



## Asia – Human Health Risks from the Human-Animal Interface



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# 1 Introduction

By 2050 global human population will be 50% greater than in 2000 (Table 1) with a 2.4 times higher per capita income. Growing populations and rising living standards in ‘developing countries’ fuel increasing consumption of food, particularly of higher value food items such as fruit, vegetables, and animal source food (meat, milk, eggs and fish). Asia, with more than half of the world’s population and its high growth in disposable incomes (average incomes have grown three and five-fold between 1990 and 2008 in India and China respectively) takes a central position in shaping global development of the agri-food sector.

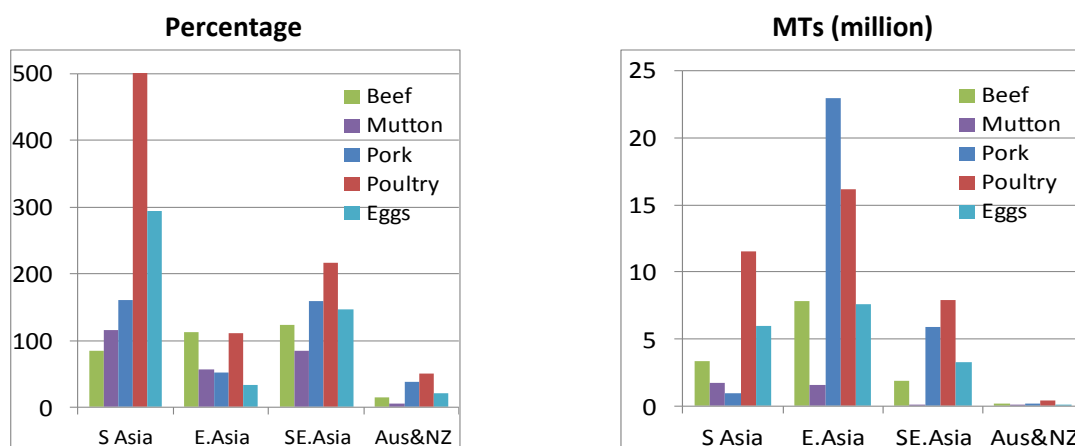
Table 1: Human populations in Asian sub-regions, 1990 to 2050 (in thousands)

Region	Population	1990	2000	2010	2030	2050
<b>S.Asia</b>	Total	1,195,985	1,460,200	1,704,146	2,141,801	2,393,885
	Rural	879,375	1,037,150	1,164,215	1,252,262	1,064,340
	Urban	316,614	423,052	539,932	889,540	1,329,544
<b>E.Asia</b>	Total	1,359,149	1,495,281	1,573,970	1,625,464	1,511,963
	Rural	922,977	892,840	784,738	587,970	385,733
	Urban	436,172	602,440	789,231	1,037,492	1,126,228
<b>SE.Asia</b>	Total	445,362	523,831	593,414	705,987	759,208
	Rural	304,694	323,514	344,189	330,591	259,060
	Urban	140,666	200,318	249,226	375,397	500,145
<b>Aus&amp;NZ</b>	Total	20,494	23,022	26,636	32,982	37,063
	Rural	3,014	3,013	3,028	2,879	2,452
	Urban	17,480	20,010	23,608	30,103	34,611
<b>WORLD</b>	Total	5,296,249	6,122,769	6,895,888	8,321,382	9,306,131
	Rural	3,044,820	3,287,027	3,412,018	3,405,370	2,906,691
	Urban	2,251,425	2,835,751	3,483,869	4,916,004	6,399,422

Source: FAOSTAT, 2012.

Global demand for animal source food is projected to nearly double to 2030 and to almost treble to 2050 (from 2000 as base year). Projections of increases in demand for ASF in South, East and Southeast Asia are shown in Fig. 1 (Australia and New Zealand are included as example of trends in ‘developed’ countries). Global grain demand is projected to double until 2050, mostly due to the increased demand for ASF, much of which will be grain-fed.

Fig. 1: Projected demand growth for different types of meat and eggs by Asian sub-regions, 2000 to 2030



Source: FAO, 2006.

Increasing livestock production by 270% and doubling global grain production without compromising environmental integrity, social stability / equity and public health is a tremendous challenge, complicated by the multiple and intricate linkages between these public goods. Given the magnitude of the challenge and its implications for human welfare, animal welfare, public policy at local, national and international levels has to guide and set boundaries for individual actions. Effective policy-making requires judicious analysis of economic and ecological trends, technical and policy options, their impacts and trade-offs and the acceptance of these by various stakeholder groups.

Environmental and social impacts of Asia's dynamic livestock sector growth and development are dealt with elsewhere. The focus of this paper is on potential risks to humans occasioned by infectious disease from microorganisms and parasites originating in animals and foreseeable changes in these risks resulting from livestock sector growth and development trends in Asia. The paper does not address food security and economic aspects of transboundary animal diseases that do not infect humans nor risks to human health associated with excessive consumption of animal products.

The paper starts with an overview of livestock sector development trends in Asia, broken down into three major sub-regions, namely South, East and Southeast Asia. Section three reviews the human health consequences of Asia's livestock sector growth and development stemming from emerging infectious diseases, established (endemic) zoonoses and from emergence and proliferation of antimicrobial resistance associated with production of ASF. Section 4 attempts to qualify and to some degree quantify the impact of the above health consequences while section 5 outlines responses required to mitigate the above risks to human health. Section 6 provides a brief synthesis and some conclusions.

## **2 Growth and development of Asia's livestock sectors**

Asian livestock populations (including farmed aquatic animals) have exhibited remarkable growth over the past 20 years (Table 2). This growth has however not been uniform across Asia's sub-regions, livestock types and time. Poultry numbers have shown the strongest growth in all three sub-regions and over both decades, numbers doubling in South Asia over the past decade. In East Asia, the growth of livestock numbers appears to be decelerating across all species (and in the case of large ruminants numbers are even declining), while in South and Southeast Asia livestock population growth was stronger in the decade 2000-2010 than in the decade 1990-2000 (with the exception of pig populations in India, which have declined). In South Asia, small ruminant populations have exhibited the second largest increase in numbers, 45% growth over 20 years, while in Southeast Asia pig populations have grown by 75% over the same period. East Asia saw a strong growth in small ruminant populations in the decade 1990-2000 but small ruminant numbers appear to have stabilized while pig populations still exhibited moderate growth in the decade 2000-2010.

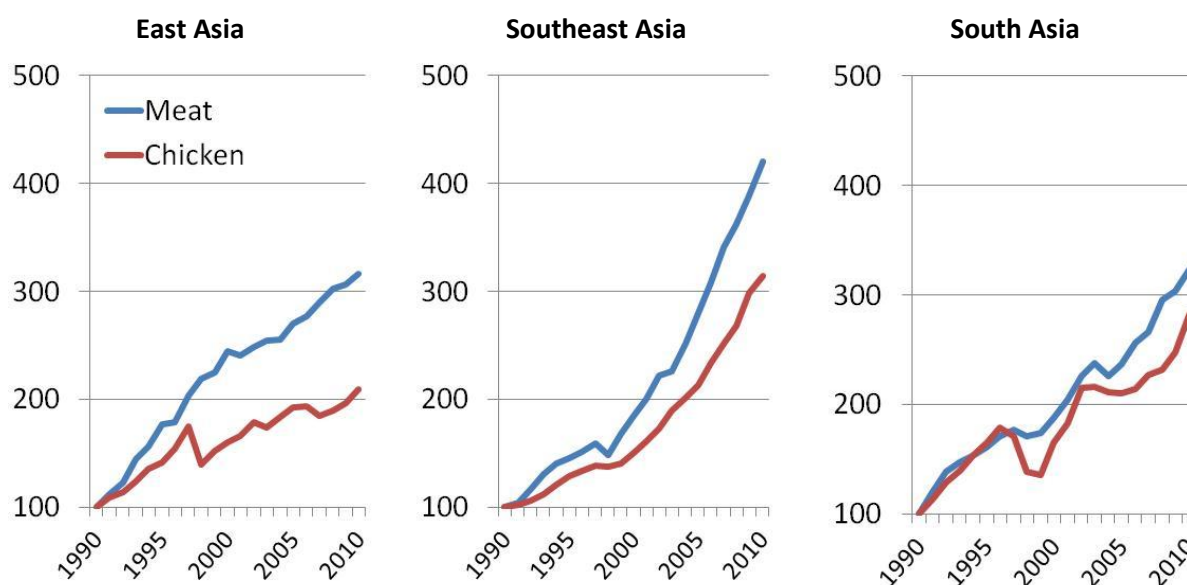
Table 2: Livestock populations and livestock population growth in Asian sub-regions, 1990 to 2010  
(poultry in 1,000s)

Region	Species	1990	2000	2010	2000/1990	2010/2000
<b>S.Asia</b>	LRs	364,129,592	377,647,557	438,780,010	104	116
	SRs	338,641,353	399,416,661	490,289,416	118	123
	Pigs	12,618,795	14,392,882	10,798,645	114	75
	Poultry	670,637	997,164	2,031,550	149	204
<b>E.Asia</b>	LRs	111,497,086	138,273,996	117,880,685	124	85
	SRs	232,475,823	308,750,212	317,103,367	133	103
	Pigs	383,235,180	460,065,244	498,190,472	120	108
	Poultry	2,970,138	4,866,944	6,387,309	164	131
<b>SE.Asia</b>	LRs	52,065,904	52,652,421	62,521,339	101	119
	SRs	24,898,510	29,392,005	38,106,884	118	130
	Pigs	40,577,003	52,374,400	71,361,625	129	136
	Poultry	1,042,326	1,719,507	2,871,319	165	167
<b>Aus&amp;NZ</b>	LRs	31,196,180	36,603,000	36,596,970	117	100
	SRs	230,842,100	162,899,840	105,243,381	71	65
	Pigs	3,042,270	2,879,754	2,624,404	95	91
	Poultry	70,652	100,110	100,288	142	100
<b>WORLD</b>	LRs	1,446,587,011	1,478,928,044	1,622,804,906	102	110
	SRs	1,799,113,925	1,811,199,498	2,000,380,066	101	110
	Pigs	855,962,572	898,813,265	965,855,414	105	107
	Poultry	11,791,809	16,078,447	21,488,551	136	134

Source: FAOSTAT, 2012.

Asia's livestock sectors are not only growing but also intensifying, a process that has started earlier and progressed furthest in East Asia as illustrated for poultry in Fig. 2 by comparing increments in chicken meat production with increases in chicken numbers. In contrast to East Asia, where chicken numbers have double while meat output has tripled, much of the growth in chicken meat production South Asia was a result of increasing chicken numbers, many of which are raised in extensive systems. Robinson et al. (2011) estimated that in 2005 80% of poultry in East Asia were reared under intensive conditions while in South Asia the corresponding figure was 30%. In terms of intensification process, Southeast Asia lies between the East and South Asian regions.

Fig. 2: Poultry sector growth, chicken numbers and chicken meat in Asian sub-region, 1990 to 2010 (1990 = 100)



Source: FAOSTAT, 2012.

The pig sectors of East and Southeast Asia are undergoing similar processes, again with higher rates of intensification in East Asia vis-à-vis Southeast Asia.

Larger farming units and concentration of units in proximity of feed sources, increased animal throughput / turnover and stratification of production (breeders, multipliers, finishers), often with vertical integration and contract farming are hallmarks of livestock sector intensification. Increases in animal turnover in intensive livestock production systems are the result of selection for production traits, enhanced management, particularly disease control, and rations with a higher nutrient density compared to traditional livestock raising systems. As Asia's agricultural areas have little potential for expansion, intensification of livestock production has led to major increases in feed imports as can be seen in Table 3. China now accounts for almost 60% of global soy meal imports (up from 8% in 1990).

