H2020-DSR-4-2014

PANDEM

Pandemic Risk and Emergency Management

D5.4 PRIORITIES FOR RESEARCH AND TRAINING

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1. BACKGROUND

Infectious diseases with pandemic potential are emerging at a greater pace than ever before as is the threat for deliberate use of biological weapons. These threats to global health security are impacted by factors that drive disease emergence, amplification and dissemination which include increased population density, and international travel. Pandemics have the capacity both to cause high numbers of cases, which would stress health systems to the limit, and cause serious disruption to social, economic and political systems. With the potential emergence of new threats growing all the time, the capacity and capability to conduct and translate research to protect health and increase health security must improve at the same rapid pace.

Central to effective pandemic response is a competent well trained health workforce which works in close collaboration with the security, civil protection and other relevant sectors and across national boundaries. Research and training to build interoperability is essential to support this cross-sectoral and cross-border work. This paper outlines research and training priorities identified by the PANDEM consortium with the aim of detecting pandemic threats early and responding in a timely and effective manner.

2. OBJECTIVES

The objectives of this report is to deliver on the two tasks outlined below.

Task 5.4 Priorities for research and training

1. To consolidate research findings from WP 2-4 in the areas of pandemic surveillance, communications and governance and identify where further research is required. The report will focus on research necessary to support effective cross-sectoral coordination and collaboration at transnational and European Union (EU) level.

2. To identify transnational opportunities for capacity building and training especially where EU-wide solutions require more standardization and predictability in risk assessment and management for cross-border response.

3. METHODOLOGY

The Integrated Gap Analysis (D5.2) analysed gaps and improvement needs identified in work packages 2-4. These improvement needs were further investigated by conducting a literature review of lessons learned from previous epidemics and pandemics. Lessons on research and training from that search will be outlined in this report. The literature search was mainly directed purposefully as many of the reviews on lessons learned following epidemics or pandemics are not found in formal literature searches but are on the websites of EU and international organisations such as European Centre for Disease Prevention and Control (ECDC), European Commission (EC), European Medicines Agency (EMA), World Health Organization (WHO). However, both PubMed and Embase were searched to answer the question: "What are the results/lessons from evaluations of effectiveness and impact of preparedness and responses by national EU governments and EU institutions".

This question was translated to a search on:

Lessons OR Learning OR Learn* OR Evaluation OR Effectiveness OR Impact

AND Preparedness OR Planning OR Prevention OR Response OR Control

AND Disease Outbreaks OR Epidemic OR Pandemic

AND European Union OR WHO OR EFSA OR ECDC OR EMA OR European Commission OR (Name of each Member State).

The search was restricted to the past 10 years and the English language.

This report also synthesizes research recommendations outlined in more recent deliverables including D4.3 on Gaps and Solutions for Pandemic Governance and D5.5 on Report of Workshop on Integrated Solutions for Pandemic Management. In addition to the literature reviewed in D5.2, a limited google scholar search was performed on serious gaming in health to support recommendations of the workshop in D5.5.

Recent publications by the EC including the European Council of Auditors report on "Dealing with serious cross-border threats to health" (1) were also reviewed for relevance to the PANDEM project and research and training priorities.

4. RESULTS ON PRIORITIES FOR RESEARCH AND TRAINING

4.1 GOVERNANCE, PLANNING AND COMMUNICATIONS

Report D4.3 presented an evaluation of knowledge, capability and capacity gaps, priorities and candidate solutions for pandemic governance. A number of research topics were identified including a model legal framework for pandemic preparedness and response, research into factors relevant to increasing trust in public health authorities, supporting the EU's role in international pandemic governance and finally the development of a model for pandemic resource allocation to ensure equity in access to scarce resources.

4.1.1 Legal basis for pandemic governance

In a review of current trends in promoting legal preparedness for emergencies and their relevance in view of the recent Ebola crisis, Cohen *et al* note that much of this preparedness has been well developed in the United States (2). Due to factors stemming from the complexity of the European Union and the variability of the Member States' (MS) health systems, the authors consider that legislative interventions inadequately promote public health preparedness and response within Europe. They advocate that efforts to improve health preparedness in legal planning must be supported by adequate research. The PANDEM consortium has also identified a need for further research in Europe on the legal underpinning for proposed pandemic control measures. D4.3 discusses the value of a model emergency act which could lead to more coherent, coordinated and transparent measures across Member States in the EU and yet is flexible enough to be used in different legal systems. The process with input from all Member States would enhance public health legal capacity in Europe and would provide guidance for national emergency legislation with safeguards for individual rights.

The PANDEM consortium advised that agreement on a common language for preparedness plans or a repository where translated national plans are accessible to all would support effective pandemic preparedness and response. While ECDC and the WHO Regional Office for Europe have a repository for pandemic plans, many are not translated and not all EU countries have revised their plans since the 2009 pandemic.

The Commission on a Global Health Risk Framework for the Future was initiated in early 2015 under the leadership of the U.S. National Academy of Medicine. The report of the Commission on the "Neglected Dimension of Global Security" advises governments to revise public health law to facilitate the implementation of core capacities required for implementation of the IHR (3). The importance of adequate legislation to act as a foundation for a resilient health system was also emphasised by Kruk *et al* when drawing lessons from the Ebola epidemic (4).

4.1.2 Pandemic planning

Holmberg and Lungdren examined eight European pandemic plans published after 2009 in terms of framing of visions associated with the plans (5). They especially looked at signs of securitization of pandemic influenza. They argue that securitization was led by the WHO in the updated guidelines of 2013 where each WHO Member State is encouraged to conduct its own risk assessment and to adopt a framework of 'Emergency Risk Management for Health'. The examined plans varied in length from 47-247 pages. The national plans of Czech Republic, France and Switzerland all had official versions translated into English and the Scandinavian authors examined the plans of Denmark, Finland, Sweden and Norway. They also studied the United Kingdom plan published in 2011. The Swiss, Norwegian and UK plans describe how stakeholders have been consulted in the development of the plans but stakeholder involvement was not outlined in the remaining plans. The authors describe both the British and the French plans as the most securitized and that these plans use uncertainty about the nature of future pandemics in a strategic way, accepting that there are many unknowns about the future pandemic and that we must learn to deal with the crisis in a very uncertain context. Three of the countries use pandemic phases published by WHO in 2009, rather than the updated phases in the new 2013 WHO guidance (6). The other plans use a different system and number of phases or stages e.g. 4 in France and 5 in the UK. The authors describe the French and the UK as using risk-based staging and Denmark and Switzerland as using epidemiologically based staging. They also describe a difference in emphasis on the possibility to delay spread in a country describing the Danish and the UK plans as most pessimistic in that regard. The plans also differ in the prioritisation or main strategic objective; some plans prioritise protection of life and health of the population whereas others give equal weight to societal functions. Not all countries include mass vaccination of the total population while four countries mention this as a possibility. Some countries describe wide

