Workshop report
Brussels, May 3\textsuperscript{th} 2013

Organised by
European Scientific Working group on Influenza
## Programme

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<td>Prof. Dr. Marc Van Ranst, University of Leuven; Belgian Influenza Commissioner</td>
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FOREWORD

The pandemic outbreak of H1N1 influenza that started in 2009 provided an important test of Europe’s preparedness activities and ability to respond to a large-scale public health emergency with the potential for huge health consequences. Experts (scientists and public health authorities alike) agreed that the pandemic had been handled well in Europe, the US and Japan. Since then, few national authorities have evaluated their pandemic response processes. To get a clear view on the issue, the European Scientific Working group on Influenza (ESWI) organized an evidence-based comparison of pre-pandemic plans in Europe (with the US and Japan serving as points of reference), the level of implementation during the pandemic and the current status of evaluation/update of these plans.

The results of that effort were presented during a dedicated FluQuest Workshop. On 3 May 2013, 45 public health officials and other influenza stakeholders gathered in the Institute of European Studies at the Free University of Brussels. Eight speakers, who had all been closely involved in collecting the FluQuest survey data, addressed their audience about the trends, caveats and differences in the approach to pandemic preparedness planning that had emerged from the survey. Their findings sparked the debate on pandemic response in Europe. To fuel that debate, this magazine provides a report of the lectures and the discussions held at the FluQuest workshop. The text can be copied and distributed freely.

ABOUT ESWI

The European Scientific Working group on Influenza (ESWI) is a partnership organization of stakeholders with a clear mission: to reduce the number of influenza victims in Europe.

Partnership organizations like ESWI are established to meet specific objectives and to undertake projects to address problems that neither partner could tackle adequately on his own. A successful long-term partnership is built on common grounds. In the case of ESWI, this common ground is a social concern to improve public health in Europe.

If you need further information please check the ESWI website at www.eswi.org or contact the ESWI manager, Mr. David De Pooter, at david.depooter@eswi.org or +32 479 45 74 46.

Also visit:
www.flucommunity.org
www.flucentre.org
www.eswiconference.org
Will H7N9 Spark the Next Pandemic?

The sudden emergence of H7N9 bird flu in China illustrates the unpredictability of influenza viruses. Whether it will cause a new pandemic, however, is just impossible to say. “Scientists and public health authorities take the H7N9 bird flu virus very seriously,” Osterhaus said. “It is better to be safe than sorry.”
CROSSING THE SPECIES BARRIER
There are three different presentations of flu: seasonal, avian and pandemic influenza. Seasonal influenza outbreaks occur annually and involve an influenza subtype that has been circulating among humans for a longer time. Avian flu comes from birds, usually poultry. Avian flu viruses do not transmit from human to human effectively. But influenza viruses are unpredictable. Pandemics are all caused by an avian flu virus that acquired the ability, by mutation or reassortment, to become transmissible among humans.

Influenza A viruses are divided into subtypes depending on the type of haemagglutinin and neuraminidase (two distinct proteins) that make up the virus surface. At present, seventeen haemagglutinins and nine neuraminidases have been identified. Virtually all of these proteins have been found – in different combinations – in migratory birds. Avian flu viruses are usually low pathogenic, meaning that they hardly cause any disease in birds. But when such a virus of the H5 or H7 subtype spills over to poultry, like chickens or turkeys, it may mutate into a highly pathogenic flu virus, killing all the poultry that are infected”, Osterhaus explained the workshop audience.

THE H5N1 THREAT
“Since H5N1 emerged in 1997, more than 650 people have been hospitalized with this bird flu virus, more than 50% of whom have died,” said Osterhaus. “Virtually all H5N1 victims had contracted the virus directly from birds, not from humans. We hence might ask ourselves why H5N1 hasn’t caused a pandemic yet. Well, for H5N1 to become transmissible between humans, for example through sneezing, it must gain the capability to efficiently replicate in the upper respiratory tract, just like a seasonal influenza virus does. Now it only replicates well in the lungs, which makes it very lethal, but not transmissible.”

Within Ab Osterhaus’ Viroscience team at the Erasmus MC, a ferret-to-ferret model was built to examine what the virus would need to efficiently replicate in the upper respiratory tract of a ferret and thus to allow aerosol transmission. “By applying reverse genetics, we found out that the virus only needs a handful of mutations to become transmissible through the air. All of these mutations are present in birds in Asia, but they have just not all come together yet.”

LOW PATHOGENIC H7N9
The H7N9 bird flu virus emerged in early 2013. Its hotspot is located around Shanghai, and the virus has originated from wild birds, ducks and bramblings. In fact, the H7N9 flu virus that is responsible for human infection is a reassortment of viruses found in these three bird groups. “To date (May 3rd, 2013) 128 people have been hospitalised, of whom 27 have died, and it continues its spread”, Osterhaus said. “But all cases seem sporadic from bird-to-human. There is no evidence yet of sustained human-to-human transmission. And in contrast to the H5N1 virus, H7N9 is a low pathogenic virus for poultry. An H7N9 infected chicken doesn’t just drop dead. The low pathogenic character makes the virus more illusive and hence it becomes more difficult to trace the virus to its main host source. Indeed, we just don’t know if poultry are the main host. We also don’t know if there is an intermediate host. It is very important that we now find out which mutations would be...
necessary to make the H7N9 bird flu virus transmissible among humans. In the meantime, preventive measures are being taken in China, where among other measures poultry markets have been closed and cleaned out.”

