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Spotlight on measles 2010: Preliminary report of an ongoing measles outbreak in a subpopulation with low vaccination coverage in Berlin, Germany, January-March 2010

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Since early January 2010, Berlin has been experiencing a measles outbreak with 62 cases as of 31 March. The index case acquired the infection in India. In recent years, measles incidence in Berlin has been lower than the German average and vaccination coverage in school children has increased since 2001. However, this outbreak involves schools and kindergartens with low vaccination coverage and parents with critical attitudes towards vaccination, which makes the implementation of public health interventions challenging.

Background

Since the implementation of the new national Protection Against Infection Act (Infektionsschutzgesetz; IfSG) in Germany in 2001, clinically suspected measles cases as well as laboratory confirmation for measles has to be reported to the District Health Offices [1]. The District Health Office evaluates the information according to the case definition for measles [2] and enters case-based data into the electronic reporting system. Since 2001, the number of measles cases and the annual measles incidences in Berlin have been low compared with the national average. The highest annual number of measles cases in Berlin was reported in 2006 (n=57). The annual incidences ranged from 0.06 to 1.51 cases per 100,000 inhabitants in Berlin compared with 0.15 and 7.32 per 100,000 country-wide (Table) [3]. The measles vaccination coverage in children at school entrance examination has increased significantly during the past years. In 2001, 91.2% of children presented with at least one measles vaccination at school entry and only 24.0% had two vaccinations [4]. In 2008, 95.2% were vaccinated once and 88.2% twice against measles [5]. In the neighbouring Federal State of Brandenburg the vaccination coverage is significantly higher: 93.4% of children had two measles vaccinations at school entry in 2008 [6]. Despite these efforts, a measles outbreak with so far 62 cases was observed in Berlin between early January and 31 March 2010.

Outbreak description

The index case of this outbreak, a secondary school student from Berlin was diagnosed on 5 January 2010. The patient was not vaccinated against measles and the medical history pointed to travel-related acquisition of the infection, since he had travelled to India at the end of 2009. The diagnosis was laboratory-confirmed on 14 January 2010 and the result was reported to the responsible District Health Office on 15 January 2010. Since samples of the index case were not available, PCR was performed at the National Reference Centre for Measles, Mumps and Rubella at the Robert Koch-Institute (RKI) on a sample of a related case diagnosed on 19 January 2010. This analysis confirmed measles virus genotype D8 (MVs/Berlin.DEU/03.10) which is identical to viruses endemic in India (MVs/Imphal.IND/19.09) and therefore supported introduction from the Indian subcontinent. To date, genotyping revealed measles virus genotype D8 in 13 cases. However, genotyping is not yet completed for all cases. There is evidence that some of the measles cases currently observed in Berlin are not linked to the outbreak. These infections might be concurrently imported from other regions (e.g. Bulgaria, South Africa). Epidemiological and laboratory investigations are ongoing to clarify the situation thoroughly.

As of week 12, 2010, the total number of cases has reached 62. So far, the outbreak has affected 52 residents living in four of the twelve Districts of Berlin (Figure 1) and 10 residents of the surrounding Federal State of Brandenburg. The number of cases per week related to the outbreak is shown in Figure 2. The index patient is attending a private school (Waldorf-Schule; anthroposophic education). The proportion of students vaccinated against measles in this school is estimated to be significantly below 70%. Parents sending their children to Waldorf schools and kindergartens are known for their critical attitudes towards vaccinations in general and especially with regards to measles vaccination. Thus, the outbreak spread mainly among unvaccinated children and adolescents attending Waldorf institutions (schools and kindergartens in two districts) and their siblings. In addition, children and adolescents attending public schools and kindergartens were exposed and infected via direct contacts with Waldorf students and their families. None of the reported cases had been vaccinated against measles before being exposed during this outbreak (some children received an active post-exposure vaccination). All measles cases resident in Brandenburg were students attending schools in Berlin or unvaccinated siblings of such students. No measles transmission was observed in schools and kindergartens in this Federal State. The mean age of the cases was 10.5 years (range: 1-18 years). To date, there have not been any reports of hospitalisations or complications due to measles infections in connection with this outbreak.

Public health intervention and challenges

After diagnosis of the index case in early January the responsible District Health Offices implemented public health interventions according to the Protection Against Infection Act to interrupt the spread of measles. The measures included:

- Temporary exclusion of students and teachers without measles vaccination or naturally acquired immunity from schools with confirmed measles cases;
- Offering measles vaccination for unvaccinated students and teachers in affected schools (vaccinations in collaboration with private practitioners);
- Equivalent measures in kindergartens with measles cases;
- Active detection of contacts and exposed persons;
- Sampling of clinical material from measles patients to confirm diagnosis and perform genotyping at the National Reference Centre for Measles, Mumps and Rubella;
- Recommendation of temporary restrictions of private contacts with unprotected persons and of any public activities in groups for patients and their unvaccinated family members;
- Public health information to increase regional clinicians' alertness regarding measles in their area;
- Enhanced communication with educational institutions and parents with critical attitudes towards vaccination of the children.

These measures showed some success. The peak of the outbreak was seen in the week 5, 2010 (n=17), with decreasing case numbers in the following weeks. However, only few of the offered measles vaccinations were accepted (numbers are currently not available because the exposed unvaccinated children were sent to private practitioners for measles vaccinations). Four students developed measles after receiving a post-exposure measles vaccination (vaccination 4–5 days after the last contact). This observation underlines the importance to apply active vaccination earlier after exposure (preferably within three days after first exposure); furthermore passive vaccination with the specific immunoglobulin should be considered for effective individual post-exposure measles prevention. After the initial peak, the outbreak continued to spread on a relatively low level, and the first case in a district not directly neighbouring the district of residence of the index case occurred at the end of week 11 (Figure 1). Currently most concern is directed towards a

Table

Number of reported measles cases, measles incidence and measles vaccine coverage at school entry examination in the Federal State of Berlin and in Germany 2001–2008

	Case reports				Vaccination coverage	
	Berlin		Germany			Germany
	n	n/100,000	n	n/100,000	1st/2nd dose (%)	1st/2nd dose (%)
2001	51	1.51	6,037	7.32	91.2 / 24.0	91.4 / 25.9
2002	24	0.71	4,656	5.64	not available	91.3 / 33.1
2003	2	0.06	777	0.94	not available	92.5 / 50.9
2004	11	0.32	123	0.15	93.4 / 71.7	93.3 / 65.7
2005	39	1.15	781	0.95	93.5 / 78.8	94.0 / 76.6
2006	57	1.67	2,308	2.80	93.8 / 83.6	94.5 / 83.2
2007	8	0.23	566	0.69	94.5 / 86.8	95.4 / 88.4
2008	29	0.85	916	1.11	95.2 / 88.2	95.9 / 91.3

Source: [3-5].

Waldorf kindergarten in a neighbouring district with a measles vaccination coverage of less than 60%.

In early February, parents whose children were affected by the temporary school exclusion filed an action against the respective District Health Office at the Berlin Administration Court. The claim argued that the health authority's decision impeded the unvaccinated children's rights to visit school and to acquire immunity against measles through natural infection. Measles was claimed to be a harmless infection in children without severe complications and possible long-term disabilities. The specific vaccination against measles was perceived to be inefficient and dangerous. However, in mid-February the Berlin Administrative Court decided to dismiss the claim and declared that the measures taken by the public health authorities had been adequate to contain the outbreak. However, further claims are pending at the Berlin High Administrative Court.

For now, parents must be aware that their unvaccinated children can acquire the infection while travelling in regions with endemic measles or ongoing measles outbreaks. Physicians should be encouraged to focus on parents with unvaccinated children and strongly recommend active measles vaccination before travelling.

Conclusion

We give a preliminary overview of a measles outbreak in Berlin. There is epidemiological and laboratory-confirmed evidence that the index case acquired the infection when travelling in India. The outbreak affected unvaccinated children and adolescents whose parents

Figure 1

Measles outbreak, cases by district, Berlin, 5 January-31 March 2010 (n=52)

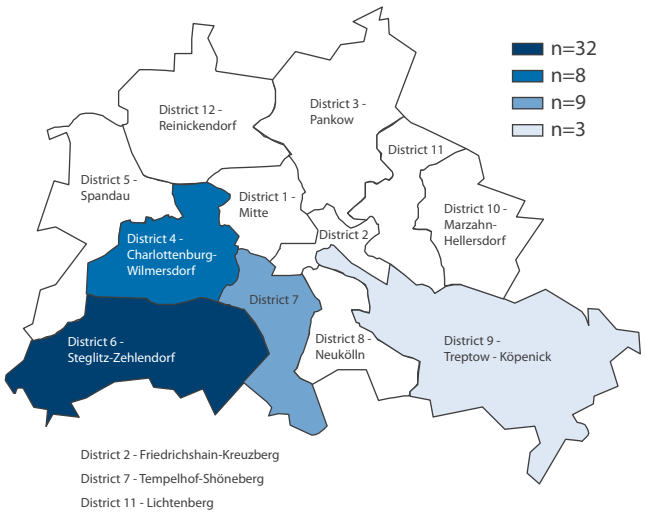
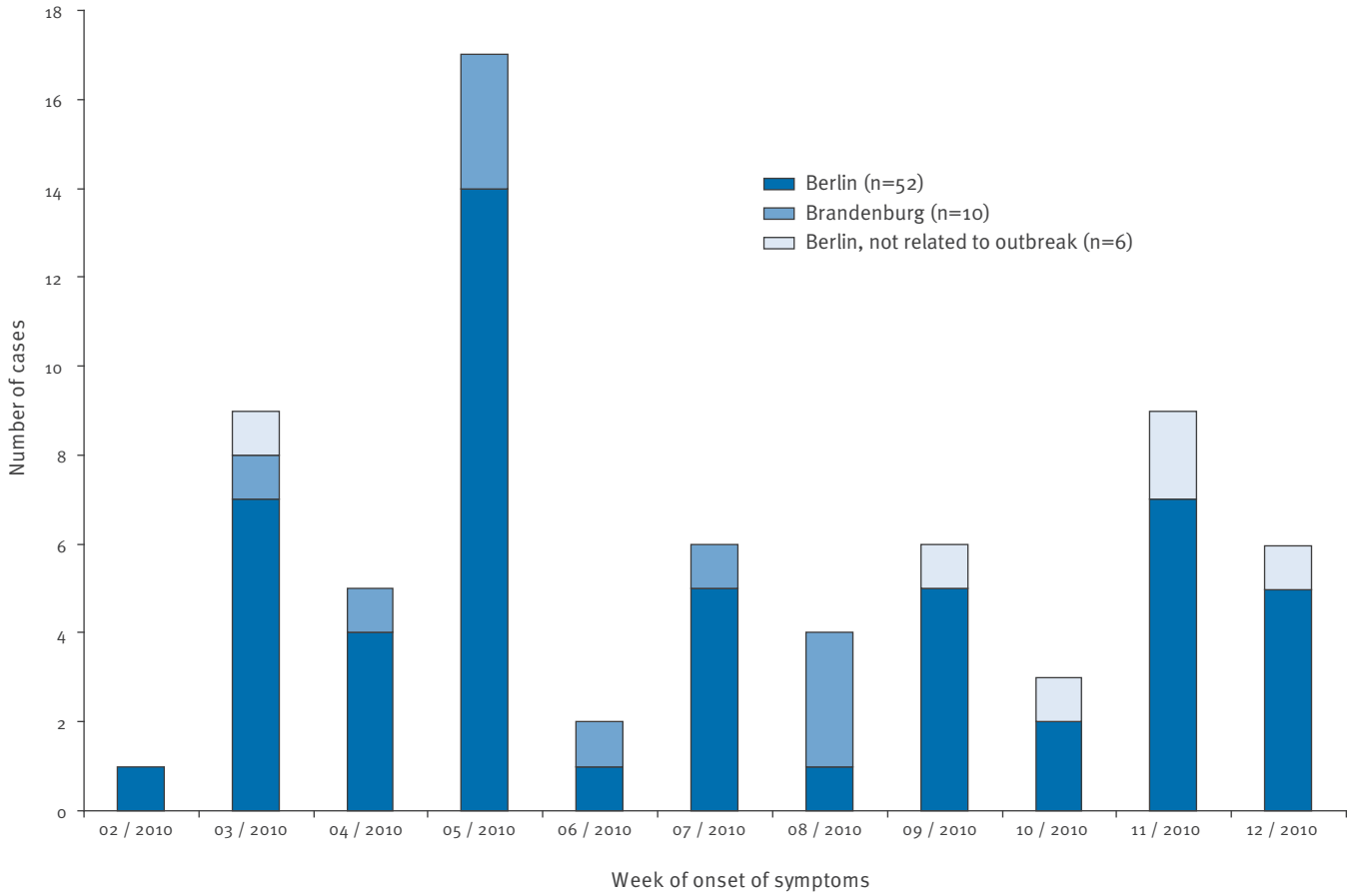


Figure 2

Measles outbreak, cases by week of onset of symptoms and place of residence including reported cases from week 2 to 12 2010 (n=62 outbreak-related cases, n=6 cases not related with the outbreak)



are known to have critical attitudes towards measles vaccination. Although vaccination coverage in Berlin has increased significantly in general, measles transmission chains can still be established in schools and kindergartens with high proportions of unvaccinated children. Public health authorities were extremely challenged in this situation because the measures taken according to infectious disease protection legislation were not generally accepted by the parents. Thus measles could be re-introduced and continue to spread on a low level within the unvaccinated parts of the population in Berlin for a not clearly foreseeable time.

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Chikungunya fever in two German tourists returning from the Maldives, September, 2009

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This report describes the first isolation and molecular characterisation of a chikungunya virus from two German tourists who became ill after a visit to the Maldives in September 2009. The virus contained the E1 A226V mutation, shown to be responsible for an adaptation to the Asian tiger mosquito *Aedes albopictus*. The E1 coding sequence was identical to chikungunya virus isolates from Sri Lanka and showed three nt-mismatches to the only available E1 nt sequence from the Maldives.

Introduction

Since the start of the current chikungunya fever pandemic on the east coast of Africa in 2005, many cases have been reported in countries in Asia and south-east Asia [1,2]. These cases were attributed to a particular chikungunya virus (CHIKV) strain that has adapted to very efficient transmission to humans via the Asian tiger mosquito (*Aedes albopictius*) due to a A226V mutation in the E1 envelope protein [3,4]. The Maldives were first hit by the chikungunya virus pandemic in late 2006 after the wet season which usually lasts until September. Based on almost 12,000 suspected cases of chikungunya fever the disease was reported on 121 of the 197 inhabited islands with incidence rates between 82 and 722 per 1,000 population [5]. A small set of blood samples from febrile patients with symptoms meeting the chikungunya fever case definition at that time confirmed CHIKV as causative agent in 64 of 67 cases by reverse-transcription PCR (RT-PCR) [5]. However, no further characterisation of the virus strain responsible for the 2006-7 outbreak was performed. One case of a traveller returning to Singapore in January 2007 was confirmed by RT-PCR and the nt sequence of the E1 gene was determined [6]. In early 2009, an outbreak of a viral fever with symptoms including myalgia or arthralgia and rash occurred on several islands of the Laamu Atoll about 400 km south of Malé [7], but no further virological investigation was carried out to determine whether this was due to dengue or chikungunya fever.

Case report and laboratory findings

Between 1 and 10 September 2009, a German couple visited the Dhiffushi Holiday Island resort at the southern tip of the Ari Atoll, the Maldives (Figure 1), together with their seven year-old son. They flew directly from Munich to Malé with a stopover in Dubai, United Arab Emirates.

Two and three days respectively after the family had returned to Munich, the son and the 35 year-old father developed symptoms compatible with either dengue or chikungunya fever (Table) while the wife stayed healthy. A test for dengue virus showed neither virus RNA nor anti-dengue virus (DENV) IgM for both patients, but the father had IgG antibodies reactive against DENV indicating an earlier anamnestic dengue fever or a cross-reaction with an earlier flavivirus vaccination. CHIKV-specific real-time RT-PCR yielded ct-values of 23 (son) and 22.5 (father) in the respective acute serum samples obtained on 14 September, indicating high-level viremia [8,9]. Chikungunya virus was isolated in Vero B4 cells from both sera and the entire nucleotide sequence of the isolate from the father was determined. The viral genome was 11,811 nucleotides in length and showed high levels of identity with the pandemic CHIKV that is circulating in many parts of the Indian subcontinent and other parts of Asia since 2006. Most interestingly the CHIKV isolate from the Maldives contained the A226V change in the E1 glycoprotein which has been shown to be responsible for shorter extrinsic incubation periods in *Aedes albopictus* mosquitoes [4]. While the son made an uneventful recovery after one week of symptoms, the father developed persisting arthralgias with limited mobility in the affected extremities and still requires analgesic treatment (Table).

