



COVID-19 and lessons learned – Preparing for future pandemics

This paper has been drafted by a group of 12 mandated scientists from six large multidisciplinary Research Performing Organisations located in Europe, the Consiglio Nazionale delle Ricerche, the Centre National de la Recherche Scientifique, the Consejo Superior de Investigaciones Científicas, the Helmholtz-Gemeinschaft Deutscher Forschungszentren, the Leibniz-Gemeinschaft and the Max-Planck-Gesellschaft. Written under the impression of the current SARS-CoV-2 pandemic, it focuses on future pandemics similar in magnitude, the risk of spreading, and impact from a scientific perspective.

I. Introduction

The pandemic hit a world that was mentally and politically not prepared for this challenge. We thought that infectious diseases that had influenced people's lives for decades had been overcome. When a pandemic is on the horizon, a fast reaction is required. Various scenarios and simulations can and should be analyzed in advance and the global governance for a consistent and coordinated reaction needs to be re-considered. While mankind cannot take specific preventions for each and every possible infectious disease event, it can learn from this pandemic, as it provides illustrative material and empirical insights into the effects of political decisions taken. The scientific reappraisal will take years, even after the pandemic. However, the pandemic has demonstrated the importance of broadly applicable tools. We have started to recognize that the availability of a wealth of scientific and technological knowledge and of great economic potential and resources of the world society are quintessential to react successfully to challenges that cannot be planned or predicted in their specific form. The following chapters summarize some of the more specific, but still preliminary insights that can be drawn from the recent experience of the COVID-19 pandemics.

II. Striking the right balance between local and global intervention measures

(D. Corda, G. Maga, M. Meyer-Hermann, U. Protzer)

A critical element of coping with a developing pandemic is a rational and fast reaction. This reaction, however, must take economic and societal costs in the different parts of the world into account. Therefore, a coordinated international response is needed as soon as signs of a possible pandemic appear. In view of the subsequent costs in health, economy, and society, a rapid initial reaction preventing the worldwide spread of a pathogen is of the highest priority. At this point in time, it is critical to contain the infection to prevent a pandemic spread without cutting off parts of the world from support chains or harming human rights. At this very moment, nations must be prepared to support each other with know-how, experienced personnel, and essential goods. Once a full pandemic has developed, globally coordinated interventions are needed. As this development can be very rapid, different intervention plans of regional, national, European, and global scope need to be prepared and put in place to be rapidly activated and start appropriate measures when needed. At all stages, policymakers

must provide comprehensive information to the general public on the reasons, the goals and the criteria for measures to be taken as this is key for the compliance with and the success of such measures.

Improve knowledge on pathogens with pandemic potential

To prevent the development of a pandemic, pathogens with a pandemic potential need to be identified and monitored. This requires systematic detection systems on various levels. A pathogen with epidemic or pandemic potential will most likely be from those groups of viruses that are either transmitted via the respiratory tract or by insect vectors such as *influenza*, *corona*, or *flaviviruses* and reside in animal reservoirs. Thus, potential animal reservoirs, i.e. farm animals, bats or, wild animals humans are in contact with should be under systematic surveillance by health authorities. A focus should be on close relatives to known human pathogens because these have the highest probability to cross the species barrier with the potential to cause an epidemic. A basic characterization of these viruses by expert laboratories with the highest safety standards is highly recommended in order to better read the early signs of a newly emerging pathogen. Particularly important pathogens also include antibiotic-resistant bacteria which are principally able to colonize humans as well as animals. This know-how should be openly shared among the scientific community and health authorities worldwide.

Early detection must be coordinated on the European and international scale

Early detection of an outbreak and fast reactions to an evolving epidemic or pandemic can be substantially improved by developing an efficient communication structure among countries worldwide. Interdisciplinary expert groups across different countries in Europe and beyond should interact on a regular basis and exchange knowledge about potentially harmful viruses using the European Centre for Disease Prevention and Control (ECDC), the recently established European Health Emergency preparedness and Response Authority (HERA), and the World Health Organization (WHO) as communication structures. Based on experience from this and past pandemics, different means will be required to contain different pathogens most efficiently. To this end, different local, European and global action plans should be elaborated by and exchanged among interdisciplinary teams, and successful containment strategies should be adapted according to the pathogen in question. Here, it is of utmost importance to take potential economic and societal costs in the different parts of the world into account.

Coordinated European and international strategies to increase compliance with the measures

In the case of a developing pandemic, European and international coordination of measures to contain the spread of the pathogen is essential (Priesemann et al., The Lancet 2021 a.b.c). The challenge here is to adapt the communicated information to the correct scientific advance during the development of a pandemic and maintain compliance by all affected authorities, stakeholders, and the general public based on such information.

