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Pandemic Preparedness: A Proposal for a Research Infrastructure and its Functionalities for a Resilient Health Research System

Pandemic Preparedness – Ein Vorschlag für eine Forschungsinfrastruktur und ihre Funktionalitäten für ein resilientes Gesundheitsforschungssystem

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Keywords

pandemic preparedness, capacity building, epidemic response plan, crisis management, health services research, scientific research infrastructure

Schlüsselwörter

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ABSTRACT

During a pandemic, resilience must be considered not only as an attribute of the health care system, but also of the surrounding research environment. To provide reliable evidence-based advice from university medicine to health policy and decision makers, scientific evidence must be generated, synthesized and communicated in a rapid, integrative and multidisciplinary manner. The resilience of public health systems and the health research systems are thus closely linked. However, the response to the SARS-CoV-2 pandemic in Germany was hampered by the lack of an adequate health research infrastructure. The Network University Medicine (NUM) was founded at the beginning of the pandemic with the aim of preparing Germany for future pandemics. The aim of the project "PREparedness and PAndemic REsponse in Deutschland (PREPARED)" is to develop a holistic concept for a cooperative, adaptable and sustainable health research infrastructure within the NUM and thus contribute to pandemic preparedness and rapid response. The proposed concept for a health research infrastructure includes four core and three supporting functionalities in four different fields of action. The functionalities aim to ensure efficient functioning within the health research system and a rapid translation to other systems in future health crises. The four fields of action are (a) monitoring and surveillance, (b) synthesis and transfer, (c) coordination and organization, and (d) capacities and resources. The seven functionalities include 1) a monitoring and surveillance unit, 2) a pathogen competence platform, 3) evidence synthesis and trustworthy recommendations, 4) a regional networking and implementation unit, 5) a strategic communication unit, 6) human resources management, and 7) a rapid reaction and response (R^3)-cockpit. A governance will be established as a control and regulatory system for all structures and processes, testing agile management in non-pandemic times to improve responsiveness and flexibility and to investigate the suitability of the methods for scientific pandemic preparedness. The establishment of the PREPARED health research infrastructure must take place before the next pandemic, as training and regular stress tests are its fundamental prerequisites.

ZUSAMMENFASSUNG

Während einer Pandemie muss Resilienz nicht nur als Eigenschaft des Gesundheitssystems, sondern auch des umgebenden Forschungsumfelds betrachtet werden. Um verlässliche, evidenzbasierte Empfehlungen aus der Universitätsmedizin an die Gesundheitspolitik und die Entscheidungsträger bereitstellen zu können, müssen wissenschaftliche Erkenntnisse schnell, integrativ und multidisziplinär generiert, synthetisiert und kommuniziert werden. Die Resilienz der öffentlichen Gesundheitssysteme und der Gesundheitsforschungssysteme sind somit eng verknüpft. Die Reaktion auf die SARS-CoV-2-Pandemie in Deutschland wurde jedoch durch das Fehlen einer adäquat vernetzten Gesundheitsforschungsinfrastruktur erschwert. Das Netzwerk Universitätsmedizin (NUM) wurde zu Beginn der Pandemie mit dem Ziel gegründet, Deutschland auf zukünftige Pandemien vorzubereiten. Ziel des Projektes "PREparedness and PAndemic REsponse in Deutschland (PREPARED)" ist es, ein ganzheitliches Konzept für eine kooperative, adaptierbare und nachhaltige Gesundheitsforschungsinfrastruktur innerhalb des NUM zu entwickeln und damit einen Beitrag zu einer umfassenden Pandemiebereitschaft zu leisten. Das vorgeschlagene Konzept dieser Infrastruktur vereint vier Kern- und drei Unterstützungsfunktionalitäten in vier verschiedenen Handlungsfeldern. Die Funktionalitäten gewährleisten im Falle zukünftiger Gesundheitskrisen ein effizientes Funktionieren des Gesundheitsforschungssystems und eine rasche Übertragung entsprechender Implikationen in andere Systeme. Die vier Handlungsfelder sind (a) Monitoring und Surveillance, (b) Synthese und Transfer, (c) Koordination und Organisation sowie (d) Kapazitäten und Ressourcen. Die sieben Funktionalitäten umfassen 1) eine Monitoring- und Surveillance-Einheit, 2) eine Pathogenkompetenz-Plattform, 3) Evidenzsynthese und vertrauenswürdige Empfehlungen, 4) eine Einheit zur regionalen Vernetzung und Implementierung, 5) eine Strategische Kommunikationseinheit, 6) Human Resources Management und 7) ein Rapid Reaction and Response (R^3)-Cockpit. Die Governance wird als Kontroll- und Regulierungssystem eingerichtet, wobei agile Management-Methoden in interpandemischen Phasen trainiert werden, um die Reaktionsfähigkeit zu verbessern sowie die Eignung agiler Methoden für die wissenschaftliche Infrastruktur für die Pandemiebereitschaft zu untersuchen. Der Aufbau der PREPARED-Forschungsinfrastruktur muss vor der nächsten Pandemie erfolgen, da Training und regelmäßige Stresstests grundlegende Voraussetzungen für deren Funktionieren sind.