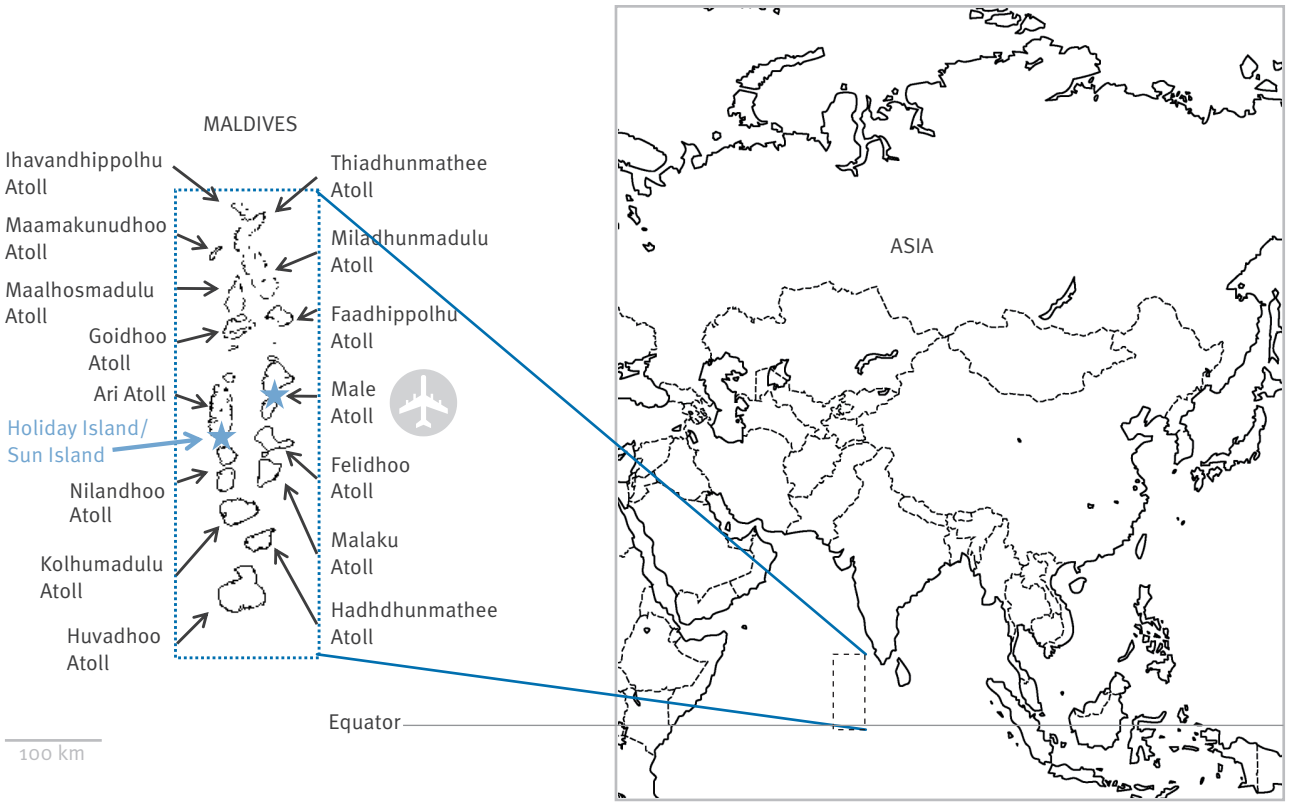
Discussion

Together with a very recent report on chikungunya fever in a French traveller returning from the northern part of Malé Island, Maldives, in October 2009 [10], our findings suggest a continuous circulation of CHIKV also in other parts of the Maldives. The family stayed

on Dhiffushi Holiday Island throughout their holidays with a daytrip to the neighboring Sun Island. Malé with its international airport was only visited for the intercontinental flight connection, leaving not much time to become exposed to mosquito bites. We cannot rule out that both infections were acquired while waiting at the airport, because this would fit well with both the incubation period of the disease and with the previous case

Figure 1

Location of Holiday and Sun Islands on the southernmost rim of the south Ari Atoll, about 100 km away from Male International Airport



Table

Clinical and laboratory data of patients diagnosed with chikungunya fever, Germany, September 2009

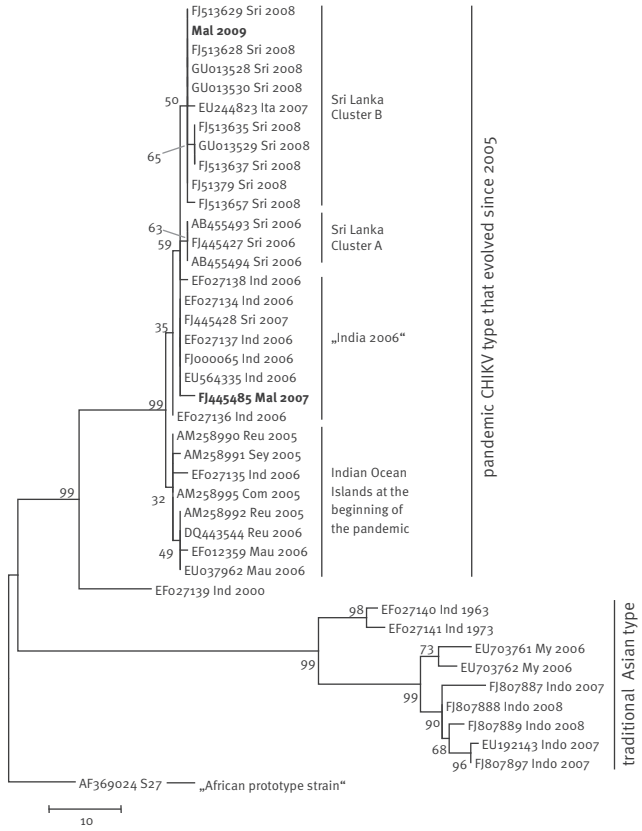
Patient	Son (7 years)	Father (35 years)
Travel schedule	Munich-Dubai-Male and back on 1-10 September, 2009	Munich-Dubai-Male and back on 1-10 September, 2009
Onset of disease	12 September 2009	13 September 2009
Clinical presentation	Fever 39.5°C	Fever 39.0°C
	Headache	Ague, retrobulbar pressure and pain, arthritis of both wrists and ankles
	Macular and partially confluent exanthema (mainly on face and torso)	Erythema, macular and partially confluent exanthema (mainly on torso and arms)
Laboratory findings	Leucocytes 2,700/µl CRP 2.5 mg/dl	Leucocytes 5,300/µl CRP 13 mg/dl Creatinine 1.4 mg/dl
	CHIKV RT-PCR positive	CHIKV RT-PCR positive
	DENV RT-PCR negative	DENV-PCR negative; anti-DENV IgG 15E
Therapy	Paracetamol, Ibuprofen	Paracetamol, Ibuprofen
Further course	Since 16 September fever-free, exanthema gone on 17 September, no further complications since then	Since 16 September fever-free and creatinin back to normal (1.1 mg/dl), exanthema gone, but arthralgias of ankles, wrists, and digital joints persist for more than six months including limited mobility and requiring NSAID treatment

CRP: C-reactive protein; CHIKV: Chikungunya virus; DENV: Dengue virus; RT-PCR: reverse transcription-polymerase chain reaction; NSAID: non steroidal anti-inflammatory drugs

report of the French traveller, who became infected while staying at the Malé Atoll. However, given the high incidence rates of 65.2 per 1,000 population previously reported for the Ari Atoll [5], both infections could likewise have been acquired on Holiday Island. Further, a considerable number of people travel constantly between India and Sri Lanka and the tourist resorts on the Atolls' islands of the Maldives where they are employed. This frequent exchange may argue for a repeated and renewed introduction of CHIKV from India or Sri Lanka via viraemic workers or tourists and limited local transmission through aedine mosquitoes at the respective islands. Analyses of the E1 gene revealed three nt-mismatches when compared to the 2007 case that was analysed in Singapore [6], but identical nt sequences to a series of CHIKV strains from Sri Lanka (Figure 2) [6,11].

Figure 2

Phylogenetic relationship generated by Maximum Parsimony method as implemented in MEGA4 based on the complete E1 protein coding sequence (1314 nt) of a set of CHIKV of different geographic origin



Sequence data are provided with their accession number, country and year. The term Cluster A and B for sequence data from Sri Lanka is adapted from [10]. Please note that the only available CHIKV E1 sequence from the Maldives from 2007 clusters together with CHIKV from India from 2006, while the CHIKV reported here is part of the Cluster B from Sri Lanka in 2008. Sri = Sri Lanka, Mal = Maldives, Ita = Italy (imported from India in 2007), Ind = India, Reu = Reunion, Sey = Seychelles, Com = Comores, Mau = Mauritius, My = Malaysia, Indo = Indonesia. The percentage of replicate trees in which the associated taxa clustered together in the bootstrap test (100 replicates) are shown next to the branches. The branch lengths are informative (bar length corresponds to 10 nt- differences)

It will be seen in the near future whether more cases of chikungunya fever will be reported for the Maldives, but we feel that this is already an issue in travel medicine although the German Robert Koch Institute reported only three chikungunya fever cases in returning travellers from the Maldives in 2009 (two of which we describe here). A crucial question concerning the current global situation on chikungunya fever is the adaptation of the pandemic CHIKV strain to *Ae. albopictus*. *Aedes aegypti* has been long known to occur on several islands of the Maldives and seems to be the predominant vector on Malé itself while *Ae. albopictus* has established foci on other islands where it seems to be the main mosquito vector species [5]. We do not know which Aedes species has infected the German tourists, but we do know that the A226V mutation is suggestive for *Ae. albopictus* as the vector. This particular mosquito is present in many areas around the Mediterranean Sea and was responsible for a CHIKV outbreak in Italy in 2007 resulting in more than 300 cases [12,13]. With a continuing circulation of CHIKV in major tourist destinations in Asia and Africa, imported cases of chikungunya fever will also be seen in Europe and North America. In countries were *Ae. albopictus* is abundant, returning viraemic tourists could cause smaller outbreaks.

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First evidence of a food poisoning outbreak due to staphylococcal enterotoxin type E, France, 2009

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At the end of 2009, six food poisoning outbreaks caused by staphylococci were reported in France. Soft cheese made from unpasteurised milk was found to be the common source of the outbreaks. Staphylococcal enterotoxin type E was identified and quantified in the cheese using both official and confirmatory methods of the European Union Reference Laboratory (EU-RL). To our knowledge, this is the first report of food poisoning outbreaks caused by staphylococcal enterotoxin type E in France.

Introduction

Staphylococcal food poisoning is one of the most common food-borne diseases worldwide [1] resulting from the ingestion of staphylococcal enterotoxins preformed in food by enterotoxigenic strains of coagulase-positive staphylococci, mainly *S. aureus*. As staphylococcal enterotoxins are heat stable, they may be present in food when *S. aureus* are absent [2]. Moreover, not all strains of *S. aureus* are enterotoxigenic. Therefore, a conclusive staphylococcal food poisoning diagnosis is mainly based on the detection of staphylococcal enterotoxins in food. To date, 21 staphylococcal enterotoxins have been described: staphylococcal enterotoxin (SE) A (SEA) to SEIV all possess superantigenic activity whereas only some (SEA to SEI, SER, SES and SET) have been proven to be emetic [3]. These toxins are produced by enterotoxigenic strains of coagulase-positive staphylococci (mainly *S. aureus*) in food with high protein content.

In October and November 2009, six household staphylococcal food poisoning outbreaks were notified in six French metropolitan départements. During the investigation, which was carried out by interviewing cases specifically focussing on food consumed, it became clear that a soft cheese made from unpasteurised cow milk was the likely common and single source of these outbreaks as all cases had eaten the same cheese. Cheese samples were available from six outbreaks and the staphylococcal food poisoning diagnosis was confirmed through (i) the high count of coagulase-positive staphylococci, (ii) the detection of staphylococcal enterotoxin E in the incriminated cheese type and (iii) the detection of the *see* gene in coagulase-positive staphylococci isolates from the suspected cheese samples.

Methods

Epidemiological data

All the epidemiological data concerning these outbreaks (number of cases, symptoms, location, type of potentially incriminated food) were collected by interviews or questionnaires by the local health authorities (DDASS). At the same time, the tracing of incriminated food was performed by the local services of the French Ministry of Food, Agriculture and Fishery.

Counts and characterisation of coagulase-positive staphylococci strains

Coagulase-positive staphylococci were counted in suspected cheese samples by laboratories involved in food surveillance using the standard method EN ISO 6888 part 2 as described in the relevant European Union (EU) legislation [4]. Coagulase-positive staphylococci isolates were tested for enterotoxin genes by PCR targeting the *S. aureus* 23S rRNA gene and biotyped as described by Kerouanton *et al.* [5]. The isolates were tested for *sea-e*, *seg-j*, *ser* and *sep* genes using two multiplex PCR assays according to the procedures of the EU Reference Laboratory (EU-RL) for coagulase-positive staphylococci. The isolates were also typed by pulsed-field gel electrophoresis (PFGE) according to Kerouanton *et al.* [5].

Sample preparation and immunoenzymatic detection of staphylococcal enterotoxins

The detection of staphylococcal enterotoxin types A to E was performed according to the EU-RL screening method for coagulase-positive staphylococci [6]. This method consists of an extraction step followed by dialysis concentration and an immuno-enzymatic detection using the Vidas SET2 kit (BioMérieux, Marcy l'Étoile, France). Staphylococcal enterotoxins were quantified

according to the EU-RL confirmatory method which uses a quantitative indirect sandwich enzyme-linked immunosorbent assay (ELISA) in order to separate and quantify staphylococcal enterotoxins type A to E [6].

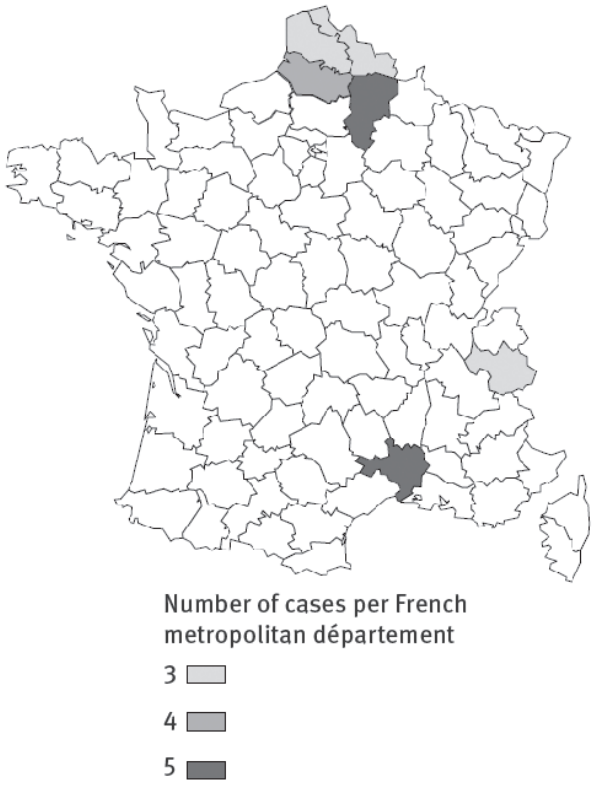
Results

Epidemiological information

Between 29 October and 14 November 2009, six outbreaks comprising 23 cases with gastrointestinal symptoms were reported through the network for mandatory notification of food-borne outbreaks, in six French districts (Figure 1).

Figure 1

Geographic distribution of food poisoning outbreaks due to staphylococcal enterotoxin type E, France, October-November 2009 (n=23)



A total of 23 persons of 26 persons who had consumed cheese (attack rate 88.5%) suffered from nausea, vomiting, abdominal cramps and diarrhoea, in some cases associated with fever. The period between the ingestion of the cheese and the onset of symptoms ranged from 1h15 to 8h. The investigation, performed by the Directorate General for Food of the Ministry of Agriculture using interviews and/or questionnaires, showed that a soft cheese made from unpasteurised cow milk distributed in supermarkets was the most likely source of food poisoning. Three cheese batches (I, II and III), produced during weeks 40 and 41 (2009) by the same producer and coming from a single milk storage tank, were involved in the six outbreaks (Table 1).

