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**Zoonotic emergence at the animal-environment-human interface:  
the forgotten urban socio-ecosystems**

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1 **Abstract**

2

3 Zoonotic emergence requires spillover from animals to humans, hence animal-human  
4 interactions. A lot has been emphasized on human intrusion into wild habitats (e.g., deforestation,  
5 hunting) and the development of agricultural and farming activities. However, the highly human-  
6 modified urban and peri-urban socio-ecosystems are also of great concern due to huge amounts of  
7 pet, domesticated and wild animals (e.g., birds, rodents and bats) that live in very close contact to  
8 very ~~densities-dense of~~ human ~~beingspopulations~~. This adds to the existence of wet wildlife markets,  
9 urban parks and wastelands, zoos and even labs, where spillover from wildlife to humans may also  
10 occur. Furthermore, cities are transport hubs that form hotspots of import/export of living resources  
11 including animals, thus potentially promoting rapid and wide-scale spread of reservoir and vectors,  
12 hence pathogens, as well as pathogen admixture through viral recombination or bacterial plasmid  
13 exchanges. Finally, cities are deeply modified environments where living organisms, including  
14 reservoirs, vectors and pathogens, undergo strong selective pressures, thus opening the gate to  
15 evolutionary novelties, hence potential new infectious threats. As such, we believe urban socio-  
16 ecosystems should be paid more attention in terms of drivers of zoonotic emergence in humans  
17 needing adapted surveillance and mitigation. Accordingly, we propose and discuss several avenues of  
18 research (~~e.g., better description of extended urban socio-ecosystems in urban health ecology~~  
19 ~~studies; truly evaluated interventional researches~~) and examples of actions that could be tested or  
20 generalized (e.g., focus on hotspots of emergence risks like slumsinformal settlements, wet markets  
21 or transport hubs; development of participative surveillance programs; shift towards inter-sectoral  
22 academic courses; massive investment into education and community information) in order to  
23 operationalize effective zoonotic surveillance. We advocate that this would allow ones to add  
24 emergence-preventive and early warning to usual outbreaks response strategies, thus significantly  
25 improving our collective ability to prevent zoonotic emergence and subsequent pandemics.

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27 **Keywords:** zoonotic emergence; urbanization; spillover; health ecology; One Health; Eco Health

## 1 1. Introduction

2

3 ~~In~~During the last decades, (re)emergence of zoonotic pathogens have led to an increasing number of  
4 human epidemics, the current Covid-19 pandemics being the most recent illustration. An important  
5 amount of observational studies as well as meta-analyses of the available scientific literature clearly  
6 point towards the association of human footprints on nature with animal-to-human spillover of  
7 infectious agents (e.g., Wolfe et al., 2005; Plowright et al., 2011; Jones et al., 2013; Gottdenker et al.,  
8 2014; Johnson et al., 2020; White & Razgour, 2020). In particular, wildlife hunting and consumption,  
9 encroachment into pristine areas, deforestation and land-use switches towards agricultural land as  
10 well as industrial livestock farming have been associated with the emergence of highly deleterious  
11 diseases such as plague, Human Immunodeficiency Virus (HIV), Ebola, Nipah, influenza, Severe  
12 Respiratory Acute Syndrome (SARS), Middle-East Respiratory Syndrome (MERS) and possibly Severe  
13 Respiratory Acute Syndrome Coronavirus 2 (SARS-Cov-2).

14 Although urbanization has also been identified as a possible factor for zoonotic spillover (e.g.,  
15 Santiago-Alarcon & MacGregor-Fors, 2020; Muloi et al., 2022) and amplification of some human  
16 epidemics (e.g., Olival et al., 2017), ~~many~~much researches and calls-for-action have rather focused  
17 on the importance of surveillance and prevention of zoonotic emergences along landscapes  
18 interfaces, with special emphasis on tropical forests (Wolfe et al., 2005; Guégan et al., 2019) and  
19 agricultural and farming industries (Jones et al., 2013). We of course fully agree with these  
20 recommendations. However, several of them failed to include cities as of potential importance for  
21 zoonotic emergence in humans *per se* (e.g., see Table 1 in the seminal paper of Jones et al., 2013;  
22 Kreuder-Johnson et al., 2015; Dobson et al., 2020; see also the very limited place given to infectious  
23 diseases in the recent review of urban-associated diseases by Flies et al., 2019). Yet, despite existing  
24 studies on urban-associated zoonoses (see examples below), we believe that ~~a particular further~~  
25 attention should ~~also~~ be paid to urban, peri-urban and sub-urban areas where massive though not  
26 fully evaluated contacts between wildlife, domestic animal and inhabitants occur on a ~~n~~ everyday  
27 daily basis. Cities are also expected to be efficient incubators of evolutionary novelties, ~~too~~. Such a  
28 situation is probably extremely favorable to repeated chains of already known or still unknown  
29 microbe transmission, thus opening the gate for spillover events and potential adaptation of some  
30 pathogens to human-to-human transmission, hence (re)emergence and large subsequent epidemics  
31 and pandemics.

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## 33 2. Cities as the most important human habitat

1

2 Urbanization is not a recent phenomenon. Large cities have existed in the past, and their  
3 development has ~~besides~~ been associated with wide-scale zoonotic epidemics (Moore, 2020). During  
4 the last century, urbanization has accelerated and, for the first time in human History, more than half  
5 of humanity now lives in cities, with Asia and Africa being currently the most urbanizing continents  
6 (UN Habitat, 2019) (Fig. 1 A-B). In the last twenty years (2001-2018), built-up areas (BUA) have ~~es~~ been  
7 increasing by 5,300,000 km<sup>2</sup> (i.e., more than 1,100 standard soccer fields per day) with 9 out of the  
8 10 countries showing the highest BUA expansion being ~~of~~ low- or middle-income ones (Sun et al.,  
9 2020). During the same period, 22 large cities (i.e., >100km<sup>2</sup>) have displayed population growth of  
10 more than 2 million inhabitants, with 15, 5 and 1 of them in Asia, Africa and South America,  
11 respectively (Sun et al., 2020) (Fig. 1 C-F). In most high-income countries, anticipated and supervised  
12 urban planning usually translates into regular sanitation devices, thus allowing for a proper  
13 management of garbage and sewage. Unfortunately, in urban settings from some low- and middle-  
14 income regions, urbanization goes faster than authorities' actions and resources allocation, thus  
15 leading to the creation and sprawling of wide, precarious and often informal urban settlements (UN  
16 Habitat, 2019). As such, millions of urban and peri-urban dwellers live within unhealthy areas  
17 characterized by waste accumulation, persistent standing waters, absence of drinkable water and  
18 electricity supply, lack of education and health services (Firdaus, 2012). In 2018, an estimate ~~of~~ 4.2  
19 billion ~~of~~ people were urban dwellers, with 20-25% (up to >60% in Africa) of them living in ~~slums~~  
20 informal settlements (UN Habitat, 2019).

21

22 Thus, ~~whatever this is good news or not~~, urban habitats must be considered as the most important  
23 environment of human life, at least for the century to come, since 6.7 billion human beings are  
24 expected to live in cities by 2050 (UN Habitat, 2019). Some scholars even argue that urbanization and  
25 its developing peripheral forms (e.g. ex-urbanization, sub-urbanization) influences the fate of most  
26 non-urban areas, far beyond the sole core cities (see the concept of "extended urbanization";  
27 Tzaninis et al., 2021). Due to this matter of fact as well as the obviously radical environmental  
28 changes, hence strong selective pressures, that urbanization puts on biodiversity, urban evolutionary  
29 ecology has recently received an important renewal of interest (Alberti, 2015; Rivkin et al., 2018;  
30 Alberti et al., 2020; Verrelli et al., 2022). However, it may be that some kind of academic European  
31 and North American leadership in the field induces a Northern hemisphere-biased perception (e.g.,  
32 Parsons et al., 2017, 2020; Alberti et al., 2020; see Box 2 in Verrelli et al., 2022 showing strong under-  
33 representation of Global South researchers in urban evolutionary ecology; see Gandy, 2021 for an

1 emphasis on urban health ecology), and so a very partial view of what animal-human interactions  
2 within cities may include. This is especially critical since ~~close to~~near 90% of extant urbanization takes  
3 place in the tropics, essentially in Asia and Africa (UN Habitat, 2019).