Introduction

Coping with a new, uncertain and complex situation such as an epidemic or pandemic poses major challenges for society as a whole, but especially for the complex systems of health research and medical care. Close cooperation between institutions and actors across sectors, such as health authorities, health care institutions, policy makers, experts and other stakeholders, is crucial for a targeted, timely, effective and efficient response to the emerging challenges. Although Germany managed the SARS-CoV-2 pandemic relatively well in terms of coordinated and structured care, numerous shortcomings were identified in both preparedness and crisis management. Central pillars for coordinated trans- and interdisciplinary research at the national level were missing. Components of the needed but unavailable research infrastructure include a framework for setting research priorities, timely access to reliable health care data, outcomes and exposure data, core data sets, coordinated and consistent roadmaps for generating and synthesizing high-quality evidence, and consistent and balanced communication between the research community and health policy makers. There is a consensus, not only among German experts [1], that resources have not been used in a timely, efficient, balanced and coordinated manner. The German Council for Health and Care stated: "*Our health care system is (…) a "fair-weather system", which is not very responsive and not very adaptable, which is not only insufficiently coordinated in the event of a crisis and is often worse in outcome than would be expected given the high level of resources used*" [2].

In times of crisis, society and politicians, and health care providers expect university hospitals not only to provide excellent medical care, but also to use their research capabilities to play a central role in the timely and coordinated provision of evidence-based, consensus-driven explanations, forecasts, and recommendations for action [3]. Meeting these expectations requires a clear definition of the objectives of the pandemic response, flexibility and agility of the stakeholders, and their coordination in fit-for-purpose structures. This implies the need for clear, established modes of collaboration and communication with the various stakeholders. Currently there is no alliance of national university hospitals for better pandemic preparedness, nor is there an international blueprint for such an approach and the goals to be achieved.

In Germany, despite the existence of a national (influenza) pandemic plan, a public health service and a Federal Institute for Disease Control and Prevention (Robert Koch Institute, RKI), the special role and importance of university hospitals has not been addressed. The existing plans and structures have proven to be too inflexible or inappropriate in relevant aspects, such as for example transferability to other pathogens or coordination with other health service providers [4, 5]. It is important to note that the resilience of health systems and medical research systems are strongly interrelated. Unclear evidence with high uncertainty and mixed messages from the research community can be a driver of scientific discourse and progress, but can also act as a barrier to compliance and acceptance of societal pandemic response measures such as contact restrictions, and vaccination programs. Therefore, an appropriate infrastructure for pandemic preparedness and response, with a special focus on interdisciplinary research, transfer and implementation, is of utmost importance for the functioning of society.