BE PREPARED
Interestingly, the four pandemics that have hit the world in the last 100 years, all originated from bird flu viruses that were low pathogenic for poultry. “We’ve all been speculating about the highly pathogenic H5N1 as a possible source of a new pandemic, yet the low pathogenic H7N9 is an important candidate source as well. Of course, it is impossible to say whether H7N9 will indeed be at the basis of the next influenza pandemic. We need to prepare for the worst and hope for the best,” Osterhaus warned the workshop audience.

“The 2009 H1N1 Mexican flu pandemic had been relatively mild with a relatively low case fatality rate. It has caused between 0.3 to 0.5 million deaths, which is similar to the toll of a seasonal influenza season. The main difference, however, was that the age range of the serious and fatal cases was relatively low, implying that a lot more quality life years were lost. In contrast, H7N9 and H5N1 have case fatality rates among hospitalized cases of about 20% and 60%. So the question is whether we are prepared for a more severe pandemic. That will be at the centre of the debates today. When we compare the last pandemic with the three previous ones, we see a totally different situation in terms of preparedness. For the first time, we had a vaccine available, although for many countries it came late. Apart from the medical interventions (including the use of vaccines and antivirals), we need to focus on societal measures and surveillance in humans and animals. Therefore it is extremely important to evaluate and update national response plans at regular intervals.”

Recent Zoonotic transmissions of influenza A virus

<table>
<thead>
<tr>
<th>SUBTYPE</th>
<th>COUNTRY</th>
<th>YEAR</th>
<th># CASES</th>
<th># DEATHS</th>
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<tr>
<td>H7N7</td>
<td>UK</td>
<td>1996</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>H5N1</td>
<td>Hong Kong</td>
<td>1997</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>H9N2</td>
<td>SE-Asia</td>
<td>1999</td>
<td>&gt;2</td>
<td>0</td>
</tr>
<tr>
<td>H5N1</td>
<td>Hong Kong</td>
<td>2003</td>
<td>2?</td>
<td>1</td>
</tr>
<tr>
<td>H7N7</td>
<td>Netherlands</td>
<td>2003</td>
<td>89</td>
<td>1</td>
</tr>
<tr>
<td>H7N2</td>
<td>USA</td>
<td>2003</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>H7N3</td>
<td>Canada</td>
<td>2004</td>
<td>2</td>
<td>0</td>
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<tr>
<td>H5N1</td>
<td>SE-Asia/M-East/Europe/W-Africa</td>
<td>2003-13*</td>
<td>&gt;630</td>
<td>&gt;350* (increasing)</td>
</tr>
<tr>
<td>H7N9</td>
<td>PR China</td>
<td>2013</td>
<td>126</td>
<td>24 (increasing rapidly)</td>
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*CFR ~ 60%
Objectives, purpose and set-up of the Flu Quest survey
To get a clear picture of the pandemic preparedness situation in Europe after the 2009 H1N1 pandemic, ESWI has carried out a comparative analysis of pre and post pandemic plans in nine European countries: Austria, Belgium, the Czech Republic, Finland, France, Germany, the Netherlands, the UK and Turkey. “Data have also been collected from the US and Japan, since both countries have quite different strategies concerning the use of vaccines and antivirals”, Osterhaus said. “The US and Japanese data have been integrated in the study as points of comparison for the European countries involved. The selection criteria for the nine European countries were mainly of geographical nature: by clustering neighbouring countries that have fairly similar healthcare systems, the survey was able to reveal substantial differences in pandemic preparedness plans and in the actual pandemic response strategies.”

“Collecting the survey information has been a time-consuming effort”, continued Osterhaus. “Our ESWI members and associate members have been instrumental in providing an insight in the way their countries have handled the 2009 pandemic. In many occasions they called upon the help of high-ranked public health officials and key opinion leaders to collect actual and precise data. We complemented that work with desk research, i.e. we reviewed relevant documents that are available in the public domain. However, today’s survey results are not complete yet. Gaps still need to be filled, knowing that not all countries are willing or able to reveal all their pandemic response data. It is hence important to note that some of the data presented today are calculated estimates.” Ab Osterhaus emphasized the fact that ESWI has carried out the survey with a number of clear objectives: to learn about Europe’s level of pandemic preparedness, to gain a clear view on the rationales for changes in pandemic response policies, and—ultimately—to enhance European preparedness for the next influenza pandemic. “This also implies that ESWI explicitly did NOT aim to facilitate the establishment of new preparedness plans nor does it aim to facilitate the revision with clear guidelines. ESWI recognizes the importance of evaluation efforts currently being carried out by WHO/Europe and ECDC and does not want to duplicate their work in any way. Therefore ESWI has opted for a broader scope and a different methodology.”

In conclusion, Osterhaus informed his audience about an important publication that will highlight the survey results: a scientific article is in preparation and will be co-authored by all respondents.

RESPONDENTS IN THE VARIOUS PARTICIPATING COUNTRIES HAD BEEN ASKED TO FILL OUT AN EXTENSIVE QUESTIONNAIRE WITH QUESTIONS ORGANIZED ACCORDING TO SIX AREAS OF FOCUS:

- Seasonal Influenza Surveillance, Vaccination and Communication
- Pandemic Influenza Planning and Coordination
- Pandemic Influenza Situation Monitoring
- Pandemic Influenza Prevention, Mitigation and Treatment
- Pandemic Influenza Healthcare Capacity
- Pandemic Influenza Communication

“So some countries are not willing or able to reveal all their pandemic response data.”

