WAGENINGEN
UNIVERSITY & RESEARCH

Early Recognition and Rapid Action in Zoonotic Emergencies

A framework document for the proposed contribution of Wageningen University & Research to a global response for Early Recognition and Rapid Action in Zoonotic Emergencies

ERRAZE@WUR | December 2020

CONTENTS

Preface

Major global challenges crossing the borders of nations and sectors provide increasing evidence of the failure of current development trajectories to deliver across the full spectrum of economic growth, social inclusion and environmental sustainability objectives. Nowhere are these questions more pressing than in the agri-food sector. Food security, human nutrition and health, the livelihoods of rural communities, responses to climate change and economic growth are all intimately connected to the sector. Wageningen University & Research (WUR) provides high quality knowledge, education and research to inform and support transition pathways addressing these global challenges and to accelerate the necessary transformations. We cannot do this alone. Achieving sustainable transitions towards a safe and secure agri-food sector requires effective partnerships. Current and new, national and international.

2020 saw the world struggle with the global COVID-19 pandemic. WUR is uniquely positioned to further the scientific knowledge base required for pandemic crisis management to prevent future pandemics from reaching such devastating impact, and considers delivering on this an inextricable part of its thought leadership role and its social responsibility. This framework document sets out how WUR takes on the challenge to contribute to the generation of timely insights into the possible scenarios for pandemic crisis management, enabling informed decision making to prevent pandemics, and to respond during and after zoonotic emergencies. WUR will contribute to a better understanding of the mechanisms of spillover events, as well as to delivering practical tools to help reduce the chance of pathogen emergence and spread, and mitigate the impacts of future pandemics.

Executive summary

Background

The ongoing COVID-19 pandemic and resulting health and economic crisis has caused major disruptions in the functioning of food systems and revived the discussion on what forms balanced, effective and responsible crisis management.

As part of its thought leadership and its social responsibility in times of crisis, WUR is uniquely placed to contribute to the scientific knowledge base and data collection mechanisms required for early recognition and rapid response. In addition, WUR takes on the challenge to generate timely insights into the possible scenarios for the prevention of a crisis and during and after emergencies to enable our clients and stakeholders to make informed decisions. Lastly, WUR can provide a better understanding of the mechanisms of spillover, and tangible and practical tools to help reduce the risk of spillover events from occurring, prevent pathogen spread, or mitigate the impacts of a future pandemic.

In its research institutes and university, WUR brings together expertise in human, animal, plant and environmental health, the global agri-food system, economics, social sciences, food safety and security, ethics, and policy. Here, in the knowledge that COVID-19 will not be the last pandemic, we present WUR's ambition and capabilities towards an integrated global multi-stakeholder approach to the prevention and management of potentially pandemic diseases, across the four phases of crisis management; prevention, preparedness, response, and recovery and learning.

Pandemic prevention

Agri-food systems form a significant part of the rapidly growing and changing interface between humans, the environment, wildlife and livestock. To reduce the chance of future spillover events occurring, WUR can leverage its knowledge and understanding of the global agri-food system, (wildlife) ecosystems, environmental resilience, human behavioural systems, and pathogens. Understanding the mechanisms underpinning the chain of events and the contributing factors to emergent pathogens, allows for the smart (re-) design of agri-food systems and consumer/producer behaviour, for the creation of sustainable interventions, and the fostering of biodiverse and healthy ecosystems, that reduce the likelihood of pathogen spillover and spread.

To create sustainable preventive interventions, WUR will leverage its global partner networks to work in a broad national and international multi-stakeholder alliance, to:

- Develop maps with high-risk areas for pathogen (re-)emergence (hotspots). WUR will draw on its understanding of both the potential pathogen pool as well as relevant socio-economic factors, and build algorithms that enable the integrated analysis of wildlife distribution data, human and livestock densities, recent changeovers from natural areas to agricultural use, trade and other agri-food characteristics. New knowledge will be shared with policy makers, to underpin effective interventions that give account to cultural, social, economic, legal and policy aspects.
- Further develop and describe evidence-based sustainable preventive interventions to the agri-food system to reduce the likelihood of occurrence of emerging zoonoses and/or to mitigate the effects of zoonoses.
- Develop system models, linked to the risk maps, to simulate the effect of preventive measures in combination with human behaviour including compliance and economic impacts, to support decision making regarding the intensity of preventive measures based upon a cost-effectivity frontier.
- Continue to develop and use tools to identify stressors to the natural ecosystem and its species that could enhance pathogen shedding by reservoir hosts and similarly identify prerequisites for a healthy and resilient system. Understanding mechanisms that contribute to enhanced shedding can inform our wildlife management partners in reducing the impact and occurrence of such stressors.

Pandemic preparedness

Several ‘peace time’ actions can underpin pandemic preparedness. These include a range of activities that WUR contributes to, including surveillance to enable early warning, rapid characterisation of novel pathogens, developing plug-and-play vaccines and therapeutics, and developing contingency plans.

WUR works across scales, from detailed knowledge of pathogen genomes and traits, to global assessments of potential shocks to the agri-food system, and back to the impact of such shocks on individuals. Leveraging the vast amounts of available data, its deep understanding of zoonotic pathogens, its experience with developing diagnostic tools and vaccine platforms, and food-based immune-modulating therapeutics, and providing science-based policy advice, WUR will:

- Further develop tools and methodologies for full characterisation of new and emerging pathogens, including pathogenic and clinical manifestations, range of susceptible hosts and potential reservoirs, and risk of interspecies transmission.
- Further develop its data analysis algorithms and tools, that allow for the integrated assessment of in silico surveillance of data, that is directly related to pathogens with pandemic potential, but also of non-traditional data such as trend data, web-scrubbing data, and eDNA.
- Use this in silico surveillance to move to smarter monitoring and sampling in field studies, including using eDNA for the identification of potential equilibrium shifts signalling potential emergence of pathogens.