To reach this goal, a common European strategy effectively communicated through HERA as well as through the official channels of the national health ministries or public health institutions will be crucial. Such a strategy should be embedded in a global approach and requires close cooperation between the European Commission, HERA, and the WHO. It will increase the trust of the population in the corresponding measures and, also, provide the media with clear and correct information, amenable to being analyzed from different viewpoints. The state-of-the-art of knowledge, the uncertainty, the reasons for specific measures, and the overall strategy need to be communicated clearly.

Actions involved in reacting to a global pandemic

Dealing with the spreading of an infectious agent requires swift and coordinated actions, yet commensurate with the level of risk for the society posed by the emerging pathogen. Starting from the fundamental concept that in case of a large-scale pandemic a reduction of individual freedom is unavoidable, the scale of such reduction, i.e. the strength, timing, and quality of the countermeasures, all depend on the given epidemiological scenario. A pandemic preparedness plan should try to envisage the different scenarios and define what type of action might be appropriate, always keeping in mind that an epidemic is a dynamic process, thus often requiring to shift back and forth from a scenario to another.

A very general classification of epidemics, based on generally accepted risks assessment criteria (REF)¹ could be as follows:

Scenario	Pathogenic potential	Risk	Countermeasures	Comments
Level 1	Low infectivity and low morbidity	Very low	Monitoring. Diagnostic tools in place. Epidemiological surveillance.	Healthcare system not under pressure. No special measures needed
Level 2	Moderate or high infectivity and moderate morbidity and low lethality	Moderate (mainly on healthcare systems)	Mitigation. Diagnostic tools to trace cases. Local isolation measures to contain outbreaks.	Healthcare system might experience some pressure. Reorganization to be considered.
Level 3	High infectivity and high morbidity and medium-low lethality	High (affecting healthcare, economy, society)	Containment and mitigation. Trace cases to identify and contain outbreaks. Mobilize resources to increase healthcare system capacity. Isolation, social distancing, face masks, school closures, interruption of social and economic activities.	Limitation of mobility, education, social life, work, might be needed on regional, national or international level. Critical pressure on healthcare systems (as with COVID-19) must be avoided.
Level 4	High infectivity and high mortality	Very high/Critical (depopulation, disruption of social and economic structures, collapse of society, famine)	High-level containment. All measures including strict curfew and extreme social distancing are justified.	In this scenario, it might be necessary to take extreme measures.

It is clear that prompt action requires a precise decision-making chain. Restriction measures, even if affecting freedom and civil rights cannot be discussed for long, since they must be implemented when they are needed, so a pandemic/epidemic preparedness plan must also clearly define the chain of command. A multidisciplinary permanent European expert panel (virologists, epidemiologists, infectious disease and pediatrics specialists, biologists, psychologists, social scientists and economists, bioethical and legal experts) should be appointed under the authority of HERA, ready to be called upon to provide counseling when needed. Given the existence of numerous bodies with sometimes overlapping competencies (for example the National Institutes of Health, Civil Protection, Ministries, etc.) it is essential to define who is doing what in case an emergency arises. Coordination of national policies should be ensured at EU level (Council of the European Union) and decisions taken based on the advice of the Standing Committee. Last but not least, clear contingency plans for the reorganization of the healthcare system (from family doctors up to hospitals) must be ready-to-go to mitigate the health impact of the epidemic and prevent local health care from collapsing.

In any case, it will be very important to restrict any measures in time and extend them to the absolute minimum required to minimize collateral damage to society, education, and democracy. Here, the short- and the long-term perspective must be balanced wisely. Any acceleration plan must be accompanied by a stepwise deceleration strategy.

¹ World Health Organization. Rapid risk assessment of acute public health events. Geneva: WHO; 2012.: http://apps.who.int/iris/bitstream/10665/70810/1/WHO_HSE_GAR_ARO_2012.1_eng.pdf

The speed of the reaction to an infection spreading with exponential growth is highly critical for its containment (Dehning et al, Priesemann, SCIENCE, 2020). During the COVID-19 pandemic, several EU member states experienced legal gaps which have hampered the prompt implementation of measures. Therefore, legal provisions have to be adopted beforehand in order to allow for prompt reaction to a threat. This requires early detection systems of local outbreaks, fast communication to decision-makers, and rapid, strict and targeted reaction to prevent any further spreading to other regions. Only then local measures may suffice to contain the spreading and may avoid transition from a local to a wider and potentially intercontinental outbreak, keeping control on the infection dynamics. Also, system-relevant activities have to be maintained under strict rules that prevent further transmission.

