Taking Action - Turning Evolutionary Theory into Preventive Policies

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Abstract

The Emerging Infectious Disease (EID) crisis has been challenging global health security for decades, dealing substantial damage to all socio-economic landscapes. Control measures have failed to prevent or even mitigate damages of an accelerating wave of EIDs, leading to the emergence and devastation caused by the COVID-19 pandemic. In the wake of the pandemic we must critically review our public health policies and approaches. Current health security measures are based on the evolutionary theorem of host-parasite coevolution, which falsely deems EIDs are rare and unpredictable. The DAMA protocol is nested in a novel evolutionary framework describing how emergence can be prevented before the onset of an outbreak. In this paper, we discuss the importance of establishing efficient communication channels between various stakeholders affected by EIDs. We describe implementation strategies of preventive interventions on global, regional and local scales, and provide guidelines for using such strategies in relevant policy environments of human, livestock and crop diseases.

Keywords : Infectious disease, EID prevention, DAMA protocol, policy implementation, Living Labs, Citizen Science

The Crisis of Emerging Infectious Diseases

The past decades have seen a striking rise in the number of Emerging Infectious Diseases (EIDs) across the globe, whether it meant known diseases appearing in previously unknown areas (e.g. West Nile Virus, Diphtheria, Measles), new variants becoming resistant to treatment (e.g. malaria, MRSA) or completely novel pathogens infecting novel hosts (e.g. SARS, African Swine Fever, Phytoplasma). With the ever increasing rate of globalisation, international trade and travel, EIDs had spread faster than ever before in human history, resulting in a staggering $1 Trillion USD/year for containment costs and production losses before 2020 (1). This figure was further elevated by the recent COVID-19 pandemic, which resulted in one of the largest economic recessions since the mid-1900s (2,3). A more significant reason for concern is that the damages in both economic production and human life was highest in the United States and United Kingdom whose

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healthcare system was announced to have been best prepared for such an event (4,5). These controversial patterns highlight the dissonance between how we try to control EIDs and what we should be focusing on instead.

As is the case with most epidemics, important conclusions are drawn from each case after the fact which should lead to better preparedness for the next such event. However, our investments into disease control and surveillance methods have neither been able to even slow down, let alone stop the acceleration of the EID crisis thus far, nor prevent the COVID-19 pandemic. To understand why our efforts have not been efficient, we must understand what the requirements and limitations of current disease management strategies are, and identify the gaps which allow for new diseases to emerge.

(Wrong) lessons learned

The main way we approach an outbreak today is to gather the maximum amount of data available to suggest pathways of containment. Although effects of an epidemic are felt throughout all sectors from tourism to education all the way to the job market, proactive initiatives are typically assigned to only two key fields: research and public health (6,7). Consistent throughout the majority of the reports and studies is the general aim of increasing preparedness measures (7,8), which translates into two major suggested outputs:

Rapid response: the main direction for developments in public health is improving preparedness. This involves decreasing the time required to identify and respond to an emerging disease. Identification of a public health event of international concern (PHEIC) requires investment into outbreak surveillance, healthcare data management, reaction protocols and real-time communication channels between local health authorities and regional or global organisations (7,9). Response on the other hand warrants sufficient capacity in healthcare infrastructure to treat incoming waves of patients, and therefore relies on stockpiling equipment and medication and increasing the number of trained healthcare professionals (6,10).

Focused research: the main directions for developments in science is increasing our knowledge on the emerging disease. A typical reaction to an epidemiological emergency is the reallocation of research funds towards studies targeting the emergent pathogen, which shifts the focus of novel and existing labs. Unfortunately, analyses show that this heightened attention and support wanes with the decreasing sense of emergency and proves to be inefficient in the long term, thus often referred to as 'boom-and-bust' funding (11,12).

Both outputs have had significant results in managing re-emergence of known diseases and managing epidemics that are considered regular occurrences in particular regions, but neither has yielded any considerable advantages against the EID crisis (9,13). The reason is that all of the initiatives listed above require the prior knowledge of the emergent pathogen. Public health needs to 'know what they're looking for' to detect it and alert health systems at an early stage of the outbreak. Otherwise the only clue of a recent emergence is the sudden spike of patients producing similar symptoms with unknown aetiology, as was the case for SARS-CoV-2 (14) the 2015 Zika epidemic (15), or even the currently ongoing outbreaks of hepatitis among children (16). Response also requires data on the clinical manifestations, morbidity and mortality to adequately prepare healthcare infrastructures, and focusing research requires an already identified and defined target pathogen or disease. In case of a newly emerging disease, none of the above described information is available, crisis response is therefore constantly lagging behind the spread of the epidemic. Taking into consideration the effects of globalised travel and trade (13,17), preparatory efforts will have little success in halting an epidemic in fulfilling its pandemic potentials, and crisis response is, by definition, a reactive measure.

To successfully address the emergence of novel diseases, a new paradigm has to be introduced into global health security, shifting our main focus from preparedness over to prevention, and moving our intervention further up the infection timeline. However, in order to change our approach, we must understand the gaps that have thus far allowed EIDs to ravage our societies.

What are we missing?

Health security measures are developed by close collaboration networks between public health and fundamental science. With the constant advancements in both technology and research, numerous defence strategies have been improved. Nevertheless, the EID crisis represents a completely novel challenge, which requires understanding the limitations of our current approaches, particularly about the predictability and the scope of EIDs.

Predictability

Despite the extent to which epidemics and pandemics damage a wide range of socio-economic landscapes, there are a concerningly few initiatives aiming to prevent large scale effects of EIDs [18,19]. This is due to the prevailing evolutionary paradigm used in public health and research regarding the ability of pathogens' to colonise new hosts a.k.a. emerge as a novel disease. The traditional scientific paradigm states that there is strong selection acting on parasite characteristics, which leads to extreme specialisation to a narrow range, often a single host species. Such specialised parasites are able to better exploit host resources, but at the same time lose their ability to infect novel host organisms, therefore any novel colonisation must necessarily be preceded with the right mutation appearing at the right time [20]. Due to the random and unpredictable nature of such genetic changes, host switching events are assumed to be rare and unpredictable [1,21]. However, this co-evolutionary theory suffers from severe shortcomings, when compared to empirical data: (I) its key assumption of parasites being tightly co-adapted to a narrow range of hosts lack empirical support, (II) its prediction regarding EIDs being rare occurrences is sharply contradicted by the accelerating EID crisis [22–24] and (III) it fails to connect such novel colonizations events to environmental changes when there is evidence that emergences cluster around climate change perturbations [25,26].