- Continue the development of the required diagnostic technologies to enable catch-all surveillance and monitoring, including on site rapid and broad tests.
- Continue the development of several vaccine platforms, and extend its pipeline partnerships towards at-scale production and (pre-)clinical data-packages.
- Develop and extend knowledge of natural immune-modulatory dietary components, that may enhance vaccination responses, prevent infection (severity), or provide passive immunity in humans and livestock.
- Develop an epidemiological and economic modelling platform to evaluate the impact of different control strategies, and to improve efficacy of control by increasing insights into human behaviour (incentives, information).
- Strengthen its implementation of FAIR data management, and the underpinning data infrastructure.

Pandemic response management

Global efforts to reduce the impacts of emerging diseases are currently largely focused on post-emergence outbreak control. Successful outbreak control hinges on several key tools, which include testing, tracing, biosecurity, drug and vaccine availability, intervention strategies, control measures and tailored risk communication. WUR can provide significant inputs to strengthen several of these tools, and will:

- Further develop agile, appropriate and scalable diagnostic and data collection tools, including infectivity assays, utilising its vast experience and detailed understanding of plant, animal, and food-related pathogens, as well as infectious disease transmission dynamics.
- Develop new scenarios for biosecurity in varying global locations, across the global food system and models to underpin and evaluate their efficacy and cost-benefit impacts.
- Continue its contribution to the development of contingency plans that underpin crisis preparedness and effectivity, drawing on knowledge of effective communication, policy and institutional change, integrated epidemiological and socio-economic models, and the impact of, and options to guide and shape, human behaviour in crises.

Recovery and learnings from pandemics

Economic shocks resulting from outbreaks and pandemics occur in both high, middle and low income countries, but the burden is not evenly distributed within populations; people with a lower socio-economic status are observed to be affected most. WUR is able to rapidly assess the consequences of a crisis like the COVID-19 pandemic on local and global agri-food systems. Both for the short, medium and long term WUR has the tools for loss assessment and scenario analyses. Drawing on a systems approach to the agri-food system, knowledge of the existing internal feedback mechanisms and external spillover effects, WUR will:

- Capture changes in both producer and consumer behaviour, the simultaneous adjustments in markets and institutions, and the heterogeneous responses to policy incentives to generating agri-food system transitions.
- Inform policy and institutional change towards recovery by use of sophisticated models for scenario analyses.
- Develop insights and tools that help combine data-based evidence with expertise-based evidence to address the growing demand for integrated policy, systems, and strategy analyses.
- Ensure that appropriate pandemic crisis feedback and learning mechanisms are completed, improving future pandemic prevention, preparedness and response.
- Contribute to resilient agri-food systems.

Introduction

The ongoing COVID-19 pandemic and resulting health and economic crisis has caused major disruptions in the functioning of food systems and revived many discussions on pandemic crisis management. It is universally recognised that elements of prevention, preparedness and response are open to significant improvement, but it has proven difficult to generate investments in pandemic preparedness during 'peace time', when there was no immediate crisis. The 2020 COVID-19 crisis made it abundantly clear that the size of the investments that would have helped to prevent or enabled a more agile and effective response are eclipsed many times over by the costs of the global health and socio-economic crises resulting from the pandemic.

In its research institutes and university, WUR brings together expertise in human, animal, plant and environmental health, the global agri-food system, ecology, epidemiological modelling, economics, social sciences, food safety and security, ethics, and policy. We will continue to invest in a systematic and integrated One Health approach to the prevention and management of potentially pandemic diseases. By putting the full force of the transdisciplinary WUR approach behind this challenge, we are able to make a considerable contribution to the prevention or mitigation of future pandemics. We will focus on infectious diseases with pandemic potential, whether new or re-emerging. We will propose solutions that solve contributing weaknesses in the agri-food system, and implement adaptations to optimise surveillance and biosecurity. Such transformation of production and consumption systems is identified in the United Nations (UN) 2030 Agenda for Sustainable Development, which details the 17 Sustainable Development Goals, as the pathway to achieving its ambitious targets.

In the knowledge that COVID-19 will not be the last pandemic, we present WUR's ambition and capabilities towards a systemic and integrated global multi-stakeholder approach to the prevention and management of potentially pandemic diseases, across the four phases of crisis management: prevention, preparedness, response, and recovery and learning.