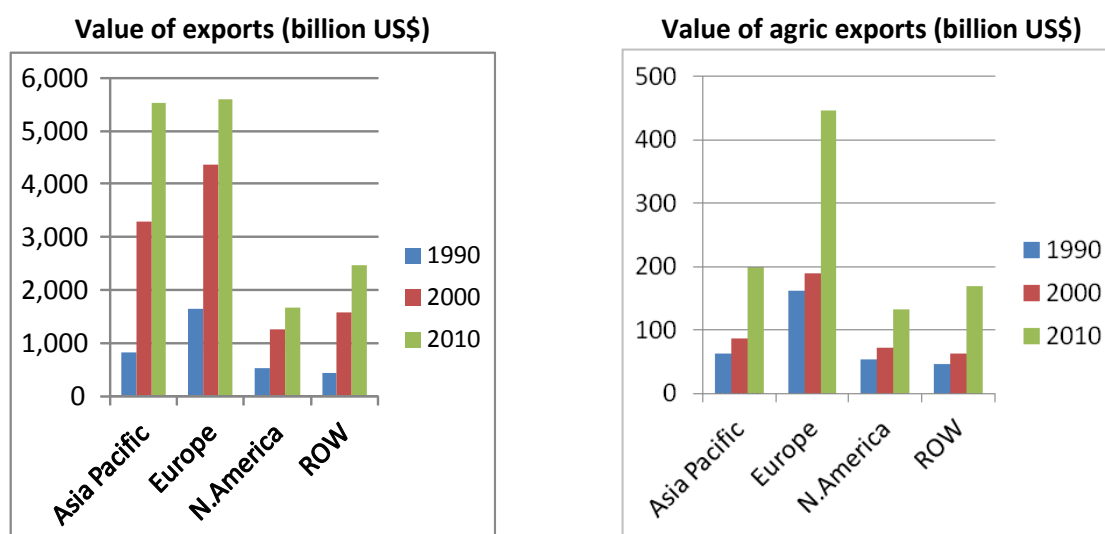
Table 3: Value (in US\$1,000) of feed imports 1990, 2000 and 2009 by Asian sub-region

Region	1990	2000	2009	2000/1990	2009/2000
<b>S.Asia</b>	112,132	214,822	959,869	192	447
<b>E.Asia</b>	1,734,245	3,023,139	5,797,128	174	192
<b>SE.Asia</b>	648,323	1,544,730	5,830,958	238	377
<b>Aus&amp;NZ</b>	55,678	124,627	687,924	224	552
<b>WORLD</b>	16,196,569	20,136,778	51,940,302	124	258

Source: FAOSTAT, 2012.

Economic development is linked to stronger integration into international supply networks, which allow for regional specialization with concomitant increase and shift of local, regional, and global trade patterns. Thus, Asia's intraregional trade and trade with the rest of the world have grown tremendously over the past two decades (trade volumes grow faster than production). Fig. 3 displays total and agricultural exports (in value terms) for 1990, 2000 and 2010.

Fig. 3: Total and agricultural export values 1990, 2000 and 2010 by major world region (exports include intra-regional trade)



Source: UN-ESCAP, 2012.

Source: FAOSTAT, 2012.

While in the 1990 more than half of Asia-Pacific exports went to other world region, presently more than 50% of Asia-Pacific exports are to other countries in the region. These export figures do not include un-official cross-border trade which, for livestock and livestock products can be quite substantial as price differentials between Asian countries are high for certain livestock types / products.

An assessment of the international agro-food trade network (IFTN) by Ercsey-Ravez et al. (2012), concludes that this network has evolved into a highly heterogeneous, complex supply-chain network, which provides a vehicle suitable for the fast distribution of potential contaminants and pathogens but unsuitable for tracing their origin. The authors warn, that even if food contamination was less frequent, for example due to better local control of production, its dispersion/spread has become more efficient.

### 3 Human health consequences of Asia's livestock sector growth

The rapid expansion of and structural changes in Asia's livestock sectors has ensured increased supplies of animal source food for Asia's growing and more affluent populations. This remarkable development has, however, come at the expense of increased risks to human health from pathogens harboured by animals, either wildlife or livestock themselves. These evolving disease risks can broadly be grouped into three interconnected categories (i) emerging infectious zoonotic<sup>1</sup> diseases, (ii) established (endemic) zoonoses and food-borne diseases transmitted via ASF and (iii) emergence of resistance of microorganisms to antimicrobial compounds used in animal production (similarly, disease vectors are developing resistance to chemicals used for their control).

The intensification of agriculture and livestock production is not always a risk amplifier and a number of zoonotic diseases actually decrease as livestock systems intensify and animals are moved into highly regulated environments (e.g. trichinellosis). However, the rapid growth and intensification of livestock production within a poorly regulated environment and without the concomitant

<sup>1</sup> Zoonoses are diseases that are naturally transmitted between humans and vertebrate hosts. Around 60% of all human infectious diseases and 75% of emerging diseases are zoonoses (Taylor et al., 2001; Woolhouse et al., 2005).

strengthening of public health systems as is the case in many Asian countries, not only generates health risks for local populations but compromises regional and global health security.

### 3.1 Emerging infectious zoonotic diseases

Humans, livestock and wildlife share large pools of microorganisms and parasites, many of which, given the opportunity, can infect and potentially establish a new host species (opportunistic invasion, e.g. SARS and Nipah virus), or, if ecological changes occur, adapt to new population structures and contact patterns of existing host species (adaptive evolution, e.g. avian influenza viruses), which in turn leads to changes in manifestation (increased incidence and / or virulence) of otherwise known diseases. Both processes result in so-called 'emerging infectious diseases' (EIDs), a phenomenon which has declined over the past two decades after increasing for the previous five decades (Grace et al., 2012). Viruses are more likely to be emerging than other types of pathogen, due to their wide host range and rapid evolution. Viruses, which have received most attention, include coronaviruses, lentiviruses, flaviviruses, paramyxoviruses and influenza A viruses. Fortunately, with the exception of the 2009 H1N1 virus, the capability of human-to-human transmission of recently emerged zoonotic diseases is moderate to low.

The majority (about 75%) of EIDs affecting humans have their origin in wildlife but livestock often play an important bridging role between wildlife and humans, either through amplification of wildlife parasites or by providing a host population in which wildlife parasites evolve and adapt. Parasite evolution and adaptation in livestock leads to increased exposure of humans, and, as livestock themselves are exposed to human pathogens, livestock provide a major 'breeding ground' for amplifying novel pathogens that are relatively well-adapted to human hosts (the continuous exchange of influenza virus genes between pigs and humans and resulting emergence of virus variants is a prime example). Livestock can also act as a 'mixing vessel' where exchange can occur between pathogens adapted to different species, for example human influenza virus and avian influenza virus can co-infect pigs allowing gene exchange and new variant emergence.

Expansion of agricultural areas, e.g. through deforestation, can lead to increased wildlife-human and livestock-wildlife contact with livestock-human transmission (e.g. Nipah virus). So far, around 2,000 viruses infecting vertebrate species have been described. Although this number appears large, it is likely to be only a small fraction of existing viruses. Given there are around 50,000 known vertebrate species and assuming each has 20 endemic viruses, there are likely over 1 million vertebrate viruses. Thus, 99.8% of vertebrate viruses remain to be discovered, and even if only 0.1% of these can infect humans, this would still represent a pool of around 1,000 undiscovered potential human pathogens (Daszak, 2009).

Intensification of agricultural land use through irrigation can lead to an increase in endemic water borne (e.g. leptospirosis) and vector-borne (e.g. Japanese encephalitis) zoonoses (which then may acquire characteristics of 'emerging' zoonoses. Similarly, the increasing scale of livestock operations, accelerated turnover ('industrialization') and the spatial concentration of these units close to feed sources or markets can lead to an increase in prevalence (e.g. *Campylobacter jejuni*, *Streptococcus suis*) and virulence (e.g. avian influenza virus) of 'endemic' zoonotic pathogens.

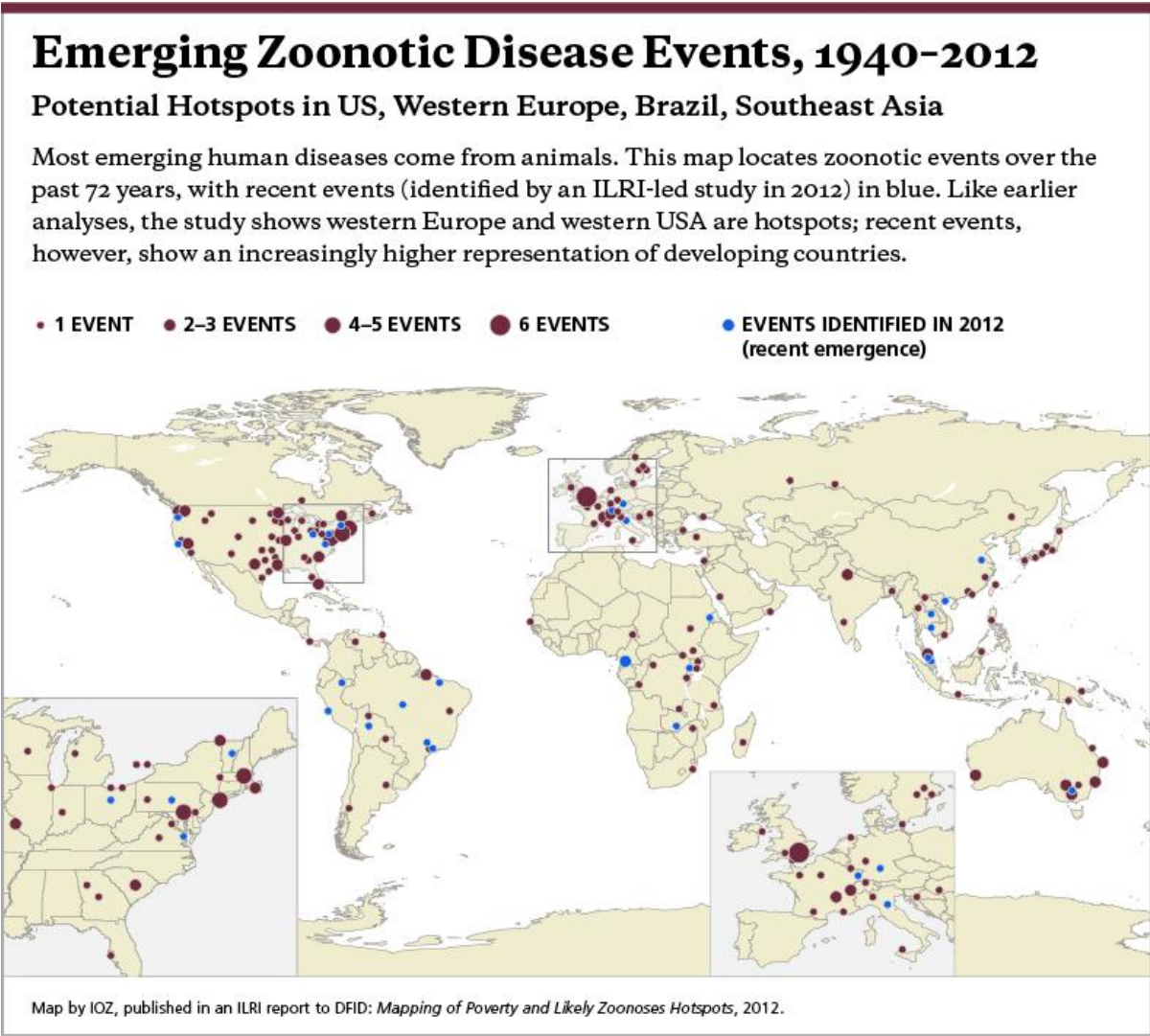
A major objective of intensive livestock production is disease control and this can paradoxically foster disease emergence. For example, salmonella serovars *Gallinarium* and *Pullorum* were an important cause of poultry mortality in emerging intensive poultry systems of Europe during the last century. Fortunately, these were virtually eradicated by vaccination. Unfortunately, but ecologically predictably this created a vacant niche and Salmonella serovar *Enteritidis* established in poultry populations. This is not associated with disease in poultry but is very commonly associated with

human disease. In the 1990s, several *Enteritidis* epidemics linked to poultry were observed in European countries and the USA (Gannon et al., 2012)

Once ‘established’ in local animal populations, new pathogens can be rapidly disseminated across a region or even the globe through trade in live animals (more than live 75,000 pigs and nearly 2,000,000 live poultry are shipped from North America to Eurasia each year (Husseini et al., 2010)), animal products and wildlife. If a novel pathogen develops the capacity for human-to-human spread, it can rapidly disseminate though ever expanding global air travel.

There is no strong link with poverty, smallholders and emerging disease. Over the last 72 years, most cases of zoonotic disease emergence have been in the western seaboard of USA and Western Europe (Fig. 4). This may reflect better reporting or it may be related to high numbers densities of genetically homogeneous livestock providing a suitable milieu for emergence.

Fig. 4: Emerging zoonotic disease events, 1940 -2012



It appears, however, that live and wet markets in which many different animal species are congregated in close proximity and also come into contact with humans may constitute a risk factor for disease emergence, maintenance and spread (e.g. bird flu, SARS).

Some examples of disease emergence and its link to agricultural intensification will be provided in the following.

### **3.1.1 Japanese Encephalitis (JE)**

JE is a vector-borne viral disease that occurs in South Asia, Southeast Asia, East Asia, and the Pacific. The JE virus (JEV) is mainly transmitted by the mosquito *Culex tritaeniorhynchus*, which prefers to breed in irrigated rice paddies. This mosquito species and members of the *Cx.gelidus* complex are zoophilic. Wading ardeid water birds (e.g., herons and egrets) serve as virus reservoirs, but the virus regularly spills over into pigs, members of the family of equidae, and humans. Humans and horses are dead-end hosts but pigs develop a high level viraemia and are amplifying hosts for human infection ([Pfeffer and Dobler, 2010](#)).

Two distinct epidemiologic patterns of JE have been described. In temperate zones, such as the northern part of the Korean peninsula, Japan, China, Nepal, and northern India, large epidemics occur in the summer months; in tropical areas of southern Vietnam, southern Thailand, Indonesia, Malaysia, the Philippines, and Sri Lanka, cases occur more sporadically and peaks are usually observed during the rainy season.

JE incidence is increasing in South Asia and Southeast Asia while in East Asian countries, which implement control programmes, incidence has declined or remained stable (Erlanger et al., 2009). Because infected pigs act as amplifying hosts, domestic pig rearing is an important risk factor in the transmission to humans. The expansion of JEV in South East Asia in the last few decades has been associated with increasing irrigated rice production and pig farming ([Pfeffer and Dobler, 2010](#)). The combination of irrigated fields, which increases the population density of mosquito vectors and water birds, and pig farming, which provides an amplifier host, increases the risk of spill-over into the human population. In Indonesia, the incidence of JE in rural communities is closely related to the ratio of humans to pigs (Xu and Liu, undated).

### **3.1.2 Nipah**

Pteropus bats (Fruit) are reservoir hosts for henipaviruses in Australasia and transmission to pigs, horses and humans (directly or indirectly) has been confirmed. Infected bats shed virus in their excretion and secretion such as saliva, urine, semen and excreta but they are symptomless carriers. As bats get stressed and hungry, their immune system gets weaker, their virus load goes up and a lot of virus spills out in their urine and saliva (WHO, undated).

Disease emergence may occur through simple host switching: bat and human isolates are identical in some outbreaks (Grace et al., 2011). Outbreaks are generally associated with changing ecology and landscapes, with habitat degradation forcing bats to encroach upon agricultural zones for survival and into contact with humans through contamination of foodstuffs ([Breed et al., 2006](#)).

Nipah outbreaks have occurred in South Asia (Bangladesh and neighbouring India) and in Malaysia. Outbreaks of Nipah in South Asia have a strong seasonal pattern and a limited geographical range (WHO, undated). A suspected mode of transmission is indirect contact with bats through contaminated palm sap.

Nipah virus (NiV) can infect pigs and other animals. The virus is highly contagious among pigs, in which it causes the porcine respiratory and neurologic syndrome (barking pig syndrome) and spreads by coughing. The amplification of NiV by pigs, with associated mortality and related human infection led to devastating economic impact and public health concern in Malaysia between September 1998 and April 1999. Direct contact with infected pigs was identified as the predominant mode of

transmission in the Malaysia outbreak. Ninety percent of the infected people were pig farmers or had contact with pigs.

The morbidity and mortality data of human NiV infection is presented in Table 4 (up to 2008). Case fatality rate of NiV ranges from 40-70% although it has been as high as 100% in some outbreaks. NiV has infected 477 people and killed 252 since 1998.

Table 4: Nipah cases and deaths 1998 to 2008

Country	Period	Cases	Deaths	CFR (%)
Malaysia	Sep. 1998 – Apr. 1999	276	106	38
India (Siliguri)	Feb. 2001	66	45	68
Bangladesh (Meherpur)	Apr. – May 2001	13	9	69
Bangladesh (Naogaon)	Jan. 2003	12	8	67
Bangladesh (Gaolando)	Jan. 2004	29	22	76
Bangladesh (Faridpur)	Apr. 2004	36	27	75
Bangladesh Tangail)	Jan. – Mar. 2005	12	11	92
Bangladesh (Thakurgaon)	Jan. – Feb. 2007	7	3	43
Bangladesh (Kushtia)	Mar. – Apr. 2007	8	5	63
India (Nadia)	Apr. 2007	5	5	100
Bangladesh (Manigonj & Rajbari)	Feb. 2008	11	6	55
Bangladesh (Shatkira & Jessore)	Apr. 2008	2	1	50

Source: WHO, undated.

There is circumstantial evidence of human-to-human transmission in India in 2001. During the outbreak in Siliguri, 33 health workers and hospital visitors became ill after exposure to patients hospitalized with Nipah virus illness, suggesting nosocomial infection. Strong evidence indicative of human- to-human transmission of NiV was also found in Bangladesh in 2004.

### 3.1.3 SARS

Severe Acute Respiratory Syndrome (SARS), caused by a coronavirus (CoV), first occurred in November 2002 in China. In March 2003 the disease (re-)emerged in Hong-Kong. Between March and July 2003, the virus dramatically spread, reaching 30 countries all over the world and rapidly obtained the status of “first pandemic of the XXI<sup>th</sup> Century”. Six months after its second emergence in Hong-Kong, more than 8,500 cases had been identified, and 800 people had died from the ‘new’ coronavirus.

The earliest human cases of SARS were associated with wildlife contact and SARS corona virus-like viruses were isolated from wild animals in a live animal market. Several surveys were conducted in domestic animals, poultry and wildlife to identify the natural reservoir of SARS corona virus and SARS corona virus-like virus was found in several species of insectivorous horseshoe bats (*Rhinolophus* sp.) from different locations in southern China (Lau et al., 2005, Li et al., 2005, Bennett, 2006).

Using genomics and phylogenetic analysis of known strains, virus transmission and adaptation have been demonstrated between bat species and between bats and other mammals e.g. palm civet, domestic animals and humans. In the case of SARS-CoV, this appears to have occurred via an intermediate, perhaps rodent, host (Guan et al., 2003).

### **3.1.4 Highly pathogenic avian influenza ('Bird Flu')**

Wild aquatic birds are believed to be the primary reservoir of influenza A viruses, and all influenza A viruses in mammals likely have ancestral links to avian lineages (Webby and Webster, 2001; Alexander, 2006). An important feature of influenza A viruses is their capacity to undergo molecular transformation through recombination and reassortment, which facilitates adaptation to new host populations and thereby the potential to cause major disease outbreaks in humans and other species (Vana and Westover, 2008). Strains that cause severe disease and high levels of mortality are classified as highly pathogenic avian influenza while viruses causing milder disease in domesticated poultry are classified as low pathogenic avian influenza (LPAI).

The introduction of LPAI viruses into domestic poultry populations usually requires direct or indirect contact with infectious wild waterfowl or from wild waterfowl to domestic ducks (Alexander, 2006). Incursions of LPAI virus into domestic poultry have been reported over the past decade, mostly in North America and Europe, but also in Mexico, Chile and Pakistan, as summarized by Capua and Alexander (2004).

The transition from LPAI to HPAI can result from a single point mutation affecting the haemagglutinin surface protein. The probability of such a mutation is amplified in the setting of industrial poultry production due to the rapid viral replication that occurs in an environment of thousands of confined, susceptible animals. In Mexico in 1994, a LPAI H5N2 virus mutated into a HPAI virus and spread to Guatemala in 2000 and to El Salvador in 2001, presumably via trade in poultry (Lee et al., 2004). LPAI H5N2 is now established in domestic chicken populations in Central America. In both the 2003 H7N7 HPAI epidemic in the Netherlands (Stegeman et al., 2004) and the 2004 H7N3 HPAI epidemic in British Columbia, Canada (Power, 2005), LPAI infections in poultry preceded the emergence of HPAI in different poultry houses on the same commercial farms. In Italy, the 1999/2000 H7N1 HPAI epidemic was preceded by 199 reported outbreaks of LPAI H7N1 in the same region. A similar process appears to have started the ongoing HPAI H7N3 epidemic in Mexico, which has led to the culling of around 8 million birds so far.

Large-scale industrial poultry production systems display many of the factors determining selection for increased virulence as identified in a review by Galvani et al. (2003). Live bird markets, with their rapid turnover of birds, may act as surrogates for 'large farms'.

HPAI caused by the notorious H5N1 virus was first reported in Southeast Asia in late 2003, although the virus is now considered to have emerged as early as 1996, when it was first identified in geese in Guangdong Province in southern China. It then caused disease in the Hong Kong Special Administrative Region, where poultry and humans were affected in 1997, poultry only in 2001 and early 2002 and poultry and captive wild birds in 2002–2003. From 2003 onwards, the disease spread widely, initially through East and Southeast Asia in 2003–2004 and then into Mongolia, southern Russia, the Middle East and to Europe, Africa and South Asia in 2005–2006, with outbreaks recurring in various countries in 2007. To date, 60 countries have reported outbreaks of HPAI H5N1 in domestic poultry, wild birds or both. In most of these, the H5N1 virus could be eliminated through swift and determined interventions of national animal health systems, or through natural burn-out (Bett et al., 2012) whereas in some countries the virus appears to have become endemic in specific eco- and production systems, probably because these have unusual epidemiological features that allow maintenance of infection (e.g. high density, clandestine vaccination, mixing poultry with ducks)

HPAI H5N1 virus has the ability to infect humans, in which it produces severe disease with a case-fatality rate of above 50%. Fortunately the H5N1 virus has not acquired the capacity of efficient human-to-human spread but recent (controversial) experiments have shown that only a limited number of mutations may be needed to acquire this trait, the consequences of which would be

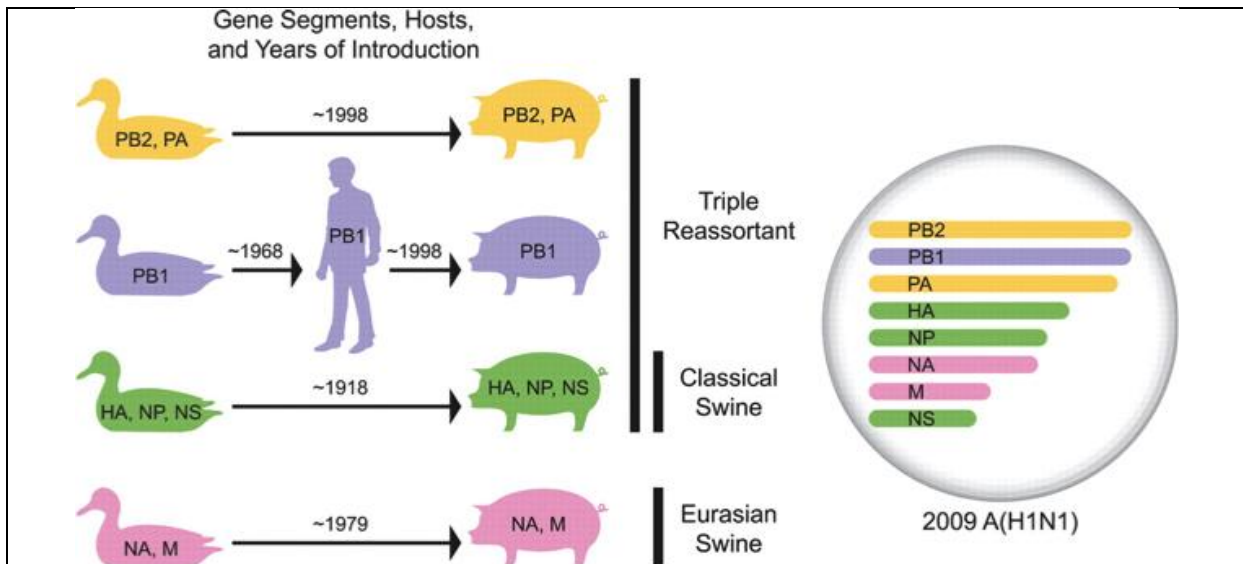
devastating. The cost of a severe global pandemic has been estimated at US\$3 trillion (World Bank, 2010).

### 3.1.5 Novel H1N1 ('Swine Flu')

Pigs may potentially assume an important role in the emergence of novel influenza A viruses as they can be infected by both avian and human viruses (Alexander, 2006; Kida et al., 1994; Schulz et al., 1991). Gilchrist et al. (2007) note the proximity of concentrated poultry and swine operations as a source of disease risk from influenza A viruses, although to date there have only been reports of avian influenza viruses in pigs, not swine influenza in poultry. Classical H1N1 swine influenza viruses are very similar to the virus implicated in the 1918 human influenza pandemic and circulate predominantly in the US and Asia. H3N2 viruses of human origin have been isolated from pigs in Europe and the Americas shortly after their emergence in humans (Webby and Webster, 2001) and are now endemic in pigs in southern China (Peiris et al., 2001), where they co-circulate with H9N2 viruses with the potential of reassortment with H5N1. Evidence for the concurrent circulation of H1N2, H1N1, and H3N2 influenza A viruses in pigs has been reported from Spain (Maldonado et al., 2006). In the United States, outbreaks of respiratory disease in swine herds have been caused by influenza A viruses which arose from reassortment of human, swine and avian viral genes (Zhou et al., 1999). Evidence for viral reassortment of avian, human and swine influenzas within pigs has been published by Zhou et al. (1999) and Shieh et al. (2008).

In March and early April 2009, a new swine-origin influenza A (H1N1) virus (S-OIV) emerged in Mexico and the United States. During the first few weeks of surveillance, the virus spread worldwide to 30 countries by human-to-human transmission, causing the World Health Organization to raise its pandemic alert to level 5 of 6. This virus was derived from several viruses circulating in swine (see Fig. 5), and the initial transmission to humans occurred several months before recognition of the outbreak (Garten et al., 2009).

Fig. 5: Host and lineage origins for the gene segments of the 2009 A(H1N1) virus (from Science)



Source: RJ Garten et al. Science 2009;325:197-201

A phylogenetic estimate of the gaps in genetic surveillance indicates a long period of unsampled ancestry before the S-OIV outbreak, suggesting that the reassortment may have occurred years before emergence in humans (Smith et al., 2009). This highlights the need for systematic surveillance of influenza in swine, and provides evidence that the mixing of new genetic elements in swine can result in the emergence of viruses with pandemic potential in humans.

Nelson et al. (2012) undertook a large-scale phylogenetic analysis of pandemic A/H1N1/09 (H1N1pdm09) influenza virus genome sequence data to determine the extent to which influenza viruses jump between humans and swine hosts. At least 49 human-to-swine transmission events occurred globally during 2009-2011, highlighting the ability of the H1N1pdm09 virus to repeatedly transmit from humans to swine, even following adaptive evolution in humans. Similarly, [reference] identified at least 23 separate introductions of human seasonal (non-pandemic) H1 and H3 influenza viruses into swine globally since 1990. These findings indicate that humans make a substantial contribution to the genetic diversity of influenza viruses in swine, and emphasize the need to improve biosecurity measures at the human-swine interface, including influenza vaccination of swine workers.

### **3.2 Established (endemic) zoonoses and food-borne diseases**

A recent study identified 56 priority zoonoses that are together responsible for around 2.5 billion cases of human illness and 2.7 million human deaths a year (Grace et al., 2012). On a global scale, the ten most important were in descending order: zoonotic bacterial gastrointestinal disease; leptospirosis; cysticercosis; zoonotic tuberculosis; rabies; leishmaniasis; brucellosis; echinococcosis; toxoplasmosis; and Q-fever. All of these are present in Asia. Food-borne trematodiasis, although globally not in the top ten, constitute an important class of zoonoses in East and Southeast Asia. We briefly review these 'top' zoonoses from the perspective of their importance in Asia and also the likely trends under intensification and climate change. In contrast to emerging zoonoses, there is a strong relation between endemic zoonoses and poor smallholder livestock keepers (Fig. 6).

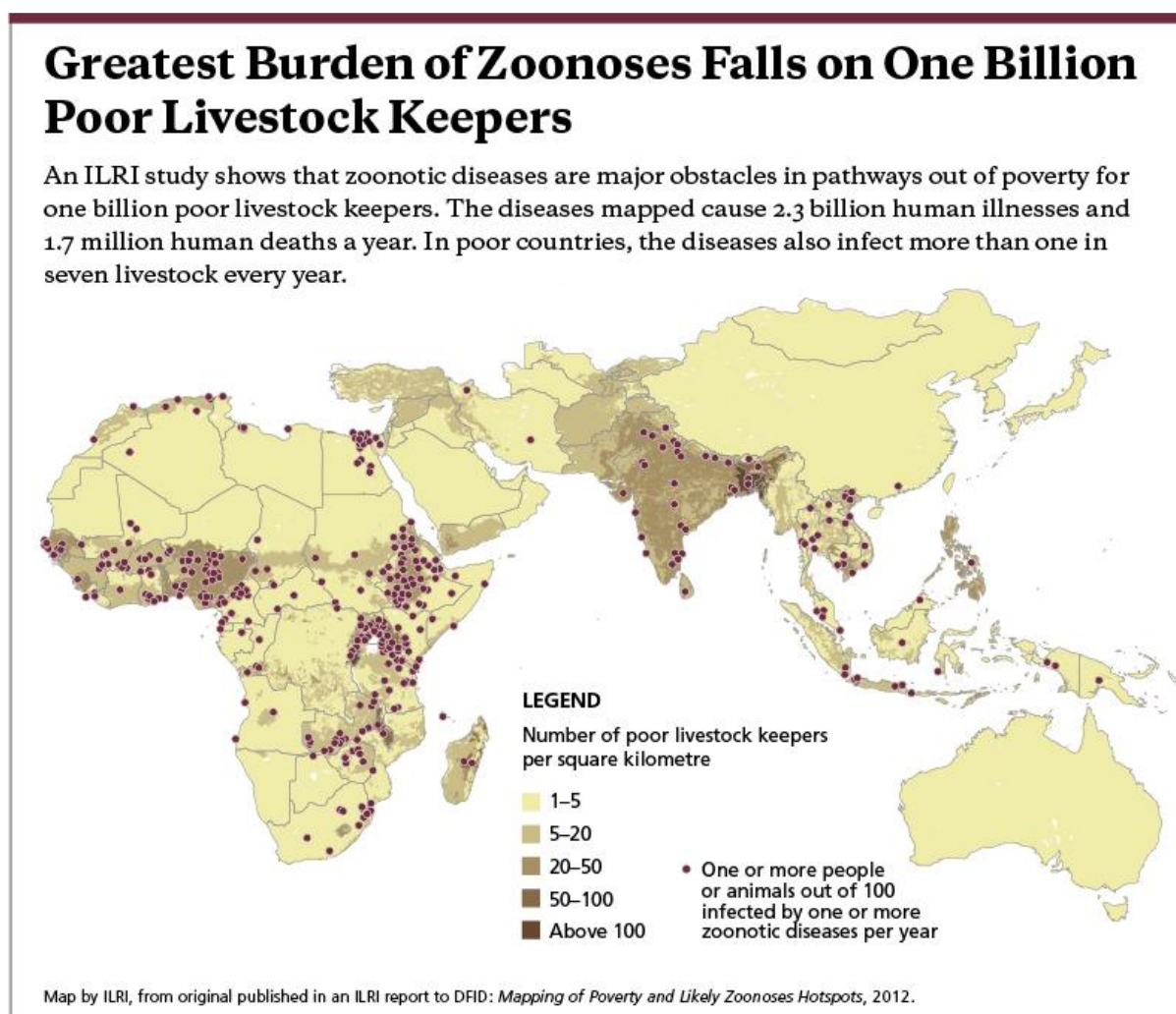
#### **3.2.1 Zoonotic gastro-intestinal disease**

This category includes the bacterial zoonotic diseases, which are transmitted mainly through food. Among the most important are *Salmonella*, toxigenic *Escherichia coli*, *Listeria*, *Campylobacter* and *Toxoplasma*. Of somewhat lesser importance are: *Staphylococcus aureus*, *Bacillus cereus*, and *Clostridium spp.* Hepatitis E is an emerging zoonoses although the role of the reservoir host (pigs) in transmission is not fully understood. Most of the classical endemic zoonoses can be food-borne (brucellosis, Q-fever, zoonotic tuberculosis) but have other important transmission pathways and are considered separately.

As animal food value chains become longer, more complex, transport larger, more diversely-sourced volumes of food, and place larger distances between producers and consumers, so food-borne hazards increase.

Food-borne diseases are expected to increase with intensification and increasing importance of monogastrics (Grace et al., 2012). With regard to climate change, campylobacteriosis and salmonellosis are thought to most likely to increase with air temperature; campylobacteriosis and non-cholera vibrio infections with water temperature; cryptosporidiosis followed by campylobacteriosis with increased frequency of rainfall; and cryptosporidiosis followed by non-cholera vibrio in association with precipitation events. *Listeria spp.* is not associated with temperature thresholds, extreme precipitation events, or temperature limits (ECDC, 2012).

Fig. 6: Burden of endemic zoonoses and density of poor livestock keepers



### 3.2.2 Leptospirosis

Leptospirosis is an infectious disease caused by pathogenic organisms belonging to the genus *Leptospira*. There are many serovars (>250) but typically only around 10-20 are found in a given region. Most mammalian species are natural carriers of pathogenic leptospirae. These include feral, semi-domestic and farm and pet animals as important infection sources. Therefore, leptospirosis is an important occupational disease, especially affecting farmers, slaughterhouse workers, pet traders, veterinarians, rodent catchers and sewer workers. The risk of acquiring leptospirosis is associated with contact with animals and the main route of infection is probably by transmission through indirect contact with leptospirae secreted into the environment. Pathogenic leptospirae survive longer in a warm and humid environment. Hence, mainly a problem in tropical countries where stagnant water can be found and where cattle, pigs or rodents are frequent.

In livestock, leptospirosis is associated with pasture grazing and may be reduced by intensification. It is considered one of the most climate sensitive zoonoses and is likely to increase with water temperature, precipitation and extreme weather events (flooding).

### 3.2.3 Cysticercosis

Cysticercosis is a systemic parasitic infestation caused by tapeworms of pigs and cattle (*Taenia solium* and *T. saginata*). The main health risk for humans is not consumption of pork with cysts but

consumption of tapeworm eggs shed by themselves or another human carrier. The disease persists in poor, pig-keeping communities where pigs have access to human faeces. Northeast India appears to be a hot spot, as is Papua New Guinea, and tribal areas of Vietnam and Thailand. Intensification of swine production would be expected to reduce prevalence of the disease; it is not climate sensitive.

#### **3.2.4 Zoonotic tuberculosis**

Worldwide and historically, most human tuberculosis (TB) is caused by *Mycobacterium tuberculosis* and maintained by human-to-human transmission. *M. bovis* is responsible for cattle tuberculosis. It affects a wide range of animals and is responsible for zoonotic TB in humans. Zoonotic TB is mainly a problem where cattle are important and is especially problematic in South Asia (Jou et al., 2008, Tipu et al., 2012). Intensification is a risk factor, but there is no special climate sensitivity, although increased temperature and humidity may increase survival in the environment.

#### **3.2.5 Rabies**

Rabies is one of the most feared zoonoses. Most cases are concentrated in a handful of countries with much of the burden in Asia (Bangladesh, India, Myanmar, Pakistan, China). The recent introduction to Bali has led to over 100 deaths and is not yet under control (Susilawathi et al., 2012). Most human infections are from canids or wildlife.

#### **3.2.6 Leishmaniasis**

Leishmaniasis are diseases caused by around 25 species of the protozoan genus *Leishmania*, and transmitted by bites of sandflies. The symptoms range from localized skin ulcers to lethal systemic disease. Outbreaks may be associated with conflict. India and Bangladesh are hotspots for visceral leishmaniasis, but disease is exclusively anthroponotic. In China and central Asia the disease is a zoonoses transmitted mainly from canids. Cutaneous leishmaniasis (dog and rodent reservoirs) is endemic in Rajasthan and has been newly recognized in South India (Singh et al., 2010). Incidence is likely to decrease with agricultural intensification (if dog and rodent populations decrease) and increase with climate change, indeed the re-emergence in India has been linked with climate change (Singh et al., 2011).

#### **3.2.7 Brucellosis**

The most important species of *Brucella* are zoonotic: *B. abortus*, responsible for bovine brucellosis; *B. melitensis*, the main etiologic agent of ovine and caprine brucellosis and an increasing cause of cattle brucellosis; and *B. suis*, causing pig brucellosis. Human brucellosis appears to be mostly a problem where ruminants are important (Africa and South Asia). However, it has been reported in Thailand, Indonesia, Malaysia and Vietnam. Brucellosis is more problematic in intensive systems than extensive and pasture-based systems. There is no marked climate sensitivity, although increased temperature and humidity may increase survival in the environment

#### **3.2.8 Echinococcosis**

Cystic echinococcosis (CE) in humans is caused by the larval stage of *E. granulosus*, *E. ortleppi*, *E. intermedium* or *E. canadensis*. All these parasites have canines (usually domestic dogs), as definitive hosts and a variety of ungulates, particularly farm animals, as intermediate hosts. Man is generally an aberrant intermediate host in which the hydatid cyst develops, usually in the liver or lungs as a space-occupying lesion, which can result in considerable morbidity. More than 90% of human cases occur in 8 endemic regions, 2 of which are found in Asia. In descending order: China (Tibetan plateau), Turkey, India, Iraq, Iran, and Afghanistan. Intensification would be expected to reduce prevalence of the disease; it is not climate sensitive.

### **3.2.9 Toxoplasmosis**

Toxoplasmosis is a disease caused by the parasite *Toxoplasma gondii* whose definitive host is felids. It is found worldwide with higher prevalences in tropical countries. Up to one third of the world's population is infected with toxoplasma, but disease is rare in otherwise healthy people. However, it is an important cause of illness in immune-compromised people and pregnant women. Consumption of under-cooked meat is a common transmission pathway. The disease may be more common in extensive and organic systems (where animals can contact cat faeces or rodents) (Jones and Dubey 2012). It is not climate sensitive.

### **3.2.10 Q-fever**

Q fever is an infectious, highly contagious, disease of animals and humans caused by a species of bacteria (*Coxiella burnetii*). *C burnetii* is most frequently found in ruminants (sheep followed by goats then cattle) but can also be detected in wildlife and companion animals. India appears to be a hot spot but it is also reported from Thailand, Lao PDR and Indonesia. It is more common in extensive systems but became a major problem in the Netherlands after intensification of goat production. Climate change may affect survival of the causative agent in the environment.

### **3.2.11 Food-borne trematodiasis**

Food-borne trematodiasis are a group of tropical diseases caused by liver, lung, and intestinal parasitic fluke infections. From a public health point of view, the most important species are *Clonorchis sinensis*, *Opisthorchis felinus*, *Opisthorchis viverrini*, *Fasciola gigantica*, and *Fasciola hepatica* among the liver flukes, *Echinostoma spp*, *Fasciolopsis buski*, *Heterophyes spp* and *Metagonimus spp* among the intestinal flukes, and *Paragonimus spp* among the lung flukes. The life-cycle of these trematodes includes two intermediate hosts, normally an aquatic snail and a fresh water fish or crustacean. Humans and animals are infected by consumption of the second intermediate host.

Pathological changes include inflammatory lesions, tissue damage, and damage of the target organs caused either directly through mechanical and chemical irritation by the parasites or indirectly through the hosts' immune response.

## **3.3 Antimicrobial use and resistance**

Increasing stocking density and confinement of livestock, a corollary of production intensification, is often accompanied by increased use of antimicrobials to treat or prevent disease or to promote growth. Long-lasting exposure to antimicrobial compounds favours selection of microbial strains which are resistant to the compound, a trait they can pass on to human pathogens. Exposure to antimicrobials occurs not only to enteric bacteria in the guts of domestic animals but also to microbes in the environment through excreted antimicrobial residues. In swine feces lagoons, liquid manure, and soil amended with manure, Tello et al. (2012) found concentrations of certain antibiotics that may act to extend the antibiotic selective pressure on bacteria within their treated hosts to wild-type bacterial populations.

Many classes of antimicrobial drugs commonly used for people are also used for farm animals to treat illnesses and prevent production losses. Antimicrobial resistance of animal pathogens thereby not only reduces the efficiency of animal production but also increases human disease burdens.

In high-income countries the largest share of total antimicrobial production is for veterinary use. In the USA for example, Mellon et al. (2001) estimated that total antibiotic use reached 17.5 thousand tonnes, of which only 1.5 million (8.5%) were used for therapy in humans, the remainder in animals.

The vast majority of veterinary antimicrobials are used in farm and aquatic animals (>90%), and in these mostly for non-therapeutic purposes. In the USA, where antimicrobials are used as growth promotants, around 80% of veterinary antimicrobial use was for non-therapeutic purposes.

A very crude estimate of the intensity of antimicrobial use in livestock production, expressed as kg of antimicrobial use per tonne of meat produced, is given in Table 5.

Table 5: Intensity of antimicrobial use in selected countries

Country	Year(s)	kg/tonne meat
Norway	2005 - 2009	0.02
Sweden	2005 - 2009	0.03
Finland	2005 - 2009	0.04
Denmark	2005 - 2009	0.06
Australia	1999 - 2001	0.10
UK	2005 - 2009	0.12
Czech Rep.	2005 - 2009	0.13
Switzerland	2004 - 2009	0.16
France	2005 - 2009	0.22
Netherlands	2005 - 2009	0.22
USA	2000 - 2007	0.27

Sources: Estimates based on reported antimicrobial sales (APVMA, 2005; EMA, 2011, and US Animal Health Institute) and meat production (FAOSTAT)

As can be seen in the above table, the lowest rates of antimicrobial use are found in the Nordic countries, in which non-therapeutic use has been banned, followed by Australia and other EU countries (which have banned antimicrobial use for growth promotion), while the highest use intensity is recorded in the USA.

For most non-OECD countries reliable data on antibiotic consumption (for both animals and humans) is not widely available. However, several studies have shown that withdrawal periods are often not observed. The amounts of antimicrobials added to feed to prevent disease or promote growth is not well known and few countries have effective policies and regulations to control antibiotic use in domestic animals.

Given the generally lower standards of animal husbandry and health, production hygiene and efficiency in Asia's intensive poultry and pig production systems vis-à-vis those in industrialized countries (in a recent survey 10% of Asian pig producers reported >25% of pigs less than 'full value' at marketing), the high ranking of disease as the main cause of underperformance (in the same survey more than half of the respondents mentioned disease reduction as most important mean to reduce losses<sup>2</sup>), the high incidence of bacterial diseases (64%, 50% and 45% of pig farms in Asia-Pacific experienced problems with *M. hyopneumoniae*, *E. coli* and *S. suis* respectively in the year of the survey) (van der Sluis, 2012) and the ease with which antimicrobials can be sourced, the magnitude of prophylactic antimicrobial use is likely to be relatively high. Applying the low rate of antimicrobial use intensity of northern European countries to East and Southeast Asia's meat output would suggest the annual use of around 4.3 and 0.8 thousand tonnes of antibiotics in the two sub-regions respectively.

Indirect evidence of widespread use of antimicrobials in livestock production is provided by the high prevalence of antimicrobial resistance found in enteric microorganisms as well as in *S. suis* isolated

<sup>2</sup> Controlling disease was also seen as best means to increase feed conversion efficiency.

from food-producing animals and retail meat in various Asian countries. Some of these findings are summarized below.

### 3.3.1 *Salmonella enterica*

Van *et al.* (2012) reviewed results of antibiotic resistance studies of non-typhoidal *S. enterica* in Southeast Asia the results of which are partly summarized in Table 6. Close to 50% of the salmonella isolates displayed multi-drug resistance.

Table 6: Resistance of non-typhoidal *S. enterica* isolates to different classes of antibiotics

Country	No of isolates	Source	Percentage of resistant isolates			
			TET	AMP	SUL	MDR
Cambodia	152	Poultry	21	17	13	ND
Malaysia	33	Various livestock	64	24	48	49
Malaysia	55	Poultry	85	29	ND	75
Thailand	211	Poultry & pigs	59	49	68	66
Thailand	131	Raw pork	67	35	55	44
Vietnam	89	Pigs	92	41	57	56
Vietnam	91	Meat & shellfish	41	22	17	21
Vietnam	241	Cattle, pigs & poultry	49	26	30	40

TET = Tetracyclines, AMP = Ampicillin, SUL = Sulfonamides, MDR = Multidrug resistance (resistance to at least three different classes

Source: Van *et al.*, 2012.

In Bangladesh, Begum *et al.* (2010) found that 9, 8, 7, 6 and 2 out of 12 *Salmonella spp.* isolates (n=12) from chicken intestines and faeces displayed resistance to Ampicillin, Nalidixic acid, Cotrimoxazole, Tetracyclines, and Kanamycin respectively while all 12 isolates were susceptible to Cephalexin, Chloramphenicol, Ciprofloxacin, Ceftriazone and Gentamycin. Rates of AMR in *Salmonella spp.* isolates from eggs (n=7) were much lower.

### 3.3.2 *Escherichia coli*

In Vietnam, a study by [Reference] found *E. coli* and *Salmonella* species to be highly prevalent in food from animal sources obtained at markets, slaughterhouses and farms, multidrug resistance reaching 50% in *E. coli*. In Thailand, Lay *et al.* (2012) analysed a total of 344 *E. coli* isolates from faecal samples of swine for antimicrobial resistance to different classes of antimicrobial agents. All isolates were resistant to at least one antimicrobial agent and 98.3% were multidrug resistant. Forty-two resistance patterns were observed.

### 3.3.3 *Campylobacter species*

Ninety-eight broiler flocks raised in Chiang Mai, Thailand, were included in a study by Chokboonmongkol *et al.* (2012) *C. jejuni* was detected as the major *Campylobacter spp.* both in broiler flocks and on broiler carcasses. In the 32 *Campylobacter* isolates, antimicrobial drug resistance to Ciprofloxacin was most common (81.3%), followed by tetracycline (40.6%), ampicillin (31.3%) and erythromycin (9.38%). Eight different antimicrobial resistance patterns were demonstrated.

In Cambodia, Lay *et al.* (2011) found high levels of resistance to Cefalotin (97%), Nalidixic acid (58%) and Ciprofloxacin (25%) in 139 *Campylobacter* isolates obtained from poultry carcasses at markets. Eleven percent of isolates were resistant to Amoxicillin while the prevalence of resistance to Azithromycin, Erythromycin and Gentamycin was below 5%.

### **3.3.4 *Streptococcus suis***

Over the past few years, the number of reported *S. suis* infections in humans has increased significantly, with most cases originating in Southeast Asia, infection being acquired through exposure to contaminated pigs or pig meat. *S. suis* strains isolated between 1997 and 2008 in Vietnam were investigated for their susceptibility to six antimicrobial agents by Hoa et al. (2011) and a significant increase in resistance to tetracycline and chloramphenicol was observed, which was concurrent with an increase in multi-drug resistance.

Li et al. (2012) examined isolates of *S. suis* from diseased pigs in China for susceptibility to nine antimicrobials, possession of virulence-associated factors (VFs), and distribution of serotypes. The association between antimicrobial resistance (AMR) and serotypes as well as VFs was subsequently assessed. It is notable that multiple antimicrobial resistance (three or more antimicrobials) was observed in 98.7% of the *S. suis* isolates, and the dominant resistance phenotype was erythromycin-tilmicosin-clindamycin-chloramphenicol-levofloxacin-ceftiofur-kanamycin-tetracycline-penicillin (35.6%). Presence of VFs and the possession of certain AMR phenotypes were significantly associated.

## **4 Disease burdens and impacts**

Zoonotic diseases and disease risk affect welfare of society through a number of pathways, some of which are not immediately apparent. Disease risk in itself imposes financial and social costs arising from publicly and privately funded disease risk mitigation (prevention) measures such as, for example, inspection, quarantines and vaccination campaigns. A major 'cost' of acute disease risk, perceived or real, is the revenue forgone through diminished economic activity in sectors and regions far removed from the original risk source. Examples of 'disease scares' impacting on sectors and regions other than those directly affected are provided by the SARS epidemic in 2002 and HPAI H5N1. Disease risk also deters investments into livestock production, thereby diminishing supply, a cost borne by consumers through higher prices for livestock products.

Disease control activities represent another element of 'the cost of disease'. Similar to prevention activities, control costs stem outlays for disease detection and quarantines (internal), to which costs of treatment and / or culling and safe disposal have to be added (see HPAI H5N1). In addition, disease outbreaks depress economic activity in the affected and associated sectors, for example feed producers and meat processors. These sector, which however may be partially compensated by increased revenues in other sectors.

The actual disease burden leading to reduced productivity and in some cases shortened life span represents a third element of 'the cost of disease'. In humans, burden of disease is of expressed in disability-adjusted life years (DALYs). This time-based measure combines years of life lost due to premature mortality and years of life lost due to time lived in states of less than full health (diseases causing mortality in children and young adults are assigned more DALYs than diseases affecting the elderly). DALYs are often used to compare the burden of disease across diseases, disease categories, regions, socio-economic groups etc. With respect to livestock, no composite standardized measure of disease burden or losses has been developed, which severely constrains comparability of figures provided by different studies.

AMR negatively affects society by leading to higher treatment costs through use of more expensive compounds and longer hospitalization and to reduced productive life (increased case fatality rates). Resistance may also affect the treatment of individuals with non-resistant organisms as in areas with

high rates of resistance physicians may change empiric therapy, increasing overall treatment costs. In some instances, these costs may exceed those attributable to treatment failure (Howard et al., 2003)

Generally, higher investments in disease prevention and control lead to lower disease burdens but usually the law of diminishing returns applies and a point is reached where the additional cost of prevention measures may outweigh the additional benefits of reduced disease burdens. Thus, although at first glance useful, disease burden alone is not the best indicator to guide health investment. Unfortunately, to date there are no systematic, comprehensive and comparative studies on the costs and benefits of the control of zoonotic diseases. Some examples of 'pathways' of disease effects and magnitude of impacts will be provided in the following.

#### **4.1 Emerging infectious zoonotic diseases**

No DALY figures have been estimated for those zoonoses that have only emerged recently such as SARS and Nipah. For these diseases, despite high case fatality rates, due to low overall case load the aggregate impact on human health is very small compared to 'established' infectious and zoonotic diseases and the main impact was caused by fear and precautionary measures.

A recent study estimated the costs of six emerging zoonoses between 1997 and 2009 (Worldbank, 2012). The average cost was US\$6.7 billion.

##### **4.1.1 SARS**

Between November 2002 and August 2003, SARS had spread from China to 29 countries and 3 regions, with a cumulative total of 8,422 cases and 916 deaths.

The main negative effects of SARS on China and Hong Kong were the drop in local demand for goods and services and the strong drop in tourism and air travel. For China, Hai et al. (2004) estimated that in 2003, tourism revenue from foreigners would decrease by about 50 to 60 percent (amounting to about US\$10.8 billion) compared with the tourism revenue in 2002 and revenue from domestic tourists would decrease by around 10 percent (amounting to about US\$6.0 billion). The same authors also concluded that SARS would cause, through a multiplier effect, a total loss of US\$25.3 billion to China's economy and that the growth rate of China's GDP in 2003 would be 1–2 percentage points lower than it would have been if the SARS outbreak had not occurred.

The above might be overestimates as initial alarmist reports and estimates about the negative economic impacts were not borne out (Siu et al., undated). Fear and panic subsided quickly once the outbreak was under control, and the economy rebounded rapidly.

##### **4.1.2 Nipah – Malaysia**

During the outbreak in 1998-99 in Peninsular Malaysia, Nipah virus affected 276 people causing 106 human deaths.

In order to control the outbreak, animal health authorities slaughtered about 1.1 million (out of 2.4 million) pigs and the evidence of infection in dogs led to the decision to shoot all dogs in infected areas. The value of destroyed pigs was about US\$97 million. The outbreak significantly reduced the number of pig farms from 1,800 prior to January 1999 to only 796 after July 21, 1999 (Nordin, 2001). An interview survey on ex-hog farmers revealed that many changed their business to poultry, dairy, beef cattle or frog farming while there are other farmers who were employed on palm farms where working conditions are poor (Hosono et al., 2006)

The outbreak led to major structural changes in the Malaysian hog industry causing 'ripple effects' in affiliated industries. The sector that suffered the greatest was the feed industry with an approximate RM67 million (US\$17.4 million) reduction in the value of its production. Next, the oils and fats sector, which uses the fat of pigs, suffered an approximately RM35 million (US\$9.1million) reduction. However, economic influence was seen not only in the industries directly related to hog raising industry but also in a wide range of business activities such as utility and real estate. The RM280 million (US\$72.8 million) reduction in the production of the hog raising industry resulted in RM541 million (US\$141 million) of economic damage nation-wide, nearly two times more than the direct damage (Hosono et al., 2006). A World Bank (2012) estimate of the economic losses related to the Malaysian Nipah outbreak is as high as US\$671 million.

#### **4.1.3 HPAI H5N1 ('Bird Flu')**

From its (re-)emergence in 2003 to June 2012, the World Health Organization has tallied 606 human cases of bird flu and 357 deaths.

A review of HPAI H5N1 impacts on livestock production was carried out by Otte et al. in 2008. In principle, the HPAI H5N1 epidemic had the same type of impacts as the Nipah outbreak in Malaysia, only at a much larger spatial and temporal scale. In the early stages of the epidemic, the main direct losses to the poultry sector were caused by the massive culling of flocks considered 'at risk'. In Thailand, for example, 63.8 million birds were culled from the onset of HPAI outbreaks in 2004 until 2006 (NaRanong, 2007) while for Viet Nam the figure amounts to around 50 million birds (McLeod and Dolberg, 2007)<sup>3</sup>. Culling not only results in the 'wastage' of birds, but carries a cost, which has been estimated to be about US\$0.25 per bird for a 200 bird flock in Vietnam. Disinfection of farms after depopulation was estimated to cost in the range from US\$22 to 110 per farm in Bangladesh.

Additional control costs were incurred through movement controls, surveillance and public awareness campaigns. In Malaysia, implementation of movement controls in form of roadblocks cost US\$50,000 per month in 2005. Some countries embarked on vaccination campaigns. In Vietnam, two mass vaccination campaigns were carried out by private agents under the supervision of public veterinary services per year. Investments were made in cold storage for vaccines, training of vaccinators and mass communication campaigns. The total costs of delivering 364.5 million vaccinations during the first year were estimated to be approximately US\$21 million.

As the HPAI H5N1 virus is able to infect humans, HPAI outbreaks in poultry have, at least in the period immediately following their notification, led to a drop in demand for poultry meat and eggs. For example a cross-country consumer survey carried out in May 2006 revealed that in most countries, not only those affected by HPAI, a significant proportion of consumers had reduced their consumption of poultry. In the European Union for example nearly 20% of respondents of a consumer survey conducted in 2006 stated that they had reduced consumption of poultry meat by an average of 18% and sales of poultry and eggs fell by 70% and 20% in Italy and France respectively.

Thailand had established itself as the fourth largest exporter of poultry meat prior to the incursion of HPAI in 2004 (only Brazil, USA and EU exported more). In 2003, Thailand exported nearly 485 thousand tonnes of poultry meat (nearly 40% of production), of which around two thirds were exported frozen and the remainder pre-cooked (NaRanong, 2007). The EU and Japan were the main export destinations for Thai poultry meat. After the notification of HPAI by Thai authorities in early 2004, Thai poultry products were immediately banned from major international trade flows and total exports in 2004 dropped to 218 thousand tonnes, or 45% of the 2003 figure.

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<sup>3</sup> In the initial waves both Thai and Vietnamese authorities applied a policy of culling all poultry within a 5km radius of an infected premises. Over time, in both countries authorities moved to much more selective culling strategies leading to much lower numbers of poultry culled in subsequent HPAI waves.

The 'ripple' effects on affiliated industries were similar to those described for Nipah in Malaysia and SARS in China. In the Mekong countries an important linkage exists between the poultry sector and rice production. Ducks are important for pest control in paddy rice and rice farmers in the Mekong Delta complained that the reductions of duck numbers in the rice fields resulted in increased damage from golden snails, increased occurrence of viral diseases in the spring-winter crop in 2006, and as a result lower net incomes of rice farmers (Men, 2007).

#### **4.1.5 2009 H1N1 ('Swine Flu')**

The 2009 pandemic influenza A H1N1 has caused an estimated excess of 201,200 respiratory deaths (range 105,700–395,600) globally with an additional 83,300 cardiovascular deaths (46,000–179,900). In contrast to seasonal influenza, 80% of the respiratory and cardiovascular deaths were in people younger than 65 years (Dawood et al., 2012). Assuming a low figure of 15 years of life lost per fatal case, and not considering disability losses in recovered cases, globally the H1N1 pandemic gave rise to at least 4.5 million DALYs in 2009, i.e. around 65 DALYs / 100,000 people.

Reports of the H1N1 epidemic in people, coupled with the use of the term "swine flu", initially caused a downturn in domestic and international pork markets. Domestic pork demand and prices dropped sharply because of consumer fears that eating pork might result in infection. Several pork-importing countries also began to consider instituting trade bans and restrictions on live pig and pork imports from certain countries, including the United States. This initial reaction further rippled throughout pork and other agricultural markets, such as feed grain and other livestock markets (Johnson, 2009). The University of Missouri estimated that the US pork industry faced losses of about US\$270 million in income in the second quarter of 2009 alone.

#### **4.1.6 Japanese Encephalitis (JE)**

An estimated 3 billion persons live in countries where the JE virus is endemic, and the annual incidence of the disease is 30,000 to 50,000 cases (Erlanger et al., 2009). The disease can cause irreversible neurologic damage. The annual number of human deaths lies between 10,000 and 15,000, and the estimated global impact from JE in 2002 was 709,000 DALYs. However, these statistics should be interpreted with care because the transmission of JE is highly dynamic; and there is considerable fluctuation in estimates of its global impact. In 1999, JE caused an estimated 1,046,000 DALYs; in the 2 subsequent years, it caused 426,000, and 767,000 DALYs, respectively (Erlanger et al., 2009). The estimated JE burden in endemic areas of affected countries and the trend of JE incidence are shown in Table 7.

Table 7: JE burden, incidence trends and control programmes in Asian countries

Country	Pop. in JE endemic areas (million)	DALYs in 2002 (thousand)	DALYs / 100,000	Trend of JE incidence	Vaccination programme
Bangladesh	106.4	24	23	Increase	No
India	597.5	226	38	Increase	No
Nepal	4.6	5	109	Stable	Yes
Pakistan	18.5	82	443	Increase	na
Sri Lanka	16.4	1	6	Decrease	Yes
China	422.5	281	67	Decrease	Yes
Japan	44.0	<1		Stable	Yes
Korea, DPR	8.6	6	70	na	na
Korea, Rep	9.2	6	65	Stable	Yes
Cambodia	11.3	4	35	Increase	No
Indonesia	116.1	23	20	Increase	No
Lao PDR	4.6	5	109	Increase	No
Malaysia	8.9	2	22	Decrease	Yes
Myanmar	35.1	13	37	Increase	No
Philippines	31.1	8	26	Stable	No
Thailand	43.4	5	12	Decrease	Yes
Vietnam	61.7	11	18	Stable	Yes
PNG	5.1	2	39	na	na
<b>Total</b>	<b>1,545.0</b>	<b>705</b>	<b>45</b>		

Source: Erlanger et al., 2009.

Underlying factors that might explain year-to-year fluctuations in JE incidence are contextual while incidence trends are likely to be determined by the expansion of irrigated rice and / or pig production and public health interventions, e.g. in the form of vaccination campaigns.

JE is not a very important disease of pigs causing only sporadic reproductive problems and pigs are asymptomatic.

## 4.2 Zoonoses and food-borne disease impact and burden

Zoonoses have negative health impacts on humans, livestock and wildlife. Classical, endemic zoonoses, present in many places and affecting many people and animals are responsible for the great majority of human cases of illness (99.9%) and deaths (96%) attributable to zoonoses as well as the greatest reduction in livestock production (Grace et al., 2012). Outbreak zoonoses are more sporadic in temporal and spatial distribution than endemic zoonoses but may be more feared because of their unpredictability and in some cases, severity. Furthermore, novel zoonoses which might be or become transmissible between humans are of concern to 'rich' countries because they threaten their own populations while endemic zoonoses are to a large extent localized and do not have the potential to assume pandemic proportions.