Counts and characterisation of coagulase-positive staphylococci strains

More than 1.5 x 10^5 colony-forming units (CFU) of coagulase-positive staphylococci/g were isolated from cheese samples from the three batches involved in the outbreaks. No cheese samples were available for outbreaks four and five. No coagulase-positive staphylococci could be detected in the cheese sample from outbreak six as this cheese had been heated before consumption. Five to ten coagulase-positive staphylococci isolates from each batch were analysed (total number n=20) and characterised. The isolates were all typed as *S. aureus* by a species-specific 23S rRNA-targeted PCR test. All were found to carry the *see* gene and none of the other *se* genes tested (Table 2, Figure 2). Four isolates were further characterised. They harboured a non-host specific biotype profile, K-β-CV:C, named NHS5 at the EU-RL, and showed the same PFGE pattern which was distinct from all other PFGE patterns available in the EU-RL database, including the pattern from the reference SEE-producing strain, FRI 326 (data not shown).

Using immunoassays to detect staphylococcal enterotoxins in samples

The EU-RL screening method using the qualitative and combined Vidas SET2 test detected SEA to SEE in the three cheese batches involved in the outbreaks.

Table 1

Epidemiological details of food poisoning outbreaks due to staphylococcal enterotoxin type E, France, October-November 2009 (n=6 outbreaks)

Outbreak	Date	Number ill/symptomatic	Symptoms	Period between ingestion of cheese and onset of symptoms	Cheese batch involved
1	3 November	3/4	AC, D, V	1h15	III
2	5 November	5/5	AC, D, V, F	8h	II
3	4 November	4/4	N, AC, D, V, F	6h	I
4	8 November	3/3	N, AC, D, V	6h	II
5	29 October	3/4	AC, D, V	2h45	II
6	14 November	5/6	AC, D, V	2h30	III

AC: abdominal cramps; D: diarrhoea; F: fever; N: nausea; V: vomiting

Moreover, the EU-RL confirmatory method detected and quantified SEE amounts ranging from 0.36 to higher than 1.14 ng/g, including the cheese sample from outbreak six where coagulase-positive staphylococci could not be detected (Table 2).

Discussion

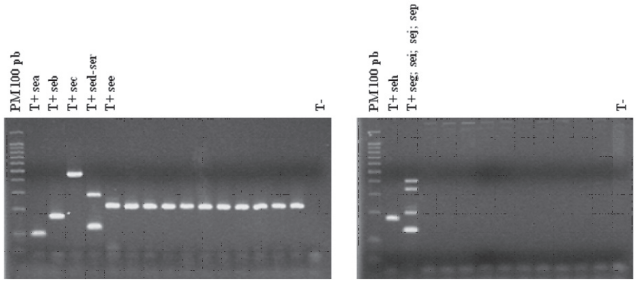
As unpasteurised cow milk cheese was the common and single food associated with all outbreaks according to the epidemiological investigation, they were obviously incriminated in the food poisonings described here. Moreover, the aetiological agent could be determined because of (i) the symptoms of the cases, (ii) the high number of coagulase-positive staphylococci recovered from remains of cheese incriminated in the outbreak and (iii) the amounts of staphylococcal enterotoxins recovered from cheese samples. In outbreak number six, the cheese had been cooked before consumption, explaining why no coagulase-positive staphylococci were recovered from this sample. Indeed, the coagulase-positive staphylococci were killed by the heat treatment whereas the staphylococcal enterotoxins, known to be heat resistant, remained active to cause a food poisoning outbreak and were actually detected in this sample.

The only type of staphylococcal enterotoxin detected in all food samples was SEE. This finding was reinforced by the fact that all tested coagulase-positive staphylococci isolates were found to carry a single *se* gene, *see*. This is the first staphylococcal food poisoning outbreak where SEE has been confirmed as the causative agent in France. The involvement of SEE seems to be also rare in other countries: to our knowledge, this staphylococcal enterotoxin has been associated to only few outbreaks. They were reported between 1960 and 1971 in USA [7] and in the United Kingdom (UK) [8] and a single case was analysed later on in the UK [9]. Otherwise, the most frequently staphylococcal enterotoxin type involved in staphylococcal food poisoning outbreaks worldwide is SEA, associated or not with other staphylococcal enterotoxins [2]. This is in agreement with the results observed by Kerouanton *et al.* [4] showing that SEA was the most frequently found (69.7%) among 31 French staphylococcal food poisoning outbreaks analysed between 1981 and 2002; out of 178 coagulase-positive staphylococci isolates tested for *se* genes, the most frequent gene was *sea* followed by *sed*, *seg*, *sei* and *seh*. The genes *seb* and *sec* were less frequent, and *see* gene was not found.

Moreover, the present study appears to be the first one where SEE was not only detected but also quantified in the food vehicle. In outbreak number six, SEE amount found in cheese sample was equal to 0.45 ng/g. Considering that symptomatic persons ingested a portion of about 200 g (data obtained from the cases interviewed in outbreak number six), the total amount of ingested SEE could be estimated to 90 ng. This dose is in accordance to those estimated in previous staphylococcal food poisoning outbreaks where SEA and/or SEA/SEH were confirmed as the causative agents [1].

Figure 2

Detection of the *see* gene on 10 *S. aureus* isolates from the cheese responsible for food poisoning outbreaks due to staphylococcal enterotoxin type E, France, October-November 2009



Left: positive controls for *sea* to *see* and *ser* genes followed by the 10 tested isolates and negative control.
Right: positive controls for *seg* to *sej* and *sep* genes followed by the 10 tested isolates and negative control.

Table 2

Analysis of cheese samples and coagulase-positive staphylococci isolates from cheese, France, October-November 2009

Outbreak number	Cheese batch number	Microbiological test in cheese samples	PCR tests on CPS isolates		SEA to SEE detection tests in cheese samples	
		CPS counts CFU/g of food sample	*S. aureus* 23S rRNA gene	*sea* to *sej* and *ser*, *sep* genes[a]	Qualitative detection[b]	Quantitative detection for SEE in food sample[c] (ng/g)[d]
1	III	$>1.8\ 10^7$	Detected (n=5)	*see* (n=5)	positive	> 0.92 (n=1)
2	II	$>1.5\ 10^5$	Detected (n=5)	*see* (n=5)	positive	> 1.14 (n=11)
3	I	$> 7.5\ 10^5$	Detected (n=10)	*see* (n=10)	positive	0.36 (n=2)
6[e]	III	$< 10^2$	Not relevant		positive	0.45 (n=1)

PCR: polymerase chain reaction; CPS: coagulase-positive staphylococci; SEA: staphylococcal enterotoxin A; SEE: staphylococcal enterotoxin E; CFU: colony forming units.
[a] The results of PCR assays for *se* genes are shown in Figure 2
[b] Global qualitative detection for SEA to SEE using Vidas SET 2 kit
[c] Confirmatory quantitative method for SEA to SEE (SEA to SED not detected)
[d] Mean of the quantitative results
[e] Cheese cooked before consumption

Considering that the coagulase-positive staphylococci isolates from the contaminated cheese samples showed the same *se* gene pattern, the same NHS5 biotype, the same PFGE profile and also the same antibiogram (data not shown), it can be considered that the same *S. aureus* strain involved in the six outbreaks came from the same origin. However, due to the non host-specific biotype detected, it was not possible to determine whether the contamination was from human, bovine or environmental source. In a previous French study [10], this NHS5 biotype was found in 8.5% of 2,021 *S. aureus* isolates from five types of raw milk cheeses; it was at the fourth rank after bovine-, NHS4- and NHS3-biotypes among the 20 distinct biotype profiles observed, indicating that its presence is not unusual in this food category.

Finally, this study illustrates that the French national surveillance system is able to detect rare events. The staphylococcal food poisoning outbreaks linked to SEE ingestion described here were quickly identified through a close collaboration between the Health Emergency Mission, the National institute for public health surveillance and the EU-RL with laboratories involved in food surveillance for coagulase-positive staphylococci and staphylococcal enterotoxins and the good cooperation of all parties involved. The rapid recall of contaminated cheese batches by the French Ministry of Food, Agriculture and Fishery prevented further cases. Due to the distribution across Europe of the incriminated type of cheese, the EU Member States were informed by the Rapid Alert System for Food and Feed (RASFF) reference 2009.1567 https://webgate.ec.europa.eu/rasff-window/portal/index.cfm?event=notificationDetail&NOTIF_REFERENCE=2009.1567.

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Impact of the routine varicella vaccination programme on varicella epidemiology in Germany

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Routine varicella vaccination with one dose for children of 11 to 14 months was recommended in Germany in 2004 to reduce disease incidence and severe complications. A country-wide varicella sentinel surveillance system was initiated in 2005 to detect trends of disease frequency and vaccine uptake and to evaluate the vaccination programme. A convenient sample of about 1,000 paediatricians and general practitioners was recruited to report on a monthly basis on varicella cases by age groups seen in their practice, and on varicella vaccine doses administered. Sentinel data from April 2005 to March 2009 show a reduction of 55% of varicella cases in all ages; 63% in the age group 0-4 years and 38% in 5-9 year-olds. The number of vaccine doses per reporting unit in all regions and physician groups increased during the same period. The number of reported cases as well as administered vaccines differed between physician groups and regions with different reimbursement policies. Where reimbursement was settled early and vaccine doses were increasing varicella cases started to decrease early as well. Besides reimbursement policies the availability and vaccination schedules influenced vaccine uptake. Sentinel surveillance provided valid data on trends for varicella associated morbidity, vaccine uptake and the age distribution of cases. The results confirm that following the introduction of routine varicella vaccination, varicella morbidity started to decline in Germany.

Introduction

Varicella vaccination was introduced for all children older than 11 months in July 2004 in Germany [1]. Besides the age group (11-14 months) for which vaccination was recommended, closing of individual immunisation gaps was generally recommended for all children and adolescents below 18 years of age. However, no systematic catch-up vaccination was foreseen.

The main aim of the routine varicella vaccination programme is the reduction of the burden of disease and of varicella related complications. However, this was not quantified [2]. Experiences from the United States (US), where varicella vaccination was introduced in the vaccination schedule already in 1996 [3,4], along with new data on the burden of disease [5] have influenced the decision to introduce varicella vaccination in Germany. Recommendations include defined antigens but not specific vaccines. All available licensed vaccines can be used according to the official information provided by the manufacturer. At the time when the recommendation was issued, two monovalent varicella vaccines were available for the administration of one dose in early childhood and two doses in children over 13 years of age. However, the costs for varicella vaccination were not covered by health insurances in all German federal states when varicella vaccination was recommended. Negotiations on reimbursement were successfully settled in spring 2006 for all states. In summer 2006, a combined vaccine against measles, mumps, rubella and varicella (MMRV) was licensed with a two-dose schedule and in 2008 licensures for the two monovalent vaccines were changed to two-dose schedules for all ages. In July 2009 the recommendation was changed to a two-dose schedule, with the second dose recommended at 15 to 23 months of age and with a minimum time interval of four to six weeks after the first dose. Thus, children in Germany have been vaccinated with different vaccines and different schedules since 2004.

Paediatricians have a key role in the immunisation of children as well as in their healthcare (including diagnosis and treatment) in Germany. Ninety-five per cent of children see a paediatrician within the first two years of life [6]. This percentage decreases with increasing age to 25% for 14-17 year-olds and general practitioners (GPs) treat up to 53% of the adolescents [6]. Therefore these two physician groups seem to be most appropriate for monitoring varicella disease and varicella vaccination. Varicella is not a notifiable disease in Germany. Therefore a country-wide varicella sentinel surveillance system was implemented in April 2005 in order to detect trends of disease frequency and vaccine uptake and to monitor the impact and the acceptance of the varicella vaccination programme.

This report reflects first results of the sentinel surveillance and describes the association between vaccine

uptake and frequency of varicella cases after introduction of routine varicella vaccination as well as factors influencing the vaccine uptake.

Methods

Sentinel surveillance

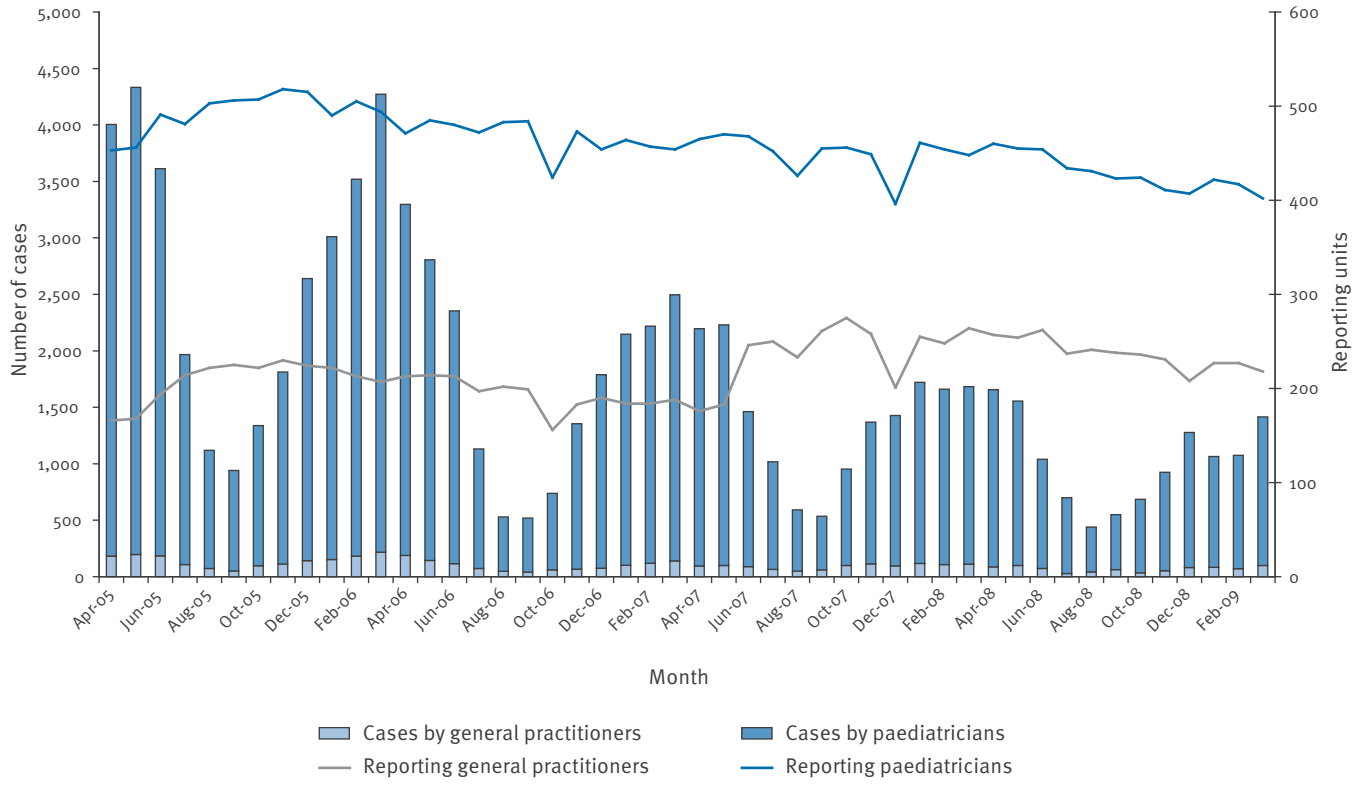
The country-wide sentinel project on varicella and zoster epidemiology is managed in public-private-partnership by the German national public health institute, the Robert Koch Institute (RKI) which is responsible for the scientific management and, the German Green Cross (DGK), responsible for the recruitment of physicians and data management. The vaccine manufactures GlaxoSmithKline and Sanofi Pasteur MSD are financing the work at DGK, the RKI receives no financial support from the manufacturers. An independent scientific board gives scientific and operational advice for running the surveillance system. The system is called "working group on measles and varicella" (Arbeitsgemeinschaft Masern und Varizellen, AGMV) [7].

A convenient sample of over 1,000 primary care physicians was recruited, consisting of 60% paediatricians and 40% GPs and accounting for about 15% of all German paediatricians and about 1% of all GPs in practice. Sentinel physicians of both groups are distributed across all 16 German federal states equally to the distribution of respective physicians in practice. Physicians participate on voluntary basis and neither doctors nor patients receive incentives. As patients are free to choose and change their physician and only a subset of physicians report to the sentinel, the population size under surveillance can not be defined. The sentinel is not population based and does aim at trends but not at incidence.

