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EDITED BY JOHN MCINTIRE AND DELIA GRACE



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CABI
Nosworthy Way
Wallingford
Oxfordshire OX10 8DE
UK

CABI
745 Atlantic Avenue
8th Floor
Boston, MA 02111
USA

Tel: +44 (0)1491 832111
Fax: +44 (0)1491 833508
E-mail: info@cabi.org
Website: www.cabi.org

Tel: +1 (617)682-9015
E-mail: cabi-nao@cabi.org

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8 Zoonoses

**Delia Grace¹, Silvia Alonso², Bernard Bett³, Elizabeth Cook³,
Hu Suk Lee⁴, Anne Liljander⁵, Jeff Mariner⁶, Florence Mutua³, Hung
Nguyen-Viet⁴, Ekta Patel³, Thomas Fitz Randolph³, Kristina Roesel³, Lian
Thomas³, Phil Toye³, Fred Unger⁴ and Barbara Wieland⁷**

¹International Livestock Research Institute, Nairobi, Kenya and University of Greenwich, UK; ²International Livestock Research Institute, Jerusalem, Israel; ³International Livestock Research Institute, Nairobi, Kenya; ⁴International Livestock Research Institute, Hanoi, Vietnam; ⁵EUROIMMUN AG, Lübeck, Germany; ⁶Cummings School of Veterinary Medicine at Tufts University, Grafton, Massachusetts, USA; ⁷International Livestock Research Institute, Addis Ababa, Ethiopia

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Executive Summary

ILRI's role in the global context

The problem

Zoonoses are diseases that are transmissible between humans and animals through either direct contact or by way of food, water or the environment. Around 60% of all human diseases and around 75% of emerging human infectious diseases are zoonotic. Zoonoses have high impacts on human health, livelihoods, animals and ecosystems. The first global syntheses on the impacts of zoonotic diseases, led by the International Livestock Research Institute (ILRI), estimated that in the least-developed countries, 20% of human sickness and death was due to zoonoses or diseases that had recently jumped species from animals to people (Grace *et al.*, 2012a). Zoonoses sicken several billion people each year and kill millions, mostly in low- and middle-income countries. While estimates of the historical burden of zoonoses are lacking, the World Bank has estimated that emerging zoonoses cost around US\$7 billion a year (World Bank, 2012).

Some zoonoses are considered neglected, classical or endemic, and others as new or emerging. Neglected zoonoses are mostly controlled or eradicated from high-income countries but impose a large burden on low- and middle-income countries. Emerging zoonoses are a global threat, but most of the economic burden falls on high-income countries. Disease categories are to some extent overlapping, and a disease may be endemic in one place and emerging in another. Many zoonoses, both neglected and emerging, are food-borne; these are discussed in Chapter 9 (this volume). This chapter focuses on zoonoses that are not transmitted primarily through food.

ILRI has worked in joint partnerships with several universities and research institutes to develop research activities on zoonoses. This area of research commenced in the 1990s with small studies on neglected zoonoses. Initial work focused on bovine tuberculosis (TB), brucellosis, human African trypanosomiasis (commonly known as sleeping sickness) and rabies. From the 2000s, an agenda on the pig tapeworm that causes the parasitic tissue infection cysticercosis emerged, while research on specific neglected zoonoses continued, including work on anthrax; the acute bacterial swine disease known as erysipeloid ('diamond skin disease'); the bacterial diseases leptospirosis, Q fever and streptococcosis; and the parasitic (roundworm) disease trichinellosis, which humans can get when consuming undercooked or raw pork products.

Work on emerging zoonoses started in the 2000s as global attention heightened following the global pandemic of highly pathogenic avian influenza (HPAI, or avian influenza, caused by influenza A virus subtype H5N1) and the high-profile outbreaks of bovine spongiform encephalopathy (BSE or 'mad cow disease') and severe acute respiratory syndrome (SARS). ILRI research on emerging diseases focused on livestock-related antimicrobial resistance, avian influenza, Ebola virus disease, Middle Eastern respiratory syndrome coronavirus (MERS-CoV) and Rift Valley fever (RVF).

As the programme matured, ILRI zoonoses research moved from a predominately veterinary public health paradigm to embrace one-health, which is predicated on the interdependence of human, animal and ecosystem health. As well as the research on high-priority zoonotic diseases, ILRI research initiatives addressed specific livestock systems, notably pastoral and urban.

In the last two decades, this work has extended from East Africa to India and South-east Asia, and in the last decade, ILRI's zoonotic research was aligned to the livestock value chains prioritized in the CGIAR Research Programmes (CRPs) on Livestock and Fish (2012–2016) and Livestock (2017–2021). Research on zoonoses has included estimating the prevalence and burden of zoonoses, identifying factors or drivers of emergence of zoonoses, understanding the risk factors of these infectious diseases, and strategies for reducing those risks and better managing these diseases.

Impacts of ILRI research

Because large-scale zoonoses research at ILRI is relatively new, ILRI's scientific impacts in this area are more notable than its impacts on development. The most-cited papers by any ILRI authors or co-authors are in the realm of climate change and human disease, emerging zoonoses and estimation of the human disease burden of zoonotic diseases. Research analytics show that ILRI research was especially dominant in MERS-CoV and RVF. There are also many important ILRI outputs on antimicrobial resistance, avian influenza, brucellosis, cysticercosis and sleeping sickness, but these diseases are the focus of considerable global research efforts, and ILRI has been a relatively minor player globally. Many syntheses chapters and papers on zoonoses have been authored or co-authored by ILRI scientists. An important scientific contribution has been development and deployment of tools as well as methodological advances. Most notable were mathematical modelling, systematic prioritization of zoonoses, use of geospatial data and participatory disease surveillance.

While many of ILRI's research activities helped to advance our basic understanding of disease, which can be anticipated to contribute to long-term improvements in human health, some had significant direct outcomes. In Uganda, ILRI scientists identified the first cases of swine erysipelas ('diamond skin disease'), established that swine brucellosis did not occur and established that trichinellosis (pork measles) might be transitioning from a wildlife to a livestock cycle. This kind of new and surprising information usefully

alerted national medical services that some diseases they did not know were present actually were present and that other diseases they suspected to be present were in fact not present.

Similarly, a study in Uganda found substantial underdiagnosis of sleeping sickness, another in western Kenya found extensive misdiagnosis of human brucellosis, and yet another in northern Kenya found substantial overdiagnosis of malaria. ILRI brought these findings to the attention of local medical authorities. While the benefits of this work have not yet been well evaluated, this work is expected to lead to better treatment for tens of thousands of sick people.

Initial work on zoonoses logically focused mostly on improving our understanding of the presence, prevalence, burden and drivers of zoonotic disease. ILRI developed a prototype diagnostic for cysticercosis, but this did not go to scale because of lack of demand; tests for bovine tuberculosis diagnosis are ongoing at ILRI. A vaccine for RVF is under development by ILRI and has potential for widespread use. Vaccination (using a commercial vaccine) for avian influenza was piloted in Java, Indonesia, with ILRI support; an ILRI evaluation showed this was effective but unsustainable purely by the market. Another ILRI evaluation of vaccination for cysticercosis in Uganda came to the same conclusion. These findings helped identify more practical solutions, some of them potentially involving public-private partnerships.

Small pilots were conducted by ILRI to train farmers, extension agents, slaughterhouse workers and street vendors to improve food safety: most showed benefits, at least in the short term. ILRI has also conducted *ex ante* and model-based assessments to compare alternative response strategies for zoonotic disease, notably for RVF and sleeping sickness.

ILRI has been involved in policy support for better controlling zoonoses at local, national, regional and international scales (UNEP and ILRI, 2020). ILRI has partnered with the World Health Organization (WHO) and other international organizations on several initiatives to better control neglected zoonoses generally and cysticercosis specifically. It has also partnered with most of the major global one-health initiatives. ILRI supported regional initiatives on rabies and cysticercosis. At national levels, ILRI has supported contingency planning and groups

working in different countries on specific zoonoses, including MERS, brucellosis and RVE, as well as working groups and task forces focused more broadly on zoonoses and one-health. In cities and decentralized countries, ILRI has worked with local authorities and in some cases has documented beneficial shifts in policy and approaches. When engaging in these policy processes, ILRI provided evidence and advocated best practice, but ILRI's contributions to health policy and the impacts of policies influenced by ILRI have not been well documented.

Estimating development impacts is more difficult. Moreover, many of the benefits of better controlling zoonotic diseases come not from increasing incomes or improving nutrition of the poor but rather from averting their losses, which is difficult to measure in the absence of a counterfactual. Certainly, individual projects demonstrated far-reaching improvements in capacity linked to development impacts. For example, projects in South-east Asia piloted a village-based approach to community control of rabies that was subsequently extended to the entire island of Bali.

Millions of people have been reached by initiatives that aimed to protect human health and reduce economic burdens as the result of timely detection of emerging diseases and an appropriate response. For example, ILRI partnered several stakeholders in Kenya to develop a decision-support tool for better managing RVE. Together with risk maps, this tool was incorporated into the country's RVE contingency plan, which is the mainstay for mitigating the impacts of an outbreak of the disease. We estimate that hundreds of millions of people lived in areas where participatory disease surveillance was active. It is difficult to quantify the impact of these preparedness activities, but our best estimates suggest that timely surveillance can reduce the impacts of a disease outbreak by 90% (Grace, 2014). Several of these programmes were operational for many years during the HPAI pandemic, and national programmes for RVE are still active in Kenya.

In several cases, ILRI's scientific outputs have been taken up by other development actors with probable benefits. For example, ILRI's contributions to research on the burden and distribution of sleeping sickness in Uganda and on management options for better control of this disease influenced major donor investments that protected the health of hundreds of thousands of cattle (although the intervention did not

prove sustainable). Zoonoses prioritizations conducted by ILRI have been directly connected to funding decisions by donors. ILRI has also led several evaluations of zoonoses control projects, most notably on avian influenza, which either endorsed national control programmes or led to improvements in how they were conducted.

Capacity development

Dozens of graduate fellows have been trained by ILRI and its partners as part of research into zoonoses. Many of these trained students have taken up important roles in ILRI and other organizations, including universities, ministries and health services. ILRI scientists also supervised and taught a novel epidemiological educational course for the Field Epidemiology and Laboratory Training Program within the Ministry of Health, Kenya, which has been evaluated positively. Veterinary staff members were trained by ILRI in several countries. ILRI also supported the establishment of one-health centres in Thailand and Indonesia and provided ongoing support to the development of similar centres in Côte d'Ivoire and Vietnam. These centres are all operational (as of 2020), providing training and conducting research in zoonoses. ILRI supported setting up and running a laboratory in the town of Busia, in western Kenya, which has helped improve understanding of livestock and human diseases and their links. In 2020, ILRI launched a major initiative, the One Health Research, Education, Outreach and Awareness Centre. Its aim is to improve the health of humans, animals and ecosystems through capacity building; strengthening local, regional and global networks; and evidence-based policy advice in the context of one-health by setting up a central facility for one-health in sub-Saharan Africa.

Introduction

This chapter considers ILRI research on zoonoses under two rubrics: (i) research on zoonoses occurring in systems; and (ii) research on high-priority emerging and neglected zoonotic diseases. Under the former, we prioritized diseases and conducted studies on disease emergence and participatory disease surveillance, investigated

multiple zoonoses occurring in systems, and collaborated in regional and international initiatives to control zoonoses. Under the latter, we conducted studies on antimicrobial resistance, avian influenza, Ebola virus disease, MERS-CoV and RVE, all of which are considered emerging disease problems, and on key neglected zoonoses including cysticercosis, brucellosis and sleeping sickness.

Zoonoses were not within the research mandate of the International Laboratory for Research on Animal Diseases (ILRAD), which, with the International Livestock Centre for Africa (ILCA), was a predecessor of ILRI. ILRAD focused on African animal trypanosomiasis and East Coast fever. ILCA did not conduct disease-specific research but frequently mentioned zoonotic diseases as key problems in Africa's livestock systems and judged them important due to the harm they cause the continent's livestock sector and public health.

When ILRI was constituted in 1994, neglected zoonoses were considered diseases well researched in high-income countries and therefore not high priorities for ILRI. However, opportunities for developing low-cost appropriate technologies for controlling neglected zoonoses in lower-income countries were not precluded from ILRI's research agenda. At that time (mid-1990s), emerging infectious diseases were not yet considered a global priority.

The first systematic approach to identify pro-poor animal health research priorities was conducted by ILRI in 2000 and identified several zoonoses as high priorities (Perry *et al.*, 2002). Following this, ILRI's new strategy identified impacts on the livestock livelihoods of the poor, including those caused by neglected zoonoses, as an important area of research. A programme on livestock impacts on human health was initiated in 2005, led by Tom Randolph. (In 2008, this programme was incorporated into a broader agenda on livestock markets research.)

Because ILRI had limited expertise dedicated to zoonoses (as distinct from veterinary public health), ILRI initiated a collaboration with the Danish Bilharziasis Laboratory and the Swiss Tropical Institute (STI) to develop a research agenda on zoonoses¹. Over the next decade, work on neglected zoonoses continued. At the same time, emerging zoonoses climbed rapidly up the research agenda, driven by concern over high-profile outbreaks of avian influenza, RVE

and SARS. Several ILRI scientists were involved in emerging zoonoses research². In 2011, following a research restructuring, zoonoses was once more the focus of a dedicated ILRI programme, namely, Animal Health, Food Safety and Zoonosis, led by Delia Grace.

In 2018, another restructuring saw this programme joined with three other units working on different aspects of health to constitute an Animal and Human Health programme, jointly led by veterinary epidemiologist Delia Grace and veterinary vaccine developer Vish Nene. Over the years, ILRI has invested substantially in several high-priority emerging and neglected zoonoses, including anthrax, avian influenza, brucellosis, COVID-19, cysticercosis, Ebola, MERS, RVE and sleeping sickness. The outputs, outcomes and impacts of this work are summarized in the next sections.

Prioritization

Priority setting is essential for directing finite resources to activities that maximize benefits. As discussed in Chapter 5 (this volume) on veterinary epidemiology, in 2002, ILRI was commissioned to conduct the first study aiming to determine the livestock diseases for which research investments were most likely to alleviate poverty. Zoonoses were considered as a separate category, and ranking was done by experts at regional workshops. The top three priorities were all neglected zoonoses: brucellosis, cysticercosis and leptospirosis. This landmark study influenced donor investment in research for development.

In 2005, WHO and the UK Department for International Development (DFID) convened the first meeting to tackle neglected zoonoses, and several ILRI experts participated (WHO, 2006). The meeting identified seven zoonoses – anthrax, bovine TB, brucellosis, cysticercosis, echinococcosis, rabies and zoonotic trypanosomiasis – as priorities. In 2012, ILRI developed the first global assessment of zoonoses and poor livestock keepers (Fig. 8.1) (Grace *et al.*, 2012b). This study combined updated maps of poor livestock keepers with a literature review on the prevalence and impacts of zoonoses. The study assessed 56 zoonoses, together responsible for around 2.5 billion cases of human illness and 2.7 million human deaths a year. The most important diseases in terms of burden and amenability to control

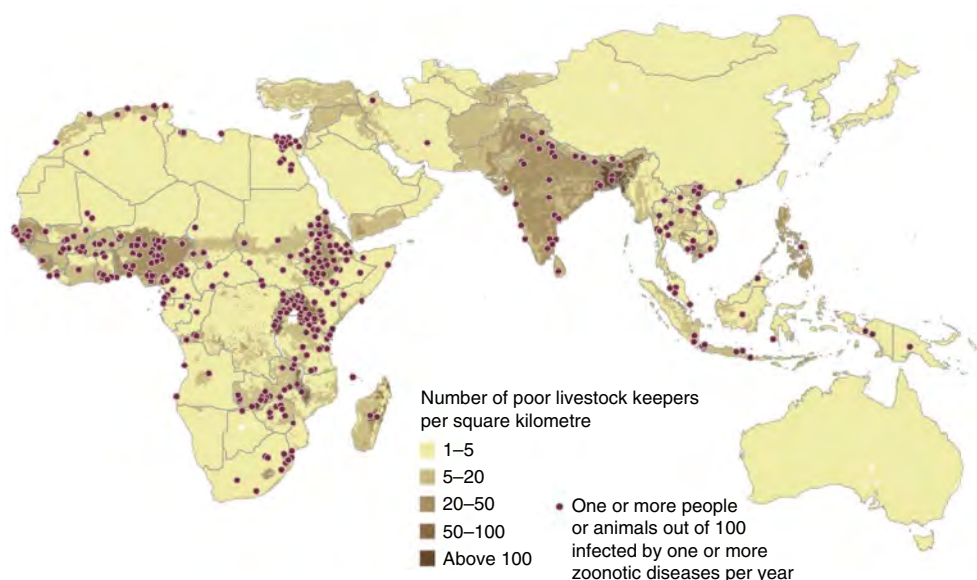


Fig. 8.1. Zoonoses and poor livestock keepers. (From Grace *et al.*, 2012b.)

were cysticercosis, leptospirosis and zoonotic gastrointestinal disease. This study was commissioned by DFID and was used to develop a major funding initiative by DFID on zoonoses.

From 2010, ILRI engaged with the Public Health Foundation of India and was a member of the Roadmap to Combat Zoonoses in India initiative. This used a systematic and validated method to prioritize a research agenda and identify priority zoonoses as well as vulnerable populations (Sekar *et al.*, 2011). Subsequently, ILRI organized a series of one-health dialogues in India with the Indian Council of Agricultural Research, the Public Health Foundation of India and other stakeholders (ILRI/ICAR, 2013; ILRI, 2014). ILRI has continued to support evidence-based one-health approaches and coordination through workshops and training in India, and one-health continues to be supported by the Bill & Melinda Gates Foundation as an important pathway to improving health care in India.

