Eurosurveillance
Europe's leading journal on infectious disease epidemiology, prevention and control

Vol. 15 | Weekly issue 18 | 6 May 2010

Rapid communications

Research articles

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ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

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Pandemic influenza A(H1N1) 2009 breakthrough infections and estimates of vaccine effectiveness in Germany 2009-2010

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Citation style for this article:
Citation style for this article: Wichmann O, Stöcker P, Poggensee G, Altmann D, Walter D, Hellenbrand W, Krause G, Eckmanns T. Pandemic influenza A(H1N1) 2009 breakthrough infections and estimates of vaccine effectiveness in Germany 2009-2010. Euro Surveill. 2010;15(18):pii=19561. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19561

This article has been published on 6 May 2010

During the 2009 influenza pandemic, a monovalent AS03-adjuvanted vaccine was almost exclusively used in Germany for immunisation against the 2009 pandemic influenza A(H1N1) virus. One-dose vaccination was recommended for all age groups. We applied the screening method for the rapid assessment of vaccine effectiveness (VE) based on reported data of vaccinated and unvaccinated pandemic influenza cases and vaccination coverage estimates. Preliminary results demonstrate excellent VE in persons aged 14-59 years (96.8%; 95% confidence interval (CI): 95.2-97.9) and moderately high VE in those 60 years or older (83.3%; 95% CI: 71.0-90.5).

Introduction

In Germany, vaccination against pandemic influenza A(H1N1) 2009 was initiated on 26 October (calendar week 44) with the monovalent AS03-adjuvanted H1N1-vaccine Pandemrix® containing 3,25 µg haemagglutinin. At the onset of the vaccination campaign, the number of reported pandemic influenza cases had just begun to rise rapidly and eventually peaked in week 47 (Figure 1).

A non-adjuvanted vaccine was introduced seven weeks later but was restricted to pregnant women. In a randomised clinical trial a higher dose of the AS03-adjuvanted vaccine (5.25 µg haemagglutinin) showed seroconversion and seroprotection rates over 96% after one shot [1]. Based on these data, the German regulatory authority recommended that one dose was sufficient for immunisation against 2009 pandemic influenza A(H1N1). While immunogenicity data remain the basis for licensure of these vaccines, it is unknown how well they correlate with protection [2]. Therefore, it is essential to estimate vaccine effectiveness (VE) from post-marketing surveillance data to confirm that the one-dose vaccination regimen induces sufficient protection in different age and risk groups [3]. Here we present results from the analysis of breakthrough infections reported through the statutory disease notification system in Germany and report VE estimated using the screening method [4,5].

Methods

With onset of the pandemic, influenza surveillance in Germany was intensified. Notified 2009 pandemic influenza A(H1N1) cases were interviewed by local public health officials for underlying chronic diseases, hospitalisation, and influenza vaccination status. Data from studies on seasonal influenza vaccines showed that protective antibodies are present in over 90% of persons 14 days after vaccination [6]. Therefore we defined vaccine failure as laboratory-confirmed pandemic influenza in a person vaccinated more than 14 days prior to illness onset. Potential risk factors for vaccine failure were assessed by comparing vaccine failure cases with persons vaccinated during the seven days prior to disease onset. The latter group was considered as representative of vaccinated persons in general and, assuming reasonably high VE it should have included only a small proportion of individuals who would have shown true vaccine failure had the infection occurred at a later point in time. For multivariate analysis, logistic regression models were applied using stepwise backward removal with inclusion of age, sex, and all variables with a p-value of ≤0.2 in univariate analysis in the first step.

To monitor pandemic influenza vaccine uptake in Germany, a computer-assisted telephone survey was carried out during the vaccination campaign starting in calendar week 47. A randomly selected representative sample of 1,000 individuals of 14 years or older was interviewed at two week intervals. Demographic information, influenza vaccination status (receipt of 2009-10 seasonal influenza vaccine or 2009 pandemic influenza vaccine, including month of vaccination), as well as knowledge of and attitude towards pandemic influenza vaccination were elicited using a standardised questionnaire. Average vaccination coverage and 95% confidence interval (CI) were weighted for representativeness of the target population. We estimated VE by using the following formula:

$$VE = (PPV-PCV) / PPV(1-PCV) \times 100\%$$

where PPV is the proportion vaccinated in the population and PCV the proportion of vaccinated cases [4]. Laboratory-confirmed pandemic influenza cases notified in all German federal states from week 47 in 2009 (the week when first vaccination coverage data were available, i.e. three weeks after initiation of the vaccination campaign) to week four in 2010 were included in the analysis. Since the exact date of vaccination and symptom onset were not available for all vaccinated cases, an expansion factor was calculated by dividing the total number of cases vaccinated against pandemic influenza by the number of vaccinated cases with available information (Table).