4 Also, cities are sometimes perceived as places of improved health following the existence of  
5 sanitation systems, the concentration of health services offer as well as more diversified and  
6 abundant food supply. However, such shortcut view fails to take into account the frequent and deep  
7 spatial and/or socio-economic inequalities which may be source of strong infectious risks, and may  
8 obscure the obvious needs of a ~~more complete~~broader apprehension-comprehension of what  
9 urbanization may represent in terms of health (Ahmed et al., 2019; Santiago-Alarcon & MacGregor-  
10 Fors, 2020). As an example, when one comes to infectious diseases and emergence risks, cities are  
11 places of millions of animal / human interactions which, by essence, are of major concern.

12

### 13 **3. Cities as places for millions of close animal-human interactions**

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15 Animals such as mammals and birds are intuitively associated with natural habitats, remote and/or  
16 protected areas that remain almost free of human disturbance. Yet, urban and peri-urban habitats,  
17 though deeply modified and densely populated by people, may shelter a wide spectrum of  
18 biodiversity, ~~as well as~~including livestock and poultry (Fig. 2). This is particularly true in “extended  
19 cities” of low- and middle-income countries, many of which lie in the intertropical zone and  
20 encompass wide zones or urban, peri-urban, sub-urban (i.e., peripheral but developing  
21 independently of the core city) and ex-urban (i.e., peripheral zones dedicated to human activities  
22 such as trade centers, airports, etc ... that densify and finally sprawl) areas (Connolly et al., 2021).

23

#### 24 **3.1 Pet and domestic animals**

25 Animal pets that may move around (such as dogs or cats) are plentiful in human settlements,  
26 including cities, and may play a major role in some diseases’ ecology (e.g., Munide et al., 2021). For  
27 instance, felids are the definitive host of *Toxoplasma gondii*; expectedly, free-living cats play a major  
28 role in the spreading of this highly human prevalent parasite within cities (e.g., in Brazil, 40% of Sao  
29 Paulo cats seropositive; Mereiles et al., 2004). Stray dogs may reach very large numbers in some  
30 urban and peri-urban areas, thus sometimes greatly contributing to rabies virus circulation and  
31 transmission within cities (e.g., Tenzin et al., 2015; Castillo-Neyra et al., 2017). In addition, many

1 urban dwellers in Africa, South America or Asia keep domestic animals such as cattle, pigs, goats,  
2 sheep, rabbits, poultries or pigeons in their households where they represent crucial food and  
3 economic resources. For instance, 56.6% of households in Banjul, Gambia, shelter poultry, while 47%  
4 of households in Dakar, Senegal, have small ruminants (Wilson, 2018). In Nairobi, Kenya, livestock is  
5 estimated to be over 1.3 million individuals: small-scale breeders represent 50-80% of cattle owners  
6 and are especially numerous in the informal settlements, with ~~slums-the latter~~ harboring 5% of dairy  
7 animals of the urban sub-counties. There, infrastructures are described as “poor and dirty” while  
8 many inhabitants even declare to share their house with their cattle (Alarcon et al., 2017). Free-range  
9 scavenging throughout insalubrious areas such as dumping sites, backyard slaughtering as well as  
10 outdoor left-over of dead animals also contribute to poor hygienic conditions (Alarcon et al., 2017).  
11 As an example, Kenyan urban farmers may sell poultry carcasses to pig farmers when massive deaths  
12 occur (Alarcon et al., 2017). Such practices are of course risky since domestic animals have been  
13 shown to play a central role in known human-mammal-virus associations network (Wells et al., 2019)  
14 and to share the highest number of viruses with our species (Johnson et al., 2020). As an example,  
15 pigs and poultry are well known domestic animals which may be influenza virus-amplifying bridge  
16 species that favor transmission to human (reviewed in Chan et al., 2013). Poultry and livestock ~~were~~  
17 ~~recently demonstrated to~~ play an important role in *E. coli* population structure at the household level  
18 across Nairobi, and inhabitants in direct contact with them had higher chance to share the same *E.*  
19 *coli* isolates, thus pointing towards livestock involvement in human transmission (Muloi et al., 2022).

20

### 21 **3.2 Wild animals including bats and rodents**

22 Although this does not seem to translate into a higher relative number of zoonotic pathogens found  
23 in urban mammals, ~~a recent meta-analysis suggests that~~ wild urban-adapted mammal species ~~tend to~~  
24 shelter an overall higher pathogen richness than their non-urban counterparts (Albery et al., 2021).  
25 Wild mammals, which were suggested as the source of transmission to humans of 86 (out of 95;  
26 91%) zoonotic viruses (Kreuder-Johnson et al., 2015), are numerous in cities (Soulsbury & White,  
27 2015). First, some cities sprawl directly into wild environments, thus favoring wildlife urban foraging.  
28 For instance, small but also very large South American or African cities develop through direct  
29 encroachment of tropical forests (e.g. Rio de Janeiro, Sao Paulo, Iquitos in South America; Franceville  
30 in Africa) and their fringes may be visited by a wide range of free-ranging wild animals. Many  
31 ~~testimonies records~~ (e.g., Barkham, 2017) demonstrate that ~~sometimes large and unexpected~~  
32 ~~animals regularly visit~~ peri-urban zones, when not core cities ~~are now regularly visited by sometimes~~  
33 ~~large and unexpected animals~~: foxes in Europe, coyotes and mountain lions in North America,

1 leopards in India, hyenas in Ethiopia, [raccoons](#), elephants, monkeys, wild boars, etc. The list could be  
2 long and may reflect a growing phenomenon, i.e. wildlife being constrained to cope with urban  
3 sprawling and/or taking advantage of easily accessible and abundant food resources through human-  
4 provide food or dumping sites (e.g., Newsome et al., 2015; see also Reed & Bonter, 2018 for a study  
5 on increased mammalian abundance on supplemented sites). This could have important  
6 consequences in terms of infectious diseases ecology. For instance, sub-urban residential habitats  
7 may provide increased food resources, thus fueling white-tailed deer densities, a keystone host for  
8 ticks that transmit borreliosis in the US (Diuk-Wasser et al., 2020). [Raccoons, reservoirs for rabies  
9 virus, also display great eco-ethological adaptation to contrasted urban landscapes and resource  
10 availability levels, thus allowing them to occur throughout some North American cities \(Gross et al.,  
11 2012\)](#). Second, some species (or populations of some species) have even adapted further and  
12 evolved a fully urban lifestyle; this includes a wide range of bird and mammal species. The latter are  
13 usually generalist, rapidly reproducing and highly adaptable species (Santini et al., 2019) which can  
14 proliferate and reach particularly elevated densities within urbanized environments (e.g., Moller et  
15 al., 2012; Tait et al., 2016). Among them, two taxonomic groups may be particularly critical for the  
16 zoonotic emergence risks, namely rodents and bats, whose urban ~~populations-communities~~  
17 display very high densities and very large [population](#) size that are expected to greatly favor pathogen  
18 transmission (Lloyd-Smith et al., 2005).

