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Dynamics of the 2009 A/H1N1 pandemic in the UK, Germany and Spain: An overview of public health interventions and recommendations

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Abstract

Background: In April 2009 a new influenza A/H1N1 virus emerged, causing the first pandemic of the 21st century. The characteristics of the pandemic A/H1N1 virus that decide the size, speed and seriousness of a pandemic were still missing when the virus emerged, but it became clear at an early stage that it met the criteria for a pandemic strain and countries started to take response measures. In order to increase the acceptance of large-scale response measures among the general public and at-risk groups, communication messages have to take into account the factors that influence human behavior. Therefore, a sub-project of the E-com@eu project aims to assess the influence of the changing A/H1N1 epidemiology, the changing pattern of risk communication, and the changing official recommendations on human protective behavior during the 2009 A/H1N1 pandemic. This work contributes to the sub-project of the E-com@eu project by exploring the dynamics of the 2009 A/H1N1 pandemic in the UK, Germany and Spain. It presents the progress of the pandemic in the UK, Germany and Spain and gives a systematically documented chronological overview of public health measures taken and official recommendations released during the pandemic. A time series analyses explores the interaction of what actually happened (epidemic curves), how the countries responded (public health measures) and what the people were recommended (official recommendations).

Methods: To obtain pandemic A/H1N1 surveillance data for the UK, Germany and Spain a systematic literature search was accomplished. In addition, grey literature and websites of national health authorities and international health agencies were searched. These data were used to draw epidemic curves for the UK, Germany and Spain. A literature search on public health measures taken and official health behavior recommendations released during the 2009 A/H1N1 pandemic was conducted. The results of this search are illustrated in a time series analysis, using the epidemic curves as a timeline along which data of the public health measures and recommendations are plotted. In order to give an in-depth description, the pandemic has been split up into five phases.

Results: The UK, Germany and Spain had different pandemic profiles during the 2009 A/H1N1 pandemic. The initial control strategies focused on limiting transmission of the virus or delaying the spread. In order to inform the general public on the pandemic A/H1N1 virus and personal protective measures, the UK, Germany and Spain developed extensive information materials at an early stage of the pandemic. The campaigns provided a basic knowledge of hygiene and personal protective measures against infection. Further, tailored information for healthcare professionals on the treatment of cases and preventive measures has been published by national authorities. In late October, Germany and the UK started its vaccination program. Spain started vaccination in mid November. The countries responded to and changed recommendations in response to available evidence on the characteristics of the virus and the pandemic vaccines. The vaccination campaigns that went alongside the vaccination programs informed the general public on the aspects of the programs. In addition, the UK and Germany issued tailored information for at-risk groups. Furthermore, information for healthcare professionals was published to inform them on the specific pandemic vaccines and on aspects for vaccine administration.

Discussion: Although a lot of information on the pandemic A/H1N1 virus, personal protective measures and the pandemic vaccine has been published, vaccination coverage rates and the uptake of recommended behavior during the pandemic were low. Several improvements have been identified regarding the vaccination and information campaigns but more work is needed to see how recommendations can be effectively translated into higher vaccination coverage and behavior change. This should also take into account the influence of varying media messages.

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Abbreviations

AEMPS	Agencia Española de Medicamentos y Productos Sanitarios (Spanish Medicines and Healthcare Products Agency)
BZgA	Bundeszentrale für gesundheitliche Aufklärung (Federal Centre for Health Education)
CCAES	Centro de Coordinación de Alertas y Emergencias Sanitarias (Coordinating Centre for Health Alerts and Emergencies at the Spanish Ministry of Health and Social Policy)
CDC	US Centers for Disease Control and Prevention
CSP	Comisión de Salud Pública (Public Health Commission)
DH	Department of Health (UK)
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
EMA	European Medicines Agency
EU	European Union
GP	General Practitioner
GSK	GlaxoSmithKline
HPA	Health Protection Agency
IfSG	Infektionsschutzgesetz (German Protection Against Infection Act)
IHR	International Health Regulations
JCVI	Joint Committee on Vaccination and Immunization (UK)
MHRA	Medicines and Healthcare products Regulatory Agency (UK)
MHSP	Ministry of Health and Social Policy (Spain)
NHS	National Health Service (UK)
NPFS	National Pandemic Flu Service
PEI	Paul-Ehrlich-Institut
PHEIC	Public Health Emergency of International Concern
PIKS	Pandemische Influenza A(H1N1) Krankenhaus Surveillance (Pandemic Influenza A(H1N1) Surveillance in hospitals)
RKI	Robert Koch-Institut
SAGE	Scientific Advisory Group for Emergencies (UK)
SISS	Spanish Influenza Surveillance System
STIKO	Ständige Impfkommission (German Committee on Vaccination)
SVA	Subcomité de Vacunas y Antivirales (Spanish Subcommittee on Vaccines and Antivirals)
WHO	World Health Organization

1 Introduction

Emergence and evolution of the pandemic A/H1N1 virus

In April 2009 a new influenza A/H1N1 virus emerged, causing the first pandemic of the 21st century. The pandemic started in Veracruz, Mexico where an outbreak of influenza-like illness was recorded in early April (European Centre for Disease Prevention and Control, 2010). A few days later other outbreaks of influenza-like illness were reported in several parts of Mexico. Analysis of samples detected an Influenza A virus but it was not possible to identify the subtype (World Health Organization, 2011). By 23 April, 120 confirmed cases of respiratory illness due to influenza and 20 deaths have been reported in Mexico (Dacey et al., 2010). The situation was of concern because especially young people and previously healthy people experienced severe disease (World Health Organization, 2011). In mid- April, the US Centers for Disease Control and Prevention (CDC) analyzed a sample from two children with respiratory illness in southern California in the USA and identified the virus as a swine influenza A/H1N1 virus. CDC stated that the virus contained a gene segment that had not yet been found in humans or swine and raised concern that this new strain of swine influenza A/H1N1 virus differs from human influenza A/H1N1 viruses. This would mean that a large proportion of people might be non-immune to this new strain of swine influenza A/H1N1 and seasonal influenza vaccine might not protect from contracting the virus (Centers for Disease Control and Prevention, 2009).

Further virological analyses confirmed that the virus isolates from Mexican patients were genetically identical to the new strain of swine influenza A/H1N1 virus discovered in California (World Health Organization, 2009b). Molecular analyses revealed that the virus was derived through a process called reassortment. In this process genetic material of various virus subtypes admixes and produces a new virus. This biological process happens when one organism is infected with two different influenza viruses at the same time. Swine are an ideal species for this process as they are susceptible to infection by both bird and human influenza viruses. The new swine influenza A/H1N1 virus was probably derived from the US triple reassortment swine influenza virus and a Eurasian H1N1 swine influenza lineage (Schaberg & Burger, 2010). The swine triple reassortment was first discovered in swine in 1998. It was derived from a swine influenza virus lineage, an avian influenza virus and a human Influenza A/H3N2 lineage. It is not clear when exactly the

reassortment took place that produced the new swine influenza A/H1N1 (Bush, 2011). Figure 1 illustrates the described evolution of the new swine influenza A/H1N1 virus.

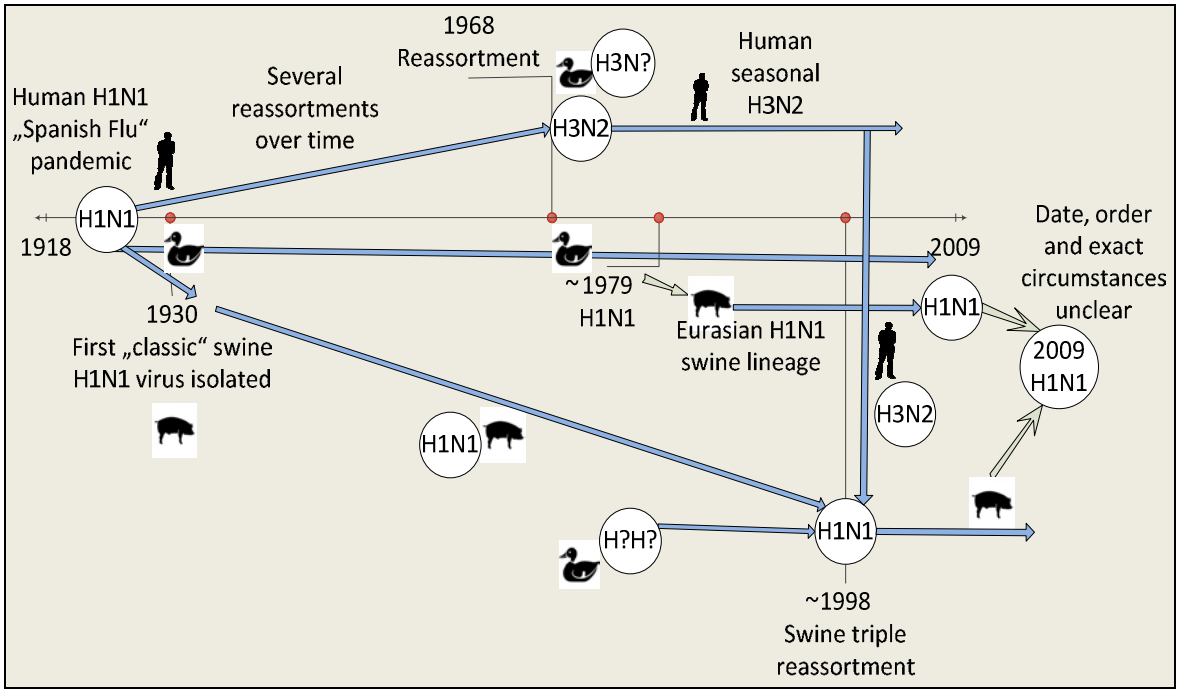

Figure 1: Evolution of the new swine influenza A/H1N1 virus (Bush, 2011; modified by author)

Global situation

The virus started to spread globally and by 28 April seven countries (Mexico, USA, Canada, Israel, New Zealand, Spain and the UK) reported confirmed cases of swine influenza A/H1N1 (World Health Organization, 2011). On 29 April, WHO raised the level of influenza pandemic alert to phase 5 and advised all countries to activate their pandemic preparedness and response plans (World Health Organization, 2009e). Although only a few countries were affected at this stage, Phase 5 was a signal that a pandemic was coming up and human to human spread of the virus into at least two countries of one WHO region was evident (World Health Organization, 2012). The number of affected countries increased steadily and by 9 June, 73 countries worldwide had reported 26.563 laboratory confirmed cases to WHO (World Health Organization, 2011). On 11 June, the WHO raised the level of influenza pandemic alert to phase 6, declaring a pandemic (World Health Organization, 2009h). This phase is defined by a high and sustained transmission in the population, in at least one other country in a different WHO region together with the characteristics of Phase 5 (World Health Organization, 2012). The severity of the

pandemic was considered to be moderate by the WHO (World Health Organization, 2009i).

To find a scientifically acceptable name for the virus, the WHO organized a teleconference with the Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health (OIE) on 15 June. The participants agreed to name the virus "pandemic influenza A/H1N1 2009 virus" (World Health Organization, 2011).

The pandemic influenza A/H1N1 2009 virus (hereafter referred to as pandemic A/H1N1 virus) continued to spread globally and became the predominant circulating influenza virus (World Health Organization, 2009m). By October, the overall number of cases started to decline but some regions of the world still experienced sustained transmission (Sekkides, 2010). An assessment of the global situation in August 2010 indicated that the levels and patterns of pandemic A/H1N1 transmission showed seasonal patterns of transmission. Therefore, on 10 August 2010 the WHO announced that the pandemic was over (World Health Organization, 2010c). By then, more than 214 countries and overseas territories have reported confirmed pandemic A/H1N1 cases and nearly 18.500 pandemic influenza A/H1N1 related deaths have been recorded (World Health Organization, 2010b). Under-reporting of deaths due to pandemic A/H1N1 infections is possible as the WHO´s number is considering patients who died, in whom pandemic A/H1N1 infection was laboratory confirmed only. Thus, many deaths were either not recognized or not reported.

Differences between pandemic A/H1N1 and seasonal influenza

The clinical presentation of a pandemic A/H1N1 infection was similar to a seasonal influenza infection. Common symptoms were: fever, cough, sore throat, body aches and headache. Additionally, patients with pandemic A/H1N1 infection reported vomiting and diarrhea (Robert Koch-Institut, 2009a). Most cases experienced mild illness. Patients experiencing severe disease had similar risk factors as for seasonal influenza complications (Louie et al., 2009; Nicoll & Coulombier, 2009).

A significant difference between pandemic A/H1N1 and seasonal influenza was that mostly younger age groups were affected. Several studies observed that many people aged ≥ 65 were immune probably due to exposure to a similar influenza virus that had been circulating before the mid 1950s (Donaldson et al., 2009; Hardelid et al., 2010). Although, the lowest incidence rate was observed in those aged 65 years or over, the case fatality ratio was highest for this age group. This means that individuals aged 65 years or over

were less likely to contract a pandemic A/H1N1 infection than younger age groups, but if they contracted the virus, they were more likely to have a severe or fatal outcome. A study on the epidemiology of 308 fatal cases in England by Pebody et al. (2010) reported a case fatality ratio of nine per 1.000 clinical cases for the ≥ 65 years age group compared to a case fatality ratio of 0.4 per 1.000 clinical cases for those aged six months to 64 years. 77% of the 308 fatal cases had underlying risk factors for severe disease. The overall case fatality rate was estimated to be 0.4 per 1.000 clinical cases. A similar finding has been reported earlier by Donaldson et al. (2009). In addition, he stated that mortality in this pandemic is lower than observed in previous pandemics.

A high percentage of fatal outcomes occurred in younger age groups (Department of Health, 2010d; Larrauri Cámara, Jiménez-Jorge, Méndez, & de Mateo Ontañón, 2010; Schaberg & Burger, 2010). Around 80% of premature deaths reported to the European Center for Disease Prevention and Control (ECDC) were in those under 65 years of age (Amato-Gauci et al., 2010). The minority of fatal cases occurred in previously healthy people. The relative risk for fatal outcome was especially high for those with underlying chronic conditions. Donaldson et al. (2009) observed a nine times greater risk of dying from pandemic A/H1N1 for people in one of the risk groups eligible for vaccination in the UK. Members of an at-risk group were people with chronic respiratory disease, chronic heart disease, chronic renal disease, chronic liver disease, chronic neurological disease, immunosuppression, diabetes mellitus and pregnant women (Department of Health, 2009g; Hine, 2010). The findings from Pedbody et al. (2010) showed that pandemic A/H1N1 patients with chronic neurological disease, chronic respiratory disease, chronic liver disease and immunosuppression were the most vulnerable group for fatal outcome. This may explain the high case fatality rate in the older age groups among whom the prevalence of underlying risk conditions is likely to be high. In addition, pregnancy has been revealed to be a risk factor for death. Similar findings on risk factors for severe disease or deaths were published in reports from other countries (Louie et al., 2009; Santa-Olalla Peralta, Cortes García, Vicente-Herrero, et al., 2010).

Although, characteristics of the pandemic A/H1N1 virus that decide the size, speed and seriousness of a pandemic (like spectrum of disease, reproduction rate, immunity, case fatality rate, age distribution, etc.) were still missing when the virus emerged (European Centre for Disease Prevention and Control, 2009g), it became clear at an early stage that it

met the criteria for a pandemic strain[1] (Amato-Gauci et al., 2010) and countries started to take response measures.

1.1 E-com@eu project

Effective measures to counter the impact of such major epidemic outbreaks include large-scale vaccination and distribution of antiviral therapy. Although scientific knowledge and technical ability to take effective response measures exist, there is still a lack in the governments' and health authorities' ability to communicate the need for such large-scale measures in a reliable way in order to increase the acceptance of these measures among the general public and at-risk groups. To bridge this gap, the project "Effective Communication in Outbreak Management: Development of an evidence-based tool for Europe (E-com@eu)" has been launched in March 2012. It brings together state-of-the-art knowledge in epidemiology, media analysis, social marketing, risk perception, and discrete choice experiments in order to develop an evidence-based behavioral and communication package that can be applied by health professionals and health agencies throughout Europe in case of major epidemic outbreaks (E-com@eu Study Group, 2011).

The different characteristics of the 2009 A/H1N1 pandemic influenza influenced people's perception on the risk of contracting the virus and the fear of the virus. In addition, the enormous amounts of varying media messages and official recommendations along with conflicting media messages of vaccine safety influenced people's perceptions, beliefs and finally people's behavior during the pandemic (Feufel, Antes, & Gigerenzer, 2010). In order to increase the acceptance of large-scale response measures among the general public and at-risk groups, communication messages have to take into account these factors that influence human behavior. Therefore, a sub-project of the E-com@eu project aims to assess the influence of the changing A/H1N1 epidemiology, the changing pattern of risk communication, and the changing official recommendations on human protective behavior during the 2009 A/H1N1 pandemic. The dynamics and interactions of these factors will be explored in a time series analysis. For this analysis, epidemic curves of the 2009 A/H1N1 pandemic in selected EU countries will be drawn. These epidemic curves provide information on the pattern of disease spread and will serve as a timeline along which data

[1] These criteria are: a new influenza A virus subtype genetically different from circulating human influenza A viruses, able to cause disease in humans and able to spread easily from one person to another (World Health Organization, 2005)

on official (national and international) public health and health behavior recommendations, information on the media content, and data on public behavior during the pandemic will be plotted. The interactions of these factors will be discussed in context. The results of this analysis will give valuable insight into the time dependent influence of the above factors and what should be taken into account when formulating uncertain risk communication messages (E-com@eu Study Group, 2011).

1.2 Purpose of this Thesis

This Thesis contributes to the E-com@eu sub-project by exploring the dynamics of the 2009 A/H1N1 pandemic in the UK, Germany and Spain. Initially, the UK and Spain were countries most affected by the pandemic in Europe but as the pandemic started to spread across Europe, Germany also reported significant numbers of cases (Nicoll & Coulombier, 2009). This Thesis presents the progress of the pandemic in the three countries and gives a systematically documented chronological overview of public health measures taken and official recommendations released during the pandemic in order to reduce the impact of the pandemic. A time series analyses explores the interaction of what actually happened (epidemic curves), how the countries responded (public health measures) and what the people were recommended (official recommendations). As described above, epidemic curves of the 2009 A/H1N1 pandemic in the UK, Germany and Spain are used as a timeline along which data on the official national and international health behavior recommendations released and public health measures taken during the pandemic are plotted. The results give valuable insight into the influence of the above aspects and are used to identify the lessons to be learned and the improvements to be made for a future pandemic. Further, the results will be included in the analysis of the E-com@EU sub-project.

2 Methods

2.1 Systematic literature search

To obtain pandemic A/H1N1 surveillance data for the UK, Germany and Spain a systematic literature search was accomplished using Medline and Google Scholar. Medline was the main source. The search terms used in Medline were: H1N1, epidemiology, population surveillance, incidence, prevalence and Europe. Two searches were conducted. The first search used the following combination: H1N1 AND (epidemiology OR population surveillance) AND Europe. The second search had the search query: H1N1 AND (prevalence OR incidence) AND Europe. The limits used were: articles published in the last three years, articles in English and German. To retrieve recent papers that are included in Medline but are not yet indexed and therefore have no assigned MeSH terms, a text words search for H1N1 was employed. Table 1 shows the search strategy in Medline.

Table 1: Search strategy in Medline

Search Term	**Combination OR**	**Combination AND**	
		Search 1	**Search 2**
H1N1 [TW][1]		**X**	**X**
Epidemiology [MeSH][2]	**X**	**X**	
Population surveillance [MeSH]			
Prevalence [MeSH]	**X**		**X**
Incidence [MeSH]			
Europe [MeSH]		**X**	**X**

[1] [tw]: Search in title, abstract, other abstract, MeSH terms, MeSH Subheadings, Publication Types, Substance Names, Personal Name as Subject, Corporate Author, Secondary Source, and Other Terms.
[2] [MeSh]: Medical Subject Heading

In Google Scholar a brief search was conducted; therefore the “allintitle”-operator was employed for each search. Except for Europe, the same search terms as for the Medline search were used. Two search terms were combined per search using the Boolean function “AND”. Same as in Medline, only articles published in the last three years were considered. Table 2 illustrates the search strategy in Google Scholar.

Table 2: Search strategy in Google Scholar

Search Term	Combination AND			
	Search 1	**Search 2**	**Search 3**	**Search 4**
H1N1	**X**	**X**	**X**	**X**
Epidemiology	**X**			
Population surveillance		**X**		
Prevalence			**X**	
Incidence				**X**

Note: For each search the „allintitle:"- operator was used. It only returns results that include your search term in the document's title.

For literature extraction the following inclusion and exclusion criteria were developed.

Inclusion criteria:

- Articles with relation to the 2009 A/H1N1 pandemic.
- Articles on epidemiological characteristics of the 2009 A/H1N1 pandemic.
- Articles with relation to the general population.
- Articles that deal with the UK, Germany and Spain.

Exclusion criteria:

- Articles that did not deal with the 2009 A/H1N1 pandemic.
- Articles that did not report epidemiological characteristics of the pandemic.
- Articles on vaccination or antiviral drugs.
- Articles on microbiological characteristics of the pandemic A/H1N1 virus.
- Articles with relation to specific risk groups only (e.g. young children, pregnant women)
- Articles in other languages (other than English or German).

Altogether, the conducted search in Medline and Google Scholar resulted in 282 articles. First a selection was made based on title whereby 207 articles were excluded. A second selection was made based on abstract. After the abstract screening another 31 articles were excluded. Finally, 44 articles on pandemic A/H1N1 surveillance data were found. Figure 2 shows this selection process.

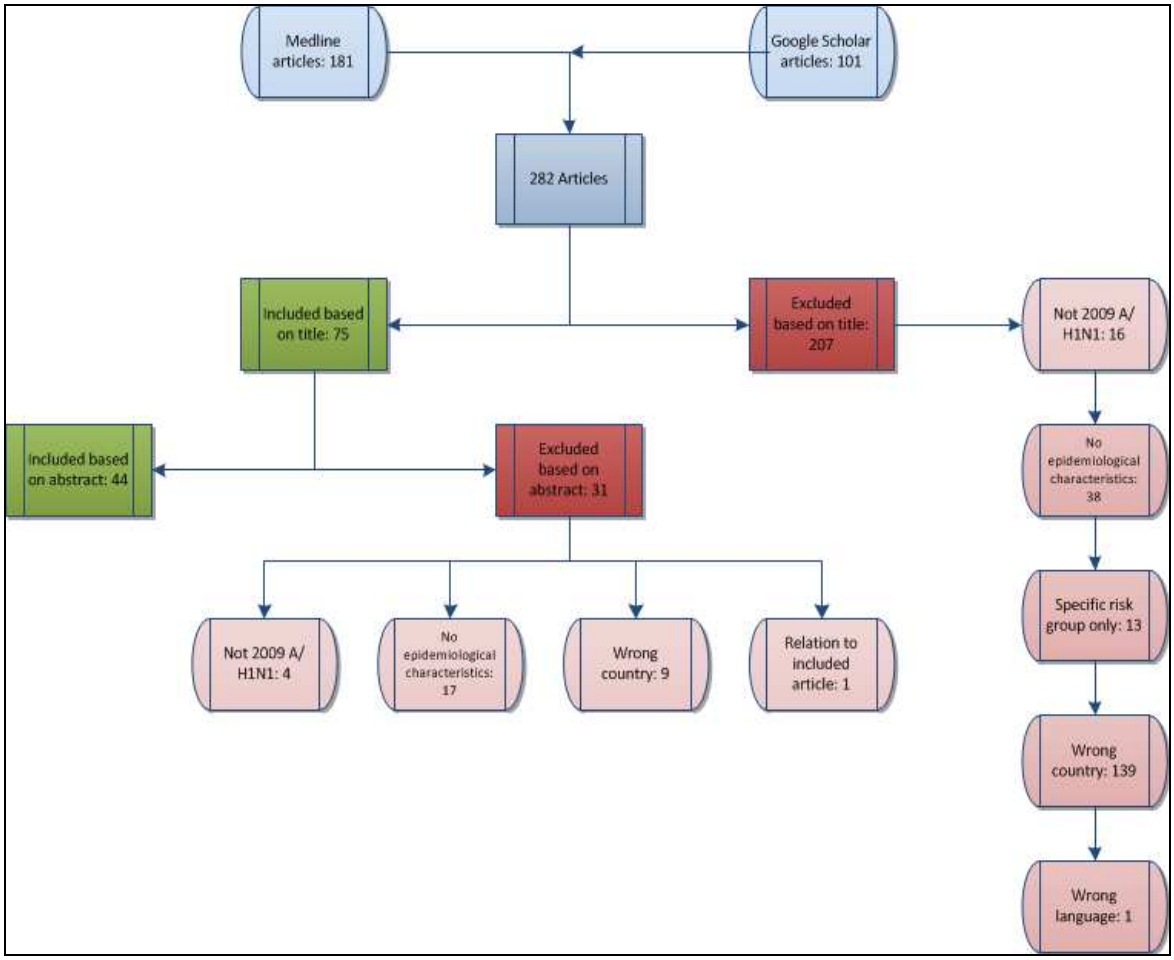

Figure 2: Selection process

In addition to the systematic literature search grey literature and websites of national health authorities (Robert Koch-Institut, Health Protection Agency, Spanish Ministry of Health and Social Policy) and international health agencies (European Centre for Disease Prevention and Control, World Health Organization) were searched to retrieve pandemic A/H1N1 surveillance data.