The following position paper proposes a concept for a comprehensive scientific research infrastructure for a coordinated response, which has been developed in the project "PREparedness and PAndemic REsponse in Deutschland (PREPARED)". The project started in 2022 and was initiated and funded by the Network University Medicine (NUM)[1]. The NUM was founded in 2020 in order to coordinate research activities on COVID-19 in university medicine on a national level and consists of all 36 university hospitals in Germany [6]. It is funded by the German Federal Ministry of Education and Research (BMBF), which, like the German government in general [7], recognized early on that the issue of *pandemic preparedness* needs to be addressed as soon as possible and therefore developed a far-sighted funding program with the goal of developing and permanently implementing an appropriate infrastructure. The proposed infrastructure is based on the preliminary work of three former NUM projects that ended in 2021 (B-FAST[2], CEOsys[3], egePan[4]).

The infrastructure concept consists of four core and three supporting functionalities, which in turn are subsumed under four fields of action in order to address the above-mentioned challenges. PREPARED follows the central goal of the NUM to prepare Germany as best as possible for the next pandemic or other health crises. The overall concept of PREPARED is based on the conceptual framework of "Capacity Building" [8, 9] and is intended to become a central pillar of future pandemic preparedness in Germany.

Not only the health care system, but also the health research system must have a high degree of resilience in order to be able to translate medical empirical evidence safely, quickly and efficiently into health care and scientific findings into decision-making systems in critical situations. The impact of research on society has been widely studied since the 1990s. However, the focus has been mainly on economic rather than societal aspects [10]. During the SARS-CoV-2 pandemic, it became clear very early on that the extent to which institutions, societies or states were prepared for new and challenging health (care) situations had a significant impact not only on the economy and the health system, but also on other areas of society. Preparedness was crucial for resilience in the face of the many resulting challenges [11–13], including management of the healthcare workforce, the supply chains for protective equipment, and the economic, cultural, and social consequences of disrupting key aspects of public life. In order to approach the term *pandemic preparedness*, a selective, critical literature review was conducted, considering scientific literature, national pandemic plans, and recommendations for pandemics. The guiding research question concerned definitions of and requirements for achieving a state of pandemic preparedness.

The results indicate, that the term "pandemic preparedness" is first and foremost a collection of processes, objectives, and conditions that serve to prepare for and respond to potential and actual

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pandemic crises. This includes activities that facilitate and improve crisis management during a given crisis, but also before a crisis occurs. Pandemic preparedness therefore describes the preparation of a society as a whole for the onset of a pandemic, which, according to the WHO, can only be achieved if all social subsystems (civil society, economy, research, health care, politics) are considered together [14]. The goal is always to avoid or minimize the negative effects of the epidemiological emergency through a rapid, targeted, effective, and efficient response. Actors can be all organizational units, e. g. public authorities, companies, and social and/or health institutions across different subsystems.

Furthermore, pandemic preparedness is considered at different levels according to institutions, actors and scope. Thus, different dimensions are addressed, which can be at the micro level (e. g. individual workers), on the meso level (e. g. organizational structure of health care institutions such as hospitals), or on the macro level (e. g. national plans or protocols). When translated into the respective policy, e. g. in the form of national pandemic plans, the individual goals of pandemic preparedness are diverse or even fragmented. Most of the literature reviewed on pandemic preparedness refers to recommendations, observations and analyses at the national level. The focus is usually on how political entities (regions, states or even the international community) can prepare more effectively to deal with a pandemic. There are also publications that discuss pandemic preparedness specifically for hospitals (less frequently for other social and health care institutions) and, in some cases, provide specific recommendations for action [11, 13–15]. The numerous objectives, tasks, processes and measures identified in the scientific literature can be systematized into four fields of action: (a) monitoring and surveillance, (b) synthesis and transfer, (c) coordination and organization, and (d) capacities and resources. These fields of action serve as the basis for the seven functionalities of a scientific research infrastructure for pandemic preparedness, which is presented (▶ **Fig. 1**) and described below.