Physicians provide aggregated numbers of varicella cases by age groups through monthly questionnaires. Age groups are divided as follows: <1 year, 1-4 years, 5-9 years, 10-14 years, 20 years and older. Doctors document the number of patients with varicella complications, vaccinated varicella cases and cases of herpes zoster. In addition, they report the monthly number of administered doses of varicella vaccines by first and second doses and since April 2007 doses are divided into monovalent and combined varicella vaccines. Zero-reporting and active reminders are included and the questionnaire provides case definitions. A case of varicella is defined as a person presenting at the physician's practice with a clinical picture resembling varicella, with skin exanthema and concomitant presentation of papules, blisters, pustules, crusts. Varicella complications are defined as varicella leading to hospitalisation, oral or parenteral antibiotic or antiviral therapy or as accompanied by neurological symptoms. Vaccinated varicella cases are persons vaccinated against varicella regardless of the time interval between vaccination and onset of varicella. Herpes zoster is defined as appearance of blisters on an exanthematic skin, confined to a spinal or cranial nerve pathway, accompanied by at least one out of the following symptoms: painful neuralgia of the affected region, fever, loss of appetite, myalgia, burning sensation

Figure 1

Number of varicella cases and reporting units by physician group, sentinel data, Germany, April 2005-March 2009



and/or itching of the affected region. Physicians are asked to report the number of patients they have seen at their practice in the respective month and categories. Laboratory confirmation is not required.

Descriptive Analysis

Data on varicella cases per age group and on varicella vaccinations by first and second doses were analysed and available from April 2005 to March 2009. Defining a varicella season as lasting from April until March of the following year, the surveillance covered four complete varicella seasons (2005-6, 2006-7, 2007-8, 2008-9). The number of reported varicella cases as well as the number of vaccine doses was related to the number of reporting physicians (units) as denominator in the respective month or season. Reporting physicians were grouped by speciality (paediatricians/GPs) and by region. Three regions were formed according to reimbursement policies (i) region 1: vaccination costs covered since general recommendation (cost regulations completed before 2005-6 season); (ii) region 2: reimbursement settled in 2005 (regulations completed during 2005-6 season) and (iii) region 3: reimbursement settled in 2006 and partly restricted for specific age or vaccine only until March 2007 (regulations completed during 2006-7 season).

For data entry and data management MS Office ACCESS version 2003 was used, descriptive data analysis was carried out by SPSS version 16.

Results

Varicella cases, vaccinations, reporting units over time

From April 2005 (start of season 1) until March 2009 (end of season 4), a total of 83,181 varicella cases were reported by 1,178 physicians. During the same time 289,327 first and 86,394 second doses of varicella vaccine were administered by sentinel physicians.

Seasonal peaks of varicella disease occurred in spring. The peaks flattened over time, whereas the total number of reporting physicians remained fairly stable. A slight decrease in the number of reporting paediatricians was balanced by an increase in the number of GPs (Figure 1). Paediatricians formed the majority of

Table 1

Mean number of varicella vaccines and varicella cases per reporting unit and month by physician group and cost cover region over four consecutive varicella seasons, sentinel data, Germany, April 2005-March 2009

Physician group	Season[1] (units)	Region 1: cost regulations before season 2005-6		Region 2: cost regulations in season 2005-6		Region 3: cost regulations in season 2006-7		All regions together	
		Vaccines per unit and month (95%CI)	Cases per unit and month (95%CI)	Vaccines per unit and month (95%CI)	Cases per unit and month (95%CI)	Vaccines per unit and month (95%CI)	Cases per unit and month (95%CI)	Vaccines per unit and month (95%CI)	Cases per unit and month (95%CI)
Paediatric reporting units	2005-6 (N=635)	13.76 (12.52-14.99)	3.72 (2.46-4.99)	13.41 (11.44-15.37)	5.54 (3.74-7.35)	6.63 (5.15-8.12)	5.73 (3.99-7.47)	11.27 (9.87-12.66)	5.00 (4.11-5.89)
	2006-7 (N=548)	15.48 (14.18-16.78)	1.99 (1.34-2.64)	16.70 (15.42-17.98)	3.2 (2.14-4.26)	13.38 (12.08-14.68)	6.03 (3.96-8.10)	15.19 (14.37-16.00)	3.74 (2.81-4.67)
	2007-8 (N=530)	21.06 (18.86-23.26)	1.93 (1.40-2.47)	20.49 (19.00-21.99)	2.37 (1.84-2.90)	14.90 (13.90-15.89)	5.03 (3.52-6.54)	18.82 (17.54-20.09)	3.11 (2.42-3.80)
	2008-9 (N=499)	24.72 (22.87-26.56)	1.91 (1.53-2.29)	25.50 (23.58-27.42)	2.07 (1.56-2.58)	20.73 (18.07-23.39)	2.98 (2.10-3.86)	23.65 (22.32-24.98)	2.32 (1.96-2.68)
GP reporting units	2005-6 (N=323)	2.04 (1.53-2.55)	0.53 (0.28-0.78)	2.09 (0.77-3.41)	0.63 (0.44-0.82)	1.29 (0.62-1.95)	0.92 (0.62-1.23)	1.8 (1.32-2.29)	0.70 (0.55-0.84)
	2006-7 (N=260)	2.92 (2.30-3.55)	0.42 (0.29-0.55)	2.72 (2.07-3.36)	0.38 (0.28-0.48)	2.22 (1.89-2.55)	0.82 (0.57-1.07)	2.62 (2.32-2.92)	0.54 (0.43-0.65)
	2007-8 (N=381)	2.83 (2.11-3.54)	0.21 (0.14-0.28)	2.82 (2.28-3.36)	0.34 (0.29-0.39)	2.43 (2.03-2.84)	0.58 (0.42-0.73)	2.69 (2.39-2.99)	0.37 (0.30-0.45)
	2008-9 (N=330)	3.34 (2.82-3.85)	0.14 (0.09-0.18)	2.81 (2.36-3.27)	0.27 (0.21-0.34)	2.82 (2.33-3.31)	0.37 (0.25-0.50)	2.99 (2.73-3.25)	0.26 (0.20-0.32)
All reporting units	2005-6 (N=958)	7.9 (5.3-10.5)	2.13 (1.22-3.03)	7.75 (5.08-10.42)	3.09 (1.74-4.44)	3.96 (2.59-5.33)	3.33 (2.01-4.64)	6.54 (5.20-7.87)	2.85 (2.17-3.52)
	2006-7 (N=808)	9.2 (6.41-11.99)	1.20 (0.75-1.66)	9.71 (6.62-12.79)	1.79 (1.01-5.57)	7.80 (5.31-10.29)	3.42 (1.95-4.90)	8.90 (7.36-10.45)	2.14 (1.55-2.73)
	2007-8 (N=911)	11.94 (7.87-16.01)	1.07 (0.62-1.52)	11.66 (7.78-15.54)	1.35 (0.85-1.86)	8.67 (5.93-11.40)	2.8 (1.62-3.99)	10.76 (8.74-12.44)	1.74 (1.27-2.21)
	2008-9 (N=829)	14.03 (9.33-18.72)	1.02 (0.6-1.45)	14.16 (9.18-19.13)	1.17 (0.72-1.62)	11.78 (7.72-15.83)	1.68 (0.98-2.37)	13.32 (10.79-15.85)	1.29 (0.99-1.59)

CI: confidence interval; GP: general practitioner.

[1] April to March of following year.

reporting units over time. Between 396 and 518 pediatricians and 156 to 275 GPs reported per month to the sentinel and the respective number of reporting units per season ranged from 499 to 635 pediatricians and 260 to 381 GPs. The mean response rate was 76% for paediatricians and 54% for GPs and was stable in both groups over time. However, the proportion of paediatric units among all reporting units declined slightly from about 66% in the seasons 2005-6 and 2006-7 to about 60% in 2007-8 and 2008-9 (Figure 1; Table 1).

The number of monthly reported varicella cases per unit in all age groups together decreased from varicella season 1 to season 4 from 2.85 to 1.29, which

Figure 2

Average number of varicella cases per month and reporting unit by age over four varicella seasons, sentinel data, Germany, April 2005-March 2009

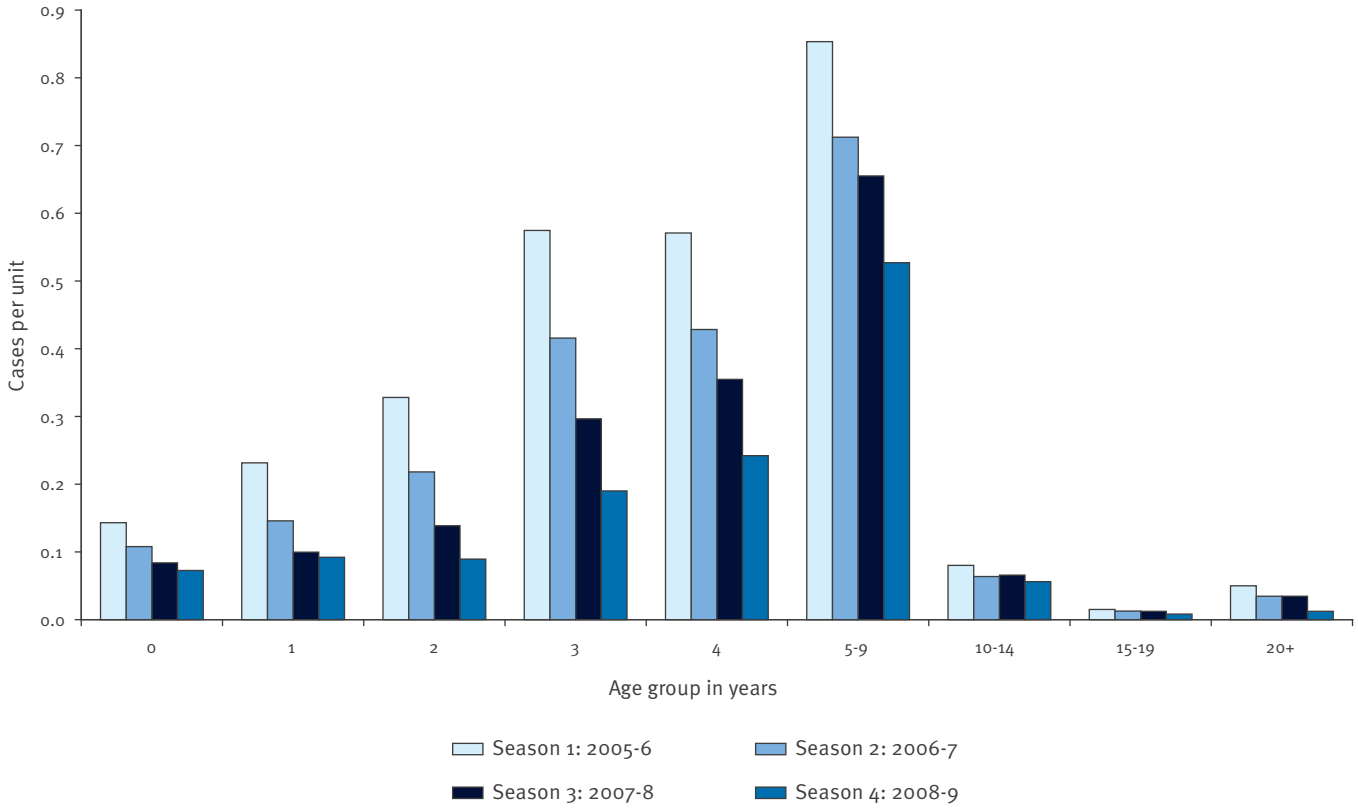


Table 2

Total number of administered varicella vaccines as first and second, monovalent and combined doses and numbers per reporting unit by season and physician group, sentinel data, Germany, April 2005-March 2009

Season[1]	Paediatricians				General practitioners			
	1st dose monovalent varicella vaccince (n per unit)	1st dose MMRV (n per unit)	2nd dose monovalent varicella vaccince (n per unit)	2nd dose MMRV (n per unit)	1st dose monovalent varicella vaccince (n per unit)	1st dose MMRV (n per unit)	2nd dose monovalent varicella vaccince (n per unit)	2nd dose MMRV (n per unit)
2005-6	64,203 (106.8)		1,914 (3.2)		1,657 (6.3)		218 (0.8)	
2006-7[2]	75,493 (143.8)		7,369 (14.0)		2,308 (10.6)		439 (2.0)	
2007-8	29,656 (59.6)	42,771 (85.6)	2,792 (5.6)	22,901 (46.0)	961 (3.8)	1,371 (5.4)	308 (1.2)	1,153 (4.5)
2008-9	19,635 (41.3)	49,305 (103.8)	13,759 (29.0)	33,928 (71.4)	546 (2.4)	1,421 (6.2)	372 (1.6)	1,241 (5.4)

MMRV: measles-mumps-rubella-varicella vaccine.

[1] April to March of following year.

[2] As MMRV was available since summer 2006 but reporting of MMRV-doses started in April 2007, an undefined no. of MMRV doses may be included in this season.

is a reduction of 55% of cases. In the age group 0-4 years cases per month and unit declined from 1.85 to 0.69 (63%), and in the 5-9-year-olds from 0.85 to 0.53 (38%). A reduction was also observed in the age group 20 years and older. However, only 1% (n=784) of all reported cases belonged to this age group and a reduction from 0.05 to 0.01 (75%) was observed between varicella season 1 and 4 (Figure 2). In all varicella seasons the majority of cases occurred in 0-4 year-olds. Proportions between age groups shifted over time; in season 1, 65% of all cases were seen in 0-4 year-olds and 30% in 5-9 year-olds, whereas the proportions were 53% and 41% respectively in season 4.

Cases and vaccinations by reporting units and cost cover groups

The number of cases and administered vaccines per reporting unit and month differed by physician group and region; in all regions paediatricians administered six to eight times more varicella vaccines and saw seven to nine times more varicella cases than GPs (Table 1). The total number of varicella cases per season (n=32,569; 21,384; 16,846 and 12,414 in varicella seasons 1, 2, 3 and 4 respectively) as well as the mean number of cases per reporting unit and month decreased steadily over the four seasons. This trend was seen in case reports by both physician groups in all regions together and by GPs alone in each of the three regions, for paediatricians this trend was also found in regions 1 and 2 but not region 3 (Table 1). In all four seasons, in region 1 (region with earliest cost regulation) all units together had less varicella cases per unit and month on average than in the other two regions; the highest number of cases per month was reported by paediatricians and GPs from region 3 (region, were cost regulation was settled last). The greatest difference in case reports between region 3 and the other two regions was calculated for seasons 2 and 3 in both physician groups. In the paediatric units of region 1 a decrease of cases per unit was seen in season 2 compared with season 1, and values remained stable on a low level in the following two seasons. In the GP units of region 1 the case numbers decreased over all four seasons but to a lesser extent than in the paediatrician group. A decrease over four seasons was also observed for both physician groups in region 2 with the above described differences between paediatricians and GPs and starting from a lower level than in region 1. However, in region 3 a remarkable decrease in cases per paediatric units did not start until season 4 and for GP units until season 3.

In all four varicella seasons, paediatricians and GPs from region 1 and 2 administered more varicella doses than those from region 3, but this difference was most prominent in season 1.

Vaccinations by physician groups over time

With 281,063 first and 82,663 second doses, 97% of all varicella vaccine doses were administered by paediatricians (Table 2). The number of first doses per paediatric reporting unit increased over three seasons and remained stable in season 4. With 35%, the increase was strongest from season 1 to 2. The number of second doses per paediatric unit increased steadily over time from 3.2 in season 1 to 100.4 in season 4. An increase in the total number of doses per unit was also seen in the GP group, however at lower level and divergent for first and second doses. Whereas first doses per unit increased from season 1 to season 2 and then slightly decreased over the following seasons, second doses per unit increased steadily over all four seasons. In season 3 less monovalent vaccine doses were administered per unit compared with season 2. This was partly balanced by the use of MMRV. The number of MMRV per unit exceeded by far the number of first and second doses of monovalent vaccine in both physician groups. Whereas MMRV vaccine use has contributed most to the increase of second doses since season 2, there

Table 3

Number of vaccinated cases, cases with complications and with Herpes zoster by physician group and by season, sentinel data, Germany, April 2005-March 2009

Season[1]	Vaccinated varicella cases, reported by paediatricians (% of all cases)	Vaccinated varicella cases, reported by GPs (% of all cases)	Complications, reported by paediatricians (% of all cases)	Complications, reported by GPs (% of all cases)	Herpes zoster, reported by paediatrician [cases per unit]	Herpes zoster, reported by GPs [cases per unit]
2005-6	283 (0.9)	6 (0.4)	130 (0.4)	12 (0.7)	505 [0.8]	1,046 [3.2]
2006-7	473 (2.3)	9 (0.8)	65 (0.3)	12 (1.0)	495 [0.9]	1,035 [4.0]
2007-8	816 (5.2)	32 (2.9)	55 (0.3)	10 (0.9)	456 [0.9]	1,100 [2.9]
2008-9	988 (8.5)	28 (3.4)	20 (0.2)	6 (0.7)	423 [0.8]	1,083 [3.3]

GP: general practitioners.

[1] April to March of following year.

was also a remarkable increase of monovalent second doses per unit from season 3 to 4.

