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Towards a conceptual framework to support one-health research for policy on emerging zoonoses

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In the past two decades there has been a growing realisation that the livestock sector was in a process of change, resulting from an expansion of intensive animal production systems and trade to meet a globalised world's increasing demand for livestock products. One unintended consequence has been the emergence and spread of transboundary animal diseases and, more specifically, the resurgence and emergence of zoonotic diseases. Concurrent with changes in the livestock sector, contact with wildlife has increased. This development has increased the risk of transmission of infections from wildlife to human beings and livestock. Two overarching questions arise with respect to the real and perceived threat from emerging infectious diseases: why are these problems arising with increasing frequency, and how should we manage and control them? A clear conceptual research framework can provide a guide to ensure a research strategy that coherently links to the overarching goals of policy makers. We propose such a new framework in support of a research and policy-generation strategy to help to address the challenges posed by emerging zoonoses.

Introduction

Nearly two-thirds of human pathogens are zoonotic and, of greater concern, nearly three-quarters of emerging and re-emerging diseases of human beings are zoonoses.¹ Emerging diseases include avian influenza, severe acute respiratory syndrome (SARS), West Nile virus, Nipah virus, and bovine spongiform encephalopathy (BSE), which have all received substantial media attention and, in the cases of avian influenza and pandemic influenza A H1N1, many resources.

New infectious diseases emerge because of a complex set of multifactorial circumstances that include population growth, changes in nutritional, agricultural, and trade practices, and shifts in land use including accelerated urbanisation, deforestation, and encroachment on wildlife.^{2–5} Additionally, ancient zoonotic diseases such as rabies, anthrax, brucellosis, bovine tuberculosis, zoonotic trypanosomiasis, and disorders associated with tapeworm infections are re-emerging because of a combination of similar factors, including transmission of pathogens from wildlife to domestic reservoir species.^{3,6,7}

Increased complexity in food chains and different systems of food production and preparation are also leading to rising importance of food-borne zoonoses such as salmonella, campylobacter, and *Escherichia coli* infections, which are all linked to livestock production and processing systems.⁸ How climate change will affect this complex dynamic mix of factors is unclear, but it is expected to affect the range, distribution, and diversity of pathogens, and possibly the associated morbidity.^{9,10}

Two overarching questions arise from these observations. Why are these problems arising with increasing frequency?¹¹ And how should we be risk-managing and controlling them? We outline some of the important changes in livestock systems and their effect on infectious diseases and describe a conceptual framework for a systematic approach to guide so-called one-health research and to aid policy formulation. We

use the term one-health to denote the collaborative effort of many disciplines—working locally, nationally, and globally—to attain optimum health of human beings, animals, and our environment.¹²

Background

During the 1990s, there was a growing realisation that the livestock sector was undergoing a so-called livestock revolution.¹³ This event was probably the second major livestock revolution, the first occurring during the 19th century as European populations grew and became increasingly urbanised. The first revolution largely affected ruminants and caused various livestock disease problems that were, especially in developed countries, controlled through creation of veterinary services, investment in research, and education systems.⁸ The benefits from these investments were felt in the control of several livestock diseases and in human health.^{14,15} There were also advances in livestock production methods and marketing systems that helped to feed a growing urban population. However, this first revolution also created major zoonotic problems, such as bovine tuberculosis and brucellosis, that were left unattended for decades. By the time they were controlled in livestock populations, these diseases had caused large-scale human morbidity and mortality.^{16–18}

