Linking animal and human health burden: challenges and opportunities

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Summary

Quantifying the human health impact due to poor animal health outcomes represents a complex challenge. Using the disability-adjusted life year (DALY) metric as an endpoint, we discuss how animal health outcomes can impact humans through three key processes: directly through zoonotic disease, indirectly via changes in yields and their impact on nutrition and wealth, and finally through indirect features associated with the agricultural industry, whether pharmaceuticals, or climate change. For each we discuss the current state-of-the-art and feasibility of global DALY-associated estimates.

For zoonoses, existing frameworks already consider some key pathogens; ensuring completeness in pathogens considered and consistency in methodological decisions is an important next step. For diet, risk factor frameworks enable a calculation of attributable DALYs, however there remain important economic methodological developments to ensure that local production changes are appropriately mapped to both local and global changes in dietary habits. With wealth-related impacts there remains much method development to happen. Industry-related impacts require a focus on key research topics such as attribution studies for animal antimicrobial resistance

contributing to human outcomes; with climate change, identifying how much of associated emissions by the industry are amenable to change should animal health outcomes improve is a critical next step.

Allocation of finite funds to improve animal health needs to consider the downstream impact on humans too. Leveraging DALYs enables comparisons with other human health-related decisions, and would represent a transformative way of approaching animal health decision making should the obstacles in this article be addressed and new methods developed.

Keywords

Antimicrobial resistance – Climate change – DALYs – Disability-adjusted life years – Global metrics – Nutrition – One Health – Zoonotic diseases.

Introduction

The means by which poor animal health can impact humans is many and varied; whether the direct impacts of transmission of pathogens from infected animal hosts into humans, the role livestock have in being disease reservoirs, or indirect aspects of animal health and agricultural outputs with the consequences they have on individual-level and population-level diets and wealth. Similarly, the livestock industry itself, and associated pharmaceutical activities, can manifest in downstream changes to human health outcomes.

Over the last thirty years or so, metrics such as the disability-adjusted life year (DALY) have proven to be a powerful perspective in evaluating decisions affecting human health. The DALY measure grew out of the desire to quantify and equate conditions that not only cause mortality, but also those with high morbidity, such as chronic diseases that impact individuals over decades of their life [1,2]. The DALY consists of the sum of the years of life lost (YLL) and the years lived with a disability (YLD) due to a specific cause. YLLs refer to prematurely lost years due to death, calculated by subtracting the age of death from the expected age limit based on a model life table [3]. YLDs are the measurement of morbidity and reflect the number of healthy years that a person loses due to illness. An essential part of this component is disability weights (DWs) where each health state related to an illness is assigned a value between zero (perfect health) and one (equivalent to death) [4].

Studies such as the Global Burden of Disease (GBD) and the Foodborne Disease Burden Epidemiology Reference Group by the World Health Organization (FERG/WHO) have demonstrated the ability for DALYs to be used to calculate the burden of disease at national, regional, and global levels for all causes of death and disability, and demonstrate to what extent these can be attributable to certain risk factors (such as tobacco smoking) or risk pathways (such as food safety) [5,6]. In examining the effects of unfavourable animal health outcomes on humans, it is essential to explore how we can convert our animal-related metrics into alterations in DALYs. This translation facilitates comparisons within the larger context of human health.

A key objective of the initial phase of the Global Burden of Animal Diseases programme is to investigate the feasibility of quantifying the various mechanisms by which human health is adversely impacted by animal diseases. While other features of impact, such as the cost-of-illness associated with human disease are important, we focus here on DALY-based assessments. As a first step, we aimed to produce a framework whereby these various pathways could be accommodated and impact a human DALY (Figure 1). Here we emphasise three core features of the livestock agricultural system – those animals currently infected with a pathogen with human transmission capabilities; the subsequent translation of animal infections (both zoonotic, and only afflicting livestock) into production losses that could be either consumable commodities or goods for sale; and the work of the agro-sector itself, with pharmaceutical products used to support growth and treat disease, emissions, effluent, and land-use changes all associated.