2.2 Literature search on official recommendations

A literature search on public health measures taken and official health behavior recommendations released during the 2009 A/H1N1 pandemic was conducted. The focus was on the UK, Germany and Spain. Thus, public health measures taken and official recommendations released by the national health authorities of the UK, Germany and Spain were searched using grey literature and websites of the authorities. These are the Health Protection Agency in the UK, the Robert Koch Institute in Germany, the

Department of Health in the UK, the Federal Ministry of Health in Germany and the Ministry of Health and Social Policy in Spain. Additionally, recommendations released by the European Centre for Disease Prevention and Control (ECDC), the World Health Organization (WHO) and the European Medicines Agency (EMA) were considered.

2.3 Epidemic curves and time series analysis

The findings from the articles, together with the finding from the additional search on official websites of national health authorities were used to draw epidemic curves for the UK, Germany and Spain. The public health measures taken and official recommendations released during the 2009 A/H1N1 pandemic are illustrated in a time series analysis, using the epidemic curves as a timeline along which key data of the events and recommendations are plotted. As already done in a similar analysis of the response measures in the Netherlands (Stein, van Vliet, & Timen, 2011), the pandemic has been split up into five phases. This split up was done to provide an in-depth description of the public health measures taken and official recommendations released during the 2009 A/H1N1 pandemic in chronological order. Each phase represents different stages in the progress of the pandemic and different response strategies. Again, each phase serves as a timeline along which data on all public health measures taken and official (national and international) health behavior recommendations released during the different phases are plotted. To structure the information of each phase, the events were allocated to the following themes: situation, surveillance, control strategy and treatment of cases, vaccination strategy and communication.

3 Results

3.1 Epidemic curves and key events

The UK, Germany and Spain had different pandemic profiles during the 2009 A/H1N1 pandemic. To show the progress of the pandemic in the respective countries epidemic curves were drawn for each country separately. In addition, to give an overview on the public health measures taken against the 2009 A/H1N1 pandemic in each country the key events that happened during the pandemic in the UK, Germany and Spain are presented together with the relative epidemic curves.

3.1.1 UK

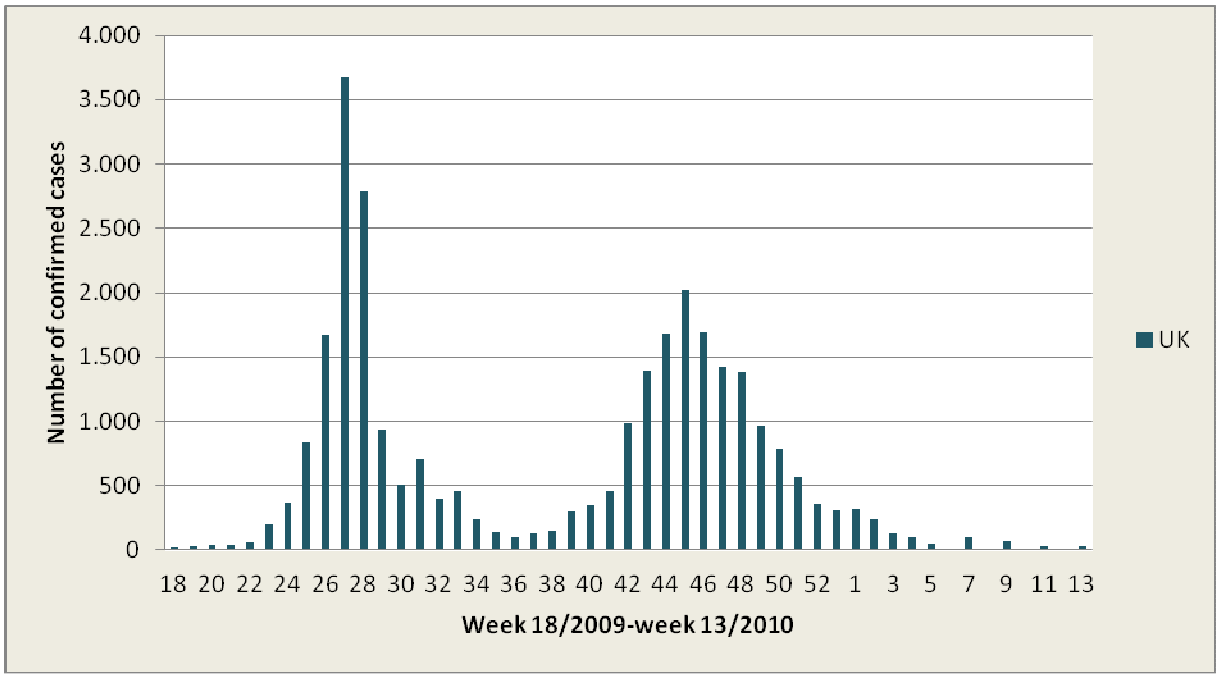

Figure 3: Weekly number of confirmed pandemic A/H1N1 cases in the UK, 2009/2010 season (Health Protection Agency, 2010a)

Influenza surveillance in the UK

For monitoring and assessing the situation, the UK used the following existing influenza surveillance systems:

For clinical surveillance through primary care the QSurveillance and Royal College of General Practitioner (RCGP) networks of sentinel General Practitioners (GP), as well as the telephone helpline NHS direct in England and Wales, and NHS 24 in Scotland were

used. These systems provided estimates of influenza incidence to detect an increase in influenza infections as early as possible (Hine, 2010).

The WHO National Influenza Reference Centre for the United Kingdom is the Respiratory Virus Unit (RVU) of the Virus Reference Department at the Health Protection Agency. It collated virological data from its reference laboratories, from a nationwide laboratory reporting system and from general practitioners (Health Protection Agency, 2012).

Progress of the A/H1N1 pandemic in the UK

Figure 3 shows weekly numbers of confirmed pandemic A/H1N1 cases and illustrates that the UK experienced two waves of pandemic A/H1N1 activity. The first confirmed case of pandemic A/H1N1 in the UK was reported on 27.04.2009 (European Centre for Disease Prevention and Control, 2009f). Initially, the UK observed sporadic importations of the pandemic A/H1N1 virus from Mexico and the US. As sustained community transmission developed in June, the number of pandemic A/H1N1 cases increased sharply until the peak of the first wave in week 27/2009. The West Midlands, London and central Scotland were most affected at the beginning of the A/H1N1 outbreak in the UK. By the end of June almost 7000 confirmed cases were reported (Health Protection Agency, 2010b). Transmission subsided as the summer progressed. The closure of schools was supposed to be responsible for this decline of infections as transmission accelerated again in late September with the return to school. The second wave peaked in week 45/2009. Thereafter the numbers of infections declined constantly until the end of the second wave in early January 2010. Throughout the pandemic, the highest infection rates were observed in children and young people. Generally, the virus caused a mild illness. More severe disease was especially experienced by those cases with underlying conditions (Department of Health, 2010a). By mid-April, the total UK number of pandemic A/H1N1 influenza related deaths was 474. Of these, 83% were in younger age groups (0-64 years) and 18% had no underlying condition (Department of Health, 2010d).

During the first wave of transmission the UK employed a containment strategy until 2 July 2009. The aim of this strategy was to delay the spread of infection and thereby get more time to develop specific countermeasures, like pandemic vaccine. Those who met the clinical and epidemiological case definition were assessed through swabbing and laboratory testing. Cases were requested to isolate at home or in hospital (depending on their clinical condition) for at least seven days. Close contacts were traced and offered antiviral prophylaxis. Additionally, information on the virus was gathered to get a better

understanding of the disease course. During this initial containment phase specimens were taken from all suspected cases for laboratory testing (Health Protection Agency, 2010c). From 2 July onwards cases were diagnosed on the basis of clinical symptoms and laboratory confirmation was not required for every patient anymore (Health Protection Agency, 2010b).

Given this information, the numbers of confirmed cases from week 27/2009 onwards shown in Figure 3 do not reflect the actual number of cases in the UK and the sharp decline in cases after week 27/2009 is, besides the school closure for summer holidays, probably due to this different testing strategy.

To still monitor the magnitude of the pandemic in the population, the Health Protection Agency (HPA) in England started to calculate estimates of the number of new clinical A/H1N1 cases in England from week 30 onwards. The estimates were generated each week using a statistical model. The data were obtained from two surveillance systems: the primary care based QSurveillance scheme and the Royal College of General Practitioners (RCGP) and HPA Regional Microbiology Network sentinel surveillance scheme. In late July data from the National Pandemic Flu Service (NPFS) were added (Health Protection Agency, 2009c). To calculate the estimates GP (General Practitioner) and NPFS age-specific consultations rates, age specific positivity rates and estimated proportions of people who contacted their GP or the NPFS were used. To take the uncertainty of proportions consulting health care into account, a range of estimates was calculated surrounding the central estimate (Health Protection Agency, 2010b). Figure 4 shows the weekly number of confirmed A/H1N1 cases and the weekly estimates in England. The figure illustrates the aforementioned under-reporting of pandemic A/H1N1 cases from 2 July onwards, as the actual number of cases was estimated to be up to a hundred times higher than the number of confirmed cases in England. However, the pandemic profile as described above is still visible in both curves.

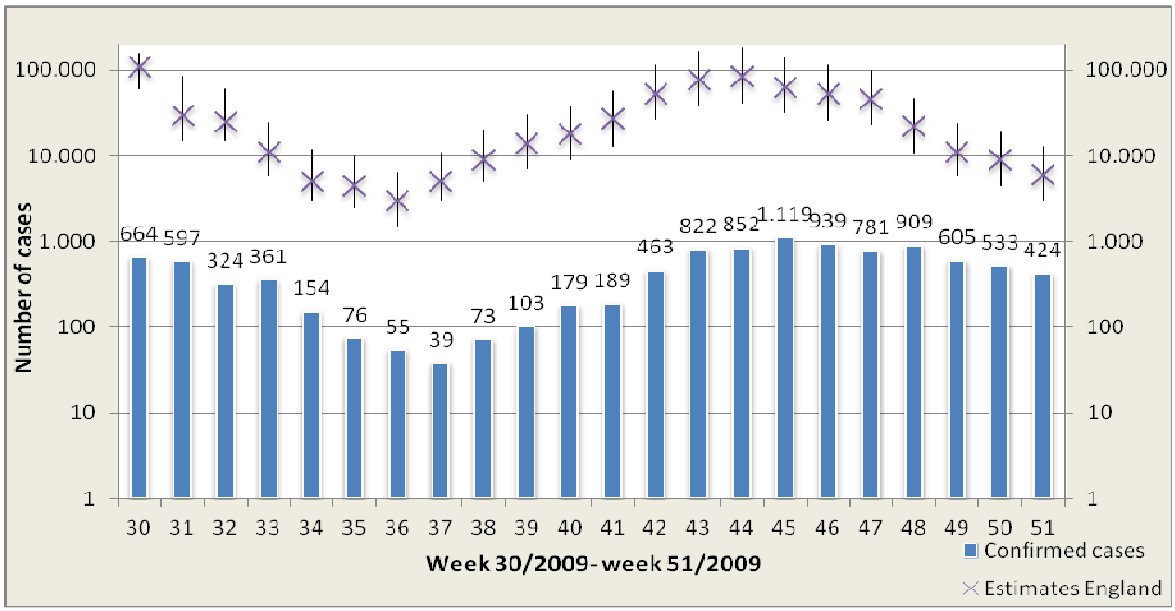

Figure 4: Weekly number of confirmed pandemic A/H1N1 cases and weekly estimates of new pandemic A/ H1N1 cases in England, 2009/2010 season (Health Protection Agency, 2010a)

Key events during the 2009 A/H1N1 pandemic in the UK

To fight the pandemic, the UK employed several public health measures and strategies. The following table gives an overview of the key events that happened during the pandemic in the UK in chronological order.

Table 3: Chronology of key events during the 2009 A/H1N1 pandemic in the UK

Month	Day	Event
April 2009	4	Outbreak of influenza-like illness started in Veracruz, Mexico (European Centre for Disease Prevention and Control, 2010)
	15	Novel Influenza A/H1N1 identified and isolated in USA (Centers for Disease Control and Prevention, 2009)
	24	WHO confirmed that the outbreak in Mexico was caused by a novel influenza virus (World Health Organization, 2009b)
	25	WHO declared the outbreak of influenza A/H1N1 in Mexico and the US as a Public Health Emergency of International Concern (PHEIC) under IHR (2005) (World Health Organization, 2009c)
	27	WHO declared influenza pandemic alert phase 4 (World Health Organization, 2009d)

		First two laboratory confirmed cases of A/H1N1 in the UK (European Centre for Disease Prevention and Control, 2009f)
		Containment strategy (Health Protection Agency, 2009d) Initially, meeting all direct flights from Mexico. Borders were not closed, no restrictions on international or domestic travel and public mass gatherings (Hine, 2010)
	29	WHO declared influenza pandemic alert phase 5 (World Health Organization, 2009e)
		Gordon Brown announced: stockpile of antivirals was to be increased from 33.5 million to 50 million doses (Hine, 2010)
		First confirmed case in England; first UK school closure (Hine, 2010)
	30	The European Union agreed on a common case definition for the new pandemic virus (European Commission, 2009a)
		Information campaign started on TV, radio and in print media. Swine Flu Information Line was set up (Hine, 2010)
May 2009	1	First case of secondary transmission in the UK and Germany (European Centre for Disease Prevention and Control, 2009i)
	2	HPA put in place regional Flu Response Centers (Health Protection Agency, 2010c)
	3	5 cases of in country transmissions in Germany, Spain and UK (European Centre for Disease Prevention and Control, 2009j)
	6	Ministers agreed that containment phase should continue (Hine, 2010)
	11	Ministers decided to procure enough pre-pandemic vaccine for 45% of the population without waiting for Phase 6 (Hine, 2010)
	15	British Foreign& Commonwealth Office stopped to advice against all but essential travel to Mexico. Agreements for up to 90 million doses of pre-pandemic vaccines were signed (Hine, 2010)
	20	HPA recommended mass prophylaxis at schools were any pupils were affected should cease (Department of Health. Scientific Advisory Group for Emergencies (SAGE), 2009a)
	21	Ministers decided not to change the prophylaxis policy at schools as recommended by HPA (Hine, 2010)

	22	HPA stopped meeting flights from Mexico (Health Protection Agency, 2009a)
June 2009	1	Scottish Flu Response Center was established to relieve the pressure on NHS 24 (Hine, 2010)
	10	Ministers agreed on policy for "hot spots" (Health Protection Agency, 2010c; Hine, 2010)
	11	WHO raised the level of influenza pandemic alert from phase 5 to phase 6 (World Health Organization, 2009h) WHO considered severity of pandemic to be moderate (World Health Organization, 2009i)
	13	Total number of cases reached 1000 (Hine, 2010)
	15	First death reported in Europe; in the UK (European Centre for Disease Prevention and Control, 2009s)
	17	Ministers agreed to procure vaccine for 100% of the population (Hine, 2010) DH`s Joint Committee on Vaccination and Immunization (JCVI) first meeting: priority groups for vaccination were discussed (Final advice on 8 October) (Department of Health. Joint Committee on Vaccination and Immunisation, 2009a)
	26	Contracts were signed with GlaxoSmithKline and Baxter Healthcare: 132 million doses of H1N1 vaccine (2 doses for the whole UK population) (Hine, 2010)
July 2009	2	Mitigation strategy started (Health Protection Agency, 2009d)
	6	MHRA developed a web-based reporting system for use by public and healthcare professionals wanting to report adverse reactions to antivirals and when available to vaccines (Medicines and Healthcare products Regulatory Agency, 2009a)
	13	Besides a few small changes, SAGE endorsed the JCVI`S advice concerning the priority groups for vaccination (Department of Health. Scientific Advisory Group for Emergencies (SAGE), 2009b)
	16	Ministers agreed that the priority groups identified by SAGE would be vaccinated (Hine, 2010) Publication of planning assumptions calculated by SAGE. Key figures: nearly 19 million cases, 2,8 million people with complications, 370.000 people hospitalized, up to 65.000 deaths (Department of Health, 2009e)

	23	National Pandemic Flu Service went live in England (Department of Health, 2009f)
	29	Ministers bought 30 million doses of additional Pandemrix vaccine to make up any possible shortfall (Hine, 2010)
August 2009	7	JCVI discussed the vaccine strategy and priority groups once more (Department of Health. Joint Committee on Vaccination and Immunisation, 2009b)
	13	UK published priority groups for the vaccination program (Department of Health, 2009g)
September 2009	3	Planning assumptions revised: reduction in hospitalization rate from 2% to 1%, reduction of upper case fatality rate from 0,35% to 0,1% (Department of Health, 2009i)
	29	Authorization of first two pandemic vaccines (Focetria & Pandemrix) by European Commission (European Commission, 2009b)
October 2009	1	Web based reporting system across England introduced to collect information on all laboratory confirmed cases admitted to NHS trusts (Health Protection Agency, 2010b)
	6	Authorization of third pandemic vaccine by EC (European Commission, 2009c)
	8	JCVI reconfirmed the priority groups for vaccination and advised on dosage of vaccine (Department of Health. Joint Committee on Vaccination and Immunisation, 2009c)
	12	SAGE discussed and agreed the JCVI recommendations (Department of Health. Scientific Advisory Group for Emergencies (SAGE), 2009c)
	14	Four health ministers agreed that vaccination program should start at the same time throughout the UK (Hine, 2010)
	21	UK begins vaccination: front-line healthcare workers and patients who fall into at-risk categories (Department of Health, 2009k)
	22	Planning assumptions revised: Reasonable worst case for the clinical attack rate was reduced from 30% to 12%. Reasonable worst case for further deaths was reduced from 19.000 to 1.000 (Department of Health, 2009m)
November 2009	5	Medicines and Healthcare products Regulatory Agency published suspected adverse reaction analysis on pandemic vaccines (Medicines and Healthcare products Regulatory Agency, 2009b)

	19	Phase two of vaccination program announced: children over 6 months and under 5 years (Department of Health, 2009u)
	30	SAGE heard from its modelers that the pandemic had now effectively peaked (Department of Health. Scientific Advisory Group for Emergencies (SAGE), 2009d)
December 2009	23	Department of Health wrote to Baxter Healthcare to stop supply of Celvapan® from 28 February (Hine, 2010)
January 2010	8	JCVI statement: vaccination of further groups of people is not recommended (Department of Health. Joint Committee on Vaccination and Immunisation, 2010)
	11	SAGE met for the last time (Department of Health. Scientific Advisory Group for Emergencies (SAGE), 2010)
	14	Agreement to start negotiating with GlaxoSmithKline (GSK) over ceasing the contract and suspending Pandemrix deliveries from 16 January (Hine, 2010)
February 2010	4	Agreement that vaccination program was not extended to other healthy age groups. Strategic reserve of 15 million doses was set up (Hine, 2010)
	11	National Pandemic Flu Service was closed down (Hine, 2010)
March 2010	12	Reported deaths across the UK: 440 (Pebody et al., 2010)
	18	H1N1 (2009) swine flu vaccine provided for protection of travelers to Southern Hemisphere countries (Department of Health, 2010c)
April 2010	1	Antivirals were no longer available from national stockpiles; Swine Flu Information Line was closed down; Treatment of cases returned to business as usual (Hine, 2010)
	6	Agreement with GSK to only take deliveries of just under 35 million doses of Pandemrix® (The Secretary of State for Health, 2010)
	15	Total number of deaths: 474 (Department of Health, 2010d)
August 2010	10	WHO Director-General: World is no longer in a pandemic (World Health Organization, 2010c)

3.1.2 Germany

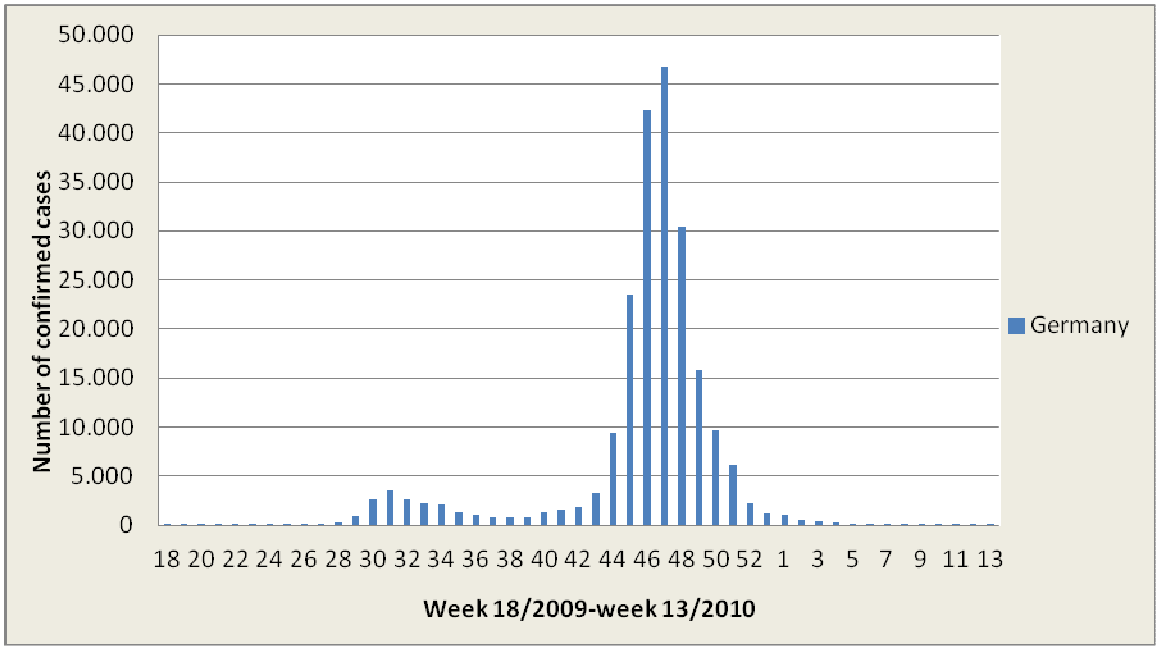

Figure 5: Weekly number of confirmed pandemic A/H1N1 cases in Germany, 2009/2010 season (Robert Koch-Institut. Arbeitsgemeinschaft Influenza, 2010)

Influenza surveillance in Germany

Figure 5 shows influenza notification data collected by the local health authorities according to the German Protection Against Infection Act (Infektionsschutzgesetz; IfSG). Influenza is a notifiable disease in Germany. According to § 7 IfSG laboratories have to report direct evidence of influenza to local health authorities and the local health authorities forward the notifications to the Robert Koch-Institut (RKI). As national reference laboratory for influenza (NRZ), the RKI performed the virological surveillance together with cooperating laboratories of four national states. To receive information on pandemic A/H1N1 infections at an early stage, a new notification regulation for physicians under § 6 IfSG came into force on 03.05.2009 saying that all suspected cases, confirmed cases and deaths from pandemic A/H1N1virus have to be reported by name to the local health authorities. In November 2009 this new regulation was revised and only deaths relating to a pandemic A/H1N1 infection had to be reported until May 2010. § 7 IfSG remained unaffected by the new regulation under § 6 IfSG, thus laboratory confirmed cases had to be reported throughout the pandemic (Buda et al., 2010).