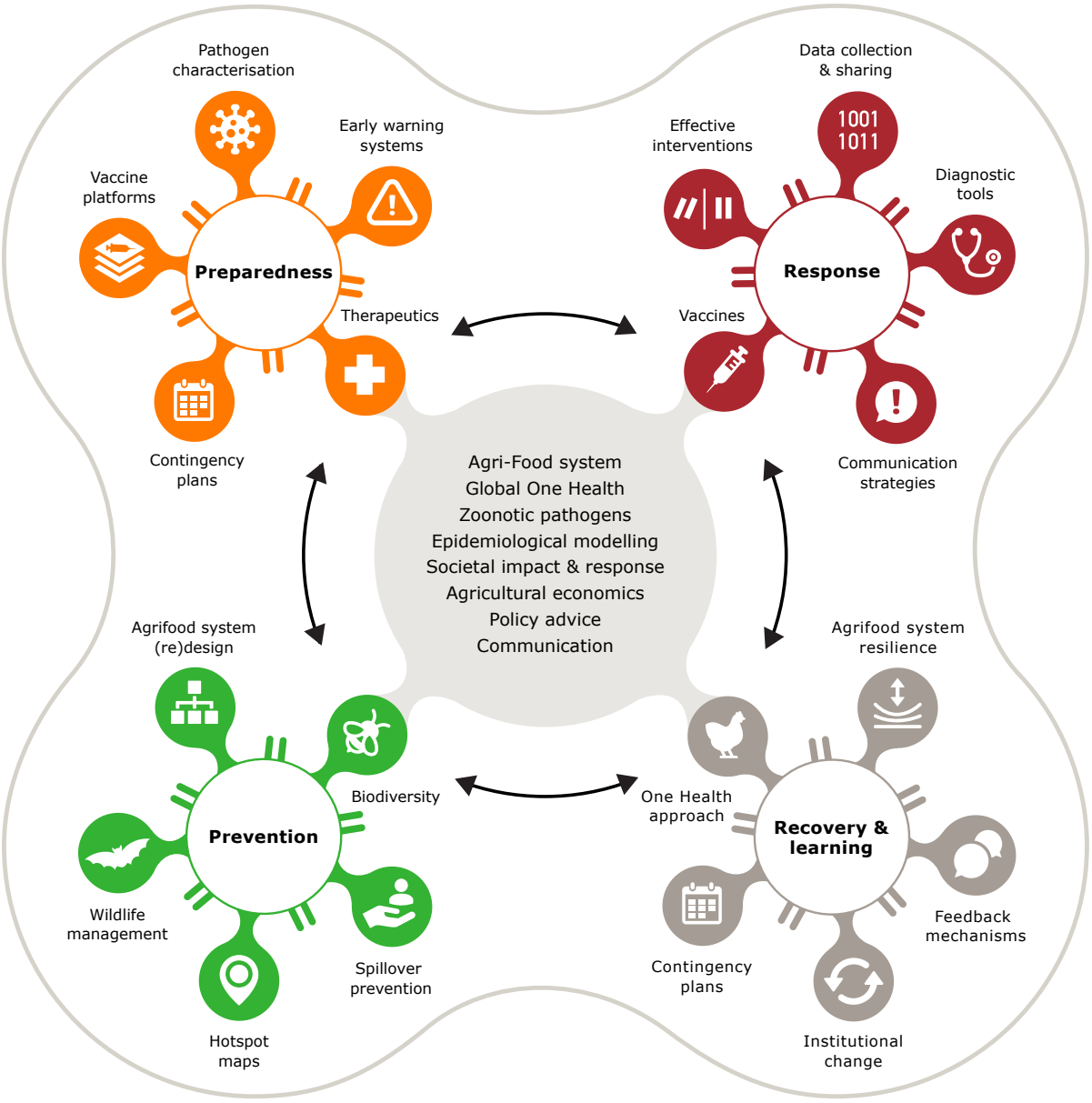
We emphasise the importance of development of agile tools for optimised surveillance, early warning, and rapid characterisation of zoonotic pathogens, vaccine and therapeutics toolboxes, and the development of new scientific insights across all WUR disciplines to underpin informed and science-based policy decisions. For all these aspects, WUR will leverage, strengthen and grow its existing network of national and international partners and stakeholders.

Outside the direct scope of the currently proposed programme, although their relevance to pandemic crisis management is recognised, are subjects like population health and nutrition and their impact on susceptibility to (severe) disease, or the risks and risk modifiers associated with the food system transition to circularity. Strong expertise on these topics exists at WUR, which will be consulted if required.

About this framework document

A crisis occurs when a system is unable to deal with a disturbance and can be characterised as transition phases during which the normal ways of operation no longer work. All crises feature severe threat, urgency, and uncertainty. But each new crisis is likely different from all previous ones. Therefore, understanding and responding to crises and their consequences will remain a recurring challenge in our society and in our research.

Early Recognition and Rapid Action in Zoonotic Emergencies



In the centre of this infographic that represents the ERRAZE@WUR programme sit the key capabilities that WUR brings to the cycle of Pandemic Crisis Management. Around the four phases of crisis management, some of the planned key outputs are depicted.

The scale and complexity of a pandemic crisis requires a systems approach, as well as a global and transdisciplinary collaboration to ensure optimal impact and results. In this document, the different aspects of preventing and managing a pandemic are discussed in the framework of the crisis prevention and management cycle. This cyclical process comprises four phases: i) the prevention phase; ii) the preparation phase; iii) the response phase, and; iv) the recovery and learning phase. These phases are all interlinked, and strongly interdependent, and illustrated along with WUR's foreseen contributions in the figure. There will be continuous evaluation and incorporation of lessons learned that subsequently feed backwards, forwards and across this cycle.

Pandemic prevention

At the basis of an outbreak, an epidemic or pandemic, lies the emergence of a pathogen to which no, or limited, immunity exists in a population, and that can then spread through the population. It is estimated that about 60% of new emerging infectious diseases in humans are zoonotic, and about 70% of those find their origin in wild animal reservoirs. The moment or event when a pathogen jumps from its existing reservoir population into a new host species is defined as a spillover event.

Spillover events are more likely to occur where and when humans or domestic animals are in frequent contact with wildlife hosts, through for example the encroachment of humans with livestock in natural areas (e.g. deforestation areas), through hunting and trade of wildlife (e.g. in wet markets) or along bird migration routes. The global agri-food system forms a significant part of this spillover interface.

WUR brings all the required expertise to the table to design sustainable and cost-effective interventions to the agri-food system that will reduce the chance of future pathogen emergence; a deep understanding of this global agri-food system, and expertise on zoonotic pathogens and animal health, wildlife and ecosystems, the mapping and risk assessments of spillover hotspots, environmental resilience, human behaviour, and transmission dynamics of pathogens.

The interfaces between wildlife, domestic animals and livestock, and humans are changing continuously due to human encroachment in natural areas. In addition, stressors on natural ecosystems are thought to affect pathogen shedding patterns by wildlife species, possibly lowering the threshold for spillover. Whilst food production in the last decades of the 20th century was characterised by significant productivity increases, this increase in yield per hectare is starting to plateau in most regions of the world. To continue to meet the growing demand for food and biofuel, further acreage expansion by conversion of natural habitats to agricultural lands is expected in a number of regions of the world, thus continuing the trend of the increasing likelihood of spillover events.

Additional factors like climate change, and the changing distributions and densities of arthropod vectors, provide further urgency to the need to develop and implement sustainable interventions to mitigate pathogen spillover and spread.