The second livestock revolution that probably began in the 1980s originated from the rapid expansion of intensive pig and poultry production systems and, to some extent, from a growth in milk production. It was facilitated by the availability of antimicrobial and antiparasitic treatments used for preventive purposes to allow high densities of animals to be kept under suboptimum husbandry conditions. Research into pig and poultry production systems has changed breeding, feeding, and management systems, leading to improvements in overall productivity and standardisation of products. These profound changes in livestock production have been broadly welcomed because they have met the

growing demand for livestock products. Initially, there were some concerns about poor livestock producers being left behind,^{19–22} and the potential negative effects on the environment.^{23,24} What was less expected were the increased problems associated with control of animal diseases that cross international borders and the resurgence, and in some cases emergence, of zoonotic diseases. Additionally, the emergence of antimicrobial resistance has led to demands to reduce or to avoid the use of antimicrobial preventive treatment in animal production.²⁵

The second livestock revolution has been concurrent with increased contact between wildlife and both livestock and people. This change has resulted from increased settlement or farming in wildlife habitats, wildlife farming, increasing diversity of animals kept as pets, and the increase of tourism in remote areas.^{3,5} Increased contact has heightened the risk of transmission of infections from wildlife to human beings and livestock. Reviews suggest that many emerging human pathogens have originated from wildlife, and that livestock intensification probably exacerbates the emergence of zoonotic diseases by amplification, irrespective of whether the infection source is livestock or wildlife.^{11,26}

Throughout human history, populations everywhere have encountered new and resurgent communicable diseases.²⁷ But, despite this history, human beings have at times been optimistic in their perceptions. Famously, in 1948, US Secretary of State George Marshall proclaimed that the conquest of all infectious diseases was imminent.²⁸ It has been widely said that, in 1969, US Surgeon General William H Stewart expressed his confidence that we had reached the frontiers of communicable diseases; although this is now dismissed as urban myth, other notable examples exist from the 1960s and 1970s of world leaders in the field proclaiming that infectious diseases had been conquered.²⁹ Since then, the number and novelty of crises associated with communicable diseases have surprised researchers, practitioners, and policy makers. And the global reach and speed of spread has challenged public health systems in ways unimagined.

At least three important lessons can be drawn from past experience with emerging zoonotic diseases. First, that progress in public health and communicable diseases is not irreversible. Second, that more of the same tactics that have emerged in the modern era to control the emergence of new diseases in animals and human beings, and their vectors, will probably be insufficient to control future threats. Third, that a changing and increasingly interconnected world means changes in ecosystems that offer unpredictable opportunities to microbes that are more varied, numerous, and adaptable than we had once hoped, with spread occurring more rapidly. Experience in the past decade with, for example, Ebola, Nipah virus, avian

influenza A H5N1, influenza A H1N1 2009, and SARS in 2002 are illustrative of new agents and zoonotic diseases associated with livestock or wild animals that are now burdening human public health systems on an international scale.

Despite the profound animal and human health and economic consequences of zoonotic diseases, until recently they have tended to be neglected. Shaw identified four reasons for this neglect.⁷ First, veterinary services had been given responsibility for control of these diseases, but had neither the farm-level economic incentives nor the societal resource allocation to fulfil this role. Second, zoonoses in both human beings and animals are generally underdiagnosed. Third, zoonoses tend to affect rural, often poor, people with poor access to health services. Fourth, mechanisms to control and to restrict food-borne diseases are difficult and complex.

We might add to this list several additional reasons: including the challenges of interdisciplinary collaboration (be it research, policy, or practice); the complex intersectoral institutional environment within which animal and human health systems operate at global, regional, national, and local levels; and the upstream nature of prevention activities and their temporal and causal distance from human consequences. To deal with this complexity requires a conceptualisation of these systems that support a visualisation of the interfaces of animal and human health, which we attempt to address. Without a common conceptualisation of the systems across which animals and human beings encounter each other, questions and challenges sit in disciplinary isolation. Moreover, strategic responses to problems risk being merely disconnected activities.

Our goal is to define health system research of policy relevance that provides a holistic systems approach that is needed for one-health.

Panel 1: Ebola in the Democratic Republic of the Congo

The Democratic Republic of the Congo is subject to several emerging infectious diseases. One that results in substantial social disruption and high mortality is Ebola. The country has had five Ebola outbreaks since the first epidemic took place in Yambuku in 1976. The fourth and fifth outbreaks took place in Mweka in 2008 and 2009.

