WP2 STUDY & ANALYSIS

TASK 2.2 REFERENCE GUIDE OF UNSOLVED SCIENTIFIC QUESTIONS RELATED TO PANDEMICS AND EPIDEMICS

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Action plan on SiS related issues in Epidemics And Total Pandemics

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D2.2 Reference Guide on Scientific Questions

Task: 2.2 Reference guide of unsolved scientific questions related to Pandemics and Epidemics

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EXECUTIVE SUMMARY

The aim of this report was to outline, from the scientific and technical literature, the main unsolved scientific questions regarding pandemics, with particular focus on influenza and, of course, by taking as particular case study the H1N1 2009 pandemic.

The global aim was to identify key points for an optimal preparedness in case of a possible future pandemic.

To structure the report, we followed the classical four-step paradigm of decision making: Decision Input, Decision Making, Decisions Output and Communication.

The analysis of decision input implied the review of the state of the art in surveillance of emerging pathogens with potential risk of causing pandemics; the analysis of decision making implied the review of the literature on decision making during H1N1 pandemics; the following step (Decisions Output) involved the review of the preparedness and response enacted during the H1N1 pandemics; finally the analysis of the communication involved a review of the processes of "Risk Communication" and a review of an important issue during pandemics and epidemics: the changes in human behavior (and its impact) following non-mandatory recommendations by Public Health Authorities.

As requested by the technical annex of the ASSET project, we complemented our analysis by means of an appropriate questionnaire, sent to experts in the field of pandemics and epidemics (virology, epidemiology, mathematical modelling, and social psychology). A focused workshop was then held in Lyon in February 2015 in order to discuss the most interesting findings of the questionnaires, and to point out main research areas that they consider as “vital” for future pandemic preparedness.

From our review, it became clear that moving forward, health care professionals at many levels will need to play a much more active role in disease surveillance than in the past. In addition, surveillance systems for infectious disease outbreaks will need to be flexible and adapted to the characteristics of the potential biological agents. Surveillance systems will also have to be sustainable, without long-term burnout. Finally, it is urgent that the traditional surveillance might be complemented by an informal surveillance that can exploit internet and its social networks.

Decision making is an iterative process i.e. each step can be investigated several times during the course of an outbreak and/or pandemic in order to adjust the approach to the situation. Our review provided evidence that the iterative process of the epidemic intelligence framework was not followed-up during the H1N1 pandemic. Another weakness during the H1N1 pandemic was the lack of enough input from modeling studies into decision process. Indeed, the large majority of modeling studies were published often too late to influence decision-making. Cost-effectiveness analysis of non-pharmaceutical interventions should also be taken into consideration.

Preparedness and response require shared responsibility and collective action on multiple fronts. We observed large heterogeneities across Europe regarding vaccine accessibility, the target population, vaccination strategy, non-pharmaceutical infection control measures and respective responsibility of organisms involved in the management of different aspects of the pandemic during the H1N1 crisis. Establishment of a real framework by the Member States to identify avenues for improvement of future influenza pandemics management is therefore warranted.

As far as communication of risk during pandemics, the analysis of risk communication (RC) during H1N1 showed that this specific pandemic has been a turning point on RC. A number of issues were raised that were specific to H1N1 pandemics and other possible future flu pandemics, and other that are in common with RC during pandemics or outbreaks of other diseases. The lack of transparency and coherence of the process and the messages transmitted by authorities was another critical issue. Overall, in order to plan effective risk communication campaigns a key point is the need of re-building the trust in the current "post-trust" society. Finally, two challenges are intimately inter-connected. First, a successful RC campaign has to take into the account the social and cultural heterogeneity of the target population. Second, the RC can no more be unidirectional but, to some extent, it ought to be bidirectional, by including feedbacks from its target population.

As far as the "non-mandatory" changes of behavior are concerned, three are the main areas of intervention. The first is the change of personal behaviors such as hand-washing, reducing behaviors at risks etc… These changes can be quite effective, and RC focusing on them can be quite successful. However, a key point is that such campaigns must not be temporally limited to the possible pandemic outbreaks, neither to the seasonal influenza outbreaks. Far more challenging is the issue of influencing the propensity to vaccinate. During H1N1 pandemics, to the traditional anti-vaccination factors permanently present (and significatively increasing in our "post-trust society"), specific new factor added. Overall, an evidence of the substantial low success of the RC campaigns during the H1N1 pandemics is the difficulty in convincing health-care workers to vaccinate. Finally, the new generation of mathematical models that take into account human behavior, which we reviewed, could be useful in designing pandemic preparedness plans.

In agreement with the findings of our report, the expert group recognized that during the last decades, rumors and suspicions regarding adverse effects of vaccines have shaken people's trust in vaccination, contributing to what is also known as a post-trust society. In this regard, rebuilding trust in vaccination by mean of well-designed communication strategies is a critical issue to restore public confidence for pandemic prevention and management. Roles and responsibilities of different players should be clarified and well defined in order to have a comprehensive message that favors compliance with recommendations. Designing a convincing communication strategy is difficult in particular, because of the fragmentation of the public to reach, the impossibility to tailor a message for everyone, and the difficult management of the media. It is therefore crucial to exploit and anticipate the role of Social Networks and Internet and integrate their use in communication strategies.

To build trust, the following points should be taken into consideration: 1) Acknowledge uncertainty and therefore to deal with the fear; 2) Have a clear message staking the burden and the risk; 3) Implement bi-directional risk strategies i.e. get a feedback from the general public; 4) Clarify and be transparent on the decision process, and 5) Make a major effort to avoid even suspicions of conflict of interest.

The most frequently research areas considered as "vital" for future pandemic preparedness stated by the expert group were more research on: the effectiveness of antiviral drugs; technology transfer, mechanism of the emergence of the viruses at the basic level; epidemiological tool to monitor early detection of outbreaks and trend; standardization and flexibility of pandemic plans; sociological aspects of vaccination including risk perception; how to improve data sharing; efficiency of social distancing and its impact on the economics; tool for real time evolution of pandemics; how to optimize the use of mathematical models.

1. INTRODUCTION

The first laboratory-confirmed case of A/2009/H1N1 virus, also known as swine influenza was reported in February 2009 in Mexico, and from April 2009 in California-USA. Less than one week later, the virus was documented in other countries including Austria, Canada, New-Zealand, UK, and Switzerland (Ficher 2011). Due to its rapid spread, the World Health Organization (WHO) raised the pandemic alert level from level 3 to level 4 on 27 April and 2 days later moved to level 5. By the beginning of June 2009, 26,000 laboratory-confirmed cases were reported from 75 (Fineberg 2014) countries in all continents. The continued spread of the virus internationally together with uncertainties as how the virus could evolve overtime has led the WHO to declare the start of swine influenza pandemic, the first global flu pandemic in 41 years, on 11 June 2009.

Contrary to a typical influenza season, the 2009 H1N1 pandemic was characterized by disproportionally affected number of young adults, children, and pregnant women who constituted the majority of hospitalized cases (Fineberg 2014; Velasco 2012). In the majority of patients, infection was a mild, self-limiting, upper respiratory tract illness, but 2–5% of cases required hospitalization (Jain 2009). The age-specific incidence was investigated by a meta-analysis of serological studies in 11 countries that found the highest age-specific incidence among 5-19 years old children (46% [36–56%]), followed by 0–4 years old (37% [30–44%]). The lowest incidence was found in those ≥65 years old (11% [5–18%]) (Van Kherkove 2013).

The pandemic was declared over in August 2010 with respectively 1 million cases and 18,449 laboratory-confirmed deaths reported to the WHO (Van Kherkove 2013). In Europe, 1975 laboratory-confirmed deaths were reported to the European Centre for Disease Contro (ECDC) (ECDC report 2012). However, the global number of deaths has been estimated to be 15 times higher (201,200 respiratory deaths, range 105,700-395,600 with an additional 83,300 cardiovascular deaths, range 46,000-179,900) than the reported laboratory-confirmed deaths and 51% occurred in Southeast Asia and Africa (Dawood 2012). The estimated case fatality rate was 0.15–0.25% (Fineberg 2014).

The pandemic ended up being milder than originally anticipated. As a result, its management in term of money, resources consumed, time and communication was the subject of considerable controversies and the WHO decision process has been heavily criticised. The Expert Group on Science, H1N1 and Society ('H1N1 Expert Group', or 'HEG'), designated by the European Commission's Directorate for Science, Economy and Society provided a detailed report on the 'Science in Society' (SiS)-related research questions raised by the H1N1 pandemic and associated crisis management.

The main findings failures identified by the expert group regarding different aspects of the H1N1 pandemics were the following:

- Insufficient knowledge in the fundamental understanding of the virus (transmissibility, severity, attack rate, risk factors for sever individual impact, etc.) at the beginning of the pandemic;
- Lack of knowledge on the efficacy of treatments, vaccines and hygiene measures;

- Lack of input from a broad variety of concerned scientific disciplines into the decision process.
- Failure in adequate risk communication

1.1 Objectives

The objective of the work-package 2 (WP2) of the ASSET project is about the state of art research and existing studies on different aspects of pandemic's management. The WP2 is subdivided into seven tasks to establish baseline knowledge about: 1) governance of flu pandemics and other similar crises; 2) unsolved scientific questions regarding influenza and pandemic situations; 3) past experiences of participatory governance; 4) ethics, law and fundamental rights in pandemics and epidemics; 5) Gender issues; and 6) intentionally caused outbreaks.

The present report focuses on task 2 by taking the example of the H1N1 influenza pandemic. The work will be conducted in coherence with the report and publication of the H1N1 Expert Group.

The objectives of the present report are to:

- ✓ Provide additional data available since the publication of the H1N1 expert group report
- ✓ Identify and summarize new research programs that aim at addressing knowledge's gaps about H1N1 that have been identified during the pandemic
- ✓ From the two previous objectives, identify what need to be done yet in case of a possible future pandemic

1.2 Plan of the report

To cover all aspects of the management of the H1N1 pandemic crisis, we will follow the classic decision making scheme. Decision making is a process of choosing the best alternative to achieve individual and organizational objectives. It concerns putting facts and evidence in order, and ranking the likelihood of various risk scenarios while taking into consideration the contextual information. It is also about providing good cost/benefit comparisons of various decision options. As represented in **Figure 1**, the general scheme follows several steps:

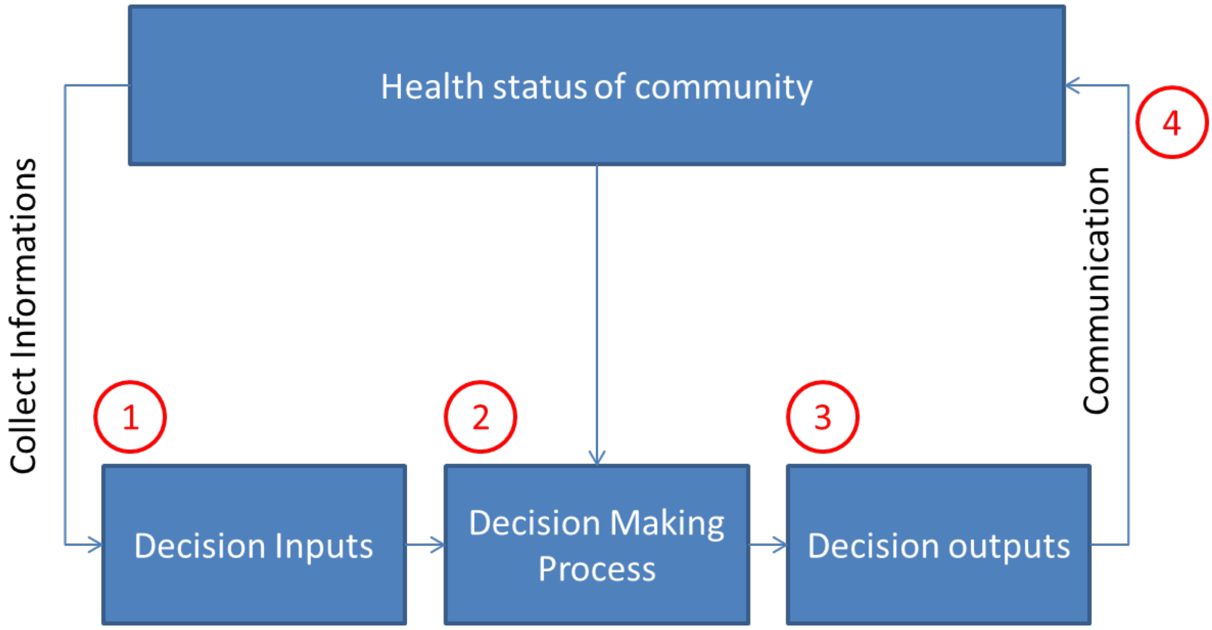

Figure 1: Decision making scheme

- ✓ The initial step consists of collecting and analysing information in order to get an evaluation of the impaired situation of the health status of the community. This part particularly focuses on analysing and characterizing the pathogen and the disease (symptoms, diagnostic tools, performance of available treatment and/or prevention tool, etc.) at early stage and during the pandemic. These points will be discussed in Section 4.
- ✓ The 2nd step i.e. decision making process, is based on information from the first step decisions are made by public health authorities and will be discussed in Section 5.
- ✓ The 3rd step i.e. response and preparedness includes the mobilisation of other organisms, response means, technical feasibility of potential responses, the choice of targets, etc. that would allow the implementation of decisions and will be detailed in Section 6.
- ✓ The last steps is to choose the most appropriate communication channel to insure efficient implementation of decisions made during step 2. Risk communication strategies and their criticalities during the H1N1 pandemic will be examined in Section 7.
- ✓ Finally, in Section 8 we will review one of the most important issues during pandemics and epidemics: the changes in human behaviour following non-mandator recommendations by Public Health Authorities.

2. SURVEILLANCE OF EMERGING PATHOGENS WITH POTENTIAL RISK OF CAUSING PANDEMICS

Background

Throughout the last few decades, emerging infectious diseases have become an increasingly important global public health problem. Examples of such outbreaks are the Severe Acute Respiratory Syndrome (SARS), which originated from Asia in 2003, the Avian influenza H5N1, and the H1N1 2009 pandemic (Morse, 2008). Therefore, effective surveillance systems for early warning are crucial. Surveillance is defined by the US CDC as follows: "Public health surveillance is the ongoing, systematic collection, analysis, interpretation, and dissemination of data regarding a health-related event for use in public health action to reduce morbidity and mortality and to improve health" (CDC, 2001). Infectious disease surveillance is an epidemiological practice used to predict, observe, and minimize the impact caused by an outbreak, epidemic or pandemic (Morse, 2008).

The surveillance systems for infectious disease outbreaks play roles at all levels of prevention (Green, 2009). At the level of primary prevention, they can reduce both the actual and perceived efficacy of deliberately caused outbreaks and can have a deterrent effect. For secondary prevention, surveillance systems can make an important contribution to the early detection of infectious disease outbreaks, thus improving the response to the outbreak and limiting its spread. Finally, at the level of tertiary prevention, the information provided by surveillance systems contributes to the evidence base for managing the epidemic, and can be especially effective in the area of risk communication. Indeed, comprehensive surveillance data from a number of different nations, examined by a central body, can increase the chances of identifying international outbreaks and warning the public in advance (Bonin, 2007). Surveillance systems may also be used for rapid detection of bioterrorist attacks. Indeed, comprehensive surveillance data from a number of different nations, examined by a central body, can increase the chances of identifying international outbreaks and warning the public in advance.

The four main goals for infectious disease surveillance are: 1) early detection of cases, 2) monitoring the progress of the outbreak, 3) providing data for risk communication, and 4) supplying data to the international health organizations. Surveillance resources can be classified into two types—formal and informal.

Formal surveillance

Formal reporting of infectious diseases is a requirement for health care providers and many national governments. During the last decade, there has been a rapid increase in the development of formal infectious disease surveillance systems. Formal surveillance measures are based on data arriving from formal organizations such as hospitals, healthcare clinics, and health agencies. At present, surveillance systems are still currently used in all countries even though they are passive in nature and are not capable of detecting disease outbreaks in real time. Furthermore, traditional infectious disease surveillance systems tend to be limited in their ability to rapidly detect and monitor spreading infectious diseases. Firstly, diagnosis of early cases may either be missed or delayed due to a failure to recognize unusual diseases. In addition, because suspected cases need to be confirmed by lab tests, there may be a long delay in reporting. Finally, the flow of information to public health authorities is often slow and a large burden is placed on health services. As such, early diagnosis and reporting by clinicians and improved sensitivity and reporting of general data on infectious diseases must occur. Due to the noted limitations of formal surveillance systems, new surveillance systems have been developed in recent years.

Informal surveillance

The rapid growth of telecommunications, media, Internet sites, and interactive social networking outlets has made it easier for public health professionals to communicate more effectively with other professionals in the field as well as with the public at large. Informal surveillance measures for the detection of infectious disease outbreaks are based on data collected through media sources such as news reports on the Internet, mailing lists, and RSS (Rich Site Summary) feeds. Informal surveillance resources are continuously evolving and increasing dramatically. Indeed, there has been impressive progress in the development of informal digital systems for disease surveillance. Examples include HealthMap, Google Flu Trends, ProMED-mail, BioCaster, Global Public Health Intelligence Network (GPHIN), MediSys, and EpiSPIDER.

Informal digital resources are characterized by their ability to mine, categorize, filter, and visualize online information regarding epidemics (Brownstein, Freifeld & Madoff, 2009). Online data mining analyzes the public via social discourse trends, noting correlations between the search words people use online, and current events. This approach, known as "Internet-based bio-surveillance", "digital disease detection", or "event-based surveillance", has been described and analyzed in the literature (Brownstein, Freifeld & Madoff, 2009; Hartley et al., 2010; Hartley et al., 2013). In the context of outbreak communication, this simple discourse surveillance tool can be used to identify people’s needs and concerns as the outbreak unfolds, both on local and international levels, even focusing on specific areas or specific group profiles.

It appears that all informal surveillance resources use similar sources of data, such as official reports and media reports, including global media resources, news aggregators, eyewitness reports, internet-based newsletters and blogs. However, they use different algorithms to create their output, and cover different geographic areas. In addition, they are diverse in the manner by which they filter and analyze the information, and may create distinctive output. Therefore, they complement each other with respect to information completeness. Still, a drawback of informal surveillance systems is that they typically accumulate a huge mass of information on a huge range of diseases, which makes it challenging to extract critical information.

Evaluation

According to the World Health Organization (CDC, 2001), the success of a surveillance system depends on factors including simplicity, flexibility, data quality, acceptability, sensitivity, predictive value, representativeness, timeliness and stability. Although there is currently little prospective evidence that existing informal systems are capable of real-time early detection of disease outbreaks, informal digital systems are widely used by the general public, as well as by health officials. Despite the increased sophistication of the surveillance systems that have been implemented in many centers, at present, early identification of infectious disease outbreaks still depend largely on the ability of primary care and emergency room physicians to diagnose and immediately report suspected cases.

It is clear that moving forward, health care professionals at many levels will need to play a much more active in disease surveillance than in the past. In addition, surveillance systems for infectious disease outbreaks will need to be flexible and adapted to the characteristics of the potential biological agents. Surveillance systems will also have to be sustainable, without long-term burnout. We have reviewed both formal and informal infectious disease surveillance by highlighting their use in the case of influenza and in the case of Ebola. Specifically, we have reviewed recent articles that address surveillance and cover new developments in the area of surveillance. As part of our bibliography, we have included websites with a comprehensive description on disease surveillance.

3. DECISION MAKING PROCESS

Decision making process is based on the idea of choosing the best alternative which allows selecting interventions that enhance quality and improve outcomes and benefits for individuals and populations. We will review the chronology of most important decisions taken by the WHO during the 2009 pandemic (Table 1) by using the so-called “epidemic intelligence framework” (Figure 2) (Paquet 2006). This framework, developed by the European Centre for Disease Prevention and Control (ECDC) in collaboration with the European Union Member States, covers all activities related to pathogens with potential epidemic and/or pandemic risk. It includes five steps from the early identification of the pathogen to assessment and investigation so that appropriate public health controls measures can be recommended (Paquet 2006). As an iterative process, each step can be investigated several times during the course of an outbreak and/or pandemic in order to adjust the approach to the situation.

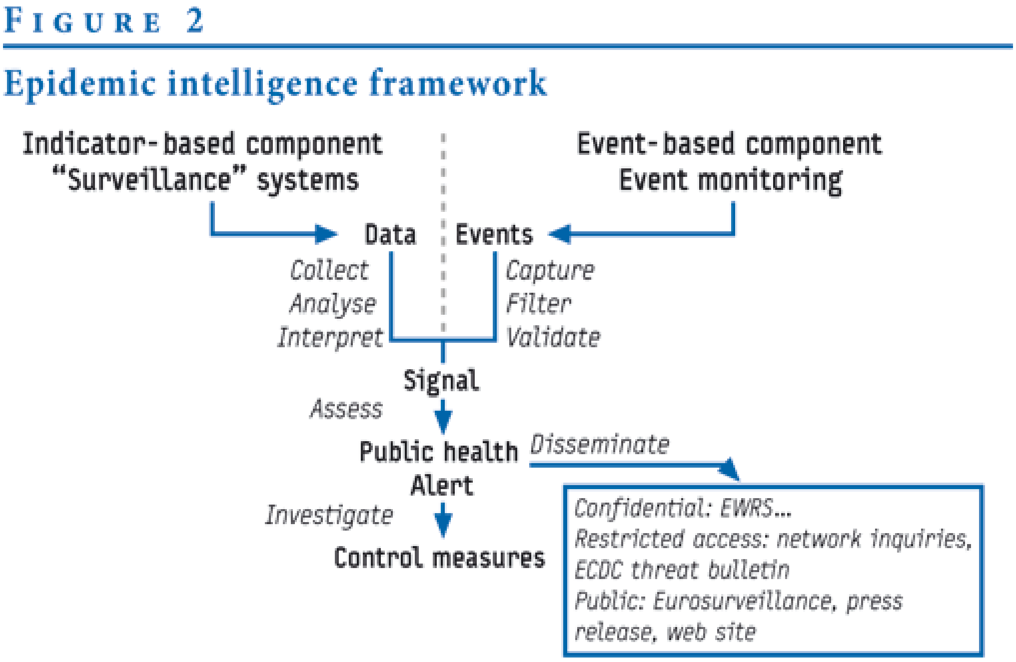

Figure2 (From Paquet et al. 2006): Epidemic Intelligence Framework

Table 1, from (Cheng 2012), provides the chronology of most important events during the 2009 pandemic. The signal for the 2009 pandemic came first from unusual increase in the incidence of respiratory diseases in Mexico (Lopez-Cervante 2009). The rapidly increasing number of infected individuals in Mexico and identification of new cases in the USA led to the set-up of a public health alert (outbreak alert) by the WHO in 24th of April 2009. The pandemic alert has been raised subsequently to phase IV (i.e. medium to high probability of pandemic), V (i.e. high to certain probability of pandemic) and VI (i.e. pandemic in progression) within two weeks.