ILRI scientists also contributed to the first estimate of the global burden of food-borne disease (Havelaar *et al.*, 2015), which estimated not only the high burden of food-borne disease but also the importance of zoonoses and animal-source foods. More recently, ILRI is a partner in an initiative to develop a global assessment of

animal disease, which will include zoonoses (Global Burden of Animal Diseases initiative). While prioritization efforts have varied in their rigour and use of evidence, they have helped build a global consensus as to which of the many hundreds of zoonoses are most important to poor people, and this has also informed research globally on neglected and emerging zoonoses. There are clear links between evidence produced by ILRI and actions taken by donors in providing funding for zoonoses research for development.

In 2015, ILRI scientists participated in a systematic prioritization of zoonotic diseases for Kenya that was coordinated by the US Centers for Disease Control and Prevention (CDC) and Kenya's Zoonotic Disease Unit. The prioritization exercise identified the top five zoonotic diseases for the country: anthrax, brucellosis, rabies, RVF and trypanosomiasis (Munyua *et al.*, 2016a). The prioritization tool has been used by government researchers to allocate resources to specific surveillance, prevention and control campaigns. ILRI scientists have partnered with the Zoonotic Disease Unit to develop elimination plans for rabies and to target research on brucellosis and RVE. ILRI scientists also sit on the Zoonosis Technical Working Group, a panel of national experts in one-health.

Understanding drivers of disease emergence

ILRI conducted broad-based research to better understand the drivers of zoonoses emergence. A foundational research paper by Jones *et al.* (2008) had mapped all disease emergence events from the 1930s to the early 2000s. In collaboration with Jones, ILRI developed an updated disease emergence database focusing only on livestock (Grace *et al.*, 2012b). This reinforced the importance of livestock in disease emergence. It also found that disease emergence appeared to be shifting from the western seaboard of Europe and the western seaboard of North America to low- and middle-income countries.

Another ILRI review summarized work linking agricultural intensification to disease emergence (Jones *et al.*, 2013). The review found strong evidence that modern farming practices and intensified systems were linked to disease emergence. However, the evidence was not sufficient to judge whether the net effect of intensified agriculture was more or less propitious to disease emergence than if land was left unused. Subsequent fieldwork helped elucidate some of the relationships between land-use change and disease. Studies in Kenya found that degraded landscapes have more disease, but the relationship between biodiversity and disease is not straightforward. Additional research addressed the hypothesis that irrigation in dry areas would increase the zoonoses burden by creating habitats suitable for diseases; however, while irrigation was associated with increased risk of some zoonoses, adjacent pastoralist areas had increased risks of other zoonoses, suggesting a more complex interaction between ecosystems and economic development (Bett *et al.*, 2017a).

ILRI scientists were also active in understanding the links between climate change and disease emergence, often with a focus on zoonoses. They were commissioned by the CRP on Climate Change, Agriculture and Food Security to develop a paper on climate-sensitive livestock diseases that was incorporated into the planning processes of the United Nations Framework Convention on Climate Change (Grace *et al.*, 2015). ILRI scientists are also members of the very influential Lancet Commission on Health and Climate Change, which has produced some of the most-cited papers from CGIAR (Watts *et al.*, 2017, 2018a,b).

Participatory disease surveillance

Participatory epidemiology is the systematic use of approaches and methods that facilitate the empowerment of people to identify and solve their health needs. It should promote the direct agency of individuals, leading to a shared learning environment that improves the understanding of their risk perception, health risks, and options for surveillance, control and health evaluation in populations. Participatory disease surveillance is a form of active clinical surveillance. It involves the use of participatory approaches and is aimed at detecting clinical cases, which can then be confirmed by specific biological tests. Participatory epidemiology evolved in the 1990s as a new approach to working across cultures in animal health surveillance and epidemiological research (Jost *et al.*, 2007).

ILRI recruited scientists active in the development of participatory epidemiology from 2005, who proceeded to introduce the approach into the institute's research programmes. ILRI has been involved in researching and supporting participatory epidemiology and participatory disease surveillance for over a decade. Some examples include the following:

- Officials from 17 African countries received training in participatory epidemiology and disease surveillance.
- In 2008, a participatory surveillance programme was introduced in Egypt to improve animal health control activities through the use of participatory epidemiology. The programme eventually covered 53 districts (30% of Egypt's districts) in 15 governorates at risk of avian influenza (Verdugo *et al.*, 2016).
- A participatory disease surveillance programme in Indonesia began as a pilot in 12 districts with 48 staff. It was rapidly scaled up, resulting in more than 2000 practitioners in 31 provinces by March 2009 (Azhar *et al.*, 2010).
- Participatory disease surveillance was established in Pakistan as part of a rinderpest eradication campaign with support from the Food and Agriculture Organization of the United Nations (FAO).
- ILRI has supported participatory epidemiology and participatory disease surveillance in Kenya for many years, including its use in control of avian influenza and RVE.

An FAO review found that ILRI was the strongest contributor to participatory disease surveillance in terms of its projects and research outputs. Allepuz *et al.* (2017) found participatory epidemiology methods in 52 countries. Countries where ILRI efforts were concentrated (Egypt, Ethiopia, Indonesia, Kenya, Nigeria and Pakistan) had more activities of that work (Fig. 8.2).

The international community of participatory epidemiology practitioners recognized the utility of establishing a network to promote good practice and to act as a training resource (Mariner *et al.*, 2011). ILRI agreed to facilitate the process, and the Participatory Epidemiology Network for Animal and Public Health (PENAPH) was formed in 2008 with nine core partners, including international agencies, non-governmental organizations and universities with demonstrated commitment to participatory epidemiology. Initially, ILRI hosted the network and the secretariat with support from the Rockefeller Foundation for establishment and activities in two projects over 4 years. PENAPH continues to operate today as a self-sustaining network working across Africa and Asia. The secretariat is now hosted by Tufts University, Massachusetts, and ILRI continues to be a core partner. PENAPH hosted its second international conference in Thailand in 2018, at which

several CGIAR scientists presented papers. ILRI's leadership thus facilitated development of a network subsequently sustained by its participants.

Through PENAPH, ILRI advocated one-health applications of participatory epidemiology; the techniques that emerged in animal health were extended and adapted to public health (Mariner *et al.*, 2014). PENAPH core partners include CDC and the African Field Epidemiology Network. Participatory approaches to surveillance for avian influenza were introduced in several countries in Africa, Egypt and Uganda in particular. The approach has had lasting impacts on epidemiological institutions in ILRI's partner countries.

Zoonoses in Systems

In 2006, ILRI started collaborating with STI (now the Swiss Tropical and Public Health Institute) to address the strategic methodological challenge of integrating veterinary and medical assessments of the impacts of zoonotic disease burden on the livelihoods of the poor. STI had found that, because zoonoses imposed costs in both the veterinary and health sectors and because these were not integrated, the benefits of zoonoses control were underestimated.

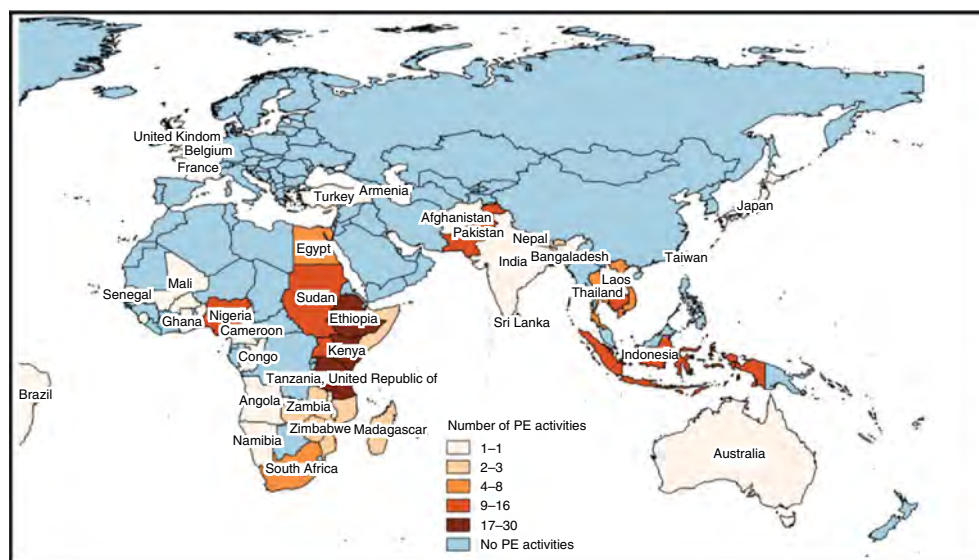


Fig. 8.2. Participatory epidemiology activities by country. (From Allepuz *et al.*, 2017.)

By integrating costs, they were able to show the 'double benefits' of brucellosis control in Mongolia (McDermott *et al.*, 2013). In collaboration with ILRI, this approach was extended to RVF in Kenya (Kimani *et al.*, 2016).

Africa is the least-irrigated continent, and it is predicted that more irrigated areas will be developed in the coming decades. However, there is long-standing concern about the health impacts of irrigation, especially in arid areas. A multi-year project in Kenya investigated links between irrigation and zoonoses. A key finding was that RVF virus (RVFV), West Nile virus and dengue virus were more prevalent in irrigated than in pastoral areas while *Leptospira* spp. and *Brucella* spp. bacteria were higher in pastoral than in irrigated areas (Bett *et al.*, 2017a). The same project investigated sociological aspects relevant to control. For example, the standard health advice was to bury animals that had died of disease, but studies in communities found that this was taboo, reporting, 'We do not bury dead livestock like human beings'; they preferred to eat them (Mutua *et al.*, 2017). This showed that the common approach to public health communication of telling people to bury dead animals was ineffective and other methods were needed to change behaviour.

In 2015, ILRI, along with the University of Edinburgh, UK, and other partners, established a field site in western Kenya for the study of zoonotic diseases. This allowed them to study neglected zoonoses in both livestock and the families that keep them, and to gather the essential baseline data about these infections and the populations affected by them that are so severely lacking. This research identified risk factors for zoonotic diseases in people and animals (Fèvre *et al.*, 2017). The diseases investigated included cysticercosis, leptospirosis, Q fever, RVF and taeniasis (tapeworm infection) (Wardrop *et al.*, 2016; Cook *et al.*, 2017).

The project identified slaughterhouse workers as high-risk groups for zoonotic diseases; this information is being used to explore interventions to reduce this occupational group's risk of exposure. The study demonstrated the existence of a socio-economic gradient within households in rural Kenya, determining individual infectious disease risk. The risk of infection with amoeba, hookworm and malaria was highest in poorer households and the risk of contracting

TB was highest in better-off families (de Glanville *et al.*, 2017). This is relevant to understanding the specific health benefits of reducing poverty.

Research on urban zoonoses started in the early 2000s with support from a CGIAR system-wide initiative. As little was known about urban zoonoses, this work focused first on generating evidence. Some findings led to further research-for-development activities. For example, *Cryptosporidium*, a protozoan zoonotic parasite, was found to be unexpectedly high in urban dairies in Nairobi, which led to another project focusing on *Cryptosporidium*. While generating additional epidemiological evidence, the project staff also engaged with policy makers and developed a behavioural approach to extension, one based on encouraging farmers to implement good practices out of concern for their social status rather than out of fear about contracting an illness. This was evaluated as successful both in improving farmer practices (Kang'ethe *et al.*, 2012a,b) and in shifting policy in a pro-poor direction (Nyangaga *et al.*, 2012). Because cryptosporidiosis is a priority disease of immunosuppressed people, Kenyan medical authorities had been wary about promoting livestock keeping among people with human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDs). An important finding was that cryptosporidiosis in Nairobi was transmitted more by person-to-person than by animal-to-human contact and that people with HIV/AIDs receiving antivirals did not have an elevated risk of cryptosporidiosis. These findings helped safeguard their access to livestock.

In Uganda, a policy-relevant finding from urban zoonoses research was that farmers who had experienced more harassment from authorities had fewer good practices (Grace *et al.*, 2008), and the project contributed to a better policy environment for urban farming (Cole *et al.*, 2008). Many of the results from this early work on urban zoonoses were summarized in a special edition of *Tropical Animal Health and Production* (Grace *et al.*, 2012c).

A more recent urbanization project focused on the emergence of zoonotic pathogens. This had several methodological innovations, including the use of a livestock value chain approach that allowed identification of the stakeholders, drivers and dynamics of urban livestock keeping, as well as the first-ever quantification of the

contribution that urban livestock keeping made to nutrition, economics and markets in the city (Alarcon *et al.*, 2017; Carron *et al.*, 2017). Another innovation in this work was the use of balloons with cameras attached to them, snapping images every second as the balloon handler walked through urban slums to map, for the first time, food kiosks, mobile street vendors and hazards such as rubbish dumps and open sewers.

At the same time, another large project focused on urban zoonoses in India and Vietnam. These projects have had scientific impacts in terms of generating both new findings and new ways of researching urban zoonoses and have helped to build local capacity in urban zoonoses issues (Bett *et al.*, 2019; Jakobsen *et al.*, 2019); it is too early to observe any development outcomes.

A large research programme in six countries of South-east Asia explicitly adopted an EcoHealth approach. Each country was supported to systematically identify priorities: for example, the Indonesian island of Bali identified rabies, the Laos team focused on pig zoonoses and the South Vietnam team identified leptospirosis. This was a strong departure from the usual mode of zoonoses research, in which donors funded projects according to their own priorities. Country teams bringing together researchers and implementers from animal health and social sciences were trained in research using EcoHealth principles, which require the involvement of the local target communities and relevant policy makers. Outcome mapping was used to identify the changes desired and to monitor success in achieving them. In all countries, there was evidence of capacity being built in these areas, and in most cases, teams were able to show community- and policy-level outcomes and impacts as well (Box 8.1). Assessment showed that this novel approach was appreciated and found useful, but its longer-term benefits and sustainability are less clear. However, the project generated actionable scientific findings such as an identification of the most common pig diseases in Laos (Holt *et al.*, 2019).

On a regional scale, ILRI played an important role in promoting the EcoHealth approach to better control zoonoses and emerging diseases in South-east Asia. A review in 2015 (Nguyen-Viet *et al.*, 2016) traced the history of EcoHealth in South-east Asia and showed the substantial role played by ILRI. It found that, in spite of barriers,

Box 8.1. A successful intervention to control zoonoses in South-east Asia.

An ILRI-supported team in Indonesia built on an existing village cadres system to establish Village Rabies Working Groups for rabies control. These groups consisted of paraprofessionals equipped to raise awareness about rabies in schools, village meetings and small groups in their own homes. They also served as first responders to dog-bite cases, ensuring that victims received rapid post-exposure prophylaxis, which is most effective when given soon after the bite. General information on rabies and what it means to be a responsible dog owner encouraged communities to register and vaccinate their dogs, two evidence-based ways of controlling rabies. The model was recognized by provincial-level leaders as a promising community intervention. As a result, a legal decree was made to adopt the village rabies cadre system by officially appointing two persons to serve in this capacity in each of the 723 villages in Bali. In addition, the ILRI team partnered with the provincial-level leaders to provide technical training for the rollout of Village Rabies Working Groups in 30 villages that were hotspots for rabies (Gilbert *et al.*, 2014).

the overall success of the use of the EcoHealth approach in the region was demonstrated by the scope and scale of activities collectively encompassed by the projects, programmes and initiatives reviewed. In a relatively short period of time, EcoHealth has been widely accepted and has gained a remarkable amount of exposure in South-east Asia. This, in turn, has led to more effective and efficient health delivery.

Zoonoses in smallholder pig systems

In 2012, the ILRI-led multicentre CRP on Livestock and Fish started and identified two smallholder pig value chains among the nine livestock value chains it considered most promising for research that would benefit poor farmers. This led to comprehensive initiatives to assess and manage pig-related zoonoses. Trichinellosis is a parasitic disease caused by nematodes in the genus *Trichinella*. This disease, commonly known as 'pork measles', historically caused outbreaks of severe illness in people, but the disease nearly disappeared when control measures were developed and adopted by many pork-producing

countries. Countries new to pork-keeping, however, had not investigated its potential risk. ILRI conducted the first study on *Trichinella* spp. in East Africa, which confirmed that trichinellosis was present and further suggested that trichinellosis might be shifting from a sylvatic transmission cycle, in which the pathogen cycles between wild animals and vectors, to a domestic cycle, in which it cycles between domestic animals and vectors, and thus might be in the process of spilling over from wildlife to establish itself in domestic pigs (Roesel *et al.*, 2016). Veterinary and medical authorities were not aware of the presence of trichinellosis or the risk that it was changing its epidemiology, so this was valuable information. In Vietnam, where pig keeping is long established, *Trichinella* spp. antibodies were detected at high levels (12%) in the serum of indigenous pigs kept in the central highlands (Unger *et al.*, 2016). Studies in Laos on trichinellosis revealed a seroprevalence in pigs of 14.4% (in Luang Prabang) and 9.3% (in Savannakhet) (Holt *et al.*, 2016).

Streptococcus suis is a leading cause of bacterial meningitis in Vietnamese adults. The major risk factors have been identified as consumption of raw pig blood in a Vietnamese dish of blood and cooked meat (*tiết canh*) and occupational exposure to pigs. ILRI conducted the first study in northern and central Vietnam and found *S. suis* type 2 in 1.4% of pig tonsils. Slaughterhouse workers were found habitually to consume raw pig blood to an even greater extent than consumers, and this was linked to excessive consumption of alcohol (Dang-Xuan *et al.*, 2015). Identifying groups at high risk allows targeted interventions. Studies in Vietnam investigated cysticercosis, dengue, leptospirosis, rabies and other zoonoses, often for the first time in a specific region (Lee *et al.*, 2020a,b). Models were also developed to inform control strategies (Bett *et al.*, 2019; Lee *et al.*, 2019). Information was shared with authorities, and high impact factor papers produced but the outcomes in terms of improvements in human health have not been evaluated.

A study on smallholder pig farmers in western Kenya was among the first to use tracer collars to understand the movement of pigs in free-ranging pig production systems. This study found that pigs move considerable distances each day (on average 4340 m) and spend almost 50% of

the day outside the home environment (Thomas *et al.*, 2013). Pigs may interact with other livestock and wild animal species, which may expose them to infectious agents. Further research in the region demonstrated a high prevalence of non-typhoidal *Salmonella* spp. and *Leptospira* spp. in pigs at slaughter, which poses a risk to both slaughterhouse workers and consumers.