At WUR an agri-food systems perspective has been advocated to create a climate smart and environmentally sustainable agri-food economy, empowering communities to create a healthy food environment (Kampers, 2017). With an eye on pandemic prevention, considerations for a safer agri-food system are integral to this perspective, and WUR is exploring what changes can help to sustainably reduce the chance of spillover.

Smart agri-food system re-design for pandemic prevention

The introduction and further transmission of zoonotic pathogens in a previously unaffected areas depend on several factors, including travel of persons, trade of goods, transport of animals and animal products, biosecurity standards implemented by surveillance agencies and livestock producers, and lifestyle, culture and tradition. In this cascade there are numerous entry points for making changes to reduce the chance of

spillover occurring. As part of a broad national and international multi-stakeholder alliance, for which WUR will leverage its existing global partner networks, WUR will:

- Develop maps with high-risk areas for pathogen (re-)emergence (hotspots). WUR will draw on its understanding of both the potential pathogen pool as well as relevant socio-economic factors, and build algorithms that enable the integrated analysis of wildlife distribution data, human and livestock densities, recent changeovers from natural areas to agricultural use, trade and other agri-food characteristics. Various factors underlying spillover hotspots should be better understood, such as the risks brought by habitat destruction, hunting, poorly regulated transport, trade and wet market operations, wildlife foraging or other wildlife interfaces in close proximity to people. Using knowledge of these hotspots, pathogen surveillance by global partners can be targeted more efficiently, and subsequently analysed in collaborative and integrated data analysis programmes. New knowledge will be shared with policy makers, to underpin effective interventions that give account to cultural, social, economic, legal and policy aspects.
- Further develop and describe evidence-based sustainable preventive interventions to the agri-food system to reduce the likelihood of occurrence of emerging zoonoses and/or to mitigate the effects of zoonoses. Examples of preventive interventions include transport restrictions, the vaccination of urban wildlife and/or companion/farm animals, and application of diagnostics in the food value-chain.
- Develop system models, linked to the risk maps, to simulate the effect of preventive measures in combination with human behaviour including compliance and economic impacts, to support decision making regarding the intensity of preventive measures based upon a cost-effectivity frontier.
- Continue to develop and use tools to identify stressors to the natural ecosystem and its species that could enhance pathogen shedding by reservoir hosts and similarly identify prerequisites for a healthy and resilient system. Understanding mechanisms that contribute to enhanced shedding can inform our wildlife management partners in reducing the impact and occurrence of such stressors.

Pandemic preparedness

Preparedness requires ongoing efforts during 'peace time', to many of which WUR already actively contributes, for example through the statutory monitoring tasks that we perform on behalf of national and international authorities. The impact of these efforts can be improved by strengthening the global surveillance infrastructure and its use that enables early warning, the creation of mitigation plans through e.g. controlling travel, trade and transport, social distancing, livestock and urban fauna clearance, and having plug-and-play vaccine technologies and therapeutics.

Early warning
Early warning comprises a multitiered surveillance system, developed to detect disturbances. Key elements are, for example, practical tools to perform risk-based targeted sampling, rapid sample analysis, and large scale data collection and analyses. We propose the information derived from these elements is analysed in an integrated approach. To inform the smart targeting of cost-effective sampling efforts, which will be undertaken in collaboration with partners of WUR, we can build on the work on hotspot mapping described in 4.1.

For rapid sample analysis, that underpins both the preparedness – early warning – phase, as well as the response phase, diagnostic tools and sample analysis workflows are required. The analytical tools that are deployed for the early warning phase should be able to detect both known and as yet unknown pathogens, but nonetheless build on a general understanding of potential zoonotic pathogens and diagnostics. In 4.3, in the context of the response phase, a more in-depth discussion of WUR's experience in the development of diagnostics is presented. Notably, the agri-food system is vulnerable not only as the wildlife interface where spillovers are likely to occur, but also as a transport vehicle for pathogens that can survive on surfaces for an extended period and which can be spread with food or food packaging and can infect the host via the consumption of food or feed.

Data collection and analysis has traditionally been guided by research-based data and data from entities with surveillance mandates (e.g., WHO, OIE, national bodies, including WUR itself). In the past decade, this has been expanded to include non-traditional information, like Google trend data, crowd-sourced data and technology derived data for example from automated sensor systems. Specifically, WUR has access to, and deep understanding of, information about local and global food value chains, that comprise indicators for early detection of disturbances to the system.

Access to reliable historic, current and real-time data is essential for hazard identification, early detection, rapid characterisation and contingency planning. However, data collected for risk assessments are often separated by application field; real-time and current data are frequently poorly documented, difficult to find, and accessible only after complicated and time-consuming procedures. Unlocking information from different data streams is typically hampered by data quality issues and comparability challenges.

To strengthen the global early warning pipeline, WUR will:

- Take an integrated approach to data analyses. Algorithms will be built that enable the interconnected analysis of historic and current traditional pathogen surveillance data, and non-traditional data from along the agri-food value chain, for the earliest possible detection of the emergence of novel pathogens.

Where needed a framework for the sharing, and the use of both traditional and non-traditional data will be developed and implemented.