“The survey revealed substantial differences in pandemic response strategies between European countries that have fairly similar healthcare systems.”
The impact of the 2009 pandemic on seasonal flu management

Effective preparedness for an influenza pandemic is only possible when effective strategies are in place to routinely manage outbreaks of seasonal influenza. The FluQuest survey therefore compared surveillance systems, communication lines and vaccine uptake for seasonal flu in Europe. “Despite the fact that flu vaccines are effective and safe, uptake rates are declining in some of the most important target groups. We urgently need to counter this worrisome trend”, Dr. Ted Van Essen warned the workshop audience.
EUROPEAN SURVEILLANCE IS AMONGST THE BEST IN THE WORLD

"Generally speaking, surveillance systems for seasonal influenza are well established in Europe. And the data generated by these networks are easily accessible via government websites. But there are some remarkable differences to be noted”, opened Van Essen.

"On the one side, we see an exceptionally high percentage of GP engagement in sentinel system in the Czech Republic, where more then 5% of general practitioners and paediatricians are part of the surveillance system. On the other hand, Finland has no surveillance network installed that reports on clinical influenza prevalence. In the post-pandemic period, surveillance systems have been expanded in some countries like Belgium and the Netherlands, but this is probably not pandemic-related. It is more likely to be part of an effort to protect citizens for a wider range of health risks.”

ESWI’S IMPACT ON STAKEHOLDER COMMUNICATION

European governments are excellent communicators as in all surveyed countries, the Ministries of Health have direct communication lines to influenza stakeholders with organizations of the elderly, healthcare organizations and at-risk patient organizations as the most obvious communication partners. "During influenza epidemics, clinical data are always available through government websites and via regularly spread influenza bulletins. Although electronic tools are by far the most widely used communication channels, it should be noted that social media are never used, except in the UK. Here is some obvious room for improvement”, continued Van Essen, “especially since social media are a cheap and effective tool to reach specific target groups.” Interestingly, ESWI has been instrumental in establishing communication lines in Finland and Turkey, two countries in which it has set up successful networks of influenza stakeholders. “The Turkish network called ‘GRIP PLATFORMU’ is really moving things forward in a country that used to have little interest in influenza prevention,” Van Essen said.

SEASONAL FLU VACCINATION: A COMPLEX STORY

“One of the remarkable outcomes of the ESWI FluQuest survey is the contrast between seasonal flu recommendations and reimbursement policies in some countries. Knowing that free access to immunisation is an important driver to encourage recommended groups to take the vaccine, it is somewhat odd to see that all EU countries recommend routine vaccination against seasonal influenza for the elderly, healthcare providers and patients with underlying conditions under 65 years of age. Yet reimbursement policies do not always correspond with these recommendations, as Austria has no reimbursement policy in place at all and few countries reimburse healthcare workers. In the Netherlands, for example, healthcare workers are supposed to be reimbursed by their employer, i.e. the hospital”, Dr. Van Essen summarizes. He continues: “The issue of healthcare worker vaccination is in fact a worrisome and painful one. In contrast to the US, healthcare workers in Europe remain reluctant to be vaccinated. However, we need to make a clear distinction between GPs and hospital workers: in all countries uptake rates in GPs
are considerably higher than the uptake rates in hospital nurses. Targeted interventions in three university medical centres in the Netherlands have led to an increased uptake among the healthcare personnel, but the increase is still largely insufficient. That is why I am strongly in favour of imposing influenza vaccination in hospital settings. We have seen some excellent examples of mandatory vaccination in Germany and the US, where uptake rates were close to 95%.”

Many countries see a decrease in seasonal vaccine uptake because of loss of credibility. Van Essen elaborates on the issue: “Before the pandemic struck, the Netherlands were the only country to reach the WHO recommendation to vaccinate at least 75% of the elderly. Today, our rate has dropped below 75% again. Flu fatigue has hit the European population quite hard. But the on-going discussions about vaccine effectiveness play an important role too. The lack of a unanimous scientific standpoint on the effectiveness issue clearly creates doubt or even aversion in the target groups. Of course, there is always room for improvement, and the entire influenza community is in strong demand for better vaccines. From yesterday’s Flu Summit sessions, we have learned that some promising scientific advances are being made in this field.”

“\textit{The on-going discussions about vaccine effectiveness clearly create doubt or even aversion in the at-risk groups.}”

### FOUR KEY ARGUMENTS FOR THE VACCINATION OF HEALTHCARE WORKERS:
- keep healthcare workers working for the sake of business continuity of the health system
- protect the healthcare workers themselves
- prevent healthcare worker/patient infection
- patients expect their healthcare worker to be vaccinated
Pandemic influenza: What was planned? What was implemented? Remarkable changes today...

“While European countries are very well equipped to monitor newly emerging strains of influenza virus, many of them are reluctant to update their pandemic response programmes,” said Dr. Meral Ciblak, addressing the FluQuest workshop audience.
In all surveyed countries, laboratories were capable of typing and subtyping all influenza strains and distinguishing H1N1 influenza early. “High quality lab facilities, including veterinary labs, are a cornerstone of Europe’s excellent surveillance system for emerging infectious diseases,” said Dr. Ciblak at the opening of her talk on pandemic preparedness in Europe. “The emergence of H5N1 influenza at the end of the 20th century and WHO’s call to prepare for a possible public health crisis, have encouraged European countries to develop detailed pandemic preparedness plans. These plans describe response scenario’s dealing with issues like vaccine procurement and distribution, antiviral stockpiling, non-medical measures, healthcare capacity and risk communication. The FluQuest survey revealed that most countries had an interministerial pandemic planning committee installed to coordinate the pandemic response. Remarkably, these committees mainly included policy makers and scientific experts, while other stakeholders, like healthcare professionals and organizations of at-risk patients and the elderly, were not involved. In that sense, collaboration could be further improved.”