A large study in pigs in Uganda found that, contrary to expectations, swine brucellosis was not present. This meant that human health services could rule out swine brucellosis and remove a potential barrier to pig marketing and trade (Erume *et al.*, 2016). Another example from Uganda shows how taking a systems approach to zoonoses studies can lead to unexpected findings and eventually to development outcomes. Systems approaches do not start by choosing a specific zoonotic disease to target but instead explore all potential disease problems. During participatory rural appraisals conducted in 2013, farmers reported symptoms suggestive of diamond skin disease. This is caused by the bacterium *Erysipelothrix rhusiopathiae* and is an economically important disease of swine that had never been reported in Uganda. If transmitted to humans, it can cause erysipeloid, which manifests as skin lesions, and in more severe cases can have systemic effects and even lead to death. The farmer reports triggered an epidemiological study in pigs and pork. Overall, 67% of the pig sera carried antibodies against *E. rhusiopathiae* and 45% of the fresh pork samples were contaminated with *E. rhusiopathiae* (Musewa *et al.*, 2018). This, in turn, led to a study to determine the prevalence and factors associated with *E. rhusiopathiae* infection among raw pork handlers, which found a prevalence of around 10%. This was the first time that the disease had been reported in humans in East Africa. Because erysipeloid is an easily diagnosed and treated disease, alerting patients and health providers to its presence was necessary. ILRI paid for the treatment of all positive human cases and all findings were communicated to stakeholders. However, these treatment impacts were not formally assessed.

Collaboration in international initiatives

In September 2005, a memorandum of understanding was signed by ILRI and WHO to better

understand links between livestock keeping and the health and general well-being of poor people in poor countries. This engagement with WHO led to a major multi-stakeholder meeting in Nairobi in 2007 hosted by ILRI. The meeting appreciated that controlling, preventing and eventually eliminating neglected zoonotic diseases would be highly cost-effective from a societal point of view, taking into account both the health and agricultural aspects. A plan of action for implementing integrated control of neglected zoonotic diseases in Africa was recommended. ILRI scientists also made major contributions, including developing a methodology for prioritizing diseases, to a WHO report on human infectious diseases of poverty (WHO, 2013).

ILRI was a lead organization in developing one-health approaches in low- and middle-income countries. As such, it engaged with international organizations promulgating one-health and Eco-Health and contributed to many of the global initiatives around one-health, including international meetings on avian influenza, the Stone Mountain Dialogue, the International One Health Congresses and meetings at Bellagio, Italy, and Chatham House, UK (Galaz *et al.*, 2015). One-health has clearly emerged as a powerful and dominant approach for managing zoonotic diseases, with most evaluations of this approach citing positive impacts, although there are some concerns about gaps between theory and implementation. Figure 8.3 shows how ILRI is embedded within one-health research groups.

In Asia, ILRI is one of the active institutional members of the Vietnamese Government's One Health Partnership for Zoonoses and a member of Gestion des Risques Emergents en Asie du Sud-Est (GREASE, Management of Emerging Risks in Southeast Asia), initiated by the Centre de Coopération Internationale en Recherche Agronomique pour le Développement (CIRAD). ILRI is also working with the Southeast Asia One Health University Network, based in Chang Mai, Thailand, to develop the capacity of partners in one-health work.

Emerging Infectious Diseases

Emerging infectious diseases are those that have newly appeared in a population or have existed

previously but are increasing in incidence or geographical range (Morens *et al.*, 2004). These diseases are caused by: (i) newly evolved pathogens; (ii) pathogens that have spread to new areas or populations; and (iii) re-emerging pathogens such as those associated with demographic, environmental or other societal changes. Emerging diseases are more likely than not to be zoonotic in origin (Woolhouse and Gowtage-Sequeria, 2005), i.e. acquired by humans from animal reservoirs, including livestock (Cleaveland *et al.*, 2001). Emerging infectious diseases are largely associated with ecological changes that destabilize existing equilibria among pathogens, hosts and vectors. These ecological changes are often the result of human intervention, such as hunting, land clearing for crops or for livestock, urbanization and irrigation.

Rift Valley fever

One new zoonotic disease is now emerging every 4 months. While many are trivial, a minority have devastating health and economic impacts (e.g. avian influenza, COVID-19, HIV/AIDS and Spanish flu). Agricultural expansion and intensification as well as climate change are driving an accelerated emergence of these new diseases. Yet without proper assessment, undue emphasis on emerging infectious diseases may deflect interest from diseases of more importance to the poor. RVF is a model emerging infectious disease because it causes severe disease in people but is not yet readily transmitted between people, it is sensitive to change in land use, and it has implications for trade and for the most poor and vulnerable populations. ILRI's geographical location also means that it has a comparative advantage in studying this important disease.

RVF is a mosquito-borne viral zoonosis that mainly affects sheep, goats, cattle, buffaloes and camels. Humans become infected following a bite from an infected mosquito or after close contact with acutely infected animals or their infected tissues. In people, the disease manifests as a mild influenza-like syndrome in most cases (over 80%) or as a severe disease with haemorrhagic fever, encephalitis or retinitis in a few cases (Njenga *et al.*, 2009). In livestock, the disease manifests as extensive abortions and perinatal mortality.

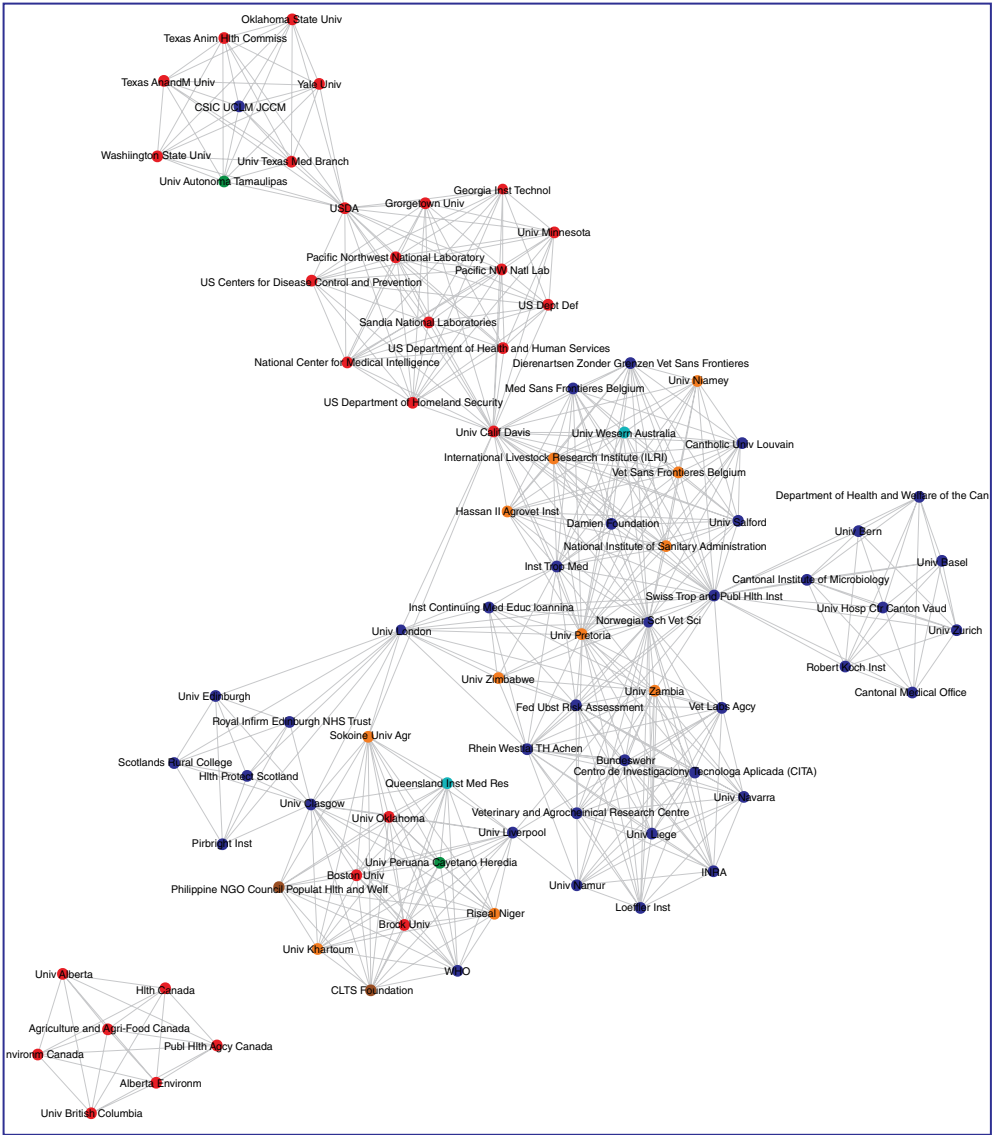


Fig. 8.3. Network digram of co-publishing patterns among organizations having six or more co-authorship relationships (ILRI in blue). (Adapted from Galaz *et al.*, 2015.)

RVF outbreaks occur after periods of above-normal precipitation associated with the warm phase of the El Niño/Southern Oscillation phenomenon (Bett *et al.*, 2017b). Outbreaks have occurred previously in Egypt, Kenya, Madagascar, Mauritania, Mayotte (French archipelago in the Indian Ocean), Saudi Arabia, Senegal, South Africa, Sudan, Zimbabwe and Yemen (Nanyingi *et al.*, 2015). In South Africa, RVF outbreaks

observed from 2008 to 2011 were associated with relentless and widespread seasonal rainfall and high soil saturation (Williams *et al.*, 2016). In Mauritania, an outbreak was associated with a fourfold increase in rainfall in a desert region in 2009–2010 and affected small ruminants, camels and people (Faye *et al.*, 2014). Similar outbreaks occurred in Senegal from 2013 to 2014, where the situation was exacerbated by

livestock movements that aided dissemination of the virus (Sow *et al.*, 2016).

Understanding transmission and burden in Kenya

Data from studies identifying rainfall patterns associated with increased risk of RVF provided the basis for development of dynamic models by ILRI and partners for evaluating the transmission dynamics of this disease (Gachohi *et al.*, 2017). The model allowed researchers to determine alternative vaccination strategies for RVF. ILRI led a related study, which revealed a positive association between flood irrigation and endemic transmission of the virus in an arid and semi-arid area of Kenya (Sang *et al.*, 2016; Bett *et al.*, 2017a; Mbotha *et al.*, 2017). The Kenya study demonstrated that standing water enhanced mosquito development, including the primary vectors of RVFV, which included *Aedes mcintoshi*, *Aedes ochraceus*, *Culex univittatus* and *Culex pipiens*.

The effects of flood irrigation on RVFV endemicity had not been explored previously. Earlier environmental impact studies of irrigation mainly considered malaria and schistosomiasis as case studies of irrigation and vector-borne diseases (Ijumba and Lindsay, 2001; Keiser *et al.*, 2005a,b). We estimated that RVF induced losses of more than US\$32 million (2.1 billion Kenyan shillings) on the Kenyan economy, based on its negative impacts on agriculture and other sectors (e.g. transport, services) alike (Rich and Wanyoike, 2010).

ILRI also made the first-ever assessment of the impact of RVF on human health in Kenya using a disability-adjusted life year (DALY) approach. (This is a standard human health metric: one DALY corresponds to 1 year of lost healthy life.) This was used to model the cost-effectiveness of livestock-based control of RVF from a public health perspective in Kenya. This ILRI assessment found that improving livestock vaccination coverage before a hypothetical outbreak could avert close to 1200 DALYs. Improved vaccinations showed cost-effectiveness values of US\$43–53 per DALY averted (Kimani *et al.*, 2016). These findings on the economic and human health impacts of RVF helped raise awareness of its importance and were cited in subsequent national policy documents and successful research proposals.

Developing a more effective vaccine

No licensed vaccines are currently available to protect humans against RVF and those widely used in livestock have major safety concerns. A one-health vaccine co-developed for multiple susceptible species is an attractive strategy for RVFV. In partnership with the Jenner Institute, UK, and the Kenya Agricultural and Livestock Research Organization (KALRO), ILRI is developing an adenovirus-vectored vaccine called ChAdOx1-GnGc to protect both livestock and humans from RVF.

The vaccine has passed critical safety and challenge studies. A single-dose immunization elicited high-titre neutralizing antibodies and provided solid protection against the disease in the most susceptible natural target species of the virus – sheep, goats and cattle (Warimwe *et al.*, 2016). The vector being used is a replication-deficient chimpanzee adenovirus (ChAd), with a high capacity to insert genomic clones and plasmids that encode desired antigens. The clone used in this case had a genetic sequence encoding the RVFV Gn and Gc envelope glycoproteins. The methods used to identify the most appropriate vector and to develop the clone are given by Warimwe *et al.* (2013). Clinical trials are still required to evaluate the vaccine before it is approved for use. Results to date suggest that the vaccine has great potential given its safety characteristics and ability to generate good levels of neutralizing antibodies. The new vaccine is likely to achieve higher levels of uptake due to its safety margin being higher than the existing livestock vaccines, which may cause abortions.

Studies on RVF vaccines have focused on the production processes, safety and efficacy standards, but those on uptake and adoption levels are rare. ILRI conducted a study that identified barriers faced by men and women farmers in the uptake of livestock vaccines (Mutua *et al.*, 2019).

Supporting response in East Africa

Studies conducted by ILRI in Kenya and Tanzania following a 2006/2007 RVF outbreak in these nations indicated that the impact of the outbreak was exacerbated by delays in recognizing the risk and in implementing prevention and

control measures (Jost *et al.*, 2010). Many stakeholders later identified the need to develop a framework to promote timely decision making and to improve targeting of prevention and control measures while encouraging closer collaboration among research and disease control institutions. In partnership with the African Union–Interafrican Bureau for Animal Resources (AU-IBAR), CDC, FAO and the Kenya Department of Veterinary Services, ILRI has developed a RVF risk map (Munyua *et al.*, 2016b), contingency plans and a decision model (Consultative Group for RVF Decision Support, 2010) to be used jointly to determine optimal interventions during an outbreak of RVF. The decision model breaks down the epidemic cycle into phases and identifies actions to manage the disease in both animals and humans. ILRI has also been a member of a RVF task force in Kenya, which coordinates surveillance and response, especially during periods of heightened risk.

A search for ‘Rift Valley fever’ in the Altmetric database (www.altmetric.com/; accessed 18 February 2020) shows that ILRI’s RVF projects have generated 91 outputs of the 632 outputs in this field overall, with the ILRI outputs being mentioned 291 out of 1986 times and being quoted in nine policy documents.

Highly pathogenic avian influenza

Highly pathogenic avian influenza (HPAI) threatens poultry industries and livelihoods worldwide as well as human health. The HPAI Asian subtype H5N1 is especially deadly for poultry. The virus was first detected in 1996 in geese in China, and human cases were first detected in 1997. Because of its ability to cause human cases and the possibility that it could evolve to cause a human pandemic, the emergence of this disease in 2003 was of great concern.

Supporting surveillance in Africa

As HPAI threatened to become a pandemic, there was concern that countries in Africa were unprepared to cope. An early ILRI activity was providing training in relevant laboratory techniques. A project on Early Detection, Reporting and Surveillance for Avian Influenza in Africa (EDRSAIA) ran from 2007 to 2012 with a main

objective of increasing the capacity of veterinary services in practical, community-focused, active surveillance in 11 countries in West and East Africa. This project developed risk maps, which were used to develop risk-targeted surveillance, and conducted risk factor analyses to inform vulnerability and control work.

There was a large capacity-building component. The training covered participatory epidemiology, data management, risk mapping using geographic information systems (GIS) software and use of risk maps. A subsequent independent assessment of the impacts of the project’s capacity building in participatory epidemiology and participatory disease surveillance on national infectious disease surveillance was generally positive. These capacity building materials were integrated into regional field epidemiology and laboratory training programmes supported by the CDC and used for additional surveillance and disease investigations. A participatory surveillance team diagnosed peste des petits ruminants in Nigeria, which led to an effective emergency disease control programme. In 2010, Nigeria chose to use participatory epidemiology practitioners trained by the EDRSAIA project to investigate animal diseases in five regions (Mariner *et al.*, 2014).

Response models in Egypt and Indonesia

Indonesia saw a major HPAI outbreak in 2004. By the end of 2005, it had spread to more than 23 provinces and more than 10 million birds had died. In January 2006, working with FAO, the government of Indonesia began a programme in Participatory Disease Surveillance and Response (PDSR) for HPAI in poultry. This project was partly driven by ILRI research on participatory epidemiology.

By 2009, the FAO/Indonesia programme was operating in 27 out of 33 provinces of Indonesia. About 20,000 villages (30% of all villages in Indonesia) and 2.5 million backyard poultry producers were covered by surveillance, control and prevention activities, indicating the ability of PDSR to deliver animal health cover at scale.

A subsequent external evaluation found that PDSR did not appear to have had a significant impact on the prevalence of HPAI, partly because it focused on the backyard sector while much of the disease was driven by commercial firms. However, the PDSR programme did introduce two valuable

approaches: (i) information, education and communication activities were well planned, supported and executed, and most targeted people had good knowledge of HPAI; and (ii) participatory and pro-poor animal health services were strengthened.

Egypt has some of the highest poultry densities on the African continent, with most birds concentrated along the River Nile. After the first Egyptian outbreaks of HPAI H5N1 in poultry in February 2006, there was widespread culling of both commercial and household poultry. In 2008, a participatory disease surveillance programme was introduced in Egypt, with technical support from ILRI. By 2014, it was covering 30% of Egyptian districts, again demonstrating the potential to deliver impact at scale. In 2011, when the overall HPAI surveillance had slowed, the PDSR programme proved resilient, contributing over 50% of the HPAI confirmed cases in 2012.