Progress of the A/H1N1 pandemic in Germany

The first laboratory confirmed cases in Germany were reported on 29.04.2009 (Robert Koch-Institut, 2009h). Initially, pandemic A/H1N1 infections occurred among travelers returning from North America. Until week 28/2009 limited spread of the diseases was observed in Germany. With the beginning of the summer holidays the number of travelers returning from affected countries, like Spain, increased. Thus numbers of confirmed cases began to rise until early August. Same as in the UK, transmission subsided as the summer progressed. As of early October, a continuous increase in case numbers due to in-country transmission of the A/H1N1 virus was observed. This autumn wave peaked in week 47/2009 and thereafter influenza A/H1N1 activity decreased steadily. The pandemic influenza wave ended in week 2/2010 but afterwards confirmed cases have still been reported. The last virus detection within the sentinel system by the influenza working group (Arbeitsgemeinschaft Influenza) for the occurrence of acute respiratory diseases in primary health care practices, in which 879 primary care physicians across Germany participated in the season 2009/2010, was in week 12/2010. By April 2010, 225.729 cases and 250 deaths of pandemic A/H1N1 virus have been reported to the Robert Koch-Institut according to IfSG (Buda et al., 2010).

The infection caused a mild illness in most cases. Infection rates were highest in children and young adults. A subset of cases experienced severe disease, especially in those with underlying risk factors. 86% of the 250 deaths attributable to pandemic A/H1N1 virus had an underlying risk factor (chronic condition or pregnancy) (Schaberg & Burger, 2010).

Key events during the 2009 A/H1N1 pandemic in Germany

The key events as well as the pandemic mitigation measures employed to contain the 2009 A/H1N1 pandemic are listed in a sequential manner in the following table.

Table 4: Chronology of key events during the 2009 A/H1N1 pandemic in Germany

Month	Day	Event
March 2009		RKI and BZgA: Information campaign “Wir gegen Viren” was developed and launched (Martin, 2010)
April 2009	4	Outbreak of influenza-like illness started in Veracruz, Mexico (European Centre for Disease Prevention and Control, 2010)
	15	Novel Influenza A/H1N1 identified and isolated in USA (Centers

		for Disease Control and Prevention, 2009)
	24	WHO confirmed that the outbreak in Mexico was caused by a novel influenza virus (World Health Organization, 2009b)
		RKI: Teleconference with infectious disease experts of the 16 German states to assess the current situation and discuss relevant infection control measures (Robert Koch-Institut, 2010a)
	25	WHO declared the outbreak of influenza A/H1N1 in Mexico and the US as a Public Health Emergency of International Concern (PHEIC) under IHR (2005) (World Health Organization, 2009c)
		RKI: First situation report (Daily report, published until 4.12.2009) (Robert Koch-Institut, 2009b)
	26	RKI distributed information on surveillance and control to local health authorities. The strategy was to contain the spread of the virus (Robert Koch-Institut, 2010a)
	27	Local health authorities started infection control measures at air-ports and distributed information leaflets for travelers (Robert Koch-Institut, 2010a)
		RKI set up an information hotline for the general public (Robert Koch-Institut, 2010a)
		WHO declared influenza pandemic alert phase 4 (World Health Organization, 2009d)
		First laboratory confirmed case of A/H1N1 announced in Europe. One in Spain and two in the UK (European Centre for Disease Prevention and Control, 2009f)
	29	WHO declared influenza pandemic alert phase 5 (World Health Organization, 2009e)
		RKI reported first confirmed cases in Germany (Robert Koch-Institut, 2009h)
	30	The European Union agreed on a common case definition for the new pandemic virus (European Commission, 2009a)
May 2009	1	First case of secondary transmission in the UK and Germany (European Centre for Disease Prevention and Control, 2009i)
		Free information hotline for the general public set up by Ministry of Health (Robert Koch-Institut, 2010a)
	3	5 cases of in country transmissions in Germany, Spain and UK

		(European Centre for Disease Prevention and Control, 2009j)
		From week 18 onwards notification regulation for all suspected cases and deaths (Bundesministerium der Justiz, 2009)
June 2009	11	WHO raised the level of influenza pandemic alert from phase 5 to phase 6 (World Health Organization, 2009h) WHO considered severity of pandemic to be moderate (World Health Organization, 2009i)
July 2009	13	Notification regulation of suspected cases revised. From week 29 onwards suspected cases did not have to be reported to state health authorities or RKI anymore; only to regional health authorities (Robert Koch-Institut, 2010a)
	15	Information campaign started (Die Beauftragte der Bundesregierung für Migration, Flüchtlinge und Integration, 2009)
August 2009	Early	Mitigation phase began (Robert Koch-Institut, 2010a)
	17	Statutory health insurances paid costs for laboratory confirmation only for cases with severe disease or cases at risk of developing severe disease (Gilsdorf & Poggensee, 2009)
	24	In week 35 infection control measures at airports were reduced (Robert Koch-Institut, 2010a)
September 2009	25	First fatal case in Germany (Robert Koch-Institut, 2009j)
	29	Authorization of first two pandemic vaccines (Focetria & Pandemrix) by European Commission (European Commission, 2009b)
October 2009	6	Authorization of third pandemic vaccine by EC (European Commission, 2009c)
	12	RKI: STIKO recommendations on priority groups for vaccination were published (Robert Koch-Institut, 2009c)
	14	Central information homepage on H1N1 was launched (Bundesministerium für Gesundheit, 2009b)
	26	Germany began vaccination (Bundesministerium für Gesundheit, 2009b)
November 2009	9	Notification regulation for suspected cases changed from week 46 onwards: Only confirmed cases and deaths had to be reported. (Robert Koch-Institut, 2010a)

	11	Germany: 1st Impfgipfel at the Ministry of Health (Martin, 2010)
	30	Week 49: Pandemic Influenza A/H1N1 Surveillance in hospitals (PIKS) started (Buda et al., 2010)
December 2009	4	RKI stopped publishing daily reports (Robert Koch-Institut, 2009b)
	7	2nd Impfgipfel at the Ministry of Health (Martin, 2010)
April 2010	1	Pandemic Influenza A/H1N1 Surveillance in hospitals (PIKS) was terminated (Buda et al., 2010)
	26	Total number of confirmed cases: 225.729 Total number of deaths: 250 Hospitalizations: 7.882 (Buda et al., 2010)
August 2010	10	WHO Director-General: World is no longer in a pandemic (World Health Organization, 2010c)

3.1.3 Spain

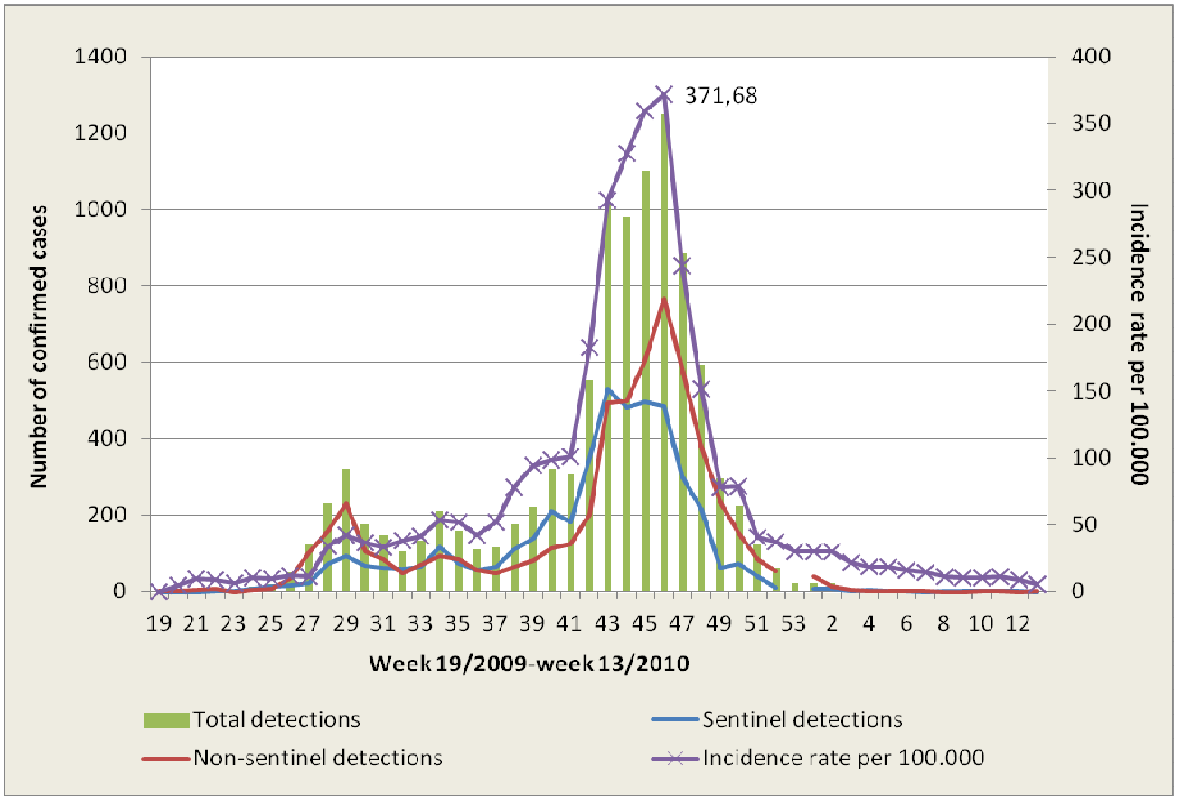

Figure 6: Weekly number of confirmed pandemic A/H1N1 cases (sentinel and non-sentinel) and weekly incidence rate per 100.000 in Spain, 2009/2010 season (Centro Nacional de Epidemiología. Instituto de Salud Carlos III, 2009a, 2010)

Influenza surveillance in Spain

The Spanish influenza surveillance system (SISS) consists of sixteen Spanish regional sentinel networks and regional laboratories, including the National Center of Microbiology at the Instituto de Salud Carlos III (WHO National Influenza Centre). In the 2008/2009 season, the system comprised over 500 general practitioners and 173 pediatricians and covered nearly 2.1% of the population of the 16 autonomous communities (ACs) in Spain. Each regional sentinel network entered data on influenza detections in a web-based application on a weekly basis and the National Centre of Epidemiology at the Instituto de Salud Carlos III in Madrid analyzed the data at central level. Pandemic A/H1N1 virus detections from non-sentinel sources (i.e. hospitals, cooperating laboratories) were also reported to the system (Larrauri et al., 2011). The data reported to the SISS were used to calculate weekly influenza incidence rates. For this calculation, the population in each sentinel network was used as the denominator (Larrauri Cámara et al., 2010). Since 1904,

Influenza is a notifiable disease in Spain but the specificity of this system is lower than the specificity of the SISS (Centro Nacional de Epidemiología. Instituto de Salud Carlos III, 2009b). Therefore, only available data of the SISS have been used to show the progress of the 2009 A/H1N1 pandemic in Spain.

Progress of the A/H1N1 pandemic in Spain

Figure 6 shows the weekly influence incidence rate per 100.000 population, the sentinel and non-sentinel detections, and the total number of A/H1N1 detections from week 19/2009 to week 13/2010 in Spain.

In Spain, the first confirmed case was reported on 27 April 2009. By 11 May, the number of confirmed cases rose to 98 cases. Of these, 76 cases had a history of travel to Mexico (Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009). In late May, the first outbreak without travel history was observed at the Military Academy of Engineering in Hoyo de Manzanares indicating the start of community transmission of the pandemic A/H1N1 virus. In July, numerous outbreaks occurred, especially in summer camps, and the numbers of infections began to increase until week 29/2009 (Sierra Moros et al., 2010). As observed in Germany and the UK, transmission decreased as the summer progressed. In early autumn transmission accelerated again and numbers of detections rose constantly. The autumn wave peaked in week 46/2009 reaching the weekly incidence rate of nearly 372 cases/ 100.000 population. Thereafter the weekly incidence rate decreased steadily and after week 2/2010 only sporadic cases have been detected in the sentinel and non-sentinel system (Larrauri Cámara et al., 2010).

In Spain, the incidence rate was highest in the under 15 years age group. The severity of the pandemic regarding lethality and mortality was characterized as mild with an estimated overall mortality rate of 0.43 deaths per 1000 pandemic cases. The 45- 64 years age group showed the highest mortality rate, with 9.35 deaths per 1.000.000 population (Larrauri Cámara et al., 2010) The total number of deaths related to pandemic A/H1N1 influenza across Spain was 348 (Ministerio de Sanidad, Politica Social e Igualdad, 2010a).

Key events during the 2009 A/H1N1 pandemic in Spain

Table 5 gives an overview of key events with respect to control measures taken by Spain to fight the 2009/H1N1 pandemic.

Table 5: Chronology of key events during the 2009 A/H1N1 pandemic in Spain

Month	Day	Event
April 2009	4	Outbreak of influenza-like illness started in Veracruz, Mexico (European Centre for Disease Prevention and Control, 2010)
	15	Novel Influenza A/H1N1 identified and isolated in USA (Centers for Disease Control and Prevention, 2009)
	24	WHO confirmed that the outbreak in Mexico was caused by a novel influenza virus (World Health Organization, 2009b)
		The Coordinating Centre for Health Alerts and Emergencies (CCAES) at the Spanish Ministry of Health and Social Policy issued a warning to the surveillance network in its daily report (Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009)
		Ministry of Health and Social Policy (MHSP) published information and advice for travelers on its website (Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009)
	25	WHO declared the outbreak of influenza A/H1N1 in Mexico and the US as a Public Health Emergency of International Concern (PHEIC) under IHR (2005) (World Health Organization, 2009c)
		National Influenza Preparedness and Response Plan activated (Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009)
		CCAES distributed a case definition and protocols for infection control and management of cases and contacts (Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009)
		Surveillance and disease control at airports started, meeting all flights from affected areas until 16 June (Dávila Cornejo et al., 2010)
	26	First 3 cases under investigation (Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009)
	27	MHSP recommended to avoid any non-essential travel to Mexico (Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009)
		WHO declared influenza pandemic alert phase 4 (World Health Organization, 2009d)

		First meeting of the Surveillance Subcommittee (Altogether 31 meetings until March 22) (Sierra Moros et al., 2010)
		First laboratory confirmed case of A/H1N1 in Spain (European Centre for Disease Prevention and Control, 2009f)
		Exclusive supply of antivirals to hospitals (Ministerio de Sanidad, Politica Social e Igualdad, 2010b)
	28	The Surveillance Subcommittee agreed on a protocol on case and contact management: Antivirals were offered to all cases and contacts. Isolation of cases and contacts was recommended (Santa-Olalla Peralta, Cortes García, Martínez Sánchez, et al., 2010; Sierra Moros et al., 2010)
		First meeting of the Subcommittee on Vaccines and Antivirals (SVA) (Ministerio de Sanidad, Politica Social e Igualdad, 2010b)
	29	WHO declared influenza pandemic alert phase 5 (World Health Organization, 2009e)
		First case of secondary transmission (Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009)
	30	The European Union agreed on a common case definition for the new pandemic virus (European Commission, 2009a)
May 2009	1	Regional Influenza laboratories started initial testing (Santa-Olalla Peralta, Cortes García, Martínez Sánchez, et al., 2010)
	7	The CSP (Comisión de Salud Pública) approved a new case definition based on the EU case definition (Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009)
	11	First confirmed tertiary case. Number of confirmed cases: 98. 76 had a history of travel to Mexico (Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009)
	13	CSP agreed on purchasing vaccine for 40% of the population. Enough vaccine for 18,3 million people (Ministerio de Sanidad, Politica Social e Igualdad, 2010b)
	20	Case and contact management protocol updated: Antivirals will be given only to cases with severe disease, those with risk factors and contacts with risk factors. Isolation of cases should be maintained. No quarantine of contacts (Santa-Olalla Peralta, Cortes García,

		Martínez Sánchez, et al., 2010)
	22	First outbreak without travel history at the Military Academy of Engineering in Hoyo de Manzanares (Ministerio de Sanidad, Politica Social e Igualdad, 2010a)
June 2009	11	WHO raised the level of influenza pandemic alert from phase 5 to phase 6 (World Health Organization, 2009h) WHO considered severity of pandemic to be moderate (World Health Organization, 2009i)
	26	The CSP approved a surveillance strategy based on 5 points: • surveillance of severe cases, • the influenza surveillance through SISS (Spanish Influenza Surveillance System), • the monitoring of cluster of cases with acute respiratory infection (confirmation of first cases only; case-based notification not required), • monitoring of influenza or acute respiratory disease from the primary care computerized database and • case-based monitoring of flu cases in the community. No need of identification, monitoring or administration of prophylaxis to contacts. (Santa-Olalla Peralta, Cortes García, Martínez Sánchez, et al., 2010)
July 2009	1	First fatal case in Spain (European Centre for Disease Prevention and Control, 2010)
	27	Mitigation phase began (Sierra Moros et al., 2010)
	28	Case-based monitoring of cases in the community was ceased (Ministerio de Sanidad, Politica Social e Igualdad, 2010a)
		SVA agreed on population groups for antiviral treatment: cases requiring hospitalization and those at risk of complications. (approved by CSP on 29. July) (Ministerio de Sanidad, Politica Social e Igualdad, 2010a)
August 2009	7	AEMPS released recommendations on the use of antivirals in children under 1 year old, pregnant and breastfeeding women and people with swallowing problems (Agencia Española de Medicamentos y Productos Sanitarios, 2009a)
	14	Information campaign “Gripe A. La prevención es la major medida” started (Ministerio de Sanidad y Politica Social, 2009a)
	31	Agreement on priority groups for vaccination (Ministerio de Sanidad, Politica Social e Igualdad, 2010b)

September 2009	9	CSP approved surveillance strategy update: Investigation of clusters of cases only in those cases deemed necessary to make a special intervention. (Ministerio de Sanidad, Politica Social e Igualdad, 2010a)
	29	Authorization of first two pandemic vaccines (Focetria & Pandemrix) by European Commission (European Commission, 2009b)
October 2009	6	Authorization of third pandemic vaccine by EC (European Commission, 2009c)
	29	Regular supply of antiviral drugs in pharmacies permitted (Agencia Española de Medicamentos y Productos Sanitarios, 2009b)
November 2009	16	Vaccination campaign started (Ministerio de Sanidad y Politica Social, 2009l)
		Authorization of a new pandemic vaccine Panenza in Spain (Agencia Española de Medicamentos y Productos Sanitarios, 2009c)
	2	AEMPS issued the first report of suspected adverse reactions associated with pandemic vaccines (Ministerio de Sanidad, Politica Social e Igualdad, 2010b)
	21	AEMPS: Official recommendations on vaccination published (Agencia Española de Medicamentos y Productos Sanitarios, 2009d)
December 2009	4	Surveillance Subcommittee eased the monitoring of severe cases (Ministerio de Sanidad, Politica Social e Igualdad, 2010a)
February 2010	1	Case-based monitoring of severe cases was suspended (Ministerio de Sanidad, Politica Social e Igualdad, 2010a)
April 2010	1	Weekly reporting of new hospitalized cases and case-based notification of fatal cases was stopped (Ministerio de Sanidad, Politica Social e Igualdad, 2010a)
		Total number of reported deaths: 348 (Ministerio de Sanidad, Politica Social e Igualdad, 2010a)
	15	End of vaccination campaign (Ministerio de Sanidad, Politica Social e Igualdad, 2010b)
August 2010	10	WHO Director-General: World is no longer in a pandemic (World Health Organization, 2010c)

3.2 In-depth description of events and recommendations

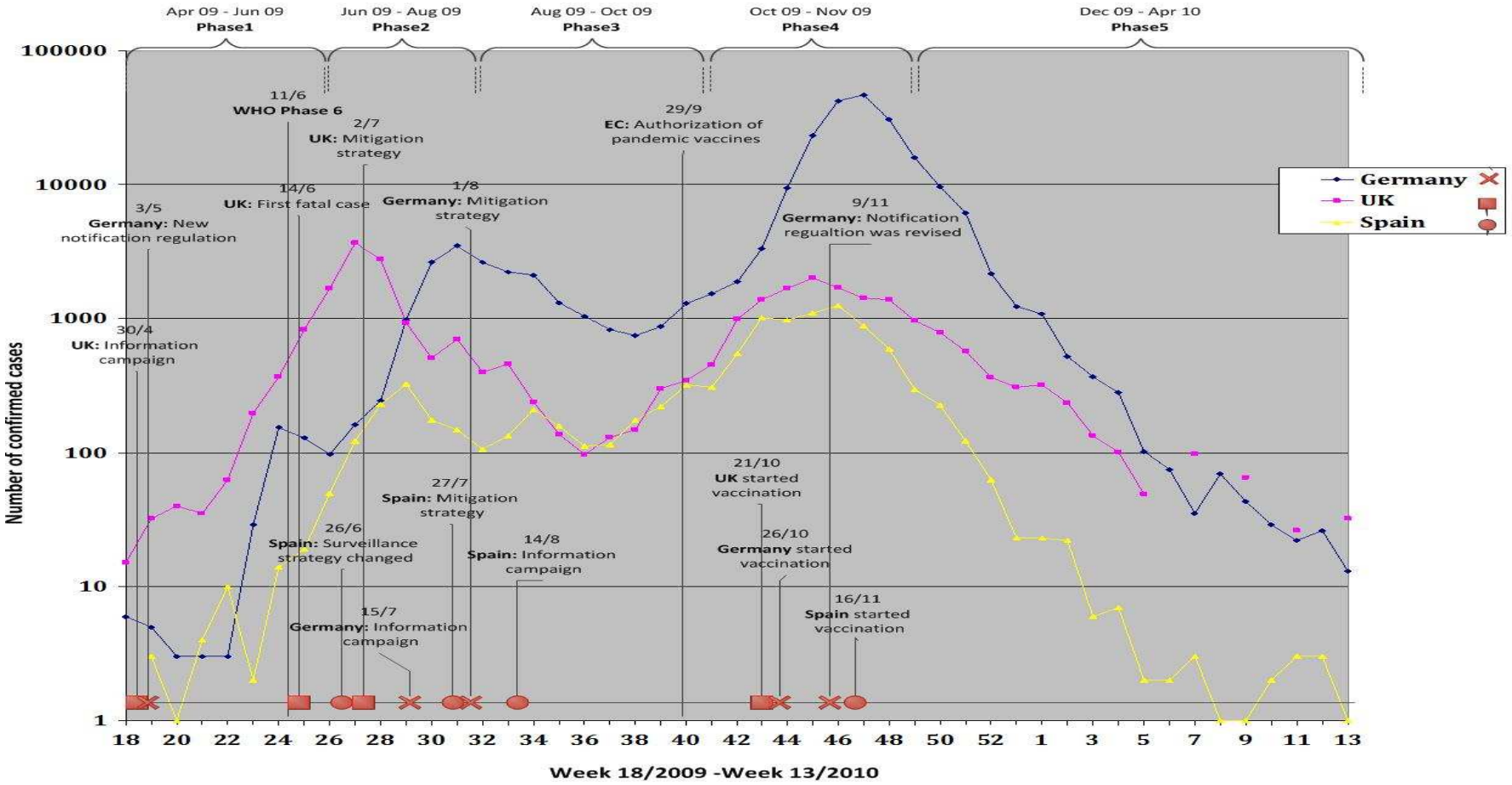

Figure 7: Weekly number of confirmed pandemic A/H1N1 cases[2] from week 18/2009 to week 13/2010 and selected key events of the UK, Germany and Spain split up into five phases

[2] Data sources: UK: A/H1N1 cases reported to the HPA; Germany: A/H1N1 cases reported to the RKI according to the IfSG; Spain: A/H1N1 cases reported to the SISS (see chapter 3.1).