deployment of antivirals in the early phases while others will mainly use them for treatment of serious disease and protection of at risk groups. Only Denmark and Finland mention adverse events following immunization, referring to the association of narcolepsy with the use of AS03-adjuvanted pandemic vaccine (Pandemrix) in 2009 in Sweden, Finland and other EU countries. While all plans state that ethical considerations are necessary, some defer further discussion to other separately published frameworks. Finally, the authors argue that to fully understand the framing it is necessary to further research the process of planning in each country. They argue that the different approaches should be further discussed between the Member States and possible reframing be considered to improve interoperability of pandemic plans within Europe.

In a review of civil-military co-operation in Ebola and beyond, the authors call for more evidence, analysis and guidelines on the type of health activities that could or should be undertaken by military personnel in humanitarian crises before we need to respond another major epidemic (7). There also needs to be discussion and further research on a redefinition of the military role along with definition of the role of civil protection entities during a pandemic. Providing support to vulnerable citizens in our societies when health systems are overwhelmed in a severe pandemic is another research priority. There needs to be a multi-agency/departmental input into pandemic plans to ensure that agreed interaction procedures with military and civil protection organizations are fully incorporated. PANDEM also recommends research to establish a shared nomenclature for disaster management and health emergency management to improve cross-sectoral collaboration and pandemic response.

4.1.3 Sharing of best practice in pandemic preparedness

The PANDEM consortium expressed concern that learning from research projects may often be lost after projects finish and expressed the need for a knowledge sharing repository for outputs from key projects. In their article 'Creating an online "promising practices" clearinghouse for pandemic influenza ', LaFrance *et al* describes efforts to create, share, and sustain an online clearinghouse of expert-reviewed "promising practices" in pandemic influenza preparedness in the United States (8). Practices were available in four areas: models for care, communication, mitigation, and at-risk groups. The authors say the clearing house enables planners to share the benefits of drawing on each other's good practices. Candidate practices were reviewed by an expert panel. To merit final inclusion,

a practice was required to (1) be promising, in the best judgment of expert reviewer(s); (2) contain useful, tangible materials; (3) be generalizable or transferable to other agencies/stakeholders; (4) have relevance beyond the jurisdiction that created it; and (5) not have any obvious flaws that would prevent it from being potentially effective. The authors say this approach may be a valuable model. In another effort to improve public health systems research, the US CDC supported the establishment of nine Preparedness and Emergency Response Centres in accredited US Schools of Public Health (9). The Centres study the main components of the public health emergency preparedness system in the United States (see figure 1 below). Examples of studies include how to better use after action reports and exercises for performance improvement. A more recent focus is on translation strategies to ensure the learning is incorporated into local use, widely disseminated and broadly accessible.

Figure 1 Main components of the US Public Health Emergency Preparedness system

''In the past year, I have been struck by how important measurement is to improving the human condition. You can achieve incredible progress if you set a clear goal and find a measure that will drive progress toward that goal'' Bill Gates.

''What gets measured gets done'' Peter Drucker (Austrian-born American management consultant, educator, and author).

In recognition of the importance of measurement, the Association of State and Territorial

Health Officials (ASTHO), through a cooperative agreement with the US Centers for Disease Control and Prevention (CDC) Office of Public Health Preparedness and Response (PHPR), is creating an annual measure of health security and preparedness at the national and state levels: the National Health Security Preparedness Index (NHSPI) (9). Within Europe, PANDEM recommends research on developing practical indices to facilitate benchmarking and quality improvement in preparedness.

4.1.4 Pandemic resource allocation

A further priority identified by the PANDEM consortium is the development of resource allocation models for pandemic planning and response. The implications of resource shortages (antivirals, vaccines, personal protective equipment (PPE), intensive care unit (ICU) beds, ventilators, staff etc.) in planning are often not explicitly understood by decision makers at national level and such modelling tools can be used for pandemic planning in conjunction with simulation exercises and training workshops. A resource modelling tool would allow Member States to select different scenarios (range of case attack rates and case fatality ratios) to support policy decision-making at national level. It would include the use of models to estimate requirements for pre-pandemic stockpiling and for response during a high-impact epidemic or pandemic. Development of such a tool in a phase II project would build on AsiaFluCap which is a publically available tool developed by the PANDEM partner LSHTM. This modelling tool focuses on pandemic influenza and allows for a comparative analysis of the effects of resource availability and consequences of different strategies of resource use, which provides guidance on resource prioritizing and/or mobilization at country level (10).

4.1.5 Trust and communication

D4.3 on the Identification of knowledge, capability and capacity gaps, priorities and candidate solutions for pandemic governance identified a need for research directed towards increasing trust in public health institutions by identifying factors which facilitate and impede the development of trust and the role of communication tools and strategies in notions of trust. In a literature review commissioned by ECDC on effective risk communication for the prevention and control of communicable diseases in Europe, the authors demonstrate that there is an impressive body of literature on risk communication relevant to the prevention and control of communicable diseases but that the "area lacks rigorous empirical evidence and is further challenged by the complex and unpredictable

ways that individuals perceive risk and the environmental, social, cultural and linguistic factors through which risk communication is viewed" (11).

D5.5 report on Workshop on Integrated Solutions for Pandemic Management recommended the development of a higher quality evidence base to enable better design, monitoring and evaluation of pandemic communication interventions for Member States. Research needs to be done to establish how countries can be most effective, clear and consistent in their messaging. Targeting specific groups can be difficult, given lack of baselines and prior systematic knowledge. Public health authorities have limited visibility over social media "outbreaks" of misinformation. Early warning systems for social media disinformation may enable mechanisms to react in a timely manner and reassure the general public in relation to myths and unfounded rumours. Terms like 'infoveillance' and 'infodemiology' have been coined to describe new approaches to analysing social media sites to determine how alerts and public health warnings have been perceived, understood and followed.