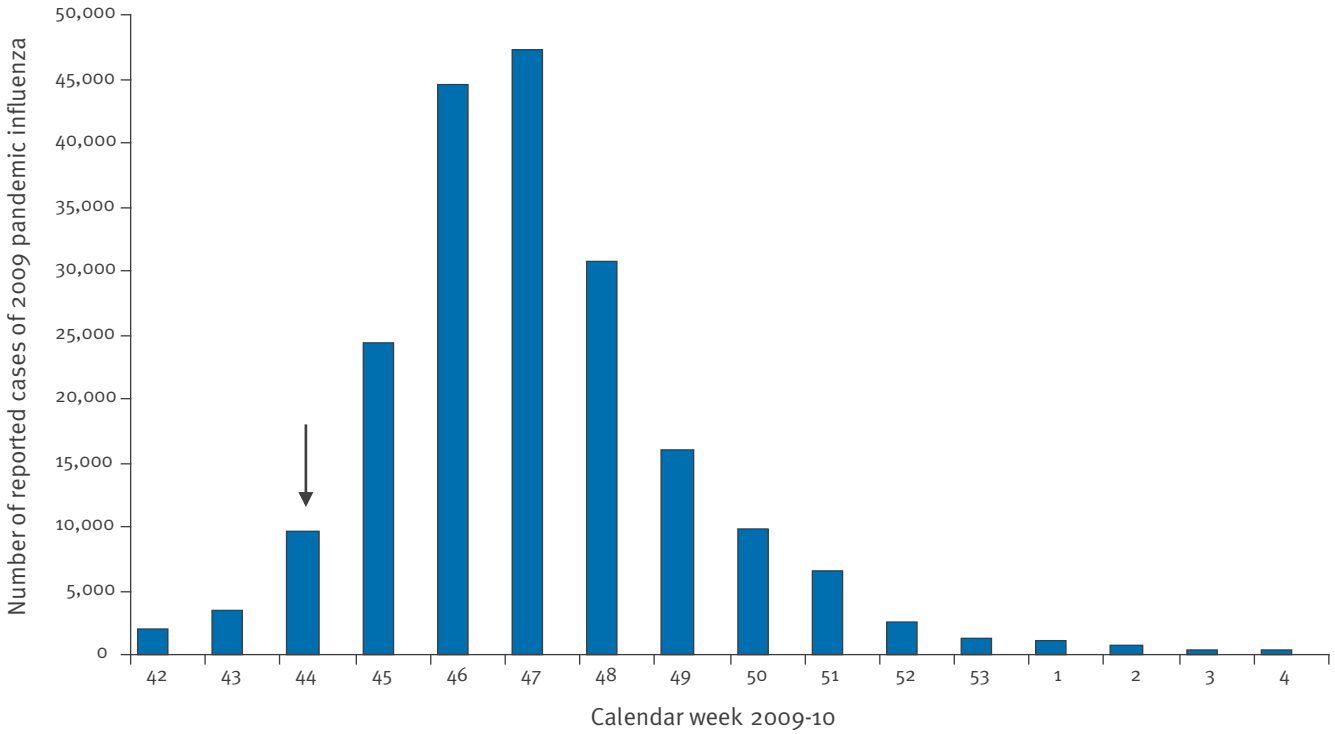
Results

From week 47 in 2009 to week four in 2010, a total of 71,315 laboratory-confirmed pandemic influenza cases were notified. Of 45,733 cases with information available, 425 (0.93%) were reported to be vaccinated against pandemic influenza. Figure 2 shows the distribution of vaccinated cases by number of days between date of vaccination and disease onset: 180 were vaccinated seven days or less, 48 cases 8-14 days, and 61 cases more than 14 days prior to disease onset (136 cases with missing data on vaccination date or symptom onset).

In univariate analysis, age (proportion of cases 60 years or older: 11.4% among vaccine failures versus 3.6% among cases vaccinated seven days or less prior

Figure 1

Number of reported pandemic influenza cases by calendar week, Germany, week 42, 2009 - week 4, 2010



The vaccination campaign was initiated in week 44, 2009 (indicated by the black arrow).