Other reporting categories

The number of varicella in vaccinated persons increased from 289 in varicella season 1 to 1,016 in season 4 and the proportion of vaccinated on all reported varicella cases went up from 0.9 to 8.2%. Although the upwards trend was seen by both physician groups, numbers and proportions of vaccinated patients were much higher in paediatricians reports in comparison to GPs (Table 3). The total number of reported complications went down from 142 cases (0.4% of all reported varicella cases) to 26 (0.2%) over the four seasons and again this trend was more distinctive in paediatricians.

Concerning herpes zoster the crude reporting numbers in all four seasons were higher from GPs than from paediatricians corresponding to about four times more cases per reporting unit. However, a steady number of cases per unit were observed over time by both physician groups.

Discussion

Germany is one of the few countries worldwide where varicella vaccination has been introduced in the routine childhood vaccination schedule. The most prominent effects in the first four years after introduction of vaccination are the decrease in number of varicella cases and the increasing acceptance of vaccination [8]. Descriptive analysis of sentinel data provided evidence of a reduction in the number of cases in four consecutive seasons following the introduction of the vaccination programme. The decrease was greatest in 0-4 year-olds, but the trend was seen in all age groups. Comparable results were reported from the US where after the introduction of varicella vaccination in the routine childhood vaccination programme in 1996 varicella incidence declined substantially between 1995 and 2000 in the sentinel regions [9].

The decrease in varicella morbidity in Germany can not be explained by secular trends. In absence of notification data this can be demonstrated by data from hospital discharges in the time from 1994 to 2004, the pre-vaccination era. The median of the annual number of hospitalised varicella cases was 1,957 and ranged from 1,806 cases in 2002 to 2,316 cases in 2004 [10]. In the three years after the general recommendation of varicella vaccination the annual number of hospitalised varicella cases steadily declined from 1,751 in 2005 to 1,269 in 2007. The decline in number of hospitalised cases per 100,000 population was largest in the age group 1-4 years old (from >20 hospitalised varicella cases per 100,000 population in 1994-2004 to 10 in 2007) and in infants (>30 in 1994-2004 to 21 in 2007). The decrease in varicella morbidity was observed in two independent sources and supported through comparison with data from the pre-vaccination era.

The rise in vaccine doses per reporting unit in all regions and all physician groups over the observed time period in the sentinel indicates an increased acceptance of varicella vaccination. Moreover, there are clear associations between reimbursements for vaccination and vaccine uptake on the one hand and the increase of vaccine uptake up to a stable level and the decrease of number of cases on the other. In the region were costs of vaccination were covered from the beginning of the programme the number of vaccines administered per physician were higher compared with the regions were reimbursement was settled at a later stage. The sentinel observations and descriptive statistics show, that when reimbursement was settled early and vaccine doses were increasing, the varicella cases started to decrease early as well. The time span between increasing number of vaccinations after cost regulations and the first visible effects on the number of varicella cases was about 1.5 seasons. Besides reimbursement policies the availability of vaccines and schedules of vaccination play an important role for vaccine uptake. While the increase of vaccinations in the first season after introduction of the programme was mainly due to negotiated reimbursement, the availability of MMRV has led to a growing number of second doses since autumn 2006. The administration of second varicella vaccine doses was further accelerated in the season four due to a change in the licensed vaccination schedule for monovalent varicella vaccines from one to two doses.

With increasing numbers of vaccinated persons, the number of patients with varicella has decreased over time in Germany. The reduction was greatest in the group targeted for vaccination, i.e. young children. The observed proportion shift in the number of varicella cases from 0-4 year-olds towards 5-9 year-old children is a result of the greater reduction of varicella disease in toddlers and pre-school-age children in comparison to school-age children. A shift in the disease rates as given by number of cases per age and reporting unit towards older age groups has not been observed in the four seasons in the sentinel. Thus, a shift towards older age groups, associated with a higher risk of complications from varicella disease, has not been observed until now. Moreover, our results show that the number of complications has declined in the sentinel.

With increasing numbers of vaccinated persons the potential for varicella disease in vaccinated persons is increasing and the proportion of vaccinated among all varicella cases will increase as well. This was shown in the US [13] and is now confirmed by the results of our sentinel surveillance in Germany. For further analysis case based data are necessary in order to differentiate between varicella shortly after vaccination and breakthrough cases. Case-based data are also necessary to investigate the reported cases of herpes zoster more thoroughly. So far no trend in the frequency of herpes zoster was detected in the sentinel.

As the sentinel system is not population based, incidence or vaccine coverage can not be estimated. For this purposes a notification system would be appropriate.

Although passive reporting (as for instance by notifications) is known to underestimate the total number of cases more than active reporting (as for instance this sentinel), the population under surveillance is clearly defined. Incidence by age and region could only be estimated if the denominator is known as in population based surveillance. Moreover, with further decreasing case numbers the sensitivity of the existing sentinel system might decrease. Therefore surveillance has to be adopted and one possible way would for instance be the introduction of varicella into statutory notifications in Germany.

In conclusion we can state that the varicella morbidity has started to decline and we are progressing towards reducing varicella morbidity and the overall burden of disease which are the main aims of the vaccination programme. Sentinel surveillance provides valid data on trends in varicella and herpes zoster morbidity in Germany and the age distribution of varicella cases so far. Furthermore, the sentinel seems to be appropriate to generate hypotheses for further investigations. If notification of varicella can not be implemented in the future, additional epidemiological data are needed to confirm sentinel results at population level and changing the current sentinel structures could ensure reliable case detection in the next years.

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The new automated daily mortality surveillance system in Portugal

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The experience reported in an earlier Eurosurveillance issue on a fast method to evaluate the impact of the 2003 heatwave on mortality in Portugal, generated a daily mortality surveillance system (VDM) that has been operating ever since jointly with the Portuguese Heat Health Watch Warning System. This work describes the VDM system and how it evolved to become an automated system operating year-round, and shows briefly its potential using mortality data from January 2006 to June 2009 collected by the system itself. The new system has important advantages such as: rapid information acquisition, completeness (the entire population is included), lightness (very little information is exchanged, date of death, age, sex, place of death registration). It allows rapid detection of impacts (within five days) and allows a quick preliminary quantification of impacts that usually took several years to be done. These characteristics make this system a powerful tool for public health action. The VDM system also represents an example of inter-institutional cooperation, bringing together organisations from two different ministries, Health and Justice, aiming at improving knowledge about the mortality in the population.

Introduction

The ongoing surveillance of mortality to detect and estimate the magnitude of deaths caused by epidemics, emergence of new diseases, or other relevant public health events or threats is envisaged as an important tool. Current efforts are in place to develop such a system at the European level [1].

In Portugal, heatwaves have been demonstrated to be an important health problem [2] and since 1999, a Portuguese Heat Health Watch Warning system (HHWW) has been operating, known as the ICARO Surveillance System (the acronym stands for ***I****mportância do* ***Ca****lor:* ***R****epercussão nos* ***Ó****bitos* – importance of heat and its repercussion on mortality) [3,4]. This ICARO system was based on models that forecast increases in mortality related to observed high temperatures [8,4] three days before the real occurrence.

Originally, the HHWW system was based on statistical models that correlated the heat occurrence with the observed mortality in the Lisbon district. Risk was conveyed to system partners in the form of a simple index called the ICARO-Index [3,5], where 0 (zero) means absence of risk and positive values added risk of mortality related with heat. Basically this index accounted for maximum temperatures above a fixed threshold of 32ºC and the number of consecutive days on which such occurrences were observed. The Lisbon ICARO-index was updated later to integrate the experience of the 2003 heatwave [4], and it is currently referred to as ICARO-Index 2005.

In the time following the first ICARO alert in 2000, public health mitigation actions tended to wait for confirmation of an impact on the population (e.g. excess mortality), and once this evidence was obtained, it was too late to act. Given that there was no rapid method available to obtain that evidence, a tool that could provide it was needed.

It was within this framework that a first mortality monitoring system was tested in the hot summer of 2003. This early version (hereafter referred as ad-hoc VDM: Vigilância Diária da Mortalidade – Surveillance of Daily Mortality) was based on the daily number of death registrations in a set of Civil Registrar Offices (CROs) that accounted for about 40% of all Portuguese mortality [6]. In fact, this early version allowed the confirmation of the excess mortality predicted by the ICARO Surveillance System in the summer 2003 [3,7].

Generation of a routine daily mortality monitoring system – the original VDM system (2004-2007)

The ad-hoc system tested during the heatwave of 2003 used a sample of 31 CROs representing all capital cities of all districts of mainland Portugal [2]. In the summer of 2004, the routine daily surveillance was launched (original VDM system). This version differed from the ad-hoc system in the set of CROs, which consisted now

of a sample of 67 CROs, the first 31 CROs plus a random sample. This original VDM system was operational from 2004 to 2007, and the data collected consisted only of the numbers of registered deaths in each CRO by date of registration (total and for individuals aged 75 years or older). Data was sent to the Portuguese National Health Institute (INSA) at the end of every day or on the following morning. Data was mainly transmitted by fax and telephone with only a few offices being able to exchange data by e-mail. This non-automated version of the system required six or seven persons at INSA to collect the basic data. Given the original interdependence of this VDM system with the ICARO system, mortality information was disseminated within the daily ICARO bulletin to its partners which consisted of National Health and Civil Protection authorities (Figure 1).

Although logistically complex, this original VDM System was functional and fully executed on a daily basis (weekdays) during the summers, and at the end of the summer of 2005 it was decided to extend the data collection period to the full year.

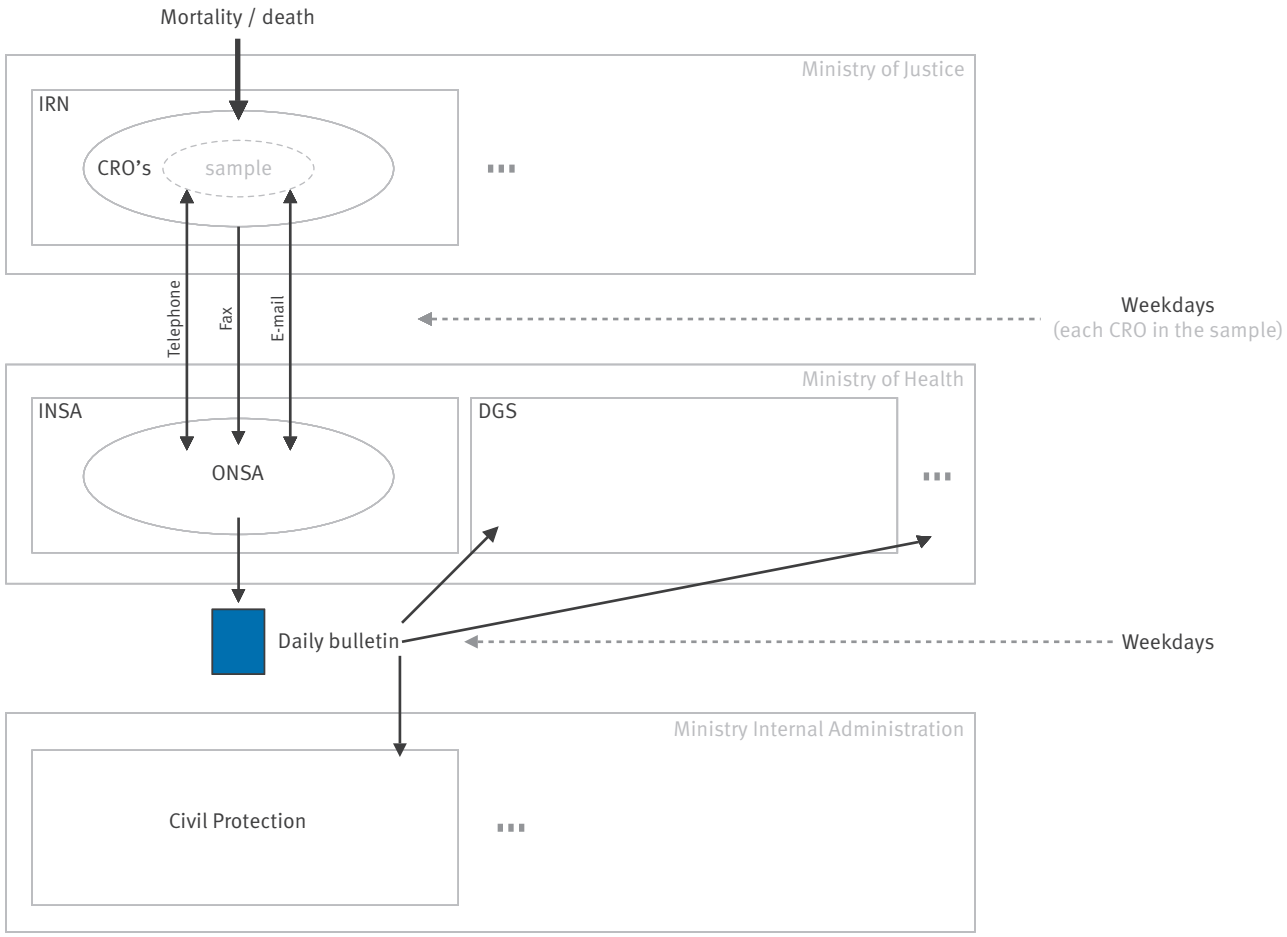
Figure 2 shows the evolution of the original VDM system. For the year 2004, the deaths registered by the 67 CROs are compared to weekday baselines of expected deaths based on information supplied by the 31 CROs involved in 2003, omitting weeks with national holidays and heatwaves. For better comparison with the baseline, the graph for the year 2004 also shows the deaths registered in 2004 by the 2003 sample of 31 CROs.

The baseline of expected deaths in the graphic for 2005 was based on information from the sample of 67 CROs in 2004, the same 67 CROs that also supplied the information on actual deaths in 2005. It is curious that the addition of 36 relatively less important CROs (with regards to the registrations of the number of deaths) led to a slightly different pattern, especially on Fridays. It is also remarkable that holidays, either national or local (in important centres like Lisbon and Porto, e.g. St. John on 24 June) caused delays in the acquisition of mortality information. Noteworthy is that a strike of the justice services in 2005 also affected the system information.

In 2006, an added feature was tested by including a mathematical model that would consider delayed information due to a holiday. This allowed an assessment of whether the observed number of death registrations

Figure 1

Original daily mortality surveillance system (VDM), Portugal, 2004-2007



CRO: Civil Registrar Offices; DGS: General Directorate of Health; INSA :National Health Institute Dr. Ricardo Jorge; IRN: Institute for Registries and Notary; ONSA: National Health Observatory (currently Epidemiology Department of INSA).

on a given day was the expected. Although this model did not have all the required statistical properties it seemed to accurately predict the real situation.

Another feature was tested: adding to the expected number of deaths those predicted by the ICARO model. Results demonstrated that it was possible to model the delay in registered mortality including excess mortality predicted by the ICARO model. But at the time the ICARO surveillance system relied on an extrapolated index for Lisbon and not on the current national weighted index (which relies on indexes for four regions of Portugal weighted according to resident population).