There is a need to examine how the impact of communications on an outbreak response can be better measured and evaluated using pre-developed study designs and toolkits. This approach to research of effective communication strategies was emphasised in a systematic review of factors associated with uptake of vaccination against pandemic influenza (12). In order to enable longitudinal studies examining changes in belief over time, "sleeping" research protocols that could be initiated at the start of the next high impact epidemic or pandemic, should be developed now. Kruk *et al* emphasise the importance of building a well of trust before any crisis develops (4). They also emphasise the importance of rigorous evaluation research on past responses to enable crucial feedback for preparing for future challenges.

The PANDEM consortium advised that in order to plan and execute effective communications interventions, capacity/skills are needed from other fields such as advertisers, sociologists and anthropologists. Research aimed at demonstrating the effectiveness of utilizing these additional skill sets could promote their wider adoption by Member States.

ECDC through its commissioned report on preparedness planning for respiratory viruses in EU Member States encouraged further work to evaluate the recipients' perceptions and

impact of messages provided by authorities (13). This could facilitate fine-tuning and maximise the impact of health communication messages.

D5.2 on Integrated Gap Analysis (building on recommendations from D4.2) addressed the research needs to be done in ethical underpinning of pandemic response and pertains to the development of pandemic plans to include an ethical dimension. Very few plans include a detailed discussion of ethics, if it is included at all. Many plans presuppose a set of ethical values without any explicit mention on what those values are. Because the EU has 28 Member States with their own distinct cultures and values, it is critical to be frank and detailed about what an ethical response to a pandemic would mean.

Most research with regard to ethics and pandemic preparedness has been done in the USA and Canada. More research needs to be done on this issue with specific regard to Europe.

This area would benefit from a comprehensive review of all EU national plans from an ethics and human rights perspective. In the future development of ethical and human rights approaches to pandemic planning, research should be done on why ethics and human rights are such a low priority and aim to make ethical concerns a foundation of pandemic planning rather than an ancillary concern at both national and international levels.

4.2   SITUATIONAL AWARENESS: DETECTION, SURVEILLANCE, RISK ASSESSMENT AND PREDICTION

4.2.1 Background

Many research priorities identified by the PANDEM project are supported in the recent book on "Transforming Public Health Surveillance: Proactive Measures for Prevention Detection and Response" (14). In the chapter on research and innovations guiding public health surveillance in the twenty first century, the authors urge public health surveillance related research to focus on strengthening the evidence base for health policies and public health interventions. Developing synergies with other stakeholders such as those working in the area of One Health (veterinarians, environmentalists etc.) is essential not only in zoonotic diseases but also improved collaboration, communication and co-ordination can benefit areas such as anti-microbial resistance. One Health is "the collaborative effort of multiple disciplines — working locally, nationally, and globally — to attain optimal health for people, animals and the environment" (15).

New innovations in surveillance will include increasing use of big data and internet related surveillance. While the potential is enormous, the authors call for careful research and development of new analytical tools to ensure the data is fit for informing public health decisions. With many new data streams becoming available, there will be increased pressure on the public health workforce (already overstretched in many areas) to investigate an increasing number of signals, some of which will be false alerts. These limitations are further discussed in the section on training.

The Report on the "Neglected Dimension of Global Security: A Framework to Counter Infectious Disease Crises" called for a more robust research and development (R&D) strategy, to be co-ordinated by WHO – including the establishment of an independent Pandemic Product Development Committee (3). This Committee should focus on diseases of pandemic or epidemic potential such as influenza or coronaviruses. They advised that research efforts should also focus on anti-microbial resistance (AMR). They note that the approach taken should be akin to that of advanced defence organizations i.e. anticipate the future threats and invest in R&D to develop countermeasures. They advocate investment in three areas:

1) Development and strengthening of core capabilities.
2) Expansion or acceleration of ongoing R&D projects – a so called plug and play strategy where some developmental work on areas such as surveillance technologies, point of care diagnostics, personal protective equipment, drugs, vaccines, medical devices, population policy and implementations research has already taken place.
3) Innovation to discover new platforms that would have broad applicability to identify, prevent and treat infectious diseases with pandemic potential.

The research based vaccine industry published their perspective on lessons learned following their experience of pandemic influenza A (H1N1) (16). They urged the further development of rapid pandemic epidemiological research capabilities to underpin assessments of the likely course and impact of future epidemics which could help inform policy decision-making and enhance modelling of vaccine demand. This supports the development of expertise in predictive modelling, a priority already identified in PANDEM. They also urged greater regional transnational collaboration combining vaccine effectiveness studies with European vaccine safety studies. Like many others, they called

for new communication approaches to address concerns over vaccine safety and build public trust. They advised that further transparency about the different roles of all stakeholders involved in immunization assessment and policy making could help avoid misconceptions about the nature of the collaboration required to protect against pandemic influenza.

At the request of its 194 Member States in May 2015, the WHO has convened a broad coalition of experts to develop an R&D Blueprint for Action to Prevent Epidemics. Already several consultations have taken place to identify bottlenecks to international collaboration, agree basic data sharing principles and explore innovative clinical trial models for the assessments of vaccines, diagnostics and medical treatments. The blueprint acts as both a convening mechanism and an instrument to articulate technical guidance for R&D preparedness (17). A database of research preparedness resources to be integrated into the WHO Global Health R&D Observatory, a central knowledge hub, has been set up (18). Initial steps have been taken to explore insurance options to address liability issues in case of use of an experimental vaccine or product during a public health emergency due to a high impact epidemic or pandemic. Further work is planned on a Material Transfer Agreement capacity building tool to inform negotiations on sharing biological samples and the concept of biobanking, a "virtual resource" of national biobanks linked by an information sharing platform, will be further developed. This process will be developed under a shared system of governance and decision making following principles of equity and benefit sharing, as are embodied in the Pandemic Influenza Preparedness Framework for the sharing of influenza viruses with pandemic potential (19) as well as in the Nagoya Protocol to the Convention on Biodiversity (20). Progress has also been made on data sharing in Public Health Emergencies. The International Committee of Medical Journal Editors has revised its policy to explicitly encourage rapid and early data-sharing, and to assuage concerns that subsequent scientific publication might be adversely affected.