Table

Pandemic influenza 2009 A(H1N1) vaccine effectiveness for individuals ≥14 years of age, estimated by the proportion of pandemic influenza cases with vaccine failure reported among all laboratory-confirmed cases in routine surveillance and the proportion vaccinated in the general population, Germany, week 47, 2009 – week 4, 2010

Age groups (years)	H1N1 cases (total)	H1N1 cases with vaccination status available		Vaccine failures (cases with disease >14 days after vaccination)	Expansion factor (total vaccinated cases / vaccinated cases with information on date of vaccination and symptom onset)	Vaccine failures (after applying expansion factors)	Proportion H1N1 cases with vaccine failure among H1N1 cases with available vaccination status	Proportion vaccinated in the general population (95%CI)	Vaccine effectiveness (95%CI)
		Cases not vaccinated against H1N1	Cases vaccinated against H1N1						
14-59	37,756	23,853	219	35	1.52 (219 / 144)	53.2	0.0022	0.064 (0.044-0.093)	96.8% (95.2-97.9)
≥60	1430	923	25	7	1.92 (25 / 13)	13.4	0.0141	0.079 (0.047-0.131)	83.3% (71.0-90.5)

to symptom onset, p=0.027) and previous seasonal influenza vaccination (61.8% versus 41.0%, p=0.008) were associated with 2009 pandemic influenza vaccine failure. Underlying chronic disease (40.0% versus 28.1%, p=0.093) and hospitalisation (9.8% vs. 12.7%, p=0.53) were not significantly associated with vaccine failure. In multivariate logistic regression only age remained independently associated with vaccine failure (odds ratio (OR)= 1.82; 95% CI 1.03-3.21). Immunosuppression was reported for two (3.3%) cases in the vaccine failure group and five (3.0%) in the control group. None of the vaccine failure cases were pregnant.

The vaccination coverage assessment included a total of 6,009 household interviews and revealed an average pandemic influenza vaccination coverage of 6.8% (95% CI 5.0-9.2) for Germany in persons 14 years and older. VE was estimated at 96.8% (95% CI 95.2-97.9) for all persons aged 14-59 years and at 83.3% (95% CI 71.0-90.5) for persons 60 years or older (Table).