This contradiction between the prevailing paradigm and empirical observations is referred to as the Parasite Paradox [27], with a significant consequence on how public health addresses EIDs: it deems emergence rare, and therefore of low global health concern, and at the same time unpredictable, thus deeming prevention efforts impossible. These wrong predictions are the main reasons public efforts aiming to address the EID crisis have been futile, and precisely why we need a novel evolutionary paradigm to resolve this paradox.

The Stockholm Paradigm

The Stockholm Paradigm (SP) [1,26,28] relies on two Darwinian principles leading to fundamentally different conclusions than the co-evolutionary theory.

First, evolutionary outcomes are always local. Pathogens are genetically capable of infecting a certain range of hosts, translated as their 'fundamental fitness space', but only infect a subset of these that are available to them in their environment, creating their 'realised fitness space'. Selection only acts on traits within the realised fitness space and has no effect on other, potential hosts in other environments. Pathogens with proportionally smaller realised fitness space therefore have a higher potential of colonising a novel host, without the necessity of evolving new capacities. This potential is referred to as ecological fitting [29]. When viewed from a public health perspective, this means emergence is a built in attribute of host-pathogen associations and is therefore expected to happen frequently, especially when environmental perturbations increase species encounters, which is what we are witnessing with the EID crisis.

Second, evolution is conservative. In order to utilise particular resources, pathogens will develop specialised traits. Since these traits are phylogenetically conservative, pathogens will be able to utilise distantly-related, naive host species upon encounter, while the same host can serve as a resource for various pathogens [30–32]. The recently emerged SARS-COV-2 uses the angiotensin I converting enzyme 2 (ACE2) as its main receptor, which is widely shared among distant groups of mammals, and is the primary reason why the pathogen had established itself in mustelids, felines and cervids, among other mammals [33,34] Translated to a practical view, conservative traits allow us to predict the risk an unknown pathogen poses to human populations without having to wait for an outbreak. Pathogenic microbes can therefore be sampled from reservoir species and action can be taken not only to contain emergence, but to prevent it all together.

The SP therefore changes the theoretical foundation on which our global health security infrastructure is

built. The bad news is that EIDs are indeed frequent and should only be expected to increase in occurrence with the intensifying globalisation and climate change. The good news, however, is that EIDs are predictable, and preventive action can and should be taken to avoid the next epidemic and pandemic.

Scope

When referring to EIDs, literature and policy refers to almost exclusively human pathogens (13,17,35). Preparatory efforts and early action plans exclusively target human diseases, which manifests in recommended actions for *Rapid Response* and *Focused Research*(36,37). However, this also narrows our view to a small subset of potentially dangerous pathogens, while we ignore those affecting crops and livestock. Infectious diseases decimating agricultural production are dealt with by food security, agri-food sciences and agricultural policies, and are barely put in the context of EIDs . Nevertheless, the loss of production and associated costs affect regions' economies just as much, if not more than human diseases do. Coconut Lethal Yellowing Disease destroyed 95% of coconut palms in a region of Mexico, killed millions of trees in Nigeria affecting the livelihood of 30000 families, and ruined 72-99% of trees in West Africa (38,39). Wheat stem rust (Puccinia graminis f. sp.) was considered eradicated until 1998, when a new, highly virulent strain emerged in Uganda (40). Since then, it has spread throughout Eastern and South Africa, the Middle East and Western Europe, and poses a threat to over 80% of the world's wheat varieties (41). From those affecting livestock, the 2014-15 avian influenza epidemic led to the culling of 45 million birds in the US, and export bans in 75 countries (42)ongoing H5N1 avian influenza outbreak already led to the loss of 77 million birds (43). Within a few years, African Swine fever (ASF) swept through Europe and Asia, destroying 20% of Vietnam's swine population and resulting in 141 billion USD economic loss for China, collapsing half the world's pork export market in a single year (44). Apart from the obvious socio-economic effects of food shortage and skyrocketing food prices, policy interventions aimed at relieving damages of ASF were suggested to have led to the emergence of COVID (45).

Although currently considered as separate issues of human wellbeing, food security and global health security are threatened by the same thing: Emerging Infectious Diseases. If we understand the dynamic allowing novel pathogens to explore and colonise new hosts, then we must also understand that this applies to not only humans invading natural habitats, but to our crops and livestock being placed in the close vicinity of natural reservoirs (46,47).

With EIDs being predictable, but much more frequent and abundant than previously thought, health security measures have to incorporate this new paradigm and adopt appropriate and much called for prevention measures (48). We therefore describe a comprehensive four-step protocol based on the SP and leading all the way to policy implementations.

The DAMA Protocol

The DAMA - Document, Assess, Monitor, Act - is a policy plan derived directly from the evolutionary framework of the Stockholm Paradigm, which aims to connect evolutionary science with applied health security. It focuses on preventing outbreaks and facilitating communication between private and public actors, knowledge institutions and communities directly affected (Fig 1, redrawn and modified from (21).

Documenting pathogens has to be extended from only those already causing diseases to those documented in wild animal and plant populations. Taking advantage of the evolutionary context provided by the SP, anticipatory research has to focus on potential reservoirs. Pathogens causing disease in humans, crops or livestock are all present in at least one other species that manifests no symptoms. Taxonomic inventories, virological and bacteriological studies have often revealed these pathogen-reservoir associations, which direct research focus on a subset of species within any given area. Pathogen transmission occurs on the interface between such reservoirs and human settlements, agricultural areas and breeding facilities (49–51). The primary step in establishing a preventive protocol is collecting all information into strategic inventories feeding into archives of host and pathogen specimens, modes of transmission and potential vectors (52,53). Finally, inventories are also to include local and traditional knowledge on the distribution, behaviour and abundance of reservoirs, which calls for the establishment of robust science-society collaborative programs (1,54,55).