The FluQuest survey revealed yet another important trend in Europe’s attitude towards pandemic planning: WHO’s set of pandemic phases was often found to be inappropriate for national response plans and have largely been abandoned. Dr. Ciblak: “Before 2009, we see that most pandemic preparedness plans strictly abide to WHO’s pandemic phases, implying that they provided response scenario’s for six levels of pandemic alert. During the pandemic, however, many governments were confronted with a situation that did not actually match WHO’s assessment. Or, quoting the UK review committee: ‘There was no easy fit between WHO phases and the UK experience of the pandemic.’ As a direct consequence, most countries that have already revised their plans, have built in some flexibility or even developed their own set of phases. The national pandemic response plan of the Czech Republic, for instance, is still organised according to WHO pandemic phases, yet the phases have now been divided in a situation A (country not affected) and a situation B (country affected). From a risk communication point of view, this multitude of different approaches will obviously lead to a multitude of different messages, i.e. it is a recipe for confusion among the European population. Secondly, one might fear that behind the focus on flexibility is mere indifference. ‘Let’s wait and see how hard the pandemic hits before we respond’, is a very dangerous attitude to take. It will simply be too late to take action.”

“Many European countries are reluctant to update their pandemic response programmes.”
Antiviral medicines: risk groups, stockpiles and distribution.
Planning versus implementation versus changes.

“The stockpiling of antiviral drugs against influenza is one of the four pillars of an effective pandemic preparedness plan. During the pandemic, however, Europe had seen a low use of antiviral drugs as compared to the previously anticipated demand and the amount of antivirals stockpiled,” said Prof. Jonathan Van-Tam. “So I can see the cheap headlines coming, something like ‘We bought them and we didn’t even need them’, but it is impossible to extrapolate future need in case we face a severe pandemic.”
“The analysis of individual patient data endorses policy decisions to stockpile and use flu antivirals in hospitalised patients.”

“The FluQuest data that we have been able to glean, clearly reveal a large variation in pre-2009 antiviral stockpiles,” Van-Tam noted. “The UK, France and Austria stockpiled enough antivirals to treat 50% of their populations, while the rest of Europe had a stockpile that covered about 10-20% of their inhabitants. However, since market supply largely sufficed to meet the demand, virtually none of the stockpiles had been touched during the pandemic. Undoubtedly, this reflects the low severity of the H1N1 pandemic as compared with predicted severity of say H5N1. It says nothing about the need for antivirals drugs in case of a future severe pandemic.”

The question now has risen of what to do with the antiviral stocks. Finland, and most probably also the UK, will renew their holdings. Other countries, however, have decided to retest the stability of the oseltamivir stockpile and will extend its shelf life. It is also interesting to note that data on the actual coverage of population groups with antiviral drugs are hardly available due to a lack of monitoring,” Van-Tam concludes.

**THE ABC OF ANTIVIRAL DRUGS AGAINST INFLUENZA**

Antiviral drugs do not kill the influenza virus, they rather inhibit replication on a cellular level, preventing spread within the respiratory track.

All countries that participated at the FluQuest survey, had stockpiles of oseltamivir and zanamivir, two brands of the so-called neuraminidase inhibitors.

Antiviral drugs can be used both for prevention and for treatment. During the 2009 pandemic, antivirals have mainly been used to treat patients with severe influenza symptoms.

Oseltamivir and zanamivir are administered orally, which makes them difficult to use in an intensive care unit. For that reason, the US and Japan licensed peramivir, a new intravenous drug, for treatment.

**Antiviral medicines: stockpiles and distribution**

Large variations in antiviral stockpile sizes currently and historically across Europe: (% of population covered by stockpile)

- **Austria** 50%
- **UK** 40%
- **France** 30%
- **Czech republic** 20%
- **Finland** 10%
- **Belgium** 0%
- **Germany** 0%
- **Netherlands** 0%
- **Turkey** 0%
- **EU average** 0%
- **Japan** 0%
- **US** 0%
SHOULD COUNTRIES STOCKPILE AGAIN OR REPLENISH?

To try and resolve this unanswered policy question, the research group at Nottingham University conducted a systematic review of published manuscripts that looked at the impact of influenza antivirals on patient outcomes during the 2009 pandemic. “In total, 44 studies contained data on 23,723 individual patients. The key outcome of this review was an important one: during the 2009-10 influenza A(H1N1) pandemic, early initiation of antivirals treatment reduced the likelihood of mortality compared with late or no treatment,” said Prof. Van-Tam, who headed the research group.

“This was the driver for carrying out an individual patient data meta-analysis to further investigate the same question.” Van-Tam’s research group has therefore set up the Post-pandemic Review of anti-Influenza Drug Effectiveness (PRIDE) Study, in close collaboration with 80 research groups from 38 countries and 6 WHO regions. PRIDE’s conclusions are of key importance to policy makers: the analysis of individual patient data confirmed the findings of the initial meta-analysis and thus endorses policy decisions to stockpile and use flu antivirals in hospitalised patients during the 2009-10 pandemic. The full study results are to be published soon.

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“THE EXCEPTIONAL UK APPROACH

Use of antiviral drugs for prevention

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“In late July 2009, the UK installed a new policy: the National Pandemic Flu Service, a novel telephone access system. If you felt ill, you just had to tick a number of boxes and provide some information about your illness. The vast majority of patients with influenza symptoms then received an authorization to pick up a box of antiviral drugs at the nearest collection point, usually a pharmacy. This system relieved the burden on primary healthcare to a large extent.”