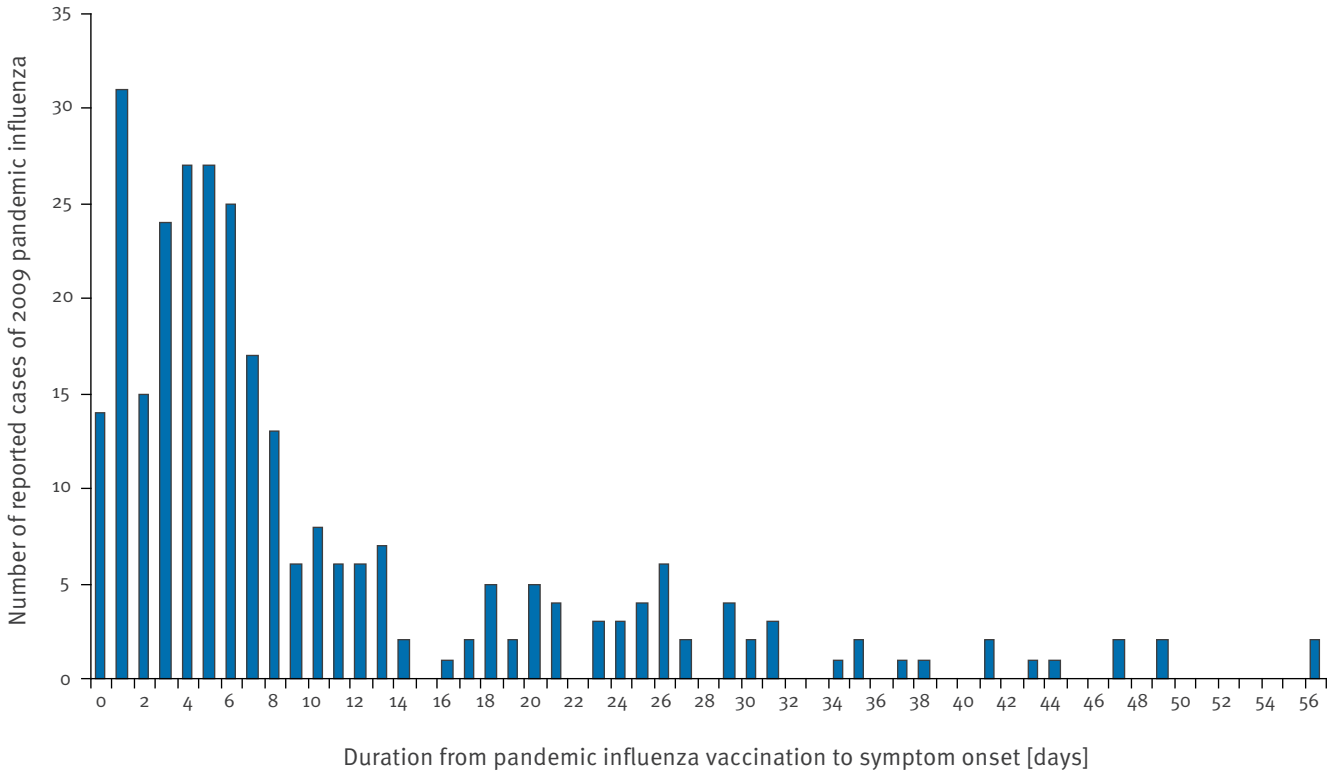
Conclusions

A comparison of the prevalence of potential risk factors for vaccine failure in the group of cases vaccinated in the seven days before disease onset (proxy for successfully vaccinated persons) with that in the group of vaccine failure cases revealed only older age to be significantly associated with vaccine failure, in keeping with the findings from the screening analysis. A Cochrane review has shown high VE of seasonal influenza vaccines up to 80% against laboratory-confirmed seasonal influenza in healthy adults aged 16 to 65 years in seasons in which the vaccine matched circulating strains [7]. In contrast, reviews on the effectiveness of seasonal influenza vaccination in the elderly have shown low or uncertain effectiveness [8, 9]. These reviews identified a lack of high quality, unbiased studies using the specific end-point of laboratory-confirmed influenza. A few studies on the effectiveness of adjuvanted seasonal influenza vaccine were included in the Cochrane review on VE in the elderly [8] and all used non-specific end-points such as preventing influenza-like illness (ILI), hospitalisation, or emergency admissions for pneumonia. However, use of adjuvanted vaccines seems to be a promising approach leading to improved immune responses compared with the conventional vaccines [10]. While lower than in younger adults, our results also suggest an acceptable effectiveness of the AS03-adjuvanted pandemic influenza vaccine in preventing laboratory-confirmed pandemic influenza in the elderly, which should be confirmed in further analytical studies.

A statistically significant association of vaccine failure with underlying chronic disease was not found, suggesting that on the whole, the vaccine is effective in chronically ill persons. However, as this group is rather inhomogeneous, an association of vaccine failure with

Figure 2

Time from pandemic influenza vaccination to date of symptom onset in 298 reported cases with laboratory-confirmed 2009 pandemic influenza A(H1N1) and information on exact date of vaccination and symptom onset, Germany , calendar week 47, 2009 - 4, 2010



certain diagnoses or therapies cannot entirely be ruled out.

The screening method is a quick and simple tool to assess VE in a population with known vaccination coverage. With reasonably accurate estimates of vaccination coverage, this technique can provide a rough guide as to whether further evaluation is necessary [5]. Strengths of our study were the statutory notification of infections with the 2009 pandemic influenza A(H1N1) virus in Germany, the occurrence of more than 70,000 laboratory-confirmed pandemic influenza cases after the implementation of the vaccination campaign, and the availability of only one vaccine type against pandemic influenza. However, it is possible that vaccinated patients with ILI might have been less frequently tested for pandemic influenza compared with unvaccinated persons, thereby potentially leading to VE overestimation. Thus, our results must be regarded as an upper-limit estimate. They nevertheless suggest excellent VE of the AS03-adjuvanted pandemic vaccine after one dose with lower but still acceptable VE in elderly persons.

Acknowledgements

The authors thank all staff of the department for infectious disease epidemiology at Robert Koch Institute who was involved in the management of the 2009 influenza A(H1N1) pandemic. All authors declare they have no conflict of interest.