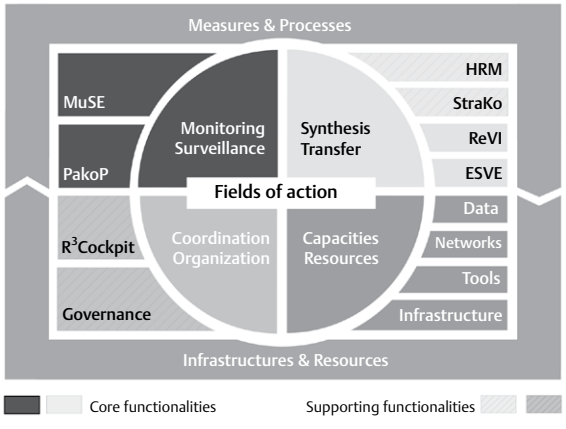
The first field of action, *monitoring and surveillance,* will bring together parameters from different relevant areas to improve guidance aimed at defining the most appropriate and balanced advice for decision making. This will include representative infection surveillance, e. g. of hospital-acquired cases and outbreaks caused by the new pathogen, and the development of appropriate infection prevention (IPC) surveillance systems [15–20] focusing on transmission networks, hospital-acquired infections including outbreaks and admissions, including risk factor analyses and sentinel surveys, e. g. on IPC measures at an institutional level. In addition, an expert group will be established to anticipate the next pandemic viruses, define laboratory resilience and develop a concept for diagnostic scalability [4].

In the second field, *synthesis and transfer*, the classification and dissemination of evidence-based recommendations to policy makers, the general population and professional communities [21] ensures informed decisions by health care providers and sound advice to policy makers [21–24], and also strengthens public awareness [23], with the aim of building trust in the population [22]. Furthermore, the rapid and trustworthy evaluation of scientific findings must be incorporated into the further training of existing employees and into the training and qualification of newly hired or non-specialist employees. The development of concepts for the protection and promotion of the physical and mental health of healthcare staff, the securing of specialist staff and the qualification of new employees as well as direct involvement in crises [15, 22, 25], exercises, simulations and training in crisis plans [15, 16, 23] strengthens resilience and leads to greater competence among healthcare staff [22, 23].

The third field of action, *coordination and organization,* includes defining the organizational structures of the hospital sector so that priority hospitals can be designated in the event of a crisis [15], as well as cross-sectoral, multidisciplinary cooperation for pandemic preparedness and management and the involvement of all relevant stakeholders [19, 23, 26] in all phases of a pandemic [23].

Adequate and flexible *capacities and resources* (4th field of action) are needed to successfully implement the required measures and processes. Relevant resources include those of the health care infrastructure (human resources, hospital beds, including reserve capacity for crises, ensuring scalability [16, 27] – such as global supply chains for consumables [19, 22] or vaccines and medicines [26] – as well as the availability and transparency of surveillance and routine health data [16, 21, 27]), the digital infrastructure of the science system [21, 27], and flexible/agile research funding capacities [21].

Based on these four fields of action, seven interrelated functionalities for the development of the PREPARED research infrastructure have been designed. Four of them are categorized as core functionalities, while three are supporting functionalities. This categorization does not reflect on their impact on the goal of pandemic preparedness (▶ **Fig. 1**)[5].



▶ **Fig. 1** Fields of action, core and supporting functionalities of the proposed PREPARED scientific research infrastructure for pandemic preparedness.