Figure 7 shows the epidemic curves of the UK, Germany and Spain from week 18/2009 to week 13/2010. The curves serve as a timeline along which selected key events during the pandemic are plotted. Figure 7 gives an overview on what happened in each country (epidemic curves) and how the countries responded (selected key events). In order to give an in-depth description of the events, the pandemic has been split up into five phases. Each phase is characterized by a different stage in the pandemic progress and different response activities of the UK, Germany and Spain:

- Phase 1 (01/04/2009 to 21/06/2009). This phase is characterized by the emergence of the pandemic A/H1N1 virus in Mexico and the spread of the virus to the UK, Spain and Germany. It also describes early response strategies to contain the spread of the virus.
- Phase 2 (22/06/2009 to 02/08/2009). Numbers of confirmed cases increased constantly, therefore a change in prevention and control policy from containment to mitigation took place in this phase.
- Phase 3 (03/08/2009 to 04/10/2009). Numbers of confirmed cases decreased during the summer. In this phase countries started to prepare the vaccination program.
- Phase 4 (05/10/2009 to week 30/11/2009). This phase is characterized by the autumn winter wave with a high number of confirmed cases. In this phase the UK, Germany and Spain started their vaccination programs and campaigns.
- Phase 5 (01/12/2009 to 15/04/2010). This is the post peak period. During this phase the numbers of confirmed pandemic cases started to decline constantly.

To structure the information of each phase, the events were allocated to the following themes: situation, surveillance, control strategy and treatment of cases, vaccination strategy and communication.

3.2.1 Phase 1

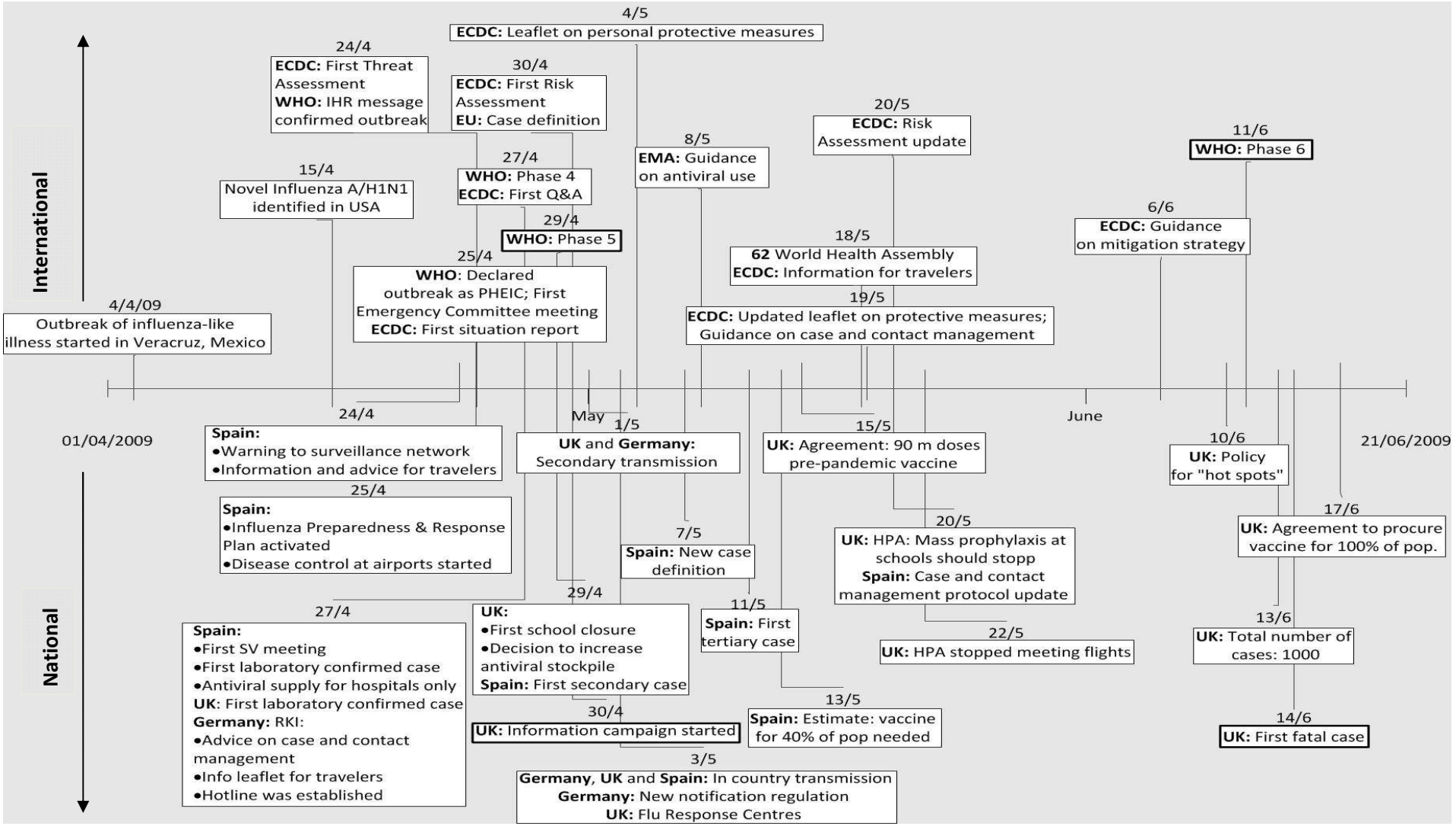

Figure 8: Chronological overview of national and international events for phase 1 (01/04/2009 to 21/06/2009)

3.2.1.1 Situation

The pandemic started in Veracruz, Mexico where an outbreak of influenza-like illness was recorded in early April 2009 (European Centre for Disease Prevention and Control, 2010). A few days later several parts of Mexico reported further outbreaks of influenza-like illness. Analysis of samples detected an Influenza A virus but it was not possible to identify the subtype (World Health Organization, 2011). In mid-April, the US Centers for Disease Control and Prevention (CDC) analyzed a sample from two children with respiratory illness in southern California, USA and identified the virus as a swine influenza A/H1N1 virus (Centers for Disease Control and Prevention, 2009). On 24 April WHO reported that virus isolates from Mexican patients were genetically identical to the new strain of swine influenza A/H1N1 virus discovered in California (World Health Organization, 2009b). On the same day ECDC published its first Threat Assessment saying that although the public health situation was still limited to Mexico and the US further vigilance was required in Europe to ensure the identification of the new virus (European Centre for Disease Prevention and Control, 2009d).

One day later, on 25 April 2009, the first WHO Emergency Committee meeting was held. International experts came together to assess the situation in Mexico and the US and to advice the WHO Director-General, Dr. Margaret Chan, on response measures. The Committee reported more information on the clinical presentation, epidemiology and virology of cases was needed, but concluded that the situation was of international concern. Thus, Dr Margret Chan declared the outbreak in Mexico and the US as a public health emergency of international concern (PHEIC) under International Health Regulations (2005) and advised all countries to intensify surveillance for influenza-like illness and respiratory disease (World Health Organization, 2009c).

On the same day, the ECDC started to publish daily situation reports in which the current epidemiological situation was summarized. So far, 8 cases of pandemic A/H1N1 have been confirmed in the United States of America. In Mexico City 854 cases of pneumonia have been reported, including 59 deaths (European Centre for Disease Prevention and Control, 2009e).

Two days later, on 27 April, the first laboratory confirmed pandemic A/H1N1 cases have been reported in Europe, one in Spain and two in the UK (European Centre for Disease Prevention and Control, 2009f). Based on available data on confirmed pandemic A/H1N1 cases in Mexico, the USA, Canada, and reports on suspected cases in other countries, the

WHO Director-General raised the level of influenza pandemic alert to phase 4 (World Health Organization, 2009d). While phase 3 is characterized by sporadic cases and limited human-to-human transmission of an influenza reassortant virus, phase 4 is defined by confirmed human-to-human transmission of an influenza reassortant virus capable to cause sustained outbreaks in a community (World Health Organization, 2012). The WHO Director-General, Dr Margaret Chan, did not recommend any trade or travel restrictions and advised to center on mitigation measures as the containment of the outbreak was not considered to be feasible (World Health Organization, 2009d).

Two days later, on 29 April, the influenza pandemic alert was raised to phase 5 (World Health Organization, 2009e). This was a signal that a pandemic was coming up and human to human spread of the virus into at least two countries of one WHO region was evident, namely Mexico and USA (European Centre for Disease Prevention and Control, 2009h; World Health Organization, 2012).

In its first risk assessment, published on 30 April, the ECDC reported missing information and data to define the seriousness of the potential pandemic. So far, the majority of pandemic A/H1N1 cases experienced a mild disease and the case fatality rate was judged not to be different than for seasonal influenza (European Centre for Disease Prevention and Control, 2009g).

As of 30 April, 19 confirmed cases have been reported in the EU: Spain (10 cases), UK (5 cases), Germany (3 cases) and Austria (1 case). Unlike all the other cases, one case in Spain had no history of travel to Mexico. This was the first evidence of human-to-human transmission within the EU (European Centre for Disease Prevention and Control, 2009h). Shortly after, secondary transmission of the virus was also notified in the UK and Germany (European Centre for Disease Prevention and Control, 2009i).

As of 12 May, Germany (12 cases), Spain (98 cases) and the UK (65 cases) have reported 175 confirmed pandemic A/H1N1 cases (European Centre for Disease Prevention and Control, 2009l). An analysis of the Spanish cases showed that of the 98 confirmed pandemic A/H1N1 cases, 21 were confirmed secondary cases and one case was a tertiary case (Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009).

At the start of the Sixty-second World Health Assembly on 18 May, members shared their experiences with the current outbreak of pandemic influenza A/H1N1. Altogether, 40 countries have reported 8829 confirmed cases of pandemic A/H1N1. 97, 9% of the total

number of cases was reported by six countries: the USA (4714 cases), Mexico (3103 cases), Canada (496 cases), Japan (125 cases), Spain (103 cases)[3] and the UK (101) (World Health Organization, 2009f).

In its risk assessment update on 20 May, the ECDC again reported a continuing lack of data on parameters needed for right risk assessment. The ECDC considered available data and stated that the pandemic A/H1N1 infections have been generally mild in Europe. Now there was more evidence that the virus was able to spread easily from one person to another and that it preferentially infected younger age groups. ECDC concluded that the spread of the pandemic A/H1N1 virus will continue (European Centre for Disease Prevention and Control, 2009p).

On 11 June, the WHO raised the level of influenza pandemic alert to phase 6, declaring a pandemic (World Health Organization, 2009h). The severity of the pandemic was considered to be moderate by the WHO (World Health Organization, 2009i).

As of 15 June, Germany, Spain and the UK have reported 1980 confirmed pandemic A/H1N1 to the ECDC: UK (1320 cases), Spain (488 cases) and Germany (127 cases). Additionally, the first fatal case in Europe was reported in Scotland (European Centre for Disease Prevention and Control, 2009s).

3.2.1.2 Surveillance:

On 30 April, the European Commission agreed on a common case definition for the European Union in order to detect cases of influenza caused by the new virus. This case definition is presented in Table 6.

[3] Please note that the number of cases shown in Figure 7 differs from this number of cases. Figure 7 only shows data on confirmed cases from the SISS as the Spanish Ministry of Health and Social Policy (MHSP) stopped reporting total numbers of cases on 28 July 2009. Hereafter, the MHSP only reported incidence rates which were calculated from the SISS data (Ministerio de Sanidad y Politica Social, 2009c).

Table 6: EU case definition for pandemic A/H1N1 infection (European Commission, 2009a)

Clinical criteria: Any person with one of the following three: • fever > 38 °C AND signs and symptoms of acute respiratory infection, • pneumonia (severe respiratory illness), • death from an unexplained acute respiratory illness.
Laboratory criteria: At least one of the following tests: • RT-PCR, • viral culture (requiring BSL 3 facilities), • four-fold rise in novel influenza virus A/H1N1 specific neutralising antibodies (implies the need for paired sera, from acute phase illness and then at convalescent stage 10-14 days later minimum).
Epidemiological criteria: At least one of the following three in the seven days before disease onset: • a person who was a close contact to a confirmed case of novel influenza A/H1N1 virus infection while the case was ill, • a person who has travelled to an area where sustained human-to-human transmission of novel influenza A/H1N1 is documented, • a person working in a laboratory where samples of the novel influenza A/H1N1 virus are tested.
Case classification: A. *Case under investigation:* Any person meeting the clinical and epidemiological criteria. B. *Probable case:* Any person meeting the clinical AND epidemiological criteria AND with a laboratory result showing positive influenza A infection of an unsubtypable type. C. *Confirmed case:* Any person meeting the laboratory criteria for confirmation.

Spain:

Based on the situation in Mexico and the US, the Coordinating Centre for Health Alerts and Emergencies (CCAES) at the Spanish Ministry of Health and Social Policy issued a national epidemiologic alert on 24 April. National and regional public health authorities were asked to enhance surveillance and to report urgently any case of influenza-like illness and severe respiratory disease among people who traveled to Mexico or who had contact with a confirmed case of pandemic A/H1N1 infection (Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009).

Following the declaration of a public health emergency of international concern (PHEIC), the Ministry of Health and Social Policy launched the National Plan for Preparedness and

Response to an influenza pandemic, including the activation of the Surveillance Subcommittee, which held its first meeting on 27 April. This committee was responsible for defining and agreeing the strategy of surveillance, although all decisions had to be presented to the Public Health Commission for approval (Sierra Moros et al., 2010).

Spain`s initial case definition was amended and finally adopted on 7 May, 2009, to accommodate to the EU case definition. The modification included the following changes: the temperature defining fever was increased from 37,5º C to 38º C and the incubation period was reduced from 10 to 7 days (Santa-Olalla Peralta, Cortes García, Martínez Sánchez, et al., 2010). To gather epidemiological data of pandemic A/H1N1 infections, a case-based surveillance was implemented which differed from the usual flu surveillance maintained by the Spanish Influenza Surveillance System (Sierra Moros et al., 2010).

Germany:

To receive information on pandemic A/H1N1 infections at an early stage, a new notification regulation for physicians under § 6 IfSG came into force on 03.05.2009 saying that all suspected cases, confirmed cases and deaths from pandemic A/H1N1 virus have to be reported by name to the local health authorities (Bundesministerium der Justiz, 2009).

3.2.1.3 Control strategy and treatment of cases

Initially, the UK, Spain and Germany employed a containment strategy. Measures focused on limiting transmission of the virus or delaying the spread in order to gain time to apply effective response measures. This strategy included the following public health measures: those who met the clinical and epidemiological case definition were assessed through swabbing and laboratory testing; cases were treated with antivirals within 48 hours after onset of symptoms and requested to isolate at home or in hospital (depending on their clinical condition) for at least seven days; close contacts were traced and offered antiviral prophylaxis. In Germany and Spain, contacts were additionally asked to self-isolate at home for seven days, or rather ten days in Spain with restrictions on visits. In the UK, contacts were asked to self-isolate only if they developed symptoms (Health Protection Agency, 2010b; Robert Koch-Institut, 2010a; Santa-Olalla Peralta, Cortes García, Martínez Sánchez, et al., 2010).

To avoid the introduction of the pandemic A/H1N1 virus through international air traffic, the UK and Spain started to meet all direct flights from Mexico at an early stage. Medical teams checked passengers and crew members on clinical symptoms and distributed information leaflets about pandemic influenza. In addition, contact details of passengers

were collected to be able to inform them if it turned out that a person with confirmed pandemic A/H1N1 infection was aboard the same flight (Dávila Cornejo et al., 2010; Hine, 2010). In Germany, health authorities agreed that instead of meeting all flights from Mexico, suspected cases had to be notified by the pilot of the plane and were examined at the airport of destination by medical teams. Same as in the UK and Spain, contact details of passengers were collected and information leaflets about pandemic influenza were distributed (Marcic et al., 2010).

Whereas in Germany and Spain school closures were not recommended as a means of reducing the spread of the virus (Ministerio de Sanidad, Servicios Sociales e Igualdad, 2009; Robert Koch-Institut, 2010a), health protection authorities in the UK advised schools to close for one week in the event of a confirmed pandemic A/H1N1 case at school and antiviral prophylaxis was given to all close contacts. The first school closure in the UK was on 29 April. On the same day, Gordon Brown announced that in order to provide antivirals for 80% of the population, the antiviral stockpile was to be increased from 33, 5 million to 50 million doses (Hine, 2010). To implement the control strategy at regional level in England, the HPA put in place Flu Response Centers staffed by HPA and NHS staff (Health Protection Agency, 2010c).

On May 20, the Surveillance Subcommittee in Spain changed the case and contact management strategy. It was agreed that antivirals will be given only to cases with severe disease, those with risk factors and contacts with risk factors. Whereas the isolation of cases should be maintained, the isolation of contacts was not considered to be necessary anymore (Santa-Olalla Peralta, Cortes García, Martínez Sánchez, et al., 2010).

On the same day, the HPA in the UK proposed to change the actions regarding the contact management at schools. Instead of offering antiviral prophylaxis to all contacts, only the closest contacts should be given antivirals to reduce the risk of viral resistance due to non-compliance with the specified course of treatment (Department of Health. Scientific Advisory Group for Emergencies (SAGE), 2009a). However, the UK maintained its initial containment actions until 22 May, at which point the first adjustment was made. Based on information on reduced prevalence of pandemic A/H1N1 in Mexico, the HPA stopped meeting all flight from Mexico (Health Protection Agency, 2009a). Spain maintained this measure until 16 June. The infection control measures at German airports were kept up until week 35/2009 (Dávila Cornejo et al., 2010; Robert Koch-Institut, 2010a).

As the numbers of cases increased steadily, the containment actions became more and more resource-intensive. Especially in the most affected areas in the UK, such as London and the West Midlands, the measures became unsustainable. Therefore, on 10 June, the initial containment approach in the UK was relaxed for “hot spot” areas. As proposed by the HPA, antiviral prophylaxis was only offered to the closest contacts. Additionally, laboratory testing was not necessary anymore if the clinical diagnosis indicated a high probability that the case was positive (Health Protection Agency, 2010c; Hine, 2010).

3.2.1.4 Vaccination strategy

As the new virus first emerged in April 2009, it was not possible to adjust the 2009/2010 seasonal influenza vaccine to this new influenza A/H1N1 strain (Robert Koch-Institut, 2009c). The production of a pandemic-specific vaccine takes four to six months and can only be started when the new strain has been isolated (Hine, 2010).

At the time the UK, Germany and Spain started to develop their vaccination strategy, the severity and infectivity of the pandemic A/H1N1 virus was still uncertain. Thus, it was difficult to decide on the quantity of required vaccine (Hine, 2010; Marcic et al., 2010). On 13 May, the Public Health Commission in Spain adopted an estimate saying that vaccine for 40% of the population would be needed. On the basis that two doses of vaccine per person were needed to achieve a sufficient immune response, the Public Health Commission planned to procure 36.6 million doses of pandemic vaccine (Ministerio de Sanidad, Politica Social e Igualdad, 2010b). The ministers in the UK decided to procure 90 million doses of pre-pandemic vaccine, enough for 45% of the population to have two doses. Pre-pandemic vaccines contain the virus strain most likely to be similar to the pandemic strain. The ministers in the UK started to negotiate with the vaccine manufactures GlaxoSmithKline and Baxter Healthcare on the supply of the pre-pandemic vaccine. In the end, no pre-pandemic vaccines were purchased, as the negotiations were still ongoing when the influenza pandemic alert phase 6 was declared by the WHO, which triggered the advance-purchase agreements (Hine, 2010). Germany and the UK had advance-purchase agreement contracts with vaccine manufacturers in order to secure sufficient vaccine supply in the event of a pandemic. These contracts were a result of the UK’s and Germany’s pre-pandemic planning and were activated with the announcement of pandemic influenza alert phase 6 (Hine, 2010; Marcic et al., 2010). On 17 June, the ministers in the UK decided to purchase pandemic vaccine for 100% of the population (Hine, 2010). In Germany, the advance-purchase agreements in place included the

assumption that enough vaccine for 100% of the population to have two doses would be needed (Marcic et al., 2010). Later, this assumption was revised downwards and only 50 million doses of pandemic vaccine were ordered (Feufel et al., 2010).

3.2.1.5 Communication

In order to give a better overview, the information published during phase 1 is grouped around the themes: personal protective measures, treatment of cases and control strategy.

Personal protective measures:

In Germany, the Robert Koch-Institut (RKI) and the Federal Centre for Health Education (BZgA) had already launched the information campaign "Wir gegen Viren" in March 2009, before pandemic A/H1N1 infections occurred in Germany. This campaign aimed to convey basic knowledge on hygiene and personal protective measures to the public in order to prevent viral infections. To disseminate the information, the RKI and BZgA developed posters, leaflets, sticker and a TV spot on hand washing (Robert Koch-Institut & Bundeszentrale für gesundheitliche Aufklärung, 2009). During the pandemic, these media were then refined and adjusted to the pandemic A/H1N1 influenza (Martin, 2010).

On 24 April, the Spanish Ministry of Health and Social Policy published information on personal protective measures for the public and for travelers on its website. The information aimed to raise early awareness of the pandemic A/H1N1 virus among the public and informed on personal protective measures, i.e. regular hand washing, respiratory hygiene and avoidance of close contacts with sick people (Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009).

On 27 April, German health authority staff at airports started to distribute information leaflets in four different languages to travelers from affected countries. The leaflets informed on pandemic A/H1N1 symptoms and advised travelers to seek medical care in case of onset of symptoms. On the same day, the RKI set up an information hotline to provide a response to inquiries from citizens (Robert Koch-Institut, 2010a).

On 30 April, the information campaign started in the UK. The campaign ran on TV, on radio and in print media. Additionally, posters and leaflets were used and an information line was set up to provide up-to-date advice to the public. Further, advice and information

was accessible on the government website. Same as in Spain and Germany, following good hygiene practices, i.e. using and disposing tissues and washing hands, was recommended as the best way to protect oneself from contracting the virus. To remember this, the UK campaign used the following slogan: “Catch it, bin it, kill it” (Department of Health, 2009a; Hine, 2010).

In addition to the public information and advice on national level, the ECDC provided information on European level. On 27 April, the ECDC published the first general questions and answers on pandemic A/H1N1 virus (European Centre for Disease Prevention and Control, 2010). In May, the ECDC published two documents on personal protective measures and information for travelers. The documents described personal protective measures to reduce the risk of acquiring influenza, i.e. regular hand washing, respiratory hygiene, avoidance of close contacts and mass gatherings (European Centre for Disease Prevention and Control, 2009k, 2009m, 2009n).

Treatment of cases:

The use of antivirals in some groups involves particularities health professionals should know. Thus, on 8 May, the European Medicines Agency (EMA) published a guidance document on the use of the antiviral medicine Tamiflu in children under one year of age and the antivirals Tamiflu and Relenza in pregnant and breastfeeding women in the case of an influenza A/H1N1 pandemic. The EMA stated that in the event of a pandemic Tamiflu can be used to treat children under the age of one and both antivirals can be used to treat pregnant women, as the benefits of their use outweigh their risks (European Medicines Agency, 2009a).

Control strategy:

On 19 May, the ECDC published a guidance document on case and contact management. The recommended measures did not differ from the measures already applied in Germany, Spain and the UK (European Centre for Disease Prevention and Control, 2009o).

On 6 June, the ECDC published a guidance document on mitigation and containment strategies for national health authorities. ECDC stated that many public health measures are common in both strategies and the implementation of a mitigation strategy would mainly mean to move away from vigorous case finding and contact tracing. Further, the ECDC acknowledged that a containment strategy is very resource-intensive and therefore not a recommended infection control strategy for human influenza beyond pandemic alert phase 4 (European Centre for Disease Prevention and Control, 2009q).