The report of the Review Committee on the functioning of the International Health Regulations (IHR) in relation to Pandemic (H1N1) 2009 called for a comprehensive influenza research and evaluation programme. Key research goals include: strengthen surveillance technology and epidemiological and laboratory capacity to improve detection, characterization and monitoring of new viruses; identify viral and host determinants of transmissibility and virulence; develop rapid, accurate, inexpensive point-of-care

diagnostic tests; enhance the accuracy and timeliness of modelling projections; create broader spectrum, highly effective, safe and longer-lasting vaccines; hasten vaccine production and increase throughput; devise more effective antiviral drugs and antimicrobials to treat bacterial complications; evaluate the effectiveness of drug, vaccine, personal protective equipment, personal hygiene and social interventions; assess the effectiveness and costs of border measures and enhance risk communication (21). The WHO public health research agenda for influenza is currently being updated (http://www.who.int/influenza/resources/research/about/en/).

4.2.2 Detection

The availability of sensitive and specific rapid point of care testing (POCT) as well as strategies for their implementation in an emergency is a priority for further research. Increased use of POCT would allow earlier detection of epidemics. Infrastructure to connect these results with the patients' electronic health care record and public health surveillance systems will be needed. Progress in public health genomics will allow recognition of host susceptibility factors and also facilitate improved typing technologies in detection of pathogens. A recent example of a POCT from Harvard University won the "Best of What's New" award for 2016. Using synthetic biology, they have developed an inexpensive test that could diagnose a patient with Zika in the field within a few hours, which they hope could be used to contain Zika or other viral outbreaks. The researchers envisioned a new class of diagnostics that is inexpensive and rapidly deployable to screen blood, urine, or saliva samples for Zika or any other RNA virus including Ebola, SARS, measles, influenza, hepatitis C, and West Nile fever. They freeze-dry synthetic gene circuits onto paper discs. These biomolecular circuits are activated when the paper is rehydrated with a droplet of sample fluid; the disc changes colour to indicate a positive result for Zika virus, similar to the visual readout of a home pregnancy test (22). So called FAST POC (facilitated fast access self-testing) is a further development where the patient obtains their own blood sample which then seals for automated testing thus limiting the chances of exposure to infectious agents (23).

The PANDEM consortium recommended that POCT should be linked with secure wireless data exchange. In addition, chain of custody should also use wireless methodology to track samples during transfer processing and reporting. This could be an adaptation of the

forensic chain of custody developed in the "Generic Integrated Forensic Toolbox (GIFT)" project, taking into account ethics and patient data confidentiality. The feasibility of incorporating these data into generic and outbreak information management system needs to be explored.

The UK Engineering and Physical Science Research Council (EPSRC) has granted I-SENSE £11M to "develop a new generation of warning systems for disease outbreaks" (24). The research uses mobile phone connected diagnostic devices to widen access to testing in GP surgeries, in the community in the developing world, and in the home. The research brings together academia, Public Health England and industrial and clinical partners and aims to promote early detection and control of outbreaks.

In D2.3 on Review of Diagnostic Technologies, the requirement for more widespread use of high-tech and up-to-date equipment [especially "open detection" equipment: electron microscopy, next generation sequencing and matrix assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry] was noted and translational research was advised to support its adoption. ECDC in a paper on a concept to integrate molecular typing into EU level surveillance data noted that molecular typing of pathogens that cause infectious diseases complements the traditional epidemiological surveillance by providing appropriate discriminatory analyses to foster the rapid and early detection of dispersed international clusters/outbreaks, to detect and investigate transmission chains and the relatedness of strains, and to detect the emergence of antimicrobial resistance and new evolving pathogenic strains. Molecular typing also supports studies to trace-back the source of an outbreak and identify new risk factors, as strains can be linked more accurately to epidemiological (incubation, route of transmission) and clinical data (severity) (25).

The PANDEM consortium also advised that semantic standards for EU laboratory information management systems (LIMS) are required to ensure interoperability between systems and ensure LIMS are capable of supplying data on epidemic and pandemic prone pathogens in commonly agreed data sharing formats.

The European Union is investing €45 million in research to fight outbreaks caused by emerging infections such as the Zika virus (26). Three consortia were selected for **EU Horizon 2020** funding for a total of €30 million: ZikaPLAN, ZIKAction and ZikAlliance. The

three research consortia will collaborate to fill the knowledge gaps on Zika infection and its consequences for pregnant women, new-born babies and adults, and they will also develop improved diagnostic tests and investigate options for treatment and prevention. Two additional projects are working on development of a safe, effective, and affordable vaccine against Zika virus infection – ZIKAVAX and INFRAVEC2. **COMPARE** is a large EU project with the intention to speed up the detection of and response to disease outbreaks like Zika among humans and animals worldwide through the use of new genome technology. If locally-transmitted Zika is detected in Europe, the clinical research project **PREPARE** (Platform foR European Preparedness Against (Re-) emerging Epidemics) has protocols ready to quickly collect crucial clinical data to improve patient management:

- The PREPARE ARBO virus study in the Balkans which started in May 2016 has been modified so that adult Zika cases, can be identified. The project is prepared to expand the study to Italy, France, Spain, Slovenia and Montenegro, areas where the *Aedes albopictus* mosquito is present, depending on how the Zika epidemic evolves.

- PREPARE has collaborated with ISARIC to establish publically available Zika research tools to collect standardised neonate and maternal clinical and laboratory data.

- Information regarding European laboratory preparedness to detect Zika infection has been collected from PREPARE and COMBACTE LAB-Net laboratory contacts through an ECDC Zika questionnaire and is currently being analysed.

ISARIC - International Severe Acute Respiratory and Emerging Infection Consortium - is a global initiative aiming to ensure that clinical researchers have the open access protocols and data-sharing processes needed to facilitate a rapid response to emerging diseases that may turn into epidemics or pandemics.

SPRINT-SARI (Short PeRiod IncideNce sTudy of Severe Acute Respiratory Infection) is an international, multi-centre, prospective, short period incidence observational study of patients in participating hospitals and intensive care units (ICUs) with SARI. The primary aim of this study is to establish a research response capability for a future epidemic/pandemic through a global SARI observational study. The secondary aim of this study is to investigate the descriptive epidemiology and microbiology profiles of patients

with SARI. The tertiary aim of this study is to assess the Ethics, Administrative, Regulatory and Logistic (EARL) barriers to conducting pandemic research on a global level. This study is supported by ISARIC, InFACT and PREPARE.