Monitoring and Surveillance Unit (MuSE)

The overall goal of the MuSE as a core functionality is to continuously improve the presentation of guidance and control parameters from infectious disease surveillance and comprehensive health

[5] The 4th field of action "capacities and resources" is not further discussed in this article.

care utilization monitoring. This includes risk factor analysis, and quality and risk management within the NUM in preparation for optimized research, but also management in the event of a pandemic or other crisis. The main objective is to provide a comprehensive and up-to-date overview of current developments in the various areas of infection prevention and control (IPC), hygiene, infectious diseases, epidemiology, quality of health care and resource monitoring, including human resources. The novelty of MuSE is the strong linkage of parameters and indicators from these different dimensions to create a comprehensive picture of the crisis, that can serve as a basis for description, prediction, modeling, evidence generation, the derivation of recommendations, and implementation review processes, and thus as the basis for a learning system. The main tasks of MuSE will be 1) to analyze the past and current course of epidemics and pandemics compared to normal circumstances including seasonal patterns (descriptive), 2) to predict the future course (modeling), 3) to conduct exploratory and hypothesis-driven analyses, and 4) to monitor the implementation of suitable measures on the basis of which advice can be provided to decision-makers in order to make the best possible decisions.

MuSE will establish certain university hospitals as sentinels for the collection and provision of key parameters to characterize the outbreak or crisis situation and crisis response. This comprehensive and up-to-date empirical resource enables PREPARED to provide the best possible evidence-based and balanced decisions to make recommendations. In order to define the extent of the direct and indirect pandemic-related health risks for the general population and/or specific subgroups and to quickly identify and reduce risk factors, it is crucial to collect standardized data across the network of all 36 German university hospitals and with the involvement of various specialist disciplines, before and especially directly at the beginning of a pandemic. MuSE works with data from: 1) other infrastructure components of the NUM, including the data integration centers of the university hospitals, 2) data provided by cooperating partner institutions, e. g. the National Reference Center for Surveillance of Nosocomial Infections (NRZ) and partner health insurance companies, 3) PREPARED/MuSE´s own data collections and 4) publicly available data. Furthermore, data sets and models developed during the SARS-CoV-2 pandemic (e. g. the standard data set for quality management [28], definitions for nosocomial infections and admission with/because of SARS-CoV-2-infection) need to be integrated. Examples of successful monitoring and surveillance processes, such as the project "Dresden information forecasting tool for bed occupancy in Saxony (DISPENSE)" [29], and work on improving the quality of guidance parameters during a pandemic [30], as well as the evaluation of guidance parameters across health care sectors [31], will provide useful experience for the implementation of MuSE. Quick surveys as a link to the scientific community can usefully complement these processes and resources. As scalability is an essential element of the PREPARED infrastructure, the relevant data is predefined according to the setting, collected, trained and tested in non-crisis times and collected and monitored at an appropriate frequency and depth, depending on the presence or absence of an acute crisis.

Pathogen competence platform (PakoP)

For effective planning of response capacities in the core program of the NUM, a pathogen-related specialized authority is needed which maintains capacities that can be activated in the event of a pandemic situation to enable a rapid, agile and (pathogen-) specific pandemic response. It is also a central point of contact for policy makers as well as researchers from other disciplines, and provides the interface between pathogen research and practical implementation. This specialized authority must be structurally anchored and implemented over the long term to provide a strong and broad basis for preparedness and response to future pandemics. The need is primarily for virology, but also for other microbiological aspects in selected areas.

The proposed Pathogen Competence Platform (PakoP) should consist of a main committee of approximately 10–15 members that meets regularly during the interpandemic phase and convenes a pathogen-specific task force for the duration of a pandemic situation/crisis in accordance with the WHO and the PREPARED governance. The composition of this task force is based on the current epidemiological situation, the perspectives represented within PREPARED, and the infrastructure and its resources are available at the various sites (e. g. pathogen-specific expertise, biosafety laboratories, animal testing facilities, special tests, diagnostics, prevention, hygiene). Depending on the latter factors, working groups register as a standby option for "their" pathogen. In the event of a pandemic, the main committee and the convened task force work on defined and time-critical tasks and ad hoc issues using agile government methods. PakoP and the Task Force can act as experts in the allocation of rapid research funding for pandemic-related research and clinical trials.