- Take an integrated approach to the understanding of the impact of human behaviour on the effectivity of surveillance systems. A framework will be created where the various components of early warning can be synthesised and integrated with knowledge on the effect of human behaviour on surveillance, and epidemiological and economic modelling. This framework can be used as a basis to simulate surveillance systems with increasing intensity in order to provide a cost-effectiveness frontier.
- Leverage the new knowledge of spillover hotspots from 4.1, to help target our partners' active surveillance efforts, as well as assessment of wildlife health and vector diversity in locations where spillover events are more likely to occur. Here WUR can build on its long-standing participation in monitoring programmes and field studies that yield a wide range of samples and associated data from wildlife, environmental, food and plant matrices. This will likely involve among other things creating affordable protocols for monitoring zoonotic safety:
  - At places of trade including at wet markets
  - In water and sewage systems, in collaboration with parties who have a shared interest in this (including national public health institutes and national water boards)
  - In aircraft air filters and wastewater tanks
  - In wildlife, environmental and food production hot spots, including surface water from wildlife foraging sites.
- Build on a previously developed genome analysis workflow for samples with a very low expected abundancy of zoonotic pathogens. The metagenome pipeline can be applied to a wider range of samples from ongoing monitoring programmes, testing it for several virus families, representing viruses known to cause respiratory and gastro-intestinal infections and whose appearance and spread is intimately associated with the food chain, as well as for emerging vector-borne viruses that are transmitted by blood sucking arthropods such as mosquitoes, biting midges and ticks. The availability of a unified protocol which is shared and supported by multiple WUR labs, and collaborator labs will yield homogeneous datasets allowing for cross comparisons of detailed virus transmission networks.
- Take a new approach to assessing genetic information contained in samples from long-standing monitoring and new surveillance efforts. If there is no pre-existing knowledge of a novel pathogen, detection can be challenging. The sequencing data obtained from samples from hotspots can be used to determine virome or microbiome shifts. Analysis of eDNA which comprises information on non-pathogenic microbe populations in a sample, may reveal a signal of equilibrium shifts caused by the presence of unknown pathogenic species, making the non-pathogenic microbes into sentinels.
- Refine the existing methods for fast and large scale tracing of pathogens through the agri-food chain, in combination with the development of new pathogen transmission models that connect the tracing and infectivity data to the design of the agri-food system. Tracking and tracing methods are in place for most foodborne pathogens, but operation is lab-bound and generally has a turnaround time of at least several hours. The character of the food supply chain, with intensive human-food contact early in the supply chain, large volume logistics, short shelf-life of the product and the non-negotiable need to maintain an uninterrupted supply, requires globally harmonised methods for sampling and sensitive, easily operable and low-cost detection methods for measuring the presence and infectivity of pathogens on food and food packaging. An integrated system for tracing, testing and intervention measures will limit disruption to the food chain, prevent food loss and diminish the negative impact on the livelihood of thousands of farmers and small companies.
- Develop and maintain the infrastructure to store and provide access to samples and data collected for, and gained from historic, current and future surveillance activities. WUR will provide fast and reliable access to data by implementing a data infrastructure based on FAIR principles: Findable, Accessible, Reusable, and Interoperable.

Rapid characterisation of novel pathogens

For many pathogen focused elements of the response phase, such as the development of specific diagnostic tools, vaccines and therapeutics, knowledge of the new pathogen is critical. Hence, during the preparedness stage, workflows will be established and tested that enable rapid characterisation and understanding of the most relevant traits of a novel pathogen. Continuing its close collaboration with global organisations and networks like the WHO, OIE, Epizone, EcoHealth Alliance, the Global Virome Project, and nationally the One Health Pact, which is part of the Netherlands Centre for One Health, WUR will:

- Build a workflow to rapidly characterise newly emerging (potentially zoonotic) pathogens for their clinical relevance, epidemiological traits and host range. In connection with this it is also important to identify additional (potential) reservoir species. Such research includes an outlook towards the further development and implementation of in vitro and ex vivo systems, complex cell systems and animal models.
- Establish a knowledge base to evaluate the pandemic potential of predicted or observed mutations. Artificial intelligence methodologies will be applied to synthesise data and feed risk models. Combining metagenomic and epidemiological (risk) models will allow the ranking of different pathogens based on the predicted epidemic risk. It will also allow scenario simulation to investigate the impact of mitigation actions. The in silico findings can be verified in in vivo or ex vivo models.
- Study both the change in transmission between species, whether or not involving humans, and within the species, by using a risk-based approach to improve the sensitivity for early detection of cross-species virus transmission and to inform mathematical models evaluating pathogen dynamics. Often a spillover event is followed by further species jumps, which implies a risk to humans as seen with BSE, Influenza, SARS and Ebola. As described above for mutation assessments, artificial intelligence methodologies will be applied. The models developed will be integrated into the centralised big data infrastructure. Due to the large amount of data and the requirement of online analysis, a high-performance computer facility compliant with the GO FAIR principles is essential.

Vaccine platforms and therapeutics

The fact that COVID-19 vaccines have reached the market within a year is astounding. Yet ideally these timelines are reduced even further to halt an outbreak before it gains pandemic potential. Proven and safe vaccine platform technologies, allowing plug-and-play with antigens of choice, are a promising avenue for accomplishing this goal. Several platform technologies have come to fruition in 2020, with both protein-, viral-vector and mRNA-based vaccines as a promising strategic choice for pandemic preparedness.

WUR has extensive experience with plug-and-play vaccine platforms for vaccination of animals and humans. This includes protein-based vaccine production using the baculovirus-insect cell expression system that is well known from commercially available vaccines. In addition, WUR spinoff BunyaVax utilises proprietary technology to develop live attenuated vaccines for bunyaviruses that optimally combine efficacy with safety.

Although vaccination remains the most efficient approach to controlling viral infections in the global population, in the absence of efficient vaccines at the immediate start of an outbreak, treatment and prevention options can be limited. Strengthening antiviral immunity through immunomodulatory nutritional approaches may thus be an important tool in preventing or reducing the clinical severity of infections or to improve the efficacy of vaccination strategies. In addition, further development of specific food components such as milk proteins and complex oligosaccharides might also contribute to enhancing immune responses to viral infection or immunisation, or provide passive immunity before vaccines become available.

To develop these technologies further, WUR will:

- Expand the agility and efficacy of the existing vaccine platforms. WUR spinoff BunyaVax and WUR, with funding from CEPI, are currently developing a Rift Valley fever virus vaccine, using the attenuated bunyavirus platform. In addition, WUR currently develops a SARS-CoV-2 nanoparticle vaccine using baculovirus-insect cell technology (H2020 Prevent-nCoV project) and improves the platform by reducing baculovirus particles prior to downstream processing of the product.
- Start the development of novel mRNA and self-replicating mRNA (‘replicon’) vaccine platforms, which induce strong protective immune responses. These plug-and-play platforms are safe-by-design and provide a rapid response during disease outbreaks. WUR develops replicon vaccines against poultry disease with industrial partners and studies the environmental safety of replicons to streamline (generic) risk assessment and speed up market authorisation.
- Further strengthen the capabilities on offer to test vaccine efficacy in pre-clinical models, in collaboration with CEPI, medial research centres and private industry, as required and desired.