We identified key human-health related endpoints of primary interest, including individuals infected with specific zoonotic pathogens, as well as populations experiencing changes in health outcomes as a consequence of changes to their wealth or diet, or the impact that agricultural systems have on the land surrounding human habitats and the broader environment. Each of these pathways represents a unique challenge with respect to necessary data, appropriate methodologies, and feasibility of quantifying their role in affecting human health, both negatively and positively, at a global scale. In the following sections, we will focus on specific linkages and discuss the current opportunities and challenges present in their possible quantification.

Direct impacts on human health due to zoonotic disease

Zoonoses encapsulate a diversity of pathogens, associated with a variety of health outcomes. Indeed, there are different types of zoonotic diseases, including those originating from wild animals, vector-borne diseases and foodborne illnesses. In this article, we have decided to group them for the sake of a comprehensive approach. DALY-based burden estimates therefore provide an essential tool for comparing their direct impact on population health.

A recent review examined the different existing DALY estimates for a selection of 26 zoonotic diseases, selected from a summary of national prioritisation exercises [7]. The review revealed that the landscape of burden estimates for these diseases remains scattered and incomplete. Several diseases lack estimates: West Nile virus, avian influenza, Marburg virus disease, plague, Lassa fever, and glanders. Conversely, numerous estimates were retrieved for non-typhoidal salmonellosis (24 studies), campylobacteriosis (22 studies) and toxoplasmosis (16 studies). Globally, discrepancies emerged between the frequency at which countries prioritised diseases and the number of estimates. For example, rabies, the most frequently mentioned disease in prioritisation exercises (highlighted 94 times), had only 12 associated studies, while *Campylobacter* spp., stated five times as a priority, had a higher number of studies. Some of these diseases are also part of other domains such as food safety, antimicrobial resistance (AMR), diarrheal disease, and maternal or neonatal health, which might contribute to their higher number of estimates. Only 16 diseases detailed the burden of disease at the global level, leaving diseases such as anthrax and Q fever without estimates despite national-level prioritisation. Indeed, most estimates were conducted at a national or subnational level, with limited global-level data available.

Two international initiatives calculated global-level DALYs, GBD and FERG/WHO [5,6]. While these projects encompass zoonotic diseases within broader categories, such as foodborne or diarrheal diseases, neither project exclusively focuses on zoonoses. The GBD has a wider scope, whereas FERG/WHO estimates DALYs for foodborne diseases, encompassing transmission routes. The WHO/FERG approach includes a structured expert elicitation for exposure route-specific proportion [8]. Other methodological differences are incidence-based *versus* prevalence-based and outcomes-based *versus* pathogen-based approaches. The GBD 2019 adopts an outcome- and prevalence-based approach, assigning disease burden to clinically defined categories in the reference period, resulting from past and present incident events [5]. On the contrary, FERG/WHO employs a pathogen- and incidence-based approach that captures the major outcomes attributable to a specific pathogen, including long-term sequelae [6]. These differences impede direct comparisons of the results of both studies, but such focuses, promote the need for ongoing source attribution research to better tease apart how specific pathways are used by pathogens.

Methodological decisions and assumptions can hinder cross-study comparability and interpretation in general. This bears implications, including misjudging disease burdens when comparing estimates from various sources and diminishing their relevance for policymakers as prioritisation tools. For instance, comparing different brucellosis burden of diseases estimates revealed methodological differences [9]. Some studies omitted mortality estimates (due to data scarcity or the assumption that brucellosis is not fatal). Also, studies used disease models with variable health states and corresponding disability weights. Variations in disease durations also emerged, ranging from 2 weeks to 4.5 years.