While cover and resilience of the initiative were high, accuracy was moderate (Verdugo *et al.*, 2016). Therefore, the results suggested that the PDSR programme might best suit epidemic situations or those where a high rate of false positives is acceptable, given a high need to detect true positives.

Identifying and supporting pro-poor interventions for disease control

An initial response to controlling HPAI worldwide was the culling of infected birds, an effective approach in high-income countries. However, if smallholders in poor countries are not compensated for the loss of their culled birds, they may be reluctant to report HPAI outbreaks and thus help spread the disease. In partnership with the International Food Policy Research Institute (IFPRI), ILRI undertook research into pro-poor interventions in Africa and South-east Asia. These interventions explicitly used a risk-based approach and built in capacity development work in the use of risk analysis. The research contributed to a better understanding of how HPAI is spread, what the critical control points for HPAI risk mitigation are, and what would be cost-effective, pro-poor risk-reduction strategies. For example, in the Mekong Delta, this information led countries to coordinate HPAI control efforts and to revise their culling strategies from 'radical' to

'targeted', substantially reducing the negative impacts of disease control on the poultry livelihoods of poor people.

Evaluation of control in Indonesia and Nigeria

When HPAI H5N1 hit Nigeria, the first African country it occurred in, in early 2006, the federal government of Nigeria requested a World Bank/International Development Association credit of US\$50 million, provided under the Global Program for Avian Influenza and Human Pandemic Preparedness and Response, to fight its ongoing outbreak. ILRI was asked to conduct an independent evaluation of Nigeria's response to avian influenza. A broad-reaching multidisciplinary evaluation found overall positive impacts but drew attention to areas that needed to be addressed to ensure that the benefits were sustainable.

In Indonesia, an FAO-coordinated response addressed the HPAI pandemic. However, as of 2007, efforts to control the disease in small-scale commercial and backyard flocks had not proven effective. ILRI was asked to evaluate intervention strategies against HPAI in backyard and small-scale commercial farms by assessing the feasibility of implementing the interventions. ILRI's evaluation consisted of a longitudinal study on intervention options and specific studies targeted to epidemiological studies. The longitudinal study found vaccination in the backyard sector was effective in backyard poultry (Bett *et al.*, 2015). The incidence of HPAI declined by 12% in the HPAI-vaccinated group and by 24% in the HPAI-plus-Newcastle disease-vaccinated group.

However, vaccination appeared to be unfeasible as an open-ended programme because the cost of avoiding one poultry death was far greater than the value of a bird (Lapar *et al.*, 2012). However, it was found that vaccination might have a role as a short-term targeted response. This information was crucial for planning public-sector control of HPAI. The targeted epidemiological studies also had useful results; for example, a study of village chicken found that vaccination was needed every 4 months due to high chicken population turnover; such information is, of course, essential for planning effective vaccination campaigns (Unger *et al.*, 2014).

Middle Eastern respiratory syndrome

Middle Eastern respiratory syndrome-coronavirus (MERS-CoV) is an emerging virus first identified in 2012 in Saudi Arabia. The case fatality rate for infected humans with overt respiratory symptoms is in the region of 30%. As with many coronaviruses, MERS-CoV is thought to have originated in bats, although camels appear to play a significant role in maintaining the virus and transmitting it to humans. While the virus appears to be poorly transmissible to humans, it can lead to human-to-human infections. Indeed, the largest outbreak of the disease was in South Korea in 2015, when human-to-human transmission resulted in hundreds of infections.

Understanding disease reservoirs and transmission

ILRI and partners have explored the role of camels in the epidemiology and transmission of MERS-CoV, with a focus on Kenya. The first important work was to mine biobanks of historical camel samples as far back as the early 1990s, which confirmed extensive exposure of camels to MERS or MERS-like viruses (Corman *et al.*, 2014; Muller *et al.*, 2014). High seroprevalences (up to 50%) were identified in herds in central Kenya (Deem *et al.*, 2015) and in herds from locations around the whole country. Liljander *et al.* (2016) identified one seropositive human in Kenya, which was the first reported human case in Africa.

The Kenya studies were important in elucidating MERS epidemiology historically and in the present. A working hypothesis is that MERS is a geographically widespread coronavirus that acquired an ability to infect humans in the Middle East, but that this zoonotic trait has not spread throughout the range of the virus. ILRI researchers have been collaborating with the government of Kenya and the Emerging Pandemic Threats-2 programmes of the US Agency for International Development (USAID) to isolate the MERS virus itself (a challenge given its transient nature in the camel host) and to carry out virus sequencing. This will allow placement of the East African virus in a global phylogeny and identification of its full host range.

Improving the national response

ILRI researchers have been members of the government of Kenya's MERS Working Group,

a reflection of the importance of ILRI's role in studies in the region. ILRI scientists have been involved in establishing MERS serodiagnostics at the Biosciences eastern and central Africa (BeCA)-ILRI Hub laboratories and hosted a regional FAO training programme for government veterinary staff to learn about MERS diagnostics.

A search of the Altmetrics database for 'MERS-CoV' indicated that ILRI generated three out of 325 outputs on this subject. The ILRI outputs have been cited in four policy documents, including FAO's *EMPRES360 Animal Health* bulletin (Issue No. 46, 2016) and the UK government's *Infectious Disease Surveillance and Monitoring System for Animal and Human Health* (Summary, March 2016).

In early 2020, ILRI started to plan a research agenda around COVID-19, caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), a virus related to SARS-CoV, which causes MERS. ILRI has contributed to evaluation of a diagnostic (Hoffman *et al.*, 2020) and is undertaking studies to understand the impact of COVID-19 on farmers, value-chain actors and consumers, their responses to the pandemic, and their knowledge, attitude and practices related to COVID-19.

Ebola

Ebola was first described in 1976 with two simultaneous outbreaks in the Democratic Republic of Congo (Zaire at the time) and South Sudan. It has since been responsible for several deadly outbreaks, most recently from 2013 to 2016 in West and Central Africa and more recently (2019–2020) in two outbreaks in eastern and north-western regions of the Democratic Republic of the Congo. Many aspects of Ebola epidemiology remain unknown, such as the virus reservoir and the role of wildlife and domestic animals in its transmission. However, there has been long-standing concern that domestic livestock, in particular swine, might have a role in its disease epidemiology (Atherstone *et al.*, 2015). Pigs in the Philippines were shown to be infected with Reston virus, one of six known viruses within the genus *Ebolavirus* and related to the Ebola virus found in Africa but that does not affect people (Marsh *et al.*, 2011). Moreover, pigs have been experimentally infected with Zaire

Ebola virus (Kobinger *et al.*, 2011) and antibodies to Ebola viruses have been found in pigs in Africa.

First risk assessment in livestock systems

Uganda has experienced four Ebola outbreaks since the disease was first identified, accounting for 606 cases (probable and confirmed) and 283 deaths (CDC, 2020). In Uganda, motivated by interest to improve risk management, ILRI has conducted *ex ante* assessments of the potential health risks associated with the pig value chain in the country (Atherstone *et al.*, 2014, 2015). This pioneering work is not only informing development of healthy and risk-free pig production and pork value chains in the country but also providing an important basis for understanding missing links in the complex epidemiology of Ebola disease.

ILRI's research has produced a policy brief that summarizes Ebola dynamics, including the role of bats (the main suspected reservoir of the Ebola virus) and a demonstration of how an integrated one-health approach is being used to address the main research gaps (Smith *et al.*, 2015). Findings from ILRI's research on Ebola in Uganda will help protect the health of the more than 1.1 million Ugandan households engaged in swine production. This research will help policy makers develop recommendations to support safe systems for pork production and supply with an emphasis on identifying suitable disease management interventions for smallholder farmers, who make up a large proportion of Uganda's pig farmers. New collaborations with Australian, Canadian and German institutions have been started to bring together expertise in developing new diagnostics for surveillance of Ebola viruses in livestock species.

Ongoing research will provide evidence on the role of pigs in Ebola transmission in Uganda and in contexts with similar agroecologies, will identify places along the pork value chain that may increase Ebola transmission to humans and will evaluate areas in the country at high risk of Ebola. This work is the first to systematically characterize and describe Ebola viruses in pigs in Africa. This information will inform policies around pork value chain development, may help to predict and prevent the spread of emerging zoonotic disease

to humans, and will provide the evidence needed to understand and manage Ebola outbreaks.

Antimicrobial resistance

Antimicrobial drugs are indispensable in managing infectious diseases in humans and animals. If these drugs stop working, millions of human lives and livelihoods are at risk because of treatment failure. Drug resistance in the microbes infecting animals could lead to economic loss and reduced yield of animal-source foods, fuelling global food insecurity. Drug-resistant pathogens – viruses, bacteria, fungi and parasites – are considered as emerging infections given that the genetic transformations that potentiate their emergence distinguish them from their parent generations. They also have the potential to spread between humans and animals and internationally through travel and trade, causing higher numbers of infections globally. Resistance to antimicrobials – here defined as substances of natural or synthetic origin that kill or inhibit the growth of microorganisms – is not a new phenomenon; it has been a concern since the discovery of antimicrobials. However, the recent increases in microorganisms developing resistance to antimicrobials and the resulting increasing threat to public health (O'Neill, 2015) warrant focused attention on the problem in both medical and agricultural sectors. ILRI research suggested that around twice as many antimicrobials are used in agriculture as in treatment of humans (Grace, 2015).

Discovery of anti-parasitic drugs

ILRI's antimicrobial resistance research aims to intensify livestock productivity while reducing its negative externalities for human health. ILRI assumes that the world's poor farmers should have access to antimicrobial drugs to safeguard the health of their livestock, upon which so many depend. These principles have guided work related to antimicrobials since the 1990s. ILRI's initial focus was on anti-parasitic drugs and problems of emerging drug resistance in parasites given the importance of parasites to smallholder livestock production. In addition to research on drug use, ILRI scientists contributed

to the development and testing of new antiparasitic compounds, such as plant compounds for the control of helminths. For example, Githiori *et al.* (2002) evaluated the effectiveness of a widely used natural compound derived from Cape myrtle (*Myrsine africana*) and Cape beech (*Rapanea melonophloeos*) against the helminth *Haemonchus contortus*, a pathogen of sheep, and showed that the effect on parasite egg count was negligible. Another study of the anthelmintic effect of *Albizia anthelmintica* showed that it, too, was not efficacious against *H. contortus* in sheep (Githiori *et al.*, 2003). This led to a widely consulted review of plants used in ethnoveterinary sources and highlighted the need for *in vivo* studies to take into account anthelmintic properties and overall effects of these plants on the performance of the parasitized hosts through potential anti-nutritional effects (Githiori *et al.*, 2006).

Understanding and improving the use of antibiotics

Initial antimicrobial work by ILRI focused on understanding the knowledge, attitudes and practices of antimicrobial use among farmers and animal health service providers. Starting in the 1990s, significant ILRI research on trypanocides had provided crucial evidence for improving control of African animal trypanosomiasis and drew attention to trypanocide resistance (Mulugeta *et al.*, 1997). Research to understand the use of trypanocides and the occurrence of resistance prompted more work on managing trypanosomiasis by evaluating different control strategies (McDermott *et al.*, 2001; Clausen *et al.*, 2010) (see also Chapters 2 and 3, this volume, on trypanosomiasis). Methodologies to evaluate use of veterinary drugs, especially participatory approaches, remain of use and are being developed further (Grace *et al.*, 2009). Further developing the capacity of farmers to better use veterinary drugs was considered promising (Grace *et al.*, 2008) but as a stand-alone intervention was found insufficient to fundamentally change farmer behaviour. As these findings are relevant to antibiotic use, this line of research has shifted over the years to antibacterial drugs.

An ILRI review highlighting a dearth of data on antimicrobial use in livestock production systems in developing countries (Grace, 2015)

led to increases in ILRI research on the use of antibiotics in these systems. ILRI scientists have closely collaborated with others to review global antimicrobial use in livestock production systems (van Boeckel *et al.*, 2015) and have led discussions highlighting the need for one-health approaches to controlling and preventing antimicrobial resistance (Robinson *et al.*, 2016). These publications have been heavily cited and have helped shape the evolving research agenda on antimicrobial use in developing countries. Documentation of antimicrobial resistance in the food value chains has become key to understand risks to public health. In Ethiopia, a study in a slaughterhouse isolated multidrug-resistant *Escherichia coli* 0157 from goats, identifying the need for surveillance of antimicrobial resistance (Dulo *et al.*, 2015). In general, ILRI has called for taking more integrated and one-health approaches to work on antimicrobial resistance and use at the interface of people, animals and the environment (Nguyen-Viet *et al.*, 2016, 2019). ILRI was the first research organization to draw attention to the worrying phenomenon of farmers in Uganda sharing their antiretroviral treatments with their livestock in the belief that it would make them gain weight and is currently researching this practice.

Understanding drug resistance emergence and transmission

More recently, research on antimicrobial use is being complemented by a growing bioscience research portfolio. For example, scientists at the BecA-ILRI Hub collaborated in genetic research on resistance mechanisms in *Salmonella* isolates for quinolones and β -lactam antimicrobials (Egualle *et al.*, 2017). To understand what is driving the emergence of antimicrobial resistance at the human–livestock–environment interface, ILRI in collaboration with academic partners has set up studies in urban settings to track antimicrobial resistance genes between species and to investigate the role of the environment in the transmission of these genes.

The CGIAR Antimicrobial Resistance Hub

ILRI's research on antimicrobial resistance focuses on developing, testing and evaluating interventions that can mitigate livestock-associated antimicrobial resistance in livestock value

chains. ILRI is increasingly involved in policy work to stem the rise of antimicrobial resistance, such as supporting the development and implementation of national action plans and supporting capacity development in various stakeholder groups. An increasing importance of livestock-associated antimicrobial resistance is reflected at the CGIAR level with two CRPs having taken up antimicrobial resistance research: Agriculture for Nutrition and Health focuses on reducing risks to public health resulting from antimicrobial resistance arising in livestock systems, while Livestock Agri-Food Systems promotes rational and effective use of antimicrobials in smallholder livestock systems to prevent future failure to treat disease in livestock and humans alike.

In both of these CRPs, ILRI scientists have assumed leading roles in antimicrobial use-related research. In early 2019, a CGIAR Antimicrobial Resistance Hub was launched at ILRI, Nairobi. It is convening stakeholders with various interests in antimicrobial resistance. It will work to influence a pro-poor antimicrobial use agenda, provide an environment fostering collaboration and new research partnerships, and streamline communications around agriculturally associated antimicrobial resistance to support evidence-based discussions.

ILRI has produced 20 out of 7967 antimicrobial resistance outputs in the Altmetrics database; one of them has been quoted in a policy document.

Neglected Zoonoses

Neglected zoonoses persist in communities with complex and interrelated development problems such as poverty, isolation, poor access to services, insecurity, political marginalization, low literacy rates, gender inequality, lack of sanitation, degraded natural resources and high dependence on livestock. In these regions, ILRI research has focused on high-priority neglected zoonoses, including bovine TB, brucellosis, cysticercosis and trypanosomiasis.

Bovine tuberculosis

Bovine tuberculosis (bovine TB) is a chronic disease of animals caused by *Mycobacterium bovis*, which is closely related to the bacteria that cause human and avian TB. This disease can affect

most mammals, causing a general state of illness and eventual death. Bovine TB is a zoonotic disease transmitted to humans mainly by their consumption of contaminated milk. Zoonotic TB makes up only a small proportion of the overall human TB disease burden but ending the TB epidemic will not be possible without combating zoonotic bovine TB.

One of ILRI's first research activities dedicated to bovine TB was evaluation of a new test for TB (interferon (IFN)- γ) in Ethiopia. The cornerstone of bovine TB control is a rapid and accurate identification of infected animals and their removal from the herd. Conventional testing for bovine TB involved injecting cattle in the neck with antigens to *M. bovis* and checking after several days to see whether the animals had a swelling on their skin, indicating they were positive for bovine TB. This test requires specialist personnel and is expensive and time consuming. The newer IFN- γ test uses blood samples, which are relatively easy and cheap to collect. Developed in Australia in the 1980s, the IFN- γ test was approved by European Union legislation for use in cattle in 2002. Comparing the conventional and new IFN- γ bovine TB tests, the ILRI study found that both tests performed similarly well and concluded that the choice of which to use depended on their relative cost and simplicity of use, as well as on livestock management and time factors (Ameni *et al.*, 2000). This finding led to further evaluation of bovine TB diagnostics in Ethiopia (Ameni *et al.*, 2006).

ILRI participated in a consortium investigating bovine TB in developing countries. ILRI's role was to determine cattle breed differences in immune responses to vaccination with BCG (bacille Calmette–Guérin vaccine, an attenuated strain of *M. bovis*) followed by infection with *M. bovis*. Previous studies and epidemiological surveys had shown a difference in susceptibility to, and disease severity in, bovine TB in Zebu and Holstein cattle (Ameni *et al.*, 2006). The BCG vaccination experiments confirmed that native African Zebu cattle were more resistant to bovine TB than exotic Holstein animals (Vordermeier *et al.*, 2012).

ILRI studies of the kinetics of IFN- γ released in the peripheral blood of calves vaccinated with the BCG vaccine showed a strong positive reaction in the calves to tuberculin inoculation 15 weeks post-vaccination, demonstrating BCG's ability to induce the release of IFN- γ in the peripheral

blood and its role in protecting calves against infection with *M. bovis* (Ameni and Tibbo, 2002).

Another area of ILRI research was surveys conducted to understand the presence, level and risk factors associated with TB. These included the following:

- A study in Narok, which vindicated a long-held official position that bovine TB was absent in Kenya (Koech, 2001).
- A study of dairy farms in central Ethiopia, which found that 45% of cattle and 13% of milk samples were positive for bovine TB, with a much higher prevalence in Holsteins than in local breeds (Ameni *et al.*, 2003). This represented a very high risk to public health. In contrast, a survey in north-eastern Ethiopia found that the prevalence of bovine TB seemed low, but there was little awareness of TB and a public health risk was present (Hadush, 2015), while a study in Gondar found a moderate but concerning prevalence of 8% (Shewatatek, 2015).
- A meta-analysis of studies in Tanzania found a prevalence of 1.8%, which was less than that of brucellosis (8.2%) or trypanosomiasis (10.2%) (Alonso *et al.*, 2016).
- A more recent project is investigating bovine TB in six cities in India, but the results are not yet available.