During the surveillance of a pandemic, accurate estimation of the per-infection severity of the new pandemic strain is a key task to define the appropriate scale of response (Lipsitch 2011).

Early data on H1N1 influenza reported high morbidity and mortality especially among children, young adults and pregnant women. However, later on new data from large number of countries reported evidence that the disease was milder than what has been thought. Based on those data, the first modeling on H1N1 published in May 2009 (Fraser 2009) estimated the basic reproductive number (R0) in the range of 1.4 to 1.6 and a case fatality rate ratio of 0.4%. Fast spread but mild character of H1N1 fact was also recognized by the WHO as early as in May 2009. Although the WHO could have scaled down the existing preparedness plan (expert report) at this time, nevertheless a phase VI pandemic was declared. This highlights that decisions made by the WHO did not follow the above-described **iterative process of the epidemic intelligence framework**. The formal criteria for advancing from one phase to another were, indeed, merely based on the spread of the disease without taking into consideration the severity. Moreover, the decision process was based on the preparedness plan for H5N1, which is very aggressive and lethal. Finally, at the crucial times when phase of pandemics had to be assessed, only a limited number of the potentially available deciders were invited (Fineberg 2014).

Probably, it was not enough stressed to national authorities that Phase VI mainly implied a judgment of speed of transmission, so that they thought it mainly was an assessment of severity. Furthermore, the lack of input from multidisciplinary scientific expertise into the decision was a negative factor.The planning framework (ratified by the World Health Assembly) was maybe excessively rigid and impeded flexible local responses, and member states did not act as independently as they could. As a consequence, the most of advance purchase orders were tied to declaration of phasing. Probably, some member states did not have fully understood the implications of the plan. These points and their impact are discussed in next sections.

In addition to saving people's lives and ensuring equity and fairness, ensuring fair procedures and accountability is another part of the three ethical decision-making principals in case of a pandemic (Forum on ethical of pandemic influenza preparedness 2008). A critical issue during the H1N1 was the lack of transparency and coherence of the process and the messages transmitted by authorities. Ideally, instead, experts involved in the decision-process should be clearly identified, and any potential conflict of interest with indusrty should be declared. During the H1N1 pandemics indeed, the lack of communication about the composition of the committee and the decision-process itself were disturbing. Because of that, authorities appeared to be unable to take enlightened and coherent decision to protect the population and fight efficiently the pathogen.

As evidence of the deep impact of these criticalities, we remind that Council of Europe passed a resolution criticizing the WHO for 'grave shortcomings' in the transparency of its decision-making processes and expressing concerns regarding potential corporate influence, lack of transparency also to maintain the level VI alert despite the evidence that the pathogen was not as lethal as previously anticipated (Parlimentary Assembly 2010).

Date	Important event[a]
Mid-February 2009	Outbreak of respiratory illness in La Gloria, Veracruz, Mexico
12 April 2009	Mexican public health authorities reported outbreak to PAHO
15 April 2009	CDC identified A/2009/H1N1 in a boy from San Diego, CA
17 April 2009	CDC identified A/2009/H1N1 in a girl from Imperial, CA
19 April 2009	Mexico declared a national alert
21 April 2009	CDC alerted doctors to a new strain of H1N1 influenza virus
24 April 2009	WHO issued Disease Outbreak Alert
27 April 2009	WHO raised the pandemic alert from phase 3 to 4
29 April 2009	WHO raised the pandemic alert from phase 4 to 5
11 June 2009	WHO raised the pandemic alert from phase 5 to 6
8 July 2009	Virus strains resistant to oseltamivir identified
13 July 2009	WHO issued recommendations on pandemic H1N1 2009 vaccines
5 November 2009	Detection of infection of farmed swine by the pandemic virus
20 November 2009	Virus mutation detected in fatal and severe cases in Norway
2 December 2009	Oseltamivir-resistant virus identified in hospitalized and immunosuppressed patients
18 February 2010	WHO issued recommendations for the composition of influenza virus vaccines for the upcoming Northern Hemisphere influenza season
10 August 2010	WHO issued recommendations for the postpandemic period

[a] CDC, Centers for Disease Control and Prevention; PAHO, Pan American Health Organization; WHO, World Health Organization.

Table 1 (From Cheng et al. 2012): Chronology of most important events during the H1N1 pandemic in 2009

Another weakness during the H1N1 pandemic was the lack of enough input from modeling studies into decision process. Modeling is a potentially powerful methodology that could guide decision-making process, if used properly. Mathematical models have been used to understand the dynamic of influenza transmission and to predict the burden of the disease in the population. They have also provided assistance in evaluating the potential beneficial effects of control measure by generation plausible scenarios (Coburn 2009). However, as illustrated in Figure 3, the large majority of modeling studies were published often too late to influence decision-making (Lee 2013).

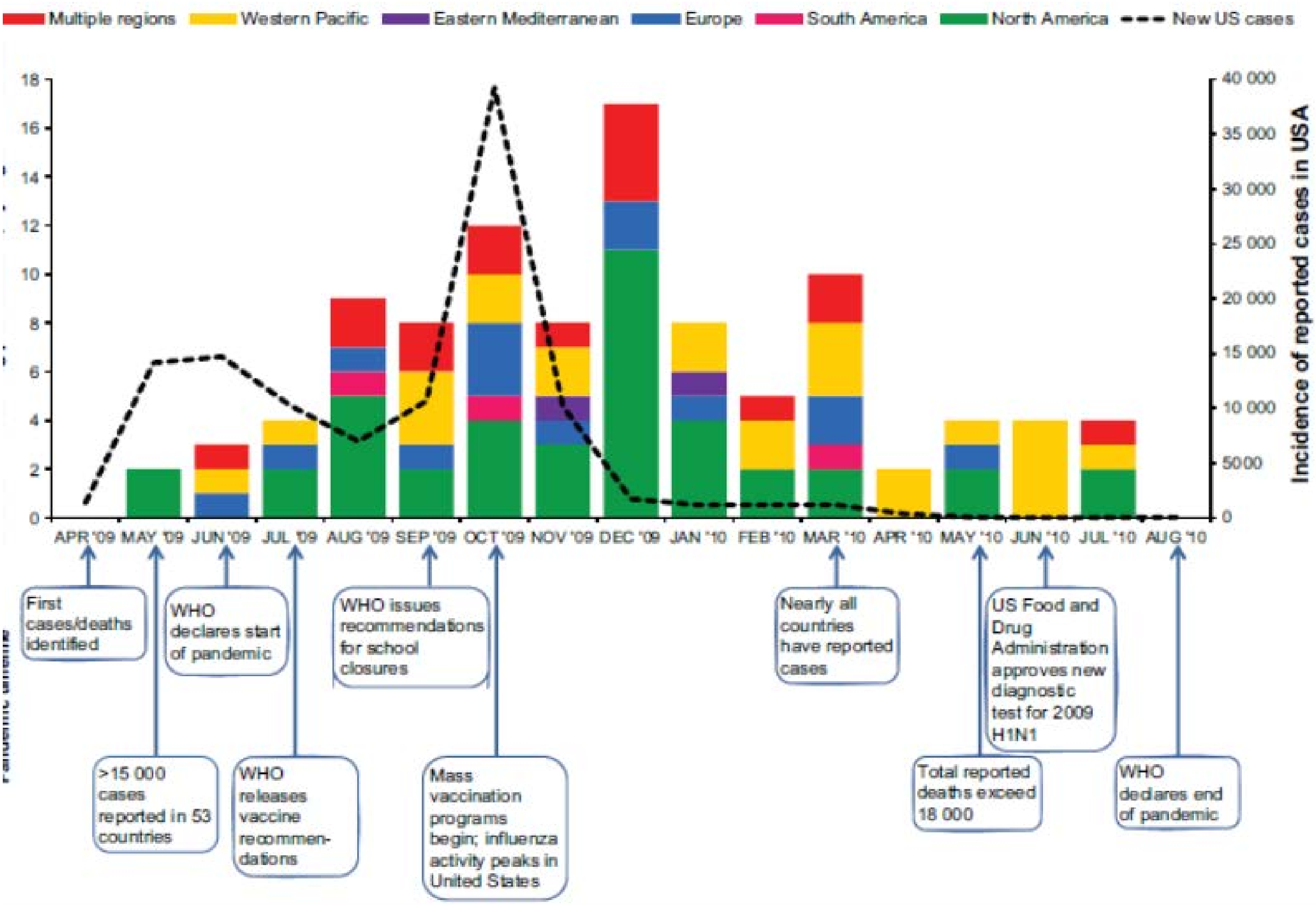

Figure 3 Dynamics of the number of modeling-based studies published during and shortly after the H1N1 pandemics (from Lee et al. 2013)

Real-time data on disease incidence and prevalence, mortality, morbidity etc. are key parameters for epidemic models to have a chance to accurately predict the course of an epidemic (Lee 2013), and of course the lack of these data delayed the model-based investigations. More in general, during the H1N1 pandemic, there was a lack of a central data repository. Therefore, putting in place data repositories at national and/or international levels using a standard approach could greatly improve the ability of modeling to assist decision-makers.

Since after H1N1 pandemics mathematical epidemiology of influenza has had a considerable impetum and many interesting studies were proposed in literature (Manfedi and d'Onofrio, 2013; Poletti et al 2011; Poletti et al, 2013; del Valle 2013). We believe that, for the preparadness of possible future pandemics, these modeling studies should be taken in serious account.

Finally, cost-effectiveness analysis of non-pharmaceutical interventions should also be taken into consideration. A systematic review of economic evaluation of influenza preparedness strategies reported the combination of pharmaceutical and non-pharmaceutical interventions as being relatively cost effective compared pharmaceutical interventions only. However, currently there is a lack of standard protocols for this purpose (Velasco Plosone 2012).

4. CRITICAL ISSUES IN RESPONSE AND PREPAREDNESS

Preparedness encompasses the achievement of a national response public health emergency plan. The historicial experience of Spanish flu pandemics (Morens 2010), the unprecedented global spread of highly pathogenic and lethal avian H5N1 influenza viruses (Webster) together with documented respiratory infection in human by other avian influenza subtypes (H9N2 and H7N7) (Guo 1999; Lin 2000; Fouchier 2004) emphasized the potential of influenza viruses to cause pandemics. To improve public health capacity and mitigate effects of emergency in case of pandemics, the WHO published the first pandemic preparedness and response guidance in 1999. These guidelines, updated in 2005 and 2009, summarize the role of the WHO and recommendations for national measures before and during pandemics. The main elements of preparedness plan considered by the WHO are organized into five basic components (WHO guideline 2009): 1) planning and coordination; 2) situation monitoring and assessment; 3) reducing the spread of disease; 4) continuity of health care provisions and 5) communications.

In Europe, as recommended by the WHO and “prescribed” in the renewed International Health Regulations (IHR), 2005, most countries had national influenza preparedness plans in place by 2005. These national preparedness plans have been subjected to evaluation exercises by the European Commission, the WHO European office and the European Centre for Disease Prevention and Control (ECDC) were considered to be potentially efficient (Pandemic Influenza Exercise 2006). The H1N1 pandemic in 2009 offered the opportunity to test the effectiveness of such preparedness plan in a real time.

Preventing spread of the disease in the community is the major component of a pandemic management crisis that involves making decisions related to:

- Preventive treatments: Are preventive treatment such as a vaccine available?
- Target population: who should be vaccinated first? (Health care workers, “at-risk” population, children…);
- Who should apply the decision? (national health authorities, healthcare worker, military forces …)
- Infection control measures: when and how public health measures (school closure, suspension of public events, etc.) should enter into force?
- How to use the available resources at best?

Critical issues in reducing the spread of disease will be discussed in the following paragraphs, as well in sections 7 and 8.

4.1 Vaccine availability

Despite the technological advances in using cell-based inactivated whole-virus vaccines and improved adjuvants, and past experience in influenza vaccine manufacturing, the first H1N1 vaccines became available only several months after the start of the pandemic (December 2009). The WHO recognized that if the H1N1 pandemic had been more virulent than the timelines for vaccine deployment would have been extremely concerning (WHO 2010).

In the European WHO region, most countries had access to vaccines. However, timing of vaccine delivery and the available quantity were highly inequitable. Comparison of the time between epidemic peak to vaccine availability by country showed that the vaccine was available from 2 months before to more than 10 months after peak transmission (Figure 4) (Jorgensen 2013). Overall, 17 (44%) countries received the vaccine after their pandemic peak has passed. Lack of advance purchase agreement (APA) with pharmaceutical companies in these countries could explain, at least partly, the observed unequal access to vaccines. Indeed, several European countries had already prepared the ground for a pandemic and had prepared APA with pharmaceutical groups which were to take effect on the declaration of a pandemic by the WHO (Parliamentary assembly 2011). These countries received vaccines several weeks (median 27.0 weeks; interquartile range (IQR), 26.7–29.3) earlier than countries without prior agreements (median 33.4 weeks (IQR, 30.6–37.0); the majority of which are classified as developing economies. Similarly, the reported number of available vaccine doses was substantially higher in countries that had APA (64.1 doses per 100 populations; IQR, 26.8–113.5) than in the others (14.3 per 100 populations; IQR, 5.1–24.4) (Jorgensen 2013).

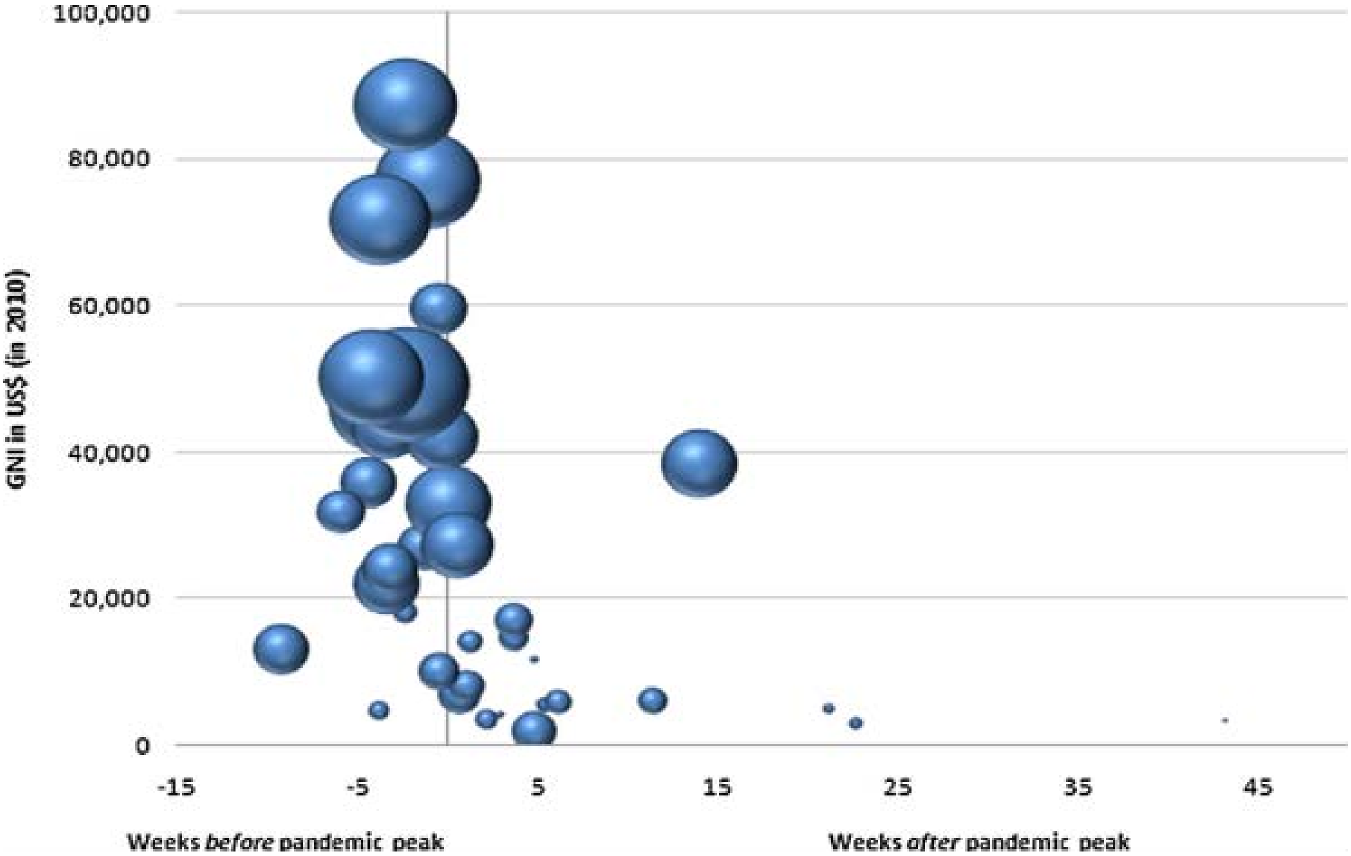

Figure 4 (From Jorgensen et al. 2013): Availability of H1N1 vaccines relative to the peak of the pandemic in each country and to country GNI per capita 2010 (size of bubble indicates quantity of vaccine doses per 100 population).

To mobilize donations of pandemic vaccines and coordinate their equitable distribution to countries that relied on vaccine donation, the WHO established the Pandemic Influenza A (H1N1) Vaccine Deployment Initiative. In the WHO European region 6 countries have been identified as being eligible. The initiative allowed delivering of over 78 million doses of H1N1 vaccine to 77 of the poorest countries in the world. However, some weaknesses in particular related to time-consuming process to obtain National deployment plan (NDPs) and satisfy other WHO requirements for donated vaccine (WHO prequalification for donated vaccines, letter of agreement between the country and WHO, letter of intent from the country to WHO), inadequate transport capacity, and complex donation process, delayed the vaccine delivery (Vaccine development initiative, WHO report 2010).

4.2 Target population

The European Union Health Security Committee and the Early Warning and Response authorities (HSC/EWRS) adopted on 25 August 2009 a policy statement proposed by the European Commission in which health care workers, persons aged ≥ 6 months with underlying chronical or other serious diseases and pregnant women (i.e. overall 19.5 % of the population) was identified for *prioritization* (EU Health Security Committee 2009). However, the responsibility to develop vaccine strategy lies with the Member States that may develop different vaccination strategies, taking into account their epidemiology, health service structures, available resources and cost-effectiveness of available vaccines (Vaccination strategy 2009). Vaccination policies and vaccination coverage in the European Union (EU), Norway and Iceland have been assessed by a survey conducted by the Vaccine European New Integrated Collaboration Effort (VENICE) consortium (Mereckiene 2012). Of the 27 countries that responded to the survey, 26 reported having had pandemic vaccination program. However, as illustrated in Figure 5, the timing varied considerably with some countries not being able to start until near the end of 2009.

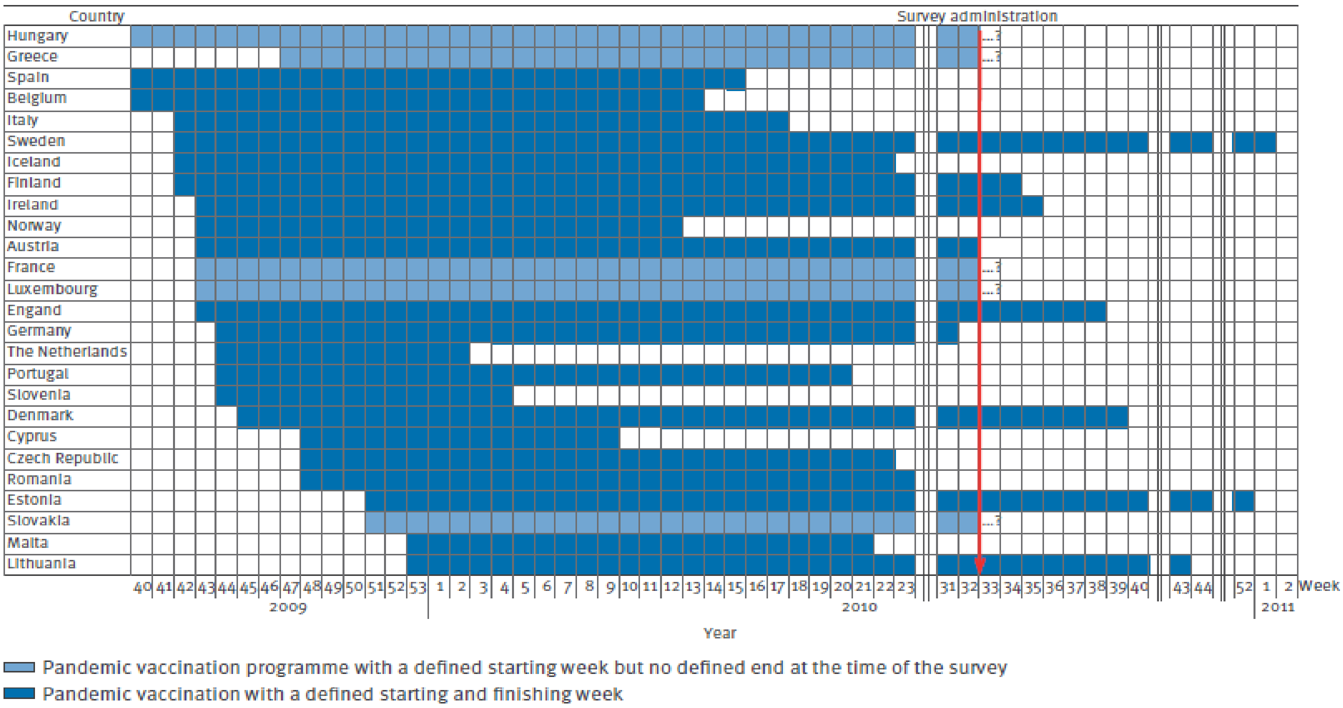

Figure 5 (Mereckiene et al. 2012): Vaccination programs for influenza vaccine among 26 European countries

At early stage of the pandemic, the recommended prioritization strategy was followed in Austria, Belgium, Cyprus, Czech Republic, Denmark, England, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Luxembourg, Malta, Norway, Portugal, Romania, Slovakia, Slovenia and Sweden. At the late phase, 7 countries switched to vaccinating the whole population. Cocooning strategy approach was implemented in five countries. In Poland, the government did not proceed to vaccination. Although the large majority of countries adopted the official recommendations, vaccine coverage varied widely, the highest being reported in the Netherlands (32.3%), Norway (45%), Sweden (50%), and Hungary (30-40%). Some countries had low vaccine coverage even if the sufficient vaccine doses were available. In France, 94 million doses have been ordered despite the statement of the French health authority saying that the disease is mild (Haute autorité de santé publique 2009). A mass vaccination campaign was launched in October 2009 and offered to the population according to a pre-defined order of priority (Bone 2010). By the first of June 2010, only 8.5% of the population has been vaccinated. Concerns about the safety and effectiveness of the vaccine, diffuse feeling among the population that the disease was not severe, and exclusion of general practitioners to provide vaccination were probably the most important barriers that led to low vaccine uptake (Bone 2010). According to the Director of health Chair at the Institute of political studies in Paris, vaccination campaign against the flu A (H1N1) was a 'missed appointment with public health' because it "has revived tensions between doctors and the Government" (Assemblée National 2010). The same findings have been reported in other European countries such as the UK, Germany and Belgium where respectively only 7.4%, 10% and 6.6% of the whole population have been vaccinated (Assemblée National 2010). These obstacles, closely related to risk communication management, which are reviewed in section 7.