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Infection with Mayaro virus in a French traveller returning from the Amazon region, Brazil, January, 2010

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Citation style for this article:
Citation style for this article: Receveur MC, Grandadam M, Pistone T, Malvy D. Infection with Mayaro virus in a French traveller returning from the Amazon region, Brazil, January, 2010. Euro Surveill. 2010;15(18):pii=19563. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19563

This article has been published on 6 May 2010

Mayaro virus (MAYV) disease is a mosquito-borne zoonosis endemic in humid forests of tropical South America. MAYV is closely related to other alphaviruses that produce a dengue-like illness accompanied by long-lasting arthralgia. A French tourist developed high-grade fever and severe joint manifestations following a 15-day trip in the Amazon basin, Brazil, and was diagnosed with MAYV infection in January 2010. This case is the first reported in a traveller returning from an endemic South American country to Europe.

Introduction

Mayaro virus (MAYV) (family Togaviridae, genus Alphavirus) is an arthropod-borne zoonotic pathogen circulating only in tropical South America [1]. The transmission cycle of MAYV in the wild is nearly similar to the continuous sylvatic cycle of yellow fever and is believed to involve wild primates (monkeys) as the reservoir and the tree-canopy-dwelling Haemagogus mosquito as the vector. Thus, human infections are strongly associated with recent exposure to humid tropical forest environments [1,2]. MAYV disease is an acute, self-limited dengue-like illness of three to five days' duration. Moreover, MAYV is closely related to chikungunya virus and produces a nearly indistinguishable, highly debilitating arthralgic disease [1-3].

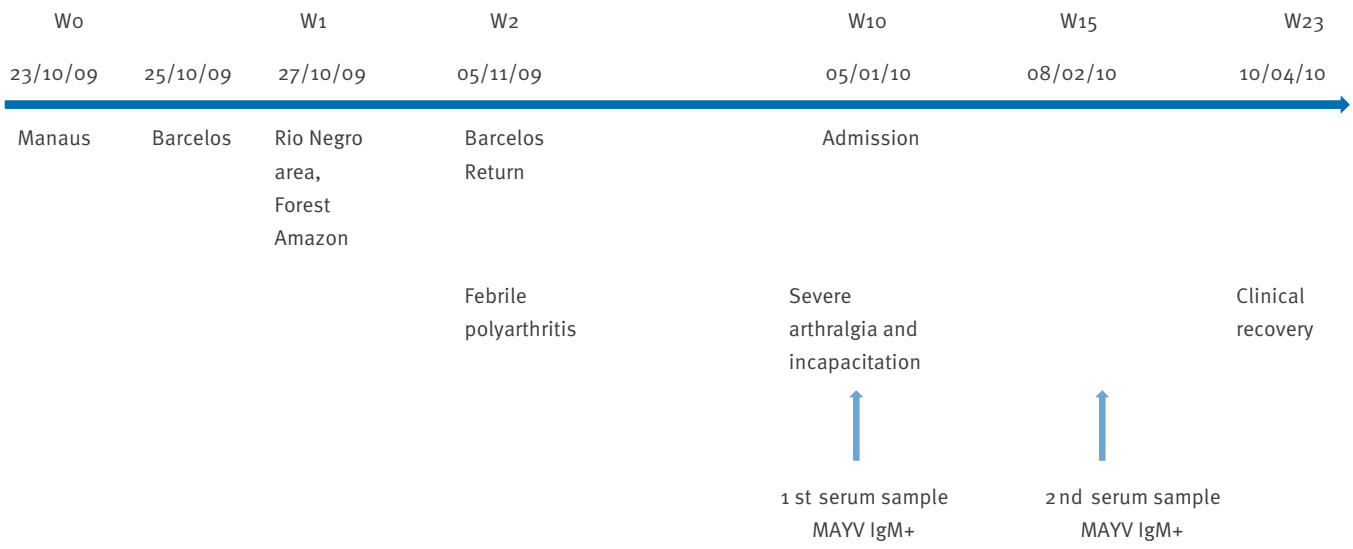
Here we report the case of MAYV disease that recently occurred in a French citizen who presented with severe rheumatologic disorders after visiting the Brazilian Amazon. This report illustrates that with increasing travel to remote areas, travellers are at risk of acquiring and importing rare diseases that are not indigenous to Europe.

Case report

The patient, a man in his late 20s, came to the travel clinic of the Department of Internal Medicine and Tropical Diseases of the University Hospital Centre, Bordeaux, France on 4 January 2010 with persistent incapacitating arthralgia for a two-month period and predominating in his knees and joints of the hands.