3.2.2 Phase 2

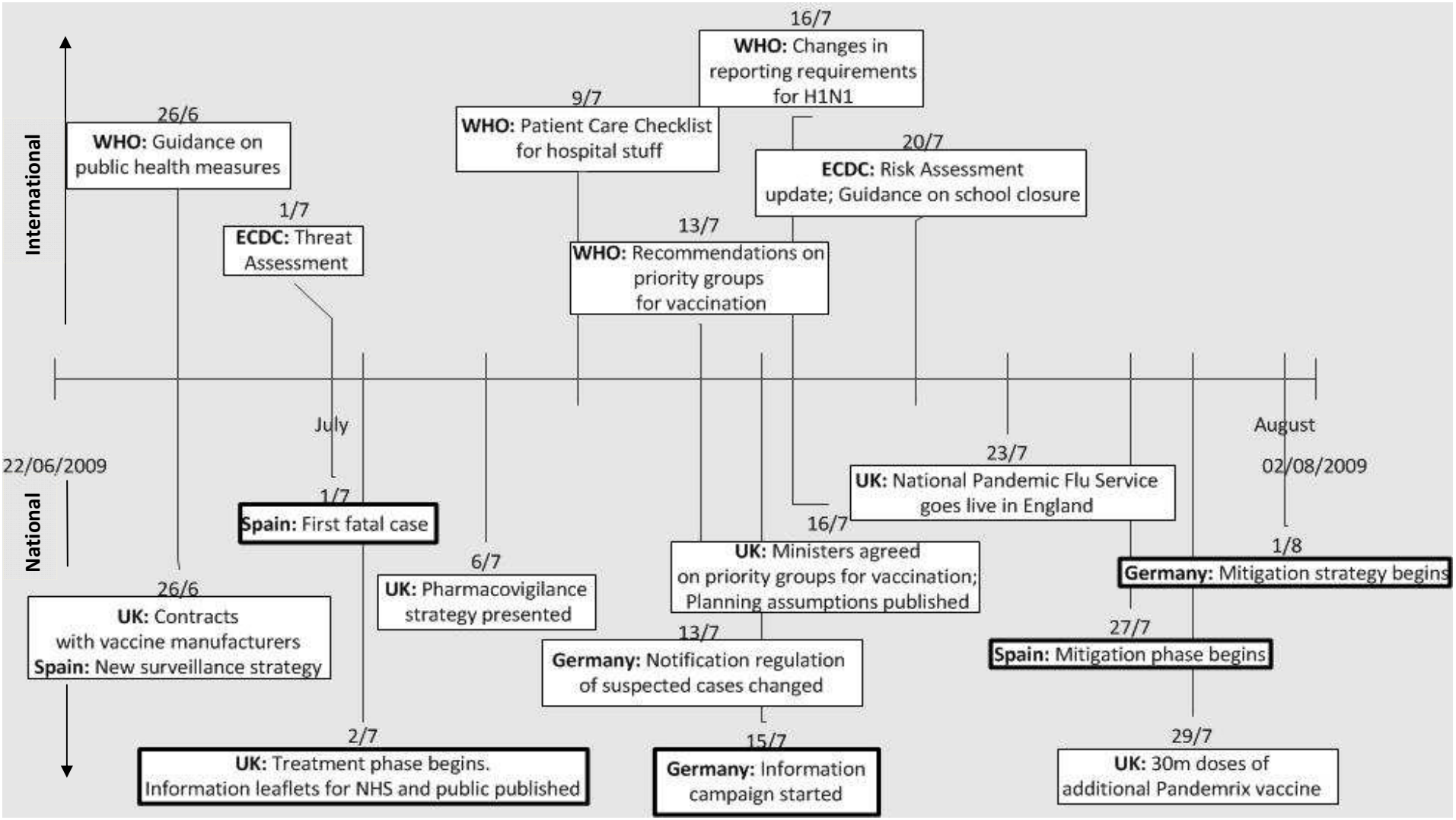

Figure 9: Chronological overview of national and international events for phase 2 (22/06/2009 to 02/08/2009)

3.2.2.1 Situation

The numbers of confirmed pandemic A/H1N1 cases increased constantly. By the end of June, Germany (429 cases), Spain (717 cases) and the UK (6929 cases) have reported 8075 confirmed cases (Health Protection Agency, 2009b; Ministerio de Sanidad y Politica Social, 2009b; Robert Koch-Institut, 2009d). On 1 July, Spain confirmed its first fatal case (European Centre for Disease Prevention and Control, 2010), which raised the cumulative number of deaths in the EU to four (UK three cases, Spain one case) (European Centre for Disease Prevention and Control, 2009u). In the UK, the number of pandemic A/H1N1 cases has increased sharply until the peak of the first wave in week 27/2009. In Spain the numbers of infections continued to increase until week 29/2009 and in Germany numbers of confirmed cases continued to rise until early August (see Figure 7).

In its Threat Assessment, published on 1 July, the ECDC announced the first isolation of an oseltamivir (also known as Tamiflu®) resistant mutant A/H1N1 virus in Denmark. The virus was not a reassortant virus and was still susceptible to zanamivir (also known as Relenza®). There was no evidence that the virus has been transmitted to other persons. ECDC stated that this phenomenon is well-known in influenza viruses and emphasized the need for continued surveillance of this problem (European Centre for Disease Prevention and Control, 2009t).

On 16 July, the Department of Health in the UK made its first planning assumptions public. The figures represented a “reasonable worst case”, not a prediction on how the pandemic will evolve. The following key planning assumptions for the first major pandemic wave were published: 18.69 million cases, 370.000 people hospitalized, 2.8 million people with complications and up to 65.000 deaths. These figures referred to the total UK population of about 62.3 million (Department of Health, 2009e).
According to an ECDC risk assessment published on 20 July, 20-30% of the population was expected to be affected over the first major wave of the pandemic. Clinical attack rates were expected to be highest in children and young adults. The estimate for hospitalization rates in Europe was 1-2% and the case fatality rate was estimated to be 0.1-0.2% of all clinical cases. ECDC stated that most cases experienced a mild and self-limiting illness, but people with chronic underlying medical conditions, pregnant women and young

children were at higher risk of experiencing severe disease and deaths (European Centre for Disease Prevention and Control, 2009v).

3.2.2.2 Surveillance

On 26 June, Spain modified its surveillance strategy. The Public Health Commission approved a strategy based on 5 points, saying that:

- a case-based surveillance of severe cases should start,
- the influenza surveillance through the SISS should be maintained,
- monitoring of clusters of acute respiratory illness should be maintained, but a case-based notification was not required anymore and only the first cases had to be swabbed for laboratory confirmation,
- monitoring of influenza or acute respiratory disease from the primary care computerized database, as well as
- case-based monitoring of flu cases in the community should be maintained.

In addition, the identification and monitoring of contacts and administration of prophylaxis to contacts was ceased. (Santa-Olalla Peralta, Cortes García, Martínez Sánchez, et al., 2010).

On 2 July, the surveillance strategy in the UK was modified as well. This change implied that laboratory testing of all cases and case-tracing was ceased (Health Protection Agency, 2009d). To monitor the safety of the medicines and vaccines that are on the market, the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK has a an on-line reporting system in place, called the Yellow Card Scheme. This system is open to members of the public as well as healthcare professionals wanting to report suspected adverse drug reactions. On 6 July, a special web-based system for reporting suspected adverse drug reactions to Tamiflu, Relenza and to future pandemic vaccine was put into operation for the duration of the pandemic (Medicines and Healthcare products Regulatory Agency, 2009a).

On 13 July, the surveillance strategy in Germany was modified as well. From week 29/2009 onwards regional health authorities were no longer required to submit reports on suspected cases to the state health authorities or to the Robert Koch-Institut (Robert Koch-Institut, 2010a).

On 16 July, the WHO announced that countries with community-wide transmission are no longer required to forward regular reports of individual confirmed cases to the WHO, as the detection, laboratory-confirmation and investigation of all cases is extremely resource-intensive and not sustainable for these countries (World Health Organization, 2009k).

On 27 July, the Spanish Surveillance Subcommittee agreed on a surveillance strategy update that suppressed the case-based surveillance of cases in the community. One day later, this new strategy was approved by the Spanish Public Health Commission (Ministerio de Sanidad, Politica Social e Igualdad, 2010a; Sierra Moros et al., 2010).

3.2.2.3 Control strategy and treatment of cases

Acknowledging that the containment of the pandemic A/H1N1 virus was no longer possible, the ministers in the UK changed the response strategy on 2 July. Due to the widespread of the virus within the UK, ministers decided to move from containment into the treatment phase. As already described in the previous chapter this change meant that laboratory testing was no longer required for all cases and case-tracing was ceased. Further, antiviral treatment was only offered to clinical cases (Health Protection Agency, 2009d). Additionally, to relieve some of the pressures on the health system, the National Pandemic Flu Service was launched in England on 23 July. This was an online and telephone self-care service that allowed people to be assessed for pandemic flu and, if required, to get access to antivirals. If symptoms were causing concern or if cases were in an at-risk group, they were advised to contact their GP. Those who were authorized to receive antivirals were able to pick up the drugs from one of the 2.000 antiviral collection points that were established across England. In Scotland, Wales and Northern Ireland A/H1N1 cases accessed antivirals through the normal primary care route, by taking a GP prescription to a pharmacy. In England, all clinical cases received antivirals, whereas GPs in the devolved administrations were advised to prescribe antivirals to cases in at-risk groups and any other cases based on clinical discretion (Department of Health, 2009f; Hine, 2010).

On 27 July, Spain moved from containment to mitigation, although response measures have already been changed towards a mitigation strategy in late June, i.e. contact tracing was ceased. Case-based reporting of cases in the community was stopped and antivirals

were only given to cases requiring hospitalization and to those at risk of complications (Ministerio de Sanidad, Politica Social e Igualdad, 2010b; Sierra Moros et al., 2010).

In early August 2009, Germany has changed its response strategy as well and moved to a mitigation strategy. The new strategy focused on risk groups and included the following changes: Contact-tracing was ceased, isolation was recommended for cases with contact to vulnerable persons only, antivirals were only given to cases in at-risk groups with signs of developing severe illness, case-based reporting requirements were relaxed and in late August infection control measures at airports were reduced (Robert Koch-Institut, 2010a).

3.2.2.4 Vaccination strategy

The UK`s initial vaccination strategy was to provide pandemic vaccine for 100% of the population. Thus, on 26 June, contracts were signed with GlaxoSmithKline and Baxter Healthcare to make available 132 million doses of pandemic vaccine, enough for the whole population to have two doses of vaccine (Hine, 2010).

As initial supplies of pandemic vaccine were limited, the WHO Strategic Advisory Group of Experts (SAGE) on Immunization recommended that the following groups should be prioritized for vaccination: health-care workers; pregnant women; individuals aged above six months with a chronic medical condition; healthy individuals aged between 15 years and up to 49 years; healthy children; healthy individuals aged between 50 years and up to 64 years; and healthy individuals aged 65 years or above. The order of priority should be based on country-specific conditions (World Health Organization, 2009j).

Three days later, on 16 July, UK ministers agreed on the following priority groups for vaccination advised by DH´s Joint Committee on Vaccination and Immunisation (JCVI) and previously endorsed by DH`s Scientific Advisory Group for Emergencies (SAGE): individuals aged between six months and 65 years in the current seasonal flu at-risk group; pregnant women; children aged between 3 years and up to 16 years; and frontline health and social care workers (Department of Health. Joint Committee on Vaccination and Immunisation, 2009a; Department of Health. Scientific Advisory Group for Emergencies (SAGE), 2009b; Hine, 2010).

At the beginning of the vaccine production, vaccine manufacturers had problems with low vaccine output. GlaxoSmithKline and Baxter Healthcare reacted to this problem by modifying their production process and thereby increased their vaccine output. Thus, on 29 July, the ministers in the UK decided to buy 30 million doses of additional pandemic vaccine from GlaxoSmithKline to ensure pandemic vaccine supply (Hine, 2010).

3.2.2.5 Communication

In order to give a better overview, the information published during phase 2 is grouped around the themes: control strategy, treatment of cases, personal protective measures and non-pharmaceutical response measures.

Control strategy:

On 26 June, the WHO published a guidance document on public health measures to help countries manage the A/H1N1 pandemic. Besides giving general advice on response measures, the WHO provided additional advice for countries with widespread community-level transmission, for countries with no reported cases and for countries in transition. The WHO advised all countries to concentrate on mitigation measures, to prepare the health-care system for a high volume of patients and to ensure antiviral medicine and vaccine supply. In addition, countries with widespread community-level transmission were advised to cease laboratory-testing of all cases, to reduce the pressure on the health-care system, to primarily focus on the treatment of ill patients, and to consider school closures or the cancellation of mass gathering on a case-by-case basis. Countries with no reported cases were advised that they may consider entry screening at airports and contact tracing, but that these measures are resource intensive and of limited benefit to prevent the spread of the disease. Countries in transition were advised to start the same control measures as countries with widespread community-level transmission (World Health Organization, 2009a).

On 2 July, the Department of Health in the UK published three documents on the new response strategy. The first document was intended for the NHS which outlined the rationale of the movement from containment to treatment and set responsibilities for the NHS during the treatment phase (Department of Health, 2009b). The second document provided clear information to the public explaining why the UK has chosen to move to a treatment phase, and the third document summarized scientific issues relevant to the new response strategy (Department of Health, 2009c, 2009d).

Treatment of cases:

On 9 July, the WHO published a patient care checklist. This was a tool intended for use by hospital stuff. It highlighted aspects of the clinical management of suspected and confirmed pandemic A/H1N1 cases and infection control measures (European Centre for Disease Prevention and Control, 2010; World Health Organization, 2009g).

Personal protective measures:

On 15 July, Germany started its A/H1N1 pandemic information campaign by publishing an information leaflet on personal protective measures in 11 languages (Die Beauftragte der Bundesregierung für Migration, Flüchtlinge und Integration, 2009). In addition, the Federal Centre for Health Education (BZgA) provided information to the public on modes of transmission, symptoms of an A/H1N1 infection and on general hygiene measures to prevent the spread of the virus (Bundeszentrale für gesundheitliche Aufklärung, 2009a). Further, the Robert Koch-Institut developed a document that aimed to inform the public about the influenza viruses and a pandemic in general, about modes of transmission of influenza viruses and about personal protective measures to prevent an influenza infection (Robert Koch-Institut, 2009i).

Non-pharmaceutical response measures:

On 20 July, the ECDC gave scientific advice on reactive and proactive school closures in Europe. ECDC highlighted that there is no consensus on the benefits from proactive school closures (school closure before transmission between the children occurs), but countries and schools were advised to at least have plans for reactive school closures (school closure when many children and/or staff are experiencing illness). These plans should consider the following issues: recommended length of time of closure; the triggers for re-opening; how to sustain teaching and learning; and potential problems that may arise for parents, if they have to take time off work (European Centre for Disease Prevention and Control, 2009w).

3.2.3 Phase 3

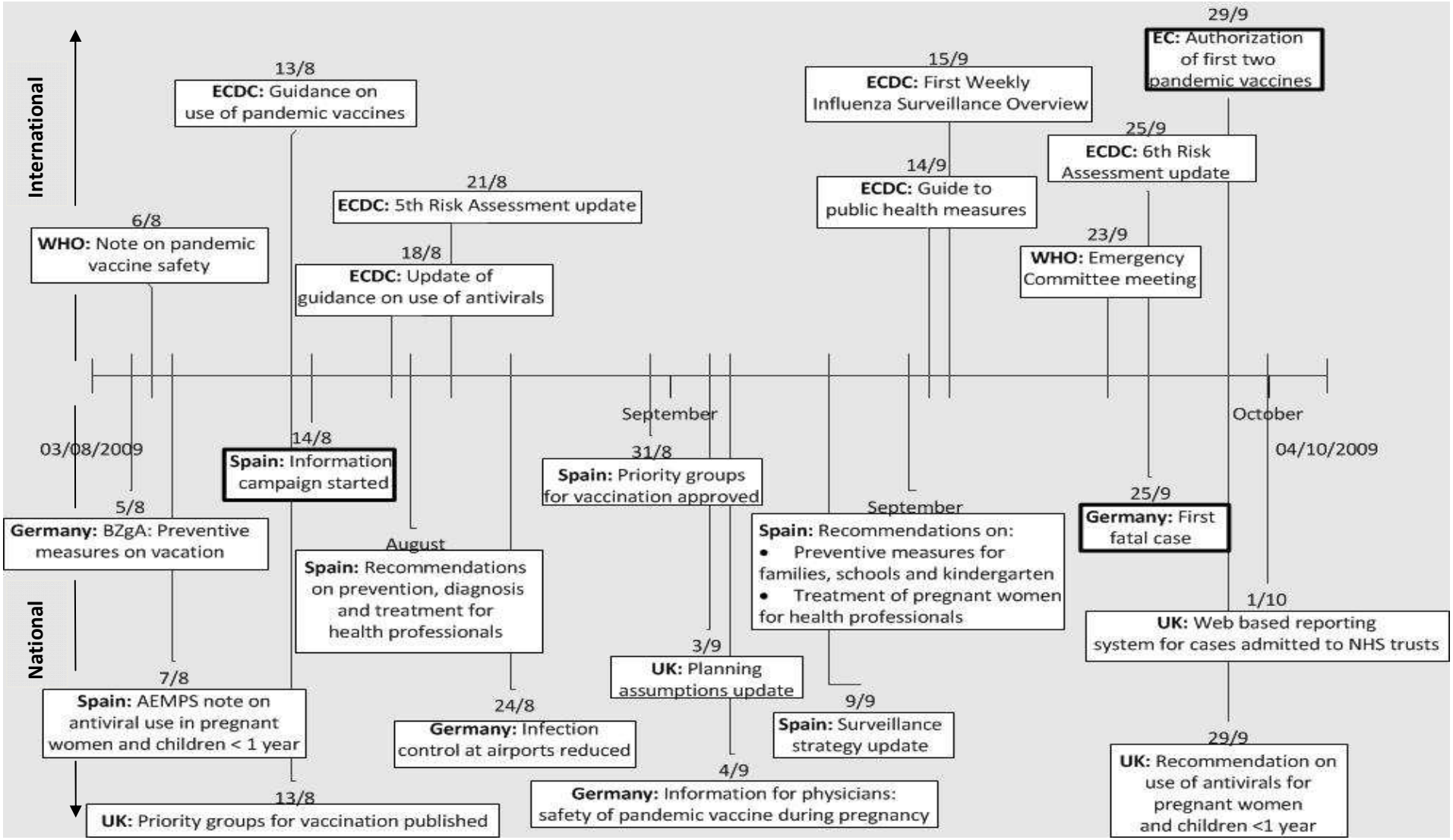

Figure 10: Chronological overview of national and international events for phase 3 (03/08/2009 to 04/10/2009)

3.2.3.1 Situation

As of 4 August, the UK (11912 cases), Spain (1538) and Germany (7177 cases) have reported 20.627 confirmed cases to the ECDC. The UK and Spain have stopped laboratory testing of all suspected cases; therefore the reported numbers severely underestimate the true figure in the two countries. So far, the UK (30 deaths) and Spain (7 deaths) have recorded 37 deaths from pandemic A/H1N1 infection (European Centre for Disease Prevention and Control, 2009z). The virus continued to spread in the three countries, but at a low level over the summer (see Figure 7). On 25 September, Germany reported the first fatal case from pandemic A/H1N1 infection (Robert Koch-Institut, 2009j).

On 21 August, the ECDC published its planning assumptions for the first major wave of infection, which was expected to take place in the autumn and winter of 2009/2010. However, these planning assumptions did not differ from those published on 20 July (European Centre for Disease Prevention and Control, 2009aa).

In contrast to the ECDC, the Department of Health in the UK has modified its planning assumptions in early September. Based on the latest evidence on the severity of the pandemic A/H1N1 virus, the following values have been revised downwards: hospitalization rate from 2% to 1% and upper case fatality rate from 0, 35% to 0, 1% (Department of Health, 2009i).

In late September, the ECDC has reduced its planning assumption as well. This decision was based on experience from Southern Hemisphere countries. It became more apparent that most pandemic A/H1N1 cases experienced a mild disease; therefore hospitalization and case fatality rates were revised downwards and were now in line with the figures published in the UK in early September (European Centre for Disease Prevention and Control, 2009ab).

3.2.3.2 Surveillance

On 9 September, the Spanish Public Health Commission revised the surveillance strategy once again. According to the new strategy, the investigation of clusters of cases was only recommended in those cases deemed necessary to make a special intervention (Ministerio de Sanidad, Politica Social e Igualdad, 2010a).

In October, the Health Protection Agency set up a web based reporting system for NHS Trusts across England to gather information on hospitalized pandemic A/H1N1 cases. With this system the Health Protection Agency aimed to collect clinical, epidemiological and demographic data on all hospitalized cases with a confirmed pandemic A/H1N1 infection (Health Protection Agency, 2010b).

3.2.3.3 Control strategy and treatment of cases

During phase 3, Germany was the only country where the control strategy has been modified. In week 35/2009 infection control measures at German airports were reduced (Robert Koch-Institut, 2010a). In the UK and Spain infection control measures at airports were already ceased in mid-June.

3.2.3.4 Vaccination Strategy

On 13 August, the priority groups for the pandemic A/H1N1 vaccination program were announced in the UK. Based on advice from the Joint Committee for Vaccination and Immunisation (JCVI) and the Scientific Advisory Group for Emergencies (SAGE) four groups have been identified to be at highest risk of developing severe disease from a pandemic A/H1N1 infection. These groups should be prioritized for vaccination in the following order:

- people aged between six months and up to 65 years in the present seasonal flu vaccine clinical at-risk groups,
- all pregnant women,
- household contacts of immunocompromised people, and
- individuals aged ≥ 65 in the present seasonal flu vaccine clinical at-risk groups.

In addition, front-line health and social care workers should be vaccinated together with the first clinical at-risk group (Department of Health, 2009g). Members of the clinical at-risk group were individuals with one of the following underlying clinical condition: chronic respiratory disease; chronic heart disease; chronic renal disease; chronic liver disease; chronic neurological disease; immunosuppression; and diabetes mellitus (Department of Health, 2009h).

In Spain, an agreement on priority groups for vaccination against pandemic A/H1N1 has been achieved on 31 August. The following population groups were considered to be priority groups for vaccination, but should not be prioritized in any order:

- health and social care workers,
- pregnant women,
- people working in essential public services (e.g. firefighters, policemen, workers at prisons, etc.), and
- individuals aged over six months in a clinical at-risk group.

Clinical at-risk groups were considered to be the same as in the UK (Ministerio de Sanidad y Politica Social, 2009l; Ministerio de Sanidad, Politica Social e Igualdad, 2010b).

On 29 September, the European Commission authorized the first two pandemic vaccines Focetria® (Novartis) and Pandemrix® (GlaxoSmithKline) for use in all Member States of the European Union and in Iceland, Liechtenstein and Norway (European Commission, 2009b).

3.2.3.5 Communication

During phase 3 a lot of information and guidance has been issued. In order to give a better overview, the publications are grouped around the themes: personal protective measures, non-pharmaceutical response measures, treatment of cases and vaccination.

Personal protective measures:

During the summer holiday season Germany observed importations of the pandemic A/H1N1 virus from affected countries, especially from Spain. Thus, in early August the Federal Centre for Health Education (BZgA) in Germany issued a press release on personal protective measures on vacation to remind holiday-maker of performing the recommended hygiene measures even on holiday (i.e. avoidance of close contacts with sick people, frequently hand washing, good respiratory hygiene, self-isolation of sick people) (Bundeszentrale für gesundheitliche Aufklärung, 2009b).

In mid-August, the pandemic A/H1N1 information campaign “Gripe A. La prevención es la major medida” started in Spain (Ministerio de Sanidad y Politica Social, 2009a). Therefore, the Ministry of Health and Social Policy has launched the information website “informaciongripea.es”. This website provided information about the disease and advice on personal protective measures for the general public. In addition, information and advice was made available to the public through posters, information leaflets, social networks and over the radio (Ministerio de Sanidad y Politica Social, 2009a, 2012). Besides the

mainstream public information campaign, the Ministry of Health and Social Policy published tailored information and guidance on preventive measures for families, schools and kindergartens (Ministerio de Sanidad y Politica Social, 2009e, 2009f, 2009g).

Non-pharmaceutical response measures:

In mid-September, the ECDC published a document on public health measures for policy and decision-makers (European Centre for Disease Prevention and Control, 2010). It provided scientific information on measures that may be applied to reduce the impact of influenza pandemics (i.e. border closures, entry restrictions, personal protective measures, social distancing measures, use of antivirals and vaccines) and aimed to help EU countries to decide on appropriate response measures (European Centre for Disease Prevention and Control, 2009a).

On 23 September, the WHO Emergency Committee held its 5th meeting and agreed on continuing the following recommendations proposed by the WHO Director-General:

- borders should not be closed and travel and trade should not be restricted,
- countries should intensify surveillance of unusual events and
- people who are ill should postpone international travel (World Health Organization, 2009n).