Low incidence strategies reduce overall damage to society

In case a global spread cannot be avoided, a low incidence strategy should be the goal because the higher the incidence, the higher the costs to the society on all levels (Priesemann et al, The Lancet). Once a low incidence has been reached in a particular region or country monitoring other countries and the exchange with HERA and the Standing Committee of European experts is critical to be alerted in case potentially more harmful pathogen variants may emerge. Such variants may be more transmissible, have an increased fatality rate, may have additional long-term effects on the health state, or escape immune responses of convalescents or vaccines. In our internationally highly interconnected societies, a variant emerging somewhere in the world will rapidly spread to other countries, requiring worldwide surveillance of emerging variants of the pathogen.

Drawing the lessons:

- A critical element of coping with a developing pandemic is a rational and fast reaction. In case a global spread cannot be avoided, a low incidence strategy should be aimed at taking economic and societal costs in the different parts of the world into account.
- A multidisciplinary permanent European expert panel on pandemics should be established under the authority of HERA.
- Clear communication of the response strategy, the current knowledge, and the reason behind each intervention, but also of potential uncertainties, is necessary to ensure public awareness and compliance.
- Legal provisions on regional, national and European level should be adopted ahead of crisis to avoid legal gaps and allow for prompt implementation of measures.
- Define, in advance, European and global coordination measures for prevention, detection, and mitigation using the ECDC, HERA, and the WHO as communication and support structures.

III. Strengthening basic knowledge of emergent pathogens and open science

(A. Alcami, S. Guerder, A. Lalo)

The COVID-19 pandemic has shown the relevance of multidisciplinary basic science to understand phenomena and find solutions. The countries that have maintained a long-term investment in basic science were better prepared. Better basic knowledge of the viruses and pathogens, in general, has already led and will lead to the efficient development of vaccines, diagnostic tests, anti-viral drugs or new treatments to reduce disease severity, also, it will help governments to control the pandemic. Basic

research leading to a better knowledge of the populations affected and the biology of pathogens, their ability to counteract the immune response, the mechanisms leading to severe pathology and animal models to understand the mechanisms of virulence is essential to prepare the world for a new pandemic. A special focus should be on studies of emergent viruses and pathogens that may transmit from animals to humans or pathogens that may spread to new regions due to climate warming.

Making scientific progress available to everyone is required to control new pandemics in the future. Sharing data, in general, and genome sequencing data, in particular, in the COVID-19 pandemic has demonstrated the value of open science to improve treatments, speed up vaccine development through sharing of the main immune targets of SARS-CoV2 and control new SARS-CoV-2 variants of concern. Similarly, sharing new advances, such as diagnostics and basic knowledge of the pathogen, is essential to move forward the identification of pathogens and means to control pandemics.

Understanding host-vector-pathogen interactions to limit the risk of pandemic

Since the '70s, epidemics linked to emerging or re-emerging infectious diseases have increased steadily mainly due to major socio-economic changes. The two major risks of emerging or re-emerging infectious diseases are zoonotic and vector-borne infectious agents (Zinsstag 2018). Zoonotic risks are increasing due to intensifying agriculture and livestock breeding (e.g. influenza or coronaviruses) and humans invading natural ecosystems leading to direct transmission of pathogens from wildlife to humans with HIV, Ebola virus and SARS-CoV being prominent examples. In addition, global warming increases the risk of emergence of insect-borne pathogens such as flaviviruses (e.g. Zika, Chikungunya, West Nile virus) or plasmodia causing malaria. Limiting these threats relies on transdisciplinary research in economy, ecology and social and human sciences to develop a sustainable but more resilient and eco-friendlier agriculture and characterize the socio-anthropological behavior associated with emergence and spreading of infectious diseases (Sinclair 2019).

Increasing our understanding of the complex host-vector-pathogen interactions is essential to control emerging diseases from the outset (Heesterbeek 2015). Most intermediate hosts supporting the replication of microorganisms are overall resistant or may even benefit from symbiotic interactions. Defining the mechanisms of resistance, including the genetic factors, may provide means to control the expansion and spreading of pathogens. The emergence of new variants, adaptation mechanisms and transmission to new hosts is central to pathogen spillover events. A better understanding of these events is required to limit zoonotic diseases.

Understanding the human host-pathogen interaction to improve treatments

All viruses and some bacteria have an intracellular life cycle and hijack the cell machinery and the cell metabolism for their replication. Combining proteomic, metabolomic and transcriptomic studies with structural studies will highlight vulnerabilities of the pathogen life cycle and possible targets of new anti-microbial agents. Given the multiplicity of microorganisms with a risk of emergence, focusing on at least one representative of a family of microorganisms likely to emerge will provide first-line therapeutics.