- Explore the safety of nutritional bovine antibody therapy for human and animal use, and investigate possible administration routes thoroughly.
- Continue work on healthy nutrition to contribute to prevention and recovery of infectious diseases.

Contingency planning for policy and societal intervention measures

For outbreak mitigation, authorities must be prepared in advance for how to implement and communicate travel, trade and transport control, social distancing, livestock and urban fauna clearance, and vaccination of livestock if available and appropriate. WUR has experience and expertise in providing science-based policy advice to national and international governments and will:

- Develop an epidemiological and economic modelling platform to evaluate the impact of different control strategies.
- Continue research on insights into human behaviour to ensure better compliance of stakeholders related to monitoring and control, both in the preparedness phase as well as during an outbreak (incentives, information). For example, willingness of farmers and other animal owners to monitor and report disease problems amongst their animals.

Pandemic response management

Global efforts to reduce the impacts of emerging diseases are currently largely focused on post-emergence outbreak control. Successful outbreak control hinges on several key tools, which include testing, tracing, biosecurity, drug and vaccine availability, intervention strategies, control measures as well as tailored risk communication.

Diagnostic tools
"Testing, testing, testing" was the mantra of the WHO from the early days of the pandemic. Who is tested, and who is not, greatly determines the inferences that can be made based on test results. Widely available, fast, appropriate and reliable diagnostics are vital in limiting personal and economic damage inflicted by new pathogens. Rapid and cheap tests would enable informed population or target group-level decision-making by governments, industries, and businesses. Highly accurate tests are needed for appropriate treatment of individual patients, and decision making on an individual level. Much remains to be gained in response time, rate of upscaling in diagnostic testing, unifying test formats, developing faster and for some uses more sensitive formats that can detect a range of food, animal and human pathogens for a range of users and test systems that discriminate between infectious and non-infectious (debris of) agents.

WUR has a track record in developing new diagnostics formats for plant, animal and human pathogens associated with food production, and animal disease with a zoonotic potential. As an example of a recent development, WUR, together with start-up Scope Biosciences, has developed proprietary CRISPR-Cas technology for fast and easy detection of any DNA or RNA target. Detection of SARS-CoV-2 in human samples, for example, was successfully set up within one week, enabling detection of a few copies of the genome in 30-40 minutes, making this test on par with, or better than current alternatives.
With respect to developing diagnostic tools (which are also required during the early warning phase, see 4.2) and the associated pipeline, WUR aims to:

- Develop diagnostic platforms for fast testing, applicable in a range of sample matrices. A plug-and-play platform for nucleic acid-based testing using the combination of isothermic LAMP amplification and subsequent CRISPR-Cas detection is agile and versatile, improving specificity and speed relative to detection platforms based on LAMP alone.
- Develop broad serological tests using synthetic peptide antigens, to detect infections with potentially zoonotic viruses both in animals (for the purpose of surveillance) and humans, to design and underpin the implementation of isolation measures. Depending on the scope of the assay and the demands of the end-user different formats will be developed (on-site, do-it-yourself, fast, sensitive, cheap or multiplex).
- Use bioinformatics for development and in silico validation of new zoonotic virus tests. In silico procedures will be developed to test the fit for purpose of broadly targeted, nucleic acid and protein-based diagnostics methods for new virus types. Such an in silico pipeline will provide a head start in the development of diagnostics for newly emerging viruses and allow fast revalidation of existing test concepts for new virus variants.
- Develop rapid infectivity assays for viruses, expanding the methods used for the recently developed plant virus infectivity assay, that combines DNA based and protein based detection, to human and veterinary

viruses. Such a test would allow for infectivity testing of viral materials on surfaces or in patient materials, and is expected to have great utility in determining the efficacy of decontaminating agents and antivirals. To put this in the context of the current pandemic, the test could be adjusted for use in ascertaining whether people recovered from SARS-CoV-2 symptoms, are still carrying infectious virus.

Roll-out of platform vaccines

Access to, and experience with, platform technologies for plug-and-play vaccines, with safety data packages available (see 4.2), puts WUR in a good position to use these platforms to rapidly develop vaccine candidates. Proven expertise is available to discover new vaccines, perform medium-size bioreactor scale up and develop downstream processing protocols. In order for these vaccine candidates to be quickly and effectively deployed, access to at-scale production and pre-clinical and clinical testing is needed. WUR itself does not have the capabilities for this, and therefore will:

- Continue to build its networks with organisations and consortia that may help facilitate access to funding, trials and GMP production facilities, as well as required assay development in as far this expertise is not available in house. These connections include the TRANSVAC consortium, ongoing strong collaborations with CEPI, QIMRB Australia for arbovirus vaccines (Chikungunya, Zika and Mayaro virus), University of Copenhagen (COVID-19 vaccine), MSD Animal Health (replicon vaccines).
- Work to establish and maintain relevant in vivo and ex vivo models for pre-clinical safety studies of vaccines, developed by others as well as by WUR itself.

Effective control measures, and communication

Although testing is important in creating insight into the onset and spread of a disease, the inferences made and the actions taken based on the results determine the outcome of the outbreak. A large number of different actors are involved in implementing measures, both in 'peace time' as well as during an outbreak. Therefore, the efficacy of mitigation measures is critically dependent on both the actions of organisations and individuals, as well as on the willingness of people to get tested, and adhere to the implemented measures. Because communication shapes the interpretation of the message around measures, both with policy makers and the public, it is a key dimension of outbreak response management. Established communication channels and strategies can reduce the length of time required to bring full resolution to a crisis situation. Predefined, modelled and well understood intervention measures are critical as long as therapeutics and vaccines are not available. Incentives, positive as well as negative, will be needed to ensure that stakeholders adopt the desired behaviour.