Evidence syntheses and trustworthy recommendations (ESVE)

In addition to the monitoring and surveillance of comprehensive information for primary evidence generation, the derivation of evidence-based and trustworthy policy recommendations through evidence synthesis plays a central role for clinical questions as well as for public health issues and health-related political decisions [1]. The main objective of the ESVE core functionality is to develop (ultra-)rapid, high-quality, interdisciplinary, evidence-based and trustworthy recommendations in a multistep process. During the SARS-CoV-2 pandemic, it became clear that decisions, such as the introduction of mandatory masks or curfews could not be adequately supported by the traditional methods of evidence-based medicine (EbM) due to the inherent time lag of such approaches [32]. Therefore, "ultra-rapid" evidence syntheses will be used to provide a preliminary overview of the current situation within a very short time frame (e. g. one week). Subsequently, the question to be answered can be addressed with more rigor, e. g. by more detailed evidence syntheses (possibly living evidence syntheses), mathematical modeling, or filling evidence gaps by activating related functionalities such as primary data analysis in the MuSE or the planned NUM cooperative study network. Evidence syntheses and recommendations for action will adhere to the principles of

transparency, multidisciplinarity and appropriate methodological standards and need to be adaptable to the availability as well as type and quality of studies at different points in time during the pandemic. It must be understood as a dynamic, iterative process, with substantial involvement of a multidisciplinary recommendation group representing relevant disciplines and with links to relevant guideline groups and organizations such as the Association of the Scientific Medical Societies in Germany (AWMF).

Regional networking and implementation (ReVI)

The experience of the SARS-CoV-2 pandemic has shown that infections can spread very differently in different regions and that containment is a local task. Networking with regional stakeholders is essential to define the dynamics of spread within a region and to rapidly identify and reduce risk factors. This function is performed by the core functionality Regional Networking and Implementation (ReVI). The unit creates prototypes for multi-professional and multi-perspective networks in health regions (*clusters*) and acts as a direct link between MuSE and ESVE. The transfer of recommendations from the other PREPARED functionalities (especially MuSE, ESVE, HRM and StraKo) to the respective regions plays an important role in order to address regional developments. In a bidirectional manner of communication, emerging questions from regional clusters are communicated to the respective functionalities in the PREPARED infrastructure, which may allow recommendations on regional issues and challenges to be derived. The ReVI therefore operates at the meso level between the regional partners within a cluster (micro level) and the PREPARED infrastructure (macro level) and focuses on establishing a bidirectional connection of information and data exchange between the regions and the PREPARED infrastructure in order to build a network as a communication platform. In order to fulfill these tasks, the ReVI needs locally appropriate networks to realize the targeted exchange of information between the relevant regional partners.

Strategic communication unit (StraKo)

In any pandemic or other health crisis, consistent, transparent and targeted communication by the NUM and all associated stakeholders is essential. This can counter the dangers of information overload, including false or misleading information ("Infodemic" [33]) and mixed messages to the public. The supporting functionality StraKo therefore aims to bundle statements from the health and healthcare research so that scientists are not only able to speak as individuals, but also as spokespersons for and on behalf of PREPARED within the NUM. Further tasks of the StraKo include collecting and bundling inquiries from politics, society and the media and forwarding them to the research networks integrated in PREPARED. The StraKo is also tasked with prioritizing these inquiries, presenting scientific evidence in a target-group-oriented manner, especially for policy makers and the media, training communicators, and producing position papers on a regular basis. The members of the StraKo will also be responsible for drafting a code-of-conduct that will define the basic communicative actions (in terms of external communication) of the NUM and will be binding for all actors involved. Key component of the code-of-conduct will be to clarify whether or not a statement or position taken in public is an official position of PREPARED. Despite the implementation of the StraKo, certainly no one will be denied their (scientific) freedom to express their personal position in the media or elsewhere.