DALY estimates demand high-quality data for all the different parameters, posing challenges for many zoonoses due to data gaps. Coping with uncertainties and data gaps significantly influences estimates, with global studies, like the GBD and FERG/WHO study, addressing missing data and uncertainty using extrapolation and stochastic models. These choices impact the estimates produced, and could lead to underestimating or overestimating disease burden, an issue common in estimating zoonotic disease burden. However, not all local studies consider uncertainty and missing data. A recent review of the methodological choices for cysticercosis revealed that only four of eight national or subnational studies included scenario analysis to reflect epidemiological parameter uncertainty or preferences for time discounting and age weighting [10]. Similarly, in the review analysing brucellosis burden of disease studies, four out of thirteen studies conducted a scenario analysis using different life expectancy tables, discounting and age weighting and different degrees of underestimation [9]. Uncertainties and data gaps can be expected in all pathways connecting animal to human health. The experience with addressing these issues in studies assessing the direct impacts of zoonotic disease on human health can serve as a valuable guide for other pathways where methods have been less well established.

While global estimation of the direct impact of some zoonotic disease already occurs, at a global scale, we see that future efforts should aim to converge not only in terms of the composition of pathogens considered, but also key methodological decisions and parameter values that influence model-to-model differences just as much as different data inputs do. The highlighted reviews underscore the importance of enhancing routine reporting, collecting improved national data, and conducting further research on parameters essential for estimating disease burdens, including source attribution estimates.

Agro-system related impacts: considering antimicrobial resistance and climate change

Antimicrobial resistance is on the rise and a leading global health threat, with estimates indicating 1.27 million human deaths worldwide in 2019 due to bacterial AMR alone [11]. AMR resistance genes can spread within and between microorganism species, which facilitates their transmission across human, animal, and environmental domains. AMR links human and animal health directly, via the transmission of resistant pathogens or mobile genetic elements carrying resistance genes through consumption of animal products or direct contact between humans and animals. Animals can also indirectly contribute to the rise of AMR in humans, for example via the excretion of antimicrobial residues into the environment following antimicrobial use (AMU), which fuels the development of environmental resistance reservoirs [12,13]. These links are especially relevant when considering that there are several antibiotic classes that have been classified to have high or critical importance in both the human and animal sector, such as 3rd and 4th generation cephalosporins or fluoroquinolones [14,15]. There is evidence that AMU-reducing interventions in livestock have a decreasing effect on AMR in humans and associations between AMU and AMR in different livestock species and humans have been found for many pathogen-antibiotic drug combinations [16,17].

However, to quantify the relative importance of animals for human AMR, sound data from both domains is needed. As outlined in the WHO global action plan on AMR resistance, integrated surveillance programmes are key to this [18]. To guide future research and data collection efforts, it is thus important to map out the current status of data availability for AMR in the animal and human sector around the globe, as well as opportunities and hindering factors in linking them. Source attribution studies and risk assessments are important avenues for assessing the extent of the contribution of animals to human AMR and help provide specificity in the animal sources that are most relevant in AMR transmission [19].

Climate change similarly represents an important consideration that is only relatively recently starting to be quantified in a manner amenable to integration into DALY frameworks. Estimates of global emissions associated with the livestock industry are being produced, however, determining to what extent these emissions are compounded by animal health losses remains to be determined. DALY estimates for all climate-sensitive conditions have not yet occurred. While for specific diseases, we have seen estimates showing how different climate pathways may alter the range and prevalence of certain conditions, within the GBD, treating temperature as a risk factor, a variety of non-communicable conditions have been evaluated as having currently attributable burden from non-optimal temperature [20,21]. As such there exists no singular-resource for characterising all possible impacts.

Both these aspects of livestock production demonstrate the complexity of how some features related to animal health impact human health outcomes. Even within the animal health space though it is not necessarily clear how mitigating animal health losses will directly impact industry-related mechanisms for changing human health.