The original Global Burden of Disease Study (GBD) was commissioned by the World Bank in 1991 to provide a comprehensive assessment of the burden of 107 diseases and injuries and ten selected risk factors for the world. The GBD study, published by WHO in 2004 represents the most authoritative source of information on human illness.

There are some challenges in using the GBD to assess the burden of zoonoses.

- Firstly, zoonoses (especially in poor countries) are widely unreported, and under-reporting is relatively greater for zoonoses than for non-zoonotic diseases of comparable prevalence

(Schelling et al., 2007). As the GBD report is based on national information for levels of mortality and cause of illness, this under-reporting is reflected in the GBD.

- Secondly, several zoonoses with considerable burdens are not included in the GBD assessment. For example rabies, echinococcosis, cysticercosis, leptospirosis and brucellosis.
- Thirdly, the GBD is organised around diseases and not pathogens or transmission pathways. For example, diarrhoeal diseases, among the highest causes of morbidity and mortality in poor countries, comprise one category. Although the majority of important diarrhoeal pathogens are zoonotic (Schlundt et al., 2004) it is not currently possible to identify the zoonotic component of diarrhoeal disease from GBD figures.

Table 8 shows the burden (000 DALYs) associated with selected zoonoses in the GBD for Asian sub-regions. It can be seen that South Asia, by a high margin, carries the highest total as well as *per capita* burden of infectious and parasitic (I&P) diseases, diarrhoea, leishmaniasis and JE.

Table 8: Burden associated with selected zoonotic diseases by Asian sub-regions (2004) (figure in brackets indicates percent of infectious and parasitic disease burden)

	I&P Diseases		Diarrhoea		TB		Leishmaniasis		JE	
	DALYs (1,000)	DALYs / 100,000	DALYs (1,000)	DALYs / 100,000	DALYs (1,000)	DALYs / 100,000	DALYs (1,000)	DALYs / 100,000	DALYs (1,000)	DALYs / 100,000
<b>S.Asia</b>	81,440	5,453	25,084 (31)	1,680	10,923 (13)	731	1,408 (2)	94	416	82
<b>E.Asia</b>	13,383	884	3,957 (30)	261	3,892 (29)	257	1	0	136	9
<b>SE.Asia</b>	19,708	3,584	3,542 (18)	644	4,860 (25)	884	40 (1)	7	121	22
<b>Aus&amp;NZ</b>	36	151	6 (17)	26	1 (2)	3	0	0	0	0

Source: extracted from WHO 2004

The estimated burden caused by diarrhoeas surpasses the burden of nutritional deficiencies (energy-protein malnutrition, iodine, Vitamin A and iron deficiency), which the same study estimated at 13.3, 3.3 and 3.2 million DALYs for South, East and Southeast Asia respectively (891, 248, and 580 DALYs / 100,000 population).

#### 4.2.1 Zoonotic bacterial gastro-intestinal disease

Several important bacterial zoonoses have minimal impact in livestock, notably toxigenic *E. coli* in cattle and *S. enteritidis* in poultry (Listeria, Staphylococcus, Bacillus spp, other Salmonella spp).

In humans, as summarized in Table 8, diarrhoea, from all causes, accounts for nearly one third of disability attributed to infectious and parasitic diseases in South and East Asia and thus is the leading cause of disability related to infectious conditions. In Southeast Asia, diarrhoea is only surpassed by TB (zoonotic and non-zoonotic) as infectious cause of human disability.

Unfortunately, the WHO 2004 GBD does not provide information on age-specific burden or cause of diarrhoea. With respect to age-specific incidence of diarrhoea, Fischer Walker et al. (2012) report that incidence is highest in children of 6 to 11 months, 4.5 episodes / child /year, thereafter declining to 2.3 episodes / child /year in children aged 24 to 59 months. Diarrhoea is responsible for slightly above 20% of child mortality in Asia (Boschi-Pinto et al., 2008), diarrhoea-specific mortality per 100 child-years being 0.12 in the region (i.e. around 120 child deaths per 100,000 children per year from diarrhoea) (Fischer Walker et al., 2012). Adult mortality from diarrhoea is considerably lower at around 0.03 deaths per 100 person years.

The pathogens causing most diarrhoeal disease are *Entamoeba histolytica*, (10.7%), *Shigella* spp. (9.3%) and enterotoxigenic *Escherichia coli* (4.6%) (reference). In developing countries, most deaths due to diarrhoea are attributed to enterotoxigenic *E coli* (28.2%) and *Vibrio cholerae* (20.7%); while in developed countries most deaths are caused by *Campylobacter* (14%) and *Salmonella* spp. (11.5%). These estimates are however based limited data and do not account for regional differences. In developed countries, several reviews (Schlundt et al., 2004, Flint et al., 2005) argue the majority of gastrointestinal disease burden is due to zoonotic pathogens (>50%). A recent study from the US estimated that 75% of the food-borne disease burden was due to bacterial or protozoal zoonoses (Hoffman et al., 2012).

Given the lack of age-cause-region specific information on diarrhoea DALYs, any estimate of the burden of zoonotic diarrhoea is highly uncertain. Taking 10% attribution to zoonotic pathogens as lower bound and 33% as upper bound would yield intervals of 168-560, 26-87 and 64-215 DALYs / 100,000 population in South, East and Southeast Asia respectively.

#### 4.2.2 Leptospirosis

In livestock, leptospirosis is associated with abortion, still-birth, infertility and milk reduction in cattle and swine. There is little good data on losses associated with leptospirosis in developing countries. In Australia, total loss was estimated at 2.2% at herd level (Holroyd, 1980). In Vietnam, infection with some serovars correlated with one less live pig per litter, equivalent to 8% loss of production (Boqvist et al., 2002).

In humans the median global incidence of endemic leptospirosis is 5 cases per 100,000 population with incidence in males exceeding that in females (WHO, 2011). Table 9 displays estimated annual incidence classes of human leptospirosis in Asian countries.

Table 9: Human leptospirosis incidence in Asian countries

Country	Cases / 100,000	Cases
Bangladesh	>10	> 15,050
Nepal	>10	> 2,650
India	1 to 10	11,170 to 111,700
Sri Lanka	>10	> 1,900
China	1 to 10	13,120 to 131,200
Mongolia	1 to 10	25 to 250
Cambodia	>10	> 1,370
Lao PDR	>10	> 550
Indonesia	1 to 10	2,230 to 22,300
Malaysia	1 to 10	250 to 2,500
Philippines	1 to 10	830 to 8,300
Thailand	>10	> 6,250
Vietnam	>10	> 8,380

Source: Victoriano et al., 2009.

Humans infected with leptospira spp normally suffer from acute febrile illness, which may be accompanied by acute renal injury (36% of cases) and or acute lung injury (17% of cases) with case fatalities of 12% and 25% respectively (WHO, 2011).

#### 4.2.3 Cysticercosis

In livestock, losses are associated with condemnation of affected meat. In Mexico, prevalence of around 1.6% was associated with losses of US\$68 million (Stabenow et al., 1987) while in Cameroon a prevalence of 5.6% was estimated to cost the pig industry nearly €500,000 a year (Praet et al., 2009).

In humans, the most significant aspect of the findings on neuro-cysticercosis burden, which was undertaken by way of a comprehensive review of 567 research articles between 1990 and 2008, reinforced the association between the disease and epilepsy. It showed that 30% of all people with epilepsy in countries where the pork tapeworm is frequent also had neuro-cysticercosis, which implied that successful interventions that reduced the burden of neuro-cysticercosis could result in concomitant decline in the burden of epilepsy.

#### 4.2.4 Tuberculosis

Muller (2010) summarizes a range of early reviews from Europe and North America before control was widespread. Infected cattle lost 10% of milk production and 4% of meat production and infected cows had one fewer calf. Unfortunately, good economic data is missing from developing countries but similar losses could be anticipated. TB lesions are also an important reason for carcass condemnation but it seems likely that routine meat inspection misses most cases (Biffa et al., 2010). Agricultural losses worldwide have been estimated at US\$3 billion (Garnier et al., 2003).

Taking the conservative estimate of Cosivi (1998), who estimated worldwide the proportion of TB caused by *M. bovis* at 3.1%, zoonotic TB is responsible for at least 330, 115 and 15 thousand DALYs per year in South, East and Southeast Asia (22, 8 and 27 DALYs / 100,000 population). The literature review of Grace et al. (2012) suggests the proportion of zoonotic TB to actually be higher.

#### 4.2.5 Rabies

The recorded incidence of rabies deaths in Asian countries in 2004 is displayed in Table 10. Most (60%) cases of rabies occur in children between 0 and 12 years of age and Coleman et al. (2004) estimate a weighted average DALY of 33.1 for rabies associated mortality. This estimated DALY impact is conservative because it considers only the YLL component and does not take into account YLDs resulting from the illness associated with the trauma of animal bites and post-exposure therapy, if available.

Table 10: Human rabies deaths and post-exposure prophylactic treatments (PEP), Asia, 2004

Country	Deaths	DALYs <sup>1</sup>	DALYs / 100,000	Post-exposure treatments	PEP cost <sup>2</sup> (US\$ million)
Bangladesh	1,550	50,568	33.6	60,000	2.70
India	17,000	554,621	49.7	2,500,000	11.25
Nepal	44	1,435	5.4	25,000	1.13
Pakistan	2,490	81,236	52.3	69,000	31.05
Sri Lanka	76	2,479	13.0	80,000	36.00
China	2,009	65,543	5.9	7,000,000	315.00
Mongolia	2	65	2.6	62	2.79
Cambodia	2	65	0.5	12,000	0.54
Lao PDR	2	65	1.2	3,000	0.14
Indonesia	40	1,305	0.6	8,800	0.40
Philippines	248	8,091	9.8	102,148	4.59
Thailand	26	848	1.4	200,000	9.00
Vietnam	30	979	1.7	635,000	28.56

<sup>1</sup> @ 33.1 YLL/rabies death

<sup>2</sup> @ US\$ 45/treatment

Source: Miranda, 2006.

The cost of post-exposure treatments, which typically is around US\$40 to 49, amounted to around US\$500 million in 2004.

#### **4.2.6 Leishmaniasis**

Equids are occasionally infected by leishmaniasis but it is not a significant disease in other livestock. According to the WHO GBD study, DALYs for leishmaniasis in Asia's sub-regions are 1.4 million in South Asia, one thousand in East Asia and 40 thousand in Southeast Asia (Table 8).

#### **4.2.7 Brucellosis**

Sero-positive animals have higher rates of abortion, stillbirth, infertility, calf mortality and lameness. This is associated with lower milk yields (around 25% milk loss in aborted cows). The losses are estimated at 6-10% of the annual value produced per animal (Mangen et al., 2002).

The World Health Organization (WHO) estimates that half a million cases are reported worldwide every year, and that for every case diagnosed there are four cases which go undetected (Puvar, 2007). Disease incidence and prevalence rates vary widely among nations. Because of variable reporting, true estimates in endemic areas are unknown. Incidence rates of 1.2-70 cases per 100,000 people are reported. Human brucellosis carries a low mortality rate (< 5%), however, brucellosis can cause chronic debilitating illness with extensive morbidity. Worldwide, brucellosis is more common in males than in females, with a ratio of 5:2-3 in endemic areas. Brucellosis in children comprises 3-10% of reported cases worldwide, with a heavier burden in endemic areas.

#### **4.2.8 Echinococcosis**

The loss to the global livestock industry is estimated at around US\$2 billion annually and the cost of illness in people is around the same (Torgerson et al., 2010).

A preliminary estimate of the global disease burden due to alveolar echinococcosis (AE) put the number of cases at 30,300 per year of which 10,381 cases were food related. More recently, Torgerson et al. (2010) estimated that there are approximately 18,235 (CIs 11,900–28,200) new cases of AE per annum globally with 16,629 (91%) occurring in China and 1,606 outside China. Most of these cases are in regions where there is little treatment available and therefore will be fatal. Based on disability weights for hepatic carcinoma and estimated age and gender specific incidence AE a median of 666,434 DALYs per annum (CIs 331,000-1.3 million) has been estimated (idem).