Human Resource Management (HRM)

During the SARS-CoV-2 pandemic, limitations in human resources management have been a key factor compromising adequate reactions by healthcare systems [2, 34–49]. Even before the pandemic, adequate staffing with qualified healthcare workers (HCW) has been challenging the German healthcare system. This situation is still prevailing, as discussed in detail e. g. in the current report of the German Expert Council for Health and Care [42]. For promoting health system resilience and crisis preparedness [2], three aspects have been proven important in a pandemic: 1) protecting and supporting physical health of HCW, 2) maintaining and supporting mental health of HCW, and 3) securing skilled labor and qualifying new workforce. These aspects are addressed in the proposed supporting functionality Human Resource Management (HRM) unit within the proposed PREPARED infrastructure.

For protecting and supporting physical health of healthcare workers, experts in the fields of Infection Prevention and Control, Hospital Hygiene, Occupational Medicine, Medical Psychology, Virology, and Microbiology will cooperate within HRM. They will provide training materials and implementation concepts to address challenges caused by newly evolving pathogens and other crisis threats in an agile way [46]. HRM will work together with MuSE, ESVE, PakoP and ReVI in order to be able to consider the most recent information and evidence, and distribute recommendations and trainings to affected HCW teams.

For maintaining and supporting mental health of healthcare workers, experts in the fields of Psychiatry and Psychotherapy, Psychosomatic Medicine, Medical Psychology, and Occupational Medicine will cooperate within HRM. Together with MuSE and ReVI, HRM will identify regional needs and burdens based on the data-driven regional surveillance (e. g. by combining indicators of mental health, intention to leave the job, and adequate staffing). Based on the new S3 Guideline "Mental Health of Healthcare Workers in Persisting Disaster Situations" [50] and its guidance in the fields of structural prevention, health knowledge and behavioral prevention, HRM will adapt the guidance to newly evolving threats, i. e. update and focus it, distribute implementation and teaching materials, offer consultations for regional teams and support and monitor guideline implementation.

For securing skilled labor and qualifying new workforce, experts in the fields of Intensive Care, Emergency Medicine, Anesthesiology, Infection Prevention and Control and further affected disciplines will work together in order to provide the foundations and materials (e. g. in an up-to-date training library) for evidence-based programs to further qualify existing employees and train and qualify newly recruited or non-specialist healthcare staff to handle newly emerging threads and challenges. The S1-Guideline „Empfehlungen zu Schulungen von Mitarbeitenden im Gesundheitswesen bei Einsatz während der COVID-19-Pandemie" [51] can serve as an example. Together with MuSE,

HRM will monitor resources and needs for qualified healthcare workforce. Additionally, HRM will facilitate consultation to infection prevention and control teams ("consult the consultants").

Rapid Reaction- and Response-Cockpit (R^3-Cockpit)

The objective of the R^3-Cockpit is to ensure that all processes and measures within a PREPARED infrastructure and between the individual core functionalities interact consistently, comprehensively and with as little redundancy as possible. To achieve this, both administrative and scientific processes are monitored, bundled and structured there. Central tasks of the *scientific coordination* are the systematic compilation of transfer-relevant findings and corresponding recommendations for action from the core functionalities MuSE, PakoP and ESVE as well as the integration of scientific networks and the corresponding resources. *Administrative coordination* includes the management of contracts and agreements, of contacts and networks to the relevant stakeholders and institutions as well as the technical, editorial and content maintenance of the R^3-Hub. The Hub is the virtual manifestation of a part of the R^3-Cockpit and its core function is the semantically useful bundling, updating and provision of all information generated within PREPARED (networks, data access, literature, networking of experts, etc.) for all involved stakeholders on a corresponding platform (or dashboard). In addition, basic tools are provided in the R^3-Cockpit. These include, for example, strategic links to networks such as the modeling network MONID or quick survey tools, that should be used to obtain the expertise of relevant stakeholders in a standardized, structured and systematic manner in quick surveys on currently urgent issues. Moreover, the R^3-Cockpit provides toolboxes that are continuously developed within the core functionalities of PREPARED. The toolboxes include systematic compilations of concrete methods, standardized operating procedures (SOPs), templates, flowcharts, manuals, etc., which provide the research actors with tools for the rapid collection, and above all, synthesis and integration of scientific evidence as well as trustworthy recommendations for action in acute situations. Appropriate technical implementation should ensure that all stakeholders can access and use these tools quickly and without barriers.

