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# Epidemiology and economics of brucellosis in northern Tanzania

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Submitted in fulfilment of the requirements for the Degree of Doctor of Philosophy

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June 2023

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*For Joana and Ilda.*

# Abstract

Brucellosis is a bacterial zoonosis endemic in many low-resource settings where communities depend highly on livestock for their livelihood. In livestock, infection with *Brucella* spp. causes production impacts, including abortion and perinatal mortality. In humans, the disease is characterised by acute or intermittent symptoms, often followed by long-term complications. The social and economic impacts of brucellosis are often stated as significant, yet little empirical evidence exists to substantiate this claim and inform investment in disease control.

This study focused on northern Tanzania, where brucellosis is endemic. The main study objectives were to estimate (i) the production losses attributable to livestock brucellosis, (ii) the cost and disease burden attributable to human brucellosis, and (iii) the costs and benefits of potential interventions for brucellosis control.

In Chapter 2, key dynamics in models of livestock disease were explored. In Chapter 3, datasets with prevalence and production data were harmonised, and households were classified into pastoral and non-pastoral production systems using a clustering algorithm. In Chapter 4, a herd-growth model was used to estimate production losses attributable to livestock brucellosis in both systems. In Chapter 5, a Markov model was used to estimate the cost and disease burden (disability-adjusted life years, DALYs) attributable to human brucellosis in a pastoral context. In Chapter 6, a disease transmission model of livestock and human brucellosis was used to estimate the costs and benefits of livestock vaccination in the pastoral context.

The median (95% uncertainty interval) annual losses attributable to brucellosis in cattle, sheep, and goats, per infected animal, were 74.4 (26.2-211.7), 9.7 (3.4-23.1), and 10.6 (3.7-25.0) international dollars (int. $) in the pastoral system, and 62.3 (16.8-228.6), 6.3 (1.8-17.1), and 7.0 (2.2-17.9) int. $ in the non-pastoral system, respectively. The median cost and disease burden attributable to human brucellosis were estimated at 448.3 (345.2-577.8) int. $ and 1.6 (1.0-2.4) DALYs, per case. An investment of 1.4 (1.2-1.7) million int. $ in livestock vaccination would mitigate livestock and human impacts, averting 6.0 (2.9-14.5) million int. $ in monetary costs and 6,271 (2,492-12,362) DALYs.

This study has generated new and robust estimates that demonstrate the considerable impacts of brucellosis and the potential benefits of control interventions in northern Tanzania. The epidemiological-economic models developed in this study can be used to inform policy and decision-making for the control of brucellosis and other zoonoses in similar settings.

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# Acknowledgement

I want to convey my profound appreciation to everyone who supported me throughout my PhD at the School of Biodiversity, One Health & Veterinary Medicine (SBOHVM). Here, I found an exceptionally nurturing academic environment. I feel privileged for the support that I received and will always feel indebted to those who welcomed me so warmly at the Graham Kerr building and at the OHRBID (One Health Research in Bacterial Infectious Diseases) lab.

I want to express my deep gratitude to my supervisor, Jo Halliday, for believing in me and for being a constant source of inspiration and guidance throughout my PhD journey. Jo´s exceptional leadership, critical thinking and interdisciplinary skills were instrumental to my research. It has been an honour to work under Jo´s supervision. Thanks for the constant support, encouragement, and relentless effort to help me improve my work.

I am extremely grateful to Nick Hanley and Emma McIntosh, my co-supervisors, for their invaluable guidance and support as I began my journey in the fascinating field of economics. Their expertise, generosity, and patience enabled me to take my first steps in this field with confidence and enthusiasm.

I would like to extend my utmost appreciation to Dan Haydon, for teaching me the wonders of mathematical modelling and the importance of asking the right questions. I could not have done this PhD without Dan´s constant willingness to listen and answer my questions.

I feel indebted to the following members of the University of Glasgow community, at SBOHVM and School of Health and Wellbeing, for addressing many of my queries, generously providing feedback and, in many cases, sharing data resources: Simon Babayan, Francesco Baldini, Rebecca Bodenham, Stefano Catalano, Fergus Chadwick, Gemma Chaters, Jessica Clark, Sarah Cleaveland, Alicia Davis, Manuella Deidda, Will de Glanville, Eleanor Grieve, Katie Hampson, Paul Johnson, Stefanie Krauth, Tiziana Lembo, Kathrin Loosli, Chengetai Mpamhanga, David Pascall, Mafalda Viana, and Jennika Virhia.

I thank my colleagues and friends at the OHRBID lab for enriching my life with daily inspiring conversations, science discussions, and engaging social events. In particular, I'd like to thank Ryan Carter, Chiara Crestani, Christina Faust, Taya Forde, Kelsey Kiernan, Davide Pagnossin, Sreejith Radhakrishnan, Mohammad Sajib, and Maha Shalaby for their collegiality.

At the Kilimanjaro Clinical Research Institute and Kilimanjaro Christian Medical University College (Tanzania), I would like to thank Victor Katiti, Eliza Kussaga, Blandina Mmbaga, Fadhili Mshana, and Rigobert Tarimo for all the help during the expert elicitation exercise.

I greatly benefited from the constructive feedback and discussions with several members of the Global Burden of Animal Diseases (GBADs) programme, particularly Ben Huntington and Jonathan Rushton.

I am also deeply grateful for the contribution and support provided by many collaborators around the world. During my PhD, I was fortunate to receive inputs from (and often worked closely with) Justine Assenga (Ministry of Livestock and Fisheries, Tanzania), Abigail Colson (University of Strathclyde, United Kingdom), John Crump (University of Otago, New Zealand), James Hammond (International Livestock Research Institute, Kenya), Abdul Lukambagire (Sokoine University of Agriculture, Tanzania), Charles Mayenga (Tanzania Vaccine Institute, Tanzania), Nestory Mkenda (Endulen Hospital, Tanzania), Pilar Muñoz (Aragon Health Sciences Institute, Spain), Jamie Prentice (University of Edinburgh, United Kingdom), and Gabriel Shirima (The Nelson Mandela African Institution of Science and Technology, Tanzania).

My deepest heartfelt thanks go to my family and closest friends, especially my daughter, wife, parents, brother, Vera, Tó, Ana, and Lucinda, for all the unconditional love, trust, and patience during my absence.

Finally, I would like to acknowledge the financial support I received from the University of Glasgow, through the Lord Kelvin/Adam Smith (LKAS) PhD Scholarship.

# Author’s declaration

I declare that, except where explicit reference is made to the contribution of others, this thesis is the result of my own work and has not been submitted for any other degree or professional qualification at the University of Glasgow or any other institution.

# Abbreviations and acronyms

| | |
|---|---|
| Acc | Accuracy |
| AIDS | Acquired immune deficiency syndrome |
| ALE | Animal loss equivalent |
| ALL | Albanian lek |
| AT | Agglutination test other than RBT or BAPA |
| BA | Disease burden averted |
| BAPA | Buffered acidified plate antigen test |
| BBSRC | Biotechnology and Biological Sciences Research Council |
| BCR | Benefit-cost ratio |
| CAHW | Community animal health worker |
| CBA | Cost-benefit analysis |
| CBC | Complete blood count |
| CDC | Centers for Disease Control and Prevention |
| cELISA | Competitive enzyme-linked immunosorbent assay |
| CER | Cost-effectiveness ratio |
| CFR | Case-fatality ratio |
| CI | Confidence interval |
| Comm | Communication |
| CPC | Cost per case |
| CUA | Cost-utility analysis |
| DALY | Disability-adjusted life year |
| DNA | Deoxyribonucleic acid |
| DPC | Duration per case |
| DRC | Democratic Republic of Congo |
| ECDC | European Centre for Disease Prevention and Control |
| EE | Expert elicitation |
| EFSA | European Food Safety Authority |
| ELISA | Enzyme-linked immunosorbent assay |
| EQ-5D | European quality of life five-dimensional |
| EROS | Earth Resource Observation and Science |
| ESRI | Environmental Systems Research Institute |
| EU | European Union |
| EVI | Enhanced vegetation index |
| Exp | Expenditure |
| EZ | Eastern Zone |
| FAME | Foundation for African Medicine and Education |
| FAO | Food and Agriculture Organization of the United Nations |
| FBAT | Febrile *Brucella* agglutination test |

| | |
|---|---|
| FERG | Foodborne Disease Burden Epidemiology Reference Group |
| GADM | Global Administrative Areas |
| GALS | Gait, Arms, Legs and Spine |
| GALVmed | Global Alliance for Livestock Veterinary Medicines |
| Gamma | Gamma distribution |
| GBD | Global Burden of Disease |
| gCDA | Gross cost per DALY averted |
| GDP | Gross domestic product |
| GHE | Global Health Estimates |
| GNI | Gross national income |
| Gov | Government |
| GPS | Global positioning system |
| HB | Averted monetary costs in humans |
| HCA | Hierarchical cluster analyses |
| HCPC | Hierarchical clustering on principal components |
| HCS | Healthcare seeking |
| HCUS | Healthcare utilisation survey |
| HLY | Proportion of human cases losing immunity per year |
| ICRAF | International Centre for Research in Agroforestry |
| IDEA | Investigate, discuss, estimate, and aggregate |
| IDSR | Integrated disease surveillance and response system |
| IL | Israeli Shekels |
| ILRI | International Livestock Research Institute |
| INR | Indian rupee |
| Int. $ | International dollars |
| JAGS | Just Another Gibbs Sampler |
| KGS | Kyrgyzstani som |
| KSH | Kenyan Shillings |
| LB | Averted production losses in livestock |
| LCA | Latent-class analysis |
| LFA | Lateral flow assay |
| LDS | Locally delivered survey |
| LFO | Livestock field officer |
| LMIC | Low- and middle-income country |
| Lnorm | Log-normal distribution |
| LRL | Locally relevant literature |
| LSMS | Living Standards Measurement Study |
| Max | Maximum |
| MCMC | Markov Chain Monte Carlo |
| MFA | Multiple factor analysis |
| Min | Minimum |
| MNT | Mongolian Tugrik |

| | |
|---|---|
| MRC | Medical Research Council |
| MRDT / mRDT | Malaria rapid diagnostic test |
| MRT | Milk ring test |
| MSK | Musculoskeletal |
| NAHDIC | National Animal Health Diagnostic and Investigation Center, Ethiopia |
| NAY | Newborns per animal per year |
| nbinom | Negative binomial distribution |
| NBS | National Bureau of Statistics |
| NCA | Ngorongoro Conservation Area |
| nCDA | Net cost per DALY averted |
| NIHR | National Institute for Health Research |
| NPV | Net present value |
| NRL | Non-locally relevant literature |
| NVI | Norwegian Veterinary Institute |
| NVSL | National Veterinary Services Laboratory |
| NZ | Northern zone |
| OECD | Organisation for Economic Co-operation and Development |
| OHCD | One Health Coordinating Desk |
| OIE | *Office International Des Epizooties* |
| PCR | Polymerase chain reaction |
| PD | Person-day |
| PERT | Program evaluation review technique |
| PPP | Purchasing power parity |
| PPR | *Peste des petits ruminants* |
| Prdl | Productivity losses |
| Prob | Probability |
| Prop | Proportion |
| QGIS | Quantum Geographic Information System |
| QOLS | Quality of life scale |
| QWB | Quality of well-being scale |
| $R_0$ | Basic reproduction number |
| RBT | Rose Bengal test |
| $R_e$ | Effective reproduction number |
| RHoMIS | Rural Household Multiple Indicator Survey |
| RPT | Rivanol precipitation test |
| RVF | Rift Valley fever |
| SEEDZ | Social, Environmental and Economic Drivers of Zoonotic disease |
| Sens | Sensitivity |
| SF-36 | 36-Item Short Form Health Survey |
| SHZ | Southern Highlands Zone |
| SI | Susceptible-infected |
| SNAP-AMR | Supporting the National Action Plan on Antimicrobial Resistance |

| | |
|---|---|
| Spec | Specificity |
| SRTM | Shuttle Radar Topography Mission |
| SVLL | Statistical value of life lost |
| syll | Expectation of life at the time of death |
| targ | Target health-related expenditure |
| TB | Tuberculosis |
| TC | Total cost |
| TL | Turkish Lira |
| TSH | Tanzanian Shillings |
| UGX | Ugandan Shillings |
| UHC | Universal health coverage |
| UI | Uncertainty interval |
| UK | United Kingdom |
| USA | United States of America |
| USAID | United States Agency for International Development |
| USD | United States dollar |
| VIP | Ventilated improved pit latrine |
| VLA | Veterinary Laboratory Agency |
| VSLY | Value of statistical life-year |
| WAHIS | World Animal Health Information System |
| WHO | World Health Organization |
| WHOQOL | World Health Organization Quality-of-Life Scale |
| WOAH | World Organization for Animal Health |
| YHEC | York Health Economics Consortium |
| YLD | Years lived with disability |
| YLL | Years of life lost |
| zDALY | Zoonosis disability adjusted life years |

# Chapter 1

# Introduction

## 1.1 Background

Brucellosis is a disease caused by bacteria of the genus *Brucella*, which can infect a wide range of mammals, including humans, livestock, and wildlife (Corbel et al., 2006). The disease is one of the most widespread zoonoses globally, causing abortion and perinatal mortality in livestock and acute febrile illness, often followed by chronic, debilitating, musculoskeletal symptoms in humans (Bosilkovski, 2014).

Many high-income countries have eliminated brucellosis through multi-year, large-scale, costly interventions targeting the livestock sector, including mass vaccination campaigns, animal movement controls, and test-and-slaughter programs (Zhang et al., 2018). In contrast, in most low-resource settings, the disease remains endemic, and several factors have halted control actions or led to the failure of those implemented (Pappas et al., 2006; Rubach et al., 2013; WHO, 2015). Human and livestock brucellosis diagnosis, incidence estimation, and disease impact assessment are complicated by non-specific clinical manifestations and inadequate diagnostic tests and surveillance systems in these settings (Halliday et al., 2015). Other challenges faced by governments and stakeholders in low- and middle-income countries (LMICs) relate to (i) the lack of effective vaccines for multiple animal hosts and against all *Brucella* species, (ii) the safety risks associated with some of the currently available vaccines, and (iii) the knowledge gaps regarding factors that influence the effectiveness of livestock vaccination (Cleaveland et al., 2017; FAO, 2014).

Overcoming these challenges is vital to mitigate the impact of brucellosis in LMICs. An increasingly advocated approach to tackle existing obstacles is the integration of principles and tools from multiple disciplines and professions, as embodied in the concept of 'one health' (Cleaveland et al., 2017; Franc et al., 2018; Hermesh, Rosenthal, and Davidovitch, 2018). By enabling costs and benefits of control actions to be estimated from society's perspective, cross-cutting initiatives are more likely to be cost-beneficial and sustainable than those that take the viewpoint of human or animal health sectors individually (Bruce, 2016; Peck and Bruce, 2017; Roth et al., 2003; van Asseldonk, Bergevoet, and Ge, 2013). Close cooperation between public health and agricultural sectors (i) promotes savings through shared infrastructure, (ii) strengthens surveillance capacity, (iii) facilitates communication with affected communities, and (iv) improves the understanding of environmental, social, and cultural factors contributing to disease spread (Martins, Rushton, and Stark, 2016; Roth et al., 2003; Zinsstag et al., 2016). However, robust evaluation methods integrating epidemiology and economics and spanning both animal and human health are needed to provide funding agencies and policymakers in LMICs with reliable and context-specific evidence of the costs and benefits of different control strategies and to support optimal allocation of scarce resources (Cleaveland et al., 2017).

## 1.2 Epidemiology of brucellosis

The genus *Brucella* comprises a wide group of Gram-negative bacteria specially adapted to mammalian hosts, including livestock, wildlife, and humans (Corbel et al., 2006). The *Brucella* species that typically cause infection in people are *B. abortus*, *B. melitensis*, *B. suis* (biovars 1, 3, and 4) and, less frequently, *B. canis* (Corbel et al., 2006). The main hosts of these *Brucella* species are cattle, small ruminants (sheep and goats), pigs (also caribou, reindeer, and rodents), and dogs, respectively (Whatmore et al., 2016). Other *Brucella* species identified in terrestrial and marine mammals are *B. ovis* (sheep), *B. neotomae* (desert wood rats), *B. microti* (voles), *B. inopinata* (unknown main host), *B. papionis* (baboons), *B. vulpis* (foxes), *B. ceti* (porpoises, dolphins, and whales), and *B. pinnipedialis* (seals) (Whatmore et al., 2016).

A frequent transmission pathway between livestock species is exposure following an abortion (Fig. 1.1). *Brucellae* shed in aborted tissues infect susceptible livestock directly or contaminate the environment, which becomes a source of infection by ingestion, inhalation, conjunctival inoculation, or skin contamination (Corbel et

al., 2006). *Brucellae* can survive in the environment for several weeks to months, depending on factors such as temperature and humidity (Kaden et al., 2018; Scholz et al., 2008). The contact of livestock with infected wildlife (e.g., buffalo and wildebeest) may be epidemiologically relevant in some settings (Godfroid, 2018; Higgins, 2015; Simpson et al., 2021).

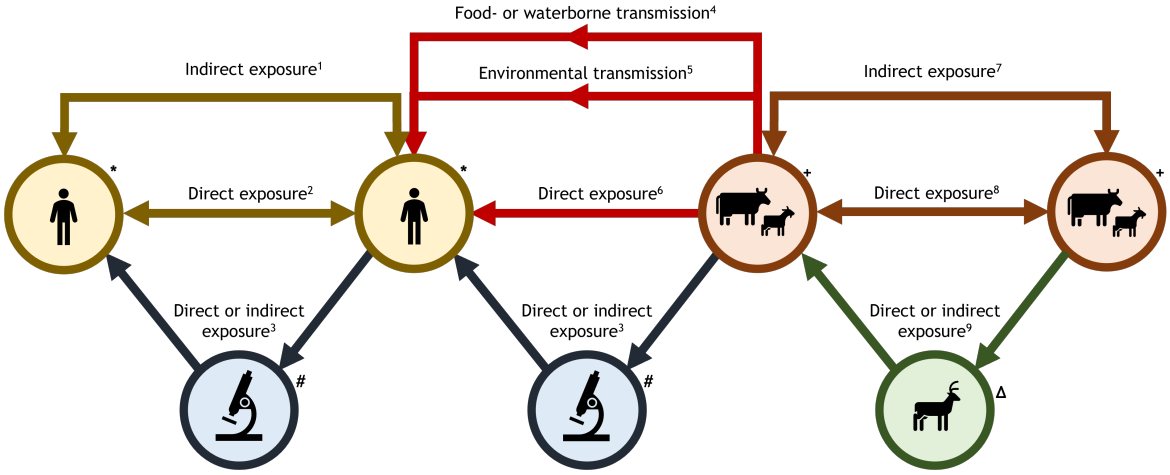



**Figure 1.1:** Main transmission pathways of brucellosis (based on Corbel et al., 2006). Examples: [1] Contamination of household or hospital surfaces. [2] Sexual transmission; breastfeeding; blood donation; tissue transplantation. [3] Diagnostic laboratory work; preparation and use of live vaccines. [4] Raw or undercooked dairy, red meat, blood and offal (liver, kidney, spleen, udder and testis); contaminated vegetables and water supplies due to abortions in the fields. [5] Contaminated surfaces due to movement of animals through populated areas; use of dry dung as fuel. [6] Assisting parturition and abortion at the farm; slaughtering animals and processing their products. [7] Contamination of pasture, livestock markets, lairages, and animal barns; pooled colostrum for newborn calves; artificial insemination. [8] Contact following an abortion; sexual transmission. [9] Contamination of pasture and contact following an abortion. * Humans. + Livestock. # Laboratory workers and technicians applying vaccines. Δ Wildlife.

Brucellosis can be transmitted from animals to humans through contact with infectious biological material (e.g., farmers assisting parturition, slaughtermen processing carcasses), contact with a contaminated environment (e.g., pastures where abortions have occurred, markets where animals are gathered, sheds where animals give birth), or consumption of contaminated water or foodstuffs (e.g., raw or

undercooked dairy and meat) (Corbel et al., 2006). Consumption of raw milk or raw dairy products is a frequent route of human infection with *Brucella* spp. globally (Béjaoui, Abdallah, and Maaroufi, 2022; Dadar, Shahali, and Whatmore, 2019; Onyango, Guitian, and Musallam, 2021).

Human-to-human transmission is rare (Mesner et al., 2007; Tuon, Gondolfo, and Cerchiari, 2017). However, this route might be overlooked in endemic areas where it is difficult to identify individual sources of infection (Meltzer et al., 2010). It has been estimated that approximately two-thirds of human-to-human transmission events are vertical (from an infected woman to the foetus) or occur during breastfeeding (Tuon, Gondolfo, and Cerchiari, 2017). Blood or organ transplantation and diagnostic work on infected material are also possible but less likely routes of transmission (Corbel et al., 2006).

Although brucellosis is often referred to as one of the most common zoonoses worldwide, the prevalence and incidence of this illness in humans and animals remain highly uncertain, and many estimates are misleading. For instance, a figure of 500,000 cases globally per year is frequently mentioned in the literature but lacks supporting evidence. Hundreds, if not thousands, of scientific articles cite this figure that was likely used for the first time by Ruiz-Castañeda in 1946 as a 'guess' for the number of human brucellosis cases in Europe and America (Laine, Scott, and Arenas-Gamboa, 2022; Moreno, Blasco, and Moriyon, 2022). Based on a systematic review of only 29 studies, a study commissioned by the WHO estimated 832,633 human brucellosis cases in 2010 globally, but the 95% uncertainty interval was between 337,929 and 19,560,440 (Kirk et al., 2015).

Inferring disease incidence estimates from routine surveillance and reporting platforms is not viable. The only intergovernmental organisation gathering information on human brucellosis incidence worldwide is the World Organization for Animal Health (WOAH). WOAH's World Animal Health Information System (WAHIS) gathers information on the number of human brucellosis cases each Member State reports annually. However, insufficient source data and poor compliance with the reporting requirements result in estimates of human brucellosis frequency worldwide that are incomplete and not representative. The reports submitted by WOAH's Members States in 2019 did not represent most of the world population (Laine, Scott, and Arenas-Gamboa, 2022). Non-compliance with the reporting requirements for notifiable livestock diseases by WOAH's Member states is also a known barrier to accurately estimating the incidence of animal brucellosis worldwide (Awada et al., 2020).

Despite the difficulties in estimating the global incidence of brucellosis in livestock and humans, patterns of spatial distributions are obvious from the WAHIS dataset and the literature in general. By the end of 2019, based on the WAHIS dataset, brucellosis, caused by *B. abortus*, *B. melitensis*, *B. suis*, or *B. ovis*, was absent in domestic animals of most northern European countries (e.g., United Kingdom, Ireland, Finland, Sweden, Norway, Denmark, and Germany), Canada, Australia, and New Zealand (World Organization for Animal Health, 2022). The disease was present in domestic animals or wildlife in southern Europe, including in Portugal, Spain, France, Italy, Croatia, Bosnia and Herzegovina, North Macedonia, and Albania. Human cases reported in Europe were often the result of infections occurring abroad or autochthonous and due to the consumption of locally produced or illegally imported raw dairy products (EFSA, 2021; Jansen et al., 2019). In the United States, *Brucella* persists in wildlife, particularly in elk and bison populations of Wyoming and Montana (Brennan et al., 2017; Proffitt et al., 2015; Rhyan et al., 2013). In contrast, brucellosis is endemic in livestock populations of many parts of Latin America, Africa, and Asia (Suresh et al., 2022). There is poor evidence of the incidence of human brucellosis in these regions (Dean et al., 2012b).

A limited number of studies have estimated the prevalence and incidence of brucellosis in livestock and humans in East Africa (Djangwani et al., 2021; Mengele et al., 2023a). In Tanzania, studies estimating the prevalence of brucellosis in livestock and humans, and published between 2009 and 2018 (Table 1.1), were (i) mostly cross-sectional, (ii) patchy in geographical coverage, and (iii) highly heterogeneous in diagnostic methodologies and prevalence estimates. The incidence of the disease in humans in the Kilimanjaro region has been estimated at 35 (range 32–93) cases per 100,000 persons annually in the period 2007-2008 and 33 (range 30-89) cases per 100,000 persons annually in the period 2012-2014 (Carugati et al., 2018). These incidence estimates were some of the first reported in sub-Saharan Africa.

**Table 1.1:** Characteristics and findings of studies estimating the seroprevalence of brucellosis in Tanzania between 2009 and 2018.

| Reference | Region | Diagnostic test / test provider / test site | % seropositive (sample size) | | | | Observations |
|---|---|---|---|---|---|---|---|
| | | | Humans | Cattle | Sheep | Goats | |
| Mellau et al. (2009)[1] | Arusha | (AT + RBT) / NR / LL | N/A | 10.0 (200) | 7.7 (13) | 11.5 (87) | Estimated prevalence is based on RBT positivity only. |
| Swai and Schoonman (2009)[1] | Tanga | RBT / VLA / LL | 5.5 (199) | N/A | N/A | N/A | Study participants were from several occupational groups. |
| Kunda et al. (2010)[1] | Arusha and Manyara | (RBT / NR / LL) + (ELISA / VLA / VLA) | 7.7 (395) | N/A | N/A | N/A | Estimated prevalence is based on ELISA positivity only. The number of tested participants was obtained from Kunda (2006) |
| Shirima et al. (2010)[1] | Arusha and Manyara | ELISA / VLA / VLA | 8.3 (460) | 5.7 (2,723) | | | Estimated prevalence in livestock combines cattle, sheep, and goats. |
| Swai and Schoonman (2010)[1] | Tanga | RBT / VLA / LL | N/A | 5.3 (654) | N/A | N/A | Traditional and smallholder dairy cattle were tested. |
| Bouley et al. (2012)[2] | Kilimanjaro | AT / NVSL / CDC | 3.5 (455) | N/A | N/A | N/A | Study participants were febrile patients. Prevalence estimate is based on a four-fold or greater rise in the antibody titer between acute and convalescent serum samples. |
| Swai and Schoonman (2012)[1] | Tanga | RBT / VLA / LL | N/A | 11.8 (51) | N/A | N/A | Sampled animals were slaughtered cattle (≥ 3 y old). |
| James (2013)[1] | Morogoro | RBT / NR / LL | 20.5 (1,807) | N/A | N/A | N/A | Most study participants (1,509) were febrile patients. |
| Lyimo (2013)[1] | Morogoro | (MRT + ELISA) / VLA / LL | N/A | 18.4 (450) | N/A | N/A | Estimated prevalence is based on MRT and ELISA positivity. |
| Shija et al. (2014)[1] | Dodoma and Morogoro | RBT / NR / LL | N/A | N/A | N/A | 0.0 (129) | Sampled animals were newly introduced Norwegian and crossbred Toggenburg goats. |
| Shirima et al. (2014)[1] | Dodoma | (RBT + ELISA) / VLA / LL | 10.0 (120) | 28.0 (483) | N/A | 0.0 (NR) | Prevalence in cattle refers to the first (year 2005) of multiple screenings and is based on RBT and ELISA positivity. |
| Assenga et al. (2015)[1] | Katavi and Rukwa | (RBT + ELISA / VLA) + (BAPA + RPT / NVSL) / LL | 0.6 (340) | 6.8 (1,103) | N/A | 1.6 (248) | Prevalence in humans is based on RBT, BAPA, and RPT positivity. Prevalence in cattle and goats is based on RBT and ELISA positivity. |
| Chipwaza et al. (2015)[1] | Morogoro | (ELISA / NovaTec®) + (AT / Span Diagnostics®) / LL | 11.4 (370) | N/A | N/A | N/A | Study participants were febrile children (2-13 y old). Estimated prevalence is based on probable prior exposure to *Brucella* spp., defined as a positive IgG ELISA result. |
| Chitupila et al. (2015)[1] | Kigoma | (RBT + ELISA) / VLA / LL | N/A | 5.6 (410) | N/A | N/A | Sampled animals were cattle aged ≥ 6 months. Estimated prevalence is based on RBT and ELISA positivity. |

Continuation of Table 1.1

| Reference | Region | Diagnostic test / test provider / test site | % seropositive (sample size) | | | | Observations |
|---|---|---|---|---|---|---|---|
| | | | Humans | Cattle | Sheep | Goats | |
| Mathew et al. (2015)[1] | Mbeya | (RBT / VLA) + (ELISA / Svanova®) / NVI | N/A | 18.0 (200) | 0.0 (35) | 0.0 (50) | Sampled animals were from one farm. Estimated prevalence is based on RBT and ELISA positivity. |
| Mfune (2015)[1] | Mbeya and Tanga | (RBT + LFA + ELISA) / (Prionics AG® + Ubio®)/ LL | N/A | 0.0 (400) | N/A | N/A | Estimated prevalence is based on RBT and LFA positivity; 21 samples (5.3%) were positive on ELISA. |
| Orsel et al. (2015)[1] | Arusha | (AT / Euromedi®) + (ELISA / Biosupply®) / LL | 5.7 (159) | N/A | N/A | N/A | Study participants were patients with malaria-like febrile illness. Estimated prevalence is based on positivity at the agglutination test. |
| Chota et al. (2016)[1] | SHZ, NZ, EZ | (RBT + ELISA) / NR / LL | 28.2 (578) | 7.2 (1,376) | N/A | N/A | Estimated prevalence in cattle is based on RBT and ELISA positivity. Human brucellosis prevalence is based on health centre records. |
| Mngumi et al. (2016)[1] | Mwanza | AT / Euromedi® / LL | 14.1 (382) | N/A | N/A | N/A | Study participants were from ten agro-pastoral villages. |
| Shirima and Kunda (2016)[1] | Mara | (RBT + ELISA) / VLA / LL | 0.0 (82) | 7.8 (296) | 0.0 (117) | | Estimated prevalence is based on RBT and ELISA positivity. Sheep and goats are combined. |
| Kassuku (2017)[1] | Morogoro | (RBT + ELISA) / NR / LL | N/A | N/A | N/A | 0.2 (478) | Estimated prevalence is based on RBT and ELISA positivity. |
| Kayombo et al. (2017)[1] | Manyara | (RBT + BAPA + ELISA) / VLA / LL | N/A | 4.2 (192) | N/A | N/A | Estimated prevalence is based on RBT or BAPA positivity, confirmed with ELISA. |
| Mathew et al. (2017)[1] | Mbeya and Njombe | ELISA / Svanova® / NVI | N/A | 5.4 (658) | N/A | N/A | Study reports prevalence estimates in Mbeya and Njombe regions separately. |
| Mhozya (2017)[1] | Geita | (RBT + ELISA) / NR / LL | N/A | 1.4 (219) | N/A | N/A | Estimated prevalence is based on RBT and ELISA positivity. |
| Nonga and Mwakapeje (2017)[1] | Arusha | AT / NR / LL | 5.8 (13,642) | N/A | N/A | N/A | Estimated prevalence is based on clinical records. |
| Sijapenda et al. (2017)[1] | Lindi | (RBT + ELISA) / VLA / LL | N/A | 5.2 (300) | N/A | N/A | Estimated prevalence is based on RBT and ELISA positivity. |
| Asakura et al. (2018a)[1] | Morogoro | (RBT / IDvet®) + (ELISA / Svanova®) / LL | N/A | 2.2 (1,340) | N/A | N/A | Study reports prevalence estimates in urban and agro-pastoral areas separately. |
| Carugati et al. (2018)[2] | Kilimanjaro | AT / NVSL / CDC | 4.8 (946) | N/A | N/A | N/A | Study participants were febrile patients. Prevalence estimate is based on a four-fold or greater rise in the antibody titer between acute and convalescent serum samples. |

Continuation of Table 1.1

| Reference | Region | Diagnostic test / test provider / test site | % seropositive (sample size) | | | | Observations |
|---|---|---|---|---|---|---|---|
| | | | Humans | Cattle | Sheep | Goats | |
| Cash-Goldwasser et al. (2018)[2] | Kilimanjaro | AT / NVSL / CDC | 6.9 (562) | N/A | N/A | N/A | Study participants were febrile patients. Prevalence estimate is based on a four-fold or greater rise in the antibody titer between acute and convalescent serum samples. |
| Mengele et al. (2018)[1] | Dodoma | (RBT / VLA / LL) + (ELISA / APHA Scientific® / NAHDIC) | N/A | 0.9 (545) | N/A | N/A | Estimated prevalence is based on RBT and ELISA positivity. |
| Mirambo et al. (2018)[1] | Mwanza | AT / Euromedi® / LL | 48.4 (250) | N/A | N/A | N/A | Study participants were abattoir workers and meat vendors. |
| Mujuni et al. (2018)[1] | Mwanza | AT / Euromedi® / LL | 37.9 (398) | N/A | N/A | N/A | Study reports prevalence estimates for women with spontaneous abortion and women with full-term delivery separately. |
| Sagamiko et al. (2018)[1] | Mbeya | (RBT / Ubio®) + (ELISA / Svanova®) / LL | N/A | 9.3 (1,211) | N/A | N/A | Study reports prevalence estimates in indigenous and exotic breeds of cattle separately. |
| Shirima et al. (2018)[1] | Morogoro | (MRT + ELISA) / VLA / LL | N/A | 21.3 (390) | N/A | N/A | Estimated prevalence is based on MRT and ELISA positivity. |

AT: agglutination test other than RBT or BAPA; BAPA: buffered acidified plate antigen test; CDC: Centers for Disease Control and Prevention, USA; ELISA: enzyme-linked immunosorbent assay; EZ: Eastern Zone; LFA: Lateral flow assay; LL: local laboratory; MRT: Milk ring test; N/A: not estimated; NAHDIC: National Animal Health Diagnostic and Investigation Center, Ethiopia; NR: not reported; NVI: Norwegian Veterinary Institute; NVSL: National Veterinary Services Laboratory, USA; NZ: Northern zone; RBT: Rose Bengal test; RPT: rivanol precipitation test; SHZ: Southern Highlands Zone; VLA: Veterinary Laboratory Agency, UK. [1]cross-sectional; [2]longitudinal. Companies: bioMérieux®, USA; Biosupply® UK Ltd, UK; Boehringer Ingelheim Svanova®, Sweden; Euromedi® Equip Ltd, UK; IDvet®, France; NovaTec® immundiagnostica GmbH, Germany; Prionics AG®, Schlieren, Switzerland; Span Diagnostics® Ltd, India; Ubio® Biotechnology Systems Pvt Ltd, India.

## 1.3 Diagnosis of brucellosis

### 1.3.1 Human brucellosis

Human brucellosis typically presents with acute or intermittent fever, malaise, sweats, and joint pain (Dean et al., 2012a). If left untreated, these symptoms often persist, progressing into chronic forms, and potentially resulting in severe complications such as meningitis and endocarditis (Jin et al., 2023). Pregnant women may suffer stillbirth while men may develop epididymo-orchitis (Akhvlediani et al., 2017; Jiang et al., 2019; Pericherla, Gupta, and Saravu, 2021; Roushan et al., 2004; Rujeni and Mbanzamihigo, 2014). Routine hemogram and biochemical analyses do not show specific changes in people with brucellosis, making it difficult to distinguish from other febrile illnesses like malaria, typhoid, and trypanosomiasis, which may be present in brucellosis-endemic settings (Crump et al., 2013; Dean et al., 2012a; Moreno, Blasco, and Moriyon, 2022). Diagnosis is further complicated by (i) the existence of multiple diagnostic protocols and criteria published or supported by international organisations and (ii) challenges in access to many of the recommended diagnostic methods, including bacterial culture (for detection of *Brucella* spp. in biological samples) and some serological tests (for detection and quantification of antibodies against *Brucella* spp. in serum samples) (Corbel et al., 2006; European Commission, 2018; Government of The United Republic of Tanzania, 2018a; U.S. Centers for Disease Control and Prevention (CDC), 2017).

In Tanzania, national guidelines for surveillance of zoonotic diseases indicate the screening of suspected brucellosis cases with the Rose Bengal Test (RBT) or Rivanol precipitation test and confirmation with molecular methods (e.g., polymerase chain reaction, PCR) or bacterial culture (Government of The United Republic of Tanzania, 2018a). However, access to these recommended diagnostic tests is limited in Tanzania and the broader East Africa region. Instead, febrile *Brucella* agglutination tests (FBATs), which have poor performance and are not recommended, are frequently used. FBATs are considered cheap, easy, and fast to process (Alumasa et al., 2021; de Glanville et al., 2017; Kiambi et al., 2020; Lukambagire et al., 2021, 2022).

In a recent survey of brucellosis testing patterns at health facilities in the Arusha region, Tanzania, the first and second most commonly used FBATs, Eurocell and Fortress, were present in 17 (94.4%) and 10 (55.6%) out of 18 surveyed health facilities, respectively (Lukambagire et al., 2022). The diagnostic sensitivity of Eurocell and Fortress has been estimated at 50.0% and 28.6%, respectively, indicating

a high probability of false negative test results, with potential delays in effective treatment prescription (Lukambagire et al., 2021). The diagnostic specificity of Eurocell and Fortress has been estimated at 55.4% and 75.0%, respectively, indicating a high probability of false positive test results in the region, with a potentially high frequency of unnecessary brucellosis treatments and associated consequences (e.g., drug toxicity, antimicrobial resistance) (Alumasa et al., 2021; Lukambagire et al., 2021). Researchers investigating the cost-effectiveness of diagnostic tests used in East Africa have called for the replacement of commercial plate agglutination tests with the Rose Bengal test (RBT), a test that performs better (with a sensitivity between 78.6% and 85.7%, and specificity between 96.6% and 99.0%; estimates of two RBT dilution protocols (Lukambagire et al., 2021)) and costs less to run (US$ 0.69–0.79 per sample, compared to US$ 1.03–1.14 with commercial plate agglutination tests) (Alumasa et al., 2021; Lukambagire et al., 2021).

### 1.3.2 Livestock brucellosis

The clinical manifestations of brucellosis in livestock include abortion, infertility, reduced milk production, and weight loss. Given the non-specific nature of these clinical manifestations, as for human brucellosis, the diagnosis of livestock brucellosis relies mainly on demonstrating the presence of *Brucella* spp. in biological samples or detecting a serological reaction to the bacterium (Corbel et al., 2006).

Bacteriological culture is the recommended method for demonstrating the presence of *Brucella* spp. in biological samples such as abortion materials, uterine discharges, and milk. Overall, the positive predictive value of culture is high, but the sensitivity is low, i.e., isolation of *Brucella* spp. provides definite diagnostic evidence of brucellosis, but many infected animals have negative culture results (Corbel et al., 2006). Culture is time-consuming, technically demanding, and poses significant safety risks to laboratory staff. Alternative methods for demonstrating the presence *Brucella* spp. include modified acid-fast staining and PCR (OIE, 2019).

Methods for serological diagnosis of brucellosis in livestock include buffered *Brucella* antigen tests (e.g., RBT), the complement fixation test, enzyme-linked immunosorbent assays (ELISA), and the fluorescence polarisation assay. RBT is likely the most economical and practical method for low-resource settings (Díaz et al., 2011). The indirect ELISA and milk ring test can detect the presence of antibodies against *Brucella* spp. in bulk milk samples, which can be used for herd-level screening in the dairy sector (OIE, 2019).

## 1.4 Treatment of brucellosis

### 1.4.1 Human brucellosis

The treatment of human brucellosis is complex and should be adapted to each patient, depending on disease severity and the presence of complications and underlying medical conditions. The core of brucellosis treatment requires a combination of antimicrobial drugs administered for several weeks (Yousefi-Nooraie et al., 2012).

In adults and children over seven years old with uncomplicated brucellosis, the standard treatment consists of doxycycline (100 mg, orally) twice a day for six weeks plus an aminoglycoside, often streptomycin (1 g, intramuscularly) daily for two to three weeks (Corbel et al., 2006). The parenteral administration of streptomycin requires repeat visits to a healthcare facility, which is inconvenient in remote areas and may cause patients to discontinue the treatment. An alternative treatment regime combines doxycycline (100 mg, orally) twice a day with rifampicin (600–900 mg, orally) daily, both for six weeks. The standard treatment with doxycycline and streptomycin is safer and more effective than the alternative treatment with doxycycline and rifampicin (del Pozo and Solera, 2012; Meng, Pan, and Tong, 2018; Yousefi-Nooraie et al., 2012). Other antimicrobial drugs and treatment regimes longer than six weeks with or without surgery may be required in cases of osteoarticular involvement or other complications such as meningitis and endocarditis. The prescription of rifampicin for treating brucellosis is not recommended in areas with high tuberculosis prevalence to avoid the emergence of multi-drug resistant *Mycobacterium tuberculosis* strains (Alavi and Alavi, 2013).

Treating brucellosis in children under the age of eight years is particularly challenging. There is little evidence of the effectiveness of antimicrobial treatments in these patients, and tetracyclines are contraindicated due to their potential inhibiting effect on bone growth (Corbel et al., 2006). In these cases, a treatment with trimethoprim-sulfamethoxazole (10 mg/kg per day of trimethoprim divided into two doses) in addition to rifampicin (15–20 mg/kg per day in one or two doses) is often recommended (Gopinathan, Menon, and Fernandes, 2022; Young, 2023).

### 1.4.2 Livestock brucellosis

The treatment of brucellosis in livestock is not recommended due to the high cost, probability of relapse, and potential consequences to public health (e.g., the emergence of antimicrobial resistance) (Caswell, Arenas-Gamboa, and Foster, 2022; Wareth et al., 2021).

## 1.5 Brucellosis impact estimation

### 1.5.1 Human brucellosis

#### 1.5.1.1 Monetary costs attributable to human brucellosis

Cost of illness studies aim to quantify the economic cost of a disease in monetary terms. These cost analyses can be performed from multiple perspectives, reflecting the multiple agents that can bear the cost of a disease, such as households, the national health service, or society in general. The types of costs considered are often classified as follows (Kernick, 2002):

- Direct: expenditure incurred by households or the health service because of the disease (e.g., drugs).
- Indirect: economic consequences of morbidity and premature mortality attributable to the disease (e.g., productivity losses).
- Intangible: consequences of a disease that are difficult to quantify in monetary terms (e.g., pain and suffering).

Cost of illness studies can be classified into different types, based on the following approaches (Jo, 2014):

- Prevalence- vs. incidence-based approaches
  Prevalence-based studies estimate the costs associated with a disease in a specific time period (e.g., a year). Incidence-based studies estimate the lifetime costs associated with individual cases of a disease.
- Prospective vs. retrospective approaches
  Retrospective studies gather cost data relative to disease events that happened in the past. Prospective studies gather cost data by following patients over time.
- Top-down vs. bottom-up vs. econometric approaches

The top-down approach applies the epidemiological concept of attributable risk to derive how much of an aggregated cost estimate (covering multiple diseases or conditions) is attributable to a specific disease. The bottom-up approach estimates the cost of a disease by multiplying the volume of health inputs used by the unit costs of health inputs. The econometric approach estimates the cost attributable to a disease as the difference between the costs in a cohort with the disease and the costs in a cohort without the disease.

In LMICs, the cost of human brucellosis has been estimated mostly through prevalence-based, retrospective, bottom-up approaches (Alshwany, 2019; Bruce, 2016; Kasymbekov, 2014; Singh et al., 2018a; Vered et al., 2015). A recurrent problem with these studies is that hospital records or national reporting data systems are often used to inform disease frequency and severity estimates. This may be misleading in many LMICs because those systems capture only a fraction of all brucellosis cases, and the recorded information is highly inaccurate. In these settings, for each person with serological evidence of *Brucella* infection at a hospital (which is not, in itself, indicative of active disease), many remain undiagnosed in the community (Gargouri et al., 2009). It has been reported that the true incidence of brucellosis in Kyrgyzstan and Mongolia may be over 10 times higher than officially recorded (Bonfoh et al., 2012; Kasymbekov, 2014; Zolzaya et al., 2014). In Kyrgyzstan, there were 77.5 new reported human brucellosis cases per 100,000 people in 2007. However, based on serological analyses, the incidence of seroconversion was approximately 11 times higher (880 per 100,000; 95% CI: 400–1,770) (Bonfoh et al., 2012). In Zavkhan, a province in Mongolia, assuming that 50% of seropositive brucellosis cases have clinical symptoms, the incidence of clinical brucellosis (1,188 per 100,000 people; 95% CI: 930–1,500) would be 59 times higher than previously reported (20 per 100,000 people). In Albania, to account for the imperfect knowledge of disease frequency, an under-reporting factor of 2.5 was used to calculate the upper estimate for the annual costs of human brucellosis (Bruce, 2016). In Iran, an under-reporting factor of 10 was used to estimate the true incidence of human brucellosis (Bakhtiar et al., 2019).

Approaches based on under-reporting factors to account for the limited data on disease frequency cannot differentiate between the economic impacts of the disease in cases that seek care and are diagnosed versus the impact in cases that do not seek care or are misdiagnosed. Although many of the latter cases, who do not seek care or are misdiagnosed, may have a mild, self-limited illness, they are likely

to incur costs of self-treatment or productivity losses that are often not considered by studies to date (Bruce, 2016; Vered et al., 2015). As a result, current approaches are likely to underestimate the true impact of brucellosis in a population, which may affect policymakers' motivation to develop targeted control interventions.

Another limitation of previously used methods to estimate the cost of human brucellosis is the inability to capture disease progression, particularly the differences between the acute and chronic stages. Capturing disease progression is important because different stages of brucellosis are associated with different levels of disability and, consequently, different impacts on productivity and healthcare costs. This limitation of current approaches may be particularly relevant in LMICs, where delayed healthcare seeking and diagnosis increase the likelihood of long-lasting and debilitating complications. Evidence from the pre-antibiotic era in Russia indicates the chronic symptoms of brucellosis were common two years after the onset of the disease (Wundt, 1968).

Despite the limitations of previous methods used to estimate the cost of brucellosis, a small number of studies have shown that the disease is likely to cause catastrophic and impoverishing healthcare expenditure and income loss in many settings (Bruce, 2016). In Kyrgyzstan, the sum of mean private health costs (including diagnosis, formal and informal treatment and travel costs) and household income loss per case (2,606 international dollars, int. $)[1] was greater than the GDP per capita (2,505 int. $ in 2006)[2] (Kasymbekov, 2014). In other countries, relatively lower but highly variable cost estimates have been reported. In Albania, the median loss of income and out-of-pocket payments per case (not including costs of self-treatment or informal healthcare) amounted to 3,150 int. $[3], which was approximately 31% of the GDP per capita (10,208 int. $ in 2011)[4] (Bruce, 2016). In East Africa, estimates of the mean cost per brucellosis case varied from 241 int. $[5] in Tanzania (health-related expenditure, including transport, diagnosis, and treatment costs, and assuming a disease duration of 12 months) (Kunda, 2006) to 648 int. $[6] in Uganda (health-related expenditure and productivity loss) (Guma et al.,

1. Based on the World Bank conversion factor of 9.847 KGS (Kyrgyzstani som) per int. $ in 2006 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=KG
2. Sourced from the World Bank at https://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD?locations=KG
3. Based on the World Bank conversion factor of 55.588 ALL (Albanian lek) per int. $ in 2011 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=AL
4. Sourced from the World Bank at https://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD?locations=AL
5. Based on the World Bank conversion factor of 385.223 TZS (Tanzanian shillings) per int. $ in 2003 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=TZ
6. Based on the World Bank conversion factor of 1,172.630 UGX (Ugandan shillings) per int. $ in 2016 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=UG

2020), which were equivalent to 17 and 31% of the GDP per capita (1,407 int. $[7] in Tanzania in 2003 and 2,092 int. $[8] in Uganda in 2016), respectively. However, these estimates of costs per case vary widely, depending on the distance from households to health facilities and number of visits made. In neighbouring Kenya, in Kajiado County, brucellosis cases in rural areas spent on average 42 int. $ just in transport to the nearest health facility, per visit (Mutua, 2017)[9].

The number of work days lost per brucellosis case is often stated as significant, but there is little quantitative evidence supporting this statement, particularly in LMICs (Buttigieg et al., 2018; Franc et al., 2018). Most available evidence on the number of work days lost due to brucellosis is from the 1970s and 1980s, in the United States and Spain (Anderson et al., 1978; Colmenero-Castillo et al., 1989; Hendricks et al., 1962; White et al., 1974). In these countries, the reported average number of work days lost due to brucellosis varied from 3 to 102 days per patient per episode.

At the household level, the productivity losses and out-of-pocket expenditure due to brucellosis are likely to reduce the consumption of non-health-related goods and services, lower investment in human and social capital (e.g., education), and, possibly, lead to liquidation of household assets and resorting to loans. These socioeconomic repercussions are likely to contribute to widening gender inequalities and worsen social oppression and dependency among women (Franc et al., 2018). In men, infertility due to brucellosis epididymo-orchitis may be associated with social stigma (Inhorn, 2004; Ntirandekura et al., 2018).

#### 1.5.1.2 Disease burden attributable to human brucellosis

Disease burden is a concept that is often used to describe the non-monetary impact of a disease on a population's health and well-being. The burden attributable to a disease is generally expressed in terms of time lost due to premature death and time lived in less-than-optimal health states (Jo, 2014). One of the most widely used metrics is the DALY (disability-adjusted life-year), which is the sum of years of life lost and years lived with disability, adjusted for disease severity (Murray, 1994).

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7. Sourced from the World Bank at `https://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD?locations=TZ`
8. Sourced from the World Bank at `https://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD?locations=UG`
9. Based on the World Bank conversion factor of 39.312 KSH (Kenyan Shillings) per int. $ in 2015 obtained from `https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=KE`

Many of the limitations and considerations mentioned concerning the monetary cost estimation methods also apply to disease burden estimation. Some of these limitations, namely those associated with the inability to capture the progressive nature of the disease, have prompted authors to argue against the usefulness of disease burden estimates in the context of brucellosis (Moreno, Blasco, and Moriyon, 2022). Additionally, studies of disease burden attributable to brucellosis are characterised by significant methodological heterogeneity, compromising the comparability purpose of such estimates for policy-making and priority setting (Di Bari et al., 2022). For brucellosis burden estimates to be useful in informing intervention development and policy decisions, the duration and disability weights must accurately represent the progressive nature of the disease in each context.

There is a large number of publications describing the clinical manifestations of brucellosis, but the direct impacts of the disease on patient's daily activities, including work and leisure, are still poorly characterised (Angle, 1935; Buzgan et al., 2010; Castaneda, 1986; Dalrymple-Champneys, 1960; De Villafañe-Lastra, 1950; Dean et al., 2012a; Evans, 1934; Karsen et al., 2012; Liu et al., 2020b; Spink, 1956; Zheng et al., 2018). The diagnostic difficulties and variable clinical presentations and disease duration have challenged the estimation of morbidity indicators for brucellosis (Moreno, Blasco, and Moriyon, 2022). There are currently no internationally published quality of life scores for people living with brucellosis in Africa, based on standard instruments such as WHOQOL (World Health Organization Quality-of-Life Scale), SF-36 (36-Item Short Form Health Survey), QWB (Quality of Well-Being Scale), QOLS (Quality of Life Scale), or EQ-5D (European Quality of Life five-dimensional). A study performed in Mexico using SF-36 found that brucellosis patients, particularly in rural areas, had a significantly lower overall quality of life than those without brucellosis (Garcia-Juarez et al., 2012). Another study in Russia found significant improvements in SF-36 scores after treatment of brucellosis orchitis patients (Lyapina et al., 2015).

A commonly used indicator of morbidity is the 'disability weight', a weighting factor that indicates the relative severity of a health state. A disability weight can take a value from 0 (reflecting a state of full health) to 1 (equivalent to death) (Mathers et al., 2001). After more than a decade of published brucellosis burden estimates, there is still no consensus regarding the disability weights that best reflect the severity of brucellosis clinical manifestations, the duration estimates to which these weights apply, and the proportion of people with brucellosis who de-

velop various complications (Moreno, Blasco, and Moriyon, 2022). A wide range of disability weights and duration estimates have been used to represent the clinical manifestations of brucellosis: from 0.092 for two weeks (Lai et al., 2020) to 0.2 for 4.5 years (Guma et al., 2020; Kunda, 2006; Singh et al., 2018a).

Evidence of brucellosis-induced mortality and age distribution of fatal cases is needed for disease burden estimation. Time loss due to death is a critical and highly influential component of the disease burden. Available estimates of human brucellosis case-fatality ratios (CFR) in LMICs are scarce and vary widely within and between settings. In a hospital-based survey in Tanzania, which likely enrolled more severe cases in contrast to a community-based survey, five out of 98 brucellosis cases (diagnosed with RBT and competitive enzyme-linked immunosorbent assay (cELISA)) died of brucellosis, which is equal to a CFR of 5.1% (Kunda, 2006). CFR estimates of 0.1%, 0.9%, 0.9%, 0.9%, and 1.5% have been reported in Egypt (using 1,364 brucellosis cases as the denominator, 1999–2003; hospital-based survey), Germany (58 deaths out of 6,269 cases, 1962–2005; national surveillance data complemented with a questionnaire-based survey), the European Union (one death out of 107 cases with reported outcome, 29.9% of all confirmed cases in the EU, 2014–2018; EU-level surveillance; most confirmed cases [71.1%] were hospitalised), Turkey (five deaths out of 536 cases, 1998-2007; hospital-based survey), and Spain (84 deaths out of 5,598 brucellosis cases, 1997-2015; survey of hospitalised cases), respectively (Afifi et al., 2005; Al Dahouk et al., 2007; Buzgan et al., 2010; EFSA and ECDC, 2019; Rodríguez-Alonso et al., 2021). Age distribution of fatal cases is seldom reported, and the global burden of foodborne disease study assumed a constant CFR by age group for brucellosis burden estimation (Kirk et al., 2015). Under this assumption, only 3% of brucellosis-induced deaths occur in the age group over 65 years old, which contrasts with evidence from a retrospective longitudinal study in Spain, which indicated that 69% of deaths occurred in this age group (Rodríguez-Alonso et al., 2021).

The methodological heterogeneity that characterises brucellosis DALYs estimation studies and the DALYs estimates obtained in these studies are shown in Table 1.2. Historically, age weighting and time discounting have been two key sources of methodological heterogeneity. Both were incorporated by the Global Burden of Diseases (GBD) 1990 study but later dropped. For the GBD 2010, experts advised against discounting future health loss (time discounting) or giving less weight to years of healthy life lost at young ages and older ages (age weighting) (WHO, 2020). Most studies in Table 1.2 also did not apply time discounting or age weighting. Other important sources of methodological heterogeneity are the inclusion of brucellosis-induced mortality, the choice of disability weights and the disease duration con-

sidered. Although most studies included years of life lost due to brucellosis-induced mortality in disease burden estimation, many studies assume that brucellosis does not cause death. The studies that included brucellosis-induced mortality often use data sources that do not clearly specify the technical methods (i.e., autopsy, clinical diagnosis, death certification) and criteria for death attribution. Fixed disability weights between 0.15 and 0.23 or disease stage-specific disability weights have been used. The disease duration considered by most studies varied from 75 days (0.21 years) to 4.5 years.

**Table 1.2:** Studies on disease burden attributable to brucellosis, methods used, and DALYs (disability-adjusted life years) per case.

| Study | | | Methods/variables included | | | | | | DALYs per case | |
|---|---|---|---|---|---|---|---|---|---|---|
| First author | Year[1] | Area | Mortality | Age weight | Discounting | Disability weight[6] | Duration (years)[7] | UR correction | Value | Mean/Median, estimated/reported[9] |
| Kunda | 2006 | Tanzania | Yes | No[5] | Yes | 0.20 | 4.50 | No | 1.36 | NR, estimated |
| Gkogka | 2011 | Greece | Yes | No | No | 0.20 | 3.11 | Yes | 0.71 | NR, estimated |
| Fèvre | 2013 | Kenya | No | NR | NR | 0.19 | 0.50 | No[8] | 0.10 | NR, estimated |
| Angara | 2014 | Sudan[2] | No | Yes | Yes | 0.20 | 3.00 | NR | 1.00 | NR, reported |
| Kirk | 2015 | Africa | Yes | No | No | Acute, severe: 0.21 | Acute: 0.04 | Yes | 0.33 | Median, estimated |
| | | | | | | Acute, moderate: 0.05 | Chronic: 0.50 | | | |
| | | | | | | Chronic: 0.08 | | | | |
| | | | | | | Orchitis: 0.10 | | | | |
| Havelaar | 2015 | Africa (E) | Yes | No | No | As in Kirk, et al. 2015 | As in Kirk, et al. 2015 | Yes | 0.30 | Median, reported |
| Counotte | 2016 | Kyrgyzstan | Yes | No | No | As in Kirk, et al. 2015 | As in Kirk, et al. 2015 | Yes | 0.29 | Median, reported |
| Singh | 2018a | India | No | No[5] | No[5] | 0.20 | 4.50 | No | 0.90 | NR, estimated |
| Piroozi | 2019 | Iran | Yes | No | Yes | 0.23 | 0.75 | Yes | 0.28 | NR, estimated |
| Alshwany | 2019 | Iraq[3] | No | NR | NR | 0.19 | 4.50 | No | 0.86 | NR, estimated |
| Charypkhan | 2019 | Kazakhstan | Yes | No | NR | 0.15 | 0.21 | No | 0.50 | Mean, reported |
| Guma | 2020 | Uganda[4] | No | NR | NR | 0.20 | 4.50 | No | 0.90 | NR, estimated |
| Lai | 2020 | Taiwan | No | No | No | 0.09 | 0.04 | No | 0.004 | NR,estimated |
| Peng | 2020 | China | Yes | NR | Yes | Acute: 0.13 | Acute: 0.04 | No | 0.13 | Mean, estimated |
| | | | | | | Chronic: 0.15 | Chronic: 2.00 | | | |
| Alumasa | 2021 | Kenya | No | No | No | 0.15 | 4.50 | No | 0.68 | NR, reported |

Africa E: Stratum defined based on child and adult mortality (Ezzati et al., 2002); for more information, see footnote in page 39. NR: Not reported. UR correction: correction of incidence for under-reporting. [1] Year of publication. [2] Khartoum State. [3] Kurdistan Region. [4] Adjumani district. [5] Estimates with age weighting or discounting may be available. [6] Fixed value or mode, rounded to two decimals places. [7] Fixed value, mode, or average, rounded to two decimals places. [8] The study may include correction for under-reporting. [9] If DALYs per case were not reported, an estimate was obtained through one of the following ways: i) the product of disability weight and disease duration if the study did not include brucellosis-induced mortality; and, ii) the quotient of total DALYs reported and number of cases if the study included brucellosis-induced mortality.

As a consequence of the methodological heterogeneity mentioned above, the estimated burden caused by brucellosis per case varies significantly between studies (Table 1.2): from 0.004 DALYs in Taiwan (Lai et al., 2020) to 1.36 DALYs in Tanzania (Kunda, 2006). At the population level (DALYs per 100,000 people), the burden attributable to brucellosis also varies significantly between studies. This could be attributed to differences in disease frequency (prevalence or incidence) and disease management practices between settings, but there is significant variation in population-level burden even where settings are similar. In a specific study commissioned by the WHO, the median burden of foodborne brucellosis in some African countries[10] was 0.3 DALYs per 100,000 people in 2010 (Havelaar et al., 2015). Assuming that the proportion of brucellosis that is of foodborne origin is 47% (30%–61%), this estimate of 0.3 DALYs per 100,000 people is equivalent to 0.6 DALYs per 100,000 people for all sources (foodborne and non-foodborne) (Kirk et al., 2015). Other studies carried out in some of these countries reported estimates of disease burden attributable to brucellosis several orders of magnitude greater (DALYs per 100,000 people): 11 in Ethiopia (FAO, 2018b), 15 in Tanzania (Kunda, 2006), 73 in Uganda (FAO, 2018c) and 117 in Kenya (FAO, 2018d).

Many of the current estimates of disease burden attributable to human brucellosis are highly uncertain (Di Bari et al., 2022). This large uncertainty compromises the applicability of these estimates in policy-making and priority setting. For instance, the global burden of foodborne disease study reported a 95% uncertainty interval (UI) of between 100,540 and 6,187,148 DALYs attributable to brucellosis globally, based on an absolute incidence (95% UI) between 337,929 and 19,560,440 cases, in 2010 (Kirk et al., 2015).

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10. Stratum E: Botswana; Burundi; Central African Republic; Congo; Côte d'Ivoire; Democratic Republic of the Congo; Eritrea; Ethiopia; Kenya; Lesotho; Malawi; Mozambique; Namibia; Rwanda; South Africa; Swaziland; Uganda; United Republic of Tanzania; Zambia; Zimbabwe

### 1.5.2 Livestock brucellosis

#### 1.5.2.1 Monetary costs attributable to livestock brucellosis

Many data gaps and methodological challenges relevant to human brucellosis impact estimation are also noticeable in the literature on livestock brucellosis. The prevalence of brucellosis in cattle, sheep, and goats remains widely uncertain in many settings. There is little empirical quantitative evidence of the direct physiological impacts of livestock brucellosis, such as abortion probability, reduction in milk yield, and perinatal mortality (Lokamar et al., 2020). These data gaps are particularly prominent in small ruminants (Bruce, 2016).

The language and methods used in livestock brucellosis impact estimation studies are highly heterogeneous. The terminology applied to describe brucellosis impacts is often inconsistent. Although clear definitions and distinctions in livestock disease impacts have been suggested and advocated for since the 1990s, many concepts, such as 'loss' and 'cost', are often used interchangeably and to describe varying outcomes from study to study. According to McInerney, Howe, and Schepers (1992), 'loss' is the production potential that is not realised over time due to the presence of the disease. For instance, a reduction in milk yield contributes to the 'production losses' caused by brucellosis. In contrast, the 'cost' of a livestock disease can be divided into two components: *ex ante* and *ex post*. *Ex ante* costs occur before a disease event (e.g., expenditure in prevention through vaccination). *Ex post* costs occur in response to a disease that has happened, and these can be divided into production losses and treatment expenditure (e.g., purchase of anti-inflammatory drugs).

Significant heterogeneity exists in the methods used to quantify costs of brucellosis in different studies, including diagnostic criteria applied, types of costs considered and outcome metrics estimated (Deka et al., 2018). This heterogeneity is especially problematic because livestock brucellosis is likely to cause low mortality but high reproductive morbidity, leading to foregone losses (e.g., the production potential of an unborn calve) that may be significant but challenging to estimate.

Despite the semantic and methodological challenges, the literature indicates that livestock brucellosis is a considerable cause of income losses in livestock-keeping households of low-resource settings. In Brazil, India, Sudan, Kenya, and Uganda, the estimated annual cost of bovine brucellosis per infected animal ranged from

126 to 734 int. $[11] (Angara et al., 2016; FAO, 2018d; Guma et al., 2020; Homem, Higa, and Neto, 2016; Patel et al., 2014; Santos et al., 2013; Singh, Dhand, and Gill, 2015). For reference, this range of estimates corresponds to 4.9% and 28.5%, of the GDP per capita in Tanzania in 2018,[12] respectively. Lower estimates have been reported in small ruminants. In India and Iraq, the estimated cost of brucellosis in sheep or goats ranged from 27 to 111 int. $[11,13] (Al Hamada et al., 2021; Alshwany, 2019; Singh, Dhand, and Gill, 2015).

In the extensive production system in Egypt, the estimated production losses due to bovine brucellosis amounted to 1,153 int. $ per case, which corresponded to approximately 23%[14] of the farm-gate price of a healthy animal (FAO, 2018e). In Ethiopia, estimated total production losses attributable to bovine brucellosis were equivalent to 0.21% of the country's annual gross domestic product (FAO, 2018b). In Colombia, each abortion due to bovine brucellosis was estimated to cost at least 4,595 int. $, including production losses and veterinary costs (Arenas and Moreno, 2016). In Malaysia, each goat culled due to brucellosis was estimated to represent an average cost of 317 int. $ to the farmer (Bamaiyi et al., 2015). These studies demonstrate that the estimated impacts of livestock brucellosis can be considerable but vary greatly between settings.

#### 1.5.2.2 Disease burden attributable to livestock brucellosis

There is a lack of standardised non-monetary metrics equivalent to the DALY that can be applied to capture the impact of livestock diseases. A modified DALY (zDALY) has been recently proposed as a non-monetary 'one health' metric to represent the burden of zoonotic diseases on society, capturing impacts to both human and animal health (Torgerson et al., 2018). This proposed metric combines DALYs with an animal loss equivalent (ALE), which represents the time required to recoup the

11. Using the country of each study, their local currency, year of data collection, and the corresponding World Bank conversion rates obtained from `https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?end`
12. GDP per capita in Tanzania in 2018 in (2,571 int. $) obtained from `https://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD?locations=TZ`
13. In Iraq, the reported cost was obtained from prevalence estimates of 9.2 and 4.9%, and costs per adult female of 2.16 and 2.56 US$, respectively (Al Hamada et al., 2021; Alshwany, 2019). The exchange rates used were US$1 = 1,190 Iraqi Dinar, 1 int. $ = 536.72 Iraqi Dinar in 2021, and 1 int. $ = 561.72 Iraqi Dinar in 2015. The first exchange rate was obtained from both publications. The latter two were obtained from the World Bank at `https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=IQ`
14. Calculated assuming a farm-gate price of a healthy animal of 5,080 int. $ (FAO, 2018e); the report indicates that the total loss per brucellosis case in the extensive production system, including 'value of animals lost' and 'value of production lost', was 3,048 int. $ or 60% of the farm-gate price of a healthy animal

production losses in the livestock sector based on the gross national income (GNI) per capita (time trade-off approach) (Torgerson et al., 2018). The disadvantage of the zDALY is that the GNI per capita may be a poor indicator for converting livestock production losses into an animal loss equivalent (Shaw et al., 2017).

## 1.6 Brucellosis control

### 1.6.1 Overview

Brucellosis prevention and control policies worldwide often encompass three core elements: a) prevention of disease transmission from livestock to humans through improvements in hygiene and sanitation (e.g., legislation requiring pasteurisation of milk for human consumption); b) prevention of disease transmission between livestock through vaccination; and, c) early detection of infection in livestock and elimination of infected animals through test-and-slaughter interventions. Vaccination of humans against brucellosis is currently not recommended because of the lack of safe and effective human vaccines (Lalsiamthara and Lee, 2017).

Strategies targeting livestock, elements b) and c) above, are required to mitigate the wide-ranging impacts of brucellosis, which span both livestock and human health. These strategies must be designed based on two key dimensions in each setting: i) the prevalence and spatial distribution of the disease; and, ii) the proficiency of veterinary services and available financial and infrastructure resources (Ducrotoy et al., 2017). If the prevalence of brucellosis in a specific country or region is high or, irrespective of the prevalence level, the veterinary services are underfunded and poorly organised, mass livestock vaccination of all species is widely recommended, rather than taking no action (Ducrotoy et al., 2017). In settings where brucellosis prevalence in livestock is relatively low and veterinary services are adequately resourced and organised, a targeted vaccination approach may be preferred, focusing on specific regions, livestock species, and age groups, with or without the test and slaughter of seropositive animals (Azami et al., 2018; Benkirane, 2006; Blasco, 2010; Blasco and Molina-Flores, 2011; FAO, 2010; Robinson, 2003; Smits, 2013).

### 1.6.2 Livestock vaccination strategies and available vaccines for brucellosis control

The safest and most effective vaccines used to control brucellosis in livestock in several countries are live-attenuated and host-specific: S19 in cattle and Rev-1 in sheep and goats (Ducrotoy et al., 2017). S19 is a spontaneously attenuated strain developed in the early 1920s through culture and selection for modified phenotypic characteristics (Buck, 1930; Graves, 1943). The Rev-1 strain was developed in the 1950s through sequential culture in media containing streptomycin (Herzberg and Elberg, 1955).

Several factors must be considered to ensure the safety and maximise the efficacy of S19 and Rev-1. The subcutaneous vaccination of adult animals may interfere with diagnostic tests, compromising the ability to differentiate vaccinated from infected animals (OIE, 2019). This limitation is highly problematic when no animal identification system exists, and vaccination is combined with or followed by a test and slaughter strategy. Additionally, if administered during pregnancy, the vaccine may cause abortion and infection of the mammary gland with excretion of the vaccine strain in the milk, which poses a risk to humans (OIE, 2019). The risk of human infection with Rev-1 is a significant concern because this strain is resistant to streptomycin, one of the first-line treatment options for brucellosis (Elberg and Faunce, 1957; Yousefi-Nooraie et al., 2012). Vaccination is also not recommended in bulls and animals younger than three months (Ducrotoy, 2014; OIE, 2019). Vaccination of bulls often results in orchitis and potential sterility (Ducrotoy, 2014; OIE, 2019). Vaccination of animals younger than three months may be ineffective because of the interference of maternal antibodies (Ducrotoy, 2014; OIE, 2019).

Several options can be considered to overcome the limitations of currently available vaccines. The conjunctival administration of the reduced dose ($5 \times 10^9$ viable organisms) of S19 in cattle and standard dose of Rev-1 in sheep and goats (between $0.5 \times 10^9$ and $2.0 \times 10^9$ viable organisms) decreases some of the risks of abortion, milk shedding, and serological interference that results from the subcutaneous administration (Fensterbank and Plommet, 1979; OIE, 2019). The probability of abortion and mammary excretion of the vaccine strain in the milk is likely below 1% in cattle vaccinated by the conjunctival route (Ducrotoy, 2014). In sheep and goats vaccinated by this route, the probability of abortion can be over 60% if animals are vaccinated in mid-pregnancy (Blasco, 1997; Fensterbank, Pardon, and Marly, 1982a,b; Zundel et al., 1992). A reduced dose of Rev-1 (lower than $1 \times 10^8$) is associated with a lower risk of abortion in sheep, but the efficacy is

largely compromised (Zundel et al., 1992). Alternatively, to further minimise the risk of abortion in animals vaccinated by the conjunctival route, particularly with the standard dose in sheep and goats, the vaccine must be administered at specific time windows when the proportion of pregnant animals is as low as possible, i.e., during calving/lambing/kidding, lactation or before mating (Bagués et al., 1989; Blasco, 1997, 2010; Blasco and Molina-Flores, 2011; Ducrotoy et al., 2017; OIE, 2019; Perez, Marín, and Grilló, 1995).

Other measures should be considered to ensure the safety and efficacy of brucellosis vaccines. The vaccine manufacturing process must comply with the World Organization for Animal Health (WOAH) quality standards to guarantee the genetic stability of vaccine strains (Blasco and Molina-Flores, 2011; Dorneles, Sriranganathan, and Lage, 2015; Ducrotoy et al., 2017; OIE, 2019). Maintenance of the cold chain during vaccine distribution, particularly in remote areas, is paramount to ensure that each vaccine dose contains the expected concentration of viable organisms (Ducrotoy et al., 2017). Only qualified staff with appropriate training and personal protective equipment must handle and administer brucellosis vaccines (Ducrotoy et al., 2017).

### 1.6.3 Brucellosis control in Tanzania

In Tanzania, reports indicate that brucellosis may have been present in livestock and humans since at least the 1920s (Mengele et al., 2023b; Shirima et al., 2014). In the 1970s, the Tanzanian Government started a brucellosis control programme based on active surveillance, livestock vaccination, and test and slaughter. However, limited resources compromised the effectiveness of official control measures, and the programme was soon discontinued (Mengele et al., 2023b; Shirima et al., 2014). Although there is local evidence of the current high willingness of livestock keepers to pay for brucellosis vaccination, farmer-led, community-based vaccination uptake has been negligible, except in some smallholder dairy systems that aim to be certified brucellosis-free for commercial purposes (Asakura et al., 2018b).

Over recent years, many documents published by the Tanzanian Government indicate the political will to bring brucellosis under control. These policy documents include the Livestock Sector Development Programme (Government of The United Republic of Tanzania, 2011), the Tanzania Livestock Master Plan (2017/2018 - 2021/2022) (Government of The United Republic of Tanzania, 2017b), the Tanzania Livestock Sector Analysis (2016/2017 - 2031/2032) (Government of The United

Republic of Tanzania, 2017c), and the One Health Strategic Plan (2015 – 2020) (Government of The United Republic of Tanzania, 2018c). In March 2017, brucellosis was classified as a 'high-priority' zoonosis based on (i) epidemiological factors, (ii) social and economic impacts, (iii) availability of control options, and (iv) disease severity in humans (U.S. Agency for International Development (USAID), USAID Preparedness and Response Project (P&R), and U.S. Centers for Disease Control and Prevention (CDC), 2017). In February 2018, the One Health Coordination Desk (OHCD) was created at the Prime Minister's Office to bridge human, animal, and environmental health sectors and help support the prevention and control of zoonoses, including brucellosis (Government of The United Republic of Tanzania, 2018c; Mtui-Malamsha, Fasina, and Aguanno, 2022).

According to Tanzania's national strategy for prevention and control of brucellosis in humans and animals (2018-2023) (Government of The United Republic of Tanzania, 2018b), some of the intended measures and activities in the livestock sector include: i) the vaccination of female calves and goats; ii) promotion of biosecurity and good husbandry practices through sensitisation of livestock keepers; iii) enhanced surveillance of brucellosis from a One Health perspective, and iv) test and slaughter of seropositive animals at specific farms. These measures and activities are still in the planning phase and do not have supported programs available for implementation yet.

The Animal Diseases (Vaccine and Vaccination) Regulations (Government of The United Republic of Tanzania, 2020a) include brucellosis as one of the eligible diseases for compulsory vaccination in Tanzania, setting and establishing (i) rules and requirements for the importation, transportation, storage, handling, pricing, quality management, and administration of vaccines, (ii) responsibilities of vaccinators and livestock keepers, (iii) potential eligibility (not currently implemented in practice) of livestock keepers to bear the costs of vaccination, and (iv) penalties for non-compliance. According to these Regulations, only veterinarians or para-veterinarians, i.e., livestock field officers, under the supervision of a District Veterinary Officer, are allowed to administer vaccines to livestock using invasive (e.g., injection) and non-invasive (e.g., topically on the conjunctiva) methods.

### 1.6.4 Barriers to brucellosis control in Tanzania

A brucellosis control and eradication programme in Tanzania, as in other countries in East Africa, is likely to face multiple barriers. Firstly, the communities most impacted by the disease in this setting require targeted outreach and engagement activities tailored to their needs and characteristics. Based on reported prevalence and incidence estimates in livestock and humans, the most impacted communities are pastoralists, who are located in remote and isolated areas, have a nomadic or semi-nomadic lifestyle, and often have deeply ingrained cultural practices identified as risk factors for human infection (e.g., close interaction with livestock, consumption of unpasteurised milk and blood) (Asakura et al., 2022; Bodenham et al., 2020, 2021; Cash-Goldwasser et al., 2018; Gustafson et al., 2015; Mburu et al., 2021; McCabe et al., 2014; Slootweg, 2018).

Secondly, there is currently insufficient surveillance capacity in both human and animal health sectors to accurately characterise the distribution and transmission dynamics of brucellosis in Tanzania. The lack of high-quality surveillance information hinders the ability of governments and stakeholders to evaluate the effect of potential control strategies and justify their implementation (Asakura et al., 2018a; Mengele et al., 2023b).

Thirdly, the interventions based on test and slaughter applied in high-income countries to achieve disease freedom may not be feasible in low-resource settings. In East Africa, veterinary services often lack the organisational structure and resources to deliver this type of interventions, and governments are likely unable to provide compensation to livestock keepers for culled seropositive animals (Bodenham, 2020; Corbel et al., 2006).

Fourthly, policies based on animal movement restrictions to prevent disease spread may be challenging to implement and ethically questionable in pastoral systems of low- and middle-income countries. Such restrictions would require enforcement capacity that is currently limited in these settings and could prevent pastoral communities from accessing critical resources for their livelihood (e.g., water and grazing land) (Bodenham, 2020; Chaters et al., 2019).

### 1.6.5 Economic analyses of livestock vaccination strategies

Policymakers considering allocating public resources to a livestock disease control intervention need information about the impacts of the disease on society and the potential intervention costs and benefits (Zinsstag et al., 2016). This type of evidence can be generated through cost-benefit analysis (CBA). The expected net present value (NPV) and the benefit-cost ratio (BCR) are two measures obtained through CBA that can be used to determine if and how cost-beneficial an intervention might be (Dijkhuizen and Morris, 1997). The NPV is calculated as the present value of expected benefits minus the present value of expected costs. The BCR is calculated as the present value of expected benefits divided by the present value of expected costs. The NPV indicates the scale of the net benefits. In contrast, the BCR indicates the relative magnitude of the benefits over costs (Dijkhuizen and Morris, 1997).

The monetary benefits often considered in CBAs of livestock vaccination are production losses and health-related expenditure averted in the livestock sector. It has been shown that livestock vaccination for controlling many infectious diseases in Africa (e.g., lumpy skin disease, foot-and-mouth disease, pasteurellosis, contagious bovine pleuropneumonia, blackleg, *peste des petits ruminants*, and contagious caprine pleuropneumonia) is generally cost-beneficial (Nuvey et al., 2022). In some cases, for zoonotic diseases such as brucellosis, the monetary benefits of livestock vaccination may also include averted productivity losses and health-related expenditure in the human health sector. Studies that considered the human health sector benefits of livestock vaccination are relatively rare, but include Roth et al. (2003) for brucellosis in Mongolia, van Asseldonk et al. (2013) for Q fever in the Netherlands, Kimani et al. (2016) for Rift Valley fever in Kenya, Okello et al. (2018) for *T. solium* taeniasis/cysticercosis in Lao People's Democratic Republic, and Olmstead and Rhode (2012) for bovine tuberculosis in the United States.

A complementary approach for evaluating a livestock vaccination programme targeting a zoonosis is through cost-utility analysis (CUA) (Hasler et al., 2014; Martins, Rushton, and Stark, 2016; Okello et al., 2018). CUA can be used to compare the programme's costs with its utility, measured as non-monetary human health gains. One of the non-monetary human health metrics used in CUAs of livestock vaccination is the number of DALYs averted in humans (Martins, Rushton, and Stark, 2016; Murray, 1994).

A systematic review of studies describing economic assessments of brucellosis control interventions focused on livestock (at national or regional levels) has recently been published (Kiiza et al., 2023). Eleven studies met the inclusion criteria, and none were conducted in Africa (Al Hamada et al., 2021; Alves et al., 2015; Amosson et al., 1981; Bardhan et al., 2020; Bernues, Manrique, and Maza, 1997; Can and Yalcin, 2014; Liu, 1979; Montiel et al., 2015; Roth et al., 2003; Singh et al., 2018b; Zeng et al., 2019). Overall, brucellosis control strategies based on livestock vaccination were cost-beneficial, with BCRs ranging from 3.2 in Tibet (species vaccinated: yaks) to 21.3 in India (species vaccinated: buffalo). Only one of these eleven studies included monetary and non-monetary human health sector benefits in the economic analysis of livestock vaccination for brucellosis: a study of the brucellosis control programme in Mongolia (Roth et al., 2003). This study in Mongolia estimated that, under a scenario of 65% vaccine efficacy and 80% of animals being vaccinated, brucellosis control would cost 627 int. $[15] per DALY averted (Roth et al., 2003).

Other existing studies of brucellosis control interventions based on livestock vaccination that were not included in the systematic review by Kiiza et al. (2023) are Camus (1980) in Ivory Coast, Rikin (1988) in Nigeria, Bernués (1997) in Spain, Astaiza-Martínez (2012) in Colombia, van Asseldonk et al. (2013) in Turkey, Bruce (2016) and Peck and Bruce (2017) in Albania, Alshwany (2019) in the Iraqi Kurdistan, and Ferreira et al. (2023) in Brazil. Except for Bernués (1997) in Spain, these additional studies concluded that livestock vaccination for brucellosis was cost-beneficial in each setting (based on a positive net present value or a benefit-cost ratio greater than one). The methods used were highly heterogeneous with respect to the types of costs and benefits included, and only two studies considered both monetary and non-monetary human health sector benefits (Bruce, 2016; van Asseldonk, Bergevoet, and Ge, 2013). The study in Turkey concluded that, under a scenario of vaccination of all young animals, brucellosis control would cost 8,278 int. $[16] per DALY averted (van Asseldonk, Bergevoet, and Ge, 2013). The study in

15. 182,701 MNT (tugrik; 5% discount rate; 8,957.3 million MNT in intervention costs over 49,027 DALYs averted); monetary values were converted to international dollars (int. $) using the World Bank conversion factor of 291.28 MNT per int. $ in 2000 obtained from `https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=MN`

16. 10,762 TL (Turkish Lira; 5% discount rate; 226 million TL in intervention costs over 21,000 DALYs averted); monetary values were converted to international dollars (int. $) using the World Bank conversion factor of 1.3 TL (Turkish Lira) per int. $ in 2013 obtained from `https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=TR`

Albania reported that small ruminant vaccination for brucellosis control (scenario 1: current national brucellosis control programme; 3% discount rate) would avert a median of 279 DALYs and cost 5.79 million Euros, which is equivalent to 53,385 int. $[17] per DALY averted (Bruce, 2016).

### 1.6.6 Modelling brucellosis control interventions

Modelling the effect of livestock vaccination and other interventions on the prevalence and incidence of brucellosis in livestock and humans is a critical step in the planning phase of any brucellosis control programme. Hypotheses that would require significant time and financial resources to test in the real world can efficiently be tested through mathematical modelling (Grassly and Fraser, 2008; Mancy, Brock, and Kao, 2017).

At the centre of any brucellosis control model is a representation of the disease transmission dynamics between relevant host species before vaccination. These dynamics must be represented as accurately as possible to avoid bias in estimating the effect of vaccination. Given that there is little evidence of the brucellosis transmission dynamics in many settings, brucellosis control models must capture uncertainty, which is often achieved by adding stochasticity and performing scenario-based analyses (Hegazy, Ridler, and Guitian, 2009; Hobbs et al., 2015; Mancy, Brock, and Kao, 2017; Roth et al., 2003).

Several models have been used over the last two decades to represent brucellosis transmission dynamics. The main differences between some of these models are shown in Table 1.3. All models in this table included at least two compartments representing groups of individuals: 'S' for susceptible and 'I' for infected and infectious. Some models also have exposed ('E') and latent ('L') infection compartments that include mostly infected and non-infectious individuals. In most models, infected individuals remain infected for the remainder of their lifespan, i.e., they do not move to a recovered ('R') or susceptible ('S') compartment. The infection process is often represented through interaction between susceptible and infected individuals at a certain rate (direct transmission, 'D'). In some cases, susceptible

17. 20,753 Euros (5.79 million Euros in intervention costs divided by 279 median DALYs averted); monetary values were converted to international dollars (int. $) using the study's exchange rate of 143 ALL (Albanian Lek) per 1 Euro in 2011 and World Bank conversion factor of 55.59 ALL per int. $ in 2011 obtained from `https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=AL`

individuals can also become infected through contact with a contaminated environment (indirect transmission, 'I'), which is often represented as an independent compartment ('C'). Transmission of disease from an infected female to their offspring can also be considered (vertical transmission, 'V').

Most brucellosis transmission models represent the progression of time continuously, which aligns with how biological processes occur (Mancy, Brock, and Kao, 2017). However, at least three studies have used a discrete representation of time (Bruce, 2016; Hobbs et al., 2015; Inchaisri et al., 2016). The main disadvantage of discrete-time models, particularly with long time steps, is the potential inability to accurately capture the sequence of certain events (Mancy, Brock, and Kao, 2017).

Only a few models in Table 1.3 (i) are age-structured, i.e., include compartments for different age groups, (ii) represent vertical transmission events, (iii) capture seasonal patterns of disease transmission, or (iv) include infection-induced infertility.

Overall, the diversity of mathematical models of brucellosis in the literature demonstrates their essential role in epidemiological research. However, it is vital to customise the model design according to each context and research question being addressed (Mancy, Brock, and Kao, 2017).

**Table 1.3:** Summary of dynamical transmission models of brucellosis published between 2003 and 2018.

| Reference | Main model compartments[1] | Model type (discrete- vs continuous-time) | Age structure (yes[2] or no) | Species[4] | Transmission (direct, D; indirect, I; vertical, V) | Seasonality (yes or no) | Infection-induced mortality (yes or no)[5] | Infection-induced infertility (yes or no) |
|---|---|---|---|---|---|---|---|---|
| Zhou et al. (2018) | SI | Continuous | No | O, H | D | No | Yes | No |
| Li et al. (2017) | SEIC | Continuous | No | O, H | D, I | No | No | No |
| Lolika et al. (2017) | SEIC | Continuous | No | A | D, I | Yes | Yes | No |
| Tumwiine et al. (2017) | SIR | Continuous | No | Bo | D, V | No | Yes | No |
| Beauvais et al. (2016) | SEIR | Continuous | Yes | Bo, O | D, V | Yes | No | No |
| Bruce (2016) | SI | Discrete | Yes | Bo, O, H | D | No | No | No |
| Hou and Sun, (2016) | SEI | Continuous | Yes | O | D | No | Yes | No |
| Inchaisri et al. (2016) | SI | Discrete | Yes | O | D, V | No | Yes | Yes |
| Lou et al. (2016) | SEI | Continuous | No | Bo, O, H | D | Yes | Yes | No |
| Alves et al. (2015) | SLI | Continuous | Yes | Bo | D, V | No | No | Yes |
| Abatih et al. (2015) | SIR | Continuous | No | Bi | D, V | No | Yes | Yes |
| Hobbs et al. (2015) | SEIR | Discrete | Yes | Bi | D, V | No | Yes | Yes |
| Nannyonga et al. (2015) | SIC | Continuous | No | O | D, I, V | No | Yes | No |
| Kang et al. (2014) | SI | Continuous | No | Bo | D | No | No | No |
| Li et al. (2014a) | SEIC | Continuous | Yes | O, H | D, I | No | Yes | No |
| Li et al. (2014b) | SEIC | Continuous | No | Bo, O | D, I | No | Yes | No |
| Nie et al. (2014) | SEIC | Continuous | No | Bo | D, I | No | Yes | No |
| Sun & Zhang (2014) | SEIC | Continuous | No | O | D, I | No | Yes | Yes |
| Zhang et al. (2014) | SEIC | Continuous | No | Bo | D, I | No | Yes | No |
| Hou et al. (2013) | SEIC | Continuous | No | O, H | D, I | No | Yes | No |
| Ainseba et al. (2010) | SIC | Continuous | No | O | D, I, V | No | No | No |
| Amaku et al. (2009) | SLI | Continuous | Yes | Bo | D, V | No | No | Yes |
| Hegazy et al. (2009) | SIR | Not reported | No | O | D | No | Yes | No |
| Roth et al. (2003) | SI | Continuous | No[3] | Bo, O, H | D | No | No | Yes |

[1] Main model compartments (may include subgroups; may differ between host species; vaccination compartments are not shown): S, susceptible; E, exposed; I, infected and infectious; R, recovered; C, contaminated environment; L, latent infection. [2] Includes at least two age-related stages. [3] Cattle and sheep populations divided into young and adult for vaccination coverage. [4] Species: Bi, bison; Bo, bovine; O, small ruminants (sheep and/or goats); H, human; A, animals in general. [5] Includes culling as a result of disease. Linked studies: the model in Amaku et al. (2009) was applied by Nepomuceno et al. (2018) and de Souza et al. (2016); the model in Roth et al. (2003) was further described in Zinsstag et al. (2005) and applied by Racloz et al. (2013); the model in Li et al. (2014a) was applied by Li, Guo, and Zhang (2017); the model in Abatih et al. (2015) was extended by Lolika et al. (2018) to include a chronic state, seasonal variation, and culling.

## 1.7 PhD objectives and thesis structure

The main objectives of this PhD were to estimate, in northern Tanzania, (i) the production losses attributable to livestock brucellosis, (ii) the cost and disease burden attributable to human brucellosis, and (iii) the costs and benefits of livestock vaccination for brucellosis control.