Figure

Timeline for travel history and symptoms in a French traveller with Mayaro virus disease, October 2009 - January 2010



The patient had travelled in the Amazon forest region for two weeks in October and November 2009 for the purpose of fishing and butterfly hunting. He stayed for two days in Manaus, Amazonas, Brazil, and for a further two days at Barcelos, Amazonas, north-western Brazil, before travelling in a dugout canoe along the Rio Negro River for ten days to the confluence area of the Demini River with the Araca River, a forest place situated 70 miles north of Barcelos. After another two days in Barcelos, he returned to France via Manaus and Sao Paulo (Figure).

During his second stay in Barcelos, in early November, he developed symptoms assumed to be related to dengue virus infection, with high-grade fever, headache, generalised myalgia and diffuse arthralgia. Macular and partially confluent transient exanthema mainly on his arms appeared around the fifth day of illness. After his return to France, the patient had increasingly difficulty walking and was severely impaired in daily activities because of severe recurrent joint pains.

The patient had received yellow fever vaccine 10 years before. During the trip to the Amazon, he had taken doxycyclin as prophylaxis for malaria.

When he presented to our centre on 5 January 2010 (two months after onset of symptoms), the patient complained of persistent headache, myalgia and severe symmetrical joint pains (wrists and ankles). At the time of presentation, laboratory tests showed a leukocyte cell count of 6,600 cells/µL and a thrombocyte count of 177,000 platelets/µL. No markers of autoimmunity were found, notably anti-citrullin peptide antibodies or antinuclear antibodies. He was negative for the major histocompatibility complex HLA B27 gene. Concurrently, serologic status for dengue, chikungunya and yellow fever viruses as well as MAYV was evaluated using IgM capture and IgG sandwich ELISA at the National Reference Centre for Arboviruses, Institut Pasteur, Paris. Serology for MAYV revealed positive results for specific IgM (optical density [OD]=0.34; serum control OD=0.122). OD values for specific IgG were negative (OD=0.082; serum control OD=0.092). The other serological results were negative, as well as tests for leptospirosis, rickettsiosis, Q fever, cytomegalovirus and Plasmodium falciparum malaria. Five weeks later, on 8 February 2010, MAYV antibody serology showed persistence of specific IgM (OD=0.494; serum control OD=0.116) and a lack of immunoglobulin switching from IgM to IgG (OD for IgG=0.076; serum control OD=0.084).

The patient recovered completely, although severe joint pain persisted for eight further weeks until 10 April despite symptomatic treatment. The diagnosis of a presumptive case of MAYV infection diagnosed by serology was established.

Discussion

To the best of our knowledge, this case is the first published report of MAYV disease in a traveller returning to Europe. The presenting symptoms and signs were almost identical to those reported in previous clinical descriptions of the disease [2,4,5]. In this case, the decision to test for a rather exotic virus such as MAYV was based on several factors: the patient's detailed travel history in tropical South America, which allowed risk factors to be identified such as potential exposure to vectors carrying diseases endemic in that area; the clinical presentation with incapacitating arthralgia following acute febrile illness; and finally, the expertise and technical tools available in the specialist clinic for tropical medicine where the patient was treated. Other viral infections with similar clinical presentation and geographical distribution were ruled out by laboratory tests.

The case illustrates the challenge of clinically differentiating MAYV disease from classical dengue fever and other febrile exanthematous diseases that also circulate in South America, as well as the role of laboratory confirmation in establishing a correct diagnosis. Indeed, dengue fever was initially suspected considering its occurrence in most cities and places on tropical America, including the Amazon basin. The pathogenesis of debilitating symptoms in MAYV disease is still a poorly understood phenomenon [5], although persistent infection of synovial macrophages has been documented for other closely related and also arthritogenic alphaviruses [6]. The results of serological studies of the two consecutive convalescent-phase serum samples showed that the patient did not seroconvert with a switch from IgM to IgG. In most acute arboviral infections, IgM class-specific antibodies are generally no longer detectable after a period of 6-12 months post infection [7,8]. Considering the period for seroconversion in MAYV infection, we can therefore assume that the time between disease onset and the last late-phase blood sampling in this patient was not long enough for to allow Ig class switching.

Interestingly, this report highlights the need for increased awareness MAYV disease as a differential diagnosis in travellers or migrants returning from endemic areas of tropical South America with febrile illnesses involving peripheral rheumatism and persistent arthralgia. Finally, it illustrates how travellers can act as signals for alert that can provide insights into the risk of transmission of infections in certain geographical areas.