The origins of the Ebola virus are difficult to establish, and prediction of where and when outbreaks are likely to occur is a challenge; therefore research into inputs might offer important strategic policy responses. Interventions to control outbreaks typically include early detection and rapid response including supportive clinical care and mass education. Research into specific pharmaceutical interventions is needed. Although the Mweka outbreak started in April, 2008, case confirmation did not occur until September, 2009. These health system delays, which were the result of inadequate mechanisms to deliver interventions, resulted in poor control for many months. 165 people died. Ineffective communication, poor stewardship, and insufficient resources contributed to delays in control. Research questions remain around which elements of the health system need to be strengthened to best support the management of such sporadic outbreaks, while the general health system is maintained and developed.

Panel 2: Rift Valley fever in Tanzania

Rift Valley fever, an episodic vector-borne viral disease affecting domestic and wild animals as well as human beings, was first reported in Tanzania in 1956. The disease re-emerged in the country in 1977, and between December, 1997, and April, 1998, an epidemic occurred that is believed to have been caused by unusually large rainfall, the result of El Niño, and subsequent expansion of the mosquito vector population.

A similar epidemic occurred in 2007. Is climate change an important input factor in the emergence of Rift Valley fever, and can interventions such as improved predictive surveillance linked to climate change or rainfall be harnessed to predict future epidemics? Although substantial delays occurred, in part because mechanisms to support interventions, including financing and logistics of laboratory testing of samples, control of the 2007 epidemic was largely the result of animal and human health agencies working in an integrated manner. Indeed, the outbreak was classified as a national disaster, thus falling under the authority of the National Disaster Preparedness and Response Unit, which involved several government departments and reported directly to the Prime Minister. Disease management units at local level were also established to support control measures across both human and animal populations. Questions remain about which elements of the health systems need to be integrated, and to what extent, to achieve policy goals that include human health protection and economic security, as well as ecological diversity. Furthermore, the response was in part dependent on a favourable and energised political context. Whether this factor is a prerequisite for effective control is unknown. Another question is how best to harness political support such that prevention through the targeted vaccination of at-risk livestock occurs before detection of clinical disease in animals or human beings.

Panel 3: Highly pathogenic avian influenza in Cambodia

From 2003, the re-emergence of the influenza A H5N1 virus in poultry and sporadically in people has emphasised the need for a comprehensive public health response integrating elements of both animal and human sectors. Since 2004, Cambodia has had 21 poultry outbreaks resulting in nine human cases including seven deaths. Backyard poultry production is widespread throughout the country and accounts for more than 90% of the poultry population. Spread of H5N1 influenza overall is driven by trade links with Vietnam in the southern parts of the country, where there is a much higher density of poultry.

Control of influenza A H5N1 is fairly well integrated across animal and human health systems at various levels, from surveillance to response coordination. For example, the Cambodian Communicable Disease Control Department hotlines can be accessed nationally and are often used by villagers to report poultry outbreaks. However, delays in reporting occur³¹⁻³³ as a result of inadequate financial reimbursement for culled poultry, an intervention that has complex and ill-understood cultural as well as economic implications. Unlike neighbouring Vietnam, which has a similar domestic poultry economy, Cambodia has not adopted a poultry vaccination campaign. Contextual factors including the dominance of international donor agencies and concerns from the international community and Cambodia's neighbour, Thailand, which has a large export market, are important considerations that could be explored through policy analysis. Also, this disease response is driven by the perceived risk of an influenza pandemic and its associated costs to Organisation for Economic Co-operation and Development countries, whereas it is ranked much lower among poultry smallholders in Cambodia. The short-term and long-term economic consequences of interventions, whether they be vaccination or culling, remain to be established. This information is likely to be important for evidence-based policy making.

Conceptual framework

Overall, zoonotic and food-borne diseases have an effect across society, with everyone sharing some burden. As in the period of the 19th century when many veterinary and human health systems were initiated, there is a need to re-examine how existing systems are structured, resourced, and managed to create synergies between animal and human health and in the process reduce the effect of zoonotic disease burdens. This process requires an evidence base to effectively, systematically, and strategically inform policy developments.

Advances in public health, veterinary, and human medicine offer benefits, but only respond to part of the struggle that we face. Many stakeholders have important roles in researching, planning, and implementing efforts to prevent, contain, and mitigate emerging infectious diseases at levels that stretch from the community to worldwide. These people work in many sectors and are involved in responding to the challenge as a primary aim, a secondary aim, or as a byproduct. They include, for example, wildlife management, farming and agriculture, veterinary medicine, the pharmaceutical industry, human public health, non-governmental organisations, the donor community, ministerial policy makers, and UN agencies, to name but a few. Moreover, many academic disciplines contribute essential knowledge (eg, climatologists, plant scientists, molecular biologists, economists, political scientists). One's understanding depends on paradigmatic and disciplinary perspective. We need an overarching or grand narrative to link all the sectors and stakeholders, and we need this narrative to have a framework.

Some of the questions that one might pose about the emergence of the global pandemic of influenza A H1N1 2009 illustrate aspects of this intersectoral, interdisciplinary complexity. For example, what upstream economic drivers contributed to the probable emergence of reassortment in hosts? How did globalisation contribute to the emergence and spread of H1N1? How has H1N1 contributed to ensuring that institutional relationships are constructive, effective, and efficient in response to the threat of an influenza pandemic? How has the industrialisation of food production affected the risk of another pandemic? Are the International Health Regulations of WHO and the International Animal Health Codes of the World Organisation for Animal Health sufficiently robust and aligned with each other to support global public health? What virological characteristics allow the virus to jump between species or person-to-person transmission? And how do characteristics of production systems or use of interventions such as vaccines influence these? What elements of veterinary and human health systems are crucially important in prevention of and response to pandemics?

Priority setting, whether research, policy, or implementation, should be based on a firm conceptual grounding with an understanding of the goals (whether

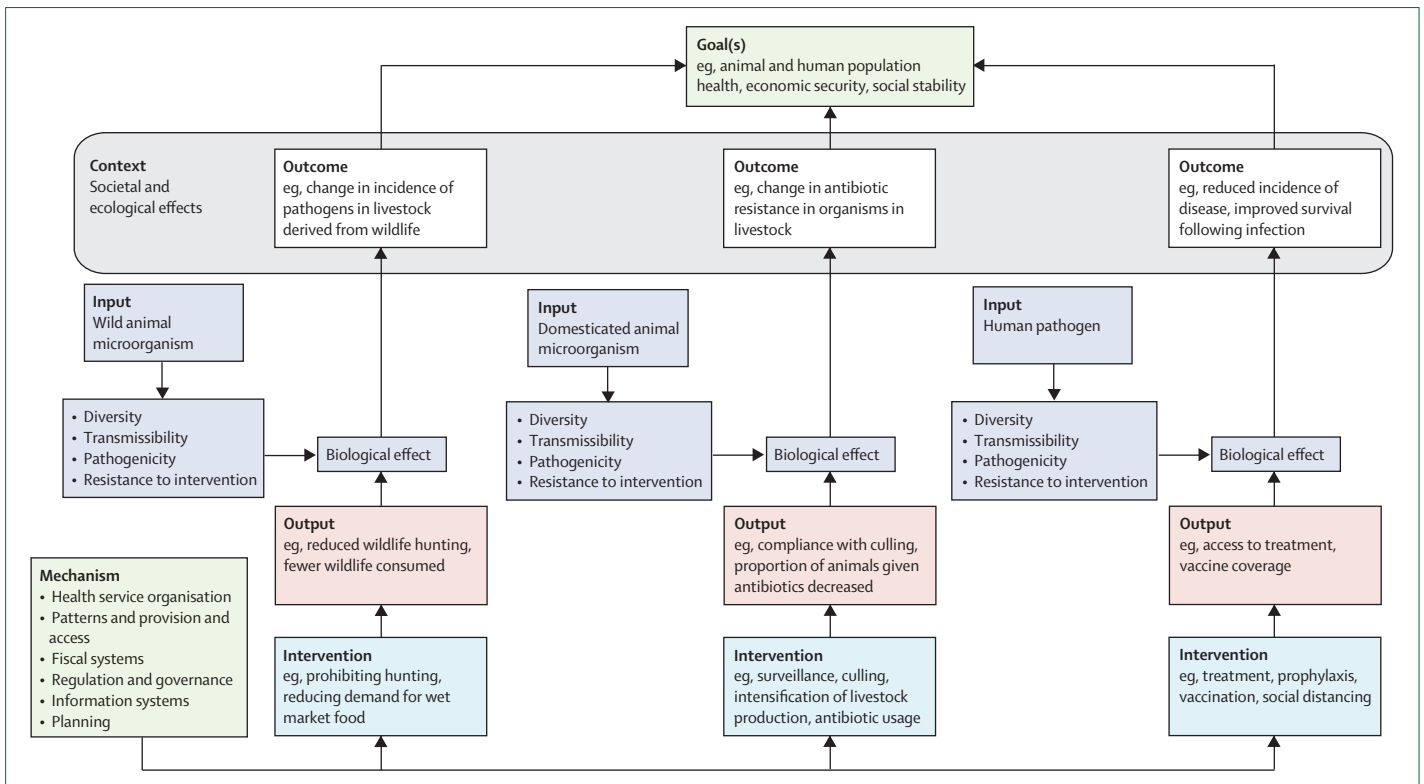


Figure: Schematic representation of a framework for research to inform one-health policy

public health, economic security, or social stability), the scale of the threat, the feasibility of the task in hand, and the likelihood of success, and with a timeline that is appropriate. The public health goal, as with other goals, is informed by sociopolitical principles including equity, sustainability, efficiency, quality, and choice.³⁰ The research agenda will be informed by researchers and others advocating for their particular disciplinary interests. Ultimately, however, decisions on funding and the allocation of resources are political. But they should, and can, be informed by a clear conceptual framework.

The framework that we propose draws on analysis of human and animal health systems during recent years. We illustrate this conceptual framework with case notes from three countries and three zoonoses to draw attention to different elements of the framework (panels 1–3).

The difficult and challenging task of understanding of complexity requires a nuanced framework for research, which acknowledges that technical, economic, policy, and systems paradigms contribute to knowledge, albeit addressing different types of to some extent overlapping research questions. Thus, in the context of research done to support policy, the figure shows in an abstract way the links between possible areas of intervention, and identifies possible areas in which research might be valued by those charged with policy making and effective practice implementation. Research questions could be

formulated at any or several intersections shown in the figure in which knowledge gaps exist to arrive at a coherent and systematically determined set of interdisciplinary research questions that could inform an overarching policy goal.

The proposed framework builds on the work of Pawson and Tilley,³⁴ who suggested five elements or components that can enable researchers to see the links between their research endeavours and others to support the achievement of a policy goal—context, input, intervention, mechanisms, and outputs.

The context is the the political, legislative, cultural, economic, and technological environment within which programmes responding to emerging infectious diseases sit. Context is also the ecological environment—for instance, changing land uses, the effect of climate change, or changes in water management. The context, global or local, can affect policy and practice or be affected by them. Research questions are defined accordingly. For example, do the International Health Regulations support or hinder Indonesia’s efforts to protect global public health? Does Thailand’s contribution to the global trade in industrially produced poultry threaten its public health? Is the poultry vaccination policy in Vietnam influenced by its trading relationship with China? What factors influence policy on beef exports from southern Africa and how do concerns in relation to foot-and-mouth disease affect policy?

Likewise, sectors with primary functions other than health are included in context. Questions might relate to the media, telecommunications, education, criminal justice, and trade agreements. Which public health messages, and through which media channels, are best delivered to rural and urban populations in Tanzania? Does legal trade in exotic animals increase the risk of the emergence of novel infectious diseases?

Input refers to infection and the characteristics of microorganisms and disease. Input might be affected by upstream threats such as the emergence of novel strains of influenza A in animals, or questions related to transmission between individuals. For example, what are the genetic markers that confer ability in microorganisms to jump between species? What are the ecological driving forces that encourage genetic shift? What is the immunological mechanisms that make strains of microorganism highly pathogenic?

Interventions are the actions intended to serve public health (or other policy goal such as economic security or stability in the event of a pandemic). In the case of influenza A H5N1, these interventions might include culling or vaccination of poultry, vaccination of the human population with pre-pandemic vaccines, treatment (or prophylaxis) with antiviral drugs, ventilation of patients with severe disease, and social distancing. There are several questions related to interventions. What is the best combination of interventions to achieve the greatest public health benefit (or economic benefit)? Or does vaccination of poultry effectively reduce transmission of influenza A H5N1? Will poultry vaccination applied at insufficient coverage result in increased selection pressure for new and resistant strains? Or is treatment with one antiviral drug sufficient to prevent development of resistance?

To the frustration of practitioners, policy makers, and health systems and health services researchers, research about how interventions shown to be useful (in clinical trials, for example) are best introduced receives little attention: 0.5% of research funding from the Wellcome Trust and 1.6% of the UK's Medical Research Council's funding was dedicated to health services or systems research in 2006.³⁵ However, the mechanisms by which interventions are delivered and the components of a programme needed to function effectively are important if policy goals are to be achieved.

Research analysing these mechanisms or functions, their interaction within human health systems, and, importantly, their interaction with animal health systems, offers the potential to gain insights into the strengths and gaps in the effective and efficient implementation of interventions. Questions relate to governance, planning, financing and payment, information systems for monitoring, and evaluation and surveillance in relation, for example, to service responses to influenza A H5N1 in poultry or human clusters. A potentially important but neglected area of research should study how human and

animal health-system resources can be mobilised both to support their primary function and to secure potential gains in integrating defined elements of these systems.

The fifth element of the conceptual framework relates to outputs—the proximal consequences produced by programmes. Typically, outputs are the amount, quality, or volume resulting from the interventions. These outputs are public health concepts that can be measured, such as the proportion of animals vaccinated, or the number of people able to access care and receive treatment. They might include notions or measures of equity, acceptability, efficiency, and effectiveness that are the direct result of interventions on populations. These outputs in turn, given biological and epidemiological assumptions, result in outcomes, such as reduced incidence of disease and broader measures of control. Outcomes ultimately lead to overarching policy goals, be they public health, security, or economic, for example.

Conclusion

Although the framework that we set out links coherently research themes that might support public health, the framework does not address policy timelines, the sometimes urgent need for evidence, issues of the feasibility of research, nor the receptivity of audiences and the willingness of research evidence to be acknowledged and embedded within policy-making processes. Such a framework does not nor can it hope to guide priority setting, nor national, regional, and global agendas for research. Other information should guide priority setting and research agendas, including timeline for results, risk of research programme failure, probable public health benefits in the short and long term, and likely beneficiaries. However, we believe that this framework offers a structure around which these issues can be discussed and from which a coherent research agenda might emerge.

Contributors

All authors contributed to the development of the conceptual framework. RC drafted the initial report and all authors subsequently contributed to its further development.

Conflicts of interest

All authors declare that they have no conflicts of interest.

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