#### **4.2.9 Toxoplasmosis**

Toxoplasmosis is a leading cause of abortion in sheep and goats. A study by Reading University estimated the costs to the sheep industry of the UK at between GBP12 million and 24 million each year. The annual economic impact of toxoplasmosis in United States livestock was estimated to be US\$7.7 billion in 1996 (Buzby et al., 1996). A study in the Netherlands found that toxoplasmosis caused the highest health burden of seven pathogens investigated (including Salmonella, Campylobacter, Norovirus and Rotavirus) (Kemmeren et al., 2006).

#### **4.2.10 Q-fever**

The economic consequences of the Q-fever epidemic that occurred between 2007 and 2010 in the Netherlands was estimated at €161 to €336 million. Loss in quality of life of affected people amounted to about €67 to €145 million and loss of work-days to €12.5 to €96.5 million (Tempelman, 2011).

Respiratory disease is a major cause of human sickness and death and a certain proportion is due to zoonotic diseases such as Q-fever. However, no reliable estimates on the possible contribution of zoonoses to the respiratory disease burden could be found.

#### **4.2.11 Food-borne trematodiasis**

Fuerst et al. (2012) estimated that in 2005 about 56.2 million people were infected with food-borne trematodes, 7.9 million had severe sequelae, and 7,158 died. Taken together, the global burden of food-borne trematodiasis was estimated at 665,352 DALYs. Food-borne trematodiasis are relatively frequent in East and Southeast Asia, where they accounted for around 440 and 160 thousand DALYs in 2005, figures that are slightly above the DALY estimates for JE.

### **4.3 Impact of AMR**

The nature of the 'cost' to society associated with resistant microorganisms has been described in the introduction to this section. Most of the losses and impacts relate to failure of treatments and disease control programmes, increased severity and longevity of diseases, increased mortality, reduced productivity, increased risk of disease spread and therefore increased costs to society as a whole.

Unfortunately no quantitative information on these costs could be found in the published literature for Asian countries and therefore some examples will be taken from other countries. In the USA, for example, Roberts et al. (2009) estimated infection with resistant microbes to be associated with an 11-day increase of hospitalization, increasing medical costs per patient by around US\$20,000 and a 2.2 fold increased risk of death. The total attributable hospital and societal cost for 1,391 patients included in the study were: hospital, US\$3.4–5.4 million; mortality, US\$7.0–9.2 million; lost productivity, US\$162,624–322,707; and total, US\$10.7–\$15.0 million (i.e. around US\$10,000 per hospitalized patient). Nationally, for the USA, the costs associated with AMR in the out-patient settings, a fraction of those for hospitalized patients, have been estimated to be between US\$400 million and US\$18.6 billion (Okeke et al., 2005).

## **5 Responses to mitigate disease risk**

The far-reaching and costly externalities of disease and disease risk warrant major public sector involvement and international cooperation and coordination in disease risk management. Current emphasis in disease control and prevention is on disrupting transmission, with early warning, early detection and early response mechanisms also targeting also emerging pathogens. Whilst critically important, this approach does in itself not confront the root causes of disease, and as such is reactive rather than pro-active leading to *post-hoc* corrective actions as opposed to farsighted *ex-ante* risk management.

Public policy and international funding agencies should address this weakness and promote a more holistic, multidisciplinary approach to agriculture and health research and risk management that addresses the root causes of disease burdens and risk. In addition to the traditional elements of 'early detection' (surveillance) and 'rapid response' (contingency plans) this more proactive approach to disease risk management would include 'foresight', 'prevention' and 'ex-ante impact mitigation'.

Foresight capacity builds on visioning exercises that systematically scan the horizons to identify sources of pathogens as well as pathways and drivers of emergence, leading to the identification of geographic 'hotspots' and 'risky practices'. A profound understanding of the demographic, cultural, economic, environmental, climatic, evolutionary, and social factors that contribute to the emergence and intensification of infectious diseases is required for this process. Given the complex dynamics of disease emergence foresight exercises require intimate interdisciplinary collaboration and build on mining and fusion of data from a broad array of sources.

'Prevention' and 'ex-ante impact mitigation' build on insights gained from improved understanding of the implications of intensification and climate change on diseases to propose preventive actions aimed at reducing the likelihood of pathogen emergence and spread by specifically tackling significantly influential drivers, and to devise interventions that increase institutional, economic, and environmental resilience against novel pathogens. Unfortunately, investments in prevention and impact mitigation face major incentive problems as: (i) today's investment costs have to be justified against the uncertainty of disease related losses avoided at some time in the future, and (ii) sources and targets of investment funding may have to diverge to achieve the highest possible global protection from emerging diseases.

Given the stochastic element of infectious disease emergence and spread, even the most massive investment in disease intelligence cannot perfectly predict or entirely prevent pathogen emergence and a comprehensive system of disease risk management that couples early detection with rapid reaction capacity to swiftly and determinately tackle diseases at, or close to, source before spread has surpassed a critical threshold is needed. Early detection of potential pathogens needs to combine active scanning of a multitude of host species, which include wildlife, food and companion animals, and humans with the rapid 'connection' of passively obtained information on unusual health events in the socio-ecological interface that link livestock, wildlife, and humans. Advances in high throughput screening and information technology systems offer the possibility of 'real-time epidemiology' for early detection of disease events. To achieve maximum benefits, such a surveillance and rapid response system needs to operate as global health network reporting to highest levels of decision-making.

Broadening of health management towards the creation of safer, more disease resilient landscapes goes beyond the veterinary and medical services. The above outlined global health management system requires significant improvements in the integration of activities of the diverse organisations and institutions involved agricultural development, food production and trade, and human and animal health protection. Alignment of activities and improvements in coordination are necessary both 'horizontally', i.e. between various actors operating on a similar scale and administrative level, e.g. province or national, as well as 'vertically', i.e. from local to national to regional and global level.

The 'divisions' between different actors involved in agricultural development and health protection and their often narrowly defined remits stand in the way of forming broad coalitions to improve health outcomes and agreement on priorities is hampered by the lack of comprehensive and systematically collected data. This dearth of information is particularly acute in the area of zoonoses, which are neither considered priority human health problems nor priority animal health problems yet can have pervasive impacts across national economies.

## **6 Synthesis**

Over the next decades global food production has to grow significantly to feed the growing and more affluent human population. Producing more food will require expansion of agricultural areas and intensification of agricultural production. Disproportionate increases in the demand for animal source food and for other higher-value food items, such as fruits and vegetables, vis-à-vis staples are major determinants of agricultural development. Both expansion of agricultural areas, e.g. through deforestation, and intensification of food production, be it through expansion of irrigation for crops or industrialization of animal production, are associated with changing risks to human health from microorganisms harboured by wildlife and / or domesticated animals. This process of disease emergence is as old as mankind itself and many infectious diseases of humans have their origins in

animals. Agricultural expansion and intensification however is a catalyst for disease emergence as established agro-ecologies are disrupted and new ecologies are established. It is therefore not surprising that over the past 70 years most zoonotic diseases emerged in 'industrialized' regions of the world, which experienced dramatic changes in their agricultural systems in the second half of the 20<sup>th</sup> century, while it appears that for more recent emergence events the balance tends to swing towards developing regions. Similar epidemiological transitions were seen when livestock were first domesticated (Wolfe et al., 2007) and when new frontiers were opened by war or transport innovations (Grace and McDermott, 2011).

A major feature of the contemporary global food system is the vast increase in trade volumes (for food and non-food commodities, the latter being a risk for vector translocation), distances and speed, greatly enhancing the potential for disease spread once 'escaped' from its original ecosystem. Increased trade in wildlife, licit and illicit, further increases the risk of microorganisms finding a niche in a new environment.

Emerging zoonoses, as well as established zoonoses, whose incidence may however also be affected by agricultural expansion and intensification (and thus qualify as 'emerging') have major direct and indirect economic and welfare impacts. One of the main economic impacts of 'novel' zoonoses is revenue foregone through diminished economic activity prompted by precautionary behaviour of large segments of society (often fuelled by mass media). This reduction in economic activity is then not limited to the sector in which the disease emerged but also affects affiliated sectors and the economy at large and has international spillovers. General precautionary and preventive measures (e.g. quarantines, import bans, pre-movement testing, restraint in antimicrobial use etc), public and private, constitute a second financial and economic burden of zoonotic (and other) diseases for society. Efforts to control diseases, either endemic or epidemic, impose further costs while the disease itself and resulting productivity and welfare losses, both in animals and humans in the case of zoonoses, represent a fourth 'category' of disease cost.

No metric combining the above elements exists nor has a 'standardized approach' for the assessment of disease costs been developed and applied. Priority setting for disease control thus remains a rather arbitrary exercise. A systematic assessment of the full cost of disease across diseases, species (including humans), countries and time would face serious difficulties from the scarcity of comprehensive and comparable data. Zoonoses especially have high under-reporting in both veterinary and medical sectors.

ENhanCE (undated) reviewed 12 methods of disease prioritisation. Two were global (FAO/OIE and WHO), one focused on Rajasthan in India, while the rest focused on developed countries. A variety of methods were used: risk assessment approach, multi-criteria decision tools, and qualitative methods. Together the studies reviewed covered animal diseases, human diseases, and zoonoses. Of the 99 diseases appearing in the rankings reviewed, 33 were zoonoses. Zoonoses appearing in multiple listings according to the ENhanCE review, in declining order of number of appearances, were:

- Salmonellosis
- Leptospirosis = rabies
- Campylobacteriosis = tuberculosis = West Nile virus = toxoplasmosis
- Listeriosis = anthrax = echinococcosis = *E. coli* infection = BSE = botulism
- Cryptosporidiosis = Japanese encephalitis = Q fever = Rift Valley fever = tetanus

The DALY developed for quantification of human disease burden is useful as a first guide to which human diseases cause relatively high 'losses', however in themselves they are insufficient to guide investment as the latter should be determined by DALYs averted per \$ investment. Nevertheless, comparison of DALYs across selected diseases and Asian sub-regions (Table 11) provides some

indications as to which endemic zoonotic diseases / disease complexes might warrant particular attention by public health systems. In South Asia, conservatively assuming 10% of diarrhoea DALYs are of zoonotic aetiology, food-borne diseases rank highest by far, followed by leishmaniasis, JE and rabies. In East Asia, in addition to zoonotic diarrhoea, food-borne parasitic diseases appear to be the cause of considerable disease burdens. In Southeast Asia, in addition to zoonotic diarrhoea, foodborne trematode infections, zoonotic TB and JE seem to be responsible for the highest human disease burdens. It should be noted that the disease list is incomplete (e.g. no DALY figures are available for leptospirosis or brucellosis) and therefore is at best indicative.

Table 11: DALYs / 100,000 for selected zoonoses in Asian sub-regions

	S.Asia	E.Asia	SE.Asia
<b>Diarrhoea (total)</b>	1,680	261	644
<b>Diarrhoea (33% zoonotic)</b>	560	87	215
<b>Diarrhoea (10% zoonotic)</b>	168	26	64
<b>TB (10% zoonotic)</b>	22	8	27
<b>TB (5% zoonotic)</b>	11	4	13
<b>Leishmaniasis</b>	94	0	7
<b>Japanese encephalitis</b>	82	9	22
<b>Rabies</b>	47	5	3
<b>Alveolar echinococcosis</b>	0	46 <sup>1</sup>	0
<b>Foodborne trematodiasis</b>	0	34	33

<sup>1</sup> Approximately 1/3 foodborne

Even if the above estimates of disease burden is only indicative, it is clear that food borne diseases cause significant disease burden enhancing food safety (and general hygiene / sanitation) should be one of the priorities of public health systems throughout Asia.

Although causing far less loss of human life and disability, recent emergence of zoonotic pathogens in East and Southeast Asia, in several cases linked to amplification of wildlife micro-organisms in livestock populations, tremendous downturn in economic activity and shock to livelihood associated with the episodes, and the relatively high ratio of pigs to humans in these regions, the former regarded as ideal 'mixing vessels' for pathogens and adaptation to humans (e.g. influenza viruses) warrant major efforts, national and international, to minimize risks of disease emergence and to implement surveillance systems, in humans and livestock, to identify emerging pathogens before they spread widely.

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