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Pandemic vaccines: priority risk groups and procurement, vaccine uptake and distribution, planning for the future

“The vaccine is the cornerstone of any successful response to the pandemic outbreak of an influenza virus,” said the director of the French national influenza center, Bruno Lina. “It is a key instrument to reduce the number of patients and ultimately to reduce the number of deaths. Unfortunately, the 2009 pandemic had a very negative impact on the general public’s perception of flu vaccines.”
PRELUDE: THE PRE-PANDEMIC H5N1 VACCINE
In order to prepare for a possible pandemic outbreak of the H5N1 flu strain, several pharmaceutical companies engaged in the production of a vaccine that would prime the human immune system against an H5N1 infection. As part of their general pandemic preparedness strategy, France, Finland, the UK and Japan had stockpiled a considerable amount of this so-called ‘pre-pandemic’ vaccine. “None of the European countries has actually used the H5N1 vaccine,” explained Bruno Lina, “but there is a correlation between the procurement of pre-pandemic vaccines and the purchase of pandemic vaccines. We will see that France, Finland and the UK did not hesitate to buy sufficient amounts of H1N1 pandemic vaccines as well.”

THE H1N1 PANDEMIC: WHO BOUGHT THE VACCINE?
As soon as the World Health Organization gives the green light for the production of pandemic vaccines, the pharmaceutical industry dedicates its entire production capacity to the manufacturing of pandemic vaccines. Countries that have no purchase agreements in place at that time, will never succeed in acquiring enough pandemic vaccines to protect their populations. “Northern and Western European countries had good access to the pandemic vaccine, due to their pre-pandemic agreements. In contrast, countries like the Czech Republic and Turkey could not cover more than 10% of their populations. These huge discrepancies in coverage levels between European countries could turn out dramatic in case of a severe pandemic,” Bruno Lina stated. “Some countries like Belgium, France and Austria were eventually able to cancel part of their purchase orders as soon as it became clear that they would not be needing the total number of ordered vaccines, which saved them some good money. But more importantly, very few governments have concluded new pandemic vaccine purchase orders after 2009. It is also interesting to note that the Czech Republic and Finland are relying on a EU joint procurement programme, rather than ordering vaccines with a manufacturing company directly. Whether this has to do with a trend towards harmonization of vaccine demand or whether it is merely an excuse to pass on the responsibility to the EU level, remains an open question.”

THE H1N1 PANDEMIC: WHO USED THE VACCINE?
Pandemic vaccine uptake varied greatly in EU countries with high uptake rates in The Netherlands and Finland on the one hand and low uptake rates in the Czech Republic, France and Germany on the other hand. “In this context, it may be surprising that countries that had good access to pandemic vaccines, like France, reached an uptake level of not more than 9% of their population,” said Bruno Lina. “The main reason for the low uptake in Germany and France was the lively public
debate on the effectiveness of the vaccine. Extremely critical and unfounded press messages poisoned the debate and had a negative impact on the general public’s opinion.”

“We also see an enormous variation when it comes to defining risk groups,” Prof. Lina continues. “In some countries, there was no difference between the list of priority groups for seasonal or pandemic vaccination, while other countries, like France, decided not to define risk groups until the start of an actual pandemic outbreak. The main lesson to be learned from the 2009 pandemic, is that none of the EU member states had similar pandemic strategies. They were all different.”

PLANNING FOR A FUTURE PANDEMIC: WHAT’S NEXT?
Many countries have adapted their pandemic priority list based on the actual pandemic experience or did not specify any priority groups at all. The latter is the case for Finland, Austria and the UK. The British review committee was quite outspoken on this topic, as its evaluation report reads: ‘The most appropriate course of action would depend on the particular circumstances.’ Prof. Lina concludes; “This points at another trend in European preparedness planning: flexibility is built in to a very large extent. I’m afraid this lenience is a symptom of indifference.”

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Health care capacity: Were we ready to cope? Did we cope? How will we cope in the future?

“As a paediatrician working at ICU during the 2009 pandemic, I do not share the optimistic view that the pandemic was a ‘whimpy’ one,” Dr. Fraaij set the scene for his review on healthcare capacity in Europe. “For those working in ICU facilities, it wasn’t a mild pandemic at all.”
FROM PRIMARY CARE TO ICU

Primary care facilities were in general very able to cope with the number of patients with flu complaints. In all surveyed countries the number of patient calls remained well below the expected numbers that had been envisaged in the pandemic preparedness plans. “It is, however, difficult to give an exact definition for a flu-related patient call,” said Dr. Fraaij. “As soon as people hear that a flu virus might be circulating in Europe, they go to the doctor. We see a very high number of GP visits in Belgium, for instance, that is because Belgian employees need a doctor’s note if they call in sick from work. Whether they all really had the flu is not quite sure.”

“We see a different picture already when we look at hospital settings. There, capacity was almost stretched to the limit. Now, the strange thing is that the revised response plans have not taken this finding into account, since they have not adapted the expected disease rates. If the next pandemic were to hit twice as hard, we will be in trouble. Then, who is going to tell the public that hospitals are no longer admitting patients because of a lack of capacity,” Dr. Fraaij asks his audience.

“But clearly, the capacity situation was worst in ICU facilities. Still, it is remarkable to see a decrease in the number of ICU upgrading plans. France, for instance, had a plan to confiscate hotel beds to accommodate ICU patients if needed, but this option was stripped from the revised version as to allow a greater deal of flexibility in response. In the pre-pandemic period 7 out of 11 countries had such an upgrade plan. Only four of them intend to also include it in the update version. That is worrisome, since ICU capacity is rather limited in all countries, additional capacity will certainly be needed in case of a severe health crisis like a severe flu pandemic.”

