

Zoonotic Diseases: The Forgotten Ones?

About 75% of the new diseases that have affected humans over the past 10 years have been caused by pathogens originating from an animal or from products of animal origin. Even though many of the zoonotic diseases have the means to spread over long distances and to become global problems (there is nowhere to hide as a result of international trade and travel), limited reliable qualitative and quantitative information on the burden of zoonotic diseases is available at the moment. There are 'high profile' diseases such as AIDS, tuberculosis and malaria – and "the others", some neglected zoonotic diseases which seem to have been almost forgotten, at least in terms of allocation of funding for research and collective action for control. But, as the experts say, one needs a problem to be quantified, otherwise it is difficult to ask the policy-makers for attention and, more importantly, funding. And as the largest outbreak of Ebola virus ever recorded has proven, when there isn't a global threat, there are no licensed drugs and vaccines.

According to WHO's 'Technical report of the TDR Disease Reference Group on Zoonoses and Marginalized Infectious Diseases of Poverty', of some 1400 species of infectious disease pathogens of humans, nearly 60% are derived from animal sources, hence the importance of recognising the role of livestock, companion animals and wildlife in the interactions between animals and humans. The WHO report represents the output of the *Disease Reference Group on Zoonoses and Marginalized Infectious Diseases of Poverty (DRG6)*, which is part of an independent think tank of international experts, established and funded by the *Special Programme for Research and Training in Tropical Diseases (TDR)* in order to identify key research priorities through review of research evidence and input from stakeholder consultation.

The review points out that zoonotic diseases, although biologically diverse, share common characteristics associated with the conditions under which people live in the world's poorer countries. The number of people who are directly dependent on livestock is estimated at somewhere around 600 million, which accounts for nearly a tenth of the world's population. Furthermore, exactly in those environments where zoonotic diseases represent the highest burden, health systems are weak, fragmented or not accessible to populations; there is inadequate surveillance and reporting of disease outbreaks, a situation exacerbated by inadequate diagnostic and therapeutic services. The efficacy of drugs for both humans and animals is not effectively monitored as a result of lack of control of imports and the widespread sale of ineffective or counterfeit products through an unregulated private sector.

It has become clear now that effective disease control for zoonotic diseases requires multisectoral collaboration between the human and veterinary health, agricultural, and water and sanitation sectors. Interventions are generally directed at both the human and the animal host, and the

approaches may be biomedical (drugs or vaccines), vector or intermediate host control, environmental, legislative (inspections) or educational. Integration must also happen across the human health and animal health sectors. The WHO report draws attention to the fact that control measures are already in place for diseases such as *rabies*, *anthrax*, *echinococcosis*, *cysticercosis* and *brucellosis*. There are several examples of major successful control programmes indicating that national, regional or even global control is (at least theoretically) possible; unfortunately, the effectiveness of these interventions in reducing human infection for some of the diseases is still unknown.

It is acknowledged that more research should be conducted to improve and develop new disease control tools. However, a tough problem seems to be adapting the diagnostic, curative, preventive and monitoring tools to the condition prevailing in developing countries and recognising the constraints of financing, affordability and delivery. And whilst there is unprecedented interest in research on diseases of the poor, the appeal of the research on zoonoses is considered still disproportionately small. Over and above the report, the needed research should be undertaken cooperatively at the international level, be multidisciplinary, involve both human and animal health research groups, and engage relevant stakeholders.

Apparently, for most diseases there is a need for development of affordable, rapid and reliable diagnostic tools, which should also be considered in the context of surveillance and monitoring and evaluation tools; a need for development of innovative strategies for disease surveillance, including the use of sentinel populations, both human and animal, adopting new approaches in communication technology and analytical tools (e.g text/data mining such as the USDA livestock disease alerts), participatory approaches such as the use of abattoir workers for surveillance and mobile phone reporting.

No doubt, there is a need for stronger advocacy and for a focused research agenda directed at improved approaches to control zoonotic diseases. In a review paper published recently in *PLoS Neglected Tropical Diseases*, a team of researchers from the *Centre for Infectious Diseases and Division of Pathway Medicine, School of Biomedical Sciences, College of Medicine and Veterinary Medicine, The University of Edinburgh, Edinburgh, United Kingdom* examined the extent of high-level political advocacy that has taken place for the NZDs since the inception of the WHO in 1948.