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Inventories then allow us to *Assess* the risk posed by potential pathogens. A three step process first separates our potential pathogens, from those already known and those considered to non-pathogenic through *phylogenetic triage* , then uses*phylogenetic assessment* to determine mode of transmission, reservoirs and potential vectors, and finally maps population genetics and rare genotypes through *population modelling* .

Potential pathogens are then *Monitored* to create a detailed distribution map in areas already confirmed as well as those deemed suitable. Changes in geographic distribution, host range, mode of transmission or disease pathology are early signs of potential emergence on interfaces between populations of reservoirs and susceptible hosts (47).

Adequate monitoring sets the stage for adequate *Action* in policy-making. Highly dependent on the context such as legal environment, policy modifications concern areas such as food safety, wildlife management, veterinary medicine, public health and education. Due to the high number of stakeholders affected by EID outbreaks, preventive action has to be designed by multi-actor task forces representing expertise from various sectors and scales. In practice, this necessitates the collaborative work of scientists, private and government practitioners, policy-makers and local experts. This collaboration can be realised by employing transdisciplinary approaches. The latter can be defined as "a critical and self-reflexive research approach that relates societal with scientific problems' ... [and] produces new knowledge by integrating different scientific and extra-scientific insights" (56) and are increasingly recognised for their potential to tackle complex real-life issues by integrating different kinds of knowledge (57,58).

Contrary to pandemics and large epidemics, emergence always takes place on a small, local scale, which calls for the facilitation of bottom-up effects and the subsequent co-accommodation of grassroots and institutional settings. When establishing task forces putting science into action, initiators have to consider implementation strategies on various scales (global, regional, local) and policy environments (human, livestock and crop health security).

Implementation strategies on different scales

Global

Current global frameworks are all based on managing existing diseases and increasing palliation and preparedness for those newly emerging (59,60). Since they are all based on the assumption that EIDs are rare and unpredictable, plans to prevent outbreaks are slim to none. Nevertheless, most of the global frameworks in use name prevention of disease as their main aim, which refers to containing diseases on the level of outbreak, halting large scale transmission and thus avoiding outbreaks from growing into epidemics. Although we can understand restricting pathogens from spreading beyond small, local outbreaks as preventing epidemics, we argue that prevention should be used in the context of avoiding emergence in the first place. This shift in epistemics is also strongly supported by the grave predictions regarding the speed with which smaller outbreaks can spread out in an increasingly globalised world (17,61,62), narrowing the time window available for containment measures.

One the one hand, global health security has to adopt a novel evolutionary paradigm to adjust risks and predictions regarding EIDs. On the other hand, the epistemology and definition of prevention needs to be unified across all global guidelines to focus efforts in both containing and preventing diseases in an evolutionary context. Therefore, current measures have to be evaluated to determine their applicability and limitations, and prevention has to be contextualised within global health security.

The Prevent - Prepare - Palliate (3P) framework offers a comprehensive, systemic characterization of existing health security initiatives and describes how prevention can be adopted into current infrastructures (21). Implementing prevention into global healthcare frameworks will help identify gaps that allow EIDs to emerge at an accelerating rate and would provide guidelines for healthcare infrastructures to intervene on a regional level.

Regional

Managing diseases on a regional level faces the challenge of having to act in various different policy and cultural environments. Ranging from upper regional levels such as international alliances (e.g. European Union) operating within large scale legal environments such as EU regulations through mid-regional levels concerning one or a few neighbouring countries to lower regional levels involving small municipalities managing local communities, regional scales are the most diverse in terms of expertise, jurisdiction and policies. Nevertheless, epidemics of national concern are dealt with on regional levels, involving municipalities directly affected as well as national health care infrastructures and public health institutions (9). Therefore, implementing the DAMA protocol on a regional scale requires carefully selected methods facilitating intersectoral collaboration and defining outcomes accommodating local policy environments.

Living Labs

From the toolkits of transdisciplinary methods, Living Labs (LLs) provide an opportunity to establish solid, well thought out task forces bringing the skills and capacities of different actors required for addressing a particular issue together (63). Living Labs can be defined as both "an arena (i.e., geographically or institutionally bounded spaces) and . . . an approach for intentional collaborative experimentation of researchers, citizens, companies and local governments" (64). It makes them suitable for dealing with healthcare issues, as they are designed to foster intersectoral communication and collaboration, and thus increase the feasibility of intervention plans by fitting them to local policy environments and interests of affected stakeholders (65). If designed and implemented well, the LL approach can also help avoid stumbling blocks (e.g. disciplinary boundaries and silos between science, practice and society, low feasibility in diverse policy environments, low level of adaptability to local cultural, societal, environmental settings, decreasing trust in policy and politics, etc.) by involving diverse experts on legal limitations, local settings and market conditions, and finally foster knowledge exchange and widen professional networks.

Containing outbreaks or epidemics requires a joint collaboration between private and public sectors, as well as science and society, and prevention is no different. Current solutions are mostly characterised by hasty and temporary collaborations formed under the pressure of a health emergency. Living Labs are potentially a very impactful approach for dealing with EID crises. They have been proliferating in Europe since 2006, when the European Network of Living Labs (ENoLL) was founded as a platform for best practice exchange, and have since been successfully adopted in domains such as food bioeconomy, agriculture, environmental, urban and rural development (64,66,67). However, to date Living Labs have hardly ever been applied to the area of EIDs. Apart from the benefits of the LL approach discussed above more generally, LLs can also enable and foster discussion between authorities, science and the public thereby addressing the dire consequences of public distrust in science and science-based policies revealed by the COVID-19 pandemic has revealed the dire consequences of public distrust in science and science-based policies (68,69).

