the MDGs [456]. Government officials, non-governmental organisations, and funding agencies have also not been able to explicitly acknowledge the links between environment and health nexus issues, such as the health impacts of agricultural land use.

While efforts to meet the MDG-related health goals should clearly continue considering the vast improvements in global health (e.g. reductions in maternal and child mortality, improvements in education, improvements in HIV control) that have been made, more serious efforts and focus are now needed to meet the SDGs. This will require broader financing and effective work across several sectors throughout national and global governance [457]. These ambitious global agreements and targets also rely on ensuring we maximise the benefits and minimise the costs of global agricultural production and trade and this can only begin by quantifying the impact extractive industries have on global health.

Based on the links established in this body of work between agriculture and infectious disease, the lowest hanging fruit includes increasing funding and implementation of public health measures in rural areas [458, 459]. Governments must also ensure equitable access to health services [457]. However, access to health services in these agricultural landscapes is often limited due to factors such as shortages of medicines or public health interventions, shortage of health personnel and facilities, poor health workers' attitudes, distance and transportation difficulties, and perceived poor quality of health services [460]. Reducing such barriers to healthcare for agricultural populations can help reduce the risk of agriculture induced infectious diseases.

It has often been suggested that prevention-based interventions are extremely cost-effective from a human health perspective. Key measures from a supply perspective that may mitigate agriculture induced burdens of disease could include Universal Health Coverage (UHC), vaccines and immunisation for all, Water Sanitation and Hygiene (WaSH) interventions, improvements in housing and drainage, improving education in children and educating communities on environmental exposures. Improving the funding streams of such programmes will be essential in meeting sustainable development and health indicators [461]. Such measures also have the possibility of deriving co-benefits where improving maternal education or WaSH interventions can reduce childhood malaria risk (Chapter 4) and also help meet other sustainable development goals [430, 431, 432].

From the demand side, appetite for claiming responsibility or implementing measures may be low amongst high income countries importing disease implicated agricultural commodities considering these countries already fund public health programmes in low- and middle-income countries through international development aid. However, an initial starting point can be the inclusion of agriculture-disease indicators within sustainability certification to effectively incorporate human health into sustainable development and land use policy making [347, 348]. Sustainable diets and inducing consumer behaviour change can also help ensure global awareness of the epidemiological risks associated with agricultural production [252].

Improving global food and agricultural systems is essential to addressing multiple SDGs that include climate change, mitigating biodiversity loss, and meeting both sustainability and human development goals [267]. Research has often highlighted the environmental impact of certain agricultural production and its supply chains (e.g. beef, palm oil and staple crops) on the environmental side; however, little research has quantified the human health impact of global food supply chains or agriculture [138, 265, 267, 462]. Characterizing the links between agriculture and human health is essential to understand the true cumulative impact of agricultural production. Without doing so, society risks unknowingly exceeding regional, or even global, environmental boundaries or missing opportunities to steer food consumption and policy toward more sustainable foods and practices [267].

The final policy recommendation is the construction of governance mechanisms to ensure that these environmental and health impacts due to consumption are mitigated. Such mechanisms will require global co-operation and intersectoral coordination between multilateral agencies such as the WHO, World Bank, World Trade Organisation, Food and Agriculture Organisation and the International Labour Organisation. Specifically, these multilateral organisations should aim to evaluate all evidence and recognise the environmental, social and human health impacts of agricultural production and provide a platform for generating dialogue on sustainable agriculture between member state governments, the private sector, civil society organizations and non-governmental organizations and most importantly, local communities engaged in agriculture.

5.2 Conclusion

This thesis offers a comprehensive evaluation of the relationships between agricultural land use and infectious diseases in humans, with the aim of facilitating improvements in agricultural sustainability. Using a variety of methods, I consistently find associations between differing agricultural land uses and infectious disease risks whilst controlling for multiple confounders. I further highlight the small, yet significant burden of disease linked to agricultural land use and trade. Findings from this thesis will form a base to guide further research questions revolving around how to integrate health metrics into agricultural sustainability and provide a framework to quantify the health impacts of other extractive industries. Finally, the findings from this thesis provide robust evidence on the current impacts that agriculture is having on human health and provides decision makers with new data and evidence to bring environmentally mediated health risks higher up the sustainable development agenda. My hope is that this can aid governments in securing co-benefits and mitigating trade-offs when trying to achieve multiple SDGs simultaneously.

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Appendix A

Appendix

A.1 Southeast Asia Exposure Based Subgroup Analysis

Table A.1: Exposure based subgroup analysis

Exposure Subgroups	Disease Subclass	No of Studies	OR	CI Low	CI High	P Value	E Value	Q Test	P Value	I2
Bovine Exposure	All Diseases	3	2.09	0.80	5.49	0.130	2.96	15.96	<0.001	84.51
Bovine Exposure	Bacterial	2	2.40	0.57	10.12	0.230	3.39	15.39	<0.001	93.50
Bovine Exposure	Vector-Borne	3	2.09	0.80	5.49	0.130	2.96	15.96	<0.001	84.51
Bovine Exposure	Zoonotic	3	2.09	0.80	5.49	0.130	2.96	15.96	<0.001	84.51
Livestock exposure	All Diseases	8	2.54	1.37	4.72	<0.001	3.57	32.25	<0.001	76.02
Livestock exposure	Bacterial	5	4.47	1.30	15.39	0.020	6.05	18.61	<0.001	88.05
Livestock exposure	Vector-Borne	6	2.52	1.48	4.28	<0.001	3.55	14.04	0.020	60.55
Livestock exposure	Viral	3	1.55	0.83	2.91	0.170	2.17	4.98	0.080	58.51
Livestock exposure	Zoonotic	8	2.46	1.35	4.48	<0.001	3.46	33.79	<0.001	77.23
Non-specific Agriculture	All Diseases	21	1.71	1.38	2.13	<0.001	2.42	76.09	<0.001	85.94
Non-specific Agriculture	Bacterial	5	1.79	0.97	3.31	0.060	2.53	27.05	<0.001	89.41
Non-specific Agriculture	Parasitic	16	1.74	1.41	2.13	<0.001	2.45	47.65	<0.001	82.77
Non-specific Agriculture	Vector-Borne	7	1.85	1.18	2.90	0.010	2.61	32.40	<0.001	88.83
Non-specific Agriculture	Zoonotic	15	1.63	1.19	2.24	<0.001	2.30	61.69	<0.001	84.30
Oil Palm Plantation	All Diseases	2	3.25	2.29	4.61	<0.001	4.51	0.16	0.690	0.00
Oil Palm Plantation	Vector-Borne	2	3.25	2.29	4.61	<0.001	4.51	0.16	0.690	0.00
Oil Palm Plantation	Zoonotic	2	3.25	2.29	4.61	<0.001	4.51	0.16	0.690	0.00
Porcine Exposure	All Diseases	7	3.57	0.84	15.23	0.090	4.92	33.97	<0.001	95.59
Porcine Exposure	Bacterial	3	3.08	0.26	35.92	0.370	4.29	8.88	0.010	95.07
Porcine Exposure	Vector-Borne	5	3.09	0.58	16.46	0.190	4.29	23.80	<0.001	94.90
Porcine Exposure	Viral	4	4.31	0.49	37.81	0.190	5.85	24.62	<0.001	96.27
Porcine Exposure	Zoonotic	7	3.57	0.84	15.23	0.090	4.92	33.97	<0.001	95.59
Poultry Exposure	All Diseases	2	0.91	0.24	3.45	0.890	0.00	6.59	0.010	84.83
Poultry Exposure	Vector-Borne	2	0.91	0.24	3.45	0.890	0.00	6.59	0.010	84.83
Poultry Exposure	Zoonotic	2	0.91	0.24	3.45	0.890	0.00	6.59	0.010	84.83
Rice Paddy	All Diseases	5	1.34	0.81	2.23	0.250	1.84	21.78	<0.001	87.15
Rice Paddy	Bacterial	3	1.40	0.71	2.77	0.330	1.93	10.83	<0.001	82.33
Rice Paddy	Vector-Borne	4	1.17	0.62	2.21	0.620	1.54	14.73	<0.001	80.86
Rice Paddy	Zoonotic	4	1.17	0.62	2.21	0.620	1.54	14.73	<0.001	80.86
Rubber Plantation	All Diseases	5	2.27	1.82	2.82	<0.001	3.20	1.33	0.860	0.00
Rubber Plantation	Bacterial	2	2.27	1.79	2.89	<0.001	3.21	0.04	0.830	0.00
Rubber Plantation	Parasitic	3	2.24	1.35	3.74	<0.001	3.17	1.28	0.530	0.00
Rubber Plantation	Vector-Borne	5	2.27	1.82	2.82	<0.001	3.20	1.33	0.860	0.00
Rubber Plantation	Zoonotic	3	2.31	1.83	2.94	<0.001	3.27	0.99	0.610	0.00

A.2 Southeast Asia Exposure Based Subgroup Publication Bias Test Results

Table A.2: Exposure based subgroup publication bias test results

Exposure Subgroups	Disease Subclass	No of Studies	Trim Fill OR	Trim Fill P Value	Trim Fill CI Low	Trim Fill CI High	Eggers T Statistic	P Value
Bovine Exposure	All Diseases	3	2.09	0.134	0.80	5.49	-0.06	0.9645
Bovine Exposure	Vector-Borne	3	2.09	0.134	0.80	5.49	-0.06	0.9645
Bovine Exposure	Zoonotic	3	2.09	0.134	0.80	5.49	-0.06	0.9645
Livestock exposure	All Diseases	8	1.62	0.209	0.76	3.43	1.33	0.2324
Livestock exposure	Bacterial	5	2.31	0.274	0.51	10.39	0.86	0.4518
Livestock exposure	Vector-Borne	6	2.52	0.001	1.48	4.28	0.13	0.9063
Livestock exposure	Viral	3	0.98	0.963	0.49	1.98	3.59	0.1731
Livestock exposure	Zoonotic	8	1.96	0.072	0.94	4.09	1.58	0.1659
Non-specific Agriculture	All Diseases	21	1.48	0.001	1.18	1.86	-0.88	0.3904
Non-specific Agriculture	Bacterial	5	1.79	0.062	0.97	3.31	-0.11	0.9222
Non-specific Agriculture	Parasitic	16	1.62	<0.001	1.32	1.99	-0.85	0.4088
Non-specific Agriculture	Vector-Borne	7	1.85	0.008	1.18	2.90	0.34	0.7471
Non-specific Agriculture	Zoonotic	15	1.37	0.060	0.99	1.92	-0.20	0.8422
Porcine Exposure	All Diseases	7	3.57	0.086	0.84	15.23	4.56	0.0061
Porcine Exposure	Bacterial	3	3.08	0.369	0.26	35.92	2.21	0.2700
Porcine Exposure	Vector-Borne	5	3.09	0.187	0.58	16.46	3.69	0.0346
Porcine Exposure	Viral	4	4.31	0.187	0.49	37.81	4.00	0.0572
Porcine Exposure	Zoonotic	7	3.57	0.086	0.84	15.23	4.56	0.0061
Rice Paddy	All Diseases	5	1.81	0.037	1.04	3.17	-1.58	0.2129
Rice Paddy	Bacterial	3	1.40	0.333	0.71	2.77	-0.14	0.9107
Rice Paddy	Vector-Borne	4	1.40	0.285	0.76	2.57	-0.70	0.5571
Rice Paddy	Zoonotic	4	1.40	0.285	0.76	2.57	-0.70	0.5571
Rubber Plantation	All Diseases	5	2.27	<0.001	1.82	2.82	0.33	0.7632
Rubber Plantation	Parasitic	3	1.84	0.004	1.21	2.78	4.41	0.1420
Rubber Plantation	Vector-Borne	5	2.27	<0.001	1.82	2.82	0.33	0.7632
Rubber Plantation	Zoonotic	3	2.31	<0.001	1.83	2.94	0.62	0.6473

A.3 Southeast Asia Disease Subgroup Analysis

Table A.3: Disease subgroup analysis

Disease	No of Studies	OR	CI Low	CI High	Pvalue	I2	E Value	Trim Fill OR	Trim Fill P Value	Trim Fill CI Low	Trim Fill CI High	Eggers T Statistic	p value
Ascaris lumbricoides	4	1.27	0.59	2.73	0.540	96.52	1.71	1.49	0.344	0.68	3.06	-1.45	0.28
Entamoeba histolytica	3	1.01	0.73	1.4	0.930	0	1.13	1.01	0.945	0.73	1.40	0.01	0.99
Giardia intestinalis	2	0.51	0.17	1.52	0.230	39	0	NA	NA	NA	NA	NA	NA
Hookworm	3	2.42	1.56	3.75	<0.001	91.96	3.41	2.42	<0.001	1.56	3.75	1.20	0.44
Leptospirosis	4	1.36	0.55	3.32	0.500	90.6	1.86	1.71	0.204	0.75	3.93	-0.16	0.88
Malaria	5	2	1.46	2.73	<0.001	46.02	2.83	1.57	0.007	1.13	2.19	1.38	0.26
Opisthorchis viverrini	7	1.51	0.84	2.7	0.170	78.14	2.1	1.20	0.497	0.71	2.04	-0.22	0.83
Orientia tsutsugamushi	5	2.37	1.41	3.96	<0.001	85.83	3.34	2.37	0.001	1.41	3.96	-0.24	0.82
Rickettsia typhi	2	1.12	0.5	2.5	0.780	0	1.42	NA	NA	NA	NA	NA	NA
Schistosoma japonicum	2	1.71	1.18	2.48	<0.001	63.92	2.41	NA	NA	NA	NA	NA	NA
Spotted fever group	2	3.91	2.61	5.85	<0.001	55.23	5.35	NA	NA	NA	NA	NA	NA
Trichuris trichuria	4	1.4	1.27	1.53	<0.001	0	1.93	1.41	<0.001	1.29	1.55	-1.25	0.34

A.4 Information theory approach linking agriculture to disease

References that discuss and potentially support the hypothesis that exposure to agriculture is linked with changes in risk of infectious disease. Only the country level burdens for these diseases were incorporated into our analysis. Burdens for diseases such as HIV or measles that have no biologically plausible link to agricultural exposure were excluded.