Both the WHO and the European Commission advised pregnant women to be vaccinated regardless of stage of pregnancy. To investigate whether these advises were followed-up by Member States, a survey was conducted in Europe (Lutejin 2011). Overall, 24 countries responded to the survey, of which 20 reported having an official vaccination policy against H1N1 for pregnant women. Vaccination policy followed advises given by the European Commission in 8 countries while in 12 countries the policy included only second and third trimester pregnant women. In Croatia and Czech Republic, pregnant women in the second or third trimester of pregnancy could apply for vaccination even if the country did not have vaccination policy for this population. In total 7 different vaccines were used for pregnant women of which 4 were adjuvanted. The highest vaccination coverage rates among pregnant women were achieved in the Netherlands and Ireland (Mereckiene 2012).

Children without underlying chronical or serious diseases were not part of the priority groups by official (WHO/EU) institutions. However, 13 Member States recommended the pandemic vaccination for this population either as part of the overall population (n=13) or as age specific groups (n=6) (Mereckiene 2012). Again, the highest coverage rates were reached in the Netherlands and Nordic countries (Mereckiene 2012).

4.3 Who should apply the decision?

As illustrated in previous paragraphs, the large majority of European countries had pandemic vaccination program. Nevertheless, their implementation could be optimal if they were in coherence with national systems of public health law. The extent to which laws across Europe support or constrain pandemic preparedness planning, and whether national differences are likely to constrain control efforts has been investigated by a survey across Europe (Martin 2010). The results showed significant differences in legislation and in the legitimacy of strategic plans; insufficient link between pandemic plans (mainly addressed to public health services) and public health laws (handled by public authorities); lack of precision with regard to the respective responsibility of organisms involved in the management of different aspects of a pandemic crisis. As a result, effectiveness of the prevention campaigns could be limited.

4.4 Infection control measure

Infection control measures i.e. non pharmaceutical interventions are another important point of preparedness that should be evaluated and anticipated in case of pandemic crisis. They may slow down the introduction and spread of the pandemic virus if instituted early enough (Cheng 2012). Early in the influenza A (H1N1) 2009 outbreak, the WHO issued guidance on non-pharmaceutical interventions (WHO technical consultation 2010) such as social distancing methods (school closures for example), and behavioral interventions. The latter is fully discussed in Section 8.

The implementation of school closure, considered as a public measure to mitigate the pandemic, was extensively considered in national pandemic plans developed prior to the start of the H1N1 pandemic and received considerable attention during the pandemic. In Europe, the Health Security Committee/ Early Warning and Response System (HSC/EWRS) considered that there was no need for mass school closure and concluded that school could be reactively closed upon infection being found among students (HSC/EWRS 2009). The diversity of school closure during the H1N1 pandemic was investigated in 12 countries and administrative regions (Bulgaria, China, France, Hong Kong Special Administrative Region, Italy, Japan, New Zealand, Serbia, South Africa, Thailand, United Kingdom, and United States) through a meeting organized by the European Centres for Disease Control (Cauchemez 2014). All study participants had national recommendations for reactive school closure i.e. when children or staff of the school start experiencing illness. However, there was wide heterogeneity in the policy decision: reactive closure was decided at the school level in the UK and Thailand, while it was made by local governments or local representatives of the state in China, France and South Africa. The extent and duration of school closure differed also considerably.

There is currently no consensus about the impact of school closure but it is well known that school closure may be effective when the pathogenic agent is highly transmissible and/or severe. School closure may have some benefits that should be balanced against their economic and social consequences (Cauchemez 2009; Jackson 2013). Published mathematical modeling that addressed questions related to the timing and duration of school closure as well different school closure strategies to control influenza pandemics have been the subject of a recent systematic review (Jackson 2014). Despite the heterogeneity of results of the reviewed modeling, overall most models predicted that school closure would be beneficial in (Table 2):

- Delaying the epidemic peak (but no more than 1 to 3 weeks);
- Reducing the peak incidence (ranging from 20% to 60%);
- Reducing the cumulative attack rates;

Giving the fact that school closure reduce contacts but does not eliminate transmission, the reduction in peak incidence was consistently predicted to be larger the overall reduction of cumulative attack rate. Particular school closure strategy to be adopted has been shown to depends on the disease transmissibility: when transmissibility is low (R0 = 1.2), attack rates remain high unless closures last 8 weeks or more while in case of high transmissibility (R0 = 1.6 and 2.0), closure duration has little effect on attack rates. With regard to the optimal timing, it seemed that school closure could be relatively ineffective if decided very late in the course of the epidemic.

Parameter/scenario	Predicted influence on impact of school closures (assuming that factors other than those specified remain unchanged)
R_0	Over the range of values of R_0 investigated in the studies (up to approximately R_0 = 3.5), the higher the value of R_0, the smaller the effect of school closure
Age-specific attack rates	School closure is more effective if baseline attack rates are higher amongst children than amongst adults, than if baseline attack rates among children equal or are smaller than those among adults
Effect of school closures on contact patterns	The greater the reduction in contact resulting from school closure, the greater the effect of the intervention *
Timing and duration of closure	
Individual versus area school closures	Results differed between models
Age-specific effects	The effect of school closures is greater on incidence amongst children than that amongst adults
Effect on peak compared to cumulative attack rate	School closures have a greater effect on the peak attack rate than on the cumulative attack rate

Table 2 (From Jackson et al. 2014): Summary of the key factors influencing the impact of school closure

Another simulation study investigated the effects of the type of authority involved in the school closure decision making (Potter 2012). The results showed that decentralized, local control of school closure is not a limiting factor and may even improve responsiveness to local needs.

The overall conclusion was that school closure should remain as an influenza mitigation strategy and might be combined with other pharmacological and/or non-pharmacological interventions.

4.5 Utilization of available resources

Increased health care demand during an influenza epidemic can exceed the existing capacity. Optimizing the use of available medical resources is therefore an important aspect in efficient response to a pandemic. As emphasized by the WHO, the benefits of an effective, hospital-based epidemic/pandemic response include (WHO hospital preparedness checklist 2009): (1) the continuity of essential services; (2) the well-coordinated implementation of priority action at every level; (3) clear and accurate internal and external communication; (4) swift adaptation to increased demands; (5) the effective use of scarce resources; and (6) a safe environment for health workers. National pandemic preparedness plans include contingencies for surge capacity including reducing non-urgent activity and expanding critical care facilities and the use of triage system. Triage can be applied both in the community and in hospitals. The purpose is to decrease patient flow-though and to provide increased 'surge' capacity in order to best allocate the limited resources (ICU beds, equipments, and manpower).

During the course of the H1N1, different triage systems have been used in hospital setting. In the UK, the CURB-65 pneumonia score, the Pandemic Medical Early Warning Score (PMEWS) and the Department of Health community assessment tool (CAT) that have been used during the 2009 H1N1 pandemic were subject of an evaluation (Challen 2012). The authors concluded that current triage methods for suspected pandemic influenza did not reliably discriminate between patients with good and poor outcomes. On the contrary, among laboratory-confirmed cases, CAT was the best predictor for need for higher level of care and/or death in both adult and children (Myles 2012). In Mexico, a scoring system for influenza-like illness (ILI) was implemented to be used as a triage system. The ILI-score turned out to be successful for clinicians to decide who needed hospital care and antiviral treatment when timely laboratory confirmation of influenza was not available (Rodriguez-Noriega 2010). Telephone triage in an obstetric service improved efficiency of resource utilization without incurring apparent influenza-like illness morbidity (Eppes 2012). Nurse triage line proved also to be efficient in reducing patient flow-though during the H1N1 pandemic (Spaulding 2013)

The use of coordinated network of nurse triage telephone lines during a pandemic is being currently explored by the US Centers for Disease Control and Prevention (Koonin 2013)

5. CRITICAL ISSUES CONCERNING RISK COMMUNICATION DURING EPIDEMICS/PANDEMICS/ENDEMICS

One of the most important and challenging core elements forming the process of preparedness to pandemics is the communication of the underlying risk, meant as exchange (see later) of communication about the health risks (ECDC Report, 2013) that were or could be caused by the pandemics. The relevance of Risk Communication (RC) in the context of pandemics is mirrored by the statement by Barry (2005): "(against) next influenza pandemics… the most important weapon will be a vaccine. The second will be communication". Indeed risk communication is the key to make the general public switch from the irrational fear and rumours-based behaviour to a rational information-based-behaviour. More in detail, apart the general aim of limiting morbidity and mortality and economic losses caused by the target communicable disease (ECDC Report, 2013), the ideal aim of RC during a pandemic is to "maximize the public's capacity to act as an effective partner by encouraging prevention, promoting containment, fostering resilience and recovery" and to "prepare the public to adapt to changing circumstances or uncertainty", as described by (Vaughan and Tinker, 2009). Finally, it is of relevance to mention different communicators' perspectives. Bodemeier and Gassmaier, (2012), classify RC strategies in two (apparently mutually exclusive) categories: persuasive or informative RCs. However, in the practice, an optimal RC strategy should contain both these components.

Before SARS epidemics the study of RC to control serious epidemics and pandemics was scarce (Abraham, 2013; ECDC Report 2013). A milestone was, of course, also the H1N1 epidemics, which triggered a number of investigations on RC and which showed that many unsolved questions exist concerning RC during pandemics (Barrelet et al, 2013). Indeed, many new specific issues concerning RC were raised during and shortly after the H1N1 pandemics.

5.1 Some Key Challenges and Unsolved Problems concerning Risk communication during Pandemics

Pandemics are characterized by both temporal and geographical scales that are larger than those of normal epidemic outbreaks. Risk Communication during pandemics has thus to be effective at both scales. This represents a first challenge and a partially unsolved problem.

First, RC tools, usually designed at the short temporal scales of the duration of epidemic outbreaks, have to be re-engineered for the long duration of pandemics (Aiello et al, 2010).

The second critical elements in pandemic RC is that guidelines are proposed across various geographical scales: international, continental (e.g. EU), national, and in some cases there is, at least theoretically also the possibility of regional scale, due to legislative processes of partial or total devolution of the administration of public health from national to regional level (e.g. in Italy and Germany).

This multi-level structure cause a challenge into the challenge, in that the guidelines emitted to a larger scale cannot (or can badly) be implemented at a lower geographical scale, causing discrepancies. This, for example, has been stressed by Gesser-Edelsburg et al (2014): we are far from the ideal collaboration between international coordinating bodies with local ones (ECDC Report, 2013). These authors identified as main cause of these heterogeneities between international guidelines and their national versions and implementations in the fact that the structure of international guidelines is excessively top-down with scarce consideration of local problems in implementation and of possible local concerns. Seldom preliminary informative evaluations are performed and an insufficient attention is given to the results and recommendations of scientific literature on communication strategies (Gesser-Edelsburg et al., 2014).

A two-way communication strategy would largely lessen these challenges of RC (Barrelet et al, 2013; Gesser-Edelsburg et al 2014) with respect to the current one-sided approach (Bodemer and Giassmaier, 2012) in that feedback from local entities and from public would become an integral part of the process of communication strategies. This approach would be more appropriate given the inherent dynamic nature of communication (Barrelet et al, 2013). Note that the two-way adaptive decision making is an increasingly important part of general political decision making and communication, where political decision-makers are shifting from the traditional top-down approach to the two-ways paradigms of governance and communication (Sabel, 2012; Barca, 2013). A more dialogue-based RC is indeed considered important in general and not only in relation to health risks (Markon et al, 2013). Note that the one-to-many traditional communication approach is easier and, such as, it is the preferred communication approach of practitioners of communication (Veil et al, 2011). We note that, also in absence of risk, many political/governmental scenarios are characterized by the provisionality of available information, which is a characteristic feature of pandemic scenarios (Vaughan and Tinker, 2009). We note also that a two-way risk communication is the optimal RC because only with a two-way approach the authorities responsible of RC can stay tuned with the risk perception of the public. Indeed, all major studies showed as theories underlying RC are strictly related to theories concerning risk perception (ECDC Report, 2013). Risk perception and health risk communication, in particular, are so consustancial that in their "Handbook of Risk Theory" (Roeser et al, 2012) the chapter on health risk communication is included in the chapter on theories of risk perception.

It is of interest to note that some countries are slowly moving toward the implementation of a two-way risk communication strategy. For example, in May 2010, in New Zealand shortly during the H1N1 pandemic (May is in late autumn in New Zealand) the public health authorities designed a rapid response initiative to have feedback from population on their communication campaign and on their risk perception (Gray et al, 2012). The need of more substantial involvement was, not surprisingly, one of the major feedbacks that emerged from this study.

Another major feedback reported in (Gray et al, 2012) is that RC should recognize that public are different and that initiatives must be "appropriate for different communities" (Gray et al, 2012). In other words, one leading challenge is related to the "choosing the channel and tailoring the message" (Gesser-Edelsburg et al, 2014; see also: ECDC Report, 2013 and Lin et al, 2014) based on socio-demographic and other characteristics (Lin et al, 2014). In doing this one has also and mainly to take into the account that the most vulnerable subjects or even entire communities may happen to experience communication gaps (Vaughan and Tinker, 2009; Aiello et al, 2010), for example due to disadvantageous geographical location or social inequalities. More in general, a number of social and individual determinants may result in unequal exposure to communication messages, as stressed by Lin and colleagues (2014), who also identified a number of predictors of behavioural compliance to the conveyed RC during H1N1 pandemics. Quite surprisingly, they showed the older age was positively associated with information on H1N1 pandemics and also with willingness to be vaccinated.

Building the trust and being identified as a credible source is another fundamental challenge (Aiello et al, 2010; Abraham, 2013; Gray et al, 2012). Indeed, in absence of trust the communication of the risk is not followed by the implementation of the recommendations (Gray et al, 2012; Gesser-Edelsburg et al, 2014), whereas where the trust is strong there the recommendations, for example concerning the enacting of behavioural changes (see next section), are more widely and coherently followed (Aiello et al, 2010). Here a major problem distinguishing RC during pandemics from other health risk communication is that under distress people "become distrustful and are less likely to accept the validity of communication" especially from authorities (Glik, 2007). Of course missteps by authorities automatically trigger a further loss of trust (Vaughan and Tinker, 2009). It is interesting to note that international organizations may be perceived as more trustable that National Health authorities (Gesser-Edelsburg et al, 2014), because the latter are perceived as political organization acting more following political interests than for the benefit of the general public. This is in agreement with data collected on public trust on general governmental authorities (Markon et al, 2013). This is a very serious issue since public trust in authorities is a crucial factor in effective RC: in case of doubts on competence and/or also on the honesty of health authorities or the government then the messages diffused by them are disregarded by the public (Abraham, 2013).

Maybe one of the most difficult challenges in RC is to overcome the "sensation of conspiracy" (Gesser-Edelsburg et al, 2014) that has been formed in the public and sometime among the health-care workers in last years. This attitude to suspect conspiracies probably reflects similar feelings in a wide spectrum of relationship of the public and of professionals of various categories with respect to political organizations, organs and with respect to many - and competing (Barrelet et al, 2013) - sources of information. These kind of negative and untrusty attitudes are generalized and one decade ago led the sociologist of risk management Loefstedt (2005) to define our society as a "post-trust society". In particular, during H1N1 pandemics public authorities had to face recurrent rumours in the traditional media and on the Internet on conspiracy between them and pharma industries (Barrelet et al, 2013), leading to allegations - reported by (Abraham, 2011) - that H1N1 was a "fake epidemics". Thus, to some extent part of RC during H1N1 pandemics showed communication failures (Abraham, 2011), and suffered from communication failures of previous years. During and especially after the H1N1 pandemics this resulted in a wave of lack of trust in governments and agencies and other agencies that propagated in EU public undermining future RC (Barrelet et al , 2013).

Indeed, counteracting/dispelling rumours is one of the most important and up to date unsolved challenges in RC during epidemics (Vaughan and Tinker, 2009; Barrelet et al, 2013): how can rational information emitted/produced in RC propagate faster than rumours ? How to help the public to discriminate between rumours and correct information?

Especially in first phases of pandemics, where the factuality and severity of the pandemics is unclear, and where the data are non-complete and possibly contradictory experts' interpretations of data exist, an important challenge concerns whether or not this uncertainty has to be transparent when communicating risks (Markon et al. 2013; ECDC Report, 2013). This issue is currently being debated and there is no consensus in research whether a transparent approach is welcome or not by the general public, and if it can enhance or decrease the trust in health authorities. Although much literature is based more or belief on public reactions than on the field data, some experimental investigations seems to indicate that a careful communication of uncertainty is positively appreciated (ECDC Report, 2013). This is particularly true if the uncertainty directly involves the individual decision-making or if it concerns side-effects of drugs or actions (Markon et al. 2013), whereas is negatively perceived when the "concerned risks are outside of individual citizen control" (Markon et al. 2013) and also when uncertainty involves the actions of the organisms communicating the risk (Markon et al. 2013). As far as the issue of the communication of uncertainty is concerned, trust in the authorities in charge of risk communication is crucial (Gray et al, 2012). An important study on how uncertainty was managed in the context of risk communication during the H1N1 pandemics is Fogarty et al. (2011), which focused on Australia. Their conclusion is that the health authorities had a responsible behaviour where uncertainties are acknowledged together with reassuring on the government preparedness.

The risks related to pandemics have intrinsic scientific complexity and it is not easy to understand and communicate them (Markon et al, 2013). It is fundamental to give to the public intelligible tools in order that they can correctly interprete the delivered health RC (Vaughan and Tinker, 2009) given their heterogeneous current cultural, social and socioeconomic frameworks. Another layer of complexity derives from the fact that ideally in decision making also public should know health statistics (Bodemeier and Gessmaier, 2012), of course appropriately simplified and verbalized. E.g. in risk communication towards public instead of say "rare event" one should say "event with 1% of probability" etc… The idealized risk communication model of Bodemeier and Gessmaier (2012), however, is of difficult applicability during pandemics, where the quantification of risk is uncertain and subject to updates as long as data accumulates.

In other cases some messages are not intrinsically complex but they are disturbing (Vaughan and Tinker, 2009). This forms another important challenge, which consists in overcoming the trade-off between conveying disturbing communication and the maintaining of the cooperation of the public (Vaughan and Tinker, 2009)

Coping with internet is a fundamental challenge for pandemic RC (Abraham, 2011; 2013). Many actors for long times did not exploit internet (Barrelet et al 2013) and social networks (Veil et al, 2011), which is unacceptable in the age of digital native (Betsch, 2011) and of the access to the Net and, in particular, to net-based social media on mobile phones. This is a negative point since, on the contrary, groups spreading rumours, which as anti-vaccines groups, employ general internet and social media in an optimal way. As far as this point is concerned, Reyna (2009) showed theoretically that anti-vaccination information sources provide more coherent accounts of the “gist” (i.e. essential meaning in opposition to the “surface form”) of the vaccination “filling a need to understand rare adverse events”. Moreover, Betsch (2011) noticed that even if individual does not report internet as a major factor in the vaccine decision, or even if they explicitly assert that they give low importance to internet-gathered information, yet the information acquired on Internet can be influential. Indeed the influence of information on individual’s perception and individual’s behaviour can be asymmetric (Betsch, 2011) in favour of the behaviour. In other words, the influence of information acquired through Internet and social media can be very effective but it may remain unconscious. This confirms that Internet has an important role in forming behaviour and risk perception (although, as we have seen, often in a non-conscious way), given that a large portion of population “surf Internet” (Betsch, 2011) to collect health information. These figures imply that the majority of people that has access to Internet use it as a source of health-related information. Ringel et al (2009) noticed during the H1N1 pandemic a geographic scale issue also in the RC on the Web in USA. Indeed, they found that the velocity in communicating risk at state health department was double than the one measures on the website of local health authorities. Veil and collegues (2011) stressed that the incorporation of social media in RC during pandemics and other health emergencies might allow to better manage risks. Of course, a central point of the incorporation is actively using social media as operative communication tools (Veil et al, 2011), of course of two-way type.

Finally, a RC strategy is very likely to fail if it does not take into the account how risk is perceived in the target population and if, more in general, the deciders in charge of the RC does not take into the account its broad cultural values (Vaughan and Tinker, 2009; Barrelet et al, 2013). This is an intrinsic critical challenge to effective RC in the multi-lingual and multi-cultural European Union (ECDC Report, 2013). However, note that cultural differences across groups are not intrinsically negative and some authors think that RC strategies should exploit them by adopting strategies that enforce community beliefs and traditions (Vaughan and Tinker, 2009).

6. HUMAN BEHAVIOUR DURING EPIDEMICS/PANDEMICS/ENDEMICS

Preparedness to pandemics does not only require being able to provide primary services such as vaccine and drugs delivery, hospitalizations, etc… but also being able to understand the population behaviour and influence it in order to make the population compliant with the established public health measures and reduce the burden of the pandemics (Balinska and Rizzo, 2009; Rizzo et al, 2013).

Understanding and governing behaviour during a pandemic is, thus, a major challenge for EU Public Health

Two outstanding examples from the recent history of public health showing the effectiveness of public health campaigns aimed at containing the spread of an infectious disease by means of pure diffusion of awareness and at inducing behavioural changes come from HIV and Ebola epidemics.

The setting up of disease awareness by public health authorities and NGOs in Uganda induced in the citizens changes in their sexual behaviours, which in turn remarkably decreased the HIV prevalence in this country in early 2000s (Green 2006). Similar patterns of awareness campaigns-triggered reduction of HIV prevalence were also observed in Zimbabwe (Gregson et al 2006; Halperin et al 2011).