Nutrition and wealth as key pathways for indirect impacts on human health

In contrast to zoonotic disease, where global estimation pathways exist, indirect impacts have not been considered at a global scale. Given the key role that livestock have served throughout human civilisation, it is important to consider the relation that poor animal health has on subsequent human consumption patterns, and ability to contribute to local and global economies. Whether livestock die prematurely, are culled to mitigate further spread, or are afflicted by disease so as to reduce yields, or the quality of these yields, much animal health loss can be translated into some sort of commodity. Either through direct estimation leveraging economic approaches, or through more simulation-based assessments of how perturbations in local, regional, and global commodities result in the redistribution of existing resources, and possible gaps where there is a deficit, we can translate animal health loss into changes in available food, individual-level wealth, and national-level economic measures [22].

Existing DALY-related frameworks typically consider diet as a metabolic risk factor, leveraging relative risks calculated for intake of specific macro- and micronutrients, as well as foodstuffs such as red meats, and pair these with consumption surveys to evaluate the prevalence of certain consumption patterns, to derive a summary exposure value that enables a calculation of a population attributable fraction [23,24]. Given these requirements, should we be able to provide estimates of the change in yield, we can initiate a series of calculations to translate this into DALYs associated with this loss of yield. Addressing yield losses and altering subsequent diets has both the opportunity to mitigate health loss due to undernutrition, or exacerbate existing poor diets by allowing further overnutrition – frameworks like the GBD can estimate the opportunity space for gains, or the negative consequences of continued excesses however, using the DALY.

With risk factors that are micronutrients related, we need to leverage food composition tables to convert units of product into units of nutrients [25]. While global production losses can be used to determine a total amount of lost nutrients, the potential for that loss to change the health of a specific population, in the absence of strong assumptions, requires the leveraging of global supply chain models, and further diet intake statistics – due to wastage, overconsumption in some communities, and global inequities in trade, it is not necessarily true that food losses in a specific location translate into poor diet related health outcomes in that same community [26]. Different communities are more or less dependent on local food production chains, and if we do not accommodate that, we can produce statistics where poor animal health in highly mechanised livestock production systems could be naively translated into possible health losses in the local community when in reality those losses mean reduced exports to other communities reliant on imported produce.

Beyond consumption, livestock and their outputs can play an important role in wealth generation for people and households, estimated to support the livelihood of 1.3 billion people worldwide [27]. Livestock can contribute with food, income, draught power, as an input to other agricultural activities, and can provide insurance and asset storage. In low-and-middle income countries, livestock keeping has been recognised as a pathway out-of-poverty [28].

Disease in animals and losses in animal production can therefore have multiple negative ramifications on economic status for households that go beyond short-term losses of outputs. One of those pathways of impact extends to access to healthcare, particularly affordability of out-of-pocket payments for health care services. For households facing financial constraints due to animal diseases, out of pocket spending in health might translate into financial hardship or to healthcare foregone, indirectly leading to negative effects in mortality and morbidity [29]. In communities heavily reliant on livestock as a main livelihood stream, continuous losses of livestock due to disease, disasters, predation and other causes, can perpetuate a cycle of poverty for livestock owners, which is also in itself an important social determinant of health with consequences on exposure to disease and access to healthcare [30].

Quantifying the contributions of these wealth effects at a global scale is not currently a feature of global estimation exercises such as the GBD or FERG. These frameworks often consider socio-economic features as covariates (such as the socio-demographic index within the GBD framework) and as such, the consequences of changes in wealth on the various activities outlined above are indirectly manifested in estimation exercises through these covariate effects [5]. Currently wealth is not featured as a risk factor within the GBD or FERG.

For these key indirect mechanisms when related to health, we see two very different pictures of feasibility. For wealth there does not exist a methodology to tap into existing DALY frameworks – other forms of evidence, such as tracking healthcare expenditure profiles, seem a more feasible way of tracking impact, and this problem space has specific importance for Universal Health Coverage, particularly when we think of agricultural communities and their ability to avoid catastrophic healthcare expenditure when also facing substantial animal losses [31]. For diet-related impacts, there exists approaches that can be co-opted, however recommendations related to taking specific actions require further integration of economic aspects in order to more realistically account for market-dynamics and consumption patterns. Regardless, even with strong assumptions on the mapping of losses to diet change, a DALY perspective can be a powerful accompanying framing of the consequences of this wastage.