Treatment of cases:

The use of antivirals in some groups involves particularities health professionals should know. Therefore, the following recommendations on the use of antivirals in children, pregnant women and women who are breastfeeding were published in Spain and the UK:

- zanamivir (Relenza®) or oseltamivir (Tamiflu®) can be used in pregnant women, but zanamivir was recommended as first choice for treatment and prophylaxis,
- the preferred antiviral medicine for breastfeeding women is oseltamivir,
- children under the age of one year should only be treated with oseltamivir,
- post exposure prophylaxis for children under the age of one should only be offered after a thorough benefit-risk assessment (Agencia Española de Medicamentos y Productos Sanitarios, 2009a; Department of Health, 2009j)

Besides the guidance on the use of antivirals, the Spanish Ministry of Health published recommendations on the treatment of cases with severe acute respiratory failure, recommendations on the clinical management of adults with pneumonia and recommendations on the treatment of pregnant women. The three documents aimed to

inform health professionals on diagnostic tests, general and severe symptoms, antiviral treatment or the treatment of complications, and personal protective measures (Ministerio de Sanidad y Politica Social, 2009d, 2009h, 2009i).

On 18 August, the ECDC published general guidance on the use of antivirals during influenza pandemics. The document aimed to inform those deciding on antiviral use strategies about the effectiveness of antivirals, side effects of antivirals, priority groups for antiviral use and about necessary arrangements for antiviral delivery and administration (European Centre for Disease Prevention and Control, 2009x).

Vaccination:

Referring to media reports that have displayed concern about the safety of pandemic vaccine, the WHO has issued a note on pandemic vaccine safety on 6 August. In this statement the WHO outlined the procedures for approval and licensing of vaccines and confirmed that these procedures are strict and do include safety and quality controls. The WHO also stated that the data on influenza vaccine safety collected during the last 60 years do not show a special safety issue. Nonetheless, the WHO advised countries to closely monitor the safety and efficacy of the pandemic vaccine, as rare adverse events may only come to light when large numbers of people got vaccinated (World Health Organization, 2009l).

On 13 August, the ECDC published a document on the use of influenza pandemic vaccines during the 2009 A/H1N1 pandemic. The document aimed to inform those deciding on vaccination policies in the European countries on vaccine use and options for prioritization in order to maximize the benefit of available vaccine (European Centre for Disease Prevention and Control, 2009y).

On 4 September, the German Paul-Ehrlich-Institut issued information for physicians and pharmacists on the safety of pandemic vaccines during pregnancy. The Paul-Ehrlich-Institut considered existing scientific evidence and concluded that the pandemic A/H1N1 vaccines do not pose a risk to pregnant women. However, the Paul-Ehrlich-Institut stated that this conclusion did not involve the recommendation of vaccinating all pregnant women at this point; and recommended to only vaccinate pregnant women if the potential benefits of the vaccine outweigh its potential risks (Paul-Ehrlich-Institut, 2009).

3.2.4 Phase 4

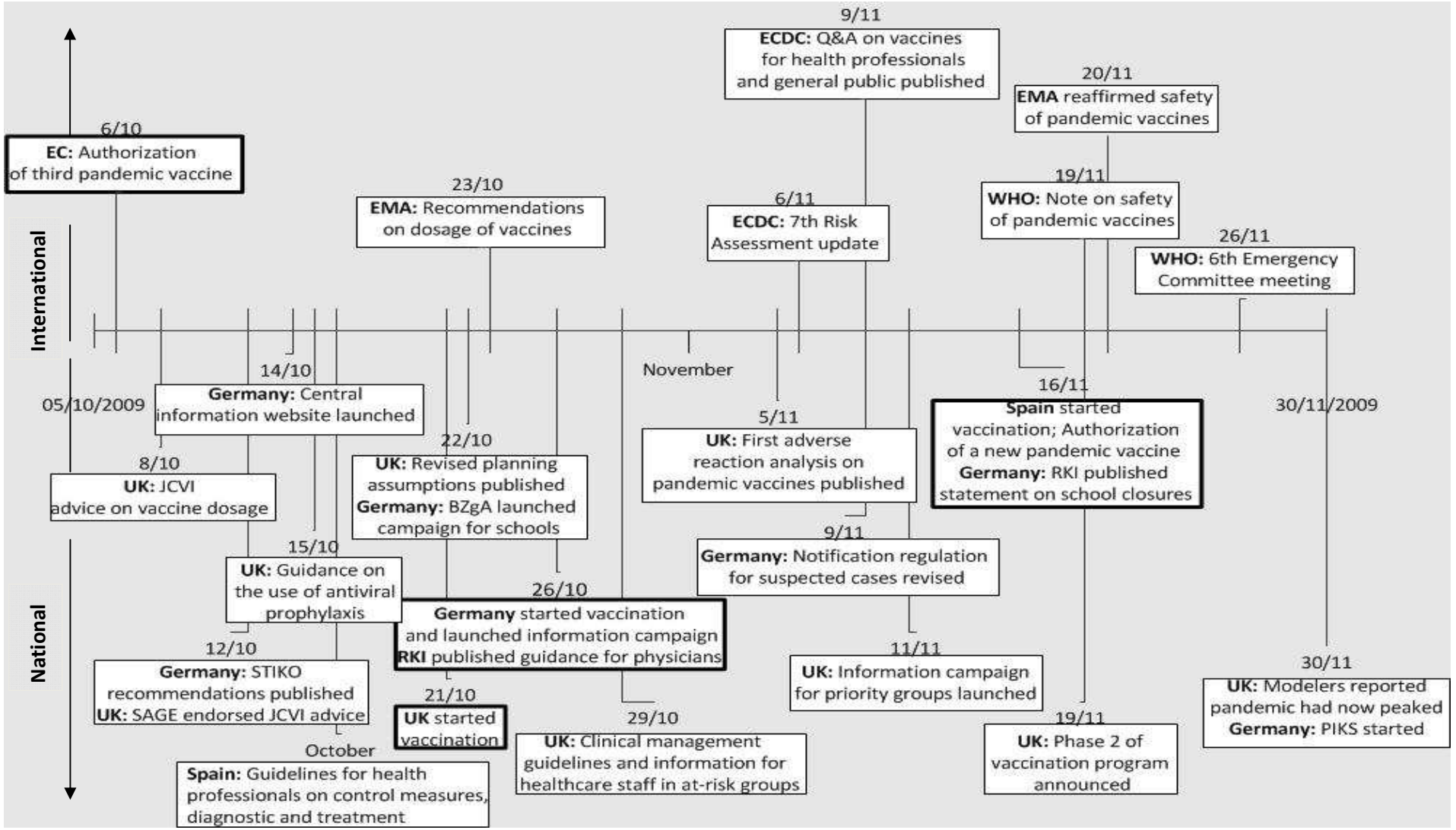

Figure 11: Chronological overview of national and international events for phase 4 (05/10/2009 to 30/11/2009)

3.2.4.1 Situation

In early autumn, the numbers of pandemic A/H1N1 infections in the UK, Germany and Spain have started to increase again, indicating the beginning of the expected autumn/winter wave (see Figure 7). In the UK the second wave peaked in week 45/2009 (Department of Health, 2010a). In Spain the autumn wave peaked in week 46/2009 reaching the weekly incidence rate of nearly 372 cases/ 100.000 population (Larrauri Cámara et al., 2010), and in Germany the peak was reached in week 47/2009 (Buda et al., 2010).

As more information on the pandemic A/H1N1 virus became available showing that it remains relatively mild for most people and suggesting that the second peak may not be as high as actually thought, the worst-case planning assumptions for the UK were revised downwards once more. In the new planning assumptions, published on 22 October, the reasonable worst case for the clinical attack rate was reduced from 30% to 12% and the reasonable worst case for further deaths was reduced from 19.000 to 1.000 (Department of Health, 2009m).

In its 7th risk assessment issued on 6 November, the ECDC has revised its planning assumptions as well. The following EU reasonable worst case planning assumptions for the first year up to mid-May 2010 were published: clinical attack rate: up to 20% of population, hospitalization rate: up to 100 per 100.000 population and case fatality rate: up to 3 per 100.000 population (European Centre for Disease Prevention and Control, 2009ac).

On 30 November, the UK`s Scientific Advisory Groups for Emergencies held a meeting in which modelers announced that the pandemic had now peaked and that the recently published worst case assumptions will not be reached (Department of Health. Scientific Advisory Group for Emergencies (SAGE), 2009d).

3.2.4.2 Surveillance

In view of increasing numbers of A/H1N1 infections, the German surveillance strategy was modified. From week 46/2009 onwards only laboratory confirmed cases and deaths relating to a pandemic A/H1N1 infection had to be reported to the RKI (Buda et al., 2010). To reduce the reporting effort for local health authorities, it was possible to only forward weekly aggregated case numbers to state health authorities and the RKI. In addition, laboratory testing was only recommended and reimbursed for cases with a high risk of

developing severe disease, in order to ensure laboratory capacity and to reduce costs (Robert Koch-Institut, 2010a). The UK and Spain have already stopped laboratory confirmation of all cases in July.

In order to gather information on hospitalizations and deaths due to pandemic A/H1N1 infections, the RKI set up the Pandemic Influenza A/H1N1 Hospital Surveillance System (Pandemische Influenza A(H1N1) Krankenhaus Surveillance; PIKS). From week 49/2009 onwards all hospitals were able to forward weekly aggregated numbers of hospital admission and deaths relating to a pandemic A/H1N1 infection to the RKI on a voluntary basis (Buda et al., 2010).

3.2.4.3 Control strategy and treatment of cases

During phase 4, no control strategy modifications have been implemented.

3.2.4.4 Vaccination strategy:

On 6 October, the European Commission authorized a third pandemic vaccine, Celvapan®, for use in all EU Member States, Iceland, Lichtenstein and Norway (European Commission, 2009c).

As the European Commission has now authorized both vaccines procured by the UK (Pandemrix® and Celvapan®), the DH`s Joint Committee on Vaccination and Immunization gave the following advice on vaccine dosage: one dose of Pandemrix® for those aged 10 years and above; two doses for immunocompromised individuals; two half adult doses for children aged below ten years and over six months; and two doses of Celvapan® for all age groups (Department of Health. Joint Committee on Vaccination and Immunisation, 2009c). Four days later, on 12 October, this advice was endorsed by DH`s Scientific Advisory Group for Emergencies (SAGE) (Department of Health. Scientific Advisory Group for Emergencies (SAGE), 2009c).

On the same day, the Robert Koch-Institut published the priority groups for vaccination recommended by the German Committee on Vaccination (Ständige Impfkommission; STIKO). According to the STIKO, three groups were identified that should be prioritized for vaccination in the following order: front-line health and social care workers; individuals aged six months and above in a clinical at-risk group; and pregnant women. Clinical at-risk groups were considered to be the same as in the UK. The Robert Koch-Institut and Paul-Ehrlich-Institut recommended a one dose schedule for Pandemrix® for those aged 10 and up to 60 years. Individuals above 60 years of age should receive two

doses and children aged below ten and over six months two half adult doses of Pandemrix® (Robert Koch-Institut, 2009c).
While the DH`s Joint Committee on Vaccination and Immunization, the Robert Koch-Institut and the Paul-Ehrlich-Institut considered a one dose schedule for Pandemrix® to be sufficient for those aged 10 years and above, the European Medicines Agency (EMA) recommended a two dose schedule for all three authorized vaccines (European Medicines Agency, 2009b).

On 21 October, the UK started its vaccination program (Department of Health, 2009k). The German vaccination program started five days later, on 26 October (Bundesministerium für Gesundheit, 2009b), and the Spanish vaccination program commenced only four weeks later, on 16 November (Ministerio de Sanidad y Politica Social, 2009l).

Just in time for the Spanish vaccination program the new pandemic vaccine Panenza® was authorized in Spain. It has been authorized by a decentralized procedure in which national agencies of Spain, France, Germany, Italy, Belgium and Luxembourg have participated. Panenza® is a vaccine without an adjuvant and was administered to pregnant women (Agencia Española de Medicamentos y Productos Sanitarios, 2009c). Pandemrix® was recommended to be administered to adults aged between 18 and 60 years only. The first choice for the other age groups was Focetria®. The Spanish Medicines and Healthcare Products Agency (Agencia Española de Medicamentos y Productos Sanitarios; AEMPS) recommended a one dose schedule for Pandemrix® and Focetria® for individuals aged over six months (Agencia Española de Medicamentos y Productos Sanitarios, 2009d).

On 19 November, phase two of the UK`s vaccination program was announced by the Department of Health. Chief Medical Officer Liam Donaldson stated that the vaccination program will be extended and vaccine will also be offered to all children over six months of age and under five years old. This decision was based on evidence showing that this age group is at higher risk of developing severe disease from an A/H1N1 infection than other healthy age groups (Department of Health, 2009u).

3.2.4.5 Communication

Same as during phase 3 a lot of information and guidance has been issued during phase 4. In order to give a better overview the publications are again grouped around the themes: personal protective measures, non-pharmaceutical response measures, treatment of cases and vaccination.

Personal protective measures:

Before the start of the vaccination program the Federal Ministry of Health in Germany has revised its offer of information. In order to provide solid information for the general public and for health professionals, the Federal Ministry of Health, together with the Robert Koch-Institut, the Federal Centre for Health Education and the Paul-Ehrlich-Institut, launched the central information website www.neuegrippe.bund.de (Bundesministerium für Gesundheit, 2009b). This website provided information on the pandemic A/H1N1 virus, personal protective measures and the pandemic vaccine.

In late October, the Federal Centre for Health Education developed a media package on hygiene practices for schools and kindergartens, called “schütz ich mich-schütz ich dich”. Posters, stickers and leaflets aimed to inform children and adolescents on proper hand and respiratory hygiene. The materials were produced in two different designs to ensure age-appropriate speech of children and adolescents (Bundeszentrale für gesundheitliche Aufklärung, 2009c).

Non-pharmaceutical response measures:

Due to increasing numbers of pandemic A/H1N1 cases, the Robert Koch-Institut received many queries regarding the effectiveness of school closures as a means to contain the spread of the virus. Thus, on 16 November, the RKI published a brief overview on aspects of reactive and proactive school closures and stated that with respect to the current epidemiological situation proactive school closures were not recommended. Further, the RKI stated that decisions on reactive school closures should depend on the epidemiological situation but an effect on the progress of the pandemic wave cannot be expected from reactive school closures (Robert Koch-Institut, 2009e).

On 26 November, the WHO Emergency Committee held its 6th meeting and agreed that delaying international travel was no longer recommended for ill persons, because pandemic A/H1N1 infections were already widespread (World Health Organization, 2009p).

Treatment of cases:

In October, the Spanish Ministry of Health and Social Policy published two documents for health professionals. The first document aimed to inform health professionals on diagnostic procedures and the treatment of pandemic A/H1N1 infections. It contained recommendations regarding the criteria for hospitalization, the organization of care, the treatment with antivirals and personal protective measures (Ministerio de Sanidad y Politica Social, 2009j). The second document included recommendations on prevention and control measures in retirement homes. It informed on general hygiene measures, the management of cases and on available pandemic vaccines (Ministerio de Sanidad y Politica Social, 2009k).

The Department of Health in the UK published clinical management guidelines for adults and children and for pregnant women (Department of Health, 2009q; Department of Health & Royal College of Obstetricians and Gynaecologists, 2009). A third document aimed to provide guidance for health professionals on the use of antiviral prophylaxis during the A/H1N1 pandemic. It informed on situations when the use of antiviral prophylaxis in pregnant women and people with underlying medical conditions was considered to be appropriate (Department of Health, 2009l). In addition, information for health and social care workers who are pregnant or in other at-risk groups was published. This document gave advice on protecting healthcare employees who are pregnant, or in one of the other at risk groups (Department of Health, 2009o).

In late October, the RKI published a guidance document for physicians. This document contained information on the epidemiological and clinical characteristics of the pandemic A/H1N1 virus, the antiviral treatment, the vaccination, the notification regulations, and preventive and control measures (Robert Koch-Institut, 2009a).

Vaccination:

Together with the start of the vaccination program, the public information campaign was launched in the UK, Germany and Spain. Information and advice was accessible on government websites and made available to the general public through leaflets (Bundesministerium für Gesundheit, Bundeszentrale für gesundheitliche Aufklärung, Robert Koch-Institut, & Paul-Ehrlich-Institut, 2009e; Department of Health, 2009n; Ministerio de Sanidad y Politica Social, 2009l). In addition to the mainstream public

information, the Federal Ministry of Health in Germany published tailored information for specific target groups (i.e. people with chronic underlying conditions; health professionals; pregnant women; and fire fighters and policemen) (Bundesministerium für Gesundheit et al., 2009a, 2009b, 2009c, 2009d). In the UK tailored information was produced for health professionals and pregnant women (Department of Health, 2009r, 2009s). Furthermore, clinical professional briefs on pandemic vaccination were published in the UK and Germany (Department of Health, 2009p, 2009t; Robert Koch-Institut & Paul-Ehrlich-Institut, 2009).

On 5 November, the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK published its first adverse reaction analysis on pandemic vaccines. In this report, the MHRA stated that there have been no new safety issues identified and that the benefits for Celvapan® and Pandemrix® still outweigh their risks (Medicines and Healthcare products Regulatory Agency, 2009b).

On European level, information on vaccination was provided by the ECDC. In November the ECDC published questions and answers on vaccines for health professionals and for the general public on its website (European Centre for Disease Prevention and Control, 2009b, 2009c, 2010).

On 19 November, the WHO issued a briefing note on pandemic vaccines in which the safety of the vaccines was reaffirmed (World Health Organization, 2009o). The European Medicines Agency (EMA) did hold the same opinion. In a press release published on 20 November, the EMA reasserted the efficacy and safety of pandemic vaccines. Further, the EMA revised its advice on vaccine schedules and published the following recommendations: Pandemrix® and Focetria® may be used as a single dose in adults (18-60 years) and in children and adolescents (Focetria®: from the age of 9 years; Pandemrix®: from the age of 10 years). Individuals aged over 60 years may also receive one dose of Pandemrix®, but younger children and immunocompromised people should receive two doses (European Medicines Agency, 2009c).

3.2.5 Phase 5

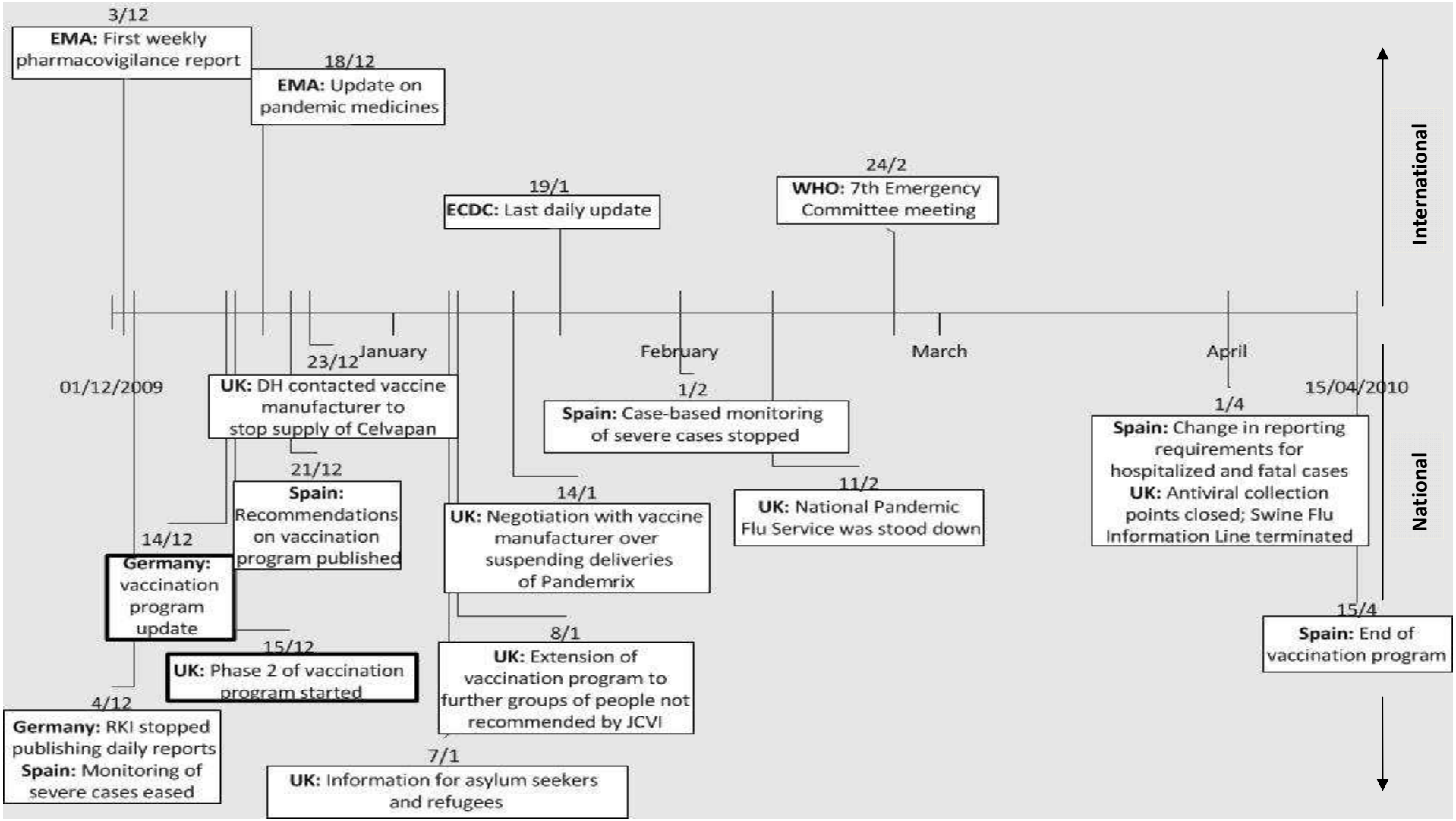

Figure 12: Chronological overview of national and international events for phase 5 (01/12/2009 to 15/04/2010)

3.2.5.1 Situation

The number of pandemic A/H1N1 infections decreased constantly in the UK, Germany and Spain. The end of the autumn wave was in early January 2010. Afterwards only sporadic cases have been reported (Buda et al., 2010; Department of Health, 2010a; Larrauri Cámara et al., 2010).

In February 2010, evidence showed decreasing or low pandemic A/H1N1 activity in many countries, but the WHO Emergency Committee agreed that it was too early to conclude that the pandemic A/H1N1 virus has run its course. Thus, the pandemic influenza alert phase was not changed (World Health Organization, 2010a). On 10 August 2010, the WHO Emergency Committee assessed the global situation again. This time the Committee concluded that the world was entering the post-pandemic period (World Health Organization, 2010c).

Altogether, Germany has reported 225.729 cases and 250 deaths of pandemic A/H1N1 virus. In the UK 474 pandemic A/H1N1 influenza related deaths have been reported and the total number of reported deaths due to pandemic A/H1N1 influenza across Spain was 348 (Buda et al., 2010; Department of Health, 2010d; Ministerio de Sanidad, Politica Social e Igualdad, 2010a).

3.2.5.2 Surveillance

On 4 December, the Spanish Surveillance Subcommittee eased the reporting requirements for severe cases. Two month later, on 1st February, the case-based monitoring of severe cases was stopped in favor of weekly aggregated reports of severe pandemic A/H1N1 cases. On 1st April, this new reporting requirement was ceased as well. Additionally, the notification of pandemic influenza A/H1N1 related deaths was stopped (Ministerio de Sanidad, Politica Social e Igualdad, 2010a).

3.2.5.3 Control strategy and treatment of cases

The National Pandemic Flu Service (NPFS) was launched in England in order to reduce the pressure on primary care. With decreasing numbers of pandemic A/H1N1 cases this service was not required anymore and was closed down on 11 February. During its operation, the NPFS distributed antivirals to 1.1 million people.

Two months later, on 1st April, antiviral collection points in England closed and the Swine Flu Information Line was stood down. Further, it was no longer possible to obtain antivirals from national stockpiles (Hine, 2010).