Given the various actors impacted by infectious disease outbreaks, LL setups are able to generate solutions across disciplines, making them a 'proliferating approach to working in a transdisciplinary fashion' (57). Stakeholders are selected based on their expertise and involvement in the context of EIDs, making them highly adaptable and specific to the issue investigated. Selection must also consider the highest-level decision-makers needed for efficient intervention (municipality governance and policy-makers, national government officials, regional public health authorities, etc.) Participants generally represent four larger sectors (Figure 1.).

1. **Public actors** - policy- and decision-makers, legal experts and government officials; expertise in the legal environment and regulatory role in the long-term management of the outcome. Typical actors for disease management are Public Health Authorities, Municipality Governance or Food Safety Control.
2. **Private actors** - private institutions, organisations and companies affected by the emergence; insights into practical and industrial implementability of intervention plans. Managing disease will be of interest to agricultural organisations and farmers' associations, livestock breeders and food production companies, travel agencies or pharmaceutical companies.
3. **Knowledge institutions** - scientific expertise on the emerging pathogen generate predictions related to transmission, epidemic and pandemic potential and risk assessment. Partners to consider in relation

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to EID are university research groups, independent research institutions and scientific organisations (e.g. Chatham House, Milken Institute).

4. **Local citizens** - it is crucial to include members of the community directly affected by potential emergence. In addition to increasing feasibility of the intervention plans among local conditions, involvement raises awareness of healthcare threats and provides the community with a sense of ownership over the situation. An emphasis must be placed on reaching out to local Citizen Science Programs who have extensive experience in not only local settings, but research processes.
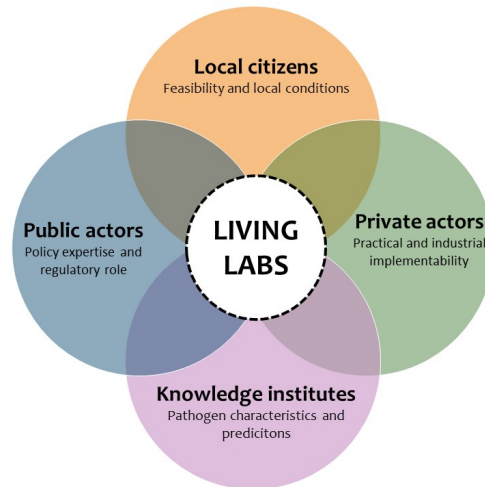

Figure 1. The stakeholder groups constructing Living Labs targeting EIDs, adapted and updated from Steen & van Bueren, 2017 (70).

LLs are fit to address the issue of feasibility and temporary collaborations through an inclusive, planned process, where solutions are planned in a precautionary manner. Participants representing diverse stakeholders and sectors jointly create an intervention plan, which aims to accommodate interests of all sides and respects limitations. Given the highly diverse legal environment on various regional levels, LLs consist of a select group of stakeholders with expertise relevant to the scientific, legal, geographical, economical and social conditions of a well-defined pathogen system. This creates a highly flexible and adaptable tool operating based on specific guidelines, but always adopted to the local environment.

LLs addressing disease prevention on a regional level should furthermore always be in close collaboration with Citizen Science and community programs engaging members of the exposed, susceptible population. The following section described the tools necessary for dealing with EIDs on a local scale.

Local

In case of a novel emergence, the initial absence of available information leaves an extremely narrow time window for reactive action. Additionally, due to the cultural and socio-economic diversity of directly affected communities, disease management often suffers from low feasibility and inefficient implementation (71–73). Similar as described for the regional scale, the DAMA protocol facilitates bottom-up processes and the involvement of local actors in both data gathering and generating solutions. Building working relationships with members and local experts of exposed communities creates mutual benefits by increasing the efficiency of implementing disease control measures, and building trust and collaboration between authorities, science and society.

Citizen/Community Science

Citizen or Community Science (CS) initiatives are founded to include locals as active participants in research projects targeting their direct environment. With insights provided by patients, farmers, students, hunters

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and hikers, CS has been invaluable in tracking insect and tick vectors (55,74), avian influenza in urban environments (54) and wildlife health (75).

Similar to preparation, disease prevention also relies heavily on completing scientific data with traditional insights and observations regarding reservoirs. CS programs provide an opportunity for outreach and contact with communities most exposed to emergence (e.g. urban minorities, underserved communities, students, rural farmers, etc.). Emphasis is placed on establishing communication channels and training programs between susceptible communities, public health and scientific research, creating long-term science-practice collaborations, which will serve as a foundation for continued monitoring and early warning systems. When mapping the distribution of a reservoir and/or vector of a suspected pathogenic microbe, local expertise and traditional insights on reservoir behaviour and distribution will be fundamental to conducting efficient monitoring. A further benefit of such initiatives is building the science - society trust bridge, which faces a difficult test during a public health emergency. Finally, including locals in the process, including in LLs (see above), grants ownership over outcomes and intervention plans to those on whom policies are acted on.

When targeting a community, it is just as important to make sure the members involved are relevant to the research and policy issue at hand, as it is to contact groups that are likely to positively respond to this research collaboration. Local organisations not only have in-depth knowledge about their community members, they already have the relevant network and infrastructure for reaching out and advertising opportunities. Although each program should consider the local setting and structure of the community, good examples to reach out to are (Figure 2.):

Community-based organisations - these organisations are founded and run by members of the community advocating for particular issues and rights, and therefore collect proactive groups of locals that could be approached with a CS initiative. Typical examples are Environmental Protection Groups, Neighbourhood Associations or Volunteering Clubs.

Educational institutions - gathering young members of the community who are currently or have been exposed to scientific knowledge makes educational institutions a prime target for CS programs, often building cohorts of volunteers who remain active in the research program even after leaving the institution. High schools, GED (General Educational Development) programs or colleges are only a few examples.

When designing a CS program, we aim to establish a long-term mutually beneficial relationship with key members of the community. This requires not only initial investment into recruiting data samplers, but must also run parallel with feedback and networking activities. The long-term goal of successful CS programs is not necessarily constant data influx, but the foundation of a dynamic network of locally trained experts and researchers which remain in touch and can be mobilised or expanded. This permanent working relationship is further fostered by selecting reliable and committed participants for leadership positions within the CS program.