A better understanding of the pathophysiology and immune pathology of emerging diseases is needed to limit their health impact. As illustrated in the COVID-19 pandemic, an exacerbated immune response may be deleterious for the host. A global understanding of the inflammatory and adaptive immune responses to specific pathogens and the clinical impact of infection is therefore essential to optimize treatments. Defining the diversity of innate immune factors and the different arms of the adaptive immune response that restrict pathogen replication will support the development of new therapeutic strategies, including optimal vaccine platforms.

State-of-the-art medicinal chemistry is essential for the development of anti-microbial agents. The development of bioinformatic algorithms is essential for molecular modelling and extensive in silico screening of libraries following structural characterization of targets of interest. Increasing the diversity of libraries (natural compounds and new chemicals generated by synthetic chemistry) and providing access to these libraries within the European research area will be essential to accelerate the response

to emerging diseases. Combining the high-resolution mapping of the molecular networks of host-pathogen interactions with the high-power computational and AI tools will also facilitate repurposing efforts of approved drugs and help streamlining and accelerating the drug development process.

The COVID-19 pandemic has highlighted the need for Europe-wide coordination of clinical trials and the importance of cohort studies. European guidelines regarding inclusion criteria and size of the cohorts to collect meaningful results and to accelerate filing and approval of clinical trials are essential.

Drawing the lessons:

- Open science and sharing of data and reagents have been instrumental for our rapid understanding of the pathophysiology of SARS-CoV-2 infection. Open science should, therefore, be further enhanced to prepare for new pandemics and improve human health in general.
- Given that we cannot predict which pathogen may emerge and will initiate a future epidemic or pandemic, multidisciplinary funding for basic research of host-pathogen interaction with a focus on candidate emerging pathogens should be sustained at national and European levels.
- Funding for transdisciplinary research in economy, ecology and social and human sciences is essential to develop a sustainable but more resilient and eco-friendlier agriculture and to better understand the socio-anthropological behavior associated with the emergence and spreading of infectious disease.
- The COVID-19 pandemic has highlighted the need for European coordination of clinical trials following common guidelines.

IV. Enhancing monitoring systems

(A. Alcamí, S. Guerder, A. Lalo, G. Maga, V. Priesemann, D. Ramiro)

Need for Europe-wide faster and efficient data monitoring systems.

The pandemic has accelerated many changes in data production that have already taken place in Europe, thereby creating a new paradigm in statistical production, moving from a data-scarce world to a data-rich world. These developments have made governments and statistical agencies focus on getting the maximum benefits of data extraction from multiple sources. At the same time, they had to develop new methodologies to deal with such vast amounts of information while complying with the EU's legal framework and respecting individual privacy. During the pandemic, most of the traditional statistical production has shown to be obsolete, as high-frequency data (weekly, daily or hourly data) was requested to comply with the information needed to tackle and monitor the pandemic. Some of the traditional health and mortality data collection systems were severely affected by the pandemic, thereby disrupting and delaying crucial information for the monitoring of mortality evolution. Measures to avoid this in the future need to be implemented via a more efficient electronic certificate system. Some information has shown to be scarce and limited, especially regarding statistics on the number of retirement homes and the health and living conditions of its residents. This data, integrating also societal aspects, was needed to provide policy-makers with evidence-based information that allows for rapid reaction and implementation of measures in a more coordinated way. Statistical offices played a key role in this change and adapted quickly to the new needs, but the depth and speed of information provision differed between countries. Part of this new information came from a more efficient use of the different administrative data already available for the citizens from governmental sources, while other

information came from an increased Business to Government (B2G) transfer of information such as mobile phone data to measure mobility, credit card use to estimate private consumption, etc. The use of this data is not new, but it becomes ever more important and frequent. Thus, it needs to comply with the rules on data privacy and anonymization, limitation and proportionality of its use, homogeneity and regularity in its production across Europe. This will result in modernized data access. To ensure trustworthiness, statistical offices will need to comply with common methodologies and quality standards, data security and protection as well as the legislative framework for B2G. The forthcoming European Data Governance Act will need to take into account this new approach. Finally, a sustained monitoring effort and understanding of the long-term effects - e.g. on health, education, economy (accumulation of non-performing loans, shifts of risks from firms to banks to sovereigns, forbearance of losses due to subsidy programs, bankruptcy gap...) and people (pension systems) - need to be undertaken. Such a monitoring system should integrate both administrative and electronic medical records. Standardization in medical recording procedures is also needed among different countries at EU level in order to ensure full homogeneity of the reported information and compliance with data quality procedures.