IMPORTANT LESSONS FROM THE ICU WARDEN

“The reason why I’m focussing on ICU facilities, is our own 2009 pandemic experience. First of all, about 30% of ICU admissions during the pandemic were previously healthy people, they had no underlying conditions at all. But what is really remarkable, is the exceptionally high number of ICU admissions of patients with an acute respiratory distress syndrome (ARDS), caused by the H1N1 flu virus. ARDS is a severe lung syndrome that has a 90% death rate in untreated patients. With treatment, the death rate is up to 50%. Usually, treatment is ventilation or extracorporeal membrane oxygenation (ECMO). Now, ECMO is a technique to provide oxygen to a patient whose lungs are so severely diseased that they can no longer serve their function. ECMO gives the lungs time to heal by themselves, which is not always possible using a ventilator. However, ECMO is a very specialised technique, requiring specific know-how and hence very few paediatric intensive care units use it. Since ECMO has proven so valuable during the H1N1 pandemic, several countries, like the UK and France, now have invested in an expansion of their numbers of ECMO facilities. It is important, however, to cluster ECMO facilities in order to create regional centres of expertise.”

HOW TO DEFINE ICU CAPACITY?

An important hurdle to compare ICU capacity in countries, is the ICU definition. Some parameters:

- Ventilators availability. Intensive care units may have many beds, but the number of patients that can be treated depends on the number of ventilators available. Those numbers do not always match.
- Staff availability. Will all patients receive adequate care when the ICU is stretched to its maximum capacity? It is hence best to measure the number of caring hands instead of the number of beds.
Communication to stakeholders and the public: main lessons learnt.

Public confidence in the provision of health care is modulated by many things, but one of the most obvious – and volatile – factors is the influence of the media. “About 50% of the attention of the officials who are responsible for managing a flu pandemic crisis goes out to communication,” said Marc Van Ranst, professor of Virology at the University of Leuven who was Belgium’s Flu Commissioner during the 2009 pandemic.
"Claiming the media attention and getting the right messages out is easiest achieved when you have a single flu spokesperson appointed."

"If you as a health policy official are not there on Day One of the crisis, the media certainly will be. They will yank the rug out right from under you by finding other people who will comment on the situation – and you will have lost your first chance to shape the perception agenda," said Prof. Van Ranst. "Claiming the media attention and getting the right messages out is easiest achieved when you have a single flu spokesperson appointed prior to the pandemic outbreak. Since not all governments had chosen to install a spokesperson, I hope my story will convince them to do so in the future."

"You have to give interviews to whoever wants it. The public craves for information about influenza, vaccines, risks, treatment, etc. And they prefer to get that information from one, reliable source. You have to be there on-site to answer any and all questions, even if it disrupts your holiday which it constantly did during mine, by the way" he said. "But if you do this, then you’ll generate a perception that ‘Yes, our country is ready to go’ and you’ll be on a good footing with your press." Noting that many researchers are afraid of live interviews, Van Ranst said public health officials and scientists “must grasp these opportunities” but only in accordance with a pre-agreed general narrative for explaining the health event’s complexities.

To avoid confusion over WHO’s pandemic phases, the Belgian Flu Commissioner applied an old communication trick. “The general public tends to believe that the pandemic phases are like Richter’s scale. In their perception, phase 6 is dramatically worse than phase 5. They do not get the notion of geographical spread. But this is easily solved. As a flu commissioner, you know when a phase change is about to happen. The trick is then to bring the news to the media a day before WHO does. This keeps the news away from the headlines, because WHO just confirms what you had already said.”

"Our mantra from the start was: ‘This pandemic is comparable to seasonal influenza though we have to prepare for worst’", Van Ranst said. Thus the Belgian government focused on low-cost basic hygienic measures, no school closures, antivirals only for high-risk groups and the purchase of only one dose of vaccine per capita. "If you do something ‘in the middle’ as a policy, the press leaves you alone. If you do too little or too much, the press will always dog you," he observed. This approach to promoting vaccination had its effects peculiar to Belgium, however. Flanders, the country’s northern Dutch-speaking half, got way more vaccinations than Wallonia, its southern francophone half. "One of the reasons was the media,” said Van Ranst. "In Flanders, people mainly listen to the Flemish news. But in Wallonia, they also get their news from France, where anti-vaccination sentiment is strong.”

And Van Ranst’s tips for dealing with a country’s anti-vaccination groups? "Never debate with them in front of the public media because that creates the impression that there is balanced discussion, when there is not," he said. “I do engage with the anti-vaccination lobby at their own meetings or in front of their office but never in front of the general media,” he warned his listeners. “It’s a hostile
“If you do something ‘in the middle’ as a policy, the press leaves you alone. If you do too little or too much, the press will always dog you.”

Did he get much support from his government?
“Of course, political support is essential. You have to work with government agencies as if you were a team. But it is equally essential to sometimes openly disagree with your political allies. As soon as people suspect you belong to this or that political party, you die. That’s the power of a non-political flu commissioner: the political opposition has no interest in making you look bad. At the same time, you’re the politician’s life insurance. If things turn for the worse, your head will roll, not theirs.”

Asked to comment on whether his policy office exploited social media to deal with the pandemic, he said “we were quite active on Twitter and Facebook. It is important to see what people are thinking – to see how they react the next day to what you say. You should have a presence in these outlets. In this context, it was astonishing to see the FluQuest survey results on the communication strategies used in Europe. It seems like we all freely experimented with communication channels.”