The specific objectives of this PhD were as follows:

- To illustrate interdependencies between key epidemiological and economic factors that are not consistently taken into account in models of livestock diseases (Chapter 2);
- To develop and evaluate a data-driven approach to support data harmonisation and identification of livestock production systems in northern Tanzania (Chapter 3);
- To estimate the production losses attributable to livestock brucellosis in pastoral and non-pastoral systems of northern Tanzania (Chapter 4);
- To estimate the personal monetary costs and disease burden attributable to human brucellosis in a pastoralist community of northern Tanzania (Chapter 5);
- To estimate and compare the monetary costs, monetary benefits, and utility of a hypothetical livestock vaccination programme to control brucellosis in a pastoralist community of northern Tanzania (Chapter 6).

This thesis comprises five data chapters (Chapters 2 to 6), each addressing a specific objective, followed by a general discussion chapter (Chapter 7). A graphical representation of the thesis structure and linked outputs between chapters is shown in Fig. 1.2.

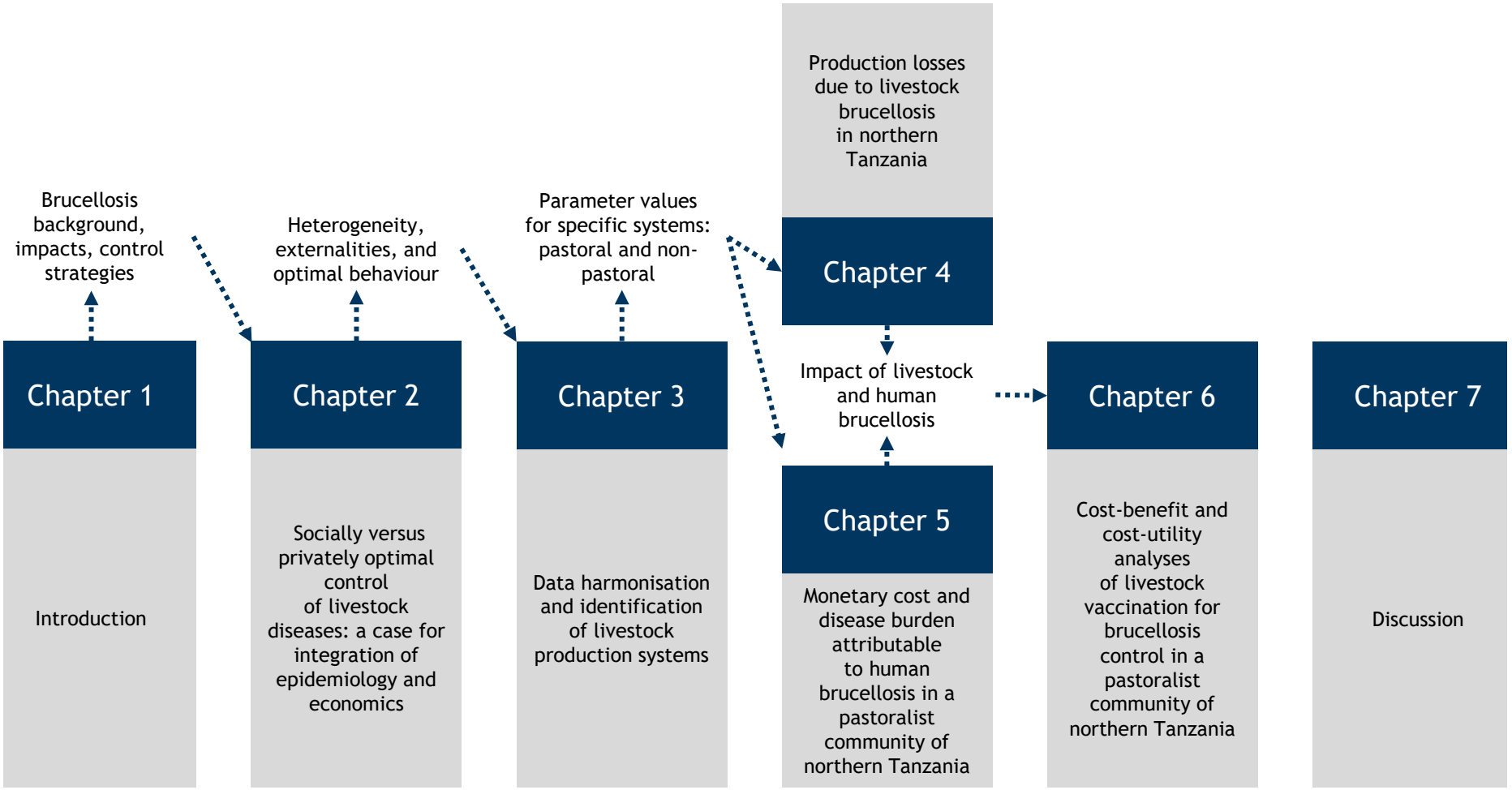



**Figure 1.2:** Thesis structure and linked outputs between chapters.

# Chapter 2

# Socially versus privately optimal control of livestock diseases: a case for integration of epidemiology and economics

A version of the work presented in this chapter has been previously published and is available in Appendix A.1: Mendes, Â. J., Haydon, D. T., McIntosh, E., Hanley, N., and Halliday, J. E. B. (2020). Socially vs. Privately Optimal Control of Livestock Diseases: A Case for Integration of Epidemiology and Economics. Frontiers in veterinary science, 7, 558409. https://doi.org/10.3389/fvets.2020.558409

## 2.1 Introduction

Livestock production is vital to economic development in many low-income countries, contributing to poverty alleviation, investment in children's education, and food security (FAO, 2018f; Marsh et al., 2016). Infectious diseases jeopardise these societal functions, yet their control has become increasingly reliant upon privately funded actions (Chilonda and Van Huylenbroeck, 2001; Ilukor, 2017; Leonard et al., 1999; Perry, 1997; Rushton and Leonard, 2009; van Veen and de Haan, 1995). This 'voluntary approach' to disease control distributes costs and responsibility between private agents (farmers that invest in control measures) and the government (animal health authorities that promote and often regulate farmers' actions) (Sok and Fischer, 2019). The problem of the voluntary approach is that self-

interested behaviour can fail to produce a socially optimal level of disease control (i.e., the level of disease control that maximises the sum of all agents' payoffs in society, the social optimum) (Hanley, Shogren, and White, 2007; Rushton and Leonard, 2009). The market thus 'fails' to achieve the social optimum.

One reason for such 'market failure' in disease control is the presence of externalities: costs and benefits borne by agents who are not parties to a market transaction (Rushton and Leonard, 2009). Externalities can be positive (e.g., a farmer enjoys a lower risk of disease incursion into his herd when neighbouring farmers vaccinate their animals) or negative (e.g., a farmer has a higher risk of disease incursion into his herd when other farmers sell sick animals into a livestock market). One farmer's investment in animal health can thus influence other farmers' levels of disease risk. The way individual farmers perceive and act upon their level of risk may fail to produce a social optimum: some farmers free-ride on the control efforts of others, and the potential benefits of one farmer's actions can be limited by others' inaction (Kristensen and Jakobsen, 2011; Sok and Fischer, 2019). Achieving the socially optimal level of disease control often requires governments to intervene (e.g., through financial incentives and regulation) in a way that accounts for the nature of farmers' decision-making processes and the interdependencies between farmers' choices and disease dynamics (Chilonda and Van Huylenbroeck, 2001; Fournie, Rushton, and Pfeiffer, 2012; Gilbert and Rushton, 2018; Horan, Wolf, and Fenichel, 2012; Mongoh, Hearne, and Khaitsa, 2008; Morin et al., 2018; Rat-Aspert and Fourichon, 2010; Roberts, Peck, and Ritten, 2012; Rushton and Leonard, 2009; Sok and Fischer, 2019; Stott et al., 2005).

The way farmers perceive and respond to disease risks is not only affected by disease spread but also impacts upon it. There are feedback processes between how a disease spreads and the responses of farmers to changing risks (Bucini et al., 2019; Delabouglise et al., 2020; Hidano et al., 2018). When the inter-dependent dynamics of economic, behavioural, and epidemiological factors are not understood or well-represented in models of disease transmission, then policies aimed at promoting farmers' action may have perverse effects (Barnes et al., 2015; Bicknell, Wilen, and Howitt, 1999; Gramig and Horan, 2011; Wolf, 2017). These effects can result, for instance, from (i) reduced individual incentive by farmers to take control action in the presence of compensation payments for infected animals (Bicknell, Wilen, and Howitt, 1999), or (ii) sale of infected animals, and potential disease spread, if less than full compensation is paid (Barnes et al., 2015).

The objective of this chapter is to illustrate interdependencies between key epidemiological and economic factors that are not consistently taken into account in models of livestock diseases: i) farmer heterogeneity (i.e., differences between farmers in how they respond to perceived risks); ii) associated externalities; and, iii) misalignment between privately and socially optimal control efforts. We demonstrate the impact of farmer heterogeneity on disease prevalence over time. We quantify the externalities associated with farmer heterogeneity and show how the outcome of any individual farmer's control effort depends on the behaviour of others. Finally, we examine a farmer's decision in trading-off *ex ante* disease prevention expenditure and *ex post* treatment expenditure and output loss, to estimate the probability that adoption of privately optimal behaviour will achieve a socially optimal disease control target. The consequences of a socially sub-optimal control level depend on, among other factors, the population at risk. Here, for simplicity and to illustrate the general case, groups of farmers represent society.

## 2.2 Methods

We explore the relationships between epidemiological and economic factors using a deterministic compartmental model (Mancy, Brock, and Kao, 2017). The model assumes a chronic infectious disease of livestock with a low basic reproduction number ($R_0$ = 1.11), a livestock species with an average lifespan of five time units, and a constant herd size over time (250 animals on farm). We apply the model in three scenarios that explore farmer heterogeneity, quantify externalities, and examine differences between privately and socially optimal control efforts. In all scenarios, the animal-level prevalence in each farm starts at 10% (the endemic equilibrium, i.e., when prevalence remains steady and the effective reproductive number, $R_e$, is 1.00). We simulate the time required to achieve a prevalence of less than 2% following a hypothetical awareness-raising event (e.g., information provision) and a time horizon of 25 time units. This target prevalence of less than 2% represents an economic optimum from society's perspective (i.e., the socially optimal level of disease control). A 2% threshold can also be considered a prevalence level below which costly government-led strategies aimed at eliminating the disease (e.g., test-and-slaughter) are required (European Commission, 2001). In our simulations, for simplicity and without loss of generality, we assume infected animals show chronic symptoms and lose productivity, but there is no disease-associated mortality or infertility. Individuals can be either susceptible or infected; once infected, they remain infected and infectious for the remainder of their lives. Complete recovery from the disease is not possible.

The model set-up is as simple as possible for demonstration purposes. The basic features are (i) two states (susceptible - S; and, infected - I), (ii) continuous time steps, (iii) equal birth and death rates ($\alpha = \mu = 0.20$), and (iv) an initial transmission rate ($\beta$) of approximately $8.89\times10^{-4}$, reflecting the endemic equilibrium. The model can be run with one or more farms, and disease transmission can occur within farm only or both within and between farms. The proportion of the initial overall $\beta$ attributable to between-farm transmission ($q$) is 0.0 when there is no transmission between farms, and 0.1 when between-farm transmission is included. The amount of control effort applied on farm $i$ is represented by a proportionate reducer on $\beta$ ($r_i^{\beta}$). The model's differential equations are as follows:

$$\begin{aligned}\frac{dS_i}{dt} &= \alpha(S_i + I_i) - (1-q)\left(1 - r_i^{\beta}\right)\beta S_i I_i - q\beta S_i \sum_{\substack{j=1 \\ j\neq i}}^{n} I_j - \mu S_i \\ \frac{dI_i}{dt} &= (1-q)\left(1 - r_i^{\beta}\right)\beta S_i I_i + q\beta S_i \sum_{\substack{j=1 \\ j\neq i}}^{n} I_j - \mu I_i\end{aligned} \tag{2.1}$$

The differential equations were solved in R (R Core Team, 2019) (version 3.6.2) with the package deSolve (Soetaert, Petzoldt, and Setzer, 2010) (version 1.27.1). All plots were generated using the ggplot2 package (version 3.3.0) (Wickham, 2016).

We demonstrate the effect of farmer heterogeneity on the predicted prevalence of disease over time by simulating transmission-reducing measures in three farms following a hypothetical awareness-raising event. As farmers continually assess the benefits and costs of their actions over time, the amount of control effort in each farm is set to be a function of disease prevalence ($p_i$). We assume that (i) disease transmission occurs within each farm only, and (ii) as the prevalence (and disease impact) at the farm declines, the control effort applied ($r_i^{\beta}$) also falls (McInerney, Howe, and Schepers, 1992), as follows:

$$r_i^{\beta} = \frac{1}{1 + e^{-100(p_i - \gamma_i)}} \tag{2.2}$$

where $\gamma_i$ represents the farmer responsiveness. $\gamma$ was set at 0.025, 0.100, and 0.175 for the farmer that is 'highly responsive', 'moderately responsive', and 'slightly responsive', respectively. Note that, as the prevalence decreases in any farm due to the control effort applied, the farmer responsiveness does not change - it is a characteristic of each individual farmer.

We then estimate the off-farm effects (externalities) of livestock disease control in two of the above farms: one in which the farmer is highly responsive and the other in which the farmer is slightly responsive. Firstly, we quantify the *ex post* cost of disease over time at the farm level by assigning a monetary value ($\delta$) to the cost of each infected animal per time unit. We assume that the *ex post* cost of the disease varies linearly with prevalence (i.e., the cost per time unit is the product of the number of infected animals and the cost per infected animal). We then compare the *ex post* cost of disease over time in each farm when the transmission rate between farms (b$\beta$) is 0% ($q$ is 0.0) and 10% ($q$ is 0.1) of the initial within-farm transmission rate (w$\beta$). Actions taken by each farmer to reduce transmission in their farms only reduce the w$\beta$ – and do not influence b$\beta$, which is kept constant over time. By holding the b$\beta$ constant over time and at a common value for the two farms, we demonstrate the off-farm effects of on-farm actions only – this assumes that (i) the contact rate between farms is kept constant, and (ii) the force of infection is proportional to the number of infected animals on each farm. Variation in farm number and density is unlikely to affect the qualitative inferences from this simulation.

We define 'cost of disease' as the sum of disease-related output loss (production potential that is not realised over time) and expenditure on treatment of infected animals, plus the cost of control. Treating infected animals does not affect their infectiousness. Cost of control refers to money spent on reducing the w$\beta$ to prevent new cases, for instance, through improvements in hygiene and biosecurity. The cost of disease can thus be split into *ex ante* cost (cost of control) and *ex post* cost (disease-related output loss and treatment-related expenditure).

We demonstrate the market failure in livestock disease control by comparing the private net profit of farmer $i$ ($\Pi_i$) with the social net profit ($\Pi_s$), the sum of the private net profits of $n$ farmers ($\Pi_s = \sum_{i=1}^{n} \Pi_i$). $\Pi_i$ denotes the private net profit of farmer $i$ for the whole simulation period of 25 time units ($\Pi_i = \sum_{t=1}^{25} \Pi_{it}$). The example has only two farmers for simplicity, so $\Pi_s = \Pi_R + \Pi_r$; the social net profit is the net profit of the highly responsive farmer ($R$) plus the net profit of the slightly responsive farmer ($r$). Considering that the benefit ($b_i$, the number of animal in-

fections averted) enjoyed by the highly responsive farmer as a result of disease control effort is a function of control effort applied in their farm ($r_R^\beta$) as well as in the other farm ($r_r^\beta$) (i.e., $b_R = f(r_R^\beta, r_r^\beta)$), the net profit $\Pi_{Rt}$ (at time t) is given by $\delta b_R - \theta r_R^\beta$, where $\delta$ is the *ex post* cost per infected animal (treatment expenditure and output loss), and $\theta$ is the unit price of control action (the price of reducing the transmission rate by 1%). For this simulation, we assume that $\delta$ and $\theta$ are fixed at 50 and 0.10 monetary units, respectively.

We examine the effect of optimising behaviour on disease prevalence by assuming that the farmer reduces the w$\beta$ so that the total cost of the disease (the sum of *ex ante* and *ex post* costs) at each time unit is minimised (McInerney, Howe, and Schepers, 1992). This process is repeated iteratively for each level of the unit price of control ($\theta$, ranging from 0.00 to 1.25 monetary units per time unit) and *ex post* cost per infected animal ($\delta$, ranging from 10 to 85 monetary units per time unit). We assume (conservatively) that (i) the farmer has perfect information of both the *ex ante* and *ex post* costs of disease, and (ii) their behaviour is no longer determined by a pre-specified logistic function. Instead, at each unit, the farmer reviews and optimises their control effort given the prevalence. The short planning horizon (one time unit, equivalent to one-fifth of the animals' average lifespan) reflects the generally high time-preference rates in low-income countries (Anderson and Gugerty, 2009).

The qualitative inferences drawn from the model outputs are observed under a range of alternative scenarios and assumed parameter values. Readers can explore different scenarios and assumptions in the interactive web application, which is available at `http://boydorr.gla.ac.uk/eemodel/epiecon`. This application was developed with *shiny* (Chang et al., 2019) (version 1.4.0) and shinydashboard (Chang and Ribeiro, 2018) (version 0.7.1) packages in R (R Core Team, 2019). The R script for all the simulations is available at `https://doi.org/10.5281/zenodo.4108335`.

## 2.3 Results

### 2.3.1 The impact of farmer heterogeneity

The prevalence of the disease is estimated over time within three model farms managed by three different 'types' of farmers who vary in their responsiveness to an awareness-raising event. The responsiveness level of each farmer type is given by a behavioural parameter ($\gamma_i$). The model uses this parameter in a logistic func-

tion that determines the reduction in transmission rate caused by each farmer's different actions at any given level of prevalence (Fig. 2.1, panel A). For instance, at the initial prevalence of 10%, (i) the highly responsive farmer reduces transmission by 100% (red solid line), (ii) the moderately responsive farmer reduces transmission by 50% (green dotted line), and (iii) the slightly responsive farmer does not reduce transmission at all (blue dashed line). The impacts of these three levels of responsiveness on disease prevalence over time are shown in Fig. 2.1, panel B. The heterogeneity in farmer responsiveness has an impact on the level of control effort applied and thus on the reduction in prevalence achieved. Among the three farmer types, only the highly responsive type achieves the target prevalence (i.e., less than 2%) within 25 time units.

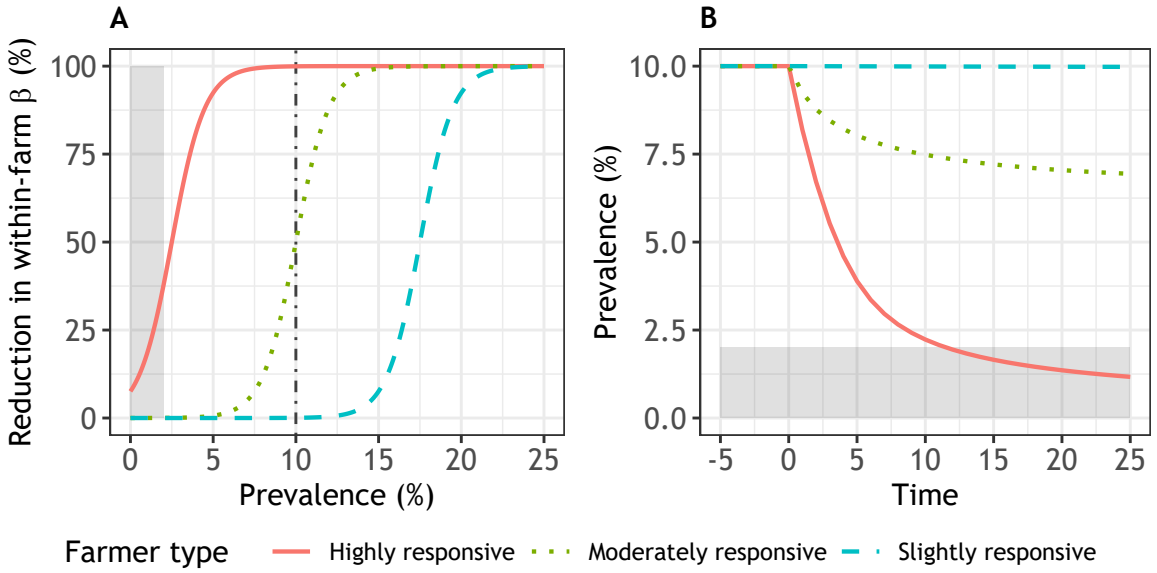



**Figure 2.1:** Effect of farmer type on disease prevalence following a common starting prevalence and a hypothetical awareness-raising event (at time zero). Panel A: control effort applied (percentage reduction in transmission rate - $\beta$ - within the farm in relation to the initial $\beta$ in endemic equilibrium) as a function of disease prevalence for three different farmer types. The vertical dash-dotted line indicates initial prevalence. Panel B: disease prevalence over time within the three farms. In both panels, the grey shaded area indicates the target prevalence level from society's perspective (less than 2%).

### 2.3.2 Externalities: the off-farm effects of farmers' control actions

Now we model disease prevalence in two neighbouring farms (managed by highly and slightly responsive farmers, respectively), allowing for between-farm transmission, to explore the off-farm effects of farmers' control actions upon within-farm and societal costs of disease, represented by the sum of costs over the two neighbouring farms.

The disease transmission rate within (w$\beta$) and between (b$\beta$) farms, in the absence (b$\beta$ = 0) and in the presence (b$\beta$ > 0) of off-farm effects, is shown in Fig. 2.2. Following an awareness-raising event (at time zero), in the scenario of no off-farm effects (i.e., b$\beta$ = 0), the highly responsive farmer (solid red line) rapidly reduces the w$\beta$ by approximately 100% (from 0.0009 to close to 0), and then gradually relaxes their control action over time. This relaxation leads to a rebound in the w$\beta$, which reaches approximately 0.0007 at the end of the simulation (25 time units). The transmission rate in the farm managed by the slightly responsive farmer (dotted blue line) remains constant over time (at 0.0009). When the off-farm effects or externalities are included (i.e., b$\beta$ > 0, transmission between farms is possible), the highly responsive farmer rapidly reduces the w$\beta$ by approximately 100% (from 0.0008 to close to 0), and then gradually relaxes their control action over time. This relaxation leads to a rebound in the w$\beta$, which reaches approximately 0.0005 at the end of the simulation (25 time units). The lower transmission rates recorded in the farm managed by the highly responsive farmer in the presence of off-farm effects, compared to the same farm in the scenario of no off-farm effects, demonstrate the overall greater control effort applied during the simulation that includes off-farm effects. The transmission rate in the farm managed by the slightly responsive farmer (dotted blue line) remains constant over time (at 0.0008). The farmers' actions within their respective farms do not affect the transmission rate between farms, which remains constant over time at approximately 0.0001.

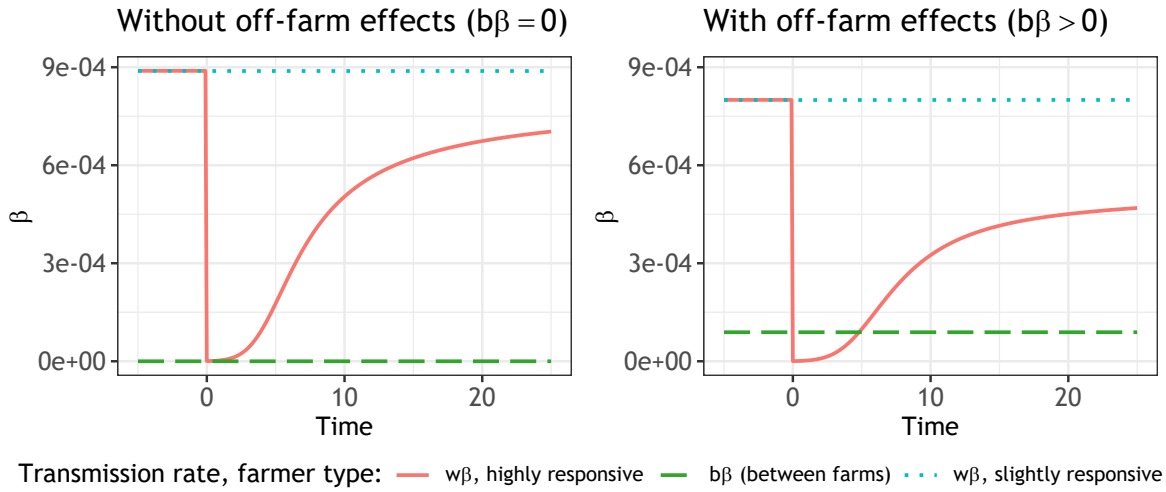



**Figure 2.2:** Transmission rates within (w$\beta$) and between (b$\beta$) two neighbouring farms (managed by highly and slightly responsive farmers, respectively) in scenarios with (b$\beta$ > 0) and without (b$\beta$ = 0) off-farm effects of control actions. Variation in the transmission rate over time results exclusively from changes in control effort applied at the farm by the respective farmers, as prevalence changes.

Fig. 2.3 shows the estimated *ex post* cost of disease over time in the two farms with and without between-farm transmission. With no off-farm effects (i.e., b$\beta$ = 0, and thus no effects of neighbour's actions on costs), a highly responsive farmer (solid red line) reduces prevalence and *ex post* cost. In contrast, for a slightly responsive farmer (dotted blue line), the prevalence and the *ex post* cost are unchanged over time. When the off-farm effects or externalities are included (i.e., b$\beta > 0$, transmission between farms is possible), the highly responsive farmer sees a reduced benefit of their actions, and the slightly responsive farmer benefits from their neighbour's actions (compared to the equivalent costs when b$\beta$ = 0). The extent by which the first farmer (highly responsive) reduces the prevalence of disease (and its associated cost) is limited by the force of infection originating from the second farm, where the farmer is only slightly responsive. Also, despite the lack of control action, the prevalence and *ex post* cost of disease at the second farm drops over time as a result of a decreasing force of infection originating from the first farm, where the prevalence is decreasing due to the control measures applied.

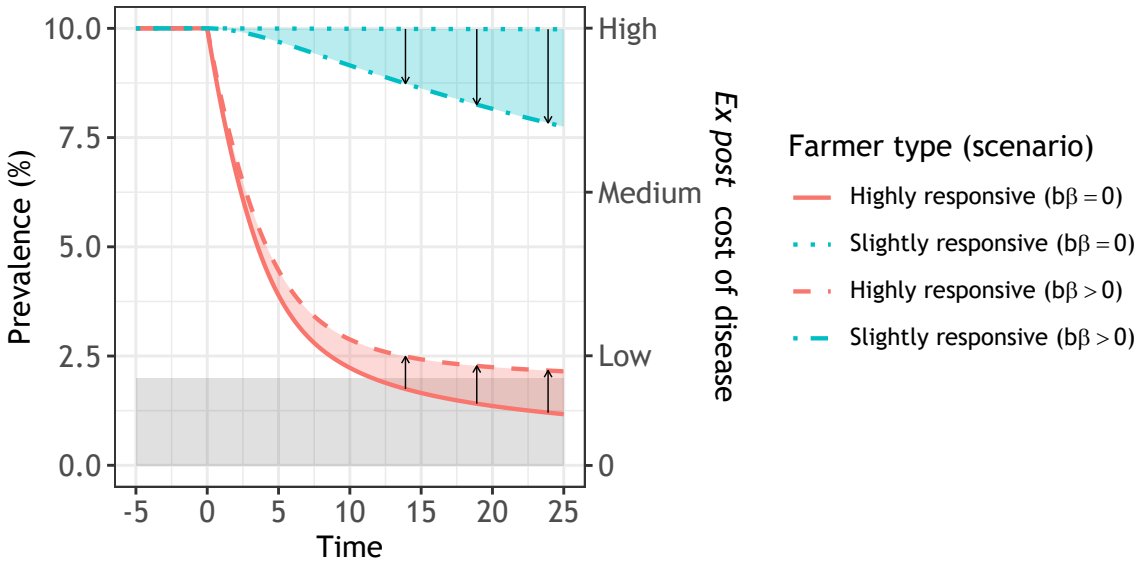



**Figure 2.3:** Externalities occurring as a result of different effort to achieve disease control in two neighbouring farms. Arrows indicate a simulation scenario shift, from absence of transmission between farms (b$\beta = 0$) to a situation in which between-farm transmission is possible (b$\beta > 0$). Assuming an *ex post* cost per infected animal per time unit ($\delta$) of 50 monetary units, the labels 'Low', 'Medium', and 'High' on the right vertical axis correspond to 313, 781, and 1,250 monetary units. Blue and red shaded areas correspond to the positive and negative externalities, respectively. The grey shaded area indicates the target prevalence level from society's perspective (less than 2%).

The benefits, costs, and net profit of the highly responsive farmer, the slightly responsive farmer, and society (made of the highly responsive farmer and the slightly responsive farmer) are shown in Table 2.1. Using a discount rate of 5%, which accounts for the decreasing value of benefits and costs over time in 'real terms', as viewed from the present, the extent of market failure is 154 monetary units, the difference between the social net profit ($\Pi_s$, 849 monetary units) and the private net profit of the highly responsive farmer ($\Pi_R$, 695 monetary units)[1]. This difference is due to the benefits enjoyed by the slightly responsive farmer, who does not incur any costs of control. Using a discount rate of 10%, the extent of market failure is 95 monetary units, the difference between the social net profit ($\Pi_s$, 692 monetary units) and the private net profit of the highly responsive farmer ($\Pi_R$, 598 monetary units)[2].

**Table 2.1:** Private net profit of a highly responsive farmer and social net profit resulting from disease control action. Values are in monetary units.

| | Discount rate† | Benefit | Cost | Net profit |
|---|---|---|---|---|
| Highly responsive farmer | 5% | 794 | 99 | 695 |
| | 10% | 667 | 70 | 598 |
| Slightly responsive farmer | 5% | 154 | 0 | 154 |
| | 10% | 95 | 0 | 95 |
| Society* | 5% | 948 | 99 | 849 |
| | 10% | 762 | 70 | 692 |

Values were obtained from a simulation with 25 time units, with $\delta$ (*ex post* cost per infected animal) and $\theta$ (the unit price of control) assumed to be fixed at 50 and 0.1 monetary units, respectively. Values may not exactly add up due to rounding. For more information, see `http://boydorr.gla.ac.uk/eemodel/epiecon`.
* It considers the benefits and costs to both the highly responsive farmer and the slightly responsive farmer. † The discount factor was given by $\frac{1}{(1+d)^t}$, where $d$ is the discount rate, and $t$ is the simulation year.

### 2.3.3 Privately optimal behaviour and reductions in prevalence

Here we model disease prevalence (with a single farm and b$\beta = 0$) to establish if privately optimal actions of a farmer will achieve the socially optimal target prevalence (i.e., less than 2%). The prevalence over time assuming privately optimal behaviour for different unit prices of control (from 'free' to 'high') is shown in Fig. 2.4. Following an awareness-raising event (at time zero) and assuming a fixed *ex post* cost per infected animal ($\delta = 50$ monetary units), the extent by which the within-farm prevalence is reduced varies inversely with the unit price of control ($\theta$). Achieving the socially optimal target prevalence is possible if the unit price

1. More details available here: `http://boydorr.gla.ac.uk/eemodel/epiecon`
2. Values may not exactly add up due to rounding.

of control is very low. Disease elimination (prevalence below 0.4% or less than one infected animal in a herd of 250; note that the predicted prevalence is strictly continuous) only occurs when the unit price of control is equal or less than 0.05 monetary units (first line above 'free' in Fig. 2.4). When the unit price of control is above 0.05 monetary units, the farmer's optimal control effort either reduces the prevalence until it reaches a new endemic equilibrium or does not reduce it at all (shown as the uppermost flat line in Fig. 2.4; the prevalence remains at the initial endemic equilibrium level). This model of optimising behaviour shows that self-interested farmers, who optimise their private investment in disease control, as assumed here, may not achieve the target prevalence from society's perspective in the absence of an intervention by, for example, the government.

In our simulations, under the assumption of optimising farmer behaviour, as prevalence drops, the marginal cost of control actions (i.e., the cost of reducing the prevalence by an additional unit, 1%), increases sharply. It is more expensive to reduce the prevalence from 3% to 2% than from 10% to 9% because the number of cases prevented per time unit by reducing the transmission rate depends on the number of currently infected individuals. If the number of currently infected individuals is high (e.g., 10% prevalence), the prevention of new cases yields a quick reduction in prevalence. If the number of currently infected individuals is low (e.g., 3% prevalence), further reductions of the prevalence rely to a greater extent on the elimination of currently infected individuals. Under the assumption of optimising behaviour, as the marginal costs of control increase, the farmer's investment in control therefore gradually declines until an equilibrium is reached in both epidemiological and economic terms (shown as the plateau for each line in Fig. 2.4). This equilibrium prevalence level is reached when the *ex ante* expenditure in one time unit equals the averted *ex post* cost of disease.

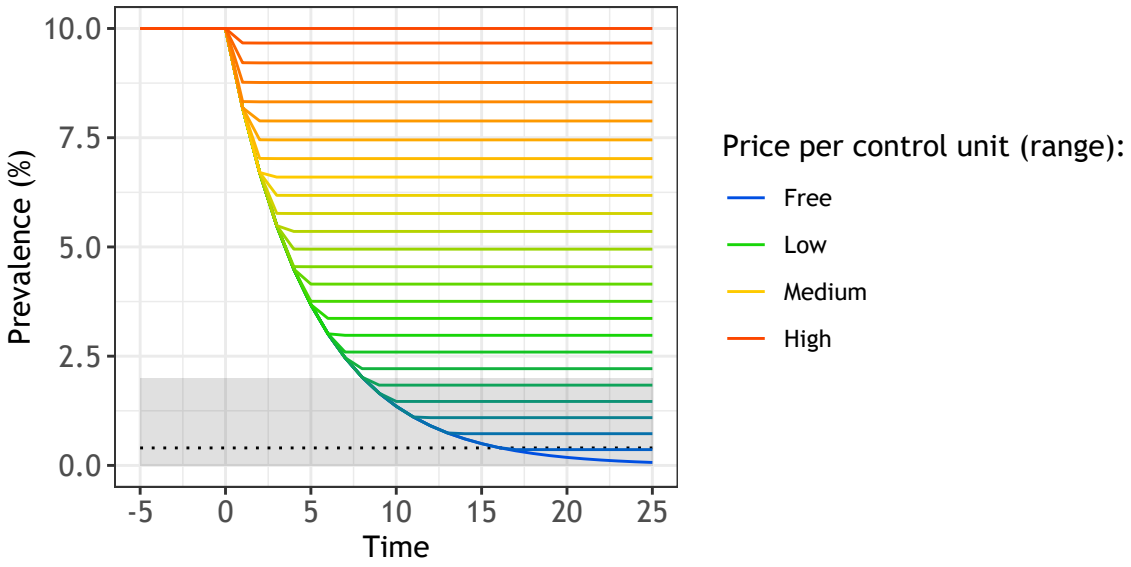



**Figure 2.4:** Disease prevalence over time, assuming privately optimal behaviour in a single farm for a range of prices per control unit. This simulation assumes a cost of one infected animal per time unit ($\delta$) of 50 monetary units. The price of reducing the transmission rate by 1% ($\theta$) ranges from "Free" (0.00 monetary units) to "High" (1.25 monetary units). "Low" and "Medium" correspond to 0.40 and 0.85 monetary units, respectively. Coloured lines represent increases by 0.05 monetary units. The grey shaded area indicates the target prevalence level from society's perspective (less than 2%). The black dotted horizontal line indicates a prevalence consistent with disease elimination (0.4%; less than one infected animal in a herd of 250 animals).

The achievement of a socially optimal outcome prevalence depends on the specific values of the unit price of control and cost per infected animal selected. The results shown in Fig. 2.4 considered a fixed *ex post* cost of one infected animal ($\delta = 50$ monetary units). However, for the same disease and animal species, this value could in practice vary with the price of livestock, cost of production inputs, type of production system, etc. Fig. 2.5 shows the predicted prevalence at the end of the simulation (25 time units) for a range of values of price per control unit and a range of values of *ex post* cost per infected animal. When we allow the cost per infected animal to vary in plausible ranges in relation to the price of control unit (e.g., eliminating disease transmission by 100% would cost a maximum of 125 monetary units per time unit, which is less than 1.5 times the highest *ex post* cost of one infected animal, i.e., 85 monetary units), the previously observed pattern holds: farmers who optimise their control effort may not achieve the target prevalence from society's perspective.

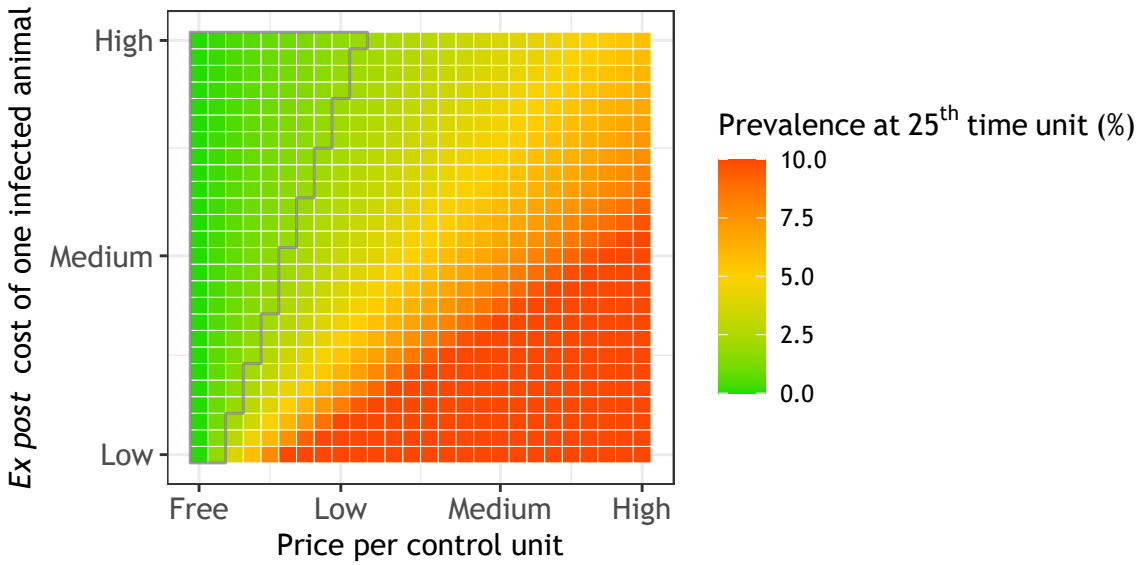



**Figure 2.5:** Predicted prevalence at 25$^{th}$ time unit for different values of price per control unit ('Free' = 0.00; 'Low' = 0.40; 'Medium' = 0.85; and, 'High' = 1.25 monetary units) and *ex post* cost per infected animal ('Low' = 10; 'Medium' = 46; and, 'High' = 85 monetary units), assuming privately optimal behaviour in a single farm. The polygon with grey border indicates the target prevalence level from society's perspective (less than 2%).

## 2.4 Discussion

Analytical frameworks introducing human behavioural dynamics in the field of livestock infectious disease modelling have emerged in the last two decades. From the pioneering works of McInerney, Howe, and Schepers (1992) and Bicknell, Wilen, and Howitt (1999) to the most recent individual-based, network-based, and game-theoretic models (Delabouglise and Boni, 2020; Hennessy, 2007; Sok and Fischer, 2019; Tago et al., 2016), many significant contributions have improved our understanding of the interplay between human behaviour and livestock disease spread (and the likelihood of disease control). However, this study is unique and contributes to that body of knowledge for two reasons. Firstly, it provides a simple but robust framework for exploring key factors in the control of livestock diseases: farmer heterogeneity, externalities, and private-social misalignment of control optima. Secondly, we apply this framework to the control of endemic chronic diseases through privately funded actions in a low-resource setting.

Despite the growing literature on livestock infectious disease modelling, very little attention has been given to the assumption of homogeneous human behaviour, the validity of which we evaluate here. Models of livestock disease typically assume that the farmers' perception of risk and the way they respond to that level

of perceived risk remain unchanged over time (Hidano et al., 2018). In addition, many epidemiological models entirely ignore the effects of changing prevalence on privately optimal spending on disease control (Barnes et al., 2015; Hidano et al., 2018). However, several empirical studies have shown that a farmer's likelihood to take control actions is the result of a dynamic and complex interplay between epidemiological, economic, environmental, cultural, and social factors (Ahmed et al., 2017; Chaters et al., 2019; Ifft, Roland-Holst, and Zilberman, 2011; Manyweathers et al., 2017; Oparinde and Birol, 2012). Models of disease transmission that ignore such heterogeneity are likely to be misleading, resulting in reduced value for informing control efforts. Like many decision-makers, farmers make decisions based on conscious and unconscious, cognitive and affective shortcuts or rules of thumb (Findlater, Satterfield, and Kandlikar, 2019; Gigerenzer and Gaissmaier, 2011; Manyweathers et al., 2017). We model the implications of this type of individual decision-making process by simulating the effects on prevalence and costs of different levels of farmer responsiveness. These simulations quantify the consequences of heterogeneous behaviour, the occurrence of externalities, and the consequent disparities between privately and socially optimal control efforts.

The simulations of our theoretical scenario of optimising behaviour assumed perfect information and rational behaviour by the individual farmer. In this scenario, the farmer was able to accurately choose the optimal control effort at any point in time by trading off the marginal benefits of reducing the prevalence against the marginal costs of their actions. These models assume a conservative range of values for the unit price of control action (from 0.00 to 1.25 monetary units to reduce the transmission rate by 1% per time unit) and cost of one infected animal (from 10 to 85 monetary units per time unit). For example, without administration and overhead charges, the annual cost of vaccinating a herd of 250 cattle for brucellosis in India (167.50 USD; 0.67 USD times 250) would be over twice as much as the average loss caused by brucellosis per infected animal (73.44 USD) (Singh et al., 2018b). The values that we used are considered appropriate and conservative for this evaluation because the highest possible cost of eliminating disease transmission completely would be equivalent to less than 1.5 times the highest *ex post* cost of one infected animal per time unit. Despite these conservative assumptions, the societal disease control target was only achieved for high disease cost to price of control ratios (less than 25% of all price-cost combinations; Fig. 2.5). Given these findings, we can infer that effective disease control through voluntary actions is unlikely to be privately optimal in many real-world cases. Additionally, as prevalence decreases, there is a sharp increase in the marginal costs of control action, which leads to a fall in optimal control effort. This result is consistent with the economic principle of diminishing returns and has also been reported by

other theoretical (McInerney, Howe, and Schepers, 1992) and empirical studies, namely those that analysed control actions against tuberculosis (Bicknell, Wilen, and Howitt, 1999; Hone, 2013) and brucellosis (Peck and Bruce, 2017; Peck, 2010) in cattle.

Our model illustrates the misalignment of private and social optima for livestock disease control through a basic trade-off between the benefits of reductions in herd prevalence and the costs of transmission-reducing actions. Essentially, farmers 'buy reductions in disease transmission', which is a simple and logical representation of many disease control actions. However, this approach is likely to underestimate the gap between private and social optima in many cases: the model does not capture many of the benefits of farmers' actions such as (i) the control of multiple pathogens through improved biosecurity, and (ii) the human health benefits in the cases of zoonoses. For instance, brucellosis is a bacterial zoonosis that causes abortion in livestock and debilitating symptoms (e.g., fever, joint pain, myalgia) in humans (Corbel et al., 2006; Dean et al., 2012a). Given this burden on human health, in addition to animal health, voluntary actions taken by farmers to control the disease in their livestock (e.g., through vaccination) generate positive externalities, as society benefits from farmers' actions whilst not bearing the costs of these actions. This is a market failure that requires coordinated action to achieve socially optimal outcomes in terms of both human and animal health and productivity (Peck and Bruce, 2017). Hence, the benefits enjoyed and the costs born by both public and private sectors must be considered throughout the planning phase of control interventions, which can include, among others, the provision of subsidised goods and services (e.g., vaccination), creating and enforcing regulations (e.g., movement restrictions) and setting compensation schemes (e.g., for culled seropositive animals) (Peck and Bruce, 2017; Rushton and Leonard, 2009).

## 2.5 Conclusion

To enable private farmers' actions to achieve a socially optimal disease control target, policy design and development must consider the heterogeneity of farmer behaviour, the associated off-farm effects or externalities, and the predicted uptake of control measures under optimised farmer behaviour. Failure to acknowledge these factors may result in potentially misleading predictions about disease transmission and the associated economic costs. This, in turn, perpetuates conditions in which private investments by farmers are inadequate to achieve disease con-

trol from society's perspective. For multi-host diseases that can impact multiple sectors (e.g., multi-host livestock diseases and zoonoses), inadequate disease control can have profound repercussions on international trade and, indeed, threaten human health.

# Chapter 3

# Data harmonisation and identification of livestock production systems

## 3.1 Introduction

Livestock diseases cause significant impacts on animal health and welfare globally (Pradère, 2014). Understanding the magnitude of these impacts is vital to support disease control initiatives and, subsequently, mitigate the adverse effects of diseases on food security, livelihoods, and sustainable development. The impacts of livestock diseases can be direct and tangible, such as production losses and treatment costs, or indirect and less tangible, such as restricted market access and losses that occur beyond the farm gate (e.g., in supply chains and tourism) (Barratt et al., 2019).

Estimating the impacts of livestock diseases, including those that are direct and tangible, is challenging for many reasons. Firstly, estimating these impacts requires an interdisciplinary approach, encompassing both biological and social sciences (Rushton, Perry, and Anton, 2018). The impact of livestock diseases on society varies with their prevalence and physiological consequences, the value of the livestock production outputs, the type of production systems affected, and the cost of disease management (Delabouglise et al., 2017). The nature of livestock disease impacts is multidimensional and context-specific (Rich and Perry, 2011). Collaborative processes leveraging the various dimensions of animal health and blending research methods from different sciences are needed.

Secondly, studies aimed at estimating the impacts of livestock diseases generally use market prices (e.g., price of livestock products, price of preventive and treatment drugs) (Abdulhameed et al., 2018; De Aquino et al., 2017; Singh, Dhand, and Gill, 2015). This practice is grounded on the assumption that market prices reflect the true value of inputs and outputs of livestock production and disease management (Jarvis and Valdes-Donoso, 2018). However, from a household's perspective, this assumption is vulnerable because the extent to which market prices reflect the value of livestock varies with (i) the production system (e.g., a subsistence farmer and a commercially-oriented cattle farmer in East Africa are likely to value the same production output differently), and (ii) the spatial scale (e.g., the mean market price of cattle in Tanzania may not reflect the value of cattle to households in a specific region). Methods aimed at estimating the impacts of livestock diseases should then consider the specific characteristics of the different production systems and spatial scales.

Thirdly, and finally, the collection and access to high-quality, livestock disease and production data is difficult. The traditional sampling procedures for primary data may not be applicable in many areas where a sample frame for animals is absent (Viscarra and Rushton, 2009). This constraint may be particularly relevant in poor and remote areas of low-and-middle-income countries or in nomadic communities, where many livestock diseases are endemic, and the systems for enumeration of livestock and quantification of offtake are weak (Donadeu et al., 2019). The most effective way to estimate the impact of livestock diseases is through longitudinal surveys, which collect data continuously or repeatedly over time (Viscarra and Rushton, 2009). However, this method can be costly and laborious to deliver, and may not be feasible in many settings. Cross-sectional surveys, which collect data at a single point in time, and secondary data from these surveys may be affordable and accessible, but these sources rarely provide both disease (e.g., prevalence) and production parameters (e.g., offtake and birth rates) (Viscarra and Rushton, 2009). New methods aimed at combining disease and production data from independent cross-sectional surveys are then required.

Statistical methods for combining information from multiple surveys may be useful to overcome some of the above challenges in estimating the impacts of livestock diseases. Many of these methods have been developed over the last few decades, but each is usually best suited to address a specific type of research question (Dong, Elliott, and Raghunathan, 2014; Elliott and Davis, 2005; Raghunathan et al., 2007; Schenker et al., 2002; Schenker and Raghunathan, 2007; Schenker, Raghunathan, and Bondarenko, 2010). For instance, when different sources keep records from a common set of individuals, linking these records can be a very efficient way of

combining data but it may violate personal data rights (Lohr and Raghunathan, 2017). Multivariate models can be used to 'fill in' or impute missing observations of datasets that are to be combined, but a number of issues due to incomparability may arise (e.g., differences in sampling design, survey context, and questionnaire wording) (Lohr and Raghunathan, 2017). Guidelines for data harmonisation, i.e., the process of improving comparability of data collected from different surveys, have been published, broadening the applicability of multivariate models (Fortier et al., 2017). However, some problems may occur during the data harmonisation process, including in (i) the access to information on study designs, (ii) the consideration of sampling and non-sampling error properties, and (iii) the definition of an acceptable level of heterogeneity between surveys (Dong, Elliott, and Raghunathan, 2014; Fortier et al., 2017).

The impacts of the above incomparability issues are often specific to the research question and likely more important when a high level of precision and granularity of estimates is needed (e.g., to analyse correlational relationships between variables) (Lohr and Raghunathan, 2017). A systems approach that focuses on shared characteristics between individuals may then be useful to combine data sources where incomparability issues are common and the research questions are not too ambitious in terms of the precision and granularity needed. For instance, a hierarchical clustering algorithm, an unsupervised machine learning technique, has been recently applied to classify livestock production systems in northern Tanzania (de Glanville et al., 2020). The ability to distinguish households that belong to different production systems is useful because livestock productivity and disease prevalence are likely to be different between systems (Bodenham et al., 2021; Shirima et al., 2010). Thus, if a survey X estimated the prevalence of a livestock disease in production systems A and B, and a survey Y measured the production of livestock in the same systems and geographical area, combining data from surveys X and Y at the system level can be useful to estimate the system-specific losses attributable to the disease.

In East Africa, livestock production systems can be classified into three main categories: pastoral, agro-pastoral, and smallholder (de Glanville et al., 2020). Other typologies and variations of these categories have been suggested, but the same general defining criteria apply. These criteria usually include the level of integration and intensification of crop and livestock production, the ecosystem conditions, and main production purposes (Cecchi et al., 2010; Otte and Chilonda, 2003; Pandey and Upadhyay, 2022; Robinson et al., 2011). In the pastoral system, households keep livestock as the primary means of subsistence, and interactions between humans and animals are marked by deeply ingrained cultural practices.

The households in this system often keep large herds and move them over long distances according to water and pasture availability (de Glanville et al., 2020; Lind et al., 2020). In the agro-pastoral system, households typically own fewer animals than pastoralists and practice mixed crop and livestock agriculture (Cibils et al., 2015; de Glanville et al., 2020). In the smallholder system, households keep relatively small herds, often for dairy purposes, and are located in peri-urban areas, where the population density is high, and land is scarce and fragmented (de Glanville et al., 2020; Habanabakize et al., 2022).

In northern Tanzania, the prevalence of brucellosis is higher in pastoral than in non-pastoral livestock (Bodenham et al., 2021; Shirima et al., 2010). Brucellosis is a bacterial zoonosis that is endemic in the region, affecting livestock productivity as well as human health and welfare (Bodenham et al., 2020; Cash-Goldwasser et al., 2018; Makala et al., 2020; Ntirandekura et al., 2020). Surveys delivered across Tanzania (and other countries) capture key livestock production metrics. Combining livestock brucellosis prevalence data with production data could enable the quantification of system-specific losses attributable to the disease, i.e., production losses attributable to brucellosis in pastoral and non-pastoral systems separately. This information could then be used to inform policy- and decision-making for disease control.

The objectives of this chapter were first to develop, apply, and evaluate harmonisation approaches to integrate multiple datasets from household surveys delivered in northern Tanzania between 2013 and 2019. Clustering analyses were then performed to classify households across the harmonised datasets into different production systems.

## 3.2 Methods

A protocol based on the Maelstrom Research guidelines for retrospective data harmonisation was followed (Fortier et al., 2017). This protocol was divided into four iterative and interrelated steps:

- Step 1: assemble information and select surveys;
- Step 2: define variables and evaluate harmonisation potential;
- Step 3: process data;
- Step 4: estimate the quality of the harmonisation process.

Before steps 1 to 4 were executed, an informal review of the literature on (i) household surveys in northern Tanzania, (ii) classification of livestock production systems, and (iii) clustering algorithms was carried out. Researchers with experience in these literature topics were also contacted for feedback on methodological issues. These preliminary steps enabled the identification of candidate surveys and the definition of survey selection criteria.

### 3.2.1 Step 1: assemble information and select surveys

General information about the candidate surveys, including research design, data collection procedures, questionnaires, and data processing and evaluation methods, was documented. Survey data were obtained from the official survey websites or directly requested from researchers or data custodians.

The 'Social, Environmental, and Economic Drivers of Zoonotic disease' (SEEDZ) project delivered a large-scale, cross-sectional survey, dedicated to the analysis of risk factors of several human and animal zoonoses, between February and November 2016, in two regions of northern Tanzania: Arusha and Manyara. In SEEDZ, households were classified by production system, and livestock were tested for brucellosis. The study design and the methods used have been described in detail elsewhere (Bodenham et al., 2021; de Glanville et al., 2020).

The SEEDZ survey was used as a contextual, spatial, and temporal reference for the definition of survey selection criteria. Thus, the additional selected household surveys were those that met each of the following conditions: (i) were delivered in the SEEDZ study area (Arusha and Manyara) or neighbouring regions (Kilimanjaro, Tanga, Dodoma, Singida, Simiyu, and Mara), (ii) collected information on the number of livestock kept and their production (e.g., wholesale price, milk yield, lactation length, and milk price), household demographics, crop agriculture, livestock management practices, food consumption practices, and indicators of household vulnerability (e.g., crop losses, illness in livestock and people), (iii) took place between 2013 and 2019 (three years before and after SEEDZ), and (iv) had publicly accessible survey data that included approximate geolocation of the households.

The following criteria were applied for the selection of households contributing data in the candidate surveys: i) living in the SEEDZ study area (Arusha and Manyara) or neighbouring regions (Kilimanjaro, Tanga, Dodoma, Singida, Simiyu, and Mara), and, ii) ownership of cattle, sheep, or goats at the time of the interview.

### 3.2.2 Step 2: define variables and evaluate harmonisation potential

The definition and availability of variables across survey datasets were compared and analysed. This step enabled an initial evaluation of the potential for running harmonised household classification models, i.e., clustering models based on de Glanville et al. (2020) applied to households from candidate surveys and those in SEEDZ. The clustering analyses of the SEEDZ dataset by de Glanville et al. (2020) served as a basis for data harmonisation and identification of livestock production systems in candidate datasets.

#### 3.2.2.1 Definition and availability of variables across survey datasets

The definition and availability of variables in the candidate survey datasets were compared with those in SEEDZ to identify equivalent variables across datasets. The corresponding questionnaires and the number of missing observations were analysed. To indicate availability in each dataset, variables were categorised as follows: 'A' (absence of variable/question), 'I' (incomplete, if $>$ 5% of the observations were missing, or if the question/item was potentially biased), and 'C' (complete availability of question/variable, or $\leq$ 5% of the observations missing). The criteria for categorising variables were specific to each question/variable and are available in Appendix B.1. Efforts were made to maximise data usage while also ensuring an acceptable balance between (i) some level of heterogeneity in variable specifications, based on question wording, (ii) the eligibility of the surveys, and (iii) the legitimacy of the harmonisation procedure.

For all datasets, the common variables used for clustering were divided into eight domains (as per de Glanville et al., 2020): 1) local household environment; 2) household demographics; 3) crop agriculture; 4) numbers of cattle, sheep, and goats owned; 5) other livestock owned; 6) livestock management practices; 7) household food consumption practices; and, 8) indicators of household vulnerability. Domains 1 (local environment) and 4 (number of livestock owned) include only numerical variables. The other domains include only categorical variables (binary variables that indicate the presence or absence of an attribute).

#### 3.2.2.2 Environmental data

Data on variables in domain 1 (local household environment) were sourced from third-party datasets. A summary description of each environmental variable (and data sources) is available in Table 3.1. The methods and sources used to gather these variables were the same as those described by de Glanville et al. (2020) for SEEDZ. However, some methods were not applicable due to the relatively low precision of GPS locations of households in the candidate surveys. For such cases, buffers were created around the approximated GPS locations of households using the 'sf' package (Pebesma, 2018) in R (R Core Team, 2019). The mean data value for all environmental variables within each buffer was extracted using the 'exactextractr' package (Baston, 2020) in R. The proportion of the buffer area classified as each landcover type was extracted using the 'sf' package in R. The village area to which the households belonged was calculated as the weighted mean of the areas of the villages covered by the buffer.

**Table 3.1:** Description of environmental variables used in clustering models based on de Glanville et al. (2020) and corresponding data sources. Defined spatial extent: northeastern Tanzania (Arusha, Manyara, Kilimanjaro, Tanga, Dodoma, Singida, Simiyu, and Mara).

| Environmental variable | Description | Data source |
|---|---|---|
| Annual precipitation | Annual precipitation in mm | www.worldclim.org/bioclim |
| Average temperature | Annual average mean temperature in $^{o}$C | www.worldclim.org/bioclim |
| Average vegetation cover | Annual average enhanced vegetation index (EVI) | https://lpdaac.usgs.gov/products/mod13q1v006 |
| Cattle density | Number of cattle per km$^2$ | www.fao.org/ag/againfo/resources/en/glw/GLW_dens.html |
| Chicken density | Number of chicken per km$^2$ | www.fao.org/ag/againfo/resources/en/glw/GLW_dens.html |
| Cropland cover | Proportion of an area with 1 km radius classified as cropland* | https://landsat.gsfc.nasa.gov/data$^{\diamond}$ |
| Distance to main road | Euclidean distance to the nearest trunk road (in km) using the Distance Matrix tool in QGIS | www.fao.org/geonetwork/srv/en/main.home |
| Forest cover | Proportion of an area with 1 km radius classified as forest* | https://landsat.gsfc.nasa.gov/data$^{\diamond}$ |
| Goats density | Number of goats per km$^2$ | www.fao.org/ag/againfo/resources/en/glw/GLW_dens.html |
| Grassland cover | Proportion of an area with 1 km radius classified as grassland* | https://landsat.gsfc.nasa.gov/data$^{\diamond}$ |
| Human population density | Human population per km$^2$ in 2016 | www.worldpop.org.uk |
| Maximum slope | Maximum slope (in degrees) within 1 km radius$^{\dagger}$ | https://lta.cr.usgs.gov/srtmgl3.html |
| Pigs density | Number of pigs per km$^2$ | www.fao.org/ag/againfo/resources/en/glw/GLW_dens.html |
| Sheep density | Number of sheep per km$^2$ | www.fao.org/ag/againfo/resources/en/glw/GLW_dens.html |
| Travel time to market centre | Travel time (in hours) to a town of greater than 20,000 people | https://harvestchoice.org/labs/travel-time-major-marketcities |
| Village area | Area of the village (in decimal degrees) | www.nbs.go.tz |

* For the candidate datasets, the proportion of the buffer area classified as each land cover type (cropland, grassland, and forest) was used. $^{\diamond}$ For the candidate datasets, the land cover data were downloaded from https://lpdaac.usgs.gov/products/mcd12q1v006. $^{\dagger}$ For the candidate datasets, SRTM (Shuttle Radar Topography Mission) data were downloaded using the SRTM-Downloader plugin (Duester, 2021) in QGIS (QGIS.org, 2020), and the mean slope within the buffer was used.

#### 3.2.2.3 Spatial and statistical analyses

General descriptive statistics were computed to compare the characteristics of households across datasets. This analysis aimed to identify any gross differences between datasets, particularly in key variables, which could compromise the legitimacy of the classification models. Key variables were considered those that were available across datasets and contributed the most (within the upper decile of the contribution scores) to the inertia of the first factor at the multiple factor analysis (MFA) of SEEDZ households by de Glanville et al. (2020). MFA is a procedure that simplifies and denoises the informative value of continuous and categorical variables that are organised in meaningful groups, e.g., in domains (Lê, Josse, and Husson, 2008).

The preliminary search for differences in key variables between datasets was carried out visually, through the inspection of boxplots of continuous variables (domains 1 and 4) and forest plots of categorical variables (domains 2, 3, and 5 to 8). The boxplots and forest plots were made with the 'ggpubr' and the 'ggforestplot' packages in R, respectively (Kassambara, 2020; Nightingale Health, 2020). The confidence intervals of the observed proportions were estimated with the 'exact' method of the 'binom.confint' function of the 'binom' package in R (Dorai-Raj, 2014). Differences in mean attribute values or proportion of households reporting attribute presence across datasets were assessed with the Wilcoxon rank-sum test and the Pearson's Chi-squared test with Yates's continuity correction, respectively (Chan, 2016). The significance level was set at 5%.

The spatial distribution of households from each dataset was analysed in R. The manipulation and processing of spatial and environmental data were conducted in R, except for calculating the Euclidean distance of households to the nearest trunk road, which was performed in QGIS. The polygons used to demark the border of regions were extracted from the GADM database (`https://gadm.org/`), version 3.4, April 2018.

### 3.2.3 Step 3: process data

#### 3.2.3.1 Harmonised household classification models

A set of harmonised household classification models, based on the two-stage clustering algorithm implemented by de Glanville et al. (2020), were run with different combinations of datasets and variables. A number of integration procedures were also tested, using the clustering of SEEDZ households as reference: i) adding all datasets to the clustering algorithm altogether; ii) adding only one dataset at a time; or, iii) adding one household at a time to the original model (M0), which initially contained SEEDZ data only, as reported by de Glanville et al. (2020).

As performed in M0 by de Glanville et al. (2020), all continuous variables were scaled in each of the harmonised models either through a Z-score or log transformation, depending on the distribution of the variable. All models were run with imputation of missing values using the regularised iterative MFA algorithm of the 'missMDA' package (version 1.17) (Josse and Husson, 2016) in R. The number of observations by dataset is available in Appendix B.1.

The first stage of the clustering algorithm consisted of dimension reduction using MFA. This stage was carried out with the 'MFA' function of the 'FactoMineR' package (version 2.3), in R (Lê, Josse, and Husson, 2008). In the second stage, the low-dimensional data obtained from the MFA (factors) were used to identify clusters of households, i.e., households sharing similar characteristics, through hierarchical cluster analyses (HCA). A statistically significant v-test result ($> 1.96$, or p-value $< 0.05$; the v-test is a criterion with a Normal distribution (Lê, Josse, and Husson, 2008)) was used as indicative of a difference in the mean value of the variable within a cluster, as compared to the mean value of the variable in the population. This second stage was carried out with the 'HCPC' (Hierarchical Clustering on Principal Components) function of the same package ('FactoMineR') in R. The partition of the hierarchical tree was automated, based on higher relative loss of inertia, which ensured the ability to identify a production system other than those obtained with M0. For those models with which the automated partition gave rise to more than three clusters (the number of clusters obtained with M0), a version of the model constrained to three clusters (named 'manual', distinct from 'auto', with automated partition) was also run. In any case, only factors associated with 'large' eigenvalues, based on the presence of a natural break on a scree plot, were included in the HCA. Depending on the model run, between three and six factors associated with 'large' eigenvalues were included in the clustering procedure.

### 3.2.4 Step 4: estimate the quality of the harmonised household classification models

The quality or performance of each model was evaluated with reference to the classification of SEEDZ households derived with M0. The performance metrics estimated were the following:

- sensitivity: the probability of a household that had been classified in cluster 1, pastoral, with M0, being assigned to the same cluster, with an alternative model;
- specificity: the probability of a household that had been classified in cluster 2 or 3, non-pastoral, with M0, being assigned to one of the same clusters, with an alternative model;
- accuracy: the probability of a model classifying a household correctly as pastoral (cluster 1) or non-pastoral (cluster 2 or 3), using M0 as reference, i.e., the classification of SEEDZ households as per de Glanville et al. (2020).

Descriptive statistics and spatial analyses by production system (as generated by the best-performing model with three clusters) in each of the candidate datasets, as compared to SEEDZ, were also run to assess the quality of the classification. Whenever necessary to evaluate inconsistencies in the household classification, additional candidate survey data, i.e., variables not used in the models, were analysed.

## 3.3 Results

### 3.3.1 Survey information

Two candidate surveys were identified for analysis at the preliminary steps of this study's protocol: (i) the 'Living Standards Measurement Study' (LSMS), and (ii) the 'Rural Household Multiple Indicator Survey' (RHoMIS).

The LSMS is a multi-country, nationally-representative, household survey programme led by the World Bank since 1980s (World Bank, 2021). This programme has a longitudinal design, which allows the living conditions of a sample of households to be tracked over time, in 'waves'. In Tanzania, four waves of the programme have been delivered since 2008. In the first three waves, the cohort sample was based on the enumeration areas of the 2002 population and housing census. In the fourth

wave (October 2014 to November 2015), given the availability of a new sampling frame from the 2012 population and housing census and the need to adjust the representativeness of the survey, a new set of households were also interviewed (National Bureau of Statistics (NBS), 2016). Data from this new set of households in wave four (LSMS4) and from the previous cohort in wave three (LSMS3, October 2012 to November 2013) were used in this study due to their temporal proximity to the SEEDZ survey. In LSMS, a 'household' is defined as 'people who live together and share income and also basic needs' (National Bureau of statistics (NBS), 2012, 2014).

RHoMIS is a standard survey tool focused on household socioeconomic characteristics, which has been applied in more than 30 countries, since 2015 (van Wijk et al., 2020). Access to data is possible upon request in the official website (`www.rhomis.org/`). In northern Tanzania, based on GPS location data, two applications of the RHoMIS tool were available by June 2020: i) RHoMIS1 - a survey funded by the Global Alliance for Livestock Veterinary Medicines (GALVmed) and led by the International Livestock Research Institute (ILRI) interviewed livestock keepers randomly selected from community animal health service records in 2017; and, ii) RHoMIS2 - a survey funded by the United States Department of Agriculture's Foreign Agriculture Service and led by the International Centre for Research in Agroforestry (ICRAF) interviewed randomly selected households based on village lists obtained from the village elders in 2018. GPS locations were unavailable for another RHoMIS application, which was then not included in this study: a survey led by the International Livestock Research Institute, in 2015, in the Tanga region of northern Tanzania. In RHoMIS, a 'household' is defined as people 'who usually live, sleep and eat' at a house or compound and includes 'anyone who is temporarily away for less than 3 months, or anyone who is staying for more than 3 months' (van Wijk et al., 2020).

All households surveyed in SEEDZ were included in this study (n=404). A total of 1,137 households were selected from LSMS and RHoMIS. A summary of the data used in this study is available in Table 3.2. All surveys gathered data through face-to-face interviews with either household heads or other household members.

**Table 3.2:** Timing, spatial extent, and number of households included in each survey selected for data harmonisation and identification of livestock production systems.

| | Survey* | | | | |
|---|---|---|---|---|---|
| | SEEDZ | LSMS3 | LSMS4 | RHoMIS1 | RHoMIS2 |
| Year | 2016 | 2012-2013 | 2014-2015 | 2017 | 2018 |
| Spatial extent of the full survey in Tanzania (regions) | Arusha, Manyara | Nationwide | Nationwide | Nationwide | Dodoma, Iringa, Tabora, Zanzibar |
| Households in the full survey (n) | 404 | 5,010 | 3,352 | 994 | 841 |
| Households surveyed in the study area (n)◇ | 404 | 935 | 712 | 302 | 206 |
| Livestock-keeping households surveyed in the study area (n)◇,† | 404 | 427 | 319‡ | 302 | 89 |

* SEEDZ refers to the Social, Environmental, and Economic Drivers of Zoonotic disease project. LSMS3 and LSMS4 refer to the third and fourth waves of the Living Standards Measurement Study, respectively. RHoMIS1 and RHoMIS2 refer to the Rural Household Multiple Indicator Survey applications led by the International Livestock Research Institute and the International Centre for Research in Agroforestry, respectively. ◇ Confirmed by GPS location, i.e., located in one of the following regions of northern Tanzania: Arusha, Manyara, Kilimanjaro, Tanga, Dodoma, Singida, Simiyu, and Mara. † Number of households from each survey that were included in this study. ‡ One household with the same identification number as in wave 3 was excluded.

In addition to the location of the villages visited in SEEDZ, the spatial distribution of households in LSMS3, LSMS4, RHoMIS1, and RHoMIS2 that were included in this study is shown in Fig. 3.1. The GPS coordinates of the households surveyed in LSMS are provided in their modified form, which relies on a random offset of cluster centre-point coordinates, i.e., the observed locations in Fig. 3.1 represent the average of household GPS locations by enumeration area. The offset in LSMS coordinates ranged from 0-2 km in urban areas and 0-5 km in rural areas. Additionally, 1% of the LSMS coordinates in rural areas were offset between zero and 10 km. Moreover, the offset LSMS coordinates are constrained at the district level (National Bureau of statistics (NBS), 2012, 2014). The GPS coordinates in the RHoMIS dataset are rounded to three decimal places (equivalent to approximately 1.1 km) (RHoMIS, 2019).

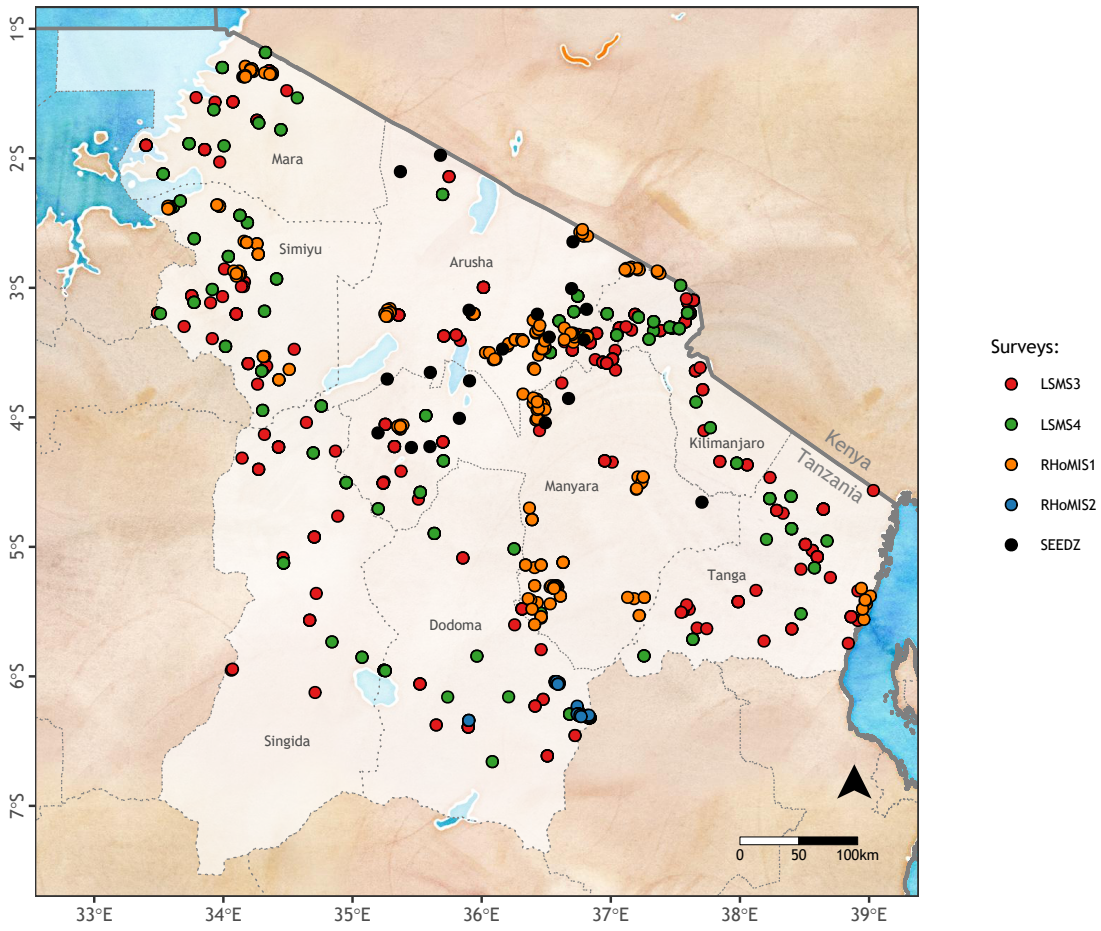



**Figure 3.1:** Spatial distribution of households from each survey included in this study. SEEDZ refers to the Social, Environmental, and Economic Drivers of Zoonotic disease project (black points represent villages visited). LSMS3 and LSMS4 refer to the third and fourth waves of the Living Standards Measurement Study, respectively. RHoMIS1 and RHoMIS2 refer to the Rural Household Multiple Indicator Survey applications led by the International Livestock Research Institute and the International Centre for Research in Agroforestry, respectively. White-filled translucent polygons indicate the study area. Dashed lines delineate regions. Solid lines indicate national borders. The polygon shapefiles were obtained from GADM, the Database of Global Administrative Areas (`https://gadm.org/`). Map tiles by Stamen Design, under CC BY 3.0. Data by OpenStreetMap, under CC BY SA.

Given that the questions asked (and the options available to answer) were mostly the same within LSMS and RHoMIS, the two waves of the LSMS (LSMS3 and LSMS4) and the two applications of the RHoMIS survey (RHoMIS1 and RHoMIS2) were analysed together, i.e., the comparator datasets were SEEDZ, LSMS, and RHoMIS.

### 3.3.2 Variable availability and harmonisation potential

The reference household classification model (M0) included 76 variables. Out of these 76 variables, 12 (15.8%) were absent in LSMS, and 28 (36.8%) were absent in RHoMIS. All the variables that were absent in LSMS were also absent in RHoMIS. It was then possible to set up the following harmonised household classification models:

- Models:
  - M0 (model 0): the original model with SEEDZ only, as reported by de Glanville et al. (2020);
  - M1: model with all SEEDZ variables except those that were missing (category 'A', absence of variable/question) in RHoMIS;
  - M2: model with all SEEDZ variables except those that were missing (category 'A', absence of variable/question) in LSMS;
- Integration process:
  - '1b1': LSMS and RHoMIS households are added 'one by one' to the whole SEEDZ dataset, minimising the impact of LSMS and RHoMIS on the inertia (an indicator of internal cluster coherence) of SEEDZ clustering;
  - 'sl': SEEDZ and LSMS datasets (excludes RHoMIS) are analysed altogether;
  - 'sr': SEEDZ and RHoMIS datasets (excludes LSMS) are analysed altogether;
  - 'all': SEEDZ, LSMS, and RHoMIS datasets are analysed altogether.

A total of 48 (63.2%) and 64 (84.2%) variables out of 76 in M0 were included in M1 and M2, respectively. All variables in domains 1, 4, and 5 were present in LSMS and RHoMIS, and were thus included in M1 and M2. The highest percentage of absent variables in LSMS and RHoMIS for one single domain was recorded in domain 2 (6 out of 11, i.e 54.5%), which included demographic characteristics such as education, gender, and tribe of the household head. The availability of all variables by dataset and their inclusion in the three main household classification models is shown in Table 3.3.

**Table 3.3:** Availability of variables by dataset and their inclusion in the three household classification models: M0, M1, and M2.

| | | | Availability by dataset* | | |
|---|---|---|---|---|---|
| Variable | Domain◇ | Model usage† | SEEDZ | LSMS | RHoMIS |
| Annual precipitation | 1 | M0; M1; M2 | C | I | C |
| Average temperature | 1 | M0; M1; M2 | C | I | C |
| Average vegetation cover | 1 | M0; M1; M2 | C | I | C |
| Cattle density | 1 | M0; M1; M2 | C | I | C |
| Chicken density | 1 | M0; M1; M2 | C | I | C |
| Cropland cover | 1 | M0; M1; M2 | C | I | C |
| Distance to main road | 1 | M0; M1; M2 | C | I | C |
| Forest cover | 1 | M0; M1; M2 | C | I | C |
| Goats density | 1 | M0; M1; M2 | C | I | C |
| Grassland cover | 1 | M0; M1; M2 | C | I | C |
| Human population density | 1 | M0; M1; M2 | C | I | C |
| Maximum slope | 1 | M0; M1; M2 | C | I | C |
| Pigs density | 1 | M0; M1; M2 | C | I | C |
| Sheep density | 1 | M0; M1; M2 | C | I | C |
| Travel time to market centre | 1 | M0; M1; M2 | C | I | C |
| Village area‡ | 1 | M0; M1; M2 | C | I | C |
| Arusha tribe | 2 | M0 | C | A | A |
| Barabaig tribe | 2 | M0 | C | A | A |
| Government title for land | 2 | M0; M2 | C | C | A |
| Head primary education | 2 | M0; M1; M2 | C | C | C |
| Household head male | 2 | M0; M1; M2 | C | C | I |
| Iraqw tribe⋆ | 2 | M0 | C | A | A |
| Latrine ownership⋆ | 2 | M0; M2 | C | C | A |
| Maasai tribe⋆ | 2 | M0 | C | A | A |
| Meru tribe | 2 | M0 | C | A | A |
| Treat drinking water | 2 | M0; M2 | C | C | A |
| Turu tribe | 2 | M0 | C | A | A |
| Grow beans | 3 | M0; M1; M2 | C | C | C |
| Grow cowpeas | 3 | M0; M1; M2 | C | C | C |
| Grow maize | 3 | M0; M1; M2 | C | C | C |
| Grow millet | 3 | M0; M1; M2 | C | C | C |
| Grow no crops | 3 | M0; M1; M2 | C | C | C |
| Grow onions | 3 | M0; M1; M2 | C | C | C |
| Grow potato | 3 | M0; M1; M2 | C | C | C |
| Grow sesame | 3 | M0; M1; M2 | C | C | C |
| Grow sorghum | 3 | M0; M1; M2 | C | C | C |

Continuation of Table 3.3

| | | | Availability by dataset* | | |
|---|---|---|---|---|---|
| Variable | Domain◇ | Model usage† | SEEDZ | LSMS | RHoMIS |
| Grow sunflower | 3 | M0; M1; M2 | C | C | C |
| Grow wheat | 3 | M0; M1; M2 | C | C | C |
| Growing crops $>$ 10 years | 3 | M0 | C | A | A |
| Own plough | 3 | M0; M2 | C | C | A |
| Sell crops | 3 | M0; M1; M2 | C | C | C |
| Staple crops last $>$ 6 m | 3 | M0 | C | A | A |
| Number of cattle‡ | 4 | M0; M1; M2 | C | C | C |
| Number of goats‡ | 4 | M0; M1; M2 | C | C | C |
| Number of sheep | 4 | M0; M1; M2 | C | C | C |
| Chickens | 5 | M0; M1; M2 | C | C | C |
| Donkeys‡ | 5 | M0; M1; M2 | C | C | C |
| European breed cattle | 5 | M0; M1; M2 | C | C | C |
| European breed small stock | 5 | M0; M1; M2 | C | C | C |
| Pigs‡ | 5 | M0; M1; M2 | C | C | C |
| Cattle transhumance⋆ | 6 | M0 | C | A | A |
| Graze cattle with small stock | 6 | M0 | C | A | A |
| Sell milk | 6 | M0; M1; M2 | C | I | I |
| Small stock transhumance⋆ | 6 | M0 | C | A | A |
| Tether cattle | 6 | M0; M2 | C | I | A |
| Tether small stock | 6 | M0; M2 | C | I | A |
| Vaccinate against any disease | 6 | M0; M2 | C | I | A |
| Zero graze cattle | 6 | M0; M1; M2 | C | I | C |
| Zero graze small stock | 6 | M0; M1; M2 | C | I | C |
| Any animal source food | 7 | M0; M1; M2 | C | C | I |
| Blood | 7 | M0 | C | A | A |
| Dairy | 7 | M0; M1; M2 | C | C | I |
| Eggs | 7 | M0; M1; M2 | C | C | I |
| Fats | 7 | M0; M2 | C | C | A |
| Fish | 7 | M0; M2 | C | C | A |
| Legumes | 7 | M0; M1; M2 | C | C | I |
| Meat | 7 | M0; M2 | C | C | A |
| Poultry | 7 | M0; M2 | C | C | A |
| Roots | 7 | M0; M2 | C | C | A |
| Vegetables | 7 | M0; M1; M2 | C | C | I |
| Crop losses | 8 | M0; M1; M2 | C | C | I |
| Hunger | 8 | M0; M2 | C | I | A |
| Illness in livestock | 8 | M0; M2 | C | I | A |

Continuation of Table 3.3

| | | | Availability by dataset* | | |
|---|---|---|---|---|---|
| Variable | Domain◇ | Model usage† | SEEDZ | LSMS | RHoMIS |
| Illness in people | 8 | M0; M2 | C | I | A |
| Land loss | 8 | M0; M2 | C | I | A |
| Livestock losses | 8 | M0; M1; M2 | C | I | I |

* SEEDZ refers to the Social, Environmental, and Economic Drivers of Zoonotic disease project. LSMS refers to the Living Standards Measurement Study. RHoMIS refers to the Rural Household Multiple Indicator Survey. Each category indicates the availability of each variable by dataset, as follows: 'A' (absence of question/variable), 'I' (incomplete, if more than 5% of the observations were missing, or if the question/item was potentially biased), and 'C' (complete availability of question/variable). ◇ Eight domains as per de Glanville et al. (2020): 1 - local household environment; 2 - household demographics; 3 - crop agriculture; 4 - numbers of cattle, sheep, and goats owned; 5 - other livestock owned; 6 - livestock management practices; 7 - household food consumption practices; and, 8 - indicators of household vulnerability. † Model usage indicates the models in which each variable was used: M0 - the original model with SEEDZ data only, as reported by de Glanville et al. (2020); M1 - model with all SEEDZ variables except those that were missing in RHoMIS (category 'A' for RHoMIS); M2 - model with all SEEDZ variables except those that were missing in LSMS (category 'A' for LSMS). ‡ Key variables, i.e., variables that were available across datasets and contributed the most to the inertia of the first factor at MFA of SEEDZ households by de Glanville et al. (2020). ⋆ Variables that would be classified as 'key' if they were present in LSMS and RHoMIS.

The key variables, i.e., those that were available across datasets and contributed the most to the inertia of the first factor at MFA of SEEDZ households by de Glanville et al. (2020), were the following (indicated with ‡ in Table 3.3): i) village area; ii) number of cattle; iii) number of goats; iv) donkeys; and, v) pigs. Several variables in M0 would have been classified as 'key', based on their contribution scores, if they were present in LSMS and RHoMIS (indicated with ⋆ in Table 3.3): i) latrine ownership; ii) Iraqw tribe; iii) Maasai tribe; iv) cattle transhumance; and, v) small stock transhumance.

### 3.3.3 Descriptive statistics and household classification

#### 3.3.3.1 Descriptive statistics by dataset

Descriptive statistics by dataset are shown in Fig. 3.2, for numerical variables, and in Fig. 3.3, for categorical variables. The visual inspection of these figures did not indicate the presence of gross differences between datasets that could affect the legitimacy of applying the household classification models. However, compared to SEEDZ, there were some differences in key variables in LSMS and

RHoMIS identified through the Wilcoxon rank-sum or Pearson's Chi-squared tests. These differences were as follows: i) LSMS households kept fewer cattle and goats (Fig. 3.2); ii) RHoMIS households kept fewer goats, but more cattle (Fig. 3.2); and, iii) LSMS and RHoMIS were located in larger villages (Fig. 3.2) and were less likely to keep donkeys or pigs (Fig. 3.3).

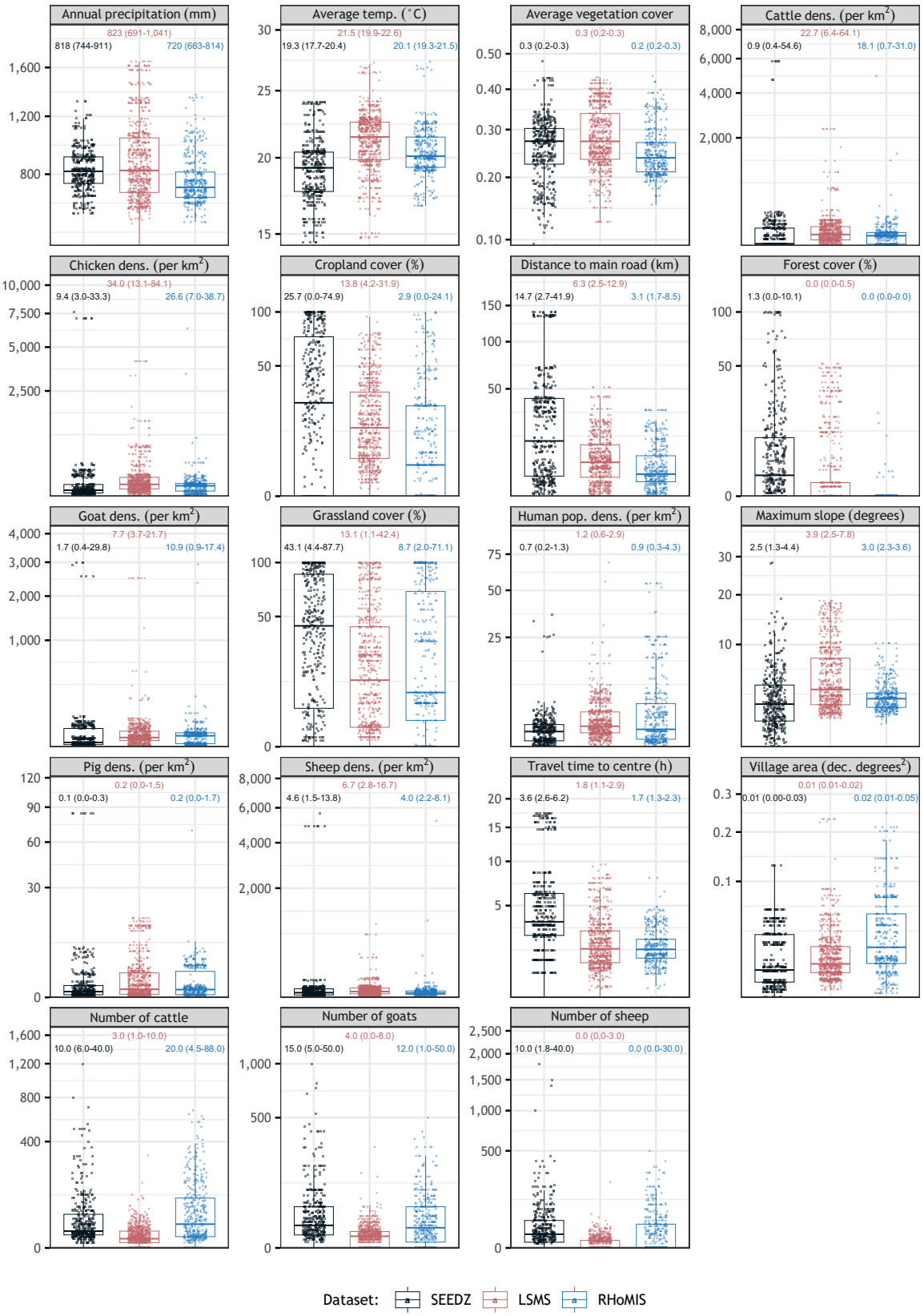



**Figure 3.2:** Boxplots of continuous variables, by dataset. Each shaped and coloured dot indicates an individual household observation. The median and the interval between the first and the third quartiles are shown at the top of each panel, for each dataset. The y-axis is on the square root scale.

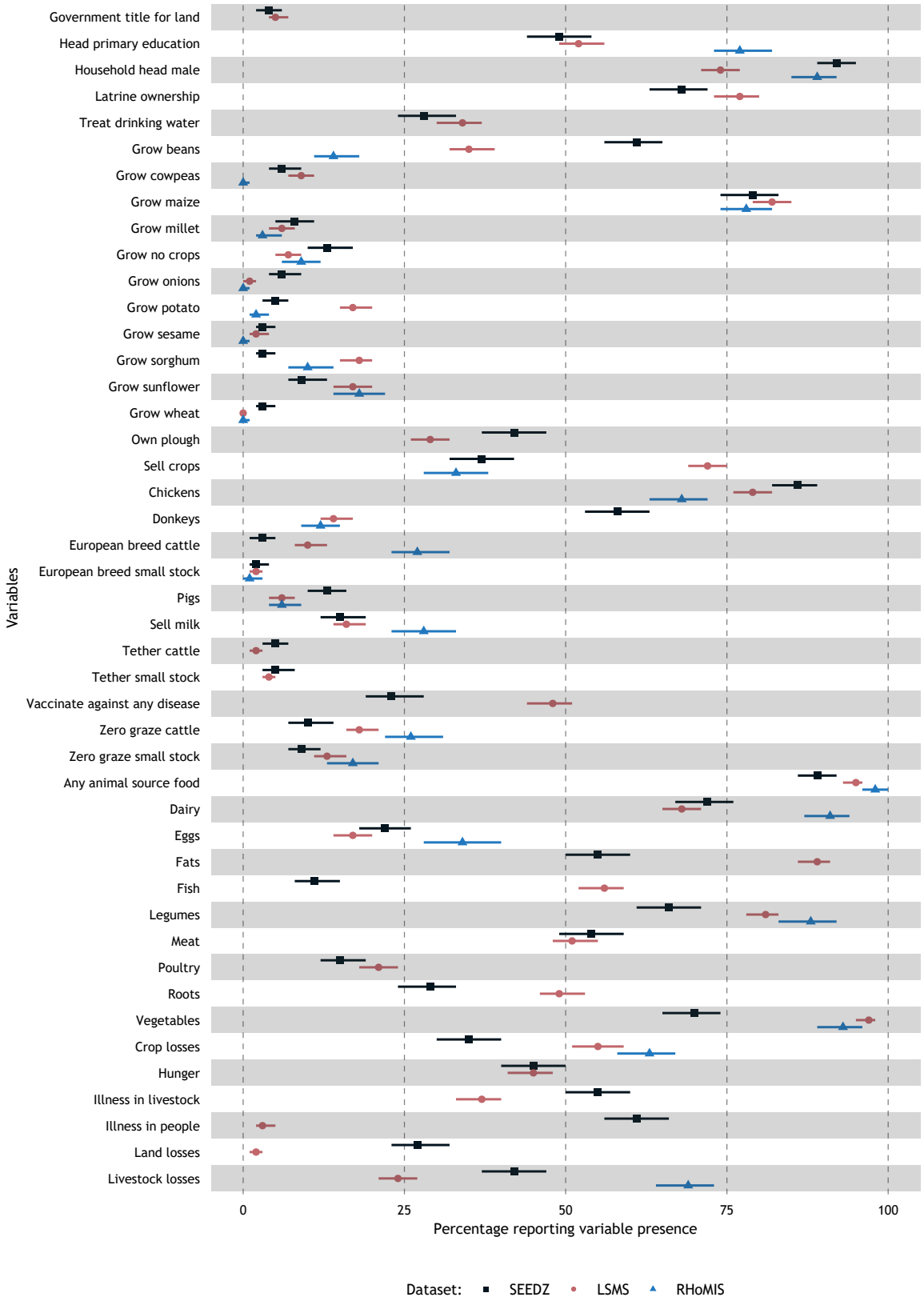



**Figure 3.3:** Forest plots of categorical variables, by dataset. Each shaped and coloured dot indicates the percentage of households with the attribute. The horizontal, coloured lines indicate the 95% confidence interval of the percentage estimate.

#### 3.3.3.2 Quality of the harmonised household classification models

Despite the reduced number of variables in M1 and M2, the classification of households with these models was highly accurate (Table 3.4). The accuracy estimates ranged from 86.6% to 95.0%. The models with the highest accuracy were the M2 models with LSMS and RHoMIS households being added one by one ('1b1' process) to SEEDZ and with partition of the hierarchical tree constrained to three clusters ('manual' partition; model hereafter referred to as 'M2_1b1_manual') or with automated partition ('auto' partition; 'M2_1b1_auto'), which both correctly classified 95.0% of SEEDZ households. In five out of eight integration processes tested, the automated partition of the hierarchical tree generated three clusters. With the other three integration processes tested, an additional cluster was created.

Compared to the 'M2_1b1_manual', 'M2_1b1_auto' created a fourth cluster with only two households, but the performance estimates were the same. The best-performing model with three clusters, 'M2_1b1_manual', was selected for classifying LSMS and RHoMIS households by production system. The characteristics of households by production system, as derived from this classification, are described next and further explored in Chapter 4 for the estimation of production losses attributable to livestock brucellosis in each system.

**Table 3.4:** Classification of households in each survey and performance (sensitivity, specificity, and accuracy) of each classification model.

| Model* | | | | | Households by cluster◇ | | | | Performance (%)† | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Name | Process | Partition | Dataset | n | 1 | 2 | 3 | 4 | Sens. | Spec. | Acc. |
| M0 | NA | auto | SEEDZ | 404 | 171 | 177 | 56 | | Ref. | Ref. | Ref. |
| M1 | 1b1 | auto | SEEDZ | 404 | 125 | 51 | 185 | 43 | 70.8 | 98.3 | 86.6 |
| | | | LSMS | 746 | 38 | 180 | 337 | 191 | | | |
| | | | RHoMIS | 391 | 72 | 78 | 134 | 107 | | | |
| | | manual | SEEDZ | 404 | 157 | 200 | 47 | | 86.5 | 96.1 | 92.1 |
| | | | LSMS | 746 | 63 | 457 | 226 | | | | |
| | | | RHoMIS | 391 | 95 | 164 | 132 | | | | |
| | sl | auto | SEEDZ | 404 | 171 | 193 | 40 | | 91.2 | 93.6 | 92.6 |
| | | | LSMS | 746 | 65 | 508 | 173 | | | | |
| | sr | auto | SEEDZ | 404 | 152 | 208 | 44 | | 81.9 | 94.8 | 89.4 |
| | | | RHoMIS | 391 | 140 | 13 | 238 | | | | |
| | all | auto | SEEDZ | 404 | 186 | 177 | 41 | | 95.3 | 90.1 | 92.3 |
| | | | LSMS | 746 | 71 | 519 | 156 | | | | |
| | | | RHoMIS | 391 | 120 | 154 | 117 | | | | |
| M2 | 1b1 | auto | SEEDZ | 404 | 173 | 184 | 47 | | 94.7 | 95.3 | 95.0 |
| | | | LSMS | 746 | 96 | 427 | 221 | 2 | | | |
| | | | RHoMIS | 391 | 115 | 148 | 128 | | | | |
| | | manual | SEEDZ | 404 | 173 | 184 | 47 | | 94.7 | 95.3 | 95.0 |
| | | | LSMS | 746 | 96 | 433 | 217 | | | | |
| | | | RHoMIS | 391 | 115 | 148 | 128 | | | | |
| | sl | auto | SEEDZ | 404 | 205 | 159 | 40 | | 97.1 | 83.3 | 89.1 |
| | | | LSMS | 746 | 74 | 492 | 180 | | | | |
| | sr | auto | SEEDZ | 404 | 173 | 30 | 193 | 8 | 91.8 | 93.1 | 92.6 |
| | | | RHoMIS | 391 | 35 | 245 | 4 | 107 | | | |
| | | manual | SEEDZ | 404 | 180 | 204 | 20 | | 92.4 | 90.6 | 91.3 |
| | | | RHoMIS | 391 | 113 | 4 | 274 | | | | |
| | all | auto | SEEDZ | 404 | 197 | 178 | 29 | | 95.9 | 85.8 | 90.1 |
| | | | LSMS | 746 | 73 | 523 | 150 | | | | |
| | | | RHoMIS | 391 | 115 | 138 | 138 | | | | |

* Model name: 'M0' - original model, as reported by de Glanville et al. (2020); 'M1' - model with all SEEDZ variables except those that were missing in RHoMIS; 'M2' - model with all SEEDZ variables except those that were missing in LSMS. Integration process: 'NA' - not applicable; '1b1' - LSMS and RHoMIS households added 'one by one' to the whole SEEDZ dataset; 'sl' - SEEDZ and LSMS datasets only (excludes RHoMIS) are analysed altogether; 'sr' - SEEDZ and RHoMIS datasets only (excludes LSMS) are analysed altogether; and, 'all' - SEEDZ, LSMS, and RHoMIS datasets are analysed altogether. Partition mechanism: 'auto' - automated partition; and, 'manual' - partition constrained to three clusters. Dataset: SEEDZ - Social, Environmental, and Economic Drivers of Zoonotic disease project; LSMS - Living Standards Measurement Study; and, RHoMIS - Rural Household Multiple Indicator Survey. n: number of households. Ref: reference model. ◇ Number of households by cluster. † Performance of the household classification model as compared to M0: 'Sens.' - sensitivity (the probability of a household that had been classified in cluster 1, pastoral, with M0, being assigned to the same cluster); 'Spec.' - specificity (the probability of a household that had been classified in cluster 2 or 3, non-pastoral, with M0, being assigned to one of the same clusters); and, 'Acc.' - accuracy (the probability of a model classifying a household correctly as pastoral (cluster 1) or non-pastoral (cluster 2 or 3), with reference to M0).

The individual LSMS and RHoMIS households scores on the first and second factors at the multiple factor analysis of the best-performing model with three clusters (M2_1b1_manual) followed, broadly, the distribution of SEEDZ households scores of M0. This result is shown in Fig. 3.4, where three distinct clusters are visible in LSMS and RHoMIS, overlapping those in SEEDZ: i) cluster one, predominately negative scores on dimension 1, consistent with pastoral households; ii) cluster two, predominately positive scores on dimension 1, consistent with agro-pastoral households; and, iii) cluster three, predominately positive scores on dimensions 1 and 2, consistent with smallholder households.

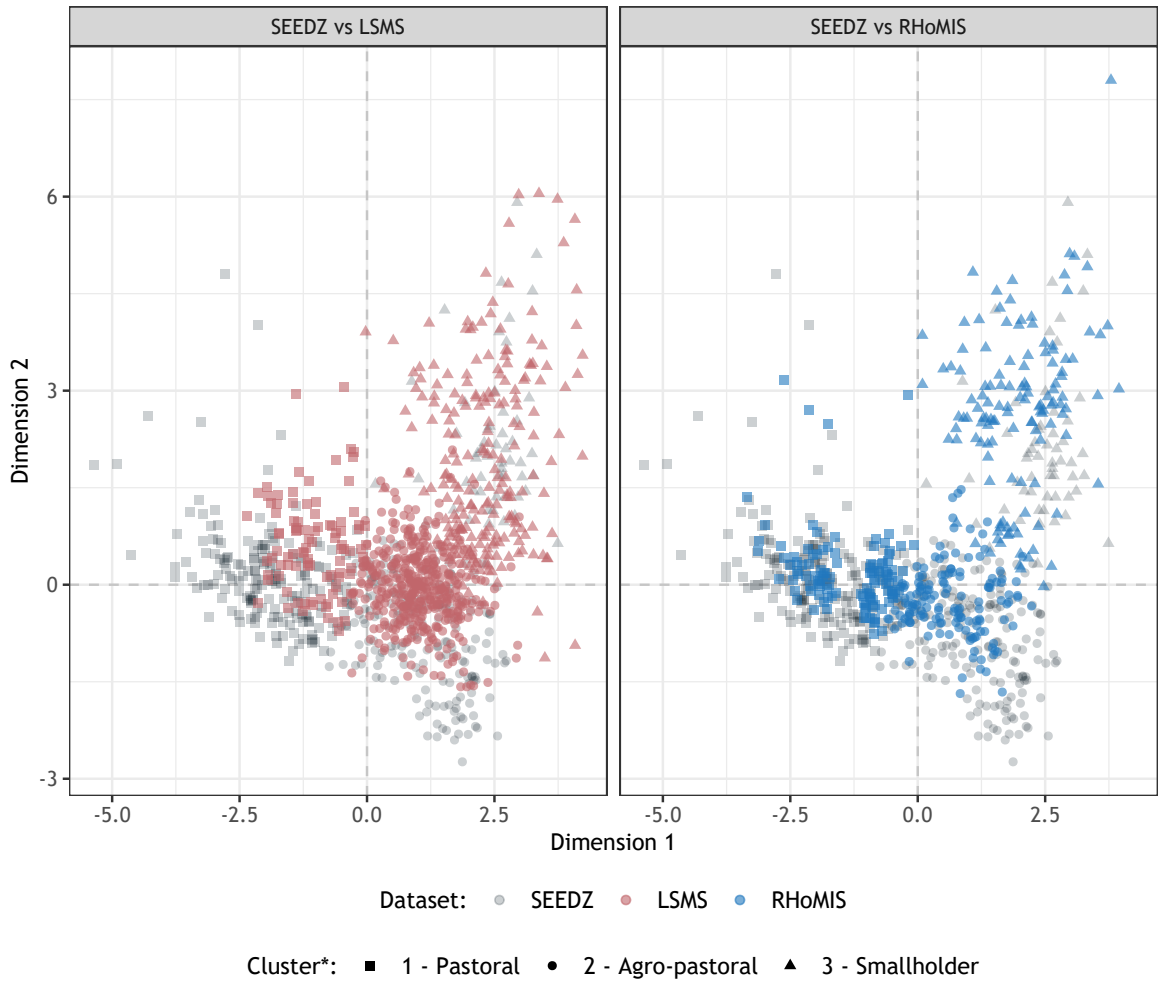



**Figure 3.4:** Individual scores of LSMS and RHoMIS households in shaped and coloured dots, as compared to SEEDZ's (grey squares, as per de Glanville et al. (2020)), on the first and second factors of the multiple factor analysis, and the membership of each household to a cluster*, with M2_1b1_manual: a model with all SEEDZ variables, except those that were missing in LSMS, integrated 'one by one' to the whole SEEDZ dataset, and with partition of the hierarchical tree constrained to three clusters. SEEDZ refers to the Social, Environmental, and Economic Drivers of Zoonotic disease project. LSMS refers to the Living Standards Measurement Study. RHoMIS refers to the Rural Household Multiple Indicator Survey.

Given that the purpose of this study was the classification of households into two predefined production systems (pastoral and non-pastoral), agro-pastoral (cluster two) and smallholder (cluster three) households were merged and characterised together as non-pastoral households. With the M2_1b1_manual model, the percentage of households that were classified as pastoral in SEEDZ, LSMS, and RHoMIS was 42.8% (173 out of 404), 12.9% (96 out of 746), and 29.4% (115 out of 391), respectively. Other descriptive statistics by dataset and production system, using the same model, are shown in Fig. 3.5, for numerical variables, and in Fig. 3.6, for categorical variables.

Overall, the differences in SEEDZ household characteristics between pastoral and non-pastoral production systems were also observed in LSMS and RHoMIS. Based on the Wilcoxon rank-sum or Pearson's Chi-squared tests, the differences in key variables between production systems in LSMS and RHoMIS were as follows (compared to non-pastoral households): i) pastoral households were located in larger villages (Fig. 3.5); ii) pastoral households kept a greater number of cattle and goats (Fig. 3.5); and, iii) pastoral households were more likely to keep donkeys and less likely to keep pigs (Fig. 3.6).

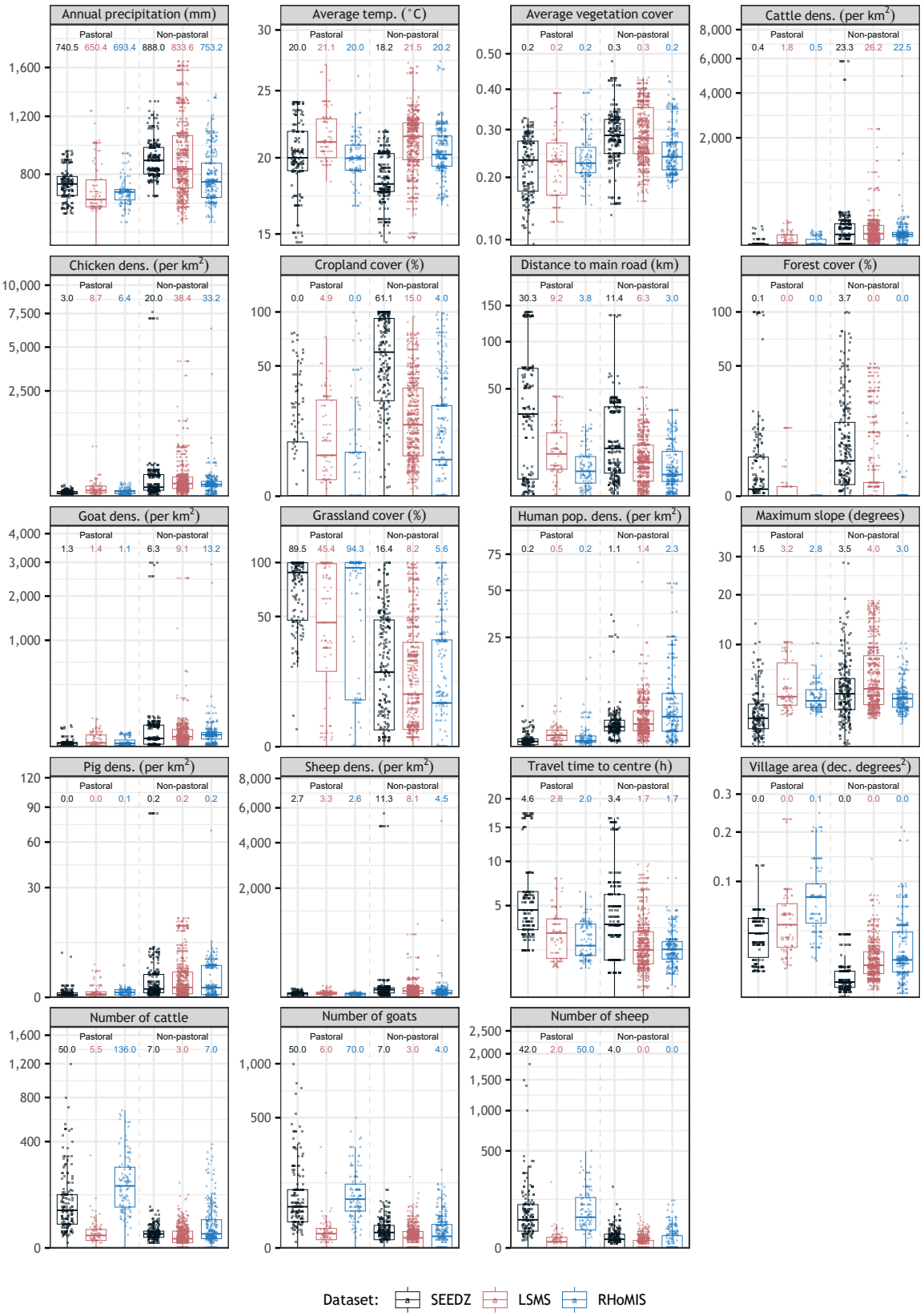



**Figure 3.5:** Boxplots of continuous variables, by dataset and production system (M2_1b1_manual model). Each shaped and coloured dot indicates an individual household observation. The median is shown at the top of each panel, for each dataset and production system. Dec: decimal. The y-axis is on the square root scale.

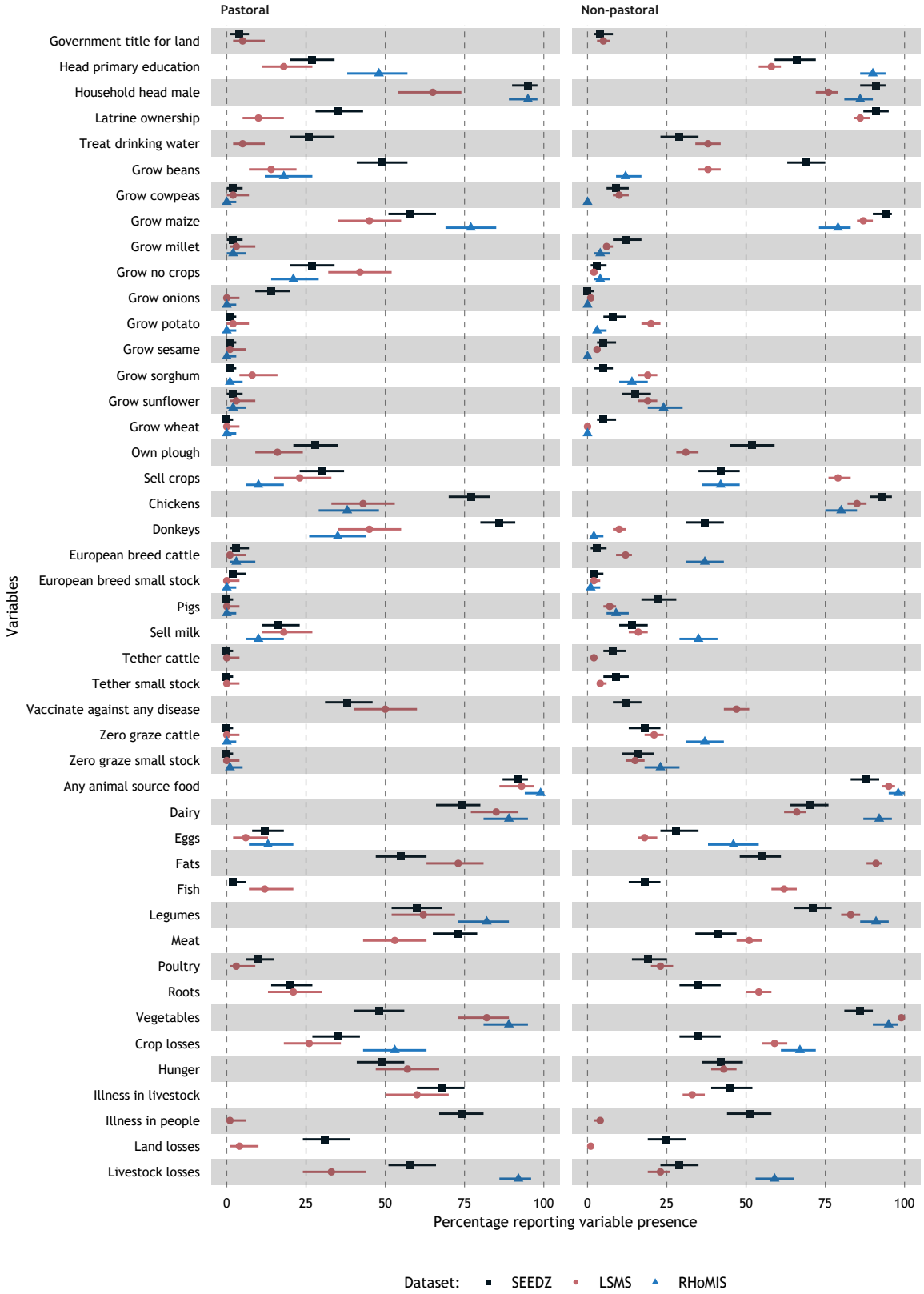



**Figure 3.6:** Forest plots of categorical variables, by dataset and production system (M2_1b1_manual model). Each shaped and coloured dot indicates the percentage of households with the attribute. The coloured lines indicate the 95% confidence interval of the percentage estimate.

The spatial distribution of LSMS and RHoMIS households by production system, as per classification using the M2_1b1_manual, is shown in Figs. 3.7 and 3.8. The majority of households that were classified as pastoral were from Arusha and Manyara. Approximately 75% (72 out of 96) and 96% (110 out of 115) of all pastoral households in LSMS and RHoMIS, respectively, were from these two regions.

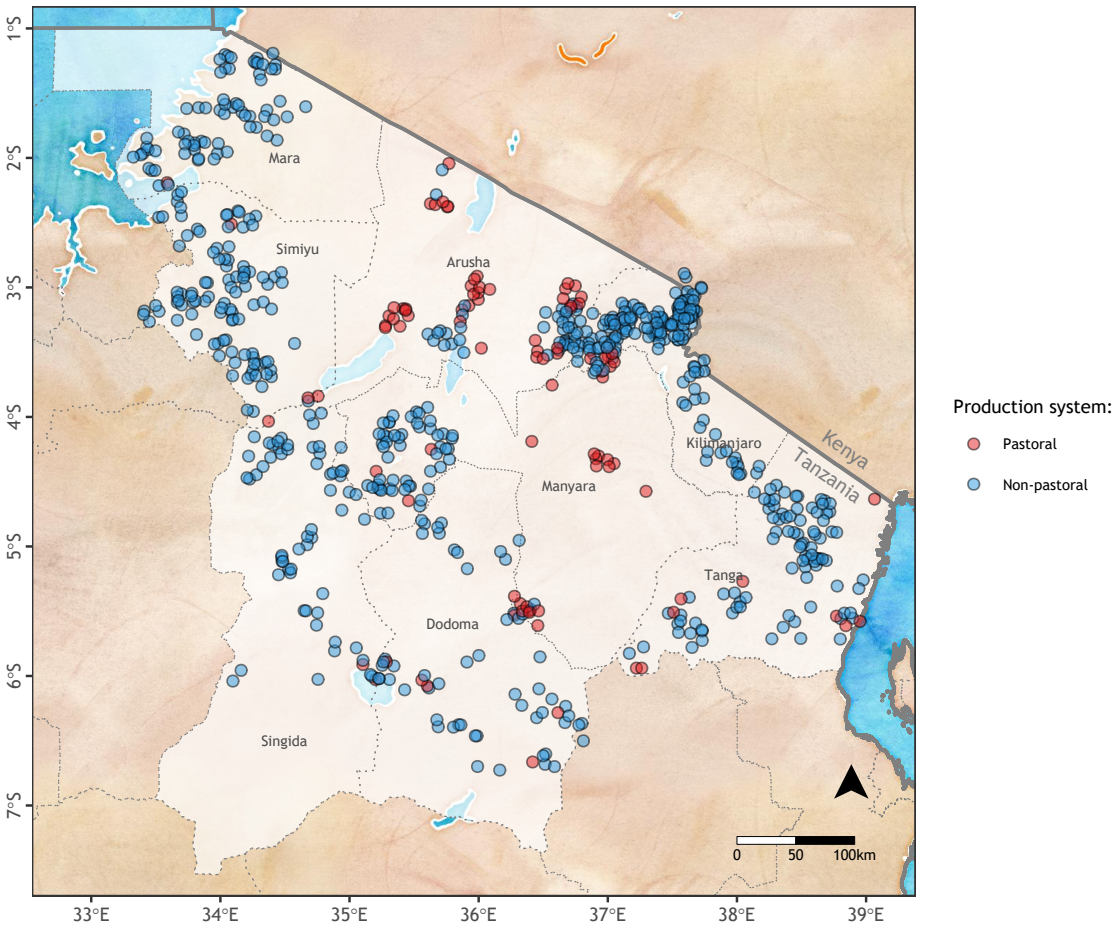



**Figure 3.7:** Spatial distribution of LSMS households by production system (M2_1b1_manual model). Overlapping points were randomly displaced for visualisation. White-filled translucent polygons indicate the study area. Dashed lines delineate regions. Solid lines indicate national borders. The polygon shapefiles were obtained from GADM, the Database of Global Administrative Areas (`https://gadm.org/`). Map tiles by Stamen Design, under CC BY 3.0. Data by OpenStreetMap, under CC BY SA.

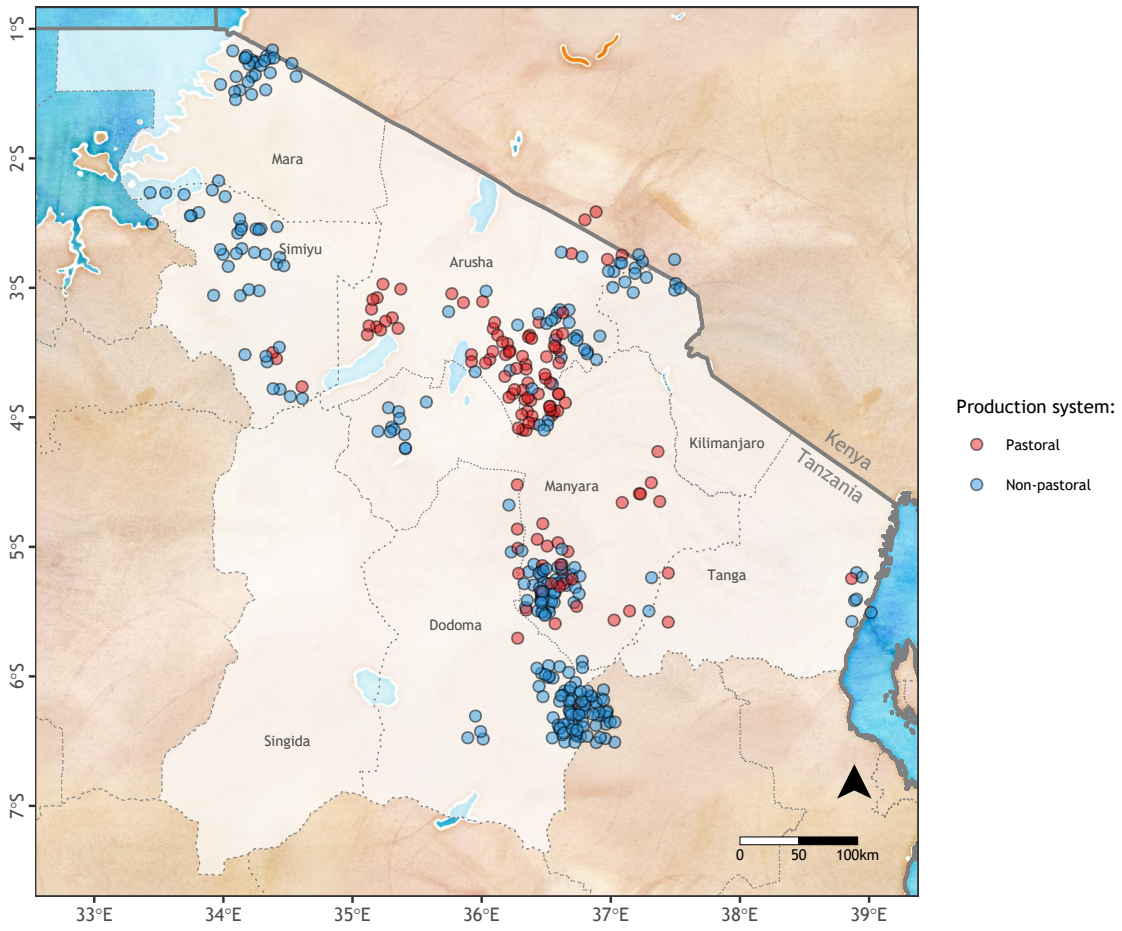



**Figure 3.8:** Spatial distribution of RHoMIS households by production system (M2_1b1_manual model). Overlapping points were randomly displaced for visualisation. White-filled translucent polygons indicate the study area. Dashed lines delineate regions. Solid lines indicate national borders. The polygon shapefiles were obtained from GADM, the Database of Global Administrative Areas (`https://gadm.org/`). Map tiles by Stamen Design, under CC BY 3.0. Data by OpenStreetMap, under CC BY SA.

## 3.4 Discussion

This study successfully developed and applied a harmonisation approach to integrating multiple datasets from household surveys delivered in northern Tanzania. Households from different surveys were grouped into two distinct traditional livestock production systems, pastoral and non-pastoral, each of them sharing a set of characteristics. The shared characteristics can be used to generate system-specific estimates of livestock disease prevalence and productivity. This approach is particularly useful in low-resource settings where data collection is challenging, and the potential for using secondary data remains to be fulfilled.

Although a number of statistical approaches for combining data from multiple sources are currently available, their application is mostly limited to cases where it is reasonable to assume unbiased estimates and overlapping sampling frames (Elliott, Raghunathan, and Schenker, 2018). The method proposed here used the construct of pastoralism, captured through a clustering algorithm, to overcome these limitations, particularly the non-overlapping sampling frames. This method can be used to estimate system-level parameters of livestock production. In combination with the Bayesian method for prevalence estimation described by Bodenham et al. (2021), also system-specific, it is then possible to estimate system-specific losses attributable to brucellosis (see Chapter 4).

Several comparability issues need to be highlighted due to their potential effect on the harmonisation process:

- Type of respondents and source of responses. The survey data combined in this study were all gathered through interviews with household heads, or other household members. However, the environmental data were gathered from third-party sources through methods that were not exactly the same across datasets due to the differing levels of precision in household geolocation information.
- Modes of data collection: Although all the surveys in this study were delivered face-to-face, the research instruments and devices used for questioning and recording answers differed in ways that are impractical to ascertain precisely.
- Survey context: All the surveys in this study were delivered by reputable Institutions and had well-characterised objectives, but the geographical extent of the surveys, the level of training and supervision of interviewers, and the components of the questionnaire were not always the same.
- Survey design: Different sampling approaches were used by each survey; LSMS3 and LSMS4 used a sampling design that was nationally representative of the general population; RHoMIS1 used a sampling design that was nationally representative of livestock keepers; RHoMIS2 used a sampling design that was regionally representative of the general population; and, SEEDZ used a sampling design that was regionally representative of livestock keepers.
- Question wording or the placement of the questions: the definition of an acceptable level of heterogeneity in wording and placement of questions between surveys was vulnerable to subjective interpretation (all differences in questions are shown in Appendix B.1).

Given that the method described in this study used a multivariate model to partition households into broad production systems (pastoral and non-pastoral), irrespective of the survey of origin, rather than attempting to draw household-level inferences, the effects of the above comparability issues are likely minimal. However, other model-based approaches formally account for these issues and could potentially be used to combine the same surveys in the future if a different level of granularity is needed (Raghunathan et al., 2007; Schenker, Raghunathan, and Bondarenko, 2010).

Although the purpose, the methods, and the data collected by SEEDZ, LSMS, and RHoMIS were specific to each survey, the approach described here was highly accurate at classifying LSMS and RHoMIS households as pastoral and non-pastoral, using previous SEEDZ classifications (model M0) as the reference (de Glanville et al., 2020). Many of the previously reported differences between production systems regarding the local environment, geographical distribution, livestock management practices, and food consumption were observed in LSMS and RHoMIS. Compared to non-pastoral households, pastoralists in LSMS and RHoMIS (i) tended to be located in remote dry lands, (ii) kept a relatively large number of livestock that included donkeys but not pigs, and (iii) relied significantly less on crop farming (based on the lower proportion of households that reported growing crops, or selling them).

Several SEEDZ variables describing key features of pastoral households were absent in LSMS and RHoMIS: those associated with ethnicity and transhumance (de Glanville et al., 2020). According to de Glanville et al. (2020), the majority of pastoral households in SEEDZ (i) were headed by someone of Maasai ethnicity (152 out of 171; 88.9%) and (ii) practised cattle (131 out of 171; 76.7%) or small stock (102 out of 171; 59.7%) transhumance. Although such variables were absent in M1 and M2, these models were highly accurate at identifying pastoral households. Between 70.8% and 95.9% of SEEDZ households initially classified as pastoral remained in that group with different M1 and M2 models (range of sensitivity estimates in Table 3.4). The good performance of these models (i) suggests that, even without highly influential variables, the classification of households is meaningful and reliable, and (ii) implies redundancy in the influence of variables identified as important. These classification models are then likely to help link data between household surveys even when key variables are absent, particularly variables that capture the transhumance dimension or other equally relevant dimensions to the construct of pastoralism (de Glanville et al., 2020; Pica-Ciamarra et al., 2014).

Despite the overall effectiveness (based on the accuracy estimates) of the methodology used in this study, some inconsistencies in the classification of LSMS and RHoMIS households require further consideration. Compared to SEEDZ, the significantly greater proportion of RHoMIS households that reported (i) owning European breeds of cattle (26.9%), (ii) practising zero grazing for cattle (26.1%), and (iii) selling milk (27.7%), combined with the larger number of cattle kept per household (median of 20), could indicate the presence, in the RHoMIS dataset, of households from non-traditional types of production system, in particular, intensive dairy farming. The possibility of identifying a potential fourth cluster in RHoMIS was accounted for in the methods by allowing an automated partition of the hierarchical tree. However, the RHoMIS households with characteristics of dairy farms kept a relatively small number of cattle (a median of six, and a maximum of 27), which indicates that they were smallholders rather than large intensive dairy farms. This result is consistent with the greater proportion of smallholders (128 out of 391, 32.7%) in RHoMIS, with the best-performing model (M2_1b1_manual), compared to SEEDZ (47 out of 404, 11.6%; p-value$<$0.001). Additionally, among the 115 pastoral households in RHoMIS, based on the same model, only four had European breeds of cattle, none practised zero-grazing, and only 12 sold milk.

The RHoMIS dataset had only 48 out of 76 (63.2%) variables available in SEEDZ. This reduced number of variables in RHoMIS, coupled with the large number of households reporting ownership of European breeds of cattle and the practice of zero grazing, could also indicate the presence of another non-traditional production system: intensive beef farming. This could indicate misclassification of pastoral households in RHoMIS, many of which kept a larger number of cattle than pastoral households in SEEDZ. However, the analyses of RHoMIS data not included in the classification models showed that the households within the group that keeps the highest number (in the upper decile, i.e., over 230) of cattle per household consumed 95.3% of their livestock production, whilst the remaining households consumed the equivalent to 71.7%. This indicates that intensive beef farming, a non-traditional type of production system emerging in Tanzania, is unlikely to be present in significant numbers in the RHoMIS dataset (Kibona and Yuejie, 2021).

The distribution of scores obtained at the MFA of LSMS and RHoMIS households within cluster 1 (Fig. 3.4) seems to indicate the presence of two groups of pastoral households. The distinction between these two groups is clear in RHoMIS: 52 households had a score below -1.25 in dimension 1 and were completely isolated; and, 63 households had a score above -1.25 in the same dimension and were closer to households in cluster 2 (agro-pastoral) than the remaining households in cluster 1. This bi-modal distribution of dimension 1 scores in pastoral households was not

visible in SEEDZ, but it is likely to indicate the presence of two types of pastoral households in RHoMIS. The distinctive features between these two groups of households were that those isolated, farther away from cluster 2, (i) had a greater number of cattle, goats, and sheep, (ii) were less likely to be headed by someone who had completed primary education or sold crops, and, (iii) were more likely to own donkeys. These two subsets of pastoral households may indicate diversification of activities and livelihoods. This possibility is consistent with prior knowledge that pastoral households have diversified over the last two decades in response to challenges posed by environmental, socioeconomic, and political change (McCabe et al., 2014). The diversification of pastoral livelihoods has been marked by the adoption of crop agriculture and commercialisation of livestock and livestock products, especially, milk (Homewood, Kristjanson, and Trench, 2009; McCabe, Leslie, and Deluca, 2010; McCabe et al., 2014). These two groups of pastoral households were handled as one population for representing production characteristics of the pastoral system in Chapter 4.

Irrespective of the production system, LSMS households tended to keep fewer cattle, sheep, and goats than those in SEEDZ or RHoMIS. A potential explanation for this result is a methodological problem, which might be considered a limitation in this study. The concept of livestock ownership may be more restrictive in LSMS than in SEEDZ or RHoMIS because, in the latter two surveys, the number of livestock kept at the 'boma' (compound or enclosure that may contain more than one household) was explicitly recorded. In LSMS, instead, a household was comprised of members of the 'immediate (nuclear) family who normally live and eat their meals together' (definition extracted from the household questionnaire). In Maasai communities, this is consistent with the concept of a 'sub-household', which is headed by one of the wives of the compound's (household's) head and occupies a single 'hut' (Allegretti, 2015). This potential explanation for fewer livestock owned by LSMS 'households', compared to SEEDZ and RHoMIS, is substantiated by the differences in gender of the 'household head' between datasets. 'Households' in LSMS were more likely to be headed by a female than households in the other datasets.

Given the likely bias in household definition, and the issues around the concept of livestock ownership, particularly in pastoral communities, where some animals may be shared for several purposes (e.g., transport and milk), the density of livestock in the vicinity of the household location can help validate the household classification model results. Livestock density tended to be different between systems

and similar within the same system and across datasets. For instance, although the number of cattle kept by LSMS households was lower than in SEEDZ and RHoMIS, as explained above, the density of cattle in the vicinity of household locations was similar within the same system and across datasets (Fig. 3.5).

The method described and evaluated here was designed specifically to enable the harmonisation of SEEDZ data with two secondary data sources: LSMS and RHoMIS. By building on the clustering algorithm initially developed for SEEDZ, this method is vulnerable to its limitations, as described by de Glanville et al. (2020). Firstly, SEEDZ did not sample households from urban areas. As a result, a relatively small, homogeneous population of smallholders, characterised by low levels of intensification (based on the infrequent ownership of European breed dairy cattle or milk sales) may have been obtained. Secondly, the distinction between subsistence-oriented and market-oriented households could have been improved if more variables on market integration, many of which are available in LSMS and RHoMIS, other than crop and milk sales, had been collected in SEEDZ. Finally, SEEDZ invited households to bring their animals to a pre-selected point within the village for interview and collection of laboratory samples. This sampling approach might have introduced a selection bias if the likelihood of accepting the invitation differed with the type of production system. It is reasonable to suspect that smallholder households in SEEDZ keeping high-value cattle, such as some European breed cattle, were less likely to be interviewed than pastoral households.

## 3.5 Conclusion

A method for harmonising data from multiple surveys and identifying common livestock production systems was developed and evaluated in this study. Despite the heterogeneity in research design and variable availability between surveys, the method was highly accurate at classifying pastoral from non-pastoral households. The ability to distinguish these types of households, irrespective of the survey of origin, is valuable to link the epidemiology and economics of livestock diseases in low-resource settings. In these settings, where estimating the impact of many livestock diseases is needed and delivering large-scale surveys is challenging, the method presented here can be used to combine disease and production data from relatively small, independent cross-sectional studies.

# Chapter 4

# Production losses due to livestock brucellosis in northern Tanzania

## 4.1 Introduction

The livestock population in Tanzania is one of the largest in Africa, contributing to food security, and providing draught power, transport, and manure (FAO, 2021). Livestock also serve as a capital asset, replacing the standard financial markets where these are inaccessible, and providing a buffer or a form of insurance in times of need (Randolph et al., 2007). However, keeping livestock is not risk-free, and many factors, such as disease, may cause reduced productivity and mortality, with knock-on effects on household income, food security, and living conditions (Government of The United Republic of Tanzania, 2015a).

One of the diseases hampering livestock productivity in Tanzania is brucellosis, which can cause low mortality but high reproductive morbidity (e.g., abortion, infertility, and sterility) (Franc et al., 2018). Given the insidious nature of the disease, the impact of brucellosis on productivity is often under-appreciated by households, particularly by those facing numerous other sources of risk, such as drought and diseases that cause higher mortality than brucellosis (e.g., East Coast fever and contagious bovine pleuropneumonia) (Alhaji et al., 2020; Cleaveland et al., 2017; Gustafson et al., 2015; Homewood et al., 2006; Swai et al., 2021). Being a zoonotic disease, brucellosis also causes a significant impact on human health and productivity, but this dual burden (on livestock and human health) is often not recognised by those most at risk (Mangesho et al., 2017).

Many studies have analysed the epidemiology of brucellosis in livestock in several parts of Tanzania, but little evidence is available on the losses attributable to the disease in this context (Asakura et al., 2018a; Assenga et al., 2015; Chitupila, Komba, and Mtui-Malamsha, 2015; Sagamiko et al., 2018; Shija et al., 2014; Shirima et al., 2010; Shirima and Kunda, 2016; Sijapenda, Komba, and Nonga, 2017; Swai and Schoonman, 2010, 2012; Viana et al., 2016). In other settings, with prevalence estimates of bovine brucellosis similar to those reported in Tanzania (mean individual-level prevalence below 10%), the annual losses caused by the disease are often greater than 100 international dollars (int. $; purchasing power parity) per infected animal or as high as 10% of the household income (Angba, Traore, and Fritz, 1987; Bardhan et al., 2020; Eşki, Demir-Ayvazoğlu, and Günaydın, 2021; Santos et al., 2013; Singh, Dhand, and Gill, 2015). This implies that substantial losses may be occurring in Tanzania. However, making direct inferences across contexts has limitations for three main reasons. Firstly, there is significant heterogeneity in the methods used to quantify losses in different countries (Deka et al., 2018). Secondly, the prevalence, the market prices of livestock and livestock products, and the type of production systems that dominate the livestock sector may differ between countries (Santos et al., 2013; Zeng et al., 2019). Finally, the concept of 'loss' is not uniformly defined between studies. In many cases, 'loss' and 'cost' are used interchangeably (Angara et al., 2016; Santos et al., 2013). This chapter uses the definition of 'loss' by McInerney, Howe, and Schepers (1992), i.e., the production potential that is not realised over time due to the presence of the disease. In contrast, the definition of 'cost' includes 'loss' as well as expenditure on disease prevention and treatment (McInerney, Howe, and Schepers, 1992).

The prevalence of brucellosis varies between production systems in northern Tanzania (Bodenham et al., 2021; Shirima et al., 2010). In the regions of Arusha, Manyara, and Kilimanjaro, the median (95% Bayesian credibility interval) prevalence of brucellosis in pastoral and non-pastoral cattle has been estimated at 6.3% (4.5-9.0) and 0.9% (0.1-2.1), respectively (Bodenham et al., 2021). The number and type of livestock kept as well as the livestock management practices in Arusha and Manyara differ between pastoral and non-pastoral households (de Glanville et al., 2020). Thus, efforts to estimate the losses attributable to the disease should consider the differences between these production systems. However, most published studies that estimate losses attributable to brucellosis, or the associated costs and benefits of its control, entirely ignore the production system-specific epidemiological and economic characteristics. This is the case when, for instance, herd sizes per household or disease prevalence are assumed to be equal across

systems (Singh, Dhand, and Gill, 2015). Information on the relative losses due to brucellosis in pastoral and non-pastoral production systems may help support the planning, design, and prioritisation of potential control interventions. It may also help inform future extrapolation of impact estimates at broader scales.

This chapter aims to estimate the production losses attributable to livestock brucellosis in pastoral and non-pastoral systems of northern Tanzania. Three levels of losses are considered here: i) at the individual level, i.e., the losses per infected animal; ii) at the household level, i.e., the losses per livestock-keeping household; and, iii) at the regional level, i.e., the sum of household losses in each region of northern Tanzania.

## 4.2 Methods

### 4.2.1 Study area

This study used data collected in eight regions of northern Tanzania: Arusha, Manyara, Kilimanjaro, Tanga, Dodoma, Singida, Simiyu, and Mara. These regions cover an area equivalent to approximately 29% of mainland Tanzania but include around half of the livestock in the country (Government of The United Republic of Tanzania, 2013b, 2017a). In October 2017, there were 13.0, 10.6, and 3.2 million cattle, goats, and sheep in these regions, respectively, which correspond to 42.6%, 55.8%, and 57.9% of the total population of each species in mainland Tanzania (Government of The United Republic of Tanzania, 2017a). The map of the study area is shown in Fig. 4.1.

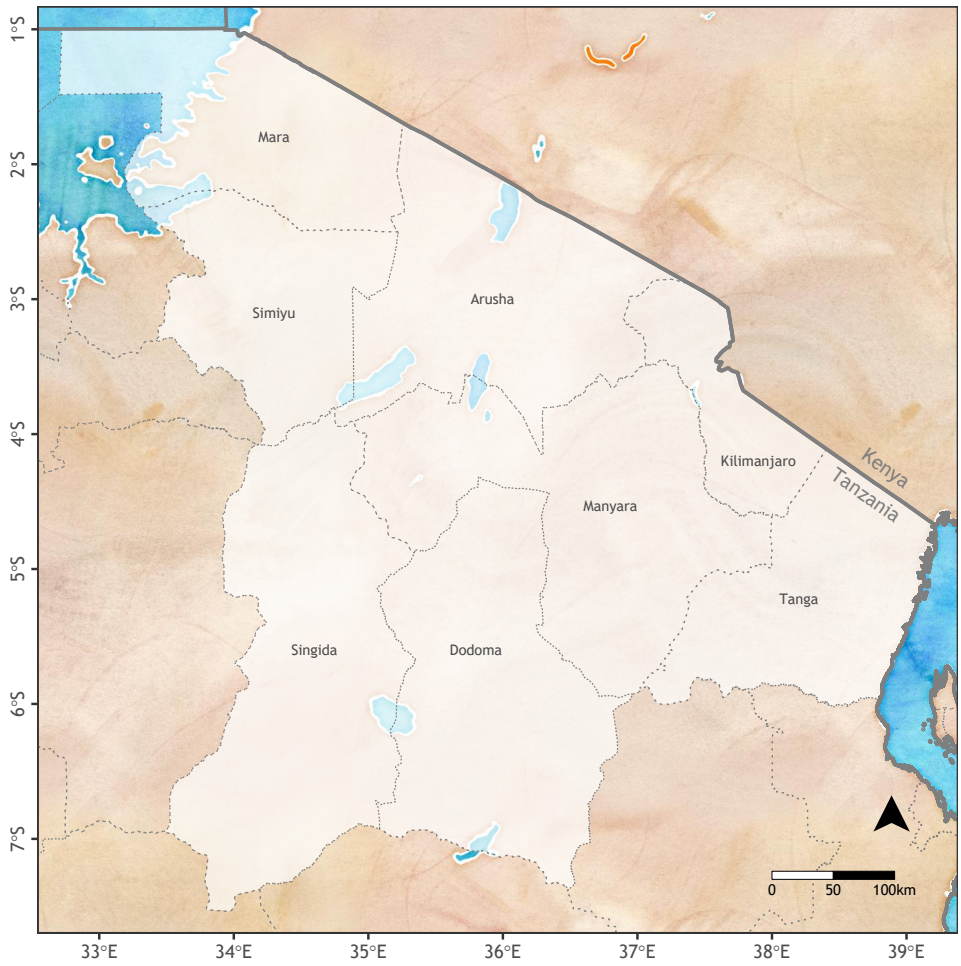



**Figure 4.1:** Map of the study area in northern Tanzania (white-filled translucent polygons). Dashed lines delineate regions. Solid lines indicate national borders. The polygon shapefiles were obtained from GADM, the Database of Global Administrative Areas (`https://gadm.org/`). Map tiles by Stamen Design, under CC BY 3.0. Data by OpenStreetMap, under CC BY SA.

This large study area has highly diverse socio-economic and geo-climatic settings. The regional average human population density is close to the national average (51 people/km$^2$), except in Kilimanjaro, where there are approximately 124 people/km$^2$ (Government of The United Republic of Tanzania, 2013a). Kilimanjaro is also the region with the smallest average household size (4.3 people per household) in the study area, contrasting with Simiyu, where the average household size is the largest nationally (6.9 people per household) (Government of The United Republic of Tanzania, 2013a). The area is dominated by savannas, grassland and, to a lower extent, small-scale crop cultivation (Friedl and Sulla-Menashe, 2019). The mean annual temperature ranges from 20.2 $^o$C in Arusha to 23.2 $^o$C in Tanga (Fick and Hijmans, 2017). The mean annual precipitation ranges from 616 mm in Dodoma to 1,060 in Mara (Fick and Hijmans, 2017). The elevation ranges from the sea-level

values in the Tanga region to the highest point of the African continent: Mount Kilimanjaro (5,895 m) (U.S. Geological Survey Center for Earth Resource Observation and Science (EROS), 2006). Arusha and Manyara are dominated by livestock-only, grassland-based systems, whilst the other regions include predominantly rainfed mixed crop/livestock systems (Robinson et al., 2011).

### 4.2.2 Study design

Data on livestock production characteristics, including demography of livestock populations, were obtained from three independent survey datasets: i) the Social, Environmental, and Economic Drivers of Zoonotic disease survey (SEEDZ); ii) the Living Standards Measurement Study (LSMS); and, iii) the Rural Household Multiple Indicator Survey (RHoMIS). Data on livestock brucellosis prevalence were sourced from the SEEDZ dataset only. Two subpopulations of households belonging to distinct production systems were considered: pastoral and non-pastoral. The classification of SEEDZ, LSMS, and RHoMIS households into these two production systems has been described in detail elsewhere (see Chapter 3).

SEEDZ is a large-scale, cross-sectional survey delivered between February and November 2016 in Arusha and Manyara regions. The study design has been described in detail by de Glanville et al. (2020). In summary, a multistage sampling design was used, selecting villages from national census data. This process excluded villages in urban wards, as per census definition, as well as those within the Ngorongoro Conservation Area. Livestock from 404 livestock-keeping households were tested for brucellosis, and information on household socioeconomic characteristics was gathered. Out of these households, 171 (42.3%) were characterised as pastoral and the remaining as non-pastoral (Chapter 3).

LSMS is a nationally representative household survey led by the World Bank that has been delivered in multiple countries since the 1980s (World Bank, 2021). Four waves of the survey have been delivered in Tanzania since 2008 (National Bureau of Statistics (NBS), 2016). This study used data from two waves of the LSMS survey: i) wave three (October 2012 to November 2013); and, ii) wave four (October 2014 to November 2015). A total of 746 livestock-keeping households provided data on livestock production in the study area. Out of these households, 96 (12.9%) were characterised as pastoral and the remaining as non-pastoral (Chapter 3).

RHoMIS is a standard household survey tool that has been applied in more than 30 countries since 2015 (van Wijk et al., 2020). Data on livestock production from two surveys that applied the RHoMIS tool were used in this study: i) RHoMIS1: a survey funded by the Global Alliance for Livestock Veterinary Medicines (GALVmed) and led by the International Livestock Research Institute (ILRI), in 2017; and, ii) RHoMIS2: a survey funded by the United States Department of Agriculture's Foreign Agriculture Service and led by the International Centre for Research in Agroforestry (ICRAF), in 2018. A total of 391 livestock-keeping households provided data on livestock production in the study area. Out of these households, 115 (29.4%) were characterised as pastoral and the remaining as non-pastoral (Chapter 3).

These data (from SEEDZ, LSMS, and RHoMIS) were used to parametrise a model aimed at estimating the losses attributable to livestock brucellosis in the study area and, specifically, in the two production systems considered.

### 4.2.3 Workflow

#### 4.2.3.1 Overview

The workflow for this study had two main objectives: i) to gather system-specific demographic, prevalence, and production parameter values from the three survey datasets; and, ii) to run herd production simulations in the presence and in the absence of brucellosis, using literature-based information on disease impacts and additional production characteristics. The losses attributable to brucellosis were calculated as the difference between the estimated value of livestock production simulated in the absence and in the presence of the disease. The same workflow was used to estimate losses in cattle, sheep, and goats. However, whilst only offtake (wholesale, home slaughter, or gifts given away) and milk contributed to production or income from sheep and goats, draught power and dung (e.g., to be used as manure, cooking fuel, feed to other animals, and in construction) were also considered in cattle.

The workflow was divided into two main layers (global and system-specific parameters) and seven interrelated steps (from A to G), as shown in Fig. 4.2. Steps A to F consisted of processes that gathered and selected parameter values through several mechanisms: i) probabilistic distributions (system-specific distributions fitted to survey data - steps A and C; or non-system-specific, literature-based, uniform distributions - step D); and, ii) fixed values (system-specific demography - step B). The parameter values gathered and selected in steps A to D were used to estimate

demography and production characteristics that would be expected in the absence of brucellosis (steps E and F). These steps were then followed by the modelling of herd production (simulations) in the presence and in the absence of brucellosis to estimate the losses attributable to the disease (step G). The whole sequence of steps was repeated 50,000 times to fully explore the multidimensional parameter space.

Data on the prevalence of brucellosis (step A; section 4.2.3.2) and demographic characteristics (step B; section 4.2.3.3) of livestock populations were obtained from the SEEDZ survey. Data on most of the production characteristics (step C; section 4.2.3.4; e.g., wholesale price, milk yield, and lactation length) of livestock were obtained from LSMS and RHoMIS surveys.

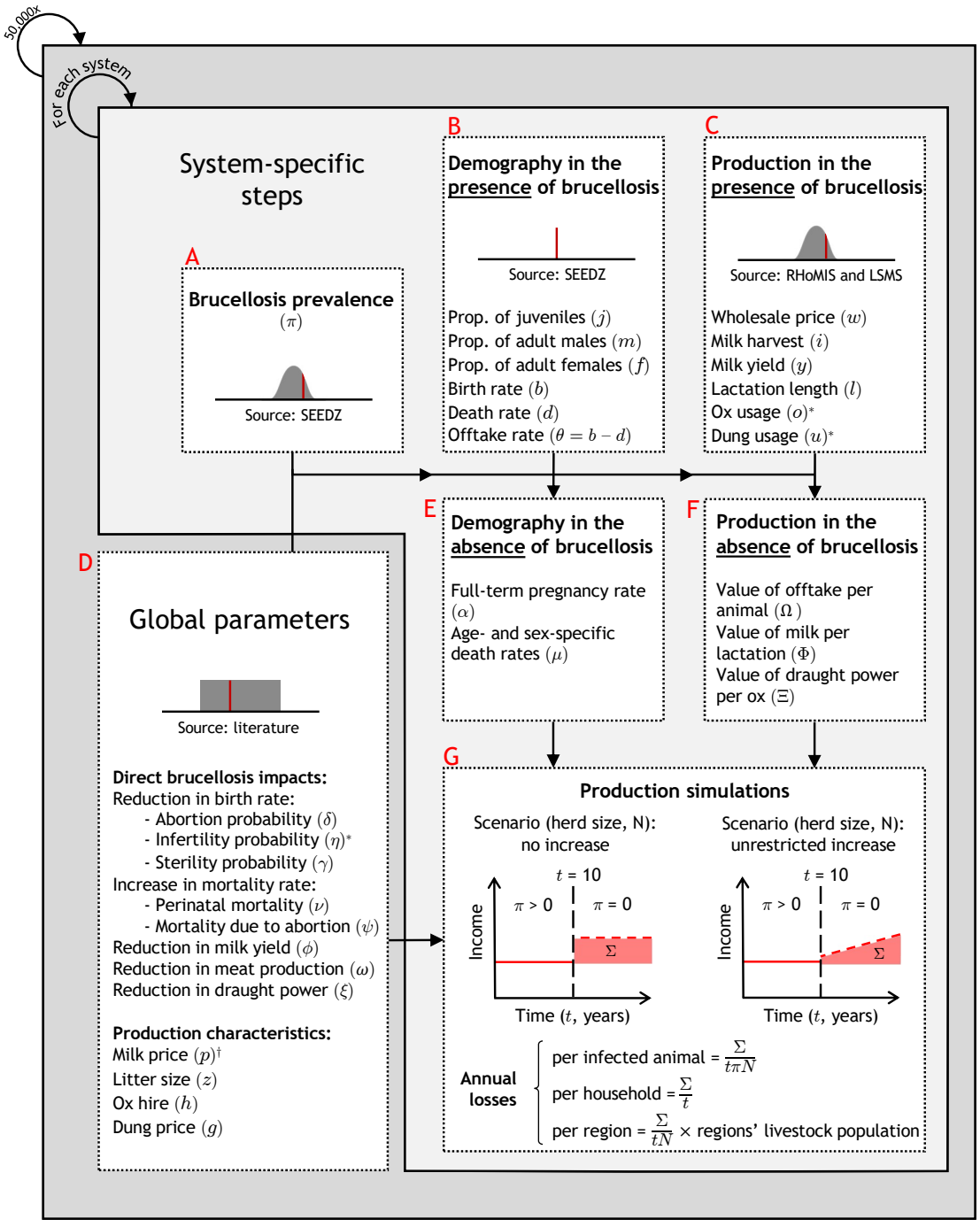



**Figure 4.2:** Workflow used to estimate losses attributable to brucellosis in livestock in northern Tanzania. Fixed parameter values are represented with a vertical red line. Parameter values obtained from distributions fitted to data are represented with a vertical red line in a grey normal distribution. Parameter values obtained from uniform distributions are represented with a vertical red line in a grey horizontal rectangle. Boxes A to G represent the step-wise processes. In the panel for step G (the model), the red shaded areas indicate the losses estimated in one iteration of the simulation ($\Sigma$), under the two model scenarios considered: no increase (left) and unrestricted increase (right). * Parameters that entered the model as fixed values. † The values of milk price ($p$) were obtained from LSMS and RHoMIS and entered the model as distributions fitted to data.

#### 4.2.3.2 Step A: Brucellosis prevalence

The first step of the analysis was the sampling of the probability distributions of brucellosis prevalence. These distributions of prevalence in cattle, sheep, and goat populations of pastoral and non-pastoral production systems were obtained from SEEDZ data through a Bayesian latent-class analysis (LCA) model. This model has been described in detail by Bodenham et al. (2021), who used data from SEEDZ and another survey to estimate (i) the sensitivity and specificity of two serological tests (Rose Bengal test - RBT, and a competitive enzyme-linked immunosorbent assay - cELISA), and (ii) the prevalence of exposure to *Brucella* spp. in the same production systems: pastoral and non-pastoral. The classification of households by production system in Bodenham et al. (2021) was based on agro-ecological definitions, in consultation with district-level government officials (i.e., District Veterinary Officers or District Livestock Officers). In the current study, instead, the household classification derived from the harmonised clustering algorithm with SEEDZ, LSMS, and RHoMIS households (Chapter 3) was used.

The LCA model used to estimate brucellosis prevalence in livestock was specified exactly as per Bodenham et al. (2021), and was applied to the SEEDZ dataset only. This model can be briefly described in three parts:

- Model framework and assumptions:
  Separate models were set up for cattle, goats, and sheep. The overall model framework was adapted from the Hui-Walter model (Bodenham et al., 2021; Bronsvoort et al., 2009; Mazeri et al., 2016; Toft, Jørgensen, and Højsgaard, 2005), using RBT and cELISA outcome probabilities and prior information on (i) test performance (sensitivity and specificity), and (ii) prevalence of exposure to *Brucella* spp. in animals originating from the two production systems (Bodenham et al., 2021; Branscum, Gardner, and Johnson, 2005; Mazeri et al., 2016).
  Two of the three core assumptions in the Hui-Walter model (Bodenham et al., 2021; Hui and Walter, 1980) were considered not violated: i) the prevalence of exposure to *Brucella* spp. was different between production systems; and, ii) the diagnostic tests perform the same across production systems. A third assumption that the diagnostic tests were conditionally independent was conservatively considered not met because RBT and cELISA detect the presence of antibodies against *Brucella*. As a result, conditional dependence was added to the model through covariance parametrisation (Bodenham et al., 2021; Toft, Jørgensen, and Højsgaard, 2005; Vacek, 1985).

- Prior distributions:
  Priors following a beta distribution were specified in this model. Three sets of priors were used: i) the performance of RBT and cELISA (sensitivity and specificity); ii) the prevalence of exposure to *Brucella* spp.; and, iii) the covariance variables.
  The priors of test performance in Bodenham et al. (2021), which were selected based on a literature search and sensitivity analysis of posterior distributions, were used in this model and are shown in Appendix C.1.
  The priors for the prevalence of exposure to *Brucella* spp. were specified as vague uniform distributions (0, 0.49), enabling wide parameters space exploration.
  The priors for the covariance variables were specified as uniform distributions with maximum and minimum limits dependent on the priors of test performance (as shown in Appendix C.1).
- Model implementation and diagnostics:
  The model was implemented in R version 3.6.2 (R Core Team, 2019) with JAGS (Plummer, 2003), using the rjags package (Plummer, Stukalov, and Denwood, 2019). Three Markov Chain Monte Carlo (MCMC) chains with different starting values were run for 250,000 iterations, discarding the first 50,000 as burn-in, and retaining every $100^{th}$ iteration.
  The Gelman and Rubin's diagnostic and the visual inspection of the Gelman-Rubin, density and trace plots were used to assess chain convergence, using the coda R package (Plummer et al., 2019).
  A sample of the posterior distribution of brucellosis prevalence for each species was used in each iteration of the production losses model. It was assumed that the prevalence of the disease was equally distributed across age and sex groups.

#### 4.2.3.3 Step B: Demography in the presence of brucellosis

The age-sex distribution as well as the birth and death rates of livestock were obtained from SEEDZ data at the survey level, i.e., including all households in each production system, and were used in the model as fixed values. Adults were distinguished from juveniles in this survey based on the presence of permanent incisors. The parameter values in this step were obtained as follows:

- Proportion of juveniles ($j$), adult males ($m$), and adult females ($f$):

The values of $j$, $m$, and $f$ were obtained by dividing the number of animals in each age-sex group by the total number of animals kept at the time of the interview.

- Birth rate ($b$) and death rate ($d$):
  The values of $b$ and $d$ were obtained by dividing the total number of animals that were born and died in the 12 months preceding the interview, respectively, by the total number of animals kept at the time of the interview.

#### 4.2.3.4 Step C: Production in the presence of brucellosis

Data on a range of production variables for each livestock species and production system were obtained from LSMS and RHoMIS datasets and used to inform model parameters.

The monetary variables originally recorded in the local currency (Tanzania Shillings) were converted to international dollars (int. $) based on purchasing power parity, using the year of data collection and the World Bank conversion rates for Tanzania.[1]

Given the scarce data on milk-related variables and the collection of data on these variables for sheep and goats together in LSMS, the proportion of households that harvested milk, the milk yield, and the lactation length were obtained as common values from both species in LSMS and RHoMIS.

The system-specific production data in the presence of brucellosis were obtained as follows (for each species, except ox and dung usage, which applied only to cattle):

- Wholesale price ($w$):
  The values of $w$, the price of livestock, in Tanzania Shillings, at farm gate, were obtained from LSMS and RHoMIS. To calculate these values for each household, the income generated from the sale of live animals during the 12 months preceding the interview was divided by the number of animals sold within the same period.
- Milk harvest ($i$):

1. https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?end&locations=TZ

The values of $i$, the proportion of households that harvest milk (for consumption or sale), were obtained from LSMS and RHoMIS. To calculate these values, the number of households that reported harvesting milk from livestock at least once in the 12 months preceding the interview was divided by the number of households that kept livestock at the time of the interview.

- Milk yield ($y$):
  The values of $y$, the volume of milk, in litres, produced daily per milked animal, were obtained from LSMS and RHoMIS through distinct ways. In LSMS, these values were obtained as reported by each household that harvested milk. In RHoMIS, each household reported the volume of milk produced in the 'good season' and in the 'bad season', as defined by the respondent, at the herd or individual level. Therefore, the values of $y$ were calculated as the milk production in the 'good season', plus the milk production in the 'bad season', divided by two. These values were further divided by the number of animals milked if the volume reported by the household was at the herd level.
- Lactation length ($l$):
  The values of $l$, the number of days on average that animals were milked for, were obtained from LSMS only. This variable was available from the dataset in units of months. To convert it into days, the variable was multiplied by 30.
- Ox usage ($o$):
  The value of $o$, the average area ploughed per year, in acres, by each ox owned, was obtained from LSMS only. To calculate this value, the total area of land owned or cultivated by households that reported using animals for ploughing the fields in the 12 months preceding the interview was divided by the total number of bulls or steers kept at the time of the interview (at survey level, i.e., including all households in each production system).
- Dung usage ($u$):
  The value of $u$, the average quantity of dung used, in kilograms, per animal per year, was obtained from LSMS only. To calculate this value, the total quantity of dung used for any purpose (e.g., manure, cooking fuel, feed to other animals, and construction) in the 12 months preceding the interview was divided by the total number of animals kept at the time of the interview (at survey-level, i.e., including all households in each production system).

The production parameter values used in each iteration of the production losses model were sampled from distributions fitted to LSMS and/or RHoMIS data by maximum likelihood, using the fitdistrplus package in R (Delignette-Muller and Dutang, 2015), with some exceptions:

- the milk harvest ($i$) was used as a beta distribution with shape parameters ($\alpha = k + 1,\ \beta = n - k + 1$), where $k$ and $n$ are the number of households that reported harvesting milk from livestock at least once in the 12 months preceding the interview and the number of households that kept livestock at the time of the interview, respectively (Chan, 2016);
- the ox and dung usage ($o$ and $u$, respectively) entered the model as fixed values - some uncertainty around the draught power and dung values was accounted for in the uniform distributions of the prices of oxen hire and dung in step D.

The probability density functions that resulted from fitting distributions and that were sampled from in the model (wholesale price, milk yield, milk price, and lactation length) are shown in Appendix C.2.

#### 4.2.3.5 Step D: Global parameters

Global parameters covering information on direct brucellosis impacts and some production characteristics were gathered from the literature, except the milk price, which was gathered from LSMS and RHoMIS. The same set of parameter values was used across production systems. The available data on direct brucellosis impacts and some production characteristics (milk price, litter size, ox hire, and dung price) was not sufficient to partition them by production system.

To gather information on direct brucellosis impacts, a systematic search of the literature was carried out through backward and forward chaining, as described by Hinde and Spackman (2015). References and citation indices were used to find documents that cited or were cited by two recent studies that estimated losses caused by livestock brucellosis: Alves et al. (2015) and Singh et al. (2015). Once the initial pool of references was scanned for brucellosis impacts in livestock, the process was repeated to gather additional references and citations until no new relevant documents were found. Additional targeted searches were carried out to identify further references. Minimum and maximum values of the following model parameters reported in the literature were used to set up uniform distributions of brucellosis impacts:

- Probability of abortion in infected females that have become pregnant ($\delta$);
- Probability of infected females being (temporarily) infertile ($\eta$; a fixed value was used, rather than a uniform distribution, because a period of two months per year was consistently reported in the literature as the duration of infertility of infected females);

- Probability of infected females becoming sterile (permanently infertile) after an abortion event ($\gamma$);
- Proportional increase in perinatal mortality rate in offspring from infected females ($\nu$);
- Proportional increase in mortality rate of infected females that aborted ($\psi$);
- Proportional reduction in daily milk yield in infected animals ($\phi$);
- Proportional reduction in meat production in infected animals ($\omega$);
- Proportional reduction in draught power in infected oxen ($\xi$).

The following parameter values on some production characteristics were used across production systems:

- Milk price ($p$):
  The values of $p$, the price of milk, in Tanzania Shillings per litre, at farm gate, were obtained from LSMS and RHoMIS, differently for cattle and sheep and goats.
  In cattle, distributions were fitted to data on milk price by maximum likelihood, as described for parameters in step B. The data in LSMS and RHoMIS were processed through distinct ways, as follows:
  - In LSMS, the daily income from sales of milk in the 12 months preceding the interview included income from sales of both liquid milk and processed dairy products. Therefore, only households that reported not converting milk into processed dairy products were used in the calculation of $p$. The values of $p$ were obtained by dividing the daily income from sales of milk in the 12 months preceding the interview by the volume of milk, in litres, sold per day in the same period.
  - In RHoMIS, the volume of milk sold is recorded in mostly qualitative terms (e.g., 'all', 'most', 'half', 'little', 'under half, 'none') and the income from milk sales is recorded in several units of time (e.g., daily, weekly, monthly, yearly). Additionally, no information on lactation length is provided in RHoMIS. Therefore, only responses on income from milk sales that were recorded in daily time units and related to 'large' volumes (i.e., 'all', 'most', or 'half') were used to calculate $p$. It was assumed that 'all', 'most', and 'half' referred to 100%, 75%, and 50% of the average volume of milk produced daily, respectively. The values of $p$ were obtained by dividing the daily income from milk sales by the average volume of milk sold per day.

Given the scarce data on milk sales in the study area, particularly on sales of sheep and goat milk, and the fact that milk-related variables were collected for sheep and goats together in LSMS, the approach for gathering data on milk price for sheep and goats combined was different from that of cattle. A PERT distribution was parametrised with the sheep and goat milk prices available in the unfiltered (i.e., unrestricted to the study area) RHoMIS1 and RHoMIS2 datasets (Bergevoet et al., 2009).

- Litter size ($z$):
  The values of $z$, the average number of offspring per term pregnancy, were obtained from the literature using the same method as described for the direct brucellosis impacts. Searches were also carried out to identify references specifically from Tanzania. Given that twining is a relatively rare event in cattle in Tanzania, a fixed value of 1 was used in this species model. In the goats and sheep models, uniform distributions were set up with values obtained from the literature.
- Ox hire ($h$):
  The values of $h$, the cost of hiring oxen for ploughing one acre of land, in Tanzania Shillings, were obtained from the literature through 'Google' searches, using the search string 'ox*', 'hir*', and 'Tanzania'. Uniform distributions were set up with these values obtained from the literature.
- Dung price ($g$):
  The values of $g$, the price of dung, in Tanzania Shillings per kilogram, were obtained from the literature through 'Google' searches, using the search string 'price', 'dung', 'manure', and 'Tanzania'. Uniform distributions were set up with these values obtained from the literature.

#### 4.2.3.6 Step E: Demography in the absence of brucellosis

The data described in steps A, B, and C were used to estimate the full-term pregnancy rate ($\alpha$) and the age- and sex-specific death rates ($\mu$) that would be expected in the absence of brucellosis. Note that $b$ (section 4.2.3.3) is the number of animals born divided by the number of animals kept, in the presence of brucellosis, whilst $\alpha$ is the proportion of adult females that are expected to complete a full-term pregnancy each year in the absence of brucellosis, assuming one breeding season per year. It was also assumed that each full-term pregnancy leads to the birth of $z$ (litter size; section 4.2.3.5) live offspring. The $\alpha$ and $\mu$ parameters were estimated

as follows:

$$\begin{aligned}\alpha &= \frac{bz^{-1}N}{((1-\pi)+\pi(1-\delta-\eta-\gamma^*))F} \\ \mu_J &= \frac{dJ}{J+\nu\pi\alpha(1-\delta-\eta-\gamma^*)zF} \\ \mu_M &= d \\ \mu_F &= \frac{d}{1+\psi\pi\alpha\delta(1-\eta-\gamma^*)}\end{aligned} \tag{4.1}$$

where $N$ is the sum of the number of juveniles ($J$), adult males ($M$), and adult females ($F$) in the modelled herd; the subscripts $J$, $F$, and $M$ in $\mu$ indicate sex- and age-specific mortality rates; and, $\gamma^*$ is the proportion, in equilibrium, of infected females that are sterile due to a previous abortion event. $\gamma^*$ was calculated assuming that the disease is in endemic equilibrium and the number of sterile females ($S = \gamma^*\pi F$) is constant over time, so that $\frac{dS}{dt}$ in Eq. 4.2 is equal to zero:

$$\frac{dS}{dt} = \gamma\delta\alpha((1-\eta)\pi F - S) - (d+\theta)S \tag{4.2}$$

where $\theta$ is the offtake rate, given by the difference between the birth ($b$) and death ($d$) rates, i.e., the offtake in each year was given by the difference between the number of animals born and the number of animals that died for reasons other than slaughter. It was assumed that the death and offtake rates of sterile females were not different from that of the general population.

Given the equation for $\alpha$ (Eq. 4.1) and the assumption of endemic equilibrium, $\frac{dS}{dt} = 0$, and that $\theta = b - d$, Eq. 4.2 can be simplified as follows:

$$0 = \frac{\gamma\pi\delta(1-\eta-\gamma^*)bz^{-1}N}{(1-\pi)+\pi(1-\delta-\eta-\gamma^*)} - b\pi\gamma^*F \tag{4.3}$$

Eq. 4.3 can then be solved for $\gamma^*$ as follows, knowing that $F = fN$ and $0 \leq \gamma^* < 1$:

$$\gamma^* = \frac{(1-\pi(\delta+\eta))f + \gamma\delta z^{-1} - \sqrt{((1-\pi(\delta+\eta))f + \gamma\delta z^{-1})^2 - 4\pi\gamma\delta(1-\eta)z^{-1}f}}{2\pi f} \tag{4.4}$$

#### 4.2.3.7 Step F: Production in the absence of brucellosis

The value of production per animal (offtake, milk, and, in the case of cattle, draught power) that would be expected in the absence of brucellosis was estimated. It was assumed that animals infected by brucellosis were less valuable due to the lower weight, lower milk yield, and lower draught power. These three direct impacts of brucellosis were accounted for in the following model parameters:

- Value of offtake per animal in the absence of brucellosis ($\Omega$):
  $\Omega$ is the income, or the equivalent monetary metric of utility, gained by a household, in the absence of brucellosis, from each animal that is sold, slaughtered or given away as a gift. It was assumed that brucellosis causes a proportional reduction in meat production (and live weight) in infected animals ($\omega$; section 4.2.3.5). However, data on the live weight of animals at the moment of sale were not available in the survey datasets, so a linear relationship between live weight and wholesale price ($w$) was assumed.
- Value of milk per lactation in the absence of brucellosis ($\Phi$):
  $\Phi$ is the income, or the equivalent monetary metric of utility, gained by a household, in the absence of brucellosis, from the milk produced by each adult female in one lactation period. It was assumed that each pregnancy was followed by a lactation period, i.e., the reduction in milk production by infected females that conceived each year was only affected by the parameter $\phi$ (section 4.2.3.5).
- Value of draught power per ox in the absence of brucellosis ($\Xi$):
  $\Xi$ is the income, or the equivalent monetary metric of utility, gained by a household, in the absence of brucellosis, from using an ox for ploughing an average area of land ($o$; section 4.2.3.4) each year.

The parameters $\Omega$, $\Phi$, and $\Xi$ were calculated as follows:

$$\Omega = \frac{w}{(1-\pi)+\pi(1-\omega)}$$

$$\Phi = ylp\frac{(1-\pi)+\pi(1-\eta-\gamma^*)}{(1-\pi)+\pi(1-\eta-\gamma^*)(1-\phi)} \tag{4.5}$$

$$\Xi = \frac{ho}{(1-\pi)+\pi(1-\xi)}$$

#### 4.2.3.8 Step G: Production simulations

To model the effects of brucellosis on livestock reproduction and mortality (lower birth rate, higher perinatal mortality, and higher female mortality), a set of differential equations were used (Eqs. 4.6). These differential equations enabled estimating the number of animals in each age and sex group and the number of events (births, deaths, abortions, etc.) at any point in time for the duration of the simulation (10 years). Animals could (i) leave the system through death (at a rate $\mu$), or offtake (at a rate $\theta$), and (ii) enter the system through birth (at a rate $\alpha$).

$$\begin{aligned}
\frac{dJ}{dt} =& \left(\left(1-\pi\right)+\pi\left(1-\delta-\eta-\gamma^{*}\right)\right)\alpha_{z}F - \\
& \mu_{J}\left(J+\nu\pi\left(1-\delta-\eta-\gamma^{*}\right)\alpha_{z}F\right)-\left(\theta+\sigma_{M}+\sigma_{F}\right)J \\
\frac{dM}{dt} =& \sigma_{M}J-\left(\mu_{M}+\theta\right)M \\
\frac{dF}{dt} =& \sigma_{F}J-\left(\mu_{F}\left(1+\psi\pi\alpha\delta\left(1-\eta-\gamma^{*}\right)\right)+\theta\right)F
\end{aligned} \tag{4.6}$$

where $\pi$ is the prevalence of brucellosis (constant for all age and sex groups), and, $\sigma_F$ and $\sigma_M$ are the transition rates from juveniles to adult females and adult males, respectively. Given that sex-specific mortality and offtake rates for juveniles were not available in SEEDZ, the transition rates $\sigma_F$ and $\sigma_M$ were updated numerically to ensure a stable sex structure in the livestock population over time.

The model herd size ($N$) in each system, i.e., the initial number of animals of each species per household, was given by the median number of animals observed per household in each system in the SEEDZ survey. The expected consequences of the hypothetical, sudden elimination of brucellosis from the system on the herd size at the end of the tenth year ($t = 10$ years) were modelled through two different model scenarios: i) 'no increase in herd size': all excess stock due to brucellosis elimination was valued as offtake (sold, slaughtered, or given away as gifts) - the offtake rate $\theta$ was numerically adjusted to ensure a stable herd size after disease elimination; and, ii) 'unrestricted increase in herd size': the herd size was allowed to increase indefinitely - the offtake rate $\theta$ was the same before and after disease elimination. Unless otherwise stated, results refer to the first model scenario ('no

increase in herd size'; reference scenario) as this is likely the most appropriate to represent how households would manage herd size in the event of a sudden elimination of brucellosis. Given the scarcity of resources and limited labour availability at the household, the unrestricted increase in herd size over ten years is unlikely.

The household production values, i.e., income or utility (e.g., in the form of livestock given away as gifts) from offtake, milk, and, in cattle, from draught power and dung, derived from livestock were estimated for the period of ten years, before and after the elimination of brucellosis from the system. The dung value only changed upon brucellosis elimination in the model scenario of 'unrestricted increase in herd size'. These estimates of household production were obtained from the following set of equations:

$$\begin{aligned} \text{Milk value} &= ((1-\pi)+\pi(1-\eta-\gamma^*)(1-\phi))\,\Phi\alpha i F \\ \text{Offtake value} &= ((1-\pi)+\pi(1-\omega))\,\Omega\theta N \\ \text{Draught power value} &= ((1-\pi)+\pi(1-\xi))\,\Xi M \\ \text{Dung value} &= ugN \end{aligned} \tag{4.7}$$

All monetary values were discounted over time ($t$, in years) at a rate ($r$) of 3%, as per Eq. 4.8:

$$\text{Discounted value} = \frac{\text{Non-discounted value}}{(1+r)^t} \tag{4.8}$$

The losses due to brucellosis per household, per year, were estimated as the production difference between the periods before and after disease elimination ($\sum$, red shaded area in box G of Fig. 4.2, which is the sum of the values of milk, offtake, and, in cattle, draught power and dung), divided by the duration of the simulation ($t = 10$ years).

The losses per infected animal, per year, were estimated as the losses per household, divided by the number of infected animals within the household ($\pi N$) at the start of the simulation.

The losses per region, per year, were estimated as the losses per animal kept (losses per household divided by the number of animals kept, $N$), multiplied by the livestock population in each region, for each species and production system. The distribution of the number of livestock by species, production system, and region is shown in Table 4.1.

**Table 4.1:** Estimated number of livestock by region, production system (pastoral and non-pastoral), and species (cattle, sheep, and goats), in northern Tanzania.

| | Pastoral | | | Non-pastoral | | |
|---|---|---|---|---|---|---|
| Region | Cattle | Sheep | Goats | Cattle | Sheep | Goats |
| Arusha | 808,849 | 503,569 | 2,008,281 | 364,595 | 155,649 | 571,736 |
| Dodoma | 636,560 | 140,920 | 565,250 | 1,175,867 | 178,498 | 659,458 |
| Kilimanjaro | 38,654 | 12,632 | 49,755 | 755,370 | 169,266 | 614,088 |
| Manyara | 1,321,002 | 304,687 | 1,252,187 | 880,668 | 139,286 | 527,236 |
| Mara | 98,076 | 27,091 | 69,025 | 2,059,591 | 390,107 | 915,490 |
| Simiyu | 112,683 | 57,412 | 124,713 | 1,659,734 | 579,857 | 1,160,158 |
| Singida | 109,872 | 26,362 | 108,062 | 1,762,530 | 289,977 | 1,094,837 |
| Tanga | 286,377 | 76,996 | 284,424 | 918,791 | 169,390 | 576,333 |

The total number of animals in each region for each species was extracted from the report of the Annual Agricultural Sample Survey 2016-2017 (Government of The United Republic of Tanzania, 2017a). The values in this table are based on the following assumptions: i) the proportion of households that belong to pastoral and non-pastoral production systems in each region are the same as those in the LSMS household classifications, and, ii) the median number of animals of each species kept by each household is the same as in the SEEDZ survey.

### 4.2.4 Statistical analyses

General descriptive statistics were calculated for each of the main model outputs: i) losses per infected animal; ii) losses per household; and, iii) losses per region. The contribution of each livestock production output (i.e., offtake, milk, draught power, and dung) to the estimated losses at the household level was also assessed.

Pearson's Chi-squared test was used to assess differences between production systems in (i) demographic attributes of animal populations (e.g., proportion of animals in each age-sex group) and (ii) the proportion of households harvesting milk (Chan, 2016). The herd sizes, the productivity of livestock (e.g., milk yield) as well as the estimated losses per infected animal and per household were compared between production systems using the Wilcoxon rank-sum test (Chan, 2016). The significance level was set at 5%. These comparative analyses were also carried out visually, through the inspection of violin and bar plots, which were made with the 'ggpubr' and 'ggplot2' packages, in R (Kassambara, 2020; Wickham, 2016).

The influence of the model parameter values on the estimated losses was assessed through elasticity analyses (Åberg et al., 2009). Elasticity analyses estimated the percentage change in production losses per infected animal that resulted from a percentage change in parameter values. These analyses were performed separately for the two model scenarios: 'no increase in herd size' and 'unrestricted increase in herd size'.

Elasticity was calculated using a log-log function, as follows (Dayal, 2015):

$$ln(y) = I + E \times ln(x) \tag{4.9}$$

where $y$ is the production loss per infected animal in each species, $I$ is the regression intercept, $E$ is the elasticity (percentage change in production loss that results from a percentage change in the parameter value), and $x$ is the input parameter.

## 4.3 Results

### 4.3.1 Inputs for production simulations

#### 4.3.1.1 Brucellosis prevalence

The estimates of individual-level brucellosis prevalence by species and production system, obtained with the latent-class analysis model, are shown in Fig. 4.3. The highest prevalence estimates were found in pastoral cattle (median of 5.1%), which were over seven times more likely to be infected than those in the non-pastoral system (median of 0.7%). In small ruminants, the prevalence estimates were similar across production systems, being slightly higher in goats (median of 2.5% in both systems) compared to sheep (median of 1.3 and 1.6% in pastoral and non-pastoral systems, respectively).

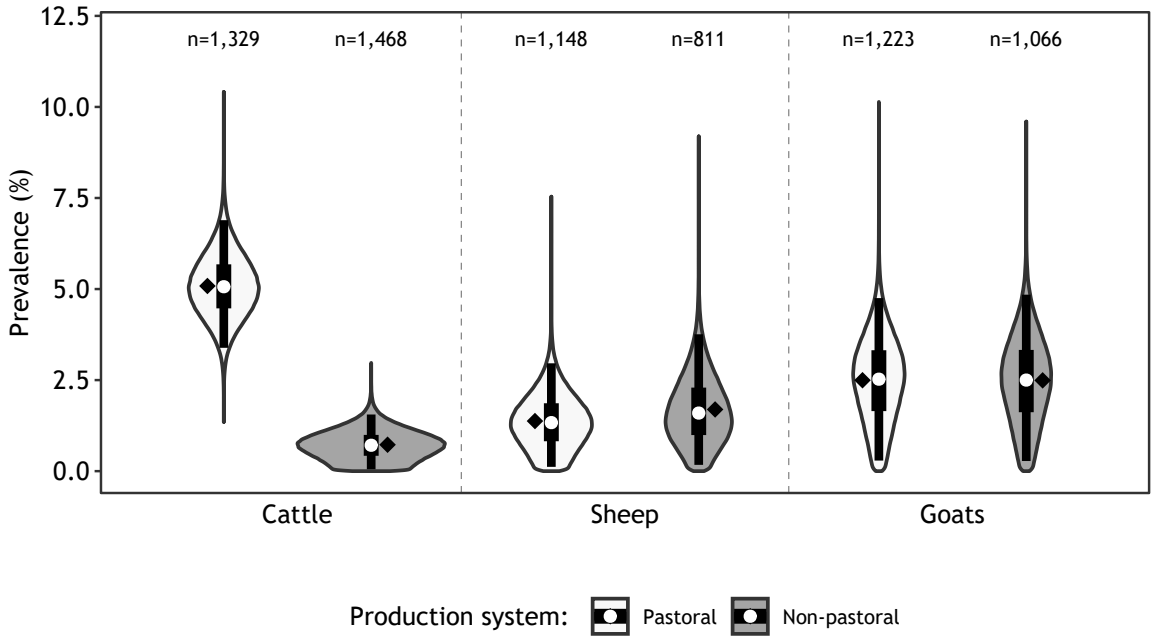



**Figure 4.3:** Latent-class analysis-derived brucellosis prevalence estimates by production system (pastoral and non-pastoral) and species (cattle, sheep, and goats). White dots indicate the median, black diamonds the mean, black boxes the 50% credible interval, and black lines the 95% credible interval. 'n' indicates the number of animals sampled and tested for brucellosis with both the Rose Bengal test (RBT) and competitive enzyme-linked immunosorbent assay (cELISA).

#### 4.3.1.2 Demography

The number of animals kept by households surveyed in SEEDZ as well as the age-sex distribution of these animals and the corresponding birth, death, and offtake rates are shown in Table 4.2. The median number of animals kept by pastoral households was 82 (24 cattle, 20 sheep and 38 goats), which was significantly greater than the number reported in the non-pastoral system (18 in total: seven cattle, four sheep, and seven goats) ($p$-value $< 0.001$).

The distribution of sheep by age and sex group was similar across systems. Regarding cattle and goats, pastoral households tended to keep relatively more adult females and fewer adult males than those in the non-pastoral system ($p$-value $< 0.001$).

For the three species, the birth and death rates were greater in pastoral households ($p$-value $< 0.001$), indicating a higher animal population turnover in this group of households, compared to the non-pastoral system. The difference between birth and death rates resulted in relatively low offtake rates in both production systems.

**Table 4.2:** Demography in the presence of brucellosis, by production system (pastoral and non-pastoral) and species (cattle, sheep, and goats), as calculated from the SEEDZ dataset.

| | Pastoral | | | Non-pastoral | | |
|---|---|---|---|---|---|---|
| | Cattle | Sheep | Goats | Cattle | Sheep | Goats |
| Total number of animals kept | 10,108 | 8,697 | 9,934 | 2,334 | 1,839 | 2,679 |
| Herd size per household* | 24 | 20 | 38 | 7 | 4 | 7 |
| Prop. of juveniles ($j$) | 0.34 | 0.29 | 0.28 | 0.28 | 0.28 | 0.27 |
| Prop. of adult males ($m$) | 0.12 | 0.15 | 0.10 | 0.24 | 0.15 | 0.16 |
| Prop. of adult females ($f$) | 0.54 | 0.56 | 0.62 | 0.48 | 0.57 | 0.57 |
| Birth rate ($b$) | 0.23 | 0.33 | 0.38 | 0.18 | 0.29 | 0.28 |
| Death rate ($d$) | 0.15 | 0.31 | 0.32 | 0.11 | 0.19 | 0.19 |
| Offtake rate ($\theta$) | 0.08 | 0.02 | 0.06 | 0.07 | 0.10 | 0.09 |

* Median number of animals kept per household.

#### 4.3.1.3 Production characteristics

The production characteristics reported by households in the RHoMIS and LSMS surveys are shown in Table 4.3. For sheep and goats, the milk-related variables (milk harvest - $i$, milk yield - $y$, and lactation length - $l$) combine data for the two species.

Only a small number of differences between production systems were identified. The milk yield of cattle in the pastoral system (median = 1.3 L/day) was significantly lower ($p$-value $< 0.001$) than the yield reported by non-pastoral households (median = 3.0 L/day). The milk yield of sheep and goats did not differ between production systems, but pastoral households were significantly more likely ($p$-value $<$ 0.001) to harvest milk (29 out of 132, 22%) from these species than non-pastoral households (23 out of 591, 3.9%).

Regarding the ox and cattle dung usage variables, the values reported by non-pastoral households were approximately twice as high as those reported by pastoral households.

**Table 4.3:** Production characteristics in the presence of brucellosis, by production system (pastoral and non-pastoral) and species (cattle, sheep, and goats), as calculated from the LSMS and RHoMIS datasets.

| | Pastoral | | | | | | Non-pastoral | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cattle | | Sheep | | Goats | | Cattle | | Sheep | | Goats | |
| | Value | n | Value | n | Value | n | Value | n | Value | n | Value | n |
| Wholesale price ($w$; int. $) | 467 (207-1,389) | 145 | 57 (19-103) | 20 | 57 (16-99) | 41 | 464 (117-1,170) | 351 | 42 (8-109) | 65 | 54 (11-110) | 181 |
| Milk harvest ($i$; %) | 82.3 | 192 | 22.0 | 132 | 22.0 | 132 | 76.6 | 725 | 3.9 | 591 | 3.9 | 591 |
| Milk yield ($y$; L/day) | 1.3 (0.3-8.0) | 157 | 1.0 (0.0-2.6) | 30 | 1.0 (0.0-2.6) | 30 | 3.0 (0.3-15.0) | 522 | 1.0 (0.1-3.0) | 20 | 1.0 (0.1-3.0) | 20 |
| Lactation length ($l$; days) | 180 (60-360) | 67 | 120 (46-360) | 23 | 120 (46-360) | 23 | 180 (30-360) | 352 | 105 (30-197) | 18 | 105 (30-197) | 18 |
| Ox usage ($o$; acres) | 1.3 | 78 | NA | | NA | | 2.6 | 490 | NA | | NA | |
| Dung usage ($u$; kg) | 59.7 | 78 | NA | | NA | | 102.7 | 490 | NA | | NA | |

For the $w$, $y$, and $l$, the values shown are the median and, inside parenthesis, the 95% uncertainty interval. 'n' indicates the number of households from which values were obtained. 'NA' indicates a parameter that is not applicable to a species. The data on $i$, $y$, and $l$ for sheep and goats combines the two species. Int $: international dollars. L/day: litres per day.

#### 4.3.1.4 Global parameters

The majority of production parameters that were not allowed to vary between production systems are shown in Table 4.4. In addition, the following median prices (95% uncertainty interval) of milk ($p$) were estimated:

- cattle milk = 0.81 (0.13-2.65) int. $/L; and,
- sheep and goats milk = 0.55 (0.36-0.74) int. $/L.

The values obtained from the literature on direct brucellosis impact probabilities (e.g., abortion, sterility, and perinatal mortality) had a relatively narrow range, i.e., the minimum and maximum values were relatively close. The parameter for which there was greatest variation in the estimates identified was the probability of abortion in infected animals ($\delta$), which varied from 0.1 to 0.5.

Most of the evidence used to inform global parameters on direct brucellosis impacts originated from the 1970s and 1980s, with more recent studies regularly citing these earlier source studies, e.g., Hugh-Jones, Ellis, and Felton (1975), Carpenter (1976), Shepherd, Simpson, and Davidson (1980), Capdevilla (1989), and, Bernues, Manrique, and Maza (1997).

**Table 4.4:** Range of values (minimum and maximum) identified in the literature and used to parametrise uniform distributions of global parameters.

| Global parameters | Minimum | Maximum | References |
|---|---|---|---|
| Abortion probability ($\delta$) | 0.100 | 0.500 | Astaiza-Martínez, Benavides-Melo, and Díaz-Rojas (2012) and Bernues, Manrique, and Maza (1997) |
| Sterility probability ($\gamma$) | 0.100 | 0.300 | Bernues, Manrique, and Maza (1997), Capdevilla (1989) and Singh, Dhand, and Gill (2015) |
| Proportional increase in perinatal mortality ($\nu$) | 0.050 | 0.200 | Alves et al. (2015), Astaiza-Martínez, Benavides-Melo, and Díaz-Rojas (2012), Bernues, Manrique, and Maza (1997), Capdevilla (1989), Hugh-Jones, Ellis, and Felton (1975) and Singh, Dhand, and Gill (2015) |
| Proportional increase in mortality due to abortion ($\psi$) | 0.005 | 0.015 | Alves et al. (2015), Bernues, Manrique, and Maza (1997) and Singh, Dhand, and Gill (2015) |
| Proportional reduction in milk yield ($\phi$) | 0.100 | 0.250 | Alves et al. (2015), Astaiza-Martínez, Benavides-Melo, and Díaz-Rojas (2012), Bernues, Manrique, and Maza (1997), Carpenter (1976), Shepherd, Simpson, and Davidson (1980) and Singh, Dhand, and Gill (2015) |
| Proportional reduction in meat production ($\omega$) | 0.000 | 0.150 | Alves et al. (2015), Astaiza-Martínez, Benavides-Melo, and Díaz-Rojas (2012), Bernues, Manrique, and Maza (1997), Capdevilla (1989), Shepherd, Simpson, and Davidson (1980) and Singh, Dhand, and Gill (2015) |
| Proportional reduction in draught power ($\xi$) | 0.000 | 0.040 | Singh, Dhand, and Gill (2015) |
| Litter size ($z$) in sheep | 1.020 | 1.180 | Dadi et al. (2008) and Safari et al. (2008) |
| Litter size ($z$) in goats | 1.100 | 1.640 | Kosgey, van Arendonk, and Baker (2003) and Tungu et al. (2017) |
| Ox hire ($h$; int. $) | 35.40 | 56.60 | Mutabazi (2014) |
| Dung price ($g$; int. $) | 0.010 | 0.040 | Kangondo (2015) |

### 4.3.2 Outputs from production simulations

#### 4.3.2.1 Losses attributable to brucellosis

The estimated losses per infected animal, by species, production system, and model scenario, are shown in Fig. 4.4. Under the model scenario of 'no increase in herd size', the median (95% uncertainty interval) annual losses attributable to brucellosis in cattle, sheep, and goats, per infected animal, were 74.4 (26.2-211.7), 9.7 (3.4-23.1), and 10.6 (3.7-25.0) international dollars (int. $) in the pastoral system, and 62.3 (16.8-228.6), 6.3 (1.8-17.1), and 7.0 (2.2-17.9) int. $ in the non-pastoral system, respectively. In cattle, the estimated losses were approximately seven to ten times as high as those estimated in sheep and goats. For all species, greater losses were estimated in the pastoral system, compared to the non-pastoral system. Additionally, within the same system, the losses per infected goat were significantly greater than the losses per infected sheep ($p$-value $< 0.001$).

Under the model scenario of 'unrestricted increase in herd size', the median (95% uncertainty interval) annual losses attributable to brucellosis in cattle, sheep, and goats, per infected animal, were 66.0 (21.1-329.2), 3.6 (0.5-29.2), and 6.9 (1.9-33.2) int. $ in the pastoral system, and 65.9 (22.3-445.0), 4.2 (1.3-10.8), and 4.0 (1.3-9.8) int. $ in the non-pastoral system, respectively. The difference in losses between cattle and the other species was slightly greater in the model scenario of 'unrestricted increase in herd size', compared to the scenario of 'no increase in herd size'.

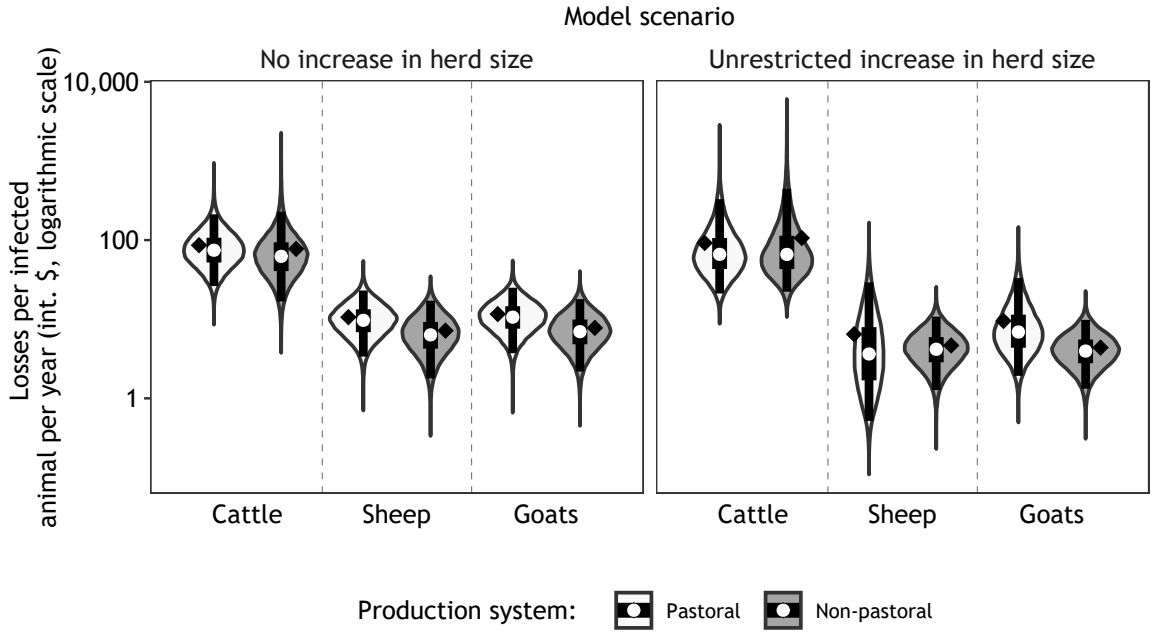



**Figure 4.4:** Estimated monetary losses attributable to brucellosis per infected animal per year, by production system (pastoral and non-pastoral), species (cattle, sheep, and goats), and model scenario ('no increase in herd size' and 'unrestricted increase in herd size'). White dots indicate the median, black diamonds the mean, black boxes the inter-quartile range (50% UI), and black lines the 2.5 and 97.5 percentiles (95% UI). Uncertainty intervals were obtained from Monte Carlo simulation (50,000 iterations). The values in the y-axis are on the logarithmic scale. Int. $: International dollars.

The estimated losses per household, by species, production system, and model scenario, are shown in Fig. 4.5. Assuming a typical herd size and species composition per household as indicated in Table 4.2, the median losses per household in the pastoral system were over 20 times as high as those in the non-pastoral system in both model scenarios. Cattle contributed the most to household-level losses in both production systems and model scenarios. Sheep and goats jointly contributed around one-tenth and less than one-fourth of the household-level losses in pastoral and non-pastoral systems, respectively.

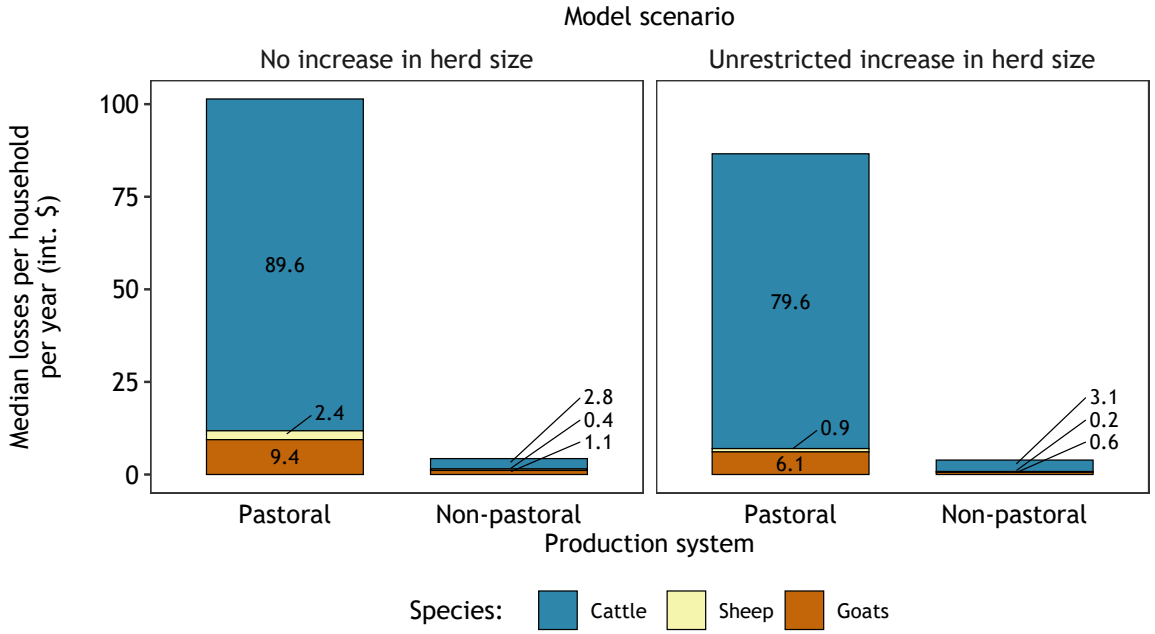



**Figure 4.5:** Estimated monetary losses attributable to brucellosis per household per year, by production system (pastoral and non-pastoral), species (cattle, sheep, and goats), and model scenario ('no increase in herd size' and 'unrestricted increase in herd size'). The numbers within each bar or connected to it with a line segment indicate the median household-level losses attributable to brucellosis in each species. Estimates of household-level losses assume a herd size of 24 cattle, 20 sheep, and 38 goats in the pastoral system, and seven cattle, four sheep, and seven goats in the non-pastoral system. Int. $: International dollars.

The contribution of each of the livestock production outputs (offtake, milk, draft power, and dung) to the household-level losses, by species, production system, and model scenario, is shown in Fig. 4.6. Under the model scenario of 'no increase in herd size', the majority of household-level losses were the result of lower offtake value, in all species and both production systems. Under the scenario of 'unrestricted increase in herd size', the majority of household-level losses were the result of lower milk value, except for sheep and goats in the non-pastoral system.

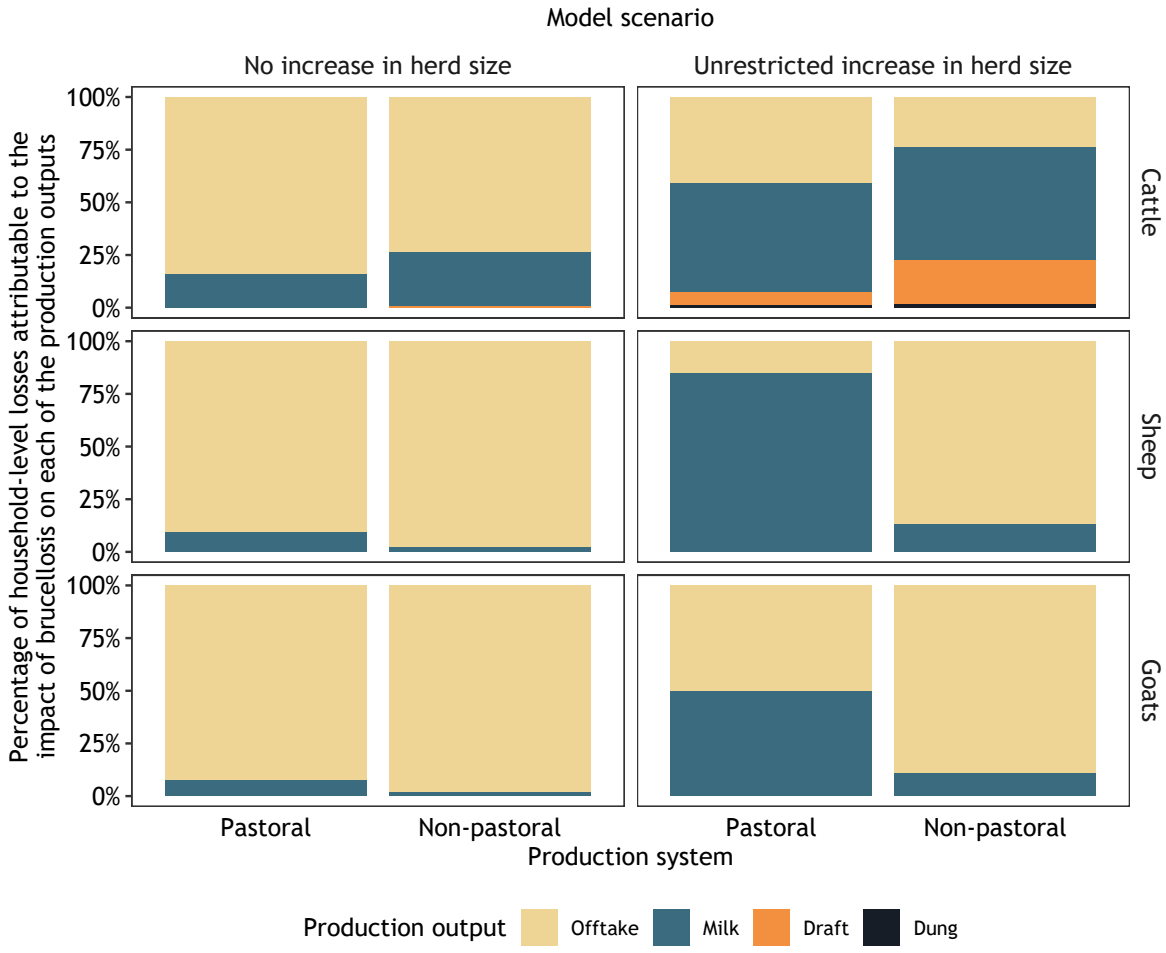



**Figure 4.6:** Estimated contribution of each of the livestock production outputs (offtake, milk, draft power, and dung) to the household-level losses, by production system (pastoral and non-pastoral), species (cattle, sheep, and goats), and model scenario ('no increase in herd size' and 'unrestricted increase in herd size').

The annual, region-level losses attributable to brucellosis in northern Tanzania are shown in Fig. 4.7. Manyara was the region with the highest estimated losses per year (5.7 M int. $), followed by Arusha (3.8 M int. $) and Dodoma (3.1 M int. $). These three regions were those with the largest population of livestock kept by pastoral households, as indicated in Table 4.1. Kilimanjaro was the region with the lowest estimated losses, at 0.6 million int. $ per year. In this region, livestock were kept predominantly by non-pastoral households.

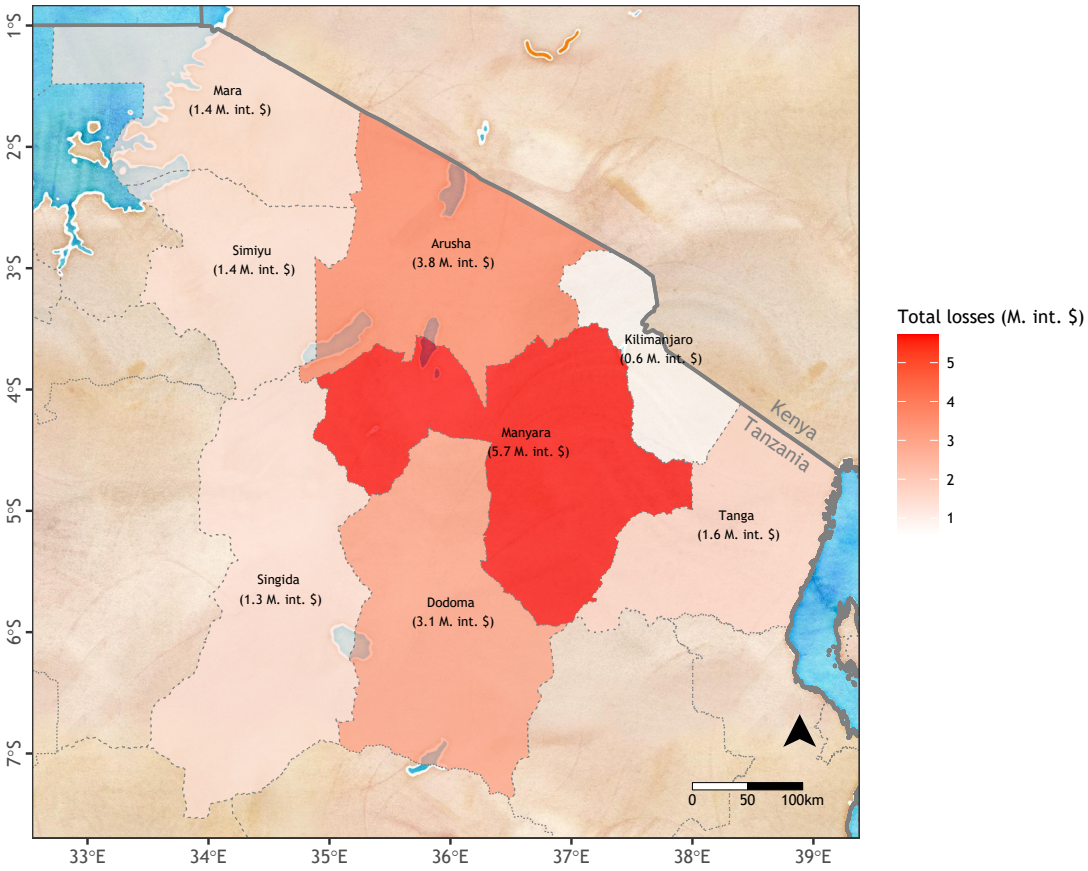



**Figure 4.7:** Choropleth map of the median losses attributable to brucellosis in the study area, northern Tanzania, by region. The estimates of losses were obtained from the reference model scenario ('no increase in herd size'). Dashed lines delineate regions. M. int. $: million international dollars. Solid lines indicate national borders. The polygon shapefiles were obtained from GADM, the Database of Global Administrative Areas (`https://gadm.org/`). Map tiles by Stamen Design, under CC BY 3.0. Data by OpenStreetMap, under CC BY SA.

### 4.3.2.2 Determinants of losses attributable to brucellosis

The results of the elasticity analyses of production losses per infected animal per year, under the model scenario of 'no increase in herd size', are shown in Fig. 4.8. The parameters for which variation affected the estimated losses per infected animal the most were the wholesale price and the abortion probability. This was consistent for all species (cattle, sheep, and goats) and both production systems (pastoral and non-pastoral). The next most influential variables were related to milk value (milk yield, lactation length, milk price, and milk harvest) in cattle and litter size in sheep and goats.

The results of the elasticity analyses of production losses per household per year, under the model scenario of ‘no increase in herd size’, are shown in Fig. 4.9. The most influential parameter to the estimated losses per household per year was the prevalence, followed by the wholesale price and abortion probability. The results of the elasticity analyses under the model scenario of ‘unrestricted increase in herd size’ are shown in Appendix C.3.

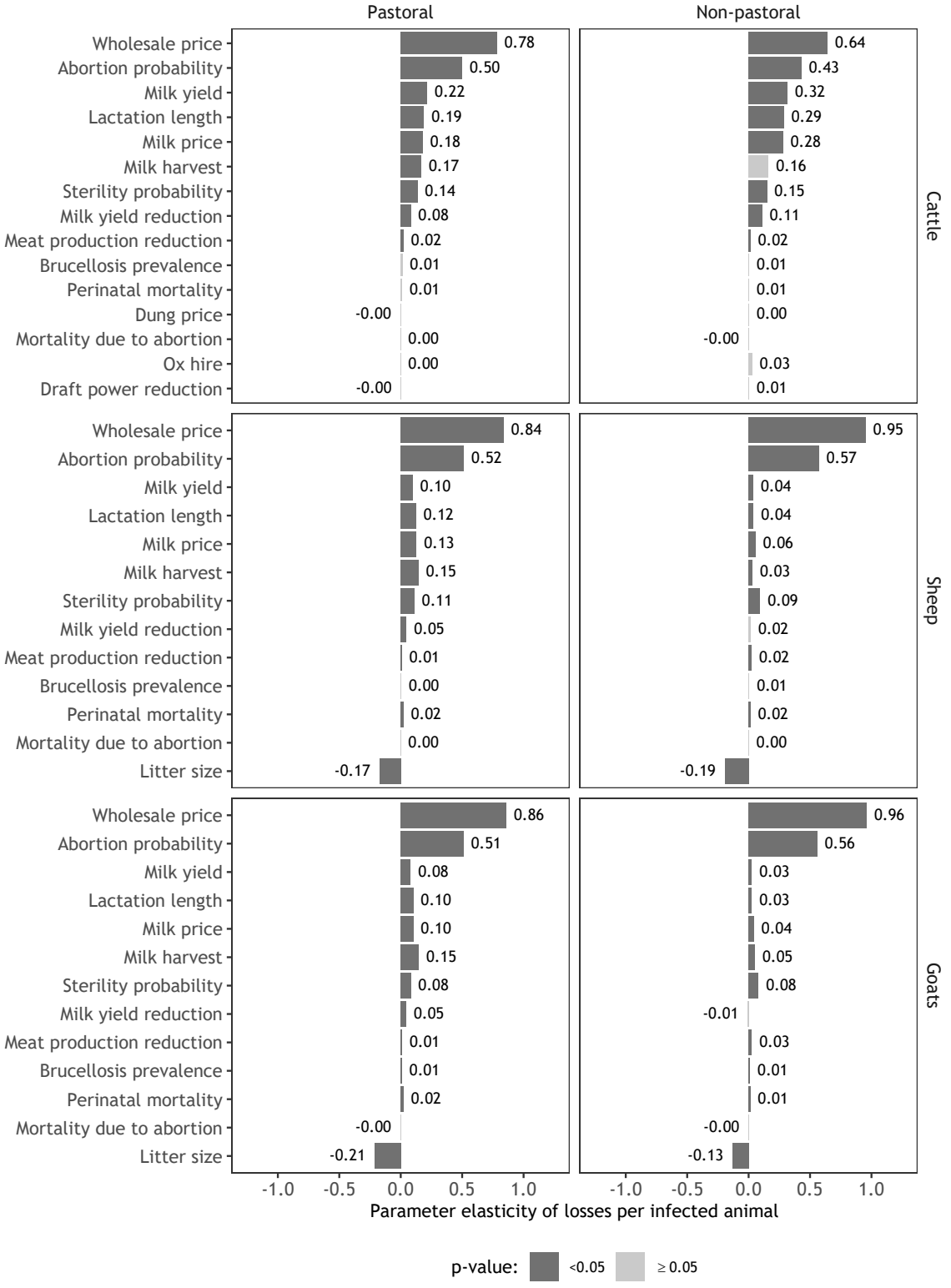



**Figure 4.8:** Tornado plot showing the parameter elasticity of production losses (int. $) per infected animal (percentage change in production losses per infected animal per year when parameter values change by 1%), by production system (pastoral and non-pastoral) and species (cattle, sheep, and goats) (50,000 model iterations, scenario of 'no increase in herd size'). The colours of the bars indicate the significance of the parameter elasticity estimate (dark and light grey indicate p-value $< 0.05$ and p-value $\geq 0.05$, respectively).

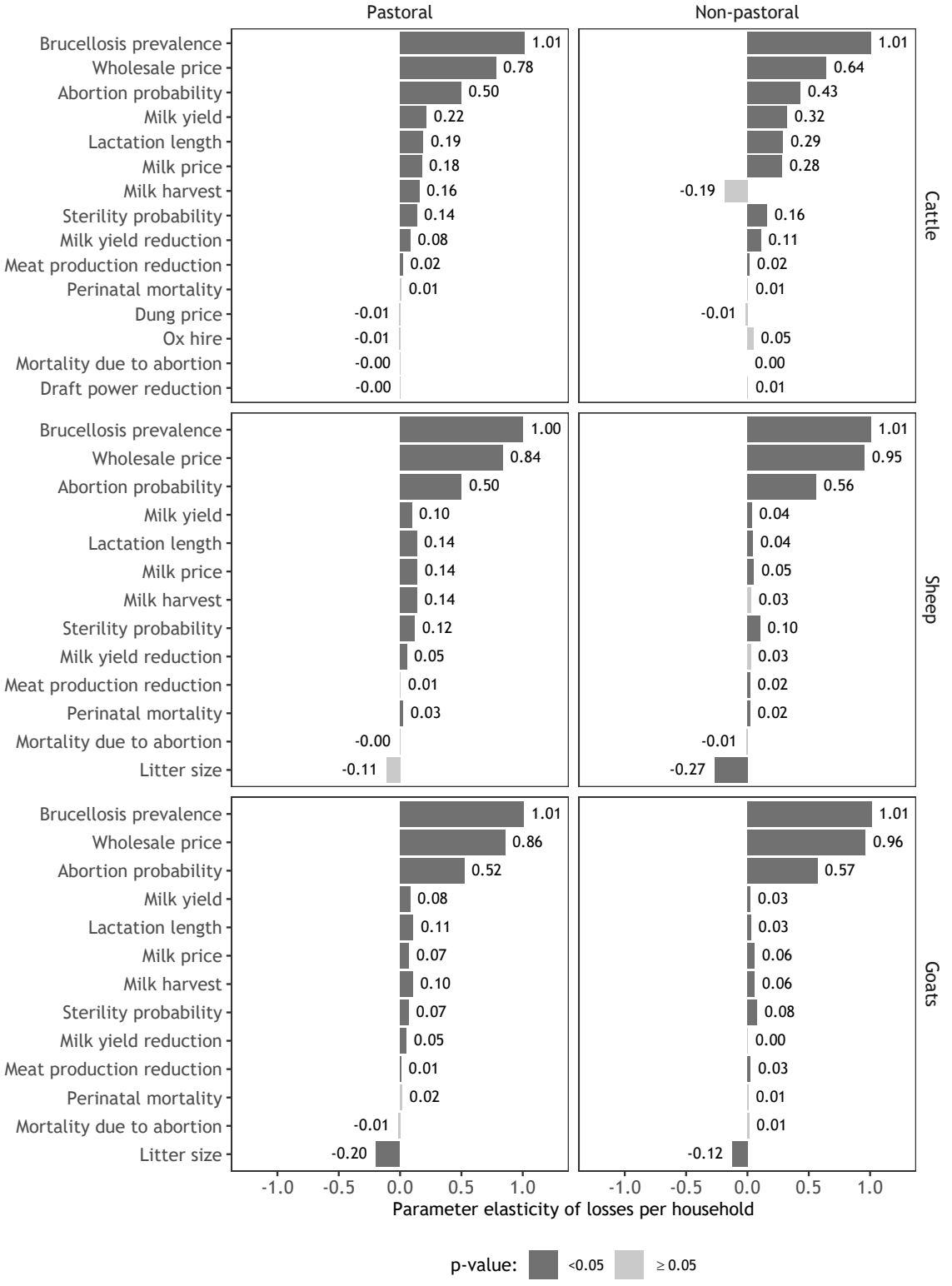



**Figure 4.9:** Tornado plot showing the parameter elasticity of production losses (int. $) per household (percentage change in production losses per household per year when parameter values change by 1%), by production system (pastoral and non-pastoral) and species (cattle, sheep, and goats) (50,000 model iterations, scenario of 'no increase in herd size'). The colours of the bars indicate the significance of the parameter elasticity estimate (dark and light grey indicate p-value $< 0.05$ and p-value $\geq 0.05$, respectively).

## 4.4 Discussion

This study estimated the production losses attributable to livestock brucellosis in pastoral and non-pastoral systems of northern Tanzania, at three different levels: i) at the individual level, i.e., the losses per infected animal; ii) at the household level, i.e., the losses per livestock-keeping household; and, iii) at the regional level, i.e., the sum of household losses in each region.

The median estimated losses per infected animal per year were equivalent to approximately 20% of the median wholesale price (model parameter $w$) in the pastoral system, for all species, and lower (closer to 10%) in the non-pastoral system (model scenario of 'no increase in herd size'). Alternatively, these losses per infected animal were equivalent to 39%, 15%, and 16% of the value of each lactation (milk yield times lactation length times milk price) in cattle, sheep, and goats in the pastoral system, respectively, and approximately 10% of the median value of each lactation for all species in the non-pastoral system.

The median household-level losses attributable to brucellosis (101.4 int. $ per year) were equivalent to around 4.5% of the median annual, livestock-derived, household income expected in the absence of the disease (approximately 2,265 int. $; model scenario of 'no increase in herd size'). In the non-pastoral system, the median household-level losses attributable to brucellosis (4.3 int. $ per year) were equivalent to around 0.6% (near eight-fold lower than in the pastoral system) of the median annual, livestock-derived, household income expected in the absence of the disease (approximately 755 int. $; model scenario of 'no increase in herd size'). The impact of livestock brucellosis on households is then inextricably linked with the context in which livestock are raised. The production system plays a clear role in determining the losses attributable to brucellosis. The higher prevalence of the disease, at least in cattle, as well as the greater dependency on livestock and livestock products for their livelihoods, as measured by livestock and livestock product harvest rates (e.g., number of animals converted into offtake and volume of milk harvested per year), results in significantly greater losses in pastoral households, compared to those in the non-pastoral system. These results indicate the importance of deriving context-specific estimates in future assessments of livestock brucellosis impacts.

The total estimated loss attributable to brucellosis per year in the study area was 19.0 million int. $ (the sum of the median estimated losses in the eight regions: Arusha, Manyara, Kilimanjaro, Tanga, Dodoma, Singida, Simiyu, and Mara), equivalent to 0.71 int. $ per animal kept (including all species: cattle, sheep, or goats). Given the differences in household-level losses between production systems and the relative distribution of livestock by regions, considerable heterogeneity in regional losses was identified. A near ten-fold difference was estimated between the regions with the highest and the lowest estimated losses (Manyara, with 5.7 million int. $ per year, and Kilimanjaro, with 0.6 million int. $ per year). The spatial heterogeneity in livestock production losses may be relevant for designing and prioritising potentially targeted control interventions.

The contribution of each type of livestock production output to the estimated household-level losses differed between model scenarios. The impact of brucellosis on offtake was greater under the reference model scenario ('no increase in herd size'), compared to the alternative scenario ('unrestricted increase in herd size'), in which overall losses were dominated by the impact of brucellosis on milk production. In the reference model scenario, all excess stock that resulted from the hypothetical brucellosis elimination was converted into offtake, hence the high importance of this production output to the household-level losses. In the alternative model scenario, not all excess stock that resulted from brucellosis elimination was converted into offtake, hence the relatively low importance of this production output (offtake) to the household-level losses. Instead, as the herd size increases after brucellosis elimination in the alternative model scenario, more milk is produced by the herd, which explains the relatively high importance of this production output (milk) to the household-level losses. This is the case, at least, where milk is harvested to a significant extent, which excludes sheep and goats in the non-pastoral system. In this system, less than 4% of households reported harvesting milk from small ruminants (Table 4.3). The differences in results between model scenarios highlight the need for future studies on the impacts of livestock brucellosis (and other diseases causing reproductive morbidity) to consider the effect of herd size management decisions on estimated losses.

The livestock production losses estimated in this study were lower than those reported elsewhere. The median losses per infected animal in the reference model scenario were between 62.3 and 74.4 int. $ per year in cattle (non-pastoral and pastoral systems, respectively) and below or equal to 10.6 int. $ per year in sheep and goats in both pastoral and non-pastoral systems. Elsewhere, the losses per infected animal have been estimated at over 100 int. $ in cattle (India, Brazil, Colombia, Uganda, Turkey, and Sudan) and over 20 int. $ in sheep and goats (India, Iraq, and

Malaysia) (Al Hamada et al., 2021; Alshwany, 2019; Angara et al., 2016; Bamaiyi et al., 2015; Bardhan et al., 2020; Eşki, Demir-Ayvazoğlu, and Günaydın, 2021; Guma et al., 2020; Homem, Higa, and Neto, 2016; Patel et al., 2014; Santos et al., 2013; Singh, Dhand, and Gill, 2015).[2]

Several reasons can explain the relatively low losses estimated in this study. Firstly, there is significant heterogeneity in methods to estimate the losses attributable to livestock brucellosis, which hampers comparisons between study systems (Deka et al., 2018). In contrast to the present study, other studies estimating the impact of livestock brucellosis often value specific impacts of the disease (e.g., temporary infertility or sterility) at the cost, at least partially, of the replacement animal (e.g., the price of a fertile adult animal) (Santos et al., 2013; Singh, Dhand, and Gill, 2015). This practice overestimates the loss caused by brucellosis because the offtake value of an infected animal is, in many cases, not depreciated by the occurrence of sterility (Ducrotoy, 2014). Another recurring practice is the use of fixed market prices collected at national or sub-national levels to value livestock and livestock products (Santos et al., 2013; Singh, Dhand, and Gill, 2015). The use of fixed market prices to estimate losses attributable to brucellosis has two disadvantages: i) market prices may be time- and context-specific, varying with factors such as supply and demand, and may not reflect the value that households put on their animals (FAO, 2018a); and, ii) as shown in the present study, the value of livestock and livestock products is the most important determinant of the losses per infected animal. Studies that use fixed livestock and livestock product market prices may fail to capture the likely substantial variation and uncertainty in estimated losses, which can influence the accuracy of central-point estimates. The central-point estimate most commonly reported is the mean, which tends to be greater than the median when the distribution of losses is skewed to the right (Chan, 2016). The present study used distributions of the actual prices reported by households based on sales instead of fixed market prices.

Secondly, a potential source of differences in results between studies is the way authors value the foregone losses. Given the long-term effects of brucellosis on reproduction and demography, foregone losses, which include, for instance, the milk loss from unborn female offspring, are a non-negligible part of the overall impact of the disease on livestock productivity (Singh, Dhand, and Gill, 2015). Foregone losses are also intrinsically challenging to estimate because they are (i) dependent on herd management decisions, (ii) time-bounded, and (iii) difficult to separate

2. Using the country of each study, their local currency, year of data collection and the corresponding World Bank conversion rates at `https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?end`

from current production losses (e.g., due to reduced growth rate). For these reasons, modelling approaches such as the one described in the present study that (i) take into account the herd-growth dynamics, (ii) simulate livestock production for a period of time in the presence and in the absence of the disease, and (iii) estimate current and foregone losses simultaneously may be good alternatives to previously used models. Additionally, most studies that estimated the losses attributable to brucellosis do not discount foregone losses over time, which overestimates these losses, as viewed from the present (Angara et al., 2016; Patel et al., 2014; Santos et al., 2013; Singh, Dhand, and Gill, 2015).

Thirdly, this study aimed to estimate losses attributable to brucellosis, as defined by McInerney, Howe, and Schepers (1992), i.e., the production potential that is not realised over time due to the presence of the disease. This definition of 'losses' excludes prevention and treatment expenditures and other reaction costs due to the presence of the disease. However, some studies have included these costs (e.g., cost of veterinary assistance, or cost of repeat breeding) in the estimation of losses (Angara et al., 2016; Santos et al., 2013). Other studies have used the definition of losses by McInerney, Howe, and Schepers (1992), but the livestock products to which such definition applied were different to those considered here. For instance, in the present study, for sheep and goats, only the losses in offtake and milk values were estimated because these are the main, if not the only, sources of income from these species to households in the study area. In other studies, for the same livestock species, losses from other outputs (e.g., wool) were also considered (Singh, Dhand, and Gill, 2015).

For these reasons, it can be inferred that the current study employed robust methodology and generated relatively more accurate estimates of production losses attributable to brucellosis than often reported elsewhere. This study would have likely overestimated production losses if it applied the same methods and definitions as previous studies.

However, several limitations of this study need to be highlighted. One of the main limitations was the uncertain representativeness of prevalence data. The SEEDZ survey tested 7,045 livestock (cattle, sheep, and goats) from 404 households in Arusha and Manyara. SEEDZ did not sample animals from other regions. The degree to which the prevalence data in SEEDZ were representative of the other regions in the study area is likely high but truly unknown. The study by Bodenham et al. (2021) applied the same latent-class model to analyse prevalence data from SEEDZ and another survey (BacZoo) delivered in Kilimanjaro. Prevalence data from BacZoo were not included in the present study because the survey excluded many

variables needed for the clustering algorithm (Chapter 3). The prevalence estimates reported by Bodenham et al. (2021) in the pastoral system were higher than in the current study (6.3% vs 5.1% in cattle; 3.3% vs 1.3% in sheep; and, 5.1% vs 2.5% in goats). Other epidemiological studies carried out in northern Tanzania or elsewhere in the country often report a higher prevalence than estimated in the present study (Asakura et al., 2018a; Assenga et al., 2015; Chitupila, Komba, and Mtui-Malamsha, 2015; Sagamiko et al., 2018; Shija et al., 2014; Shirima et al., 2010; Shirima and Kunda, 2016; Sijapenda, Komba, and Nonga, 2017; Swai and Schoonman, 2010, 2012). In cattle, the prevalence of brucellosis has been estimated at 11.8% in the Tanga region (Swai and Schoonman, 2012). In small ruminants, prevalence estimates of 1.6% and 6.5% were reported in Katavi and Rukwa regions (Assenga et al., 2015) and Arusha and Manyara regions (Shirima et al., 2010), respectively. Greater production losses would have been estimated if the current study had used the prevalence estimates in Bodenham et al. (2021) and other studies.

The small number of households providing information on production characteristics, particularly of sheep and goats, is another limitation of this study. For instance, the wholesale prices of sheep and goats in the pastoral system were obtained from 20 and 41 households only, respectively (Table 4.3). It could be argued that this small sample of households may have provided a biased estimate of wholesale prices. The median prices reported by these households (57 int. $ for both sheep and goats) were lower than reported nationwide in the latest livestock sector analysis led by the Tanzania Government: between 80 and 119 int. $ for adult male sheep and goats (Government of The United Republic of Tanzania, 2017c).[3] However, the median wholesale price of goats in the non-pastoral system in the present study (54 int. $), which was based on answers from many more households (n=181), was also lower than in the livestock sector analysis report. This indicates that the wholesale prices used in the present study are likely specific to the study area, rather than potentially biased.

Finally, the cross-sectional nature of the survey that provided data on demographic characteristics of the livestock population (SEEDZ) is another potential limitation of the present study. It is unclear whether the year in which the SEEDZ survey was delivered (2016) accurately represented the demographic characteristics of the same livestock population in other years. If there were abnormal birth and death rates in 2016, the losses estimated in 10-year simulations could be biased. Note that the offtake rate ($\theta$) was given by the difference between the birth ($b$) and death ($d$) rates. If 2016 was a 'good' year, with higher birth rates and lower death

3. Using the World Bank conversion rates for Tanzania in 2017 at `https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?end&locations=TZ`

rates than usual, the losses reported here are likely overestimated. In contrast, if 2016 was a 'bad' year, with lower birth rates and higher death rates than usual, the losses reported here are likely underestimated. The latter (2016 being a 'bad' year) is plausible because higher offtake rates ($> 10\%$) have been reported in other years and for all species in Tanzania (Government of The United Republic of Tanzania, 2017c).

## 4.5 Conclusion

Brucellosis causes significant economic impacts in the livestock sector of northern Tanzania, with estimated annual losses amounting to approximately 19 million int. $. These estimated losses can be useful to inform cost-benefit analyses of potential brucellosis control interventions, such as livestock vaccination (see Chapter 6).

The distribution of estimated losses across households and geographical areas is highly heterogeneous. A key determinant of this heterogeneity is the production system, with losses occurring predominantly in pastoral households and in regions where these households are concentrated (Arusha and Manyara). Future research projects aimed at estimating the impact of livestock brucellosis in a similar context should then be designed taking into account the differences between production systems.

A new model framework for estimating the losses attributable to brucellosis was proposed in this study. By enabling the simulation of livestock production for an observed disease prevalence as well as for a hypothetical scenario of disease absence, this model framework can estimate the production potential that is not realised due to the presence of the disease. This approach may help estimate losses attributable to other livestock diseases in Tanzania and similar settings. Given the ability to capture foregone losses due to low reproductive performance, the proposed method is particularly relevant in the context of diseases characterised by high reproductive morbidity and low mortality.

# Chapter 5

# Monetary cost and disease burden attributable to human brucellosis in a pastoralist community of northern Tanzania

## 5.1 Introduction

### 5.1.1 Background

Human brucellosis is a bacterial infection that causes acute or intermittent fever, often associated with progressive, debilitating symptoms that include arthralgia, myalgia, back pain, and malaise (Bouley et al., 2012; Dean et al., 2012a; Eroglu and Kandemir, 2020; Liu et al., 2020a,b; Qie et al., 2020). A considerable number of people suffering from brucellosis develop severe complications, including endocarditis and meningitis (approximately 5% globally, but highly dependent on the setting) (Dean et al., 2012a). Reproductive complications of brucellosis are common. Approximately 10% of men with brucellosis develop epididymo-orchitis (Akhvlediani et al., 2017; Jiang et al., 2019; Pericherla, Gupta, and Saravu, 2021; Roushan et al., 2004). Pregnant women with brucellosis are more likely to develop obstetric complications, including spontaneous abortion and stillbirth, than pregnant women without brucellosis (Elshamy and Ahmed, 2008; Gulsun et al., 2011; Kurdoglu et al., 2010).

Despite the debilitating nature of the clinical manifestations, there is currently poor evidence of the socio-economic impacts of human brucellosis, particularly in low- and middle-income countries (LMICs). Some of the reasons that explain the limited evidence on these impacts in Tanzania are the (i) sparse data on disease incidence due to the absence of effective surveillance systems (Laine, Scott, and

Arenas-Gamboa, 2022), (ii) poor sensitivity and specificity of tests widely used in clinical practice (Lukambagire et al., 2021), (iii) low healthcare-seeking rates[1] (Carugati et al., 2018), (iv) inadequate scientific evidence of morbidity and mortality caused by brucellosis (Moreno, Blasco, and Moriyon, 2022), and (v) lack of robust methodology to estimate costs (i.e., healthcare expenditure and productivity losses) and disease burden (e.g., disability-adjusted life-years, DALYs) attributable to brucellosis from available data (Moreno, Blasco, and Moriyon, 2022).

Evidence of the socio-economic impact of human brucellosis is key to informing health-policy development and control interventions in Tanzania. Disease burden estimates are particularly relevant for policy makers aiming to allocate scarce resources optimally. Metrics such as DALYs (disability-adjusted life years), based on years of life lost due to premature death or disability, enable standardised comparison and prioritisation of health conditions and potential control interventions. Estimating the magnitude of health-related expenditure and productivity losses attributable to brucellosis in poor communities would be helpful to justify investment in control.

### 5.1.2 Surveillance of human brucellosis

In Africa, the largest disease surveillance platform is the Integrated Disease Surveillance and Response (IDSR) system, which was initially adopted by the World Health Organisation (WHO) Regional Committee for Africa in 1998 (Mremi et al., 2021). Since then, 44 out of 47 countries in the WHO African region, including Tanzania, have used this platform for disease surveillance activities, including case investigation, confirmation, registration, notification/reporting, as well as data analysis and response (Fall et al., 2019; Mremi et al., 2021; Nkowane, 2019). Currently, Tanzania's IDSR system includes surveillance and response protocols for 34 priority diseases and conditions, including many zoonoses (e.g., rabies and anthrax) (Nkowane, 2019). Brucellosis is not routinely included in this list of priority diseases and conditions, despite being one of six high-priority zoonoses in Tanzania (U.S. Agency for International Development (USAID), USAID Preparedness and Response Project (P&R), and U.S. Centers for Disease Control and Prevention (CDC), 2017). Thus, no reliable data on brucellosis prevalence or incidence can be drawn from the IDSR system in Tanzania.

1. 'healthcare-seeking rates' and 'healthcare-seeking probability' are concepts that are used here instead of 'healthcare resource use / consumption' to capture the whole healthcare-seeking process and associated costs from the perspective of the patients and their families, including especially relevant aspects in low- and middle-income countries such as expenditure in transport, accommodation and subsistence

Recent hospital-based febrile surveillance studies have produced some evidence of the acute brucellosis prevalence and incidence in northern Tanzania (Bodenham et al., 2020; Bouley et al., 2012; Carugati et al., 2018; Cash-Goldwasser et al., 2018). However, there have been just a small number of these studies and incidence estimates were predominantly from urban populations. Exceptionally, a recent study has estimated human brucellosis incidence in a rural setting, the Ngorongoro Conservation Area (NCA; Fig. 5.1), from hospital-based surveillance and healthcare-seeking behaviour (Will de Glanville, personal communication). The estimated incidence of brucellosis in the NCA was approximately 413 per 100,000 person-years. The NCA is a protected ecosystem of woodland and plains in the Ngorongoro district, Arusha region, with an estimated population of about 100,000 people, predominantly Maasai pastoralists (Government of The United Republic of Tanzania, 2019; Manzano and Yamat, 2018; Tanzania Wildlife Research Institute, 2016). In the wider areas of the Ngorongoro district, a survey of pregnant women receiving antenatal care concluded that 34 (10.9%) out of 313 participants had evidence of *Brucella* spp. exposure (Makala et al., 2020). Eight (23.5%) out of the 34 seropositive participants had likely been exposed recently, based on high IgM titres on enzyme-linked immunosorbent assay (ELISA).

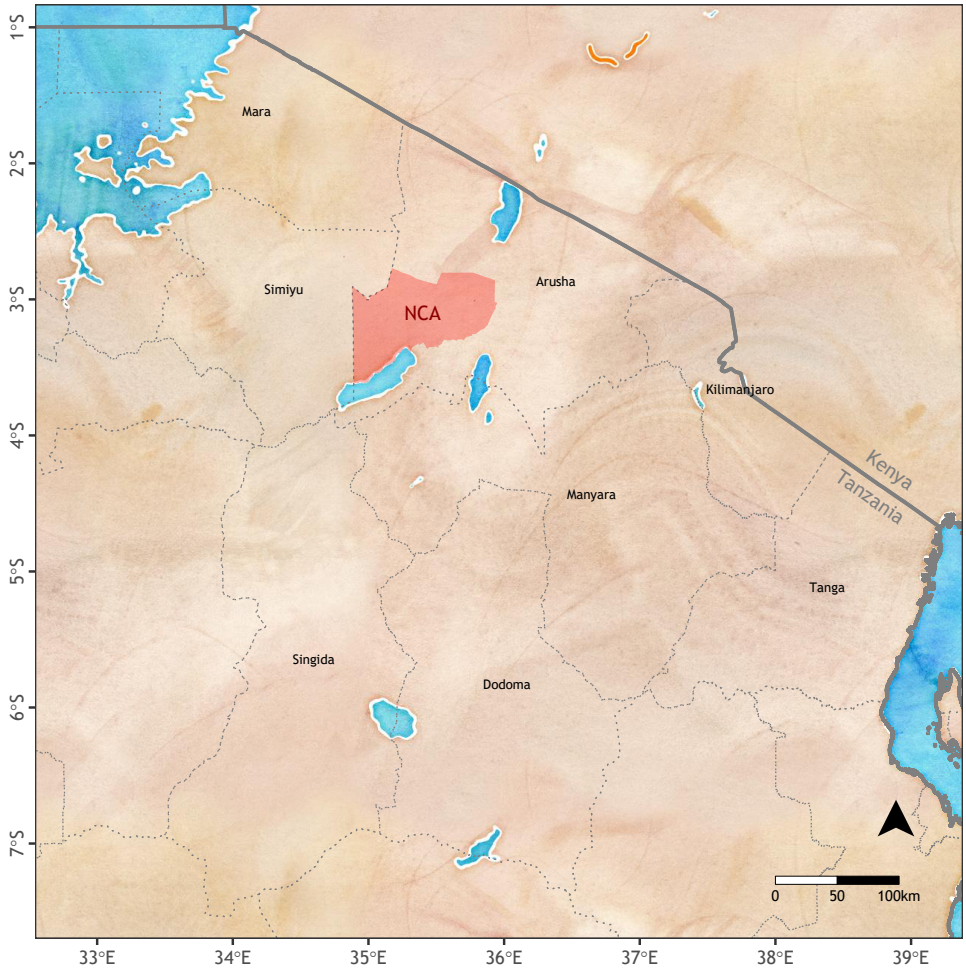



**Figure 5.1:** Map of northern Tanzania indicating the location of the Ngorongoro Conservation Area (NCA, red-filled polygon). Dashed lines delineate regions. Solid lines indicate national borders. The region- and country-level polygon shapefiles were obtained from GADM, the Database of Global Administrative Areas (`https://gadm.org/`). The polygon shapefile of the NCA was obtained from the National Bureau of Statistics of Tanzania (https://www.nbs.go.tz/index.php/en/). Map tiles by Stamen Design, under CC BY 3.0. Data by OpenStreetMap, under CC BY SA.

### 5.1.3 Healthcare seeking for human brucellosis

Many people suffering with brucellosis (brucellosis cases, i.e., people experiencing signs and/or symptoms caused by the infection with *Brucella* spp., irrespective of whether they have been formally diagnosed at a healthcare facility) in LMICs do not seek healthcare before the disease progresses to a chronic or complicated stage. In Tanzania, a study reported that the majority of cases delayed visiting a hospital by up to three months since the onset of symptoms (Kunda et al., 2007).

In another survey also delivered in Tanzania, only 41.2% of households (334 out of 810) reported that a household member 15 years old or over would go to a hospital that could diagnose brucellosis if they developed a fever that lasted for longer than three days (Carugati et al., 2018).

Many factors may contribute to delayed healthcare seeking for brucellosis in Tanzania. The country has one of the lowest Universal Health Coverage (UHC) indices in the East African region (WHO, 2019). The healthcare financing system in Tanzania is highly fragmented, which causes inequalities in affordability and access: the poorest in rural areas, where brucellosis is likely more prevalent, depend mostly on out-of-pocket payments to access services of perceived poor quality, whilst the least poor in urban areas, where brucellosis is likely less prevalent, are mostly covered by health insurance (e.g., from the National Health Insurance Fund) and can access services of perceived better quality (Mhagama, 2017; Mtei et al., 2012). The perceived poor quality of the healthcare service in some areas, often affected by staff shortages, variable levels of staff training, and problems of drug supply and effectiveness, coupled with cultural preferences, motivate many households to seek alternative services (e.g., traditional healers or herbalists), which also require households to incur out-of-pocket costs (Brinda, Andrés, and Enemark, 2014; Loosli et al., 2021). Access to healthcare services is further complicated by poor road infrastructure, high transportation costs, and seasonal weather conditions (Kunda et al., 2007; Loosli et al., 2021). Ultimately, many people suffering from brucellosis are at risk of either financial hardship due to healthcare-related expenditure or morbidity and mortality due to poor, absent or delayed disease management.

### 5.1.4 Adverse obstetric outcomes attributable to human brucellosis

In pregnant women, brucellosis is a cause of adverse obstetric outcomes, including spontaneous abortion (foetal death that occurs up to the 24$^{th}$ week of gestation), stillbirth (foetal death that occurs after the 24$^{th}$ week of gestation), and preterm delivery (the birth of a baby before the 37$^{th}$ week of gestation) (Bosilkovski, Arapović, and Keramat, 2020; Karcaaltincaba et al., 2010). None of the studies summarised in Table 1.2 estimated the burden of obstetric complications attributable to brucellosis. In fact, the global burden of disease study does not count loss of 'potential' life years due to any foetal death, even if it happens during labour. Practical reasons, including the lack of data in many settings, explain why foetal deaths, even during labour, have not been considered. However, ignoring such deaths seems ethically unacceptable and potentially biased (Phillips and Millum,

2015). Two of the key principles of DALYs estimation methods are (i) *to the extent possible, any health outcome that represents a loss of welfare should be included in an indicator of health status*, and (ii) *treating like health outcomes as like* (Murray, 1994). It can be argued that a population health measure should account for the well-being of a fully developed foetus unless it can be shown that such well-being is not as equally important as that of an infant (Phillips and Millum, 2015).

### 5.1.5 Dynamical modelling to estimate the cost and disease burden attributable to human brucellosis

Markov models are commonly used in decision analysis of healthcare interventions. Examples of Markov modelling applications include cost-effectiveness analyses of prevention and therapeutic interventions against a wide range of infectious, endocrine, musculoskeletal, cardiovascular, neurological, immunological, and psychiatric disorders or diseases (Bankar et al., 2020; Chen et al., 2021; Lindholt and Søgaard, 2021; Lokkerbol et al., 2021; Peersman et al., 2014; Pesonen, Kankaanpää, and Vottonen, 2021). Although these models provide the ability to represent features of disease management (e.g., healthcare-seeking probability and diagnostic sensitivity), they are rarely applied to estimate costs of infectious diseases (Benčina et al., 2017; Bereza et al., 2012; González, Walker, and Einarson, 2009; Herrick et al., 2012). A typical Markov disease model simulates the transition of patients through a sequence of mutually exclusive states over time. Transitions occur between fixed time steps (Markov cycles), which are clinically relevant (e.g., days for acute diseases, weeks or months for chronic diseases) (York Health Economics Consortium (YHEC), 2023). By simulating the progression through this chain of disease states (i.e., a Markov chain) and the costs or disability associated with each state, it is possible to estimate the total cost of a disease.

A Markov model was developed and applied to predict mortality, morbidity, and cost of a salmonellosis outbreak (Herrick et al., 2012). This salmonellosis model was a significant improvement over previously existing methods that did not consider disease duration and progression as determinants of cost and morbidity (Herrick et al., 2012). For many communicable and non-communicable diseases, the duration of symptoms is often positively associated with healthcare-seeking probability, healthcare-related expenditure, and productivity losses (Chevreul et al., 2015; Jordan et al., 2009; MacDougall et al., 2008; Sharma et al., 2016). This model framework is very flexible but so far has not been applied in the context of brucellosis cost estimation.

### 5.1.6 Study objective and scenarios

Estimates of the current socioeconomic impact of brucellosis in northern Tanzania and the potential benefit of increased case detection probability are needed to inform future disease management and control strategies. Increased case detection probability could be achieved through increased diagnostic sensitivity (e.g., replacing currently used commercial plate agglutination tests by the RBT) and increased healthcare-seeking probability (e.g., through the promotion of healthcare access). It can be hypothesised that increased case detection probability will reduce (i) the probability of progression to chronic brucellosis, (ii) the case-fatality ratio, and (iii) the productivity losses significantly. To test this hypothesis, novel approaches that overcome the limitations of previous methods (e.g., inability to represent disease incidence uncertainty and capture disease progression) need to be taken.

This study aimed to estimate the personal monetary costs (costs borne by the patient or their household) and disease burden (DALYs per case and DALYs per 100,000 people) attributable to human brucellosis in the Ngorongoro Conservation Area (NCA), northern Tanzania. For estimating these costs and disease burden, three scenarios were considered:

- the 'status quo' scenario, with current diagnostic sensitivity (of commercial plate agglutination tests) and healthcare-seeking probability;
- the 'RBT' scenario, a hypothetical scenario in which brucellosis diagnosis is made with RBT, rather than with a commercial plate agglutination test, with current healthcare-seeking probability; and,
- the 'RBT + increased healthcare seeking (HCS)' scenario, a hypothetical scenario in which brucellosis diagnosis is made with RBT and the probability of a brucellosis case seeking healthcare is increased by 10%.

The diagnosis of all forms of brucellosis is significantly more complex than serological testing alone. However, in this study, it is assumed that the result of a serological test is diagnostic and determines if a patient is prescribed a treatment (for a positive test result and all types of brucellosis presentations) or not (for a negative test result).

Note that, in this modelling study, all patients included are assumed to have brucellosis. This study does not capture the potential socioeconomic impact of the poor specificity (probability of a negative test result when the disease is absent) of commercial plate agglutination tests currently in use in northern Tanzania. People

without brucellosis who test positive with a commercial plate agglutination test are likely to incur monetary costs and disease burden that are not accounted for in this study: the socioeconomic impacts of the true disease cause remaining untreated and toxicity of unnecessary medicines, for instance (Alumasa et al., 2021).

## 5.2 Methods

### 5.2.1 Modelling framework, parametrisation, and analyses

A Markov Chain Monte Carlo (MCMC) model was set up and run for 50,000 iterations, under each of the scenarios considered ('status quo', 'RBT', and 'RBT + increased HCS'). The diagnostic test and healthcare-seeking probability in each scenario are shown in Table 5.1. The workflow that describes the model parameterisation and output analyses is shown in Fig. 5.2. This workflow comprised two main levels, consisting of 'global values', i.e., parameter values that did not differ between scenarios, and 'specific values', i.e., parameter values (diagnostic test sensitivity and healthcare-seeking probability) that differed between scenarios (section 5.2.4). Global and specific parameter values were used to estimate the average expected probability, duration, and cost of each Markov path, a sequence of Markov states representing the progression of brucellosis cases through different disease stages and healthcare-seeking behaviour.

**Table 5.1:** Diagnostic test and healthcare-seeking probability assumptions in each model scenario.

| Model scenario | Healthcare-seeking probability | Diagnostic test |
|---|---|---|
| 1 | From survey data | FBATs |
| 2 | From survey data | RBT |
| 3 | From survey data + 10% (arbitrary value) | RBT |

FBAT: febrile *Brucella* agglutination tests; RBT: Rose Bengal test

In each model iteration, the outputs were i) the monetary cost, i.e., healthcare-related expenditure (clinical exams, treatments, and additional costs) and productivity loss (loss of income due to loss of work days), and ii) the disease burden, i.e., DALYs. The calculation of these model outputs is described in detail in sections 5.2.5 and 5.2.6, respectively.

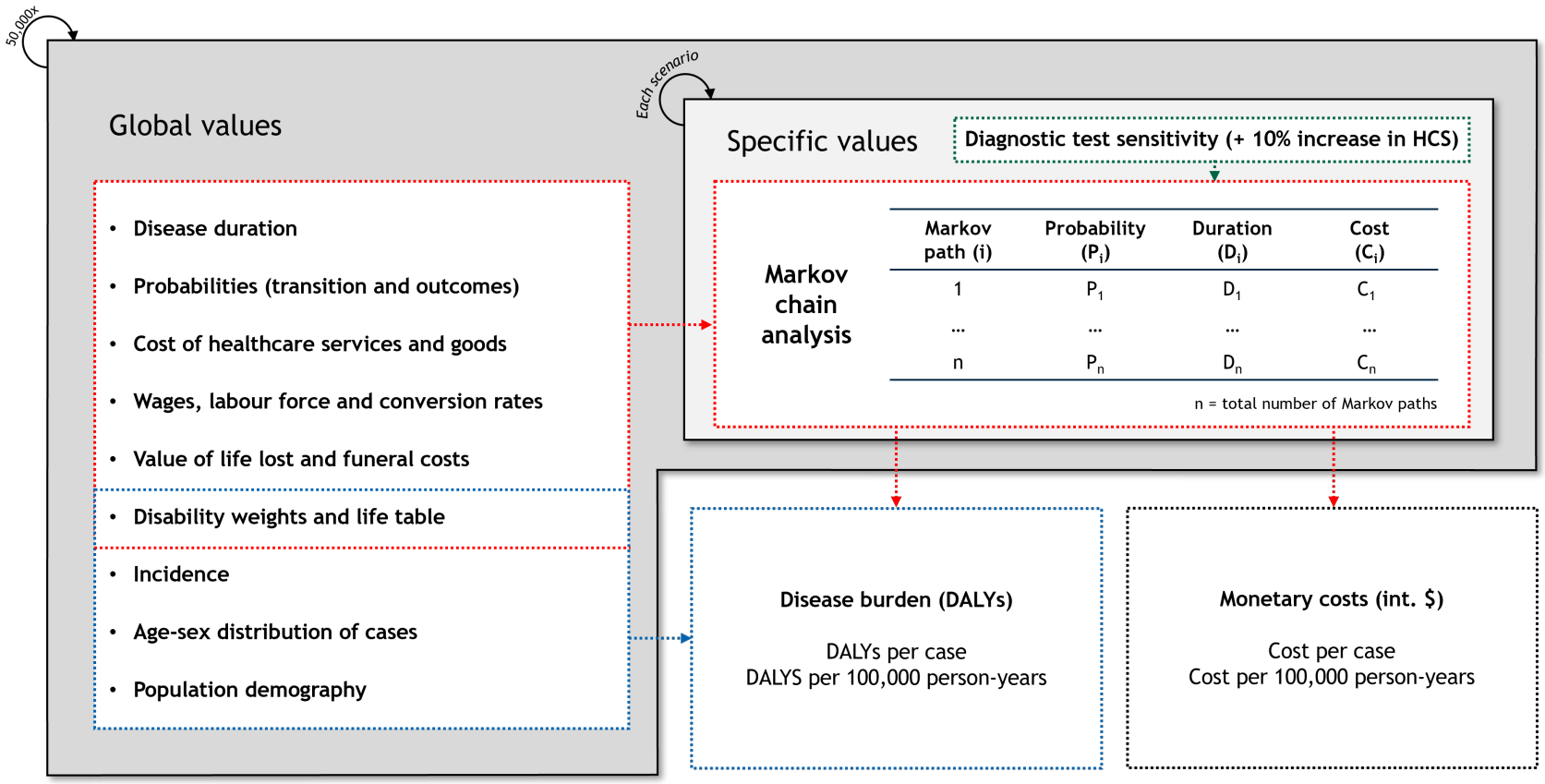



**Figure 5.2:** Workflow representing the parameters used in the Markov Chain Monte Carlo (MCMC) simulation model for estimation of the monetary costs and disease burden attributable to brucellosis in the NCA (Ngorongoro Conservation Area). Boxes delimited with a red dashed line indicate parameters and processes required for the Markov model. The box delimited with a blue dashed line indicates parameters and processes required for the DALYs burden estimation. The box delimited with a black dashed line indicates the monetary cost estimation. The box delimited with a green dashed line indicates the parameters that differ in alternative scenarios (different diagnostic test sensitivity and healthcare-seeking probability). HCS: Healthcare-seeking probability. DALYs: Disability-adjusted life years. int. $: International dollars.

### 5.2.2 Markov Chain Monte Carlo (MCMC) simulations

To identify current methods suitable for assessment of the impact of brucellosis on households, a literature search for Markov models estimating the cost of infectious diseases was performed in Ovid[2] and Web of Science[3], on 24th May 2021. Only one model was identified that explicitly accounted for disease progression and healthcare-seeking: a model used to estimate morbidity, mortality, illness duration, and costs attributable to salmonellosis (Herrick et al., 2012). This paper was selected as a reference and adapted for this study.

Given that not all healthcare facilities have the capacity to diagnose and manage brucellosis, the Markov model included two types of health management: target and non-target management. A target management state represents healthcare provision by a health facility that can diagnose and manage brucellosis in the NCA or neighbouring areas. In this definition of target management, brucellosis diagnosis requires laboratory testing either through serological methods or bacterial culture. The ability to 'manage' brucellosis requires the provision of treatments intended to treat brucellosis. A non-target management state represents no healthcare seeking (self-treatment) or healthcare provision by a health facility that cannot diagnose and manage brucellosis.

Besides the two types of health management, two disease types were considered: acute and chronic. Acute illness was defined as the initial clinical manifestation of brucellosis (up to three weeks), which includes symptoms and signs such as fever, chills, sweats, weakness, and headache. Chronic illness was defined as the longer-term clinical manifestation of brucellosis (over three weeks), which includes symptoms and signs such as joint, back, and muscular pain and others related to localised and complicated forms of the disease (e.g., epididymo-orchitis, endocarditis, meningitis or encephalitis).

The two types of health management and the two types of disease resulted in four transitive states (S) in the Markov model ($S_1$ to $S_4$). In addition to these states, two absorbing states were used to represent recovery ($S_5$) and death ($S_6$). The model diagram is shown in Fig. 5.3. The transitive states were named as follows: non-target management of acute illness ($S_1$), target management of acute illness ($S_2$),

2. https://ovidsp.ovid.com/
3. https://www.webofscience.com/

non-target management of chronic illness ($S_3$), and target management of chronic illness ($S_4$). At any time, brucellosis cases in transitive states could recover or die, with probabilities $p_{x5}$ and $p_{x6}$, respectively, where x is a transitive state number (between 1 and 4).

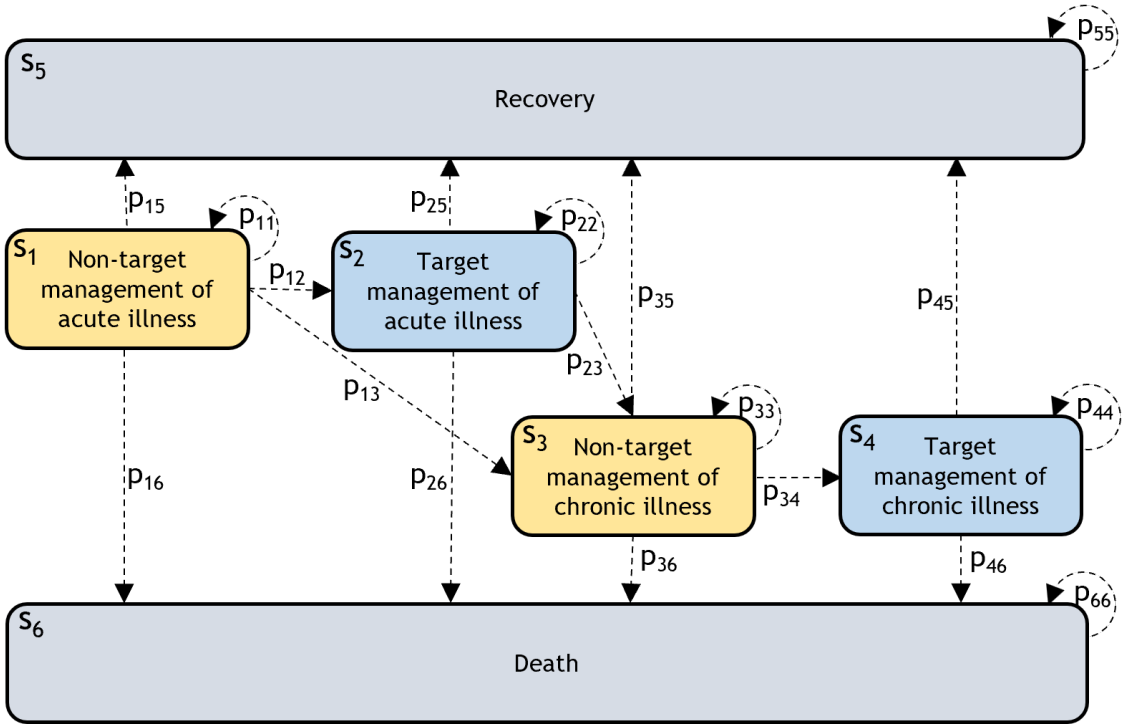



**Figure 5.3:** Diagram of the brucellosis Markov chain model representing two disease stages (acute and chronic), two disease management types (non-target management and target management), and two absorbing states (recovery and death). $p_{xy}$ represents the transition probability from $S_x$ to $S_y$ during each Markov cycle. $p_{xx}$ represents the probability of an individual remaining in the state $S_x$ from one Markov cycle to the next.

All brucellosis cases began in $S_1$, non-target management of acute illness, and progressed through the Markov chain until they reached $S_5$ or $S_6$. The time spent in $S_1$ represented the acute disease duration before cases (i) sought healthcare at a target healthcare facility, which occurred with probability $p_{12}$, (ii) developed chronic brucellosis, which occurred with probability $p_{13}$, (iii) recovered, which occurred with probability $p_{15}$, or (iv) died, which occurred with probability $p_{16}$.

Once cases reached $S_2$, target management of acute illness, the probability of recovery ($p_{25}$) was a function of test sensitivity and treatment success - described in detail in section 5.2.4. Irrespective of the model scenario, once cases reached $S_2$, it was assumed that all cases were tested and remained in $S_2$ for an average period corresponding to the brucellosis treatment duration. If cases in $S_2$ did not recover,

because of (i) misdiagnosis due to a false negative test result or (ii) treatment failure, they could die, which occurred with probability $p_{26}$. Alternatively, cases in $S_2$ that did not recover or die transitioned to $S_3$, which occurred with probability $p_{23}$.

The time spent in $S_3$, non-target management of chronic illness, represented the chronic disease duration before cases (i) sought healthcare for chronic disease at a target healthcare facility, which occurred with probability $p_{34}$, (ii) recovered, which occurred with probability $p_{35}$, or (iii) died, which occurred with probability $p_{36}$.

In $S_4$, target management of chronic illness, the probability of recovery ($p_{45}$) was assumed to be the same as $p_{25}$, for acute disease. In each Markov cycle, if cases in $S_4$ did not recover, they could die, which occurred with probability $p_{46}$, or stay in $S_4$, which occurred with probability $p_{44}$. Note that if cases entered $S_4$, and were misdiagnosed or failed the treatment, they remained in that state until recovery, instead of returning to the non-target management of chronic illness, as experienced by brucellosis cases that entered the target management for acute illness ($S_2$), and were misdiagnosed or failed the treatment.

Brucellosis cases could progress through the Markov Chain following twelve mutually exclusive paths ($i \in 1{:}12$), six leading to recovery and six leading to death. Each path and its corresponding probability are shown in Table 5.2.

**Table 5.2:** Markov chain model paths, probabilities, and outcomes.

| Path (i) | States ($S_x$) | Path probability ($P_i$) | Outcome |
|---|---|---|---|
| 1 | $S_1$-$S_5$ | $\frac{p_{15}}{1-p_{11}}$ | Recovery |
| 2 | $S_1$-$S_2$-$S_5$ | $\frac{p_{12}p_{25}}{(1-p_{11})(1-p_{22})}$ | Recovery |
| 3 | $S_1$-$S_2$-$S_3$-$S_5$ | $\frac{p_{12}p_{23}p_{35}}{(1-p_{11})(1-p_{22})(1-p_{33})}$ | Recovery |
| 4 | $S_1$-$S_2$-$S_3$-$S_4$-$S_5$ | $\frac{p_{12}p_{23}p_{34}p_{45}}{(1-p_{11})(1-p_{22})(1-p_{33})(1-p_{44})}$ | Recovery |
| 5 | $S_1$-$S_3$-$S_5$ | $\frac{p_{13}p_{35}}{(1-p_{11})(1-p_{33})}$ | Recovery |
| 6 | $S_1$-$S_3$-$S_4$-$S_5$ | $\frac{p_{13}p_{34}p_{45}}{(1-p_{11})(1-p_{33})(1-p_{44})}$ | Recovery |
| 7 | $S_1$-$S_6$ | $\frac{p_{16}}{1-p_{11}}$ | Death |
| 8 | $S_1$-$S_2$-$S_6$ | $\frac{p_{12}p_{26}}{(1-p_{11})(1-p_{22})}$ | Death |
| 9 | $S_1$-$S_2$-$S_3$-$S_6$ | $\frac{p_{12}p_{23}p_{36}}{(1-p_{11})(1-p_{22})(1-p_{33})}$ | Death |
| 10 | $S_1$-$S_2$-$S_3$-$S_4$-$S_6$ | $\frac{p_{12}p_{23}p_{34}p_{46}}{(1-p_{11})(1-p_{22})(1-p_{33})(1-p_{44})}$ | Death |
| 11 | $S_1$-$S_3$-$S_6$ | $\frac{p_{13}p_{36}}{(1-p_{11})(1-p_{33})}$ | Death |
| 12 | $S_1$-$S_3$-$S_4$-$S_6$ | $\frac{p_{13}p_{34}p_{46}}{(1-p_{11})(1-p_{33})(1-p_{44})}$ | Death |

$S_1$: non-target management of acute illness; $S_2$: target management of acute illness; $S_3$: non-target management of chronic illness; $S_4$: target management of chronic illness; $S_5$: recovery; and $S_6$: death.

### 5.2.3 Data sources, literature search strategies, and data selection

To parametrise the Markov model (e.g., probabilities, durations, costs), this study obtained data from many sources, including locally delivered surveys, locally and non-locally relevant literature, and expert elicitation. For more information on specific parameters, see section 5.2.4.

#### 5.2.3.1 Selection of data sources

The selection of data sources to inform each model parameter was based on the decision tree shown in Fig. 5.4. This decision tree prioritised locally delivered surveys and locally relevant literature over non-locally relevant literature, conditional on a quality assessment: an evaluation of the degree to which the evidence available was of sufficient quality to inform each (group of) model parameter(s). This assessment considered two dimensions: i) 'external validity', i.e., the appropriateness of the studies' research question and generalisability or applicability of the reported findings; and, ii) 'internal validity', i.e., whether the studies answered the research question 'correctly' (Higgins, Altman, and Sterne, 2017). To be considered of 'sufficient quality' (level 1 classification in Fig. 5.4), data sources had to be classified as both externally and internally valid.

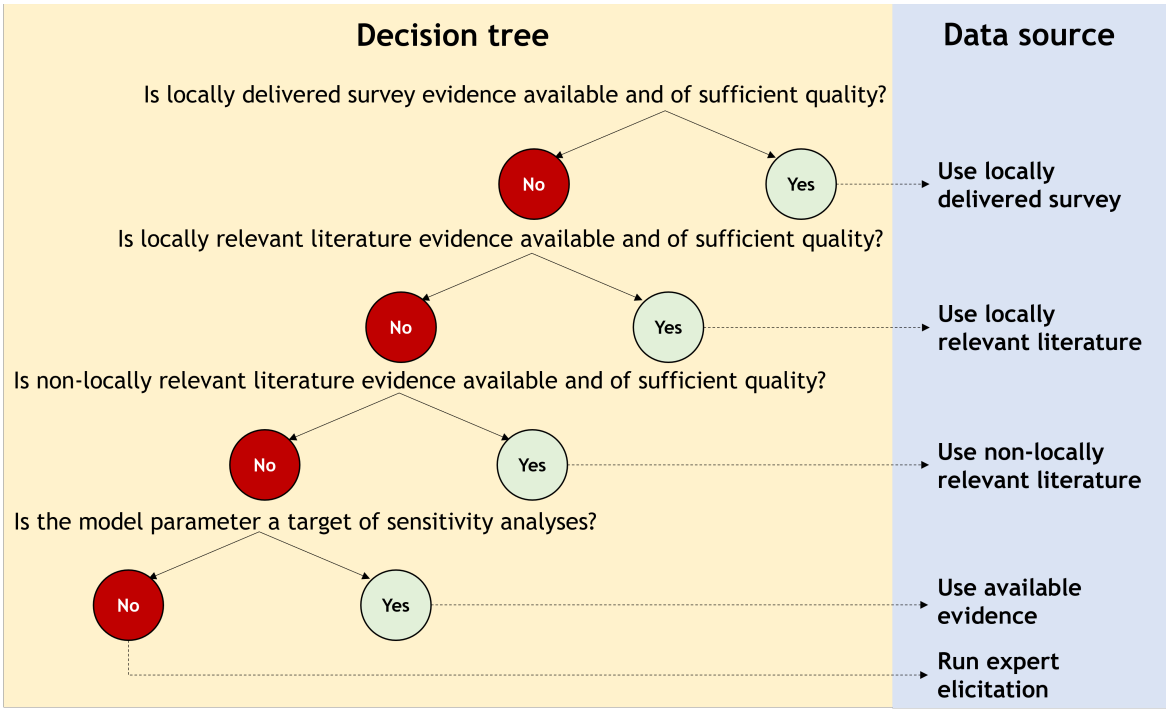



**Figure 5.4:** Decision tree for selecting data sources to inform Markov model parameters.

When none of these sources (locally delivered surveys, locally relevant literature, and non-locally relevant literature) provided evidence of 'sufficient quality' to inform certain model parameters, expert elicitation or otherwise available data (subject to sensitivity analyses) were used.

#### 5.2.3.2 Locally delivered surveys

Data from the following locally delivered surveys were used:

- BBSRC (Biotechnology and Biological Sciences Research Council) project Reference BB/S013857/1: Operationalizing One Health Interventions in Tanzania: Healthcare utilisation survey (HCUS)
  A healthcare utilisation survey was delivered in the Ngorongoro Conservation Area. Households were selected through cluster random sampling approaches.
  The reported healthcare-seeking behaviour by household members in case of a fever episode that lasted for more than three days was used in the Markov model as a proxy for the probability of brucellosis cases transitioning from non-target management to target management of acute illness ($p_{12}$).
- NIHR (National Institute for Health Research) Global Health Research Group; project reference 17/63/35: estimating the prevalence, quality of life, economic and societal impact of arthritis in Tanzania: a mixed methods study at the University of Glasgow
  A survey was delivered in Hai district (Kilimanjaro region, northern Tanzania), involving community members, to estimate the prevalence, health and economic burden of arthritis. The Gait, Arms, Legs, and Spine (GALS) screening exam assessed the presence and severity of arthritis.
  The reported probability of GALS-positive participants seeking care at a hospital was considered to be the probability of transition from non-target management to target management of chronic illness ($p_{34}$) in the Markov model. This assumes that the healthcare-seeking behaviour of GALS-positive participants in Hai district is representative of the behaviour of chronic brucellosis cases living in the NCA.
- Medical Research Council (MRC) project reference MR/S004815/1: Supporting the National Action Plan on Antimicrobial Resistance (SNAP-AMR) in Tanzania project

A survey was delivered in three districts of Tanzania (Ngorongoro, Misungwi, and Mwanga, two villages per district), to gather information on expenditure incurred by people at the time of exit from pharmacies, dispensaries, and health centres.
The price of drugs (anti-inflammatories, antibiotics, and antimalarials) purchased by survey participants was used to estimate health-related expenditure attributable to brucellosis (see price distributions in Appendix D.1).

#### 5.2.3.3 Locally and non-locally relevant literature

Locally and non-locally relevant literature on human brucellosis, its clinical manifestations, and economic impacts were obtained from targeted literature searches. The following search engines were used: Ovid[4], Web of Science[5], EBSCO[6], and Cochrane library[7].

The search strategy for locally relevant literature combined three queries (Q1, Q2 and Q3) using the Boolean operator 'AND':

- Q1:
  *brucella OR brucellosis OR melitococci OR 'malta fever' OR 'cyprus fever' OR 'mediterranean fever' OR 'intermittent typhoid' OR 'rock fever of Gibraltar' OR 'gibraltar fever' OR 'undulant fever' OR 'mediterranean phthisis'*
- Q2 (for each parameter or group of parameters, with wildcard operators):
  - Disease duration:
    *days OR weeks OR months*
  - Probability of death and age-sex distribution of fatal cases:
    *died OR death OR lethal OR mortal OR fatal*
  - Brucellosis test sensitivity:
    *accuracy OR diagnostic performance OR sensitivity*
  - Probability of treatment failure:
    *treatment OR therapy OR prescription*
  - Probability of progression to chronic brucellosis:
    *acute OR chronic*
  - Attributable risk of spontaneous abortion or stillbirth in pregnant women with brucellosis:
    *pregnancy OR gestation OR parity OR gravidity*

4. https://ovidsp.ovid.com/
5. https://www.webofscience.com/
6. https://search.ebscohost.com/
7. https://www.cochranelibrary.com/search

  - Healthcare services and goods - access and costs:
    *cost OR loss OR impact OR price OR expenditure*
  - Disability weights:
    *DALYs OR YLD OR YLL*
  - Age-sex distribution of cases:
    *epidemiology OR prevalence OR incidence*
- Q3:
  *Tanzania*

The references in the literature obtained through these searches were also scanned for additional relevant literature. For non-locally relevant literature searches, query Q3 was dropped. Descriptive demographic statistics for the NCA were extracted from census data (Government of The United Republic of Tanzania, 2013a, 2015b) and the multiple land use model of the NCA (Government of The United Republic of Tanzania, 2019).

#### 5.2.3.4 Expert elicitation

Expert elicitation is an established, structured approach to elicit scientific and technical judgements from experts (Morgan, 2014). In Tanzania, expert elicitation has been applied on many occasions, including epidemiological and economic studies of malaria, trypanosomiasis, and leptospirosis (Abro et al., 2021; Beerbohm, 2007; Maze et al., 2018).

An expert elicitation exercise using the IDEA (Investigate, Discuss, Estimate, and Aggregate) protocol was conducted (Hemming et al., 2017). Fourteen (out of 16 initially invited) health professionals from Kilimanjaro and Arusha regions in northern Tanzania participated in a workshop that took place in Karatu, in 2022. The group of participants included district medical officers, clinical officers, and medical doctors. The protocol was cleared by the Ethics Committees of the College of Medical, Veterinary and Life Sciences (University of Glasgow), the Kilimanjaro Christian Medical University College, and the National Institute for Medical Research.

Following an introduction of the expert elicitation methodology, participants were invited to complete an online questionnaire (round 1) that had been previously shared in advance of the workshop (Appendix D.2). The questionnaire covered several topics on brucellosis diagnosis, management, and impacts, such as disease duration, healthcare-seeking behaviour, probability of death, and loss of work days.

Both English and Swahili versions of the questionnaire were made available, and participants were given the opportunity to select the language version that they preferred. Qualtrics (version September 2022; Provo, UT) and R (version 4.1.1; 2021-08-10; R Core Team, 2021) were used to gather participants' answers and to generate a summary report, respectively. The report containing summary statistics and plots of answers anonymously given by each participant was used as a platform for reflection and debate during the workshop. This was an opportunity for participants to exchange knowledge and share experiences about brucellosis diagnosis and management that could justify answers given. After the discussion, participants completed a second round of the same questionnaire. A report with answers and summary statistics from this questionnaire round was produced and sent to participants for their information (See Appendix D.3 for an anonymous version of the report).

### 5.2.4 Model parameter values and distributions

#### 5.2.4.1 Parameter distributions

Parameter values in the MCMC model were randomly picked from distributions of parameter estimates in each iteration. The distributions used and the corresponding justification for each model parameter are shown in Appendix D.4. Unless otherwise stated, the following criteria were applied for constructing the distributions:

- *Uniform* distributions
  Model parameters for which there was little supporting evidence or high uncertainty in the literature or survey data were assigned *Uniform* distributions. These distributions were constructed with minimum and maximum values obtained from the survey, literature or expert elicitation data.
- *PERT* distributions
  Model parameters for which there was survey data or evidence in the literature that indicated a most common value (with some level of uncertainty) were assigned PERT distributions. These distributions were constructed with the following parameters: minimum, mode (in most cases, assuming a mode equal to the mean), and maximum values (Pouillot, Delignette-Muller, and Denis, 2021).
- *Beta* distributions

For some of the probability estimates, *Beta* distributions were constructed with the following shape parameters (shape 1 and shape 2, respectively) for $1 \leq k \leq n$: $k + 1$, and $n - k + 1$; where $k$ is the expected number of successes (e.g., number of brucellosis cases with a positive test result or number of brucellosis cases that seek healthcare at a target health facility) and $n$ is the number of trials (e.g., number of brucellosis cases) (Gelman et al., 2013).

### 5.2.4.2 Transition probabilities

The transition probabilities used to parametrise the Markov chain model were classified into two different types: i) type 1, obtained directly from surveys and literature data (Appendix D.4); and, ii) type 2, calculated from type 1 probabilities, under certain assumptions.

Type 1 probabilities were obtained from data sources that provided the probability of brucellosis cases moving from one Markov state to the next during a certain time period ($\pi$ weeks e.g., $\alpha_1$ for the probability of target healthcare seeking for acute brucellosis). This probability ($p_{xy}(\pi)$) was time-adjusted to a weekly probability ($p_{xy}$) using Eq. 5.1 (adapted from Eq. 10.2 and 10.3 in Drummond et al. (2015)).

$$p_{xy} = 1 - exp\left(\frac{log\left(1 - p_{xy}(\pi)\right)}{\pi}\right) \tag{5.1}$$

Time-adjusted type 1 probabilities were $p_{12}$, $p_{16}$, $p_{26}$, $p_{34}$, $p_{36}$, and $p_{46}$.

Type 2 probabilities included the probability of a brucellosis case remaining in the same transitive state from one Markov cycle to the next ($p_{xx}$: $p_{11}$, $p_{22}$, $p_{33}$, and $p_{44}$) as well as all other probabilities of cases moving between states ($p_{xy}$: $p_{13}$, $p_{15}$, $p_{23}$, $p_{25}$, $p_{35}$, and $p_{45}$).

The probabilities of cases under target management recovering ($p_{25}$ and $p_{45}$) were given by Eqs. 5.2:

$$\begin{aligned} p_{25} &= 1 - exp\left(\frac{log\left(1 - \gamma(1 - \varepsilon)\right)}{\alpha_2}\right) \\ p_{45} &= 1 - exp\left(\frac{log\left(1 - \gamma(1 - \varepsilon)\right)}{\alpha_4}\right) \end{aligned} \tag{5.2}$$

where $\gamma$ is the diagnostic test sensitivity (the joint sensitivity of commercial plate agglutination tests or the sensitivity of RBT, depending on the scenario under evaluation), $\varepsilon$ is the probability of treatment failure, i.e., persistence or relapse of symptoms or signs of disease after the end of treatment, $\alpha_2$ is the target health facility treatment duration for acute illness, and $\alpha_4$ is the target health facility treatment duration for chronic illness.

To calculate $p_{15}$, Eq. 5.3 was used, ensuring that the probabilities of paths 1 ($S_1$-$S_5$), 2 ($S_1$-$S_2$-$S_5$), 7 ($S_1$-$S_6$), and 8 ($S_1$-$S_2$-$S_6$) (Table 5.2) add up to $1-\lambda$, where $\lambda$ is the probability of progression to chronic brucellosis (Appendix D.4).

$$\frac{p_{15}}{1-p_{11}} + \frac{p_{12}p_{25}}{(1-p_{11})(1-p_{22})} + \frac{p_{16}}{1-p_{11}} + \frac{p_{12}p_{26}}{(1-p_{11})(1-p_{22})} = 1-\lambda \tag{5.3}$$

$p_{15}$ was calculated by solving Eq. 5.3, assuming that $p_{11} = 1-\frac{1}{\alpha_1}$ and $p_{22} = 1-\frac{1}{\alpha_2}$ (adapted from equation 3 in Herrick et al., 2012):

$$p_{15} = \frac{1-\lambda}{\alpha_1} - p_{16} - p_{12}\alpha_2(p_{25}+p_{26}) \tag{5.4}$$

The remaining probabilities determining transitions from states $S_1$, $S_2$, and $S_3$ were given by Eqs. 5.5.

$$\begin{aligned} p_{13} &= \frac{1}{\alpha_1} - p_{12} - p_{15} - p_{16} \\ p_{23} &= \frac{1}{\alpha_2} - p_{25} - p_{26} \\ p_{35} &= \frac{1}{\alpha_3} - p_{34} - p_{36} \end{aligned} \tag{5.5}$$

The probability of cases remaining in a transitive state from one cycle to the next ($p_{xx}$) was given by Eq. 5.6.

$$p_{xx} = 1 - \sum_{y=1}^{y=6} p_{xy}, y \neq x \tag{5.6}$$

The following probability limits were applied to ensure that $p_{23}$, $p_{35}$, $p_{13}$, and $p_{15}$ are equal or greater than zero, and $p_{45}$ yields a target health facility treatment duration for chronic illness not below $\alpha_4$:

$$\begin{gathered} p_{25} \leq \frac{1}{\alpha_2} - p_{26} \\ p_{34} \leq \frac{1}{\alpha_3} - p_{36} \\ p_{45} \leq \frac{1}{\alpha_4} - p_{46} \\ \alpha_1 p_{12} \left(1 - \alpha_2 \left(p_{25} + p_{26}\right)\right) \leq \lambda \leq 1 - \alpha_1 \left(p_{16} + p_{12} \alpha_2 \left(p_{25} + p_{26}\right)\right) \end{gathered} \tag{5.7}$$

Model scenarios directly or indirectly affected some of the transition probabilities (compared to the *status quo*, the RBT scenario affected $p_{25}$, $p_{45}$, $p_{23}$, $p_{22}$, and $p_{44}$; in addition to these, the RBT + inc. HCS affected $p_{12}$, $p_{34}$, $p_{13}$, $p_{11}$, and $p_{33}$). All of these transition probabilities ($p_{25}$, $p_{45}$, $p_{23}$, $p_{22}$, $p_{44}$, $p_{12}$, $p_{34}$, $p_{13}$, $p_{11}$, and $p_{33}$) were recalculated for each model scenario.

### 5.2.4.3 Population demography

The NCA includes seven wards (Kakesio, Enduleni, Ngorongoro, Olbalbal, Nainokanoka, Alailelal, and Naiyobi) of the Ngorongoro district, Arusha region (Jones et al., 2020). It has been estimated that the human population in the NCA in 2016/2017 was approximately 100,000 people (Government of The United Republic of Tanzania, 2019; Slootweg, 2018), which corresponds to around half of the population reported to live in the Ngorongoro district (Government of The United Republic of Tanzania, 2013a). It was then assumed for this study that the age-sex distribution of people in the NCA was the same as in the Ngorongoro district (2012 Population and Housing Census). The age-sex distribution of people in the healthcare utilisation survey (NCA-specific; project reference BB/S013857/1; n=2,055) and in the Ngorongoro district (2012 Population and Housing Census; n=174,278) are shown in Appendix D.5.

### 5.2.5 Personal monetary cost and disease duration

The personal monetary cost of brucellosis was the sum of health-related expenditure and productivity loss attributable to the disease.

The health-related expenditure in target and non-target management states included costs incurred with clinical exams, treatments, and other goods or services. These expenditures were estimated by multiplying the probability of a brucellosis case incurring a cost (from expert elicitation) and the price of the good or service (Appendix D.1). The total health-related expenditure in a pathway was denoted with $\eta_{\mathrm{t}}$ for target healthcare seeking and $\eta_{\mathrm{n}}$ for non-target healthcare seeking.

It was assumed that all health-related expenditure attributable to brucellosis was out-of-pocket. This is consistent with previously observed low health insurance coverage in the study area: - only 147 (7.2%) out of 2,055 household members in the healthcare utilisation survey (project reference BB/S013857/1) were covered by some form of health insurance; - only 4 (9.1%) out of 44 Ngorongoro-based participants in the SNAP-AMR survey (project reference MR/S004815/1) purchased medicines through health insurance.

To estimate the probability of catastrophic expenditure due to brucellosis, households' monthly non-food expenditure was obtained from waves three (2012-2013) and four (2014-2015) of the Tanzania National Panel survey (Living Standards Measurement Study, LSMS; sections K and L). Only data from LSMS households classified as pastoral in Chapter 3 were used to estimate the probability of catastrophic expenditure. Given the availability of expenditure information for different recall periods (one week, one month, and one year) depending on the type of non-food item, non-food expenditure and health-related expenditure were calculated as the average per month. Sampling with replacement of the distribution of LSMS households' monthly non-food expenditure was performed. The probability of catastrophic expenditure was calculated as the proportion of iterations (n=50,000) in which the estimated monthly health-related out-of-pocket expenditure per brucellosis case under the 'status quo' scenario was greater than 40% of the monthly non-food expenditure sampled from the LSMS dataset (Brinda, Andrés, and Enemark, 2014).

To estimate productivity losses, a method similar to the approach described by Frick et al. (2015) was adopted, replacing the gross domestic product (GDP) per capita per week with the weekly wage in the agricultural sector in rural areas of Mainland Tanzania ($\zeta$), because this wage is likely to reflect productivity better in the NCA setting than the national GDP per capita per week. A productivity loss multiplier ($\phi$) was used to ensure that the median productivity loss per brucellosis case was equivalent to 28 work days lost (based on expert elicitation outcome) in wages. Disability weights ($\omega$) were used as a surrogate for disease severity and, consequently, the relative extent of productivity loss by disease type. The productivity loss per case per week by disease type (k) was given by $\nu_{\mathrm{k}}$ in Eq. 5.8, where k can be 'ac' for acute ($S_1$ and $S_2$) or 'ch' for chronic ($S_3$ and $S_4$):

$$\nu_{\mathrm{k}} = \zeta \phi \omega_{\mathrm{k}} \tag{5.8}$$

where $\omega_{\mathrm{a}}$ comprised 50% severe and 50% moderate disability weights, and $\omega_{\mathrm{c}}$ comprised 10% of adult (over 15 years old) males with orchitis disability weight and remaining males and females with chronic disability weight (Appendix D.4).

The path duration was calculated as the sum of the expected residence time in each transitive state ($\tau_{\mathrm{x}}$), using equation 3 in Herrick et al., 2012, as follows:

$$\tau_{\mathrm{x}} = \frac{1}{1 - \mathrm{p}_{\mathrm{xx}}} \tag{5.9}$$

The personal monetary costs along each path are shown in Table 5.3. Given that the mean disease duration was expected to be short (shorter than one year), the cost along each path ($C_{\mathrm{i}}$) was not discounted.

**Table 5.3:** Disease duration and personal monetary costs along each path in the Markov model.

| Path (i) | States ($S_x$) | Duration ($D_i$) | Cost along path ($C_i$) |
|---|---|---|---|
| 1 | $S_1$-$S_5$ | $\tau_1$ | $\tau_1 v_{ac} + \eta_n$ |
| 2 | $S_1$-$S_2$-$S_5$ | $\tau_1 + \tau_2$ | $\tau_1 v_{ac} + \tau_2 v_{ac} + \eta_t$ |
| 3 | $S_1$-$S_2$-$S_3$-$S_5$ | $\tau_1 + \tau_2 + \tau_3$ | $\tau_1 v_{ac} + \tau_2 v_{ac} + \tau_3 v_{ch} + \eta_t$ |
| 4 | $S_1$-$S_2$-$S_3$-$S_4$-$S_5$ | $\tau_1 + \tau_2 + \tau_3 + \tau_4$ | $\tau_1 v_{ac} + \tau_2 v_{ac} + \tau_3 v_{ch} + \tau_4 v_{ch} + \eta_t$ |
| 5 | $S_1$-$S_3$-$S_5$ | $\tau_1 + \tau_3$ | $\tau_1 v_{ac} + \tau_3 v_{ch} + \eta_n$ |
| 6 | $S_1$-$S_3$-$S_4$-$S_5$ | $\tau_1 + \tau_3 + \tau_4$ | $\tau_1 v_{ac} + \tau_3 v_{ch} + \tau_4 v_{ch} + \eta_t$ |
| 7 | $S_1$-$S_6$ | $\tau_1$ | $\tau_1 v_{ac} + \eta_n$ |
| 8 | $S_1$-$S_2$-$S_6$ | $\tau_1 + \tau_2$ | $\tau_1 v_{ac} + \tau_2 v_{ac} + \eta_t$ |
| 9 | $S_1$-$S_2$-$S_3$-$S_6$ | $\tau_1 + \tau_2 + \tau_3$ | $\tau_1 v_{ac} + \tau_2 v_{ac} + \tau_3 v_{ch} + \eta_t$ |
| 10 | $S_1$-$S_2$-$S_3$-$S_4$-$S_6$ | $\tau_1 + \tau_2 + \tau_3 + \tau_4$ | $\tau_1 v_{ac} + \tau_2 v_{ac} + \tau_3 v_{ch} + \tau_4 v_{ch} + \eta_t$ |
| 11 | $S_1$-$S_3$-$S_6$ | $\tau_1 + \tau_3$ | $\tau_1 v_{ac} + \tau_3 v_{ch} + \eta_n$ |
| 12 | $S_1$-$S_3$-$S_4$-$S_6$ | $\tau_1 + \tau_3 + \tau_4$ | $\tau_1 v_{ac} + \tau_3 v_{ch} + \tau_4 v_{ch} + \eta_t$ |

$S_1$: non-target management of acute illness; $S_2$: target management of acute illness; $S_3$: non-target management of chronic illness; $S_4$: target management of chronic illness; $S_5$: recovery; and $S_6$: death; $\tau_x$ is the expected residence time in the transitive state $S_x$; $\eta_t$ is the total health-related expenditure in a target healthcare-seeking pathway; $\eta_n$ is the total health-related expenditure in a non-target healthcare-seeking pathway; $v_k$ is the productivity loss per case per week by disease type (k), where k can be 'ac' for acute ($S_1$ and $S_2$) or 'ch' for chronic ($S_3$ and $S_4$).

The expected personal monetary cost per case (CPC, int. $) was estimated by adding up the product of path (i) probabilities ($P_i$, in Table 5.2) and costs ($C_i$, in Table 5.3), as follows:

$$\mathrm{CPC} = \sum_{i=1}^{n} P_i C_i \tag{5.10}$$

The expected personal monetary cost per 100,000 person-years was calculated as the product of CPC and incidence. Note that model scenarios do not affect the incidence, just the pathway probabilities. The median, mean, inter-quartile range (50% uncertainty interval), and 2.5 and 97.5 percentiles (95% uncertainty interval) of the personal monetary cost are reported.

The expected disease duration per case (DPC, weeks) was estimated by adding up the product of path (i) probabilities ($P_i$, in Table 5.2) and duration ($D_i$, in Table 5.3), as follows:

$$\mathrm{DPC} = \sum_{i=1}^{n} P_i D_i \tag{5.11}$$

The durations of acute and chronic disease ($\mathrm{DPC}_k$) were calculated separately.

### 5.2.6 Disease burden

The burden of brucellosis was estimated in DALYs, a measure of time lost due to premature death and time lived in less than optimal health states (Murray, 1994). DALYs were calculated as the expected sum of the years of life lost (YLLs) and years lived with disability (YLDs) in a cohort of 100,000 people in the NCA. Given the differences in disability weights between disease states, the DALYs caused by acute and chronic brucellosis were calculated separately, as follows:

$$\mathrm{DALYs} = \mathrm{YLL}_{\mathrm{acute}} + \mathrm{YLL}_{\mathrm{chronic}} + \mathrm{YLD}_{\mathrm{acute}} + \mathrm{YLD}_{\mathrm{chronic}} \tag{5.12}$$

As outlined by Fox-Rushby and Hanson (2001), the equations for calculating YLLs (Eq. 5.13) and YLDs (Eq. 5.14) incorporate weights for life expectancy, age, future time, and disability.

$$\begin{aligned}\mathrm{YLLs}[r,K,\beta] = &\frac{KCe^{ra}}{(r+\beta)^2}\{e^{-(r+\beta)(S+a)}[-(r+\beta)(S+a)-1] \\ &- e^{-(r+\beta)a}[-(r+\beta)a-1]\} + \frac{1-K}{r}\left(1-e^{-rS}\right)\end{aligned} \tag{5.13}$$

where $r$ is the discount rate, $K$ is the age weighting modulation factor, $\beta$ is a parameter from the age weighting function (standard age weights use 0.04), $C$ is a constant (0.1658), $a$ is the age of death, and $S$ is the standard expectation of life at age $a$ (obtained from the WHO GHE life table, in Appendix D.4).

The equation for calculating YLDs (Eq. 5.14) is similar to Eq. 5.13 but includes a disease stage-specific disability weight ($\omega_{\mathrm{k}}$).

$$\begin{aligned}\mathrm{YLDs}[r,K,\beta] = &\omega_{\mathrm{k}}\frac{KCe^{ra}}{(r+\beta)^2}\{e^{-(r+\beta)(L+a)}[-(r+\beta)(L+a)-1] \\ &- e^{-(r+\beta)a}[-(r+\beta)a-1]\} + \frac{1-K}{r}\left(1-e^{-rL}\right)\end{aligned} \tag{5.14}$$

where $a$ is the age of onset of disability (according to age distribution of cases in Appendix D.4), and $L$ is the duration of disability by disease type ($\mathrm{DPC_k}$).

The discount rate ($r$) and the age weighting modulation factor ($K$) were assumed to be zero, simplifying equations Eqs. 5.13 and 5.14, as follows:

$$\begin{aligned} \mathrm{YLLs} &= \mathrm{S} \\ \mathrm{YLDs} &= \omega_{\mathrm{k}} \mathrm{L} \end{aligned} \tag{5.15}$$

The reference (baseline) age distribution of deaths for DALYs estimation was obtained from a retrospective, longitudinal survey of hospitalised cases in Spain (Rodríguez-Alonso et al., 2021) and is shown in Appendix D.4. DALYs were estimated per brucellosis case and per 100,000 people. The median percentage contribution of YLLs and YLDs to the DALYs per case estimate is reported.

### 5.2.7 Sensitivity analyses

A series of sensitivity analyses were performed to assess the influence of the methodological choices and parameter uncertainty and variability on the results obtained. The following variations in methods used to estimate monetary costs and disease burden were analysed using the 'status quo' scenario as the 'base case': (i) inclusion of the cost of death in the estimation of the monetary cost per case, (ii) replacement of the age distribution of deaths in the estimation of disease burden, and (iii) inclusion of brucellosis-induced stillbirth in the estimation of disease burden.

#### 5.2.7.1 Cost of death due to brucellosis

A proxy of the monetary cost per fatal case was calculated as the sum of statistical value of life lost (SVLL) and funeral costs ($\rho$). SVLL was calculated as the product of the value of statistical life-year (VSLY) and standard years of life lost, which, in turn, was obtained through random sampling, with replacement, in each iteration, of the WHO GHE life table, using a vector of probability weights equal to the age distribution of deaths (Appendix D.4). SVLL was not discounted because the VSLY is provided in its discounted format.

#### 5.2.7.2 Disease burden under alternative age distribution of deaths due to brucellosis

Disease burden was estimated with an alternative age distribution of deaths, equal to the age distribution of cases (Appendix D.4), as considered in the FERG study that estimated the global and regional burden of brucellosis in 2010 (Kirk et al., 2015).

#### 5.2.7.3 Disease burden including brucellosis-induced stillbirth

The burden (DALYS per case and DALYs per 100,000 people) of brucellosis-induced stillbirths in the NCA was estimated using a method derived from Phillips and Millum (2015). This method requires data on the incidence and timing of stillbirth by causative agent. Given that these data are not available for brucellosis, the disvalue of life lost due to foetal death in the 'third trimester' of pregnancy (stillbirth, as commonly defined) was weighted at 50% the disvalue of life lost due to death at the time of birth, instead of gradually between 28 to 40 weeks of foetal age, as proposed by Phillips and Millum (2015). This method adaptation assumes that all stillbirths occur halfway through the third trimester. The burden of spontaneous abortion, foetal death occurring before the beginning of the third trimester, coincidental with the onset of sentience, is not considered. The burden of preterm delivery and congenital brucellosis to the infant and all obstetric complications (spontaneous abortion, stillbirths, and preterm delivery, among others) to the pregnant women, both in terms of physical and mental health impacts, are not considered in this study due to the lack of evidence on the magnitude and risk of induced morbidity and mortality.

Given a reported number of annual live births in the NCA ($B$), from the literature (Government of The United Republic of Tanzania, 2015b), it is possible to estimate the expected number of live births per female in the NCA in the hypothetical absence of brucellosis ($\theta$), as follows:

$$\theta = \frac{B}{F\left((1-\delta)+\delta\left(1-\mu-\upsilon\right)\right)} \tag{5.16}$$

where $F$ is the female population in the NCA, $\delta$ is the proportion of $F$ that are newly infected each year (incidence times proportion of cases that are female divided by $F$), $\mu$ is the attributable risk of spontaneous abortion in pregnant women with brucellosis, and $\upsilon$ is the attributable risk of stillbirth in pregnant women with brucellosis. The values used for the proportion of cases that are female, $\mu$ and $\upsilon$ are shown in Appendix D.4.

The number of brucellosis-induced stillbirths ($S$) in the NCA per year can then be estimated as follows:

$$S = F\theta\delta\upsilon \tag{5.17}$$

The estimation of the number of stillbirths ($S$) in the NCA from Equations 5.16 and 5.17 assumes that (i) the probability of a woman conceiving is independent of brucellosis infection status, (ii) only new brucellosis infections in each year (not historical infections) cause obstetric complications (spontaneous abortion and stillbirth), iii) the probability of infection with brucellosis and the probability of brucellosis-induced stillbirth in pregnant women with brucellosis are independent of females' age and reproductive status, iv) all pregnancies are single (i.e., it excludes twins, triplets), and v) pregnant women with brucellosis who seek care at a target health facility are equally likely to suffer a brucellosis-induced stillbirth as pregnant women with brucellosis who do not seek care at a target health facility.

### 5.2.8 Elasticity analyses

The influence of input parameters on the monetary cost and disease burden per case was assessed through elasticity analyses. Elasticity analyses were performed in addition to sensitivity analyses because of the differences in parameter input ranges and units (Åberg et al., 2009). Elasticity analyses estimated the percentage change in monetary costs and disease burden that results from a percentage change in parameter values. These analyses were performed for each input parameter at a time, using exclusively the outputs of the 'status quo' scenario (50,000 iterations).

Elasticity was calculated using a log-log function, as follows (Dayal, 2015):

$$ln(y) = I + E \times ln(x) \tag{5.18}$$

where $y$ is either the monetary cost or disease burden per case, $I$ is the regression intercept, $E$ is the elasticity (percentage change in monetary costs or disease burden that results from a percentage change in parameter value), and $x$ is the input parameter.

### 5.2.9 Model implementation and statistical analyses

The Markov chain Monte Carlo simulation model was implemented in R version 4.1.1 (2021-08-10) (R Core Team, 2021). Graphics were produced with ggplot2 version 3.3.5 (Wickham, 2016).

Two-sample Wilcoxon rank-sum tests were performed to assess differences between model scenarios in (i) monetary cost and DALYs per case, and (ii) weekly transition probabilities (Chan, 2016). Spearman's correlation coefficients between transition probabilities and between model inputs and outputs were computed to assess multicollinearity and dependencies between variables (Chan, 2016).

## 5.3 Results

### 5.3.1 Data source selection and model parametrisation

The outcome of the quality assessment and selection of data sources for each model parameter group is shown in Appendix D.6. The parameters or variables for which locally delivered survey or literature data of 'sufficient quality' were unavailable (and thus targeted by sensitivity analyses or sourced from expert elicitation) included the following: duration of non-target management of chronic illness, probability of death due to brucellosis, probability of treatment failure, probability of progression to chronic brucellosis, attributable risk of spontaneous abortion and stillbirth, health-related expenditure attributable to brucellosis, productivity losses (loss of work days), and age-distribution of deaths.

### 5.3.2 Personal monetary cost, disease duration, and probability of disease progression and death

The estimates of the monetary cost of human brucellosis per case are shown in Fig. 5.5. In the 'status quo', 'RBT', and 'RBT + increased HCS' scenarios, the median (95% uncertainty interval within brackets) monetary cost of brucellosis per case was 448 [345-578] int. $, 424 [325-549] int. $, and 421 [327-534] int. $, respectively. The mean was slightly greater than the median: 452 int. $, 428 int. $, and 423 int. $ in the 'status quo', 'RBT', and 'RBT + increased HCS' scenarios, respectively. The systematic use of RBT in the study area would reduce the current ('status quo') median cost of brucellosis per case by 5.4%. If the systematic use of RBT was accompanied by an increase in target healthcare seeking of 10%, the current median cost of brucellosis per case would be reduced by 6.2%.

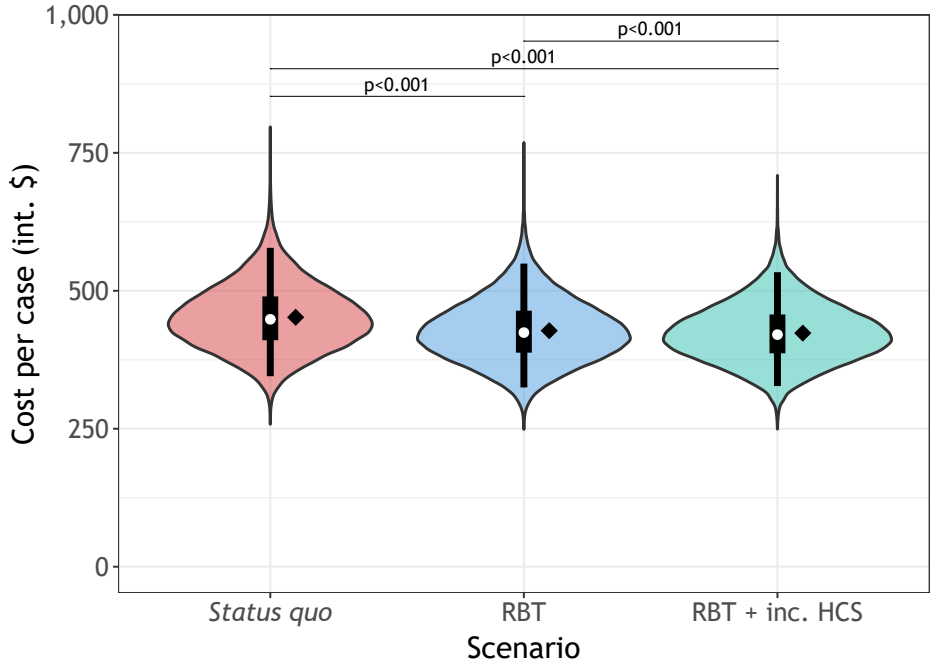



**Figure 5.5:** Monetary cost of brucellosis per case, in each model scenario, in the Ngorongoro Conservation Area (50,000 model iterations). int. $: international dollars. RBT: Rose Bengal test. inc. HCS: Increased healthcare seeking. White dots indicate the median, black diamonds the mean, black boxes the inter-quartile range (50% UI), and black lines the 2.5 and 97.5 percentiles (95% UI). p-values indicate the significance of the two-sample Wilcoxon rank-sum test for differences between model scenarios.

The partition of median monetary cost per case by productivity losses and health-related out-of-pocket expenditure is shown in Fig. 5.6. The median monetary cost per case was divided almost equally between productivity losses and out-of-pocket expenditure. In the 'status quo', 'RBT', and 'RBT + increased HCS' scenarios, the share of monetary costs attributable to out-of-pocket expenditure was 51.8%,

54.6%, and 56.3%, respectively. Compared to the 'status quo' scenario, the share of costs attributable to productivity losses decreased by 2.8% (from 48.2% to 45.4%) and 4.5% (from 48.2% to 43.7%) in the 'RBT' and 'RBT + increased HCS' scenarios, respectively.

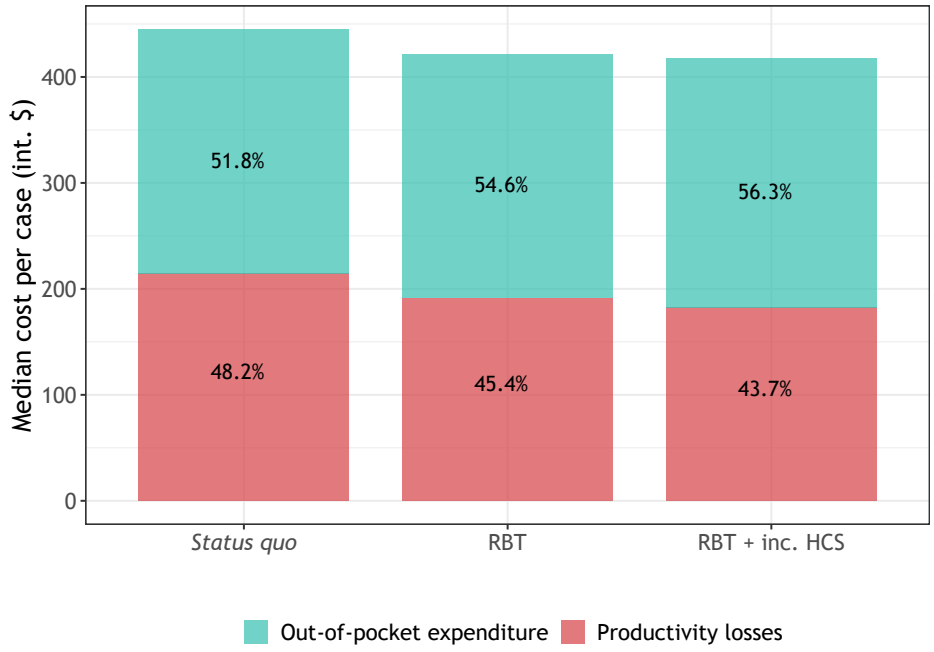



**Figure 5.6:** Partition of the median monetary cost of human brucellosis per case, by productivity losses and health-related expenditure, in the Ngorongoro Conservation Area (50,000 model iterations). Percentage values inside bars indicate the contribution of productivity losses and health-related expenditure to the median cost per case. int. $: international dollars. RBT: Rose Bengal test. inc. HCS: Increased healthcare seeking.

Assuming an incidence of 412 cases per 100,000 person-years (Appendix D.4), the median annual population-level cost (per 100,000 person-years) of brucellosis in the NCA, under the 'status quo' scenario, was 184,576 int. $ (448 int. $ times 412 cases per 100,000 person-years). With 'RBT' and 'RBT + increased HCS', the median annual population-level cost (per 100,000 person-years) in the NCA would be reduced by 9,888 int. $ and 11,124 int. $, respectively.

Under the 'status quo', 'RBT', and 'RBT + increased HCS' scenarios, the median (95% uncertainty interval within brackets) disease duration was 1.9 [1.4-2.4] months, 1.6 [1.2-2.1] months, and 1.5 [1.0-2.0] months, respectively. The mean disease duration was 1.9 months, 1.6 months, and 1.5 months, respectively. The systematic use of RBT in the study area would reduce the current median disease duration per case by 12.9%. If the systematic use of RBT was accompanied by an increase in target healthcare seeking of 10%, the current median disease duration per case would be reduced by 20.3%. The median percentage of acute brucellosis cases

developing chronic brucellosis would be reduced from 60.0% to 44.5%, from the 'status quo' to the 'RBT + increased HCS' scenarios. The median percentage of brucellosis cases that die would be reduced from 6.7% to 5.3%, from the 'status quo' to the 'RBT + increased HCS' scenarios.

The estimated probability, cost, and duration of each pathway under all scenarios are shown in Fig. 5.7. A graphical representation of estimated transition probabilities by model scenario is available in Appendix D.7. A correlation matrix of transition probabilities is available in Appendix D.9. The most likely pathways followed by brucellosis cases in the 'status quo' scenario were $S_1$-$S_5$ (pathway 1) and $S_1$-$S_3$-$S_5$ (pathway 5), which included non-target management states ($S_1$ and $S_3$) exclusively. Pathways 1 ($S_1$-$S_5$) and 7 ($S_1$-$S_6$) were the only pathways with the same probability, cost, and duration across model scenarios.

The pathways that ended in recovery (first six columns in Fig. 5.7) had equal cost and duration as the corresponding pathways that ended in death (last six columns in Fig. 5.7). The below description then focuses on pathways that ended in recovery.

Compared to the *status quo* scenario, with RBT use, pathways 2 ($S_1$-$S_2$-$S_5$) and 6 ($S_1$-$S_3$-$S_4$-$S_5$) became more likely, in contrast with pathways 3 ($S_1$-$S_2$-$S_3$-$S_5$) and 4 ($S_1$-$S_2$-$S_3$-$S_4$-$S_5$), which became less likely. Pathways 4 ($S_1$-$S_2$-$S_3$-$S_4$-$S_5$) and 6 ($S_1$-$S_3$-$S_4$-$S_5$) were shortened by RBT use due to a reduction in expected residence time in $S_4$ (target management of chronic illness).

Besides these effects of RBT use on pathways' probability and duration, in the scenario of RBT use and increased healthcare seeking, compared to the *status quo* scenario, pathway 5 ($S_1$-$S_3$-$S_5$) became less likely. Pathways 3 ($S_1$-$S_2$-$S_3$-$S_5$) and 5 ($S_1$-$S_3$-$S_5$) were shortened by RBT use and increased healthcare seeking due to a reduction in expected residence time in $S_3$ (non-target management of chronic illness).

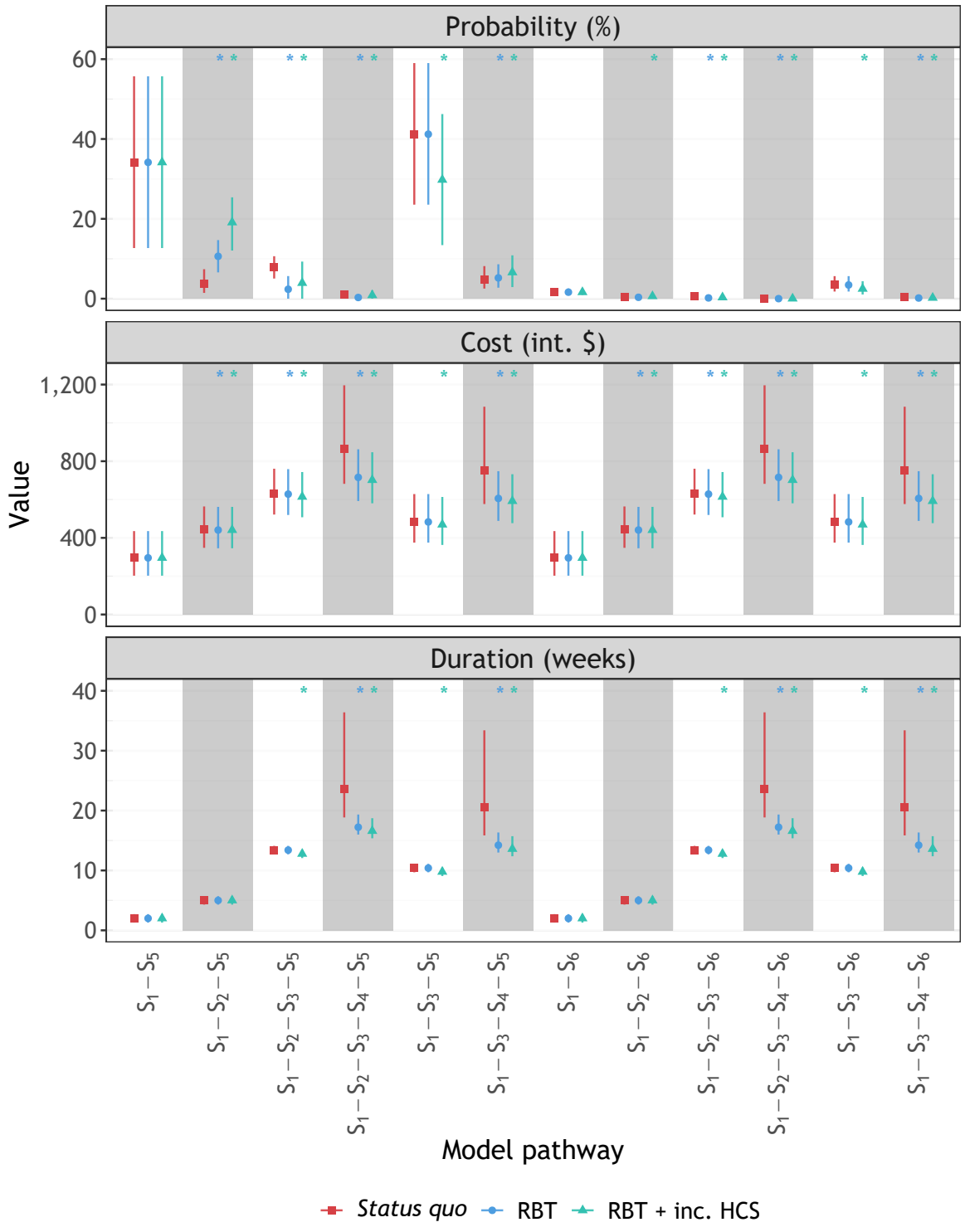



**Figure 5.7:** Probability (%), cost (international $), and duration (weeks) of each pathway and model scenario. Median point estimates (dots) and 95% uncertainty intervals (vertical bars) were obtained from the simulations. States (S): non-target management of acute illness ($S_1$), target management of acute illness ($S_2$), non-target management of chronic illness ($S_3$), target management of chronic illness ($S_4$), recovery ($S_5$), and death ($S_6$). RBT: Rose Bengal test. inc. HCS: Increased healthcare seeking. Coloured asterisks indicate the significance (p-value $< 0.05$) of the two-sample Wilcoxon rank-sum test comparing the *status quo* scenario and RBT or RBT+inc. HCS scenarios.

The median monthly non-food expenditure by pastoral households in northern Tanzania, calculated from the Tanzania National Panel survey dataset, was 61 (95% UI: 6-419; n=96 households) int. $. Under the 'status quo' scenario, the median monthly health-related expenditure due to brucellosis per case was 123 (95% UI: 78-203; n=50,000 iterations) int. $, and the percentage of model iterations with monthly health-related expenditure due to brucellosis greater than 40% the monthly non-food expenditure (probability of catastrophic health expenditure) was 94.8%.

### 5.3.3 Disease burden

The disease burden per case, in DALYs, attributable to human brucellosis is shown in Fig. 5.8. Under the 'status quo', 'RBT', and 'RBT + increased HCS' scenarios, the median (95% uncertainty interval within brackets) DALYs per case was 1.62 [1.01-2.42], 1.41 [0.86-2.12], and 1.29 [0.77-1.97], respectively. The mean DALYs per case was 1.65, 1.43, and 1.31, respectively. The systematic use of RBT in the study area would reduce the current median disease burden per case by 13.2%. If the systematic use of RBT was accompanied by an increase in target healthcare seeking of 10%, the current median disease burden per case would be reduced by 20.6%. Irrespective of the model scenario, years of life lost (YLLs) contributed 99% to the DALYs per case estimate. The remaining 1% were due to years lived with disability (YLDs).

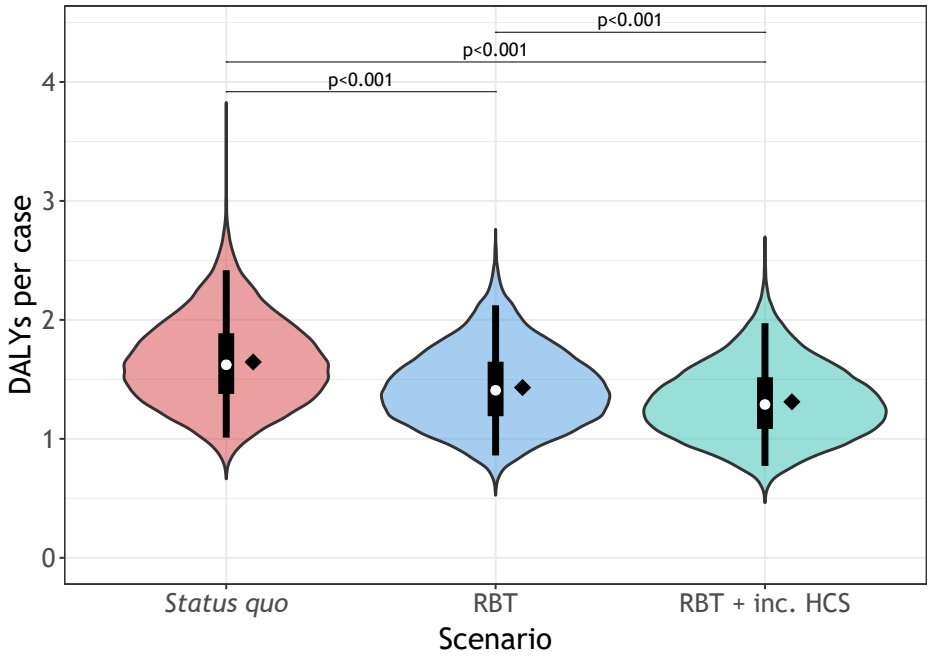



**Figure 5.8:** Disease burden per brucellosis case in DALYs (disability-adjusted life years), under each model scenario, in the Ngorongoro Conservation Area (50,000 model iterations). RBT: Rose Bengal test. inc. HCS: Increased healthcare seeking. White dots indicate the median, black diamonds the mean, black boxes the inter-quartile range (50% UI), and black lines the 2.5 and 97.5 percentiles (95% UI). p-values indicate the significance of the two-sample Wilcoxon rank-sum test for differences between model scenarios.

Under the 'status quo', 'RBT', and 'RBT + increased HCS' scenarios, the median population-level disease burden in the NCA (per 100,000 people) was estimated at 654 [261-1,284] DALYs, 567 [225-1,123] DALYs, and 519 [204-1,038] DALYs, respectively. The mean DALYs per 100,000 people were 686, 596, and 546, respectively.

### 5.3.4 Sensitivity analyses

The cost of human brucellosis per case, under the 'status quo' scenario, including (alternative definition) and excluding (reference definition) the cost of death (statistical value of life lost and funeral costs) is shown in Fig. 5.9. The median (95% uncertainty interval within brackets) cost of brucellosis per case including the cost of death was 13,125 [4,129-43,825] int. $. The cost of brucellosis per case with the cost of death is 29 times greater than without the cost of death (Fig. 5.5).

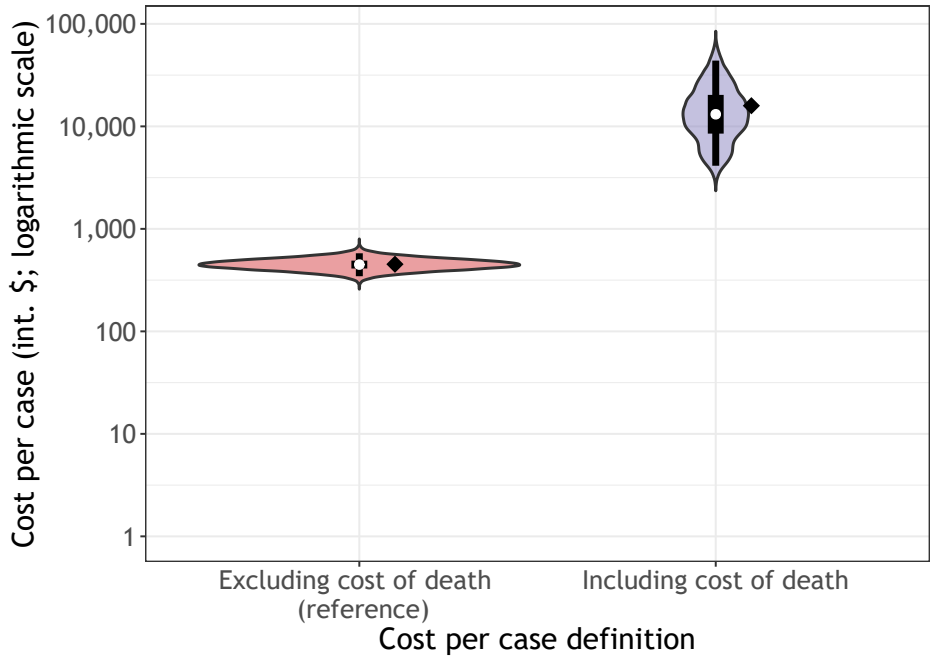



**Figure 5.9:** Median monetary cost of human brucellosis per case, including and excluding (reference) the cost of death (statistical value of life lost and funeral costs) in the Ngorongoro Conservation Area (50,000 model iterations, 'status quo' scenario). int. $: international dollars. White dots indicate the median, black diamonds the mean, black boxes the inter-quartile range (50% UI), and black lines the 2.5 and 97.5 percentiles (95% UI). The y-axis is on the logarithmic scale.

Fig. 5.10 shows estimates of brucellosis burden (per case and 100,000 people) under three options: i) the reference age distribution of deaths (baseline; age distribution of deaths differs from the age distribution of cases); ii) the alternative age distribution of deaths (age distribution of deaths is equal to the age distribution of cases); and, iii) the baseline plus brucellosis-induced stillbirth burden. Both the alternative age distribution of deaths and the stillbirth burden led to increased brucellosis burden estimates (per case and 100,000 people) compared to the baseline. Under the alternative age distribution of deaths, DALYs per case and DALYs per 100,000 people estimates were over twice as high as the baseline. Accounting for stillbirths under baseline increased the median estimates of DALYs per case and DALYs per 100,000 people by 2.9%. This increase of 2.9% due to stillbirth is equivalent to 0.05 (95% UI: 0.01-0.12) DALYs per case, and 19 (95% UI: 4-49) DALYs per 100,000 people. One brucellosis-induced stillbirth was estimated to occur in the NCA every two to three years (median rate of 0.4 [95% UI: 0.1-1.1] brucellosis-induced stillbirths per year).

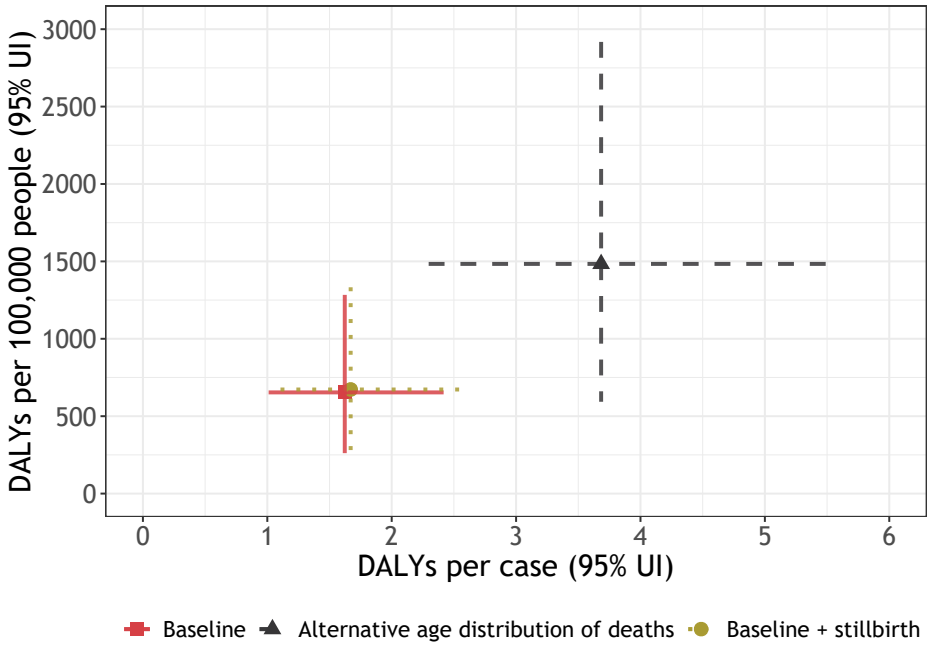



**Figure 5.10:** Disease burden attributable to brucellosis per case and per 100,000 people (dots), in the Ngorongoro Conservation Area (50,000 model iterations, 'status quo' scenario), under alternative methodological approaches. DALYs: disability-adjusted life-years. Lines indicate 95% uncertainty intervals. Baseline: reference age distribution of deaths (age distribution of deaths differs from the age distribution of cases). Alternative age distribution of deaths: age distribution of deaths is equal to the age distribution of cases. Baseline + stillbirth: disease burden estimation includes baseline plus the burden of brucellosis-induced stillbirth.

### 5.3.5 Elasticity analyses

The results of elasticity analyses on the monetary costs and disease burden attributable to human brucellosis are shown in Figs. 5.11 and 5.12. The range of parameter values that entered the elasticity analyses is shown in Appendix D.8. A correlation matrix of model inputs and outputs is available in Appendix D.9.

The input parameters most influential to estimates of the monetary cost per case (elasticity greater than 0.2) were the non-target health-related expenditure, probability of chronic progression, and chronic disability weight. An increase of 1% in the non-target health-related expenditure, the most influential input parameter, increased the cost per case by 0.40%. Among the other variables with a significant p-value (p-value$<$0.05), increasing acute disease duration, acute (moderate and severe) and orchitis disability weights, target health-related expenditure,

healthcare-seeking probability (for fever and for musculoskeletal symptoms), and probability of treatment failure increased the monetary cost per case estimate. Increasing the diagnostic test sensitivity decreased the monetary cost per case estimate.

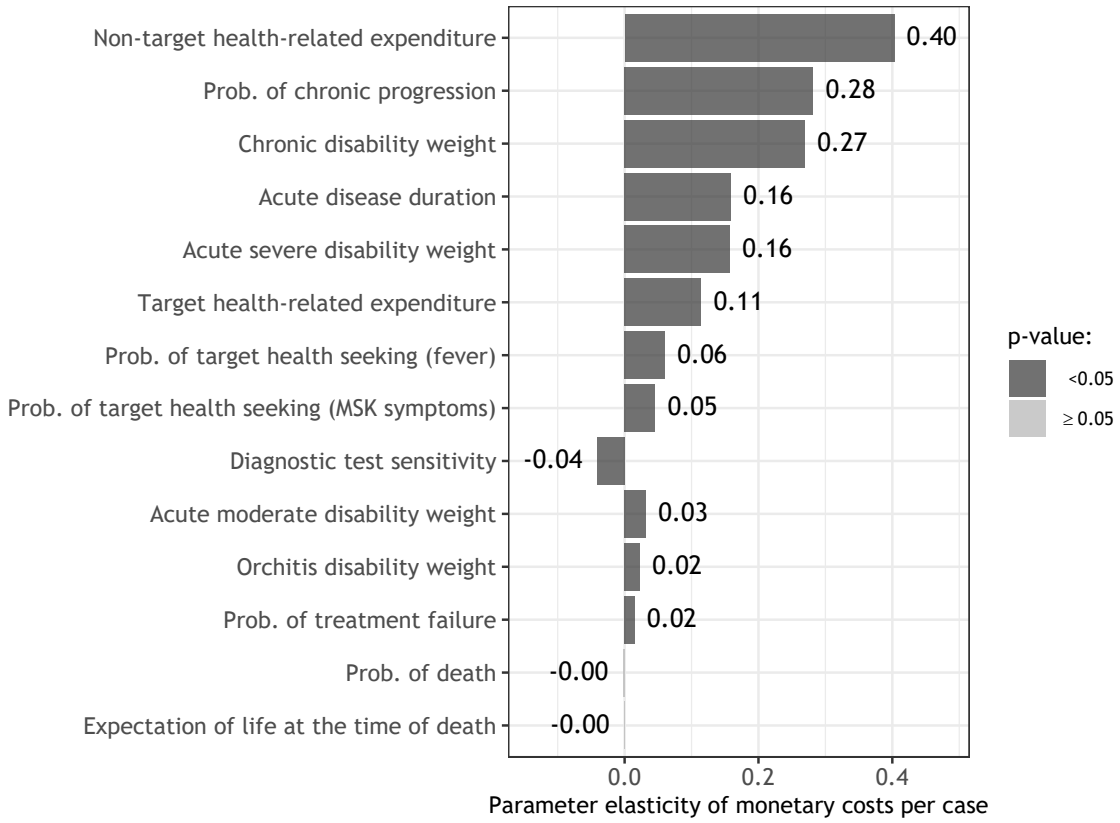



**Figure 5.11:** Tornado plot showing the parameter elasticity of monetary cost (int. $) per brucellosis case (percentage change in costs per case when parameter values change by 1%) in the Ngorongoro Conservation Area (50,000 model iterations, 'status quo' scenario). The colours of the bars indicate the significance of the parameter elasticity estimate (dark and light grey indicate p-value $< 0.05$ and p-value $\geq 0.05$, respectively). Prob.: probability. MSK: musculoskeletal.

The input parameters that were most influential to estimates of the disease burden per case (elasticity greater than 0.2) were the probability of death, probability of chronic progression, and acute disease duration. The probability of death was a highly influential parameter. An increase of 1% in the probability of death, which was a relatively uncommon event (between 4.1 to 10.0%, as per Appendix D.8) increased the DALYs per case by 1.02%. Among the other variables with a significant p-value, increasing the healthcare-seeking probability (for fever and for musculoskeletal symptoms), probability of treatment failure, and acute severe disability weight increased the disease burden per case estimate. Increasing the diagnostic test sensitivity and acute moderate disability weight decreased the disease burden per case estimate.

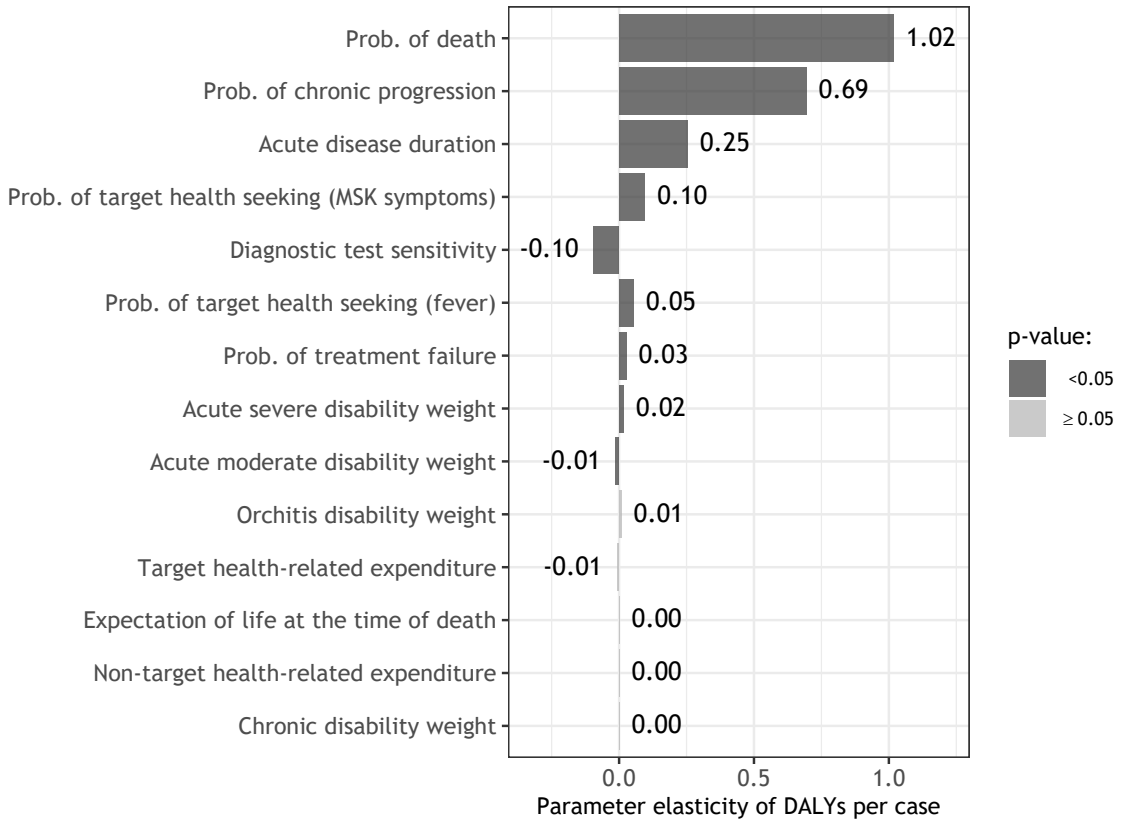



**Figure 5.12:** Tornado plot showing the parameter elasticity of disease burden (DALYs, disability-adjusted life-years) per brucellosis case (percentage change in DALYs per case when parameter values change by 1%) in the Ngorongoro Conservation Area (50,000 model iterations, 'status quo' scenario). The colours of the bars indicate the significance of the parameter elasticity estimate (dark and light grey indicate p-value $< 0.05$ and p-value $\geq 0.05$, respectively). Prob.: probability. MSK: musculoskeletal.

## 5.4 Discussion

### 5.4.1 Personal monetary cost and disease duration

This study estimated the personal monetary costs (healthcare-related expenditure and productivity losses) and disease burden (disability-adjusted life-years, DALYs) attributable to brucellosis in the Ngorongoro Conservation Area (NCA), northern Tanzania. The estimated current ('status quo') median cost of brucellosis per case was 448 int. $, which is 16.2% of the GDP per capita in Tanzania (2,773 int. $ in 2019).[8] Productivity losses and health-related expenditure contributed 48.2% and 51.8% to the current median cost per case, respectively.

8. Sourced from the World Bank at `https://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD?locations=TZ`

Although differences in methods between studies hamper strict comparisons, the estimated current median cost per case as a proportion of GDP per capita (16.2%) obtained in this study is in line with an estimate previously reported for Tanzania (Kunda, 2006). Based on data from 41 brucellosis cases in Arusha and Manyara, the mean direct and indirect costs (including diagnosis, treatment, subsistence, and transport) incurred by each case amounted to 241 int. $[9] in 2003, which was equivalent to 17% of the GDP per capita[10] at the time (Kunda, 2006). In studies carried out in other settings, the median or mean cost of brucellosis per case, including health-related expenditure and productivity loss, ranged from 200 to 2,606 int. $[11,12] (Alshwany, 2019; Guma et al., 2020; Kasymbekov, 2014; Singh et al., 2018a). In Kenya, the cost of brucellosis treatment charged to patients was estimated at 34 int. $ (90% CI: 6-93)[13] (Alumasa et al., 2021). In Israel, the median annual healthcare utilisation cost per brucellosis case from the insurer's perspective was 42 int. $ before diagnosis and 260 int. $ after diagnosis (Vered et al., 2015)[14].

Compared to the cost of other endemic diseases in Tanzania, the cost of brucellosis estimated in the present study is considerable. For instance, studies carried out in Lindi rural district of southern Tanzania in 2003-2004 estimated that households spent on average 7 int. $[15] per illness episode of any aetiology (including health-care service fees, drugs, diagnostic tests, transport, and accommodation) (Save the children, 2007). More recently, according to data from the Tanzania National Panel survey delivered between October 2008 and October 2009, the mean out-of-pocket expenditure, including on private outpatient clinics, preventive health services, over-the-counter medications and traditional healer services for any health

9. Based on the World Bank conversion factor of 385.223 TZS per int. $ in 2003 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=TZ
10. Sourced from the World Bank at https://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD?locations=TZ
11. 200 int. $ in India calculated from healthcare-related expenditure and productivity losses of 627.5 million Indian rupee (INR) in a population of 1,210,193,422 people, incidence of 17 per 100,000 person-years, and a World Bank conversion factor of 15.283 INR per int. $ in 2011 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=IN
12. 2,606 int. $ in Kyrgyzstan calculated from health-related expenditure and productivity losses assuming 4,412 cases, and a World Bank conversion factor of 9.847 KGS per int. $ in 2006 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=KG
13. Based on the World Bank conversion factors 101.991 KSH (Kenyan Shillings) per 1 USD (United States Dollars) and 43.979 KSH per int. $ in 2019 obtained from https://data.worldbank.org/indicator/PA.NUS.FCRF?locations=KE and https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=KE, respectively
14. Based on the World Bank conversion factor of 4.427 IL (Israeli Shekels) per int. $ in 2013 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=IL
15. Based on the World Bank conversion factor of 392.947 TZS (Tanzanian Shillings) per int. $ in 2004 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=TZ

reason, among adult participants, was 6 int. $[16] per month (Brinda, Andrés, and Enemark, 2014). Regarding chronic diseases specifically, a study estimated that the mean health expenditure among households affected by illnesses such as acquired immunodeficiency syndrome (AIDS), Tuberculosis (TB) and, potentially, brucellosis, was 104 int. $[17] per year, between 1991 and 2010, in the Kagera region, northwestern Tanzania (Counts and Skordis-Worrall, 2015). The mean monetary cost of typhoid fever in Zanzibar, Tanzania, has been estimated at 410 int. $[17] per episode, being 340 int. $ attributable to productivity losses and 70 int. $ to expenditure for treatment, travel, and meals before, during, and after hospitalisation (Riewpaiboon et al., 2014). In another study, the cost of a malaria episode (including direct and indirect household costs and health system costs) in Tanzanian children aged under five ranged from 13 to 353 int. $,[16] depending on disease severity and presence of complications, and only 55% of this cost was borne by the households (Sicuri et al., 2013). The healthcare-related expenditure and productivity losses due to a stroke event in Tanzania have been estimated at 618 and 598 int. $,[18] respectively (Kabadi et al., 2013).

Recently, a large cross-sectional survey of TB patients (n=777) who were diagnosed and treated under the Tanzania's national TB programme gathered data on direct medical costs (e.g., medicines, diagnostic tests), direct non-medical costs (e.g., travel fees, accommodation), and indirect costs (e.g., time lost while seeking and receiving care) (Kilale et al., 2022). The median cost incurred by TB patients during their illness was estimated at 461 int. $ (interquartile range: 288–767).[19] Although differences in methodology between studies hamper direct comparisons, the results of our study indicate that the cost of brucellosis per case (median of 434 int. $) is unlikely to be of a considerably different magnitude to that of TB.

The disease duration under the 'status quo' scenario (median of 1.9 months), as obtained from the expert elicitation, is lower than expected based on previous reports from northern Tanzania. In a study carried out in Arusha and Manyara, Tanzania, brucellosis cases often reported symptoms that lasted for over one year (Kunda, 2006). However, strict comparisons between studies may be hampered by many factors, such as enrolment criteria, study period, location, and case defini-

16. Based on the World Bank conversion factor of 515.829 TZS (Tanzanian Shillings) per int. $ in 2009 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=TZ
17. Based on the World Bank conversion factor of 538.972 TZS (Tanzanian Shillings) per int. $ in 2010 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=TZ
18. Based on the World Bank conversion factor of 414.752 TZS (Tanzanian Shillings) per int. $ in 2006 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=TZ
19. Based on the average annual exchange rate during 2019 of US$ 1 = 2,307.06 TZS (Tanzanian Shillings) (Kilale et al., 2022), and the World Bank conversion factor of 774.74 TZS per int. $ in 2019 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=TZ

tion. The expert elicitation outputs might have been biased towards a median disease duration shorter than real if experts were used to diagnose and treat patients early in the course of their illness. The median duration of the acute, non-target health-seeking phase in the present study (approximately two weeks) was in line with the findings from previous studies carried out in Moshi, Kilimanjaro region, Tanzania, where the median duration of febrile illness due to brucellosis, before hospital presentation or admission, was approximately seven days (Bouley et al., 2012; Carugati et al., 2018). In contrast, the study in Arusha and Manyara reported that two thirds of brucellosis cases presented to hospital at least three months after the onset of symptoms (Kunda, 2006).

### 5.4.2 Disease burden

The estimated current median burden of brucellosis per case in the NCA was 1.62 (95% UI: 1.01-2.42) DALYs. This value is greater than previously reported for other settings using incidence-based approaches for DALYs estimation that included mortality, no discounting, and no age-weighting. For instance, reported estimates of the median DALYs per brucellosis case in Kyrgyzstan and Africa vary from 0.29 to 0.33 (Counotte et al., 2016; Havelaar et al., 2015; Kirk et al., 2015). In Greece, 0.71 DALYs per brucellosis case can be calculated from a reported incidence of 69.9 per 100,000 person-years and a population-level burden of 49.3 DALYs per 100,000 people (Gkogka et al., 2011). Based on hospital survey data in Tanzania, 1.36 DALYs per brucellosis case can be calculated from a reported incidence of 11 per 100,000 person-years and a population-level burden of 15 DALYs per 100,000 people (3,645 DALYs in a population of 24,392,862 people) (Kunda, 2006).

The estimated current median population-level burden attributable to brucellosis in the NCA (654 [95% UI: 261-1,284] DALYs per 100,000 people) was also greater than previously reported in Tanzania (15 DALYs per 100,000 people; hospital-based survey; Kunda, 2006) or elsewhere. Values of population-level brucellosis burden greater than 15 DALYs per 100,000 people but lower than the 689 DALYs per 100,000 people estimated in this study have been reported in Kyrgyzstan (18, likely mean), Iraqi Kurdistan region (27, median), Greece (49, likely mean), Uganda (73, mean),[20] and Kenya (117, mean)[21] (Alshwany, 2019; FAO, 2018c,d; Gkogka et al., 2011; Torgerson et al., 2018). Despite focusing on an extremely high incidence area, our

20. Uganda (73 DALYs per 100,000 people) estimate obtained from 136,266 DALYs per year in 746,029 prevalent cases, 9,696,623 cattle keepers plus 9,016,656 consumers at risk and 10 years seropositivity

21. Kenya (117 DALYs per 100,000 people) estimate obtained from 502,801 DALYs per year in 1,275,917 prevalent cases, 42,961,187 population at risk and 10 years seropositivity

study estimated a population-level burden for brucellosis that is small compared to other endemic diseases in Tanzania. For instance, the Global Burden of Disease Study 2019 estimated that AIDS, malaria, and tuberculosis cause 2,715 (95% UI: 2,250-3,400), 2,480 (95% UI: 1,054-4,824), and 1,551 (95% UI: 1,208-2,005) DALYs per 100,000 people, respectively (Vos et al., 2020).

Compared to previous studies, the high disease burden per case estimate in this study is likely due to the high probability of death obtained in the expert elicitation. According to clinicians who regularly manage brucellosis cases in the study area, on average, 7 out of 100 brucellosis cases die due to brucellosis. This value is close to a case-fatality ratio (6.67%) used by the FAO to estimate the disease burden attributable to brucellosis in Ethiopia (FAO, 2018b). It is plausible that given the low probability of cases reaching a health facility that can diagnose and manage brucellosis, low test sensitivity, and poor treatment outcomes, brucellosis cases in the NCA are more likely to develop serious complications of the disease, including meningitis and endocarditis, with high mortality risk, than in other places. Case-fatality ratios of brucellosis endocarditis have been estimated between 16.7% and 79.5% in other settings (Harthi, 1989; Jacobs et al., 1990; Keshtkar-Jahromi et al., 2012; Peery and Belter, 1960). Even if the true case-fatality ratio in the NCA is lower than the 7% used in the present study, it is possible that the disease burden per case was underestimated because a conservative age distribution of deaths from a study carried out in Spain was used (Rodríguez-Alonso et al., 2021). In the study carried out in Spain, 69.0% of brucellosis deaths were in the over-65 age group (Rodríguez-Alonso et al., 2021). Based on the sensitivity analyses, if a constant case-fatality ratio across age groups was considered, as assumed in the FERG study (Kirk et al., 2015), the DALYs per case under the 'status quo' scenario would more than double.

Brucellosis-induced stillbirth caused a median of 19 (95% UI: 4-49) DALYs per year in the NCA (100,000 people), which corresponds to an increase of 2.9% in relation to the baseline burden estimate under reference age distribution of deaths (age distribution of deaths differs from the age distribution of cases) for all brucellosis clinical outcomes (654 DALYs per 100,000 people). This estimated brucellosis-induced stillbirth burden is greater than the previously reported disease burden estimate in Tanzania, nationally, for all brucellosis clinical outcomes (15 DALYs per 100,000 people; hospital-based survey; Kunda, 2006). It is worth highlighting that the distribution of the attributable risk of brucellosis-induced stillbirth used in this study is most likely conservative (ranging from 0.0% to 8.9%) (Elshamy and Ahmed, 2008; Gulsun et al., 2011; Kurdoglu et al., 2010). This distribution of attributable risk, which yields an estimated rate of 0.4 (95% UI: 0.1-1.1) brucellosis-induced still-

births per year in the NCA, was obtained from three case-control studies in Turkey and Saudi Arabia. Many other studies suggest that the link between brucellosis infection in pregnant women and obstetric complications might be underappreciated (Ali et al., 2016; Khan, Mah, and Memish, 2001; Kurdoglu et al., 2010; Liu et al., 2020b; Rujeni and Mbanzamihigo, 2014; Vilchez et al., 2015). The present study provides evidence of the need to account for stillbirth in brucellosis burden estimation methodology.

### 5.4.3 Effect of diagnostic test sensitivity and healthcare-seeking probability on monetary cost and disease burden estimates

The current median monetary cost per case estimated in the present study would be reduced by 5.4% under the scenario of increased diagnostic sensitivity (using RBT for diagnosis, instead of commercial plate agglutination tests) and 6.2% under the scenario of both increased diagnostic sensitivity and healthcare-seeking probability. Reductions of greater magnitude under these alternative scenarios were estimated for disease burden per case (13.2% under the scenario of increased diagnostic sensitivity, and 20.6% under the scenario of both increased diagnostic sensitivity and increased healthcare-seeking probability). These results indicate that diagnostic sensitivity and healthcare-seeking probability are important determinants of cost and disease burden. Acute brucellosis cases that (i) do not reach a health facility that can diagnose and manage the disease or (ii) receive a false negative test result are likely to progress to a chronic stage, with its associated productivity loss and mortality risk. Under the alternative scenarios, the increased probability of correct diagnosis and effective disease management led to a reduction in disease duration, productivity loss, and probability of death. In addition to published evidence indicating that RBT is both more accurate and cheaper to run than commercial plate agglutination tests, the magnitude of the potential monetary costs and disease burden averted with RBT, as estimated in our study, strongly supports recommendations for the standardised application of RBT for human brucellosis testing in northern Tanzania (Lukambagire et al., 2021).

The elasticity analyses aimed to assess the influence of input parameters on the monetary cost and disease burden per case, under the ‘status quo’ scenario only. These analyses indicated that the probability of target healthcare seeking (for fever and for musculoskeletal symptoms) was positively associated with the monetary cost and disease burden per case estimates (Figs. 5.11 and 5.12). This association seems to be contrary to the observed reduction in monetary cost and disease burden estimates in the ‘RBT + increased healthcare seeking (HCS)’ scenario, com-

pared to the 'RBT' scenario. This apparent inconsistency occurred because numerical trade-offs between transition probabilities were computed (through Eqs. 5.2 to 5.7) in each iteration to respect, among other conditions, the expected overall disease duration (8.2 weeks from expert elicitation) and probability of progression to chronic disease (e.g., $\lambda$ parameter). These trade-offs resulted in associations between transition probabilities, model inputs, and model outputs, which are visible in Appendix D.9. For instance, the probability of transition from non-target management of chronic illness to target management of chronic illness ($p_{34}$) was strongly and negatively associated (Spearman's coefficient = -0.82) with the probability of recovery from non-target management of chronic illness ($p_{35}$) so that the duration of chronic illness was consistent with the corresponding input parameter ($\alpha_3$) and overall expected disease duration. The target healthcare-seeking probability was positively correlated with disease duration (probability of healthcare seeking for fever was positively correlated with acute disease duration; and, probability of healthcare seeking for musculoskeletal symptoms was positively correlated with chronic disease duration) and, consequently, productivity losses. Target management of acute and chronic brucellosis was assumed to last at least three weeks (Kunda, 2006), a considerable proportion of the average disease duration obtained from the expert elicitation. Note that one week spent in a target management state and one week spent in a non-target management state contributed equality to disease duration, productivity loss, and DALYs estimation. Finally, in the absence of a reduction in disease duration and productivity losses with increased target healthcare-seeking probability in each iteration, the overall cost of the disease increased because the target health-related expenditure was greater than non-target health-related expenditure (Appendix D.1).

The present study estimated costs and disease burden potentially avoidable under different scenarios of healthcare seeking and test sensitivity. In practice, our scenarios could represent many dimensions of the healthcare-seeking process that include availability, accessibility, affordability, adequacy, acceptability, and quality aspects (e.g., accuracy of diagnosis and treatment) (Loosli et al., 2021; Obrist et al., 2007). Improvements in any of these dimensions will likely result in substantial benefits to households that are not specific to brucellosis. Our methodological approach may help estimate the true economic impact of multiple underdiagnosed illnesses and conditions in northern Tanzania. This evidence is key to comprehensively analysing the cost-effectiveness of public health interventions that affect any of the dimensions of healthcare seeking.

This study did not estimate the monetary cost and disease burden attributable to false positive test results (indicating disease presence when that is not true), which often occur due to the poor specificity of commercial plate agglutination tests (55.4% specificity with Eurocell, and 75.0% with Fortress) (Lukambagire et al., 2021). In neighbouring Kenya, it has been estimated that unnecessary treatments due to false positive test results cost 785,917 (95% CI: 108,997-2,664,628) int. $[22] nationally per year, without considering the cost of the true illness remaining untreated (Alumasa et al., 2021). Further studies are needed to quantify the magnitude of this problem in Tanzania.

### 5.4.4 Limitations

This study applied novel approaches to estimate the monetary costs and disease burden attributable to brucellosis and provided key evidence to inform policy development for disease control, but several limitations need to be highlighted. Firstly, based on the elasticity analyses, some of the most influential parameters to the monetary cost or disease burden estimation were poorly supported by literature evidence and were sourced from the expert elicitation: probability of progression to chronic disease and probability of death. The information elicited from experts may be biased for several reasons. The experts' knowledge of the brucellosis status of patients that they examine is imperfect due to the lack of adequate clinical infrastructure, and poor diagnostic performance (low diagnostic sensitivity and specificity) of tests widely used in northern Tanzania. Not all clinicians were based in the Ngorongoro district, which might imply heterogeneity in brucellosis clinical presentations that they have experience with. Also, without routine pathological investigations, the experts' ability to determine the cause of death of brucellosis cases may be compromised.

Self-limiting brucellosis infections have been reported, particularly during the pre-antibiotic era (early 1900s), but it is not clear yet how often this outcome occurs currently in northern Tanzania (Davies and Anderson, 1929; Huddleson, 1931; Poole, 1975). In a 6-year survey of human brucellosis in England and Wales, at least four (7.1%) out of 56 patients with active brucellosis infection recovered without treatment (Poole, 1975). However, the proportion of cases with self-limiting disease may be greater than 7.1% because evidence of previous exposure or infection

22. Based on the World Bank conversion factors 101.991 KSH (Kenyan Shillings) per 1 USD (United States Dollars) and 43.979 KSH per int. $ in 2019 obtained from `https://data.worldbank.org/indicator/PA.NUS.FCRF?locations=KE` and `https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=KE`, respectively

is often detected in cross-sectional sero-surveys in endemic areas, indicating that many people may have had short, mild or asymptomatic brucellosis (Hu et al., 2021). In Jilin Province, a region with endemic brucellosis in China, 25% (25 of 100) of blood samples from asymptomatic people in a high-risk group had *Brucella* DNA (Zhen et al., 2013). In a prospective epidemiological survey in Turkey, 12 (10.9%) out of 110 family members of confirmed brucellosis cases were seropositive and asymptomatic without treatment during a follow-up period of 6–12 months (Tabak et al., 2008). Further research is needed to determine the probability of recovery among symptomatic cases of brucellosis that do not reach a health facility that can diagnose and manage the disease.

The duration of non-target management of chronic illness and target management (for acute and chronic illness) used in this study were informed from the expert elicitation and locally-relevant literature (Kunda, 2006), respectively. The duration of the non-target management of acute illness was obtained from the global burden of foodborne disease study (FERG). FERG considered an average of two weeks for acute disease and six months for chronic disease. The mean illness duration (including acute and chronic stages) obtained from the expert elicitation was approximately 8.2 weeks. Neither of these values likely captures well the duration of symptoms experienced by brucellosis cases in the NCA. Most cases in a study in northern Tanzania had symptoms of brucellosis for more than two years, and the average hospitalisation time was five days (Kunda, 2006). In other settings, mean or median duration of hospitalisation between eight and 13 days have been reported (Afifi et al., 2005; Ariza et al., 1995; Mancini et al., 2014; Shi et al., 2018).

Thirdly, for estimating productivity losses, the approach described by Frick et al. (2015) was adopted. This approach applied disability weights as a surrogate for disease severity and the magnitude of inability of brucellosis cases to generate income. A multiplier was used to adjust the median productivity loss estimate so that it was consistent with 28 work days lost (expert elicitation output) in wages. The number of work days lost due to brucellosis in Tanzania and other settings has rarely been quantified, which compromises the validity assessment of these results. The small number of available estimates of work days lost due to brucellosis are mostly from the 1970s and are highly variable. The number of work days lost ranged from seven to 56 in a brucellosis outbreak at a meat packing plant in Virginia, US (White et al., 1974). In another brucellosis outbreak at a meat packing plant, in Iowa, US, the mean number of work days lost per brucellosis case was three (Anderson et al., 1978; Colmenero-Castillo et al., 1989). In contrast, in Malaga, Spain, between 1984 and 1986, the mean number of work days lost per brucellosis case was 102 (Colmenero-Castillo et al., 1989).

Finally, the reported healthcare-seeking behaviour by GALS-positive participants in a survey delivered in the Hai district was used in the Markov model as a proxy for the probability of brucellosis cases transitioning from non-target to target management of chronic illness. The extent to which GALS-positive participants in the Hai district are representative of chronic brucellosis cases in the NCA is unclear. The decision to use a healthcare-seeking probability from the Hai district to represent healthcare-seeking behaviour in the NCA is likely conservative. The population in the Hai district is primarily urban, wealthier, and has more accessible healthcare facilities than the population in the NCA (Bank of Tanzania, 2021). As a result of this assumption, chronic brucellosis cases in the NCA may be (i) less likely to seek care at a target health facility and receive the appropriate treatment, and (ii) consequently more likely to suffer long-lasting symptoms and productivity losses than modelled in this study.

## 5.5 Conclusion

This study demonstrates that brucellosis is a cause of considerable economic impact in a pastoralist community living in the Ngorongoro Conservation Area of northern Tanzania. The estimated disease burden attributable to human brucellosis was greater than previously reported in Tanzania and elsewhere. The disease is likely to cause catastrophic health expenditure and extensive productivity loss in the study area.

These results may be used to inform analyses of the potential benefits of future control interventions. Strategies aimed at reducing transmission of *Brucella* spp. (between livestock and from livestock to people) and at improving diagnosis and management of human cases are likely to reduce the impact of the disease remarkably. Potential strategies include (i) livestock vaccination to reduce disease spread, (ii) community outreach programs to raise awareness and educate communities on brucellosis prevention and treatment, and (iii) RBT use by healthcare facilities for improved diagnosis and management of human brucellosis patients.

The Markov model used in this study may be useful to estimate the impact of brucellosis in similar settings where the disease remains underdiagnosed and poorly managed. This flexible model can be used to simulate the effect of public health interventions that affect any transition probabilities (e.g., healthcare seeking, progression to chronic disease, recovery, and death). The Markov states used to represent the natural history of the disease, by healthcare seeking and disease

progression, could also be appropriate to estimate the cost and disease burden attributable to other infectious diseases such as Q fever, leptospirosis, malaria, and dengue, in this or similar settings. The Monte Carlo process captures the uncertainty in many of the Markov model input parameters. It provides a mechanism for studying the relative influence of each input parameter on the overall monetary cost and disease burden. Analysing such insights can support identifying key research priorities and selecting the suitable methods for data collection.

Future research on the impact of brucellosis should (i) gather more data on key uncertain variables that proved highly influential to the disease burden estimation (e.g., probability of death, age distribution of deaths, and disease duration), and (ii) take into account the non-negligible risk and burden attributable to brucellosis-induced stillbirth. Exploring these research paths poses considerable practical challenges and ethical questions that need to be addressed first. In the absence of better evidence, this study used data elicited from experts to inform the probability of death and disease duration in the Markov model. A potential approach to improving the quality of evidence available is a longitudinal cohort study of brucellosis patients in endemic areas where access to healthcare services is limited. Despite the obvious limitations of such a study, e.g., cost and time, it could help better estimate the mortality risk and duration of symptoms of brucellosis patients in low-resource settings and directly gather information on health-related out-of-pocket expenditure and loss of work days. Alternatively, conducting either a hospital-based or a community-based case-control study would enable estimating the monetary cost and disease burden attributable to brucellosis. Such a study would also allow estimation of brucellosis impact on households, compared to other conditions. This information could aid in the development of targeted control policies.

The findings of this study provide valuable information to guide policymakers in developing strategies to alleviate the impact of brucellosis on both public health and the economy in Tanzania and similar settings.

# Chapter 6

# Cost-benefit and cost-utility analyses of livestock vaccination for brucellosis control in a pastoralist community of northern Tanzania

## 6.1 Introduction

Brucellosis is a bacterial zoonosis that remains endemic in many countries despite considerable investment in control and eradication efforts (Pappas et al., 2006; Zhang et al., 2018). Several livestock and wildlife species can be infected and represent a source of infection to humans. Contact with or ingestion of contaminated products, including unpasteurised dairy and meat, are the most common transmission pathways from animals to humans (Corbel et al., 2006). In livestock, brucellosis causes mainly abortion and perinatal mortality, with the consequent reduction in milk and meat production. In humans, the disease is characterised by variable, acute or intermittent, clinical manifestations, including fever, headache, and fatigue, often followed by chronic symptoms resulting from long-term complications (e.g., joint, back, and muscular pain) (Corbel et al., 2006).

In Tanzania, brucellosis is considered a high-priority zoonosis based on, among other factors, the widespread distribution, and social and economic impacts (U.S. Agency for International Development (USAID), USAID Preparedness and Response Project (P&R), and U.S. Centers for Disease Control and Prevention (CDC), 2017). Epidemiological surveys indicate that the prevalence of brucellosis is particularly high in the pastoral communities of northeastern regions. In this part of the country, the disease is one of the most common bloodstream infections in humans and

over 6% of cattle are seropositive (Bodenham et al., 2020, 2021). Findings from the studies described in Chapters IV and V demonstrate that brucellosis causes significant monetary costs and disease burden in these communities, including in the Ngorongoro Conservation Area (NCA). The NCA is a protected area with an estimated population of about 100,000 people, 80% of which are Maasai pastoralists, who keep around 115,000 cattle and 180,000 sheep and goats (Government of The United Republic of Tanzania, 2019; Manzano and Yamat, 2018; Tanzania Wildlife Research Institute, 2016).

Mass livestock vaccination is often recommended to control brucellosis in settings such as northeastern Tanzania, where the prevalence is high and veterinary services have limited resources (Bodenham et al., 2020, 2021; Ducrotoy et al., 2017; Mtui-Malamsha, Fasina, and Aguanno, 2022). The safest and most effective brucellosis vaccines currently available are live-attenuated and host-specific. These include *B. abortus* strain 19 (S19) in cattle and *B. melitensis* strain Rev-1 in sheep and goats. Both vaccines can be administered subcutaneously or topically on the conjunctiva (Ducrotoy et al., 2017).

Several factors must be considered to develop a safe and successful vaccination strategy. The subcutaneous administration of S19 in cattle and Rev-1 in sheep and goats may cause severe adverse reactions. These include abortion, particularly if the vaccine is given mid-pregnancy, milk shedding of the vaccine strain, and serological interference, which makes it difficult to differentiate infected from vaccinated animals. The conjunctival administration of the reduced dose ($5 \times 10^9$ viable organisms) of S19 in cattle and standard dose of Rev-1 in sheep and goats (between $0.5 \times 10^9$ and $2.0 \times 10^9$ viable organisms) minimises some of these adverse effects (Fensterbank and Plommet, 1979; OIE, 2019). The probability of abortion and mammary excretion of the vaccine strain in the milk is likely below 1% in cattle vaccinated by the conjunctival route (Ducrotoy, 2014). In contrast, vaccination of sheep and goats through this route during mid-pregnancy can result in a probability of abortion that exceeds 60% (Blasco, 1997; Fensterbank, Pardon, and Marly, 1982a,b; Zundel et al., 1992). A reduced dose of Rev-1 (lower than $1 \times 10^8$) is associated with a lower risk of abortion in sheep, but the efficacy is largely compromised (Zundel et al., 1992). Alternatively, to minimise the risk of abortion in animals vaccinated by the conjunctival route, particularly with the standard dose in sheep and goats, the vaccine must be administered at specific time windows when the proportion of pregnant animals is as low as possible, i.e., during calving/lambing/kidding, lactation or before mating (Bagués et al., 1989; Blasco, 1997, 2010; Blasco and Molina-Flores, 2011; Ducrotoy et al., 2017; OIE, 2019; Perez, Marín, and Grilló, 1995).

One dose of S19 or Rev-1 is sufficient to confer long-term immunity against brucellosis, which likely lasts the entire lifespan of the vaccinated animal (Díaz-Aparicio, Hernández, and Suárez-Güemes, 2004; Manthei, 1968; Plommet and Fensterbank, 1976). In northern Tanzania, the livestock population turnover rate is between 20 and 35%, depending on the species and production system (SEEDZ dataset, Chapter 4). At this rate, only around one-third of the livestock population is unprotected the year after a first successful (with high coverage) mass vaccination campaign for brucellosis. This is a relatively small proportion of mostly sexually immature animals that play a minor role in disease transmission and can reasonably be excluded from vaccination to maximise the cost-effectiveness of the control programme. However, in the second year after the mass vaccination campaign, this proportion of unprotected, unvaccinated livestock increases to more than half, and many may become infected and transmit the disease. A mass vaccination campaign against brucellosis every two years is then recommended in this setting (Ducrotoy et al., 2017).

This study aimed to estimate and compare the monetary costs, monetary benefits (in averted production losses in the livestock sector and averted productivity losses and health-related out-of-pocked expenditure in the human sector), and health utility (in DALYs averted) of a hypothetical livestock vaccination programme to control brucellosis in the NCA, northern Tanzania.

## 6.2 Methods

### 6.2.1 Reference and alternative scenarios of livestock vaccination for brucellosis

The main hypothetical strategy for livestock vaccination under evaluation in this study (reference scenario) consisted of mass vaccination, through conjunctival instillation, of cattle, sheep, and goats, every two years. Sheep and goats were considered together as a single species throughout this study. In each vaccination year, the vaccine would be administered immediately after a calving, lambing, and kidding season, or before mating. The vaccines S19 (supplied by the Tanzania Vaccine Institute) and Rev-1 (under the commercial name Ocurev, supplied by CZ Vaccines, Spain) were assumed to be used in cattle ($5 \times 10^9$ viable organisms; reduced dose) and sheep and goats ($1\text{-}2 \times 10^9$ viable organisms; standard dose), respectively (Blasco, 2010; OIE, 2019). The reduced dose (in cattle), route, and time

windows for vaccination aimed to (i) minimise the possible side effects of the vaccine, including abortion, mammary infection, and excretion of the vaccine strain in the milk, and (ii) avoid a persistent antibody response that could potentially affect the ability to distinguish vaccinated from infected animals in the future.