Finally, it is worth to note that social mobilitation and spreading of the awareness of the outbreak was one of the most important measures enacted by Uganda during the Ebola epidemics in 2000 (Lamunu et al 2004).

Many lessons can be learned by these examples.

Behavioural response to the spread of vaccine-preventable infectious diseases has usually two key components: vaccine propensity and enacting of non-pharmaceutical steps related to the infection, i.e. interaction with other people (social distancing and changes on mobility) or hygienic habits such as handwashing, nutritional patterns etc.. Moreover, both pharmaceutical and non-pharmaceutical steps can be either effective (e.g. H1N1 vaccination, more frequent and accurate handwashing) or ineffective or dubious (avoiding cold places, seasonal influenza vaccination). Moreover, for zoonoses such as Influenza it is of relevance a third important component of HB: the interplay with animals that carry the virus.

A vast body of historical evidences (Bauch, d'Onofrio and Manfedi, 2013) exists concerning the role of behaviour changes during epidemics or in relation to endemic infectious diseases. These evidences show that both positive and negative outcomes can emerge from behavioural changes of individuals.

We mentioned above the success stories of Uganda and Zimbabwe. As far as negative outcomes are concerned, probably the most known and documented example of negative impact on the burden of a disease of a change of behaviour is the drastic reduction of vaccine propensity at population level known as "the MMR vaccine scare". A long standing rumour on possible links between MMR vaccination and forms of autism, amplified by a fraudulent paper published on a high impact journal (see Godlee 2011 for a summary of the facts), caused during many years a remarkable reduction of MMR vaccine uptake in UK and various western countries (Jansen 2003; Friedrichs et al 2006; Pearce 2008, MMRW 2011,Bauch 2012) This ultimately resulted in outbreaks of measles in countries where this disease was close to eradication (Jansen 2003; MMRW 2011, AnonymousEditorial 2012) and to a delay of five years in the esteemed date of measles eradication in Europe (MMRW 2011).

Influencing the human behaviour during a pandemic is a multi-faceted challenge, requiring the substantial interplay of many scientific fields alongside public health science and epidemiology. Indeed, apart economic issues, sociology, psychology and even anthropology are needed to investigate these issues. Moreover, since the impact of Human Behavioural Changes (HBC) can potentially affect the dynamics of the spread, the contribution of mathematical models cannot be neglected. In order to pave the way to a clear understanding of the HB-related needs for the setting up of effective preparedness plans, in next section we shall review empirical evidences of spontaneous HBC during influenza pandemics. Forms of mandatory HBC, such as school closing or other force “community mitigation” measures (Aiello et al, 2010), have been reviewed in section 6. In the same section we also discussed another factor that did not help in favouring positive changes in human behaviour: the large and country-dependent delay in the availability of H1N1 vaccine.

Although we will mainly focus on 2009 H1N1 pandemics, however, following (Balinska and Rizzo, 2009) we shall not neglect the influenza pandemics of the past century (i.e. the 1918-1919 “Spanish flu”) as well as the SARS outbreaks in 2003. Evidences of HBC during 1957-1958 and the 1968-1969 pandemics are, unfortunately scarcely documented, as stressed in 2009 by Balinska and Rizzo, and we were not able to find any new work on this topic in the 2009-2013 literature

6.1 Enacting of non-pharmaceutical steps

Remarkable behavioural changes have been adopted by populations during pandemic influenza such as H1N1 in 2009 (Eastwood 2010; Rubin 2010; SteelFisher, 2010; Setbon et al., 2011; Rizzo et al, 2013) as well as during SARS outbreak (Ferguson 2006; Sadique 2009): increased number of daily hand-washing, hand sanitizing with alcoholic solutions, changes of patterns of mobility, social distancing, etc... It has also been reported an increasing number of General Practictioners consulting by people affected by flu-like symptoms (Miller et al, 2010). Wearing masks was a measure taken by many citizens during the “Spanish flu” pandemics (Balinska and Rizzo, 2009). All these measures, spontaneously adopted by individuals that have been informed on their usefulness, substantially contribute to the so-called “community mitigation” (Aiello et al, 2010) of pandemics. Moreover, it has also stressed that the vast majority of such protective behaviours can be effectively taught through campaigns of community health education (Aiello et al, 2010). For wearing masks the degree of acceptance is, instead, thought to be low (Aiello, 2010).

Short-time behavioural response after outstanding events has particular interest. Goodwin and colleagues (Goodwin, 2010) investigated behavioural response in Europe and in Malaysia during the first six days after WHO declared pandemic alert 5 during the H1N1 pandemics. They showed remarkable changes in behaviour, with a 22% and a 17% of responders that, respectively, had reduced the use of public transportation and had cancelled flights. The studies also showed marked differences in behaviours and anxiety between the European and the Malayisian samples. This study also stressed that 64% respondents of European sample remarkably under-rated the death risk from normal seasonal flu.

Marked behavioural changes were measured in a UK-based survey held in early days of May 2009 (Rubin et al, 2009), with increase of social distancing measures and recommended protective behaviours, such as increased hand-washing. People that had enacted social distancing or recommended protective behaviours had significantly higher levels of anxiety than participants that had not. Remarkably, anxiety was significantly smaller in subjects that had read a leaflet sent by British government, with respect to subject that had not red or received it. However, reading this publication had not direct effect on the behaviour.

Probably the largest behavioural changes during 2009 pandemics were observed in France, where a survey in the general public led by (Setbon et al, 2011) only the 17.7% of responders declared that they did not protect themselves at all, or had no intention to protect them. In particular 73.5% declared to enact non pharmaceutical steps, in 27.4% of cases in combination with H1N1 vaccination (intention or action). Among the non-pharmaceutical steps, 59.7% declared and increased frequency of hand-washing, 43.7% the use of anti-microbial solutions, whereas a minority of responders indicated measures of social distancing (avoiding crowded places: 14.6%, avoiding public transportation: 12.8%). As far as those that did not want to change their behaviour reported assertions of fatalism, distrust and belief in conspiracy (Setbon et al, 2011).

Scarce behavioural response was evidenced in Hong Kong (Cowling et al, 2010) and in Rajstan (India) (Kamate et al, 2010).

A remarkable change of behaviour was observed among Italian healthcare workers in a survey by La Torre and colleagues (2009) were 64.7% of physicians and 79.5% of nurses declared that they washed their hands and used hand sanitizers more frequently.

During H1N1 epidemics, the change of behaviour was at least in part in line with suggestions by the public health authorities, as noticed in USA (SteelFisher, 2010), in part of UK (England, Scotland and Welsh) (Rubin, 2009) and in France (Setbon et al, 2011; Caille et al, 2014). Rubin and colleagues (2009) also evidenced that in UK ethnic minorities were more likely to adopt recommended changes of behaviour. In France, Setbon and colleagues (2011) stressed that although a large majority of people responding to their survey adopted behavioural changes or get vaccinated suggested by public health authorities, yet in majority (50.8%) they adopted a single strategy (i.e. they only vaccinated, 8.8%, or took non-pharmaceutic steps, 42.0%) instead of the cumulative one, which was the suggestion of the public health authorities.

However, due to the dichotomy – stressed by the committee- between mildness of the pandemics and the diffusion of social alarm, at the end of the pandemics a negative trend of willingness of adopting vaccination has been observed when comparing two surveys in four EU countries, one done at the beginning and one at the end of the 2009 pandemics. Instead, as far as the adoption of precautionary measures, no decrease was observed between the two surveys: in both cases increases in protective behaviours were observed. Note that the trends observed in (Rizzo et al, 2013) were not uniform but nation-dependent. Indeed, patterns of change of behaviour are influenced by local public health politics as well as by cultural factors influencing beliefs on the disease and on the mechanisms of contagion, as it was evidenced by Rizzo et al, (2009).

Waning of propensity to adopt self-protective behaviours has also been evidenced by (Holland Jones and Salathe, 2009) who, in the framework of a survey held between April 29 and May 5 2009, stressed that emotional status mediated behavioural response, and that accurate monitoring of both self-protective behaviours and factors mediating them might be an important pillar for strategies of control of epidemics.

Concerning self-protective behaviours during H1N1 pandemics, Remschmidt et al (2013) showed that in German households where a subject with influenza was present a marked increase of hand-washing frequency was measured with respect to the previous year (55% vs 30%). In general, increasing of non-pharmaceutical steps in households and hospitals where one or more patients with influenza is present are very effective in reducing the local contagion (Aiello et al, 2010).

In contrast to many papers focusing on early phases of the pandemics, Gaygisiz and coworkers (2012) studied behavioural reactions in Turkey (applicant country to EU, member of EU council) during a late stage of H1N1 spread, i.e. when the peak of the feelings of anxiety caused by the first news on H1N1-related deaths had disappeared. Although effective recommended behaviours (such as increased hand-washing with hot water and soap (70.4%) were largely adopted (globally by the 87.9% of the investigated sample), the majority of subjects (59.8%) reported to have enacted ineffective behaviours (such as: avoiding cold surfaces: 49%; avoiding sitting close to open doors and windows: 37%). Social distancing behaviours (such as: staying away from crowds: 32.5%; using less public transportation: 18%) were also largely present (41.2%). Quite interestingly: i) anxiety was a statistically significant predictor for both avoidance and ineffective behaviours; ii) individual's awareness of being able to modulate his/her own risk of being infected was a significant predictor of adopting recommended protective behaviours. As far as anxiety is concerned, note that in this case the anxiety was not significant for people enacting recommended protective behaviour, at variance with the British study (Rubin et al, 2010), which had been done in early phase of epidemics (and, of course, in another country). Finally, low levels of trust in the information provided by the government and in its ability in managing the epidemics in the future were observed.

Disease-related risk perception and the consequent changes in the behaviours impact onto the transmission of the disease, which implies that it can modulate its population dynamics (d'Onofrio and Manfredi, 2009).

The increasing qualitative consciousness of this phenomenon and the subsequent start of inflow of related epidemiologic data led in last ten year to a deep rethinking of the mathematical modelling of infectious diseases. These models are not only of intrinsic scientific interest, but they also are a useful tool actively employed by national and international public health agencies to decipher epidemic dynamics, and to assess the impact of prevention measures (Ward et al, 2014; Basu and Andrews, 2013; Anderson and May, 1991; Bailey, 1975).

An intrinsic limitation of epidemic models is that they are based on a statistical mechanics approach: the contagion is abstracted as a chemical reaction that can or cannot occur upon the random encounter of two "particles": the infectious and the susceptible subjects.

However useful it may be to describe many epidemic scenarios, this approach misses the behavioural component that we described in the previous sections. This led in last ten years to the birth of a new branch of epidemiology: the behavioural epidemiology of infectious diseases, aimed at investigating the changes of behaviour of individuals of a population where an infectious disease is spreading, and their impact on the spread itself of the disease. As clearly shown by contributes of the first book ever published on this topic (Manfredi and d'Onofrio, 2013), the behavioural epidemiology is intrinsically multi-disciplinary, requiring the intervention not only of applied mathematics and statistical epidemiology but also of economy, sociology and anthropology.

The first pioneering model that took into the account human behaviour-based modulation of the contagion probability was due to (Capasso and Serio, 1978), where the transmission rate decreases as the prevalence of the disease increases. In (d'Onofrio and Manfredi, 2009) it was evidenced the role of the memory: as we have seen for the H1N1 pandemics, often the changes of behaviour are of short duration, whereas in other scenarios a long memory is possible. In (Bootsma and Ferguson, 2007) it is proposed a model of the Spanish Flu in 1918-1919, where the behaviour transmission is a decreasing function of the number of disease-related deaths in a given time interval.

Of course, H1N1 pandemics as well as SARS triggered in behavioural epidemiology a number of theoretical investigations. Furthermore, many research works have also been devoted to assess the role and impact of changes of behaviour during the major world pandemics: the Spanish flu in 1918-1919.

Merler and coworkers (Poletti et al, 2011; Poletti et al., 2013) noticed that the time series of Influenza-Like-Illness (ILI) during the H1N1 pandemics in Italy cannot be fit by a model where the disease transmission rate is constant: a time varying rate is needed. This led them to model the behaviour during pandemics as the risk-perception-driven switching between normal and reduced risk behaviours. At population level, this means the unconscious adoption by the population of an imitation game dynamics. This model perfectly fits the ILI time-series, thus giving a mechanistic explanation of the changes in transmission rates. In particular, in the model suggest that in the first phase of the pandemics the altered behaviour was prevalent, whereas in the second phase a normal behaviour was restored. This despite the increase of the number of cases of ILI. In particular, they analysis suggest that an initial overestimation of the risk led to an initial delay which, however, was followed to a sudden return to normal behaviour and, as a consequence, to a sharp increase of the number of ILI cases.

A model with spontaneous switching between a baseline behaviour and a prudent behaviour during pandemic influenza has been developed by Del Valle and coworkers (2013), and applied to evaluate the impact of extreme social distancing (remaining at home) and forced social distancing (school closure). These models predict that if the behaviour change is temporary then epidemic waves are generated, i.e. multiple epidemic peaks. Two peaks had been, for example observed during the SARS epidemics in Toronto in 2002-2003 season (Ofner-Agostini et al., 2008) and during the Spanish influenza pandemics in 1918-1919. And indeed data analysis of Spanish flu time series by Hatchcett and coworkers (2007) suggests that in USA only in cities were multiple and long-lasting measures of forced social distancing had been introduced had a significant reduction in mortality peaks; and that relaxation of these measures induced the above mentioned epidemic waves. Chowell and coauthors (2006) investigated the time-series of the Spanish influenza in 1918-1919 in Geneva

(Switzerland), which was characterized by two peaks, one in the spring and one in the fall. They showed that although the second peak was larger than the first, the estimated transmission rate was smaller in the fall with respect to the spring, which they attributed to a multiple spontaneous and forced changes of behaviour. However no mechanistic model of the behaviour change was provided.

Funk and Jansen (2009, 2013) investigated the spontaneous spread of awareness and its impact on disease spread during an epidemic. Not surprisingly, Funk and Jansen (2009, 2013) showed that the important parameter is the relative velocity of the spread: if the spread of the awareness is faster than the spread of the disease the impact of the disease is smaller. Although this result is theoretical and only refers to the spread of an infectious diseases in absence of vaccination, it suggest that the rapidity and quality spread of awareness is a crucial parameter for the success of a vaccination campaign.

Another issue of relevance suggested by theoretical models concerns the local vs global awareness of the spread (Perra et al., 2011; Perra and Vespignani, 2013; Funk and Jansen, 2013): to minimize the burden of the disease is it better to obtain information on the spread or information on a larger spatial scale (e.g. country-wide) ?

6.2 Vaccine Propensity

As far as the vaccination behaviour is concerned, there are quite clear evidences that the awareness campaigns enacted during the H1N1 pandemics were not successful in reversing the poor baseline score of anti-influenza vaccinations. For example, Rodriguez-Rieiro and colleagues (2011) showed that in Madrid province (Spain) of all those for whom the H1N1 vaccination was indicated (1,114,000 subjects over a total population of 6,366,000 in the region), only 14.6% were vaccinated. Among under 30 this percentage is only 5%. Even among the subject suffering three or more chronic conditions for whom vaccination is warmly suggested only 31.3% got vaccinated. Quite interestingly, as a possible explanation of the low vaccination rates in Spain (Rodriguez-Rieiro et al, 2011) formulates the hypothesis that a vaccination strategy focused (as the one against seasonal flu) on age groups would have been more effective of the one enacted, which was, instead targeted at risk groups. This change of target might have induced confusion among the population. For France, different estimates are available.

Vaulx and coworkers (2011) estimated that the pandemic influenza vaccination coverage in France –where the H1N1 vaccine was given for free - was only 11.1% about in the general population and 12.2% among individuals with health conditions associated with higher risk from influenza. Privileggio et al (2013) estimated, instead, coverage of 23% in persons with high risk of severe influenza. Although very different, both these estimates are even lower than the usual rates of seasonal influenza vaccine uptake in people at risk in France, which was 56% in 2008 (Tuppin et al, 2011) .

These data concerning France exemplify very well the dichotomy between intention to vaccinate and action. Indeed, in the above mentioned survey in France (Setbon et al, 2011) among responders 27.4% declared they had or had the intention of vaccinating themselves against H1N1. Thus we may infer that the majority of the responders to the survey by (Setbon et al, 2011) have been not vaccinated against H1N1. Maybe instead of the H1N1 vaccine many have chosen the vaccine against the seasonal flu, since the 25.6% of responders had indicated the intention to take this step.

On the other side of the spectrum of H1N1 vaccine coverages in EU were Sweden, Finland and Norway where, respectively, 60%, 52% and 45% of the general populations decided to get vaccinated against H1N1 (Bjorkman and Sanner, 2012; Finnish NHI, 2010; Waalen, 2010).

Adherence to H1N1 vaccination campaign was also low among the healthcare workers (HCWs) in EU, especially among nurses (Wicker and Rabenau, 2010). This means that the awareness campaigns during the pandemics were not able to remarkably reverse the trend of low vaccination rates against seasonal influenza among HCWs, which ranges in some European country between 14% (UK) up to a maximum of 48% in France (Venice Report, 2008).

An evidence of the markedly different attitude among HCWs towards pandemic influenza vaccinations was pointed out in the Italian survey by La Torre and coworkers (2009): although 79.5% of nurses declared in a large majority that they had started to sanitize and/or wash their hands more frequently versus the 64.7% of physicians, who reported a comparable percentage of vaccine acceptance (67%), the acceptance of vaccine for nurses was very low: only 31%.

In a survey among nurses in London (Zhang et al, 2012), only the 35.3% of responders reported receiving the H1N1 vaccine. Of them 48.6% reported the intention of being again vaccinated the next season, 31.4% was unsure and 20% answered 'No'. In a similar survey conducted at the University Hospital in Madrid (Spain) only the 16.5% reported having been vaccinated for H1N1 (Virseda et al., 2010). At the University Hospital of Frankfurt, where large campaign in favour of seasonal influenza are enacted since 2003 with excellent results, only 30.2% of nurses were vaccinated against H1N1 versus the 80% of vaccinations among physicians (Wicker and Rabenau, 2010). As far as physicians are concerned, in a survey on the vaccination behaviour of Health care workers in the region of Thessaly, Greeces, showed that only 26.7% of the medical doctors were going to be vaccinated against H1N1, and only 4.2 of interviewed nurses (Rachiotis et al, 2010). Globally the 83% of interviewed healthcare workers declared that they were going to refuse vaccination (Rachiotis et al, 2010).

Note that the above reported differential vaccine behaviours in EU was at variance with the one reported in USA were the same percentage of vaccination among both physicians and nurses (44.7% vs 44.5%) was reported (CDC, 2010)

H1N1 "mild pandemics" stimulated a large number of investigations aimed at understanding the reasons underlying the poor responses to the awareness campaigns aimed at building up a consistent vaccination coverage. One of the earliest surveys was conducted during the H1N1 pandemic in France (Schwarzinger et al, 2010) yet clearly pointed out two major causes of this poor response. The first was the "dissonance" between the alarm signals communicated by public health messages and the "daily experience which did not confirm the threat": only 36% of responders perceived H1N1 as a severe disease. The second issue is the general concerns raised by the public on safety of the vaccine (Schwarzinger et al, 2010), a well-known major factor in opposition to vaccination (d'Onofrio et al, 2011; d'Onofrio et al, 2012; d'Onofrio and Manfredi, 2013). In the study by (Schwarzinger et al, 2010) the 71% of respondents that refused vaccinations raised concerns on possible vaccine-related side effects. As a local factor, (Schwarzinger et al, 2010) also stressed the lack of involvement of General Practicioners in the awareness campaign, as also mentioned in Section 6. The relevance of the role of GPs for mass vaccination and vaccine awareness campaigns in France was also pointed out by (Privileggio et al, 2013).

In the above mentioned survey on nurses in Madrid (Virseda et al., 2010), "doubts about vaccine efficacy" and "fear of adverse reactions" were the two main reasons underlying non-acceptance of vaccine. Quite surprisingly, membership of a priority group was strong factor for vaccine refusal with an OR close to 6 (OR 5.98, CI: 1.35-26).

In the survey in Tessalony Rachiotis and colleagues (2010) reported that 75% of interviewed health care workers that were not going to be vaccinated against the pandemic influenza raised concerns over vaccine safety, and 16.5% refused the vaccine since they self-assed their status as not at risk of serious illness. One fifth of the people fearing vaccine side-effects specifically indicated that they had specific concerns on the possible association between H1N1 vaccination and Guillan-Barre' syndrome (Rachiotis et al, 2010), some cases of which had been reported in December 2009, for example in France (Setbon et al, 2011). Finally, about 58.5% of the interviewed HCWs complained for the scarceness of available information on the pandemic influenza vaccine.

A large survey among the HCWs working in four university hospitals of Lyon (France) (Valour et al, 2012) showed that 75.7% of interviewed HCWs had concerns on lack of sufficient number of studies on the H1N1 vaccine, and 51.5% of interviewed perceived H1N1 influenza as a benign disease. Moreover, 24.6% of vaccinated nurses and 10% of vaccinated physicians regretted for being vaccinated.

Finally it is worth of note mentioning that, in their systematic review on H1N1 pandemic vaccination (on papers not included in the present one, apart Virseda et al., 2010), Prematurge and coworkers (2012; 2014) stressed that during H1N1 pandemics occurred a number of factors concurring to vaccine refusal that was unique to that pandemic, such as: i) belief that vaccine development was too rapidly developed and authorized by national health authorities; ii) inhibitory role of media; iii) many HCWs used mass media as their main source of information on H1N1; iv) negative influence by political leaders, such as the prime minter of Turkey (applicant country to EU) that publicly rejected H1N1 vaccine. All mentioned points but (iii) were likely to act also on general population.

This widely reported lack of knowledge and also misconception about vaccine among health professions should be taken into the account when planning an awareness plan.

Following (Bjorkman and Sanner, 2012) "a prerequisite for taking the vaccine would be that people feel involved in the vaccination enterprise to make a sensible decision regarding whether their health will be best protected by vaccination".

Not differently from recent evidences in Africa, also in Europe it seems important to move from the traditional statistical-based epidemiological surveys to new generation of investigations where the statisticians cooperate with anthropologists and psychologists.

An important question arising from the current literature on vaccine behaviour is whether the vaccine refusal is more due to an instinctive or superficially motivated reasoning or it is the result of a full rational reasoning. Concerning this question a survey conducted on Israel many months after the H1N1 epidemic peak showed that 30% of the non-vaccinated responder provided reasoned arguments for their decision, usually based on balancing threats vs actual risks (Velan et al, 2011).