ILRI collaborated in a study describing best practices for diagnosing and assessing livestock productivity losses due to bovine TB and summarized the methodology of assessment for this particular disease (Tschoopp *et al.*, 2009).

Cysticercosis

Cysticercosis, a parasitic tissue infection caused by larval cysts of a tapeworm (*Taenia solium*) that infect brain, muscle and other tissue, is a major cause of adult-onset seizures in most low-income countries. The adult tapeworm lives in the human gut and the larval stages develop in pig muscle. However, if humans ingest the egg of the adult tapeworm, then cysts may develop in the human skin, eye, brain and other tissues resulting in serious illness. Endemic areas are located predominately across Latin America, sub-Saharan Africa and South-east Asia where pigs are raised under 'traditional' extensive systems

and where latrine coverage and meat hygiene capacity may be low.

T. solium cysticercosis is often ranked among the top priorities of neglected zoonoses and was an early focus for ILRI research. Initial priorities, formulated and led by Lee Willingham, were on better defining the health and economic burden of cysticercosis and supporting an important regional collaboration to better control it. When Phil Toye joined ILRI, a multi-year effort focused on developing lateral-flow diagnostics for this disease, as well as testing simpler approaches to its diagnosis. Meanwhile, extensive epidemiological surveys were conducted in Kenya, Mozambique, Tanzania and Uganda in Africa, and in India, Laos and Vietnam in Asia. The participation of Lee Willingham and subsequently of Eric Fèvre in WHO-led initiatives has given ILRI an influential position in the global one-health phalanx of efforts to control cysticercosis.

A collaboration with the University of Guelph in Canada included a component on training local extension officials, farmers and pork butchers on cysticercosis control, as well as ways to improve pig productivity. Engaging stakeholders in workshops and one-on-one training sessions at the farm level was associated with improved knowledge about cysticercosis (Wohlgemut *et al.*, 2010). Three PhD students were trained under the collaboration, and several undergraduate students were exposed to relevant research activities in western Kenya.

Cysticercosis causes illness and productivity losses in both people and livestock. Estimates of the burden of this disease provide essential, evidence-based data for conducting cost-benefit and cost-utility analyses that should help secure political will and financial and technical resources. ILRI led work on developing frameworks for assessing and combining health and economic information (Carabin *et al.*, 2005). Several of the scientists involved went on to participate in landmark assessments of the global burden of diseases. The methods were also used to estimate disease burdens in proof-of-concept studies. For example, an estimate of the impact in the Eastern Cape Province of South Africa found that there were an estimated 34,662 cases of epilepsy due to cysticercosis in 2004. The overall monetary cost was estimated to vary between US\$18.6 million and US\$34.2 million in a population of about 7 million people, depending on the method used to estimate productivity losses. The agricultural

sector contributed an average of US\$5 million (Carabin *et al.*, 2006).

Epidemiological studies on prevalence and risk factors were conducted in several countries generating evidence, often for the first time, on the presence and prevalence of cysticercosis. These findings led to further research and stimulated efforts to improve control. Among the highlights were the following:

- In Tanzania, the prevalence of swine cysticercosis was found to be 7.6%, 8.4% and 16.9% for Chunya District, Iringa Rural District and Ruvuma Region, respectively. Risk factors were free-ranging of pigs, home slaughtering of pigs, pork not being inspected before consumed, lack of latrines and barbecuing pork (Boa *et al.*, 2006).
- A study of 1051 epileptics in western Kenya found that one-third had observed nodules in pork meat and one-half had observed tapeworm segments in their own faeces, suggesting a possible role of cysticercosis (Grace and Downie, 2011). Another study in Homa Bay confirmed that cysticercosis was endemic (Eshitera *et al.*, 2012).
- A study in western Kenya found that 34.4–37.6% of pigs at slaughter were positive for *Taenia* spp. using an HP10 antigen enzyme-linked immunosorbent assay (Ag-ELISA). All pigs, however, were reported to have passed routine meat inspection, raising considerable concern over the effectiveness of current public health measures (Thomas *et al.*, 2016). In contrast, an earlier study found that only 4% of pigs were positive using a B158/B60 Ag-ELISA and no slaughtered pigs were positive (Kagira *et al.*, 2010). A study in slaughterhouse workers found a low but concerning prevalence for both *Taenia* spp. and cysticercosis (Cook, 2014).
- While an abattoir study in Nairobi found the prevalence of *Taenia* spp. was 8.5%, all the carcasses were passed for human consumption. Furthermore, the abattoir had no facilities for handling *T. solium*-infected carcasses (Akoko *et al.*, 2016).
- A study in south-east Uganda found that 8.6% of pigs screened were seropositive for cysticercosis. In addition, 26% of homes did not have pit latrines, indicating a high

probability of pigs having access to human faeces and thus *T. solium* eggs (Waiswa *et al.*, 2009).

- A later study in Uganda found a prevalence of 14% in the Lake Kyoga Basin (Nsadha *et al.*, 2014). Subsequently, one of the largest and most rigorous and representative studies found a high prevalence of *T. solium* in rural production settings (10.8%) and an even higher prevalence in urban settings (17.1%) (Kungu *et al.*, 2017).
- A review suggested that cysticercosis was problematic in Mozambique. Human serological studies found that 15–21% of apparently healthy adults were positive for cysticercosis antibodies or antigen, while in neuropsychiatric patients, seroprevalence was as high as 51%. Slaughterhouse records indicated a countrywide occurrence of porcine cysticercosis, while studies have shown that 10–35% of pigs tested were seropositive for cysticercosis antibodies or antigen (Afonso *et al.*, 2011).
- A study in the state of Nagaland, in north-east India, found an alarmingly high prevalence of cysticercosis in marketed pork (Fahrion *et al.*, 2014).
- A study in Laos found a low but concerning prevalence of cysticercosis in people and pigs that was associated with poor hygiene (Holt *et al.*, 2016).

Field studies in Uganda identified additional risk factors for cysticercosis. Much pork is consumed in 'pork joints', typically with alcohol. Because pork fat is thought to absorb alcohol, some customers prefer undercooked pork, believing that when pork is fully cooked, the fat drips off and therefore will not fully 'neutralize' the alcohol. This undercooked pork can expose customers to several zoonotic pathogens, including *T. solium* (Thomas *et al.*, 2017).

The Cysticercosis Working Group of Eastern and Southern Africa was founded in 2001 by scientists from Kenya, Mozambique, South Africa, Tanzania, Uganda, Zambia and Zimbabwe with the purpose of collaborating against cysticercosis. This cysticercosis working group had considerable success in organizing workshops, obtaining funding, conducting studies, agreeing on a regional action plan and developing a widely used standard questionnaire about the

disease (Gabriël *et al.*, 2017). The group has been described as one of the notable successes of Danish aid (Johansen and Mukaratirwa, 2013) and is now recognized internationally, serving as a model for other similar networks.

A promising avenue for control of cysticercosis is the development of rapid and cheap diagnostics for the disease in live pigs, which could be made readily available to farmers and meat inspectors. This would allow infected animals to be identified and rejected either before transport to slaughter or at slaughter. Infected pigs could then be treated (e.g. with the anthelmintic oxfendazole) and re-presented for slaughter when its cysts had become non-viable. This would safeguard public health while allowing pig farmers to retain an important source of their income. ILRI undertook development and validation of a pen-side lateral-flow assay to detect porcine cysticercosis, which showed that the assay performs acceptably well compared with standard laboratory-based assays.

A second round of funding was obtained for further development of the assay, in particular to convert to a format that would allow whole blood to be tested instead of serum. The lateral-flow assay is now undergoing further developments; with an initial sensitivity of 73.84% and specificity of 66.7%, and a κ index of 0.38, it has clear potential to be developed and used for diagnosis of cysticercosis in the field (Kivali *et al.*, 2013). ILRI scientists are now establishing a 'gold standard' sera bank collected from known cysticercosis-positive and -negative pigs, achieved through fine dissection of carcasses after slaughter to identify cysts. This sera bank will be used for the validation of current and future diagnostics for cysticercosis.

Cysticercosis has traditionally been diagnosed by lingual palpation, a technique the utility of which was confirmed in an early study by ILRI (Mutua *et al.*, 2007). A subsequent meta-analysis found that all areas with more than 10% of pigs having cysts in their tongues had at least 30% seroprevalence of cysticercosis, and assessing the prevalence of tongue cyst-positive pigs is a potentially rapid epidemiological tool for identifying areas at high risk of cysticercosis, although further refinement and validation is required using standardized data sets (Guyatt and Fèvre, 2016).

In resource-constrained developing countries, it is often difficult to obtain the funding

needed to support public health campaigns. This has led to interest in public-private or market-based solutions to controlling diseases. These are most likely to be effective for diseases such as cysticercosis that inflict costs on farmers and traders. ILRI collaborated with the Global Alliance for Livestock Veterinary Medicines (GALVmed) to evaluate an approach to cysticercosis control based on marketing pig vaccines and wormers to farmers in Uganda. A series of surveys, auctions and economic studies showed that farmers were unwilling to pay for cysticercosis prevention (vaccine and wormer), suggesting that these vaccines would have to be highly subsidized to make them attractive to pig keepers (Dione *et al.*, 2019).

Given the failure to achieve the WHO goal for a validated strategy for *T. solium* control and elimination by 2015, ILRI continued to work with international partners to develop alternative frameworks for the development of realistic control goals for endemic areas (Braae *et al.*, 2019).

Human African trypanosomiasis

Human African trypanosomiasis, known commonly as sleeping sickness, is caused by a protozoan parasitic infection of public health importance. In East Africa, sleeping sickness presents as an acute syndrome caused by the *Trypanosoma brucei rhodesiense* parasite, which is maintained in an animal reservoir. Where wildlife is not abundant, domestic livestock species, particularly cattle, are the main reservoir. West African sleeping sickness is caused by *T. b. gambiense* and is transmitted in a human-tsetse-human cycle. The role of an animal reservoir still needs to be clarified. ILRI work focused on East African sleeping sickness and global control.

Uganda and the Congo experienced a massive sleeping sickness outbreak from 1900 to 1920 and a more recent outbreak from 1976 to 1989. Building on its long history of trypanosomiasis research, ILRI has collaborated with local partners, the University of Edinburgh, UK, and FAO to better understand the potential role of veterinary interventions in controlling sleeping sickness in Uganda.

An early desk study produced the first-ever one-health assessment of the burden of tsetse-transmitted trypanosomiasis by combining

economic losses in livestock with impacts on human health measured in DALYs (Odiit *et al.*, 2000). This led to studies of the risk factors for transmission of *T. b. rhodesiense* sleeping sickness in endemic regions and to identification of new endemic areas (2004). Importantly, closeness to a reporting health unit was a major determinant for detecting early rather than advanced cases (Odiit *et al.*, 2004). A related study investigated late diagnosis of sleeping sickness, which typically results in a worse outcome for patients. This found long delays in diagnosis (and therefore in treatment), much of it due to the service provider failing to diagnose sleeping sickness among symptomatic individuals (Odiit *et al.*, 2004). Following this work, a model was developed to quantify underdetection of sleeping sickness in Uganda during a 1988–1990 epidemic. This showed that, of 73 undetected deaths, 62 entered the healthcare system but were not diagnosed and 11 died without seeking healthcare from a recognized health unit (Odiit *et al.*, 2005). This evidence of under detection stimulated an initiative to upgrade 12 facilities to perform confirmatory testing for sleeping sickness, resulting in a substantial reduction in the distance necessary to travel to get a diagnosis for sleeping sickness (Wamboga *et al.*, 2017). The work was also used by the WHO to support the argument that zoonoses were neglected.

Further work helped to identify the distribution of villages at risk of sleeping sickness using GIS and remote sensing (Odiit *et al.*, 2006). Distribution maps based on archival and contemporary data showed that the disease focus had moved from lakeshore Buganda (1905–1920) to the Busoga and south-east districts (Berrang-Ford *et al.*, 2006). This information was used by medical services to better understand risk.

A model of *T. b. rhodesiense* infections transmitted by a single tsetse species between cattle and humans was developed at ILRI using empirical data (Coleman *et al.*, 1999) to assess the relative impact of mass treatment of cattle versus treatment of human cases on the prevalence of *T. b. rhodesiense* sleeping sickness in south-eastern Uganda. Mass treatment of cattle with a coverage of 80% was predicted to break the transmission to humans. This evidence contributed to a major public–private partnership campaign

called ‘Stamp out Sleeping Sickness’ that aimed to slow the spread of sleeping sickness, which itself was driven by cattle movements.

The campaign helped private-sector animal health providers to treat cattle with preventive drugs and insecticides. Between 2006 and 2010, nearly 200,000 cattle were treated, and the intervention was shown to reduce sleeping sickness in people and to halt its expansion. However, both the human and animal forms significantly increased after the intervention, and uptake by farmers was low. These disappointing results were attributed to a lack of community concern about sleeping sickness, the cost of treating cattle, insufficient incentives for private-sector disease control, a lack of control infrastructure, the seasonality of the disease and poor targeting, among other factors (Bardosh, 2018).

While the development impacts of this large-scale, low-technology, private sector-based intervention were disappointing, ILRI’s evidence on the burden, distribution, under-reporting and potential of managing sleeping sickness through treatment of the livestock form of the disease helped to draw attention to the importance of sleeping sickness and to increase efforts to control it, which were globally spearheaded by WHO.

ILRI scientists contributed to the WHO Expert Committee Report on Human African Trypanosomiasis and the WHO stakeholder meetings on *T. b. rhodesiense* human African trypanosomiasis. Work continued with the first geographically delimited estimation of the burden of sleeping sickness disease at the subcounty scale in Uganda (Hackett *et al.*, 2014). Importantly, this work found that, whereas the relative burden of sleeping sickness was low at the national level, in some districts it was a high-priority disease. Human sleeping sickness was also considered in economic analyses of the control of African animal trypanosomiasis in East Africa (Shaw *et al.*, 2015). More recently, ILRI has been involved in evaluating diagnostic tools for sleeping sickness (Lejon *et al.*, 2017).

Brucellosis

Brucella spp. infect many animals, including cattle, small ruminants, camels, water buffaloes,

yaks and pigs. Different *Brucella* spp. infect different animal species, but most have the potential to infect humans, with some species causing more disease than others. *Brucella* spp. infection rates in some developing countries can reach more than 10% of the human population, making it a serious public health disease. In livestock, *Brucella* spp. cause diseases that reduce animal production and cause abortions in females and reduced fertility in males. The most common method by which humans are infected is through ingestion of unprocessed milk products from infected animals, but direct contact with infected animals and meat can also be a source of infection.

Initial work at ILRAD and ILCA identified brucellosis as one of many constraints to livestock production in Africa and Asia. Surveys on brucellosis in livestock and marketed milk were conducted in the late 1990s in Ethiopia and Kenya (Asfaw *et al.*, 1998; Kang'ethe *et al.*, 2000). These surveys confirmed the presence and importance of the *Brucella* pathogen and also revealed problems with the commonly used diagnostics for this disease. In Kenya, *Brucella abortus* antibodies were not detected in raw milk sold in urban areas but were found at low levels (2–5%) in milk sampled from consumers in rural areas, and at higher levels (25%) in pasteurized milk (Omoro *et al.*, 2000). This finding added to the body of evidence being developed by ILRI that formal milk is not always safe and informal milk is not always risky. These results were instrumental in a radical, pro-poor shift in Kenyan dairy policy (Leksmono *et al.*, 2006).

ILRI produced important syntheses of research on brucellosis in developing countries. The first assessment of brucellosis in Africa found that the incidence of the disease was highest in pastoral production systems, that this incidence decreased with decreases in herd size and size of landholding, that little was known of brucellosis in other species and that control of brucellosis was largely inadequate (McDermott and Arimi, 2002). A systematic review of the economics of brucellosis control found that the benefits of control always exceeded its costs (McDermott *et al.*, 2013). Interestingly, *ex post* assessments had relatively higher benefits than *ex ante* assessments, and control in lower-income countries had relatively higher benefits than control in higher-income countries.

A workshop held by ILRI and USAID in 2013 brought together participants from 16 countries to identify gaps in brucellosis epidemiology, diagnosis, surveillance and control (USDA/USAID/ILRI, 2013). The workshop provided information to help design brucellosis research programmes and intervention strategies at national and regional levels.

A landmark study of brucellosis tested 825 patients for the disease at the Busia County Referral Hospital and the KEMRI Alupe Research Centre, located in the same area (de Glanville *et al.*, 2017). The team used the regular government febrile antigen *Brucella* agglutination test and a second called the rose Bengal test, while another two kits were used to confirm the results. Of the 825 cases, 196 patients (19.6%) were found positive for brucellosis from the regular tests. However, when the positive cases were tested with the second and other confirmatory tests, only eight people (1%) of the total were found to have been infected with *Brucella* spp. In this case, if not for the secondary and confirmatory tests, 188 people would have unnecessarily been put on the rigorous treatment to cure brucellosis. This high-profile study drew widespread attention and led to the formulation of improved guidelines for diagnosing brucellosis. In addition, ILRI scientists have worked on evaluating improved tests (Falzon *et al.*, 2019).

Brucellosis is especially problematic to manage in countries where the culling of cattle is not acceptable, such as in India. ILRI work commenced with a systematic review to clarify the contradictory evidence on prevalence. This has been reported to be as low as 1% and as high as 60% by different researchers. The ILRI review concluded that the disease's overall prevalence in the country was probably 12% or less (Deka *et al.*, 2018), which is still high. This was followed by a number of prevalence studies to better understand the true picture of this disease (Lindahl *et al.*, 2018), which confirmed that the disease was highly heterogeneous. This information is essential for targeting control efforts to where they are needed most.