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The growing contribution of hepatitis C virus infection to liver-related mortality in Scotland

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Citation style for this article:
Citation style for this article: McDonald SA, Hutchinson SJ, Bird SM, Robertson C, Mills PR, Graham L, Dillon JF, Goldberg DJ. The growing contribution of hepatitis C virus infection to liver-related mortality in Scotland. Euro Surveill. 2010;15(18):pii=19562. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19562

This article has been published on 6 May 2010

The large number of individuals in Scotland who became infected with the hepatitis C virus (HCV) in the 1970s and 1980s leads us to expect liver-related morbidity and mortality to increase in the coming years. We investigated the contribution of HCV to liver-related mortality in the period January 1991 to June 2006. The study population consisted of 26,861 individuals whose death record mentioned a liver-related cause (underlying or contributing). Record-linkage to the national HCV Diagnosis database supplied HCV-diagnosed status for the study population. The proportion diagnosed with HCV among people dying from a liver-related cause rose from 2.8% (1995-1997) to 4.4% (2004-June 2006); the largest increase occurred in those aged 35-44 years at death (7% to 17%). Among all deaths from a liver-related cause, an HCV-positive diagnosis was more likely in those who died in 2001 or later than those who died in 1995-1997 (2001-2003: odds ratio=1.4, 95% confidence interval: 1.1-1.7; 2004-June 2006: 1.6, 1.3-2.0), and in those who died at under 55 compared with at least 55 years of age. HCV infection represents a significant, growing, public health burden in Scotland in terms of early deaths from liver disease.

Introduction

Mortality from severe liver disease, of which major contributing factors include excessive alcohol consumption and chronic infection with the hepatitis C virus (HCV), is increasing in Scotland [1,2] and in other developed countries, such as the United States of America [3]. About 1,500 new HCV diagnoses are made each year in Scotland (population 5.1 million in 2006) [4], and projection models of HCV-related liver disease forecast significant rises in morbidity and mortality over the coming decades, placing a growing clinical and economic burden on the Scottish healthcare system [5]. Given the large number of individuals chronically infected with HCV, and the fact that cirrhosis develops in 5%-15% of these individuals within 20 years of infection [6] and in about 20% within 30 years [7], it is important to ascertain the contribution of chronic HCV infection to liver-related mortality.

The existence of high-quality national HCV diagnosis and mortality databases provided the opportunity to use record-linkage methods to investigate the prevalence of diagnosed HCV infection in people who died from liver disease. The goals of this study were therefore to estimate the contribution of HCV infection to liver-related deaths in Scotland and to examine trends in this contribution over time and by age group. Up-to-date information regarding the contribution of HCV to mortality from liver disease is required to inform public health intelligence and health service planning, and as a calibration check on projections.

Methods

Study population and data sources

Death registrations are held by the General Register Office for Scotland (GROS). The study population consisted of all those who died from 1 January 1991 to 30 June 2006, and whose death certificate specified a liver-related condition.

International Classification of Diseases (ICD) codes were used to extract all records from the deaths register in which a liver-related condition was listed as either the underlying cause (i.e. the disease or injury initiating the train of events leading directly to death) or a contributing cause of death (n=26,861). We obtained underlying and contributing cause-of-death codes from ICD's ninth revision (ICD-9) for deaths between 1989 and 1999 and the tenth revision (ICD-10) for deaths between 2000 and 2006. The relevant cause-of-death categories were: liver cancer, alcoholic liver disease, nonalcoholic liver disease, viral hepatitis, and sequelae of viral hepatitis (Table 1). Specific mention of viral hepatitis C (ICD-10 B17.1, B18.2), unspecified viral hepatitis C (ICD-9 070.7), or other/unspecified viral

hepatitis (ICD-9 070.4-6, 070.9) as a cause of death was also noted, to assess the frequency with which HCV is mentioned on the death certificate. Liver-related deaths among those diagnosed HCV antibody-positive (with or without mention of HCV on the death record) were determined through record-linkage between the GROS deaths registry and the HCV Diagnosis database (details below).

Carstairs social deprivation scores (coded as quintiles) were available for each death record; deprivation score is determined from postcode sector of residence and is based on 2001 census variables [8]. The highest quintile corresponds to the 20% most deprived localities.