Of course, the presence of a reasoning is not a guarantee that the reasoning is really rational: reasoning can be irrational. Indeed, a prototypical problem in behavioural epidemiology is the pseudo rational exemption to vaccination, an example of the “free riding phenomenon” where people decide to not vaccinate themselves and their children because they over-weight vaccine-related side effects with respect to risks intrinsic to the target disease, which they perceive as low because of the low number of people affected by the disease (d’Onofrio et al 2007). This kind of decision is myopic because the prevalence of the target disease is low due to the large number of vaccinated subjects.

Mathematical models that take into the account the dynamical enhancement of vaccine propensity caused by the prevalence of the target disease are (Bauch, 2005; Reluga et al, 2006). The specific effect of information on the disease spread as well as the historical memory of past epidemics, were included in (d’Onofrio et al, 2007; 2008). For further references, see (Manfredi and d’Onofrio, 2013).

As major determinant negatively influencing the propensity to vaccinate are the vaccine-related side effects (d’Onofrio and Manfredi, 2010), and this emerges also from the above reviewed literature concerning H1N1 vaccination campaign. In a mechanistic perspective, the vaccine propensity is determined by the opposition of two “forces”: the fear of getting the disease, which is related to the perception of tis spread, and the fear of getting the side effects. This tension was modelled by coupling a classical epidemic model with an imitation game dynamics representing the temporal evolution of the average population-level propensity to vaccinate (d’Onofrio et al, 2011). The scenario depicted by these theoretical investigations is apparently negative: spontaneous behavioural changes are useful but only a mandatory vaccination is able to eradicate the epidemic spread. This result, however, does not take into the account the possible actions of public health systems in increasing the awareness of the relevance of the vaccination, which is an important factor as evidenced in the previous sections. Once included in the above-mentioned model also a vaccine awareness campaigns aimed at increasing the propensity of non-vaccinators to vaccinate, the resulting model suggest that if the campaign is appropriately intense then it can lead to eradication of the target disease (d’Onofrio et al, 2012).

6.3 Interactions with animals carrying the virus

Influenza can be considered as a zoonotic diseases since birds and pigs carry influenza viruses and can transmit some of them to human beings, and vice versa. In particular, H1N1, as it is well-known, is a Swine Influenza Virus. For this reason the behaviour of human when interacting with the animals carrying the virus is of extreme relevance, as it has been stressed in the literature. An important point for disease spread are wet markets, where people buy a living animal to be slaughtered at home by the buyer or in the market by the vendor (Alexander and McNutt, 2010). Wet markets are a great opportunity for pathogen adaptation and have been indicated as a key point for the onset of SARS outbreak (Brown 2004). Another source of animal to human transmission is the habit of householding animals.

As noticed by (Alexander and McNutt, 2010), the human behaviour at animal interface is the result of centuries of cultural practices and thus in the elaboration of a plan to act in this particular and sometime peculiar aspect of HB it is of fundamental relevance the role of anthropological studies. Indeed, we note, in some areas it is important to understand that modifying the interface human-carrier animals is similar to the enacting of social distancing between humans, because in rural areas there is a culturally shaped social dimension in the relationships human-animal.

CONCLUSIONS AND RECOMMENDATIONS

In view of difference across Europe in legal systems, various initiatives taken by the Member States and heterogeneous results obtained in terms of vaccine delivery, vaccination uptake, and infectious controls measures, establishment of a real framework by the Member States to identify avenues for improvement of future influenza pandemics management is warranted. Retrospective analysis of different vaccination strategies would provide lessons to be used for future pandemics with regard to vaccine production capacity, vaccine efficacy etc. These points should be addressed in inter-pandemic time. The WHO initiative to support for technology transfer to enable domestic influenza vaccine production in developing countries (Friede 2011) would help to decrease the observed inequity to vaccine access. Preparedness requires shared responsibility and collective action on multiple fronts. A better overall understanding of the role of the IHR, coherence between national laws and the IHR and further guidance from the EU to support design of more common legal approaches across states would be of particular importance for next influenza pandemic.

Indeed, preparing to new and efficient systems of Pandemics Surveillance is a major challenge. In recent literature investigators stressed the following issues:

- Informal surveillance by collecting and decyphering data of multiple types from Internet. This is a field of investigation where no consensus has been established and which is extremely dynamics, but nevertheless it has to be taken in serious consideration
- Development of a new generation of fast and flexible multi-level evaluation tools and plans, where health-care professionals of various types and background have to play a far more active role.
- Rethinking of classical formal surveillance plans and tools, because of their scarce reactiveness in front highly dynamical events such as those in Pandemics.

To help improvement in response and preparedness plan, the WHO together with the University of Nottingham (UK) carried out a qualitative study that reviewed and evaluated pandemic planning activities undertaken before March 2009 in seven Member States of the WHO European region (Armenia, Bosnia and Herzegovina, Denmark, Germany, Portugal, Switzerland and Uzbekistan). The outcome of the evaluation is a list of recommendations for good practices in pandemic and preparedness. Those related to the points discussed in this chapter were the following.

- WHO should intervene by supporting regional as well as national pandemic plans;
- Countries have to develop flexible plans and define “practical thresholds” to trigger action (e.g. for escalation and de-escalation).
- A revision of the WHO pandemic guidance concerning phases in order to include, apart spread also other epidemiological indicators, among which severity;

- Templates for various kinds of pandemic plannings should be provided by WHO (e.g. vaccine deployment plans).
- A key issue is the timeliness of availability of pandemic vaccines, and donation issues from the WHO stockpile;
- The regulation of vaccine distribution has to be needs-oriented more than market-oriented Equity of access during possible future pandemics is a priority.
- Across hospitals coordination of resources is now mandatory
- Triage tools linked to severity assessment are required.
- Finally, the potentially of managing large temporary influxes (triggered by pandemics) to hospitals and other health-care structures is one o the most important issues

As far as communication of risk during pandemics, the analysis of RC during H1N1 showed that that specific pandemic has been a turning point on RC during general pandemics. A number of issues were raised that were specific to H1N1 pandemics and other possible future flu pandemics, and other that are in common with RC during pandemics or outbreaks of other diseases.

Here we summarize some of the key open problems/challenges that we have illustrated in detail in the previous section 7:

- Coordination across the geographical and hierarchical scales of public health authorities
- Transition to a two-way strategies of risk communication, i.e. with feedback from lower hierarchical scales and public to the top deciders
- Knowledge and exploitation of risk perception among the public
- Knowing the communities/subpopulations that are present in the public and target the communication
- Enact a coherent build of trust in the age of the “post-trust society”
- Waning the “conspiracy sensation” and other rumours (both political and pseudo-scientific) that arose in occasion of the H1N1 pandemics
- Carefully adopt a transparent and coherent policy of communication of uncertainty
- Manage the scientific complexity of communication of risk during epidemics
- Full exploitation of Internet 2.0 through social media and smartphone-based apps
- Develop a paradigm to take care of cultural differences

Additionally and finally, it is important to stress, as in (Abraham, 2011; 2013) that the RC during influence epidemics outbreaks and during future pandemics ought to be complemented by more long-term campaigns aimed at permanently induce changes in current behaviours that may favour the spread of influenza epidemics.

Changes in behaviour are indeed noteworthy, although heterogeneous. Indeed, those changes that affect changes in personal behaviour seem to be easier to be induced (at least for a short-medium interval of time) provided that adequate justification is given to them. On the contrary, changes in vaccinating behaviour seem far more complex to be induced. H1N1 pandemics showed that two key factors synergize in case of pandemic influenza. The first is the suspicions and fear of vaccine-induced side-effects that surround all vaccines. A wrong perception of risks remarkably decreases the propensity to vaccinate in general. The second is caused by the fact that influenza is perceived as a minor disease for which it is not worthwhile to get vaccinated. This thought is so pervasive that also people cumulating more than one chronical health conditions refused, in their majority, the vaccination against H1N1. An outstanding evidence of misconceptions and fears concerning vaccinations is the fact that many medical doctors and the majority of nurses objects to vaccination. This scarce compliance of health-care workers to recommendations diffused by RC campaigns is one of main challenge, and it stresses their global scarce effectiveness. Finally, although this is a problem that marginally present in EU, a major effort has to be done in decreasing the contacts with living animal vectors of influenza, typical of other regions of the world, for example far-East.

Finally, classical statistical methodologies in epidemiology are nowadays complemented by the suggestions coming from mathematical models of the spread of infectious diseases. Increasingly trustable generations of mathematical models are being published in literature: they constitute a precious resource to be better exploited, at least in the field of preparedness of pandemics. These models in last years started including an essential factor here investigated: the human behaviour and how the information and, unfortunately, also the rumours on the spread of a disease (and on vaccine-related side-effects) induce those changes. In turn the latter modify the dynamics of the spread of the disease.

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Internet links on surveillance

ECDC http://www.ecdc.europa.eu/en/activities/surveillance/EISN/surveillance/Pages/surveillance.aspx

CDC http://emergency.cdc.gov/episurv/

WHO http://www.who.int/immunization/monitoring_surveillance/en/

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ANNEXE 1: ASSET FOCUSED WORKSHOP SUMMARY (23/02/2015)

PARTICIPATING EXPERTS

Lois BASTIDE, Department of Sociology, University of Geneva,
Member of the resarch project "Lessons from the A (H1N1) pandemic to the Ebola epidemic"

- This research projects is a cooperation between the University of Geneva and the Haute Ecole de Gestion, Geneva.
- The oubtreak response is studied from a threefold perspective: organizing practices, communication, and costing.
- The research framework includes fieldwork in Switzerland, the United States, Japan, and at WHO headquarter in Geneva.

Alberto D'ONOFRIO, Research Director at International Prevention Research Institute

- Computational biology
- Role of human behavior on the spread of communicable diseases
- Mathematical epidemiology of infectious diseases,
- Geographic epidemiology of cancer
- Epidemiology of cancer
- Cancer systems biomedicine.
- Effects of nonlinearity and randomness in biological phenomena, from microscopic to population level

Manfred GREEN, Professor, School of Public Health, University of Haifa, Israel

- Past Director, Israel Center for Disease Control
- Member, National Advisory Committee on Epidemiology and Vaccines
- Member, National Epidemic Control Team
- Head, National Committee for the Eradication of Measles and Rubella
- Member, National Committee for Pandemic Influenza Preparedness

Bruno LINA, Laboratoire de Virologie Est des HCL, CNR des virus influenza
Pandemic influenza activities :

- Surveillance of influenza
- Screening for viruses of clinical relevance and emerging viruses (Incl HRV)
- Member of the Influenza expert groups for the MoH
- Member of the Pandemic expert task group for the Ministry of Health (2009-2010)
- External expert for ECDC
- Temporary Expert for the WHO (PIP)
- Chair of the Advisory group at WHO for sharing of PIP material (2007-2009)
- French representative at the G8 for pandemic preparedness (2008-2010)

Seasonal Inlfuenza activities

- Surveillance of influenza
- Screening for viruses of clinical relevance and emerging viruses (Incl HRV)
- Biobank
- Training EUPHEM fellows (ECDC)

Piero MANFREDI, Dep. Economics & Management, Pisa University

- Formal demography & population dynamics, Demo-economic modeling.
- Mathematical modeling of infectious diseases (since 2002):
  - Transmission dynamics of measles.
  - The impact of demographic change on the transmission & control of infections.
  - Estimation of contact patterns.
  - Transmission dynamics of VZV.
  - Behavioral epidemiology.

Jonathan NGUYEN-VAN-TAM, Professor of Health Protection, Health Protection and Influenza Research Group (Honorary Consultant Epidemiologist, Public Health England)

- Medically trained specialist in public health/epidemiology with clinical background in infectious diseases and emergency medicine
- Active in influenza research since 1991; epidemiology, vaccinology, antiviral drugs, transmission, public health measures, public health policy
- Previously, Head UK Health Protection Agency Pandemic Influenza Office
- Previous consultancy to WHO, ECDC, EU Commission (DG Sanco) and vaccine/pharma industries
- Member UK Scientific Advisory Group for Emergencies (SAGE), 2009
- Former Head of Medical Affairs for Roche, UK and Medical Director of Sanofi-Pasteur MSD
- WHO Collaborating Centre (Nottingham) for pandemic influenza and research
- Chair: UK NERVTAG (New and Emerging Respiratory Virus Threat Advisory Group)
- Co-Editor of Pandemic Influenza (1st and 2nd Editions)
- Editor-in-Chief: Influenza and other Respiratory Viruses

Caterina RIZZO, National Center for Epidemiology, Surveillance and Health Promotion,
Istituto Superiore di Sanità

- Influenza and other respiratory virus: a) Surveillance; b) Epidemiology; c) Transmission dynamics; d) Evaluation of pharmaceuticals and non pharmaceutical mitigation measures; e) Computational Epidemiology
- Vector borne diseases: a) Surveillance of imported and autochthonous infections; b) Computational Epidemiology; c) Evaluation of mitigation measures using mathematical modelling techniques
- Food-Borne and water borne disease: a) Surveillance; b) Epidemiology; c) outbreak investigation; d) control measures
- Preparedness: a) contributed to the Pandemic Preparedness Plan; b) survey on the state of the art of “generic” preparedness at EU level
- Expert and Focal point for European Center for Disease Control (ECDC): Influenza and Pandemic preparedness, FWD, and VBD (2007-to date)
- WP leader and coordinator of several projects funded by the European Commission Seventh Framework Programme, DG SANCO and Italian. (2007-to date)
- Participate to the WHO Informal Network or Mathematical Modelling Working Group on influenza A(H1N1)pdm09 (2010-to date)

Mitra SAADATIAN, Epidemiologist at Lyonbiopole and at Lyon Civil Hospices

Philippe VANHEMS, Edouard Herriot University Hospital, Epidemiology and Public Health Lyon-1 university
Research activities on the epidemiology of infectious diseases (ID) including prevention and research methodology

- Healthcare acquired infections (HAI)
- Community-acquired infections
- Vaccine and prevention
- Statistical epidemiology and modeling

Surveillance of nosocomial influenza

- Outbreak investigations
- Vacccine effectiveness
- Modelisation

Maria ZAMBON, Professoor, Influenza Virologist

- UK National Microbiology Focal Point (NMFP)
- Director UK Reference Microbiology Laboratories
- Head of UK NIC
- Member of WHO IHR Emergency Committee
- UK pandemic planning

Portfolio of Operational delivery :

- 2003 UK SARS Laboratory response
- 2005 UK Lab response network for avian influenza
- 2008-2014 EU influenza reference co-ordination
- 2006-2009 EU Antiviral Resistance Programme VIRGIL
- 2009 National Incident Director Pandemic Influenza
- 2012 London Olympics Microbiology Preparation
- 2012/2013 MERS laboratory response

Pandemic planning laboratory work

- Improve detection capability for laboratory diagnostics H5, H7, H9, etc
- Clinical trials and experimental vaccines :Pandemic Vaccine development (H5, H7, H9):
- Influenza serology developments: new serology tests for population assessment of impact/individual susceptibility assessments
- New surveillance technologies : use of self sampling, WGS for surveillance
- Basic and applied work on antiviral resistance :Mechanism of action of amantadine
- Development of human Mabs in response to emerging infections

Moderator : Alberto D'ONOFRIO

Also Participating :
Elisabeth MARCHI, International Prevention Research Institute
Estelle VINCENT, Lyonbiopole

DISCUSSION SUMMARY AND RECOMMENDATIONS

The aim of the focused workshop was to challenge the main findings of the ASSET T.2.2 reference guide with a subgroup of experts bringing various key expertises (virology, epidemiology, mathematical modelling, social psychology) and who took part in the questionnaire. The purpose of the round table was to:

1- Discuss the most interesting comments of the questionnaires,

2- Point out one main research area that they consider as “vital” for future pandemic preparedness.

The outcome will complete the findings of the report related to unsolved scientific questions in pandemics and epidemics.

The key finding from the discussion are provided below:

Vaccination is part of most pandemic planning, as it is, up to date, one of the best way to fight infectious diseases. However, to be efficient, a minimum coverage rate is required. During the last decades, rumors and suspicions regarding adverse effects of vaccines have shaken people’s trust in vaccination contributing to what is also known as a post-trust society. In this regard, rebuilding trust in vaccination is a main challenge. Communication is a critical issue to restore public confidence for pandemic prevention and management. Compliance with recommendations and commitment will greatly depend on the efficacy of this communication.

In Italy a regulatory agency, let out, without consulting other agencies, that there was a death related to the MF59 adjuvanted vaccine. This had for immediate effect that the batches were suspended. This happened at the end of November 2014 when most people get vaccinated; therefore we can expect a great impact of this communication, on vaccination coverage of the elderly (which usually is around 60 %). This last example shows how much it is therefore necessary to:

- ⇨ Design, from the beginning, a communication strategy on risk and define key messages
- ⇨ Clarify the roles and responsibilities of the different players and to define who leads the communication and how this leader interacts with the other players of the health landscape

The reality of the health environment shows that we cannot prevent having multiple players but maybe those players should all follow the same script. On one hand key messages and the single route to convey them should be defined well in advance, in order to have a message as clear as possible and favor compliance with recommendations. On the other hand, experience shows that media will be looking for and publishing conflict messages and truncate or distort messages, and that scientific and professional advises can be overruled by politicians. Moreover, societal research shows that having one line of communication does not help to rebuilt trust, on the contrary, it leaves space for all rumors. The ability to communicate on uncertainty and potential risks should be part of the message.

Rumors regarding vaccination mainly concern adverse effects of vaccines. Experience shows that media will be looking for and publishing conflicted, truncated or distorted messages and those scientific and professional advices can be overruled by politicians. A way to limit the spreading of those rumors could be improve reports on the adverse effects of vaccines, with:

- ⇨ Better monitoring of the occurrence of vaccine-related adverse events and better surveillance data on their severity. In particular, clearly identify the vaccine-related death rates in EU and compare the with disease –delated death rates
- ⇨ Balance between adverse effect cases and studies on severity of adverse effect

The results would demonstrate the good safety of the products and should be communicated largely. In terms of safety one question remains open today and should be answered:

- ⇨ What is the reason for an increase of autism over the last 30 years? Is it related to vaccination?

Distrust in flu vaccine exists partly because seasonal vaccination campaigns are usually targeting the elderly and risk population but not children. And vaccines are sub-effective in the elderly and are not effective against other respiratory disease. Moreover, sometimes the vaccine does not include the right strain. The effect of those combined elements is that vaccinated people might get sick.

- ⇨ Need of a clear message on why vaccinate, what vaccine will protect people from and that getting vaccinated will not prevent from getting sick
- ⇨ Different strategies should be adopted for adults and elderlies vaccinations.

As for the pandemic vaccines, they arrived too late during the H1N1 pandemics and their novelty arose questions regarding their safety.

There is still room to **improve influenza vaccines**, in order to have:

- ⇨ longer protection
- ⇨ wider protection
- ⇨ patient stratification for the different vaccines we have so far, for example higher doses for elderly combining humoral and cellular protection, lower doses for women, or targeting pediatric use
- ⇨ Improvement in the route of administration (ex. Nasal)
- ⇨ Beside being more effective clinically new vaccines should also be cost effective (including the cost of delivery)

Political decisions to vaccinate are usually base on mathematical models in which behavioural aspects and in particular hesitancy are not taken into account. Therefore this unique source of estimation is not sufficient to constitute a founded basis for decision.

⇨ Mathematical models should be improved and include behavioural aspects, in particular, hesitancy

The recommended coverage rate of vaccination to prevent a pandemic is usually too high to reach. Studies have shown that it is impossible to reach an 85% coverage rate in a democratic country. Incentives to get people vaccinated were discussed:

- UK had implemented targets for Medical Doctors to increase vaccination rate. General practicionners could be given financial incentives for work in increasing the propensity of vaccination of their patients
- Compulsory vaccination: in France for the moment it is mandatory to have your child vaccinated against diphtheria, tetanus and poliomyelitis in order to have access to public schools. But the tendency is to make those vaccines recommended instead of mandatory. A region in Italy has tested this by suppressing mandatory vaccines and investing greatly in communication and surveillance. Despise this huge investment they are experiencing a decrease in vaccine coverage

The **general tendency to stop compulsory vaccination and to only recommend it** should have a negative impact on vaccination coverage.

Seasonal influenza vaccination versus pandemic influenza vaccination: lessons to be learned

In 2009, people were accepting seasonal influenza vaccine but not the H1N1 one. This is probably linked to the fact that:

- There was no time to prepare a proper communication strategy tailormade for pandemics, having as an effect confusing messages raising discussions and suspicion of vaccination.
- The vaccine was available too late, but due to the huge quantity of doses available vaccination was forced even though not always necessary / efficient any more.

Best examples of seasonal vaccination campaigns successes are found in UK and in the Netherlands. As for pandemic vaccines, the best achievements are found in Sweden.

Recommendations are to:

⇨ Incorporate pandemic influenza vaccine to seasonal influenza vaccine

⇨ Information on the right time to vaccinate should be included in communication strategy

⇨ Make vaccines available at the beginning of the pandemics

How to convince?

Conveying the idea that a vaccine is totally safe would be an error as it could lead to rumors and distrust.

In France there was a good communication campaign on antimicrobial which gave excellent results: it explained to people what is the aim of antibiotics, when to take them and what is the risk in taking them when they are not needed. Finally, it had a good slogan "les antibiotiques c'est pas automatique" (Antibiotics are not automatic)

- ⇨ Communication to the general public should deal with the question of why vaccinate and inform on the burden of the disease, its impact… and what is prevented by mass vaccination. It should be made clear that the decision to vaccine or not, is a public health problem and not a self issue. People need to be reminded that fatality during epidemics does not exist and that compliance with pandemic planning gives results.

At the start of the H1N1 pandemic in France, the **commitment of carers** to follow the pandemic planning showed excellent results: for 1 month ½ until 15 June, every flue case even mild was contained in hospital to slow down the emergence of the epidemic to have time to run the vaccine. The effect was that there was no H1N1 summer wave in France in 2009.

Designing a convincing communication strategy is difficult in particular, because of the fragmentation of the public to reach, the impossibility to tailor a message for everyone, and the difficult management of the media. Finally one should not underestimate the influence of Internet. A lot of studies prove that the unconscious influence of Internet is very important. The message has to be simple to be understandable by the general public but not too simple otherwise you risk giving the wrong message. Moreover it is difficult to know how the population will receive the message.

- ⇨ It is important to exploit and anticipate the role of Social Networks and Internet
- ⇨ The use of social media and Internet should be integrated in the communication strategy

Whom to convince?

It seems unnecessary to try to convince the "anti-vaccine" people. Efforts should be focused on persuading the "undecided" and keeping the "pro-vaccine" people.