4.2.3 Participatory surveillance

Traditional public health surveillance depends on notification of infectious disease events from clinicians and laboratories. Increasingly non-traditional sources are supplementing capacity to enhance our assessment of public health situational awareness. For example, community engagement with partners in the corporate and educational sectors can deliver information on absenteeism from work and schools. Biedrzycki describes engaging communities to transform public health surveillance, and training and exercises with airport administrators to address specific infectious disease threats such as novel pathogen introduction via an arriving air flight (14). The building of stronger relationships with key community/cross-sectoral partners such as law enforcement and defence forces, civil protection, veterinarians, entomologists, NGOs, transport, corporate entities, environmental and meteorology experts, food safety agencies and academia is needed to strengthen early warning and detection as well as improved collaborations for response. Participatory surveillance also includes public participation of web-based infectious disease reporting sites. Ideally such a system would incorporate the addition of laboratory sampling to estimate accurately the proportion of such cases that have been truly infected. This would provide the Member States with the ability to quickly assess the impact of a pandemic, be it influenza or other pathogen, at community level, identify implications for essential services and plan response in real-time in collaboration with all stakeholders.

The PANDEM consortium recommended that a combination of tools be developed that could monitor large company absenteeism, school absenteeism and social media/internet based voluntary participatory population surveillance. The toolbox could be a manual of methodologies and tools to collect and present the data. It would be useful for business continuity and estimations of susceptibility in the population. This type of surveillance would be most helpful in the early stages of a pandemic when serological data is not yet available, but could also monitor the impact of mitigation in later stages. Participants advised that new tools could link health messaging to those who reported illness on the web just as retailers target advertising to those seeking information on the web. The

PANDEM consortium has advised further research into these non-traditional sources of surveillance to validate their usefulness and to weigh costs against utilities.

Progress in informatics, including information technology, present exciting opportunities to harness new data streams for more effective and efficient public health surveillance. Developments in electronic health care records can enable more timely detection of emerging disease threats if new data exchange systems and analytical procedures are in place. In CDC's vision for public health surveillance in the 21st century, global consensus standards on data exchange were recognized as essential as well as standards on ethical concerns, data sharing privacy and confidentiality (27). Even the most sophisticated and automated systems will however depend heavily on well trained human resources for analysis and interpretation of data. The role of public health informatics in enhancing public health surveillance is emphasized to enable exchange of high–value data and knowledge in a secure and timely manner. Transforming information systems from the old passive but often incomplete surveillance systems or time consuming active surveillance techniques into automated data acquisition will require resources and training. In the US, financial incentives have been put in place to encourage more meaningful use of data for public health purposes and to build the work force required.

4.2.4 Situational awareness platform

With increasing use of real-time data, dissemination of analysis results in a simple understandable display becomes increasingly important. A proactive approach would be to anticipate how such technology would be used in a major event and the US strategy on surveillance from CDC advocated further study in this area (27). The European Court of Auditors published a special report on "Dealing with serious cross-border threats to health in the EU: important steps taken but more needs to be done" (1). The report notes that there is currently no dedicated situational awareness platform or tool at EU level for maintaining a real-time overview of national public health measures taken for dealing with a serious cross-border threat (Para 61). It advises that there is scope to develop either a dedicated tool, or incorporate one as an integrated function in an enhanced version of the EWRS. Such a tool could also incorporate incident management functionality.   The PANDEM consortium has recommended careful research and evaluation to understand requirements at different phases of the emergency cycle and to assist policy makers in decision making on countermeasures and responses that are best suited

to the priorities of each of the Member States. A requirement analysis and usability study etc. could be implemented as a demonstrator/pilot for evaluation in a small number of countries. This would enable a common understanding of the decision-making challenges faced by policy makers, and a suite of customisable decision support tools designed to support stakeholder requirements.

4.2.5 Risk assessment

Risk assessments have become one of the corner stones of technical support given to Member States from organisations such as ECDC and WHO and have repeatedly been reported as important tools for decision-making. On occasion, however, risk assessments from national and international bodies have reached different conclusions. Further research is required on the process to enable understanding of different methodologies and underlying parameters studied. Standardized, ready-to-use templates would be especially useful within Member States for risk assessments of an unknown disease. For influenza and other infectious disease threats, work would be facilitated by sharing templates for the first few hundred (FF100) cases, as well as standardizing parameters so that modellers can share and compare data. There should also be consideration of designating sites for intensive monitoring of the FF100 cases.

4.2.6 Predictive modelling

The PANDEM consortium identified the need for further research and development in the area of predictive modelling to provide an informed analysis for policy makers. Chretien defines predictive surveillance as a type of surveillance that uses state of the art computer models and algorithms to predict the presence or absence of a pathogen in a geographic area (14). Current predictive surveillance applications use Bayesian methods, machine learning approaches, data assimilation, individual based modelling and other recently developed computational capabilities. Recently, developers of predictive surveillance models have adapted methods used in other fields such as weather prediction. Researchers have used these methods to predict influenza incidence using variously modified SEIR (susceptible, exposed, infected, recovered) models or individual based models. In a scoping review of influenza forecasting in human populations, Chretien *et al* make recommendations for developers of these forecasting models including to develop common practices, compare the utility of diverse models, include the likelihood of their forecasts (as in weather prediction '80% chance of rain tomorrow'), incorporate additional expertise from scientists and public health officials, incorporate research into

user acceptance and how public health officials actually use the predictions for decision support. Finally they urge efforts to link modellers and public health officials through seminars, exercises and other activities to foster mutual understanding and improve collaboration during emergencies (28). Ajelli *et al* reported that their transmission based model proved to be a valuable support for public health policy makers in planning interventions for mitigating the spread of the pandemic in Italy in 2009 (29). Similarly Baguelin *et al* report on a real time economic evaluation of vaccination against pandemic influenza/H1N1v in England using a dynamic transmission model that was used for policy makers in the United Kingdom (30). In a systematic review of mathematical modelling of combination strategies for pandemic influenza response the authors call for more evidence through targeted research (31).