3.2.5.4 Vaccination strategy

So far, in Germany the Committee on Vaccination (Ständige Impfkommission; STIKO) recommended to offer pandemic vaccines to the following groups: front-line health and social care workers, individuals aged six months and above in a clinical at-risk group and pregnant women. Based on new data suggesting that young children and adolescents have an increased risk of contracting the pandemic A/H1N1 virus and of developing severe disease from the virus, the German Committee on Vaccination extended its recommendations on priority groups for vaccination. This update was published on 14 December and included the following changes: After vaccination of the three identified priority groups, vaccine should also be offered to household contacts of people in at-risk groups, all children and adolescents aged between 6 months and 24 years, all adults aged between 25 and 59 years, and all individuals aged 60 years and over (Robert Koch-Institut, 2009f). In addition to the updated recommendations on priority groups for vaccination by the German Committee on Vaccination, the Robert Koch-Institut (RKI) and Paul-Ehrlich-Institut (PEI) updated their recommendations on vaccine dosage. So far, the RKI and PEI recommended a one dose schedule for Pandemrix® for those aged 10 and up to 60 years. Individuals above 60 years of age should receive two doses and children aged below ten and over six months two half adult doses of Pandemrix® (Robert Koch-Institut, 2009c). Now, on the basis of available data on the pandemic vaccine Pandemrix®, the RKI and PEI recommended a one dose schedule for those aged 10 and above and one half adult dose schedule for children aged between 6 months and 9 years (Robert Koch-Institut, 2009g).

In December, the UK extended its vaccination program as well. As already announced in mid November, the UK started to offer pandemic vaccine to children over 6 months and under 5 years of age. Same as in Germany, the recommendation on the vaccine dosage was updated and one half adult dose of Pandemrix® was now considered to be sufficient for children over six months (Department of Health, 2009v). In contrast to the recommendations on priority groups for vaccination by the German Committee on Vaccination, the DH`s Joint Committee on Vaccination and Immunization in the UK did not recommend to extend the vaccination program to other groups of the population. This

recommendation was based on the latest epidemiological evidence and modeling predictions, which showed that pandemic A/H1N1 activity has decreased and a third wave was unlikely (Department of Health. Joint Committee on Vaccination and Immunisation, 2010). On 4 February, ministers approved this advice, but decided to set up a strategic reserve of 15 million doses of pandemic vaccine (Hine, 2010). The Department of Health has already contacted Baxter Healthcare in late December 2009 to stop supply of Celvapan® from 28 February 2010. This was possible, because a break clause was agreed with Baxter Healthcare at the time the UK ordered the vaccine in 2009 (Hine, 2010). On 14 January 2010, ministers agreed to stop deliveries of Pandemrix® as well. As this contract did not include a break clause, the Department of Health commenced negotiations with GlaxoSmithKline over terminating vaccine deliveries. On 6 April, the Department of Health achieved agreement to only take deliveries of just under 35 million doses of Pandemrix® (The Secretary of State for Health, 2010).

3.2.5.5 Communication

During phase 5, only little information and guidance has been published. Thus, the information and guidance is only grouped around the themes: vaccination and personal protective measures.

Vaccination:

In December 2009, the UK started to offer pandemic vaccine to children over 6 months and under 5 years of age. The Department of Health developed a leaflet for parents that contained tailored information about the second phase of the vaccination program (Department of Health, 2009w).

Between December 2009 and August 2010, the European Medicines Agency (EMA) published regular updates on safety monitoring of vaccines and medicines used during the pandemic (European Medicines Agency, 2010). In its update on pandemic medicines of 18 December, the EMA reaffirmed that the available data on the three pandemic vaccines and Tamiflu® showed no unexpected serious safety issues (European Medicines Agency, 2010).

On 21 December, the Spanish Medicines and Healthcare Products Agency (Agencia Española de Medicamentos y Productos Sanitarios; AEMPS) issued official

recommendations on the vaccination program. This document informed health professionals on the priority groups for vaccination, the specific pandemic vaccines and on aspects for vaccine administration (Agencia Española de Medicamentos y Productos Sanitarios, 2009d).

Personal protective measures:

In early January, the Department of Health in the UK published information leaflets in 32 languages to provide information on the pandemic A/H1N1 virus, personal protective measures, and the vaccination program for people who cannot speak or read English and who may not have access to a regular flow of news, i.e., an asylum seeker or refugee or a member of an established migrant group (Department of Health, 2010b).

4 Discussion

This Thesis presents the progress of the pandemic in the UK, Germany and Spain and explores the interaction of what actually happened (epidemic curves), how the countries responded (public health measures) and what the people were recommended (official recommendations) in context along a timeline.

The first confirmed case of pandemic A/H1N1 in the UK, Germany and Spain was reported in late April (European Centre for Disease Prevention and Control, 2009f; Robert Koch-Institut, 2009h; Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain, 2009). Initially, the UK, Germany and Spain observed sporadic importations of the pandemic A/H1N1 virus from Mexico and the US. In the UK sustained community transmission developed in June and the number of pandemic A/H1N1 cases increased sharply until the peak of the first wave in late June. In Spain and Germany numbers of confirmed cases began to increase in July (Buda et al., 2010; Health Protection Agency, 2010b; Sierra Moros et al., 2010). Transmission subsided in all three countries as the summer progressed. In early autumn transmission accelerated again and the numbers of reported pandemic A/H1N1 cases increased constantly in the UK, Germany and Spain. This autumn wave peaked between week 45/2009 and week 47/2009 and thereafter influenza activity decreased steadily. The pandemic influenza wave ended in early to mid January. Afterwards only sporadic cases have been reported (Buda et al., 2010; Department of Health, 2010a; Larrauri Cámara et al., 2010)

Throughout the pandemic, the highest infection rates were observed in children and young people. Generally, the virus caused a mild illness. More severe disease was especially experienced by those cases with underlying conditions (Department of Health, 2010a; Larrauri Cámara et al., 2010; Schaberg & Burger, 2010).

4.1 Control strategy

The initial control strategy in the UK, Germany and Spain focused on limiting transmission of the virus or delaying the spread in order to gain time to apply effective response measures like large-scale vaccination. The measures applied during this containment approach included the laboratory testing of all suspected cases, the tracing of contacts, the provision of antivirals to cases and contacts, and the isolation of cases. Further,

information on the risk groups, severity and transmissibility of the virus was gathered through detailed analysis of the cases (Health Protection Agency, 2010b; Robert Koch-Institut, 2010a; Santa-Olalla Peralta, Cortes García, Martínez Sánchez, et al., 2010). As the first few pandemic A/H1N1 cases were imported by travelers from Mexico and the US these measures may have helped to slow the initial spread of the virus, but a conclusive proof of this assumption is not possible (Hine, 2010; Robert Koch-Institut, 2010a). Anyhow, the WHO has already advised countries in late April to center on mitigation measures as the containment of the outbreak was not considered to be feasible (World Health Organization, 2009d). In June, the ECDC acknowledged that a containment strategy is very resource-intensive and therefore not a recommended infection control strategy for human influenza beyond pandemic alert phase 4, which was announced on 27 April 2009 (European Centre for Disease Prevention and Control, 2009q). Although not recommended by both the ECDC and the WHO, the UK, Germany and Spain continued to employ a strategy of containment (the UK until early July, Spain until late July and Germany until early August). Therefore, the resource-intensive measures remained in place for longer than may have been beneficial (Hine, 2010; Krause et al., 2010). Probably, this was only possible because of the relatively mild nature of the virus. In a more severe pandemic public health professionals would probably have been overwhelmed earlier (Hine, 2010).

Although it became apparent at an early stage of the pandemic that the majority of people experienced a mild disease from the pandemic A/H1N1 virus, the lack of data on parameters needed for right risk assessment continued for a long time. Even in mid-June there were still unresolved issues relating to the severity of the disease, the specific risk groups and whether or not the virus would remain sensitive to available antivirals (European Centre for Disease Prevention and Control, 2009g, 2009r). In the absence about the clarity of the nature of the virus, the likely impact on different groups, and its potential to mutate the continuation of the containment measures seems reasonable (Robert Koch-Institut, 2010a). Additionally, the virus continued to spread in an uneven manner across the UK, Germany and Spain with some areas more affected, while others remained largely unaffected. A move away from the containment approach may have seemed premature in largely unaffected areas. However, as done in the UK for “hot spots” areas, a more tailored, localized strategy might have also been helpful in managing local circumstances in Germany and Spain (Hine, 2010; Krause et al., 2010; Marcic et al., 2010; Sierra Moros et al., 2010).

The move away from the containment approach also affected the surveillance of pandemic A/H1N1 activity. Whereas the surveillance during the containment approach aimed to gather information on the clinical, epidemiological and virological characteristics of the virus through laboratory testing and contact tracing, the surveillance during the mitigation phase rather focused on gathering information on the trend, intensity and impact of the virus. The UK, Germany and Spain introduced surveillance systems to monitor severe cases and deaths due to pandemic A/H1N1 (Buda et al., 2010; Health Protection Agency, 2010b; Santa-Olalla Peralta, Cortes García, Martínez Sánchez, et al., 2010). However, in Germany the usefulness of these data were limited as the system was introduced too late and only a few sentinel hospitals joined the system (Krause et al., 2010). As the surveillance of severe cases is also relevant for other epidemic outbreaks, these surveillance systems should be improved or implemented as routine systems (Greco, Stern, & Marks, 2011; Krause et al., 2010).

During a pandemic any changes in response measures should be communicated to the public in order to assuage public concern and maintain confidence in health authorities (Hine, 2010; Krause et al., 2010). The UK was the only country that produced special leaflets for the public and health professionals explaining why the UK has chosen to move to a treatment only phase.

Nevertheless, the majority of German, Spanish and British citizens was satisfied with the way authorities in their countries responded to the pandemic flu. This becomes evident in a survey commissioned by the European Commission. It was conducted in November 2009 and examined public opinion about the 2009 A/H1N1 pandemic across Europe. Among others, interviewees were asked how satisfied they were with preventive measures that authorities have taken so far against the pandemic A/H1N1 virus. In Germany (n=1001) 53%, in Spain (n=1003) 62.7% and in the UK (n=1000) 60.8% stated they were satisfied with the measures taken by the authorities (The Gallup Organization, 2010).

4.2 Vaccination strategy

Another intervention measure that the UK, Germany and Spain employed to counter the impact of the pandemic was large-scale vaccination.

Spain decided to procure vaccine for 40% of the population and the UK ordered vaccine for 100% of the population. Both countries decided to order enough vaccine to have two doses for each person (Hine, 2010; Ministerio de Sanidad, Politica Social e Igualdad, 2010b). Germany`s initial assumption was to procure enough pandemic vaccine for 100% of the population, although later this assumption was revised downwards to 50 million doses (Feufel et al., 2010; Marcic et al., 2010). The nature of the virus, its potential impact on different groups and the number of vaccine doses needed were still not clear when the initial decisions on vaccine procurement were made. Given the uncertainties regarding the virus at the beginning of the outbreak, it was not easy to make a decision about the amount of vaccine to procure. Although, by the end of the pandemic less vaccine has been distributed than purchased (O'Flanagan, Cotter, & Mereckiene, 2011), the initial decisions on vaccine procurement seem reasonable regarding the context in which they were made. The results in chapter 3.2.3.4, chapter 3.2.4.4 and chapter 3.2.5.4 show that the UK, Germany and Spain responded to and changed vaccination policy and recommendations in response to available evidence on the characteristics of the virus regarding the risk groups (Department of Health, 2009g; Ministerio de Sanidad y Politica Social, 2009l; Robert Koch-Institut, 2009c, 2009f), available evidence on the immunogenicity of the pandemic vaccines (Agencia Española de Medicamentos y Productos Sanitarios, 2009d; Department of Health, 2009v; Robert Koch-Institut, 2009g) and in response to the pandemic progress (Department of Health. Joint Committee on Vaccination and Immunisation, 2010; Ministerio de Sanidad, Politica Social e Igualdad, 2010b). The changes were based on advice from national expert groups.

To ensure vaccine supply, Germany and the UK had advanced purchase agreements with vaccine manufacturer. As it turned out that less vaccine was needed than ordered, the countries aimed to reduce the amount of vaccine. Vaccine manufacturers were willing to negotiate over ceasing the contract and suspending vaccine deliveries (Hine, 2010; Krause et al., 2010). However, in future, negotiations with vaccine manufacturers should attempt to include break clauses wherever possible, like it was done in the contract between the UK and Baxter Healthcare (Hine, 2010). These break clauses allow for further flexibility in vaccine procurement. This is important when new vaccines are more immunogenic than anticipated so that for most vaccines only a single dose is required, as it has been demonstrated now (Robert Koch-Institut, 2009g).

Due to problems in the manufacturing process of the pandemic vaccines initial supply was limited (Hine, 2010; Marcic et al., 2010). The prioritization of special groups in Germany and the UK allowed those at greatest risk the chance to be vaccinated first and made best use of limited supply (Department of Health, 2009g; Robert Koch-Institut, 2009c) .

The leaflets and communication on the government websites that went alongside the vaccination programs informed the general public on which groups were being vaccinated, the reasons behind this selection, the side effect and safety of the pandemic vaccine (Bundesministerium für Gesundheit et al., 2009e; Department of Health, 2009n; Ministerio de Sanidad y Politica Social, 2009l). In Addition, the UK and Germany issued tailored information for at-risk groups and health professionals (Bundesministerium für Gesundheit et al., 2009a, 2009b, 2009c, 2009d; Department of Health, 2009r, 2009s). Furthermore, information for healthcare professionals was published to inform them on the priority groups for vaccination, the specific pandemic vaccines and on aspects for vaccine administration (Agencia Española de Medicamentos y Productos Sanitarios, 2009d; Department of Health, 2009p, 2009t; Robert Koch-Institut & Paul-Ehrlich-Institut, 2009). In addition to information on national level, the ECDC published questions and answers on vaccines for health professionals and for the general public on its website (European Centre for Disease Prevention and Control, 2009b, 2009c, 2010).

Although a lot of information on the pandemic vaccine has been distributed, vaccination coverage rates were low. In Germany, only 8% of the population and 16% of healthcare workers received the vaccine (Robert Koch-Institut, 2010b). In Spain the overall vaccination coverage rate was 27%. For those aged 6 months and above with chronic disease and underlying conditions the vaccination coverage rate was 24%, for pregnant women 9% and for healthcare workers 12% (Mereckiene et al., 2012). In England, the vaccination coverage rate for people under the age of 65 years with chronic disease and underlying conditions was 37.6%, including pregnant women. Further, 23.6% of children between the age of six months and five years, and 40.3% of healthcare workers received the pandemic vaccine in England. Vaccine uptake in Wales was similar and uptake in Northern Ireland and Scotland was higher compared to that of England. 86.5% of people under the age of 65 years with chronic disease and underlying conditions received the pandemic vaccine in Northern Ireland, and up to 54.5% of this group received the vaccine

in Scotland. Coverage rates among healthcare workers were 47.7% in Northern Ireland and 55.1% in Scotland (Health Protection Agency, 2010b).

However, the methods used for calculating vaccination coverage varied between countries limiting comparability of these data. The UK and Spain used administrative data and Germany used a survey as a reliable system to monitor vaccination rates is still missing in Germany (Health Protection Agency, 2010b; Krause et al., 2010; Mereckiene et al., 2012; Robert Koch-Institut, 2010b). Comparisons are also difficult due to the different starting dates of the vaccination programs. On 21 October, the UK started its vaccination program (Department of Health, 2009k). The German vaccination program started five days later, on 26 October (Bundesministerium für Gesundheit, 2009b), and the Spanish vaccination program commenced only four weeks later, on 16 November (Ministerio de Sanidad y Politica Social, 2009l). Further, a comparison is difficult due to the different vaccination strategies, i.e. the prioritization of special groups in the UK and Germany (Department of Health, 2009g, 2009v; Robert Koch-Institut, 2009c, 2009f).

Reasons for the low vaccination coverage rates were seen in the late arrival of the vaccines, the moderate character of the pandemic, vaccine safety concerns and skepticism regarding the need for vaccination among a large part of the healthcare workers (Greco et al., 2011; Marcic et al., 2010; Martin, 2010; Stern et al., 2010).

According to a European survey on the public opinion about the pandemic, conducted in November 2009, the most German (59.3%, n=1001), Spanish (34%, n=1003) and British citizens (39.8%, n=1000) believed it was rather unlikely that they would personally contract a pandemic A/H1N1 infection. When asked about the intention to get vaccinated 31.9% of German citizens and 40.3% of Spanish citizens stated it was not likely at all that they would get vaccinated, whereas in the UK only 17.3% of the respondents stated that they would not get vaccinated. The most stated reasons behind their choice were not being in one of the priority groups and safety concerns of pandemic vaccines (The Gallup Organization, 2010).

Although the EMA and WHO reaffirmed the safety of the pandemic vaccines (European Medicines Agency, 2009c; World Health Organization, 2009o), and national authorities stated that vaccines were safe in their information leaflets (Bundesministerium für Gesundheit et al., 2009e; Department of Health, 2009n; Ministerio de Sanidad y Politica Social, 2009l), this message was obviously not effectively communicated to the public.

In a future pandemic, authorities may consider giving safety data more prominence. A more clearly risk-focused approach to communication may have helped uptake rates. In order to make informed decisions regarding vaccination, the risks associated with pandemic A/H1N1 infection versus the risk of vaccination need to be more clearly explained. Further, the use of social networking may also help to identify public concerns on vaccination and to adjust information material accordingly (Hine, 2010). So far, the UK and Germany made limited use of social networking.

The interviewees in the aforementioned European survey were also asked about the source from which they received information on the pandemic vaccine. 33.3% (n=1001) of German, 24.5% (n=1003) of Spanish and 37.3% (n=1000) of British citizens said they were informed by physicians. Only 9.6% of German and 13.8% of Spanish citizens stated that they informed themselves on vaccination through official leaflets. This number was a lot higher in the UK. The majority (64.6%) of British citizens said that they received information from official leaflets (The Gallup Organization, 2010). Another survey conducted by the Robert Koch-Institut found similar results for Germany (Robert Koch-Institut, 2010b). Furthermore, the interviewees of the European survey were asked about the most trusted sources to inform themselves about the pandemic. According to this survey, respondents had the most trust in health professionals and national authorities (The Gallup Organization, 2010). These results show that healthcare professionals need particular attention as they are a key factor informing the public and winning the trust of the population (Greco et al., 2011). According to the survey conducted by the Robert Koch-Institut, the majority of physicians advised people against getting vaccinated (Robert Koch-Institut, 2010b). This result shows how essential it is that healthcare professionals have the right information in order to make informed decisions and to pass on the right information to patients. Thus, knowledge and understanding of the medical profession regarding the goals, benefits and risks of vaccination should be encouraged in the future (Krause et al., 2010). Therefore, in a future outbreak, professional bodies should be more involved in informing healthcare professionals and the public and in promoting vaccine uptake (Schaade et al., 2010).

4.3 Communication

In order to inform the general public on the pandemic A/H1N1 virus and personal protective measures, the UK, Germany and Spain developed extensive information materials at an early stage of the pandemic (see chapter 3.2.1.5, chapter 3.2.2.5 and chapter 3.2.3.5). The campaigns provided a basic knowledge of hygiene and personal protective measures in order to prevent a pandemic A/H1N1 infection. To disseminate the information various materials have been developed (flyers, posters, stickers) and the campaigns ran on TV and radio. The tonality of the communication was calm and factual. The information was understandable, short and concise (Martin, 2010).

To meet the information needs of the population, information and advice was also accessible on government websites (Bundesministerium für Gesundheit, 2009b; Hine, 2010; Ministerio de Sanidad y Politica Social, 2009a). These websites contained all the necessary information in a clearly structured and concise manner.

It has been possible to bring the basic information widely in the population. This becomes evident in the European survey that examined the public opinion about the pandemic. The majority of German (56.8%, n=1001), Spanish (56.1%, n= 1003) and British (55.2%, n=1000) citizens stated that they felt well informed about the pandemic A/H1N1 influenza (The Gallup Organization, 2010). Other surveys found similar results (Hine, 2010; Robert Koch-Institut, 2010b).

Although the public felt well informed about the pandemic A/H1N1 virus and about what they can do to protect themselves against it, the uptake of recommended behavior during the 2009 A/H1N1 pandemic was low. According to the European survey 75% of the interviewees in Germany (n=1001), 86.2% of the interviewees in Spain (n=1003) and 73.9% of the interviewees in the UK (n=1000) did not change their behavior to protect themselves against pandemic flu. Among those who changed their behavior, the most commonly adopted preventive measures were regular hand washing and good respiratory hygiene. Further, the majority of interviewees felt that seasonal flu and pandemic flu are equally dangerous and stated that it was rather unlikely that they will catch the pandemic flu (The Gallup Organization, 2010).

According to several surveys, factors independently associated with the adoption of the preventive measures are high perceived susceptibility to infection, high perceived effectiveness of the measures and high perceived usefulness of the information provided by

the government (Agüero, Adell, Giménez, Medina, & Continente, 2011; Rubin, Amlot, Page, & Wessely, 2009; Rubin, Potts, & Michie, 2010). Thus, in any future campaign, raising levels of worry about the possibility of contracting the virus, emphasizing the efficacy of recommended behaviors, reducing uncertainty and providing clear information on the practical things that people can do to reduce their risk should help to maximize the campaign's impact on preventive behaviors. Additionally, in times of rapid dissemination of opinion through the internet, this information channels should be better used to detect false information and disseminate reliable information (Krause et al., 2010).

Further, factors like gender, educational level, ethnicity, age, household size, health status, and socioeconomic status do also affect behavioral responses during major outbreaks (Agüero et al., 2011; Rubin et al., 2010). These factors should also be taken into account in any future campaign. As the interaction of these factors is likely to be complex, the consultation of behavioral scientists would be of value.

Public understanding of a pandemic and what it will be like supports an effective response (Hine, 2010), but some of the terminology used during the pandemic was misunderstood by the public. For example the term pandemic was often assumed to refer to the severity of the disease (Feufel et al., 2010; Hine, 2010; Krause et al., 2010). The communication did not clarify that the term pandemic does refer to geographic spread of the virus, rather than to the severity of the disease (Hine, 2010). The moderate character of the pandemic should have been better communicated to the public as people might have been confused with what they have expected and what was observable on the ground (Hine, 2010; Krause et al., 2010).

In the absence of any other figures that described the possible development of the pandemic, the UK and the ECDC published planning assumptions of only the "reasonable worst-case". This term was often assumed to refer to likely events, which then have not been observed in the countries (Hine, 2010). The UK published the following key planning assumptions for the first major pandemic wave: 18.69 million cases, 370.000 people hospitalized, 2.8 million people with complications and up to 65.000 deaths. (Department of Health, 2009e). The ECDC estimate for hospitalization rates in Europe was 1-2% and the case fatality rate was estimated to be 0.1-0.2% of all clinical cases (European Centre for Disease Prevention and Control, 2009v). What the UK and ECDC were saying and what was observable in the countries was not consistent. Generally, the virus caused a mild

illness and mortality levels were low (Buda et al., 2010; Department of Health, 2010a, 2010d; Larrauri Cámara et al., 2010; Ministerio de Sanidad, Politica Social e Igualdad, 2010a; Schaberg & Burger, 2010). Although, the UK and ECDC revised their planning assumptions downwards as more information on the characteristics of the virus became available, this gap could have risked weakening public trust in the response (Hine, 2010). Instead of publishing planning assumptions which were easily misunderstood, existing and missing evidence should have been communicated in a transparent way (Feufel et al., 2010). Thus, a more accurate picture of the pandemic would have been provided to the public.

In addition to the public information campaigns, tailored information for healthcare professionals on the treatment of cases and preventive measures has been published by national authorities (see chapter 3.2.2.5, chapter 3.2.3.5 and chapter 3.2.4.5). Regarding the vaccination program, appropriate information for healthcare professionals on the priority groups for vaccination, the specific pandemic vaccines and on aspects for vaccine administration has been published (Agencia Española de Medicamentos y Productos Sanitarios, 2009d; Department of Health, 2009p, 2009t; Robert Koch-Institut & Paul-Ehrlich-Institut, 2009). As already observed in the previous chapter, healthcare professionals as the primary contact have an important role in informing the public and promoting the adoption of preventive measures. But the exchange of information between health authorities and healthcare professionals could have been improved (Hine, 2010; Krause et al., 2010; Schaade et al., 2010; Sierra Moros et al., 2010). According to a review of the response in the UK, some healthcare professionals stated that they did not receive timely information on the response measures from the authorities. Others stated that too much information and guidance was published (Hine, 2010). The issue that healthcare professionals did not receive timely information was also observed in Germany. Here, especially information materials on the vaccination program appeared too late (Krause et al., 2010; Schaade et al., 2010). Thus, to ensure timely and coordinated information for healthcare professionals a source of direct clinical advice, e.g. a hotline or secure internet site, would be helpful in a future outbreak (Hine, 2010).