19 Many studies have identified bats as major potential sources of zoonotic pathogens, especially RNA  
20 viruses (e.g., Olival et al., 2017; Nieto-Rabiela et al., 2019; Wells et al., 2019; reviewed in Hayman,  
21 2016). Bats are usual urban dwelling mammals, including in large metropolises. In a meta-analysis, a  
22 (probably underestimated) total of 84 bat species were identified in Brazilian cities, 70% of which  
23 may roost (and 12% roosting exclusively) within human infrastructures, and at least 32.1% of which  
24 harbored zoonotic pathogens (Nunes et al., 2017). In many tropical towns, thousands of bats gather  
25 in trees that stand along streets, above houses, markets and squares where millions of people live  
26 and work every day (Ayivor et al., 2017). Among other species, the straw-coloured fruit bat (*Eidolon*  
27 *helvum*) is known to shelter several zoonotic viral lineages (e.g. Paramyxoviruses: Baker et al., 2013;  
28 Rotavirus: Esona et al., 2010; Lyssaviruses: Suu-Ire et al., 2017; Ebolaviruses: De Nys et al., 2018). The  
29 species was found to form one single continental Africa-wide panmictic [hence freely mixing](#)  
30 population (Peel et al., 2013). This suggests that viral transmission could be facilitated across its  
31 whole [geographical](#) range (as supported by similar virus seroprevalence values observed in West,  
32 Central and East Africa; Peel et al., 2013) which encompasses many tropical African cities, including  
33 very large metropolises where colonies routinely reach several thousand individuals (Peel et al., 2016).  
34 In Eastern Australian cities, fruit bats of the *Pteropus* genus may form roosts of several thousands of

1 individuals. While globally decreasing in Eastern Australia, the flying-foxes populations show a shift  
2 towards more urban lifestyle, thus increasing conflicts with humans (Westcott et al., 2015) and  
3 spillover of Hendra paramyxoviruses (Plowright et al., 2011). In addition, maybe unexpectedly, direct  
4 contacts between wild bats and human may not be rare within cities. As an example, 31 cases of  
5 human injuries due to bats were reported in the heart of Salvador, Brazil, between 2012 and 2015  
6 (Santos et al., 2019), thus reflecting a poorly documented but potentially important source of  
7 spillover of bat-borne pathogens to humans. The West African Ebola epidemics, that affected  
8 >28,000 and killed >11,000 persons between 2013 and 2015, most probably started in a kid playing in  
9 close proximity to a tree that sheltered insectivorous bats (Mari-Saez et al., 2015). Though unknown,  
10 we suspect ~~the probability~~ that such ~~a~~ promiscuity-mediated bat-to-human transmission of RNA  
11 viruses ~~occurrences is~~ may be quite high in many urban settlements in the world.

12 Although viral network analyses often identify bats as major sources of zoonotic viruses, especially  
13 RNA viruses (Nieto-Rabiela et al., 2019; Wells et al., 2019; Johnson et al., 2020), a higher proportion  
14 of zoonotic viruses are found in rodents than in bats (Nieto-Rabiela et al., 2019). The ~~latter-former~~  
15 are known to be reservoirs for a wide panel of known zoonotic pathogens (reviewed in Meerburg et  
16 al., 2009), with 400 million human infections by pathogens whose ecology involve rodents each year  
17 (Colombe et al., 2019). A very recent study on 50 zoonotic viruses ranked rodent-specific Lassa  
18 Mammarenavirus and Seoul Orthohantavirus as the first and fourth biggest risks of animal-to-human  
19 viral spill-over (Grange et al., 2021). Though representing only a limited fraction of global rodent  
20 specific diversity, the urban-adapted rodent species were recently demonstrated to share  
21 significantly more pathogens and parasites with humans than their non-urban counterparts (Gibb et  
22 al., 2020). Urban rodent assemblages are usually simplified and dominated by highly competitive,  
23 often invasive species, such as rats and mice that may replace native taxa within core cities (e.g.  
24 Dalecky et al., 2014; Garba et al., 2014b; Hima et al., 2019; Blasdell et al., 2022). They also consist in  
25 particularly competent species (Gibb et al., 2020). For instance, Norway rats from New York were  
26 found to shelter an important viral diversity, including many undescribed viruses that belong to  
27 genera pathogenic for humans (e.g., Firth et al., 2014). In a similar manner, black rats are abundant in  
28 central Kuching, Malaysia, and host a wide panel of zoonotic pathogens, especially pathogens with  
29 environmental transmission (Blasdell et al., 2022). Among existing rodent-borne diseases with  
30 possible shifts to human-to-human transmission, the recent plague epidemics in Madagascar also  
31 reminds us about the risk associated with this deadly bacterial disease, especially in large and  
32 overcrowded urban areas (e.g., Majunga: Boisier et al., 1997; Antananarivo: Randremanana et al.,  
33 2019). Lassa hemorrhagic fever is usually considered as a rural disease, but its rodent reservoir,  
34 *Mastomys natalensis*, is widespread in many African cities (e.g. Garba et al., 2014b) where it may



1 display quite high prevalence (e.g. close to 23.3% in N'Zerekore, Guinea; Karan et al., 2019). Although  
2 the 'historical strain' of SARS-CoV-2 was poorly infective in mice and rats due to its poor ability to  
3 bind to the murine ACE2 cellular receptor, some very recent pieces of evidence suggest that  
4 laboratory mice may be able to replicate some of its variants (at least the B.1.1.7 and other N501Y-  
5 carrying ones) in their lungs at high levels, suggesting that SARS-CoV-2 evolution may occur in  
6 commensal rodents as secondary hosts with potential subsequent spill-back to humans (Shuai et al.,  
7 2021; see also Wei et al., 2021 for a similar scenario involving the Omicron variant). Urban rodents  
8 were also shown to be important reservoirs for a wide panel of parasites: for instance, 15.3% of  
9 Durban rodents carry *Angiostrongylus cantonensis* (Archer et al., 2017); in Kuala Lumpur, 28.4% of  
10 rats are infected by *Hymenolepis nana* (Mohd Zaïn et al., 2012) while up to 94% of *H. diminuta*  
11 prevalence was observed in rats from some Ibadan areas, Nigeria (Akinbodae et al., 1981). Worms  
12 are not necessarily emerging pathogens, but they are under-documented though massively infecting  
13 urban human dwellers (Jariwala et al., 2017) and they are expected to remain a major public health  
14 issue in cities where rodents and humans coexist in high numbers. The absolute numbers of rats and  
15 mice in the different cities of the world remain astonishingly unknown, but they are obviously  
16 millions in many of them. In Chicago, the Bureau of Rodent Control of Chicago, USA, registered  
17 between 35,000 and 49,000 rodent-associated complaints per year between 2008 and 2017 (Murray  
18 et al., 2018). In only five boroughs of New York City, USA, 514 rodent bites were reported to the  
19 Department of Health in less than four years (Childs et al., 1998). Exceptionally high numbers of rat-  
20 seeing regularly trigger public reactions and subsequent press releases in most European and North  
21 American cities, thus reflecting the abundance of rodents in these urban settlements. Yet, in most of  
22 them, underground sewers provide some kind of physical separation between rats and human  
23 beings, thus probably greatly limiting direct human / rodent contacts. Unfortunately, in many low- or  
24 middle-income countries, sanitation system are lacking or very poorly developed, and when they do  
25 exist, they often consist in large open sewers. In slums-informal settlements, garbage management is  
26 very limited or inexistent, thus providing omnipresent, sustainable and open-air food resources for  
27 rodents all year long. As a direct consequence, rats, mice and other commensal rodents are plentiful  
28 in most poor urban settings, especially slums-informal ones, where they regularly forage in close  
29 contact with people, and even nest inside houses. For instance, in the Pau da Lima favela, Salvador,  
30 Brazil, 109 out of 185 (59%) of households are infested by Norway rats (Costa et al., 2014). In Luang  
31 Prabang, Lao DR, 61.5% of interviewed inhabitants declared rodent sighting indoor within the week  
32 preceding the survey (Promkerd et al., 2008). During a two year-long study in Cotonou, Benin, small  
33 mammals were trapped in 91.8% of the investigated households (Dossou, Houéménou & Dobigny,  
34 unpublished results). In Niamey, Niger, rodents were trapped in 125 out of the 170 households  
35 investigated (73.5%), while rodent-associated issues were reported in 164 of them (96.5%) by the

1 inhabitants (Garba et al., 2014a). In the same survey, 5% of interviewed inhabitants declared to have  
2 been bitten by wild rodents at least once at home (Garba et al., 2014a). In Osogbo, capital of Osun  
3 State in SW Nigeria where Lassa fever occurs each year, 55.4% of 500 slum-informal settlements  
4 inhabitants declare that they seeing rodents moving around freely in their own houses, with 43.3%  
5 having observed at least one rodent in their home within the last 24 hours before the interview, and  
6 20.2% having already eaten wild rats (Olalekan, 2015).

7 Altogether, these studies illustrate how abundant pathogen-carrying wildlife, especially small flying  
8 and terrestrial mammals, may be in cities where human density reaches its maximum. This sets the  
9 scene for billions of everyday wildlife-human interactions, hence spill-over opportunities (Fig. 2).

10

### 11 **3.3 Captive animals, bush meat and wet wildlife meat and wildlife meat markets**

12 Kreuder-Johnson et al. (2015) pointed towards the risk of viral emergence in places where  
13 taxonomically diverse mammal species coexist in close promiscuity and where trans-species  
14 transmission is plausible. They mainly quoted such risks in zoos, labs -that usually lie within cities- as  
15 well as wet markets/wildlife meat markets. Relying on current data about of two viruses that display  
16 only rodent-to-human transmission in nature, namely the Lymphocytic Chorio-Meningitis  
17 Mammarenavirus and the Seoul Orthohantavirus, Childs et al. (2019) alerted on the importance of  
18 pet-, lab- and even transplant-associated risks of zoonotic viral spillover. Accidental human  
19 contaminations within research laboratories where infectious agents are investigated and  
20 manipulated are not infrequent (Peng et al., 2018), with 100-275 potential releases of pathogen each  
21 year in the US (Kaiser, 2014). Famous examples of lab-escapees or wrong uses include agents of SARS  
22 (Normile, 2004), anthrax, small pox, flu, etc (Owens, 2014). Among other hypotheses, a lab-escapee  
23 as a possible origin for the ongoing Covid-19 pandemics remains to be fully addressed (Harrison &  
24 Sachs, 2022).

25 Manipulation and consumption of bushmeat-wildlife meat have also been identified as a major risk  
26 for zoonotic spillovers (Wolfe et al., 2005; Katani et al., 2019), with wildlife markets being identified  
27 as potential spillover hotspots due to numerous interspecific contacts and poor sanitary and hygienic  
28 conditions (e.g., Saylor et al., 2021). Although wildlife consumption may be more important in rural  
29 areas, especially remote ones (Kurpiers et al., 2015), urban wet-wildlife markets are not rare and  
30 surprisingly under-represented in studies that quantify the demand for bushmeat-wildlife meat  
31 (McNamara et al., 2019). Yet, urban demand for bushmeat-wildlife meat is underpinned by a wide  
32 panel of socio-cultural drivers (Shairp et al. 2016; Chausson et al., 2019) and is likely to increase in  
33 the coming decades (Kurpiers et al., 2015; McNamara et al., 2019). This may imply intensifying rural-

1 to-urban socio-economic connections, from hunters to city-dwelling consumers. As an example,  
2 Kamins et al. (2011) showed that ca. 130,000 bats were sold each year along a 400 km-long economic  
3 network in Ghana (see other African examples in Kurpiers et al., 2015). It should be kept in mind that  
4 Ebola virus remains viable on monkey carcasses for at least a week, and viral RNA is detectable for up  
5 to 10 weeks (Prescott et al., 2015). In addition, many urban markets group living wild animals, thus  
6 probably greatly enhancing the chances of infectious pathogens spillover ~~and as well as~~ the number  
7 of persons potentially involved, thus favoring epidemics early stages. For instance, it is plausible that  
8 SARS coronavirus has jumped from wild horseshoe bats to small carnivores, and then to humans in  
9 Chinese wet markets (Guan et al., 2003; Lau et al., 2005). ~~In the same manner~~ Likewise, though still  
10 uncertain, the ~~still hypothetical~~ hypothesis of the emergence of SARS-CoV-2 at Wuhan wet market,  
11 China, would be another example of the potential role played by that-such places are susceptible to  
12 play-in zoonotic chains of transmission from wildlife to humans (Li et al., 2020).

13

14 Interestingly, many of the animals listed here above belong to a panel of mammalian lineages,  
15 namely Artiodactyla, Carnivora, Chiroptera, Eulipotyphla and Rodentia, that were all shown to have a  
16 critical role in zoonotic emergence, especially viral emergence (Olival et al., 2017; Nieto-Rabiela et  
17 al., 2019; Wells et al., 2019). Such a biodiversity, together with very close promiscuity between  
18 animals and people, both at very high densities, result in constant interspecific contacts within cities  
19 around the world. ~~It may even be that u~~ Urban habitats may even offer the highest number of  
20 opportunities of wildlife / domestic animals / human contacts. This, of course, provides optimal  
21 conditions for pathogen exchanges between people, domestic and wild animals, hence zoonotic  
22 emergence and subsequent epidemics.

23

#### 24 **3.4 Arthropod vectors**

25 Many infectious diseases are vector-borne (usually involving diptera, coleoptera, fleas, mites, lice or  
26 ticks; reviewed in Huttington et al., 2016; Semenza & Suk, 2018) with 40% of zoonotic viruses of wild  
27 animals being vector-transmitted to humans (Kreuder-Johnson et al., 2015) and the majority of  
28 emerging vector-borne diseases being transmitted by ticks and mosquitos (Swei et al., 2020).  
29 Although recent meta-analyses suggest that complex parasitological cycles may have higher chances  
30 than simple cycle to be disrupted within cities, especially in carnivores and primates (Werner &  
31 Nunn, 2020), many vectors of primary health importance show clear trends of adaptation to urban  
32 ecological conditions (e.g., Triatomine bugs: Parra-Henao et al., 2021; Anopheles spp.: Azrag &  
33 Mohammed, 2018; Takken & Lindsay, 2019; Aedes spp.: Wilke et al., 2020), sometimes taking

1 advantage of remnant forests, urban parks and increasing city greenings (e.g. ticks and tick-borne  
2 diseases: Lydecker et al., 2019; Heylen et al., 2019; [typhus-transmitting chiggers: Wulandary et al.,](#)  
3 [2021; Aedes spp.: Huynh & Minakawa, 2022](#)). Accordingly, several studies have clearly pointed  
4 towards the existence of urban zoonotic cycles of vector-transmitted pathogens, thus suggesting  
5 increasing city-specific infectious risks (e.g., tick-borne *Borrelia*: Reye et al., 2010; mosquito-  
6 transmitted Zika virus: Musso & Gubler, 2016; [Gandy, 2021; triatomine-borne Trypanosoma cruzi:](#)  
7 [Dye-Braumuller et al., 2019](#)). The agents of murine (*Rickettsia typhi*) and cat-flea (*R. felis*) typhus  
8 were detected in rodents, tree-shrews and shrews from seven urban parks of Bangkok, Thailand  
9 (Rungroj et al., 2021), while urban parks have also been associated with 20.5% of human cases of  
10 scrub typhus (due to another Rickettsiale bacterium *Orientia tsutsugamushi*) in Seoul, South Korea  
11 (Park et al., 2015).

12 The great heterogeneity of urban landscapes may deeply impact the arthropod vectors distribution  
13 and biology, including transmission characteristics such as competence, biting rate or incubation  
14 time, among others, thus making incidence of vector-borne infectious diseases quite evenly  
15 distributed within and among cities (review in LaDeau et al., 2015). The wildland-urban interface has  
16 been identified as a unique ecotone critical for ticks due to habitat heterogeneity hence increased  
17 ecological opportunities (the “intermediate disturbance hypothesis”), thus potentially leading to  
18 increased tick-borne diseases risk (Diuk-Wasser et al., 2020). There is little doubt that, in the decades  
19 to come, increasing processes of land-use change, especially peri-urbanization, sub-urbanization and  
20 ex-urbanization will be accompanied by a wide range of vector species proliferation in close  
21 proximity to high densities of both animals (see above) and humans, thus contributing to the growing  
22 range of infectious diseases that may emerge in core cities or their peripheries.

23

#### 24 **4. Cities as incubators for evolutionary novelties**

25

26 By essence, cities are the socio-ecosystems with the highest human densities and population growth,  
27 and they are the receptacles for large human rural-urban or post-conflicts migrations; consequently,  
28 they are privileged places for epidemic amplification of human-human transmitted pathogens  
29 (Connolly et al., 2021) ~~(Fig3)~~. The 2014-2015 West African epidemics of Ebola fever, which was  
30 responsible for a death toll that had never been faced before, was essentially due to the  
31 unprecedented migration of human cases from rural areas into urban centers: at the outbreak peak,  
32 51% of the cases identified in Liberia were from the capital city, Monrovia (Fallah et al., 2018; see  
33 also Wilkinson & Leach, 2015, [and Gandy, 2021](#)).

1

2 Importantly, even before human contamination, One-one also expects that very high numbers of  
3 available hosts, as may typically be the case within cities, translate into more intensive pathogen  
4 multiplication, hence genetic mutation and subsequent evolutionary changes. This should be  
5 particularly true for viruses, as illustrated by the SARS-CoV-2 variants evolution (Blackstone et al.,  
6 2020; Bandy & Wermer, 2021). As such, cities may be particularly favorable for human pathogen  
7 evolution simply due to higher number of infections, hence increased genetic change opportunities.  
8 Unfortunately, little is known about these aspects (Verrelli et al., 2022). In addition, cities are very  
9 deeply modified habitats and display radically reorganized landscapes structure and connectivity,  
10 highly constrained hydrographic networks, usually very elevated levels of air, water and soil  
11 pollution, fully reshaped species communities and interactions, and even locally modified  
12 microclimates (Grimm et al., 2008). For instance, in central France, urban temperatures may be up to  
13 3-4°C higher than their peripheral counterparts, and heat islands effect induces up to extra 3-4°C in  
14 some circumstances (Richard et al., 2021). While the average increase in global temperatures (i.e.,  
15 1.5-4°C in the coming decades) is expected to be associated with enhanced infectious risks (Hess et  
16 al., 2020), the resulting impacts of local climatic anomalies such as urban heat islands on processes  
17 like pathogen replication, reservoirs and vector population dynamics, hosts immunity and  
18 competence, hence infectious diseases transmission and trans-species zoonotic spillover, remain  
19 largely unknown (LaDeau et al., 2015; see e.g., Misslin et al., 2016, for an example on *Aedes*  
20 mosquito-transmitted dengue; Mironova et al., 2019, for an example on *Plasmodium vivax* malaria).  
21 Another very poorly understood aspect of city life is the effect of air, soil and water pollution on  
22 genetic mutation rate in pathogens, and the consequences in terms of multiplication,  
23 contagiousness, host-specificity and virulence. Following overconsumption and subsequent release  
24 of antibiotics in the urban environment (Buelow et al., 2021), repeated exposure of pet and domestic  
25 animals as well as urban wildlife to a wide spectrum of antibacterial molecules is highly probable,  
26 and would greatly contribute to antibio-resistance evolution. Moreover, commensal microbiotes are  
27 inter-related with the environmental microbial biodiversity as well as widely impacted by lifestyle  
28 (Flandroy et al., 2018). Accordingly, although a lot remains to be described and understood, it is  
29 expected that urban lifestyle and habitats induce important changes in animal symbiotic microbial  
30 communities, thus potentially driving many evolutionary changes that may have consequences in  
31 terms of health (Flandroy et al., 2018; Mills et al., 2019), for instance through impacts on reservoir  
32 immune systems and their capacity of acquiring zoonotic agents (Pickard et al., 2017), or on vector  
33 ability to multiply and transmit pathogens (Yin et al., 2020).

1 From what precedes, urban socio-ecosystems' characteristics are expected to induce very strong  
2 selective pressures on living organisms, thus setting the stage for very new eco-evolutionary  
3 trajectories and scenarios in the decades to come (Alberti et al., 2020). This of course involves  
4 reservoir and vector species as well as zoonotic pathogens (Bradley & Alitzer, 2006). A recent meta-  
5 analysis suggested that urban environment may disrupt transmission cycle of some parasites,  
6 especially those displaying complex cycles (Werner & Nunn, 2020). However, some zoonoses tend to  
7 urbanize (e.g., leptospirosis: Lau et al., 2010; Blasdel et al., 2019; scrub typhus: Park et al., 2015),  
8 sometimes following the abundance of a few but highly competent reservoir species that are well-  
9 adapted to deeply human-modified habitats (Morand et al., 2019; Gibb et al., 2020). We still do not  
10 know much about evolutionary fate of zoonotic systems under urban selective regimes (Verrelli et  
11 al., 2022), and it may be cautious and wise to keep aware that one cannot really predict what may  
12 emerge from urban-driven novelties in terms of parasite diversity, hosts/parasite associations and,  
13 ultimately, zoonotic emergence.

14 Another crucial characteristic of cities is that they are transport hubs, so critical nodes for  
15 dissemination of reservoirs, vectors and pathogens, hence long-distance expansion of infectious  
16 diseases (Bradley & Alitzer, 2006; Alirol et al., 2011; Neiderud, 2015; e.g. plague: Zietz & Dunkelberg,  
17 2004; hantavirus: Lin et al., 2012, Castel et al., 2021). This adds to the increasing supply of cities with  
18 living animals for food human consumption, as well as to the many urban-rural linkages through  
19 human movements, thus opening the gate to human- and animal-mediated import of rural  
20 pathogens into cities (Alirol et al., 2012; Ahmed et al., 2019; Connolly et al., 2021). Such multi-scale  
21 redistributions of reservoirs, vectors and pathogens (i.e., the "global biological cauldron"; Gandy,  
22 2021) may greatly foster the evolution of host-pathogen interactions and dynamics to some extent  
23 that remain poorly understood and quantified.

24 In addition, increased exchanges between and within cities may deeply impact microbial interactions.  
25 First, they may favor exchange of genetic material between sometimes highly divergent lineages of  
26 bacteria. In particular, bacterial communities may share antibiotic-resistant plasmids, thus potentially  
27 conferring antibiotic multi-resistance to wide diversity of pathogens such as gastro-enteric ones  
28 (Partridge et al., 2018), especially at the human-livestock-wildlife interface (Hassel et al., 2019).  
29 Taking the risk associated with plague (Stenseth et al., 2008) as an example, the identification of  
30 antibiotic-resistant strains of *Yersinia pestis* in Malagasy black rats, including rats from the capital city  
31 Antananarivo (Cabanel et al., 2018) and the probable horizontal transfers within flea mid gut  
32 (Galimand et al., 2006) provide another example that undoubtedly deserves a particular attention.  
33 Second, cities may also favor the coexistence of viruses, hence recombination between viral strains  
34 which facilitates host jumps and immune evasion (Vijaykrishna et al., 2015; Gandy, 2021). This may

1 be particularly true for a wide panel of coronaviruses and influenza A viruses that actively circulate  
2 among bats and birds, respectively (reviewed in Chan et al., 2013). Much less documented but  
3 potentially worrisome, the presence of influenza A viruses in bats (Tong et al., 2012) as well as in 11%  
4 of Norway rats from Boston, USA (Cummings et al., 2019), probably deserves special attention, too.