According to the researchers, years of advocacy for the neglected tropical diseases (NTDs) have succeeded in focusing the world's attention on these diseases of the poor, resulting in the 2012 "London Declaration" and more recently, the *World Health Assembly Resolution WHA66.12 on NTDs* in May 2013. Control of the endemic neglected zoonotic diseases



(NZDs) would certainly benefit from such a campaign, which needs the support of a global community. As to the perception that the NTDs and NZDs have been historically “neglected” by decision-makers in terms of their political profile and allocation of funding for research, the study shows that such neglect is largely driven by the fact that their burden is often solely found in developing countries, where the majority of effort in recent years has focused on HIV/AIDS, tuberculosis, and malaria. Then again, it is also difficult to gather information about the extent and impact of these diseases of the poor due to ineffective diagnostic capacity and poor health delivery systems, hence the underestimation of disease burden. Well, unless a problem can be quantified, it is difficult to argue for funding and attention by policy-makers.

The passing of the recent *World Health Assembly Resolution WHA66.12* is seen as a key step in the advocacy process for the neglected tropical diseases, acknowledging the research and efforts of those involved in their control. Five of the eight neglected zoonotic diseases — *cysticercosis*, *rabies*, *echinococcus*, *human African trypanosomiasis*, and *leishmaniasis* — are now included in the list of NTDs identified by *Resolution WHA66.12*. However, *anthrax*, *bovine tuberculosis*, and *brucellosis* are still lacking the high-level advocacy required to rally political support for their control in endemic countries. Global advocacy for control of the NZDs as a whole would similarly benefit from adoption of a *One Health* approach as is promoted for the NTDs under *WHA66.12*.

The priority is ... to prioritise

At the *Centre for Public Health and Zoonoses, Department of Population Medicine, Ontario Veterinary College, University*

of Guelph, Guelph, Canada, Victoria Ng and Jan M. Sargeant used a well-established quantitative method in market research (CA), to identify the relative importance of 21 key characteristics of zoonotic diseases for their prioritisation in Canada and the US. As their study shows, although zoonotic outbreaks are a significant burden of disease in North America (for example, outbreaks of *West Nile virus*, *SARS*, *H1N1 influenza* and *Lyme disease* in the past decade), there are limited resources available for their control and prevention, making the development of a scientifically driven framework for the prioritisation of zoonoses essential.

Apparently, everyone agrees on the need to prioritise zoonoses, to establish a universally accepted priority list, but there are a lot of challenges to the process: it is not easy to compare the overall public health impact of zoonoses when they vary so significantly in incidence, clinical manifestations, control measures, transmission potential and socio-economic impact in humans and animals. Additionally, there are multiple stakeholders involved, each with their own prioritisation objectives and beliefs, and there is even a lack of agreement concerning prioritisation methodologies .

The principle behind the novel quantitative approach used by the researchers, Conjoint Analysis (CA), is that a product (goods or service) can be described by a set of characteristics and the extent to which an individual values a product is determined by the level of each of those characteristics and the combination of those characteristics together. A CA study presents individuals with competing products containing both desirable and undesirable characteristics and forces them to state a preference, usually as a choice between products. In doing so, they make a trade-off between the desirable and undesirable characteristics in

the products through their choices, revealing the true value of each characteristic relative to each other.

In the context of zoonoses, a disease can be treated as a product described by a set of disease criteria (characteristics), and the value of the disease can be determined by the level and the combination of those criteria.

For their study, the researchers recruited 707 participants from Canada and 764 from the US from relevant professional disciplines that would provide some prior knowledge of infectious diseases: epidemiologists, public health practitioners and policy-makers in the human and animal health disciplines at the local, provincial/state and national level, academic and practising physicians and veterinarians, infectious disease researchers, human and animal health laboratory microbiologists, pathologists and technicians and registered nurses. This study represents the first zoonoses prioritisation exercise involving public health, veterinary and medical professionals in North America, and the results illustrate that CA can indeed be used as a tool for the prioritisation of zoonoses, particularly as a method to overcome subjective weighting and scoring of disease criteria.