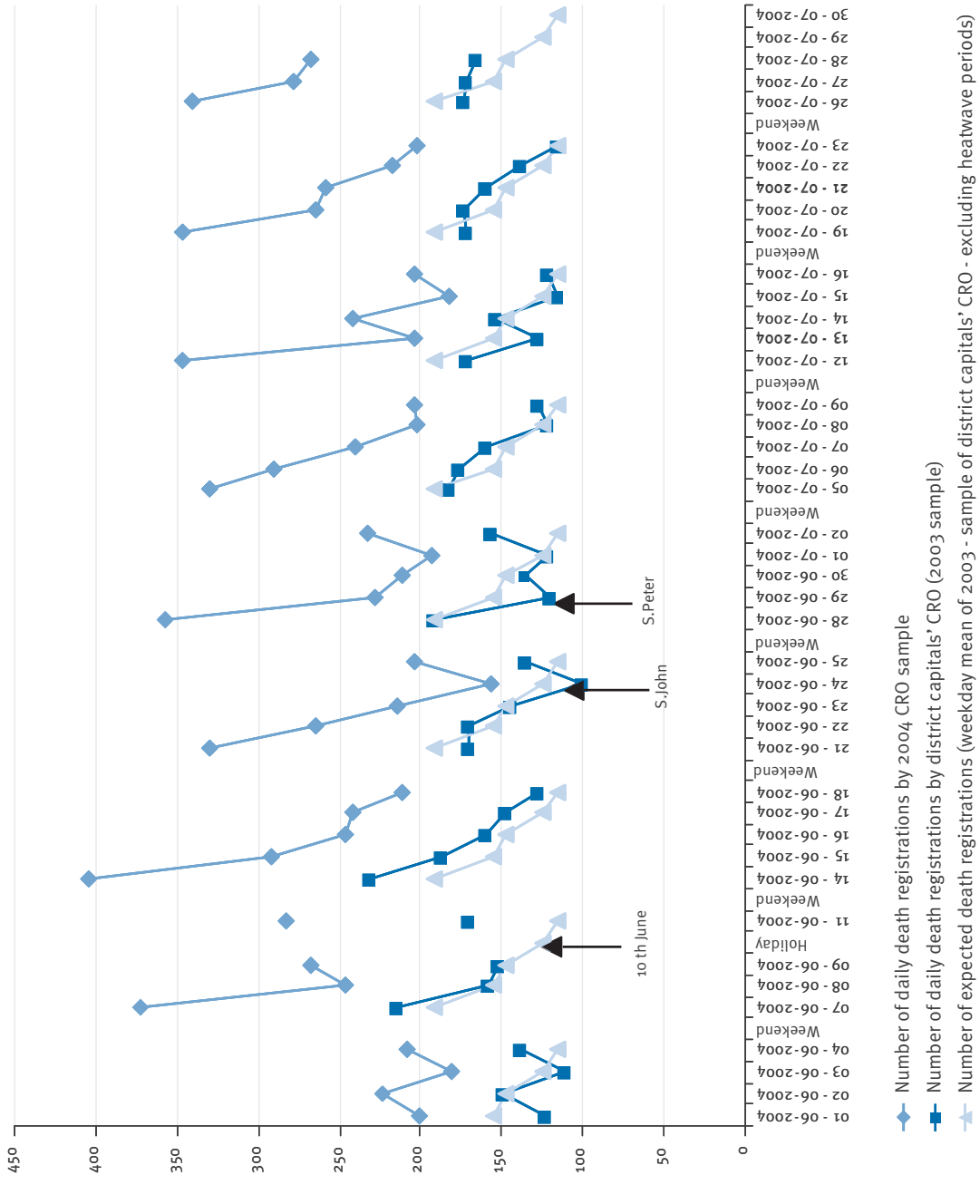
Several estimates of excess deaths due to heat episodes have been made using the mortality surveillance system (original VDM). For example, heatwave data analysis for 2003 was done comparing several reference periods of mortality data with the observed data in that particular heatwave period, deriving the respective confidence intervals and calculating exact Poisson probabilities to obtain p-values [3].

Although this mortality system was in place and functional, the detection and calculation of excess mortality due to an event was not straightforward. The main limitation of this system was the use of daily number of death registrations instead of daily number of deaths. The use of the former is heavily dependent on the weekday, with mortality on weekends and holidays registered later (Figure 2). Consequently, it was only possible after the experience of three summers (2003-2005) to establish a rationale that allowed modelling the expected delayed mortality registration.

Figure 2

Evolution of the Portuguese daily mortality surveillance system (VDM) system, 2004-2006

Daily Mortality Surveillance System CRO-ICARO 2004



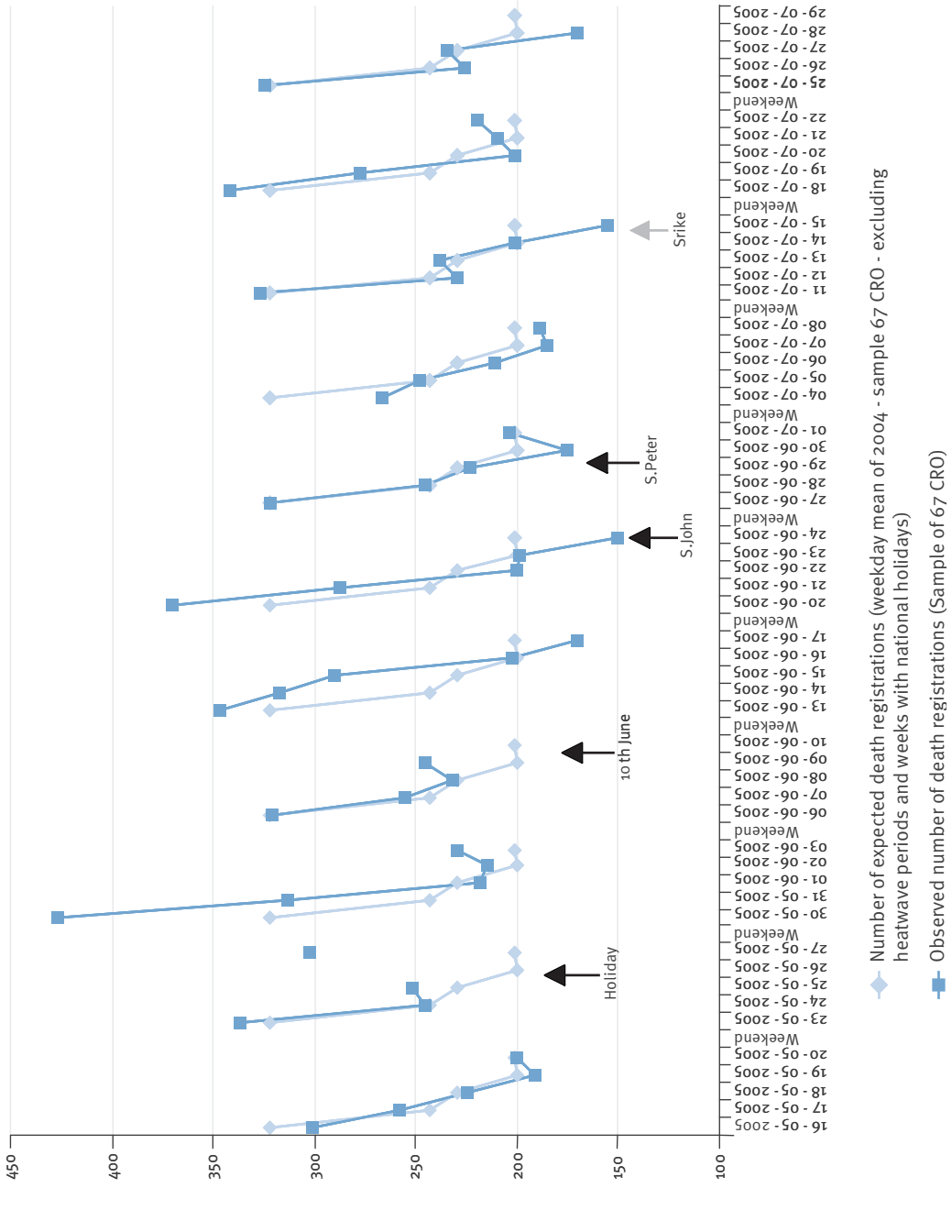
The new VDM system (in place since 2007)

The new VDM system was only possible because of a technical change in 2006 within the Ministry of Justice through a system called SIRIC (Integrated system for civil registries and identification) that aimed at connecting all civil CROs and collecting their data in a centralised way. SIRIC included information from the Institute for Registries and Notary (IRN), which is responsible for the CROs and was implemented and maintained by the Institute for Information Technologies of Justice (ITIJ).

Although SIRIC included only half of the existing CROs (those that were already computerised), IRN asked INSA in mid-2006 to test an automated version of the VDM system using exchange between INSA and ITIJ of data collected centrally by SIRIC. For this test, only of few variables (date of death, age, gender, and geographical code for location of death registration) were circulated by e-mail. The experience was satisfactory and the automated system was deemed feasible and useful as it would save resources at both ends.

The two systems, old and new, coexisted from September 2006 to May 2007 when the original VDM system was discontinued. By June 2007, all Portuguese CROs were reporting to SIRIC. Data flow consisted of a single e-mail, containing information for the previous day, sent by ITIJ on a daily basis, including weekend days and holydays (Figure 3). With this paper we aim to demonstrate that the new VDM system, fully automated since early 2008, allows quick detection of events and rapid estimates of their impact using reduced resources.

Figure 2
Continued
Daily Mortality Surveillance System CRO-ICARO 2005



Methods

Definition of events

Influenza activity

The definition of influenza epidemic periods relied on information of influenza activity that consisted on weekly estimates of influenza-like illness (ILI) incidence rates obtained by the Portuguese General Practitioner (GP) Sentinel Network (Rede Médicos-Sentinela) [8]. The study period comprised the seasons 2006-7, 2007-8 and 2008-9. The epidemic periods were defined as the set of consecutive weeks with estimates of ILI incidence rates above the 95% upper confidence limit of the baseline levels [9] (see Table 1).

Heat periods

For the determination of the heat periods, data of observed maximum temperatures in a given district were considered. Temperature data were made available by the Meteorological Institute in Portugal. Heat periods, summarised in Table 2, were defined according to one of two criteria:

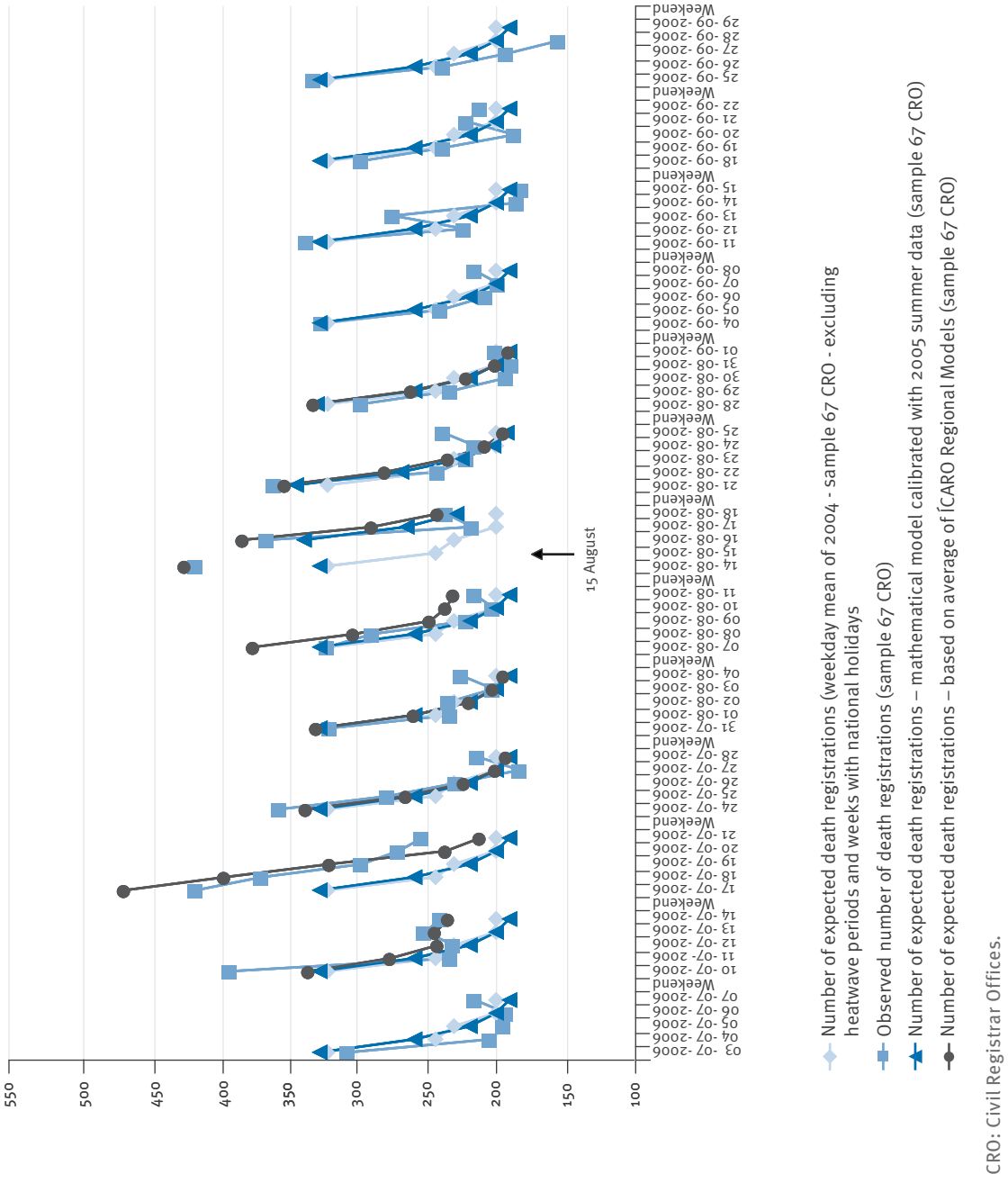
1. Two or more consecutive days with temperature above 35°C in two (of 18) districts (or temperature above 36° in one district)
2. Two or more consecutive days with ICARO index above zero.

Mortality

Mortality data were generated by the new VDM system from January 2006 to June 2009. Depending on the event studied, data was aggregated on a daily (heat event) or weekly (influenza activity event) basis.

FIGURE 2
Continued

Daily Mortality Surveillance System Portugal Mainland 2006



CRO: Civil Registrar Offices.

Data was stratified by gender, age group (65-74 and ≥75 years) and by Nomenclature of Territorial Units for Statistics (NUTS) 2 regions (North, Centre, Lisbon and Tagus Valley, Alentejo and Algarve).

Determination of VDM system delay

To determine the VDM system delay, daily data by date of registration, date of death and the respective number of days of delay were considered. The period from 5 June 2007 (1st day with all CROs included in the system) to 4 June 2009 was covered. Analysis by weekday and month of death was performed using relative percentages for each weekday or month.

Statistical methods

For confirmation and detection of impact, cyclical regression models [10] were fitted to complete mortality data (January 2007 to June 2009) using the Flubase package [11]. For the confirmation approach, models were fitted to data excluding the event periods (Tables 1 and 2), and for event detection, all data was used without considering known event periods.

The mortality predicted by the model was considered as the baseline mortality. A confirmed excess mortality period was defined as a set of consecutive days or weeks (depending on data level being used) that began with two values of observed number of deaths above the upper 95% confidence limit of the baseline and ended with two consecutive mortality values below this limit. For heat periods impacts, a single day or week of mortality above the 95% confidence interval, within a marked heat event period, was also regarded as a confirmed excess mortality.

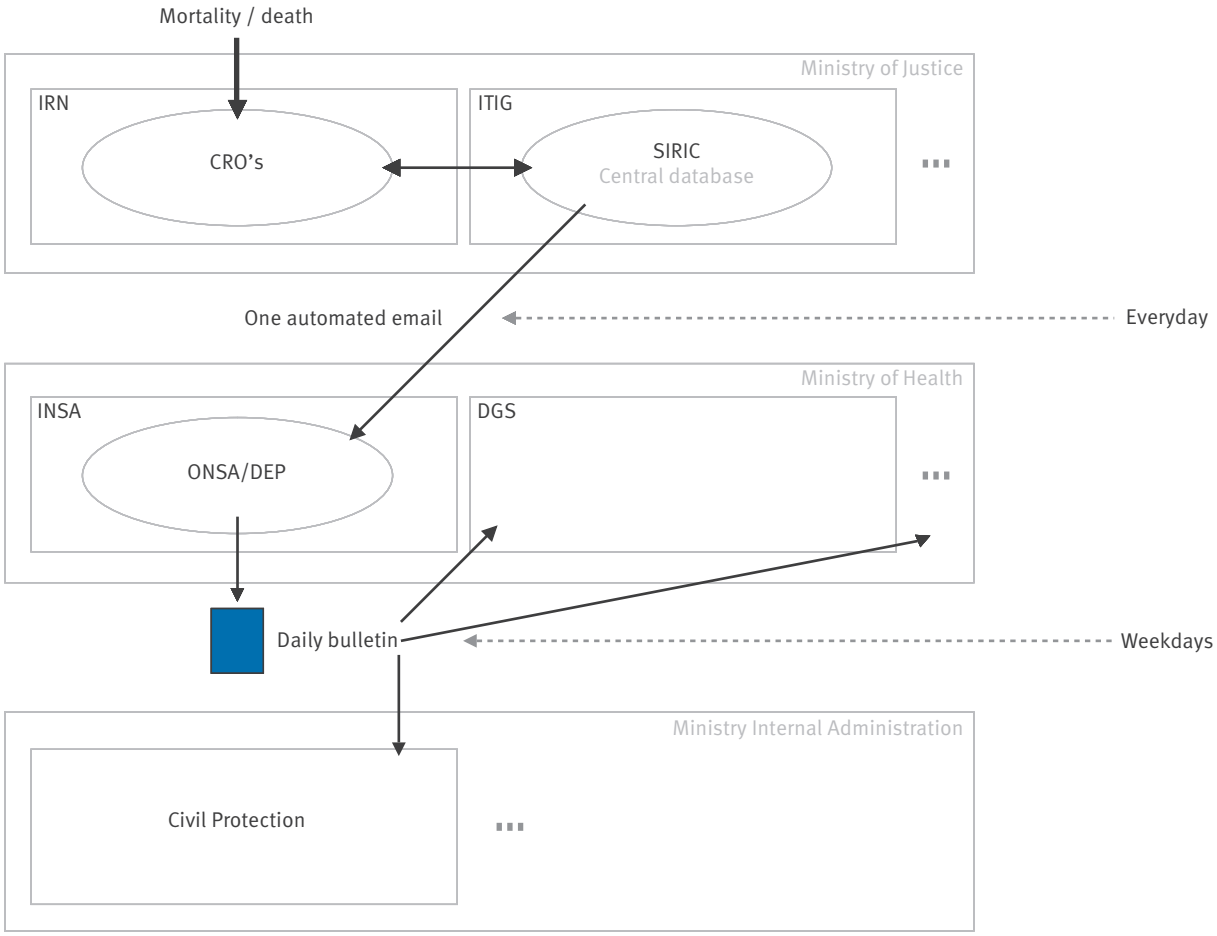
Results

New VDM system overview

Figure 4 shows mortality series, identifying the influenza epidemics and heat periods as well as the evolution of the ICARO system. The evolution of ILI incidence rate per 100,000 inhabitants is presented elsewhere [10]. From January 2006 to June 2007, several CROs were added to the SIRIC system, resulting in several steps visible in Figure 4 as abrupt increases in the number of reported deaths. Mortality peaks identi-

Figure 3

New daily mortality surveillance system (VDM) system, Portugal, since 2007



CRO: Civil Registrar Offices; DGS: General Directorate of Health; INSA: National Health Institute Dr. Ricardo Jorge; IRN: Institute for Registries and Notary; ITIJ: Institute for Information Technologies of Justice; ONSA/DEP: National Health Observatory/ Epidemiology Department of INSA;
SIRIC: Integrated system for civil registries and identification.

fied by the system coincide with important events of heatwaves and influenza activity.