1. Diarrheal Diseases - [90, 174, 175, 176, 198, 273, 282, 463, 464]
2. Hepatitis E - [91, 465, 466]
3. Malaria - [86, 89, 138, 161, 184, 224, 239, 259, 288, 289, 290, 371, 443, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480]
4. African Trypanosomiasis - [481]
5. Schistosomiasis - [112, 482, 483, 484, 485]
6. Leishmaniasis - [486, 487, 488]
7. Cysticercosis - [489, 490, 491]
8. Echinococcosis - [492, 493]
9. Dengue - [494, 495, 496, 497]
10. Yellow fever - [411, 498]
11. Ascariasis - [176, 464, 499, 500]
12. Trichuriasis - [175, 270, 464, 499, 500, 501]
13. Hookworm disease - [184, 270, 484, 499, 501, 502]
14. Food-borne trematodes - [185, 503, 504, 505, 506, 507, 508]
15. Lower respiratory infections - [280, 321, 509, 510]
16. Upper respiratory infections -[280, 321, 509, 510]

A.5 Global Geographic Subgroup Analysis Results

Table A.4: Global geographic subgroup analysis results

Geographic Subgroup	Disease Category	No of Studies	OR	CI LOW	CI HIGH	P value	I2	E Value	Q Test	P Value	Trim Fill OR	Trim Fill P Value	Trim Fill CI LOW	Trim Fill CI HIGH
Global	Diarrheal	31	1.630	1.230	2.170	0.000	86.09	2.29	155.56	0.00	1.632	0.001	1.229	2.167
Global	Parasitic & Vector Borne	67	1.980	1.600	2.440	0.000	92.06	2.79	573.8	0.00	1.976	0.000	1.600	2.441
Global	Nematodes	12	1.980	1.170	3.350	0.010	96.56	2.8	154.7	0.00	2.927	0.000	1.713	5.002
Global	All Diseases	81	2.070	1.720	2.500	0.000	90.47	2.93	618.87	0.00	2.072	0.000	1.720	2.496
Americas	Diarrheal	12	1.550	0.880	2.760	0.130	80.78	2.18	56.92	0.00	1.200	0.555	0.655	2.198
Americas	Parasitic & Vector Borne	27	1.990	1.320	2.980	0.000	88.02	2.81	206.09	0.00	1.986	0.001	1.325	2.978
Americas	Nematodes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Americas	All Diseases	35	2.130	1.540	2.950	0.000	82.99	3.01	212.18	0.00	2.133	0.000	1.542	2.950
African	Diarrheal	5	1.390	0.540	3.540	0.490	86.15	1.91	39.18	0.00	1.387	0.493	0.544	3.537
African	Parasitic & Vector Borne	9	2.430	1.130	5.250	0.020	93.31	3.43	152.04	0.00	2.434	0.023	1.129	5.245
African	Nematodes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
African	All Diseases	13	2.680	1.500	4.790	0.000	91.79	3.76	173.02	0.00	2.683	0.001	1.504	4.787
South East Asia	Diarrheal	3	2.200	1.340	3.600	0.000	0	3.1	0.62	0.73	1.839	0.003	1.234	2.740
South East Asia	Parasitic & Vector Borne	10	1.690	1.150	2.480	0.010	76.66	2.38	26.06	0.00	1.364	0.069	0.976	1.907
South East Asia	Nematodes	7	1.530	0.920	2.550	0.100	85.48	2.14	23.92	0.00	1.287	0.283	0.812	2.039
South East Asia	All Diseases	11	1.580	1.110	2.240	0.010	76.69	2.21	30.69	0.00	1.290	0.120	0.936	1.777
Western Pacific	Diarrheal	11	1.680	1.150	2.440	0.010	89.07	2.36	54.36	0.00	1.679	0.007	1.154	2.444
Western Pacific	Parasitic & Vector Borne	21	1.850	1.430	2.400	0.000	90.55	2.62	136.65	0.00	1.852	0.000	1.427	2.405
Western Pacific	Nematodes	4	1.780	1.140	2.790	0.010	88.66	2.52	12.22	0.01	2.240	0.002	1.332	3.767
Western Pacific	All Diseases	22	1.880	1.460	2.410	0.000	89.86	2.52	137.22	0.00	1.878	0.000	1.463	2.410

A.6 Global Agriculture Exposure Subgroup Analysis Results

Table A.5: Global agriculture exposure subgroup analysis results

Geographic Subgroup	Disease Category	No of Studies	OR	CI LOW	CI HIGH	P value	I2	E Value	Q Test	P Value	Trim Fill OR	Trim Fill P Value	Trim Fill CI LOW	Trim Fill CI HIGH
Agriculture	Diarrheal Disease	24	1.650	1.220	2.240	0.000	85.93	2.33	117.75	0.000	1.281	0.144	0.919	1.785
Agriculture	Parasitic & Vector Borne	53	2.250	1.770	2.860	0.000	93.33	3.18	516.85	0.000	2.249	0.000	1.772	2.855
Agriculture	Nematodes	14	2.290	1.390	3.780	0.000	96.16	3.23	161.83	0.000	2.292	0.001	1.390	3.778
Agriculture	All Diseases	62	2.360	1.900	2.930	0.000	92.09	3.33	539.66	0.000	1.649	0.000	1.287	2.111
Hunting	Diarrheal Disease	1	3.340	1.040	10.700	0.040	0	4.62	0	1.000	NA	NA	NA	NA
Hunting	Parasitic & Vector Borne	4	2.710	1.580	4.640	0.000	47.22	3.79	5.55	0.140	1.875	0.036	1.041	3.376
Hunting	Nematodes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Hunting	All Diseases	4	2.710	1.580	4.640	0.000	47.22	3.79	5.55	0.140	1.875	0.036	1.041	3.376
Oil Palm	Diarrheal Disease	2	3.250	2.290	4.610	0.000	0	4.51	0.16	0.690	NA	NA	NA	NA
Oil Palm	Parasitic & Vector Borne	2	3.250	2.290	4.610	0.000	0	4.51	0.16	0.690	NA	NA	NA	NA
Oil Palm	Nematodes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Oil Palm	All Diseases	2	3.250	2.290	4.610	0.000	0	4.51	0.16	0.690	NA	NA	NA	NA
Rice Paddy	Diarrheal Disease	4	1.150	0.650	2.020	0.630	78.47	1.48	13.4	0.000	1.148	0.630	0.654	2.016
Rice Paddy	Parasitic & Vector Borne	6	1.370	0.880	2.130	0.170	77.24	1.88	20.32	0.000	1.534	0.066	0.972	2.419
Rice Paddy	Nematodes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Rice Paddy	All Diseases	6	1.370	0.880	2.130	0.170	77.24	1.88	20.32	0.000	1.534	0.066	0.972	2.419
Rubber	Diarrheal Disease	4	2.270	1.830	2.830	0.000	0	3.21	1.29	0.730	2.238	0.000	1.801	2.781
Rubber	Parasitic & Vector Borne	5	1.880	1.240	2.860	0.000	55.25	2.66	9.2	0.060	1.659	0.008	1.138	2.419
Rubber	Nematodes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Rubber	All Diseases	5	1.880	1.240	2.860	0.000	55.25	2.66	9.2	0.060	1.659	0.008	1.138	2.419

A.7 Global Livestock Exposure Based Subgroup Analysis Results

Table A.6: Global livestock exposure based subgroup analysis results

Geographic Subgroup	Disease Category	No of Studies	OR	CI LOW	CI HIGH	P value	I2	E Value	Q Test	P Value	Trim Fill OR	Trim Fill P Value	Trim Fill CI LOW	Trim Fill CI HIGH
Livestock	Diarrheal Disease	4	1.120	0.300	4.200	0.860	89.92	1.43	21.16	0.000	1.123	0.863	0.300	4.199
Livestock	Parasitic & Vector Borne	8	1.320	0.620	2.810	0.480	81.63	1.79	28.62	0.000	1.124	0.777	0.501	2.520
Livestock	Nematodes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Livestock	All Diseases	10	1.470	0.820	2.630	0.200	76.52	2.04	31.23	0.000	1.172	0.611	0.636	2.163
Bovine	Diarrheal Disease	4	3.270	1.930	5.540	0.000	37.11	4.53	4	0.260	3.267	0.000	1.927	5.539
Bovine	Parasitic & Vector Borne	5	2.400	1.220	4.720	0.010	67.07	3.38	11.6	0.020	2.398	0.011	1.219	4.719
Bovine	Nematodes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bovine	All Diseases	6	2.090	1.150	3.810	0.020	68.14	2.96	16.14	0.010	2.092	0.016	1.147	3.814
Ovine	Diarrheal Disease	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ovine	Parasitic & Vector Borne	2	1.020	0.570	1.840	0.940	0	1.16	0.64	0.420	NA	NA	NA	NA
Ovine	Nematodes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ovine	All Diseases	2	1.020	0.570	1.840	0.940	0	NA	0.64	0.420	NA	NA	NA	NA
Pig	Diarrheal Disease	5	1.030	0.400	2.640	0.960	83.08	1.17	25.3	0.000	0.637	0.341	0.251	1.613
Pig	Parasitic & Vector Borne	7	1.030	0.460	2.350	0.930	80.88	1.21	34.58	0.000	1.035	0.934	0.456	2.347
Pig	Nematodes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Pig	All Diseases	10	1.360	0.670	2.790	0.390	84.41	1.87	48.6	0.000	1.133	0.774	0.484	2.649
Poultry	Diarrheal Disease	3	0.680	0.270	1.720	0.410	79.31	0	8.61	0.010	0.680	0.415	0.268	1.720
Poultry	Parasitic & Vector Borne	5	0.970	0.460	2.050	0.940	77.13	0	18.33	0.000	0.973	0.942	0.461	2.052
Poultry	Nematodes	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Poultry	All Diseases	5	0.970	0.460	2.050	0.940	77.13	0	18.33	0.000	0.973	0.942	0.461	2.052

A.8 Global Disease Based Subgroup Analysis Results

Table A.7: Global disease based subgroup analysis results

Disease	No of Studies	OR	CI LOW	CI HIGH	P value	I2	E Value	Q Test	P Value	Trim Fill OR	Trim Fill P Value	Trim Fill CI LOW	Trim Fill CI HIGH
Ascaris lumbricoides	5	1.470	0.790	2.740	0.220	94.6	2.05	71.69	0.000	1.613	0.131	0.867	3.001
Brucellosis	3	3.780	1.420	10.050	0.010	78.61	5.18	9.78	0.010	3.776	0.008	1.419	10.052
Entamoeba histolytica	3	1.010	0.730	1.400	0.930	0	1.13	0.14	0.930	1.011	0.945	0.731	1.400
Giardia intestinalis	2	0.510	0.170	1.520	0.230	39	0	1.64	0.200	NA	NA	NA	NA
Hantavirus	2	3.180	1.080	9.340	0.040	0	4.41	0	0.990	NA	NA	NA	NA
Hepatitis E	2	1.430	0.660	3.100	0.360	79.51	1.98	4.88	0.030	NA	NA	NA	NA
Hookworm	5	2.340	1.700	3.200	0.000	76.73	3.29	7.95	0.090	2.335	0.000	1.701	3.205
Leishmaniasis	6	3.330	1.180	9.430	0.020	94.28	4.61	53.33	0.000	3.329	0.024	1.175	9.432
Leptospirosis	5	1.420	0.680	2.960	0.350	86.16	1.96	30.22	0.000	1.420	0.349	0.682	2.956
Malaria	10	1.540	0.990	2.380	0.050	87.92	2.15	62.42	0.000	1.538	0.054	0.993	2.380
Mansonella ozzardi	6	4.590	2.570	8.180	0.000	54.77	6.2	11.11	0.050	4.585	0.000	2.571	8.179
Onchocerciasis	2	5.590	4.040	7.740	0.000	0	0	0.33	0.560	NA	NA	NA	NA
Opisthorchis viverrini	7	1.510	0.840	2.700	0.170	78.14	2.1	24.03	0.000	1.201	0.497	0.707	2.040
Orientia tsutsugamushi	5	2.370	1.410	3.960	0.000	85.83	3.34	22.98	0.000	2.366	0.001	1.414	3.960
Paracoccidioidomycosis	2	2.540	1.020	6.300	0.040	0	3.57	0.41	0.520	NA	NA	NA	NA
Rickettsia typhi	2	1.120	0.500	2.500	0.780	0	1.42	0.59	0.440	NA	NA	NA	NA
Schistosomiasis	7	1.960	1.170	3.310	0.010	86.59	2.78	29.11	0.000	1.963	0.011	1.165	3.307
Spotted fever group	2	3.910	2.610	5.850	0.000	55.23	5.35	2.23	0.140	NA	NA	NA	NA
Trichuris trichuria	4	1.400	1.270	1.530	0.000	0	1.93	4.21	0.240	1.410	0.000	1.286	1.546
Toxoplasmosis gondii	2	1.240	0.920	1.680	0.160	0	1.66	0.4	0.530	NA	NA	NA	NA

A.9 Sample Characteristics

Table A.8: Sample characteristics

Author	Year	Country	exposure	Disease	caseexpyes	caseexpno	controlexpyes	controlexpno	log odds ratio	samplin variance	All_Diseases	Other_Diseases	Diarrheal	ParVecBorne	Nematode	patho_region	WHO_region
Abad-Franch	2012	Brazil	Agriculture	Mayaro virus	105	14	137	14	-0.266020576	0.159680222	Yes	Yes	Yes	Yes	No	Neotropical	Americas
Adami	2014	Brazil	Agriculture	Mansonella ozzardi	37	4	115	50	1.391714429	0.305722679	Yes	Yes	No	Yes	No	Neotropical	Americas
Aguiar	2006	Brazil	Bovine Exposure	Leptospirosis	16	7	27	21	0.575364145	0.290013228	Yes	Yes	Yes	Yes	No	Neotropical	Americas
Akogun	1999	Nigeria	Agriculture	Onchocerciasis	402	5	415	22	1.449778109	0.250351746	Yes	Yes	No	Yes	No	African	African
Amoah	2016	Ghana	Agriculture	Hookworm	27	5	265	147	1.097101714	0.247613343	Yes	Yes	Yes	Yes	No	African	African
Arzubiaga	1984	Peru	Agriculture	Leishmaniasis	17	1	8	41	4.467343869	1.208213773	Yes	Yes	No	Yes	No	Neotropical	Americas
Basano	2016	Brazil	Agriculture	Mansonella ozzardi	34	20	15	47	1.672725652	0.167355027	Yes	Yes	No	Yes	No	Neotropical	Americas
Cadavid	1993	Colombia	Agriculture	Paracoccidioidomycosis	20	6	17	10	0.673344553	0.375490196	Yes	Yes	No	No	No	Neotropical	Americas
Cermeno	2004	Venezuela	Agriculture	Histoplasmosis	6	7	14	32	0.672527893	0.412202381	Yes	Yes	No	No	No	Neotropical	Americas
Cermeño	2009	Venezuela	Agriculture	Histoplasmosis	4	17	7	247	2.116559205	0.455729255	Yes	Yes	No	No	No	Neotropical	Americas
Chaiputcha et al	2015	Thailand	Agriculture	Opisthorchis Viverrini	17	56	2	30	1.5159	0.61	Yes	Yes	No	Yes	Yes	Oriental	South East Asia
Chan et al	2008	Malaysia	Agriculture	Toxoplasmosis gondii	127	133	189	250	0.2336	0.0247	Yes	Yes	No	Yes	No	Oriental	Western Pacific
Chudthaisong et al	2015	Thailand	Agriculture	Opisthorchis Viverrini	107	198	10	36	0.6655	0.1422	Yes	Yes	No	Yes	Yes	Oriental	South East Asia
Costa	1991	Brazil	Agriculture	Schistosomiasis	58	18	140	290	1.898309753	0.083388068	Yes	Yes	Yes	Yes	No	Neotropical	Americas
Coura-Filho	1994	Brazil	Agriculture	Schistosomiasis	12	28	12	91	1.178654996	0.213369963	Yes	Yes	Yes	Yes	No	Neotropical	Americas
Cruz	2012	Bolivia	Agriculture	Hantavirus	25	3	142	54	1.153420525	0.398894105	Yes	Yes	Yes	No	No	Neotropical	Americas
Czechowicz	2011	Peru	Agriculture	Cardiovirus A	8	64	14	325	1.065326311	0.215130495	Yes	Yes	No	No	No	Neotropical	Americas
Dao et al	2016	Vietnam	Agriculture	Opisthorchis Viverrini	27	207	2	18	0.1603	0.5974	Yes	Yes	No	Yes	Yes	Oriental	Western Pacific
Diniz	2016	Brazil	Livestock Farming	Bartonella	4	12	69	415	0.695559727	0.350235726	Yes	Yes	No	Yes	No	Neotropical	Americas
Dozie	2007	Nigeria	Agriculture	Onchocerciasis	526	42	602	278	1.754995263	0.030968916	Yes	Yes	No	Yes	No	African	African
Eid	2018	Bolivia	Agriculture	Leishmaniasis	77	42	76	79	0.644850316	0.062612659	Yes	Yes	No	Yes	No	Neotropical	Americas
Erhart et al	2005	Vietnam	Agriculture	Malaria	1245	2176	65	376	0.4216	0.0124	Yes	Yes	Yes	Yes	No	Oriental	Western Pacific
Ferreira	2012	Brazil	Agriculture	Malaria	43	17	91	32	-0.117136832	0.124318354	Yes	Yes	Yes	Yes	No	Neotropical	Americas
Fuhrimann et al	2016	Vietnam	Agriculture	Hookworm	43	15	239	384	1.5273	0.0967	Yes	Yes	Yes	Yes	No	Oriental	Western Pacific
Garcia	1992	Peru	Pig Exposure	Taenia solium	21	3	48	29	1.442004968	0.436268473	Yes	Yes	Yes	Yes	No	Neotropical	Americas
Grigg et al	2017	Malaysia	Agriculture	Malaria	64	89	165	591	0.9461	0.0346	Yes	Yes	Yes	Yes	No	Oriental	Western Pacific
Gurtler	1998	Argentina	Livestock Farming	Chagas disease	4	34	25	32	-1.893206086	0.350661765	Yes	Yes	Yes	Yes	No	Neotropical	Americas
Guthmann	2001	Peru	Agriculture	Malaria	83	240	278	691	-0.151279605	0.02125916	Yes	Yes	No	Yes	No	Neotropical	Americas
Hinjoy et al	2012	Thailand	Pig Exposure	Hepatitis E	39	79	132	263	-0.0165	0.0497	Yes	Yes	No	No	No	Oriental	South East Asia
Huong et al	2015	Vietnam	Agriculture	Streptococcus Suis	47	32	68	115	0.9098	0.0759	Yes	Yes	No	No	No	Oriental	Western Pacific
Junaid	2014	Nigeria	Agriculture	Hepatitis E	73	52	37	57	0.771349078	0.077500286	Yes	Yes	No	No	No	African	African
Kaewpitoon et al	2016	Thailand	Agriculture	Opisthorchis Viverrini	16	0	849	53	0.7315	2.0805	Yes	Yes	No	Yes	Yes	Oriental	South East Asia
Kalu	2012	Nigeria	Agriculture	Malaria	165	38	34	35	1.497346851	0.090359589	Yes	Yes	Yes	Yes	No	African	African
Kawaguchi et al	2008	Lao PDR	Rice Paddy	Leptospirosis	86	11	280	29	-0.211	0.1406	Yes	Yes	Yes	Yes	No	Oriental	Western Pacific
Kenu	2014	Ghana	Agriculture	Buruli Ulcer	70	34	43	93	1.49353409	0.077705981	Yes	Yes	No	No	No	African	African
Kho et al	2017	Malaysia	Livestock Farming	Ricketsia felis	14	0	73	61	3.189	2.0988	Yes	Yes	No	Yes	No	Oriental	Western Pacific
Marques	2008	Brazil	Agriculture	Toxoplasmosis gondii	48	10	13	2	-0.303186259	0.69775641	Yes	Yes	No	Yes	No	Neotropical	Americas
Martin	2010	Brazil	Agriculture	Mansonella ozzardi	28	6	121	39	0.408216141	0.236286441	Yes	Yes	No	Yes	No	Neotropical	Americas
Matthys	2007	Cote d'Ivore	Agriculture	Schistosomiasis	68	8	55	10	0.435318071	0.257887701	Yes	Yes	Yes	Yes	No	African	African
Medeiros	2014	Brazil	Agriculture	Mansonella ozzardi	69	18	186	419	2.155858993	0.077811288	Yes	Yes	No	Yes	No	Neotropical	Americas
Medeiros	2007	Brazil	Agriculture	Mansonella ozzardi	18	4	20	35	2.063693185	0.384126984	Yes	Yes	No	Yes	No	Neotropical	Americas
Medeiros	2011	Brazil	Agriculture	Mansonella ozzardi	72	2	81	6	0.980829253	0.692901235	Yes	Yes	No	Yes	No	Neotropical	Americas
Membrive	2012	Brazil	Pig Exposure	Leishmaniasis	1	13	98	260	-1.589235205	1.090973312	Yes	Yes	No	Yes	No	Neotropical	Americas
Mngumi	2016	Tanzania	Agriculture	Brucellosis	44	10	107	241	2.29357264	0.136222445	Yes	Yes	No	No	No	African	African
Mngumi	2016	Tanzania	Bovine Exposure	Brucellosis	43	11	251	77	0.181657326	0.131135982	Yes	Yes	No	No	No	African	African
Mogaji	2013	Nigeria	Agriculture	Malaria	58	84	69	45	-0.797817803	0.065861117	Yes	Yes	Yes	Yes	No	African	African
Moro	2008	Peru	Ovine Exposure	Echinococcosis	20	14	21	20	0.30788478	0.219047619	Yes	Yes	No	Yes	No	Neotropical	Americas
Moro	1997	Peru	Ovine Exposure	Echinococcosis	74	69	18	14	-0.18135584	0.154990394	Yes	Yes	No	Yes	No	Neotropical	Americas
Ngoc dinh et al	2006	Vietnam	Poultry Exposure	H5N1	18	10	52	54	0.6255	0.1933	Yes	Yes	Yes	Yes	No	Oriental	Western Pacific
Nguyen et al	2006	Vietnam	Agriculture	Ascaris lumbricoides	1400	1938	770	2666	0.9168	0.0029	Yes	Yes	No	Yes	Yes	Oriental	Western Pacific
Nwakor	2008	Nigeria	Rice Paddy	Guinea worm	104	12	1977	289	0.236575114	0.096914742	Yes	Yes	No	Yes	No	African	African
Oliveira	2006	Brazil	Livestock Farming	Leishmaniasis	79	30	74	32	0.12992128	0.090755075	Yes	Yes	No	Yes	No	Neotropical	Americas
Oliviera	2013	Brazil	Agriculture	Schistosomiasis	12	14	316	259	-0.353064832	0.161787466	Yes	Yes	Yes	Yes	No	Neotropical	Americas
Ong et al	2016	Thailand	Agriculture	Opisthorchis Viverrini	0	0	0	0	-0.820980552	0.084252912	Yes	Yes	No	Yes	Yes	Oriental	South East Asia
Parashar et al	2000	Malaysia	Pig Exposure	Nipah Virus	40	8	71	38	0.9843	0.1904	Yes	Yes	No	Yes	No	Oriental	Western Pacific
Pattasin et al	2012	Thailand	Rubber Plantation	Malaria	0	0	0	0	0.832909123	0.168568461	Yes	Yes	Yes	Yes	No	Oriental	South East Asia
Pham Duc et al	2011	Vietnam	Agriculture	Entamoeba histolytica	30	16	93	45	-0.0973	0.1288	Yes	Yes	Yes	Yes	Yes	Oriental	Western Pacific
Pham Duc et al	2013	Vietnam	Agriculture	Trichuris Trichiura	302	271	401	451	0.2258	0.0117	Yes	Yes	No	Yes	No	Oriental	Western Pacific
Ramos	2008	Brazil	Livestock Farming	Brucellosis	18	8	297	312	0.860201265	0.187127687	Yes	Yes	No	No	No	Neotropical	Americas
Rangsin et al	2009	Thailand	Agriculture	Opisthorchis Viverrini	59	105	24	89	0.7342	0.0794	Yes	Yes	No	Yes	Yes	Oriental	South East Asia
Ridzuan et al	2016	Malaysia	Bovine Exposure	Leptospirosis	0	0	0	0	1.615419984	0.07674818	Yes	Yes	Yes	Yes	No	Oriental	Western Pacific
Ron-Roman	2014	Ecuador	Livestock Farming	Brucellosis	63	7	2946	717	0.784096821	0.160464302	Yes	Yes	No	No	No	Neotropical	Americas
Rosas-Aguirre	2015	Peru	Agriculture	Malaria	18	99	14	103	0.290923566	0.146793875	Yes	Yes	Yes	Yes	No	Neotropical	Americas
Ross et al	2016	Philippines	Agriculture	Any Helminth	962	1545	160	507	0.6796	0.0099	Yes	Yes	Yes	Yes	Yes	Oriental	Western Pacific
Rukmanee et al	2008	Thailand	Agriculture	Trichuris Trichiura	157	120	768	908	0.4362	0.0171	Yes	Yes	No	Yes	Yes	Oriental	South East Asia
Satitvipawee et al	2012	Thailand	Rubber Plantation	Malaria	60	10	186	57	0.6091	0.1396	Yes	Yes	Yes	Yes	No	Oriental	South East Asia
Silva	1997	Brazil	Agriculture	Schistosomiasis	25	46	54	169	0.531149097	0.086174809	Yes	Yes	Yes	Yes	No	Neotropical	Americas
Somboon et al	1998	Thailand	Agriculture	Malaria	0	0	0	0	1.172482137	0.389205875	Yes	Yes	Yes	Yes	No	Oriental	South East Asia
Täger Frey	2003	Chile	Agriculture	Hantavirus	4	1	337	270	1.16463339	1.256671063	Yes	Yes	Yes	No	No	Neotropical	Americas
Tan et al	1979	Malaysia	Agriculture	Leptospirosis	30	562	174	3880	0.1742	0.0411	Yes	Yes	Yes	Yes	No	Oriental	Western Pacific
Tarafder et al	2006	Philippines	Agriculture	Schistosomiasis	0	0	0	0	0.277631737	0.052893951	Yes	Yes	Yes	Yes	No	Oriental	Western Pacific
Tay et al	1999	Malaysia	Rubber Plantation	Orientia tsutsugamushi	45	25	150	80	-0.0408	0.0814	Yes	Yes	No	Yes	No	Oriental	Western Pacific
Tay et al	2000	Malaysia	Agriculture	Orientia tsutsugamushi	226	66	399	420	1.2822	0.0245	Yes	Yes	No	Yes	No	Oriental	Western Pacific
Tay et al	2013	Malaysia	Agriculture	Orientia tsutsugamushi	14	36	35	195	0.7732	0.1329	Yes	Yes	No	Yes	No	Oriental	Western Pacific
Thayaparan et al	2015	Malaysia	Agriculture	Leptospirosis	39	32	82	45	-0.4022	0.0913	Yes	Yes	Yes	Yes	No	Oriental	Western Pacific
Tuyizere	2018	Rwanda	Agriculture	Strongyloides Stercoralis	90	4	434	10	-0.656944132	0.363415259	Yes	Yes	Yes	Yes	No	African	African
Udonsi	1992	Nigeria	Agriculture	Hookworm	233	42	192	498	2.66647354	0.035317735	Yes	Yes	No	Yes	Yes	African	African
Vallee et al	2010	Lao PDR	Agriculture	Orientia tsutsugamushi	24	357	23	1567	1.5217	0.0886	Yes	Yes	No	Yes	No	Oriental	Western Pacific
Wattanayingcharoenchai et al	2011	Thailand	Agriculture	Opisthorchis Viverrini	737	103	2617	660	0.5903	0.013	Yes	Yes	No	Yes	Yes	Oriental	South East Asia
Weigle	1993	Colombia	Agriculture	Leishmaniasis	187	40	76	151	2.228775659	0.050128005	Yes	Yes	No	Yes	No	Neotropical	Americas
Yadon	2003	Argentina	Agriculture	Leishmaniasis	63	108	65	243	0.779677673	0.044632117	Yes	Yes	No	Yes	No	Neotropical	Americas

A.10 Country-specific Agricultural Land Use Deaths

See next page.