Need for a Europe-wide pandemic surveillance system

Europe needs a strategic plan to better predict, prevent and respond to future viral pandemic threats. This requires a coordinated multidisciplinary approach from various partners to build a framework of shared global strategies, in order to be able to better respond to both international and local needs. Constant epidemiological surveillance of areas at risk of emergence is required for early detection of emerging pathogens. Early detection is essential to slow down the international spread of a novel virus or virus variant. Such real-time monitoring systems need to be integrated into European and worldwide systems with all countries providing data and accessing data in a common, machine-readable framework.

Global prevention strategies and proactively developed countermeasures to mitigate the impact of future pandemics should be built on the following key pillars: i) identifying where viral threats are; ii) understanding what are the risks of exposure for the population, iii) studying the effectiveness of interventions and iv) identifying vulnerabilities in the response systems. Last but not least, it has turned out that freedom in basic research was essential to enable a multitude of researchers to swiftly address the challenges of the COVID-19 pandemic. It is not known, what the precise challenges in the next crisis will be, yet, a flexible and strong basic research community is an invaluable resource for effective and fast crisis response.

To achieve the specific pandemic preparedness goals, we must urgently fill our existing knowledge gaps of the global virome through a multidisciplinary basic science approach. Strategic plans must be developed in order to detect and identify possible zoonotic viral threats to human health, in particular at the animal/human interfaces to understand their transmission and pathogenicity characteristics, to explore the ecological niches where these viral threats circulate in terms of host range and evolutionary relationships and to identify behaviors and practices potentially increasing the risk of spillover. From the public health perspective, we need to better understand how and under which conditions people can be empowered best to protect themselves against an infection and thereby contribute to mitigation of the spread (Priesemann et al, 2021a, b, c). In general, maintaining low incidence has advantages in all respects: it minimizes the risk of infection, severe course and death, increases the trust of the general public and thereby fosters social and economic activity. Also, technically, the mitigation is facilitated as the health authorities can concentrate on stopping the remaining infection chains locally, fast and efficiently (Contreras et al. 2021; Kretzschmar et al. 2020). To maintain low incidence, the advantage of pandemic control over an uncontrolled spread needs to be clearly communicated. Socio-economic factors need to be taken into account when designing and communicating mitigation and support measures. A set of clear, fair and comprehensive mitigation measures which are communicated univocally, fosters the cooperation of the population and thereby contributes to mitigation (Katrine Bach Habersaat, et al. 2021).

During a viral pandemic timely availability and reliability of data are key. Therefore, a centralized, harmonized pandemic surveillance system for Europe is required. Regular, randomized and representative testing fosters comparability of data across Europe. The database should integrate the European data in one single place and be machine-readable, open and fast, while respecting individual privacy. In case of a viral pandemic, such a database should include e.g. the daily number of infections, hospitalization, intensive care and death; test reasons and strategies; local responses, details on the course of disease and viral genomes. It should be broken down by localization and age, contain governmental mitigation measures, mobility statistics, interfaces for socio-economic information and results of systematic surveys.

As mobility spreads viruses and variants across the world, virus surveillance for long-distance and international travelers is particularly important and informative. It would (i) provide core information on local distribution of viral strains, and (ii) the impact of travel on spreading variants. Moreover, for COVID-19, mandatory testing and sequencing for any long-distance travel could slow down the spread of novel variants of concern. These rules should apply also to vaccinated or immunized people, as they might accelerate the spread of variants of concern with partial immune escape.

The pandemic has emphasized the critical role of diagnostic tests to control the spread of new pathogens. The development of rapid diagnostic tests based on new technologies (biosensors, colorimetric detection) should be prioritized, since the faster we can detect infected individuals the easier it will be to control the pandemic (Kevadiya 2021, Tang 2021).

The COVID-19 pandemic has shown that we are not prepared to prevent transmission of pathogens through aerosols, which facilitates rapid spread in the population, whereas we control better surface transmission through fomites (Greenhalgh 2021; Wang 2021). There is, therefore, an urgent need to develop methods for the detection of pathogen-containing aerosols in public places (hospitals, schools, transport) (Bhardwaj 2021). Rapid detection of airborne pathogens will help to identify emergent viral infections and bacteria such as tuberculosis and antibiotic-resistant strains, and to control their spread. As our society is asking for better microbiological air quality, research on new technologies to inactivate airborne pathogens is required and should, thus, be supported (Morawska 2021).