Pandemic flu vaccination 2009 in Belgium
WHO reflections on the Flu Quest outcomes

“The world is ill-prepared to respond to a severe influenza pandemic or to any similarly global, sustained and threatening public-health emergency.” This was one of the conclusions of the IHR review committee’s assessment of the global response to the 2009 pandemic. “To be better prepared for the next, potentially more severe pandemic, European countries need to use the lessons learned during the 2009 pandemic to improve pandemic preparedness”, WHO’s Michala Hegermann-Lindencrone told the FluQuest workshop audience.
“ESWI conducted a very interesting and important survey, which raises many issues regarding pandemic preparedness. The result of the survey is a reminder that there is still work to be done in Europe to improve pandemic preparedness.” The recent outbreaks of avian influenza A(H7N9) in China and the ongoing outbreaks of Middle East respiratory syndrome coronavirus (MERS-CoV) also remind us that Member States continuously need to strengthen their capacities to detect and respond to emerging pathogens. Over the past years, laboratory capacities, surveillance systems and pandemic plans have substantially improved in the WHO European Region but there are still important gaps to be filled and the FluQuest survey highlighted some of these gaps.

One of the findings in the survey was that only a few countries have published updated pandemic preparedness plans following the 2009 pandemic. WHO encourages its Member States to update their pandemic plans incorporating lessons learned during the pandemic. However, many countries are awaiting the revised WHO global guidance on pandemic preparedness. Another interesting finding from FluQuest is that some countries have decided not to replenish expiring stockpiles of antivirals.

Yet another result highlighted during the presentation was that the 2009 pandemic seems to have created more awareness about pregnant women as a risk group for severe influenza infections. This is reflected in some countries including pregnant women as one of their target groups for seasonal influenza vaccination, in line with WHO recommendations.

**WHO/EUROPE INITIATIVES**

The WHO European Region is continuously working with its Member States to strengthen pandemic preparedness and update pandemic plans. The Region is diverse covering 53 Member States from the European Union countries in the West to central Asian republics in the East wherefore the work of the Regional Office needs to be tailored to meet the needs of the different parts of the Region. In relation to the ongoing events with A(H7N9) and MERS-CoV, trainings are conducted in selected countries to strengthen outbreak response capacities including laboratory detection of new respiratory pathogens and clinical management of severe acute respiratory infections.

The Regional Office is working to finalize its European guidance on pandemic preparedness which is aimed at supporting countries in applying lessons learned from the 2009 pandemic. At the same time, the new global WHO guidance on pandemic influenza risk management which places greater emphasis on national risk assessment and integration of pandemic preparedness in all-hazards risk management, is about to be published.

In the autumn 2013, the Regional Office, together with ECDC, is organizing a meeting on pandemic and generic preparedness to address areas such as risk assessment. The meeting is part of the Regional Office’s strategy to further strengthen European preparedness to the next pandemic.
Prof. Masato Tashiro,
WHO Collaborating Centre for Reference and Research on Influenza,
Tokyo

The Japanese perspective
“Japan received a serious warning during the H1N1 pandemic, since we were very lucky that the virus was relatively mild”, Prof. Tashiro opens his comment on the Japanese pandemic strategy. “We therefore think it is very dangerous to make pandemic preparedness plans more flexible. On the contrary, we still continue to strengthen our national pandemic plan. This is partially due to the Fukushima experience. While experts had warned for a worst-case scenario with a tsunami and a nuclear power plant breakdown, our government had not paid attention to these warnings. Obviously, they do not want to make this mistake twice.”

“In April 2013, the Japanese government passed a new law on health emergency,” Prof. Tashiro continues. “That too is a direct consequence of the 2009 pandemic, when the government was confronted with the fact that most of the non-medical interventions that were included in the preparedness plan had in fact no legal basis.”

No other country in the world has such a large stockpile of H5N1 vaccines. Prof. Tashiro elaborates: “The stockpile will expire in three years time, and discussions are now going on whether we should destroy the vaccines or whether we should use the stockpile anyway to immunise healthcare workers and essential service workers. Action groups have prevented this from happening, but the idea of inducing immunity against H5N1 as a protective measure against other flu virus strains is quite interesting, I think.”

80% OF GLOBAL FLU ANTIVIRAL DRUGS PRODUCTION USED IN JAPAN

“The Japanese authorities approved zanamivir and oseltamivir for use in 2000. Since then, we have used about 80% of the global production. I don’t know exactly why antiviral drugs are so popular in Japan, but paediatricians especially prescribe antivirals very easily. We now have a stockpile of 50 million courses and that is enough to cover about 40% of our population. It is interesting to note that two additional drugs have been approved for use in Japan during the pandemic: peramivir and laninamivir.”
“In its present form, the FluQuest survey has brought together a substantial set of relevant data already, yet additional input from the respective countries will be needed. What is important, however, is that we see some clear messages emerging,” Prof. Osterhaus starts his concluding overview.
1. **FLU VIRUS IS UNPREDICTABLE**

   “An important lesson to be learned is that, whilst we were all bracing for the H5N1 pandemic, we faced the H1N1 pandemic. Now we are bracing for both H5 and H7 based pandemics, but it might as well be that we get an H2 or an H3 pandemic. Influenza viruses are just so unpredictable.”

2. **OVERALL DECREASE IN SEASONAL VACCINE UPTAKE IS WORRISOME**

   “The decrease is due to an overall lack of confidence in the vaccine effectiveness, but has also to do with the role of healthcare workers. The uptake rate in this target group should be raised considerably in all countries. Vaccine reimbursement and GP incentives are essential drivers to reach this goal.”

3. **EUROPEAN COUNTRIES ARE WELL EQUIPPED TO MONITOR NEWLY EMERGING STRAINS OF INFLUENZA VIRUS**

   “This is true for influenza viruses emerging both in the animal world and in the human world. The WHO surveillance network has proven to be very instrumental for the early identification of new human influenza viruses. Although improvements are still to be made, especially in the veterinary field, European surveillance is among the best in the world.”