China's Yunnan Province is at particular risk of brucellosis because ruminants are increasingly introduced to the province from other parts of the country in response to increasing demand for milk. ILRI developed an EcoHealth approach to control brucellosis.

ILRI conducted studies on brucellosis in a range of species, products, and countries:

- A study in camel-rearing areas of Ethiopia found that around 6% of camels were seropositive for *Brucella* spp. As camel milk here is rarely boiled before being consumed, this represents a significant public health risk (Teshome *et al.*, 2003).
- Brucellosis was detected in just under half of the cows' milk samples tested in Tanga, Tanzania (Shija, 2013).
- An anthropological study in Mali provided a key insight – that brucellosis was common but that pastoralists believed milk to be intrinsically 'pure' and hence incapable of being a source of disease (Fokou *et al.*, 2010).
- Brucellosis was not found in goats in western Kenya (Akoko *et al.*, 2013).

Other neglected zoonoses

Neglected zoonotic diseases are commonly associated with poverty and greatly impact in particular the lives and livelihoods of millions of poor livestock keepers, processors and consumers of livestock products. WHO has identified a subgroup of eight 'neglected zoonotic diseases': anthrax, bovine TB, brucellosis, cysticercosis, hydatidosis, leishmaniasis, rabies and sleeping sickness. ILRI research has focused mostly on bovine TB, brucellosis, cysticercosis, rabies and sleeping sickness. (ILRI's work on rabies is noted in Chapter 5, this volume.) Limited ILRI research has been conducted on other zoonoses on the WHO list, as well as other zoonoses that fit a broader definition of neglected.

Anthrax is a bacterial zoonosis, caused by *Bacillus anthracis*. It primarily affects herbivores and is highly lethal to them. Humans contract the disease from contact with infected or dead animals, and infections can result in a high mortality rate for people as well, if not diagnosed and treated promptly. Anthrax is also of interest as a 'dreaded disease', a climate-sensitive disease and a possible 'bioterrorist' agent. When alarming outbreaks of anthrax occurred in Nakuru, Kenya, ILRI was part of the team sent to investigate. Participatory epidemiology was used to map current and previous outbreaks, with the results suggesting a long history of outbreaks (Muturi

et al., 2018). ILRI is currently (2020) developing an anthrax risk map for the country for use in developing prevention and control measures aimed at reducing the public health and economic impact of anthrax.

In many low- and middle-income countries, it is a common practice to consume animals that have died of an illness because they are a valuable and scarce source of protein. An assessment in Zambia found that the risk to humans of contracting illness due to consuming meat from animals that have died of disease was rather low and could be reduced by taking precautions, including careful butchery and ensuring that meat is cooked properly (Simpson, 2015). This example illustrates the complexity of work aiming to change behaviour, especially when people do not have sufficient incentives to change their behaviour.

Human cystic echinococcosis is a neglected zoonotic parasitic disease caused by the larval stage of the dog tapeworm, *Echinococcus granulosus*. Ungulates are intermediate hosts, but if a human consumes tapeworm eggs, they may develop into fluid-filled cysts in organs and tissues. The infection is most common in pastoral communities, where it causes considerable socio-economic impact. A systematic literature review showed its widespread occurrence in small ruminants in Ethiopia (Asmare *et al.*, 2016). A study in abattoirs in Narok, Kenya, found that 16% of sheep had cysts, which was considered a high level of infection constituting a public health risk (Odongo *et al.*, 2018).

Q fever, caused by *Coxiella burnetii*, is an old zoonotic disease believed to be widely present in ruminant populations worldwide. It is a common cause of abortion in ruminants, and in people can cause flu-like illness. There is little detailed knowledge of its presence in livestock systems in low- and middle-income countries. ILRI conducted or supported surveys of Q fever in Kenya and Tanzania. These showed a high prevalence (20%) in camels in Laikipia, Kenya (Browne *et al.*, 2017), and in livestock (13%) and people (27%) in Tana River, Kenya (Mwologolo, 2016). A moderate prevalence was found in cattle (10%) and humans (2.5% in slaughterhouse workers) in western Kenya (Cook, 2014; Wardrop *et al.*, 2016) and in cattle reported as sick (15%) by farmers in northern Tanzania (Alonso *et al.*, 2015).

A study of hospital patients in Kenya found acute Q fever in 16% of patients, a finding unsuspected by the treating clinicians. A diagnostic tool was developed based on symptoms and was shown to be reasonably accurate (sensitivity 93.1%, specificity 76.1%) (Njeru *et al.*, 2016). This tool has obvious potential to improve diagnosis and hence healthcare, but its impact has not been evaluated. Other studies have looked at farmer awareness of Q fever, finding it low (Nyokabi *et al.*, 2017), while studies looking at the disease risk and economic impacts found they were high (Oboge, 2016).

Conclusions and the Future

ILRI research has contributed to an emerging consensus about neglected and emerging zoonotic diseases. It is clear that zoonotic diseases associated with livestock and livestock production are constraints to human health, well-being and economic development. Many of these diseases pose risks to wildlife and to the ability of ecosystems to provide services. However, for many of these diseases, basic epidemiological data are unavailable. ILRI research has often overturned conventional wisdom by finding zoonoses absent where they were believed to be common and to be major problems when their existence was unsuspected.

Establishing systematic data collection is the first step to manage zoonoses. Management is complicated by heterogeneity: zoonoses may have a significant and debilitating effect on some communities but not on others. Understanding the spatial distribution of the burden of zoonoses is important to better focus control efforts. A significant constraint is the lack of collaboration between medical and veterinary authorities: institutionally speaking, zoonoses typically find themselves homeless and ignored. There is a need for one-health thinking and research to overcome inter-sectoral barriers to effective control of zoonoses.

We can suggest some future directions. A first step is to develop cheap and efficient diagnostics in human and animal hosts to assist in understanding zoonoses and in managing them. Another important step is to develop metrics that capture the societal burden of zoonoses,

recognizing the high dependence of the poor on livestock. DALYs and economic costs of livestock and human disease are important metrics, but good information is expensive and difficult to collect, and even when available, we lack agreed ways of combining epidemiological and economic metrics. Moreover, other aspects of the zoonoses burden, such as the cost of a high-impact, low-probability and civilization-altering pandemic, are difficult to capture. ILRI is involved in new and ongoing initiatives to measure the multiple burdens of zoonotic diseases.

It is generally accepted that zoonoses are best tackled in their livestock rather than human hosts. This avoids human suffering, has been shown to be more cost-effective in studied cases (e.g. rabies) and historically was the main means of eliminating many neglected zoonoses from high-income countries. However, most developing countries still lack comprehensive programmes to tackle zoonoses in their livestock reservoirs. To generate additional investment, more information is needed on the costs, benefits, acceptability and scalability of interventions, including those targeting animals. Malaria and water research show how credible, comparable information on control options can underpin action.

The majority of emerging human diseases are zoonotic, often following amplification in a farmed animal host. The current (as of 2020) COVID-19 pandemic is just one of a series of emerging zoonoses over the last decades that has resulted in enormous impacts, both health and economic. ILRI long-standing research into the drivers of disease emergence and into more timely and effective surveillance and response can contribute to a new urgency around the need to prevent and manage pandemics.

Zoonotic diseases are particularly complex disorders involving the environmental sciences, agriculture and public health. Policy frameworks for managing zoonoses are sometimes weak, and there are often gaps between policy and implementation. Successful control of zoonoses requires a judicious legal and policy framework, well-functioning institutions, adequate financing, rapid detection and an intervention implementation plan. The failure of the public sector to manage neglected zoonoses in developing countries has led to interest in public-private partnerships and market-based solutions. Although harnessing market or social forces has

great potential in improving human health in resource-scarce environments, they have not yet been shown to be sustainable or scalable, and further innovation is required. The role of behavioural sciences is therefore an active area of ILRI.

Notes

¹ This work was led by Arve Lee Willingham and Esther Schelling, respectively, both of whom shared joint appointments at their home institutions and ILRI.

² These included Silvia Alonso (Spain), Bernard Bett (Kenya), Delia Grace (Ireland), Joerg Jores (Germany), Lucy Lapar (Philippines), Anne Liljander (Germany), Johanna Lindahl (Sweden), Jeff Mariner (USA), Karl Rich (USA), Fred Unger (Germany) and Francis Wanyoike (Kenya). A later collaboration involved the University of Edinburgh, and later the University of Liverpool, led by Eric Fèvre (UK).

References

- Afonso, S.M.S., Vaz, Y., Neves, L., Pondja, A., Dias, G., *et al.* (2011) Human and porcine *Taenia solium* infections in Mozambique: identifying research priorities. *Animal Health Research Reviews* 12, 123–129.
- Akoko, J.M., Kiyong'a, A.N., de Glanville, W.A., Thomas, L.F. and Fèvre, E.M. (2013) The seroprevalence of caprine brucellosis in western Kenya. Poster presented at the 47th annual scientific conference of the Kenya Veterinary Association, 24–27 April 2013, Mombasa, Kenya. ILRI, Nairobi.
- Akoko, J.M., MacLeod, E., Kang'ethe, E., Muinde, P., Alarcon, P., *et al.* (2016) Serological survey of porcine cysticercosis and associated risk factors in pigs slaughtered at Ndumbuni abattoir in Nairobi, Kenya. *International Journal of Infectious Diseases* 45 (Suppl. 1), 464.
- Alarcon, P., Fèvre, E.M., Muinde, P., Murungi, M.K., Kiambi, S., *et al.* (2017) Urban livestock keeping in the city of Nairobi: diversity of production systems, supply chains, and their disease management and risks. *Frontiers in Veterinary Science* 4, 171.
- Allepuz, A., de Balogh, K., Aguanno, R., Heilmann, M. and Beltran-Alcrudo, D. (2017) Review of participatory epidemiology practices in animal health (1980–2015) and future practice directions. *PLoS One* 12, e0169198.
- Alonso, S., Msalya, G., Toye, P., Grace, D. and Unger, F. (2015) Ancient farming styles and old zoonoses: brucellosis and Q fever among pastoralist and smallholder cattle herds in Tanzania. Poster prepared for the European College of Veterinary Public Health (ECVPH) annual scientific conference, 7–10 October, Belgrade, Serbia. ILRI, Nairobi.
- Alonso, S., Dohoo, I., Lindahl, J., Verdugo, C., Akuku, I. and Grace, D. (2016) Prevalence of tuberculosis, brucellosis and trypanosomiasis in cattle in Tanzania: a systematic review and meta-analysis. *Animal Health Research Reviews* 17, 16–27.
- Ameni, G., Miorner, H., Roger, F. and Tibbo, M. (2000) Comparison between comparative tuberculin and γ -interferon tests for the diagnosis of bovine tuberculosis in Ethiopia. *Tropical Animal Health and Production* 32, 267–276.
- Ameni, G. and Tibbo, M. (2002) Kinetics of interferon-gamma (IFN- γ) release in the peripheral blood of calves vaccinated with BCG. *Journal of Immunoassay and Immunochemistry* 23, 245–251.
- Ameni, G., Bonnet, P. and Tibbo, M. (2003) A cross-sectional study of bovine tuberculosis in selected dairy farms in Ethiopia. *Journal of Applied Research in Veterinary Medicine* 1, 253–258.
- Ameni, G., Aseffa, A., Engers, H., Young, D., Hewinson, G. and Vordermeier, M. (2006) Cattle husbandry in Ethiopia is a predominant factor affecting the pathology of bovine tuberculosis and gamma interferon responses to mycobacterial antigens. *Clinical and Vaccine Immunology* 13, 1030–1036.
- Asfaw, Y., Molla, B., Zessin, K.H. and Azage, T. (1998) A cross-sectional study of bovine brucellosis and test performance in intra- and peri-urban production systems in and around Addis Ababa, Ethiopia. *OAU/STRC Bulletin of Animal Health and Production in Africa* 46, 217–224.
- Asmare, K., Sibhat, B., Abera, M., Haile, A., Degefu, H., *et al.* (2016) Systematic review and meta-analysis of metacestode prevalence in small ruminants in Ethiopia. *Preventive Veterinary Medicine* 129, 99–107.

- Atherstone, C., Picozzi, K. and Kalema-Zikusoka, G. (2014) Seroprevalence of *Leptospira hardjo* in cattle and African buffalos in southwestern Uganda. *American Journal of Tropical Medicine and Hygiene* 90, 288–290.
- Atherstone, C., Smith, E., Ochungo, P., Roesel, K. and Grace, D. (2015) Assessing the potential role of pigs in the epidemiology of Ebola virus in Uganda. *Transboundary and Emerging Diseases* 64, 333–343.
- Azhar, M., Lubis, A.S., Siregar, E.S., Alders, R.G., Brum, E., *et al.* (2010) Participatory disease surveillance and response in Indonesia: strengthening veterinary services and empowering communities to prevent and control highly pathogenic avian influenza. *Avian Diseases* 54, 749–753.
- Bardosh, K.L. (2018) Towards a science of global health delivery: a socio-anthropological framework to improve the effectiveness of neglected tropical disease interventions. *PLoS Neglected Tropical Diseases* 12, e0006537.
- Berrang-Ford, L., Odiit, M., Maiso, F., Waltner-Toews, D. and McDermott, J.J. (2006) Sleeping sickness in Uganda: revisiting current and historical distributions. *African Health Sciences* 6, 223–231.
- Bett, B., McLaws, M., Jost, C., Schoonman, L., Unger, F., *et al.* (2015) The effectiveness of preventative mass vaccination regimes against the incidence of highly pathogenic avian influenza on Java Island, Indonesia. *Transboundary and Emerging Diseases* 62, 163–173.
- Bett, B., Said, M.Y., Sang, R., Bukachi, S., Wanyoike, S., *et al.* (2017a) Effects of flood irrigation on the risk of selected zoonotic pathogens in an arid and semi-arid area in the eastern Kenya. *PLoS One* 12, e0172626.
- Bett, B., Kiunga, P., Gachohi, J., Sindato, C., Mbotha, D., *et al.* (2017b) Effects of climate change on the occurrence and distribution of livestock diseases. *Preventive Veterinary Medicine* 137, 119–129.
- Bett, B., Grace, D., Lee, H.S., Lindahl, J., Nguyen-Viet, H., *et al.* (2019) Spatiotemporal analysis of historical records (2001–2012) on dengue fever in Vietnam and development of a statistical model for forecasting risk. *PLoS One* 14, e0224353.
- Boa, M.E., Mahundi, E.A., Kassuku, A.A., Willingham, A.L. and Kyvsgaard, N.C. (2006) Epidemiological survey of swine cysticercosis using ante-mortem and post-mortem examination tests in the southern highlands of Tanzania. *Veterinary Parasitology* 139, 249–255.
- Braae, U.C., Gabriël, S., Trevisan, C., Thomas, L.F., Magnussen, P., *et al.* (2019) Stepwise approach for the control and eventual elimination of *Taenia solium* as a public health problem. *BMC Infectious Diseases* 19, 182.
- Browne, A.S., Fèvre, E.M., Kinnaird, M., Muloi, D.M., Wang, C.A., *et al.* (2017) Serosurvey of *Coxiella burnetii* (Q fever) in dromedary camels (*Camelus dromedarius*) in Laikipia County, Kenya. *Zoonoses and Public Health* 64, 543–549.
- Carabin, H., Budke, C.M., Cowan, L.D., Willingham, A.L. and Torgerson, P.R. (2005) Methods for assessing the burden of parasitic zoonoses: echinococcosis and cysticercosis. *Trends in Parasitology* 21, 327–333.
- Carabin, H., Krecek, R.C., Cowan, L.D., Michael, L., Foyaca-Sibat, H., *et al.* (2006) Estimation of the cost of *Taenia solium* cysticercosis in Eastern Cape Province, South Africa. *Tropical Medicine & International Health* 11, 906–916.
- Carron, M., Alarcon, P., Karani, M., Muinde, P., Akoko, J., *et al.* (2017) The broiler meat system in Nairobi, Kenya: using a value chain framework to understand animal and product flows, governance and sanitary risks. *Preventive Veterinary Medicine* 147, 90–99.
- CDC (Centers for Disease Control and Prevention). (2020) 40 years of Ebola disease around the world. <https://www.cdc.gov/vhf/ebola/history/chronology.html> (accessed 16 August 2020).
- Clausen, P.H., Bauer, B., Zessin, K.H., Diall, O., Bocoum, Z., *et al.* (2010) Preventing and containing trypanocide resistance in the cotton zone of West Africa. *Transboundary and Emerging Diseases* 57, 28–32.
- Cleaveland, S., Laurenson, M. and Taylor, L. (2001) Diseases of humans and their domestic mammals: pathogen characteristics, host range and the risk of emergence. *Philosophical Transactions of the Royal Society of London B: Biological Sciences* 356, 991–999.
- Cole, D., Grace, D. and Diamond, M. (2008) Researcher approaches to evidence on urban agriculture and human health. Cole, D., Lee-Smith, D. and Nasinyama G. (eds) *Healthy City Harvests: Generating Evidence to Guide Policy on Urban Agriculture*. International Potato Center (CIP), Lima, and Makerere University Press, Kampala, pp. 31–47.
- Coleman, P., McDermott, J. and Mauldin, I. (1999) The public health impact of controlling *Trypanosoma brucei rhodesiense* in cattle. Paper presented at the 25th International Scientific Council on Trypanosomiasis Research and Control (ISCTRC) Meeting, Mombasa, Kenya, 1999.