Although differences were observed between countries, both groups considered incidence of the disease in the last five years in humans and case-fatality in humans to be the most influential criteria in the decision to prioritise zoonoses. Similarly, both groups judged high-risk groups in animals to be the least influential criteria in the decision to prioritise zoonoses.

Canadian professionals were more strongly influenced by severity of disease in humans, economic burden in humans, duration of illness in humans, case-fatality in animals and high-risk groups in animals. US professionals were more strongly influenced by incidence of the disease in the last five years in humans, incidence of the disease in the last five years in animals, disease trend in the last five years, and economic and social burden on trade in animals.

Canadians deemed rabies to be the most important of the zoonoses to prioritise, followed by *Nipah virus encephalitis*, *H1N1 influenza*, *variant Creutzfeldt-Jakob disease* and *listeriosis*. These were also the top five priority diseases in the US, ranked in a different order. There was also consensus between the bottom five diseases on the priority list with three of the five least important diseases appearing in both priority lists.

Canadians considered *leishmaniasis*, *Hendra virus*, *salmonellosis*, *cryptosporidiosis* and *Crimean-Congo hemorrhagic fever* of higher priority than Americans. Conversely, Americans considered *babesiosis*, *anaplasmosis*, *paralytic shellfish poisoning*, *coccidioidomycosis*, *cysticercosis* and *Rocky Mountain spotted fever* of higher priority than Canadians. According to the researchers, this can be explained by regional differences in both human and animal disease incidence: for example, *babesiosis* does not occur naturally in Canada but is endemic in the US, *anaplasmosis* is extremely rare in Canada but endemic in the US, and *Rocky*

Mountain spotted fever is found only in Western Canada but is distributed throughout the US. Regional differences in disease trend also likely contributed to different rankings, for example, *paralytic shellfish poisoning* has been increasing in the US but is stable in Canada.

Seven of the top ten diseases were common across all groups (*rabies*, *Nipah virus encephalitis*, *Ebola virus hemorrhagic fever*, *Marburg hemorrhagic fever*, *H1N1 influenza*, *variant Creutzfeldt-Jakob disease* and *listeriosis*) while five of the bottom ten diseases were common across all groups (*bovine tuberculosis*, *cyclosporiasis*, *Dengue fever*, *La Crosse encephalitis* and *St Louis encephalitis*). Despite more similarities in demographics, model fit, disease criteria importance scores and part-worth utility values between the two public and the two professional groups, there was more uniformity across priority lists between the Canadian public and Canadian professionals and between the US public and US professionals than between the Canadian and US public groups and between the Canadian and US professional groups.

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References

1. WHO — “Research Priorities for Zoonoses and Marginalized Infections – Technical report of the TDR Disease Reference Group on Zoonoses and Marginalized Infectious Diseases of Poverty”
2. “Neglected Zoonotic Diseases — The Long and Winding Road to Advocacy” - Hayley E. Mableson, Anna Okello, Kim Picozzi, and Susan Christina Welburn*, Centre for Infectious Diseases and Division of Pathway Medicine, School of Biomedical Sciences, College of Medicine and Veterinary Medicine, The University of Edinburgh, Edinburgh, United Kingdom. *PLoS Negl Trop Dis*. Jun 2014; 8(6): e2800. Published online Jun 5, 2014. doi: 10.1371/journal.pntd.0002800 PMID: PMC4046968
3. “Quantitative Approach to the Prioritization of Zoonotic Diseases in North America: A Health Professionals’ Perspective”, by Victoria Ng and Jan M. Sargeant. Centre for Public Health and Zoonoses, Department of Population Medicine, Ontario Veterinary College, University of Guelph, Guelph, Canada and Université Catholique de Louvain, Belgium. *PLoS One*. 2013; 8(8): e72172. Published online Aug 21, 2013. doi: 10.1371/journal.pone.0072172 PMID: PMC3749166