Table A.9: Country-specific agricultural land use deaths

	All Diseases		Diarrheal Disease		Intestinal Nematodes		Parasitic & Vector-Borne Diseases		Other Diseases	
Country	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Afghanistan	3337	1274	2665	731	13	6	78	31	433	163
Albania	15	6	3	1	0	0	3	1	9	4
Algeria	398	73	167	105	0	0	21	4	89	16
Andorra	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Angola	3436	1274	919	619	6	0	1072	234	244	90
Antigua	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Argentina	211	126	7	3	0	0	25	17	167	105
Armenia	7	3	3	1	0	0	1	1	3	1
Aruba	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Australia	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Austria	16	8	4	1	0	0	0	0	11	6
Azerbaijan	121	53	86	25	0	0	2	1	28	13
Bahamas	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bahrain	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bangladesh	11530	5601	10511	542	30	13	350	148	3515	1554
Barbados	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Belarus	6	3	1	0	0	0	1	1	4	2
Belgium	13	8	4	2	0	0	0	0	9	5
Belize	2	0	1	1	0	0	0	0	0	0

Benin	7937	1041	2483	1231	33	0	3259	436	856	106
Bermuda	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bhutan	68	26	32	9	0	0	2	1	33	13
Bolivia	310	51	224	88	1	0	12	7	29	5
Bosnia and Herzegovina	5	2	1	0	0	0	1	1	3	1
Botswana	203	59	97	53	0	0	8	1	19	5
Brazil	3500	595	450	195	3	1	498	94	2288	389
British Virgin Islands	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Brunei	0	0	0	0	0	0	0	0	0	0
Bulgaria	14	7	2	1	0	0	6	3	6	3
Burkina Faso	27790	672	4397	2183	41	0	14432	1383	2500	58
Burundi	11212	1890	3668	1622	29	0	3746	367	754	138
Cambodia	949	391	518	132	21	10	100	42	391	157
Cameroon	15964	1758	5198	2534	141	2	5386	597	2163	229
Canada	160	34	34	25	0	0	0	0	95	20
Cape Verde	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Cayman Islands	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Central African Republic	6146	1067	1851	869	29	0	2638	283	277	48
Chad	18462	1802	6898	3123	46	0	5299	587	1633	165
Chile	92	59	42	18	0	0	4	3	60	38
China	7810	3418	1809	588	657	305	3535	1570	1312	596
Colombia	840	116	95	39	2	0	68	21	388	52

Congo	2605	639	803	400	5	0	1023	144	181	42
Costa Rica	54	8	11	5	0	0	1	0	14	2
Cote dIvoire	19346	558	5208	2435	140	2	5540	682	2667	78
Croatia	15	7	3	1	0	0	0	0	11	6
Cuba	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Cyprus	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Czech Republic	37	17	10	3	0	0	0	0	27	12
Denmark	15	8	3	1	0	0	0	0	11	6
Djibouti	199	61	86	52	0	0	14	2	20	6
Dominican Republic	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
DR Congo	82578	17635	20552	10083	398	5	39354	4370	5960	1206
Ecuador	255	49	53	20	2	0	25	9	127	24
Egypt	2254	354	856	489	1	0	190	32	565	88
El Salvador	108	17	50	30	0	0	3	1	17	3
Eritrea	2078	428	1005	493	2	0	209	25	193	40
Estonia	1	0	0	0	0	0	0	0	1	0
Ethiopia	47962	8991	21791	9659	115	1	6732	714	3411	698
Fiji	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Finland	6	3	1	0	0	0	0	0	5	3
Former USSR	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
France	287	116	42	20	0	0	2	1	190	79
French Polynesia	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Gabon	341	100	90	56	1	0	140	26	30	9
Gambia	841	46	201	113	1	0	269	43	101	5
Gaza Strip	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Georgia	21	9	4	1	0	0	7	3	10	4
Germany	133	72	51	19	0	0	2	1	75	39
Ghana	13469	468	1991	1067	17	0	6698	895	1403	49
Greece	149	72	4	1	0	0	0	0	142	69
Greenland	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Guatemala	1086	154	489	265	6	0	110	17	186	26
Guinea	15992	415	2686	1173	74	1	7682	837	1847	46
Guyana	39	9	6	3	0	0	5	1	15	3
Haiti	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Honduras	429	58	163	88	1	0	31	5	64	9
Hong Kong	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Hungary	19	10	13	4	0	0	0	0	4	2
Iceland	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
India	148085	63421	130144	12385	117	52	15171	6448	13442	5620
Indonesia	18417	3416	11218	4484	31	15	1746	328	3834	731
Iran	328	159	230	78	0	0	4	2	64	31
Iraq	494	234	375	119	0	0	23	11	63	30
Ireland	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Israel	22	8	2	2	0	0	0	0	17	6

Italy	322	137	39	13	0	0	0	0	263	114
Jamaica	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Japan	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Jordan	9	4	3	2	0	0	0	0	3	1
Kazakhstan	61	28	39	13	0	0	2	1	16	7
Kenya	29518	6302	12996	6096	17	0	5983	673	1510	327
Kuwait	4	2	0	0	0	0	0	0	4	2
Kyrgyzstan	48	20	30	9	0	0	8	4	7	3
Laos	1177	448	689	76	44	18	103	38	346	136
Latvia	2	1	0	0	0	0	0	0	1	1
Lebanon	28	10	9	5	0	0	1	0	10	3
Lesotho	802	187	422	221	1	0	10	1	40	10
Liberia	3220	104	759	407	11	0	1132	157	310	10
Libya	52	8	14	9	0	0	10	2	17	3
Liechtenstein	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Lithuania	13	7	1	0	0	0	2	1	10	5
Luxembourg	0	0	0	0	0	0	0	0	0	0
Macao SAR	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Madagascar	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Malawi	9081	1915	2628	1206	9	0	4275	418	330	64
Malaysia	149	32	41	18	0	0	35	7	67	14
Maldives	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Mali	25910	1311	6119	2782	15	0	12001	1465	1304	63
Malta	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Mauritania	2112	189	719	354	1	0	615	88	253	23
Mauritius	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Mexico	1268	230	495	284	1	0	71	13	395	69
Moldova	7	3	1	0	0	0	2	1	4	2
Monaco	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Mongolia	20	9	15	5	1	0	0	0	2	1
Montenegro	0	0	0	0	0	0	0	0	0	0
Morocco	719	98	340	195	0	0	43	7	125	18
Mozambique	18145	3590	4226	1898	75	1	9416	949	1248	264
Myanmar	3178	1567	2722	455	82	39	170	83	827	405
Namibia	349	93	155	86	0	0	28	4	34	9
Nepal	4983	1777	3780	965	4	1	149	55	872	307
Netherlands	43	23	10	4	0	0	0	0	30	16
Netherlands Antilles	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
New Caledonia	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
New Zealand	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Nicaragua	159	18	49	19	0	0	5	2	14	2
Niger	22630	2490	6354	3048	35	0	10529	1211	2129	235
Nigeria	115769	17257	38546	22748	553	9	42031	6645	10729	1520
North Korea	329	126	195	54	36	15	12	5	54	23

Norway	13	7	3	1	0	0	0	0	10	5
Oman	6	3	1	0	0	0	0	0	4	2
Pakistan	24170	10185	16927	5028	14	6	561	248	5163	2155
Panama	114	15	17	7	0	0	4	1	52	7
Papua New Guinea	1839	272	792	269	9	4	807	122	126	20
Paraguay	53	34	30	12	0	0	16	11	6	4
Peru	388	122	265	101	1	0	49	18	75	23
Philippines	3270	748	1416	331	NA	NA	670	159	1189	267
Poland	73	37	50	17	0	0	1	0	16	8
Portugal	132	26	16	10	0	0	0	0	106	20
Qatar	0	0	0	0	0	0	0	0	0	0
Romania	177	81	33	10	0	0	74	34	63	28
Russia	64	32	22	8	0	0	11	6	30	16
Rwanda	5470	1097	1491	652	8	0	2549	263	372	78
Samoa	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
San Marino	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sao Tome and Principe	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Saudi Arabia	34	17	19	6	0	0	3	1	11	5
Senegal	7045	302	1814	911	6	0	2340	306	848	33
Serbia	48	24	27	9	0	0	2	1	17	8
Seychelles	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sierra Leone	14173	374	2774	1256	65	1	5727	631	2038	53

Singapore	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Slovakia	6	3	1	0	0	0	0	0	5	2
Slovenia	9	4	0	0	0	0	0	0	8	4
Somalia	13630	2718	6011	2713	27	0	1786	186	1287	240
South Africa	2235	819	863	588	0	0	102	22	289	104
South Korea	179	92	30	11	29	15	5	3	86	47
South Sudan	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Spain	278	58	37	25	0	0	0	0	209	43
Sri Lanka	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sudan	8210	1112	2459	1349	21	0	3450	514	773	101
Suriname	2	0	0	0	0	0	0	0	1	0
Swaziland	231	68	112	67	1	0	7	1	18	5
Sweden	30	16	4	2	0	0	0	0	24	13
Switzerland	21	10	7	2	0	0	1	1	12	5
Syria	618	180	204	76	0	0	10	4	92	28
Taiwan	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Tajikistan	447	176	289	80	0	0	17	7	126	50
Tanzania	32620	6698	10959	4947	109	1	11611	1329	2197	432
TFYR Macedonia	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Thailand	1476	368	1407	381	93	44	54	12	512	132
Togo	6982	194	1423	689	19	0	2853	308	822	22
Trinidad and Tobago	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Tunisia	83	15	30	18	0	0	7	1	25	5
Turkey	308	149	105	33	0	0	26	12	179	85
Turkmenistan	117	54	83	30	0	0	0	0	23	11
UAE	4	2	1	0	0	0	0	0	2	1
Uganda	22853	4287	6684	3032	63	1	8644	936	2263	498
UK	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ukraine	106	49	39	13	0	0	9	4	49	25
Uruguay	16	11	9	4	0	0	1	0	4	3
USA	1844	301	273	163	0	0	6	1	1340	229
Uzbekistan	310	141	173	54	0	0	14	6	109	49
Vanuatu	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Venezuela	564	107	86	37	1	0	25	5	204	37
Viet Nam	1943	303	907	260	129	60	149	30	689	106
Yemen	1545	673	991	310	1	1	227	100	251	107
Zambia	9214	1947	2790	1285	18	0	3814	448	566	130
Zimbabwe	5077	1076	1870	902	10	0	1572	164	175	37

A.11 Country-specific Agricultural Land Use DALYs

See next page.