Under this reference scenario, mass vaccination of cattle, sheep, and goats would happen five times in ten years (at years one, three, five, seven, and nine). The benefits and costs of vaccination were estimated over this period and the subsequent ten years. It was assumed that the efficacy (proportion of vaccinated animals that become protected from infection with *Brucella* spp.) of both S19 and Rev-1 was 70% (El Idrissi et al., 2001; Fensterbank, Pardon, and Marly, 1982a; Oliveira et al., 2021), and the proportion of eligible animals that would be vaccinated was 75%. It was assumed that the immunity conferred by the vaccine would cover the entire lifespan of the vaccinated animal (Alton, 1968; Manthei, 1968).

It was assumed that the prevalence of brucellosis in livestock and the incidence of brucellosis in humans would be monitored via a pre-existing surveillance system throughout the vaccination programme at no additional cost. A target control prevalence in livestock at the end of the vaccination programme (ten years) was set at 2%, a value below which strategies based on test and slaughter are often recommended (European Commission, 2001).

In many settings where reproduction is highly synchronised, all animals over three months old, except bulls, are eligible for vaccination. In this study, given that reproduction in the NCA is often not well synchronised, it was assumed that animals in the second or third third of pregnancy were known to livestock keepers and excluded from vaccination. The proportions of cattle, sheep, and goats eligible for vaccination in the NCA, calculated assuming a constant birth rate throughout the year (worst-case scenario; high expected number of adult females in the second or third third of pregnancy at any time), are shown in Table 6.1. In total, 33% of cattle and 17% of sheep and goats were not eligible for vaccination. The livestock population in the NCA was made of 115,562 ($\pm$ 16,053) cattle and 181,281 ($\pm$ 23,947) sheep and goats (Tanzania Wildlife Research Institute, 2016).

**Table 6.1:** Proportion of animals in the NCA eligible (and non-eligible) for vaccination, by species and age-sex group.

| Species | Age-sex group | Eligible(%) | Non-eligible (%) |
|---|---|---|---|
| Cattle | Juveniles | 75 | 25 |
| | Adult male | 0 | 100 |
| | Adult female | 78 | 22 |
| | Total | 67 | 33 |
| Sheep and goats | Juveniles | 75 | 25 |
| | Adult male | 100 | 0 |
| | Adult female | 84 | 16 |
| | Total | 83 | 17 |

Non-eligible juveniles (cattle, and sheep and goats) are animals younger than three months old. Non-eligible adult females (cattle, and sheep and goats) are pregnant animals in the second or third third of the pregnancy. The values assumed a constant birth rate over time and were obtained from the Social, Environmental, and Economic Drivers of Zoonotic disease project (SEEDZ project; University of Glasgow).

To assess the influence of key variables on the outcomes of cost-benefit and cost-utility analyses, alternative scenarios of livestock vaccination were evaluated. Each scenario was the result of different combinations of (i) species to be vaccinated (variable 'S'), (ii) frequency of vaccination (variable 'F'), (iii) efficacy of the vaccine used (variable 'E'), and (iv) proportion of eligible animals to be vaccinated (variable 'P'). The following options were considered:

- Species to be vaccinated: cattle only ($S_C$), sheep and goats only ($S_S$), and both ($S_B$, cattle and sheep and goats)
- Frequency of vaccination: annual ($F_A$), and biennial ($F_B$)
- Efficacy of the vaccine used: 50% ($E_{50}$), 70% ($E_{70}$), and 90% ($E_{90}$)
- Proportion of eligible animals to be vaccinated: 50% ($P_{50}$), 75% ($P_{75}$), and 100% ($P_{100}$)

The content inside the parenthesis is used for scenario identification. For instance, a scenario in which 50% of eligible cattle only (not sheep or goats) are vaccinated annually with a vaccine that has an efficacy of 50% is named $S_CF_AE_{50}P_{50}$. All the assumptions of the reference vaccination programme (e.g., duration, vaccines, dose, administration route, and time window for vaccination) also applied to the alternative scenarios.

### 6.2.2 Model estimation of the costs of the livestock vaccination programme

The cost of the livestock vaccination programme was made up of two cost types: i) information campaigns; and ii) vaccination.

Before each vaccination run, an information campaign is assumed to support communication of the programme's objectives to the community, promote engagement with livestock keepers, and increase adherence to the programme. The main activities in this information campaign were (i) large two-day meetings with village leaders, executive staff (i.e., government officials), livestock keepers, and other community members, (ii) radio programmes disseminating interviews with village leaders, and (iii) circulation of video clips about the control programme on social media. The detailed costing of one information campaign is shown in Appendix E.1.

The cost of livestock vaccination was estimated as the sum of consumables, transport, labour, and cold chain costs. All costs were assumed to occur in each vaccination run, except the cold chain costs (purchase of two fridges and eight cool boxes), which were assumed to occur in the first year only. The detailed costing of the first vaccination run is shown in Appendix E.2. It was assumed that eight teams of vaccinators would be needed. Each team comprised two livestock field officers and two community animal health workers. Four cars, with one driver each, would be used to transport the eight teams of vaccinators (two teams per car). Each team of vaccinators was expected to vaccinate an average of 500 animals per day (PERT distribution; minimum: 250; maximum: 750) (personal communication with governmental officials).

The cost of the livestock vaccination programme in each vaccination year ($C_t$) was discounted at 3%, using the following equation:

$$DC_t = \frac{C_t}{(1+0.03)^t} \tag{6.1}$$

where $DC_t$ is the present value (discounted) cost of the livestock vaccination programme in year $t$. The total cost of the livestock vaccination programme (TC) is the sum of present value costs in all vaccination years.

### 6.2.3 Model estimation of the benefits and utility of the livestock vaccination programme

A compartmental, discrete-time, susceptible-infected (SI) model was designed to represent brucellosis transmission dynamics between livestock (cattle and sheep and goats) and from livestock to humans. In addition to susceptible and infected compartments for each host species, a vaccinated compartment was used to represent the immunisation of livestock against brucellosis. It was assumed that human-human transmission does not occur. The model diagram is shown in Fig. 6.1.

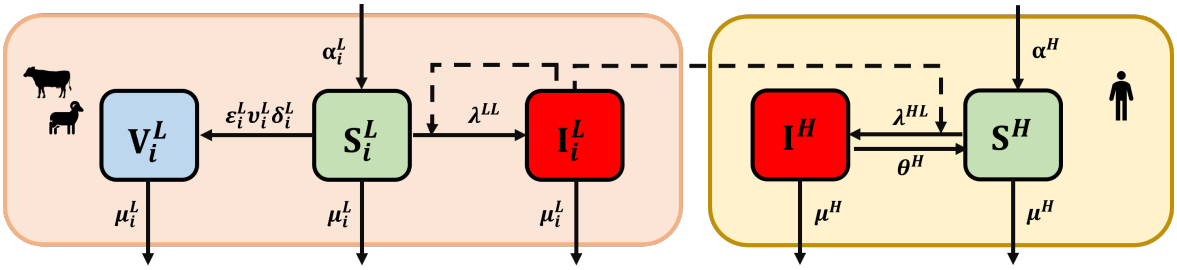



**Figure 6.1:** Diagram of the compartmental, discrete-time, brucellosis transmission model used to estimate the effect of livestock vaccination on disease prevalence in livestock (left, orange box) and humans (right, yellow box). Subscript $i$: livestock species - cattle or sheep and goats; superscript $L$: livestock; superscript $H$: humans; $V$: number of vaccinated individuals; $S$: number of susceptible individuals; $I$: number of infected individuals; $\alpha$: birth rate; $\mu$: death rate; $\varepsilon$: vaccine efficacy (variable 'E'); $v$: proportion of eligible animals that is administered a vaccine (variable 'P'); $\delta$: proportion of animals eligible to be vaccinated (Table 6.1); $\theta$: waning immunity rate in humans; $\lambda^{LL}$: force of infection within and between livestock species; $\lambda^{HL}$: force of infection from livestock to humans.

The population sizes of livestock and humans were kept constant by setting the death rate ($\mu$) equal to the birth rate ($\alpha$). A susceptible individual is equally likely to be vaccinated as is an infected or previously vaccinated individual. The difference equations used were as follows (Eqs. 6.2):

$$
\begin{aligned}
S^L_{i,t+1} &= S^L_{i,t} + \alpha^L_i N^L_{i,t} - \beta_{ii} S^L_{i,t} \frac{I^L_{i,t}}{N^L_{i,t}} - \sum_{\substack{j=1 \\ j\neq i}}^{n} \beta_{ij} S^L_{i,t} \frac{I^L_{j,t}}{N^L_{j,t}} - \mu^L_i S^L_{i,t} - \varepsilon^L_i \nu^L_{i,t} \delta^L_i S^L_{i,t} \\
I^L_{i,t+1} &= I^L_{i,t} + \beta_{ii} S^L_{i,t} \frac{I^L_{i,t}}{N^L_{i,t}} + \sum_{\substack{j=1 \\ j\neq i}}^{n} \beta_{ij} S^L_{i,t} \frac{I^L_{j,t}}{N^L_{j,t}} - \mu^L_i I^L_{i,t} \\
V^L_{i,t+1} &= V^L_{i,t} + \varepsilon^L_i \nu^L_{i,t} \delta^L_i S^L_{i,t} - \mu^L_i V^L_{i,t} \\
S^H_{t+1} &= S^H_t + \alpha^H N^H_t - \sum_{i=1}^{n} \beta_{Hi} S^H_t \frac{I^L_{i,t}}{N^L_{i,t}} - \mu^H S^H_t + \theta^H I^H_t \\
I^H_{t+1} &= I^H_t + \sum_{i=1}^{n} \beta_{Hi} S^H_t \frac{I^L_{i,t}}{N^L_{i,t}} - \mu^H I^H_t - \theta^H I^H_t
\end{aligned}
\tag{6.2}
$$

where $t$ is the time (simulation year, from zero to 19), the subscripts $i$ and $j$ indicate livestock species, the superscripts $L$ and $H$ indicate livestock and humans, respectively, $N$ is the total number of individuals, $V$ is the number of vaccinated individuals, $S$ is the number of susceptible individuals, $I$ is the number of infected individuals, $\varepsilon$ is the vaccine efficacy (variable 'E'), $\nu$ is the proportion of eligible animals that is administered a vaccine (variable 'P'), $\delta$ is the proportion of animals eligible to be vaccinated (Table 6.1), $\theta$ is the waning immunity rate in humans, $\beta_{ii}$ is the transmission rate between animals of species $i$, $\beta_{ij}$ is the transmission rate from animals of species $j$ to animals of species $i$, and $\beta_{Hi}$ is the transmission rate from animals of species $i$ to humans.

The transmission rates ($\beta_{ii}$, $\beta_{ij}$, and $\beta_{Hi}$) were calculated assuming that brucellosis is in endemic equilibrium, i.e., the incidence in livestock ($Y^L_i$) and humans ($Y^H$) remains steady and the effective reproductive number ($R_e$), is 1.00. The equations used to calculate the transmission rates were as follows (Eqs. 6.3):

$$
\begin{aligned}
\beta_{ii} &= \frac{Y^L_i \rho}{S^L_i \frac{I^L_i}{N^L_i}} \\
\beta_{ij} &= \frac{Y^L_i (1-\rho)}{S^L_i \frac{I^L_j}{N^L_j}} \\
\beta_{Hi} &= \frac{Y^H \pi_i}{S^H \frac{I^L_i}{N^L_i}}
\end{aligned}
\tag{6.3}
$$

where $i = 1,2$, $j = 1,2$, and $j \neq i$. $\rho$ is the proportion of livestock infections that occur due to transmission within species (cattle to cattle, or sheep and goats to sheep and goats), and $\pi_i$ is the proportion of human infections due to transmission from livestock species $i$.

The basic reproductive number ($R_0$) is *the average number of secondary infections produced when one infected individual is introduced into a host population where everyone is susceptible* (Anderson and May, 1991). The $R_0$ of the brucellosis transmission model was calculated as the spectral radius (largest eigenvalue) of the next-generation matrix $Q$ (Diekmann, Heesterbeek, and Metz, 1990; Diekmann, Heesterbeek, and Roberts, 2010) (Eq. 6.4):

$$Q = \begin{bmatrix} \frac{\beta_{11}}{\mu_1} & \frac{\beta_{12}}{\mu_2}\frac{N_1}{N_2} \\ \\ \frac{\beta_{21}}{\mu_1}\frac{N_2}{N_1} & \frac{\beta_{22}}{\mu_2} \end{bmatrix} \tag{6.4}$$

The disease transmission model was run for 20 years, firstly under the assumption of no vaccination (*status quo*), and then under reference and alternative scenarios of livestock vaccination. The monetary benefits (averted production losses in livestock, and averted productivity loss and health-related out-of-pocket expenditure in humans) and utility (averted disease burden in disability-adjusted life years, DALYs) of livestock vaccination were estimated as the difference between the outputs of (i) the model run without vaccination (*status quo*) and (ii) the model run with vaccination (reference and alternative scenarios). The production losses per infected animal per year were obtained from Chapter 4. The monetary cost and disease burden per human case were obtained from Chapter 5.

The averted monetary costs in humans in each year ($B_t^H$) were discounted at 3%, using the following equation:

$$DB_t^H = \frac{B_t^H}{(1+0.03)^t} \tag{6.5}$$

where $DB_t^H$ is the present value (discounted) benefits in year $t$, i.e., averted monetary cost in humans in year $t$. The base year ($t$ =0) was assumed to be the present.

The averted production losses in livestock were not discounted because the production losses per infected animal per year were estimated in Chapter 4 in its discounted format. The total benefit of the livestock vaccination programme is the sum of the present value averted monetary costs in humans (HB; averted productivity losses and health-related out-of-pocked expenditure) and present value averted production losses in livestock (LB).

The input parameters and variables in the disease transmission model are shown in Appendix E.3. Given considerable uncertainty around the likely values some model parameters and variables could take, Monte Carlo simulations were run (50,000 iterations) for each model scenario (*status quo*, reference vaccination, and alternative vaccination scenarios).

### 6.2.4 Cost-benefit and cost-utility measures

Two main indicators of the cost-beneficialness and cost-effectiveness of the reference livestock vaccination strategy were computed: the benefit-cost ratio (BCR) and the gross cost per DALY averted (gCDA). Three supplementary indicators were computed: the net present value (NPV), the net cost per DALY averted (nCDA; aggregate net cost approach), and the cost-effectiveness ratio (CER; separable costs approach) (Shaw et al., 2017). These indicators were calculated as follows:

$$
\begin{aligned}
NPV &= \text{LB+HB} - \text{TC} \\
BCR &= \frac{\text{LB+HB}}{\text{TC}} \\
gCDA &= \frac{\text{TC}}{\text{BA}} \\
nCDA &= \frac{\text{TC-LB-HB}}{\text{BA}} \\
CER &= \frac{\frac{\text{HB}}{\text{LB+HB}}\text{TC}}{\text{BA}}
\end{aligned}
\tag{6.6}
$$

where TC is the total present value cost of the livestock vaccination programme (the sum of information campaign and vaccination costs in all vaccination years), and BA is the disease burden (DALYs) averted in humans.

The median, mean, inter-quartile range (50% uncertainty interval), and 2.5 and 97.5 percentiles (95% uncertainty interval) of the NPV, BCR, gCDA, nCDA, and CER are reported. For conciseness, the comparison between the economic viability and effectiveness measures of different alternative livestock vaccination strategies was restricted to BCR and gCDA. Vaccination scenarios with a BCR greater than one were considered cost-beneficial. Vaccination scenarios with a gCDA lower than 2,836 int. $ (the gross domestic product per capita in Tanzania in 2021, World Bank)[1] were considered cost-effective.

### 6.2.5 Elasticity analyses

The influence of input parameters and variables on the BCR and gCDA was assessed through elasticity analyses, which are particularly useful when dealing with a variety of input parameter ranges and units (Åberg et al., 2009). These analyses estimated the percentage change in BCR and gCDA that resulted from a percentage change in input parameters or variable value. These analyses were performed for each input parameter and variable at a time, using the outputs of the reference vaccination scenario ($S_BF_BE_{70}P_{75}$), exclusively.

Elasticity was calculated using a log-log function, as follows (Dayal, 2015):

$$ln(y) = I + E \times ln(x) \tag{6.7}$$

where $y$ is either the BCR or gCDA, $I$ is the regression intercept, $E$ is the elasticity (percentage change in BCR or gCDA that results from a percentage change in input parameters or variable value), and $x$ is the input parameter or variable.

Elasticity analyses to assess the influence of input parameters and variables on the NPV were not performed because NPV varies linearly with BCR, and the logarithm of potentially negative NPV results (indicating that a strategy is not cost-beneficial) is undefined.

1. International Comparison Program, World Bank, World Development Indicators database, Eurostat-OECD PPP Programme: https://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD?locations=TZ

### 6.2.6 Model implementation and statistical analyses

The disease transmission model and Monte Carlo simulations were implemented in R version 4.1.1 (2021-08-10) (R Core Team, 2021). Graphics were produced with ggplot2 version 3.3.5 (Wickham, 2016).

The spearman correlation coefficient was computed using the cor.test function in R to assess the correlation between the basic reproductive number ($R_0$) and the benefit-cost ratio.

## 6.3 Results

### 6.3.1 Reference scenario of livestock vaccination for brucellosis

#### 6.3.1.1 Cost of the livestock vaccination programme

The estimated cost of the information campaigns was 23,049 int. $ per vaccination year. Approximately 60% of this cost was allocated to cover allowances, transportation, venue hire, and food and beverages in the large two-day meeting with village leaders, executive staff (i.e., government officials), livestock keepers, and other community members (more details in Appendix E.1).

The estimated cost of vaccination was 287,319 (95% UI: 246,468-364,151) int. $ in the first year, and 282,916 (95% UI: 242,066-359,748) int. $ in subsequent years. The difference (4,403 int. $) between the median cost of the vaccination in the first year and subsequent years was attributed to capital expenditure (the purchase of fridges and cool boxes in the first year).

The total present value cost of the 10-year vaccination programme (including information campaigns and vaccination) was estimated at 1,368,390 (95% UI: 1,186,279-1,710,905) int. $. The information campaigns were estimated to cost approximately 7.5% (95% UI: 6.0-8.7) of the total cost of the vaccination programme. Approximately 170,930 (95% UI: 158,688-183,188) vaccine doses were estimated to be administered in each vaccination year. Thus, the present value cost of the vac-

cination programme (five vaccination years; including information campaigns and vaccination) per administered vaccine would be 1.6 (95% UI: 1.4-2.0) int. $. All vaccine doses were expected to be administered within 42.7 (95% UI: 31.2-66.3) days in each vaccination year.

#### 6.3.1.2 Epidemiological outcomes, monetary benefits, and utility of the livestock vaccination programme

The estimated basic reproductive number ($R_0$) of brucellosis in the Ngorongoro Conservation Area was 1.04 (95% UI: 1.02-1.06). The expected prevalence of brucellosis over time in livestock and humans under the reference vaccination scenario is shown in Fig. 6.2. The vaccination programme would reduce the estimated prevalence of brucellosis in cattle, sheep and goats, and humans. Over the 20-year time horizon, the prevalence of brucellosis in cattle would decrease from 5.1% (95% UI: 3.4-6.9) to 1.3% (95% UI: 0.9-1.9). In sheep and goats, the prevalence would decrease from 2.2% (95% UI: 0.2-4.6) to 0.6% (95% UI: 0.1-1.2). In humans, the prevalence would decrease from 3.4% (95% UI: 1.4-7.1) to 1.4% (95% UI: 0.5-3.6).

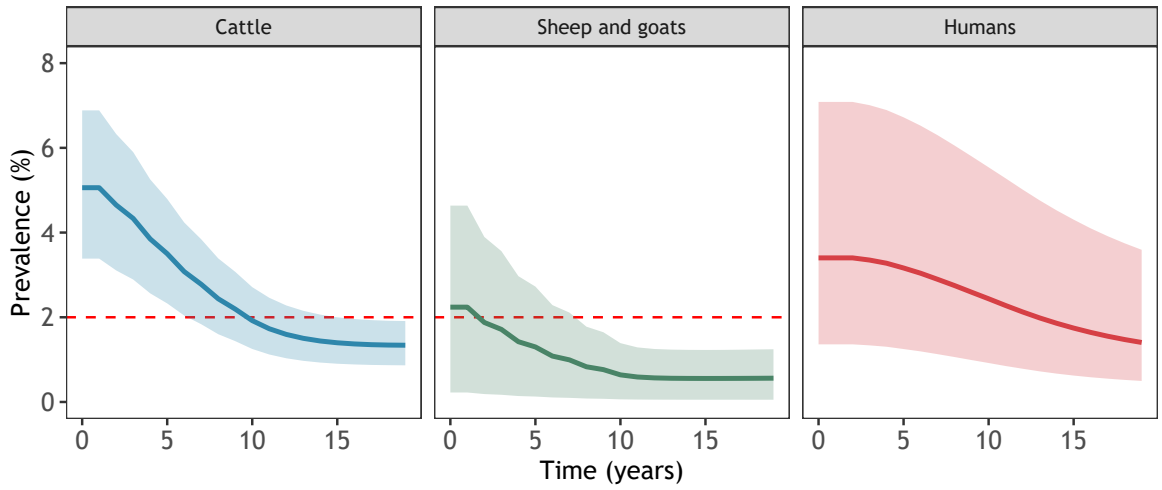



**Figure 6.2:** Estimated prevalence of brucellosis in cattle, sheep and goats, and humans, over the 20-year time horizon, in the Ngorongoro Conservation Area, under the reference vaccination programme (vaccination of 75% of eligible cattle, and sheep and goats, every two years, with a vaccine that has an efficacy of 70%). The solid lines indicate the median. The coloured bands indicate the 95% uncertainty interval obtained from Monte Carlo simulation (50,000 iterations). The red dashed line indicates the target control prevalence in livestock (2%) at the end of the vaccination programme (ten years).

Over the 20-year time horizon, the vaccination programme would reduce monetary costs and disease burden attributable to brucellosis considerably. The effect of the programme on these costs and disease burden are shown in Fig. 6.3. The livestock production losses averted due to the vaccination programme were estimated at 4,718,926 (95% UI: 1,780,506-13,260,088) int. $, 88.6% of which in cattle. The averted monetary costs (productivity losses and health-related out-of-pocket expenditure) in humans were estimated at 1,218,113 (95% UI: 517,654-2,180,499) int. $. The averted disease burden in humans was estimated at 6,271 (95% UI: 2,492-12,362) DALYs.

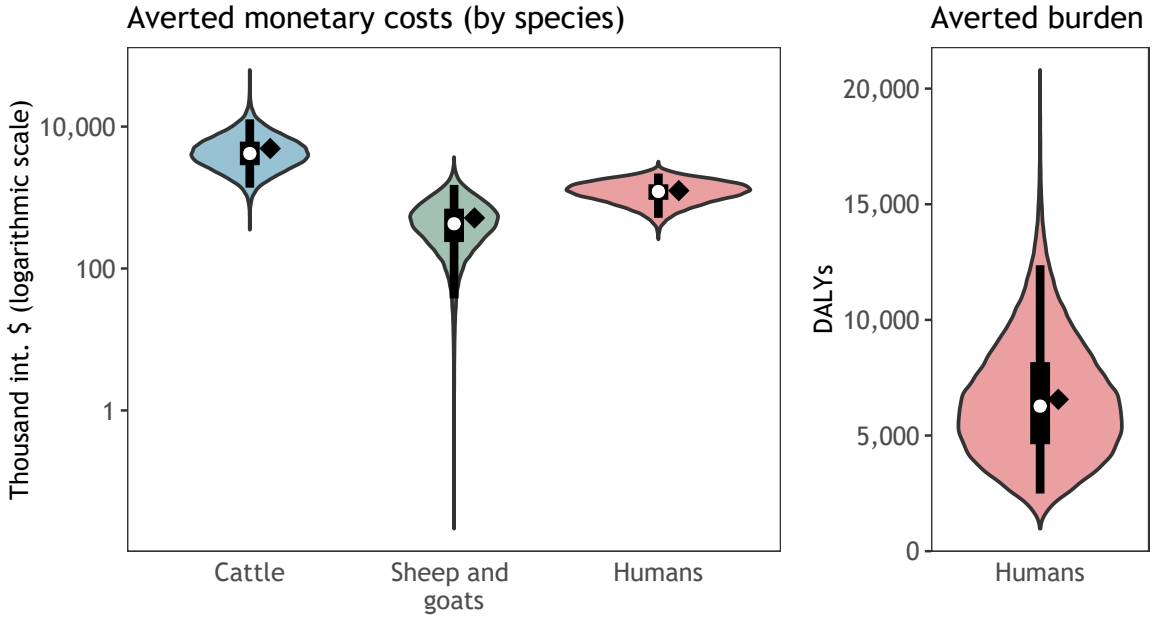



**Figure 6.3:** Estimated averted monetary costs (production losses in livestock, and productivity losses and health-related out-of-pocket expenditure in humans) and disease burden (humans) attributable to brucellosis due to vaccination (reference scenario: vaccination of 75% of eligible cattle, and sheep and goats, every two years, with a vaccine that has an efficacy of 70%), in the Ngorongoro Conservation Area. White dots indicate the median, black diamonds the mean, black boxes the inter-quartile range (50% UI), and black lines the 2.5 and 97.5 percentiles (95% UI). Uncertainty intervals were obtained from Monte Carlo simulation (50,000 iterations). The monetary costs in the y-axis are in present values and on the logarithmic scale. Int. $: International dollars. DALYs: Disability-adjusted life-years.

### 6.3.1.3 Cost-benefit and cost-utility measures

The monetary benefits and health utility of the vaccination programme would likely outweigh its costs (Fig. 6.4). The benefit-cost ratio (BCR) was estimated at 4.3 (95% UI: 2.0-10.6). The gross cost per DALY averted (gCDA) was estimated at 222 (95% UI: 109-566) int. $. The net present value (NPV) was estimated at 4.6 (95% UI: 1.5-13.1) million int. $. The net cost per DALY averted (nCDA) was estimated at -736 (95% UI: -2,800 - -227) int. $. The cost-effectiveness ratio (CER) was estimated at 45 (95% UI: 16-110) int. $.

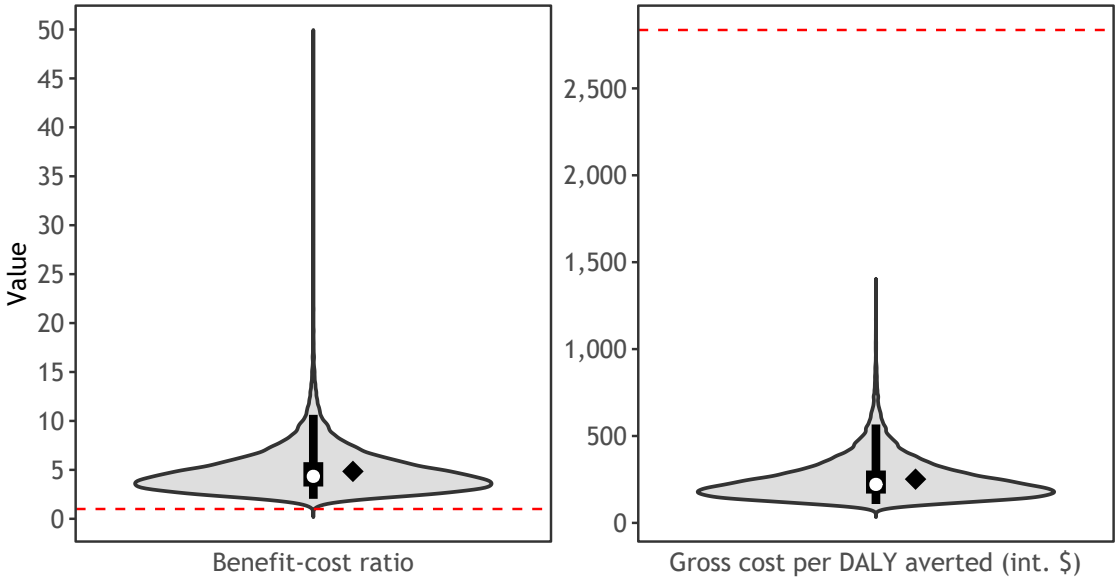



**Figure 6.4:** Estimated benefit-cost ratio (BCR, left) and gross cost per DALY averted (gCDA, right) of the vaccination programme (reference scenario: vaccination of 75% of eligible cattle, and sheep and goats, every two years, with a vaccine that has an efficacy of 70%) in the Ngorongoro Conservation Area. White dots indicate the median, black diamonds the mean, black boxes the inter-quartile range (50% UI), and black lines the 2.5 and 97.5 percentiles (95% UI). Uncertainty intervals were obtained from Monte Carlo simulation (50,000 iterations). The horizontal, red, dashed lines indicate a BCR of 1.0 (the monetary benefits equal the monetary costs) on the left panel and 2,836 int. $ (the gross domestic product per capita in Tanzania in 2021, World Bank)[1] on the right panel.

The BCR was positively correlated with the basic reproductive number ($R_0$). The Spearman's correlation coefficient between BCR and $R_0$ was 0.26 (p-value $< 0.001$).

The monetary benefits of the vaccination programme to the livestock sector alone (excluding the monetary benefits to humans) would outweigh its costs, as shown in Fig. 6.5. The monetary benefits to humans were slightly lower than the costs of the vaccination programme.

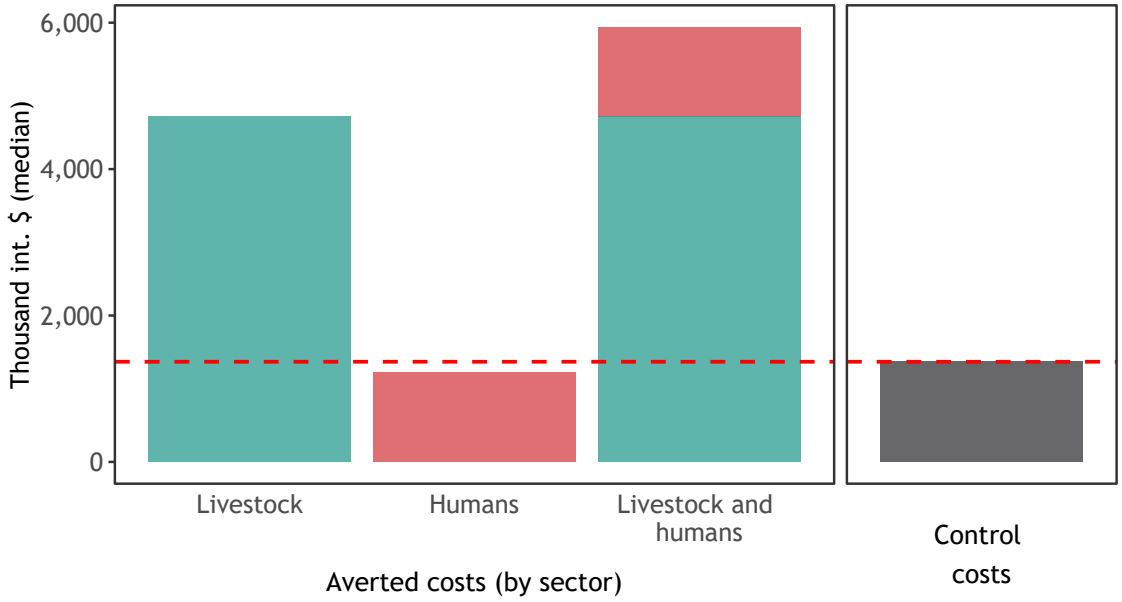



**Figure 6.5:** Median monetary benefits (averted monetary costs, left panel) and control costs (right panel) of the livestock vaccination programme by sector (livestock, humans, and joint livestock and humans). The horizontal, red, dashed line indicates the median cost of the livestock vaccination programme (control costs).

### 6.3.1.4 Elasticity analyses

The results of elasticity analyses on the BCR and gCDA are shown in Figs. 6.6 and 6.7. The range of parameter values that entered the elasticity analyses is shown in Appendix E.4.

The input parameters most influential to estimates of BCR (parameter elasticity greater than 0.5) were the production losses (per infected animal per year) and brucellosis prevalence, in cattle. An increase of 1% in the production losses in cattle, the most influential input parameter, would increase the BCR by 0.70%. Other variables positively and significantly associated with BCR were the brucellosis prevalence in sheep and goats and humans, the birth and death rates of the

cattle and human populations, the number of animals vaccinated per team per day, the cattle population size, the monetary cost per human case, and the production losses in sheep and goats. In contrast, increasing the population size of sheep and goats would decrease the BCR.

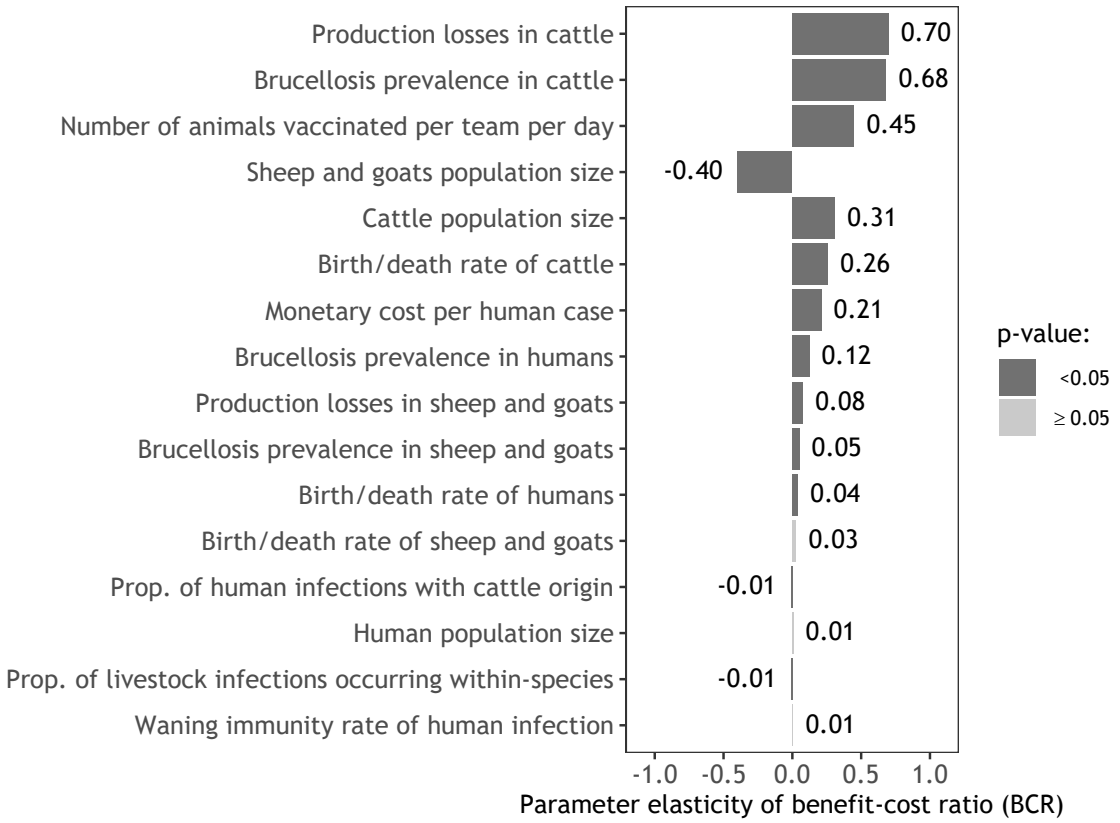



**Figure 6.6:** Tornado plot showing the parameter elasticity of benefit-cost ratio (percentage change in benefit-cost ratio when parameter values change by 1%) of the livestock vaccination programme (reference scenario: vaccination of 75% of eligible cattle, and sheep and goats, every two years, with a vaccine that has an efficacy of 70%) in the Ngorongoro Conservation Area (50,000 model iterations). The colours of the bars indicate the significance of the parameter elasticity estimate (dark and light grey indicate p-value $<$ 0.05 and p-value $\geq$ 0.05, respectively). Prop.: proportion.

The most influential input parameter to estimates of gCDA (parameter elasticity greater than 0.5, in absolute terms) was the brucellosis prevalence in humans. An increase of 1% in the brucellosis prevalence in humans would decrease the gCDA by 0.66%. Among the other variables with a significant p-value (p-value$<$0.05), increasing the population size of cattle and sheep and goats, the proportion of human infections with cattle origin, and the brucellosis prevalence in cattle would increase the gCDA. In contrast, increasing the number of animals vaccinated per team per day, the birth/death rates of the livestock (cattle, sheep, and goats) and human populations, and the human population size would decrease the gCDA.

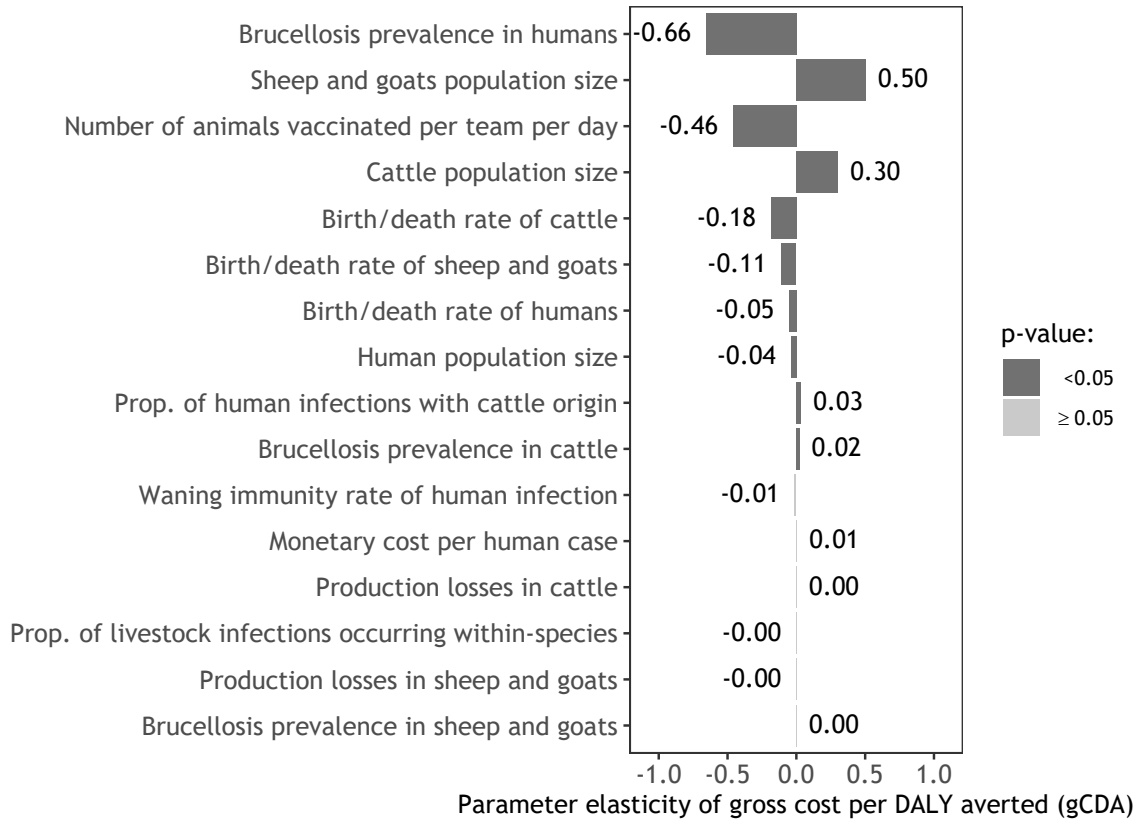



**Figure 6.7:** Tornado plot showing the parameter elasticity of gross cost per DALY averted (percentage change in the gross cost per DALY averted when parameter values change by 1%) of the livestock vaccination programme (reference scenario: vaccination of 75% of eligible cattle, and sheep and goats, every two years, with a vaccine that has an efficacy of 70%) in the Ngorongoro Conservation Area (50,000 model iterations). The colours of the bars indicate the significance of the parameter elasticity estimate (dark and light grey indicate p-value $< 0.05$ and p-value $\geq 0.05$, respectively). Prop.: proportion.

## 6.3.2 Alternative scenarios of livestock vaccination for brucellosis

### 6.3.2.1 Outcome prevalence, benefit-cost ratio (BCR), and gross cost per DALY averted (gCDA)

The estimates of benefit-cost ratio (BCR) and gross cost per DALY averted (gCDA) and whether the prevalence of brucellosis in livestock (in cattle, and sheep and goats) was below the control target (2%) at the end of the vaccination programme (ten years), for each vaccination scenario, are shown in Fig. 6.8.

All scenarios had a median BCR greater than 1.0 and a median gCDA lower than 2,836 int. $ (the gross domestic product per capita in Tanzania in 2021)[1]. The 95% uncertainty intervals of BCR and gCDA estimates also did not cross these thresholds (1.0 and 2,836 int. $, respectively), except for 12 scenarios in the case of BCR ($S_SF_AE_{50}P_{50}$, $S_SF_AE_{50}P_{75}$, $S_SF_AE_{50}P_{100}$, $S_SF_AE_{70}P_{50}$, $S_SF_AE_{70}P_{75}$, $S_SF_AE_{70}P_{100}$, $S_SF_AE_{90}P_{50}$, $S_SF_AE_{90}P_{75}$, $S_SF_AE_{90}P_{100}$, $S_BF_AE_{50}P_{100}$, $S_SF_BE_{50}P_{75}$, and $S_SF_BE_{50}P_{100}$). Nine out of these 12 scenarios consisted of annual vaccination of sheep and goats only.

The vaccination scenarios that were most cost-beneficial were those that consisted of cattle-only vaccination every two years, using a vaccine with high efficacy ($S_CF_BE_{90}P_{50}$, $S_CF_BE_{90}P_{75}$, $S_CF_BE_{90}P_{100}$, $S_CF_BE_{70}P_{50}$, $S_CF_BE_{70}P_{75}$, and $S_CF_BE_{70}P_{100}$). These scenarios would also result in a relatively low gCDA.

Only 13 (24.1%) out of 54 scenarios would result in a median prevalence of brucellosis at ten years below the 2% target in both cattle and sheep and goats. These 13 successful scenarios had the following characteristics: i) four included vaccination of cattle only, and nine included vaccination of both cattle and sheep and goats; ii) nine consisted of annual vaccination, and four of biennial vaccination; iii) 12 scenarios included a vaccine with a minimum efficacy of 70%, while one included a vaccine with an efficacy of 50%; and, iv) 12 scenarios had a minimum proportion of eligible animals to be vaccinated of 75%, while one would only cover 50%.

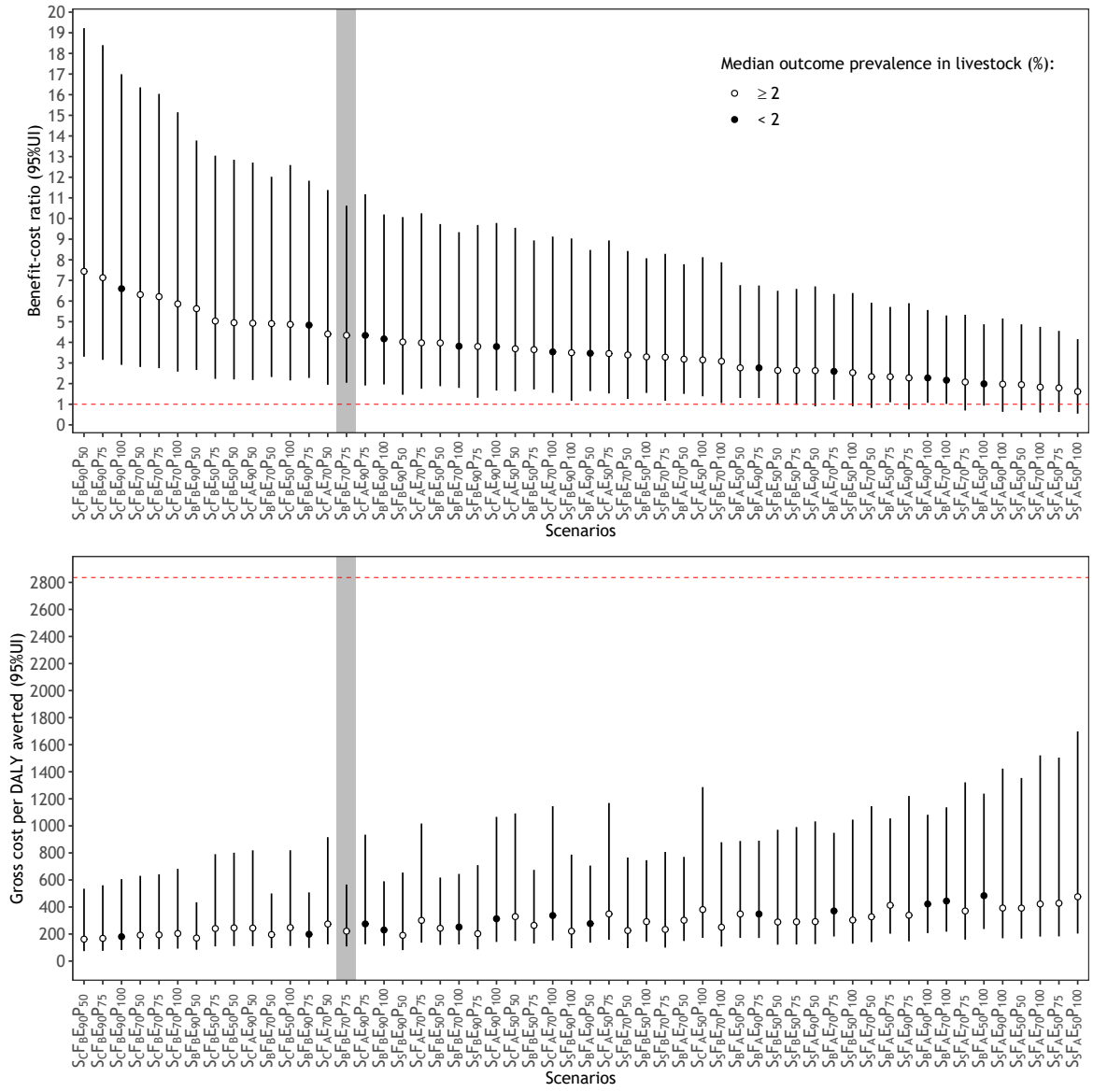



**Figure 6.8:** Estimates of benefit-cost ratio (BCR) and gross cost per DALY averted (gCDA) and whether the median prevalence of brucellosis in livestock (in cattle, and sheep and goats) was below the control target (2%) at the end of the vaccination programme (ten years), for each vaccination scenario, in the Ngorongoro Conservation Area. Dots indicate the median. Empty dots indicate a median outcome prevalence greater than or equal to 2%. Full dots indicate a median outcome prevalence lower than 2%. Vertical black lines indicate the 95% uncertainty intervals obtained from Monte Carlo simulation (50,000 iterations). The horizontal, red, dashed lines indicate a BCR of 1.0 (the monetary benefits equal the monetary costs) on the upper panel, and 2,836 int. $ (the gross domestic product per capita in Tanzania in 2021, World Bank)[1] on the lower panel. The grey vertical band indicates the reference scenario: vaccination of 75% of eligible cattle, and sheep and goats, every two years, with a vaccine that has an efficacy of 70%. The scenarios were named based on the following variables: i) species to be vaccinated - cattle only ($S_C$), sheep and goats only ($S_S$), and both ($S_B$, cattle and sheep and goats); ii) frequency of vaccination - annual ($F_A$), and biennial ($F_B$); iii) efficacy of the vaccine used - 50% ($E_{50}$), 70% ($E_{70}$), and 90% ($E_{90}$); and, iv) proportion of eligible animals to be vaccinated - 50% ($P_{50}$), 75% ($P_{75}$), and 100% ($P_{100}$).

## 6.4 Discussion

### 6.4.1 Interpretation of results

This study estimated the monetary costs, monetary benefits (in averted production losses in the livestock sector and averted productivity losses and health-related out-of-pocked expenditure in the human sector), and utility (in DALYs averted) of a hypothetical livestock vaccination programme to control brucellosis in the Ngorongoro Conservation Area (NCA), northern Tanzania. Under the reference control strategy, 75% of eligible cattle, and sheep and goats in the NCA would be vaccinated on the conjunctiva every two years, over a period of ten years, with a vaccine that has an efficacy of 70%. The benefits and costs of vaccination were estimated over this period and the subsequent ten years (20-year time horizon).

The total monetary benefits of the livestock vaccination programme (as averted disease costs) would likely outweigh its costs. An investment of around 1.4 million int. $ (present value) in the 10-year vaccination programme would yield a median of approximately 6.0 million int. $ (present value) in monetary benefits, representing a significant return on investment. The benefits of brucellosis control would be over four times greater than its costs. If the benefits in the livestock sector alone were considered (excluding averted productivity losses and health-related out-of-pocket expenditure in humans), the control programme would likely still be cost-beneficial. The benefits of livestock vaccination to the livestock sector were greater than those to the human sector.

According to the cost-utility analyses of livestock vaccination for brucellosis in the NCA, the median gross cost per DALY averted was 222 (95% UI: 109-566) int. $. This value indicates the 'price' of avoiding one DALY and must be compared to a threshold to decide whether the intervention is cost-effective (Leech et al., 2018). The threshold used in this study was Tanzania's gross domestic product per capita in 2021 (2,836 int. $[1]), based on recommendations from the World Health Organization's Choosing Interventions that are Cost–Effective project (WHO-CHOICE) (Bertram et al., 2016; Hutubessy, Chisholm, and Edejer, 2003; Robinson et al., 2017). According to these recommendations, interventions that cost, per DALY averted, less than three times the GDP per capita can be considered cost-effective (and highly cost-effective if costing less than once the GDP per capita). However, this per capita GDP-based threshold has several weaknesses (Marseille et al., 2015). Firstly, although livestock vaccination for brucellosis would be considered highly cost-effective under this threshold, it might not indicate best use of public funds.

It is essential to know how such cost-effectiveness estimates compare with those of other potential interventions targeting different diseases and conditions (Marseille et al., 2015). In Tanzania, this comparison exercise as a tool for determining healthcare priorities in the country is challenging, though. The currently available evidence of the cost-effectiveness of health interventions in Tanzania is insufficient, particularly in areas other than malaria, HIV-AIDS, maternal and perinatal health, and tuberculosis (Robberstad and Hemed, 2010). Other problems of per-capita GDP-based thresholds are that (i) they are often easily reached, which means that only a small number of interventions can be dismissed, (ii) they assume that a country is willing to pay that value to avoid one DALY, without application of appropriate revealed- and stated-preference methods, and (iii) they do not adequately reflect affordability, i.e., a country might not necessarily afford to deliver an intervention that costs, for instance, as much as the GDP-per capita to avoid one DALY (Leech et al., 2018; Marseille et al., 2015).

### 6.4.2 Comparison with previous research

The results obtained in this study are consistent with those obtained by other researchers in different settings, where brucellosis control interventions have generally been reported as cost-beneficial, even if the studies considered the benefits to the livestock sector only (excluding the benefits to the human health sector) (Kiiza et al., 2023). The benefits of brucellosis control interventions based on livestock vaccination, with or without additional measures (e.g., test and slaughter), were found to outweigh its costs in studies conducted in England and Wales (cattle), the United States (cattle), Ivory Coast (cattle), Nigeria (cattle), Mongolia (cattle, sheep, and goats), Colombia (cattle), Turkey (cattle, sheep, and goats), Brazil (cattle), Albania (sheep and goats), Mexico (goats), India (cattle and buffalo), Tibet (yaks), and Iraq (sheep and goats) (Al Hamada et al., 2021; Alshwany, 2019; Alves et al., 2015; Amosson et al., 1981; Astaiza-Martínez, Benavides-Melo, and Díaz-Rojas, 2012; Bardhan et al., 2020; Bruce, 2016; Camus, 1980; Can and Yalcin, 2014; Dietrich, Amosson, and Crawford, 1986; Ferreira et al., 2023; Hugh-Jones, Ellis, and Felton, 1975; Liu, 1979; Montiel et al., 2015; Peck and Bruce, 2017; Rikin, 1988; Roth et al., 2003; Singh et al., 2018b; van Asseldonk, Bergevoet, and Ge, 2013; Zeng et al., 2019).

Studies conducting cost-benefit analyses of livestock vaccination for brucellosis in Mongolia, Turkey, and Albania have explicitly included private human health sector costs averted (out-of-pocket expenditure and loss of income) in the definition of benefits of livestock vaccination (Bruce, 2016; Peck and Bruce, 2017; Roth et al.,

2003; van Asseldonk, Bergevoet, and Ge, 2013). In the three countries, the benefits of livestock vaccination to the livestock sector were greater than those to the human sector. This knowledge of the greater share of benefits to the livestock sector compared to the human sector may help inform policy decisions around the relative contribution of each sector to cover the vaccination costs.

A study conducted in the Mvomero District of the Morogoro Region in Tanzania found that nearly 60% of livestock keepers were willing to pay 3,000 Tanzania Shillings (4.1 int. $[2]) to vaccinate cattle of all ages (Asakura et al., 2018b). A higher percentage of livestock keepers (around 90%) would be willing to pay for the vaccination of newborn calves only. This vaccine price (3,000 Tanzania Shillings) was set based on pricing information obtained from a private veterinary medicines shop, and it would be considerably more expensive than the S19 sold by the Tanzania Vaccine Institute (800 Tanzania Shillings) (personal communication from a local veterinary officer). Thus, a brucellosis control strategy that relies on at least some contribution from livestock keepers to cover vaccination costs could potentially be viable in this agro-pastoral community of the Morogoro Region. However, some of the problems of willingness-to-pay methodology need to be highlighted. Participants may have a tendency to overestimate their willingness to pay in an effort to conform to social norms (social desirability bias) (Schläpfer, Roschewitz, and Hanley, 2004). Livestock keepers' willingness to pay for vaccination may be influenced by their income and knowledge of brucellosis, which are context-specific. In the same study, only 29 (48.3%) out of 60 Maasai households were willing to accept vaccination of all cattle, demonstrating that the viability of a farmer-led strategy might not hold in an exclusively pastoral setting, such as the NCA.

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2. Based on the World Bank conversion factor of 735.66 TZS (Tanzania Shillings) per int. $ in 2016 obtained from `https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=TZ`

This study in the NCA estimated a gross cost per DALY averted (median of 222 int. $) that was equivalent to 7.8% of Tanzania's gross domestic product per capita in 2021 (2,836 int. $)[1]. In Mongolia and Turkey, the gross cost per DALY averted as a percentage of GDP was 17.2%[3] and 37.2%[4], respectively.

If the Ministry of Health in Tanzania contributed to the livestock vaccination intervention costs in proportion to the monetary benefits to human health (averted productivity losses and health-related out-of-pocket expenditure), the cost-effectiveness ratio (CER) would be 45 (95% UI: 16-110) int. $ per DALY averted (1.6% of GDP per capita, median). Under a similar cost-sharing scenario, in Mongolia, where 34.9%[5] of monetary benefits of the intervention would be to the private human health sector (averted productivity losses and health-related out-of-pocket expenditure), the CER would be 219 int. $[6] per DALY averted (6.0% of GDP per capita)[7]. Similarly, in Turkey, where 10.3%[8] of monetary benefits of the intervention would be to the human health sector (averted out-of-pocket payments for hospitalisation and loss of income), the CER would be 850 int. $[9] per DALY averted (3.8% of GDP per capita)[10].

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3. Under a scenario of 65% vaccine efficacy and 80% of animals being vaccinated; gross cost per DALY averted obtained as 8,957.3 million MNT (tugrik) over 49,027 DALYs; monetary units were converted to international dollars (int. $) using the World Bank conversion factor of 291.28 MNT per int. $ in 2000 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=MN; Mongolia's gross domestic product per capita was 3,643.6 int. $ in 2000: https://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD?locations=MN
4. Under a scenario of vaccination of all young animals; gross cost per DALY averted obtained as 226 million TL (Turkish Lira) over 21,000 DALYs; monetary values were converted to international dollars (int. $) using the World Bank conversion factor of 1.3 TL per int. $ in 2013 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=TR; Turkey's gross domestic product per capita was 22,248.1 int. $ in 2013: https://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD?locations=TR
5. 8,901.5 million MNT (tugrik) of private human health sector benefits (sum of averted out-of-pocket contribution to health costs and household income losses) and 16,611.6 million MNT of private livestock sector benefits
6. Under a scenario of 65% vaccine efficacy and 80% of animals being vaccinated; 63,744 MNT (tugrik; 5% discount rate; 8,957.3 million MNT in intervention costs times 34.9% over 49,027 DALYs averted); monetary values were converted to international dollars (int. $) using the World Bank conversion factor of 291.28 MNT per int. $ in 2000 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=MN
7. Mongolia's gross domestic product per capita was 3,643.6 int. $ in 2000: https://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD?locations=MN
8. 53 million TL (Turkish Lira) in human costs averted and 463 million TL in agricultural loss averted
9. 1,105 TL (Turkish Lira; 5% discount rate; 226 million TL in intervention costs times 10.3% over 21,000 DALYs averted); monetary values were converted to international dollars (int. $) using the World Bank conversion factor of 1.3 TL per int. $ in 2013 obtained from https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=TR
10. Turkey's gross domestic product per capita was 22,248.1 int. $ in 2013: https://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD?locations=TR

### 6.4.3 Potential conservative nature of study findings

The benefits and utility of livestock vaccination for brucellosis estimated in this study are likely conservative. Firstly, the benefits of increased community awareness around brucellosis that would result from the vaccination programme, particularly the information campaign, were not quantified. The information campaign aimed to promote engagement with livestock keepers and increase adherence to the programme to ensure enough vaccination coverage. However, it would also be an opportunity to raise awareness and increase the adoption of safe husbandry practices that would likely reduce disease transmission between livestock and from livestock to humans. Behavioural changes that could significantly reduce disease transmission include hygienic disposal of abortion products and avoiding consumption of raw or undercooked milk and blood (Corbel et al., 2006).

Secondly, the investment in staff training and infrastructure to deliver the brucellosis vaccination campaign would likely yield unmeasured benefits to the control and surveillance of other infectious diseases of livestock. For instance, the fridges and cool boxes budgeted for the brucellosis control programme in the NCA could also be used to store and deliver other vaccines and medicines (e.g., anthrax and foot-and-mouth disease vaccines). This equipment would only be required for a few months each year in the brucellosis vaccination programme.

Thirdly, the expected reduction of livestock and human brucellosis incidence in the NCA due to the livestock vaccination programme would likely have positive downstream effects on the household economy and health service that were not quantified. By reducing household production losses, livestock vaccination for brucellosis in the NCA could enable many children, particularly girls, to access education, as reported in the case of vaccination for East Coast fever in a pastoralist community in Kenya (Marsh et al., 2016). By reducing the incidence of human brucellosis, the livestock vaccination programme could also minimise the impact of the disease on the health service, freeing human and other healthcare resources (e.g., beds) in local hospitals and health centres, which would be available for other medical needs.

Fourthly and finally, the current knowledge of the brucellosis transmission dynamics in the NCA is limited. The transmission rates used in the disease transmission model were calculated for the observed prevalence and livestock population turnover rates (assuming a death rate equal to the birth rate) in a pastoralist community of northern Tanzania. As a result, a basic reproductive number $R_0$ of 1.04

(95% UI: 1.02-1.06) was obtained. This $R_0$ estimate in the NCA was lower than estimated or assumed to be in an agro-pastoral area of the Morogoro region, Tanzania (1.07; cattle), Mongolia (1.09; cattle), Albania (1.13; sheep and goats), northern Iraq (2.18; sheep and goats), and China (cattle in Jilin province: 2.13 between 1998 and 2005; cattle and sheep in Xinjiang province: 2.55) (Al Hamada et al., 2021; Bruce, 2016; Lou et al., 2016; Nie et al., 2014; Ukita et al., 2021; Zinsstag et al., 2015). Given the positive correlation between $R_0$ and the benefit-cost ratio (page 206) in the NCA, a greater $R_0$ in this setting would likely yield higher benefit-cost ratio estimates.

### 6.4.4 Study limitations

This study produced novel evidence of the benefits, costs, and utility of a hypothetical livestock vaccination programme for brucellosis in the Ngorongoro Conservation Area. However, it is important to highlight a few limitations.

Firstly, some critical assumptions were made to overcome existing knowledge gaps. It was assumed that the proportion of livestock infections that occur due to transmission within species ($\rho$; cattle to cattle, or sheep and goats to sheep and goats) and the proportion of human infections due to transmission from each livestock species ($\pi_i$) follow a uniform distribution between zero and one. This assumption implies that, on average, half of livestock infections occur due to transmission within species, and humans are as likely to be infected by cattle as by sheep and goats.

Little is known about brucellosis transmission dynamics within and between livestock species in northern Tanzania and elsewhere. Although, in Sub-Saharan Africa, *B. abortus* is predominantly isolated in cattle, and *B. melitensis* in sheep and goats, *B. melitensis* has often been isolated in cattle and *B. abortus* in sheep and goats (Ducrotoy et al., 2017). Cross-species transmission is possible and likely to happen in settings where cattle, sheep, and goats graze together, such as in the pastoral setting of northern Tanzania. More evidence of the *Brucella* species circulating in each livestock species in this setting could help inform the parameters in the disease transmission model (Viana et al., 2016). However, the predicted reduction in prevalence due to the mass vaccination programme, which targeted cattle, sheep, and goats, would likely still hold under different assumptions of transmission dynamics because, at least for cattle, the vaccination with S19 confers protection against both *B. abortus* and *B. melitensis* (OIE, 2019).

The current knowledge of the relative importance of *B. abortus* and *B. melitensis* infecting humans in Sub-Saharan Africa is currently limited. Most epidemiological studies on human brucellosis analyse the serological response to *Brucella* infection, which does not enable the identification of the infecting species (Moreno, Blasco, and Moriyon, 2022). *B. melitensis* has been isolated more often than *B. abortus* in bacteriological studies of human brucellosis in Sub-Saharan Africa (Ducrotoy et al., 2017). In a pastoralist community of northern Tanzania, seven out of eight *Brucella* isolates obtained from humans with febrile illness were identified as *B. melitensis* (Bodenham et al., 2020). It is unclear, though, to which extent the greater disease severity caused by *B. melitensis* in humans might have contributed to bias in the relative frequency of identified *Brucella* species in these studies. Nonetheless, the cost-benefit analyses of brucellosis control interventions in Mongolia, Turkey, and Albania (the studies that included monetary and non-monetary human health benefits of livestock vaccination) assumed that most human cases originated from small ruminants (Bruce, 2016; Roth et al., 2003; van Asseldonk, Bergevoet, and Ge, 2013; Zinsstag et al., 2005). The contact rate between sheep and humans ($1.13x10^{-8}$) was over five times greater than between cattle and humans ($2.11x10^{-9}$) in the study in Mongolia, which resulted in 90% of human cases being of small ruminant origin (Roth et al., 2003; Zinsstag et al., 2005). This result is consistent with values reported in Turkey and Albania, where 70% and 80% of human cases were of small ruminant origin, respectively (Bruce, 2016; van Asseldonk, Bergevoet, and Ge, 2013). More research is needed to characterise brucellosis transmission dynamics in low-resource settings comprehensively.

Another critical model assumption was the stable and closed nature of the livestock and human populations in the NCA. The disease transmission model did not account for the possibility of changes in population sizes and the potential effect of livestock and human migration on the prevalence estimates over time. The size of the livestock population in the NCA has been relatively stable over the last half-century (Slootweg, 2018), with occasional high mortality events often associated with droughts (Manzano and Yamat, 2018). It is unknown how these events affect the dynamics of brucellosis transmission in this setting. The potential movement of livestock infected with brucellosis into the NCA from neighbouring areas could affect the brucellosis prevalence and the estimated monetary benefits of disease control. Future modelling studies of brucellosis control in the NCA should evaluate the impact of livestock movement. The Endulen ward in the NCA has been identified as a highly connected node in a network model in northern Tanzania, indicating that this ward is likely to play an important role in livestock movement and trade in the region (Chaters et al., 2019).

Secondly, based on the elasticity analysis, a relatively uncertain and critical parameter determining the efficiency of livestock vaccination for brucellosis in the NCA was the number of animals vaccinated per team per day. This parameter was drawn from a PERT distribution with the following minimum, mode, and maximum values: 250, 500, and 750, respectively. The most likely rate of 500 vaccinated animals per team per day was four times lower than previously assumed in a study of livestock vaccination for anthrax in the NCA (unpublished study; 2,000 animals vaccinated per team per day) because of the extra safety precautions needed with the brucellosis vaccines and the potential additional time needed for conjunctival administration as opposed to the subcutaneous route. A costing analysis of vaccination for *peste des petits ruminants* (PPR) in Senegal assumed that, in the worst-case scenario, the most likely number of animals vaccinated per team per day would be 316 (Tago et al., 2017). This study in Senegal concluded that the number of animals vaccinated per team per day is a critical parameter for the cost of a vaccination campaign, highlighting the need for adequate training to improve performance. However, studies that estimate the costs and benefits of livestock vaccination for brucellosis rarely report the expected number of animals vaccinated daily or assume a relatively high vaccination rate. A cost-benefit analysis of small ruminant vaccination for brucellosis in northern Iraq assumed that the vaccination teams (one veterinarian, two veterinary nurses, and one driver) would vaccinate an average of 1,400 animals per day (Al Hamada et al., 2021). A risk-based decision tool for prevention and control of Rift Valley fever in the Greater Horn of Africa assumed that each team of five people would vaccinate 2,500 animals per day (Group for RVF decision support, 2010). An evidence-based definition of the number of animals that can be vaccinated per day is critical in cost-benefit analyses of disease control interventions.

Thirdly, a vaccine efficacy (proportion of vaccinated animals that become protected from infection with *Brucella* spp.) of 70% was assumed for S19 and Rev-1 in the NCA. A systematic review and meta-analysis estimated that the efficacy of S19 in cattle was 72% (Oliveira et al., 2021). Rev-1 was found to confer protection (from abortion and excretion of the challenge strain) to 12 (86%) out of 14 pregnant ewes (El Idrissi et al., 2001). Other studies of the costs and benefits of livestock vaccination for brucellosis have assumed efficacy values of 60% (minimum; sheep and goats in Albania), 65% (minimum; cattle and sheep in Mongolia; and, sheep in Turkey), 70% (cattle, India), 75% (minimum; sheep and goats in Iraq; and, yaks in Tibet), and 86% (baseline scenario; goats in Mexico) (Al Hamada et al., 2021; Alshwany, 2019; Bardhan et al., 2020; Bruce, 2016; Montiel et al., 2015; Roth et al., 2003; van Asseldonk, Bergevoet, and Ge, 2013; Zeng et al., 2019). There are no published efficacy and stability data for the S19 and Rev-1 vaccines produced

by the Tanzania Vaccine Institute (Tanzania) and CZ Vaccines (Spain). It is possible that the S19 produced by the Tanzania Vaccine Institute (Tanzania) might have sub-optimal efficacy and stability under field conditions due to potential issues with the cold chain during the vaccine delivery stage. On the other hand, CZ Vaccines (Spain) indicates that their Rev-1 is highly thermostable, i.e., it can be kept in warm conditions, at a maximum of 37 $^{o}$C, for up to seven days.[11] Therefore, the outcomes of the current brucellosis control modelling study need to be interpreted based on the premise that field staff strictly follow the instructions provided by the vaccine manufacturers.

Fourthly, the brucellosis control programme evaluated in this study excluded from vaccination animals younger than three months old, pregnant animals in the second or third third of the pregnancy, and bulls. As a result of these exclusion criteria, only 67% of cattle and 83% of sheep and goats were eligible for vaccination. Under the reference scenario evaluated in this study, the proportion of eligible animals to be vaccinated was 75%, which means that only approximately 50% (67% times 75%) of cattle and 62% (83% times 75%) of sheep and goats would be vaccinated in each vaccination year. This level of vaccination coverage aligns with assumptions made in previous studies. For instance, the estimated vaccination coverage was 48% of cattle in India and 60% of sheep and goats in Iraq (Al Hamada et al., 2021; Bardhan et al., 2020). However, it is possible that many livestock keepers would fail to exclude pregnant animals, particularly small ruminants, from vaccination. These animals might suffer abortion and potentially excrete the vaccine strain in the milk. This study did not account for the costs of these adverse reactions (production losses and human exposure to the vaccine strain) and their potential effect on livestock keepers' willingness to accept vaccination in subsequent years. These negative impacts of vaccination need to be accounted for in future cost-benefit analyses of brucellosis control interventions, particularly if vaccination is targeted at small ruminants with low prevalence. Under these circumstances, the marginal benefit of vaccination may be limited and the cost of adverse reactions potentially large.

11. https://preventingwithexperts.com/vaccine/ocurev/

Finally, this study used a discount rate of 3% to account for the lower value of future benefits and costs compared to the present. Higher discount rates (e.g., 6%), representing the often high time-preference rates in low- and middle-income countries, would likely affect the estimated cost-benefit and cost-utility analyses metrics (Anderson and Gugerty, 2009). Future evaluations of brucellosis control interventions based on livestock vaccination in northern Tanzania should analyse the impact of the discount rates on the estimated costs and benefits.

## 6.5 Conclusion

Livestock vaccination for brucellosis in the Ngorongoro Conservation Area is likely cost-beneficial. The monetary benefits of a hypothetical vaccination programme would exceed its costs in most circumstances. This would be true even if the vaccine efficacy and coverage were relatively low, and if the losses averted in the livestock sector alone were considered, as opposed to both livestock and human health sectors.

The purpose of this study was not to determine whether or not livestock in the NCA should be vaccinated for brucellosis. The cost-benefit and cost-utility analyses indicate that a brucellosis control strategy based on livestock vaccination is economically feasible. However, many social, cultural, and political barriers to implementation and sustainability specific to the NCA context would need to be overcome. Overcoming these challenges and achieving effective and sustainable brucellosis control in this context requires expert contributions from multiple fields, including behavioural economics, biodiversity conservation, and health systems management.

The relative distribution of monetary benefits of livestock vaccination to the livestock and human health sectors in this setting may help inform the establishment of cost-sharing scenarios. The co-funding of livestock vaccination by the relevant ministries for human and animal health in proportion to the benefits is likely justifiable from society's perspective.

The NCA could be used as a pilot for co-funding before scaling up to other regions. Larger scale cost-sharing scenarios for livestock vaccination in other regions would benefit from lessons learned from initial implementation in the NCA. These lessons would likely cover aspects such as stakeholder engagement, communication between funding bodies, surveillance systems, and monitoring and evaluation of intervention outcomes.

More research into the epidemiology and impacts of brucellosis in northern Tanzania is needed to reduce uncertainty in key variables and parameters used in the cost-benefit and cost-utility analyses. The methodological framework applied in this study may be adapted to estimate the benefits of brucellosis control in similar settings in Tanzania and elsewhere.

# Chapter 7

# Discussion

Brucellosis is considered one of the most prevalent zoonoses worldwide, despite the availability of effective control strategies (Enkelmann, Stark, and Faber, 2020; Nawaz et al., 2021; Pappas et al., 2006). Many high-income countries have eliminated brucellosis through large-scale, government-funded interventions targeting the livestock sector (Zhang et al., 2018). In contrast, brucellosis control efforts in low-income settings have generally been unsuccessful or non-existent. The lack of brucellosis control actions in these settings is partly due to limited resources and poor evidence on the impact of the disease and potential benefits of disease control measures (McDermott, Grace, and Zinsstag, 2013).

In Tanzania, brucellosis is endemic in livestock and humans, with higher prevalence in pastoral communities that rely primarily on livestock for their subsistence (Bodenham et al., 2020, 2021). The country has 4.9 million farming households, and one of the largest livestock populations in Africa (Mtui-Malamsha, Fasina, and Aguanno, 2022). The Government of Tanzania has published a national strategy for brucellosis prevention and control in humans and animals (Government of The United Republic of Tanzania, 2018b). This strategy is built on three pillars: i) provision of information on brucellosis prevention and control to affected communities; ii) strengthening of disease surveillance mechanisms; and, iii) livestock vaccination. There are also provisions for test-and-slaughter interventions at specific farms. To the author's knowledge, no formal economic evaluations of livestock vaccination for brucellosis control have been conducted in Tanzania prior to this study (Kiiza et al., 2023).

This PhD research focused on northern Tanzania, and aimed to estimate (i) the production losses attributable to livestock brucellosis, (ii) the cost and disease burden attributable to human brucellosis, and (iii) the costs and benefits of livestock vaccination for brucellosis control. These objectives align with the three pillars

mentioned above. To achieve these objectives, a holistic, 'one health' approach was taken, integrating data on environmental factors (Chapter 3), animal health (Chapter 4), and human health (Chapter 5). The study required the application of interdisciplinary methodology, blending concepts and tools from epidemiology and economics, and benefited from close collaboration with local researchers and communities. The outcomes of this research are relevant to local livestock keepers, other occupationally exposed groups, farmer associations, healthcare professionals, researchers, non-governmental organisations, and policymakers in Tanzania and similar settings.

## 7.1 Main study findings

This study has made novel contributions in four critical areas of brucellosis research: i) it has estimated the monetary costs and disease burden attributable to livestock and human brucellosis in northern Tanzania; ii) it has estimated the costs and benefits of livestock vaccination for brucellosis control in the Ngorongoro Conservation Area; iii) it has developed a new methodological framework that can be applied in the context of other zoonoses and similar settings to estimate disease impacts and benefits of control actions; and, iv) it has identified critical knowledge gaps and research priorities relevant to the potential development and implementation of sustainable and cost-effective brucellosis control strategies in northern Tanzania.

This study's results indicate that brucellosis causes considerable monetary costs and disease burden in northern Tanzania. In the pastoral setting, the median production losses attributable to livestock brucellosis per household were equivalent to nearly 5% of the household income derived from livestock. Cattle were the main livestock species contributing to household-level losses. The personal monetary cost of healthcare due to human brucellosis in this setting was likely to exceed 40% of the non-food expenditure, meeting the definition of catastrophic expenditure (Brinda, Andrés, and Enemark, 2014). The median disease burden attributable to human brucellosis (1.62 DALYs per case and 654 DALYs per 100,000 people) was greater than previously reported in Tanzania and elsewhere.

This study demonstrates that the benefits of a mass livestock vaccination programme for brucellosis in a pastoral community of northern Tanzania would almost certainly outweigh the programme's costs. Substantial benefits would be gained in both the livestock and human sectors. The study's findings on the distribution of these benefits by sector may help inform cost-sharing scenarios for livestock vaccination. One such scenario could involve the Ministry of Health and the Ministry of Agriculture jointly funding livestock vaccination for brucellosis control.

The methodological framework developed in this study to estimate disease impacts and benefits of control may be applied in similar settings and for other zoonoses. This framework could be suitable for estimating the impact of zoonoses such as Rift Valley fever (RVF), Q fever, and leptospirosis, which cause high reproductive morbidity in livestock and febrile illness in humans. Research conducted in northern Tanzania suggests that these zoonoses are present in the region and may be causing considerable and underappreciated production losses in livestock and disease burden in humans (de Glanville et al., 2022a,b; Pisharody et al., 2022; Thomas et al., 2022).

## 7.2 Identified knowledge gaps and future research priorities

This study identified critical knowledge gaps and areas that need further research. Chapter 2 demonstrated that models of livestock disease control need to account for the heterogeneity in farmer behaviour, the associated externalities, and the effects of privately optimal uptake of disease control measures. Chapter 3 applied a data-driven approach to account for the heterogeneity in livestock production and management. More research is needed to capture the effects of externalities and optimised farmer behaviour in models of livestock disease control. Chapters 4, 5, and 6 identified key research priorities specific to brucellosis in northern Tanzania and other low-resource settings: i) the epidemiology of the disease (e.g., species-specific prevalence and incidence, and transmission rates); ii) its clinical and pathological features in livestock and humans (e.g., abortion probability in infected animals, case-fatality ratio in humans); and, iii) standardisation of disease impact estimation methodology (e.g., current methods and outputs vary widely). In light of the findings presented here, filling these knowledge gaps is critical for informing the best possible resource allocation for brucellosis control in Tanzania and similar settings.

### 7.2.1 Effects of externalities and privately optimal behaviour

More research is needed (i) to characterise the factors that influence the uptake of disease risk mitigation and control measures, and (ii) to incorporate understanding of these factors into models of livestock and zoonotic disease control. These research priorities are particularly relevant in the context of privately funded control actions that have potentially significant public health benefits (positive externalities), such as farmer-led vaccination of livestock against zoonotic diseases (Hasler, Delabouglise, and Babo Martins, 2017). To address these priorities effectively, researchers must establish collaborative networks and interdisciplinary teams that involve experts from various fields, such as human medicine, veterinary medicine, environmental science, behavioural economics, psychology, sociology, and political science.

Various factors influence an individual's decision-making process related to disease control in each setting (Mankad, 2016; Ritter et al., 2017). These factors include perception of disease impacts, socioeconomic conditions, cultural practices, education, access to resources, and confidence in government institutions (Chilonda and Van Huylenbroeck, 2001; Gizaw et al., 2020). A better understanding of these factors is needed for designing and delivering effective interventions, educational campaigns, and policies in low-resource settings. Failure to account for these factors in livestock and zoonotic disease control models may lead to misleading estimates of the costs and benefits of potential control interventions.

### 7.2.2 Epidemiology of brucellosis

More research is needed to fully understand the epidemiology of brucellosis in livestock and humans in Tanzania and other LMICs. Obtaining accurate estimates of the prevalence and incidence of brucellosis in these areas is often challenging. The epidemiology of brucellosis in different livestock production systems is insufficiently characterised. The role of wildlife, camels, and pigs as reservoirs of *Brucella* spp. is poorly understood. Limited evidence is available to estimate transmission rates between host species and to describe trends and temporal patterns in transmission dynamics, and circulating *Brucella* species and genotypes.

Research pathways for overcoming these challenges can be suggested based on the outcomes of this study. Research that prioritises isolation and whole genome sequencing of *Brucella* spp., rather than simply identifying serological evidence of exposure, is needed to understand the epidemiology of brucellosis in each setting.

Obtaining and characterising *Brucella* spp. isolates is challenging for many reasons (e.g., low sensitivity of bacteriological culture, safety risks for laboratory staff), but it would generate critical evidence for informing disease control interventions. While this detailed evidence may not have been necessary to inform brucellosis control in many high-income countries, it would reduce uncertainty in estimated control costs and benefits in LMICs, potentially strengthening the rationale for implementing effective control measures and enabling the best possible allocation of limited available resources. It is important to note that many benefits of brucellosis control in high-income countries are not yet attainable in other settings. For instance, brucellosis elimination enabled high-income countries to access international markets, a benefit not applicable in many low-resource settings due to the presence of other livestock diseases affecting trade (e.g., foot-and-mouth disease) (Franc et al., 2018; Jamal and Belsham, 2013). A better understanding of the epidemiology of brucellosis in each setting may help inform the vaccination of targeted livestock species and age groups to break key transmission cycles. It would also help ascertain the need for additional control measures such as test-and-slaughter and movement restrictions in specific areas.

In livestock, classical and molecular bacteriology analyses of samples collected through syndromic (e.g., abortion-focused) and abattoir-based surveillance platforms would help estimate the prevalence of the disease in each host species and the associated transmission rates (Viana et al., 2016). In humans, hospital-based surveys of febrile illness have proven useful in detecting brucellosis cases and identifying *Brucella* species (Bodenham et al., 2020; Bouley et al., 2012; Crump et al., 2013). When coupled with community-level surveys of healthcare utilisation behaviour, hospital-based surveys of febrile illness may help generate accurate community-level incidence estimates for human brucellosis. Finally, a likely cost-effective solution would be a ‘one health’ approach integrating livestock and human health surveillance platforms. Such an integrated surveillance strategy could encompass testing members of households keeping livestock that suffered brucellosis-induced abortion. Another potentially viable integrated approach would be to test livestock kept by households with human brucellosis-confirmed cases.

### 7.2.3 Clinical and pathological features of brucellosis

Chapters 4 and 5 revealed the need to investigate further the physiological consequences of *Brucella* spp. infection in livestock and humans, respectively. The probability of abortion in livestock and the case-fatality ratio, disease duration, and probability of chronic progression in humans were key determinants of monetary costs and disease burden attributable to brucellosis. In livestock, evidence of the likelihood of brucellosis-induced abortion and other consequences of brucellosis (e.g., infertility, sterility, perinatal mortality) is limited (Bruce, 2016). In humans, several estimates of the brucellosis case-fatality ratio, disease duration, and probability of chronic progression are available in the literature, but these are predominantly from high-income countries (Afifi et al., 2005; Al Dahouk et al., 2007; Buzgan et al., 2010; Dean et al., 2012a; EFSA and ECDC, 2019; Rodríguez-Alonso et al., 2021). Disease outcome data from high-income countries are not representative of low-resource settings due to differences in the quality of healthcare systems, access to medical care, and the prevalence of comorbidities (Kruk et al., 2018).

Prospective cohort and case-control studies can help fill these knowledge gaps in low-resource settings. This type of research is known to be costly, but even small and well-designed studies are likely to generate better evidence than is currently available (Jo, 2014). In livestock, evidence of the physiological consequences of *Brucella* spp. infection could be gathered alongside a randomised control trial to evaluate a livestock vaccination intervention. Components of this evaluation could include the study of locally produced vaccines' efficacy and stability. In humans, data on case-fatality ratio, disease duration, and probability of chronic progression could be obtained alongside trial implementation of improved diagnostic (e.g., Rose Bengal test, RBT) and management protocols.

### 7.2.4 Disease impact estimation methodology

There is a need to standardise methods and parameters used to estimate the costs and disease burden attributable to brucellosis in livestock and humans. Significant heterogeneity characterises the literature on brucellosis impact assessments. This heterogeneity makes it difficult to compare brucellosis impact estimates with other diseases and health hazards, thereby limiting policymakers' ability to prioritise disease control measures effectively.

The 'DALY' metric originated from the need to standardise disease burden assessments and help inform the optimal allocation of scarce resources for disease control (Murray, 1994). However, when assessing the burden attributable to human brucellosis, strong assumptions on key uncertain variables, such as the case-fatality ratio, disease duration, and disability weights, and significant differences in parameter values used between studies weaken the power of DALYs outputs in public health priority setting and policy development. The case-fatality ratio and disease duration, in particular, are highly influential parameters for brucellosis burden estimation (see elasticity analyses in Chapter 5). Researchers have called for the development of guidelines and checklists for clearly reporting methodological choices and assumptions in DALYs estimation studies (Di Bari et al., 2022).

More evidence for informing disability weights used in assessments of the burden attributable to human brucellosis is needed. This evidence can be gathered by applying standardised instruments for quality-of-life evaluation (Salomon et al., 2012). To the author's knowledge, this type of research has rarely been conducted, despite the potential for generating valuable insights into the quality-of-life impacts of brucellosis at a relatively low cost (Garcia-Juarez et al., 2012; Lyapina et al., 2015).

Currently, there is a lack of standardised metrics analogous to the DALY to evaluate animal health loss. It is crucial to address this issue so that society can make informed decisions about resource allocation for animal health. The Global Burden of Animal Diseases (GBADs) Programme is an ongoing international initiative that seeks to address this problem (Huntington et al., 2021). GBADs aims to develop conceptual frameworks, international guidelines, and systematic methodology to estimate the burden of animal diseases. The anticipated inclusion of such guidelines in the World Organisation for Animal Health's Terrestrial Animal Health Code will mark a significant milestone in animal health economics, with many potential downstream benefits to animal, human, and environmental health.

## 7.3 Policy recommendations

In Tanzania, there is a recognised need for integrated, multi-sectoral strategies to prevent and control zoonotic diseases (Government of The United Republic of Tanzania, 2018c). The successful implementation of these strategies is expected to have several beneficial outcomes, such as (i) improving human health and well-being, (ii) increasing livestock productivity, protecting livelihoods, and ensuring

food security, (iii) reducing trade barriers and potentially opening up export markets, (iv) boosting resilience against climate change, and, ultimately (v) contributing to sustainable, equitable, and inclusive economic growth and development (Auty et al., 2021; McLeod and Rushton, 2007; Pica-Ciamarra, 2005; Pica-Ciamarra et al., 2014).

Brucellosis is considered a 'high-priority' zoonosis in Tanzania (U.S. Agency for International Development (USAID), USAID Preparedness and Response Project (P&R), and U.S. Centers for Disease Control and Prevention (CDC), 2017). The findings of this PhD research can inform policy development for improving brucellosis surveillance, diagnosis, prevention, and control in the country.

The 2020 surveillance guidelines identified brucellosis as a key human disease for integrated surveillance and response (Government of The United Republic of Tanzania, 2020b). Chapters 4 to 6 addressed data generation priorities in line with these guidelines. Better data on brucellosis frequency are needed to accurately assess the impacts of the disease and evaluate potential control interventions. This could be achieved through improved access to human and veterinary healthcare, enhanced diagnostic capacity and, ideally, the establishment of an animal identification system (e.g., ear tagging). Improved access to healthcare and enhanced diagnostic capacity would simultaneously contribute to disease frequency estimation and improvement in disease outcomes. The animal identification system would facilitate monitoring seroconversion post-vaccination and enforcement of potential future regulations based on movement restrictions and test and slaughter.

To improve brucellosis diagnosis, a standardised application of a brucellosis case definition and recommended diagnostic algorithms is needed. In Tanzania, the guidelines for the surveillance of prioritised zoonoses recommend using the RBT as the initial diagnostic tool for suspected human brucellosis cases (Government of The United Republic of Tanzania, 2018a). Despite this indication, healthcare facilities in northern Tanzania often opt for tests that have poor diagnostic performance and cost more than RBT (Lukambagire et al., 2021, 2022). It is crucial that policies regarding brucellosis diagnosis promote and enable testing of suspected human brucellosis cases with RBT, ensure appropriate training of laboratory staff, and guarantee a reliable supply chain for test reagents. Chapter 5 demonstrated that replacing currently used plate agglutination tests with RBT would significantly reduce the personal monetary costs and disease burden attributable to brucellosis in the study area.

Finally, this PhD research may help inform the development of two policy areas: firstly, the prevention and control of livestock diseases in general (based on Chapter 2), and secondly, the prevention and control of brucellosis specifically (based on Chapter 6).

Chapter 2 modelled several scenarios of livestock disease control. The common feature of all scenarios was a change in the behaviour of livestock keepers towards disease control following an awareness-raising event. The livestock keepers decided whether to 'invest in reductions in the transmission rate' of a hypothetical disease. The modelled reductions in the transmission rate were used as a proxy for the effect of improvements in hygiene and biosecurity. Policies aimed at providing information and raising awareness can achieve this effect, which applies to many livestock infectious diseases. Thus, such policies can yield multiple benefits at a relatively low cost. For instance, encouraging the hygienic disposal of placentas and birth products may reduce transmission of numerous diseases, including brucellosis and other zoonoses such as Q fever, Rift Valley fever, leptospirosis, and toxoplasmosis (Cavalerie et al., 2021; Cleaveland et al., 2017; Thomas et al., 2022).

Chapter 6 estimated the costs and benefits of livestock vaccination for brucellosis control in a pastoral community of northern Tanzania. The analyses revealed that the benefits outweighed the costs, even when solely considering the benefits to the livestock sector (excluding human health benefits derived from livestock vaccination). However, these results *per se* do not necessarily indicate that the Government of Tanzania should invest in livestock vaccination for brucellosis or if such investment would be the most efficient use of available resources. It is crucial to interpret the findings of this study in the context of other diseases and health hazards (Marseille et al., 2015). This study did not compare the cost-effectiveness of brucellosis control with that of interventions targeting other diseases and health hazards.

The successful implementation of a livestock vaccination programme for brucellosis control in low-resource settings depends on multiple factors. These include funding sources and strategies, targeted livestock species, the level of trust livestock keepers have in government institutions, and the perceived benefits of control interventions (Auty et al., 2021; Davis et al., 2021; Hermesh, Rosenthal, and Davidovitch, 2020; Kiiza et al., 2023; Zhang et al., 2018).

In high-income countries, large-scale brucellosis control interventions have been financed almost entirely by the respective governments or inter-governmental organisations (e.g., European Union) (Auty et al., 2021; European Commission, 2011). In low-income countries, government funding alone is often insufficient due to limited resources (McDermott, Grace, and Zinsstag, 2013). To overcome this problem, the establishment of public-private partnerships for delivering animal health services, such as livestock vaccination, has been proposed (Auty et al., 2021). Such partnerships can enhance access to animal health services in remote communities, which is critical since livestock keepers are often willing to pay for these services (Ahuja et al., 2020; Asakura et al., 2022). Disease freedom certification and subsidy schemes for livestock vaccination can also be effective (Cardenas et al., 2019; FAO, 2018a). However, these schemes have some limitations. In Tanzania, disease freedom certification programmes, often led by farmers' associations, tend to benefit mainly production systems with relatively low brucellosis prevalence (e.g., smallholder dairy production, compared to pastoral systems) (Professor Gabriel Shirima, personal communication). Government subsidies may help correct the market failure that results from livestock vaccination (Chapter 2) but do not solve the problem of insufficient access to animal health services and vaccine supply chains in some areas (Sok and Fischer, 2019; Wolf, 2017).

Mass livestock vaccination, covering cattle and small ruminants, is often recommended for brucellosis control in low-resource settings, such as northern Tanzania (Ducrotoy et al., 2017). However, a more focused vaccination approach, targeting certain livestock species should not be excluded. Although recent evidence suggests that sheep and goats play an important role as a source of human infection in northern Tanzania, a vaccination strategy focused on small ruminants only may not be economically viable, based on the results reported in Chapter 6 (Viana et al., 2016). In contrast, cattle-only vaccination is likely to be highly cost-beneficial, in this setting. Compared to sheep and goats, cattle have a higher prevalence of brucellosis, and the disease causes greater losses per infected animal (Chapter 4). The marginal benefits of vaccinating cattle are likely to be much higher than those of sheep and goats (Chapter 6).

Building and maintaining trust between livestock keepers and the government is vital for successful disease control. Trust in government institutions influences the likelihood of livestock keepers (i) adhering to recommended preventive measures, (ii) complying with regulations (e.g., mandatory testing and vaccination), (iii) cooperating with animal health services, and, (iv) contributing to disease surveillance. Trust is particularly relevant in the case of brucellosis because of the potentially severe adverse reactions associated with livestock vaccination (e.g.,

abortion). To ensure the safety of brucellosis vaccines, it is imperative that the manufacturing process adheres to high-quality standards, including those set by the World Organization for Animal Health (WOAH). It is equally important to maintain the cold chain during vaccine distribution and to ensure that only qualified personnel administer the vaccines.

The perceived knowledge of disease impacts is a key determinant of the willingness to pay for livestock vaccination (Hermesh, Rosenthal, and Davidovitch, 2020; Zhang et al., 2018). Therefore, the future availability of multivalent vaccines offering protection against brucellosis as well as other diseases considered more important by livestock keepers, such as malignant catarrhal fever and foot-and-mouth disease, could lead to high vaccination uptake rates (Auty et al., 2021). While not yet commercially available, ongoing research is exploring the development of a multivalent vaccine for this purpose (GALVmed, 2023). Another option for improving the uptake and potential cost-effectiveness of government-funded livestock vaccination for brucellosis could be the combination with other zoonoses control interventions. Examples of interventions that could be combined with livestock vaccination for brucellosis include the distribution or administration of preventive medicines (e.g., praziquantel for human schistosomiasis and *Taenia solium* taeniasis), and dog vaccination for eliminating dog-mediated human rabies.

## 7.4 Conclusion

In conclusion, brucellosis causes considerable monetary costs and disease burden in northern Tanzania. Pastoral communities that depend primarily on livestock for their livelihood are particularly impacted by the disease. Livestock vaccination for brucellosis control in these communities is likely cost-beneficial.

For the first time in northern Tanzania, this study applied a ‘one health’ approach to evaluate the impact of brucellosis and estimate the benefits of potential disease prevention and management actions. In poor resource settings, a comprehensive understanding of the impacts of brucellosis and the costs and benefits of disease control is of utmost importance. The outcomes of this study can support the delivery of Tanzania’s national strategy for brucellosis prevention and control, contributing to poverty alleviation, food security, and improved health and well-being.

The methodological framework developed and described in this study can be applied in the context of brucellosis and other zoonoses in similar settings. The application of this framework in the context of other endemic zoonoses in LMICs would enable comparison of impacts between diseases and settings, which is key to prioritising control strategies and allocating resources accordingly. The framework's 'one health' perspective enables estimation of the benefits of potential control interventions to livestock and human health sectors separately. The ability to estimate the relative distribution of control benefits by sector may help inform co-funding scenarios for zoonoses control. A potential scenario could involve the Ministry of Health and the Ministry of Agriculture financing livestock vaccination.

This study identified key research priorities to support evidence-based policy development for brucellosis surveillance, diagnosis, prevention, and control in Tanzania. These priorities span areas such as (i) the epidemiology of brucellosis (e.g., species-specific prevalence and transmission pathways), (ii) the physiological consequences of infection with *Brucella* in livestock and humans, and (iii) the factors that influence the uptake of disease prevention and control measures. More research in these areas is critical to inform best possible resource allocation for brucellosis control in Tanzania and other low-resource settings.

# Appendices

## A Socially versus privately optimal control of livestock diseases

### A.1 Mendes et al., 2020

frontiers in Veterinary Science

BRIEF RESEARCH REPORT
published: 25 November 2020
doi: 10.3389/fvets.2020.558409

# Socially vs. Privately Optimal Control of Livestock Diseases: A Case for Integration of Epidemiology and Economics

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This paper aims to illustrate the interdependencies between key epidemiological and economic factors that influence the control of many livestock infectious diseases. The factors considered here are (i) farmer heterogeneity (i.e., differences in how farmers respond to a perceived disease risk), (ii) off-farm effects of farmers' actions to control a disease (i.e., costs and benefits borne by agents that are external to the farm), and (iii) misalignment between privately and socially optimal control efforts (i.e., privately optimal behavior not conducive to a socially optimal outcome). Endemic chronic diseases cause a wide range of adverse social and economic impacts, particularly in low-income countries. The actions taken by farmers to control livestock diseases minimize some of these impacts, and heterogeneity in those actions leads to variation in prevalence at the farm level. While some farmers respond to perceived disease risks, others free-ride on the actions of these individuals, thereby compromising the potential benefits of collective, coordinated behavior. When evaluating a plausible range of disease cost to price of control ratios and assuming that farmers choose their privately optimal control effort, we demonstrate that achievement of a socially optimal disease control target is unlikely, occurring in <25% of all price-cost combinations. To achieve a socially optimal disease control outcome (reliant on farmers' voluntary actions), control policies must consider farmer heterogeneity, off-farm effects, and the predicted uptake of control measures under the assumption of optimized behavior.

**Keywords: livestock, infection, disease control, model, epidemiology, economics**

OPEN ACCESS

***Edited by:***
*Kimberly VanderWaal, University of Minnesota Twin Cities, United States*

***Reviewed by:***
*Karun Kaniyamattam, Cornell University, United States*
*Arata Hidano, University of London, United Kingdom*

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***Specialty section:***
*This article was submitted to Veterinary Epidemiology and Economics, a section of the journal Frontiers in Veterinary Science*

***Received:*** *02 May 2020*
***Accepted:*** *19 October 2020*
***Published:*** *25 November 2020*

***Citation:***
*Mendes ÂJ, Haydon DT, McIntosh E, Hanley N and Halliday JEB (2020) Socially vs. Privately Optimal Control of Livestock Diseases: A Case for Integration of Epidemiology and Economics. Front. Vet. Sci. 7:558409. doi: 10.3389/fvets.2020.558409*

## INTRODUCTION

Livestock production is vital to economic development in many low-income countries, contributing to poverty alleviation, investment in children's education, and food security (1, 2). Infectious diseases jeopardize these societal functions, yet their control has become increasingly reliant upon privately funded actions (3–8). This "voluntary approach" to disease control distributes costs and responsibility between private agents (farmers that invest in control measures) and the government (animal health authorities that promote and often regulate farmers' actions) (9). The problem of the voluntary approach is that self-interested behavior can fail to produce a socially optimal level of disease control (i.e., the level of disease control that maximizes the sum of all

agents' payoffs in society, the social optimum) (8, 10). The market thus "fails" to achieve the social optimum.

One reason for such "market failure" in disease control is the presence of externalities: costs and benefits borne by agents who are not parties to a market transaction (8). Externalities can be positive (e.g., a farmer enjoys a lower risk of disease incursion into his herd when neighboring farmers vaccinate their animals) or negative (e.g., a farmer has a higher risk of disease incursion into his herd when other farmers sell sick animals into a livestock market). One farmer's investment in animal health can thus influence other farmers' levels of disease risk. The way individual farmers perceive and act upon their level of risk may fail to produce a social optimum: some farmers free-ride on the control efforts of others, and the potential benefits of one farmer's actions can be limited by others' inaction (9, 11). Achieving the socially optimal level of disease control often requires governments to intervene (e.g., through financial incentives and regulation) in a way that accounts for the nature of farmers' decision-making processes and the interdependencies between farmers' choices and disease dynamics (3, 8, 9, 12–19).

The way farmers perceive and respond to disease risks is not only affected by disease spread but also impacts upon it. There are feedback processes between how a disease spreads and the responses of farmers to changing risks (20–22). When the inter-dependent dynamics of economic, behavioral, and epidemiological factors are not understood or well-represented in models of disease transmission, then policies aimed at promoting farmers' action may have perverse effects (23–26).

Our objective in this paper is to illustrate interdependencies between key epidemiological and economic factors that are not consistently taken into account in models of livestock diseases: (i) farmer heterogeneity (i.e., differences between farmers in how they respond to perceived risks); (ii) associated externalities; and (iii) misalignment between privately and socially optimal control efforts. We demonstrate the impact of farmer heterogeneity on disease prevalence over time. We quantify the externalities associated with farmer heterogeneity and show how the outcome of any individual farmer's control effort depends on the behavior of others. Finally, we examine a farmer's decision in trading-off *ex ante* disease prevention expenditure and *ex post* treatment expenditure and output loss, to estimate the probability that adoption of privately optimal behavior will achieve a socially optimal disease control target. The consequences of a socially sub-optimal control level depend on, among other factors, the population at risk. Here, for simplicity and to illustrate the general case, groups of farmers represent society.

## METHODS

We explore the relationships between epidemiological and economic factors using a deterministic compartmental model (27). The model assumes a chronic infectious disease of livestock with a low basic reproduction number ($R_0 = 1.11$), a livestock species with an average lifespan of five time units, and a constant herd size over time (250 animals on farm). We apply the model in three scenarios that explore farmer heterogeneity, quantify externalities, and examine differences between privately and socially optimal control efforts. In all scenarios, the animal-level prevalence in each farm starts at 10% (the endemic equilibrium, i.e., when prevalence remains steady and the effective reproductive number, $R_e$, is 1.00). We simulate the time required to achieve a prevalence of <2% following a hypothetical awareness-raising event (e.g., information provision at time zero) and a time horizon of 25 time units. This target prevalence of <2% represents an economic optimum from society's perspective (i.e., the socially optimal level of disease control). A 2% threshold can also be considered a prevalence level below which costly government-led strategies aimed at eliminating the disease (e.g., test-and-slaughter) are required (28). In our simulations, for simplicity and without loss of generality, we assume infected animals show chronic symptoms and lose productivity, but there is no disease-associated mortality or infertility. Individuals can be either susceptible or infected; once infected, they remain infected and infectious for the remainder of their lives. Complete recovery from the disease is not possible.

The model set-up is as simple as possible for demonstration purposes. The basic features are (i) two states (susceptible—*S*; and infected—*I*), (ii) continuous time steps, (iii) equal birth and death rates ($\alpha = \mu = 0.20$), and (iv) an initial transmission rate ($\beta$) of approximately $8.89 \times 10^{-4}$, reflecting the endemic equilibrium. The model can be run with one or more farms, and disease transmission can occur within farm only or both within and between farms. The proportion of the initial overall $\beta$ attributable to between-farm transmission (q) is 0.0 when there is no transmission between farms, and 0.1 when between-farm transmission is included. The amount of control effort applied on farm is represented by a proportionate reducer on $\beta$ ($r_i^{\beta}$). The model's differential equations are as follows:

$$\frac{dS_i}{dt} = \alpha (S_i + I_i) - (1 - q)\left(1 - r_i^{\beta}\right)\beta S_i I_i - q\beta S_i \sum_{\substack{j=1 \\ j \neq i}}^{n} I_j - \mu S_i \quad (1)$$

$$\frac{dI_i}{dt} = (1 - q)\left(1 - r_i^{\beta}\right)\beta S_i I_i + q\beta S_i \sum_{\substack{j=1 \\ j \neq i}}^{n} I_j - \mu I_i \quad (2)$$

The differential equations were solved in *R* (29) (version 3.6.2) with the package *deSolve* (30) (version 1.27.1). All plots were generated using the *ggplot2* package (version 3.3.0) (31).

We demonstrate the effect of farmer heterogeneity on the predicted prevalence of disease over time by simulating transmission-reducing measures in three farms following a hypothetical awareness-raising event. As farmers continually assess the benefits and costs of their actions over time, the amount of control effort in each farm is set to be a function of disease prevalence ($p_i$). We assume that (i) disease transmission occurs within each farm only, and (ii) as the prevalence (and disease impact) at the farm declines, the control effort applied ($r_i^{\beta}$) also

falls (32), as follows:

$$r_i^{\beta} = \frac{1}{1 + e^{-100(p_i - \gamma_i)}} \quad (3)$$

where $\gamma_i$ represents the farmer responsiveness. $\gamma$ was set at 0.025, 0.100, and 0.175 for the farmer that is "highly responsive," "moderately responsive," and "slightly responsive," respectively. Note that, as the prevalence decreases in any farm due to the control effort applied, the farmer responsiveness does not change—it is a characteristic of each individual farmer.

We then estimate the off-farm effects (externalities) of livestock disease control in two of the above farms: one in which the farmer is highly responsive and the other in which the farmer is slightly responsive. Firstly, we quantify the *ex post* cost of disease over time at the farm level by assigning a monetary value ($\delta$) to the cost of each infected animal per time step. We assume that the *ex post* cost of the disease varies linearly with prevalence (i.e., the cost per time step is the product of the number of infected animals and the cost per infected animal). We then compare the *ex post* cost of disease over time in each farm when the transmission rate between farms (bβ) is 0% (q is 0.0) and 10% (q is 0.1) of the initial within-farm transmission rate (wβ). Actions taken by each farmer to reduce transmission in their farms only reduce the wβ—and do not influence bβ, which is kept constant over time. By holding the bβ constant over time and at a common value for the two farms, we demonstrate the off-farm effects of on-farm actions only—this assumes that (i) the contact rate between farms is kept constant, and (ii) the force of infection is proportional to the number of infected animals on each farm. Variation in farm number and density is unlikely to affect the qualitative inferences from this simulation.

We define "cost of disease" as the sum of disease-related output loss (production potential that is not realized over time) and expenditure on treatment of infected animals, plus the cost of control. Treating infected animals does not affect their infectiousness. Cost of control refers to money spent on reducing the wβ to prevent new cases, for instance, through improvements in hygiene and biosecurity. The cost of disease can thus be split into *ex ante* cost (cost of control) and *ex post* cost (disease-related output loss and treatment-related expenditure).

We demonstrate the market failure in livestock disease control by comparing the private net profit of farmer $i$ ($\Pi_i$) with the social net profit ($\Pi_s$), the sum of the private net profits of $n$ farmers ($\Pi_s = \sum_{i=1}^{n} \Pi_i$). $\Pi_i$ denotes the private net profit of farmer $i$ for the whole simulation period of 25 time units ($\Pi_i = \sum_{t=1}^{25} \Pi_{it}$). The example has only two farmers for simplicity, so $\Pi_s = \Pi_R + \Pi_r$; the social net profit is the net profit of the highly responsive farmer ($R$) plus the net profit of the slightly responsive farmer ($r$). Considering that the benefit ($b_i$, the number of animal infections averted) enjoyed by the highly responsive farmer as a result of disease control effort is a function of control effort applied in their farm ($r_R^{\beta}$) as well as in the other farm ($r_r^{\beta}$) (i.e., $b_R = f\left(r_R^{\beta}, r_r^{\beta}\right)$), the net profit $\Pi_{Rt}$ (in time step $t$) is given by $\delta b_R - \theta r_R^{\beta}$, where $\delta$ is the *ex post* cost per infected animal (treatment expenditure and output loss), and $\theta$ is the unit price of control action (the price of reducing the transmission rate by 1%). For this simulation, we assume that $\delta$ and $\theta$ are fixed at 50 and 0.10 monetary units, respectively.

We examine the effect of optimizing behavior on disease prevalence by assuming that the farmer reduces the wβ so that the total cost of the disease (the sum of *ex ante* and *ex post* costs) at each time step is minimized (32). This process is repeated iteratively for each level of the unit price of control ($\theta$, ranging from 0.00 to 1.25 monetary units per time step) and *ex post* cost per infected animal ($\delta$, ranging from 10 to 85 monetary units per time step). We assume (conservatively) that (i) the farmer has perfect information of both the *ex ante* and *ex post* costs of disease, and (ii) their behavior is no longer determined by a pre-specified logistic function. Instead, at each time step, the farmer reviews and optimizes their control effort given the prevalence. The short planning horizon (one time step, equivalent to one-fifth of the animals' average lifespan) reflects the generally high time-preference rates in low-income countries (33).

The qualitative inferences drawn from the model outputs are observed under a range of alternative scenarios and assumed parameter values. Readers can explore different scenarios and assumptions in the interactive web application, which is available here: http://boydorr.gla.ac.uk/eemodel/epiecon. This application was developed with *shiny* (34) (version 1.4.0) and *shinydashboard* (35) (version 0.7.1) packages in R (29). The R script for all the simulations is available at: https://doi.org/10.5281/zenodo.4108335.

## RESULTS

### The Impact of Farmer Heterogeneity

The prevalence of the disease is estimated over time within three model farms managed by three different "types" of farmers who vary in their responsiveness to an awareness-raising event. The responsiveness level of each farmer type is given by a behavioral parameter ($\gamma_i$). The model uses this parameter in a logistic function that determines the reduction in transmission rate caused by each farmer's different actions at any given level of prevalence (**Figure 1A**). For instance, at the initial prevalence of 10%, (i) the highly responsive farmer reduces transmission by 100% (red solid line), (ii) the moderately responsive farmer reduces transmission by 50% (green dotted line), and (iii) the slightly responsive farmer does not reduce transmission at all (blue dashed line). The impacts of these three levels of responsiveness on disease prevalence over time are shown in **Figure 1B**. The heterogeneity in farmer responsiveness has an impact on the level of control effort applied and thus on the reduction in prevalence achieved. Among the three farmer types, only the highly responsive type achieves the target prevalence (i.e., <2%) within 25 time units.

### Externalities: The Off-Farm Effects of Farmers' Control Actions

Now we model disease prevalence in two neighboring farms (managed by highly and slightly responsive farmers, respectively), allowing for between-farm transmission, to explore the off-farm effects of farmers' control actions upon within-farm and societal costs of disease, represented by the sum of costs over the two neighboring farms.

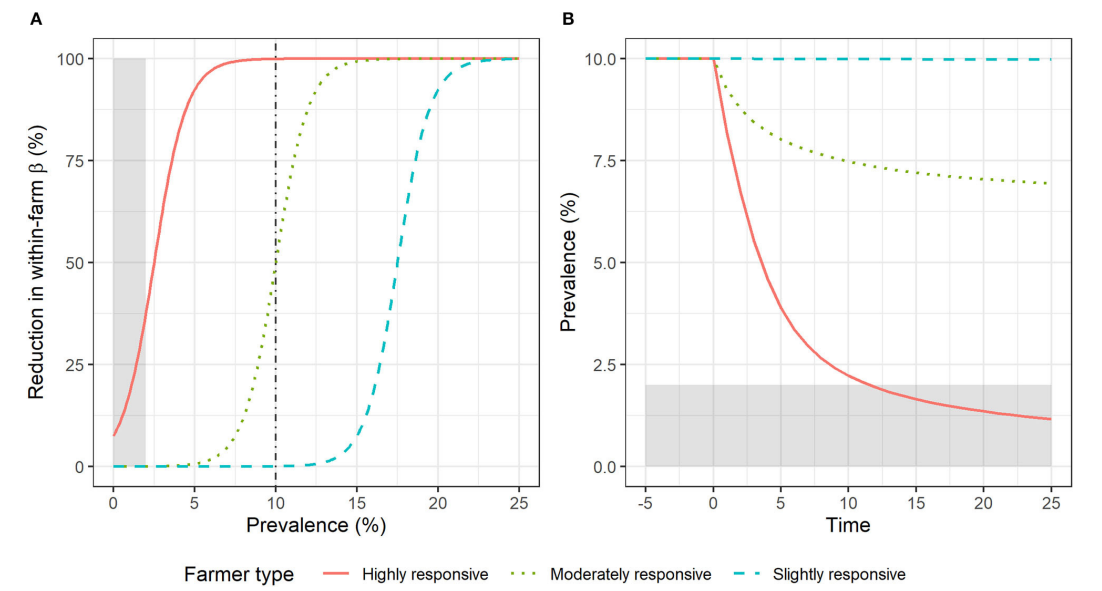



**FIGURE 1 |** Effect of farmer type on disease prevalence following a common starting prevalence and a hypothetical awareness-raising event (at time zero). **(A)** Control effort applied (percentage reduction in transmission rate—β—within the farm in relation to the initial β in endemic equilibrium) as a function of disease prevalence for three different farmer types. The vertical dash-dotted line indicates initial prevalence. **(B)** Disease prevalence over time within the three farms. In both panels, the gray shaded area indicates the target prevalence level from society's perspective (<2%).

For each farm, we estimate the *ex post* cost of disease over time following an awareness-raising event. **Figure 2** shows the estimated *ex post* cost in two farms with and without between-farm transmission. With no off-farm effects (i.e., $b\beta = 0$, and thus no effects of neighbor's actions on costs), a highly responsive farmer (solid red line) reduces prevalence and *ex post* cost. In contrast, for a slightly responsive farmer (dotted blue line), the prevalence and the *ex post* cost are unchanged over time. When the off-farm effects or externalities are included (i.e., $b\beta > 0$, transmission between farms is possible), the highly responsive farmer sees a reduced benefit of their actions, and the slightly responsive farmer benefits from their neighbor's actions (compared to the equivalent costs when $b\beta = 0$). The extent by which the first farmer (highly responsive) reduces the prevalence of disease (and its associated cost) is limited by the force of infection originating from the second farm, where the farmer is only slightly responsive. Also, despite the lack of control action, the prevalence and *ex post* cost of disease at the second farm drops over time as a result of a decreasing force of infection originating from the first farm, where the prevalence is decreasing due to the control measures applied. Using a discount rate of 5%[1], the extent of market failure[2] is the difference between the $\Pi^S$ (849 monetary units) and $\Pi^R$ (695 monetary units). This difference is due to the benefits enjoyed by the slightly responsive farmer, who does not incur any costs of control.

[1]The discount rate accounts for the decreasing value of benefits and costs over time in "real terms," as viewed from the present.

[2]More details available here: http://boydorr.gla.ac.uk/eemodel/epiecon.

## Privately Optimal Behavior and Reductions in Prevalence

Here we model disease prevalence (with a single farm and $b\beta = 0$) to establish if privately optimal actions of a farmer will achieve the socially optimal target prevalence (i.e., <2%). The prevalence over time assuming privately optimal behavior for different unit prices of control (from "free" to "high") is shown in **Figure 3**. Following an awareness-raising event (at time zero) and assuming a fixed *ex post* cost per infected animal ($\delta = 50$ monetary units), the extent by which the within-farm prevalence is reduced varies inversely with the unit price of control ($\theta$). Achieving the socially optimal target prevalence is possible if the unit price of control is very low. Disease elimination (prevalence below 0.4% or <1 infected animal in a herd of 250; note that the predicted prevalence is strictly continuous) only occurs when the unit price of control is equal or <0.05 monetary units (first line above "free" in **Figure 3**). When the unit price of control is above 0.05 monetary units, the farmer's optimal control effort either reduces the prevalence until it reaches a new endemic equilibrium or does not reduce it at all (shown as the uppermost flat line in **Figure 3**; the prevalence remains at the initial endemic equilibrium level). This model of optimizing behavior shows that self-interested farmers, who optimize their

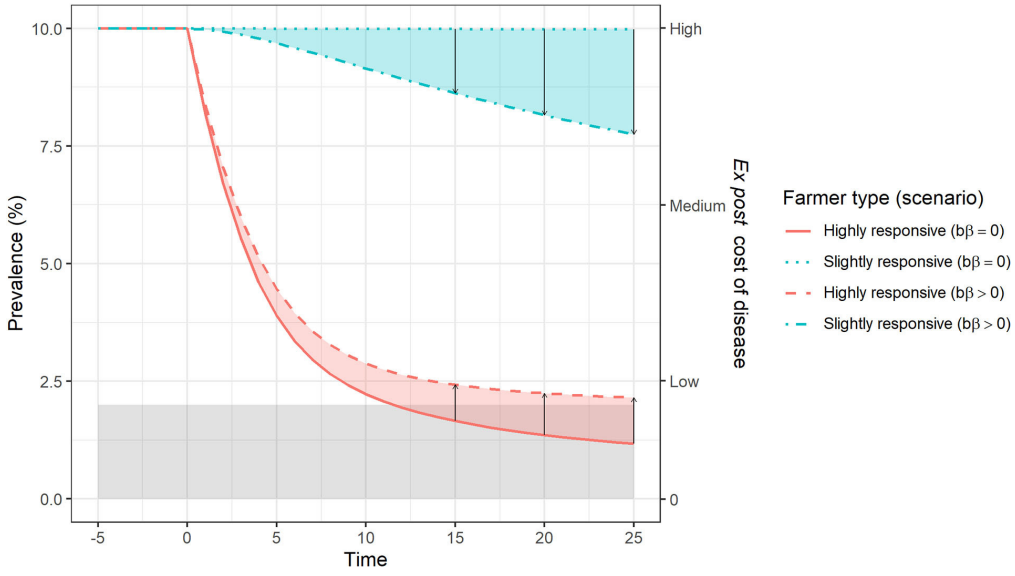



**FIGURE 2 |** Externalities occurring as a result of different effort to achieve disease control in two neighboring farms. Arrows indicate a simulation scenario shift, from absence of transmission between farms ($b\beta = 0$) to a situation in which between-farm transmission is possible ($b\beta > 0$). Assuming an *ex post* cost per infected animal per time step ($\delta$) of 50 monetary units, the labels "Low," "Medium," and "High" on the right vertical axis correspond to 313, 781, and 1,250 monetary units. Blue and red shaded areas correspond to the positive and negative externalities, respectively. The gray shaded area indicates the target prevalence level from society's perspective (<2%).

private investment in disease control, as assumed here, may not achieve the target prevalence from society's perspective in the absence of an intervention by, for example, the government.

In our simulations, under the assumption of optimizing farmer behavior, as prevalence drops, the marginal cost of control actions (i.e., the cost of reducing the prevalence by an additional unit, 1%), increases sharply. It is more expensive to reduce the prevalence from 3 to 2% than from 10 to 9% because the number of cases prevented per time step by reducing the transmission rate depends on the number of currently infected individuals. If the number of currently infected individuals is high (e.g., 10% prevalence), the prevention of new cases yields a quick reduction in prevalence. If the number of currently infected individuals is low (e.g., 3% prevalence), further reductions of the prevalence rely to a greater extent on the elimination of currently infected individuals. Under the assumption of optimizing behavior, as the marginal costs of control increase, the farmer's investment in control therefore gradually declines until an equilibrium is reached in both epidemiological and economic terms (shown as the plateau for each line in **Figure 3**). This equilibrium prevalence level is reached when the *ex ante* expenditure in one time step equals the averted *ex post* cost of disease.

The achievement of a socially optimal outcome prevalence depends on the specific values of the unit price of control and cost per infected animal selected. The results shown in **Figure 3** considered a fixed *ex post* cost of one infected animal ($\delta$ = 50 monetary units). However, for the same disease and animal species, this value could in practice vary with the price of livestock, cost of production inputs, type of production system, etc. **Figure 4** shows the predicted prevalence after 25 time units for a range of values of price per control unit and a range of values of *ex post* cost per infected animal. When we allow the cost per infected animal to vary in plausible ranges in relation to the price of control unit (e.g., eliminating disease transmission by 100% would cost a maximum of 125 monetary units per time step, which is <1.5 times the highest *ex post* cost of one infected animal, i.e., 85 monetary units), the previously observed pattern holds: farmers who optimize their control effort may not achieve the target prevalence from society's perspective.

## DISCUSSION

Analytical frameworks introducing human behavioral dynamics in the field of livestock infectious disease modeling have emerged in the last two decades. From the pioneering works of Bicknell et al. (24) and McInerney et al. (32) to the most recent individual-based, network-based, and game-theoretic models (9, 36–38), many significant contributions have improved our understanding of the interplay between human behavior and livestock disease spread (and the likelihood of disease control). However, this study is unique and contributes to that body of knowledge for two reasons. Firstly, it provides a simple but robust

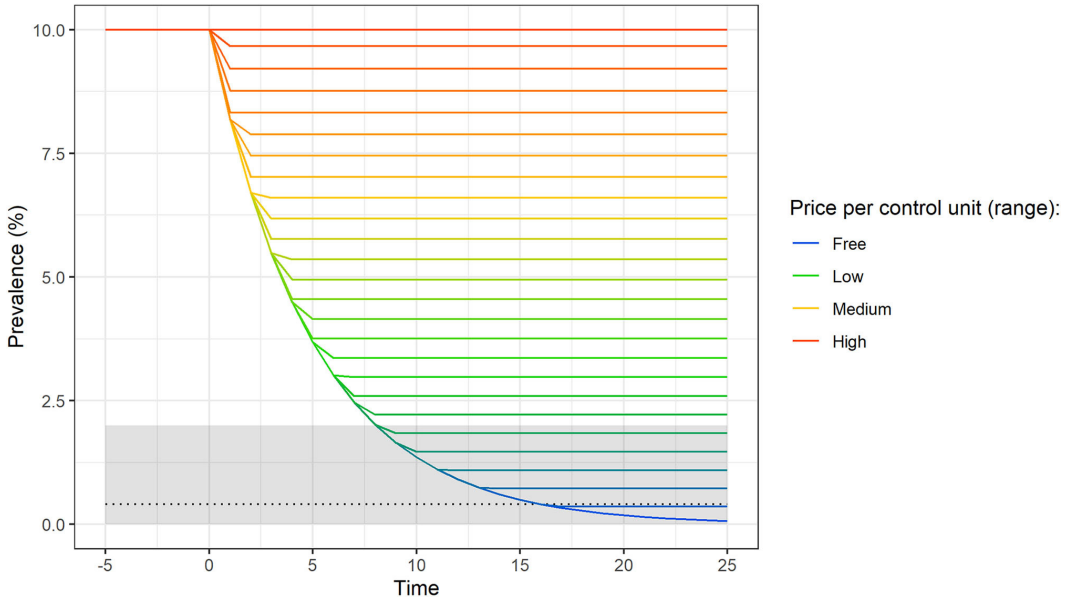



**FIGURE 3 |** Disease prevalence over time, assuming privately optimal behavior in a single farm for a range of prices per control unit. This simulation assumes a cost of one infected animal per time step ($\delta$) of 50 monetary units. The price of reducing the transmission rate by 1% ($\theta$) ranges from "Free" (0.00 monetary units) to "High" (1.25 monetary units). "Low" and "Medium" correspond to 0.40 and 0.85 monetary units, respectively. Colored lines represent increases by 0.05 monetary units. The gray shaded area indicates the target prevalence level from society's perspective (<2%). The black dotted horizontal line indicates a prevalence consistent with disease elimination (0.4%; <1 infected animal in a herd of 250 animals).

framework for exploring key factors in the control livestock diseases: farmer heterogeneity, externalities, and private-social misalignment of control optima. Secondly, we apply this framework to the control of endemic chronic diseases through privately funded actions in a low-resource setting.

Despite the growing literature on livestock infectious disease modeling, very little attention has been given to the assumption of homogeneous human behavior, the validity of which we evaluate here. Models of livestock disease typically assume that the farmers' perception of risk and the way they respond to that level of perceived risk remain unchanged over time (22). In addition, many epidemiological models entirely ignore the effects of changing prevalence on privately optimal spending on disease control (22, 23). However, several empirical studies have shown that a farmer's likelihood to take control actions is the result of a dynamic and complex interplay between epidemiological, economic, environmental, cultural, and social factors (39–43). Models of disease transmission that ignore such heterogeneity are likely to be misleading, resulting in reduced value for informing control efforts. Like many decision-makers, farmers make decisions based on conscious and unconscious, cognitive and affective shortcuts or rules of thumb (42, 44, 45). We model the implications of this type of individual decision-making process by simulating the effects on prevalence and costs of different levels of farmer responsiveness. These simulations quantify the consequences of heterogeneous behavior, the occurrence of externalities, and the consequent disparities between privately and socially optimal control efforts.

The simulations of our theoretical scenario of optimizing behavior assumed perfect information and rational behavior by the individual farmer. In this scenario, the farmer was able to accurately choose the optimal control effort at any point in time by trading-off the marginal benefits of reducing the prevalence against the marginal costs of their actions. These models assume a conservative range of values for the unit price of control action (from 0.00 to 1.25 monetary units to reduce the transmission rate by 1% per time step) and cost of one infected animal (from 10 to 85 monetary units per time step). For example, without administration and overhead charges, the annual cost of vaccinating a herd of 250 cattle for brucellosis in India (167.50 USD; 0.67 USD times 250) would be over twice as much the average loss caused by brucellosis per infected animal (73.44 USD) (46). The values that we used are considered appropriate and conservative for this evaluation because the highest possible cost of eliminating disease transmission completely would be equivalent to <1.5 times the highest *ex post* cost of one infected animal per time step. Despite these conservative assumptions, the societal disease control target was only achieved for high disease cost to price of control ratios (<25% of all price-cost combinations; **Figure 4**). Given these findings, we can infer that

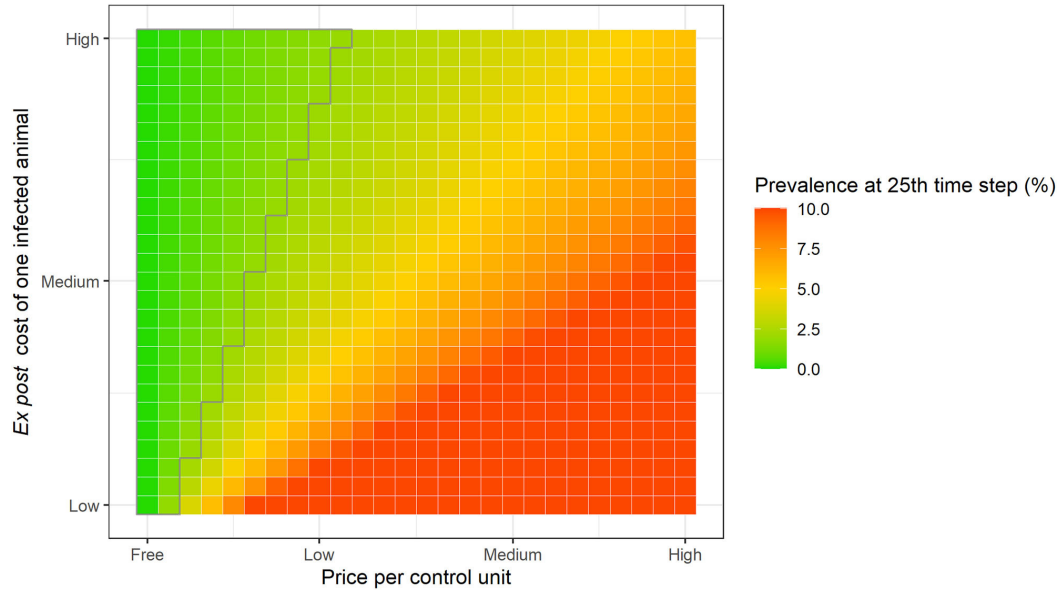



**FIGURE 4 |** Predicted prevalence at 25th time step for different values of price per control unit ("Free" = 0.00; "Low" = 0.40; "Medium" = 0.85; and, "High" = 1.25 monetary units) and *ex post* cost per infected animal ("Low" = 10; "Medium" = 46; and, "High" = 85 monetary units), assuming privately optimal behavior in a single farm. The polygon with gray border indicates the target prevalence level from society's perspective (<2%).

effective disease control through voluntary actions is unlikely to be privately optimal in many real-world cases. Additionally, as prevalence decreases, there is a sharp increase in the marginal costs of control action, which leads to a fall in optimal control effort. This result is consistent with the economic principle of diminishing returns and has also been reported by other theoretical (32) and empirical studies, namely those that analyzed control actions against tuberculosis (24, 47) and brucellosis (48, 49) in cattle.

Our model illustrates the misalignment of private and social optima for livestock disease control through a basic trade-off between the benefits of reductions in herd prevalence and the costs of transmission-reducing actions. Essentially, farmers "buy reductions in disease transmission," which is a simple and logical representation of many disease control actions. However, this approach is likely to underestimate the gap between private and social optima in many cases: the model does not capture many of the benefits of farmers' actions such as (i) the control of multiple pathogens through improved biosecurity, and (ii) the human health benefits in the cases of zoonoses. For instance, brucellosis is a bacterial zoonosis that causes abortion in livestock and debilitating symptoms (e.g., fever, joint pain, myalgia) in humans (50, 51). Given this burden on human health, in addition to animal health, voluntary actions taken by farmers to control the disease in their livestock (e.g., through vaccination) generate positive externalities, as society benefits from farmers' actions whilst not bearing the costs of these actions. This is a market failure that requires coordinated action to achieve socially optimal outcomes in terms of both human and animal health and productivity (48). Hence, the benefits enjoyed and the costs born by both public and private sectors must be considered throughout the planning phase of control interventions, which can include, among others, the provision of subsidized goods and services (e.g., vaccination), creating and enforcing regulations (e.g., movement restrictions) and setting compensation schemes (e.g., for culled seropositive animals) (8, 48).

To enable private farmers' actions to achieve a socially optimal disease control target, policy design and development must consider the heterogeneity of farmer behavior, the associated off-farm effects or externalities, and the predicted uptake of control measures under optimized farmer behavior. Failure to acknowledge these factors may result in potentially misleading predictions about disease transmission and the associated economic costs. This, in turn, perpetuates conditions in which private investments by farmers are inadequate to achieve disease control from society's perspective. For multi-host diseases that can impact multiple sectors (e.g., multi-host livestock diseases and zoonoses), inadequate disease control can have profound repercussions on international trade and, indeed, threaten human health.

## DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary materials, further inquiries can be directed to the corresponding author/s.

## AUTHOR CONTRIBUTIONS

ÂM, DH, EM, NH, and JH contributed to conception and design of the study and writing of the manuscript. ÂM and DH wrote the code in R. ÂM developed the interactive web application. All authors contributed to the article and approved the submitted version.

## FUNDING

This publication was supported by the University of Glasgow's Lord Kelvin/Adam Smith (LKAS) Ph.D. Scholarship.

## ACKNOWLEDGMENTS

We thank the members of the OHRBID lab (Univ. of Glasgow) for their useful feedback on the epidemiological-economic model presented here.

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**Conflict of Interest:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# B Data harmonisation and identification of production systems

## B.1 Availability of variables by dataset and criteria for validity.

**Table B.1.1:** Availability of numerical variables by dataset and criteria for the validity of observations.

| Numerical variable* | Dataset◇ | n† | Description | Criteria for the validity of observations |
|---|---|---|---|---|
| Annual precipitation | SEEDZ | 402 | Annual precipitation in mm | Valid geolocation in spatial dataset |
| | LSMS | 746 | Annual precipitation in mm | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 391 | Annual precipitation in mm | Coverage of the buffer by the spatial dataset |
| Average temperature | SEEDZ | 402 | Average annual mean temperature in $^{o}$C | Valid geolocation in spatial dataset |
| | LSMS | 746 | Average annual mean temperature in $^{o}$C | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 391 | Average annual mean temperature in $^{o}$C | Coverage of the buffer by the spatial dataset |
| Average vegetation cover | SEEDZ | 402 | Annual average enhanced vegetation index (EVI) | Valid geolocation in spatial dataset |
| | LSMS | 746 | Annual average enhanced vegetation index (EVI) | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 391 | Annual average enhanced vegetation index (EVI) | Coverage of the buffer by the spatial dataset |
| Cattle density | SEEDZ | 402 | Number of cattle per km$^2$ | Valid geolocation in spatial dataset |
| | LSMS | 746 | Number of cattle per km$^2$ | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 391 | Number of cattle per km$^2$ | Coverage of the buffer by the spatial dataset |
| Chicken density | SEEDZ | 402 | Number of chicken per km$^2$ | Valid geolocation in spatial dataset |
| | LSMS | 746 | Number of chicken per km$^2$ | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 391 | Number of chicken per km$^2$ | Coverage of the buffer by the spatial dataset |
| Cropland cover | SEEDZ | 402 | Proportion of an area with 1 km radius classified as cropland | Valid geolocation in spatial dataset |
| | LSMS | 746 | Proportion of the buffer area classified as cropland | Coverage of the buffer by the spatial dataset |

Continuation of Table B.1.1

| Numerical variable* | Dataset◇ | n† | Description | Criteria for the validity of observations |
|---|---|---|---|---|
| | RHoMIS | 391 | Proportion of the buffer area classified as cropland | Coverage of the buffer by the spatial dataset |
| Distance to main road | SEEDZ | 402 | Euclidean distance to the nearest trunk road (in km) | Valid geolocation in spatial dataset |
| | LSMS | 746 | Euclidean distance to the nearest trunk road (in km) | Valid distance from the center of the buffer |
| | RHoMIS | 391 | Euclidean distance to the nearest trunk road (in km) | Valid distance from the center of the buffer |
| Forest cover | SEEDZ | 402 | Proportion of an area with 1 km radius classified as forest | Valid geolocation in spatial dataset |
| | LSMS | 746 | Proportion of the buffer area classified as forest | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 391 | Proportion of the buffer area classified as forest | Coverage of the buffer by the spatial dataset |
| Goats density | SEEDZ | 402 | Number of goats per $km^2$ | Valid geolocation in spatial dataset |
| | LSMS | 746 | Number of goats per $km^2$ | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 391 | Number of goats per $km^2$ | Coverage of the buffer by the spatial dataset |
| Grassland cover | SEEDZ | 402 | Proportion of an area with 1 km radius classified as grassland | Valid geolocation in spatial dataset |
| | LSMS | 746 | Proportion of the buffer area classified as grassland | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 391 | Proportion of the buffer area classified as grassland | Coverage of the buffer by the spatial dataset |
| Human population density | SEEDZ | 402 | Human population per $km^2$ in 2016 | Valid geolocation in spatial dataset |

Continuation of Table B.1.1

| Numerical variable* | Dataset◇ | n† | Description | Criteria for the validity of observations |
|---|---|---|---|---|
| | LSMS | 746 | Human population per $km^2$ in 2016 | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 391 | Human population per $km^2$ in 2016 | Coverage of the buffer by the spatial dataset |
| Maximum slope | SEEDZ | 402 | Maximum slope (in degrees) within 1 km radius | Valid geolocation in spatial dataset |
| | LSMS | 746 | Mean slope within the buffer of uncertainty | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 391 | Mean slope within the buffer of uncertainty | Coverage of the buffer by the spatial dataset |
| Pigs density | SEEDZ | 402 | Number of pigs per $km^2$ | Valid geolocation in spatial dataset |
| | LSMS | 746 | Number of pigs per $km^2$ | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 391 | Number of pigs per $km^2$ | Coverage of the buffer by the spatial dataset |
| Sheep density | SEEDZ | 402 | Number of sheep per $km^2$ | Valid geolocation in spatial dataset |
| | LSMS | 746 | Number of sheep per $km^2$ | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 391 | Number of sheep per $km^2$ | Coverage of the buffer by the spatial dataset |
| Travel time to centre | SEEDZ | 402 | Travel time (in hours) to a town of greater than 20,000 people | Valid geolocation in spatial dataset |
| | LSMS | 746 | Travel time (in hours) to a town of greater than 20,000 people | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 390 | Travel time (in hours) to a town of greater than 20,000 people | Coverage of the buffer by the spatial dataset |
| Village area | SEEDZ | 402 | Area of the village (in decimal degrees) | Valid geolocation in spatial dataset |
| | LSMS | 746 | Area of the village (in decimal degrees) | Coverage of the buffer by the spatial dataset |
| | RHoMIS | 391 | Area of the village (in decimal degrees) | Coverage of the buffer by the spatial dataset |
| Number of cattle | SEEDZ | 404 | How many animals of the following species and type are managed together at this compound? | Answered a non-negative integer |

Continuation of Table B.1.1

| Numerical variable* | Dataset◇ | n† | Description | Criteria for the validity of observations |
|---|---|---|---|---|
| | LSMS | 746 | How many [ cattle ] does this household currently own? | Answered a non-negative integer |
| | RHoMIS | 391 | How many head of cattle does your household own | Answered a non-negative integer |
| Number of goats | SEEDZ | 404 | How many animals of the following species and type are managed together at this compound? | Answered a non-negative integer |
| | LSMS | 746 | How many [ goats ] does this household currently own? | Answered a non-negative integer |
| | RHoMIS | 391 | How many head of goats does your household own | Answered a non-negative integer |
| Number of sheep | SEEDZ | 404 | How many animals of the following species and type are managed together at this compound? | Answered a non-negative integer |
| | LSMS | 746 | How many [ sheep ] does this household currently own? | Answered a non-negative integer |
| | RHoMIS | 391 | How many head of sheep does your household own | Answered a non-negative integer |

* Numerical variables ordered by domain (domain 1, local household environment, and domain 4, number of livestock. ◇ SEEDZ refers to the Social, Environmental and Economic Drivers of Zoonotic disease project. LSMS refers to the Living Standards Measurement Study. RHoMIS refers to the Rural Household Multiple Indicator Survey. † Number of valid observations.

**Table B.1.2:** Availability of categorical variables by dataset and variable attribute definition.

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| Arusha tribe | SEEDZ | 404 | What is your tribe? | Answered 'Arusha' |
| | LSMS | 0 | Not available | Not available |
| | RHoMIS | 0 | Not available | Not available |
| Barabaig tribe | SEEDZ | 404 | What is your tribe? | Answered 'Barabaig' |
| | LSMS | 0 | Not available | Not available |
| | RHoMIS | 0 | Not available | Not available |
| Government title for land | SEEDZ | 404 | Do members of the household have a title for this land? Where is the land title from? | Household members have a government title for the land (local (traditional); government; other) |
| | LSMS | 745 | Do you have any documentation of ownership of the dwelling? | Answered one of the following options: i) offer of the right of occupancy; ii) title deed for land; iii) letter or allocation from village government; or, iv) settlement permit. |
| | RHoMIS | 0 | Not available | Not available |
| Head primary education | SEEDZ | 404 | What is the highest level of education of the head of the household? | Answered primary or above |
| | LSMS | 746 | What is the highest grade completed by [household head]? | Completed primary education if answered D7, D8, OSC or above (prior to independence, there used to be a D8) |
| | RHoMIS | 381 | What is the highest level of education the head person has completed? | Answered primary or above. If 'illiterate' was answered, did not complete primary education |
| Household head male | SEEDZ | 404 | Sex of household head | Household head is male |
| | LSMS | 746 | Sex of household head | Household head is male |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| | RHoMIS | 367 | Sex of respondent | Questionnaire only asked sex of respondent. If the respondent is female and was married with the household head, it is assumed that the household head is male |
| Iraqw tribe | SEEDZ | 404 | What is your tribe? | Answered 'Iraqw' |
| | LSMS | 0 | Not available | Not available |
| | RHoMIS | 0 | Not available | Not available |
| Latrine ownership | SEEDZ | 404 | What type of toilet system do members of this household use? | Answered one of these: flush or pour toilet with septic tank, including squat toilet; flush or pour toilet connected to sewer pipe; pit latrine with covering slab; pit latrine without covering slab; ventilated improved pit latrine (VIP); bucket or plastic bags. |
| | LSMS | 746 | What is the main toilet facilities usually used in this household?[1] | Answered one of these: pit latrine without slab, pit latrine with slab (not washable), pit latrine with slab (washable), VIP, pour flush, flush toilet, ecosan.[2] |
| | RHoMIS | 0 | Not available | Not available |
| Maasai tribe | SEEDZ | 404 | What is your tribe? | Answered 'Maasai' |
| | LSMS | 0 | Not available | Not available |
| | RHoMIS | 0 | Not available | Not available |
| Meru tribe | SEEDZ | 404 | What is your tribe? | Answered 'Meru' |
| | LSMS | 0 | Not available | Not available |
| | RHoMIS | 0 | Not available | Not available |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| Treat drinking water | SEEDZ | 404 | How frequently do you treat water before drinking it? | Answered other than never |
| | LSMS | 746 | What measures does this household take to ensure the safety of drinking water?[3] | Answered a treatment other than none[4] |
| | RHoMIS | 0 | Not available | Not available |
| Turu tribe | SEEDZ | 404 | What is your tribe? | Answered 'Turu' |
| | LSMS | 0 | Not available | Not available |
| | RHoMIS | 0 | Not available | Not available |
| Grow beans | SEEDZ | 404 | Which crops did members of the household grow in the past 12 months? | Beans was one of the crops mentioned |
| | LSMS | 746 | For each plot list all annual crops cultivated (in the long rainy season 2012 and in the last completed short rainy season)[5] | Beans was one of the crops cultivated in any plot in any season |
| | RHoMIS | 391 | Which crops were grown by your household during the last 12 months? | Beans was one of the crops mentioned |
| Grow cowpeas | SEEDZ | 404 | Which crops did members of the household grow in the past 12 months? | Cowpeas was one of the crops mentioned |
| | LSMS | 746 | For each plot list all annual crops cultivated (in the long rainy season 2012 and in the last completed short rainy season)[5] | Cowpeas was one of the crops cultivated in any plot in any season |
| | RHoMIS | 391 | Which crops were grown by your household during the last 12 months? | Cowpeas was one of the crops mentioned |
| Grow maize | SEEDZ | 404 | Which crops did members of the household grow in the past 12 months? | Maize was one of the crops mentioned |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| | LSMS | 746 | For each plot list all annual crops cultivated (in the long rainy season 2012 and in the last completed short rainy season)[5] | Maize was one of the crops cultivated in any plot in any season |
| | RHoMIS | 391 | Which crops were grown by your household during the last 12 months? | Maize was one of the crops mentioned |
| Grow millet | SEEDZ | 404 | Which crops did members of the household grow in the past 12 months? | Millet was one of the crops mentioned |
| | LSMS | 746 | For each plot list all annual crops cultivated (in the long rainy season 2012 and in the last completed short rainy season)[5] | Bulrush millet or finger millet were two of the crops cultivated in any plot in any season |
| | RHoMIS | 391 | Which crops were grown by your household during the last 12 months? | Millet was one of the crops mentioned |
| Grow no crops | SEEDZ | 404 | Were any crops grown by members of this household during the last 12 months? | Answered ‘no’ |
| | LSMS | 746 | Does anyone in the household cultivate any plot? | Answered‘no’ |
| | RHoMIS | 391 | Does your household grow any crops? | Answered ‘no’ |
| Grow onions | SEEDZ | 404 | Which crops did members of the household grow in the past 12 months? | Onions was one of the crops mentioned |
| | LSMS | 746 | For each plot list all annual crops cultivated (in the long rainy season 2012 and in the last completed short rainy season)[5] | Onions was one of the crops cultivated in any plot in any season |
| | RHoMIS | 391 | Which crops were grown by your household during the last 12 months? | Onions was one of the crops mentioned |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| Grow potato | SEEDZ | 404 | Which crops did members of the household grow in the past 12 months? | Potato was one of the crops mentioned |
| | LSMS | 746 | For each plot list all annual crops cultivated (in the long rainy season 2012 and in the last completed short rainy season)[5] | Sweet potatos or irish potatos were two of the crops cultivated in any plot in any season |
| | RHoMIS | 391 | Which crops were grown by your household during the last 12 months? | Potato was one of the crops mentioned |
| Grow sesame | SEEDZ | 404 | Which crops did members of the household grow in the past 12 months? | Sesame was one of the crops mentioned |
| | LSMS | 746 | For each plot list all annual crops cultivated (in the long rainy season 2012 and in the last completed short rainy season)[5] | Sesame was one of the crops cultivated in any plot in any season |
| | RHoMIS | 391 | Which crops were grown by your household during the last 12 months? | Sesame was one of the crops mentioned |
| Grow sorghum | SEEDZ | 404 | Which crops did members of the household grow in the past 12 months? | Sorghum was one of the crops mentioned |
| | LSMS | 746 | For each plot list all annual crops cultivated (in the long rainy season 2012 and in the last completed short rainy season)[5] | Sorghum was one of the crops cultivated in any plot in any season |
| | RHoMIS | 391 | Which crops were grown by your household during the last 12 months? | Sorghum was one of the crops mentioned |
| Grow sunflower | SEEDZ | 404 | Which crops did members of the household grow in the past 12 months? | Sunflower was one of the crops mentioned |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| | LSMS | 746 | For each plot list all annual crops cultivated (in the long rainy season 2012 and in the last completed short rainy season)[5] | Sunflower was one of the crops cultivated in any plot in any season |
| | RHoMIS | 391 | Which crops were grown by your household during the last 12 months? | Sunflower was one of the crops mentioned |
| Grow wheat | SEEDZ | 404 | Which crops did members of the household grow in the past 12 months? | Wheat was one of the crops mentioned |
| | LSMS | 746 | For each plot list all annual crops cultivated (in the long rainy season 2012 and in the last completed short rainy season)[5] | Wheat was one of the crops cultivated in any plot in any season |
| | RHoMIS | 391 | Which crops were grown by your household during the last 12 months? | Wheat was one of the crops mentioned |
| Growing crops $>$ 10 years | SEEDZ | 404 | How many years have members of this household been growing crops | Growing crops $>$ 10 years |
| | LSMS | 0 | Not available | Not available |
| | RHoMIS | 0 | Not available | Not available |
| Own plough | SEEDZ | 404 | Do members of this household own any of the following items? | Answered ox plough or other |
| | LSMS | 746 | How many [ITEMS] does your household own? | Answered more than zero 'plough etc.' |
| | RHoMIS | 0 | Not available | Not available |
| Sell crops | SEEDZ | 404 | Did this household sell any crops in the last 12 months? | Answered 'yes'. If the household did not grow crops, it is assumed that it did not sell. |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| | LSMS | 743 | Did you sell any of the crops produced in the long rainy season 2012? Did you sell any of the crops produced in the last completed short rainy season?[6] | Answered 'yes' for at least one crop in any season. If the household did not grow crops, it is assumed that it did not sell. |
| | RHoMIS | 391 | What did you do with the main harvest of during the last 12 months? Did you eat it, use at home, sell it? | Answered 'sell it' for at least one crop. If the household did not grow crops, it is assumed that it did not sell. |
| Staple crops last $>$ 6 m | SEEDZ | 401 | How many months do staple crops (e.g. beans, maize, rice, bananas) support your family in an average year? | If answered '6 or more months' |
| | LSMS | 0 | Not available | Not available |
| | RHoMIS | 0 | Not available | Not available |
| Chickens | SEEDZ | 404 | [Do you own] chickens? | Answered 'yes' |
| | LSMS | 746 | How many [ chickens ] does this household currently own? | Answered more than zero |
| | RHoMIS | 391 | How many head of chicken does your household own | Answered more than zero |
| Donkeys | SEEDZ | 404 | [Do you own] donkeys ? | Answered 'yes' |
| | LSMS | 746 | How many [ donkeys ] does this household currently own? | Answered more than zero |
| | RHoMIS | 391 | How many head of donkeys or similar does your household own | Answered more than zero |
| European breed cattle | SEEDZ | 404 | How many of these cattle are exotic breeds? | Answered more than zero |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| | LSMS | 746 | How many [ cattle ] does this household currently own? | Includes improved or exotic cattle |
| | RHoMIS | 386 | Are they (cattle) local breeds? | Answered 'improved' or 'both' (local and improved) |
| European breed small stock | SEEDZ | 404 | How many of these goats are exotic breeds? | Owns exotic goats |
| | LSMS | 746 | How many [ goats ] does this household currently own? | Includes improved or exotic (goats) |
| | RHoMIS | 391 | Are they (goats) local breeds? | Answered 'improved' or 'both' (local and improved) goats |
| Pigs | SEEDZ | 404 | [Do you own] Pigs? | Answered 'yes' |
| | LSMS | 746 | How many [ pigs ] does this household currently own? | Answered more than zero |
| | RHoMIS | 391 | How many head of pigs does your household own | Answered more than zero |
| Cattle transhumance | SEEDZ | 384 | Are cattle from this compound regularly taken to seasonal camps for grazing? | Answered 'yes' |
| | LSMS | 0 | Not available | Not available |
| | RHoMIS | 0 | Not available | Not available |
| Graze cattle with small stock | SEEDZ | 404 | Which of the following best describes the way you manage the herding of animals in this compound? Cattle, sheep and goats together; Cattle separately, sheep and goats together; Cattle with goats, sheep separately | Graze cattle with goats and/or sheep |
| | LSMS | 0 | Not available | Not available |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| | RHoMIS | 0 | Not available | Not available |
| Sell milk | SEEDZ | 404 | In the past month have you sold milk from animals in this household? | Answered 'yes' |
| | LSMS | 746 | During this period (12 months), how many litres of [ANIMAL] liquid milk did you sell per day? | Sold more than zero litres of liquid milk per day from any species (cattle or small ruminants) |
| | RHoMIS | 379 | What does your household do with the [livestock_label] milk? Drink it at home, sell it, make dairy products. | Answered 'sell it' for at least one of the species. |
| Small stock transhumance | SEEDZ | 385 | Are goats from this compound regularly taken to seasonal camps for grazing? Are sheep from this compound regularly taken to seasonal camps for grazing? | Answered 'yes'. Includes sheep or goats. |
| | LSMS | 0 | Not available | Not available |
| | RHoMIS | 0 | Not available | Not available |
| Tether cattle | SEEDZ | 403 | How are cattle in this compound grazed during the wet and dry season? Free grazing (no herdsperson); Herded; Tethered; Zero grazed | Answered 'tethered' in wet or dry season |
| | LSMS | 745 | What have been for this household the major feeding practices for [ small ruminants ] in the last 12 months? | Answered 'tethering' only |
| | RHoMIS | 0 | Not available | Not available |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| Tether small stock | SEEDZ | 404 | How are sheep and goats in this compound grazed during the wet and dry season? Free grazing (no herdsperson); Herded; Tethered; Zero grazed | Answered 'tethered' in wet or dry season |
| | LSMS | 745 | What have been for this household the major feeding practices for [ small ruminants ] in the last 12 months? | Answered 'tethering' only |
| | RHoMIS | 0 | Not available | Not available |
| Vaccinate against any disease | SEEDZ | 397 | Have any animals in your herd been vaccinated in the past 24 months? | Answered 'yes' |
| | LSMS | 745 | Did you vaccinate your [ANIMAL] in the past 12 months? | Answered 'yes, at least once' or 'yes, some' |
| | RHoMIS | 0 | Not available | Not available |
| Zero graze cattle | SEEDZ | 403 | How are cattle in this compound grazed during the wet and dry season? Free grazing (no herdsperson); Herded; Tethered; Zero grazed | Answered 'zero grazed' in wet or dry season |
| | LSMS | 745 | What have been for this household the major feeding practices for [ cattle ] in the last 12 months? | Answered only 'feeding (no grazing and no scavenging)' |
| | RHoMIS | 391 | Does your household use any grazing land for your animals? | Answered 'no grazing' and own cattle |
| Zero graze small stock | SEEDZ | 404 | How are sheep and goats in this compound grazed during the wet and dry season? Free grazing (no herdsperson); Herded; Tethered; Zero grazed | Answered 'zero grazed' in wet or dry season |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| | LSMS | 745 | What have been for this household the major feeding practices for [ small ruminants ] in the last 12 months? | Answered only feeding (no grazing and no scavenging) |
| | RHoMIS | 391 | Does your household use any grazing land for your animals? | Answered 'no grazing' and own sheep or goats |
| Any animal source food | SEEDZ | 404 | In the past 4 days, have you or anyone else in the household eaten the following foods? | Answered meat, dairy, blood, poultry, fish, or eggs |
| | LSMS | 746 | Within the past 7 days, did the members of this household eat/drink any [. . .] within the household? | Answered meat, meat products, fish, milk and milk products, butter, margarine, ghee or other fat products |
| | RHoMIS | 255 | How often were these eaten in your household during the last month? | Answered meat, dairy, or eggs (eaten daily or weekly) |
| Blood | SEEDZ | 404 | In the past 4 days, have you or anyone else in the household eaten the following foods? | Answered blood from livestock, either fresh or processed |
| | LSMS | 0 | Not available | Not available |
| | RHoMIS | 0 | Not available | Not available |
| Dairy | SEEDZ | 404 | In the past 4 days, have you or anyone else in the household eaten the following foods? | Answered cheese, yoghurt, milk or other milk products |
| | LSMS | 746 | Within the past 7 days, did the members of this household eat/drink any [. . .] within the household? | Answered fresh milk, milk products (like cream, cheese, yoghurt, etc), or canned milk/milk powder |
| | RHoMIS | 254 | How often were these eaten in your household during the last month? | Answered milk or dairy foods (eaten daily or weekly) |
| Eggs | SEEDZ | 404 | In the past 4 days, have you or anyone else in the household eaten the following foods? | Answered eggs |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| | LSMS | 746 | Within the past 7 days, did the members of this household eat/drink any [. . .] within the household? | Answered eggs |
| | RHoMIS | 253 | How often were these eaten in your household during the last month? | Answered chicken eggs, guinea fowl eggs, duck eggs, kalukuluku eggs, or any eggs (eaten daily or weekly) |
| Fats | SEEDZ | 404 | In the past 4 days, have you or anyone else in the household eaten the following foods? | Answered foods made with oil, fat, or butter |
| | LSMS | 746 | Within the past 7 days, did the members of this household eat/drink any [. . .] within the household? | Answered cooking oil, butter, margarine, ghee or other fat products |
| | RHoMIS | 0 | Not available | Not available |
| Fish | SEEDZ | 404 | In the past 4 days, have you or anyone else in the household eaten the following foods? | Answered fresh or dried fish or shellfish |
| | LSMS | 746 | Within the past 7 days, did the members of this household eat/drink any [. . .] within the household? | Answered fresh fish and seafood (including dagaa), dried/salted fish or seafood (incl. dagaa), package/canned fish |
| | RHoMIS | 0 | Not available | Not available |
| Legumes | SEEDZ | 404 | In the past 4 days, have you or anyone else in the household eaten the following foods? | Answered foods made from beans, peas, lentils, nuts |
| | LSMS | 746 | Within the past 7 days, did the members of this household eat/drink any [. . .] within the household? | Answered peas, beans, lentils and other pulses, nuts or seeds. |
| | RHoMIS | 255 | How often were these eaten in your household during the last month? | Answered beans, peas, lentils, nuts or seeds (eaten daily or weekly) |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| Meat | SEEDZ | 404 | In the past 4 days, have you or anyone else in the household eaten the following foods? | Answered beef, pork, lamb, goat, rabbit, wild game or liver, kidney, heart or other organ meats from these animals. Excludes Chicken and other poultry |
| | LSMS | 746 | Within the past 7 days, did the members of this household eat/drink any [. . .] within the household? | Answered goat meat, beef, including minced sausage, pork, including sausages and bacon, wild birds and insects, or other domestic/wild meat products |
| | RHoMIS | 0 | Not available | Not available |
| Poultry | SEEDZ | 404 | In the past 4 days, have you or anyone else in the household eaten the following foods? | Answered chicken, duck or other birds (including liver, kidney, heart, or other organ meats from such animals) |
| | LSMS | 746 | Within the past 7 days, did the members of this household eat/drink any [. . .] within the household? | Answered chicken or other poultry |
| | RHoMIS | 0 | Not available | Not available |
| Roots | SEEDZ | 404 | In the past 4 days, have you or anyone else in the household eaten the following foods? | Answered potatoes, yams, cassava, or any other foods made from roots or tubers |
| | LSMS | 746 | Within the past 7 days, did the members of this household eat/drink any [. . .] within the household? | Answered cassava fresh, cassava dry/flour, sweet potatoes, yams/cocoyams, or irish potatoes |
| | RHoMIS | 0 | Not available | Not available |
| Vegetables | SEEDZ | 404 | In the past 4 days, have you or anyone else in the household eaten the following foods? | Answered vegetables or fruits |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| | LSMS | 746 | Within the past 7 days, did the members of this household eat/drink any [. . .] within the household? | Answered onions, tomatoes, carrots and green pepper, other viungo, spinach, cabbage and other green vegetables, canned, dried and wild vegetables, ripe bananas, citrus fruits (oranges, lemon, tangerines, etc.), mangoes, avocadoes or other fruits, and sugarcane |
| | RHoMIS | 255 | How often were these eaten in your household during the last month? | Answered leafy green vegetables (rape, kale, cabbage, spinach, greens), orange coloured vegetables or fruits (orange maize, orange sweet potato, pumpkin, ripe papaya) or other vegetables (eggplant, mushrooms, onion, tomato, cucumber) eaten daily or weekly |
| Crop losses | SEEDZ | 404 | Did your household experience any of the following situations during the past year? | Answered loss of crops |
| | LSMS | 745 | Were there any losses of crops before the harvest? | Answered 'yes' for the long rainy season 2012 or last completed short rainy season[7] |
| | RHoMIS | 385 | During the 12 months, was the harvest good or bad? | Answered 'bad' for at least one of the crops |
| Hunger | SEEDZ | 404 | Did your household experience any of the following situations during the past year? | Answered 'yes' to hunger |
| | LSMS | 745 | In the last 12 months, have you been faced with a situation when you did not have enough food to feed the household? | Answered 'yes' |
| | RHoMIS | 0 | Not available | Not available |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| Illness in livestock | SEEDZ | 404 | Did your household experience any of the following situations during the past year? | Answered 'yes' to livestock illness |
| | LSMS | 745 | Have you lost any [ANIMAL] to disease in the past 12 months? | Answered 'yes' |
| | RHoMIS | 0 | Not available | Not available |
| Illness in people | SEEDZ | 404 | Did your household experience any of the following situations during the past year? | Answered 'yes' to long illness (people) |
| | LSMS | 746 | Over the past two years, was your household severely affected negatively by any of the following events?[8] | Answered 'yes' to chronic/severe illness or accident of household member |
| | RHoMIS | 0 | Not available | Not available |
| Land losses | SEEDZ | 404 | Did your household experience any of the following situations during the past year? | Answered 'yes' to loss of land |
| | LSMS | 746 | Over the past two years, was your household severely affected negatively by any of the following events?[8] | Answered 'yes' to loss of land |
| | RHoMIS | 0 | Not available | Not available |

Continuation of Table B.1.2

| Categorical variable* | Dataset◇ | n† | Question | Variable attribute definition |
|---|---|---|---|---|
| Livestock losses | SEEDZ | 404 | Did your household experience any of the following situations during the past year? | Answered 'yes' to loss of livestock (death, predation, theft, etc.) |
| | LSMS | 746 | Over the past two years, was your household severely affected negatively by any of the following events?[8] | Answered 'yes' to 'livestock died' or 'were stolen' |
| | RHoMIS | 391 | Did any of the [livestock] die during the last 12 months? How many? | Answered 'yes' (or more than zero) for at least one of the livestock species. |

* Categorical variables ordered by domain (from domain 2 (household demographics) to domain 8 (indicators of household vulnerability), excluding domain 4, which is made of numerical variables (number of livestock)). ◇ SEEDZ refers to the Social, Environmental and Economic Drivers of Zoonotic disease project. LSMS refers to the Living Standards Measurement Study. RHoMIS refers to the Rural Household Multiple Indicator Survey. † Number of valid observations. [1] In wave 4, 'what kind of toilet facility do members of your household generally use?' [2] In wave 4, 'answered one of these: pit latrine without slab/open pit, pit latrine with slab (not washable), pit latrine with slab (washable), VIP, pour flush, flush toilet, ecosan.' [3] In wave 4, 'what do you usually do to the water to make it safer to drink in the rainy season? What do you usually do to the water to make it safer to drink in the dry season?' [4] In wave 4, answered a treatment other than none in at least one of the seasons. [5] In wave 4, 'for each plot list all annual crops cultivated (in the long rainy season 2014 and in the last completed short rainy season).' [6] In wave 4, 'did you sell any of the crops produced in the long rainy season 2014? Did you sell any of the crops produced in the last completed short rainy season?' [7] Answered 'yes' for the long rainy season 2014 or last completed short rainy season. [8] In wave 4, 'over the past five years, was your household severely affected negatively by any of the following events?'

# C Production losses due to livestock brucellosis in northern Tanzania

## C.1 Model step A - brucellosis prevalence

**Table C.1.1:** Beta distribution (dbeta) shape parameters ($\alpha$, $\beta$) used to specify priors for sensitivity and specificity of the Rose-Bengal test (RBT) and competitive enzyme-linked immunosorbent assay (cELISA) for cattle, sheep, and goat models, as per Bodenham et al. (2021).

| | Shape parameters ($\alpha$, $\beta$) in each species model | | |
|---|---|---|---|
| | Cattle | Sheep | Goats |
| RBT sensitivity | (8,1) | (4,1) | (4,1) |
| RBT specificity | (1,1) | (1,1) | (1,1) |
| cELISA sensitivity | (30,2) | (8,1) | (12,1) |
| cELISA specificity | (1,1) | (1,1) | (1,1) |

The covariance variables ($\gamma_{Se}$ and $\gamma_{Sp}$) were specified as uniform distributions with the maximum and minimum limits given below, as per Branscum et al. (2005), Mazeri et al. (2016), Dendukuri and Joseph (2001), and Bodenham et al. (2021):

$$\begin{aligned} (Se_1 - 1)(1 - Se_2) \leq \gamma_{Se} \leq min(Se_1, Se_2) - Se_1 Se_2 \\ (Sp_1 - 1)(1 - Sp_2) \leq \gamma_{Sp} \leq min(Sp_1, Sp_2) - Sp_1 Sp_2 \end{aligned} \quad (1)$$

where $Se$ and $Sp$ refer to sensitivity and specificity, respectively, and the subscripts $_1$ and $_2$ refer to the Rose-Bengal test (RBT) and a competitive enzyme-linked immunosorbent assay (cELISA), respectively.

## C.2 Model step C - production in the presence of brucellosis

**Table C.2.1:** Probability density functions used to parametrise the production losses model. Int. $: international dollars.

| | | Production system | |
|---|---|---|---|
| Species | Parameter | Pastoral | Non-pastoral |
| Cattle | Wholesale price ($w$, int. $) | lnorm(6.21, 0.50) | gamma(3.15, 0.01) |
| | Milk yield ($y$, litres per day) | lnorm(0.34, 0.79) | lnorm(0.94, 0.98) |
| | Milk price ($p$, int. $/L) | gamma(2.04, 2.39) | gamma(2.04, 2.39) |
| | Lactation length ($l$, days) | nbinom(3.95, 208.65) | nbinom(3.48, 198.29) |
| Sheep | Wholesale price ($w$, int. $) | gamma(5.24, 0.09) | gamma(3.84, 0.08) |
| | Milk yield ($y$, litres per day) | gamma(0.98, 1.11) | gamma(1.85, 1.43) |
| | Lactation length ($l$, days) | nbinom(2.77, 161.74) | nbinom(2.50, 106.69) |
| Goats | Wholesale price ($w$, int. $) | gamma(5.35, 0.10) | gamma(4.64, 0.08) |
| | Milk yield ($y$, litres per day) | gamma(0.98, 1.11) | gamma(1.85, 1.43) |
| | Lactation length ($l$, days) | nbinom(2.77, 161.74) | nbinom(2.50, 106.69) |

'lnorm' refers to the log-normal distribution, with parameters $\mu$ and $\sigma$, which are the mean and standard deviation, respectively; 'gamma' refers to the gamma distribution, with parameters $\alpha$ (or shape) and $\beta$ (or scale or 1/rate), respectively; 'nbinom' refers to the negative binomial distribution, with parameters 'size' and $\mu$, which are the dispersion parameter and the mean, respectively.

## C.3 Determinants of losses attributable to brucellosis

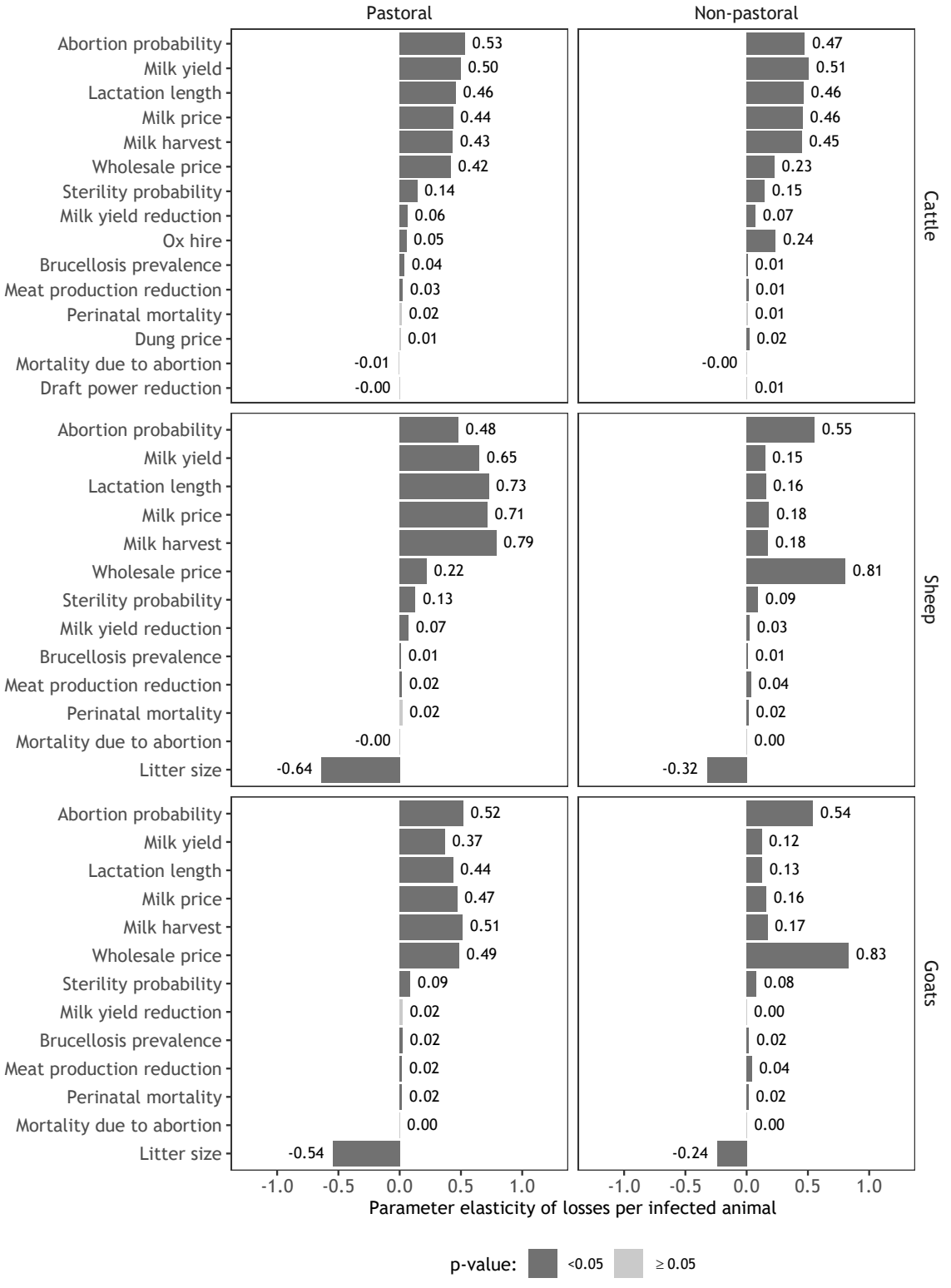



**Figure C.3.1:** Tornado plot showing the parameter elasticity of production losses (int. $) per infected animal (percentage change in production losses per infected animal per year when parameter values change by 1%), by production system (pastoral and non-pastoral) and species (cattle, sheep, and goats) (50,000 model iterations, scenario of 'unrestricted increase in herd size'). The colours of the bars indicate the significance of the parameter elasticity estimate (dark and light grey indicate p-value $< 0.05$ and p-value $\geq 0.05$, respectively).

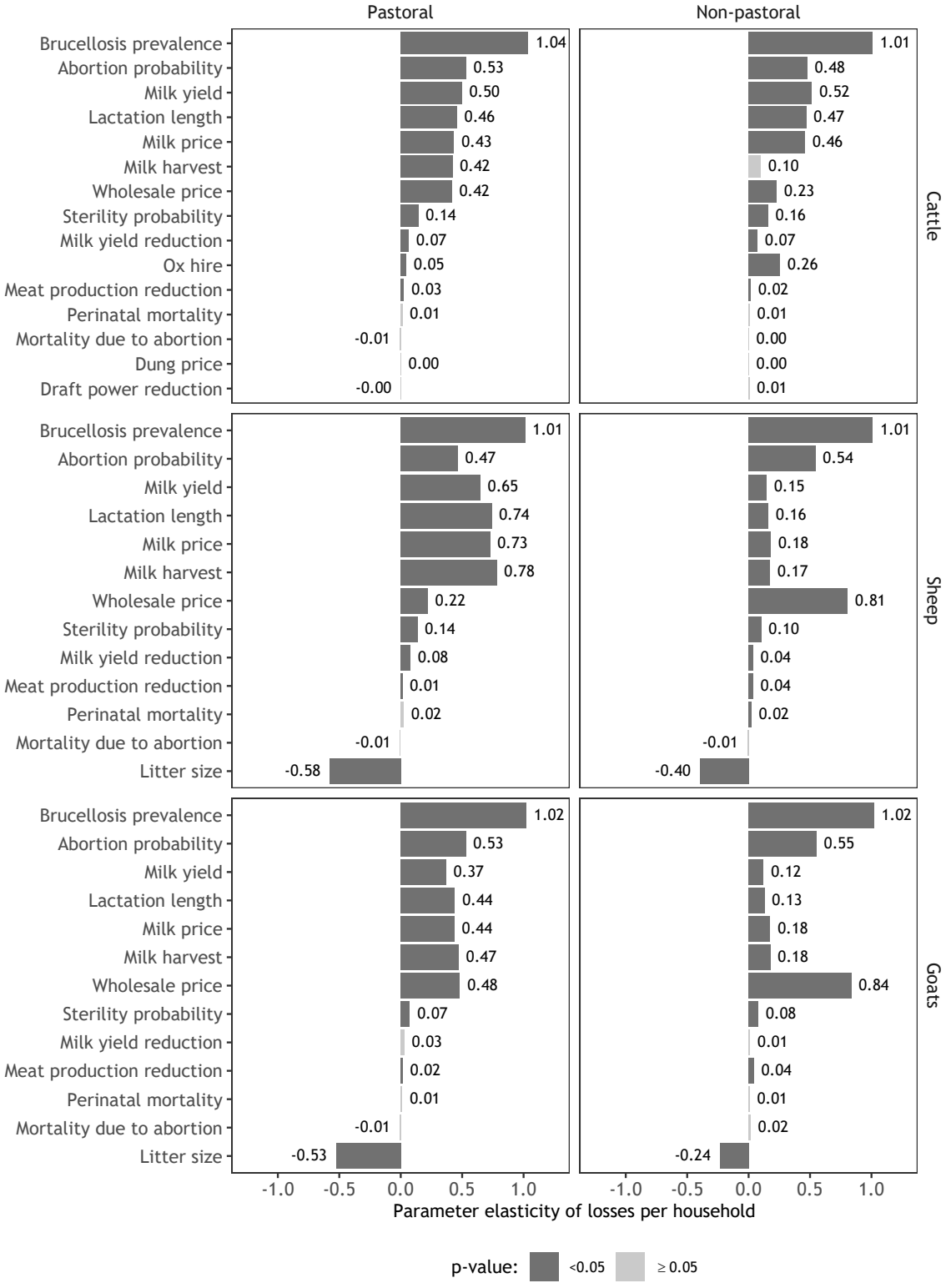



**Figure C.3.2:** Tornado plot showing the parameter elasticity of production losses (int. $) per household (percentage change in production losses per household per year when parameter values change by 1%), by production system (pastoral and non-pastoral) and species (cattle, sheep, and goats) (50,000 model iterations, scenario of 'unrestricted increase in herd size'). The colours of the bars indicate the significance of the parameter elasticity estimate (dark and light grey indicate p-value $< 0.05$ and p-value $\geq 0.05$, respectively).

# D Monetary cost and disease burden attributable to human brucellosis

## D.1 Health-related expenditure calculation

The health-related expenditure was calculated separately for target and non-target healthcare-seeking cases. Brucellosis cases that take pathways 1 ($S_1$-$S_5$), 5 ($S_1$-$S_3$-$S_5$), 7 ($S_1$-$S_6$) and 11 ($S_1$-$S_3$-$S_6$) incur non-target health-related expenditure. Brucellosis cases that take other pathways incur target health-related expenditure.

Target and non-target health-related expenditures were calculated as the sum of the expenditures incurred with all relevant goods and services (listed in Table D.1.1). The expenditure incurred with each good or service was calculated by multiplying the probability of a case incurring a cost (with the health-related good or service) by the price of the good or service, as follows:

$$\text{Expenditure} = \sum_{i=1}^{n} P_i Q_i \tag{2}$$

where i is a good or service listed in Table D.1.1, $P_i$ is the probability of a case incurring a cost with good or service i, and $Q_i$ is the price of the good or service i.

The probability of a target or non-target healthcare-seeking case incurring a cost was obtained from the expert elicitation (*PERT* distributions; the group mean for mode, and the minimum and maximum values corresponding to the minimum and maximum estimates from experts). The price of each good or service (*PERT* distributions; the mean value for mode, and the minimum and maximum values corresponding to the minimum and maximum values reported from each source) was

obtained from the SNAP-AMR survey (project reference MR/S004815/1; price of antimalarials, anti-inflammatories and antibiotics), healthcare utilisation survey (project reference BB/S013857/1; price of treatments from traditional healers or herbalists), and personal communication with service providers.

It was assumed that all brucellosis cases reaching a target health facility incurred a cost with either a febrile antigen *Brucella* agglutination test (FBAT) or Rose-Bengal test (RBT), depending on the model scenario. The price of the FBAT was fixed at 5,000 Tanzania Shillings (6.33 int. $), which was the price charged to patients per test at a designated district hospital, a district health centre, and a private hospital in the Ngorongoro district (supplementary information gathered by a survey of testing patterns at health facilities in Arusha region (Lukambagire et al., 2022)). Given that RBT is not routinely used in this setting (there are no reported prices of RBT in the study area), and that the running cost of RBT is approximately 65% the running cost of FBATs (Lukambagire et al., 2021), the price of RBT was fixed at 3,250 Tanzania Shillings (4.11 int. $).

**Table D.1.1:** Parameters (minimum, mode and maximum) of the PERT distributions used to represent usage probabilities and prices of services and goods, for target and non-target health-related expenditure.

| | Probability distribution ($P_i$) | | |
|---|---|---|---|
| Good/service (i) | Target | Non-target | Price ($Q_i$; int. $) |
| *Clinical exams* | | | |
| mRDT | 0.00,0.30,1.00 | 0.00,0.35,1.00 | 0.63,2.53,6.33* |
| Widal test | 0.50,0.69,1.00 | 0.00,0.29,1.00 | 6.33,12.65,25.30* |
| CBC | 0.35,0.64,1.00 | 0.00,0.29,1.00 | 6.33,12.65,25.30* |
| Biochemical | 0.10,0.52,1.00 | 0.00,0.26,1.00 | 12.65,25.30,37.95* |
| Urinalyses | 0.20,0.61,1.00 | 0.00,0.34,1.00 | 0.63,2.53,6.33* |
| X-ray | 0.02,0.44,1.00 | 0.00,0.16,1.00 | 6.33,18.98,37.95* |
| Ultrasound | 0.00,0.35,1.00 | 0.00,0.17,1.00 | 12.65,18.98,37.95* |
| *Treatments* | | | |
| Traditional | 0.00,0.48,1.00 | 0.00,0.67,1.00 | 2.53,6.33,12.65† |
| Anti-inf. | 0.02,0.83,1.00 | 0.00,0.51,1.00 | 0.25,1.27,3.80‡ |
| Antimal. | 0.00,0.34,1.00 | 0.05,0.38,1.00 | 1.14,2.53,6.33‡ |
| Antibiotics | 0.50,0.82,1.00 | 0.00,0.45,1.00 | 1.90,4.43,7.59‡ |
| Hospital | 0.02,0.40,1.00 | 0.00,0.22,1.00 | 31.63,63.25,379.52* |
| Surgery | 0.00,0.07,0.42 | 0.00,0.11,1.00 | 63.25,189.76,442.77* |
| *Additional costs* | | | |
| Health c. | 0.00,0.88,1.00 | 0.00,0.78,1.00 | 3.80,6.33,18.98* |
| Transport | 0.50,0.83,1.00 | 0.20,0.78,1.00 | 12.65,101.20,189.76* |
| Accommod. | 0.20,0.47,1.00 | 0.00,0.26,1.00 | 25.30,37.95,50.60* |
| Food | 0.10,0.69,1.00 | 0.00,0.46,1.00 | 12.65,25.30,37.95* |

Probability distributions ($P_i$) were obtained from the expert elicitation. * Personal communication with service providers. † Healthcare utilisation survey (project reference BB/S013857/1). ‡ SNAP-AMR project (project reference MR/S004815/1). mRDT: malaria rapid diagnostic test. CBC: complete blood count. Traditional: treatments from traditional healers / herbalists. Anti-inf: anti-inflammatories. Antimal: antimalarials. Antibiotics: first-line antibiotics (targeting brucellosis specifically or not). Hospital: hospitalisation (for five days). Health c: health centre file and consultation fees. Accommod: accommodation (one night, double bedroom).

## D.2 Expert elicitation questionnaire (round 1)

**Expert elicitation**
**Protocol A**
**Round 1 questionnaire**

**Responsible researcher:** Dr. Jo Halliday.

**Co-researchers (facilitators):** Rigobert Tarimo, Fadhili Mshana and AbdulHamid Lukambagire.

**Ethics approval:** National Institute for Medical Research, project reference NIMR/HQ/R.8a/Vol.IX/2079. Kilimanjaro Christian Medical University College, research ethical clearance certificate n. 829. University of Glasgow, College of Medical, Veterinary & Life Sciences Ethics Committee, project n. 200210099.

**Objective:** To collect expert judgements on clinical manifestations, management, and prognosis of human brucellosis in the Ngorongoro Conservation Area, Tanzania.

**Introduction:** You have attended an inception meeting where the research project and protocols have been explained. You have been given a copy of the instructions sheet, where guidance on how to fill this questionnaire was provided. Please read the instructions sheet carefully before completing this questionnaire. Please complete the questionnaire by answering each question in the order presented. If you have any queries during the completion or after completing this questionnaire, please contact the research team at brucellosis.meeting@gmail.com.

**Please write a code name made of four uppercase letters** (a name that cannot be used to identify you; do not share this code name with anyone, not even the facilitators):

_____

**You can detach this page whenever you finish completing the questionnaire. Please keep this page in a safe place for future reference** – you will need to use the same code name in round 2; please destroy this page once round 2 is completed.