The information collected by the new VDM system, by sex, age group and region of death registration is summarised in table 3 below.

VDM system delay

In order to understand the potential and applicability of the generated data, it was important to determine the system delay (time in days from death until inclusion in the VDM system). Overall, 14.1% of deaths were included on the day of occurrence, 58.0% within one day, 77.9% within two days, 94.2 within three to four days, and 98.0% were included within seven days of occurrence.

While each weekday had a specific information delay (Figure 5), the different patterns seemed to be the simple consequence of the weekend when only a reduced number of CROs are available. The greatest proportion of mortality included on the day of occurrence was observed on Fridays. Fridays were also the weekdays on which it took longer to include all information in the system, with only 87.3% of complete information available within four days.

Table 1

Influenza epidemic periods potentially associated to excess mortality, Portugal, 2006-9

Influenza epidemic season	Period (weeks)	Number of weeks
2006-7	Weeks 3 to 9/2007	7
2007-8	Weeks 3 to 7/ 2008	5
2008-9	Week 49/2008 to week 6/2009	10

Table 2

Heat periods potentially associated to excess mortality, Portugal, 2007-2009

Year	Period	Beginning	End
2007	p1	09-05-2007	11-05-2007
2007	p2	17-05-2007	20-05-2007
2007	p3	02-06-2007	08-06-2007
2007	p4	04-07-2007	16-07-2007
2007	p5	25-07-2007	13-08-2007
2007	p6	17-08-2007	20-08-2007
2007	p7	23-08-2007	29-08-2007
2007	p8	02-09-2007	14-09-2007
2008	p1	13-06-2008	16-06-2008
2008	p2	25-06-2008	03-07-2008
2008	p3	14-07-2008	26-07-2008
2008	p4	30-07-2008	16-08-2008
2008	p5	20-08-2008	30-08-2008
2009	p1	25-05-2009	04-06-2009
2009	p2	11-06-2009	24-06-2009

Confirmation and detection of an event's impact

Detection

Figures 6 and 7 show the results of a cyclical model fitting total data, stratified at various levels (sex, age group and two major Portuguese regions) both daily and weekly. It is noteworthy that the main known events (influenza activity and heat) were identified by the system as expected.

The influenza periods 2006-7 and 2008-9 and the heat periods of 2007 and 2008 were identified using both daily and weekly data. However, daily data seemed to generate better evidence of the occurrence of these events than the VDM data aggregated by week.

There was a consistent lack of evidence for any impact on mortality of the observed influenza activity during the season of 2007-8. This was expected, since the estimated incidence rates were low and within the sentinel influenza surveillance 95% confidence interval limits. The consistent increase of mortality identified in the daily data series (Figure 6) at the end of year of 2007 did not correspond to any known event.

Confirmation

Figures 8 and 9 demonstrate the impact on mortality of known events, namely the influenza seasons 2006-7 and 2008-9, the heat periods of 2007 and 2008, and provide some evidence of an impact on mortality of the heat period observed in the summer of 2009.

Both approaches (daily and weekly) were suitable for the confirmation of events. The weekly aggregated data confirmed an impact of influenza activity in 2006-7 and 2008-9 and the heat periods of 2007 and 2008. The daily data on the other hand showed less excess mortality related to the 2008 heat period and better evidence of impact of the 2009 heat period. Also here, both approaches did not reveal any impact of the influenza activity of 2007/8 and showed increased mortality at the end of 2007.

Figure 8. Cyclical regression on daily mortality data generated by the daily mortality surveillance system (VDM), with defined event periods (respective data omitted in model fitting), by total mortality, sex, age group and two major regions in Portugal, January 2007-June 2009

Discussion and conclusion

Our results show the advantages of the VDM system: lightness, timeliness, rapidity and completeness. By lightness we mean that very little information on a registered death is exchanged, consisting only of date of death and registration, sex, age and region of death registration. The residence of the individual was not considered in order to enforce confidentiality of data.

The system obtains information very quickly and in a very complete way. It collects 94.2% of the total number of deaths within four days of their occurrence and 98% within seven days; it allows detecting impacts on mortality in a very timely manner; and it seems to be sensitive to phenomena that are generically considered for the construction of such mortality surveillance systems, i.e. it is sensitive to extreme weather events and to winter influenza activity [7,10]. In fact, in a year with moderate summer temperatures as in 2007, the VDM system data without additional information could point out even some of the events with low impact in mortality within a framework of event detection (Figures 6 and 7).

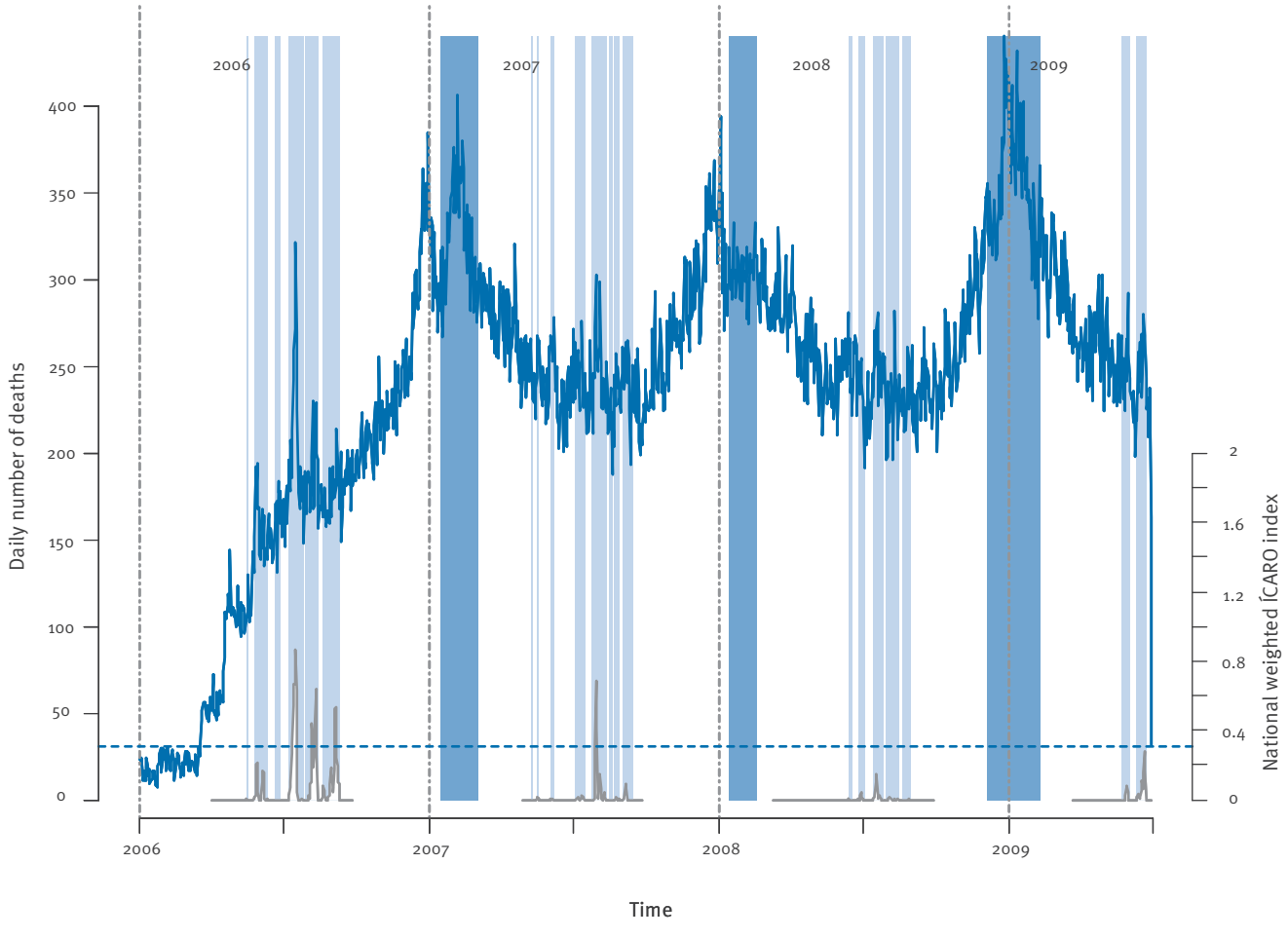
We showed that the reporting delay was dependent on the weekday, with deaths occurring on Fridays entered into the VDM system with the greatest delay (three or more days), although mortality registration on the same day of death occurrence was highest on Fridays. This pattern might indicate that mortality monitoring is least influenced by delay on Thursdays, when most of the weekend mortality is already integrated. This would probably be the optimal day for monitoring of mortality data from the preceding week.

Mortality data delay also showed some dependence on the month of registration (data not shown). January to March had the minimum delay with at least 14.7% of the data registered on the day of the mortality event and more than 80% within two days. Greater delays occurred in April, August and December, which was expected because these months are associated with holiday periods. The minimum mortality registered on the day of death occurrence was 12.2% in December, followed by the summer months with about 13%. In months associated with holidays (April, August and December), arrival of data within two days was always below 75%, with December reaching only 71.5%.

The system delays related to weekdays and months are basically a reflection of society's organisation of time. This time structure remains unaltered through the years, therefore detection and determination of event impacts should be done using within-system data for the definition of baselines and thresholds. Overall, the identified system delays are not expected to dramatically change monitoring or surveillance schemes using VDM system information. Empirically, past experience of VDM system management, both in the old and the new version, showed that residual impacts on

Figure 4

Daily observed mortality data collected by the new daily mortality surveillance system (VDM) and ICARO Index, Portugal, 2006-2009



Blue line: new VDM system; grey line: ICARO Index; light blue bars: heat periods; medium blue bars: influenza epidemic periods.

mortality (like those of the moderate heat periods of 2007 and 2008) are usually only identifiable about four or five days after the event.

It seems widely accepted to study winter/influenza activity using weekly aggregated mortality data and heatwaves of moderate proportion using daily mortality data. For heatwaves, the daily level is very important in order to quickly confirm the impact and initiate mitigating measures. Our results, albeit contradictory, indicated that daily data may be better suited to confirm and detect events in general. The contradiction lay in the fact that best confirmation of an event, both influenza activity and moderate or mild heat periods, was obtained from daily data, while these daily data were of limited use for the purpose of detecting heatwaves. This latter limitation may be due to the fact that the system so far only covers a short time series of 2.5 years. It is reasonable to expect that as the VDM time series gets longer, its ability to model cyclical patterns, detect and confirm relevant events will improve.

The apparently unexplainable increase in mortality at end of the year 2007 may in fact have been a result of the short length of the VDM data series at the time. The increased mortality may reflect a cyclical pattern that has not yet been picked up because many other events occurred in the relatively short studied period.

The current status of the new VDM system allows us to look forward convinced that it can be used in a timely and useful manner no matter what public health problems arise (provided they have a detectable impact on mortality). But there were challenges during the development of the current system: The first version of the automated VDM system was not fully automatic and relied on human intervention. With the increase of data and work, it had to be improved and the used XML data structure had to be changed. That posed problems because the simple solutions previously adopted and implemented in Microsoft Excel were not able to deal with the new data structure. The problem could not be solved by the use of statistical packages. Basically, the system received partial records of different tables, relating to the same individual but not connected. A solution was found using an open source database management system called MySQL. Although the solution was not complex, it took more than six months to have the system completely operational and re-establish of the data flow.

In early 2009, when trying to check if the number of records for full years was correct, about 5% of data was found to be missing. The explanation for this was that only records with registration and confirmation on the same day were being sent to VDM. Records registered on one day, but with administrative confirmation on a different day were not sent. What must be stressed is that both parties intended to exchange all the information, but the implementation was done in a different way. This was easily corrected and now all is working correctly. Such quality control must be implemented in early phases of these systems.

The construction of an automated system for mortality surveillance requires strong inter-institutional will and awareness of the potential downfalls to ensure that such a system is fully operational all year round. This seems to be more important than financial resources, seeing as the successive versions of the Portuguese

Table 3

Number of deaths registered in the daily mortality surveillance system (VDM) by sex, age group and region of death registration, Portugal, January 2006-June 2009

		n	%
Total		**264,427**	**100%**
Sex			
	Male	135,832	51,4%
	Female	128,475	48,6%
	Unknown	120	0,045%
Age group (years)			
	0 - 14	1,462	0,6%
	15 - 24	1,366	0,5%
	24 - 44	9,393	3,6%
	45 - 64	34,991	13,2%
	65 - 74	43,896	16,6%
	75+	169,717	64,2%
	Unknown	3,602	1,4%
Region (of death registration)			
	Norte	76,880	29,1%
	Centro	65,017	24,6%
	Lisboa	69,075	26,1%
	Alentejo	22,441	8,5%
	Algarve	12,022	4,5%
	Açores	5,814	2,2%
	Madeira	6,546	2,5%
	Other/foreign	6,632	2,5%

Figure 5

Delay of data inclusion in the daily mortality surveillance system (VDM) from date of death occurrence to registration, by weekdays, Portugal, 5 June 2007 to 4 June 2009