Drawing the lessons:

- Rapid development of diagnostic tools to detect a pathogen and antibodies indicating a prior infection are critical to control the spread of a pathogen and a growing pandemic.
- Rapid and efficient monitoring systems, including early detection assays, genomic sequencing of pathogens, and representative pandemic surveillance, must be integrated into European and worldwide monitoring systems.
- Europe should develop a framework of strategies that involves policy-makers, scientists and relevant stakeholders at regional, national and European level in order to be better prepared for future pandemics.
- New technologies to monitor aerosols and to inactivate airborne pathogens are needed and should, thus, be funded at the European level.
- Researchers from many areas of basic research contributed essential knowledge to the pandemic response by flexibly shifting their research focus. In order to be prepared for future, as yet unknown crises, strong basic research is therefore the key to being able to quickly close knowledge gaps.

V. Research infrastructures to react to new pandemics

(A. Alcamí, S. Guerder, A. Lalo, G. Maga, D. Ramiro)

A central European viral genomes database

Data generated through metagenomic environmental investigations must be set up, consolidated and made publicly available to the health research community for phylogenetic/ecological studies and potential pathogenicity biomarkers identification. The ECDC analysis teams must be strengthened to coordinate data collection and key risk assessment analyses.

National surveillance networks should be integrated at European level to rapidly detect anomalies (outbreaks of new human/animal viral pathogens), including the capacity to quickly deploy multidisciplinary field teams of experts to assess the nature of the potential threat and implement mitigation measures.

Resources should be allocated to the creation or upscale of high biosafety level/high-tech virology laboratories to be integrated into a European network in order to increase our capability to examine the biology and be ready to respond to the emergence of highly pathogenic viruses.

National healthcare systems should be provided with emergency response plans addressing new viral outbreaks in order to avoid or mitigate the disruption of essential services due to overwhelming pressure on the healthcare system.

Initiatives such as COG-UK (COVID-19 Genomics UK Consortium) and G2P-UK (genotype to phenotype UK Consortium) should be expanded to the European level to allow for real-time monitoring of the evolution of the viral population in the course of the epidemics through the sequencing of a relevant number of clinical samples. The genomic surveillance information should be integrated and become a core element of the national surveillance systems to allow individual viral genomic data to be linked to case clinical and epidemiological data.

European infrastructures dedicated to all emerging or re-emerging infectious agents

The European Virus Archive (EVA) has been decisive during past virus-driven health crises and the international InfraVec infrastructure focusing on insect vectors is of major interest for the research community in this field. Infrastructures dedicated to archiving parasites and bacteria, including antibiotic-resistant strains, need to be created and implemented at the European level. Continued support to the European INFRAFRONTIER research infrastructure to accelerate the human genome project is required. In addition, to maintain a strong international position, Europe must build infrastructures for the dissection of the pathophysiology of infection and for the validation of therapeutic candidates and vaccines, from *in vitro* to *ex vivo* and *in vivo* experimental models.

The impact of such actions will be: i) to generate accurate datasets essential to develop new vaccines, pharmaceuticals and diagnostic tools; ii) to make available better tools to inform European and national health policies, environmental conservation strategies and pre-pandemic plans. A continuous investment effort on these lines must be made particularly in non-pandemic times so that the local, national and European health systems are ready for the next pandemic.

Translation of basic research to the private sector

Basic science investment is required to advance our ability to control pandemics. However, the transfer of this knowledge to society requires the participation of both non-profit and for-profit private sectors (start-up and pharma companies). Thus, private-public collaborations must be strengthened.

Drawing the lessons:

- Europe should develop and support data infrastructures to allow for phylogenetic/ecological studies and the identification of biomarkers indicating pathogenicity.
- The role of the ECDC analysis teams must be strengthened with regard to the coordination of data collection and risk assessment analyses.
- European/international research infrastructures such as EVA, InfraVec or INFRAFRONTIER have been decisive in past virus-driven health crises and are of major importance for the research community in this field. Therefore, political commitment and a sustained investment effort at national and European level are required.

VI. Protecting our people and economy in the long term

(K. Konrad, M. Kunter, L. Tonzer)

While taking measures to prevent the infection was an acute necessity, the impact on other areas of life should always be considered, both, in the short- and long term. The pandemic and the mitigation measures have directly or indirectly affected people's well-being, their general health, education or the economy. In order to learn for the future, it is of utmost importance to monitor and understand these side effects, in particular regarding long-term developments. This section focuses on serious side effects of the pandemic beyond its medical dimensions. In particular, it addresses the social and economic consequences of the disruption in education, the risks posed by the pandemic to financial stability and the lessons that can be learned, and provides general considerations on how our society should strengthen its crisis resilience.

Education

As one measure to control the pandemic, most states closed their educational institutions (early education institutions, schools, universities) with varying lengths of the closures and different compensation layouts, with most countries resorting to online distance learning. Along with the closing of educational institutions, most of the extracurricular activities and child and youth welfare structures have also been closed or access was narrowly restricted. This worldwide and in many cases long-term closing of educational facilities is unprecedented in history.