Increasingly another source of data for incorporation into models includes genetic sequencing data of pathogens. Linking these massive amounts of data to routine more traditional epidemiological surveillance data is increasingly used to understand what drives transmission of infection through populations. This has huge potential to better guide control measures. In his chapter on using genetic sequence data for public health surveillance, Koopman urges greater collaboration on research between academic users of phylodynamics (the study of how epidemiological, immunological, and evolutionary processes act and potentially interact to shape viral phylogenies) and public health agencies (14).

D5.3 on Integrated Solution Specifications recommended the development of an integrated predictive modelling tool to provide timely estimates on pandemic evolution. The tool would draw from Big Data including vector data, animal health data, online feeds as well as traditional data sources

4.3 TRAINING AND NETWORKS

In order to respond effectively to pandemics, a knowledgeable skilled and effective workforce with the right skill mix is essential. Innovation is required to develop teaching practices and methods that can quickly reach and continuously update the public health workforce to respond to current and future health security threats.

4.3.1 Workforce capacity

The CDC surveillance strategy in the US called for a systematic approach for monitoring the public health work force (27). The strategy also documents the need for continuous learning and the use of teaching approaches to allow enhanced participation in the educational process by those in senior practice positions, combining distance learning with face to face instruction. The strategy includes evaluation to enable continuous improvement and also programme accountability. The need is no less in Europe to identify workforce gaps and the diversity and balance of disciplines required to counter infectious disease threats. Many health systems lack the capacity to systematically and dynamically quantify their own workforce shortages and assess the core competencies required to perform essential public health functions. Linked to this is ensuring adequate numbers of well trained staff. Enumeration studies of the public health work force in Europe are hampered by the different systems and nomenclature used in the different Member States.

In calling for a framework to counter infectious diseases, the report on the "Neglected Dimension of Global Security" advises the development of precise definitions and bench marks for core capacities against which countries can be independently assessed (3). The report highlights the importance of developing and implementing a public health system work–force strengthening strategy and plan. Strengthening disease surveillance systems require professional context of continuous learning and updating of guidelines based on changing needs and priorities. Integration of laboratory diagnostics with public health surveillance is essential as is collaboration between human, environmental and animal sectors in a One Health approach. There is a need for greater use of transdisciplinary One Health collaborative research to identify likely scenarios with increased risk of zoonotic epidemic/pandemic potential.

Training and capacity development needs also to be established across sectors prior to the emergence of a high-impact epidemic or pandemic to enable effective collaboration between all relevant sectors. Capacity should be developed also among staff in national public health agencies with anthropological, social science and crisis communication expertise. Multidisciplinary collaboration in training and exercises is seen as key to ensuring a synergistic approach to tackling emerging infectious disease threats in Europe. Joint public health and military exercises with cross-border components should be developed and implemented. The PANDEM has identified the need for improved laboratory

training, particularly in field situations. Training on biosecurity and biosafety should include use of personal protective equipment, management of stress and hazards, and accident avoidance and management.

The Advisory Group on Reform of WHO's work in Outbreaks and Emergencies encourages "long-term investments to increase integrated national, regional and global capabilities for risk assessment, management, communication and outbreak response in the Global Outbreak Alert and Response Network, as well as preparedness and prevention - especially in relation to risks posed by unfamiliar and potentially dangerous pathogens" (32). The second report of this group emphasized that governments have the primary role and responsibility to train national workforces who will be the first responders in an outbreak or an emergency (33). However, support should be provided through the provision of training and technical guidance. They also advised that more work is required to build robust capacity for systematized information management and protocols to enable sharing of information from multiple sources. This supports the need for trained health informaticians.

The PANDEM consortium identified a gap in the development of online and e-learning resources for training of health, security and civil protection professionals including first responders. Linking these to continuing professional development requirements in the Member States would encourage early adoption. The use of MOOCS (massive online open courses) is particularly suited for continuing education because they enable interaction, including quiz taking and online discussions with fellow course takers. In addition busy working professionals can take them at times convenient to themselves (34). Others have explored the effectiveness of a flipped classroom model, a type of blended learning where in class learning is integrated with on-line experiences. The defining characteristic of the flipped classroom model is that content and material are delivered primarily prior to the in-class time which can then be devoted to advanced concepts and collaborative learning (35). In a webinar for health care professionals on training for good clinical practice in clinical trials, Buckley advised that e-training needs to be protocol-directed, comprehensive, targeted at individual needs and deficiencies, individually paced, entertaining, brief, monitored, evaluated, and capable of providing certified competence as an outcome. A highly structured and integrated solution needs to use validated instructional design, engaging highly interactive presentations, tailored to individual needs and localized to language and culture of the learning site (36).

The Global Health Network was established to create a subject specific online community of researchers who can build collaborations, develop documents, share resources and exchange information (37). Its Global Health Training Centre provides links to online training resources across many relevant areas in laboratory sciences, disease surveillance and infectious diseases among others (38). The Global Health Network has recently announced the launch of a new seven-module eLearning course which has been adapted from the WHO training manual and resources on: 'Ethics in epidemics, emergencies and disasters: Research, surveillance and patient care'. The course offers comprehensive training exploring the wide range of ethical issues faced by health professionals and policy makers working in the context of epidemics/pandemics and disaster situations, focusing primarily on the key areas of research, surveillance and patient care.

Increasingly e-learning is seen as a way to increase access to good learning resources and reduce inequities in availability of life-long learning materials. In addition, user-oriented e-learning platforms offer the possibility to connect learners virtually, across organisational and geographical boundaries. In order to support continuous learning, the consortium considers the promotion of 'virtual communities of practice' of value. These approaches are potentially useful for the broad spectrum of sectors with a role to play in pandemic response.

4.3.2 Serious Gaming

Serious gaming was also suggested as a user friendly and innovative method for training. This has the added advantage of enabling training to take place without the added cost of travel and could be translated into commonly used languages.