Table A.10: Country-specific agricultural land use DALYs

	All Diseases		Diarrheal Disease		Intestinal Nematodes		Parasitic & Vector-Borne Diseases		Other Diseases	
Country	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Afghanistan	379398	144826	256464	70387	7224	3157	58817	23485	38160	14379
Albania	1073	449	561	167	0	0	83	36	378	164
Algeria	38003	7010	16297	10266	108	2	1434	276	8324	1535
Andorra	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Angola	265772	98526	68815	46370	1662	38	83887	18316	20854	7650
Antigua	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Argentina	5351	3184	502	219	85	17	801	526	3204	2006
Armenia	1212	520	739	226	2	1	61	28	342	148
Aruba	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Australia	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Austria	418	212	163	61	0	0	8	5	221	114
Azerbaijan	13592	5933	9898	2874	12	6	122	53	3013	1335
Bahamas	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bahrain	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bangladesh	680447	330533	488061	25169	58773	25672	28896	12228	230545	101927
Barbados	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Belarus	819	424	468	162	0	0	46	23	268	135
Belgium	247	139	86	32	0	0	1	0	155	85
Belize	308	54	115	69	11	0	39	7	61	10

Benin	627435	82327	170979	84768	3764	52	291204	38970	74164	9220
Bermuda	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bhutan	5359	2090	2605	693	22	9	175	67	2494	985
Bolivia	32567	5360	18978	7427	4274	679	2004	1130	3194	505
Bosnia and Herzegovina	472	229	267	89	0	0	39	19	138	64
Botswana	13447	3891	5198	2829	630	11	1683	280	1557	433
Brazil	194405	33073	48597	21050	9116	1694	38073	7214	69175	11762
British Virgin Islands	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Brunei	7	2	2	1	0	0	2	0	3	1
Bulgaria	784	365	361	112	0	0	158	76	225	107
Burkina Faso	2183487	52825	282885	140410	5378	55	1224906	117386	217376	5024
Burundi	824163	138961	243910	107869	9361	86	302620	29659	65802	12022
Cambodia	74575	30756	35825	9119	1131	521	11426	4800	32094	12924
Cameroon	1309075	144154	367462	179131	23382	284	525355	58260	179088	18952
Canada	2821	602	561	411	0	0	7	2	1745	373
Cape Verde	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Cayman Islands	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Central African Republic	473142	82105	119532	56141	6419	71	237366	25453	21948	3823
Chad	1443721	140919	510995	231356	10378	107	445263	49317	138034	13938
Chile	2678	1701	1276	557	224	43	117	79	1496	944
China	719237	314790	193264	62757	158375	73649	180051	79981	95641	43489
Colombia	71875	9912	9625	3969	5944	1037	4789	1495	16041	2137

Congo	173199	42496	43719	21779	3448	49	77104	10820	15208	3491
Costa Rica	4693	727	847	389	286	55	142	47	678	103
Cote dIvoire	1551386	44738	376538	176066	21168	260	493113	60740	221605	6442
Croatia	542	263	266	93	0	0	7	4	213	112
Cuba	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Cyprus	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Czech Republic	957	441	448	126	0	0	5	2	488	216
Denmark	244	134	68	26	0	0	0	0	162	90
Djibouti	12266	3741	4994	3013	83	1	882	140	1720	509
Dominican Republic	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
DR Congo	6948337	1483848	1505801	738768	81964	928	3647524	405052	493020	99757
Ecuador	28081	5421	8107	3124	4867	828	1711	623	3852	737
Egypt	221682	34817	80382	45884	9985	165	21774	3648	48396	7527
El Salvador	8860	1380	3629	2200	548	10	855	155	1027	170
Eritrea	119122	24554	53333	26177	355	4	12816	1521	17041	3563
Estonia	87	44	57	22	0	0	1	0	18	9
Ethiopia	3170207	594275	1303415	577751	42586	453	564835	59906	297141	60828
Fiji	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Finland	212	117	95	35	0	0	1	0	112	59
Former USSR	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
France	4992	2017	877	426	0	0	50	20	2969	1232
French Polynesia	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Gabon	23475	6898	4831	3038	672	13	11133	2099	2335	683
Gambia	64413	3532	14523	8161	157	2	20742	3337	9222	482
Gaza Strip	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Georgia	1809	731	899	264	3	2	247	105	598	243
Germany	2319	1258	891	341	0	0	42	23	1302	687
Ghana	1015029	35277	137610	73737	2916	41	511097	68303	120631	4227
Greece	2281	1104	311	107	0	0	12	6	1896	924
Greenland	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Guatemala	82822	11771	33605	18207	12672	195	6508	974	8591	1199
Guinea	1301702	33768	182974	79933	13010	146	690547	75266	135176	3370
Guyana	2243	494	442	187	16	3	383	69	565	125
Haiti	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Honduras	34869	4689	10746	5806	3222	52	3307	532	5063	708
Hong Kong	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Hungary	677	355	462	164	0	0	14	7	137	71
Iceland	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
India	8068249	3455398	6387348	607843	139094	61791	1035185	439988	983212	411045
Indonesia	978709	181549	464268	185594	16888	7986	140701	26440	284554	54279
Iran	36485	17727	26877	9083	137	66	862	418	5077	2437
Iraq	53149	25137	38436	12208	9	5	2717	1315	8552	4024
Ireland	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Israel	390	139	52	37	0	0	3	1	278	102

Italy	5081	2157	776	246	0	0	25	11	3939	1704
Jamaica	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Japan	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Jordan	1079	462	358	236	32	8	20	8	311	136
Kazakhstan	8449	3939	4863	1628	416	202	111	54	2320	1095
Kenya	1687468	360242	643541	301864	5827	65	450108	50642	138642	30001
Kuwait	242	124	103	38	0	0	4	2	121	63
Kyrgyzstan	5726	2449	3451	1091	240	117	358	162	1214	504
Laos	101817	38731	57708	6369	5752	2307	8977	3312	28944	11393
Latvia	194	98	121	43	0	0	5	3	50	27
Lebanon	2176	746	730	468	2	0	59	12	630	223
Lesotho	49690	11600	24457	12807	1674	23	875	115	3295	842
Liberia	265773	8584	47230	25344	3439	47	117225	16280	24606	823
Libya	7576	1217	2151	1332	13	0	2329	417	1544	262
Liechtenstein	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Lithuania	579	283	276	99	0	0	41	21	218	108
Luxembourg	6	4	2	1	0	0	0	0	5	3
Macao SAR	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Madagascar	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Malawi	620325	130823	152028	69748	1881	20	323346	31615	36047	7019
Malaysia	19391	4174	4668	2064	4667	2429	2897	618	4512	954
Maldives	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Mali	2057430	104067	395563	179851	3420	43	1086769	132650	117058	5645
Malta	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Mauritania	147759	13218	47424	23370	200	3	43615	6274	21759	1992
Mauritius	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Mexico	77342	14003	28320	16243	5587	109	7817	1397	17665	3092
Moldova	793	343	439	137	0	0	70	31	230	105
Monaco	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Mongolia	2824	1274	1807	569	42	20	419	197	435	193
Montenegro	32	14	18	6	0	0	1	1	9	5
Morocco	64946	8816	29817	17121	447	7	4564	704	11634	1682
Mozambique	1498667	296531	307070	137934	29768	312	807881	81409	117696	24939
Myanmar	205023	101069	152639	25531	9970	4725	10926	5354	64940	31770
Namibia	24064	6409	9673	5347	561	9	2693	429	2638	711
Nepal	240234	85678	136539	34840	14245	5753	10556	3906	68210	23998
Netherlands	779	420	248	91	0	0	2	1	468	255
Netherlands Antilles	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
New Caledonia	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
New Zealand	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Nicaragua	15409	1787	4368	1706	111	19	941	280	1278	149
Niger	1791679	197119	441491	211780	3501	41	922474	106085	182547	20149
Nigeria	8870603	1322304	2515060	1484237	88708	1434	3855131	609514	881306	124828
North Korea	38764	14866	26938	7398	2014	872	720	293	6010	2548

Norway	188	105	54	20	0	0	0	0	129	69
Oman	594	302	266	94	0	0	18	10	265	136
Pakistan	1788712	753717	1176087	349326	11792	5342	55675	24669	434692	181414
Panama	7802	1028	1647	675	31	5	373	113	1824	243
Papua New Guinea	139846	20710	46860	15930	10238	4275	62770	9507	10212	1589
Paraguay	5771	3635	3823	1521	278	50	936	603	602	359
Peru	41930	13134	22629	8654	8460	1490	4361	1604	5892	1840
Philippines	251176	57430	116768	27309	NA	NA	60978	14445	52603	11816
Poland	4473	2245	3284	1121	0	0	51	26	765	380
Portugal	2340	468	345	215	8	0	15	3	1755	340
Qatar	25	13	11	4	0	0	0	0	11	6
Romania	7460	3424	3308	1014	0	0	1638	755	2085	930
Russia	10333	5213	6348	2229	67	33	580	298	2792	1474
Rwanda	379142	76032	89414	39092	11796	126	181796	18773	31855	6696
Samoa	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
San Marino	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sao Tome and Principe	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Saudi Arabia	3983	2060	2206	747	74	39	188	102	1306	674
Senegal	488620	20969	113968	57263	1256	16	166075	21699	76307	2968
Serbia	1952	977	1198	411	0	0	62	30	571	268
Seychelles	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sierra Leone	1088739	28764	179995	81482	8218	93	502851	55424	143300	3711

Singapore	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Slovakia	269	135	128	47	0	0	1	1	113	59
Slovenia	267	134	120	43	0	0	7	4	121	61
Somalia	1054289	210262	457265	206355	9631	102	131713	13719	111292	20756
South Africa	141191	51713	48471	33045	6765	142	10412	2280	17392	6260
South Korea	4148	2127	591	211	838	437	149	77	1830	995
South Sudan	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Spain	4936	1031	808	555	1	0	37	8	3405	695
Sri Lanka	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sudan	634885	85957	205793	112880	5888	90	219527	32722	74370	9739
Suriname	115	22	30	13	3	1	30	6	29	6
Swaziland	17691	5217	7755	4637	1000	17	584	95	1560	470
Sweden	476	251	107	41	0	0	1	1	335	178
Switzerland	470	211	203	58	0	0	20	9	220	102
Syria	67457	19683	20558	7654	570	192	3948	1422	8698	2596
Taiwan	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Tajikistan	41455	16318	27457	7634	65	29	781	316	11743	4636
Tanzania	2270961	466346	657622	296854	41028	477	897762	102775	202335	39744
TFYR Macedonia	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Thailand	79958	19936	53497	14481	17456	8321	5635	1220	26852	6947
Togo	544635	15124	91164	44127	2140	25	251854	27169	68382	1812
Trinidad and Tobago	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Tunisia	6067	1099	2327	1411	30	1	547	105	1574	291
Turkey	31778	15382	15964	5073	64	32	1392	663	13909	6606
Turkmenistan	11567	5356	8348	3000	5	3	31	16	2158	1062
UAE	720	326	436	121	1	0	8	4	236	109
Uganda	1811501	339853	469943	213200	13672	151	757494	82016	199413	43927
UK	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ukraine	11686	5431	7092	2393	22	11	379	184	2956	1498
Uruguay	357	238	190	86	0	0	18	12	109	80
USA	43514	7107	7344	4387	0	0	231	42	29883	5100
Uzbekistan	34062	15461	18416	5756	17	8	920	434	13152	5974
Vanuatu	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Venezuela	54145	10227	8897	3795	3827	733	2950	564	7102	1293
Viet Nam	201050	31369	82505	23684	34032	15722	17989	3649	51762	7977
Yemen	152981	66632	92575	28940	1018	478	22933	10094	29223	12421
Zambia	687790	145366	185238	85330	11033	132	301830	35421	51747	11885
Zimbabwe	403158	85439	138633	66868	11022	118	127864	13374	16946	3563

A.12 Country-specific International Agricultural Trade Deaths

See next page.

Table A.11: Country-specific international agricultural trade deaths

	All Diseases		Diarrheal Disease		Intestinal Nematodes		Parasitic & Vector-Borne Diseases		Other Diseases	
Country	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Afghanistan	1545	25	1234	23	6	2	36	5	200	10
Albania	6	2	1	1	0	0	1	1	3	2
Algeria	64	4	27	4	0	0	4	1	14	2
Andorra	0	0	0	0	0	0	0	0	0	0
Angola	368	13	98	12	1	0	113	7	26	4
Antigua	0	0	0	0	0	0	0	0	0	0
Argentina	99	6	3	1	0	0	13	3	78	6
Armenia	1	1	1	0	0	0	0	0	1	1
Aruba	0	0	0	0	0	0	0	0	0	0
Australia	0	0	0	0	0	0	0	0	0	0
Austria	8	3	2	1	0	0	0	0	5	2
Azerbaijan	57	5	41	4	0	0	1	1	13	3
Bahamas	0	0	0	0	0	0	0	0	0	0
Bahrain	0	0	0	0	0	0	0	0	0	0
Bangladesh	3894	70	3550	13	10	3	114	9	1187	20
Barbados	0	0	0	0	0	0	0	0	0	0
Belarus	6	2	1	0	0	0	1	1	4	2
Belgium	11	3	3	2	0	0	0	0	7	3

Belize	2	1	1	1	0	0	0	0	0	0
Benin	1880	17	588	21	8	0	767	11	203	6
Bermuda	0	0	0	0	0	0	0	0	0	0
Bhutan	17	3	8	2	0	0	1	1	8	3
Bolivia	95	4	69	6	0	0	4	2	9	1
Bosnia and Herzegovina	2	1	0	0	0	0	0	1	1	1
Botswana	23	1	11	3	0	0	1	1	2	1
Brazil	553	12	71	7	1	0	78	5	361	11
British Virgin Islands	0	0	0	0	0	0	0	0	0	0
Brunei	0	0	0	0	0	0	0	0	0	0
Bulgaria	11	3	1	1	0	0	5	2	5	2
Burkina Faso	8007	17	1267	32	12	1	4153	29	720	7
Burundi	2495	26	816	29	6	0	838	10	168	7
Cambodia	561	19	307	12	13	3	59	7	231	12
Cameroon	9741	48	3172	43	86	2	3297	28	1320	14
Canada	97	5	21	4	0	0	0	0	57	4
Cape Verde	0	0	0	0	0	0	0	0	0	0
Cayman Islands	0	0	0	0	0	0	0	0	0	0
Central African Republic	2005	21	604	20	9	0	865	6	90	6
Chad	10315	35	3854	60	26	1	2973	23	912	11
Chile	44	5	20	3	0	0	2	1	28	3
China	816	22	189	6	69	7	355	11	137	10

Colombia	0	0	0	0	0	0	0	0	0	0
Congo	1017	17	313	19	2	0	402	10	71	6
Costa Rica	45	4	9	2	0	0	1	1	12	2
Croatia	5	2	1	1	0	0	0	0	4	2
Cuba	0	0	0	0	0	0	0	0	0	0
Cyprus	0	0	0	0	0	0	0	0	0	0
Czech Republic	20	4	5	1	0	0	0	0	15	3
Cote dIvoire	18075	25	4865	45	131	2	5201	22	2491	12
North Korea	193	11	115	6	21	3	7	2	32	5
DR Congo	11137	70	2772	38	54	1	5283	29	804	16
Denmark	11	4	2	1	0	0	0	0	8	2
Djibouti	59	6	25	6	0	0	4	1	6	2
Dominican Republic	0	0	0	0	0	0	0	0	0	0
Ecuador	68	3	14	3	0	0	7	2	34	3
Egypt	841	8	319	17	1	0	71	4	211	9
El Salvador	52	4	24	5	0	0	1	1	8	1
Eritrea	322	9	156	11	0	0	32	2	30	4
Estonia	0	1	0	0	0	0	0	0	0	1
Ethiopia	47959	127	21789	105	115	2	6746	39	3410	26
Fiji	0	0	0	0	0	0	0	0	0	0
Finland	4	2	0	0	0	0	0	0	3	1
France	118	10	17	4	0	0	1	1	78	8