5

## 6 **5. Call for some actions**

7

8 From what precedes, it appears that already known as well as still unknown microbes may arrive to,  
9 and get amplified in cities, or even emerge *in situ* following local evolutionary innovations as well as a  
10 very high number of ~~everyday-daily~~ interactions between humans and animals, both wild and  
11 domestic. There is little doubt that these multiple animal-human contacts provide excellent  
12 conditions for “microbial chatter” (extending the “viral chatter” concept proposed by Wolfe et al.,  
13 2005), i.e. ~~repeated-iteration of~~ animal-human human-animal transmission events until the  
14 pathogen’s adaptation opens the gate to human-to-human infectious routes and subsequent rapid  
15 and large-scale epidemics. As such, we believe that, together with the already well-identified risks  
16 associated with deforestation and zones of intensifying agricultural and livestock or poultry farming  
17 activities, urban areas as places of zoonotic emergence should be considered as another priority in  
18 terms of surveillance and risk mitigation measures. As a first step, Tthis requires a better knowledge  
19 of the urban-specific zoonotic danger, ~~an appropriate management of the exposure as well as a~~  
20 ~~decrease of the vulnerability of city inhabitants.~~

21

### 22 **5.1 A better understanding of pathogen evolution at the animal-human interface within extended** 23 **urban socio-ecosystems**

24

25 Following the rapid urbanization and increase in urban lifestyle, the chances of zoonotic spillovers  
26 within urban and peri-urban regions will probably increase (Blasdell et al., 2019). However, the  
27 monitoring of all cities and urban zones is unrealistic. In order to prioritize urban zoonotic risk and  
28 guide surveillance networks’ implementation, researches ~~are-is~~ needed to identify which urban  
29 features and/or activities are the most favorable ones for disease emergence. Indeed, a lot remains  
30 to be understood about the selective pressures and resulting adaptive trajectories that may shape  
31 urban-dwelling organisms’ ecology and evolution. For instance, recent experimental credit has been

1 given to the pivotal role of selection on the distribution of *E. coli* and their resistance to antibiotics  
2 across an African city (the so-called “everything is everywhere, the environment selects” hypothesis;  
3 Muloi et al., 2022). Such studies are very useful for our understanding of pathogen ecology at the  
4 human-animal interface within urban environments and should be extended to other geographic  
5 contexts and wider panels of zoonotic pathogens. More generally, increased eco-evolutionary  
6 researches ~~are is~~ crucial in order to anticipate and to cope with the new zoonotic threats to come  
7 (Roche et al., 2020). In this context, moving towards studies that consider urban ‘extended’ socio-  
8 ecosystems in their full complexity and diversity would be very useful, as ~~has been~~ recently  
9 recommended in the fields of urban health (Flies et al., 2019), urban ecology (Alberti et al., 2020) and  
10 urban political ecology (Gandy, 2021; Tzaninis et al., 2021). In particular, it appears much too  
11 simplistic to consider cities as one single hence homogeneous ecosystem (e.g., urban vs. non-urban  
12 conditions; Blasdell et al., 2022), as what is sometimes done in meta-analyses that are yet published  
13 in very high standard scientific journals (e.g., Werner & Nunn, 2020; Albery et al., 2021). Cities are  
14 still too often perceived as essentially human socio-ecosystems that are to be opposed to natural  
15 environments. ~~Although the influence of man is obviously massive there, a better understanding of~~  
16 ~~infectious diseases ecology in extended urban environments firmly require that one moves beyond~~  
17 ~~this so-called “urbanization of nature” paradigm and adopt a “more than human” view of the urban~~  
18 ~~world (Tzaninis et al., 2021).~~ Clearly, health ecology investigations in cities must take extended urban  
19 socio-environmental heterogeneity and historical trajectories into much better consideration (Gandy,  
20 2021; Blasdell et al., 2022; Verrelli et al., 2022).

21

## 22 5.2 From response to epidemics towards densified surveillance and prevention networks

23

24 The Covid19 crisis has ~~been~~ deeply ~~questioning~~ questioned social models and their resilience  
25 abilities. A recent UN report (UN Habitat, 2021) highlights the importance of pre-existing and well  
26 established institutionalized bodies and governance to set up and drive ~~riposte~~ appropriate response  
27 policies against the epidemics in cities of the world. It also shows that, in addition to task forces that  
28 were created *ad hoc*, local networks drawn from preceding crises were successfully re-leveraged in  
29 some countries (e.g., DRC and its Ebola experience). However, it may be that the Covid19 pandemics  
30 have exacerbated some limits of ~~riposte~~ response-based systems that may be insufficient to respond  
31 quickly enough in our extremely connected world, and should be supplemented by prevention-  
32 targeting actions. Such a shift towards prevention rather than sole ~~riposte~~ response is not a new idea



1 (e.g., Patz et al., 2004), but its operationalization through inter-sectorial One Health approaches still  
2 remains limited.

3 From a surveillance perspective (in cities, but also in other socio-environments), human sciences  
4 should take the scene early in the process of building One Health actions. In particular, they should  
5 have a leading role in showing biomedical experts and health ecologists which socio-ecosystems  
6 (hence where, when, who and what) to investigate from the biological and medical perspectives.  
7 Indeed, one priority should be to identify fine-scale habitats and associated uses as well as historical,  
8 demographic and socio-environmental dynamics that are associated with the most extensive  
9 microbial interaction and evolution, as well as with human / animal contacts that are the most  
10 significant in terms of spillover potential. From there, “sentinel spaces” and “sentinel uses” (rather  
11 than sentinel species) cshould be targeted for the monitoring of microbial chatting, thus constituting  
12 a solid science-guided basis for emergence-preventive strategies. For instance, a recent surveillance  
13 system of 15 zoonotic diseases was recently implemented and evaluated in three counties of  
14 Western Kenya where husbandry practices are currently moving from subsistence to intensive  
15 market-oriented production (Falzon et al., 2019). It builds on hierarchical sampling protocols of  
16 sentinel markets, slaughterhouses and human health centers. Like others (e.g., MonkeyFeverRisk on  
17 tick-borne viral Kyasanur Forest Disease that affects low-income communities in the Western Ghats,  
18 India; Burthe et al., 2021; <https://www.monkeyfeverrisk.ceh.ac.uk/>), this remarkably integrated  
19 device involves veterinarians and medical doctors, founded on a good understanding of the local  
20 socio-economic context and bets on a long-term confidence relationships between academic,  
21 operational and community stakeholders. In the same mannerLikewise, in-depth analysis of urban  
22 livestock keeping uses and supply chains permits the clear understanding of economic constraints  
23 and opportunities that characterize urban livestock economy in Southern cities, thus pointing  
24 towards an urgent need to accompany urban farmers in animal management in order to reach both  
25 food security and safety (Alarcon et al., 2017). Other emblematic One Health programs were  
26 conducted on rabies (such as in Chad, Mali and Côte d’Ivoire: reviewed in Lechenne et al., 2021) and  
27 have led to important improvement in terms of both human and animal surveillance as well as of  
28 showing the interest of some strategies over others. For instance, they were useful in identifying  
29 some sources of improvement, such as the good reporting of data in main cities -where labs usually  
30 exist- that contrasts with the mass of knowledge and data that are collected in peripheral areas but  
31 fail to reach national hence international monitoring systems (Lechenne et al., 2021). Robust  
32 epidemiologically structured sampling procedures focusing on the human-animal interface within  
33 cities are also very informative to identify scales at which microbial spillover may occur (e.g.,  
34 household vs. city; Muloi et al., 2022), and so at which scales preventive actions may be tailored.