Paraprofessional networks

Although initiatives targeting health disasters have been widely introduced, including the integrated 'One Health' surveillance, a common issue is barriers in the way of societal implementation, such as lack of efficient communication, fluctuating compliance and engagement, and territorial fragmentation (76). Disease prevention relies on long-term monitoring of both pathogen and reservoir populations; it is therefore crucial to have a permanent program in place that engages citizens, collects data and knowledge and feeds information back to the community.

After establishing a CS program, opportunities must be provided for consistently involved, engaged members to immerse within the project, gain agency and ownership over the issue at hand. Selecting candidates for leadership positions creates a network of so-called paraprofessionals who are then able to head particular tasks, assist with training, lead recruitment and participate in feedback. A regular income assigned to such positions also increases livelihood, as well as trust and cooperation with authorities. Paraprofessionals have been indispensable in addressing livestock (77) and human diseases (78), and should therefore be cornerstones
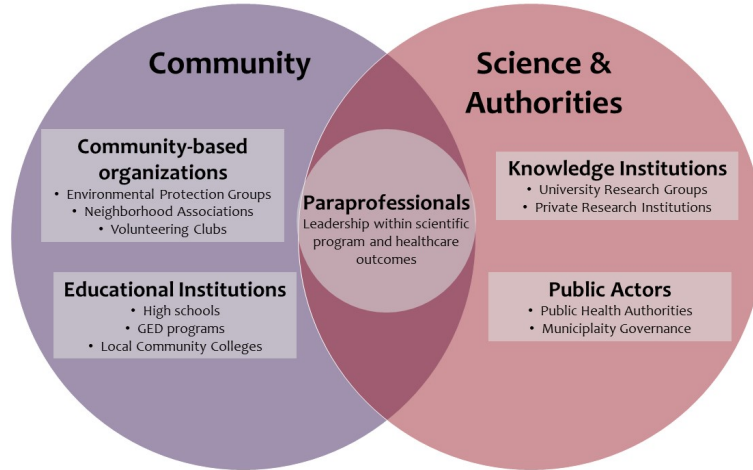
of EID prevention efforts.

Figure 2. The stakeholders participating in Community Science initiatives.

The strategies listed above provide guidance in implementing prevention measures of different scales of society. Nevertheless, efficient prevention requires the close collaboration of not only partners within a certain program and scale, but partners across diverse scales. Information and expertise coming from grassroot science must be utilised to design and implement intervention plans on regional levels, which will feed into global frameworks collecting exemplary cases and efficient methods to be applied on other reservoir-pathogen systems in diverse policy environments.

Implementation strategies in different policy environments

When reviewing various EIDs, outbreaks and epidemics are often dealt with by different legal and economic frameworks depending on not only the scale they manifest on, but also on the newly infected host. Pathogens emerging in human communities, for instance, will come under the jurisdiction of public health and healthcare institutions, which has already resulted in the false interpretation that the EIDs are exclusively human diseases (79). Pathogens damaging livestock and crops are therefore seldom connected to those creating illness in humans, despite the anthropogenic drivers of their emergence (globalisation, climate change, international travel and shipping, human intrusion, etc.) and the socioeconomic impacts being the same in both severity and magnitude (18,46,51,80). Policy silos can further be observed in livestock diseases being addressed by food safety regulations and production management, while crop diseases being the concern of agricultural policies. Nevertheless, not only are the drivers of disease emergence the same, but pathogens colonising livestock and crops can increase the probability of emerging human diseases (45).

The One Health initiative considers all novel diseases a direct threat to human wellbeing and has been working to implement the One Health approach to medical, veterinary and wildlife disease management, urging for large scale, merged databases, expanding research focus to wild populations and reservoirs and preparing for future emergences (73,81,82). In line with these efforts, the DAMA calls for preventive intervention against all pathogens with a potential to emerge in human, livestock or crop populations. At the same time, this also means that prevention has to be planned and executed in three different policy environments. In the following sections, we will present the main focus points, target stakeholders and typical stumbling blocks of establishing LLs and CS programs in different policy infrastructures.

Human pathogens

Human diseases come under the deepest scrutiny and attract the most attention from authorities and the public alike. Nevertheless, there is major divergence between countries and regions in terms of healthcare

infrastructure, pathogen diversity and sources of potential emergence. While temperate zone regions are more exposed to air-travel related infections being introduced (17), tropical and mediterranean areas have a higher potential for wildlife originated emergences (83). These patterns are then further complicated by climate change driving both species and human migration, providing opportunity for disease to expand their geographic, vector and host range. Chikungunya is an arboviral infection spread by the yellow fever mosquito (*Aedes aegypti*) and was therefore referred to as a 'tropical fever' due its distribution area limited to that of its vector. However, 2010 saw the virus establish itself in the tiger mosquito (*Aedes albopictus*) and produce autochthonous cases in Southern Europe (84), where it has since developed self-sustaining populations (85). Also an arbovirus moving from the *Ae. aegypti* to the *Ae. albopictus* , the ZIKA virus has seen its first local cases in Europe in 2019 (86) and is likely to threaten over a billion people with its recent range expansion (87). Finally, with the recent outbreaks of hepatitis of unknown aetiology (16) and the ongoing monkeypox outbreaks (88), it is clear that preparation for the barrage of human EIDs is unsustainable. The focus needs to shift towards prevention by launching multi-actor task forces handling emergence within a local and regional setting.

Living Labs preventing human pathogens

Preventing EIDs directly threatening human health will focus on the interfaces between human communities and identified reservoir populations where pathogens are expected to switch over to their new, susceptible host. Exposure will often be increased by living and working in close contact with wildlife (e.g. rural farming and hunting communities) and/or limited access to healthcare services coupled with improper maintenance of hygienic standards (e.g. urban poverty, marginalised communities) (1). Main focus points are to control and minimise the chances of pathogens switching over to humans, by either

targeting a specific host-pathogen system (e.g. Zika virus in *Aedes albopictus* mosquitos) in which case we identify the stakeholders affected by this system, or

targeting people whose circumstances (living conditions, occupation, habits, etc.) supposedly place them at higher exposure (e.g. jobs during COVID-19 that do not carry a home office option), in which case we identify stakeholders connected to our target community.