4.4 Conclusion

Although, several improvements have been identified regarding the vaccination and information campaigns more work is needed to see how recommendations can be effectively translated into higher vaccination coverage and behavior change. This should also take into account the influence of varying media messages (main stream media, internet, new social media) during the pandemic and more data on public perceptions and changing behavioral patterns during the different phases of the pandemic.

4.5 Limitations

4.5.1 Data on pandemic A/H1N1 cases and deaths

The data on confirmed pandemic A/H1N1 cases in the UK, Germany and Spain are not comparable between the countries as there is variability in the data sources, size and representativeness of the surveillance systems (Buda et al., 2010; Health Protection Agency, 2012; Hine, 2010; Larrauri et al., 2011). In addition, the shape of the epidemic curves is influenced by changes in the testing and control policies throughout the pandemic. The steep decline in confirmed pandemic A/H1N1 cases, as was the case in the UK after week 27/2009, can be partly explained by changing testing policies with a general move away from intense contact tracing and laboratory testing of all suspected cases (Health Protection Agency, 2009d). This decline was also observed in Germany after the notification regulation of suspected cases has been revised in week 46/2009 (Buda et al., 2010). Also, cases with infections so mild that they did not seek medical care were not reported. As such, there was an under-reporting of pandemic A/H1N1 cases and the epidemic curves do not present the true figure of pandemic A/H1N1 cases. However, the intention of this work was to present the trend of the pandemic in the UK, Germany and Spain and the epidemic curves do reflect this trend. This becomes evident in Figure 4, which presents the weekly number of confirmed pandemic A/H1N1 cases and weekly estimates of new pandemic A/ H1N1 cases in England. The figure shows that the actual number of cases was estimated to be up to a hundred times higher than the number of confirmed cases, but the pandemic profile is still visible in both curves.

Just as reported cases are an underestimate, so is the data on deaths due to the 2009 pandemic influenza. A serious limitation of reporting the number of deaths was the attribution of cause of deaths to the pandemic A/H1N1 virus. A large proportion of deaths caused by pandemic influenza occurred in individuals who suffered from one or more

chronic underlying medical condition (Department of Health, 2010a; Larrauri Cámara et al., 2010; Schaberg & Burger, 2010). Thus, many deaths might have been recorded as due to the chronic underlying medical condition, and not to the pandemic A/H1N1 virus (World Health Organization, 2009q).

4.5.2 Systematic literature search

To obtain pandemic A/H1N1 surveillance data for the UK, Germany and Spain a systematic literature search was accomplished using only Medline and Google Scholar. Therefore, there might have been more articles on pandemic A/H1N1 surveillance data in other databases (e.g. Embase) which have been neglected. In addition, one exclusion criteria was to eliminate articles in languages other than English and German. Thus, potential articles on Spanish pandemic A/H1N1 surveillance data might have been eliminated. Further, the additional search for pandemic A/H1N1 surveillance data on websites of national health authorities and international health agencies might have missed information that has already been removed from the websites.

4.5.3 Literature search on public health measures and official recommendations

Although a lot of information on public health measures taken and official health behavior recommendations released during the 2009 A/H1N1 pandemic was retrieved from grey literature and websites of the national health authorities and international health agencies, this search might have missed information that has already been removed from the websites or was not published. In addition, some information published in Spanish might have been neglected due to the language barrier.

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Annex

I Guidelines and recommendations released during the 2009 A/H1N1 pandemic

Guidelines	Spain	UK	Germany	International
March			**Information campaign:** "Wir gegen Viren" Campaign http://www.wir-gegen-viren.de/ [Accessed on 16.05.12] http://www.bzga.de/presse/pressearchiv/?jahr=2009&nummer=513	
April		**Information leaflet:** Important information about swine flu http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_098680.pdf [Accessed on 14.03.12]		
May **To be continued on next page**			**Information for general public:** Presentation on RKI website: Influenza Typ A/H1N1 http://www.pandemierisiko.info/ [Accessed on 15.03.12]	**Information for general public:** ECDC Health Information. Influenza A(H1N1) virus: how to protect yourself. http://www.ecdc.europa.eu/en/healthtopics/Documents/0905_Influenza_A%28H1N1%29_how_to_protect_yourself.pdf [Accessed on 11.03.12] ECDC Information for Travellers. Influenza A(H1N1). http://www.ecdc.europa.eu/en/healthtopics/Documents/0905_Influenza_AH1N1_Info_for_Travellers.pdf [Accessed on 11.03.12]

Guidelines	Spain	UK	Germany	International
May				ECDC Health Information. Personal protective measures for reducing the risk of acquiring or transmitting human influenza. http://ecdc.europa.eu/en/healthtopics/Documents/09_07_personal_protective_measures_ECDC-2009-0001-00-00-ENEN_final.pdf [Accessed on 11.03.12] **Information for policy makers:** ECDC public health guidance on case and contact management for the new influenza A(H1N1) virus infection. http://www.ecdc.europa.eu/en/publications/Publications/0905_GUI_Influenza_AH1N1_Public_Health_Guidance_on_Case_and_Contact_Management.pdf [Accessed on 11.03.12] Eurpoean Medicines Agency. Guidance for use of antiviral medicines http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2009/11/WC500011127.pdf [Accessed on 12.04.2012]

Guidelines	Spain	UK	Germany	International
June				**Information for policy makers:** ECDC Interim Guidance. Mitigation and delaying (or 'containment') strategies as the new influenza A(H1N1) virus comes into Europe. http://ecdc.europa.eu/en/publications/publications/0906_gui_influenza_ah1n1_mitigation_and_delaying_strategies_for_the_influenza_in_europe.pdf [Accessed on 11.03.12] New influenza A (H1N1) virus: WHO guidance on public health measures, 11 June 2009. http://www.who.int/wer/2009/wer8426.pdf [Accessed on 25.04.12]
July **To be continued on next page**		**Leaflets on control strategy:** Swine flu pandemic: from containment to treatment - guidance for the NHS http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_102021.pdf [Accessed on 14.03.12] Swine Flu: From Containment to Treatment. http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_101955.pdf [Accessed on 14.03.12]	**Information leaflets:** Tipps und Informationen zur Neuen Grippe A/H1N1 http://www.bundesregierung.de/Content/DE/Artikel/IB/Artikel/Themen/Gesellschaft/Gesundheit/2009-07-15-neue-grippe.html [Accessed on 16.05.12] And http://www.bundesregierung.de/Content/DE/Artikel/IB/Anlagen/2009-07-15-neue-grippe-englisch.pdf?__blob=publicationFile&v=2 [Accessed on 16.05.12]	**Information for healthcare professionals:** World Health Organization. Patient Care Checklist. http://www.who.int/csr/resources/publications/swineflu/ah1n1_checklist.pdf [Accessed on 18.02.12]

July		Swine Flu: From Containment to Treatment- Scientific Issue http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_101988.pdf [Accessed on 14.03.12] Swine Flu. UK Planning Assumptions http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_102891.pdf [Accessed on 14.03.12] (Updated 3 September, 22 October)	Schweinegrippe. Empfehlungen zum Verhalten im Verdachts- und Krankheitsfall http://www.bzga.de/presse/pressearchiv/?jahr=2009&nummer=538 [Accessed on 15.03.12] Influenza Typ A/H1N1 http://www.bundesaerztekammer.de/downloads/InfluenzaAH1N1.pdf [Accessed on 15.03.12]	**Information for policy makers:** European Centre for Disease Prevention and Control. Managing schools during the current pandemic (H1N1) 2009 – Reactive and proactive school closures in Europe. http://www.ecdc.europa.eu/en/activities/sciadvice/Lists/ECDC%20Reviews/ECDC_DispForm.aspx?List=512ff74f-77d4-4ad8-b6d6-bf0f23083f30&ID=631 [Accessed on 20.05.12] WHO recommendations on pandemic (H1N1) 2009 vaccines. http://www.who.int/csr/disease/swineflu/notes/h1n1_vaccine_20090713/en/index.html [Accessed on 16.05.12]
August **To be continued on next page**	**Public information campaign:** Gripe A. La prevención es la mejor medida http://www.msssi.gob.es/campannas/campanas09/informacionGripeA.htm [Accessed on 25.05.12] And http://www.informaciongripea.es [Accessed on 16.03.12] And http://www.facebook.com/informaciongripea [Accessed on 16.06.12]		**Press release:** Influenza A/H1N1: Hygiene- und Verhaltenstipps im Urlaub http://www.bzga.de/presse/pressearchiv/?jahr=2009&nummer=540 [Accessed on 15.03.12]	**Information for policy makers:** ECDC Health Education. On public health use of influenza antivirals during influenza pandemics (with particular reference to the pandemic (H1N1) 2009). http://www.ecdc.europa.eu/en/healthtopics/Documents/0908_Influenza_AH1N1_On_Public_Health_Use_of_Influenza_Antivirals_during_Influenza_Pandemics.pdf [Accessed on 25.05.12]

August	**Information for healthcare professionals:** Management of severe acute respiratory failure in patients with pneumonia caused by the new virus influenza A (H1N1) in the ICU http://www.msps.es/va/profesionales/saludPublica/gripeA/guiasProtocolosInf/pdf/ProtocoloGripeAenUCI.pdf [Accessed on 15.04.12] AEMPS. Use of antivirals in children under 1 year old, pregnant and breastfeeding women http://www.aemps.gob.es/informa/notasInformativas/medicamentosUsoHumano/2009/docs/NI-Oseltamivir-Zanamivir_agosto-2009.pdf [Accessed on 22.05.12]			ECDC Interim Guidance. Use of specific pandemic influenza vaccines during the H1N1 2009 pandemic. http://www.ecdc.europa.eu/en/publications/Publications/0908_GUI_Pandemic_Influenza_Vaccines_during_the_H1N1_2009_Pandemic.pdf [Accessed on 25.05.12] WHO: Safety of pandemic vaccines http://www.who.int/csr/disease/swineflu/notes/h1n1_safety_vaccines_20090805/en/index.html [Accessed on 23.04.2012]
Guidelines	**Spain**	**UK**	**Germany**	**International**
September **To be continued on next page**	**Information on preventive measures:** Guide for families http://www.msc.es/servCiudadanos/alertas/pdf/09-09-10_guia_gripe_A_Familias.pdf [Accessed on 16.04.12] Guide for schools http://www.msc.es/servCiudadanos/alertas/pdf/09-09-10_Recomendaciones_AmbitoEscolar.pdf [Accessed on 16.04.12]	**Information for policy-makers:** Swine Flu. UK Planning Assumptions http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_104843.pdf [Accessed on 13.05.12] **Information for healthcare professionals:** Pandemic influenza. Recommendations on the use of antiviral medicines for pregnant women, women who are breastfeeding and children under the age of one year. http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_106148.pdf [Accessed on 14.03.12]	**Information for healthcare professionals:** Fachliche Information für Ärzte und Apotheker: Pandemie-Impfstoffe in der Schwangerschaft – Sicherheitsaspekte http://www.pei.de/cln_101/nn_158122/DE/arzneimittelsicherheit-vigilanz/archiv-sicherheitsinformationen/archiv-infos-influenza-pandemie-2009-2010/schwangerschaft-04-09-2009-pandemie-impfstoffe.html [Accessed on 11.06.12]	**Information for policy-makers:** ECDC Technical Report. Guide to public health measures to reduce the impact of influenza pandemics in Europe: 'The ECDC Menu' http://www.ecdc.europa.eu/en/publications/Publications/0906_TER_Public_Health_Measures_for_Influenza_Pandemics.pdf [Accessed on 12.04.2012]

September	Guide for kindergarten http://www.msc.es/servCiudadanos/alertas/pdf/09-09-11-Guarderias.pdf [Accessed on 16.04.12] **Information for healthcare professionals:** Prevention measures and treatment of pregnant women http://www.msc.es/profesionales/saludPublica/gripeA/guiasProtocolosInf/pdf/09-10-09_Embarazada.pdf [Accessed on 18.04.12] Clinical management of adults with pneumonia during the H1N1 pandemic http://www.msc.es/profesionales/saludPublica/gripeA/guiasProtocolosInf/pdf/neumonia.pdf [18.04.12]			
Guidelines	**Spain**	**UK**	**Germany**	**International**
October **To be continued on next page**	**Information for healthcare professionals:** Guideline for Prevention and control measures in retirement homes http://www.msps.es/va/profesionales/saludPublica/gripeA/guiasProtocolosInf/pdf/09-12-02_ResidenciasPersonasMayores.pdf [Accessed on 05.04.12]	**Information for healthcare professionals:** Antiviral prophylaxis. Guidance on the use of prophylaxis with antiviral medicines during the H1N1 (swine flu) pandemic http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_107132.pdf [Accessed on 14.03.12]	**Information for healthcare professionals:** STIKO-Empfehlung zur Impfung gegen die Neue Influenza A (H1N1) http://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2009/Ausgaben/41_09.pdf?__blob=publicationFile [Accessed on 26.04.12] **Information campaign for children:** Das Medienpaket „schütz ich mich - schütz ich dich“ http://www.bzga.de/presse/pressearchiv/?jahr=2009&nummer=551 [15.03.12]	

October **To be continued on next page**	Recommendation for primary care professionals on diagnostic and treatment of H1N1 infections http://www.msc.es/profesionales/saludPublica/gripeA/guiasProtocolosInf/pdf/09-12-02-atencionPrimaria.pdf [Accessed on 19.04.12]	Swine Flu. Guidance for planners http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/@sta/@perf/documents/digitalasset/dh_107428.pdf [Accessed on 14.03.12] **Vaccination campaign:** Swine flu vaccination: what you need to know. http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/@sta/@perf/documents/digitalasset/dh_109109.pdf [Accessed on 14.03.12] **Information for healthcare professionals:** Health and Social Care Workers and Pandemic Influenza. Information for staff who are pregnant or in other at-risk groups http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_108365.pdf [Accessed on 14.03.12] Clinical Professionals Brief on Swine Flu Vaccination http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_107651.pdf [Accessed on 14.03.12] Pandemic H1N1 2009 Influenza: Clinical Management Guidelines for Adults and Children http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/@sta/@perf/documents/digitalasset/dh_110617.pdf [Accessed on 14.03.12]	**Information for healthcare professionals:** RKI-Ratgeber Infektionskrankheiten – Merkblätter für Ärzte: Influenza http://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2009/Ausgaben/43_09.pdf?__blob=publicationFile [15.03.12] Die Impfung zum Schutz vor der Neuen Influenza A (H1N1) – Hinweise für das medizinische Personal http://www.aerztekammer-hamburg.de/aerzte/Pandemie/Hinweise_medizinisches_Personal_092010.pdf [Accessed on 19.04.12] or http://www.dkgev.de/dkg.php/aid/6630/cat/43 [Accessed on 19.04.12] **Information on website:** Was Sie über die Neue Grippe („ Schweinegrippe“) wissen müssen https://www.bundesgesundheitsministerium.de/fileadmin/redaktion/pdf_publikationen/62100211-Neue-Grippe-Faltblatt_200912.pdf [Accessed on 15.03.12] **Vaccination campaign:** Impfung gegen die Neue Grippe („ Schweinegrippe“) https://www.bundesgesundheitsministerium.de/fileadmin/redaktion/pdf_publikationen/62100212-Neue-Grippe-Impfen-Faltblatt_200912.pdf [Accessed on 22.02.12]	

October		Pandemic H1N1 2009 Influenza: Clinical Management Guidelines for Pregnancy http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/@sta/@perf/documents/digitalasset/dh_110618.pdf [Accessed on 14.03.12]	**Leaflets for specific target groups:** Impfung gegen die Neue Grippe („Schweinegrippe“). Information für Menschen mit chronischen Erkrankungen http://www.thueringen.de/imperia/md/content/tmsfg/aktuell/h1n1/rz_final_chron.erkrankungen.pdf [Accessed on 16.05.12] Impfung gegen die Neue Grippe („Schweinegrippe“). Information für medizinisches Personal http://www.cremlingen.de/content/files/downloads/merkblatt_med_pers.pdf [16.05.12] Impfung gegen die Neue Grippe („Schweinegrippe“). Information für Angehörige von Polizei und Feuerwehr http://www.muenster.de/stadt/gesundheitsamt/pdf/neue-grippe_polizei-feuerwehr.pdf [Accessed on 16.05.12] Impfung gegen die Neue Grippe („Schweinegrippe“). Information für Schwangere http://www.berlin.de/imperia/md/content/landesverwaltungsamt/beihilfe/formulareundmerkblaetter/mb_bm_ges_schweinegrippeinfo_fuer_schwangere.pdf?start&ts=1256892413&file=mb_bm_ges_schweinegrippeinfo_fuer_schwangere.pdf [16.05.12]	

Guidelines	Spain	UK	Germany	International
November	**Vaccination campaign:** http://www.informaciongripea.es [Accessed on 16.03.12] And http://www.informaciongripea.es/descargas/fichas/fase2/FICHA_VACUNACION_INGLES_baja.pdf [Accessed on 28.11.11]	**Information for specific target groups:** Swine Flu and Pregnancy. How to protect yourself and your baby. http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_108154.pdf [Accessed on 14.03.12] **Leaflets for health professionals:** Swine Flu. If you can´t catch it, you can´t pass it on http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/@sta/@perf/documents/digitalasset/dh_108392.pdf [Accessed on 14.03.12]	**Information on non-pharmaceutical response measures:** Zur Schließung von Kinder-gemeinschaftseinrichtungen im Zusammenhang mit Neuer Influenza A/H1N1 http://edoc.rki.de/documents/rki_fv/rewA1WUoUgosU/PDF/217OmEJPp5k2g_01.pdf [Accessed on 11.11.11]	**Information on vaccination:** ECDC: Q&A for the general public on vaccines and vaccination in relation to the A(H1N1) pandemic. http://www.ecdc.europa.eu/en/healthtopics/pandemic_preparedness/2009_pandemic_vaccines/Pages/QA_gp_pandemic_vaccines.aspx [Accessed on 18.02.12] ECDC: Q&A for health professionals on vaccines and vaccination in relation to the A(H1N1) pandemic. http://www.ecdc.europa.eu/en/healthtopics/pandemic_preparedness/2009_pandemic_vaccines/Pages/QA_hp_pandemic_vaccines.aspx [Accessed on 18.02.12] European Medicines Agency reaffirms efficacy and safety of H1N1 pandemic vaccines http://www.emea.europa.eu/docs/en_GB/document_library/Press_release/2009/11/WC500015558.pdf [Accessed on 21.04.2012] WHO: Safety of pandemic vaccines http://www.who.int/csr/disease/swineflu/notes/briefing_20091119/en/index.html [23.04.2012]

Guidelines	Spain	UK	Germany	International
December	**Information for healthcare professionals:** Agencia Española de Medicamentos y Productos Sanitarios. Official recommendations on the vaccination program http://www.aemps.gob.es/informa/notasInformativas/medicamentosUsoHumano/vacunas/2009/docs/NI_campana-vacunacion-H1N1_recomendaciones-oficiales.pdf [25.05.12]	**Information for specific target groups:** Swine Flu Vaccination: information for parents of children over six months and under five years old http://www.direct.gov.uk/prod_consum_dg/groups/dg_digitalassets/@dg/@en/documents/digitalasset/dg_183752.pdf [Accessed on 14.03.12]	**Information for healthcare professionals:** Mitteilung der Ständigen Impfkommission (STIKO) am Robert Koch-Institut. Impfung gegen die Neue Influenza A (H1N1). Erneute Bewertung der Daten am 24.11.2009 **And** Ergänzende Hinweise des Paul-Ehrlich-Instituts und des Robert Koch-Instituts zur Impfung gegen die Neue Influenza A (H1N1) http://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2009/Ausgaben/50_09.pdf?__blob=publicationFile [Accessed on 26.04.12]	
January		**Information leaflet:** Swine Flu. Information for asylum seekers, refugees and foreign nationals in the UK http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_110808 [Accessed on 14.03.12]		

II Data used for epidemic curves

Week	New A/H1N1 cases per week Germany	New A/H1N1 cases per week UK	New A/H1N1 cases per week England	Total number England	Estimated A/H1N1 cases in England	Estimates lower limit England	Estimates upper limit England	A/H1N1 sentinel detections Spain	A/H1N1 non sentinel detections Spain	Total number per week Spain	A/H1N1 incidence rate per 100.000 Spain
27.04.2009	0	2									
29.04.2009	3	3									
18	6	15									
19	5	32						0	3	3	0
20	3	40						0	1	1	4,63
21	3	35						0	4	4	9,27
22	3	63		171				1	9	10	8,34
23	29	196	142	313				2	0	2	6,44
24	154	369	164	477				8	6	14	10,74
25	129	832	585	1.062				12	7	19	9,21
26	97	1.672	1.480	2.542				16	34	50	11,63
27	162	3.675	3.162	5.704				21	101	122	11,46
28	243	2.789	2.500	8.204				72	158	230	33,75
29	984	931	681	8.885	100.000			94	229	323	41,84
30	2.627	510	664	9.549	110.000	60.000	160.000	69	106	175	36,04
31	3.518	705	597	10.146	30.000	15.000	85.000	63	85	148	32,89
32	2.637	397	324	10.470	25.000	15.000	60.000	59	47	106	37,67
33	2.230	459	361	10.831	11.000	6.000	25.000	64	70	134	41,17
34	2.110	237	154	10.985	5.000	3.000	12.000	115	94	209	53,61
35	1.321	138	76	11.061	4.500	2.500	10.000	72	86	158	51,75
36	1.051	97	55	11.116	3.000	1.500	6.500	56	55	111	41,97
37	829	130	39	11.155	5.000	3.000	11.000	66	49	115	52,35
38	750	149	73	11.228	9.000	5.000	20.000	109	66	175	77,88

39	873	299	103	11.331	14.000	7.000	30.000	139	83	222	94,72
40	1.294	344	179	11.510	18.000	9.000	38.000	209	112	321	98,65
41	1.535	455	189	11.699	27.000	13.000	58.000	182	125	307	101,22
42	1.875	987	463	12.162	53.000	27.000	115.000	350	202	552	182,45
43	3.318	1.389	822	12.984	78.000	39.000	169.000	529	493	1022	292,94
44	9.435	1.678	852	13.836	84.000	42.000	181.000	482	498	980	327,92
45	23.480	2.024	1.119	14.955	64.000	32.000	140.000	496	605	1101	359,85
46	42.261	1.693	939	15.894	53.000	26.000	114.000	484	767	1251	371,68
47	46.767	1.422	781	16.675	46.000	23.000	99.000	303	585	888	243,71
48	30.494	1.380	909	17.584	22.000	11.000	47.000	215	378	593	151,42
49	15.881	968	605	18.189	11.000	6.000	24.000	63	234	297	77,72
50	9.624	783	533	18.722	9.000	4.500	19.000	72	153	225	78,55
51	6.160	571	424	19.146	6.000	3.000	13.000	38	84	122	40,8
52	2.182	362	324	19.470				10	53	63	37,5
53	1.233	309	243	19.713						46 (23 week53 + 23 week 1)	29,8
1	1.088	321	282	19.995				8	38		29,8
2	519	234	174	20.169				8	14	22	29,92
3	369	133	103	20.272				1	5	6	21,6
4	282	101	77	20.349				5	2	7	18,41
5	102	49	28	20.377				1	1	2	18,69
6	75							1	1	2	15,74
7	35	98		20.458				0	3	3	14,51
8	69							1	0	1	11,32
9	43	65		20.511				1	0	1	10,33
10	29							1	1	2	10,01
11	22	26		20.533				1	2	3	10,94
12	26							3	0	3	8,6
13	13	32		20.565				0	1	1	5,25

(Source: Centro Nacional de Epidemiología. Instituto de Salud Carlos III, 2009a, 2010; Health Protection Agency, 2010a; Robert Koch-Institut. Arbeitsgemeinschaft Influenza, 2010)

Erklärung zur eigenständigen Verfassung der vorliegenden Thesis

Ich versichere hiermit, dass ich die vorliegende Master Thesis mit dem im Ausgabeantrag formulierten Thema ohne fremde Hilfe selbständig verfasst und nur die angegebenen Quellen und Hilfsmittel verwendet habe. Wörtlich oder dem Sinn nach aus anderen Werken entnommene Stellen sind unter Angabe der Quellen kenntlich gemacht.

Datum: 17.10.2012

Verena Keßler