When the implementation of control measures is likely to have a large socio-economic impact, they might need to be combined with (economic) support measures to limit the consequences of most affected stakeholders and ensure compliance with the control measures.

Building on extensive experience in crisis communication, developing incentive schemes and evaluating the efficacy of intervention measures, and evaluating the socio-economic impact of a crisis, WUR will:

- Inform governments and policy makers on developing effective crisis communication and incentives tools and pathways, aimed to inform and modify the behaviour of producers and consumers.
- Develop up-to-date epidemiological and socio-economic models to be used during an outbreak to monitor the effect of control strategies and to predict the outcomes of alternative scenarios.
- Show, by epidemiological and simulation modelling, the effect of various response activities consisting of the application of diagnostic tools, implementation of (financial) incentives, communication on the development and possible outcomes of the outbreak with an explicit role for human behaviour.
- Develop models to get real time insight into the economic consequences of a crisis and the effect of support measures.

Recovery and learnings from pandemics

Outbreaks and pandemics do not only cause public health crises, but also form shocks to economies and food systems. These shocks occur in high, middle and low income countries alike, but the burden is not evenly distributed within populations. It is commonly observed that people with low socio-economic status are affected disproportionately. For instance, recent assessments of the impacts of COVID-19 by WUR clearly indicate profound effects on the income and nutritious status of low-income groups in several sub-Sahara African countries (Unique country assessments show direct effects COVID-19 crisis on food systems, 2020) (WUR Rapid Appraisal Covid19 Food systems, 2020). Failures to adequately respond to shocks can be attributed to a (lack of) response capacity by policy makers at food system level, or to vulnerabilities at lower levels of aggregation, such as small- and medium sized enterprises, stakeholder organisations or at individual levels due to e.g. social disaggregation and gender inequalities.

If public interventions by policy makers are limited in their efficacy, this is typically due to one of two constraints: i) lack of understanding of the behaviour itself and the underlying drivers and motives of stakeholders in food systems, or ii) limited insights in feed-back loops, stakeholder interactions and trade-offs in the food system. Better understanding of food systems' performance may enhance prospects for supporting food system transformations. These aforementioned constraints are caused by methodological problems related to the interdisciplinary nature of the resilience challenges at hand. A consequence is that national governments haven't developed integrated food policies that unify the interests of ministries of public health, economic development, social affairs, environment and agriculture.

During a crisis and in its aftermath, a thorough monitoring and evaluation of the crisis and the response is of pivotal importance. The outcome of this evaluation does not only consist of lessons learned regarding the actions performed but should also address fundamental questions on the resilience of the current ecosystem, economy and food system to effectively cope with a major crisis. Moreover, contingency plans and the simulation models used to test contingency plans should be evaluated and validated using data from past crises, in order to improve the models that we are using and have better preparedness for the next crisis. With the adagio "never waste a good crisis" in mind, we find ourselves on a crossroads. We can keep the current system, but fundamentally strengthen our preparedness, including the actions outlined in 4.2. Or, in addition to being better prepared, we rethink the set-up of parts of the agri-food system, as outlined in 4.1.

Food system resilience
Because WUR houses all different expertise areas required for this work, it is able to rapidly assess the consequences of a crisis like COVID-19 for agriculture. Here, we intend to focus on evaluations and learnings, taking into account all aspects of food systems and their challenges from an interdisciplinary perspective. During the recovery phase of a crisis, frequently the focus is on a quick return to normal. Given our extensive and highly diverse track record on empirical, normative and applied interdisciplinary research on food system resilience, WUR has the tools for short and long term loss assessment and scenario analysis. Recently, upon the request by the Dutch Ministry of Foreign Affairs, WUR coordinated various working groups on COVID-19 and food system responses. A rapid assessment tool was developed and applied to provide immediate insights in the effects of COVID-19 on food systems, components and

stakeholders in various Sub-Saharan African countries (WUR Rapid Appraisal Covid19 Food systems, 2020).

Moreover, WUR has strong knowledge on human behaviour and communication as relevant to food production and consumption, and has initiated and led many projects on optimisation and preparedness of animal disease mitigation and eradication programmes.

To address knowledge gaps that currently hinder effective policy roll-out, WUR will work with national and international governments, multilateral agencies, NGO's and civil society, to:

- Capture changes in both producer and consumer behaviour, the simultaneous adjustments in markets and institutions, and the heterogeneous responses to policy incentives to generating agri-food system transitions.
- Develop and provide sophisticated models for scenario analyses to inform policy and institutional change towards recovery.

Contingency and preparedness plans

Contingency and preparedness plans are living documents, typically developed and maintained by national and international governments such as the European Commission and the UN, that support the coordination of rules and actions in both 'peace time' and during a health crisis. They aim to underpin decisiveness and the ability to respond effectively by having alternative plans, and contribute to preparedness. They provide guidelines at each value chain level on how to act in the event of a crisis. Besides specific actions to take and instruments to implement, they describe the chain of command. Although the moment, location and precise nature of outbreaks cannot be foreseen, these plans comprise detailed procedures on how to control outbreaks.

Most contingency plans are aimed at specific situations about which a relatively large amount of knowledge is available. These contingency plans, in general, are well developed and, if updated regularly, suitable to be used immediately. For less well known, emerging risks, knowledge is more generic and scenario-based and the uncertainties are much larger. Development of contingency plans is therefore much more complex and should consist of generic, format-based plans. Development of these types of plans is challenging and should focus on finding the right balance between intervening too early or unnecessarily, with high costs and inconvenience, or intervening too late, resulting in possible loss of human or animal health or lives. Especially for unknown risks, this balancing is important but difficult. Other aspects of contingency plans detail the level and intensity of the use of the tools in the toolbox (rules/regulations, diagnostics, movement restrictions etc.) where the costs (in more than only monetary terms) and effects should be weighed versus the risk of negative consequences of under-response. Human behaviour, i.e., compliance with rules, regulations and advice are important aspects in estimating the effect of interventions. Therefore communication aspects in order to increase and maintain social licence should be part of such contingency plans as well.