From the groups outlined for LLs in general, the following actors should be considered relevant to preventing high risk human EIDs.

Public actors - government authorities addressing public health related matters, such as health services and public health authorities, national laboratories and epidemiological surveillance facilities, district health systems and district public health authorities and food safety institutions.

Private actors - private companies and organisations affected by potential emergence or connected to endangered communities. Relevant examples include pharmaceutical companies producing treatment or vaccines against the potential threat, travel agencies mapping international routes of concern, or software development and data management companies offering digital tools for tracking and monitoring human-pathogen interfaces.

Knowledge institutions - scientific institutions focusing on human pathogens, for instance epidemiology research laboratories, veterinary research groups working on reservoirs or vectors of the pathogen in question, and medical research institutions for human diseases.

Local citizens - community members should be involved in multi-actor task forces to represent local interest and expertise. Priority should be given to those already participating in CS programs or civil organisations, with an emphasis on engaging students and early career youth.

LLs handling human diseases will rely heavily on personal data regarding local workforce, financial status, access to health services, medical history and connectivity, it is therefore crucial to secure data protection and privacy. Furthermore, resources should be dedicated to communicating the process to the local community through paraprofessionals involved in the LL to establish solid working relationships and trust between the

task force and locals. Relying on a collaborative foundation will not only facilitate implementation but also foster long-term engagement for maintaining preventive monitoring and screening.

Community Science programs preventing human pathogens

The focal point of disease prevention measures is engaging and working with communities directly exposed to the emergence of a novel pathogen. As described for LLs (see above), the target population for CS programs is identified (i) either through their contact with a particular reservoir or (ii) their circumstances making them susceptible to emergence of potential pathogens. Main focus points are to engage members of a community and initiate bidirectional communication channels between locals and researchers. On the one hand, prevention research relies heavily on knowledge of local habits and lifestyle, traditions, knowledge of reservoir behaviour and the interface between potential pathogens and community members. On the other hand, researchers can raise awareness on the lurking healthcare threat, establish educational and training programs, involve locals in the project and solidify collaboration by assigning leadership positions to paraprofessionals.

When planning recruitment within the community, factors to be considered include setting (e.g. rural vs. urban), occupation (local trade unions, commonalities between employment types, working conditions), socio-economic status (access to healthcare, level of education, household income) and cultural background (ethnicity, language, cultural habits and traditions, religion, etc.). Recruiting and training programs should be designed to be accessible and comprehensible for the target population, with a clear explanation of why they had been selected as participants.

Attention should be given to providing regular and thorough feedback on the process to all members of the community. Activities should be planned to ensure bidirectional flow of information: benefiting from community engagement should always be coupled with feedback sessions planned around delivering preliminary results, reflecting on experience of involved (academic and community) members and discussing potential impacts. This bidirectional discussion builds the trust and engagement required to establish long-term programs and networks, and builds a reliable network of non-scientific, local experts. Feedback should be constant during the actual sampling/collection to not only give back to the community, but to collect reflections and observations that can improve methods and communication strategies. A public facing website that is accessible for all stakeholders at all times is ideal, but regular newsletters or social media are popular ways to communicate effectively.

Contrary to LLs, CS programs are widely used to target infectious disease threats by monitoring bacterial pathogens polluting water bodies (89), preventing Lyme-disease (90), or monitoring viruses in urban environments (54). Methods and practices developed in previous programs should be implemented into newly established initiatives focusing on prevention.

Livestock pathogens

Diseases emerging in livestock have been just as impactful as those affecting humans directly. The past decades have seen an increase in both frequency and magnitude, with pandemics plaguing livestock across regions and continents (91,92). However, studies often focus on zoonoses rather than diseases affecting livestock directly, creating a lack of available information on pathogens of domesticated species (93). This bias in research is fueled by preferential funding for zoonotic diseases, which also manifests in lack of veterinary healthcare infrastructure, low efficiency or high priced medications, lapses in vaccination programs and knowledge discrepancies in breeders regarding diseases (94,95). Adding to the effects of this asymmetry in knowledge and research is the management of livestock diseases, which primarily aims to eliminate infected individuals from breeding stock, with extremely limited efforts dedicated to treatment development (96,97). Although there have been suggestions to introduce preemptive hunting strategies to avoid livestock being contaminated from wild populations (98), prevention still has a lot of ground to cover regarding livestock disease. This is further certified by the major economic effects livestock pandemics have, which add to the costs and damages caused by human EIDs. Foot and mouth disease of cattle resulted in up to 88% market value losses, affecting all actors along the cattle marketing chain in Uganda (99), while leading to the culling

of 3.4 million animals during the UK epidemic (100). African Swine Fever has led to major economic losses in South-East Asia, and has triggered policy modifications linked to the emergence of SARS-CoV-2 (45,51). Avian influenza has not only led to dire losses in poultry production (80) but also to pandemic potential in humans (101). Therefore, in line with the One Health approach calling for integrated investigation of livestock, wildlife and human systems (102,103), the DAMA protocol calls for precautionary and preventive policies addressing livestock diseases.

Living Labs preventing livestock pathogens

Livestock disease will be of concern to different stakeholders than human pathogens, although a considerable overlap is to be expected. The drivers behind any preventive or managing intervention are mostly to maintain production and livelihood of breeders and production plants. Exposure will increase in free range breeding stocks and those housed partly in external enclosures, while outbreaks will be more likely to occur among high density stocks (104). Main focus points are to control and minimise the chances of pathogens switching over to livestock, by either

targeting a specific host-pathogen system (e.g. ASF in wild boar populations) in which case we identify the stakeholders affected by this system, or

targeting breeding facilities and game populations whose circumstances (housing conditions/distribution area, species, immediate surroundings etc.) supposedly place them at higher exposure (e.g. frequent encounters with (other) wildlife, limited access to veterinary/wildlife services, lack of knowledge regarding livestock/wildlife diseases, etc.), in which case we identify stakeholders connected to our target facilities.