1 ~~Finally, such long-term and integrative works are very useful in showing which caveats should be~~  
2 ~~avoided, and which leverages may be activated, thus being critical to guide One Health~~  
3 ~~implementation.~~ Consequently, this type of long-term inter-sectorial programs should be strongly  
4 encouraged by funding bodies and then put forward in order to convince socio-economic  
5 stakeholders and decision makers to invest in their generalization and institutionalization.

6 More specifically, interventional research could fuel similar programs by targeting strategic urban  
7 sites (e.g., wet-wildlife meat markets, slums/informal settlements) as well as urban/non-urban  
8 interfaces. The new forms of extended urbanization, that usually take place at (peri-urbanization),  
9 when not beyond (sub- and ex-urbanization) core cities' margins, especially in the global South,  
10 should also be carefully scrutinized due to potentially high levels of wild and domestic biodiversity  
11 together with dense, rapidly growing and vulnerable human populations (Diuk-Wasser et al., 2020;  
12 Connolly et al., 2021). ~~In order to setup reciprocally beneficial multi-stakeholder relationships, a~~  
13 ~~better understanding of the spatial and demographic patterns as well as political-economic~~  
14 ~~governance that influence the spread of infectious diseases in these new frontiers of our urban world~~  
15 ~~would be very useful (see the landscape political ecology approach proposed by Connolly et al.,~~  
16 ~~2021).~~

17 In addition, as discussed above, entry points and transport hubs also deserve a particular attention.  
18 For instance, dedicated actions could be launched to train and enroll transport and trans-border  
19 stakeholders (e.g. seaport and port industrial networks, custom services, import/export firms), taking  
20 advantage of their operational "savoir-faire" and tools which would probably be of great help in the  
21 surveillance of transport means, hubs and networks, hence of the prevention of long distance  
22 dissemination of zoonotic agents. In essence, this is the purpose of the International Health  
23 Regulation (WHO, 2005) that is in fact inherited from quite old international debates (Howard-Jones,  
24 1975) and texts – e.g., the 1903 International Sanitary Convention already preconized rat control on  
25 ships, and desinsectization was added in the subsequent versions in 1912 and 1923 (Lembrez, 1966).

26 It could be interesting to capitalize on concepts and approaches developed for biological invasion  
27 management (e.g., see the special issue of Biological Invasions on Early Detection and Rapid  
28 Response of invasive organisms, eds. Meyerson, A. & Simberloff, D., 2020). For instance,  
29 Collaborative-collaborative platforms of surveillance managed jointly by academic, institutional and  
30 operational stakeholders could be implemented within transport stations, ports and seaports (e.g.  
31 Port Platform of Environmental Surveillance currently settled in Cotonou seaport, Benin; Adamjy et  
32 al., 2020).

33

### 1 5.3 A special role for local community-based networks?

2

3 ~~In a more general manner, p~~Prevention and early warning before spillover and subsequent spread of  
4 emerging pathogens ~~is probably key to avoid major zoonotic epidemic events. This~~ cannot be  
5 achieved without a dense surveillance network at the closest from the field. The only realistic option  
6 is to take advantage of already existing operational networks, starting with local veterinary and  
7 health care centers and staffs. Surveying cities, where human / animal interactions are daily and  
8 widespread, requires massive human resources. In such a context, community-based early alert  
9 systems intuitively appear as a promising way to leverage surveillance networks within urban settings  
10 (e.g., Toledo-Romani et al., 2007; Costa et al., 2014; Urioste-Stone et al., 2015; Carvalho Parente et  
11 al., 2017; Ouédraogo et al., 2018; Valdez et al., 2020). This requires strong inhabitants' trust in order  
12 to reach ownership, hence long-term enrollment and implication in participative actions which  
13 remains a critical challenge (e.g., Webb Hooper et al., 2019; Valdez et al., 2020). The latter should be  
14 facilitated by political goodwill and supportive leadership through a national structure dedicated to  
15 One Health actions (Falzon et al., 2019). Participative approaches are promising and further  
16 experimental attempts should be made in a wide panel of socio-cultural contexts, especially urban  
17 ones, to consolidate the corpus of knowledge and "savoir-faire" in such actions which may be  
18 particularly challenging in cities (Ridde et al., 2014; Saré et al., 2018). Indeed, though usually  
19 beneficial, community-based approaches to health improvement may have limited or incomplete  
20 effects (Nickel & von dem Knesebeck, 2020). For instance, limitations of community-based actions  
21 against urban vectors or reservoirs may arise from the lack or poor engagement of local  
22 champions/leaders, especially in absence of financial incentives (e.g., Espino et al., 2012; Saré et al.,  
23 2018 for examples in Cuba, Philippines and Burkina-Faso). This may sometimes be overcome through  
24 more adapted communication, iterative processes, local capacity building as well as political support  
25 and investment in order to help the poorest communities to overpass the socio-economic constraints  
26 that prevent them to self-adapt for disease prevention purposes (Nickel & von dem Knesebeck, 2020;  
27 Asaaga et al., 2021). Such debates highlight the crucial importance of the evaluation of these types of  
28 interventional researches (Ridde et al., 2020), especially within cities where heterogeneous socio-  
29 economic contexts may require specific community-based approaches (e.g., formal vs. informal  
30 areas: Ridde et al., 2014) and where the choice of the leaders may be particularly critical (Espino et  
31 al., 2012; Saré et al., 2018). This implies that more knowledge, hence research, about the real  
32 efficiency and adaptability of participatory programs aiming at reducing animal-human contacts and  
33 mitigating zoonotic risks within urban areas are conducted. It also raises the issue of rapid sharing of

1 knowledge from the communities to the Health authorities in charge, whoever they might be, in  
2 order to trigger immediate and coordinated higher-level responses.

#### 4 5.4 Wide-scale empowerment on the One Health concept

6 Thinking forwards, as many people as possible need to be empowered, especially young generations.  
7 To do so, generalizing the teaching of One Health concept and approach in educational and academic  
8 courses is probably the only way to achieve massive, efficient, wide-scale and long term capacity  
9 building and awareness raising at a reasonable cost. In universities, this will mean to adapt existing  
10 or create *de novo* courses in a ~~trans-sectorial~~transdisciplinary manner, far beyond the sole  
11 biomedical and environment sciences, i.e. including socio-economical, anthropological, urban  
12 planning, logistical and political aspects. Accordingly, the creation of Centers (or Networks) of  
13 Excellence in Ecology and Health Research and Training housed in regional universities and/or  
14 research institutes had already been advocated more than fifteen years ago (Patz et al., 2004);  
15 unfortunately, to our knowledge, they are still rare (e.g., One Health Center of Excellence, University  
16 of Florida, USA; One Health Frontier Graduate School of Excellence, Hokkaido University, Japan; One  
17 Health Research Center of Excellence for Research and Training, Sun Yat-sen University, Guangzhou,  
18 China; One Health European Joint Program, European Union network). Large-scale education is also a  
19 critical issue to question and potentially reshape people's habits and uses since the latter factors are  
20 central in the zoonotic spill-over process (Epstein, 2020; Hassel et al., 2021). This will require huge  
21 funding investments in education in universities and schools as well as at the community level (e.g.,  
22 Hancke & Suarez, 2014). Importantly, it should benefit from significant inputs from socio-  
23 anthropologists, linguists (to transfer specialized concepts and semantics to local languages), experts  
24 in education and communication sciences. For such investments to be prioritized, an important  
25 lobbying towards national and local political leaders will be necessary. Media support through  
26 adapted channels (e.g., national TVs, community radios, social media, social workers' campaigns) will  
27 be another important way to reach a maximum of people and stakeholders.