Governance

Studies during the SARS-CoV-2 pandemic have shown that, regardless of the specific leadership style, supportive leadership can have a positive impact on the health care system, the healthcare professionals, and related processes [18, 52–54]. At a higher level, the German health care system is governed by a joint self-administration. At the level of large providers such as university hospitals, this self-governance is implemented through hierarchical governance. However, during the SARS-CoV-2 pandemic it became clear that top-down (hierarchical) governance systems have a negative impact on responsiveness, especially under uncertain and constantly changing circumstances [55–57].

This indicates the need for a paradigm shift in the governance of at least the health research system, combining top-down clarity (leadership) with bottom-up co-determination and decision-making (participation) [55]. The aim of the PREPARED governance is therefore to explore contemporary governance for pandemic preparedness and response, in particular whether leadership can be faster, more innovative and more resilient in crisis situations by applying agile methods and strengthening resilience through a combination of top-down leadership and bottom-up participation. To investigate this question and to ensure a combined approach of leadership and participation, PREPARED develops potentially suitable agile methods, integrates them into its governance and organization and evaluates these measures on an ongoing basis. The governance of PREPARED is based on a clear, hierarchical structure and an unconditional commitment to collaboration between relevant stakeholders. In the interpandemic phases, agile methods will be used for training purposes in order to keep the democratically legitimized partners and the system flexible and highly adaptable in the event of a future pandemic or other crisis. In addition, agile methods will be trained and used for organizational development during interpandemic phases. In times of crisis, agile methods can be actively used in order to achieve the central goals of PREPARED.

All functionalities have been ethically assessed and evaluated during the concept development. From NUM´s perspective and with regard to already existing components, the PREPARED infrastructure will add a missing component, probably best described as a *Surveillance and Rapid Reaction and Response Platform*, which 1) will increase the resilience of research and health system in crises situations, addressing the needs of the constant and seasonal challenges, 2) will use 1) to train all functionalities and interactions, and will thus 3) increase performance during crises situations based on 1) + 3) and through stress tests, thus improving resilience.

CONCLUSIONS AND OUTLOOK

The organization of scientific research and health policy advice during the SARS-CoV-2 pandemic was characterized by slow and inefficient processes in the implementation of conventional methods of evidence-based medicine and insufficient coordination in the communication of evidence. Starting from this problem, the concept for a research infrastructure for pandemic preparedness in Germany developed by PREPARED aims at a collaborative, rapid, efficient and sustainable response to social and medical threats caused by (health-)crises. It addresses the challenges faced by the university-based health research system during the past SARS-CoV-2 pandemic. The proposed PREPARED research infrastructure will provide a framework and basis for efficient collaboration, targeted cooperation and communication in both interpandemic and pandemic phases. The four core and three supporting functionalities cover all relevant fields of action for improving the resilience of the health research system. In a next step, the infrastructure will undergo a proof-of-concept phase by testing two hypothetical but realistic use cases (A: antimicrobial

resistance due to a sudden increase in Carbapenemase-producing bacteria – a “slow but accentuated pandemic”; B: (classical course) pandemic with a newly introduced zoonotic influenza A virus (respiratory transmission) reaching Europe). The PREPARED infrastructure will be implemented permanently after a comprehensive scientific evaluation, considering these results. Once the PREPARED concept has been successfully implemented, it will serve as a collaborative national infrastructure that complements the RKI´s pandemic concept to maintain the preparedness of the German health research system in future crises and thus increase its resilience.

Compliance with ethical guidelines

In preparing this manuscript, the authors have adhered to the latest version of the “World Medical Association Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects”.

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Conflict of Interest

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