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Towards a 'One Health' research and application tool box

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Summary

The 'One Medicine' concept by Calvin Schwabe has seen an unprecedented revival in the last decade and has evolved towards 'One Health' conceptual thinking, emphasising epidemiology and public health. Pathologists rightly recall the contribution of their discipline by close genomic relationship of animals and humans e.g. in cancer genetics. We need to change our 'us versus them' perspective towards a perspective of 'shared risk' between humans and animals. Professional organisations have declared their adhesion, governments have created joint public and animal health working groups and numerous research and surveillance programmes have been incepted as demonstrated on the 'One Health Initiative' website. Above all these beneficial developments, we should not forget however, that there remains a huge divide between human and veterinary medicine borne from unprecedented (over) specialisation of disciplines and increasingly reductionist approaches to scientific inquiry. What is required now is a radical paradigm shift in our approach to global public health with practical approaches and 'hands-on' examples to facilitate its application and accelerating necessary leverage of 'One Health'. We propose elements of an open 'tool box' translating the 'One Health' concept into practical methods in the fields of integrated disease surveillance, joint animal-human epidemiological studies and health services development, which we hope might serve as a discussion basis for mutually agreed practical cooperation between human and animal health with special emphasis on developing countries.

Keywords

Animal health, Disease, Epidemiology, Health, One Health, Public health, Services, Surveillance.

Verso una guida "Una sola salute" per l'applicazione pratica e la ricerca

Riassunto

Negli ultimi dieci anni si è assistito a una rinascita senza precedenti del concetto "Una sola medicina" coniato da Calvin Schwabe, con l'evoluzione verso la filosofia "Una sola salute" incentrata su epidemiologia e salute pubblica. A giusta ragione, i patologi evidenziano le strette relazioni genomiche tra uomo e animali, ad esempio nella genetica tumorale. E' necessario passare da una prospettiva di confronto "noi contro loro" a una prospettiva di "rischio condiviso" da uomo e animali. Le organizzazioni professionali hanno annunciato la propria adesione, i governi hanno creato gruppi di lavoro congiunti su salute pubblica e animale e

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sono nati numerosi programmi di ricerca e sorveglianza, come evidenziato nel sito Web dell'iniziativa "Una sola salute". A prescindere da questi sviluppi positivi, non si deve tuttavia dimenticare l'ampio distacco che permane tra medicina umana e quella veterinaria, dovuto a una (iper)specializzazione delle discipline, mai verificatasi in precedenza, e ad approcci sempre più riduzionisti all'indagine scientifica. Attualmente c'è la necessità di un radicale cambio di vedute e paradigmi nell'approccio alla salute pubblica globale, con strategie d'intervento ed esempi "pratici" che ne facilitino l'applicazione e accelerino il necessario impiego della prospettiva "Una sola salute". Propone l'utilizzo di una guida aperta per tradurre il concetto "Una sola salute" in metodi pratici da applicare alla sorveglianza integrata delle malattie, agli studi epidemiologici congiunti su uomo e animali e allo sviluppo dei servizi sanitari, auspicando che possa servire come base di discussione per l'avvio di una collaborazione pratica, concordata tra specialisti della medicina umana e animale, con particolare enfasi nei paesi in via di sviluppo.

Parole chiave
Epidemiologia, Malattia, Salute, Salute animale, Salute pubblica, Servizi, Sorveglianza, Una sola salute.

Introduction

The 'One Medicine' concept by Calvin Schwabe (54) has seen unprecedented revival in the last decade and has evolved, by extending into health systems aspects towards 'One Health' conceptual thinking, emphasising epidemiology and public health (64). Pathologists involved in comparative medicine rightly recall that their discipline 'One Pathology' illustrates 'One Medicine' by close genomic relationship of animals and humans e.g. in cancer genetics. Many cancer genes were discovered in animals prior to identifying similar pathologies in humans. Currently functional genomics of human and animal genes are pulled together by a huge International Knockout Mouse Consortium (IKMC) (Table I) (8). Such a highly specialised process should however, not lead to an 'other One Medicine' (17), but should contribute to the convergence of an integrated approach to health of all species at the levels of pathogens, patients, populations and their cultural and natural environments.