While the impact of these closures on the spread of the infection remains unclear, it is without any doubt that this has had a substantial impact on the education and the well-being of young people. Research clearly shows negative effects on learning time and on short-term learning outcomes (e.g., Pensiero et al, 2020; Engzell et al., 2021). If not compensated, these are likely to lead to long-term disadvantages in educational trajectories (e.g., grades, degrees, skill acquisition, income). This is not only relevant for individual children and adolescents, but also has long-term consequences for the economy as a whole (Fuchs-Schündeln et al., 2020). The loss of familiar daily structures in combination with the lack of opportunities for exchange with peers also has a negative impact on the well-being of children and adolescents (Ravens-Sieberer, 2021) and recent data shows that during the pandemic, clinically relevant depression and anxiety increased, particularly among younger people (COVID-19 Mental Disorders Collaborators (2021)). Overall, there is great variability in how well children and families cope with the limitations. For children and adolescents who were already disadvantaged before the pandemic due to poverty, lack of family support, or difficulties with school learning, the pandemic situation has had a particularly negative impact.

Countries were differently well prepared for phases of school closures. While some countries already had an effective digital infrastructure in place before the pandemic, others had to adjust to the new

situation completely unprepared. Furthermore, within Europe alone, clear differences can be seen in the relevance attributed to education and the situation of children and young people. While some states gave high priority to the education system and avoided long-term school closures, other states closed educational institutions for much longer than other areas of public or commercial life. The findings from ongoing international large-scale school achievement studies will reveal the consequences of these different approaches. A particular challenge for all countries will be to develop meaningful support strategies specifically for those children and adolescents who showed particularly adverse developments in the pandemic due to individual or family risk factors, as these disadvantages will deepen without further intervention, and thus contributing to educational and social inequality within and between countries. Individual countries have already launched more or less comprehensive aid packages; an exchange on the different approaches or a pan-European program would be a useful way to support a group of people currently suffering particularly from the pandemic.

The pandemic and financial stability risks

Financial stability is key to maintaining financial intermediaries' credit supply to the real economy, which in turn fosters investment activity and thus contributes to economic growth. While the global financial crisis starting in 2007/08 had its roots in the financial system, banks started relatively well into the pandemic such that it was argued that banks could this time be part of the solution rather than the problem. Especially the lessons learnt from the financial crisis have resulted in a more stringent regulatory and supervisory framework. Consequently, increased capital and liquidity ratios as well as the establishment of the European Banking Union in the Euro Area setting up rules for restructuring and resolution of banks in distress have contributed to systemic stability and created buffers.

Importantly, policy responses to the pandemic have been significant to stabilize credit supply by banks, avoid liquidity shortages and waves of insolvencies in the real sector. Especially in the financial system, quick intervention and the avoidance of panics is key to mitigating severe disruptions in financial intermediation with potentially long-lasting effects for economic development. Therefore, the European Central Bank (ECB) has responded promptly by setting up the pandemic emergency purchase programme (PEPP) and the pandemic emergency longer-term refinancing operations (PELTRO). These measures ensured that liquidity is available and eased credit supply to the real sector. From a regulatory perspective, conditions for banks have been relieved by lowering capital and liquidity requirements and by loosening macroprudential policies. Additionally, supervisors introduced some flexibility for banks regarding the classification of loan losses and they postponed stress tests. Such measures aimed at mitigating the build-up of constraints for banks have been complemented by government support programs targeting non-financial firms as well as job retention programs.

This set of newly introduced schemes and tools have certainly helped maintaining financial stability, credit and liquidity, as well as jobs in the short run. However, over the longer term, risks might build up and have to be carefully monitored. Data reveal already now that there is a significant bankruptcy gap (Banerjee et al. 2021). This observation can be explained by, for example, the temporary removal of insolvency reporting duties and Covid-19 related moratoria. It might also reflect that weaker banks continue to support weaker firms to avoid that loan losses materialize in their balance sheet. Such kind of "zombie" lending is detrimental as it hinders the efficient allocation of resources to productive and innovative firms with relevant research and development activity (Acharya et al. 2019). One key lesson is thus that rescue programs should be implemented quickly but in a targeted way stabilizing illiquid but solvent banks and non-financial firms, which are hit more severely by the exogenous shock that the pandemic constitutes. Here, a certain degree of flexibility is needed to support also smaller firms and span the social security net as well for, e.g., self-employed individuals and weak groups in the society, which tend to be hit more severely during crisis times (Tonzer 2019).

Looking forward and regarding the recovery phase, the right moment for phasing out support measures and tightening regulatory measures has to be found. Already before the pandemic, the banking sector has been struggling with major challenges such as i) low profitability in a low-interest rate environment, ii) overcapacity and difficulties when it comes to cross-border consolidation, and iii) increased pressure

due to digitalization and the entry of new types of non-bank financial intermediaries into the market (Beck and Carletti 2021). Too early would hence increase constraints, raise uncertainty and probably delay economic recovery. Too late could foster the build-up of risks in banks' balance sheets and support zombie lending. Sustainable debt management is, however, needed to avoid long-lasting spillovers of risks amongst different sectors, e.g., from banks to sovereigns. Therefore, tightening previously loosened standards is key in good times to have buffers in bad times. Beyond that, a well-functioning secondary market for non-performing loans (NPL) as well as harmonized and clear insolvency rules could reduce incentives for "evergreening" of NPLs and align the level playing field (Kasinger et al. 2021, Laeven et al. 2020).

Multiple global risks and the role of adaptability

Infectious diseases in their many different manifestations are only one risk from a whole group of global risk categories. The Global Risks Report by the World Economic Forum typically names cyberattacks, breakdowns in the information structure, climate change, the loss of biodiversity and other natural disasters as risks that experts assessed as similarly likely events with an impact comparable to that of infectious diseases.

In crisis prevention policy, all these risks compete with each other, as well as with other general societal welfare goals (e.g. education, nutrition, general health, etc.) for the available economic resources. Comprehensive specific prevention against individual risks, therefore, has high (opportunity) costs in terms of the degree of achievement of prevention goals for other risks such as financial stability and for general welfare.

The "finite pool of worry" hypothesis, for instance, suggests that the high visibility and immediacy of the current pandemic situation may cause excessive attention given to the risk of infectious diseases and a reduction in attention to other risks. (See e.g. Weber [2010], Botzen [2021] and Evensen et al. [2021] who focus on changes in the assessment of the risk of climate change during the pandemic.) As a result, an unbalanced policy response too specific to the current pandemic can easily occur.

In the short term, a massive response to a pandemic is without alternative. But in the long run, the non-specific crisis response capacity of the global community for a whole spectrum of known or yet unknown risks could be more valuable than very specific prevention measures that help only against risks similar to the Covid-19 pandemic.

To illustrate: the rapid vaccine development success in the pandemic was based on technologies that were not developed specifically for Covid-19. The digital economy was also not developed as a treatment tool for the pandemic. However, digital technologies were of tremendous use and prevented the worst economic damage in the pandemic, despite the complexity and the high degree of division of labor of the modern economy. They prevented the collapse of supply of essential goods, and working from home made it possible to maintain economic activity. In previous pandemics, society could not resort to such technologies. In this respect, the examples show how a large pool of technologies that were not developed for specific crises can make society more resilient and increase society's crisis response capacity.

Schelling [1992] who made this argument in a different context, additionally highlights the importance of societal wealth along other dimensions, such as human capital and economic power the capacity of which can be redirected in response to a large variety of crises as they occur. Spending on measures aimed at very specific risk scenarios may make sense in individual cases, but in view of the general competition in the use of finite economic resources, it is in sharp competition with such spending that strengthens general crisis resilience.

Drawing the lessons:

- Side effects of the pandemic and mitigation measures on areas other than health need to be monitored and considered, especially regarding long-term development.
- A thorough cost-benefit analysis regarding the closures in the educational sector is warranted, as children and adolescents have been particularly affected, with possible detrimental long-term effects.
- Over the longer term, financial stability risks might build up and have to be carefully monitored. Harmonized rules on how to deal with non-performing loans and insolvencies across European countries are key to avoiding forbearance and sluggish recovery.
- Specific prevention for all future infectious diseases and other major risks will hardly be possible. Mankind should therefore strengthen its crisis response capacity through general prosperity and a wealth of general scientific and technological knowledge.

VII. Conclusion

The COVID-19 pandemic has demonstrated how unexpectedly a pandemic or crisis of any other kind can hit mankind, and we have to admit that we were not prepared for this. A crisis of this magnitude requires political decisiveness and action based on scientific knowledge. The scientific community has, thus, an important responsibility and it can and wants to assume it. Epidemiologists, physicists, biologists and scientists from all disciplines have been working together across disciplines and borders, and this not just since yesterday. The COVID-19 pandemic has shown, however, that much more needs to be done in terms of improved preparedness and resilience, and that these challenges cannot be met by individual regions or member states. This concerns in particular decision-making structures, the provision of expertise, the legal basis for a rapid response and, last but not least, the expansion of scientific knowledge. The EU Institutions, together with the EU member states, are currently discussing the future of Europe. It is, thus, the right time to reflect on the lessons learned from COVID-19 and, together, better prepare for future pandemics.

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ANNEX

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