From the groups outlined for LLs in general, the following actors should be considered relevant to preventing high risk livestock EIDs.

Public actors - government agencies involved in food safety, including national level institutions (e.g. Food Safety and Inspection Service (FSIS; US), Federal Institute of Risk Assessment (BIR; Germany), Austrian Agency for Health and Food Safety (AGES; Austria), Fish and Wildlife Department, as well as municipality level department of public health, agriculture, hunting and food safety.

Private actors - private companies and enterprises whose main activity is related to the livestock and/or game exposed to emergence. A few examples include farms, processing plants, hunting associations, suppliers and veterinary institutions providing vaccinations and medication. In case they are active in the area of potential emergence, companies offering digital tracking services recording movement, development and other data on individual animals, will also have valuable expertise in identifying interfaces and location of possible intervention to reduce encounters between livestock and reservoirs.

Knowledge institutions - research groups targeting the livestock and game pathogen under investigation as well as those conducting research in livestock and wildlife vaccination, treatment, methods to increase production and environmental effects on stock yield. Furthermore, veterinary science is also a key stakeholder contributing to knowledge on transmission, morbidity and mortality, and to potential direction of treatment and/vaccine development.

Local citizens - required expertise will be found among individual farmers and workers at breeding and processing facilities, as well as hunters, who not only hold valuable insights regarding animal behaviour and diseases but are also directly exposed to any emerging pathogen due to their constant close contact with the breeding stock and wildlife.

LLs handling livestock and game diseases must always consider that, contrary to those dealing with human pathogens, they will have dual priorities of preventing emergence and maintaining or even increasing production. As livelihood of most stakeholders is closely connected to yield of breeding stocks and game populations, tools such as culling or restricting stock size, increasing hunting bag size or applying targeted hunting should be used with extraordinary caution to establish long-term feasibility of prevention methods.

Community Science programs preventing livestock pathogens

CS programs targeting livestock diseases are far less common than those addressing human pathogens, since the community affected by them is much smaller and consists almost exclusively of citizens working in livestock breeding or processing and hunters. Whether a CS initiative is designed to target (i) a particular pathogen and the livestock or game exposed to it or (ii) breeding stocks and game populations whose circumstances make them susceptible to emergence of potential pathogens, the initiative will be of interest to a narrower community of local experts.

Main focus points are to engage breeding experts and individual hunters that work in close contact with animals and are aware of the day-to-day issues and conditions of a breeding/processing facility or a particular hunting area. Livestock experts will be able to identify interfaces between the stock and wildlife accurately, while hunters will be familiar with movement and behavioural patterns of game and potential reservoirs, as well as population sizes and demography.

When planning recruitment strategies, a close collaboration is required with the management of the breeding facility(s) for efficient study design and institutional encouragement to participate. It is also necessary to align interests of larger breeding enterprises and small-scale, local farmers to ensure the homogeneity of data collected. An additional opportunity lies in designing studies for the general audiences, targeting those that are active outdoors and therefore have occasional encounters with wildlife. Recruiting and training programs should be designed to be accessible and comprehensible for the target population, with a clear explanation of why they had been selected as participants.

To avoid unnecessary investment, planning must always consider existing data collected by breeders and hunters, as both institutions collect particular types of data on a permanent basis. This is available either from government institutions overseeing wildlife management or private breeders keeping their own records, both subject to restricted access. Similarly, feedback sessions and reports have to be targeted to both citizen participants and the institutional board overseeing the stock in question, which can alter the format of the feedback.

CS programs have been introduced into research focusing on wildlife health surveillance (75) as well as monitoring invasive vector species (55). Studies have also used CS methods to target diseases plaguing wildlife and livestock simultaneously (105) and to identify shortcomings of policies addressing foot and mouth disease (106).

Crop pathogens

Crop pathogens are commonly the most neglected EIDs since they pose no immediate health risk to humans and therefore mostly manifest in indirect effects due to decreased production. Crop pathogens have typically been addressed by palliative efforts eliminating them from the cultivated plant stock (107,108) or later applying defence priming against known crop diseases (109). Macroscopic pests of crops have a longer history of defence strategies, as microscopic pathogens had only been discovered to coincide with plant diseases in the late XIXth century and named as a cause decades later (110). Initial research focus gradually shifted from epidemiology towards control and founded commercial disease control with a wide range of bactericide, fungicide and virucide treatments, as well as extensive gene-modification research breeding resistant crops lineages (110). Although without such protection measures, losses in crop production could increase five-fold in Europe (111), it has now become clear that global demand as well as changing climate and globalised trade have subjected crops to EIDs unmanageable by current measures. Additional to coconut yellow disease and wheat stem rust described above, tomatoes are plagued by rapidly spreading, diverse viral diseases (112), grapevine downey mildew has spread from Europe and now threatened vineyards worldwide (113), and the Fusarium incarnatum-equiseti species complex had invaded leafy vegetable crops in novel European areas (114). Although still treated as an agricultural and production issue, more studies are connecting plant diseases to the larger context of EIDs (115–117). In line with this, evidence shows that plant pathogens follow similar evolutionary trajectories to those described in the Stockholm Paradigm, for instance Phytoplasmas using common receptors distributed across several insects that serve as vectors to infect plants (118,119).

Although the overlap between plant and human pathogens is presumably negligible, the effect of emerging

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plant pathogens on global food security is devastating, which justifies their inclusion within the preventive measures of the DAMA protocol.