While animals are commonly used as sentinels for human health, documented by the unique Canary database by Yale University (Table I), one of its creators, Peter Rabinowitz, suggests that, as humans, we should change our 'us versus them' perspective of the entire environment, including animals as determinants of 'risk to human health' towards a perspective of 'shared risk' between humans and animals (41). The American Medical Association (AMA) and the American Veterinary Medical Association (AVMA) have both adopted endorsing resolutions leading to the creation of the 'One Health initiative' (16). This was further emphasised at the recent conference of the American Society of Tropical Medicine in Philadelphia in November 2007 and at the Convention of the American Veterinary Medical Association in New Orleans in July 2008 (28). Additional organisations that have endorsed the 'One Health initiative' are given on the 'One Health Initiative' website (2).

Joint working groups have been established in many countries. For example, the United Kingdom Zoonoses Group was set up at the ministerial level, bringing together representatives of veterinary and public health and other services on a permanent basis in 2001. Innovative research, like the zoonoses research programme of the German government, required compulsory cooperation between physicians and veterinarians in their application process. Numerous other research programmes were instigated, such as the European Union focus on zoonotic diseases, by addressing both the public health and veterinary sectors. 'One Health' has received recognition by the World Conservation Union in the Manhattan declaration considering that the survival of wildlife requires healthy animals and healthy people. The Consultative Group of International Agricultural Research has set up a focus on agriculture and health. The food industry has internalised human health considerations of animal source foods

Table I
Summary of major 'One Health' activities since 1998

Type of cooperation	Initiative	Institutions involved	Reference/website (sites accessed on 28 February 2009)
Awareness	Endorsing resolution	American Medical Association	(18)
Awareness	Endorsing resolution	American Veterinary Medical Association	(18)
Awareness	Advocacy	'One Health initiative'	www.onehealthinitiative.com
Awareness	Manhattan declaration	World Conservation Union	www.oneworldonehealth.org
Scientific debate	Scientific conference	Society for Tropical Veterinary Medicine	www.soctropvetmed.org
Scientific debate	Scientific conference	Convention of the American Veterinary Medical Association, 2008	(27)
Research programme	National Centers for Competence North South	Public health and veterinary partners in Kyrgyzstan, Ethiopia, Chad, Mali, Mauritania	www.nccr-north-south.unibe.ch
Research programme	Zoonoses Research Programme	German ministry of research	www.bmbf.de/foerderungen/12275.php
Research programme	FP-7 focus on zoonotic diseases	European Union	ftp.cordis.europa.eu/pub/fp7/docs/call2-so-topic.pdf
Research programme	Agriculture and Health Program	Consultative Group for International Agricultural Research (CGIAR)	www.ifpri.org/ahrp/ahrp.asp
Research programme	International Knockout Mouse Consortium (IKMC)	Knock-out mouse programmes of the United States, Canada and Europe	www.knockoutmouse.org/
Disease surveillance	Canary database	University of Yale, Occupational Medicine	www.canarydatabase.org
Disease surveillance	United Kingdom Zoonoses Group	Government public health and veterinary authorities	www.defra.gov.uk/animalh/diseases/zoonoses/ukzg/index.htm
Disease surveillance	Global early warning for animal diseases transmissible to humans (GLEWS)	World Health Organization (WHO), Food and Agriculture Organization of the United Nations (FAO), World Organisation for Animal Health (*Office International des Épizooties*: OIE)	www.who.int/mediacentre/news/new/2006/nw02/en/index.html
Disease surveillance	ProMed mail	International Society for Infectious Diseases	www.promedmail.org
Surveillance of enteric pathogens	C-Enternet, National Integrated Pathogen Surveillance Program	Public Health Agency of Canada, together with a large group of partners in agriculture and environmental sectors	www.phac-aspc.gc.ca/publicat/2007/c-enternet05-06/areport05-06-eng.php
Surveillance of antimicrobial resistance	The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)	Government of Canada	www.phac-aspc.gc.ca/cipars-picra/index-eng.php

from animal feed issues to the consequences of health economics (22). The World Health Organization (WHO), the Food and Agricultural Organization of the United Nations (FAO) and the World Organisation for Animal Health (*Office International des Épizooties*: OIE) cooperate in a global early warning system for animal diseases transmissible to humans (GLEWS) since 2006 (Table I).

Above all these beneficial developments, we should not forget that there remains a huge divide between human and veterinary medicine borne from unprecedented (over)specialisation of disciplines and increasingly reductionist approaches to scientific inquiry. Even within human medicine, there appears to be a growing divide between disciplines of mental and somatic health in such a way that Marusic and Bhugra recently felt the need to recall that mental and physical health are indeed related – a change in one provokes a change in the other – hence, it is indeed worthwhile to consider human health as 'One Health' among others and get away from Cartesian dichotomy of mind-body dualism (36). This example shows the extent of the current fragmentation of medical sciences, leading to an underestimation of the interplay of somatic and mental health.

In the same way and to a much greater extent is the divide between human and veterinary medicine, leading to misinterpretation in the fields of comparative pathology (8) or by lack of cooperation to delayed recognition of infectious disease outbreaks (12). Communication between physicians and veterinarians is nearly absent or very weak and medical doctors do not feel competent to talk to their patients about sources of zoonotic infection. Risks of zoonotic transmission between animals and humans, although in the same context, are perceived differently by veterinarians and physicians (23, 24).

Despite the importance of understanding the life cycle of pathogens in humans and both domestic and wild animals, most national and international health organisations monitor only human or domestic animal disease but not both together (29). Quantitative methods to link animal and human surveillance require further development (41). Public health and veterinary government authorities often only start cooperating when facing outbreaks of emerging zoonoses, e.g. Ethiopian public health and veterinary departments started collaboration during outbreaks of Rift Valley fever in 2006 (65) and, in Tajikistan, on anthrax surveillance in 2007 (43). Furthermore, H5N1 avian influenza outbreaks certainly fostered cooperation between public health and veterinary authorities worldwide in an unprecedented way.

Against the above-mentioned divide of human and veterinary medicine, integrative concepts exist and extend far beyond the direct animal-human interconnectedness and include the environment as a whole, coined as 'Eco-Health' approaches which have many beneficial consequences for the health of populations by recognising health effects within complex social and environmental interactions, e.g. by showing that mercury poisoning of fish and its corresponding risk for public health in the Amazon was much less due to gold mining, but due to soil erosion following deforestation (19, 30, 46, 47, 57). They recognise that complex challenges cannot be solved by reductionist approaches alone and are geared towards systems thinking (31). We have restricted this paper, however, to animal-human interfaces because, as shown above, its assessment is still highly deficient and requires particular attention prior to attempting further extensions. What is required now are practical approaches and hands-on examples to facilitate its application and accelerating necessary leverage (27). We propose elements of an open 'tool box' translating the 'One Health' concept into practical methods and approaches in the fields of integrated disease surveillance, joint animal-human epidemiological studies and health services development, which we hope can serve as a discussion basis for mutually agreed practical cooperation between human and animal health also in many other domains of joint interest, with a special emphasis on developing countries.

Integrated surveillance

Today, information technology provides opportunities beyond belief for collecting, storing and dissemination of data for disease surveillance, e.g. the Livestock Early Warning System of the Center for Natural Resource Information Technology (CNRIT) (cnrit.tamu.edu/lews/). While most of the surveillance data is still collected separately by public health or veterinary services, joint aggregate surveillance databases are being developed such as the above-mentioned GLEWS (Table I) by the WHO, FAO and OIE, the Program for Monitoring Emerging Diseases (ProMED)-mail electronic early warning system (11), or the Canary database documenting animals as sentinels of human environmental health hazards which goes beyond the surveillance of infectious disease and includes cancers and environmental toxicology (41). A multi-partner initiative facilitated by the Public Health Agency of Canada and funded by Agriculture and Agri-Food Canada (C-Enternet) is designed to support activities that will reduce the burden of enteric (gastrointestinal) disease by integrated sentinel site surveillance. Moreover, the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) is a comprehensive and unified approach monitoring the use of antimicrobials and antimicrobial resistance across the country. The two latter public initiatives are certainly a model for integrated surveillance and have the potential to include other hazards, e.g. as included by the Canary database (Table I).

From a global perspective, huge gaps in coverage for individual countries persist however (11) and the WHO study group on future trends in veterinary public health, emphasising the need to expand the links between human and animal medicine, recognises that developing countries, especially in Africa, may lack the necessary technology, infrastructure and resources leading to poor or non-existent surveillance and even inappropriate setting of priorities (60). As a consequence of the acute human resources crisis affecting the health sector (61) and the structural adjustment programmes followed by the privatisation of most of the services, large areas cannot be covered by sufficient qualified public and animal health professionals to ensure surveillance and reporting of new outbreaks. Under these circumstances, a central question that remains is how to address integrated surveillance at community levels in developing countries?

Communities play an essential role at the first level of any surveillance system (32, 60) and are often excellent observers and know the priority diseases of humans and animals in their context. For example, thanks to livestock holder reports on perceived anthrax vaccine quality, contamination problems in the local vaccine production were detected in Chad (53). Mobilising communities for disease surveillance requires culturally and gender sensitive, participatory approaches. They involve multiple disciplines, ideally including anthropological and social scientists along with physicians and veterinarians. Ownership by the communities for such endeavours requires their participation in knowledge generation as equal partners, together with local authorities and scientists in a transdisciplinary approach (53) (Fig. 1). In this way, e.g. differentials of human and animal vaccination coverage, or sources of zoonotic diseases were identified much more rapidly than by standard sectoral epidemiological studies (50, 52). To convert such transdisciplinary research into continuous surveillance systems yielding meaningful indicators of disease incidence, they should best be connected to demographic surveillance.

Figure 1
Participatory stakeholder meeting between nomadic pastoralist communities, veterinary and public health authorities and scientists in Chad, 2005
(Photo: J. Zinsstag)

In 1998, an international network of field sites with continuous demographic evaluation of populations and their health in developing countries (INDEPTH) was founded. Its mission is to harness the collective potential of the world's community-based longitudinal demographic surveillance initiatives in resource constrained countries to provide a better, empirical understanding of health and social issues, and to apply this understanding to alleviate the most severe health and social challenges (www.indepth-network.org). Today INDEPTH has more than 37 demographic surveillance sites in 19 countries. Of these, 25 sites are located in Africa, 10 sites in Asia , 1 in Oceania and 1 in Central America. INDEPTH is hence an excellent framework for human demographic and health data collection. We suggest here to extend this approach to animal populations living with the surveyed human populations. Survey teams can be complemented with trained livestock personnel simultaneously assessing the health and demography of dogs (10, 37), poultry, pigs, horses, donkeys, camels, goats, sheep (1) and cattle (63). Potentially, this approach can also be extended to wildlife in a given context (communities living along boundaries to game reserves). Periodically, biological samples (sera, faeces) can be collected to assess specific pathogens. Special cases are mobile populations, such as nomadic pastoralists for which so far no demographic surveillance system (DSS) exists. New technologies utilising electronic finger print devices and hand held computers, combined with capture-mark-recapture methods and geographic information systems enable the monitoring of demographic parameters in mobile populations and could easily be extended to animal populations using ear tags or other marking devices (58). Integrated DSS, assessing demographic and health parameters of sedentary and possibly mobile communities and their animals is thus quite possibly more cost-effective than separated human and animal disease surveillance, it is feasible and has a huge potential addressing persistent and emerging zoonoses, food-borne diseases, potential for joint health services (6), environmental toxicological (41) or even chemical and bio-terrorist threats (40, 42). An important conceptual advantage and synergism of an integrated surveillance system to conventional DSS is the potential of animals as sentinels for human disease (10, 41), but also the reverse, humans as sentinels for disease in animals.

Epidemiological study designs: potential and pitfalls

Potential

In many cases, we are not primarily interested in the surveillance of emerging diseases, but the incidence and control of specific disease in humans and animals. Investigating human and animal health simultaneously is justified if the incremental knowledge generated is higher compared to two separated human and animal health studies and if there are no concessions made with regard to the quality of methods used on either side. The interfaces between species can be straightforward or at different levels, e.g. by occupational or consumer exposure. In-depth assessments are then necessary to understand life cycles and to understand drivers of reservoir or maintenance host populations. A variety of longitudinal and cross-sectional designs exist to monitor animal-human transmission using proxy indicators, such as dog bites for rabies (9) or questionnaires of exposure (25) or comparative seroprevalence in humans and potential animal reservoirs (50). Studies at the animal-human interfaces should aim primarily at high risk human populations considering the particular context of exposure, such as encroaching habitat, live animal markets and risk groups of professional exposure e.g. livestock workers or veterinarians. In the text below, we present a case example of the study design of a representative, national human and animal brucellosis seroprevalence study and cost of disease to society for Kyrgyzstan.

The example of brucellosis in Kyrgyzstan

Kyrgyzstan has one of the highest brucellosis incidences worldwide (annual incidence 2007: >50 per 100 000 (Venera Maitieva, personal communication). An increase of the disease has been reported since the end of Soviet system in 1990, but knowledge of the representative incidence and prevalence of brucellosis was lacking. Livestock farmers indicated that brucellosis was known to be in the herd when found in humans. Within a partnership of the Institute of Livestock, Veterinary Sciences and Pastures, the State Republican Central Veterinary Laboratory, the Republican Centre for Quarantine and especially dangerous diseases, the State Sanitary Epidemiological Department of the Kyrgyz Republic, the Swiss Red Cross in Bishkek and the Swiss Tropical Institute (Table I), a representative cross-sectional animal and human brucellosis study was agreed, after successful liaison by Tobias Schüth of the Swiss Red Cross.

The sampling frame was the national census of the sheep population. A multi-stage cluster sampling proportional to size (4), analogous to Schelling *et al.* (50), was performed by levels of Oblast (Province), Rayon (District) and village. Villages were sampled proportional to the size of the sheep and goat populations, suspected to be the main reservoir of brucellosis in Kyrgyzstan. Selected villages were informed of the contents of the study and asked for their informed consent. In randomly selected households, 20 sheep and goats were sampled. If a livestock species was not present in a village, then no other completion of the sample was sought. If there were cattle in the household, they were sampled equally up to a total number of 20 in the same way as the sheep (Fig. 2).

In every village, up to 40 human blood samples were collected (Fig. 2c). In the selected households, all humans were sampled after informed consent was given, following National brucellosis examination guidelines (Decree 240, Epidemiology and surveillance of brucellosis of the Kyrgyz Republic). Humans were sampled by public health physicians under supervision of the Republican Centre for Quarantine and especially dangerous diseases. A questionnaire was filled in with herders on the following:

- observed abortion rates within herds
- life-history of sampled animals
- vaccination status of herds
- predominant animal health problems
- occurrence of human brucellosis in the family, including reproductive disorders.

For the economic analysis, animal serological data was related to productivity as proposed by Bernues *et al.* (5) and as used by Roth *et al.* (49). The economic analysis assesses the cost of disease to households and to the livestock production. The burden of brucellosis on the

a) Blood sampling of sheep

b) Blood sampling of cattle

c) Blood sampling of humans

Figure 2
Sampling of sheep, cattle and humans in a simultaneous animal and human brucellosis serological study in Kyrgyzstan
(Photos: J. Kasymbekov)

human population is stratified by age group and sex from data on morbidity and mortality and on the duration of the disease (49).

The theoretical base for the control of brucellosis exists over fifty years and comprehensive elimination schemes have been successfully operated in many countries. However, these schemes cannot be transferred directly to low income countries. Representative simultaneous investigation of human and animal brucellosis provides an evidence base for the development of the most cost-effective national brucellosis control strategy for Kyrgyzstan. Other zoonotic or livestock diseases could be assessed at the same time, e.g. echinococcosis (55, 62). In-depth knowledge of the transmission of multiple zoonotic diseases may lead towards intervention packages e.g. against brucellosis and echinococcosis during the same farm visit, which are very likely more cost-effective than single interventions. Most importantly, this study was agreed jointly between the Kyrgyz public health and veterinary authorities and provides a common evidence base for future intersectoral decision-making and policy. Moreover, if future joint surveillance of human and animal brucellosis could take place, considerable reductions of surveillance costs can be expected.

Pitfalls

While such animal-human outcome linkages often appear biologically plausible and commonsensical, in practice they can be difficult to prove. Obstacles include the mobility, heterogeneity and diverse exposure histories of human populations (41). While at the household level, a direct relationship of disease outcome in animals and humans is often not evident, higher levels of geographic aggregation are more likely to show an animal-human linkage. Studies on social contact networks (48) of animals including humans, combined with molecular genetic analysis of transmitted pathogens (26) may contribute to ascertain causality. Despite the relatively high prevalence of bovine tuberculosis in Chad (14) however, no human cases of *Mycobacterium bovis* has been detected to date (13). Assessing non-transmission between animals and humans thus sometimes becomes as interesting as to understand transmission (56). Within the 'One Health' concept, genomics shows its power not only between humans and animals (8) but also for the pathogens transmitted between them. The dynamics of interactions of animal and human pathogens often require broader ecological and societal considerations, such as climate change, political transitions and their economic consequences, human behaviour and changing agricultural land use as has been perfectly demonstrated by the example of tick-borne diseases in Eastern Europe (44, 45).

Joint health and social services development

Health services for humans and animals are provided, in most cases, in forms that are strictly separated from each other. Veterinarians are generally not allowed by law to treat humans and physicians only rarely treat animals. While overlapping issues are evident with regard to the transmission and control of zoonoses, joint health service provision is much less obvious and is likely restricted to specific cases and situations. In remote rural areas of many developing countries, health services of any kind are rare and hardly accessible. It is thus not surprising that the 'One Medicine' idea was first formulated within an African context. It was conceived and conceptually consolidated during Calvin Schwabe's work with Dinka pastoralists (34). McCorkle (33) argues that, especially for remote or rural peoples of the developing countries, an intersectoral approach partly modelled along the lines of traditional, non-Western patterns for the joint delivery of basic health care services to both humans and animals would be more appropriate and feasible than attempting to impose a dualistic 'Western-style' structure on services. In this way, observations of higher vaccination coverage in cattle than in children in nomadic pastoralists in Chad have led to joint livestock and human vaccination campaigns through cooperation between the expanded programme on immunisation (EPI) and the veterinary services in Chad (51) (Figs 3 a and b). Novel models of integrated social services exploiting links between education, public health, animal health and natural resource management (59) could contribute to improved rural health service coverage (6, 7, 65). Generalisations can hardly be made and we refer to the transdisciplinary method by Schelling *et al.* (53), where communities interact with the authorities in a participatory process to identify acceptable institutional (18) and legal frameworks and arrangements for social service development in a given context (Fig. 1). Cooperation or joint services may be limited to information exchange but can also result in joint activities, especially in remote areas with limited access to any service, which are roamed only by illegal drug peddlers (65).

a) Vaccination of cattle by the Veterinary Services of Chad

b) Vaccination of women and children within the framework of the Expanded Programme of Immunization (EPI)

Figure 3
Joint human and animal vaccination services in Chad
(Photos: J. Zinsstag)

Closing circles

Restricting method development on the human-animal interface of 'One Health' may appear 'reductionist' to those involved in broader approaches of ecosystem health (20) and others interacting closely between medical and social sciences (39). While we deliberately chose this restriction to contribute to better cooperation between human and animal health, we attempt to close the circle by relating 'One Health' to 'Ecosystem Health'.

Whilst adopting a reductionist stance, we acknowledge the importance of bringing together the key decision-makers from disparate groups, especially where the scientific veterinary/medical interface meets the needs of policy makers.

Interpreting the metaphor of a 'healthy agroecosystem' by Gitau *et al.* (21) as a balanced and sustainable agricultural environment, the 'shared risk' perspective by Rabinowitz *et al.* (41) can be further extended to humans as a determinant of 'risk to ecosystem health'. For example, continuous industrial and agricultural pollution of the Saguenay fiord (Quebec, Canada), threatens the delicate eco-system of beluga (*Delphinapterus leucas*) reproduction, leading to one of the highest cancer rates in this species. Beluga cancer incidence can be considered as a proxy outcome variable for the quality of the ecosystem to which human industrial practices are a risk factor (35). Besides industrial and agricultural pollution, human and animal environmental sanitation is a good example requiring a 'shared risk' approach. Considering waste management in sanitation, combined material flow analysis (MFA) and quantitative microbial risk assessment (QMRA), together with social science vulnerability assessments, identify critical control points in a cyclical interventionist approach (38). One of the most important global issues that we will all encounter in the 21st century and which will adversely affect the ecosystems in both developing and developed regions will be in maintaining a healthy population in the face of climate change and energy shortfalls. A long-term vision would be to optimise human-environment interactions while minimising health hazards to humans and animals and preserving a balanced ecosystem. In many cases, however, changes are irreversible or long-lasting, such as the case of climate change or pollution with heavy metals (19). When dealing with irreversible changes, study approaches should be extended further to include methods based on resilience (15, 39) and adaptive management research in socio-ecological systems (3, 31).

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Conflict of interest/competing interests

The authors declare no conflict of interest.

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