Conclusions

Quantifying animal health outcomes in a manner comparable to that which has resulted from the last three decades of human health metrics represents an ambitious challenge. However, should this be achieved, there exists a large opportunity space to integrate human health measures with those of animals to begin to more comprehensively quantify the totality of global One Health outcomes. For some of the major pathways we indicated in Figure 1, we have outlined either existing mechanisms for quantifying their impacts (along with their constraints), or indicated where current methods could be newly associated, or repurposed to produce global estimates of the translation of animal health outcomes into human health metrics, such as the DALY. For some potential linkages, currently evidence is mixed or inconsistent – nevertheless, there do exist comparable analytical blueprints that could incorporate evidence as and when it becomes available or clearer to result in global estimates.

When we consider decisions on where to allocate finite resources to improve animal health outcomes, doing so with associated human health impacts is an essential requirement. While complex and multidimensional, some of these impacts are feasible to calculate should we emulate existing approaches in this population health research. Being able to quantify animal health decisions in terms of DALYs and other related human health measures will represent a transformative means of approaching animal health decision making that fully acknowledges the interdependent nature of livestock and humans.

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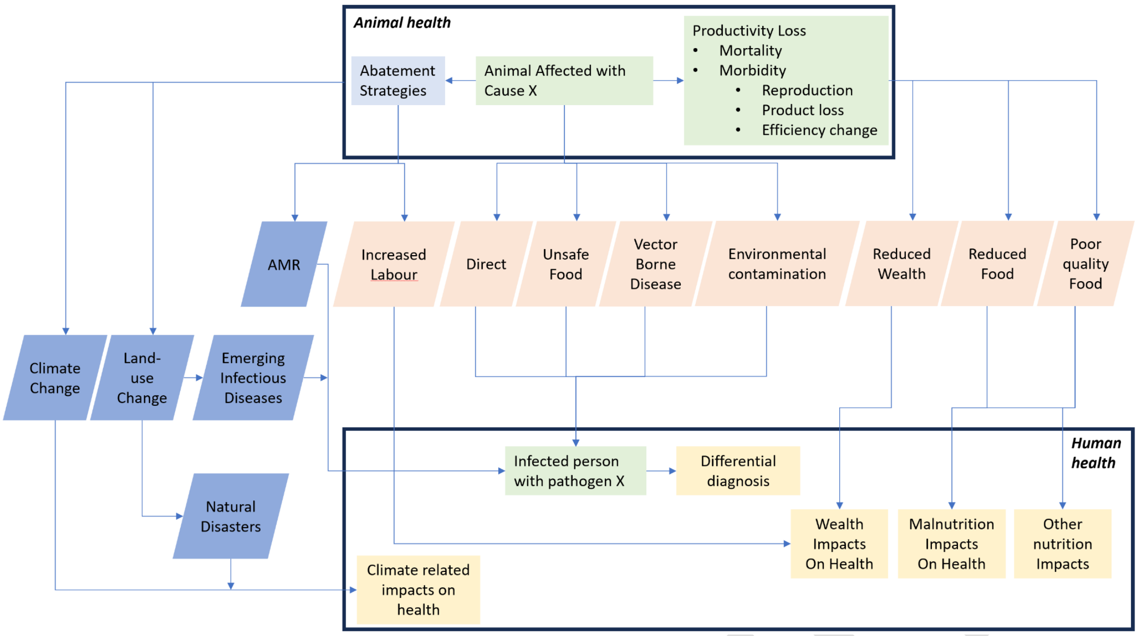

AMR: antimicrobial resistance

Figure 1

A conceptual framework for associating poor animal health outcomes with human health