Family doctors, pediatricians and more largely healthcare workers are trusted by their patients and therefore have a great influence on the decision to vaccinate or not. The vaccination coverage among this group is though quite low.

- ⇨ A special communication targeting healthcare workers, and in particular family doctors and pediatricians should be designed to get them vaccinated not only for their own benefit but also to protect their patients. If they are conviced they will also recommend vaccination to hesitant people.

Children are an important source of infection and transmission. Communication should target mothers as in most families the decision to vaccinate children is influenced by the mother. In 2014, there was an upsurge in measles in UK. To cope with it there were additional group campaign to targeted groups: twitters of Manchester United football club and mothers of children playing football in Manchester showed satisfactory results.

Recommendations are to:

- ⇨ Define a specific communication towards mothers should be set up
- ⇨ Explore the relevance of targeting children for vaccination campain

The idea to get people vaccinated or to vaccinate their children not only to protect themselves but also to protect others, as a sign of civism or public welfare concern, would mean in certain countries a total change in mentality. It also brings out the questions of how to deal with deliberately taking a risk:

- Risk and individual rationality versus population rationality: Am I willing to take a risk by vaccinating myself and my children, for the sake of the population welfare? What would be an acceptable risk? What is the risk for the global population and therefore me and my children if we don't follow recommendations? In the USA the whole society approach, make people responsible of their own safety
- Trust: Do I have all the right information to decide to vaccinate or not? Do I trust my government to take the best decision and to give the best recommendations? In Northern countries, the willingness to take a course of action is greatly linked to trust in government

Risk Perception

People usually react on experience and their risk perception is greatly linked to the answer to the question: did people died from this? It is now rare to know someone who has died from measles, influenza, or nosocomial infection. Moreover how do you know if you caught influenza or another close disease, how do you know if an elderly died from influenza or its consequences or from something else. Perception of risk for scientists and for the public is also different.

A study on the perception of the risk of an outbreak was conducted in the Rhone-Alpes population (region of France) in 2006 when there was a lot of news on avian flu. It appeared that the fear of an outbreak was very low. People's concerns were mainly cancer, diabetes, and violence but not avian flu.

- ⇨ The following topics should be investigated :
    - o How do people perceive risk?
    - o What would be an acceptable risk for people?
    - o Are people willing to take a course of action when they have perceived the risk?
    - o How to help people understand risk better?

Community versus individual rationality

⇨ In risk communication campaigns it is important to make an effort to switch citizen from an approach uniquely based on self-advantages to another where community advantages are also present in the reasoning leading to the decision of vaccinate.

It ought to be stressed that vaccinating must have an altruistic component. Of course it is not trivial to implement this switch.

Building a risk culture in population

In USA, the risk culture exists; people are responsible for their own safety.

Italy is not ready both at the political and technical level to build a risk culture. It would need to involve people from the public society, an adequate budget, a huge work for advocacy, and to be tightly driven. New communication strategies would be more efficient than building a risk culture in population.

In France, the "Principe de précaution" precautionary principle will weight on the ability to build a risk culture.

Building or "re-building"trust

In a lot of countries it is difficult to build trust due to the continuous changing environment of immunization programmes.

In UK different efforts to build trust have brought positive results: when a problem occurs people tend to think that it is more due to mess up than to a deliberate action (conspiracy). Since 2005, very clear messages about avian influenza, seasonal influenza, and pandemic influenza, have been given in order to prevent any confusion between the three. There is also a reflex response to have public inquiries which forces public structures to clarify and record how decision is made and what evidence decision is made on. A factor that hampers the possibility of reaching a full bidirectionality is the heterogeneity of the target populations, which makes heterogeneous and potentially in partial conflict the feeback towards the public health authorities.

Experts in France have to declare all their potential conflict of interest, may they be links with industry or with other stakeholders.

Conflict of interest of experts with pharmaceutical companies is another source of distrust. It is necessary to keep in mind that the best experts will automatically have a conflict of interest, because working with other stakeholder is part of how they get their expertise. Moreover public-private partnerships are necessary to progress. More transparency in this regard would help.

WHO and ECDC recommendation during the H1N1 outbreak was heavily criticized. Principal criticisms were on lack of transparency on the decision process. The distrust was mainly due to enormous amount of money spent by governments to acquire medicines and vaccines.

We can look closer at the stakes for pharmaceuticals companies and governments. In 2000 pharmaceutical companies invested millions of euros in antiviral drugs which were developed but not sold. In 2003 the pharmaceutical companies saw an opportunity to sell drugs they spent a lot on developing for the market. On the states side, it was also an opportunity of stockpiling drugs in the event of a pandemic. In 2009 the outbreak was there and drugs were brought to the market late 2009. The rules were respected but the degree of scrutiny of conflict of interest was very low. Pharmaceutical companies were under a lot of pressure to manufacture enormous amount of drugs in a very short time. Governments were also under a lot of pressure by pharmaceutical companies who needed to have orders passed soon enough to be able to supply drugs in time.

It turned out that WHO pandemic plan was not flexible enough to calibrate to what might happen. In 2008 there were a meeting on pandemic planning and preparedness. The aim of this meeting was to have a pandemic plan in every country. ECDC was to take over the pandemic planning and to harmonize planning but it appeared impossible.

- ⇨ Pandemic planning should be dealt with at the national level, in some countries even at the regional level, it cannot be taken over by EU.

Despite the efforts made by WHO to constitute an advisory board with experts from different countries who were uncoupled from the organization / countries they were from, it endured criticisms of lack of transparence.

If you look at the WHO management of the H1N1 crisis maybe, actually, nothing went wrong as the targeted goal to prevent a H1N1 pandemic was met… Today the General Director of the WHO is advised on emergency by 150 experts. WHO has also created a department which is monitoring answers from the public. It shows the population that their feedback is listened to; even if it is still unclear how it is implemented.

To build trust it is necessary to:

- ⇨ Acknowledge uncertainty and therefore to deal with the fear
- ⇨ Have a clear message staking the burden and the risk
- ⇨ Clearly separate communication on different disease
- ⇨ Implement bi-directional risk strategies: get a feedback from the general public - Set up public enquiries. Setting-up sentinel populations in order to have feed-back from the population could be an alternative as it is hard to do so in the whole population.
- ⇨ Clarify and be transparent on the decision process, and record how decision is made and on what evidence it is made

Public engagement

In UK, the public was asked to vote on how funding should be allocated for research in all fields of research (not only health) and a surprising outcome was that they voted massively for research on antimicrobial resistance. Moreover, in the Oxford University, parents were involved in the design of a vaccine clinical trial in children.

⇨ The following topics should be further investigated :

- How do we harness public engagement?
- How do we involve the public in the decision making process? in the design of clinical trial?

⇨ We could imagine that when vaccines studies are designed, mothers and fathers are involved for a reality check

<u>If you were a top EU decision maker what would be the most important research you would be supporting?</u>

Maria ZAMBON

- Investigate how much information in necessary to make decision
- Assess the severity and the understanding of the severity and adapt the answer accordingly
- Study the political decision and how are they made
- Commission industry to work or bid for projects in link with pandemic planning, like in USA where the government is co-funding projects stimulating different approaches to vaccines.
- Capitalize on the fantastic innovation we have in the EU level

Jonathan VAN TAM

- Speed up access to vaccines (technology transfer). The critical steps in the vaccine process are the regulatory steps and scale up to a million doses. It would need an investment at the EU level to take the most promising platforms and help them scale up.
- Optimize the use and effectiveness of antiviral drugs : if there was to be a pandemic tomorrow, vaccines would arrive late again and we will have to rely on antiviral drugs before vaccines are available.
- Examine the different ways to incentivize drug and vaccine manufacturers to research and produce drugs in prevision of a pandemic. Today there are no state vaccine manufacturers left. Private

manufactures have to see a commercial output (which was the case during H5N1). And stockpiles are expiring around the world. Manufacturers won't be able to produce for new stocks unless public authorities commit.

Bruno LINA

- Support research on antiviral
- Development a vaccine that mitigates pandemics even if not 100% effective
- Investigate mechanism of the emergence of the viruses at the basic level: understand how and why some viruses reassert from animals to human. There are some markers of severity, but once mutations occur, you don't know what will happen in human and transmissibility can be important. Sequencing only and having mutations and fragmentations of the virus is not enough.
- Scale up manufacturing capacity worldwide.

Philippe VAN HEMS

- Accelerate access to vaccine
- Find adequate intervention to improve vaccine coverage: identify the best mean to vaccine population and to counter opposition. Realistic mathematical models can help choose the best strategy.
- Improve epidemiological tool to monitor early detection of outbreaks and trends : involve more sources of information
- Improve education on diseases prevention and vaccines of healthcare workers but also among general population. This could start for example by educating high school children.
- Develop perception of risk and capacity to understand probabilities in the population

Lois BASTIDE

- Investigate sociological aspects in order to develop better models
    - Examine how public trust is built and distributed across society
    - How knowledge is legitimate
    - Explore how understanding shapes actions
    - Consider how to keep people mobilized/concerned between different crises. Is regular simulation/exercise the best way?

- Work on the organization of pandemic response: standardization and flexibility; organization of the different institutions who deliver pandemic plans and apply them.
- Stratify the different audiences and characterize them

A huge challenge is how to monitor the actions of people.

Manfred GREEN

In surveillance issues:

- Set up a much stronger and efficient sentinel networkto improve early identification of the virus.
- Improve data sharing. During the H1N1 pandemic it took sometimes a long time for good data to be available because researchers wanted to be able to write a paper and publish it before giving any data. The lack data sharing had a great impact on the economics of the countries

In pandemic management:

- Investigate the efficiency of social distancing and its impact on the economics. One unsolved problem is how to deal with economical impact of public closure. For example, what is the economic impact of school closure as it has for consequence that some staffs stay at home. Or, what is the economic impact in a company, of a strategy to encourage staff with sign of disease to stay at home ?

Piero MANFREDI

- Optimize the pipeline research-industry-public health
- Improve global availability of vaccines. We could imagine an International cooperation of industries for producing drugs in 3rd countries (ex : India)
- Learn more about the biology of the pandemics. Only the UK has performed serological studies using sero-bank to have an idea on the existing immunity.
- Develop a tool for real time evolution of pandemic in all EU countries (EU project / model done by Stefano MERLER). Pandemic can appear anywhere. In modeling we usually use the hypothesis that the pandemic will start in one country more than in another but reality can prove that this hypothesis can be the wrong one.
- Use already available data : anonymization and identification of parameters are fundamental
- Monitor the discrepancies between declarations (“I will get vaccinated”) and the actions (“I got/did not get vaccinated”)

- Build a Risk culture. If we have to face a real serious threat what will be the response from the front line (healthcare workers)? During the Ebola crisis NGO Emergency had to intervene is some place because Healthcare workers refused ti cure Ebola patients
- Study more the spread in relation with faith practices and believes.

Mathematical models are now very advanced and, thanks to computers, they can simulate behavior of a large number of virtuam individuals. Howeven High quality data are needed in order to fine-tune the parameters of such healthmodels.

Alberto D'ONOFRIO

In mathematical models there are 2 very important technical points: privacy, and in many models not all the parameters can be identified

ANNEXE 2: ANSWERS TO QUESTIONNAIRE

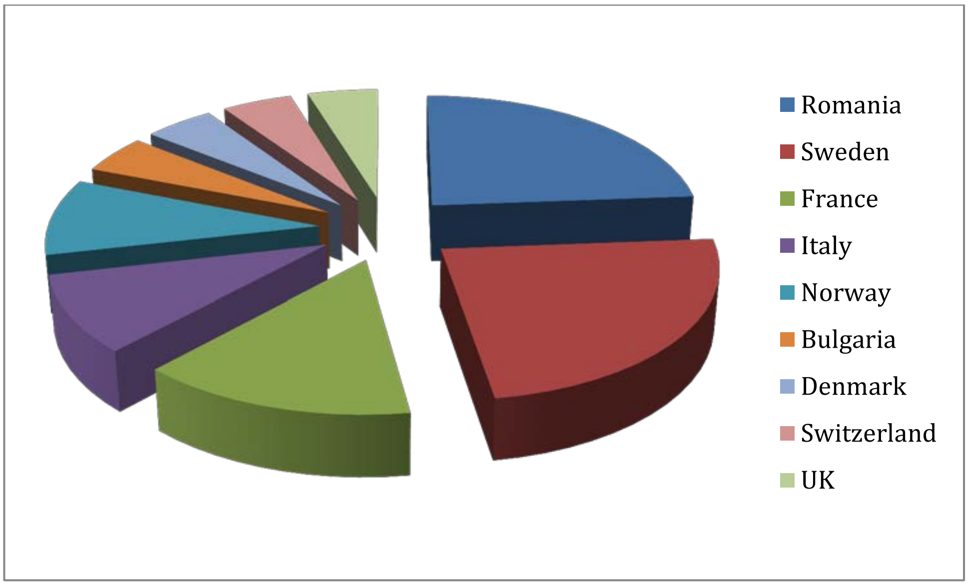
Experts involved

48 experts involved in different aspects of H1N1 pandemic were identified. They came from 14 european countries: Belgium, Bulgaria, Denmark, France, Greece, Ireland, Italy, Norway, Poland, Romania, Sweden, Switzerland, The Netherland, and UK. They covered a wide spectrum of the expertises needed to identify unsolved scientific questions related to pandemics and epidemics. They were epidemiologists, microbiologists, virologists, biologists, pharmacists, experts in pathogens identification or characterisation, diagnostics, vaccinology, communication, behavioral science, social psychology, sociology, statistics, modeling, economics, politics, surveillance, preparedness, response, crisis management...

21 of those experts representing the different fields of expertise and coming from 9 european countries answered the questionnaire:

- Bocsan Ioan from Cluj University
- Bourrier Mathilde from Université de Genève
- Britt-Marie Drottz Sjöberg from Norwegian Institute of Science and Technology - department of psychology (and Chairperson of the Expert group on "Science, H1N1 and Society")
- Brown Caroline from WHO Regional Office for Europe, Copenhagen
- Ciancio Bruno from ECDC (Center for Disease Prevention and Control)
- Ciotti Massimo from ECDC (Center for Disease Prevention and Control)
- Kojouharova Mira from National Centre of Infectious and Parasitic Diseases (NCIPD) of Bulgaria
- Lina Bruno from Lyon 1 Claude Bernard University (UCBL) Laboratoire « Virologie et Pathologies Humaines (VirPath) »
- Lopalco Pierluigi from ECDC (Center for Disease Prevention and Control)
- Merler Stefano from Intitute Bruno Kessler, Trento
- Nicoll Angus from ECDC (Center for Disease Prevention and Control)
- Palazzi Mauro from Cesena Asl
- Pranhos-Baccala Glaucia from Fondation Mérieux
- Pistol Adriana from National Center for Prevention and Control – Communicable Diseases (Romania)
- Popa Mircea from Univeristy of Medicine and Pharmacy Carol Davila
- Preben Aavitsland from the Norwegian Institute of Public Health

- Ruta Simona from Bucharest University
- Snakcen René from ECDC (Center for Disease Prevention and Control)
- Vanhems Philippe from HCL Lyon Civil Hospices
- Viorel Alexandrescu from Cantacuzino Institute
- Zambon Maria from UK Health Protection Agency



Summary of findings from questionnaire

The objective of question 2 was to identify the 3 main research needs that were not adequately investigated during the H1N1 pandemic. In agreement with what has been evidenced from our literature review, the most important points raised by the respondents were the following:

- Lack of adequate communication between national/international health authorities and populations;
- Lack of networking between different actors involved in the decision-making process;
- Lack of robust preparedness plans;
- Vaccines issues including perception, timely manufacturing and delivery;
- Lack of sufficient input from epidemiological and mathematical models;
- Lack of flexibility in strategies that have been set-up in different countries;
- Lack of animal-human research;

One special issue regarding the potential benefits of having a universal long-lasting influenza vaccine was raised by some respondents. This issue was not discussed in the present report.

The aim of question 3 was to show up the 3 mains research needs that were TOO stressed during the pandemic. Overall, 3 items were reported recurrently:

- Information on severity of the disease;
- Issues related to containments;
- Features of H1N1 virus (mutation, recombination, etc.)

Lack of the use of modelling was highlighted as a point that was not sufficiently investigated (see question 2). However, a divergent statement was found from question 3 because some respondents reported that modelling was too much stressed during the pandemic.

The main areas of research that are missing, as provided by answers from question 4, are the following:

- Vaccines issues including perception, timely manufacturing and delivery;
- Early epidemiology of pathogens with potential to cause pandemics (i.e. better surveillance are warranted);
- Strategies to improve preparedness plans;
- The role of social media;
- Importance of setting-up common database for early analysis and modelling;
- Strategies to improve transparency

The objective of questions 5 was to appreciate the opinion of respondents on whether they think their respective country is aware of pandemic's danger and if there are well prepared. We found heterogeneity among answers. Indeed, some respondents declared that their country was well prepared while others acknowledged that there is still place for improvement in their current preparedness plans and vaccine delivery. The importance for population to have a "risk culture" trough public campaigns was also highlighted.

Answer 1 (Italy)

1/ How were you or your organization involved in the H1N1 pandemic?

- Management: I'm a public health MD and work in a local health unit in Cesena. Italy. We were involved in communication to the population and management of vaccination to the people.

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

➢ In global?

1) How the people perceive the risk

2) risk communication

➢ In your country?

1) How the people perceive the risk

2) risk communication (was not transparency

3) the level of trust of population in ministry of health and other health stakeholders (industry)

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

➢ In global?

surveillance, response, preparedness

➢ In your country?

surveillance, response, preparedness

4/ What is missing in today pandemic research, identification, management?

➢ In global?

After the failure of H1N1 pandemic, the government and health authorities have to work to built trust. More transparency about the research, advantage and limit of vaccine, policy and agreement with pharmaceutical industry

- In your country?

After the failure of H1N1 pandemic, the government and health authorities have to work to built trust. More transparency about the research, advantage and limit of vaccine, policy and agreement with pharmaceutical industry. Involve in the strategy of response and communication the family doctor (General Pratictioner) who is very close to people and has to send coherent message to the citizens.

5/ how do you think your country relates to pandemic dangers?

Understand the role of risk communication and building trust.

Define a strategy to have a good surveillance and response with a communication plan. Be coherent with the message, be transparent about the agreement with the stakeholder, organize a good training for all the health worker to send correct messages and information to the citizens.

Answer 2 (Romania)

1/ How were you or your organization involved in the H1N1 pandemic?

- Identification: pandemic surveillance and response
- Management: public health management of the pandemic (SoPs)

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

- In global?

risk communication

public health measures effectivness

- In your country?

risk communication

vaccination beneffits

public health measures effectivness

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

- In global?

severity

- In your country?

Contact tracing

4/ What is missing in today pandemic research, identification, management, ...?

- In global?

risk communication

- In your country?

public health measures effectivness studies

risk communication

5/ How do you think your country relates to pandemic dangers?

surveillance- excelent

response – very good

preparedness – good

communication –satisfactory

Answer 3 (Switzerland)

1/ How were you or your organization involved in the H1N1 pandemic?

Swiss National Science Foundation

[Sept. 2013 - Sept. 2016]. Principal investigator of the research project "Organizing, Communicating, Costing in Risk Governance: Lessons learned from H1N1 pandemic" (co-principals: Claudine Burton-Jeangros; dpt of Sociology, Unige and Nathalie Brender, Geneva Business School). Award Number : FN 100017_146546.

American National Science Foundation

[Jan. 2009 - Dec. 2011]. Special partner for the project "Global Infectious Disease Response Project" (Principal investigator: Chris Ansell, University of California, Berkeley; Ann Keller, University of California, Berkeley; Art Reingold, University of California, Berkeley). Award Number SES-0826995.

World Health Organization (WHO, Geneva)

[May - September 2011]. Principal Investigator of the research mandate given by the Global Influenza Program on "Literature Review on Risk Communication Research and Mapping of Risk Communication Research Networks and institutions". (With Claudine Burton-Jeangros; Research Assistants: Clara Barrelet and Mélinée Schindler).

WHO's expert "Role of Health Risk Communication", presented by Mathilde Bourrier, based on "Literature Review on Risk Communication Research", prepared for WHO consultation on Public Health Research Agenda for Influenza (Geneva, Nov. 15 -17, 2009)

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

- In global?

The Risk communication component has not sufficiently integrated the daily experiences people had during the pandemic.

Family doctors and health care specialists have not be in the loop from the beginning. Vaccination poses new special challenges (both in rich countries and in poor countries).

They have insufficiently been taken into account by public health authorities..

Influenza is probably one of the diseases that is the best "equiped"…… in term of surveillance.

- **In your country?**

Same in Switzerland

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

- **In global?**

Applying the plans seemed to be more important than tailoring something specific for the pandemic, as it evolved into a milder one.

Maybe too much emphasis on preparedness and less on adaptation to circonstances. And local situations

- **In your country?**

this goes as well for Switzerland

4/ What is missing in today pandemic research, identification, management, ...?

- **In global?**

What is missing is a declination on how each of us can contribute to limit the spread of influenza: this is a community's call as well.

2. Top-down messages have to be articulated with current perspectives on how people think they ought to protect themselves.

3. There should be an up-dated knowledge basis of network and nods of trusted persons, be it family doctors; hospitals consultations.... Who, which groups are trusted the most, accross age, class, urban or not., professions…medias.

4. Globally, there should be a better recognition of the large spectrum of possible responses and points of view.

- **In your country?**

What is missing is a declination on how each of us can contribute to limit the spread of influenza: this is a community's call as well.

2. Top-down messages have to be articulated with current perspectives on how people think they ought to protect themselves.

3. There should be an up-dated knowldge basis of network and nods of trusted persons, be it family doctors; hospitals consultation. Who, which groups are trusted the most, accross age, class, urban or not., professions…

5/ How do you think your country relates to pandemic dangers?

There is probably a lack of interest. And a lack of trust in pre-defined plans.

Additional question for members of the Expert Group on "Science, H1N1 and Society" chaired by Britt-Marie Drottz Sjöberg:

6/ In your opinion, since your were member of the H1N1 expert group on "Science, H1N1 and Society", what happened as remarkable in pandemic research, management… in the last 3 years ?

Going from a "plan culture" to a more "adaptive culture"…, yet with too little knowldege on how to articulate multiple scenarii. ………What are the – social, political, economical – conditions under which such and such course of action might change. More importantly, whose's call is it? Pandemic planning and management if to succeed should incorporate a great deal of democratic values (openness; transparency; alternative options debated and true choice presented to the public if there is a choice) but also clear line of reasoning (based on evidence and facts). This is more than a politicans/public health experts' call. Everybody seems to agree on that, yet, how it does translate into proper recommandations for future epidemic remains a daunting task.