Gentry *et al* have published a protocol in the Cochrane library to evaluate the effectiveness of serious gaming and gamification interventions for delivering pre- and post-registration health professional education compared with traditional learning, other types of e-learning, or other serious gaming and gamification interventions (39). They describe how gamification differs from serious games in terms of the design intention, with gamification interventions involving the application of game elements to something with a utilitarian purpose, and serious games designed as full-fledged games for a purpose other than just entertainment. Multiplayer functions allow opportunities for collaborative learning. Ricciardi and De Paolis have already published a review of serious games in

health professions (40). They note that emergency services, triage and first responders are the fields where they found the highest numbers of developed serious games. They found few examples of collaborative learning but describe one game "virtual heroes" where in phase one the user is introduced to teamwork and communication skills and in phase 2 up to 32 players use these skills to play together in predetermined roles of doctor, nurse, technician etc. As most health care workers work in teams they advocate greater use of collaborative learning.

Chittaro *et al* investigated the contribution of serious games for emergency preparedness, and found that interactive simulations (games) had an advantage over non-interactive simulations, as the interactivity enhanced users' perception of threat, which is a desirable outcome in the situation when target audiences (e.g. health care workers) are known to underestimate the level of threat (41).

If properly designed, serious games can offer a dual use, both in training staff, as well as in evaluating bioterrorism and emergency readiness (42).

Besides an added value for training and education, applications of serious games for modelling and simulating population response to mass casualty events, including pandemic influenza, are being further investigated (43).

4.3.3 Networks

The PANDEM consortium has built a network of stakeholders and users working in the area of pandemic preparedness and response from a range of sectors. Front line practitioners in the public health, security, emergency management and civil protection sectors have provided invaluable input to the identification of gaps and solutions over the project duration. There will be a legacy phase when the project is completed where updates will be provided to members of the PANDEM network and this dialogue will continue through links with DG HOME's CoU on Safe, Secure and Resilient Societies.

The PANDEM consortium suggested further development of laboratory networks to share protocols/guidelines/standards/biological material in order to reach standardisation concerning: request forms, diagnostic processes, development and validation of new tests, sample inactivation, laboratory and equipment decontamination, result transmission (format and communication channels), biosecurity and biosafety. Development of EU public health legal networks working closely with public health colleagues will facilitate

training in public health law. Networks of communicators have been established under the aegis of the Health Security committee but recent experience, during the pandemic in 2009 and again during the recent Ebola and Zika epidemics, has highlighted the need for continuous training in this area. Workshop participants (as outlined in D5.5) opined that communicators can sometimes fail to follow risk communications principles, creating lack of trust when they are found to have been over-confident or to not have revealed full details to the population upon request. Additionally, politicians and officials can occasionally overrule technical guidance on using risk communications. In general, investment in training on risk communications was thought to be important.

In 2001, the EU Civil Protection Mechanism was established, fostering cooperation among national civil protection authorities across Europe (44). The Mechanism currently includes all 28 EU Member States in addition to Iceland, Montenegro, Norway, Serbia, the former Yugoslav Republic of Macedonia and Turkey. The European Emergency Response Capacity (EERC) consists of a voluntary pool of resources to be used to respond to emergencies, which are pre-committed by the countries participating in the EU Civil Protection Mechanism. The European Medical Corps is part of the EERC. The Mechanism also provides participating countries with the opportunity to train their civil protection teams. By exchanging best practices and learning, teams increase their ability and effectiveness in responding to disasters. Additionally, the Mechanism provides emergency communications and monitoring tools, overseen by the EERC through the Common Emergency Communication and Information System (CECIS), a web-based alert and notification application enabling real time exchange of information between participating states and the ERCC. The EU Civil Protection Mechanism runs an active and comprehensive training programme, offering experts from all over Europe a deeper knowledge of the requirements of European civil protection missions. The training helps experts improve their coordination and assessment skills in disaster response.

The European Commission is working with the Global Research Collaboration for Infectious Disease Preparedness (GloPID-R), a global network of major public and private funders of preparedness research. Funders, public health authorities from affected countries, as well as experts and researchers in relevant fields from the affected countries and GloPID-R members are invited to establish research priorities, track research capacity, and share any research activities that are ongoing or under development. GLOPID-R has set the goal of initiating a coordinated international research response between its members, within

48 hours of a declared public health emergency. The network has 23 members from across the globe with WHO as an observer. The secretariat of GloPID-R initiative is funded through EU's Horizon 2020 programme and ran by the Fondation Merieux and the University of Oxford. The European Commission's Directorate General for Research and Innovation is Chair with Vice Chairs coming from Brazil, Canada, France and South Africa.

The Coalition for Epidemic Preparedness Innovation (CEPI) is an initiative established following the Annual Meeting of the World Economic Forum in Davos in January 2016, where stakeholders from governments, foundations, industry and civil society discussed the urgent need for a fresh approach to the development of vaccines for infections of epidemic potential (45).

4.3.4 Exercises

ECDC commissioned a report on preparedness planning for respiratory viruses in EU Member States (13). The report suggested areas for strengthening the implementation of EU Decision 1082/2013 on serious cross-border threats to health. The authors found that many of the challenges in preparedness planning stemmed from financial pressures due to budget cuts which reduced the opportunities for conducting preparedness exercises and training and ensuring that the lessons learned from such exercises are then incorporated into protocols. "Executing table-top public health preparedness exercises could support efforts to ensure sustainability of capacities, and could be organised by national authorities, complemented by input from international organisations". They specifically recommended intersectoral simulation exercises to help enhance the interoperability of preparedness plans of the different sectors such as civil protection, transport etc. Multi-country simulation exercises which would promote cross-border collaboration could prove to be a good investment and would support Article 4 of the EU Decision 1082/2013 on serious cross-border threats to health. Such exercises could explore the effectiveness of control measures at the borders for prevention of transmission of epidemic prone diseases. For many diseases border screening is resource intensive and there is significant opportunity cost for other public health measures if border screening is in place. Communication as a border measure has been seen as a more effective means to encourage self-reporting and early detection of disease (46). In a systematic review of travel restrictions for the containment of influenza the authors advise that travel restrictions may have intuitive appeal to policy makers because they demonstrate that a tangible attempt is being made to prevent the ingress of a novel virus or prevent onward

spread. " However such an attempt is not always effective" (47). Multisectoral exercises could explore the costs and benefits of border controls, thus facilitating a more co-ordinated approach across Europe.