## Section 1

This section refers to brucellosis occurring in people currently living in the Ngorongoro Conservation Area (NCA). Please assume that a **brucellosis case** is someone (adult or child) who has signs and/or symptoms caused by the infection with *Brucella* spp., irrespective of whether they have been formally diagnosed at a healthcare facility.

This is a hypothetical exercise, as if we were watching a movie. In this movie, you can see precisely the current status of each brucellosis case in relation to the following variables: i) illness type; and, ii) healthcare-seeking behaviour.

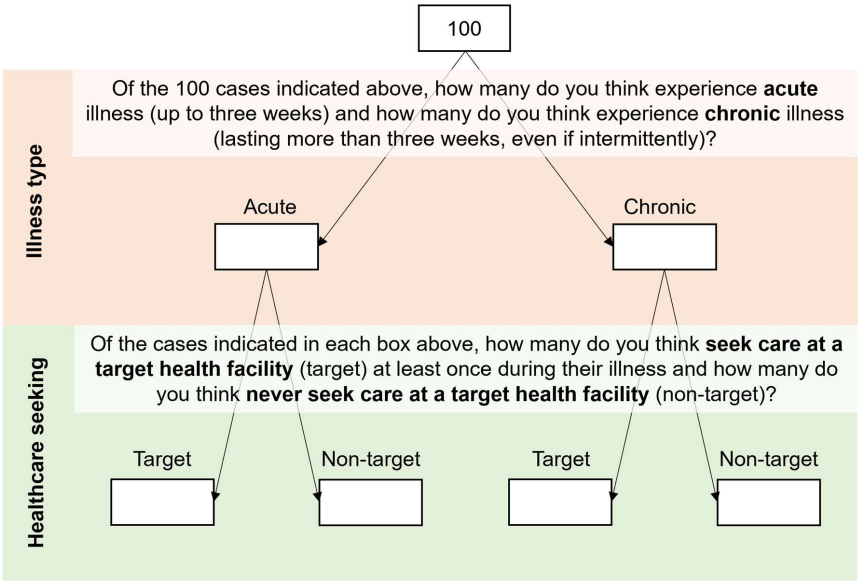
Regarding illness type, we are interested in the differences between the acute and chronic types of brucellosis. By acute illness, we mean the type of brucellosis characterised by clinical manifestations that last for up to three weeks before recovery, i.e. permanent elimination of signs or symptoms, or death. Examples of signs or symptoms of acute illness include fever, chills, sweats, weakness, and headache.

In contrast, by chronic illness, we mean the type of brucellosis characterised by clinical manifestations that last for more than three weeks, even if intermittently, before recovery or death. Examples of symptoms of chronic illness include joint, back, and muscular pain and other symptoms related to localised and complicated forms of the disease (e.g. epididymo-orchitis, endocarditis, meningitis or encephalitis). It is assumed that all chronic brucellosis cases go through an acute phase of brucellosis.

Regarding healthcare-seeking behaviour, we are interested in the proportion of brucellosis cases who seek care at a health facility that can diagnose and manage brucellosis (e.g. Endulen, FAME and Karatu Lutheran hospitals; and, Rhotia health centre). We refer to these as “target health facilities”. In this definition of “target health facilities”, brucellosis diagnosis includes laboratory testing either through serological methods (e.g. plate agglutination) or bacterial culture. Brucellosis management includes a treatment intended to treat brucellosis.

Here, we provide a diagram representing the above described variables (illness type, and healthcare seeking) that characterise brucellosis cases in the NCA. Please indicate how 100 cases of human brucellosis in the NCA can be distributed according to those variables. Please fill in the boxes in each row at a time. The sum of the numbers written in the boxes of each row must be 100, and the sum of the numbers in boxes that derive from one box in the preceding row, i.e. parent box, as indicated by arrows, needs to be equal to the number in that parent box.

**Hypothetical number of human brucellosis cases in the NCA**



## Section 2

In this section, we are interested in your judgement about the following variables:

- Illness duration: illness duration (in weeks) of brucellosis cases in the NCA i.e. time between onset of signs or symptoms of brucellosis until recovery (permanent elimination of signs or symptoms of brucellosis) or death, irrespective of type of illness or healthcare-seeking behaviour.
- Productivity impacts: number of days each person with brucellosis in the NCA is unable to carry out work activities, formal or informal, during the course of their illness, irrespective of type of illness or healthcare-seeking behaviour.
- Probability of treatment success: probability that a "target health facility" treatment intended to treat brucellosis is successful i.e. it causes permanent elimination of signs or symptoms of brucellosis. Please note the definition of a target health facility in the previous section: a health facility that can diagnose and manage brucellosis (e.g. Endulen, FAME and Karatu Lutheran hospitals; and, Rhotia health centre).
- Probability of death: probability of death of a brucellosis case in the NCA due to brucellosis, irrespective of type of illness or healthcare-seeking behaviour.

As in the previous section, we would like to know your judgement about these variables, not necessarily what you can recall from your research or professional experience in the NCA.

Please note that questions 1 and 2 require you to provide a lowest plausible value, a highest plausible value, a best estimate and a confidence level (expressed as a percentage). Your specified confidence level 'x' indicates that you think the "true" value falls within your upper and lower bounds in approximately 'x' out of 100 cases. Questions 3 and 4 just require you to provide a lowest plausible value, a highest plausible value, and a best estimate. Decimal numbers are valid answers.

**Question 1**:

| | |
|---|---|
| a. Realistically, what do you think is the lowest plausible value for the illness duration (in weeks) of each brucellosis case in the NCA? | |
| b. Realistically, what do you think is the highest plausible value for the illness duration (in weeks) of each brucellosis case in the NCA? | |
| c. Realistically, what do you think is the best estimate for the illness duration (in weeks) of each brucellosis case in the NCA? | |
| d. How confident are you that the interval you created, from lowest to highest, captures the illness duration of each brucellosis case in the NCA (enter a value between 50 and 100%)? | |

**Question 2**:

a. Realistically, what do you think is the lowest plausible value for the number of days each brucellosis case in the NCA is unable to carry out work activities during the course of their illness?
b. Realistically, what do you think is the highest plausible value for the number of days each brucellosis case in the NCA is unable to carry out work activities during the course of their illness?
c. Realistically, what do you think is the best estimate for the number of days each brucellosis case in the NCA is unable to carry out work activities during the course of their illness?
d. How confident are you that the interval you created, from lowest to highest, captures the number of days each brucellosis case in the NCA is unable to carry out work activities during the course of their illness (enter a value between 50 and 100%)?

**Question 3**:

a. Realistically, out of 100 brucellosis cases taking a "target health facility" treatment intended to treat brucellosis, what do you think is the lowest plausible number that recover because of the treatment taken?
b. Realistically, out of 100 brucellosis cases taking a "target health facility" treatment intended to treat brucellosis, what do you think is the highest plausible number that recover because of the treatment taken?
c. Realistically, out of 100 brucellosis cases taking a "target health facility" treatment intended to treat brucellosis, what do you think is the best estimate of the number that recover because of the treatment taken?

**Question 4**:

a. Realistically, out of 100 brucellosis cases in the NCA, what do you think is the lowest plausible number that die due to brucellosis?
b. Realistically, out of 100 brucellosis cases in the NCA, what do you think is the highest plausible number that die due to brucellosis?
c. Realistically, out of 100 brucellosis cases in the NCA, what do you think is the best estimate of the number that die due to brucellosis?

## Section 3

In this section, we are interested in your judgement about the health-related costs incurred due to brucellosis in the NCA, by brucellosis cases or by members of the household of brucellosis cases on their behalf. As in the previous sections, it is not a requirement that you worked at any of the health facilities in the NCA – we would like to know your judgement, not what you can recall.

This section requires you to provide the best estimate of the number of brucellosis cases that purchase a specific item. We need this estimate separately for 100 cases who seek care at a target health facility at least once during their illness (target healthcare seeking) and 100 cases who never seek care at a target health facility during their illness (non-target healthcare seeking). Please note that, as previously mentioned, a target health facility is a health facility that can diagnose and manage brucellosis (e.g. Endulen, FAME and Karatu Lutheran hospitals; and, Rhotia health centre). For instance, for the first row in the table below, please fill in the two empty cells by answering the following questions:

- **Target healthcare seeking**: out of 100 brucellosis cases who seek care at a target health facility at least once during their illness, how many do you think purchase a malaria rapid diagnostic test (MRDT)?
- **Non-target healthcare seeking**: out of 100 brucellosis cases who never seek care at a target health facility during their illness, how many do you think purchase a malaria rapid diagnostic test (MRDT)?

Empty rows are provided at the bottom of the table in case you wish to add any relevant items that have not been listed.

Please fill in the table below, one row at a time. All costs incurred must be due to brucellosis, at any point during the course of the illness.

| | Target healthcare seeking (n=100) | Non-target healthcare seeking (n=100) |
|---|---|---|
| **Clinical exams** | | |
| Malaria rapid diagnostic test (MRDT) | | |
| Widal agglutination test | | |
| Complete blood count | | |
| Blood biochemical analysis | | |
| Urinalysis | | |
| X-ray | | |
| Ultrasound | | |
| **Treatments** | | |
| Treatments from traditional healers | | |
| Anti-inflammatory drugs | | |
| Antimalarial drugs | | |
| First-line antibiotics (targeting or not brucellosis specifically) | | |
| Hospitalisation | | |
| Surgery | | |
| **Other types of health-related costs incurred** | | |
| Health centre file and consultation fees | | |
| Transportation (when the means of transport is any other than by foot) | | |
| Accommodation for the brucellosis case or someone accompanying them | | |
| **Please add any other relevant costs in the empty rows below** | | |
| | | |
| | | |
| | | |

**Section 4**

In this section, if you are interested, you can write a comment directed to the researchers (box 1) or other experts participating in this study (box 2). To the researchers, you may point out questions that you found particularly difficult to provide estimates for or highlight a question/section that was not clear to you. To other experts, you may want to provide evidence or explain the rationale for a particular answer. Only the comments written in box 2 will be shared with other experts in round 2 of the questionnaire. Although reaching a consensus is not the objective of round 2, leaving comments in box 2 is highly encouraged because it may help inform other experts' answers. Please do not write any information that could potentially be used to identify you in any of the boxes.

Box 1. Comments directed to researchers.

Box 2. Comments directed to other experts.

**Please write below the same code name that you wrote in the first page, with four capital letters** (you can now detach the first page and hand the completed questionnaire to the researcher - facilitator):

_____

## D.3 Expert elicitation - summary report

# Expert elicitation - summary report

Karatu, 13th September 2022

## Questions and answers

### Question 1: Illness type

**Question**

Out of 100 brucellosis cases in the NCA, how many do you think experience acute illness (up to three weeks) and how many do you think develop chronic illness (lasting more than three weeks, even if intermittently)?

**Results**

The attendees' mean estimate was that 60 out of 100 brucellosis cases develop chronic illness (lasting more than three weeks, even if intermittently), and the remaining 40 (out of 100 brucellosis cases) only experience acute illness (up to three weeks). The attendee's estimates of the number of chronic brucellosis cases (out of 100) varied from 30 to 90. Nine out of 13 attendees considered that the majority of brucellosis cases experience chronic illness.

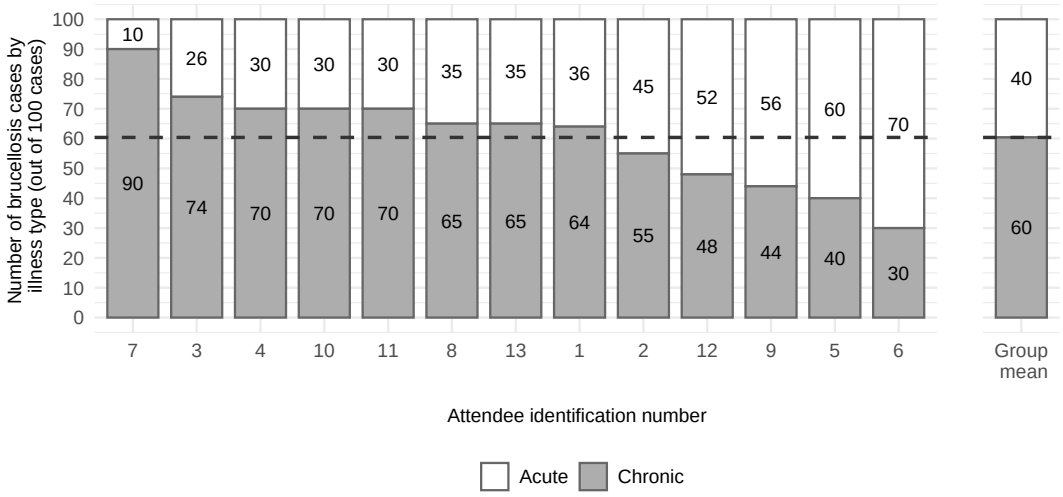



Figure 1: Attendees' responses about the number of brucellosis cases (out of 100) and group mean by illness type: acute (up to three weeks, white bars) vs chronic (lasting more than three weeks, even if intermittently, grey bars). The black dashed line indicates the group mean.

## Question 2: Healthcare-seeking behaviour

**Question**

Out of 100 acute and chronic brucellosis cases each in the NCA, how many do you think seek care, at least once during the course of their illness, at a target healthcare facility (a healthcare facility that can diagnose and manage brucellosis)?

**Results**

The attendees' mean estimate was that 51 out of 100 acute brucellosis cases seek care at a target health facility (ranging from 17 to 77). Regarding chronic brucellosis cases, the attendees' mean estimate was that 60 out of 100 cases seek care at a target health facility (ranging from 11 to 86).

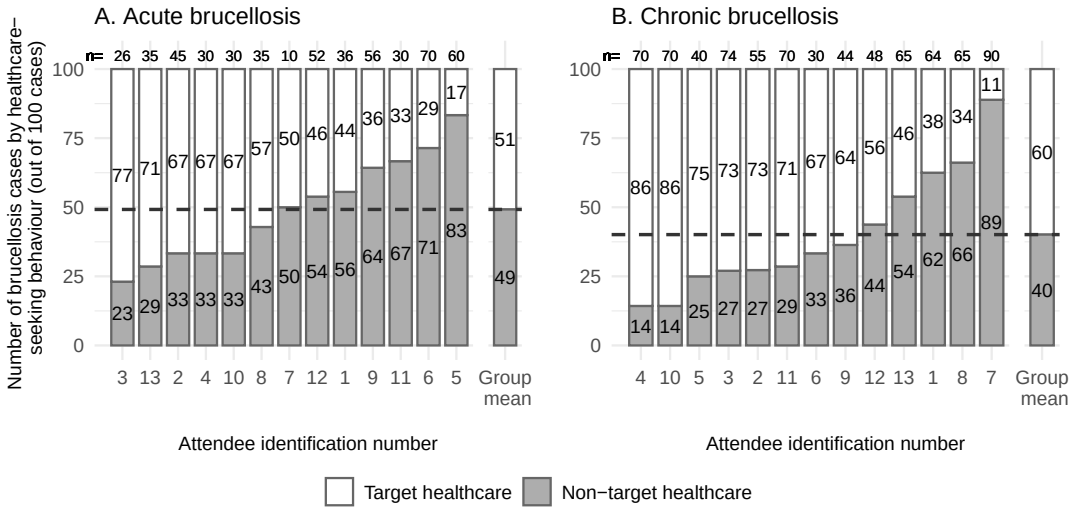



Figure 2: A. Attendees' responses about the number of acute brucellosis cases (out of 100) and group mean by healthcare-seeking behaviour: target healthcare-seeking cases (who seek care at least once during the course of their illness at a health facility that can diagnose and manage brucellosis), white bars, vs non-target healthcare-seeking cases (never seek care during the course of their illness at a health facility that can diagnose and manage brucellosis), grey bars. B. Attendees' responses about the number of chronic brucellosis cases (out of 100) and group mean by healthcare-seeking behaviour: target healthcare-seeking cases, white bars, vs non-target healthcare-seeking cases, grey bars. The black dashed line indicates the group mean. "n" is the number of brucellosis cases by illness type, as indicated by attendees and shown in Fig. 1.

## Question 3: Illness duration

**Question**

What do you think is the illness duration (in weeks) of a brucellosis case in the NCA?

**Results**

The mean estimated brucellosis duration estimate was 8.2 weeks (95% standardised uncertainty interval: 1.2-16.0). The attendee's judgement of the most likely illness duration varied from 2.0 to 27.0 weeks. The majority of attendees (seven out of 13) thought that the most likely illness duration was greater than three weeks.

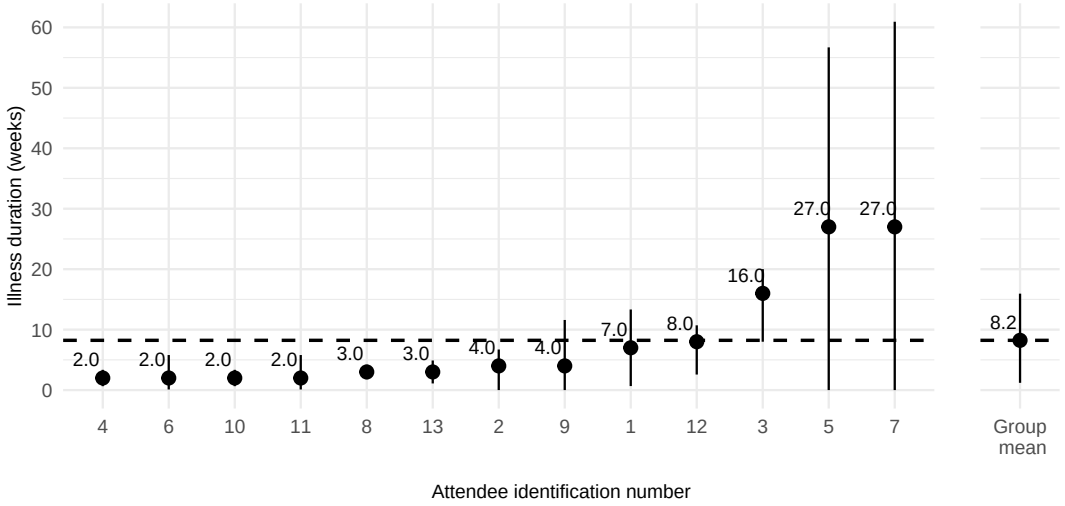



Figure 3: Attendees' responses about the brucellosis duration (weeks), and group mean. Dots represent the best estimate. Vertical bars indicate the standardised 95 percent uncertainty interval. The black dashed horizontal line indicates the group mean.

## Question 4: Loss of work days

**Question**

What do you think is the number of days each brucellosis case in the NCA is unable to carry out work activities during the course of their illness?

**Results**

The mean estimated number of work days lost due to brucellosis per brucellosis case was 28 (95% standardised uncertainty interval: 9-53 days). The attendee's judgement of the most likely number of work days lost varied from 9 to 72 days. The majority of attendees (seven out of 13) thought that the most likely number of work days lost was greater than 14 days.

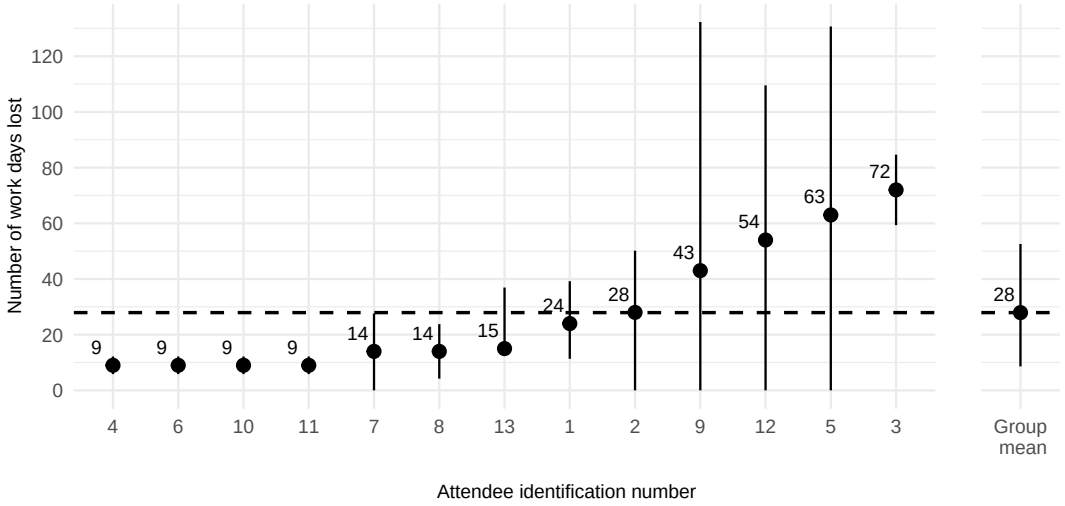



Figure 4: Attendees' responses about the number of work days lost due to brucellosis, per brucellosis case, and group mean. Dots represent the best estimate. Vertical bars indicate the standardised 95 percent uncertainty interval. The black dashed horizontal line indicates the group mean.

## Question 5: Target healthcare treatment success probability

**Question**

Out of 100 brucellosis case in the NCA taking a target healthcare facility treatment intended to treat brucellosis, how many do you think recover as intended because of the treatment taken?

**Results**

The attendees' mean estimate was that, out of 100 brucellosis cases taking a treatment intended to treat brucellosis and provided by a target healthcare facility, 73 recover as intended because of the treatment taken (range: 55-84). The attendee's judgement of the most likely number of brucellosis cases that recover varied from 50 to 95. The majority of attendees (eight out of 13) thought that the most likely number of brucellosis cases that recover was greater than 70, out of 100.

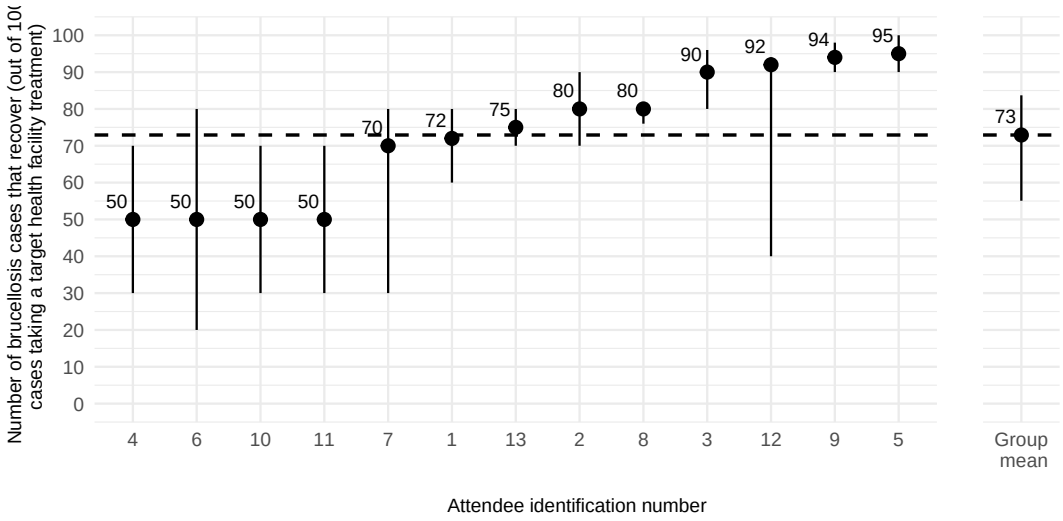



Figure 5: Attendees' responses about the success probability of a target healthcare facility treatment intended to treat brucellosis, and group mean. Dots represent the best estimate. Vertical bars indicate the range. The black dashed horizontal line indicates the group mean.

## Question 6: Probability of death

**Question**

Out of 100 brucellosis cases in the NCA, how many do you think die due to brucellosis?

**Results**

The attendees' mean estimate was that, out of 100 brucellosis cases in the NCA, 7.1 die due to brucellosis (range: 3.5-10.4). The attendee's judgement of the most likely number of brucellosis cases that die (out of 100) varied from 2.0 to 21.0. The majority of attendees (eight out of 13) thought that the most likely number of brucellosis cases that die (out of 100) was greater than 6.0.

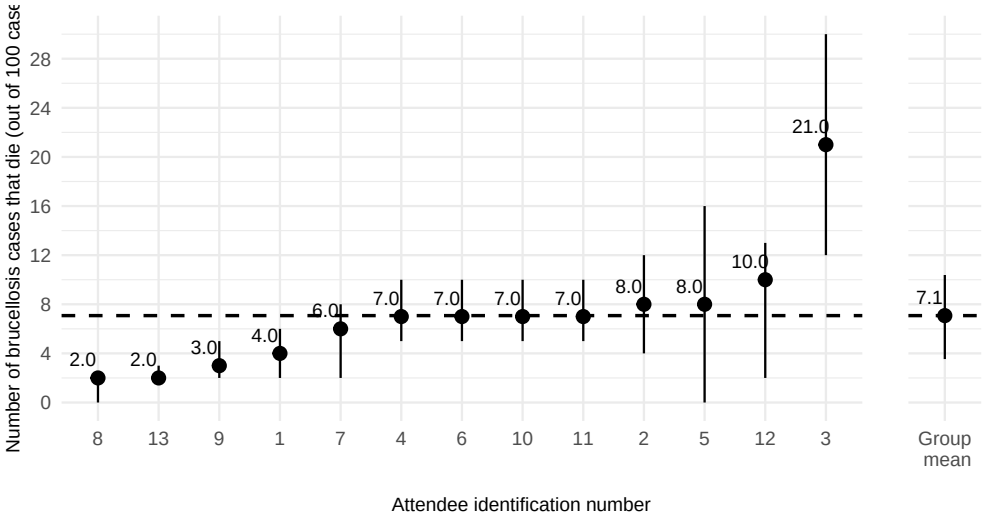



Figure 6: Attendees' responses about the number of deaths due to brucellosis, out of 100 brucellosis cases, and group mean. Dots represent the best estimate. Vertical bars indicate the range. The black dashed horizontal line indicates the group mean.

## Question 7: Health-related costs incurred by brucellosis cases

**Question**

Out of 100 brucellosis cases in the NCA who seek care at a target health facility at least once during their illness and 100 brucellosis cases in the NCA who never seek care at a target health facility during their illness, how many do you think pay for each of the following clinical exams, treatments and additional items?

**Results**

According to the attendees' mean group estimate, brucellosis cases who seek care at a target health facility at least once during their illness are more likely to incur many of the health-related costs, compared to brucellosis cases who never seek care at a target health facility during their illness. The attendees indicated that the most common costs incurred by cases who seek care at a target health facility were health centre file and consultation fees (n=88), anti-inflammatory drugs (n=83), antibiotics (n=82) and transportation (n=83). The most common costs incurred by cases who never seek care at a target health facility were transportation (n=78), health centre file and consultation fees (n=78), and treatments from traditional healers or herbalists (n=67). Fig. 7 shows the mean group answers for each cost item. Fig. 8 to 10 show the individual responses, in addition to the group mean, for each cost item.

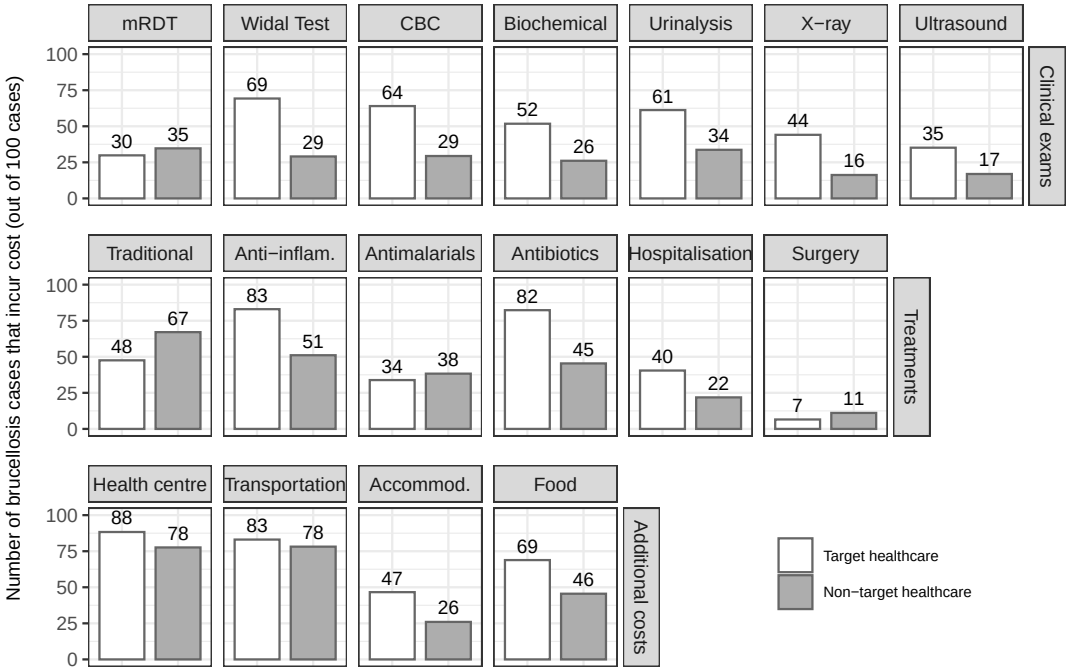



Figure 7: Attendees‘ mean estimate of the number of brucellosis cases who pay for each of the clinical exams, treatments and additional items, by healthcare-seeking behaviour (target, white bars, vs non-target healthcare seeking, grey bars). CBC: complete blood count. Traditional: treatments from traditional healers / herbalists. Anti-inflam.: anti-inflammatory drugs. Antibiotics: first-line antibiotics (targeting brucellosis specifically or not). Health centre: health centre file and consultation fees. Accommod.: Accommodation for the brucellosis case or someone accompanying them.

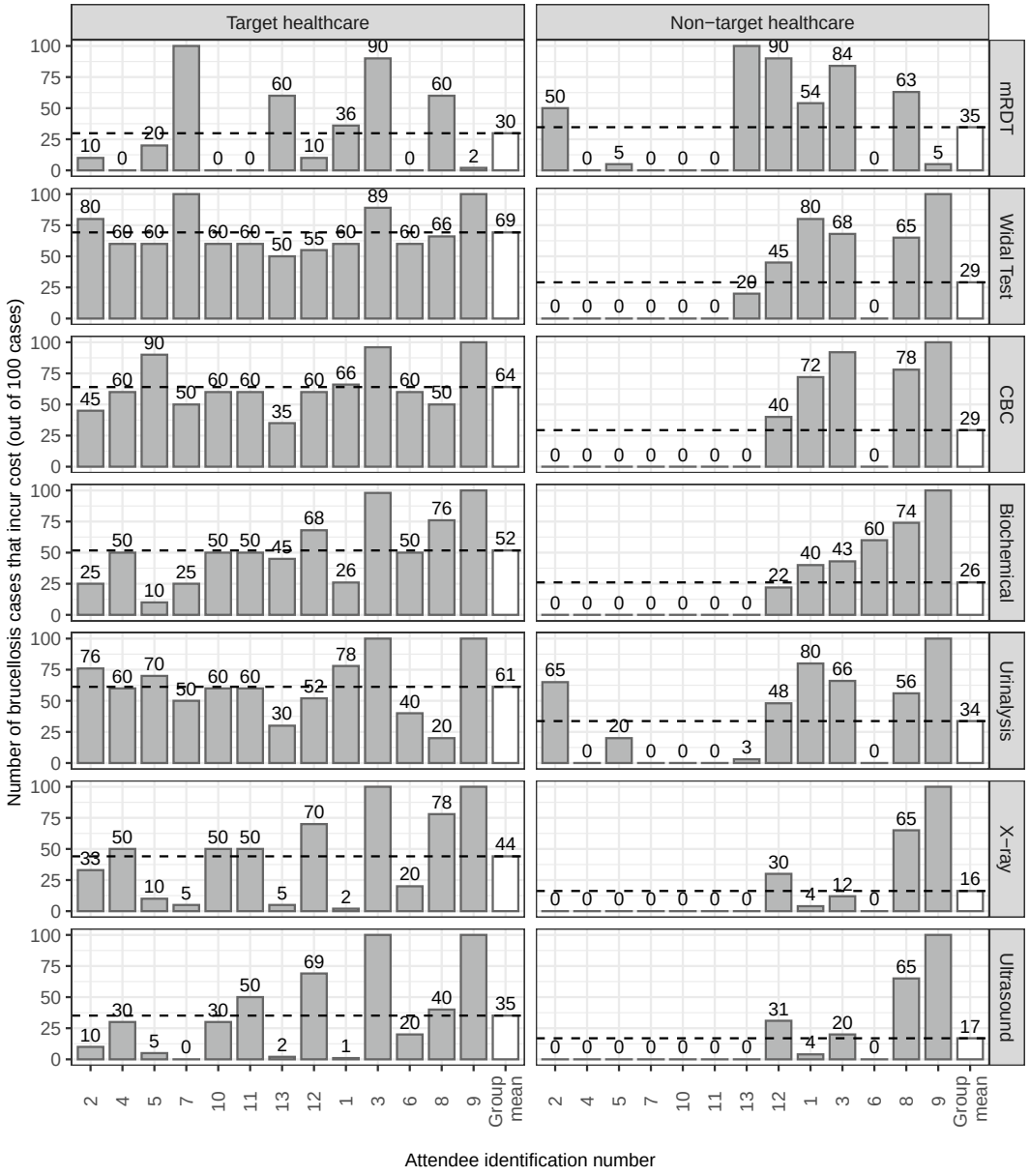



Figure 8: Attendees‘ responses (grey bars) about the number of brucellosis cases (out of 100) who pay for each of the clinical exams by healthcare-seeking behaviour (target vs non-target healthcare seeking), and group means (white bars). CBC: complete blood count.

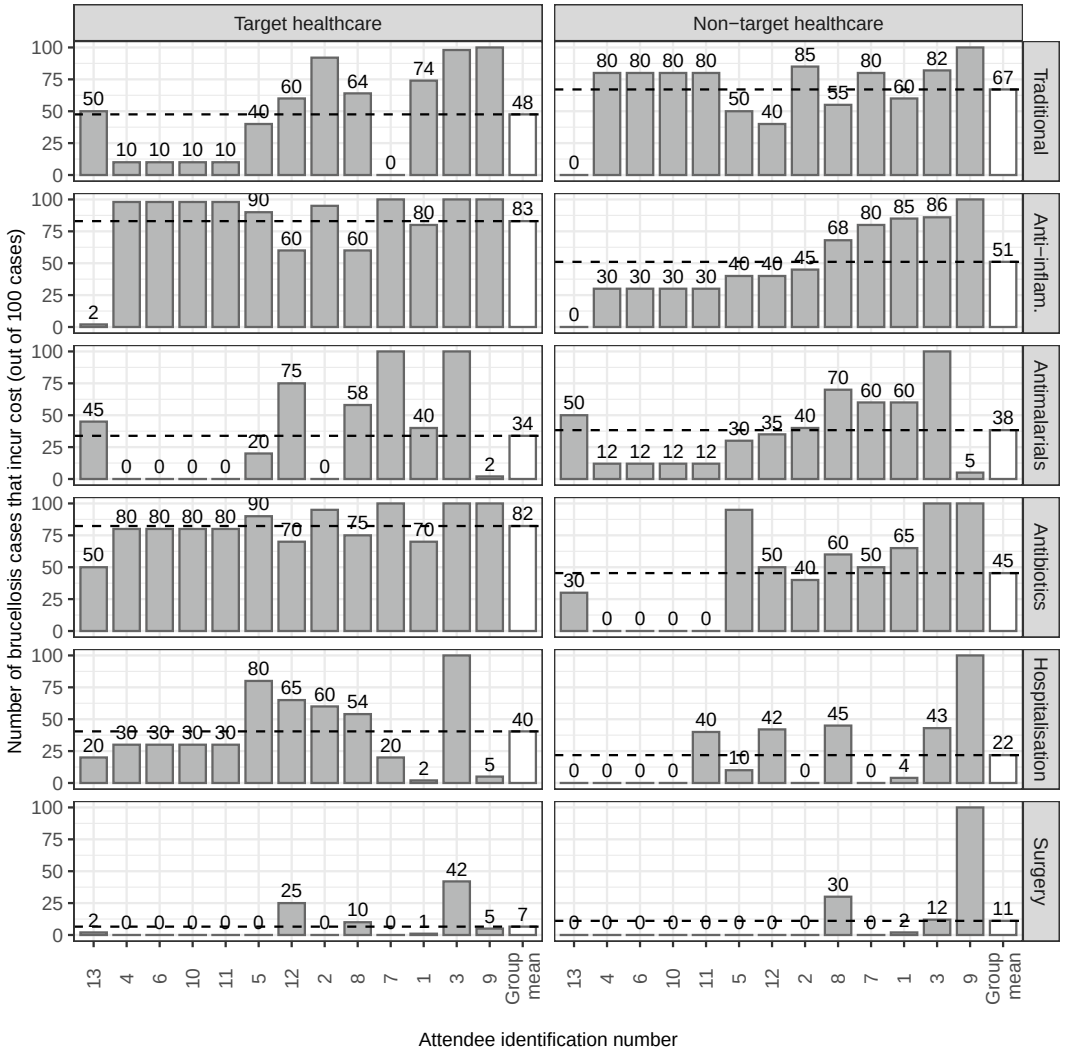



Figure 9: Attendees‘ responses (grey bars) about the number of brucellosis cases (out of 100) who pay for each of the treatments, by healthcare-seeking behaviour (target vs non-target healthcare seeking), and group means (white bars). Traditional: treatments from traditional healers / herbalists. Anti-inflam.: anti-inflammatory drugs. Antibiotics: first-line antibiotics (targeting brucellosis specifically or not).

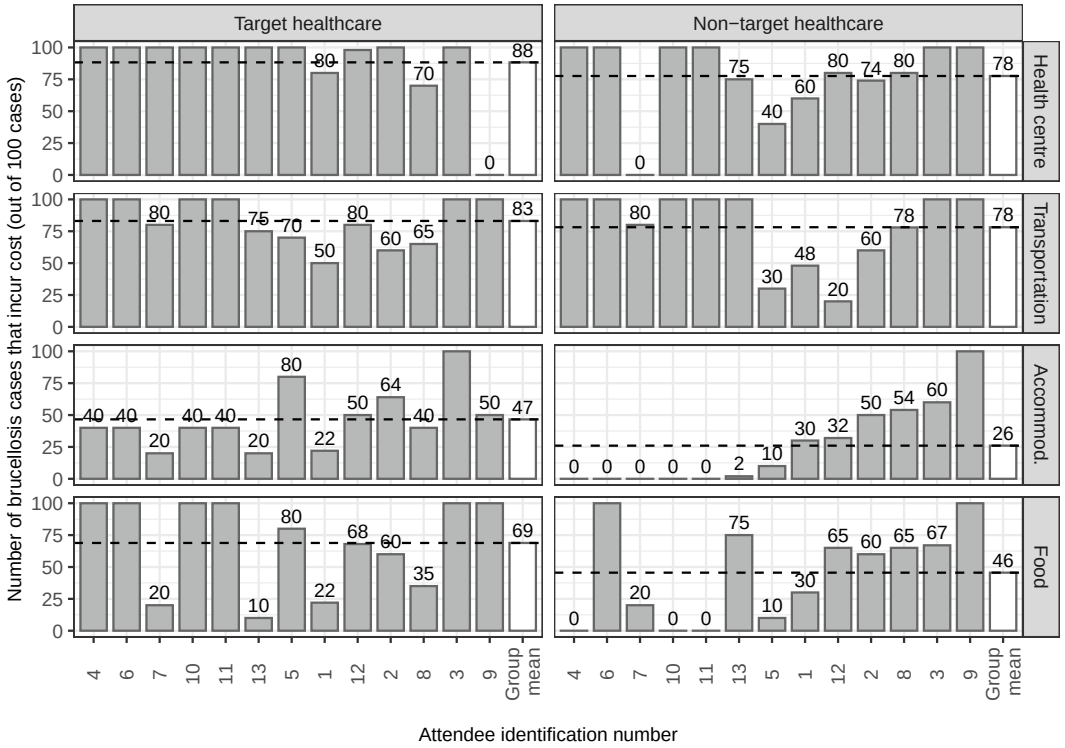



Figure 10: Attendees‘ responses (grey bars) about the number of brucellosis cases (out of 100) who pay for each of the additional items, by healthcare-seeking behaviour (target vs non-target healthcare seeking), and group means (white bars). Accommod.: Accommodation for the brucellosis case or someone accompanying them.

## D.4 Markov model parameters, distributions, units, data sources and explanation

**Table D.4.1:** Markov model parameters, distributions, units, data sources and explanation.

| Parameter(s) | Distribution | Units | Data sources and explanation |
|---|---|---|---|
| *Disease duration* | | | |
| Time spent in non-target management of acute illness ($\alpha_1$) | *PERT*(min:1.0; mode:2.0; max:3.0) | Weeks | Duration as per systematic review and meta-analysis of clinical manifestations of human brucellosis (Dean et al., 2012a) and used by FERG to estimate the global and regional burden of brucellosis in 2010 (Kirk et al., 2015); the definition (assumption) of acute illness in the expert elicitation was consistent with a duration of up to three weeks. |
| Time spent in target management of acute illness ($\alpha_2$) | *Fixed*(3.0) | Weeks | Treatment duration of acute illness as prescribed to brucellosis cases at Endulen Hospital (Streptomycin injection [1 g] once a day for two weeks in combination with Doxycycline tablets [200 mg] once a day for three weeks) (Kunda, 2006) |
| Time spent in non-target management of chronic illness ($\alpha_3$) | *Fixed*(8.4) | Weeks | Value that results in a median overall disease duration per brucellosis case of 8.2 weeks, as per the outcome of the expert elicitation |
| Time spent in target management of chronic illness ($\alpha_4$) | *Fixed*(3.0) | Weeks | Assumed to be the same as the treatment duration of acute illness (treatment prescribed to brucellosis cases at Endulen Hospital) (Kunda, 2006) |
| *Transition probabilities and linked parameters* | | | |
| Prob. of visiting a target healthcare facility for fever | *Beta*(shape 1: 123+1; shape 2: 920-123+1) | Prob. | Prob. of a household member seeking care at a target healthcare facility for fever; source: healthcare utilisation survey (project reference BB/S013857/1); numerator (123): number of household members that would 'go to a health facility to get advice or treatment', based on the question 'which of the following would you be most likely to do if [household member] developed a fever that lasted for more than 3 days?' and would choose Endulen, FAME, or Karatu hospitals or Rhotia health centre, as answered to the question 'which health facility would be your first choice?'; denominator (920): sum of the number of households with members by each age group. It is assumed that 85.7% of brucellosis cases are over 15 years old (Kunda, 2006). |

Continuation of Table D.4.1

| Parameter(s) | Distribution | Units | Data sources and explanation |
|---|---|---|---|
| Prob. of visiting a target health facility for musculoskeletal symptoms | *Beta*(shape 1:35+1; shape 2:227-35+1) | Prob. | Prop. of survey participants with musculoskeletal symptoms (abnormal GALS - gait, arms, legs and spine - examination result) that visited a hospital in the three months before the interview, for any reason; source: NIHR Arthritis project (project reference 17/63/35); numerator (35): number of study participants with abnormal GALS that reported visiting a hospital in the three months before the interview; denominator (227): number of study participants with abnormal GALS. |
| Prob. of death | *PERT*(min:0.035; mode:0.071; max:0.104) | Prob. | Outcomes of the expert elicitation (mode is equal to the group mean of the most likely value; minimum and maximum indicate the group mean of the minimum and maximum plausible values). |
| Joint sensitivity of commercial plate agglutination tests in use in the NCA | *Beta*(shape 1: 4.6+1.0; shape 2: 14.0-4.6+1.0) | Prob. | Joint prob. distribution calculated from three sources: i) a survey of local health facilities indicating brucellosis testing with Fortress at Endulen hospital and Eurocell at FAME, Karatu and Rhotia (Lukambagire et al., 2022); ii) a study that estimated the sensitivity of Fortress (28.6%) and Eurocell (50.0%) in the NCA (Lukambagire et al., 2021); and, iii) based on the healthcare utilisation survey (project reference BB/S013857/1), 80% of household members that would go to Endulen, FAME or Karatu hospitals or Rhotia health centre for a fever that lasted for more than 3 days would choose Endulen as the first choice. The joint sensitivity of commercial plate agglutination tests in use in the NCA is then equal to 33% (80% times 28.6% plus 20% times 50.0%), with denominator (number of brucellosis cases tested in Lukambagire et al., 2021) equal to 14. |
| Sensitivity of Rose-Bengal test | *Beta*(shape 1: 12+1; shape 2: 14-12+1) | Prob. | Sensitivity of RBT using the standard (undiluted sample) protocol (RBT 1:2); 12 positive test results out of 14 brucellosis cases tested (Lukambagire et al., 2021). |
| Prob. of treatment failure ($\varepsilon$) | *PERT*(min:0.16; mode:0.27; max:0.45) | Prob. | Outcomes of the expert elicitation (mode is equal to the group mean of the most likely value; minimum and maximum indicate the group mean of the minimum and maximum plausible values). |

Continuation of Table D.4.1

| Parameter(s) | Distribution | Units | Data sources and explanation |
|---|---|---|---|
| Prob. of progression to chronic brucellosis ($\lambda$) | *PERT*(min:0.30; mode:0.60; max:0.90) | Prob. | Outcomes of the expert elicitation (mode is equal to the group mean; minimum and maximum indicate the minimum and maximum individual estimates). |
| *Attributable risk of spontaneous abortion and stillbirth in pregnant women with brucellosis* | | | |
| Attributable risk of spontaneous abortion ($\mu$) | *PERT*(min:0.025; mode:0.121; max:0.166) | Prob. | Calculated as the difference between the probability of spontaneous abortion in pregnant women with and without brucellosis; 0.025 from a study of 39 pregnant with brucellosis (one of whom had spontaneous abortion) and 40 controls (none of whom had spontaneous abortion) in Turkey (Gulsun et al., 2011); 0.121 from a study of 55 pregnant with brucellosis (15 of whom had spontaneous abortion) and 395 controls (60 of whom had spontaneous abortion) in Saudi Arabia (Elshamy and Ahmed, 2008); 0.166 from a study of 29 pregnant with brucellosis (seven of whom had spontaneous abortion) and 33,936 controls[1] (2,577 of whom had spontaneous abortion) in Turkey (Kurdoglu et al., 2010) |
| Attributable risk of stillbirth ($\upsilon$) | *PERT*(min:0.000; mode:0.032; max:0.089) | Prob. | Calculated as the difference between the probability of stillbirth in pregnant women with and without brucellosis; 0.000 from a study of 39 pregnant with brucellosis (none of whom had stillbirth) and 40 controls (none of whom had stillbirth) in Turkey (Gulsun et al., 2011); 0.032 from a study of 29 pregnant with brucellosis (one of whom had stillbirth) and 33,936 controls[2] (76 of whom had stillbirth) in Turkey (Kurdoglu et al., 2010); 0.089 from a study of 55 pregnant with brucellosis (seven of whom had stillbirth) and 395 controls (15 of whom had stillbirth) in Saudi Arabia (Elshamy and Ahmed, 2008) |

1. This population is not explicitly defined as ‘control group’; instead, the wording ‘general population of pregnant women’ followed in the maternity hospital is used
2. This population is not explicitly defined as ‘control group’; instead, the wording ‘general population of pregnant women’ followed in the maternity hospital is used

Continuation of Table D.4.1

| Parameter(s) | Distribution | Units | Data sources and explanation |
|---|---|---|---|
| *Healthcare services and goods - access and costs* | | | |
| Non-target health-related expenditure | See Appendix D.1 | int. $ | Obtained from the product of expenditure probability by brucellosis cases who never visit a target health facility during their illness (expert elicitation) and price of services and goods (SNAP-AMR survey (project reference MR/S004815/1), healthcare utilisation survey (project reference BB/S013857/1), and personal communication with service providers) |
| Target health-related expenditure | See Appendix D.1 | int. $ | Obtained from the product of expenditure probability by brucellosis cases who visit a target health facility at least once during their illness (expert elicitation) and price of services and goods (SNAP-AMR survey (project reference MR/S004815/1), healthcare utilisation survey (project reference BB/S013857/1), and personal communication with service providers) |
| *Wages and conversion rates* | | | |
| Weekly wage from agricultural activities ($\zeta$) | *Fixed*(46.3) | int. $ | Mean monthly income in rural areas of Mainland Tanzania from the Integrated Labour Force Survey (2020/2021): 158,480 TSH; the weekly rate is calculated on the basis of 12 months per year, 4.3 weeks per month (National Bureau of Statistics (NBS), 2022) |
| Productivity loss multiplier ($\phi$) | *Fixed*(5.9) | NA | Multiplier used for estimation of productivity losses ensuring that the median productivity loss per brucellosis case was equal to 28 work days lost (group mean in the expert elicitation) in wages |
| Purchasing power parity (PPP) conversion factor | *Fixed*(790.5) | TZS | PPP conversion factor, private consumption (Tanzania Shillings (TZS) per int. $ in 2020) from the World Bank[3] |
| *Value of life lost and funeral costs* | | | |
| Value of statistical life-year (VSLY) | *Fixed*(9,340) | int. $ | Mean VSLY, (discounted) obtained through contingent valuation with 3,985 participants in Tanzania (Patenaude et al., 2019) |

3. https://data.worldbank.org/indicator/PA.NUS.PRVT.PP?locations=TZ

Continuation of Table D.4.1

| Parameter(s) | Distribution | Units | Data sources and explanation |
|---|---|---|---|
| Funeral costs ($\rho$) | *Uniform*(min:2,250; max:3,750) | int. $ | 3,000 int. $, $\pm$ 25%; value based on the price of a basic funeral (direct burial or direct cremation) in Tanzania: approximately US$ 1,000 (Tanzania Funeral Arrangements, 2022) |
| Life table | WHO GHE | NA | Life table based on the lowest projected age-specific mortality rates for the year 2045-2050 by the World Population Prospects 2019 (WHO, 2020) |
| Prop. of deaths in the 0-14 age group | *Fixed*(0.000) | Prop. | None of the 84 people that died in a study of 5,598 brucellosis cases in Spain was in the 0-14 age group (Rodríguez-Alonso et al., 2021) |
| Prop. of deaths in the 15-44 age group | *Fixed*(0.083) | Prop. | Seven of the 84 people that died in a study of 5,598 brucellosis cases in Spain were in the 15-44 age group (Rodríguez-Alonso et al., 2021) |
| Prop. of deaths in the 45-64 age group | *Fixed*(0.227) | Prop. | Nineteen of the 84 people that died in a study of 5,598 brucellosis cases in Spain were in the 45-64 age group (Rodríguez-Alonso et al., 2021) |
| Prop. of deaths in the over 65 age group | *Fixed*(0.690) | Prop. | Fifty-eight of the 84 people that died in a study of 5,598 brucellosis cases in Spain were in the over 65 age group (Rodríguez-Alonso et al., 2021) |
| *Disability weights* | | | |
| Acute moderate brucellosis | *PERT*(min:0.033; mode:0.053; max:0.081) | NA | Disability weight for infectious disease, acute episode, moderate (Kirk et al., 2015), experienced by 50% of acute cases, as used by FERG to estimate the global and regional burden of brucellosis in 2010 (Kirk et al., 2015) |
| Acute severe brucellosis | *PERT*(min:0.139; mode:0.210; max:0.298) | NA | Disability weight for infectious disease, acute episode, severe (Kirk et al., 2015), experienced by 50% of acute cases, as used by FERG to estimate the global and regional burden of brucellosis in 2010 (Kirk et al., 2015) |
| Chronic brucellosis | *PERT*(min:0.053; mode:0.079; max:0.115) | NA | Disability weight for musculoskeletal problems (legs, moderate) (Kirk et al., 2015), as used by FERG to estimate the global and regional burden of brucellosis in 2010 (Kirk et al., 2015) |

Continuation of Table D.4.1

| Parameter(s) | Distribution | Units | Data sources and explanation |
|---|---|---|---|
| Brucellosis orchitis | *PERT*(min:0.063; mode:0.097; max:0.137) | NA | Disability weight for infectious disease, epididymo-orchitis (Kirk et al., 2015), experienced by 10% of adult (over 15 years old) male chronic cases (Kirk et al., 2015) |
| *Incidence* | | | |
| Number of cases per 100,000 persons-year in the NCA | *PERT*(min:100; mode:400; max:800) | NA | Community-level incidence estimated by de Glanville et al (personal communication) from hospital-level surveillance data and the healthcare utilisation survey (project reference BB/S013857/1) |
| *Age-sex distribution of cases* | | | |
| Percentage of cases that are male | *Fixed*(54.1) | % | 53 out of 98 brucellosis cases - Arusha and Manyara, Tanzania (Kunda, 2006) |
| Percentage of cases that are female | *Fixed*(45.9) | % | 45 out of 98 brucellosis cases - Arusha and Manyara, Tanzania (Kunda, 2006) |
| Percentage of cases below 15 years-old | *Fixed*(14.3) | % | 14 out of 98 brucellosis cases - Arusha and Manyara, Tanzania (Kunda, 2006) |
| Percentage of cases 16-30 years-old | *Fixed*(26.5) | % | 26 out of 98 brucellosis cases - Arusha and Manyara, Tanzania (Kunda, 2006) |
| Percentage of cases 31-45 years-old | *Fixed*(31.6) | % | 31 out of 98 brucellosis cases - Arusha and Manyara, Tanzania (Kunda, 2006) |
| Percentage of cases 46-60 years-old | *Fixed*(16.3) | % | 16 out of 98 brucellosis cases - Arusha and Manyara, Tanzania (Kunda, 2006) |
| Percentage of cases over 60 years-old | *Fixed*(11.2) | % | 11 out of 98 brucellosis cases - Arusha and Manyara, Tanzania (Kunda, 2006) |

Continuation of Table D.4.1

| Parameter(s) | Distribution | Units | Data sources and explanation |
|---|---|---|---|
| *Demography* | | | |
| Population size | *Fixed*(100,000) | NA | Human population size in the NCA (Government of The United Republic of Tanzania, 2019; Slootweg, 2018) |
| Age-sex distribution | See Fig. D.5.1 | NA | Age-sex distribution of the human population in the Ngorongoro district (Government of The United Republic of Tanzania, 2013a) |
| Crude birth rate (per 1,000 people) | *Fixed*(35) | NA | Thematic report on fertility and nuptiality, based on the 2012 Population and Housing Census (Government of The United Republic of Tanzania, 2015b); data for Arusha region. |

FERG: Foodborne Disease Burden Epidemiology Reference Group, established by the World Health Organization (WHO); GHE: Global Health Estimates; min: minimum; max: maximum; prob: probability; prop: proportion; RBT: Rose-Bengal test; int. $: international dollars.

## D.5 Ngorongoro district and healthcare utilisation survey populations

This study assumed that the age-sex distribution of people in the NCA was the same as in the Ngorongoro district (2012 Population and Housing Census, Government of The United Republic of Tanzania, 2013a). Fig. D.5.1 shows that the age-sex distribution of household members in the healthcare utilisation survey (project reference BB/S013857/1) delivered in the NCA was similar to the age-sex distribution of the Ngorongoro district population (Tanzania Census 2012 data).

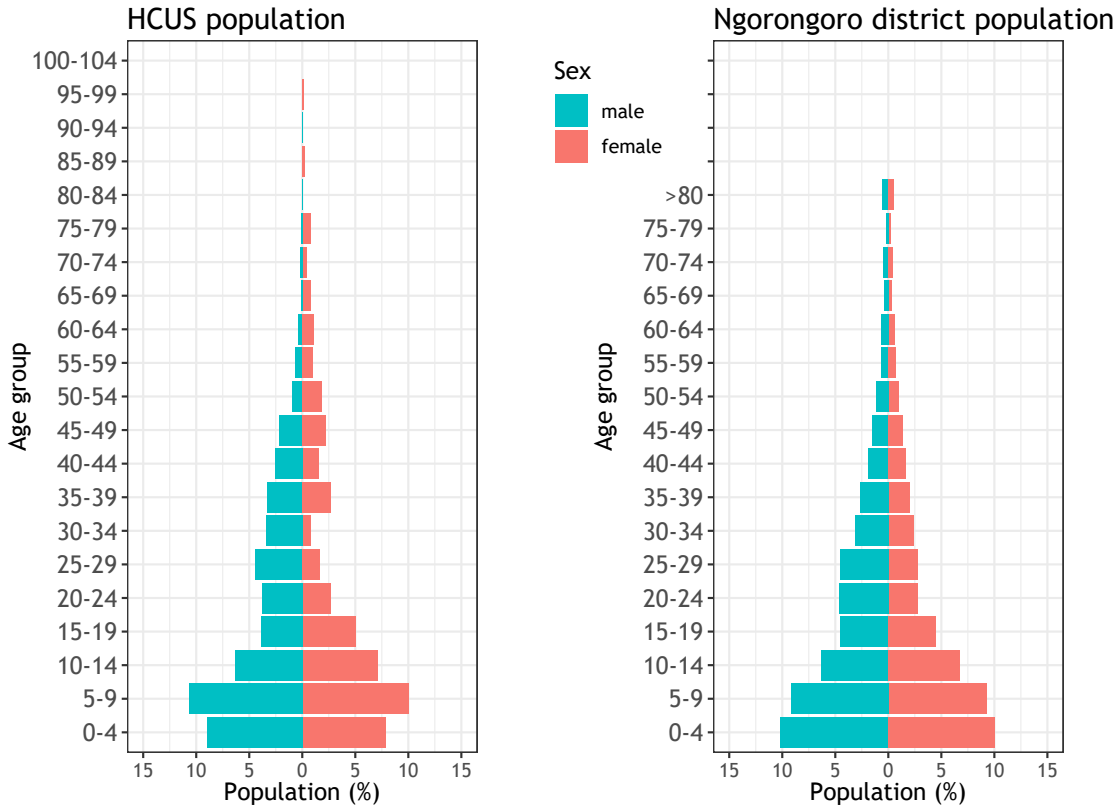



**Figure D.5.1:** Tornado plots showing the age-sex distribution of the healthcare utilisation survey (HCUS; project reference BB/S013857/1; n=2,055) participants and the Ngorongoro district population (Tanzania Census 2012 data; n=174,278).

## D.6 Quality assessment of data sources by model parameter

| Parameter (group) | Data sources | | | Decision tree | | |
|---|---|---|---|---|---|---|
| | Locally delivered survey (LDS) | Locally relevant literature (LRL) | Non-locally relevant literature (NRL)* | Sensitivity analyses? | Expert elicitation (EE)? | Data source(s) to be used |
| Duration of non-target management of acute illness | Not available | Not available | Dean et al, 2012; Kirk et al, 2015 | No | No | NRL |
| Duration of target management of acute illness | Not available | Kunda (2006) | Not applicable | No | No | LRL |
| Duration of non-target management of chronic illness | Not available | Not available | Dean et al, 2012; Kirk et al, 2015 | No | Yes | EE |
| Duration of target management of chronic illness | Not available | Kunda (2006) | Not applicable | No | No | LRL |
| Prob. of target healthcare seeking for acute brucellosis | Healthcare utilisation survey (HCUS) | Not applicable | Not applicable | No | No | LDS |
| Prob. of target healthcare seeking for chronic brucellosis | NIHR arthritis project | Not applicable | Not applicable | No | No | LDS |
| Prob. of death due to brucellosis | Not available | Kunda (2006) | Afifi et al, 2005; Al Dahouk et al, 2007; Buzgan et al, 2010; EFSA & ECDC, 2019; Rodriguez-Alonso et al, 2021 | No | Yes | EE |
| Diagnostic test sensitivity and test usage by health facilities | Lukambagire et al. 2021; Lukambagire et al. 2022 | Not applicable | Not applicable | No | No | LDS |
| Prob. of treatment failure | Not available | Kunda (2006) | Yousefi-Nooraie et al, 2012 | No | Yes | EE |
| Prob. of progression to chronic brucellosis | Not available | Kunda (2006) | Yang et al, 2020; Zinsstag et al, 2015; Ulambayar, 2001 and Damdinsuren, 1972 cited by Roth 2007 | No | Yes | EE |
| Attributable risk of spontaneous abortion and stillbirth | Not available | Not available | Gulsun et al, 2011; Elshamy & Ahmed, 2008; Kurdoglu et al., 2010 | Yes | No | NRL |
| Price of goods and services in the NCA | HCUS, SNAP-AMR, personal comm. | Not applicable | Not applicable | No | No | LDS |
| Probability of health-related expenditure attributable to brucellosis in the NCA | HCUS | Not available | Not available | No | Yes | EE |
| Productivity losses (loss of work days) | Not available | Kunda (2006) | White et al. 1974; Colmenero-Castillo et al, 1989; National Brucellosis Technical Commission et al, 1978 | No | Yes | EE |
| Wages in the agricultural sector | Not available | Integrated Labour Force Survey (2020/2021) | Not applicable | No | No | LRL |
| Value of statistical life-year | Not available | Patenaude et al, 2019 | Not applicable | No | No | LRL |
| Funeral costs | Not available | Funeral price survey | Not applicable | No | No | LRL |
| Age-distribution of deaths | Not available | Kunda (2006) | Rodriguez-Alonso et al, 2021 | Yes | No | LRL & NRL |
| Disability weights | Not available | Not available | Dean et al, 2012; Kirk et al, 2015 | No | No | NRL |
| Incidence | Not available | de Glanville et al (unpublished) | Not applicable | No | No | LRL |
| Age-sex distribution of cases | Not available | Kunda (2006) | Not applicable | No | No | LRL |
| Population size | Not available | Tanzanian gov., 2019 | Not applicable | No | No | LRL |
| Age-sex distribution | Not available | Tanzanian gov., 2013 | Not applicable | No | No | LRL |
| Crude birth rate | Not available | Tanzanian gov., 2015 | Not applicable | No | No | LRL |

* selected best quality evidence

| Evidence quality and relevance classification | |
|---|---|
| 1 | Available and sufficient quality |
| 2 | Available but insufficient quality |
| 3 | Not available |
| 4 | Not applicable |

**Figure D.6.1:** Quality assessment of data sources and decision tree outcomes for each parameter (group). For more details on the decision tree, see Fig. 5.4 in the main text. Prob: probability. NIHR: National Institute for Health Research Arthritis project (project reference 17/63/35). SNAP-AMR: Supporting the National Action Plan on Antimicrobial Resistance in Tanzania project (project reference MR/S004815/1). Personal comm.: Personal communication with service providers. Gov: Government. EFSA: European Food Safety Authority. ECDC: European Centre for Disease Prevention and Control.

## D.7 Transition probabilities

Weekly transition probabilities are shown in Fig. D.7.1. The probability of a case staying in the acute target treatment state from one cycle to the next ($p_{22}$; $S_2$ to $S_2$) is not shown because it is constant (inverse of treatment duration). In the scenario of increased healthcare seeking at a target health facility, the increase in $p_{12}$ reduced the probability of cases developing chronic disease (transitioning to $S_3$, non-target management of chronic illness, at $p_{13}$). Once cases reached $S_2$ (target management of acute illness), the improved test sensitivity in the scenarios with RBT use led to increased recovery probability ($p_{25}$) and reduced probability of cases developing chronic disease ($p_{23}$). Once cases with chronic disease reached $S_4$ (target management of chronic illness), the improved test sensitivity in the scenarios with RBT use led to increased recovery probability ($p_{45}$).

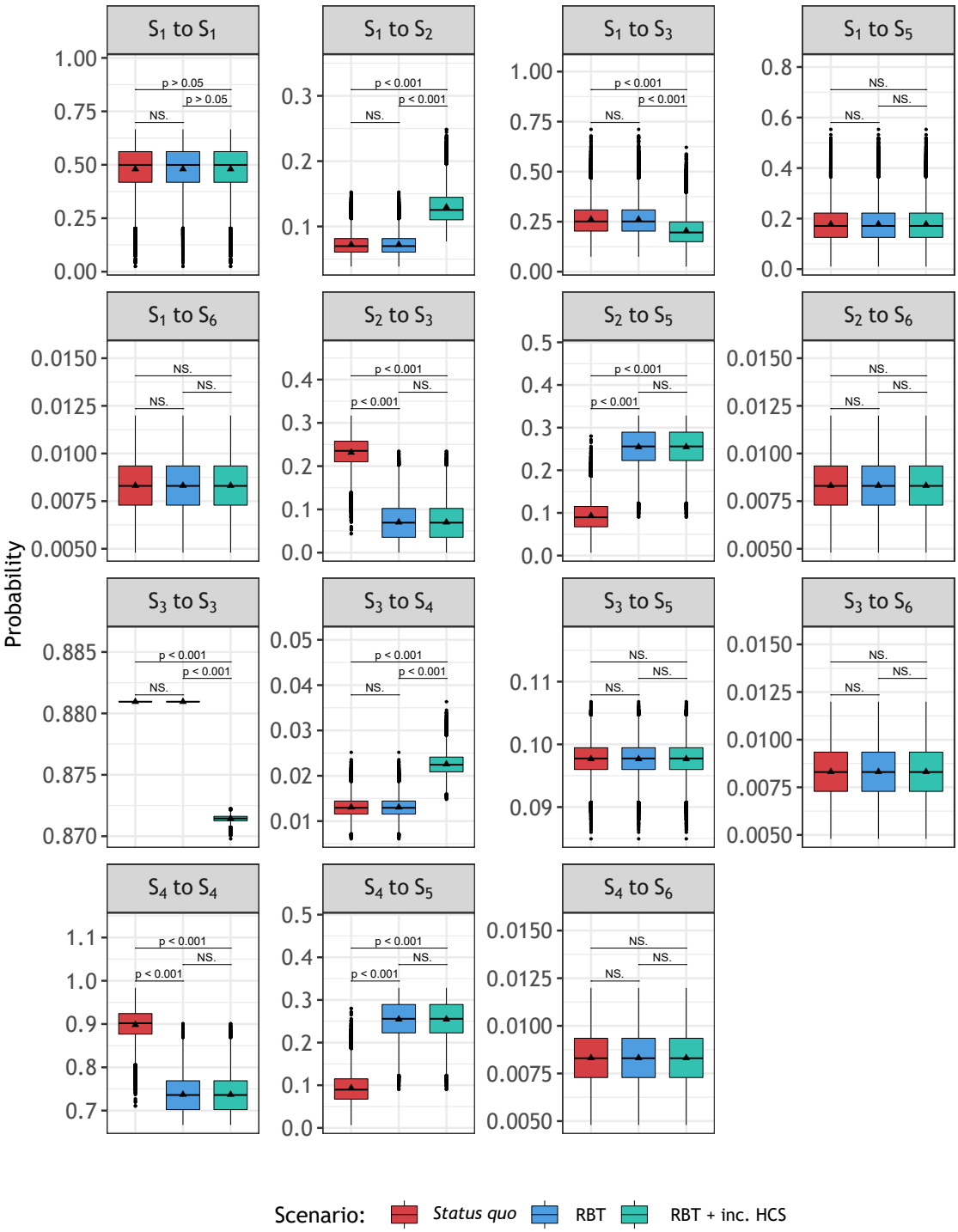



**Figure D.7.1:** Boxplots of weekly transition probabilities used in the model to estimate the monetary costs and disease burden attributable to brucellosis in the Ngorongoro Conservation Area. Panel titles indicate the transitions between states (S): non-target management of acute illness ($S_1$), target management of acute illness ($S_2$), non-target management of chronic illness ($S_3$), target management of chronic illness ($S_4$), recovery ($S_5$) and death ($S_6$). Black dots indicate outliers. Black triangles indicate the mean. p-values indicate the significance of the two-sample Wilcoxon rank-sum test. NS indicates that values are equal across two scenarios. RBT: Rose Bengal test. inc. HCS: Increased healthcare seeking.

## D.8 Elasticity analyses

**Table D.8.1:** Model input parameters, range (minimum-maximum values obtained from distributions in Appendix D.4) and units considered in the elasticity analyses.

| Input parameter | Range | Unit |
|---|---|---|
| Acute disease duration | 1.025-2.991 | Weeks |
| Prob. of target health seeking (fever) | 0.089-0.186 | Prob. |
| Prob. of target health seeking (MSK symptoms) | 0.077-0.283 | Prob. |
| Prob. of death | 0.041-0.100 | Prob. |
| Prob. of treatment failure | 0.162-0.446 | Prob. |
| Prob. of chronic progression | 0.305-0.890 | Prob. |
| Diagnostic test sensitivity | 0.031-0.811 | Prob. |
| Non-target health-related expenditure | 79.640-578.250 | int. $ |
| Target health-related expenditure | 127.300-554.300 | int. $ |
| Expectation of life at the time of death | 7.050-72.600 | Years |
| Acute moderate disability weight | 0.033-0.080 | NA |
| Acute severe disability weight | 0.139-0.296 | NA |
| Chronic disability weight | 0.053-0.114 | NA |
| Orchitis disability weight | 0.064-0.136 | NA |

Prob: probability; trad: traditional; MSK: musculoskeletal; Exp: expenditure; NA: not applicable; int. $: international dollars.

## D.9 Correlation matrices of transition probabilities, model inputs and model outputs

**Table D.9.1:** Matrix of Spearman's correlation coefficients between transition probabilities in the Markov model.

| | p11 | p12 | p13 | p15 | p16 | p22 | p23 | p25 | p26 | p34 | p35 | p36 | p44 | p45 | p46 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| p11 | 1.00 | **-0.91** | **-0.62** | **-0.49** | **0.01** | -0.00 | 0.01 | -0.01 | **0.01** | -0.01 | -0.00 | **0.01** | 0.01 | -0.01 | **0.01** |
| p12 | | 1.00 | **0.54** | **0.43** | **-0.01** | 0.01 | **-0.01** | **0.01** | **-0.01** | 0.01 | 0.00 | **-0.01** | **-0.01** | **0.01** | **-0.01** |
| p13 | | | 1.00 | **-0.33** | -0.00 | 0.00 | **-0.10** | **0.10** | -0.00 | **0.01** | -0.01 | -0.00 | **-0.10** | **0.10** | -0.00 |
| p15 | | | | 1.00 | **-0.03** | 0.00 | **0.10** | **-0.10** | **-0.03** | -0.00 | **0.02** | **-0.03** | **0.10** | **-0.10** | **-0.03** |
| p16 | | | | | 1.00 | -0.00 | **-0.04** | -0.00 | **1.00** | -0.00 | **-0.54** | **1.00** | **-0.04** | -0.00 | **1.00** |
| p22 | | | | | | 1.00 | 0.01 | -0.01 | -0.00 | 0.00 | 0.00 | -0.00 | 0.01 | -0.01 | -0.00 |
| p23 | | | | | | | 1.00 | **-1.00** | **-0.04** | -0.00 | **0.02** | **-0.04** | **1.00** | **-1.00** | **-0.04** |
| p25 | | | | | | | | 1.00 | -0.00 | 0.00 | 0.00 | -0.00 | **-1.00** | **1.00** | -0.00 |
| p26 | | | | | | | | | 1.00 | -0.00 | **-0.54** | **1.00** | **-0.04** | -0.00 | **1.00** |
| p34 | | | | | | | | | | 1.00 | **-0.82** | -0.00 | -0.00 | 0.00 | -0.00 |
| p35 | | | | | | | | | | | 1.00 | **-0.54** | **0.02** | 0.00 | **-0.54** |
| p36 | | | | | | | | | | | | 1.00 | **-0.04** | -0.00 | **1.00** |
| p44 | | | | | | | | | | | | | 1.00 | **-1.00** | **-0.04** |
| p45 | | | | | | | | | | | | | | 1.00 | -0.00 |
| p46 | | | | | | | | | | | | | | | 1.00 |

Values in bold indicate a p-value $< 0.05$.

$p_{xy}$ represents the transition probability from $S_x$ to $S_y$ during each Markov cycle. $S_1$: non-target management of acute illness; $S_2$: target management of acute illness; $S_3$: non-target management of chronic illness; $S_4$: target management of chronic illness; $S_5$: recovery; and $S_6$: death. $p_{33}$ not shown in this table because it is constant.

**Table D.9.2:** Matrix of Spearman's correlation coefficients between Markov model inputs and outputs.

| | prdl | hexp | adal | cdal | ntar | targ | actd | chrd | acud | hcsf | hcsm | fatr | tsen | tref | acpr | syll | amdw | asdw | chdw | ordw |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| prdl | 1.00 | 0.01 | **0.26** | **0.54** | 0.00 | -0.01 | **0.39** | **0.71** | **0.38** | **0.04** | **0.07** | -0.00 | **-0.15** | **0.03** | **0.68** | 0.00 | **0.07** | **0.27** | **0.48** | **0.02** |
| hexp | | 1.00 | 0.00 | **0.01** | **0.97** | **0.21** | -0.00 | **0.01** | -0.00 | **0.02** | **0.01** | 0.00 | -0.01 | 0.00 | **0.01** | -0.00 | -0.01 | -0.00 | -0.00 | **0.01** |
| adal | | | 1.00 | **0.45** | -0.00 | -0.00 | **0.68** | -0.00 | **0.68** | **0.06** | -0.01 | **0.71** | -0.01 | -0.01 | 0.00 | -0.00 | -0.00 | **0.01** | -0.00 | 0.01 |
| cdal | | | | 1.00 | 0.00 | -0.00 | **0.01** | **0.75** | **0.01** | 0.00 | **0.08** | **0.63** | **-0.16** | **0.03** | **0.73** | 0.01 | **-0.01** | 0.01 | 0.00 | 0.00 |
| ntar | | | | | 1.00 | 0.01 | -0.00 | 0.00 | -0.00 | 0.01 | 0.00 | 0.00 | -0.01 | 0.00 | 0.00 | -0.00 | -0.00 | -0.00 | 0.00 | **0.01** |
| targ | | | | | | 1.00 | -0.00 | -0.01 | -0.00 | **0.01** | -0.00 | -0.00 | **-0.01** | -0.00 | -0.01 | 0.00 | -0.01 | -0.00 | -0.00 | -0.00 |
| actd | | | | | | | 1.00 | 0.01 | **1.00** | **0.08** | -0.01 | **0.01** | -0.01 | -0.00 | 0.00 | -0.01 | -0.00 | 0.00 | 0.00 | 0.01 |
| chrd | | | | | | | | 1.00 | 0.00 | 0.00 | **0.10** | -0.01 | **-0.21** | **0.05** | **0.96** | 0.01 | **-0.01** | 0.01 | 0.00 | 0.00 |
| acud | | | | | | | | | 1.00 | -0.00 | -0.01 | **0.01** | -0.01 | -0.00 | 0.00 | -0.01 | 0.00 | 0.00 | 0.00 | 0.01 |
| hcsf | | | | | | | | | | 1.00 | -0.00 | 0.00 | 0.01 | 0.00 | 0.00 | -0.00 | -0.01 | -0.00 | 0.00 | -0.00 |
| hcsm | | | | | | | | | | | 1.00 | -0.00 | 0.00 | 0.00 | 0.01 | -0.00 | -0.01 | 0.00 | 0.00 | **0.01** |
| fatr | | | | | | | | | | | | 1.00 | -0.01 | -0.01 | 0.00 | 0.00 | -0.00 | 0.01 | -0.01 | 0.00 |
| tsen | | | | | | | | | | | | | 1.00 | 0.00 | 0.00 | -0.00 | 0.00 | 0.00 | -0.00 | -0.00 |
| tref | | | | | | | | | | | | | | 1.00 | 0.00 | 0.00 | -0.00 | 0.00 | 0.00 | 0.00 |
| acpr | | | | | | | | | | | | | | | 1.00 | 0.01 | **-0.01** | 0.01 | 0.00 | 0.00 |
| syll | | | | | | | | | | | | | | | | 1.00 | -0.01 | -0.00 | 0.01 | -0.01 |
| amdw | | | | | | | | | | | | | | | | | 1.00 | 0.00 | -0.00 | -0.01 |
| asdw | | | | | | | | | | | | | | | | | | 1.00 | 0.00 | -0.01 |
| chdw | | | | | | | | | | | | | | | | | | | 1.00 | -0.00 |
| ordw | | | | | | | | | | | | | | | | | | | | 1.00 |

Values in bold indicate a p-value $< 0.05$.

Model outputs: prdl - productivity losses; hexp - out-of-pocket expenditure; adal - acute DALYs per case (the sum of the years of life lost and years lived with disability due to acute brucellosis); cdal - chronic DALYs per case (the sum of the years of life lost and years lived with disability due to chronic brucellosis); ntar - non-target health-related expenditure; targ - target health-related expenditure; actd - acute disease duration per case; chrd - chronic disease duration per case.

Model inputs: acud - acute disease duration; hcsf - probability of healthcare seeking for fever; hcsm - probability of healthcare seeking for musculoskeletal symptoms; fatr - probability of death; tsen - diagnostic test sensitivity; tref - probability of treatment failure; acpr - probability of chronic progression; syll - expectation of life at the time of death; amdw - acute moderate disability weight; asdw - acute severe disability weight; chdw - chronic disability weight; ordw - orchitis disability weight.

# E Cost-benefit and cost-utility analyses of livestock vaccination

## E.1 Costing of the information campaign

**Table E.1.1:** Estimation of the cost of one information campaign.

| Cost item | Sub-item | Cost per unit (int. $) | Unit | Number of units | Total cost (int. $) | Observations |
|---|---|---|---|---|---|---|
| Allowances | Community leaders | 44.28 | One PD | 100 | 4,428 | 50 community leaders for a two-day meeting |
| | Executive staff | 113.85 | One PD | 20 | 2,277 | Five government officials, three livestock field officers, one district veterinary officer, one district medical officer |
| | Drivers | 63.25 | One PD | 20 | 1,265 | Two drivers during ten days to announce vaccination campaign with loudspeakers |
| | Radio program | 63.25 | One PD | 30 | 1,898 | Two village leaders per day for 15 days to participate in a radio program |
| | Video clip production | 75.90 | One PD | 45 | 3,416 | Three people working on video clip production for 15 days |
| Transport | Meeting participants | 3.16 | One person | 200 | 633 | Two-way transport for 100 community members to participate in a two-day meeting |
| | Fuel | 3.80 | One litre | 240 | 911 | Fuel (20 litres per day, 12 days) for video clip production and announcements with loudspeakers |
| Other | Stationary | 633 | One set | 1 | 633 | Stationary for the two-day meeting |
| | Flyers and posters | 1,265 | One set | 1 | 1,265 | Production and printing of flyers and posters |
| | Food and beverages | 18.98 | One PD | 320 | 6,072 | Food and beverages for 50 community leaders, 10 executive staff, and 100 community members at a two-day meeting |
| | Meeting venue | 126.51 | One day | 1 | 253 | Meeting venue hire for the two-day meeting |
| | | | | **Total:** | **23,049** | |

PD: person-day; int. $: international dollars; Unit prices were obtained from local service providers, researchers and government officials; total costs shown may not add up precisely due to rounding.

## E.2 Costing of the livestock vaccination

**Table E.2.1:** Estimation of the cost of one vaccination run.

| Cost item | Sub-item | Cost per unit (int. $) | Unit | Reference / source | Assumptions and explanation for total cost calculation |
|---|---|---|---|---|---|
| Consumables | S19 | 1.01 | One dose | Tanzania Vaccine Institute | Cost per unit times number of cattle to be vaccinated (cattle population times proportion eligible to be vaccinated [67% in Table 6.1] times proportion of the eligible population to be vaccinated [75% in the reference scenario]) plus 10% of contingency; it is assumed that each vaccine kit contains 100 doses |
| | Rev 1 | 0.49 | One dose | CZ Vaccines, Spain | Cost per unit times number of sheep and goats to be vaccinated (sheep and goats population times proportion eligible to be vaccinated [83% in Table 6.1] times proportion of the eligible population to be vaccinated [75% in the reference scenario]) plus 10% of contingency; it is assumed that each vaccine kit contains 50 doses |
| | Syringes | 10.69 | Pack of 100 | Local supplier | One syringe with needle needed per vaccine kit i.e. per 100 doses of S19 or 50 doses of Rev 1 |
| | Gloves | 5.10 | Pack of 100 | Local supplier | Five pairs of gloves used per team member per vaccination day |
| | Surgical face mask | 7.06 | Pack of 50 | Local supplier | Four masks used per team member per vaccination day |
| | Paper roll | 14.61 | One roll | Local supplier | One roll per team for each five vaccination days |
| | Overshoes | 31.37 | Pack of 100 | Local supplier | Six pieces used per team member per vaccination day |
| | Disinfectant | 130.83 | Box with 50 tablets | Local supplier | Virkon S; 20 litres per team for each vaccination year; one tablet yields 0.57 litres |

Continuation of Table E.2.1

| Cost item | Sub-item | Cost per unit (int. $) | Unit | Reference / source | Assumptions and explanation for total cost calculation |
|---|---|---|---|---|---|
| | Clinical waste container (sharps) | 117.18 | One pack of 10 boxes | Local provider | Twenty boxes for each vaccination year, including disposal |
| | Clinical waste container (general) | 483.83 | One box | Local provider | Two boxes per team for each vaccination year, including disposal |
| | Tweezers | 6.33 | Pack of five | Local supplier | One pack per team for each vaccination year |
| | Disposable gowns | 391.36 | Pack of 100 | Local supplier | Three gowns per team member per vaccination day |
| | Safety glasses | 8.63 | One pair | Local supplier | One pair per team member for each vaccination year |
| | Log books | 6.33 | One book | Local supplier | Two log books per team for each vaccination year |
| Transport | Car maintenance | 885.54 | One service | Local provider | One service every 20 days for each car (four cars in total) |
| | Fuel | 3.80 | One litre | Local supplier | 20 Litres per car (four cars in total) per vaccination day |
| Labour | Allowance for LFOs | 75.90 | One PD | Government official | Two LFO per team per vaccination or training day |
| | Allowance for CAHWs | 44.28 | One PD | Government official | Two CAHWs per team per vaccination or training day |
| | Allowance for drivers | 63.25 | One PD | Government official | Four drivers for eight teams per vaccination or training day |
| Cold chain | Cool boxes | 75.90 | One box | Local supplier | One cool box per team for the whole vaccination program (10 years) |

Continuation of Table E.2.1

| Cost item | Sub-item | Cost per unit (int. $) | Unit | Reference / source | Assumptions and explanation for total cost calculation |
|---|---|---|---|---|---|
| | Fridge | 1,897.58 | One fridge | Local supplier | Two fridges for eight teams for the whole vaccination program (10 years) |

LFOs: livestock field officers; CAHWs: community animal health workers; PD: person-day; int. $: international dollars. Local suppliers include Medeor (International Healthcare Tanzania) and ubuy.co.tz.

## E.3 Input parameters and variables in the disease transmission model and cost-benefit and cost-utility analyses

**Table E.3.1:** Input parameters and variables in the disease transmission model.

| Parameter / variable group | Sub-group | Distribution | Source and justification |
|---|---|---|---|
| Initial population | Cattle | PERT(min: 99,509; mode: 115,562; max: 131,615) | Data from an aerial census conducted in 2016 indicated that there were 115,562 ($\pm$ 16,053) cattle in the NCA (Tanzania Wildlife Research Institute, 2016) |
| | Sheep and goats | PERT(min: 157,334; mode: 181,281; max: 205,228) | Data from an aerial census conducted in 2016 indicated that there were 181,281 ($\pm$ 23,947) sheep and goats in the NCA (Tanzania Wildlife Research Institute, 2016) |
| | People | PERT(min: 75,000; mode: 100,000; max: 125,000) | Estimated human population size in the NCA in 2016/2017 ($\pm$ 25%) (Government of The United Republic of Tanzania, 2019; Slootweg, 2018) |
| Birth rate ($\alpha$) and death rate ($\mu$) | Cattle | PERT(min: 0.17; mode: 0.23; max: 0.29) | Data from the SEEDZ project (Chapter 4) indicated that 23 animals were born in one year for every 100 cattle kept; the minimum and maximum values are 0.23 $\pm$ 25% |
| | Sheep and goats | PERT(min: 0.28; mode: 0.37; max: 0.46) | Data from the SEEDZ project (Chapter 4) indicated that 37 animals were born in one year for every 100 sheep and goats kept; the minimum and maximum values are 0.37 $\pm$ 25% |
| | People | PERT(min: 0.011; mode: 0.014; max: 0.018) | A 2002 population and housing census report indicated that the life expectancy at birth in Arusha was 70.5 (1/0.014) years; the minimum and maximum values are 0.014 $\pm$ 25% |
| Waning immunity rate ($\theta^H$) | People | PERT(min: 0.05; mode: 0.10; max: 0.20) | The duration of immunity to brucellosis in people has been estimated at around 10 years (1/mode) (Bonfoh et al., 2012); the minimum and maximum values correspond to half and twice the mode, respectively |

Continuation of Table E.3.1

| Parameter / variable group | Sub-group | Distribution | Source and justification |
|---|---|---|---|
| Initial prevalence in livestock | Cattle | See Chapter 4 | Latent class analyses-derived prevalence distribution for cattle in the pastoral production system. The initial incidence was the product of initial prevalence, total cattle population, and death rate of cattle |
| | Sheep and goats | See Chapter 4 | Joint latent class analyses-derived prevalence distributions for sheep and goats in the pastoral production system, considering that 80% of sheep and goats were goats, and 20% were sheep. The initial incidence was the product of initial prevalence, total sheep and goats population, and death rate of sheep and goats |
| Initial incidence in people ($Y^H$) | People | PERT(min: 100; mode: 400; max: 800) | Community-level incidence estimated by de Glanville et al (See Chapter 5) from hospital-level surveillance data and a healthcare utilisation survey (project reference BB/S013857/1). The initial prevalence was given by $\frac{Y^H}{N^H\left(\mu^H+\theta^H\right)}$, where $N^H$ is the number of people, $\mu^H$ is the death rate of people, and $\theta^H$ is the waning immunity in people |
| Prop. of livestock infections that occur due to transmission within species ($\rho$) | | Uniform(min:0; max:1) | Assumption |
| Prop. of human infections due to transmission from livestock species $i$ ($\pi_i$) | | Uniform(min:0; max:1) | Assumption |
| Number of animals vaccinated per team per day | | PERT(min: 250; mode: 500; max: 750) | Personal communication with a veterinary officer at the Tanzania Vaccine Institute, and supported by data from an unpublished study of livestock vaccination for anthrax in the NCA |

NCA: Ngorongoro Conservation Area; min: minimum; max: maximum; Prop: proportion; SEEDZ: Social, Environmental and Economic Drivers of Zoonotic disease project.

## E.4 Elasticity analyses

**Table E.4.1:** Model input parameters, range (minimum-maximum values obtained from distributions in Appendix E.3) and units considered in the elasticity analyses.

| Input parameter | Range | Unit |
|---|---|---|
| Birth/death rate of cattle | 0.173-0.286 | NAY |
| Birth/death rate of sheep and goats | 0.280-0.461 | NAY |
| Birth/death rate of people | 0.011-0.018 | NAY |
| Production losses in cattle | 8.523-946.583 | int. $ |
| Production losses in sheep and goats | 0.744-50.222 | int. $ |
| Monetary cost per human case | 258.200-797.000 | int. $ |
| Cattle population size | 99,909-131,472 | N |
| Sheep and goats population size | 157,758-204,890 | N |
| Human population size | 75,466-124,655 | N |
| Brucellosis prevalence in cattle | 0.018-0.089 | Prop. |
| Brucellosis prevalence in sheep and goats | 0.000-0.088 | Prop. |
| Brucellosis prevalence in people | 0.006-0.130 | Prop. |
| Prop. of human infections with cattle origin | 0.000-1.000 | Prop. |
| Prop. of livestock infections occurring within-species | 0.000-1.000 | Prop. |
| Waning immunity rate of human infection | 0.050-0.195 | HLY |
| Number of animals vaccinated per team per day | 253.900-745.600 | N |

N: number of animals; NAY: newborns per animal per year; int. $: international dollars; Prop.: proportion; HLY: Proportion of human cases losing immunity per year.

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