Answer 4 (Romania)

1/ How were you or your organization involved in the H1N1 pandemic?

In 2009 I worked in "Carol Davila" University of Medicine and Pharmacy and our organization was not directly involved in the H1N1 Pandemic, as an organization. But, in CDUMP we have some disciplines (infectious diseases, epidemiology, microbiology) that were involved through their members (with double affiliation e.g. to National Infectious Diseases Institute, National Virology Institute, National Institute for Microbiology and Immunology) as will follow

- Research: virus and results of vaccination, attitudes regarding the pandemic (unpublished results)
- Identification: classical and modern techniques
- Management: in collaboration with the other institutes under the coordination of the Romanian Ministry of Health (clinical and laboratory surveillance, advertising for vaccination and follow-up)
- Other: risk communication to students, medical doctors, general population

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

- In global?

1. Risk assessment and modelling for preventing another epidemic/pandemic

2. A better vaccine, in time + methods to approach the anti-vaccination groups

3. Clinical research

- In your country?

1. Surveys in extraepidemic time and during the epidemic.

2. Better way to communicate with the general population and some medical doctors (that do not understand the importance of immunization)

3. Assessment of vaccine coverage and efficacy + ways to preserve the national capacity for vaccine production

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

- In global?

1. Risk communication

2. Risk management including quarantine

3. Clinical descriptions of hospitalised patients.

- In your country?

1. Characteristics of the virus.

2. Chemoprophylaxis

4/ What is missing in today pandemic research, identification, management?

- In global?

1. collaboration between human and animal sanitary systems

2. not enough stimulation of research in the field

3. adherence to IHR

4. vaccination of medical workers

5. new targets and molecular mechanisms for treatment

6. better vaccines

7. faster identification of viral recombinants

- In your country?

1. collaboration between human and animal sanitary systems

2. not enough stimulation of research in the field

3. adherence to IHR

4. vaccination of medical workers

5. faster identification of viral recombinants

6. insufficient communication between research and clinical facilities, insufficient involvement of general practitioners

5/ how do you think your country relates to pandemic dangers?

I can say that we are fortunate, not having dangerous threats. Even some colleagues are good specialists, the continuous political changing decreased the capacity at regional and county level and we need a multi-annual plan to be implemented. The colleagues that are still working in the field have a good mobilization capacity and they are able to react in danger – but this is not the way to prepare a system and to face a pandemic danger.

Answer 5 (Bulgaria)

1/ How were you or your organization involved in the H1N1 pandemic?

- Research: Yes.

My organization is a leading national public health institution, specialized in research and practical activities in the field communicable disease surveillance, prevention and control, including influenza. We are responsible at a national level for the epidemiological surveillance, microbiology, training and scientific advice. In 2011 the institute was appointed by the Ministry of Health to serve as a National Coordinating Competent body, working with the ECDC.

- Identification: Yes.

The National Influenza Centre is a part of the Institute. The National influenza reference laboratory, recognized by the WHO, is responsible for the identification of seasonal/pandemic influenza viral isolates. The laboratory is participating in External Quality Assessments (EQA) organized by WHO and is complying with the Terms of Reference for NIC.

- Management: Yes.

• Participation in the process of the development of the National Influenza Pandemic Preparedness Plan, approved by the Decision of the Council of Ministries № 5 on 13th January 2006;

• Experts from the Institute were members of the National Influenza Pandemic Committee, approved by the Decision of the Council of Ministries on 1st June 2006;

• Experts from the Institute participated in the development of guidelines and advises for the medical specialists and for the general population;

• The epidemiological surveillance of the Influenza A(H1N1)2009 pandemic was one of the tasks of the Institute;

• The laboratory surveillance of Influenza A(H1N1) 2009 pandemic was performed in the National Influenza Reference Laboratory.

- Other: Permanent contact with mass media during the pandemic

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

- **In global?**

1. Discussion on the possibility that the influenza pandemic could not be caused by the H5N1 strain, but by another influenza virus, regardless of the forecasts that the circulating H5N1 strains (“avian flu”) represent a potential near-term threat.

2. Insufficient focusing on the historical epidemiological experience, based on the data obtained during previous influenza pandemics. For example, the pandemic in 1977-1978, caused by virus A (H1N1) – so called "Russian influenza" was very similar to the 2009 A (H1N1) pandemic. At that time, the disease was also significantly milder, non-severe and the case fatality rate was low. The pandemic affected mainly children and young people. This fact was explained by data indicating that identical virus had circulated earlier – in the period of 1947-1956 and therefore the persons over 23 years of age already had immunity. This information was not used at all during the 2009 pandemic.

3. The terms and definitions related to influenza epidemiology were used in different way by scientists and experts. The lack of unified understanding, i.e. using a common terminology led to serious misunderstandings, such as how is it possible to have a pandemic, while having a non-severe disease and low lethality. And, while scientists were in debate on that matter and the WHO had to modify the meaning of those terms during the pandemic, the situation was simply beyond understanding for the population. This would not happen if it was made clear that epidemiology make distinction between the categories of outbreak, epidemic and pandemic based on the morbidity level. The clinical presentation of the disease in the individual patient however does not depend on the morbidity level.

- In your country?

1. Risk communication during the pandemic: Regular official communications provided up-to-date information on the pandemic activity and about the actions being undertaken by the government; nevertheless the final result was the exaggerated perception about the threat posed by the A(H1N1) pandemic influenza virus in Bulgaria. Perhaps this "result" reflected the communication skills of the sources of information:

- Information was provided by scientists that had the appropriate scientific knowledge in the subject, but did not have the experience in communications, and unintentionally or not, involved the community in scientific debates, hypotheses and suggestions that were completely out of common public understanding.

- In addition, information was also given by people with communication skills, which however did not understand the notions of pandemic, influenza strain, measures of prevention and control, coming into contradiction with the scientific knowledge available.

2. Not sufficiently was addressed the analysis of all the implemented in the country activities related to the preparedness and subsequently to the response during the H1N1 pandemic. Thus, the stage "lessons learned" was omitted.

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

- In global?

1. It is necessary to start with the period before the occurrence of the H1N1 pandemic, because it was in this period when flaws and errors were predetermined to a great extent in the preparedness, risk assessment, response and risk communication during the pandemic in 2009. The national influenza preparedness plans were in fact "H5N1 influenza pandemic plans" based on unproved assumptions that the subtype of the next pandemic strain could be predicted well before the pandemic occurs and it will be influenza A(H5N1). The pandemic was expected to be not only widespread all over the world (characteristic feature of any pandemic by definition), but also the clinical presentation of the disease was expected to be very severe (something that could not be predicted). As a result, when the real A(H1N1) pandemic started, the situation was not properly

estimated by the international organizations and all the risk assessments in the beginning were not scientific justified.

2. The potential risk of the new pandemic strain was exaggerated.

3. The communications about the severity of the disease and the need to vaccinate the whole population was contradictory in the European countries, sometimes depending on the availability of vaccine and its amount.

- In your country?

1. Control measures – however the spread of the pandemic virus was unstoppable and containment measures in the beginning were extremely resource-intensive, but poorly effective. Entry and exit screening at airports and contact tracing did not prevent the spread of the disease (asymptomatic and sub-clinical cases!). The measures mitigating the health and social impact are more appropriate for the diseases such as influenza, including during pandemic.

2. Attempts to confirm all cases through laboratory testing and the continued counting of individual cases were important to document the spread and the features of the pandemic, but led to misunderstanding about the real epidemiological situation.

3. The problem related to the abilities and ways in which influenza viruses can constantly change and mutate. Sometimes the speculations about these mutations were totally incomprehensible to public, but everybody was thus persuaded that something very scary was expected to happen, which however did not happen.

4/ What is missing in today pandemic research, identification, management, …?

- In global?

The confidence that the research work in the field of influenza is sincerely done in the interest of the development of science and in the interest of society, that the influenza pandemic is not a notion, thought up to scare people and the proposal of measures and means of prevention and control of influenza will no more be accompanied with conflict of interest.

- In your country?

Lack of confidence on the global scale is also valid for my country. Combined with the very much limited financial resources, this has seriously obstructing pandemic research, promoting influenza immunization, use of antiviral treatment drugs.

5/ How do you think your country relates to pandemic dangers?

The topic of 'pandemic' is not popular among both the wide public and politicians. The perception of threat related to the influenza pandemic dramatically changed after the real pandemic in 2009, in such a way that it went from one extremity of exaggerating the risks and fear, to the other extremity of complete disregard and denial of any, even potential, threat.

Answer 6 (Italy)

1/ How were you or your organization involved in the H1N1 pandemic?

- Research:

1. Mathematical modelling: incidence projection

2. Mathematical modelling: effectiveness of mitigation measures

3. Mathematical modelling: estimate of key epidemiological parameters

4. Mathematical modelling: restrospective analysis (effects of human mobilty, schools, susceptibility to infection)

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

- In global?

1. estimates of case fatality rate (during, in the early phase)

2. preparedness for mild pandemics (never addressed)

3. surveillance: credible estimates of actual number of cases

- In your country?

1. Serological studies (during)

2. preparedness for mild pandemics (never addressed)

3. Inappropriate risk communication strategies

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

➢ In global?

1. “alternative” surveillance systems (e.g. social networks)
2. tools for real-time prediction
3. risk communication: estimate of CFR based on the first hundreds of cases

➢ In your country?

1. “alternative” surveillance systems (e.g. social networks)
2. risk communication: (partial) failure of the vaccination campain
3. risk communication: purchase of antiviral drugs in the initial phases without being prescribed by GPs

4/ What is missing in today pandemic research, identification, management, ...?

➢ In global?

1. Understanding individual behaviour in response to health threats
2. Tools/procedures for the quick assessment of key epidemiological parameters
3. Quick collection, organization of data and diffusion to the scientific community

➢ In your country?

1. Quick collection, organization of data and diffusion to the scientific community
2. Understanding individual behaviour in response to health threats

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Answer 7 (Romania)

1/ How were you or your organization involved in the H1N1 pandemic?

Correct identification of H1N1 virus in the frame of WHO External Quality Assessment Programme for the Detection of Influenza Virus Type A by PCR

Risk communication for the general public and specialists, training of medical stidents and residents in laboratory medicine and infectious diseases

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

- In global?

- calls for grant proposals

- interest for validation of the new identification methodologies

- development of a selective anti-viral drug

- In your country?

- preparedness in multiple centers in the country (decentralization)

- continuous availability of the vaccine ,

- maintenance of the national facility for vaccine preparation

- assessment of vaccine coverage and efficacy

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

- In global?

-risk communication

- In your country?

- surveillance, response, preparedness only at centralized level

4/ What is missing in today pandemic research, identification, management, ...?

- In global?

- insuficient calls for grant proposals to stimulate the research in the field
- more efficient antivirals
- markers for predicting the disease severity and potential complications
- new targets and molecular mechanisms for treatment
- better connection between veterinary and human surveillance systems

- rapid identification of viral recombinants

➢ In your country?

- no calls for grant proposals to stimulate the research in the field

- capabilities for continous surveillance of viral isolates, assessment of resistance in multiple centers,

- good vaccine coverage , a national facility for vaccine production

- assessment of vaccine efficacy

- insufficient communication between research and clinical facilities, insufficient involvement of general practitioners

5/ How do you think your country relates to pandemic dangers?

-participation in the viral isolates surveillance programme, preparedness for a rapid response and patients management (only in several centers), good risk communication

Additional question for members of the Expert Group on "Science, H1N1 and Society" chaired by Britt-Marie Drottz Sjöberg:

6/ In your opinion, since your were member of the H1N1 expert group on "Science, H1N1 and Society", what happened as remarkable in pandemic research, management in the last 3 years ?

- I was not a member, however significant progress was made on recommended viral surveillance , vaccination, and clinical management during the post-pandemic period.

Answer 8 (Romania)

1/ How were you or your organization involved in the H1N1 pandemic?

- Research: Phase I clinical trial coordination of pandemic vaccine Romania

- Identification: detection and characterization of A(H1N1 pdm09) at national level.

- Management: coordination of laboratory diagnosis of pandemic influenza A / H1N1 at national level

- development of guidelines for the management of pandemic influenza A /H1N1-2009 Other:

- participation in the preparation and authorization of pandemic vaccine CANTGRIP in Romania

- member of the "Committee for action in pandemic “

- Participation in the elaboration of the National pandemic preparedness and response

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

- **In global?**

- development of a universal influenza vaccine

- Development of adjuvanted pandemic vaccines

- Completion of estimating potential pandemic influenza viruses by IRAT method finalizarea estimarii potentialului pandemic al virusurilor gripale prin metoda

- development of new antivirals

- **In your country?**

-Introduction of an automatic monitoring of cases, complications and deaths caused by SARI, ARI, ILI at nationwide

- extending detection of influenza viruses (including pandemic) nationwide through operationalization of regional laboratories

- improving antiviral susceptibility testing and sequencing of pandemic virus isolates

- improving communication with media, population and health care professionals.

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

- **In global?**

-at the beginning of the pandemic, the pandemic vaccine production and distribution was unequal to the different states

- Preparation of intervention suboptimal in many countries

- Unconvincing messages about the impact of the pandemic of WHO and national health authorities

- **In your country?**

-Large number of samples processed at NIC

- Small number of intensive care units in infectious hospitals

- Relatively high cost of reagents for diagnostic

4/ What is missing in today pandemic research, identification, management, ...?

- In global?

- Lack of rapid tests with high specificity and sensitivity

- Relatively long period of preparation and authorization of Pandemic vaccines - 5-6 months

- Operationalization of preparedness and response committees in all countries

- In your country?

- Lack of a national system for recording and highlighting the etiology of complications and deaths caused by influenza and lack of a cost estimation of such effects

- Limited capacity of laboratory diagnosis at regional level

- Reduced identification of co-infections virus- bacteria in SARI cases

- Lack of an organized transport of samples at national level

5/ How do you think your country relates to pandemic dangers?

- Public health authorities in Romania aware of the danger of influenza pandemic preparedness and working towards intervention in these events. Given the increased potential pandemic of avian influenza viruses, there is a close collaboration with veterinary authorities that supervise circulation of avian viruses in Danube Delta

Answer 9 (France)

1/ How were you or your organization involved in the H1N1 pandemic?

- Research: Epidemiological research on risk fators and clinical course of the disease

- Management: Organisation of care to prevent nosocomial transmission and promoting vaccination

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

- In global?

Simulation studies on the outbreak spreading

Vaccine perception by the populations

Epidemiological tools for monitoring in real time the outbreak to adjust appropriate care and to anticipate future trends

- In your country?

Same issues

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

- In global?

Inadequate results from simulation studies. These results were interesting, but too few resaerch teams were involved in this topic. Then, public health decision were based on to few results.

The spectrum of clinical severity differed with the observed data. Then, scenarii fo rpublic health decisions were biased toward a very sever disease. The communication was also done in the same direction. Then, the population and healt care authorities were suspicious when cases with a mild dieseasess occurred.

Communication between healt care authorities and media

- In your country?

Same issues

4/ What is missing in today pandemic research, identification, management, ...?

- In global?

Epidemiological tools for early cases detection

Epidemiological tools for surveillance in sentinel populations

Anticipation of vaccine perception by the populations

Simulation studies and exercises for vaccination

To anticipate the place and rules of social networks (Facebook, Twitter, etc) as informative and/or epidemiological tools for pandemic management. These tools might be also counterproductive (i.e. false trends or false informations).

- In your country?

Same issues

5/ How do you think your country relates to pandemic dangers?

It depends of the source of inforation : media, health care system, general population.

A standardized and objective information is difficult to obtain. The population is not ready to hear different messages in a short period of time. However, the population should have a "risk culture" through public health campaigns. The risk assessement in public health is not easy to share. That is more difficult for special populations (neonates, children, sick people, etc.).

Answer 10 (Norway)

1/ How were you or your organization involved in the H1N1 pandemic?

- Research: Through a EC invitation; the expert group on Science, H1N1 and Society

- Identification: HEG Expert group, September 2010 – March 2011

……

- Management: Contact person Ing. Dr. Philippe Galiay, Unit B6 "Ethics and Gender", Directorate "European Research Area, European Commission

- Other: See report on "Developments in the treatment of severe influenza: lessons from the pandemic of 2009 and new prospects for therapy"

http://www.ncbi.nlm.nih.gov/pubmed/25333476

2/ **Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?**

- In global?

The difference between geographic spread and seriousness of the disease should have been clarified early and thoroughly in relation to the pandemic. It cannot be taken for granted that medical terminology, including definitions and uses, is obvious to non-experts. This is more an information issue than a research need, but I do not rule out that expertise from various disciplines would be required to address information production in this and similar types of situations.

Maybe issues around production, ordering and management of vaccines, such as safety and reliability of products, prices and distribution, could have been more attended to. It seems like public opinions in some countries were affected by "conspiracy" thinking due to lack of transparency in these respects, sometimes leading to conclusions that special interests were more effective drivers of the process than concerns for public health and safety. Research on, and information about, effective vaccines are certainly key elements here, and such issues could perhaps be attached to research on how to best inform consumers about the origin, contents and effects of products – in line with common demands of product information from the cradle to the grave.

Also, the issue of disinformation spread via Internet (by very few actors it seems) regarding dangers connected to vaccination could have been expected and better prepared for and explained. Research on "consumer information needs" on regional, local and individual levels as well as for personnel groups central to the risk management, regarding which were their salient questions, might to some extent have counteracted early or spreading distrust in authorities and recommendations. Attached to the issue lies the more fundamental challenge of how to establish and uphold highly trusted information sources.

Thirdly, to develop international guidelines on rights and responsibilities for authorities, risk managers as well as individuals regarding behaviour in connection with suspicious or actual cases of disease. I believe quite a lot could be learnt from the current ebola epidemic.

- In your country?

Overall, I believe Norwegian authorities did a very good job, although some critics have voiced the opinion that the very early overestimation of future victims ought to have been avoided. Maybe the Norwegian situation was also quite unique since there were no major financial problems securing vaccines for the population. In addition and relatively speaking, the Nordic countries usually display high levels of trust in authorities, their recommendations and actions. An issue that could have been more thoroughly investigated in the aftermath was the immediate effect of the "crying wolf" strategy, i.e. a later public evaluation of authorities' assuming of the worst case when later developments proved the situation to be less severe. Thus, how would the public have reacted to a new, but much more severe threat shortly afterwards, given that history. However, and although this is an issue of more general interest regarding preparedness and response, it seems today as if the quick and heightened preparedness at that time did not diminish subsequent trust. That tentative conclusion should also be understood within the wider time and framework since then where various threats to health and safety have become more salient. Also, and as mentioned above, the ethical and legal aspects attached to rights and responsibilities could have been more clarified during or after the uncertain times of the situation.

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

- In global?

Can not point to any issue that gained too much attention.

- In your country?

Can not point to any issue that gained too much attention.

4/ What is missing in today pandemic research, identification, management?

- In global?

Maybe more world-wide, comprehensive, and easily available, information on health issues to business as well as leisure travellers. Such information could involve spread of diseases, precautionary measures, symptoms and risk mitigation standards.

- In your country?

Maybe it would be good to produce and publicise various kinds of continuous follow-up studies on the current actual situation (e.g. cases of serious diseases, countermeasures, etc), preparedness situation, and public information needs. The main gain with such work would be to establish a main trustworthy source of correct information that would become the natural choice for public information gathering in any situation where there is a risk of more widespread health risks.

5/ how do you think your country relates to pandemic dangers?

With a high degree of professionalism regarding authorities and a somewhat hightened awareness in the general public. It is also my understanding that local authorities do consider such situations and have a general preparedness.

Additional question for members of the Expert Group on "Science, H1N1 and Society" chaired by Britt-Marie Drottz Sjöberg:

6/ In your opinion, since your were member of the H1N1 expert group on "Science, H1N1 and Society", what happened as remarkable in pandemic research, management… in the last 3 years ?

The ebola outbreak, resulting in global attention and preparedness, is maybe the most remarkable development, but also the re-emergence of diseases, e.g. tuberculosis, are worrysome although not highly publicised. In addition, the hightened focus on antibiotica resistent bacteria is important and points to the hazard of future baceria pandemics unless effective remedies are developed.

Secondly, I find it a bit remarkable that the intense information campaines and research efforts relating to the H1N1 time period are not more, and more comprehensively, followed up nationally and internationally. It would be of general interest to have the lessons learnt and future prognoses summarised.

Answer 11 (Norway)

1/ How were you or your organization involved in the H1N1 pandemic?

In 2009 I worked at the Norwegian Institute of Public Health.

- Research: Yes, we were involved in research on the virus and effects of vaccination. We also established a cohort and biobank of people vaccinated with Pandemrix and of people infected with pandemic influenza .

- Identification: Yes, the institute is the national reference lab for influenza and was involved in both diagnostics, advice to other labs and characteristation of viruses.

- Management: Yes, the institute worked with other governmental agencies to respond to the pandemic, especially concerning surveillance, advice and vaccine produrement and distribution.

- Other: Risk assessment.

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

- In global?

1. Risk assessment: How to predict the extent and severity of a new influenza pandemic.

2. Development of new universal influenza vaccines with long-lasting immunity.

3. What is the importance of asymptomatic and mild infections in transmission and epidemic spread.

➢ In your country?

1. Surveys of seroprevalence.

2. Methods for surveillance of mortality and severe cases.

3. Studies of adverese events following immunisation.

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

➢ In global?

1. Characteristics of the virus.

2. Clinical descriptions of hospitalised patients.

➢ In your country?

1. Characteristics of the virus.

4/ What is missing in today pandemic research, identification, management?

➢ In global?

- Better systems for early risk assessment of epidemics casued by new influenza viruses and adjustment of the response to the risk level.

- Better adherence to International Health Regulations.

- More knowledge of the (probably minor) importance of border measures against international spread.

- Better vaccines at an earlier stage.

- Better surveillance of severe influenza and deaths.

- Better evidence for who are at risk of severe influenza.

➢ In your country?

- Much the same as above.

5/ how do you think your country relates to pandemic dangers?

- It wants to be prepared. There is an updated national influenza pandemic plan. There is a new procurement agreement for influenza pandemic vaccine.

Answer 12 (UK)

1/ How were you or your organization involved in the H1N1 pandemic?

- Research:
  - Field Studies
  - Antiviral Resistance
  - Vaccine Studies
- Identification:
  - Development of diagnostics
- Management:
  - Guidance and advice

Other:

- Surveillance

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

➢ In global?

- Management of severe influenza
- Pregnant women
- Assessment of impact
- Prediction of severity

➢ In your country?

- Assessment of impact
- Surveillance requirements

- Preparedness/operational response capability
- Monitoring outcomes of infection ability to use interventions

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

- In global?

- Containment strategies
- Mathematical modelling
- Worst case scenarios

- In your country?

- Containment (use 8 antiviral for preplyoxil)
- Prophylaxis

4/ What is missing in today pandemic research, identification, management?

- In global?

- Pregnant women
- Severe influenza
- Additional drugs for treatment
- Use of adjuvants for vaccines

- In poor country?

- Pregnant women
- Severe influenza
- Uptake of vaccines

5/ how do you think your country relates to pandemic dangers?

- Good for operational response
- Good for pandemic planning
- Disconnected about use of countermesures and their evaluation.

Additional question for members of the Expert Group on "Science, H1N1 and Society" chaired by Britt-Marie Drottz Sjöberg:

6/ In your opinion, since your were member of the H1N1 expert group on "Science, H1N1 and Society", what happened as remarkable in pandemic research, management… in the last 3 years ?

- Important information about ease of switching to aerosol transmission in avian strains with relatively few amino acid changes (work of Fouchier and Kawaoka)
- Adverse effects to particular vaccine adjuvants
- Recognition of impact of influenza in pregnancy

Answer 13 (Romania)

1/ How were you or your organization involved in the H1N1 pandemic?

Please detail:

- Research: no
- Identification: no (exceptions: routine aetiological diagnostic of ILI human cases; it is not scientific research itself).
- Management: no (exceptions: admission of ILI middle or high severity cases; it is not scientific research itself).
- Other: teaching, CME.

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

- In global?

- Surveillance of non-human potential reservoir of viruses, particularly pigs and pig breeders and their families, outside of epidemic season (storage of flu viruses during the summer season?).

- Surveillance of liaisons between humans and non-human potential reservoir of viruses (pigs and birds).

- Communication between healthcare sector and general population outside of pharmaceutical industry advertising campaigns with proper public information on preparedness before the epidemic season.

- In your country?

Same as above.

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

- In global?

- Need / efficiency of quarantine.

- Efficiency of early admission of most ILI cases in tertiary hospitals of infectious diseases.

- Efficiency of chemoprophylaxis at population scale.

- In your country?

Same as above.

4/ What is missing in today pandemic research, identification, management, ...?

- In global?

Early compulsory immunisation of healthcare workers, particularly those working in primary and tertiary health care units.

- In your country?

As above, plus the follow-up of morbidity by influenza-related diseases (e.g. sudden death, Guillain-Baré syndrome etc.).

5/ How do you think your country relates to pandemic dangers?

Mediocre to good. An earlier / timely purchase of vaccine would be strongly recommended; there is, every year, a significant delay in providing vaccine to populations at risk (healthcare workers included).

Additional question for members of the Expert Group on "Science, H1N1 and Society" chaired by Britt-Marie Drottz Sjöberg:

6/ In your opinion, since your were member of the H1N1 expert group on "Science, H1N1 and Society", what happened as remarkable in pandemic research, management… in the last 3 years?

- Proving and increasing the importance of hand washing as preventive / control measure.
- Proving the lack of efficacy of mass chemoprophylaxis.

Answer 14 (France)

1/ How were you or your organization involved in the H1N1 pandemic?

- Identification: development of a molecular test.
- Management: Training and transfer in the GABRIEL network

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

- In global?

Surveillance is very important. Identification of strains in severe cases and risk factors. The response in low income and emerging countries as well as in developed countries.

Antecipate preparedness is not very easy but networking is essential and relevance.

- In poor countries?

Yes, sulveillance is essential. In hospital and in outpatients.

Response to emerging respiratory infections should be follow up during the time or seasonality, depending on the country.

Of course that preparedness is important and some rules should be implemented in poor couuntries.

Network is the key of success.

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

- In global?

Preparedness, risk comminication and surveillance.

However, networking it was not very stressed and remains one of the keys of success.

- In poor countries?

More complicated! Preparedeness and risk factors, and risk of communication. Once again, networking to set-up the different steps.

4/ What is missing in today pandemic research, identification, management?

- In global?

Organization, good networking with prepared scientists, respect for countries involved in pandemic, surveillance, SOPs, protocols, trainings and... subventions!

- In poor countries ?

Trainings, harmonized protocols, implementation, surveillance, epidemiological studies

5/ how do you think your country relates to pandemic dangers?

France is well prepared. Antecipate differente actions and it seems to work.

I am more involved in actions in low income and emergent countries. In these countries the history is not the same. They need actions, education, research implementation and constant support.

Additional question for members of the Expert Group on "Science, H1N1 and Society" chaired by Britt-Marie Drottz Sjöberg:

6/ In your opinion, since your were member of the H1N1 expert group on "Science, H1N1 and Society", what happened as remarkable in pandemic research, management... in the last 3 years ?

The media here was very relevant. The association between physician and biologists. Networking and information.

Answer 15 (Denmark)

1/ How were you or your organization involved in the H1N1 pandemic?

- Management:…………Yes, at the WHO Regional Office for Europe I was a lead member of the pandemic response team, providing information, advice and tecnical guidance to Member States, coordinating surveillance in the WHO European Region, supporting laboratory capacity, deployment of influenza vaccines and antivirals

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

- In global?

What is an appropriate/correct level of preparedness for a particular risk? need to know what health authorities think and match to what the public expects/needs

To what extent were health systems prepared? Did they have the necessary capacities in place? How quickly could they ramp up or ramp down a response?

Particularly the current out break of A(H7N9)……highlights the need to intensify research…at the animal-human interface which requires collaboration between human and animal health sectors in affected countries. To identify the risk to humans etc

4/ What is missing in today pandemic research, identification, management, …?

- In global?

What is an appropriate/correct level of preparedness for a particular risk? what do health authorities think and what do the public expect/need. Particularly relevant regarding Ebola: what was the right level of preparedness for Europe considering the very low risk of persons infected with Ebola travelling to the Region?.

To what extent are health systems prepared? Often the public health authorities drive preparedness but there is too little involvement and linkage with health services. Eg. Patient information is needed for surveillance and risk assessment as well as clinical management. How is this data collection organized so that it serves both purposes? Can it be ramped up quickly in an emergency?

Research at animal-human interface.

5/ How do you think your country relates to pandemic dangers?

Speaking from the perspective of working with 53 countries in the area of pandemic preparedness, there is a whole range of actions taken depending on the country. Countries with strong systems are better prepared, better able to implement measures, deal with the media etc. Countries with weak health systems struggled with most aspects of the 2009 pandemic and were dependent on WHO for risk assessment. However, the fact that the 2009 pandemic was relatively mild caused problems particularly in better-prepared countries as they changed their vaccine and antiviral policy from what had been in the pandemic plan. This is why countries (at least ones in Europe that have revised their pandemic plans) have developed plans that cover a range of scenarios and state that the actual measures implemented will depend on the risk assessment once a pandemic occurs. This is also according to the revised WHO pandemic guidance.

Answer 16 (France)

1/ How were you or your organization involved in the H1N1 pandemic?

- Research: I was involved in a task group that was promoting the implementation of specific research programs on all aspects of emerging influenza (from basic to clinical research). In addition, I (my lab) received fonds for research.

- Identification: As a membre of the " cellule de lutte contre la grippe "for the Ministry of health, and as the head of one of the 2 National Référence Centre, I have been involved in the very early steps of the identification of the pandemic.The NRC has implemented a lab network during the early phases of the pandemic, and carried out a follow up of the technical performances of several kits. We also carried out the caracterisation of the strains along the epidemic. We were also involved in several WHO TC dealing with virus issues like antiviral resistance or identification of virulence factors

- Management: Again, as a member of the "cellule de lutte contre la grippe", I have been involved in the pandemic planning before the pandemic,and I was in the expert group of the Ministry of Health during the whole pandemic period.

- Other: In addition, I have been expert for the different research bodies in France, including INSERM, CNRS and the University of Lyon

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

- In global?

The most important gap was concerning the impact of the pandemic virus in the very early phases of the pandemic. We lacked robust epi and impact data that would have been of help to provide early estimates regarding severity and mortality. In addition, we also missed the cross-immunity protection observed in the >65 that was a key issue in the vaccine program.

The pandemic should have been a period for evaluation of novel antiviral strategies, and/or vaccine strategies. It was not use as it should.

Communication was very difficult, and very strong political voices were sometime missing. This aspect of the management of the pandemic was missed.

The pandemic plans were too rigids, and prepared for an H5N1pandemic that would have been responsable for a very high mortality. The plans were not adapted for a "milder" pandemic.

- In your country?

All the comments above are for my country as well

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

- In global?

Cannot say there was any subject that was too much stressed

4/ What is missing in today pandemic research, identification, management, …?

- In global?

Human science research program should be reinforced. Public health microbiology should be reinforced, and we should cross fertilize our experiences in emerging viruses to implement structure with cross competencies.

- In your country?

Long term public health commitment is missing

5/ How do you think your country relates to pandemic dangers?

With ups and downs. The lacks of knowledge at the top of theMoH is puzzling

Answer 17 (collective answer from ECDC)

1/ How were you or your organization involved in the H1N1 pandemic?

- Research: Facilitating cross-EU studies through a "Studies and surveys ina pandemic – SsiaP" framework

- Identification:ECDC is responsible for early detectiona and surveillance of new influenza strains in the EU

- Management: ECDC coordinates crisis management and outbreak response in the EU for communicable diseases.

- Other: Surveillance and risk assessment at EU level

2/ Which were, in your opinion, the 3 main research needs (scientific or not) which were NOT SUFFICIENTLY addressed during and / or following the H1N1 pandemic?

➢ In global?

- early asssment of severity
- risk communication (to health professionals and public as well)
- early identification of people to be vaccinated or who should receive antivirals

➢ In your country?

- Preparedness
- Guidance for continuing care
- Vaccination coverage and speed of distribution

3/ Which were, in your opinion, the 3 main research needs (scientific or not) which were TOO MUCH stressed during and/or following the H1N1 pandemic?

➢ In global?

- Role of social media

- Geographic spread
- Diagnostic procedures

  - In your country?

Management and control in developing countries

4/ What is missing in today pandemic research, identification, management, ...?

- In global?

A lot of papers on lessons learned were published but few were applied

Improving modelling of transmission and severe outcomes.

Improving mortality monitoring

Improving understanding of benefits of antivirals as a prophylactic tool

Rapid pre-approved clincial research protocols for early stages of the pandemic

Understanding of zoonotic transmission accross the animal-human interface

Understanding of the effectiveness of social distancing measures

Tools to operationalise pandemic preparedness to lcoal and regional levels

Reserch to improve personal protective equipment (PPE) in healthcare and in the public

Role of environmental drivers on transmission patterns

Role of human movement (travel etc) on transmission patterns

Socio-economic drivers of severe outcomes

Communicating uncertainty of risk in various cultures and environments

Crisis management practice in public ehalth organisations

Role of private sector (healthcare and non-healthcare) in pandemic preparedness.

Complications of severe influenza infections.

Role of co-infections and anitbiotic use in influenza infection.

Cross-border and international co-operation

Sharing of treatment and management resrouces accross administrative borders

Plans for joint procurement of medical countermeasures

Understanding genetic vs antigenci characterisations of influenza viruses

Sharing of genetic data accross administrative borders

- In your country?

Specific preparedness

5/ How do you think your country relates to pandemic dangers?

The EU and EC are well aware of risks related to pandemics and epidemics, leading, inter alia, to the establishement of ECDC in 2005. Many organisational and operational issues between the EU level and EU Member States remain to be clarified.

ANNEXE 3: FOCUS ON PROJECTS

There are and there were numerous projects founded by different organization and aiming at improving pandemic surveillance, preparedness and communication throughout the world

For example :

The **world bank** is financing several preparedness projects in developing countries such as the "Health Systems Strengthening and Ebola Preparedness Project" for Cote d'Ivoire which was approved on November 25th, 2014)

http://www.worldbank.org/projects

The **USDA (United stated department of Agriculture**) have been financing several zoonose preparedness projects such as "Influenza pandemic preparedness" which was financed from Septembre 15th, 2012 to september 30th, 2013. Its aim was to evaluate 1) Pathogenesis of avian inluenza virus isolates in swine; 2) Role of avian polymerases in adaptation of swine influenza viruses to swine; 3) Genetic characterization of swine and avian influenza viruses to swine; and 4) Preparation of reagents

http://www.usda.gov/wps/portal/usda/usdahome?contentidonly=true&contentid=Emergency_Preparedness_and_Response.html

The **National Institute of Allergy and Infectious Diseases NIAID** (part of the National Institutes of health) conducts and supports basic research into the viral biology, pathogenesis, and epidemiology of influenza viruses, and host immune responses to these agents. It also conducts and supports applied research to develop new or improved influenza vaccines and production methods; to identify new anti-influenza drugs; and to support surveillance for previously unknown influenza viruses in animals and characterize any that are found. NIAID's role is also to develop and clinically evaluate specific candidate vaccines against an emergent strain, test the activity of antiviral drugs, and, in some cases, supply vaccine manufacturers and the research community with viral reference strains and other reagents to speed vaccine development.

NIAID has lead the "Influenza Genome Sequencing Project" launch in the fall of 2004 with the Centers for Disease Control and Prevention (CDC) and several other organizations to determine the complete genetic sequences of thousands of influenza virus isolates and to rapidly provide these sequence data to the scientific community.

In 2014 a candidate vaccine to prevent Ebola virus disease was co-developed by the NIAID and GlaxoSmithKline (GSK)

https://www.niaid.nih.gov/about/Pages/default.aspx http://www.niaid.nih.gov/news/newsreleases/2014/Pages/EbolaVaxResults.aspx

PhD students of the Nottingham University are in the process of working with WHO performing funded projects to look at pandemic preparedness across Europe and Asia as well as reasons for acceptance and refusal of flu virus vaccine http://nottingham.ac.uk/research/groups/healthprotection/projects/index.aspx

Through the Innovative Medicine Initiative the European Commission supports projects aiming at improving pandemic surveillance, preparedness and communication

For example :

Accelerated development of vaccine benefit-risk collaboration in Europe (ADVANCE) : Vaccines are one of the most effective public health measures out, saving some two to three million lives worldwide every year. However, in Europe, public distrust in immunisation programs is limiting high vaccine uptake, resulting in outbreaks of vaccine-preventable infectious diseases that had almost disappeared. Bringing together the European Centre for Disease Prevention and Control and the European Medicines Agency, as well as national public health and regulatory bodies, vaccine manufacturers and academic experts, the ADVANCE project will develop and test methods and guidelines in order to pave the way for a framework capable of rapidly delivering reliable data on the benefits and risks of vaccines that are on the market. This framework should both help regulators and public health authorities make decisions on vaccination strategies, and help maintain public confidence in immunisation as an effective public health tool to control infectious disease.

http://www.imi.europa.eu/content/advance

Through its European Framework Programmes 5, 6 and 7 the European Commission has supported several projects on :

Influenza : http://ec.europa.eu/research/health/poverty-diseases/doc/influenza-research_en.pdf

Vaccines and Correlates of Protection

http://ec.europa.eu/research/health/infectious-diseases/emerging-epidemics/projects/l-vaccines_en.html

Diagnostics and Surveillance

http://ec.europa.eu/research/health/infectious-diseases/emerging-epidemics/projects/l-diagnosis_en.html

Biology, Target Search and Drug Discovery

http://ec.europa.eu/research/health/infectious-diseases/emerging-epidemics/projects/l-biology_en.html

Public Health Aspects, Networking and Training

http://ec.europa.eu/research/health/infectious-diseases/emerging-epidemics/projects/l-network_en.html

Preparedness and capacity building for emerging epidemics,

http://ec.europa.eu/research/health/infectious-diseases/emerging-epidemics/projects/l-preparedness_en.html

Denge and other haemorhagic fevers,

http://ec.europa.eu/research/health/infectious-diseases/emerging-epidemics/projects/l-denge-other-fevers_en.html

SARS

http://ec.europa.eu/research/health/infectious-diseases/emerging-epidemics/projects/l-sars_en.html

Transmissible spongiform encephalopathies

http://ec.europa.eu/research/health/infectious-diseases/emerging-epidemics/projects/l-spongiform-encephalopathies_en.html

Zoonoses, food- and waterborne emerging epidemics

http://ec.europa.eu/research/health/infectious-diseases/emerging-epidemics/projects/l-zoonoses_en.html

On April 8th and 9th 2014 the european projects **OFFLU (Network of expertise in animal influenza)** and **STAR-IDAZ (Global Network for amila Disease Research)** have partnered to develop a strategic agenda for animal influenza research. OFFLU and STAR-IDAZ convened a group of 60 key contributors to the field of influenza including animal health and public health scientists; representatives from animal production and trade (poultry, egg, and pork); the pharmaceutical sector; equine sports; policy advisers; and representatives from research funding bodies.

The experts developed their vision for animal influenza research and identified areas of research which are currently of highest priority.

The group identified whether each priority was short-term applied research (studies needed to determine effective intervention strategies with potential for immediate impact); longer-term applied research (studies most likely to reduce disease burden (economic and health)); or priority basic research (studies which may ultimately lead to effective intervention strategies or reduced disease burden).

In general three strong themes came out of the consultation

1) Research to identify the multifactorial determinants of health risk from influenza viruses is needed to support risk assessment, surveillance, and intervention strategies.

2) Integrated approaches to influenza research and surveillance across species (at the interface between animals and humans, and between animal species) should be taken and surveillance findings should be shared rapidly.

3) There is a need to improve technologies to develop more effective and universal influenza vaccines and diagnostics.

Research priorities may apply to a sector (poultry, pork, equine, wildlife or animal human interface), in which case this is specified, or cut across a number of these sectors. The priorities are not ranked in order of importance and categories of short-term applied, longer-term applied, and priority basic research, are considered to be of equal importance.

http://www.star-idaz.net/?p=859

On August 14th, 2014 the **E-com@eu, Effective Communication in Outbreak Management; development of an evidence-based tool for Europe,** project published a p paper by Crosier A., McVey D., French J. intitled :By failing to prepare you are preparing to fail': lessons from the 2009 H1N1 'swine flu' pandemic.

Background: Pandemic influenza has the potential to cause widespread death and destruction. Communications with the public have a vital role in the prevention of pandemic influenza by promoting the effective uptake of behaviours that can delay the spread of infection. This study explored the development and implementation of communications in the pandemic influenza outbreak of H1N1 ('swine flu') in 2009 in three European countries.

Methods: In-depth interviews were conducted with senior policy and communication officials involved in the planning and delivery of communications programmes in England, Italy and Hungary.

Results: The study found a lack of planning and a low value attached to the skills required to produce effective communications. In all case study countries there was a dearth of good quality audience research to inform the development of communications. Little thought had been given to the tone, targeting or channelling of messages. Instead, communications were characterized by a 'one size fits all' and a 'top down', expert-led response. There was also little effort to evaluate the impact of communications, but where this was done, very low levels of public compliance and engagement with key behavioural messages were found.

Conclusions: Policy makers should prioritize investment in the skills and expertise required to achieve desired behaviour changes. Audience research should be conducted throughout the planning cycle to inform national communications strategies. This should include insights to inform the segmentation of public audiences, targeting of messages and consideration of content and emotional tone most likely to achieve desired behavioural outcomes.

http://www.ecomeu.info/

On April 18th 2014 **TELL ME (Transparent communication in Epidemics: Learning Lessons from experience, delivering effective Messages, providing Evidence) experts published a case study of the 2009 H1N1 influenza pandemic**

A case study of the 2009 H1N1 influenza pandemic – the so-called swine flu – has been published on Disaster Medicine and Public Health Preparedness by a team of experts from the TELL ME projects. Their study compared the guidelines for risk communication in case of epidemics or pandemic from 2005 to 2008, released by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), with CDC reports from 2009 to 2011. Aim of this analysis was to assess the implementation of these guidelines during the swine flu outbreak in 2009.

The TELL ME experts shown that such guidelines were mainly based on a top-down kind of communication that did not pay sufficient consideration to individual member-state situation. This could be the main reason behind the gap the experts found between the international guidelines and their implementation at a local level. Also, the WHO and CDC recommendations were not always based on formative evaluation studies, which is something that could have undermined their validity.

TELL ME experts concluded their work with two recommendations: the first is to define the goal of a vaccination program, by taking into account the segmentation of the population and applying a two-way communication. The second is to plan communication strategies in accordance with the most current theoretical framework, thus including elements like transparency and uncertainty. They also pointed out that organizations should be more involved in the implementation of guidelines.

http://www.tellmeproject.eu/content/tell-me-experts-published-case-study-2009-h1n1-influenza-pandemic

In its H2020 programme the European Commission continue its support to projects aiming at improving pandemic surveillance, preparedness and communication:

PREPARE Platform for European Preparedness Against (Re-)emerging Epidemics : A key lesson from a series of recent epidemics of emerging pathogens of global public health importance (e.g., the 2009 H1N1 influenza pandemic) was that implementing clinical research in response to a rapidly emerging infectious disease is extremely challenging and often delayed. We currently have no European framework for ensuring clinical research is built into epidemic responses and in fact our present research culture often precludes a rapid clinical response. Because of this, clinical research studies generally miss the initial waves of an epidemic or pandemic and in many cases fail to enrol significant numbers of patients across the clinical spectrum of disease, even during subsequent waves. This in turn means the opportunity is missed to improve patient outcomes and develop high-quality evidence to inform future clinical management strategies at the 'coalface'. Indeed, in almost all epidemics over the last decades very little research directly aimed at improving clinical management or understanding pathogenesis has been able to be conducted. These experiences have demonstrated that unless something is done now to change the approach to clinical research, the next epidemic will result in a similar missed opportunity to save lives and advance medical knowledge. PREPARE has been designed to address this problem.

http://www.prepare-europe.eu/About-us/Why-PREPARE

COMPARE COllaborative Management Platform for detection and Analyses of (Re-) emerging and foodborne outbreaks in Europe is a collaboration of founding members of the Global Microbial Identifier (GMI) initiative (www.globalmicrobialidentifier.org) and institutions with hands-on experience in outbreak detection and response, including several PREPARE partners. In September 2014, COMPARE was selected for negotiation for funding under Horizon 2020 and should kick-off early 2015. COMPARE will establish a “One serves all” analytical framework and data exchange platform, that will allow real time analysis and interpretation of sequence-based pathogen data in combination with associated data (e.g. clinical, epidemiological data) in an “one health” approach.

http://www.prepare-europe.eu/Portals/0/Documents/Newsletters/PREPARE%20Newsletter%20September%202014%20-%20web.pdf