#### 29 5.5 Urban management and poverty reduction

1 Last but not least, one must recognize that many zoonotic emergence risks are associated with  
2 poverty. As a consequence, efficient prevention and early ~~riposte~~-response against nascent  
3 epidemics cannot be achieved without full political involvement and support. Decline of infectious  
4 diseases in US and European cities within the last two centuries probably owes a lot to concerted  
5 efforts of urban planners and public health stakeholders who work together towards wide-scale  
6 sanitation and waste management services, something that has been rather rare in the Global South  
7 where attention is rarely paid to infectious diseases, especially zoonoses, when it comes to urban  
8 planning (Ahmed et al., 2019). Obviously, eradication of insalubrious urban areas would immediately  
9 translate into great improvement in terms of infectious diseases burden (G. Suzan, in Robin, 2021).  
10 As such, following the One Health approach, a real dialogue between urban policy makers and health  
11 stakeholders is required to make significant progress towards better sanitation and living conditions,  
12 hence decreased zoonotic risks, for a vast number of poor urban dwellers.

13

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23

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1

2 **Authors' respective contributions**

3

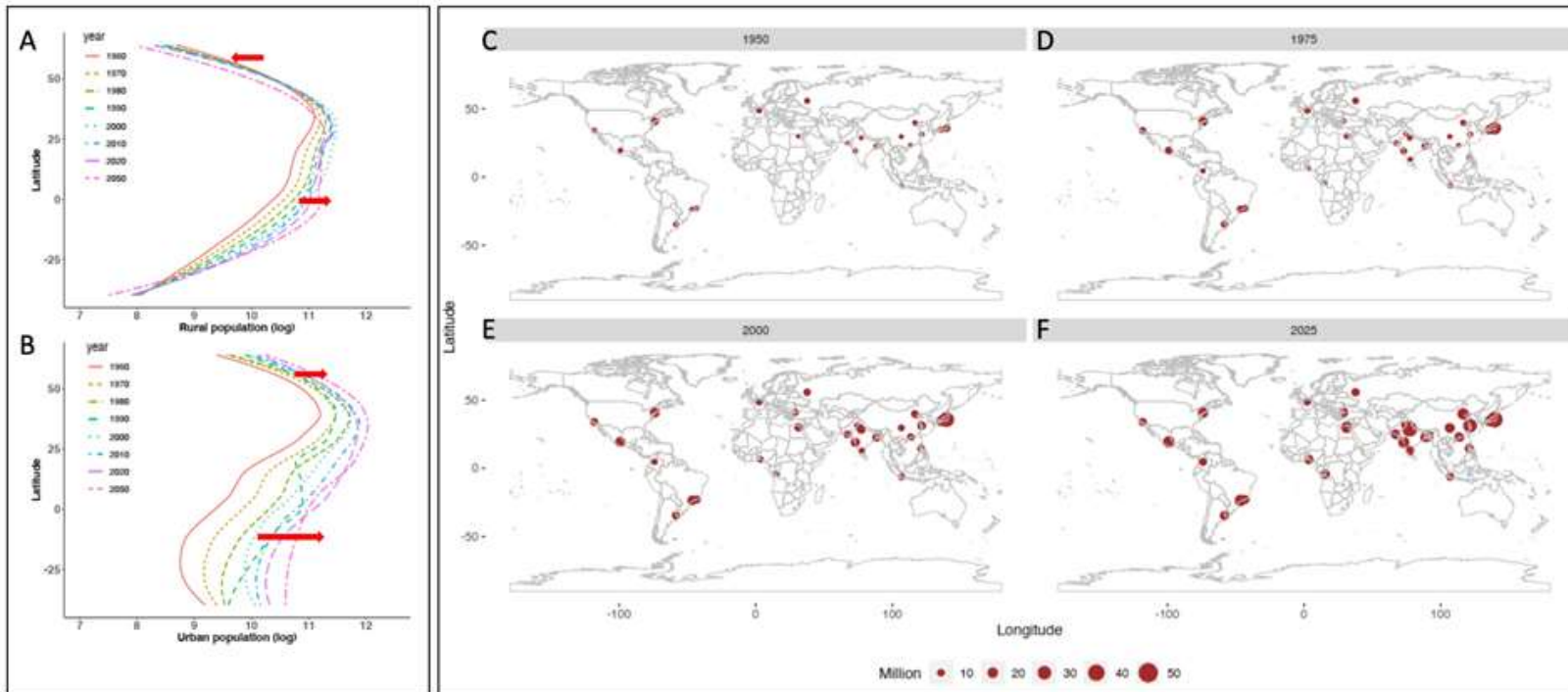
4 Gauthier DOBIGNY and Serge MORAND both conceived and wrote the paper.

5

1 **Figures**

2

3 **Figure 1.** Changes in rural (A) and urban (B) population size from 1960 to 2050 (note the sharp increase in urban population in tropical regions) and in the  
4 number and size of large cities from (C) 1950, (D) 1975, (E) 2000 and (F) 2025 (data from the World Bank, [https://databank.worldbank.org/source/world-](https://databank.worldbank.org/source/world-development-indicators)  
5 development-indicators)

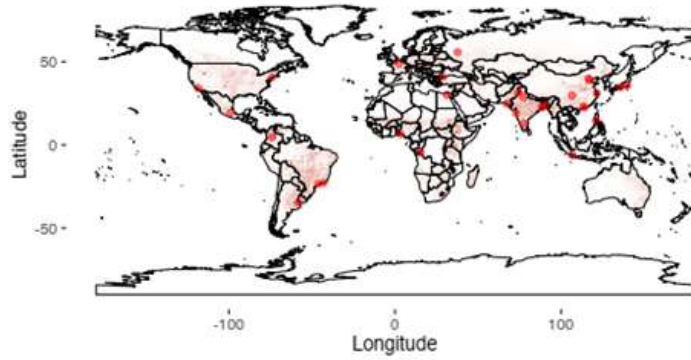


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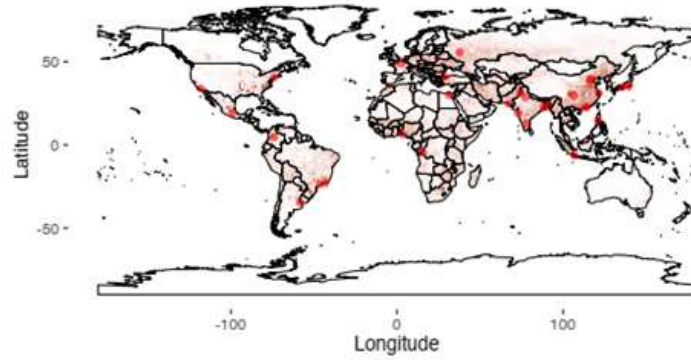
1 **Figure 2.** Global maps of livestock and wildlife with large world cities: (A) density of cattle, (B) density of chickens, (C) density of pigs, (D) number of  
2 mammal species. Data from FAO (Gridded Livestock of the World database GLW v3.1), IUCN (mammal species richness) and World Bank (large  
3 cities)Graphical summary of the main hypothetical trends in terms of animal-human interaction and zoonotic processes that we believe are expected along  
4 a rural-urban gradient.



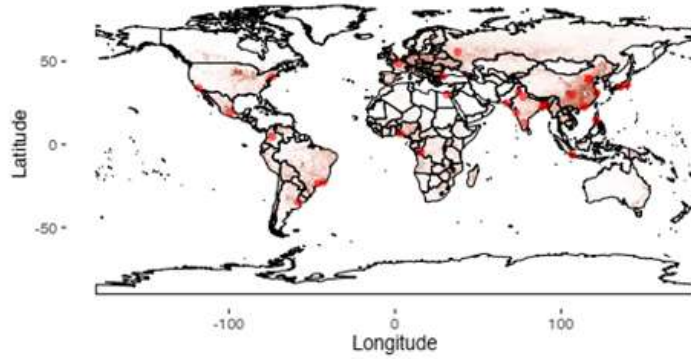
A. Density of cattle



B. Density of chickens



C. Density of pigs



D. Mammal species richness