Typically, contingency plans cannot be tested in real life. We can learn from previous outbreaks and the current pandemic, and adjust plans accordingly. We should test novel plans in epidemiological simulations where various scenarios can be trialled. Depending on the type of crisis and the stakeholders involved, these types of simulations involve cost-effectiveness, cost-utility and cost-benefit analyses. The effect of communication activities should be included in this type of testing.

In collaboration with national and international policy makers and using key evidence, WUR will develop insights and tools that help combine data-based evidence with expertise-based evidence to address the growing demand for integrated policy, systems, and strategy analyses. These insights and tools will consist of:

- A flexible epidemiological and economic modelling platform that enables us to simulate outbreaks and control strategies of diseases both in livestock and wildlife.
- Insights in the cost-effectiveness frontier of various intensities of contingency plans and intervention moments.
- Insights into human behaviour in crisis situations that consists of an understanding of farmers' or producers' behaviours and consumer choices, the often unexpected and perverse responses to well-intended policy incentives, and the difficulties of implementing effective programmes.

- State of the art scientific knowledge combined with hands-on experience during crises.
- Ultimately this should result in a coherent WUR system analysis framework that can address strategic and tactical policy questions and guide integrated resource management covering topics that require integration across WUR domains.

A global collaborative effort

The above stated aims will be receiving substantial WUR investment in the coming three years. It is strongly recognised, however, that to tackle the global scale challenges outlined WUR will need to embed its work, and play different roles within the wider architecture of local, national and global partnerships, platforms and networks. Architectures linking local to global scales will be key to achieving impacts at scale. It is thus our explicit intention to engage relevant stakeholders in pandemic preparedness research and along the agri-food value chain throughout the process. In addition, we expect to leverage external funding to supplement WUR's investment where possible, to enable the establishment of an enduring research and outreach programme.

The programme as currently envisioned, delivers outcomes to a range of stakeholders, but will focus on WUR's role of a trusted advisor to inform and support policies and actions by the UN Tripartite Plus (OIE, FAO, WHO and UNEP), national and European governments and (inter-)governmental agencies including ECDC. Moreover, WUR will build and expand collaborations with alliances such as the Coalition for Epidemic Preparedness Innovations (CEPI) and the CGIAR. Specific results will be of interest to private parties including ones spanning the food production value chain, and animal health as well as pharmaceutical companies. Lastly, but importantly, WUR is proud to be part of an international network of excellent research providers. Our investments will enable furthering our participation and leading role in such partnerships as the One Health European Joint Programme (OH-EJP), the Global One Health Research Partnership (GOHRP), and networks including the MedVetNet Association, VetBioNet, TRANSVAC, and the Netherlands Centre for One Health (NCOH).

At the time of writing, WUR is actively strengthening its linkages with, or is lead partner in, international initiatives looking to tackle pandemic preparedness challenges. We are thus, actively involved in the co-design of a global network of organisations and relevant capacities that will allow us to contribute to the different impact domains through the delivery of cutting edge and relevant science – including the Franco-German proposed creation of a One Health High-level Expert Council.

Bibliography and further reading

All pages accessed last on 22 December 2020.

Bergevoet R.H.M. et al. (2019). Improving crisis prevention and management criteria and strategies in the agricultural sector: Final report EC. 182 p.

Kampers, F. W. H. and Fresco, L. O. (2017). Food transitions 2030: How to achieve the transitions to a sustainable, affordable, trustworthy and high-quality food system in the next decade or two that will fulfil the needs of a diverse and growing world population. Wageningen University & Research.

Sustainable food systems: Concept and framework. (2018). FAO.

Unique country assessments show direct effects COVID-19 crisis on food systems. (2020).

WUR Rapid Appraisal Covid19 Food systems. (2020).

WUR Strategic Plan 2019-2022 Finding Answers Together.

Joint Opinion, Independent Expert Report, European Commission. Improving pandemic preparedness and management. (2020)

Brief overview of the EU's investments in improving epidemiology, modelling and monitoring systems in response to infectious disease outbreaks: Preparedness and response to infectious disease outbreaks. (2020)

Taking a Multisectoral, One Health Approach: The UN's Tripartite Guide to Addressing Zoonotic Diseases in Countries. (2019)

The UN's Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity. (2010)

The UN's 2030 Agenda for Sustainable Development, that introduced the 17 Sustainable Development Goals. (2017)

On the FAIR Data Principles

This document is the result of the joint effort of researchers from various disciplines within Wageningen University & Research.

It has been prepared by:
Prof. Wim van der Poel, DVM
Andries Koops, PhD
Ron Bergevoet, PhD, DVM
Prof. Frank van Langevelde
Bieneke Bron, PhD, DVM
Peter Bonants, PhD
Joukje Siebenga, PhD
Ludo Hellebrekers, PhD, DVM
Jeroen Dijkman, PhD

With contributions from:
Prof. Henk Hogeveen
Prof. Gorben Pijlman
Willem Jan Knibbe, PhD
Jose L Gonzales, PhD
Prof. Joost van Neerven
Prof. Jeroen Kortekaas
Alex Bossers, PhD
Prof. Marcel Zwietering
Prof. Marcel Verweij
Bart de Steenhuijsen Piters, PhD
Prof. Marijn Poortvliet

Photography:
PTI (p1), Delmiro Junior / Shutterstock.com (p13), Alexandros Michailidis / Shutterstock.com (p4, 15), Anthony Mujica Viera / Shutterstock.com (p4), Salvacampillo / Shutterstock.com (p3), Shutterstock (p7, 9), Suteren / Shutterstock.com (p3)