Ablah *et al* describe a multi-county multidisciplinary inter agency training exercise in the US as an innovative solution to provide training via electronic media to public health employees in their local offices (48). The exercise was designed as a simulated outbreak of an undisclosed, unintentional infectious disease and took place over the period of one month. The longer duration of this exercise encouraged participants to communicate over a period of time which reinforced functional partnerships and encouraged the sharing of real life investigation protocols and communication technologies such as conference calls etc. The funding of this exercise was provided by US federal bioterrorism funds to improve public health infrastructure.

In the EU, there is a financing mechanism for exercises in the frame of the DG ECHO Union Civil Protection Mechanism (http://ec.europa.eu/echo/en/funding-evaluations/financing-civil-protection/calls-for-proposal). This is to organize exercises between components of the EERC from at least three countries.

In a review of planning against biological terrorism: lessons from outbreak investigations, the most critical component for detections was education of frontline health care workers in order to shorten the time between outbreak onset and reporting (49). This was recognised as a problem by the PANDEM consortium where many first line responders are unfamiliar with clinical presentations of rare pathogens especially those that are only likely to be encountered in scenarios of deliberate use. It was suggested that serious gaming could deliver suitable lessons including protocols for collaborative working with law enforcement and military services.

In summary, training is recognized by the PANDEM consortium as a key factor in preparation for high-impact epidemics and pandemics. Intersectoral and multidisciplinary training is key not only to improve knowledge but also to forge relationships which will enable more effective responses during a high-impact epidemic/pandemic. New methods of sharing novel ideas and learning need to be developed, recognizing that many public health professionals are experiencing a limitation in resources and time for international travel.

5. CONCLUSIONS

The PANDEM consortium has identified the following research and training priorities to strengthen capacity for pandemic preparedness and response, with specific emphasis on research that cuts across sectors and national boundaries and training where EU-wide solutions require greater standardization to support interoperability. The final priorities selected for further consideration in a phase II project will be chosen and described in the PANDEM roadmap.

5.1 GOVERNANCE, PLANNING AND COMMUNICATIONS

- Strengthening the legal basis for pandemic governance and pandemic response measures in Member States: consideration could be given to the feasibility of developing a model emergency act.
- Expansion of the repository for pandemic plans in ECDC to include translated versions of all Member State plans.
- Development of a shared nomenclature for disaster management and health emergency management to improve cross sectoral response.
- Improve sharing of best practices by developing an EU "clearing house for promising practices" in pandemic preparedness. Building on the work of ECDC under Decision 1082, intersectoral and multi-country workshops could examine how best to widen the approach to development of pandemic plans to include sectors outside health (e.g. civil protection and military).
- Development of practical indices of Member State preparedness to facilitate benchmarking and quality improvement in EU preparedness.
- Development of a resource modelling tool for pandemic planning to support policy makers at national level in Member States in predicting impact of a pandemic and estimating requirements for pre-pandemic stockpiling.
- Identification of factors which facilitate and impede trust in public health and government institutions and the role of communications tools to build and maintain trust.
- Development of a high quality evidence base to enable better design, monitoring and evaluation of pandemic communications interventions in Member States.

- Development of early warning systems for social media disinformation and research directed at the most effective methods of early interventions to counteract such myths.

- Development and use of pre-developed study designs and toolkits to examine the impact of communications during epidemic/pandemic responses.

- Research to demonstrate the effectiveness of utilizing additional skills from fields such as advertising, sociology and anthropology in outbreak communications.

- Review of EU National Pandemic Plans from an ethics and human rights perspective.

5.2   SITUATIONAL AWARENESS: DETECTION, SURVEILLANCE, RISK ASSESSMENT AND PREDICTION

- Development of sensitive and specific rapid point of care testing with strategies for their implementation in an epidemic.

- Research to enable real time linkage of point-of-care test results with laboratories and public health surveillance systems and research into factors enabling the more widespread adoption of the newer diagnostic methodologies.

- Semantic standards for EU laboratory information management systems to ensure interoperability between systems and ensure LIMS are capable of supplying data on epidemic and pandemic pathogens in commonly agreed data sharing formats.

- Validation of the usefulness of non-traditional sources of surveillance data including the development of innovative tools to monitor large company absenteeism, school absenteeism and internet/social media.

- Identification of requirements for a situational awareness platform at EU level for maintaining a real-time overview of national public health measures for serious cross-border threats to compliment the EWRS system.

- Standardized methodologies for developing, ready-to-use risk assessment templates for Member States an unknown disease, influenza and other infectious threats. This work would be facilitated by sharing templates for FF100 cases, as well as standardizing parameters so that modellers can share and compare data. There should also be consideration of designating sites for intensive monitoring of the FF100 cases.

- Development of an integrated predictive modelling tool to provide timely estimates on pandemic evolution. The tool would draw from Big Data including vector data, animal health data, online feeds as well as traditional data sources.

5.3   TRAINING AND NETWORKS

- Systematic approach to evaluate the public health workforce capacity of Member States developed and agreed to identify workforce gaps and the diversity and balance of disciplines required to counter infectious disease threats.

- Multidisciplinary collaboration in training and intersectoral simulation exercises to enhance the interoperability of preparedness plans of the different sectors such as civil protection, transport etc. Multisectoral exercises could explore the costs and benefits of border controls, thus facilitating a more co-ordinated approach across the EU.

- Training in EU laboratories, especially in field conditions involving biosecurity and biosafety, self-protection and adequate use of PPE, stress and hazards management, accident avoidance and management.

- Training of national communicators in effective risk communication methods.

- Development of online and e-learning resources for the training of health, security and civil protection professionals on pandemic preparedness and response.

- Development of serious gaming applications to provide an interactive user friendly and innovative method for training. This has the added advantage of enabling training to take place without the added cost of travel and could be translated into commonly used languages.

- The establishment of a European modelling network to examine resource allocation models and enable predictive modelling.

Collaborative, cross-sectoral research and training will enable the development of novel approaches and innovative solutions that lead to more resilient societies to face inevitable future pandemic threats.

The PANDEM consortium is developing a roadmap for a phase II project to build capacity for pandemic management across Member States. PANDEM has built a network of stakeholders and practitioners working on pandemic preparedness and response with links to DG HOME's CoU on Safe, Secure and Resilient Societies. Working with front line users in

the public health, security, emergency management and civil protection sectors over the final stages of the project, solutions identified will be refined and developed to ensure that all sectors can collectively contribute to improving the health security of EU citizens.

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