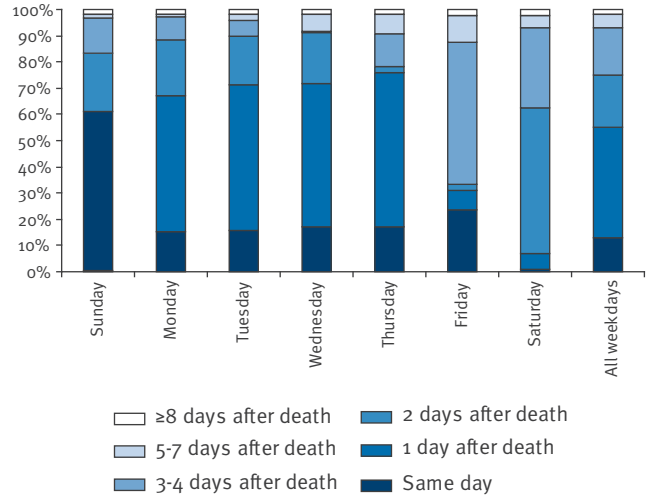
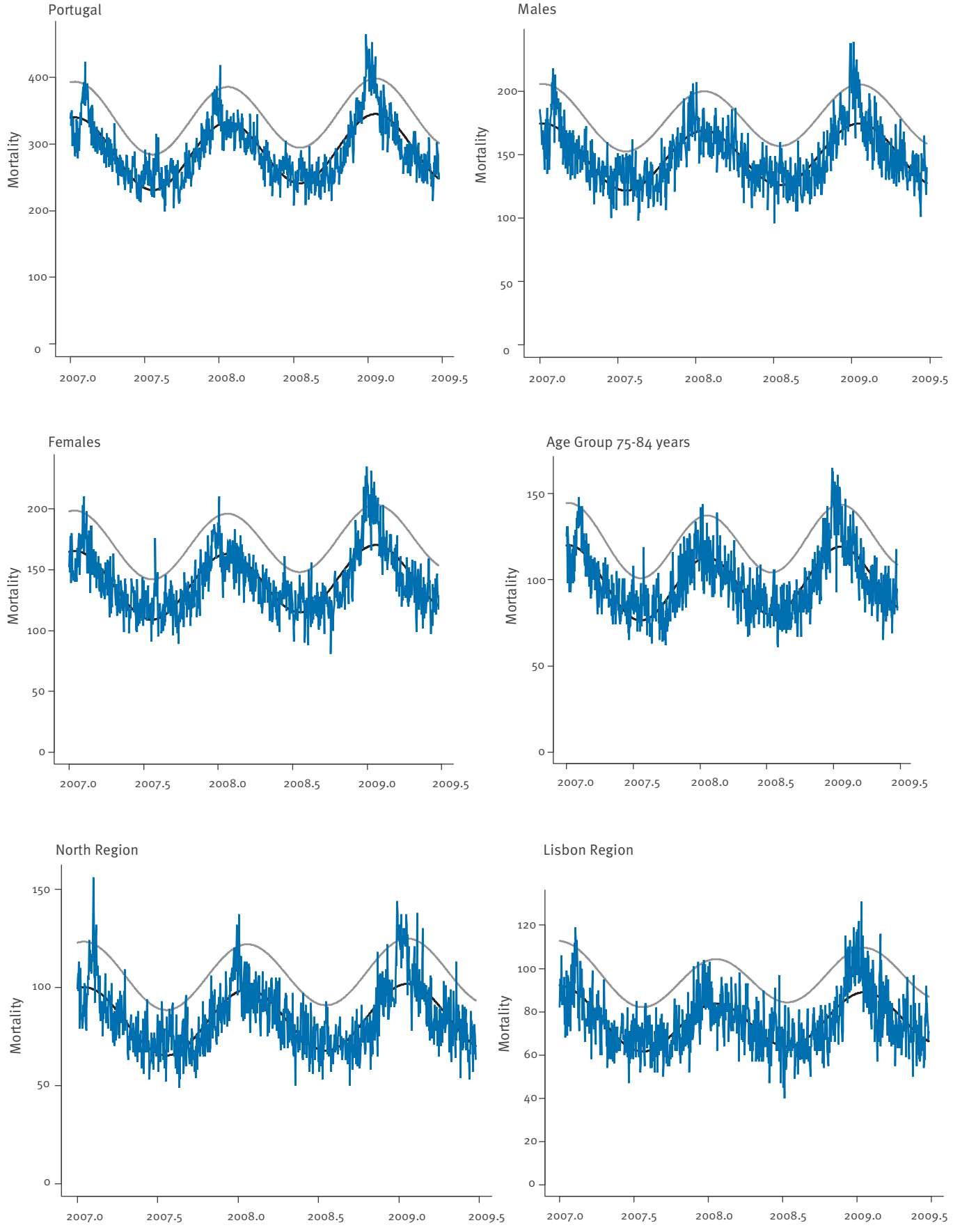


Figure 6

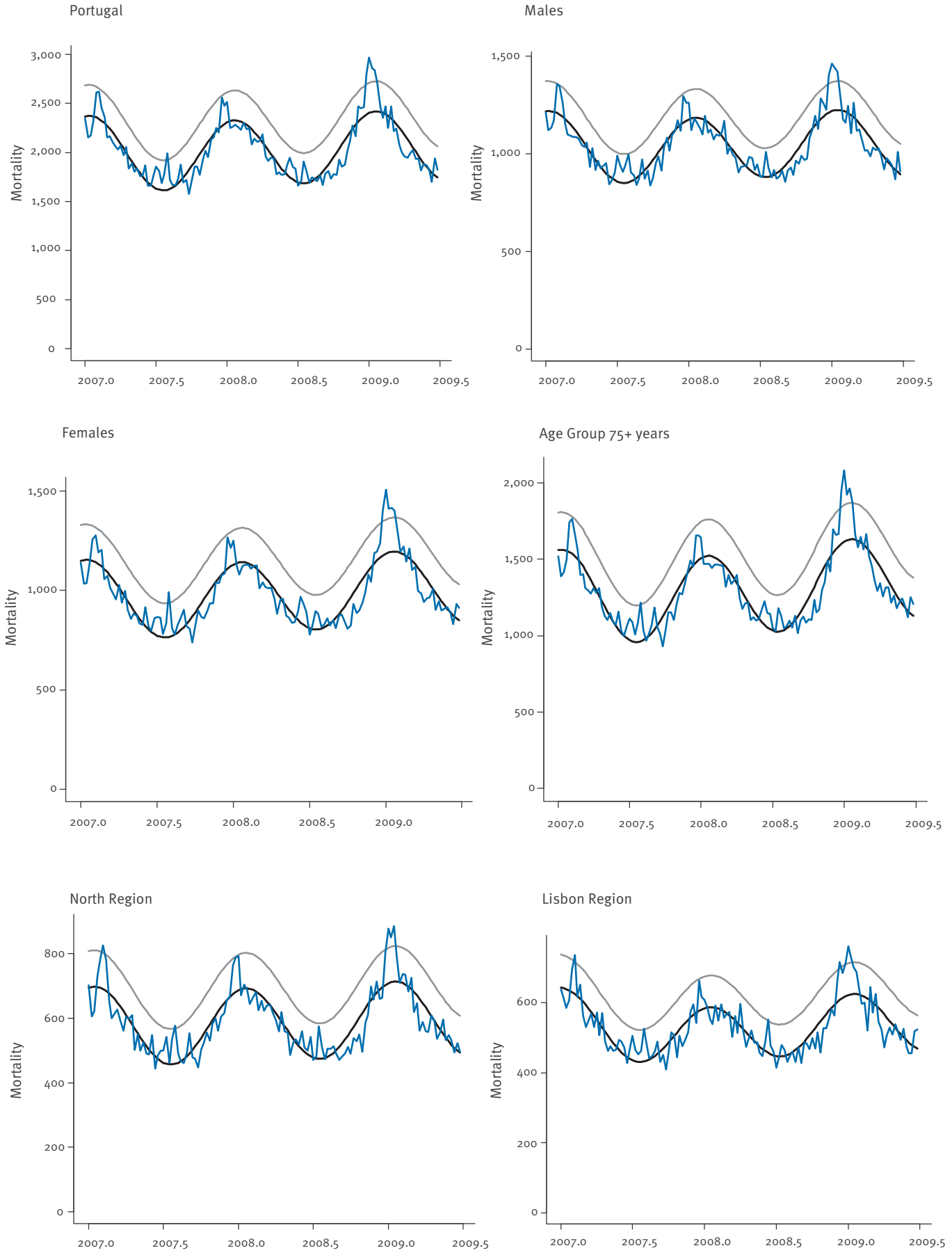
Cyclical regression of daily mortality data generated by the daily mortality surveillance system (VDM) without definition of event periods (for detection purposes) by total mortality, sex, age group and two major regions in Portugal, January 2007-June 2009



Black line: mortality baseline; blue line: observed mortality; grey line: baseline 95% confidence interval upper limit.
In the x axis, .0 stands for beginning of the year, .5 for half year.

Figure 7

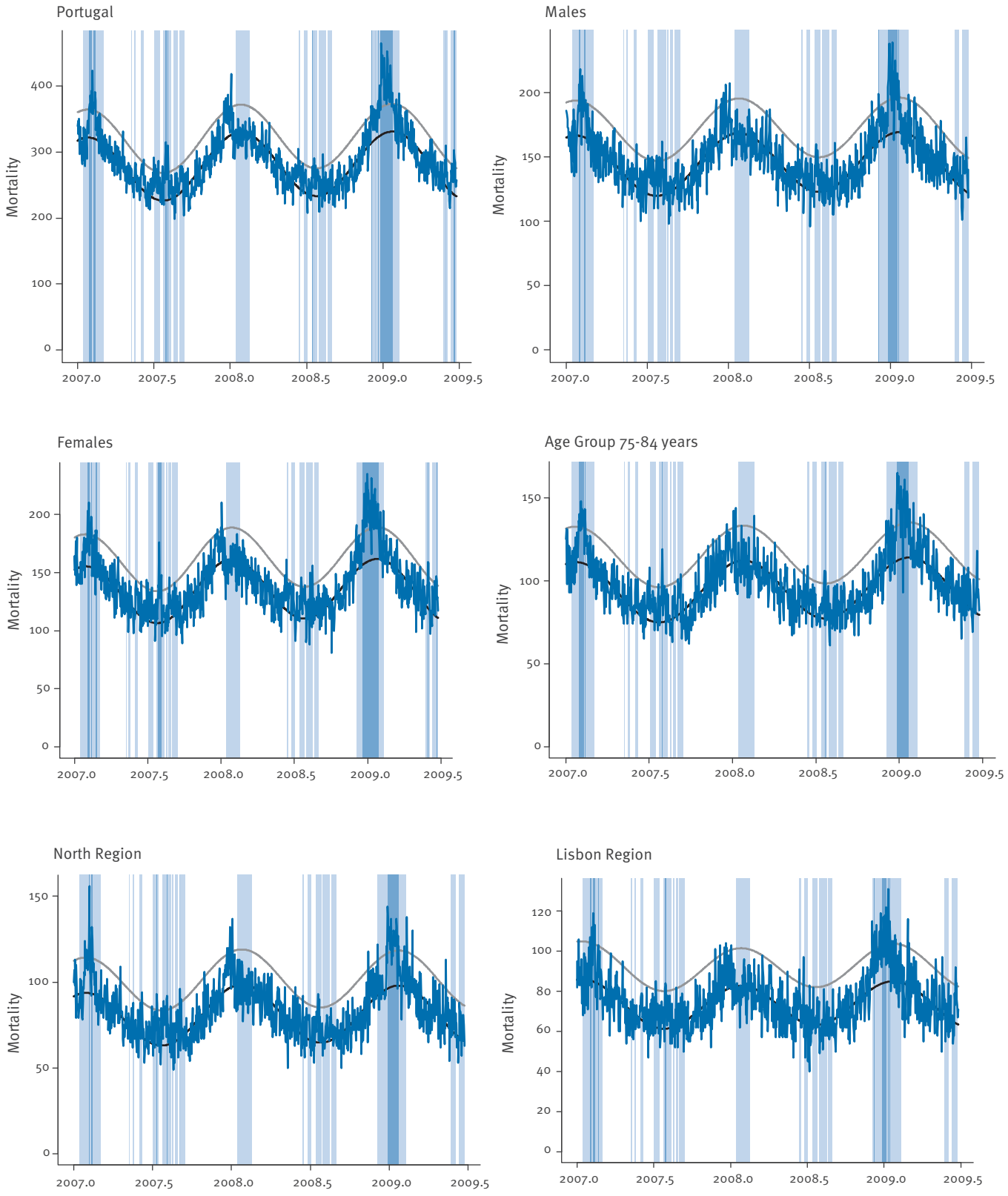
Cyclical regression on data generated by the daily mortality surveillance system (VDM), aggregated by week, without defined events periods (for detection purposes), by total mortality, sex, age group and two major regions in Portugal, January 2007-June 2009



Black line: mortality baseline; blue line: observed mortality; grey line: baseline 95% confidence interval upper limit.
In the x axis, .0 stands for beginning of the year, .5 for half year.

Figure 8

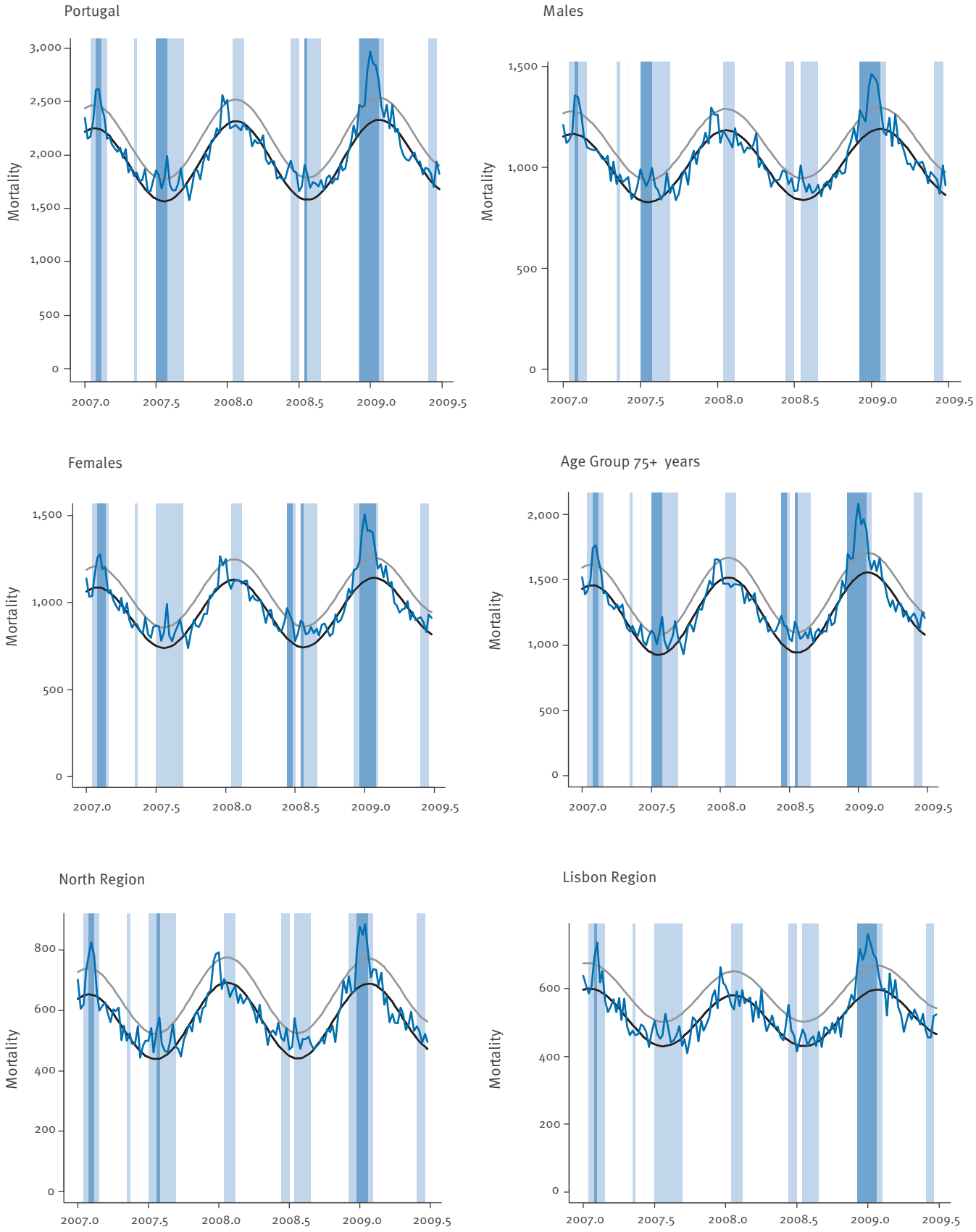
Cyclical regression on daily mortality data generated by the daily mortality surveillance system (VDM), with defined event periods (respective data omitted in model fitting), by total mortality, sex, age group and two major regions in Portugal, January 2007-June 2009



Black line: baseline as defined by cyclical regression representing expected mortality; grey line: 95% Confidence interval upper limit.
Light blue bars: known events periods; medium blue bars: confirmed excess mortality periods (two or more consecutive days).
In the x axis, .0 stands for beginning of the year, .5 for half year.

Figure 9

Cyclical regression on data generated by the daily mortality surveillance system (VDM), aggregated by week, with defined events periods (respective data omitted in model fitting), by total mortality, sex, age group and two major regions in Portugal, January 2007-June 2009



Black line: baseline as defined by cyclical regression representing expected mortality; grey line: 95% Confidence interval upper limit.
Light blue bars: known events periods; medium blue bars: confirmed excess mortality periods (two or more consecutive weeks).
In the x axis, .0 stands for beginning of the year, .5 for half year.

VDM system were developed without any specific budget using only the available manpower and computer technology. It should be possible to establish a timely mortality surveillance system such as the VDM at European level. It would probably need goodwill and coordination between institutions within and among the countries rather than resources, and faces potential technical pitfalls that would need to be solved.

Currently, the new version of the VDM system has been separated from the ICARO surveillance system, having its own bulletin that is sent on every weekday to national and regional health authorities and also to the Portuguese civil protection authorities. Some products based on this system are being studied for future application. A system for surveillance of infant mortality is currently being tested with promising results.

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