Living Labs preventing crop pathogens

Crop pathogens will be of interest to stakeholders quite different than described for human and livestock diseases, with smaller overlaps. However, some similarities will exist between motivation for preventing crop and livestock EIDs, namely the drive to maintain production and yield of crops. Also, exposure will increase in those planted in the vicinity of wild areas, with large scale monocultural fields being at elevated risk of epidemics and outbreaks. Additionally, growing similar species in close spatial or temporal proximity may further increase the chances of transferring pathogens from one to the other (120). Main focus points are to control and minimise the chances of pathogens switching over to crop plants, by either

targeting a specific host-pathogen system (e.g. phytoplasma in their vector insects) in which case we identify the stakeholders affected by this system, or

targeting areas or particular crops whose circumstances (distribution area, species, immediate surroundings etc.) supposedly place them at higher exposure (e.g. large areas bordering natural habitats, limited access to agricultural and control services, lack of knowledge regarding crop diseases, etc.), in which case we identify stakeholders connected to our target areas or species.

From the groups outlined for LLs in general, the following actors should be considered relevant to preventing high risk crop EIDs.

Public actors - government ministries involved in agricultural services, including national level institutions (e.g. National Institute of Food and Agriculture (NIFA; US), Federal Ministry of Food and Agriculture (Germany), Federal Ministry of Agriculture (Austria), as well as municipality level departments of public health, agriculture, and food safety.

Private actors - private companies and enterprises whose main activity is related to the crop and/or area exposed to emergence. A few examples include farms, plantations, suppliers and agricultural institutions providing protection methods. In case they are active in the area of potential emergence, companies offering digital mapping services recording distribution, density, species composition, and other data in high resolution, will also have valuable expertise in identifying interfaces and location of possible intervention.

Knowledge institutions - research groups involved in agri-food sciences relating to the emergent threat, working on control measures such as resistant lineages, pesticides, defence priming techniques, and ways of increasing production, as well as those studying the distribution and genetic mapping of the pathogen in question.

Local citizens - required expertise will be found among individual farmers and workers working with investigated crops or in relevant areas, as well as the general public visiting natural areas in the vicinity of the cultivated plants. Both will have direct insights into the manifestation and the distribution of the disease and will be able to point out significant interfaces between crops and wild reservoirs or hosts.

A further similarity to LLs handling livestock and game diseases, those addressing crop diseases must also aim to prevent emergence and maintain or increase production at the same time. Additionally, since current control measures hold off substantial losses in production, prevention measures must accommodate ongoing treatment protocols. Finally, different regions will often have very different infrastructure on cultivated areas, which will have a significant influence on the potential prevention plans and their feasibility.

Although particular plant pathogens have been addressed by multi-actor approaches targeting pathogens such as cassava viruses (121), the Living Lab approach is still to be utilised to its full potential in preventing and controlling emerging crop diseases.

Community Science programs preventing crop pathogens

Unlike in livestock diseases, CS programs tend to have a more thorough representation in crop disease studies. This is mainly due to the economic drivers of controlling crop pests as well as the larger community of farmers and general public that is able to contribute. Whether a CS initiative is designed to target (i) a particular pathogen and the cultivated species exposed to it or (ii) crops whose circumstances make them susceptible to emergence of potential pathogens, the initiative will be of interest to a wider audience than in the case of livestock diseases.

Main focus points are to engage farmers, cultivation experts and individuals living or frequenting endangered areas, who will possess the knowledge on crop and reservoir species as well as specifics on the area of cultivation. Training programs should primarily focus on developing skills to identify particular wild plant species and recognize signs of infection, which will also be useful in tracking invasive species in the future. Recruiting and training programs should be designed to be accessible and comprehensible for the target population, with an additional educational role in raising awareness about food security issues and conscientious consumer behaviour. Depending on the setting of the study, a long-term return can be encouraging participants to grow produce at home, thereby increasing green areas and increasing self-sustaining households.

The benefit of CS programs in crop health has been established regarding potato diseases (122) and identifying main threats of maize and soybean in the Amazon region (123). Additionally, data collected by a relatively small number of expert citizens has been demonstrated to be highly accurate (124), which makes CS programs very promising for implementing the DAMA protocol.

Conclusions

The EID crisis represents one of the largest threats to modern lifestyle, endangering human health, food security, economic and societal systems. Isolated institutions dealing with various manifestations of EIDs have thus far been unsuccessful in stopping the wave of newly emergent pathogens. The SP provides a comprehensive evolutionary framework, which replaces current, false characterization of EIDs with clear predictions. The DAMA protocol provides a general step-by-step plan for constructing preventive interventions targeting emergent pathogens before the onset of an outbreak. This paper focuses on the final step of implementing evolutionary theory into preventive policies considering scales and policy environments.

Global, regional and local scales require precise conceptualization and the introduction of adequate transdisciplinary methods to gather all relevant knowledge and expertise, and create feasible, cost-efficient intervention plans. Global integration of the DAMA protocol into existing frameworks is crucial to provide useful guidelines to regional and national institutions; this is described in the Prevent-Prepare-Palliate (3P) framework. Regional scales addressing EID threats are to introduce the widely tested approach of Living Labs, which can be seen as multi-actor platforms delivering solutions co-created by various stakeholders. Their application to infectious disease threats will be a unique contribution which has significant potential of dealing with diverging interests. Finally, local scales would benefit from a wide-range of Community Science initiatives targeting affected populations directly and the assistance of local experts on various host-pathogen systems. Although each method is most suitable for their particular scale, it is crucial that all of them operate in close collaboration with each other, circulating knowledge from the grassroots towards institutions. The key to disease prevention is ongoing monitoring that engages local experts, citizens, as well as relevant decision-makers in bidirectional communication.

Another important step towards more effectively controlling the EID crisis is eliminating the barriers among human health care, wildlife health care, livestock health care and crop health care. The current lack of a unifying scientific understanding of health issues results in divergent policies providing palliative and perhaps preparatory solutions, none of which is efficient or sustainable in the face of accelerating EIDs. By understanding the common underlying evolutionary drivers, predictions can be adjusted appropriately across the board for human, livestock and crop diseases, and prevention can be implemented onto existing infrastructures and legal environments.

Our advancements in technology have brought with them novel threats in the shape of EIDs. Climate change and globalisation have changed the evolutionary trajectory of diseases as we know them, it is therefore

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inevitable to change our approach to global health security and shift our focus from reactive approaches to those moving up the infection timeline towards prevention.

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contributions

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