French Polynesia	0	0	0	0	0	0	0	0	0	0
Gabon	255	7	67	7	1	0	107	5	22	4
Gambia	150	4	36	6	0	0	48	3	18	1
Georgia	3	2	1	1	0	0	1	1	1	1
Germany	61	6	24	4	0	0	1	1	35	5
Ghana	10852	29	1604	31	14	0	5396	37	1131	7
Greece	40	6	1	1	0	0	0	0	38	4
Greenland	0	0	0	0	0	0	0	0	0	0
Guatemala	807	13	363	14	4	0	82	4	138	6
Guinea	4932	17	828	18	23	1	2351	13	570	5
Guyana	2	1	0	1	0	0	0	0	1	1
Haiti	0	0	0	0	0	0	0	0	0	0
Honduras	285	7	108	9	1	0	21	3	42	2
Hong Kong	0	0	0	0	0	0	0	0	0	0
Hungary	11	3	7	1	0	0	0	1	2	1
Iceland	0	0	0	0	0	0	0	0	0	0
India	19005	92	16702	23	15	3	1948	24	1725	22
Indonesia	2864	22	1745	26	5	1	272	7	596	13
Iran	37	5	26	4	0	0	0	1	7	2
Iraq	6	2	4	2	0	0	0	0	1	1
Ireland	0	0	0	0	0	0	0	0	0	0
Israel	8	1	1	1	0	0	0	0	6	1

Italy	121	10	15	3	0	0	0	0	99	8
Jamaica	0	0	0	0	0	0	0	0	0	0
Japan	0	0	0	0	0	0	0	0	0	0
Jordan	5	2	2	1	0	0	0	0	2	1
Kazakhstan	7	2	4	2	0	0	0	0	2	1
Kenya	5725	38	2521	29	3	0	1164	8	293	7
Kuwait	0	0	0	0	0	0	0	0	0	1
Kyrgyzstan	5	1	3	1	0	0	1	0	1	0
Laos	940	23	550	9	35	5	82	8	276	13
Latvia	0	0	0	0	0	0	0	0	0	0
Lebanon	15	3	4	2	0	0	1	0	5	2
Lesotho	128	7	67	8	0	0	2	1	6	2
Liberia	3027	13	714	27	11	0	1061	18	292	3
Libya	8	2	2	2	0	0	1	1	3	1
Liechtenstein	0	0	0	0	0	0	0	0	0	0
Lithuania	5	2	0	0	0	0	1	1	3	2
Luxembourg	0	0	0	0	0	0	0	0	0	0
Macao SAR	0	0	0	0	0	0	0	0	0	0
Madagascar	0	0	0	0	0	0	0	0	0	0
Malawi	7623	54	2206	29	8	0	3576	26	277	7
Malaysia	39	3	11	2	0	0	9	1	18	2
Maldives	0	0	0	0	0	0	0	0	0	0

Mali	8100	30	1913	43	5	0	3720	33	408	6
Malta	0	0	0	0	0	0	0	0	0	0
Mauritania	1399	12	477	25	1	0	407	10	168	6
Mauritius	0	0	0	0	0	0	0	0	0	0
Mexico	234	8	91	6	0	0	13	1	73	4
Monaco	0	0	0	0	0	0	0	0	0	0
Mongolia	13	3	10	2	1	1	0	0	2	1
Montenegro	0	0	0	0	0	0	0	0	0	0
Morocco	462	12	218	16	0	0	28	2	80	5
Mozambique	7824	57	1822	45	32	1	4061	30	538	14
Myanmar	2004	30	1716	17	52	7	105	7	522	25
Namibia	193	11	86	9	0	0	15	2	19	3
Nepal	2266	37	1719	32	2	1	68	7	397	15
Netherlands	36	6	8	3	0	0	0	0	25	5
Netherlands Antilles	0	0	0	0	0	0	0	0	0	0
New Caledonia	0	0	0	0	0	0	0	0	0	0
New Zealand	0	0	0	0	0	0	0	0	0	0
Nicaragua	102	6	32	4	0	0	3	1	9	1
Niger	2517	26	707	21	4	0	1169	11	237	7
Nigeria	26140	99	8704	87	125	2	9546	63	2423	18
Norway	4	1	1	1	0	0	0	0	3	2
Gaza Strip	0	0	0	0	0	0	0	0	0	0

Oman	3	2	0	0	0	0	0	0	2	2
Pakistan	8965	72	6279	63	5	2	210	11	1915	35
Panama	47	4	7	2	0	0	2	1	21	2
Papua New Guinea	1702	20	733	22	8	2	751	16	117	7
Paraguay	12	3	7	2	0	0	4	2	1	1
Peru	53	6	36	5	0	0	7	2	10	2
Philippines	439	11	190	8	0	0	90	5	160	6
Poland	15	3	10	2	0	0	0	0	3	1
Portugal	45	4	6	2	0	0	0	0	37	3
Qatar	0	0	0	0	0	0	0	0	0	0
South Korea	11	2	2	1	2	1	0	0	5	2
Moldova	6	2	1	1	0	0	2	1	3	2
Romania	22	3	4	2	0	0	9	2	8	2
Russia	5	2	2	1	0	0	1	1	3	1
Rwanda	482	10	131	10	1	0	226	8	33	4
Samoa	0	0	0	0	0	0	0	0	0	0
San Marino	0	0	0	0	0	0	0	0	0	0
Sao Tome and Principe	0	0	0	0	0	0	0	0	0	0
Saudi Arabia	3	2	2	1	0	0	0	1	1	1
Senegal	3748	19	965	23	3	0	1250	14	451	4
Serbia	4	1	2	1	0	0	0	0	1	1
Seychelles	0	0	0	0	0	0	0	0	0	0

Sierra Leone	2275	7	445	12	10	0	922	16	327	3
Singapore	0	0	0	0	0	0	0	0	0	0
Slovakia	1	1	0	0	0	0	0	0	1	1
Slovenia	2	2	0	0	0	0	0	0	2	1
Somalia	1814	25	800	27	4	0	236	7	171	8
South Africa	716	23	277	15	0	0	33	3	93	7
South Sudan	0	0	0	0	0	0	0	0	0	0
Spain	116	7	15	4	0	0	0	0	87	5
Sri Lanka	0	0	0	0	0	0	0	0	0	0
Sudan	200	7	60	7	1	0	84	4	19	1
Suriname	1	0	0	1	0	0	0	0	0	0
Swaziland	127	6	61	9	0	0	4	1	10	2
Sweden	13	3	2	1	0	0	0	0	10	2
Switzerland	5	2	2	1	0	0	0	0	3	2
Syria	365	12	121	10	0	0	6	3	54	6
Taiwan	0	0	0	0	0	0	0	0	0	0
Tajikistan	372	15	241	7	0	0	14	3	105	7
Thailand	387	7	369	8	24	3	14	1	134	4
TFYR Macedonia	0	0	0	0	0	0	0	0	0	0
Togo	4191	15	854	32	11	1	1722	14	493	4
Trinidad and Tobago	0	0	0	0	0	0	0	0	0	0
Tunisia	41	3	15	5	0	0	3	1	12	2

Turkey	46	6	16	3	0	0	4	2	27	5
Turkmenistan	72	8	52	5	0	0	0	0	14	3
Former USSR	0	0	0	0	0	0	0	0	0	0
Uganda	10876	63	3181	47	30	1	4098	31	1077	21
Ukraine	12	3	5	2	0	0	1	1	6	2
UAE	1	1	0	0	0	0	0	0	1	1
UK	0	0	0	0	0	0	0	0	0	0
Tanzania	23763	53	7984	64	79	1	8509	32	1601	24
USA	342	5	51	4	0	0	1	0	249	5
Uruguay	5	2	3	1	0	0	0	0	1	1
Uzbekistan	54	5	30	4	0	0	2	1	19	4
Vanuatu	0	0	0	0	0	0	0	0	0	0
Venezuela	21	1	3	1	0	0	1	0	8	1
Viet Nam	385	5	179	7	26	3	30	2	136	4
Yemen	407	16	261	12	0	1	61	8	66	6
Zambia	4207	42	1274	21	8	0	1746	18	258	7
Zimbabwe	5076	44	1870	32	10	0	1568	16	175	7

A.13 Country-specific International Agricultural Trade DALYs

See next page.

Table A.12: Country-specific international agricultural trade DALYs

	All Diseases		Diarrheal Disease		Intestinal Nematodes		Parasitic & Vector-Borne Diseases		Other Diseases	
Country	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Afghanistan	175653	407	118737	183	3344	65	27105	119	17667	123
Albania	397	20	207	11	0	0	32	5	140	11
Algeria	6150	46	2637	53	18	1	236	11	1347	20
Andorra	0	0	0	0	0	0	0	0	0	0
Angola	28439	153	7364	82	178	3	8880	60	2231	33
Antigua	0	0	0	0	0	0	0	0	0	0
Argentina	2499	44	234	8	0	0	406	14	1496	38
Armenia	248	13	151	8	0	0	13	4	70	8
Aruba	0	0	0	0	0	0	0	0	0	0
Australia	0	0	0	0	0	0	0	0	0	0
Austria	199	12	77	7	0	0	4	1	105	8
Azerbaijan	6436	75	4687	43	0	0	59	8	1427	19
Bahamas	0	0	0	0	0	0	0	0	0	0
Bahrain	0	0	0	0	0	0	0	0	0	0
Bangladesh	229828	436	164848	140	19851	88	9434	87	77869	215
Barbados	0	0	0	0	0	0	0	0	0	0
Belarus	818	28	467	14	0	0	45	4	268	11
Belgium	196	16	69	6	0	0	0	0	124	10

Belize	254	9	94	5	0	0	0	0	50	3
Benin	148638	204	40505	186	892	5	68549	95	17569	52
Bermuda	0	0	0	0	0	0	0	0	0	0
Bhutan	1365	38	663	17	0	0	45	6	635	27
Bolivia	10009	34	5832	38	1313	13	606	18	982	12
Bosnia and Herzegovina	163	8	92	5	0	0	14	3	47	7
Botswana	1495	22	578	20	0	0	185	8	173	9
Brazil	30688	109	7671	57	1439	23	5997	33	10920	50
British Virgin Islands	0	0	0	0	0	0	0	0	0	0
Brunei	2	1	1	1	0	0	1	0	1	0
Bulgaria	592	11	273	14	0	0	121	11	170	10
Burkina Faso	629108	206	81505	273	1549	7	352522	259	62631	47
Burundi	183396	215	54276	160	2083	4	67683	120	14643	74
Cambodia	44099	179	21184	105	669	20	6819	76	18978	110
Cameroon	798777	451	224220	460	14267	15	321567	305	109277	128
Canada	1711	15	340	23	0	0	4	2	1058	20
Cape Verde	0	0	0	0	0	0	0	0	0	0
Cayman Islands	0	0	0	0	0	0	0	0	0	0
Central African Republic	154380	230	39002	159	2094	7	77836	99	7161	57
Chad	806643	364	285505	391	5799	11	249801	199	77123	158
Chile	1267	29	604	18	0	0	55	7	708	14
China	75158	198	20195	90	16550	123	18063	102	9994	93

Colombia	0	0	0	0	0	0	0	0	0	0
Congo	67577	195	17058	100	1345	7	30310	68	5934	56
Costa Rica	3890	25	702	19	237	12	119	6	562	13
Croatia	177	12	87	9	0	0	2	2	70	6
Cuba	0	0	0	0	0	0	0	0	0	0
Cyprus	0	0	0	0	0	0	0	0	0	0
Czech Republic	522	21	245	8	0	0	3	1	266	11
Cote dIvoire	1449441	253	351794	484	19777	20	462926	309	207043	97
North Korea	22815	121	15855	76	1185	29	404	16	3537	44
DR Congo	937089	629	203080	327	11054	13	489656	266	66491	137
Denmark	185	12	52	3	0	0	0	0	123	7
Djibouti	3614	43	1471	32	0	0	258	5	507	12
Dominican Republic	0	0	0	0	0	0	0	0	0	0
Ecuador	7476	41	2158	31	1296	13	449	13	1026	13
Egypt	82667	140	29975	148	3724	11	8096	37	18047	73
El Salvador	4279	27	1752	52	265	2	410	9	496	14
Eritrea	18446	56	8258	69	55	1	1992	19	2639	27
Estonia	49	7	32	5	0	0	0	1	10	3
Ethiopia	3169976	974	1303320	862	42582	30	566019	261	297120	337
Fiji	0	0	0	0	0	0	0	0	0	0
Finland	134	11	60	5	0	0	0	0	71	7
France	2061	38	362	17	0	0	20	4	1226	33

French Polynesia	0	0	0	0	0	0	0	0	0	0
Gabon	17585	97	3619	56	503	4	8489	62	1749	29
Gambia	11452	37	2582	56	28	1	3682	34	1640	13
Georgia	278	13	138	6	0	0	38	5	92	6
Germany	1073	19	413	10	0	0	20	4	603	23
Ghana	817818	236	110873	347	2349	8	411773	322	97193	74
Greece	610	27	83	7	0	0	3	2	507	20
Greenland	0	0	0	0	0	0	0	0	0	0
Guatemala	61529	142	24965	140	9414	11	4833	31	6383	45
Guinea	401473	149	56433	98	4013	10	211335	206	41691	30
Guyana	140	9	28	4	0	0	24	3	35	4
Haiti	0	0	0	0	0	0	0	0	0	0
Honduras	23183	80	7144	85	2142	5	2229	26	3366	35
Hong Kong	0	0	0	0	0	0	0	0	0	0
Hungary	383	16	261	14	0	0	8	2	77	4
Iceland	0	0	0	0	0	0	0	0	0	0
India	1035459	425	819736	207	17851	67	132927	226	126183	196
Indonesia	152213	158	72205	169	2627	43	21945	50	44255	93
Iran	4096	49	3017	38	15	3	97	5	570	17
Iraq	631	22	456	16	0	0	33	6	101	7
Ireland	0	0	0	0	0	0	0	0	0	0
Israel	150	6	20	3	0	0	0	0	107	5