4. **PREPAREDNESS PLAN UPDATES ARE OFTEN POSTPONED**

   “Few countries have their act together. While countries like Finland, France, UK, Czech Republic and Japan have updated their pre-pandemic preparedness plan, several other countries lack the sense of urgency to revise their plans, for a variety of reasons: lack of political interest, lack of scientific consensus over the pandemic evaluation or because they are waiting for a coordinated response by WHO and ECDC. The latter reason might be seen as an excuse for not having to take responsibility.”

5. **WHO PANDEMIC PHASING LARGELY ABANDONED**

   “Whereas many pre-pandemic preparedness plans chose to strictly abide to WHO’s pandemic preparedness phases, most countries which have already revised their PPPs, have built in some flexibility or even developed their own set of phases. Our survey did not ask for the reasons behind this change in attitude, it may be speculated that the way in which WHO has communicated about the implementation of its phases is part of the explanation.”

6. **VERY FEW COUNTRIES HAVE OR WILL REPLENISH THEIR ANTIVIRAL STOCKPILE**

   “Before the pandemic we have seen a lot of attention for antiviral stockpiling as part of the preparedness programmes. In fact, all countries had oseltamivir and zanamivir stockpiles, while the new antiviral peramivir was licensed for use during the pandemic in US and Japan, the same holds true for another new drug, laninamivir, which was licensed for use in Japan. However, since virtually none of the stockpiles had been touched during the pandemic, the question has risen what to do with these stockpiles. As a result, stockpile expiration dates are being extended after retesting the stability of the oseltamivir stockpiles. It is also interesting to note that data on the actual coverage of population groups with antiviral drugs are hardly available due to a lack of monitoring.”

7. **THE UK APPLIED AN EXCEPTIONAL YET SUCCESSFUL PANDEMIC STRATEGY**

   “The UK was the only European country that made antiviral drugs widely available, virtually over the counter. While 50% of the population was covered by the national antivirals stockpile, 1,1 million courses have actually been distributed for prophylactic use and for treatment. Secondly, it was the only EU country to install a telephone flu algorithm to relieve the burden on frontline health workers. And lastly, pharmacists acted as antiviral collection points in the National Pandemic Flu Service, again a measure to mitigate the burden for GPs and other primary care professionals.”
8. WIDESPREAD HESITANCE TO HAVE PANDEMIC VACCINE PURCHASE CONTRACTS IN PLACE

“While several countries were able to partially cancel their purchase order as soon as it became clear that they would not need the total number of ordered vaccine doses, few governments have concluded new pandemic vaccine purchase orders. Of course, it might well be that they are reluctant to share this information with us. It is also interesting to note that the Czech Republic and Finland are relying on the EU joint procurement programme, as opposed to ordering vaccines on a national level.”

Audience remark: “Some countries do have Advanced Purchase Agreements in place with vaccine producing companies. APA is an agreement to block a certain percentage of the company's production capacity in the event where a pandemic vaccine will be manufactured. It hence grants the right to buy a certain percentage of the vaccines produced. Although it is less binding than the traditional pandemic vaccine contracts, an APA still comes at an annual cost/fee.”

Conclusion: “It is an important post-pandemic evolution that governments are hesitant to conclude real binding contracts and that they are hesitant to openly communicate about their agreements with vaccine producing companies. This trend may be a major barrier to DG Sanco's attempts to establish joint procurement procedures in the EU.”

9. REMARKABLE VARIATION IN PANDEMIC VACCINE USE IN THE EU

“The FluQuest survey revealed that pandemic vaccine uptake varied greatly in EU countries with high uptake rates in The Netherlands and Finland on the one hand and low uptake rates in the Czech Republic and Germany on the other hand. In this context, it may be surprising that many countries have adapted their pandemic priority list based on the actual pandemic experience or did not specify any priority groups at all. The latter is the case for Finland, Austria and France. This points at another trend in European preparedness planning, where flexibility is built in to a large extent. We also see this when it comes to social distancing measures, like school closures and restrictions on social gatherings, where most countries maintain a flexible attitude, stating that “they may be imposed whenever the epidemiological situation requests it.”

10. HEALTHCARE CAPACITY HAD BEEN PUSHED TO THE LIMIT DURING THE ‘MILD’ H1N1 PANDEMIC

“Although primary care and hospital care systems were able to cope with all patients in all surveyed countries, it is estimated that many countries were close to 100% occupation of hospital capacities. Consequently, general and specialized hospital capacity would have been overstretched if the pandemic would have been worse, but surprisingly, the lack of hospital capacity is not calculated in pandemic preparedness plans. So it is clear that governments should develop emergency plans to cope with a possible shortage of ICU and hospital capacity.”

11. BELGIAN EXAMPLE UNDERSCORES THE IMPORTANCE OF INSTALLING A SINGLE FLU SPOKESPERSON

“In virtually all the countries, we have experienced a communication flaw. In part this was due to the fragmentation of responsibilities in several European countries: all the different committees issuing all the different recommendations made it hard to communicate with a single voice. In spite of the uncoordinated communication during the pandemic, where many self-proclaimed experts gave their opinion on the situation, many governments still chose not to install a single flu spokesperson to inform the public at large. The Belgian example, however, showed the obvious benefits of channelling the media attention to one single person.”
The European Scientific Working group on Influenza is a network of partner organizations that share the same goal: to reduce the burden of influenza in Europe.

To realize its objectives, ESWI works with the following organizations: