Zoonoses and marginalised infectious diseases of poverty: Where do we stand?

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Abstract
Despite growing awareness of the importance of controlling neglected tropical diseases as a contribution to poverty alleviation and achieving the Millennium Development Goals, there is a need to up-scale programmes to achieve wider public health benefits. This implementation deficit is attributable to several factors but one often overlooked is the specific difficulty in tackling diseases that involve both people and animals - the zoonoses. A Disease Reference Group on Zoonoses and Marginalised Infectious Diseases (DRG6) was convened by the Special Programme for Research and Training in Tropical Diseases (TDR), a programme executed by the World Health Organization and co-sponsored by UNICEF, UNDP, the World Bank and WHO. The key considerations included: (a) the general lack of reliable quantitative data on their public health burden; (b) the need to evaluate livestock production losses and their additional impacts on health and poverty; (c) the relevance of cross-sectoral issues essential to designing and implementing public health interventions for zoonotic diseases; and (d) identifying priority areas for research and interventions to harness resources most effectively. Beyond disease specific research issues, a set of common macro-priorities and interventions were identified which, if implemented through a more integrated approach by countries, would have a significant impact on human health of the most marginalised populations characteristically dependent on livestock.

Introduction
Infectious diseases disproportionately affect poor and marginalised populations which are subjected to a cycle of ill-health and poverty. With 60% of human infectious diseases caused by zoonotic pathogens [1] effective public health policy must recognise the importance of interactions between humans and animals [2]. The control of neglected tropical diseases (NTDs) for poverty alleviation has become an increasing priority [3,4], but endemic zoonotic diseases are still largely ignored by public health and veterinary services, despite causing a substantial health burden [2,5]. In contrast, for zoonotic diseases with pandemic potential, such as avian or swine influenza and SARS, the international community has responded vigorously with committed resources, reflecting concerns of potential consequences for higher-income countries.

Many endemic zoonoses have a dual impact on human health and livestock production. Human populations dependent on livestock are not only most at direct risk from zoonotic disease but are most vulnerable to the indirect impacts on health of reduced production on livelihoods and food security, which exacerbates the poverty cycle. It is estimated that over 600 million people globally are livestock-dependent, and represent up to 70% of the population in the most marginal areas [6]. These communities are typically isolated from political processes, communication, education and health care, due to geographic, economic and socio-cultural factors, which exacerbate problems of awareness and health-care delivery.

Effective surveillance and control of zoonotic diseases usually requires multisectoral collaboration involving the human health, veterinary, agricultural, educational,
wildlife and environment and sanitation sectors. It remains a considerable challenge to coordinate these different interests, and to achieve collaboration in policies, priorities, resourcing and communication at the national and international levels.

Over the last decade significant work on zoonoses has been undertaken; as a result policy has been articulated on prevention and control of individual neglected zoonotic diseases as a generic concept by WHO and partners at three meetings convened since 2005 [2].

In 2009 WHO UNDP World Bank Special Programme as part of its stewardship function established a Disease Reference Group to address with stakeholders’ priority research issues for Zoonotic Diseases and other marginalized infections of poverty (Figure 1). This paper summarizes the major findings of DRG6.

Burden of disease
There are four reasons why zoonotic diseases have been even more neglected than other neglected tropical diseases. Firstly, there is a lack of reliable qualitative and quantitative data on disease burden in endemic countries. This must go beyond the traditional disability-adjusted life year (DALY) assessment to measure and incorporate monetary and health burdens resulting from production losses due to disease in animals [5].

Secondly, clinicians and policy makers often have little knowledge of zoonotic causes of human disease [7] that can be confused with more widely recognized causes of common syndromes including febrile illness, or respiratory or diarrhoeal diseases. Zoonoses presenting as non-specific febrile illness, for example brucellosis, [8] leptospirosis, [9] rickettsiosis and Q-fever, [10] are often misdiagnosed as malaria [11,12]. There is also surprisingly little awareness that long-term sequelae of zoonoses include cancer (food borne trematodiases) or neurological disorders (neurocysticercosis).

Thirdly, the diagnosis of many endemic zoonoses requires capacities that may only be available in referral hospitals and reference laboratories, if at all [13]. For zoonotic schistosomiasis, neurocysticercosis, echinococcosis, opisthorchiasis and clonorchiasis, useful diagnostic imaging techniques are either unavailable or too expensive; similarly, early diagnosis of many bacterial zoonoses depends on sophisticated microbiological or molecular diagnostic methods typically not available to those at greatest risk.

Fourthly, data collection systems for zoonotic diseases are often fragmentary, collected independently by the public health, veterinary or wildlife sectors and recorded and reported separately, if they are recorded at all, resulting in a failure to identify disease outbreaks. They often occur in environments beyond the reach of formal health facilities, education systems and livestock services. Hence, reporting and certification of deaths, a prerequisite for accurate disease burden estimates, often do not exist, contributing to limited awareness and lack of interest and political will to study and control these diseases.

| 1. Helminth Infections          |
|---------------------------------|
| - Taeniasis/Cysticercosis      |
| - Echinococcosis               |
| - Food-borne Trematodiases     |
| - Zoonotic schistosomiasis     |

| 2. Protozoan Infections        |
|--------------------------------|
| - Cryptosporidiosis            |
| - Toxoplasmosis                |

| 3. Viral infections            |
|--------------------------------|
| - Rabies                       |

| 4. Bacterial Infections        |
|--------------------------------|
| - Brucellosis                  |
| - Certain enteric bacterial pathogens |
| - Bovine Tuberculosis          |
| - Anthrax                      |

Figure 1 DRG6 targeted diseases.
Standardised measures of public health burden, such as the DALY, are only currently available for some of the endemic zoonoses, such as cysticercosis, [14] echinococcosis, [15] human African trypanosomiasis [16] and rabies [17]. Such data have contributed to policy change but information on chronic impacts and non-specific sequelae of untreated zoonoses remains inadequate. A new metric that incorporates social and economic outcomes is needed to assess the societal impact of zoonotic diseases, and provide the evidence base for objective decision-making and priority-setting.

**Intervention and control of endemic zoonotic diseases**

Community-led approaches that empower families and communities to assume responsibility for aspects of disease control can result in feasible and cost-effective strategies to control and, in some cases, eliminate endemic zoonoses. Experience from other neglected disease programmes demonstrates the success of these approaches. For example, the African Program for Onchocerciasis Control (APOC), directly involves communities in decision-making, implementation and monitoring of mass drug administration programmes [18]. Community-led Total Sanitation (CLTS) is another innovative strategy for mobilising communities to completely eliminate open defecation, with sustainable impacts on enteric diseases [19]. Empowering marginalised communities through community-directed interventions offers great promise for tackling endemic zoonoses, and should be encouraged and supported by local and international technical and financial resources.

Despite these successes, an intervention vacuum still exists for many zoonoses - even when the outcome and cost-effectiveness of interventions are known - because of entrenched perceptions of health impacts and priorities. Local neglect is sometimes exacerbated by international disregard, with international priorities focusing on diseases that pose an emerging global threat, such as influenza A H5N1, but are of limited importance to impoverished communities in comparison to endemic zoonoses. Despite the promise of the Alma Ata Declaration [20] to attain ‘health for all’ by the year 2000, marginalised communities still suffer from poor access to health technologies and services, which continues to undermine all disease control efforts.

"One Health"
The ‘One Health’ philosophy, to forge inclusive collaborations between human and animal health professionals, and related environment and agricultural disciplines, currently dominates much of the discussion of zoonotic diseases. While the concept in theory has been widely embraced progress in practice to ensure genuine integration lags behind, not only across academic disciplines, but also with respect to integration of research with policy. Too often research questions are formulated without input from policy-makers, when effective ‘buy-in’ could be achieved by integration and iterative engagement throughout the research development cycle [21-23].

A clear advantage of One Health is that interventions in animal populations can result in public health and societal benefits more cost-effectively than just interventions in humans. For example, although human rabies can be prevented through timely post-exposure prophylaxis, the high cost of human vaccination places a significant burden on health budgets, in contrast to mass vaccination of domestic dog reservoirs. Similarly, a comprehensive control strategy in China based on interventions to reduce the rate of transmission of *Schistosoma japonicum* infection from bovines and humans to snails has been highly effective, [24] and has now been adopted by the Chinese government as the national strategy for the control of schistosomiasis. In Uganda, sleeping sickness caused by *Trypanosoma rhodesiense* is being controlled by the mass chemotherapy treatment of the cattle reservoir and insecticidal treatment to control tsetse populations which also reduces tick populations [5,16].

Integrated, trans-disciplinary approaches envisioned under One Health are more likely to be adopted when they provide added value. Many opportunities exist for adding value through shared resources and expertise, for example, in zoonotic disease surveillance. Investments to enhance laboratory capacity to diagnose avian influenza provided a useful opportunity to enhance the surveillance of other zoonotic diseases but there are few examples of this for endemic zoonoses. The widespread perception that testing human and animal samples must be conducted in separate laboratory facilities, for which there is little rationale, increases the cost for diagnostic facilities, and is a major barrier to integration of disease surveillance efforts between different Ministries.

Whereas One Health aims to expand our thinking beyond the confines of disciplinary silos, the way forward will not necessarily be straightforward. Traditional roles and responsibilities may need to be relinquished while financial control is shared or ceded entirely to another sector. But, potential health gains for the most impoverished surely make these changes worth pressing for.

**Macro research priorities and recommendations to policy makers**

DRG6 identified a set of macro-priorities for facilitating interactions between applied researchers to promote necessary intervention research on zoonotic diseases of marginalised populations (Figure 2).
1. There is a need to develop a comprehensive methodology for calculating the societal burden of disease attributable to zoonoses recognising that a high proportion of the population of rural (and often urban) populations in least developed countries depends on livestock.

2. More studies are required to generate data on the costs, cost-benefits and cost effectiveness of interventions for endemic zoonoses. Such studies should also incorporate the economic effect of animal disease as an indirect contributor to poverty through the impact on nutrition, loss of meat and milk products and livestock as a capital asset.

3. There is a need for operational and systems research to identify reasons for the limited communication and interaction between the key sectors - health, agriculture, livestock - particularly in countries where a large proportion of the population is dependent on livestock.

4. There is a need to evaluate effective community-based approaches and interventions for zoonotic disease, drawing on the experience and success of initiatives for water and sanitation improvements, mass drug delivery and community-based health care.

5. Experiences from separate initiatives in different geographic and epidemiological settings need to be evaluated to ensure that such experiences are amplified and synergised, with potential for integration between programmes.

6. Investing in systems for collection of reliable data on disease/infection incidence and prevalence from both veterinary and medical sectors is recognised as a priority, both for measurement of disease burden and for evaluation of control measures.

7. Investment in endemic zoonoses in least-developed countries would provide multiple benefits, not only improving health and livelihoods of marginalized communities, but also reducing threats and enhancing response capacity for emerging zoonoses that pose a threat to the global community.

8. Effective lessons are often best learned by implementation of strategies (such as the onchocerciasis control program), with research to evaluate factors leading to success measured by effectiveness and cost-effectiveness embedded within programme implementation.

9. As endemic zoonoses disproportionately affect impoverished and marginalised populations, investments need to be specifically targeted to overcome barriers to health care in these communities, including isolation, population movement or migration, social or political unrest, and conflict.

Investments in disease burden assessments for zoonotic diseases are essential to provide an advocacy base to highlight their importance. A prerequisite is country prioritisation and commitment from different sectors, including finance, national research institutions, and political commitment to stable policy supplemented by long term international support. This will allow development of national guidelines that establish and sustain veterinary public health units, and clarify their role in tandem with the human health system. These will improve public health care for, and actually beyond, the neglected zoonotic diseases.
List of Abbreviations
A HSN1: Highly pathogenic avian influenza, APOC: African Program for Onchocerciasis Control, CLTS: Community-led Total Sanitation, DALY: Disability-adjusted life year; DRGG: Disease Reference Group on Zoonoses and Marginalised Infectious Diseases; GSK: GlaxoSmithKline; TDR: The Special Programme for Research and Training in Tropical Diseases, UNDP: United Nations Development Programme; UNICEF: The United Nations Children’s Fund, WHO: World Health Organization

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Authors’ contributions
GK drafted the first version of the manuscript based on the work of the whole Disease Reference Group which was subsequently redrafted and edited with additional material from DHM, DPM, SC and OK and further reviewed by ZH. All members of the Group reviewed the final manuscript and their signatures are below

Competing interests
DHM is a Senior Professorial Fellow in the Center for Neglected Tropical Diseases, in Liverpool School of Tropical Medicine, which receives funding from the UK Department for International Development and GlaxoSmithKline (GSK) in support of the Global Programme and Global Alliance for the Elimination of Lymphatic Filariasis. He also has a consulting agreement with Pfizer and is Chair of WHO/TDR Disease Reference Group on Zoonoses and other marginalized infectious diseases of poverty. All other authors declare that they have no Conflict of Interest

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