- Consultative Group for RVF Decision Support (2010) Decision-support tool for prevention and control of Rift Valley fever epizootics in the Greater Horn of Africa. *American Journal of Tropical Medicine and Hygiene* 83, 75–85.
- Cook, E.A. (2014) Epidemiology of zoonoses in slaughterhouse workers in western Kenya. PhD thesis, University of Edinburgh, Edinburgh, UK.
- Cook, E.A., Grossi-Soyster, E.N., de Glanville, W.A., Thomas, L.F., Kariuki, S., *et al.* (2017) The sero-epidemiology of Rift Valley fever in people in the Lake Victoria Basin of western Kenya. *PLoS Neglected Tropical Diseases* 11, e0005731.
- Corman, V.M., Jores, J., Meyer, B., Younan, M., Liljander, A., *et al.* (2014) Antibodies against MERS coronavirus in dromedary camels, Kenya, 1992–2013. *Emerging Infectious Diseases* 20, 1319–1322.
- Dang-Xuan, S., Bryant, J.E., Unger, F., Bao N.-T., Ngoc, B.V.T., *et al.* (2015) Risk pathways and prevalence in slaughtered pig blood of *Streptococcus suis* in Vietnam. Poster presented at the 9th European Congress on Tropical Medicine and International Health, 6–10 September, Basel, Switzerland. Hanoi School of Public Health, Hanoi.
- Deem, S.L., Fèvre, E.M., Kinnaird, M., Browne, A.S., Muloi, D., *et al.* (2015) Serological evidence of MERS-CoV antibodies in dromedary camels (*Camelus dromedarius*) in Laikipia County, Kenya. *PLoS One* 10, 11–15.
- Deka, R.P., Magnusson, U., Grace, D. and Lindahl, J. (2018) Bovine brucellosis: prevalence, risk factors, economic cost and control options with particular reference to India – a review. *Infection Ecology & Epidemiology* 8, 1555448.
- de Glanville, W.A., Conde-Álvarez, R., Moriyón, I., Njeru, J., Díaz, R., *et al.* (2017) Poor performance of the rapid test for human brucellosis in health facilities in Kenya. *PLoS Neglected Tropical Diseases* 11, e0005508.
- Dione, M., Adediran, A.S., Colston, A., Ouma, E., Lule, P. and Grace, D. (2019) A market scoping study for porcine cysticercosis vaccine calls for a one-health approach to sustain the control of the disease in Uganda. GALVmed, Nairobi.
- Dulo, F., Feleke, A., Szonyi, B., Fries, R., Baumann, M.P. and Grace, D. (2015) Isolation of multidrug-resistant *Escherichia coli* O157 from goats in the Somali region of Ethiopia: a cross-sectional, abattoir-based study. *PLoS One*, 10, e0142905.
- Eguale, T., Birungi, J., Asrat, D., Njahira, M.N., Njuguna, J., *et al.* (2017) Genetic markers associated with resistance to β -lactam and quinolone antimicrobials in non-typhoidal Salmonella isolates from humans and animals in central Ethiopia. *Antimicrobial Resistance & Infection Control* 6, 13.
- Erume, J., Roesel, K., Dione, M.M., Ejobi, F., Mboowa, G., *et al.* (2016) Serological and molecular investigation for brucellosis in swine in selected districts of Uganda. *Tropical Animal Health and Production* 48, 1147–1155.
- Eshitera, E.E., Githigia, S.M., Kitala, P., Thomas, L.F., Fèvre, E.M., *et al.* (2012) Prevalence of porcine cysticercosis and associated risk factors in Homa Bay District, Kenya. *BMC Veterinary Research* 8, 234.
- Fahrion, A.S., Jamir, L., Richa, K., Begum, S., Rutsa, V., *et al.* (2014) Food-safety hazards in the pork chain in Nagaland, North East India: implications for human health. *International Journal of Environmental Research and Public Health* 11, 403–417.
- Falzon, L.C., Traoré, S., Kallo, V., Assamoi, J.-B., Bonfoh, B. and Schelling, E. (2019) Evaluation of the fluorescence polarization assay as a rapid on-spot test for ruminant brucellosis in Côte d'Ivoire. *Frontiers in Veterinary Science* 6, 287.
- Faye, O., Ba, H., Ba, Y., Freire, C.C.M., Faye, O., *et al.* (2014) Reemergence of rift valley fever, Mauritania, 2010. *Emerging Infectious Diseases* 20, 300–303.
- Fèvre, E.M., de Glanville, W.A., Thomas, L.F., Cook, E.A., Kariuki, S. and Wamae, C.N. (2017) An integrated study of human and animal infectious disease in the Lake Victoria crescent small-holder crop-livestock production system, Kenya. *BMC Infectious Diseases* 17, 457.
- Fokou, G., Koné, B.V. and Bonfoh, B. (2010) “Mon lait est pur et ne peut pas rendre malade”: motivations des acteurs du secteur informel et qualité du lait local au Mali. *Revue Africaine de Santé et de Productions Animales* 8, 75–86.
- Gabriël, S., Dorny, P., Mwape, K.E., Trevisan, C., Braae, U.C., *et al.* (2017) Control of *Taenia solium* taeniasis/cysticercosis: the best way forward for sub-Saharan Africa? *Acta Tropica* 165, 252–260.
- Gachohi, J.M., Njenga, M.K., Kitala, P. and Bett, B. (2017) Correction: modelling vaccination strategies against Rift Valley fever in livestock in Kenya. *PLoS Neglected Tropical Diseases* 11, e0005316.
- Galaz, V., Leach, M., Scoones, I. and Stein, C. (2015) The political economy of One Health research and policy. STEPS Working Paper 81. STEPS Centre, Brighton, UK.

- Gilbert, J., Grace, D., Unger, F., Lapar, M.L., Asse, R., *et al.* (2014) *Increasing awareness of zoonotic diseases among health workers and rural communities in Southeast Asia*. ILRI Research Brief 15. ILRI, Nairobi.
- Githiori, J.B., Höglund, J., Waller, P.J. and Baker, R.L. (2002) Anthelmintic activity of preparations derived from *Myrsine africana* and *Rapanea melanophloeos* against the nematode parasite, *Haemonchus contortus*, of sheep. *Journal of Ethnopharmacology* 80, 187–191.
- Githiori, J.B., Höglund, J., Waller, P.J. and Baker, R.L. (2003) The anthelmintic efficacy of the plant, *Albizia anthelmintica*, against the nematode parasites *Haemonchus contortus* of sheep and *Heligmosomoides polygyrus* of mice. *Veterinary Parasitology* 116, 23–34.
- Githiori, J.B., Athanasiadou, S. and Thamsborg, S.M. (2006) Use of plants in novel approaches for control of gastrointestinal helminths in livestock with emphasis on small ruminants. *Veterinary Parasitology* 139, 308–320.
- Grace, D. (2014) The business case for One Health. *Onderstepoort Journal of Veterinary Research* 81, E1–E6.
- Grace, D. (2015) *Review of evidence on antimicrobial resistance and animal agriculture in developing countries*. ILRI, Nairobi.
- Grace, D., Bett, B., Lindahl, J. and Robinson, T. (2015) Climate and livestock disease: assessing the vulnerability of agricultural systems to livestock pests under climate change scenarios. CCAFS Working Paper No. 116. CCAFS, Copenhagen.
- Grace, D. and Downie, K. (2011) Cysticercosis in a population of epileptics in Western Kenya: relating human and pig risk factors. Presentation at the 1st International One Health Congress, 14–16 February, Melbourne, Australia. ILRI, Nairobi.
- Grace D, Gilbert J, Randolph T and Kang'ethe E. (2012a) The multiple burdens of zoonotic disease and an EcoHealth approach to their assessment. *Tropical Animal Health and Production* 44 (Suppl. 1), 67–73.
- Grace, D., Kang'ethe, E. and Waltner-Toews, D. (2012c) Participatory and integrative approaches to food safety in developing country cities. *Tropical Animal Health and Production* 44 (Suppl. 1), 1–2.
- Grace, D., Mutua, F., Ochungo, P., Kruska, R., Jones, K., *et al.* (2012b) *Mapping of poverty and likely zoonoses hotspots*. Zoonoses Project 4. Report to the UK Department for International Development. ILRI, Nairobi.
- Grace, D., Nasinyama, G., Randolph, T.F., Mwiine, F. and Kang'ethe, E. (2008) City dairying in Kampala: integrating benefits and harms. In: Cole, D., Lee-Smith, D. and Nasinyama, G. (eds) *Healthy City Harvests: Generating Evidence to Guide Policy on Urban Agriculture*. International Potato Center (CIP), Lima, pp. 193–210.
- Grace, D., Randolph, T., Affognon, H., Dramane, D., Diall, O. and Clausen, P.H. (2009) Characterisation and validation of farmers' knowledge and practice of cattle trypanosomosis management in the cotton zone of West Africa. *Acta Tropica* 111, 137–143.
- Guyatt, H.L. and Fèvre, E.M. (2016) Lingual palpation for porcine cysticercosis: a rapid epidemiological tool for estimating prevalence and community risk in Africa. *Tropical Medicine & International Health* 21, 1319–1323.
- Hackett, F., Ford, L.B., Fèvre, E.M. and Simarro, P. (2014) Incorporating scale dependence in disease burden estimates: the case of human African trypanosomiasis in Uganda. *PLoS Neglected Tropical Diseases* 8, e2704.
- Hadush, A. (2015) Assessment of bovine tuberculosis in dairy farms and its public health importance in and around Adigrat District. MSc thesis, Mekelle University, Mekelle, Ethiopia.
- Havelaar, A.H., Kirk, M.D., Torgerson, P.R., Gibb, H.J., Hald, T., *et al.* (2015) World Health Organization global estimates and regional comparisons of the burden of foodborne disease in 2010. *PLoS Medicine* 12, e1001923.
- Hoffman, T., Nissen, K., Krambrich, J., Rönnerberg, B., Akaberi, D., *et al.* (2020) Evaluation of a COVID-19 IgM and IgG rapid test; an efficient tool for assessment of past exposure to SARS-CoV-2. *Infection Ecology & Epidemiology* 10, 1754538.
- Holt, H.R., Inthavong, P., Boualam, K., Blaszkak, K., Keokamphe, C., *et al.* (2016) Endemicity of zoonotic diseases in pigs and humans in lowland and upland Lao PDR: identification of socio-cultural risk factors. *PLoS Neglected Tropical Diseases* 10, e0003913.
- Holt, H.R., Inthavong, P., Blaszkak, K., Keokamphe, C., Phongmany, A., *et al.* (2019) Production diseases in smallholder pig systems in rural Lao PDR. *Preventive Veterinary Medicine* 162, 110–116.
- Ijumba, J.N. and Lindsay, S.W. (2001) Impact of irrigation on malaria in Africa: paddies paradox. *Medical and Veterinary Entomology* 15, 1–11.

- ILRI (2014) One Health, EcoHealth and agriculture associated diseases – report of a regional dialogue. New Delhi, 25 November 2013. ILRI, Nairobi.
- ILRI/ICAR (2013) Livestock research and development: summary report of the ICAR-ILRI partnership dialogue, New Delhi, 7 November 2012. ILRI, Nairobi.
- Jakobsen, F., Nguyen-Tien, T., Pham-Thanh, L., Bui, V.N., Nguyen-Viet, H., *et al.* (2019) Urban livestock-keeping and dengue in urban and peri-urban Hanoi, Vietnam. *PLOS Neglected Tropical Diseases* 13, e0007774.
- Johansen, M.V. and Mukaratirwa, S. (2013) The Cysticercosis Working Group of Eastern and Southern Africa (CWGESA). In Olsen, A., Ørnbjerg, N. and Winkel, K. (eds) *A Success Story in Danish Development Aid – DBL (1964–2012)*. Narayana Press, Odder, Denmark.
- Jones, K.E., Patel, N.G., Levy, M.A., Storeygard, A., Balk, D., Gittleman, J.L. and Daszak, P., (2008). Global trends in emerging infectious diseases. *Nature* 451(7181), 990–993.
- Jones, B.A., Grace, D., Kock, R., Alonso, S., Rushton, J., *et al.* (2013) Zoonosis emergence linked to agricultural intensification and environmental change. *Proceedings of the National Academy of Sciences* 110, 8399–8404.
- Jost, C., Mariner, J.C., Roeder, P., Sawitri, E. and Macgregor-Skinner, G. (2007) Participatory epidemiology in disease surveillance and research. *Revue Scientifique et Technique* 26, 537–549.
- Jost, C.C., Nzietchueng, S., Kihu, S., Bett, B., Njogu, G., *et al.* (2010) Epidemiological assessment of the Rift Valley fever outbreak in Kenya and Tanzania in 2006 and 2007. *American Journal of Tropical Medicine and Hygiene* 83, 65–72.
- Kagira, J.M., Maingi, N., Kanyari, P.W.N., Githigia, S.M., Ng'ang'a, J.C. and Gachohi, J.M. (2010) Sero-prevalence of *Cysticercus cellulosae* and associated risk factors in free-range pigs in Kenya. *Journal of Helminthology* 84, 398–403.
- Kang'ethe, E.K., Arimi, S.M., Omoro, A.O., McDermott, J.J., Nduhiu, J.G., *et al.* (2000) The prevalence of antibodies to *Brucella abortus* in marketed milk in Kenya and its public health implications. Paper presented at the 3rd All Africa Conference on Animal Agriculture (AACAA), 6–9 November, Alexandria, Egypt. ILRI, Nairobi.
- Kang'ethe, E.K., Kimani, V.N., McDermott, B., Grace, D., Lang'at, A.K., *et al.* (2012a) A trans-disciplinary study on the health risks of cryptosporidiosis from dairy systems in Dagoretti, Nairobi, Kenya: study background and farming system characteristics. *Tropical Animal Health and Production* 44, 3–10.
- Kang'ethe, E., Kimani, V., Grace, D., Mitoko, G., McDermott, B., *et al.* (2012b) Development and delivery of evidence-based messages to reduce the risk of zoonoses in Nairobi, Kenya. *Tropical Animal Health and Production* 44 (Suppl. 1), 41–46.
- Keiser, J., de Castro, M.C., Maltese, M.F., Bos, R., Tanner, M., *et al.* (2005a) Effect of irrigation and large dams on the burden of malaria on a global and regional scale. *American Journal of Tropical Medicine and Hygiene* 72, 392–406.
- Keiser, J., Utzinger, J. and Tanner, M. (2005b) The effect of irrigation and large dams on the burden of malaria on global and regional scale. Report prepared for the WHO commissioned study 'Burden of water-related vector-borne diseases: An analysis of the fraction attributable to components of water resources development and management' WHO, Geneva, Switzerland.
- Kimani, T., Schelling, E., Bett, B., Ngigi, M., Randolph, T. and Fuhrmann, S. (2016) Public health benefits from livestock Rift Valley Fever control: a simulation of two epidemics in Kenya. *EcoHealth* 13, 729–742.
- Kivali, V., Thomas, L., Toye, P. and Fèvre, E. (2013) Diagnosis of porcine cysticercosis using lateral flow assay and HP10 Ag ELISA. Poster presented at the 47th Annual Scientific Conference of the Kenya Veterinary Association, 24–27 April, Mombasa, Kenya. ILRI, Nairobi.
- Kobinger, G.P., Leung, A., Neufeld, J., Richardson, J.S., Falzarano, D., *et al.* (2011) Replication, pathogenicity, shedding, and transmission of Zaire ebolavirus in pigs. *Journal of Infectious Diseases* 204, 200–208.
- Koech, R.K. (2001) Epidemiology of tuberculosis in humans in Narok district with special interest on *Mycobacterium bovis*. MSc thesis, University of Nairobi, Nairobi.
- Kungu, J.M., Dione, M.M., Ejobi, F., Harrison, L.J., Poole, E.J., *et al.* (2017) Sero-prevalence of *Taenia* spp. cysticercosis in rural and urban smallholder pig production settings in Uganda. *Acta Tropica* 165, 110–115.
- Lapar, M.L., Nuryartono, N., Toan, N.N., Rafani, I., Bett, B., *et al.* (2012) Are smallholders willing to pay for animal disease control? Empirical evidence from a study of mass vaccination for avian influenza in Indonesia. *Asian Journal of Agriculture and Development* 9, 74.

- Lee, H.S., Thakur, K.K., Bui, V.N., Bui, A.N., Dang, M.V. and Wieland, B. (2019) Simulation of control scenarios of porcine reproductive and respiratory syndrome in Nghe An Province in Vietnam. *Transboundary and Emerging Diseases* 66, 2279–2287.
- Lee, H.S., Bui, V.N., Nguyen, H.X., Bui, A.N., Hoang, T.D., *et al.* (2020a) Seroprevalences of multi-pathogen and description of farm movement in pigs in two provinces in Vietnam. *BMC Veterinary Research* 16, 15.
- Lee, H.S., Pham T.L. and Wieland, B. (2020b) Temporal patterns and space-time cluster analysis of foot-and-mouth disease (FMD) cases from 2007 to 2017 in Vietnam. *Transboundary and Emerging Diseases* 67, 584–591.
- Lejon, V., Ilboudo, H., Mumba, D., Camara, M., Kaba, D., *et al.* (2017) Diagnostic tools for human African trypanosomiasis elimination and clinical trials: the DiTECT-HAT project. *BMJ Global Health* 2 (Suppl. 2), A8.
- Leksmono, C., Young, J., Hooton, N., Muriuki, H. and Romney, D. (2006) Informal traders lock horns with the formal milk industry: the role of research in pro-poor dairy policy shift in Kenya. Working Paper 266. ILRI, Nairobi.
- Liljander, A., Meyer, B., Jores, J., Müller, M.A., Lattwein, E., *et al.* (2016) MERS-CoV antibodies in humans, Africa, 2013–2014. *Emerging Infectious Diseases* 22, 1086–1089.
- Lindahl, J.F., Kumar, N.G., Deka, R.P., Shome, R. and Grace, D. (2018) Serological evidence of *Brucella* infections in dairy cattle in Haryana, India. *Infection Ecology & Epidemiology* 8, 1555445.
- Mariner, J.C., Hendrickx, S., Pfeiffer, D.U., Costard, S., Knopf, L., *et al.* (2011) Integration of participatory approaches into surveillance systems. *Revue Scientifique et Technique* 30, 653–659.
- Mariner, J.C., Jones, B.A., Hendrickx, S., El Masry, I., Jobre, Y. and Jost, C.C. (2014) Experiences in participatory surveillance and community-based reporting systems for H5N1 highly pathogenic avian influenza: a case study approach. *EcoHealth* 11, 22–35.
- Marsh, G.A., Haining, J., Robinson, R., Foord, A., Yamada, M., *et al.* (2011) Ebola Reston virus infection of pigs: clinical significance and transmission potential. *Journal of Infectious Diseases* 204, S804–S809.
- Mbotha, D., Bett, B., Kairu-Wanyoike, S., Grace, D., Kihara, A., *et al.* (2017) Inter-epidemic Rift Valley fever virus seroconversions in an irrigation scheme in Bura, south-east Kenya. *Transboundary and Emerging Diseases* 65, e55–e62.
- McDermott, J.J. and Arimi, S.M. (2002) Brucellosis in sub-Saharan Africa: epidemiology, control and impact. *Veterinary Microbiology* 90, 111–134.
- McDermott, J.J., Kristjanson, P.M., Kruska, R.L., Reid, R.S., Robinson, T.P., *et al.* (2001) Effects of climate, human population and socio-economic changes on tsetse-transmitted trypanosomiasis to 2050. In: Seed, R. and Black, S. (eds) *World Class Parasites*, Vol 1: *The African Trypanosomes*. Kluwer Academic, Boston, pp. 25–38.
- McDermott, J., Grace, D. and Zinsstag, J. (2013) Economics of brucellosis impact and control in low-income countries. *Scientific and Technical Review* 32, 249–261.
- Morens, D.M., Folkers, G.K. and Fauci, A.S. (2004) The challenge of emerging and re-emerging infectious diseases. *Nature* 430, 242–249.
- Muller, M.A., Corman, V.M., Jores, J., Meyer, B., Younan, M., *et al.* (2014) MERS coronavirus neutralizing antibodies in camels, eastern Africa, 1983–1997. *Emerging Infectious Diseases* 20, 2093–2095.
- Mulugeta, W., Wilkes, J., Mulatu, W., Majiwa, P.A.O., Masake, R. and Peregrine, A.S. (1997). Mechanisms and genetics of resistance to trypanocides in African trypanosomes. *Acta Tropica* 64, 205–217.
- Munyua, P., Bitek, A., Osoro, E., Pieracci, E.G., Muema, J., *et al.* (2016a) Prioritization of zoonotic diseases in Kenya 2015. *PLoS One* 11, e0161576.
- Munyua, P.M., Muriithi, R.M., Ithondeka, P., Hightower, A., Thumbi, S.M., *et al.* (2016b) Predictive factors and risk mapping for Rift Valley fever epidemics in Kenya. *PLoS One* 11, e0144570.
- Musewa, A., Roesel, K., Grace, D., Dione, M. and Erume, J. (2018) Detection of *Erysipelothrix rhusiopathiae* in naturally infected pigs in Kamuli District, Uganda. *Revue d'Élevage et de Médecine Vétérinaire des Pays Tropicaux* 71, 31229.
- Mutua, E.N., Bukachi, S.A., Bett, B.K., Estambale, B.A. and Nyamongo, I.K. (2017) 'We do not bury dead livestock like human beings': community behaviors and risk of Rift Valley Fever virus infection in Baringo County, Kenya. *PLoS Neglected Tropical Diseases* 11, e0005582.
- Mutua, F.K., Randolph, T.F., Arimi, S.M., Kitale, P.M., Githigia, S.M., *et al.* (2007) Palpable lingual cysts, a possible indicator of porcine cysticercosis, in Teso District, Western Kenya. *Journal of Swine Health and Production* 15, 206–212.

- Mutua, E., de Haan, N., Tumusiime, D., Jost, C. and Bett, B. (2019) A qualitative study on gendered barriers to livestock vaccine uptake in Kenya and Uganda and their implications on Rift Valley fever control. *Vaccines* 7, 86.
- Muturi, M., Gachohi, J., Mwatondo, A., Lekolool, I., Gakuya, F., *et al.* (2018) Recurrent anthrax outbreaks in humans, livestock, and wildlife in the same locality, Kenya, 2014–2017. *American Journal of Tropical Medicine and Hygiene* 99, 833–839.
- Mwololo, D.K. (2016) Seroepidemiological survey of Q fever in livestock and humans in Bura, Tana River County, Kenya. MSc thesis, University of Nairobi, Nairobi.
- Nanyingi, M.O., Munyua, P., Kiama, S.G., Muchemi, G.M., Thumbi, S.M., *et al.* (2015) A systematic review of Rift Valley Fever epidemiology 1931–2014. *Infection Ecology & Epidemiology* 5, 1–12.
- Nguyen-Viet, H., Chotinun, S., Schelling, E., Widyastuti, W., Khong, N.V., *et al.* (2016) Reduction of antimicrobial use and resistance needs sectoral-collaborations with a One Health approach: perspectives from Asia. *International Journal of Public Health* 62 (Suppl. 1), 3–5.
- Nguyen-Viet, H., Grace, D. and McDermott, J. (2019) Integrated approaches to tackling health issues-related to agri-food systems. *International Journal of Public Health* 64, 5–6.
- Njenga, M.K., Paweska, J., Wanjala, R., Rao, C.Y., Weiner, M., *et al.* (2009) Using a field quantitative real-time PCR test to rapidly identify highly viremic rift valley fever cases. *Journal of Clinical Microbiology* 47, 1166–1171.
- Njeru, J., Henning, K., Pletz, M.W., Heller, R., Forstner, C., *et al.* (2016) Febrile patients admitted to remote hospitals in Northeastern Kenya: seroprevalence, risk factors and a clinical prediction tool for Q-Fever. *BMC Infectious Diseases* 16, 244.
- Nsadh, Z., Thomas, L.F., Fèvre, E.M., Nasinyama, G., Ojok, L. and Waiswa, C. (2014) Prevalence of porcine cysticercosis in the Lake Kyoga Basin, Uganda. *BMC Veterinary Research* 10, 239.
- Nyangaga, J.N., Grace, D., Kimani, V., Kiragu, M.W., Langat, A.K., *et al.* (2012) Outcome mapping for fostering and measuring change in risk management behaviour among urban dairy farmers in Nairobi, Kenya. *Tropical Animal Health and Production* 44 (Suppl. 1), S47–S51.
- Nyokabi, S., Birner, R., Bett, B., Isuyi, L., Grace, D. *et al.* (2017) Informal value chain actors' knowledge and perceptions about zoonotic diseases and biosecurity in Kenya and the importance for food safety and public health. *Tropical Animal Health and Production* 50, 509–518.
- Oboe, H.M. (2016) Socio-economics and perceptions of Q-fever infection in a pastoralist system of Kajiado County. MSc thesis, University of Nairobi, Nairobi.
- Odiit, M., Coleman, P.G., Fèvre, E.M., Magona, J. and McDermott, J.J. (2000) Incorporating the burden of human sleeping sickness in an economic impact assessment of trypanosomiasis. In: *Proceedings of the Ninth International Symposium on Veterinary Epidemiology and Economics*, 7–11 August, Breckenridge, Colorado. ISVEE, Breckenridge, Colorado, pp. 1300–1303.
- Odiit, M., Shaw, A., Welburn, S.C., Fèvre, E.M., Coleman, P.G. and McDermott, J.J. (2004) Assessing the patterns of health-seeking behaviour and awareness among sleeping-sickness patients in eastern Uganda. *Annals of Tropical Medicine and Parasitology* 98, 339–348.
- Odiit, M., Coleman, P.G., Liu, W.C., McDermott, J.J., Fèvre, E.M., *et al.* (2005) Quantifying the level of under-detection of *Trypanosoma brucei rhodesiense* sleeping sickness cases. *Tropical Medicine & International Health* 10, 840–849.
- Odiit, M., Bessell, P.R., Fèvre, E.M., Robinson, T.P., Kinoti, J., *et al.* (2006) Using remote sensing and geographic information systems to identify villages at high risk for rhodesiense sleeping sickness in Uganda. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 100, 354–362.
- Odongo, D.O., Tiampati, C.M., Mulinge, E., Mbae, C.K., Bishop, R.P., *et al.* (2018) Prevalence and genotyping of *Echinococcus granulosus* in sheep in Narok County, Kenya. *Parasitology Research* 117, 2065–2073.
- Omoro, A.O., Arimi, S., Kang'ethe, E.K. and McDermott, J.J. (2000) Analysis of public health risks from consumption of informally marketed milk in Kenya. Paper presented at the Faculty of Veterinary Medicine Biennial Scientific Conference, 30–31 August, University of Nairobi, Kenya. ILRI, Nairobi.
- O'Neill, J. (2015) Antimicrobials in agriculture and the environment: reducing unnecessary use and waste. *Review on Antimicrobial Resistance*. Wellcome Trust.
- Perry, B.D., Randolph, T.F., McDermott, J.J., Sones, K.R. and Thornton, P.K. (2002) *Investing in animal health research to alleviate poverty*. ILRI, Nairobi.
- Rich, K.M. and Wanyoike, F. (2010) An assessment of the regional and national socio-economic impacts of the 2007 Rift Valley fever outbreak in Kenya. *American Journal of Tropical Medicine and Hygiene* 83 (Suppl.), 52–57.

- Robinson, T.P., Bu, D.P., Carrique-Mas, J., Fèvre, E.M., Gilbert, M. *et al.* (2016) Antibiotic resistance is the quintessential One Health issue. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 110, 377–380.
- Roesel, K., Nöckler, K., Baumann, M.P.O., Fries, R., Dione, M.M., *et al.* (2016) First report of the occurrence of *Trichinella*-specific antibodies in domestic pigs in Central and Eastern Uganda. *PLoS One* 11, e0166258.
- Sang, R., Lutomiah, J., Said, M., Makio, A., Koka, H., *et al.* (2016) Effects of irrigation and rainfall on the population dynamics of Rift Valley fever and other Arbovirus Mosquito vectors in the epidemic prone Tana River County, Kenya. *Journal of Medical Entomology* 54, 460–470.
- Sekar, N., Shah, N.K., Abbas, S.S. and Kakkar, M. (2011) On behalf of the Roadmap to Combat Zoonoses in India (RCZI) Initiative Research options for controlling zoonotic disease in India, 2010–2015. *PLoS One* 6, e17120.
- Shaw, A.P.M., Wint, G.R.W., Cecchi, G., Torr, S.J., Mattioli, R.C. and Robinson, T.P. (2015) Mapping the benefit–cost ratios of interventions against bovine trypanosomosis in Eastern Africa. *Preventive Veterinary Medicine* 122, 406–416.
- Shewatatek, F. (2015) Bovine tuberculosis: prevalence, economic implications and diagnostic tests comparison in smallholder dairy farms in selected districts of North Gondar Zone, Amhara Region. Thesis, University of Gondar, Gondar, Ethiopia.
- Shija, F. (2013) Assessment of milk handling practices and bacterial contaminations along the dairy value chain in Lushoto and Handeni districts, Tanzania. MSc thesis, Sokoine University of Agriculture, Morogoro, Tanzania.
- Simpson, A. (2015) Consumption of fallen stock: a risk assessment. MSc thesis, Royal Veterinary College, University of London, London.
- Smith, E., Atherstone, C. and Grace, D. (2015) One Health approach recommended in investigating and communicating the potential role of pigs in transmitting Ebola in Uganda. ILRI Policy Brief No 17. ILRI, Nairobi.
- Sow, A., Faye, O., Ba, Y., Diallo, D., Fall, G., *et al.* (2016) Widespread Rift Valley fever emergence in Senegal in 2013–2014. *Open Forum Infectious Diseases* 3, ofw149.
- Teshome, H., Molla, B. and Tibbo, M. (2003) A seroprevalence study of camel brucellosis in three camel-rearing regions of Ethiopia. *Tropical Animal Health and Production* 35, 381–390.
- Thomas, L.F., de Glanville, W.A., Cook, E.A. and Fèvre, E.M. (2013) The spatial ecology of free-ranging domestic pigs (*Sus scrofa*) in western Kenya. *BMC Veterinary Research* 9, 46.
- Thomas, L.F., Harrison, L.J.S., Toye, P., de Glanville, W.A., Cook, E.A.J., *et al.* (2016) Prevalence of *Taenia solium* cysticercosis in pigs entering the food chain in western Kenya. *Tropical Animal Health and Production* 48, 233–238.
- Thomas, L.F., de Glanville, W.A., Cook, E.A., Bronsvoort, B.M., Handel, I., *et al.* (2017) Modelling the risk of *Taenia solium* exposure from pork produced in western Kenya. *PLoS Neglected Tropical Diseases* 11, e0005371.
- Tschopp, R., Schelling, E., Hattendorf, J., Aseffa, A. and Zinsstag, J. (2009) Risk factors of bovine tuberculosis in cattle in rural livestock production systems of Ethiopia. *Preventive Veterinary Medicine* 89, 205–211.
- Unger, F., Bett, B., Siregar, E.S., Idris, S. and Randolph, T.F. (2014) Integrated HPAI control in kampung chicken in Indonesia – an overview on ILRI's research and lessons learned. Poster presented at the Tropentag 2014 Conference on Bridging the Gap between Increasing Knowledge and Decreasing Resources, 17–19 September, Prague, Czech Republic. ILRI, Nairobi.
- Unger, F., Long, C.T.M. and Khong, N.V. (2016) Prevalence of trichinellosis and cysticercosis in indigenous pigs from ethnic minorities for selected communes in the Central Highlands (Dak Lak). Summary report. ILRI, Nairobi.
- United Nations Environment Programme and International Livestock Research Institute. (2020). Preventing the next pandemic: Zoonotic diseases and how to break the chain of transmission. Nairobi, Kenya: UNEP. <https://cgspace.cgiar.org/handle/10568/108707>
- USDA/USAID/ILRI (2013) An integrated approach to controlling brucellosis in Africa: workshop report. ILRI, Nairobi.
- van Boeckel, T.P., Brower, C., Gilbert, M., Grenfell, B.T., Levin, S.A., *et al.* (2015) Global trends in antimicrobial use in food animals. *Proceedings of the National Academy of Sciences USA* 112, 5649–5654.
- Verdugo, C., El Masry, I., Makonnen, Y., Hannah, H., Unger, F., *et al.* (2016) Sensitivity and specificity estimation for the clinical diagnosis of highly pathogenic avian influenza in the Egyptian participatory disease surveillance program. *Avian Diseases* 60, 805–809.

- Vordermeier, M., Ameni, G., Berg, S., Bishop, R., Robertson, B.D., *et al.* (2012) The influence of cattle breed on susceptibility to bovine tuberculosis in Ethiopia. *Comparative Immunology, Microbiology and Infectious Diseases* 35, 227–232.
- Waiswa C., Fèvre, E.M., Nsadhwa, Z., Sikasunge, C.S. and Willingham, A.L. (2009) Porcine Cysticercosis in Southeast Uganda: seroprevalence in Kamuli and Kaliro Districts. *Journal of Parasitology Research* 2009, 375493.
- Wamboga, C., Matovu, E., Bessell, P.R., Picado, A., Biéler, S. and Ndung'u, J.M. (2017) Enhanced passive screening and diagnosis for *gambiense* human African trypanosomiasis in north-western Uganda – moving towards elimination. *PLoS One* 12, e0186429.
- Wardrop, N.A., Thomas, L.F., Cook, E.A.J., de Glanville, W.A., Atkinson, P.M., *et al.* (2016) The sero-epidemiology of *Coxiella burnetii* in humans and cattle, western Kenya: evidence from a cross-sectional study. *PLOS Neglected Tropical Diseases* 10, e0005032.
- Warimwe, G.M., Gesharisha, J., Carr, B.V., Otieno, S., Otingah, K., *et al.* (2016) Chimpanzee adenovirus vaccine provides multispecies protection against Rift Valley Fever. *Scientific Reports* 6, 20617.
- Warimwe, G.M., Lorenzo, G., Lopez-Gil, E., Reyes-Sandoval, A., Cottingham, M.G., *et al.* (2013) Immunogenicity and efficacy of a chimpanzee adenovirus-vectored Rift Valley fever vaccine in mice. *Virology Journal* 10, 349.
- Watts, N., Adger, W.N., Ayeb-Karlsson, S., Bai, Y., Byass, P., *et al.* (2017) The Lancet Countdown: tracking progress on health and climate change. *Lancet* 389, 1151–1164.
- Watts, N., Amann, M., Ayeb-Karlsson, S., Belesova, K., Bouley, T., *et al.* (2018a) The Lancet Countdown on health and climate change: from 25 years of inaction to a global transformation for public health. *Lancet* 391, 581–630.
- Watts, N., Amann, M., Arnell, N., Ayeb-Karlsson, S., Belesova, K., *et al.* (2018b) The 2018 report of the Lancet Countdown on health and climate change: shaping the health of nations for centuries to come. *Lancet* 392, 2479–2514.
- Williams, R., Malherbe, J., Weepener, H., Majiwa, P. and Swanepoel, R. (2016) Anomalous high rainfall and soil saturation as combined risk indicator of Rift Valley fever outbreaks, South Africa, 2008–2011. *Emerging Infectious Diseases* 22, 2054–2062.
- Wohlgemut, J., Dewey, C., Levy, M. and Mutua, F. (2010) Evaluating the efficacy of teaching methods regarding prevention of human epilepsy caused by *Taenia solium* neurocysticercosis in Western Kenya. *American Journal of Tropical Medicine and Hygiene* 82, 634–642.
- Woolhouse, M.E. and Gowtage-Sequeria, S. (2005) Host range and emerging and reemerging pathogens. *Emerging Infectious Diseases* 11, 1842–1847.
- World Bank (2012) People, pathogens and our planet: the economics of One Health. World Bank, Washington, D.C.
- WHO (2006) The control of neglected zoonotic diseases: a route to poverty alleviation: report of a joint WHO/DFID-AHP meeting, 20 and 21 September 2005, WHO Headquarters, Geneva, with the participation of FAO and OIE. WHO, Geneva. Available at: www.who.int/neglected_diseases/zoonoses/9789241594301/en/ (accessed 12 February 2020).
- WHO (2013) Research priorities for the environment, agriculture and infectious diseases of poverty: technical report of the TDR Thematic Reference Group on Environment, Agriculture and Infectious Diseases of Poverty. Technical report series no. 976. WHO, Geneva.