Italy	1910	39	292	10	0	0	9	2	1481	33
Jamaica	0	0	0	0	0	0	0	0	0	0
Japan	0	0	0	0	0	0	0	0	0	0
Jordan	569	14	189	18	0	0	10	2	164	10
Kazakhstan	969	31	558	15	0	0	13	2	266	13
Kenya	327293	299	124818	220	1130	4	87572	73	26890	64
Kuwait	14	3	6	2	0	0	0	0	7	2
Kyrgyzstan	569	10	343	6	0	0	35	2	121	5
Laos	81294	273	46076	106	4593	60	7117	75	23110	113
Latvia	47	5	29	4	0	0	1	1	12	4
Lebanon	1119	23	375	26	0	0	31	3	324	16
Lesotho	7919	53	3898	69	267	3	138	5	525	19
Liberia	249890	135	44407	219	3233	10	109891	155	23136	40
Libya	1178	12	334	18	0	0	360	4	240	8
Liechtenstein	0	0	0	0	0	0	0	0	0	0
Lithuania	208	11	99	9	0	0	15	3	78	8
Luxembourg	4	2	1	1	0	0	0	0	3	1
Macao SAR	0	0	0	0	0	0	0	0	0	0
Madagascar	0	0	0	0	0	0	0	0	0	0
Malawi	520687	481	127609	392	1579	6	270529	163	30257	68
Malaysia	5093	22	1226	21	1226	21	757	13	1185	13
Maldives	0	0	0	0	0	0	0	0	0	0

Mali	643191	304	123660	324	1069	3	336875	278	36595	54
Malta	0	0	0	0	0	0	0	0	0	0
Mauritania	97888	86	31417	145	132	1	28847	66	14415	45
Mauritius	0	0	0	0	0	0	0	0	0	0
Mexico	14284	64	5230	59	1032	6	1459	23	3262	23
Monaco	0	0	0	0	0	0	0	0	0	0
Mongolia	1890	34	1209	32	28	5	0	0	291	14
Montenegro	5	2	0	0	0	0	0	0	1	1
Morocco	41739	60	19162	165	288	2	2940	25	7477	41
Mozambique	646187	544	132401	282	12835	13	348400	230	50748	112
Myanmar	129251	256	96227	209	6285	62	6758	50	40940	210
Namibia	13323	94	5356	76	0	0	1494	16	1460	29
Nepal	109270	265	62104	176	6479	66	4832	58	31025	130
Netherlands	659	16	210	9	0	0	2	1	396	15
Netherlands Antilles	0	0	0	0	0	0	0	0	0	0
New Caledonia	0	0	0	0	0	0	0	0	0	0
New Zealand	0	0	0	0	0	0	0	0	0	0
Nicaragua	9919	48	2812	41	72	5	607	21	823	7
Niger	199282	140	49105	107	389	3	102395	144	20304	53
Nigeria	2002970	668	567897	667	20030	27	875536	483	198998	292
Norway	57	8	16	3	0	0	0	0	39	6
Gaza Strip	0	0	0	0	0	0	0	0	0	0

Oman	272	18	122	8	0	0	8	3	121	13
Pakistan	663473	545	436237	302	4374	78	20822	146	161237	371
Panama	3183	27	672	22	0	0	153	9	744	15
Papua New Guinea	129445	175	43375	153	9477	86	58408	149	9453	47
Paraguay	1291	43	855	22	62	3	209	13	135	7
Peru	5738	52	3097	50	1158	19	580	18	806	24
Philippines	33706	104	15669	70	0	0	8186	54	7059	47
Poland	910	28	668	12	0	0	11	2	156	10
Portugal	809	15	119	9	0	0	5	1	607	14
Qatar	2	1	1	1	0	0	0	0	1	1
South Korea	258	10	37	4	52	6	10	2	114	8
Moldova	690	22	382	13	0	0	61	8	200	15
Romania	908	22	402	14	0	0	195	9	254	9
Russia	884	35	543	20	0	0	50	7	239	12
Rwanda	33431	125	7884	71	1040	4	16097	55	2809	37
Samoa	0	0	0	0	0	0	0	0	0	0
San Marino	0	0	0	0	0	0	0	0	0	0
Sao Tome and Principe	0	0	0	0	0	0	0	0	0	0
Saudi Arabia	384	18	212	13	7	3	19	4	126	12
Senegal	259945	129	60631	244	668	4	88698	138	40595	57
Serbia	157	15	97	7	0	0	5	2	46	7
Seychelles	0	0	0	0	0	0	0	0	0	0

Sierra Leone	174762	45	28892	114	1319	4	80953	135	23002	18
Singapore	0	0	0	0	0	0	0	0	0	0
Slovakia	61	7	29	4	0	0	0	0	26	3
Slovenia	76	5	34	4	0	0	2	1	34	5
Somalia	140306	201	60853	220	1282	2	17427	54	14811	45
South Africa	45250	207	15534	124	2168	8	3338	31	5574	64
South Sudan	0	0	0	0	0	0	0	0	0	0
Spain	2058	23	337	20	0	0	15	3	1419	21
Sri Lanka	0	0	0	0	0	0	0	0	0	0
Sudan	15476	60	5016	68	144	2	5340	37	1813	16
Suriname	75	4	20	5	0	0	20	2	19	2
Swaziland	9722	71	4262	42	550	5	317	9	857	23
Sweden	202	10	46	5	0	0	0	0	143	6
Switzerland	102	9	44	5	0	0	4	2	48	3
Syria	39813	162	12134	78	336	12	2285	36	5133	51
Taiwan	0	0	0	0	0	0	0	0	0	0
Tajikistan	34530	155	22871	96	54	7	650	24	9782	51
Thailand	20944	66	14013	46	4572	46	1443	13	7033	32
TFYR Macedonia	0	0	0	0	0	0	0	0	0	0
Togo	326956	112	54728	219	1285	5	152056	164	41052	34
Trinidad and Tobago	0	0	0	0	0	0	0	0	0	0
Tunisia	3003	35	1152	25	0	0	273	11	779	15

Turkey	4751	63	2387	34	10	3	203	9	2079	41
Turkmenistan	7150	82	5160	42	0	0	20	4	1334	38
Former USSR	0	0	0	0	0	0	0	0	0	0
Uganda	862101	479	223648	319	6507	9	359102	230	94901	136
Ukraine	1365	23	828	20	0	0	44	8	345	16
UAE	199	11	120	7	0	0	0	0	65	8
UK	0	0	0	0	0	0	0	0	0	0
Tanzania	1654357	767	479067	436	29889	19	657928	262	147398	211
USA	8080	31	1364	24	0	0	42	2	5549	22
Uruguay	112	11	60	5	0	0	6	2	34	6
Uzbekistan	5933	62	3208	42	0	0	161	12	2291	45
Vanuatu	0	0	0	0	0	0	0	0	0	0
Venezuela	2021	14	332	10	143	5	109	4	265	7
Viet Nam	39806	63	16335	55	6738	50	3567	22	10248	43
Yemen	40345	193	24415	82	268	15	6159	66	7707	68
Zambia	314051	365	84581	213	5038	10	138165	152	23628	69
Zimbabwe	403047	326	138595	224	11019	17	127543	137	16941	75

A.14 Sub Saharan Africa Regional Analysis Tabulated Results

See next page.

Table A.13: Sub-Saharan Africa analysis

	Standard Error	Odds Ratio	CI LOW	CI High	Data Type
Year	1.0217	0.9532	0.9140	0.9942	Socioeconomics
Age	1.0157	1.2775	1.2392	1.3170	Socioeconomics
Population Density	1.0288	0.7728	0.7310	0.8169	Socioeconomics
Sex	1.0458	0.9958	0.9121	1.0872	Socioeconomics
Education	1.2620	0.4201	0.2662	0.6628	Socioeconomics
Has a bednet	1.0622	1.0164	0.9030	1.1441	Socioeconomics
Dwelling sprayed against mosquitoes	1.1194	0.9091	0.7288	1.1340	Socioeconomics
Wealth	1.0268	0.6903	0.6554	0.7270	Socioeconomics
Urban Rural	1.0886	0.5382	0.4557	0.6357	Socioeconomics
Water Source Unimproved	1.0933	1.3068	1.0971	1.5566	Socioeconomics
Sanitation Unimproved	1.0810	1.1476	0.9851	1.3368	Socioeconomics
Mean Temperature	1.0019	1.0040	1.0003	1.0078	Climate
Precipitation	1.0005	0.9994	0.9985	1.0003	Climate
Elevation	1.0781	0.9722	0.8390	1.1266	Climate
Rainfed Cropland	1.0388	1.1858	1.1005	1.2776	Agriculture
Irrigated or post-flooding cropland	1.0243	1.0469	0.9988	1.0972	Agriculture
Mosaic Cropland	1.0289	0.9685	0.9159	1.0241	Agriculture
Mosaic Natural Veg	1.0260	1.0406	0.9895	1.0942	Agriculture
Forest Cover	1.0441	1.3396	1.2309	1.4580	Forest Cover Change
Forest Loss	1.0151	0.9841	0.9557	1.0135	Forest Cover Change

A.15 Analysis of Rural Households Tabulated Results

See next page.

Table A.14: Analysis of rural households

	Standard Error	Odds Ratio	CI Low	CI High	Data Type
Year	1.0292	1.0062	0.9511	1.0644	Socioeconomics
Age	1.0181	1.2828	1.2385	1.3288	Socioeconomics
Population Density	1.0423	0.8112	0.7479	0.8797	Socioeconomics
Sex	1.0533	1.0112	0.9134	1.1196	Socioeconomics
Education	1.3095	0.4910	0.2894	0.8328	Socioeconomics
Has a bednet	1.0736	1.0030	0.8726	1.1528	Socioeconomics
Dwelling sprayed against mosquitoes	1.1412	0.8266	0.6381	1.0707	Socioeconomics
Wealth	1.0305	0.7590	0.7156	0.8051	Socioeconomics
Water Source Unimproved	1.1177	1.3712	1.1027	1.7053	Socioeconomics
Sanitation Unimproved	1.0947	1.0397	0.8708	1.2415	Socioeconomics
Mean Temperature	1.0024	1.0056	1.0008	1.0104	Socioeconomics
Precipitation	1.0006	0.9981	0.9969	0.9993	Climate
Elevation	1.1028	0.8743	0.7217	1.0591	Climate
Rainfed Cropland	1.0477	1.1914	1.0873	1.3054	Climate
Irrigated or post-flooding cropland	1.0203	1.0190	0.9797	1.0600	Agriculture
Mosaic Cropland	1.0254	0.9472	0.9017	0.9950	Agriculture
Mosaic Natural Veg	1.0225	1.0383	0.9940	1.0847	Agriculture
Forest Cover	1.0556	1.2394	1.1147	1.3781	Agriculture
Forest Loss	1.0161	0.9778	0.9477	1.0089	Forest Cover Change
Forest Loss	1.0151	0.9841	0.9557	1.0135	Forest Cover Change

A.16 Analysis of Urban Households Tabulated Results

See next page.

Table A.15: Analysis of urban households

	Standard Error	Odds Ratio	CI Low	CI High	Data Type
Year	1.0803	0.7640	0.6567	0.8888	Socioeconomics
Age	1.0307	1.2609	1.1885	1.3378	Socioeconomics
Population Density	1.0440	0.7824	0.7191	0.8514	Socioeconomics
Sex	1.0895	0.9177	0.7758	1.0855	Socioeconomics
Education	1.5976	0.2752	0.1099	0.6893	Socioeconomics
Has a bednet	1.1177	1.0018	0.8054	1.2459	Socioeconomics
Dwelling sprayed against mosquitoes	1.2379	1.0786	0.7099	1.6388	Socioeconomics
Wealth	1.0559	0.5448	0.4896	0.6061	Socioeconomics
Water Source Unimproved	1.1813	0.9943	0.7173	1.3782	Socioeconomics
Sanitation Unimproved	1.1831	1.6260	1.1694	2.2608	Socioeconomics
Mean Temperature	1.0009	0.9999	0.9982	1.0017	Socioeconomics
Precipitation	1.0002	1.0002	0.9999	1.0006	Climate
Elevation	1.0323	0.9649	0.9066	1.0270	Climate
Rainfed Cropland	1.0125	0.9930	0.9691	1.0176	Climate
Irrigated or post-flooding cropland	1.0300	1.0525	0.9932	1.1153	Agriculture
Mosaic Cropland	1.0101	1.0037	0.9841	1.0237	Agriculture
Mosaic Natural Veg	1.0105	0.9939	0.9737	1.0145	Agriculture
Forest Cover	1.0761	1.5520	1.3443	1.7918	Agriculture
Forest Loss	1.0213	0.9833	0.9436	1.0247	Forest Cover Change
Forest Loss	1.0151	0.9841	0.9557	1.0135	Forest Cover Change

A.17 List of models

The below list highlights the variables used per model.

1. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation
2. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , X10baseline , X20baseline , X30baseline , X40baseline
3. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , X10baseline
4. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , X20baseline
5. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , X30baseline
6. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , X40baseline
7. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , forestcover , X10baseline
8. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , forestcover , X20baseline
9. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , forestcover , X30baseline
10. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , forestcover , X40baseline

11. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , forestcover , X10baseline , X20baseline , X30baseline , X40baseline
12. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , forestcover , X10baseline , forestloss
13. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , forestcover , X20baseline , forestloss
14. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , forestcover , X30baseline , forestloss
15. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , forestcover , X40baseline , forestloss
16. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , forestcover , X10baseline , X20baseline , X30baseline , X40baseline , forestloss
17. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , X10baseline , forestloss
18. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , X20baseline , forestloss
19. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , X30baseline , forestloss
20. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , X40baseline , forestloss
21. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , meantemp , prec , elevation , X10baseline , X20baseline , X30baseline , X40baseline , forestloss

22. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation

23. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , X10baseline

24. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , X20baseline

25. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , X30baseline

26. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , X40baseline

27. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , X10baseline , X20baseline , X30baseline , X40baseline

28. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestcover , X10baseline , X20baseline , X30baseline , X40baseline

29. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestcover , X10baseline

30. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestcover , X20baseline

31. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestcover , X30baseline

32. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestcover , X40baseline

33. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestcover , X10baseline , X20baseline , X30baseline , X40baseline , forestloss

34. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestcover , X10baseline , forestloss

35. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestcover , X20baseline , forestloss

36. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestcover , X30baseline , forestloss

37. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestcover , X40baseline , forestloss

38. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestloss

39. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestcover , forestloss , meantemp , prec , elevation

40. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestloss , meantemp , prec , elevation

41. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , +X10baseline , forestloss

42. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , +X20baseline , forestloss

43. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , +X30baseline , forestloss

44. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , +X40baseline , forestloss

45. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , +X10baseline , X20baseline , X30baseline , X40baseline , forestloss
46. year , age , popdense , sex , education , bednetforsleeping , dwellingsprayedagainstmosquitoes , wealthindex , URBANRURA , watersource , sanitation , forestcover , meantemp , prec , elevation
47. meantemp , prec , elevation
48. X10baseline , X20baseline , X30baseline , X40baseline
49. X10baseline
50. X20baseline
51. X30baseline
52. X40baseline
53. forestcover
54. forestloss
55. forestcover , X10baseline
56. forestcover , X20baseline
57. forestcover , X10baseline , X20baseline , X30baseline , X40baseline
58. forestcover , X30baseline
59. forestcover , X40baseline
60. forestloss , X10baseline
61. forestloss , X20baseline
62. forestloss , X30baseline
63. forestloss , X40baseline
64. forestloss , forestcover
65. meantemp , prec , elevation , X10baseline , X20baseline , X30baseline , X40baseline
66. meantemp , prec , elevation , X10baseline
67. meantemp , prec , elevation , X20baseline

68. meantemp , prec , elevation , X30baseline
69. meantemp , prec , elevation , X40baseline
70. meantemp , prec , elevation , forestcover
71. meantemp , prec , elevation , forestloss
72. meantemp , prec , elevation , forestcover , X10baseline
73. meantemp , prec , elevation , forestcover , X20baseline
74. meantemp , prec , elevation , forestcover , X30baseline
75. meantemp , prec , elevation , forestcover , X40baseline
76. meantemp , prec , elevation , forestcover , X10baseline , X20baseline , X30baseline , X40baseline
77. meantemp , prec , elevation , forestloss , X10baseline
78. meantemp , prec , elevation , forestloss , X20baseline
79. meantemp , prec , elevation , forestloss , X30baseline
80. meantemp , prec , elevation , forestloss , X40baseline
81. meantemp , prec , elevation , forestloss , X10baseline , X20baseline , X30baseline , X40baseline

A.18 Table of AICs

Table A.16: AIC values for each model

Model	AIC	BIC	Log Likelihood	Deviance	Residuals
africa0	16987	17132	-8475	16951	24016
africa1	16968	17146	-8462	16924	24012
africa2	16969	17123	-8466	16931	24015
africa3	16986	17140	-8474	16948	24015
africa4	16987	17141	-8475	16949	24015
africa5	16987	17141	-8475	16949	24015
africa6	16929	17090	-8444	16889	24014
africa7	16944	17106	-8452	16904	24014
africa8	16945	17107	-8453	16905	24014
africa9	16947	17108	-8453	16907	24014
africa10	16927	17113	-8440	16881	24011
africa11	16930	17099	-8444	16888	24013
africa12	16945	17115	-8451	16903	24013
africa13	16946	17116	-8452	16904	24013
africa14	16947	17117	-8453	16905	24013
africa15	16927	17121	-8440	16879	24010
africa16	16971	17133	-8466	16931	24014
africa17	16988	17149	-8474	16948	24014
africa18	16988	17150	-8474	16948	24014
africa19	16988	17150	-8474	16948	24014
africa20	16971	17157	-8463	16925	24011
africa21	16989	17111	-8480	16959	24019
africa22	16975	17104	-8471	16943	24018
africa23	16990	17120	-8479	16958	24018
africa24	16991	17120	-8479	16959	24018
africa25	16991	17120	-8479	16959	24018
africa26	16975	17128	-8468	16937	24015
africa27	16932	17093	-8446	16892	24014
africa28	16934	17071	-8450	16900	24017
africa29	16948	17086	-8457	16914	24017
africa30	16949	17086	-8457	16915	24017
africa31	16950	17088	-8458	16916	24017

africa32	16932	17102	-8445	16890	24013
africa33	16934	17079	-8449	16898	24016
africa34	16949	17095	-8457	16913	24016
africa35	16950	17096	-8457	16914	24016
africa36	16952	17097	-8458	16916	24016
africa37	16989	17119	-8479	16957	24018
africa38	16946	17107	-8453	16906	24014
africa39	16988	17142	-8475	16950	24015
africa40	16976	17114	-8471	16942	24017
africa41	16991	17128	-8478	16957	24017
africa42	16991	17128	-8478	16957	24017
africa43	16991	17129	-8479	16957	24017
africa44	16975	17136	-8467	16935	24014
africa45	16945	17098	-8453	16907	24015
africa46	18325	18382	-9156	18311	24027
africa47	18294	18359	-9139	18278	24026
africa48	18300	18340	-9145	18290	24029
africa49	18367	18407	-9178	18357	24029
africa50	18365	18405	-9177	18355	24029
africa51	18366	18406	-9178	18356	24029
africa52	18230	18270	-9110	18220	24029
africa53	18365	18405	-9177	18355	24029
africa54	18164	18213	-9076	18152	24028
africa55	18231	18279	-9109	18219	24028
africa56	18163	18236	-9073	18145	24025
africa57	18232	18280	-9110	18220	24028
africa58	18232	18281	-9110	18220	24028
africa59	18300	18349	-9144	18288	24028
africa60	18366	18415	-9177	18354	24028
africa61	18365	18413	-9176	18353	24028
africa62	18365	18414	-9177	18353	24028
africa63	18295	18368	-9139	18277	24025
africa64	18224	18272	-9106	18212	24028
africa65	18249	18338	-9113	18227	24023
africa66	18257	18322	-9121	18241	24026
africa67	18325	18390	-9154	18309	24026
africa68	18324	18389	-9154	18308	24026

africa69	18327	18392	-9156	18311	24026
africa70	18172	18237	-9078	18156	24026
africa71	18325	18389	-9154	18309	24026
africa72	18107	18180	-9044	18089	24025
africa73	18168	18241	-9075	18150	24025
africa74	18174	18246	-9078	18156	24025
africa75	18174	18247	-9078	18156	24025
africa76	18099	18196	-9037	18075	24022
africa77	18258	18331	-9120	18240	24025
africa78	18324	18397	-9153	18306	24025
africa79	18324	18397	-9153	18306	24025
africa80	18326	18399	-9154	18308	24025
africa81	18249	18347	-9113	18225	24022

A.19 Correlation matrix

Please see the next page.

Table A.17: Correlation matrix

	year	sex	age	edu	bednet	dwelling	wealth	temp	prec	Rainfed	Irrigated	CMosaic	VMosaic	floss	popdense	fcover	elevatio
year	1	0	0	0	0.1	0	-0.1	0	0.1	0	-0.1	-0.1	-0.1	0.1	-0.1	0	0.2
sex	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
age	0	0	1	0.2	0	0	0	0	0	0	0	0	0	0	0	0	0
edu	0	0	0.2	1	0	0	0	0	0	0	0	0	0	0	0	0	0
bednet	0.1	0	0	0	1	0.1	0	0.2	-0.1	0.1	0.1	0	0.1	-0.1	0	-0.1	-0.2
dwelling	0	0	0	0	0.1	1	0	0	-0.1	0	0	-0.1	0	0	0	-0.1	-0.1
wealth	-0.1	0	0	0	0	0	1	-0.1	0	-0.1	0	0.1	0.1	0	0.5	0	-0.1
temp	0	0	0	0	0.2	0	-0.1	1	-0.2	0.3	0.2	0.2	-0.1	0	-0.1	-0.2	-0.7
prec	0.1	0	0	0	-0.1	-0.1	0	-0.2	1	-0.2	-0.1	0.1	-0.1	0.1	0.1	0.4	0.2
Rainfed	0	0	0	0	0.1	0	-0.1	0.3	-0.2	1	0.1	0	-0.1	-0.1	0	-0.2	-0.3
Irrigated	-0.1	0	0	0	0.1	0	0	0.2	-0.1	0.1	1	0.4	-0.1	0	0	0	-0.3
CMosaic	-0.1	0	0	0	0	-0.1	0.1	0.2	0.1	0	0.4	1	-0.1	0	0	0	-0.1
VMosaic	-0.1	0	0	0	0.1	0	0.1	-0.1	-0.1	-0.1	-0.1	-0.1	1	0	0	-0.1	-0.1
floss	0.1	0	0	0	-0.1	0	0	0	0.1	-0.1	0	0	0	1	0	0.4	0
popdense	-0.1	0	0	0	0	0	0.5	-0.1	0.1	0	0	0	0	0	1	-0.1	0
fcover	0	0	0	0	-0.1	-0.1	0	-0.2	0.4	-0.2	0	0	-0.1	0.4	-0.1	1	0.2
elevation	0.2	0	0	0	-0.2	-0.1	-0.1	-0.7	0.2	-0.3	-0.3	-0.1	-0.1	0	0	0.2	1

A.20 Description of DHS Dataset

	Rural		Urban	
	Malaria (+ve)	**Malaria (-ve)**	**Malaria (+ve)**	**Malaria (-ve)**
Total Sample	4196 (27.2%)	11212 (72.7%)	1126 (13.1%)	7500 (86.9%)
Age				
Mean	2.513	2.347	2.548	2.35
SD	1.396	1.498	1.39	1.468
Sex				
Male	2055 (48.9%)	5554 (49.5%)	524 (46.5%)	3697 (49.3%)
Female	2141 (51.0%)	5658 (50.5%)	602 (53.5%)	3803 (50.7%)
Mothers Education				
No Education	4166 (99.29%)	11112 (99.11%)	1117 (99.20%)	7402 (98.69%)
Primary	29 (0.69%)	99 (0.88%)	9 (0.79%)	97 (1.29%)
Secondary and Higher	1 (0.02%)	1 (0.009%)	0 (0.00%)	1 (0.01%)
Household has a bed-net for sleeping				
Yes	3095 (73.76%)	8674 (77.36%)	818 (72.65%)	5823 (77.64%)
No	1101 (26.24%)	2538 (22.64%)	308 (27.35%)	1677 (22.36%)
Dwelling sprayed against mosquitoes in last 12 months				
Yes	231 (5.51%)	1113 (9.93%)	57 (5.06%)	619 (8.25%)

	Rural		Urban	
No	3965 (94.49%)	10099 (90.07%)	1069 (94.94%)	6881 (91.75%)
Wealth Index				
1 = Poorest	1283 (30.58%)	3135 (27.96%)	255 (22.65%)	103 (1.37%)
2 = Poorer	1205 (28.72%)	2982 (26.59%)	104 (9.24%)	537 (7.16%)
3 = Middle	985 (23.47%)	2510 (22.39%)	259 (23.00%)	1229 (16.39%)
4 = Richer	570 (13.58%)	1870 (16.68%)	333 (29.57%)	2227 (29.69%)
5 = Richest	153 (3.65%)	715 (6.38%)	327 (29.04%)	3252 (43.36%)
Water Source				
Improved	575 (13.70%)	4177 (37.25%)	488 (43.34%)	5182 (69.09%)
Unimproved	3621 (86.30%)	7035 (62.75%)	638 (56.66%)	2318 (30.91%)
Sanitation				
Improved	1699 (40.49%)	5495 (49.01%)	718 (63.77%)	5860 (78.13%)
Unimproved	2497 (59.51%)	5717 (50.99%)	408 (36.23%)	1640 (21.87%)
Mean Temperature (°C)				
Mean	25.204	24.744	25.799	25.198
SD	2.641	3.726	2.328	3.019
Precipitation (mm)				

	Rural		Urban	
Mean	83.25	79.644	96.681	74.461
SD	98.717	88.586	96.891	96.259
Rainfed Cropland (%)				
Mean	35.592	27.583	33.605	24.345
SD	31.174	29.17	27.935	25.599
Irrigated/Post-Flooding Cropland (%)				
Mean	2.88	2.528	2.353	2.53
SD	11.847	9.833	9.864	8.644
Crop Dominant Mosaic (tree, shrub, herbaceous cover) (<50%) (%)				
Mean	6.274	6.992	5.497	8.478
SD	9.88	9.035	8.107	9.669
Veg-dominant Mosaic (tree, shrub, herbaceous cover) (>50%) / cropland (<50%) (%)				
Mean	3.226	5.799	4.08	6.426
SD	6.485	9.818	6.527	8.142
Elevation (m)				
Mean	407.1323	519.852	334.985	353.13
SD	383.7677	643.831	290.712	493.864

	Rural		Urban	
Forest Loss				
Mean	0.146	0.179	0.149	0.179
SD	0.364	0.447	0.344	0.379
Forest Cover				
Mean	16.621	14.291	15.601	10.677
SD	16.193	14.141	16.437	11.934

Table A.18: DHS data stratified by urban and rural clusters and malaria presence or absence.