The HCV Diagnosis database, maintained by Health Protection Scotland (HPS), is a database of all individuals who have been diagnosed HCV positive in Scotland since testing began in 1991 [9]; laboratory detection of hepatitis C antibody positivity is a requirement for inclusion. This database contains the following non-named information: surname Soundex (a consonant-only phonetic encoding), forename initial, date of birth, sex, and postcode district of residence, as well as data concerning risk activities and the date of the earliest positive specimen. The database contained records for 20,969 persons diagnosed HCV positive between 1 January 1991 and 30 June 2006 [4]. As no probabilistic linkages between the GROS deaths register and the HCV diagnosis database were achieved if the HCV diagnosis record was lacking date of birth and two or more other identifiers, records for 1,295 out of 20,969 HCV-diagnosed people (6%) were deemed to have insufficient identifiers for linkage. Of

Table 1

Deaths from liver-related (underlying/contributing) conditions (n=26,861), and those diagnosed hepatitis C virus-positive (n=871), by cause-of-death category, Scotland, 1 January 1991 to 30 June 2006

Underlying/contributing cause of death	n (%)	HCV[a] (%)	HCV/n %
Alcoholic liver disease (ICD-10 K70; ICD-9 571.0-571.3)	12,018 (44.7)	279 (32)	2.3
Non-alcoholic liver disease (ICD-10 K71-77; ICD-9 570, 571.4-571.9, 572-573)	17,304 (64.4)	500 (57)	2.9
Hepatocellular carcinoma (ICD-10 C22.0, ICD-9 155.0)	1,797 (6.7)	116 13)	6.5
Viral hepatitis (ICD-10 B15-19; ICD-9 070)	620 (2.3)	456 (52)	73.5
Sequelae of viral hepatitis (ICD-10 B94.2, R17, R18, I85.0, I98.2; ICD-9 789.5, 456.0)	1,811 (6.7)	85 (10)	4.7
Total	**26,861 (100)**	**871 (100)**	**3.2**

HCV: hepatitis C virus-positive.

[a] Number of deaths among those diagnosed HCV-positive, determined through linkage to HCV Diagnosis database.

Table 2

Deaths from liver-related (underlying/contributing) conditions (n=26,861), and those diagnosed HCV-positive (n=871), multifactorial logistic regression analysis, Scotland, 1 January 1991 to 30 June 2006

Factor	Level	n	HCV[a]	(%)	OR	95% CI
Sex	Female[b]	10,200	223	(2.2)		
	Male	16,661	648	(3.9)	1.70	1.45-1.99
Age at death	<25	135	8	(6)	5.47	2.63-11.39
	25-34	600	103	(17)	13.72	10.69-17.61
	35-44	2,571	274	(10.7)	7.84	6.56-9.37
	45-54	5,602	228	(4.1)	2.66	2.22-3.20
	55+[b]	17,953	258	(1.4)		
Year of death	Before 1995	4,697	51	(1.1)	0.39	0.28-0.55
	1995-1997[b]	4,657	132	(2.8)		
	1998-2000	5,519	196	(3.6)	1.23	0.98-1.55
	2001-2003	6,592	257	(3.9)	1.35	1.08-1.68
	2004-2006	5,396	235	(4.4)	1.61	1.29-2.01
Deprivation quintile	First, second[b]	6,967	147	(2.1)		
	Third	4,797	145	(3.0)	1.27	1.00-1.61
	Fourth, fifth	14,940	575	(3.8)	1.36	1.12-1.64

HCV: hepatitis C virus-positive; OR: adjusted odds ratio; 95% CI: confidence interval.

[a]Number of deaths among those diagnosed HCV-positive, determined through linkage to HCV Diagnosis database.

[b]Reference.

the records with sufficient identifiers, 68% were male, and 71% (14,018/19,674) were born between 1960 and 1979.

Linkage procedure

Linkage of records between the HCV Diagnosis database and the GROS deaths registry was carried out by the Information Services Division (a division of NHS National Services Scotland) using probabilistic record-linkage techniques [10] to determine the HCV-diagnosed status of all individuals whose cause of death included a liver-related condition. These methods allow for matches using incomplete identifiers. The linked dataset was anonymised (i.e. the only identifiers retained were, date of birth, sex and postcode district of residence) before transfer to HPS for analysis. Linkages were approved by the Privacy Advisory Committee, which oversees confidentiality issues involving data held on NHS Scotland patients.

Data analysis

Logistic regression was used to estimate the association between four epidemiological variables and diagnosed HCV status (i.e. whether or not linked to the HCV Diagnosis database). These were: sex, age at death, year of death (with 1995–1997 specified as the reference category, because HCV testing was more limited before this period), and Carstairs social deprivation quintile. We did not analyse trends in mortality rates because the HCV Diagnosis database has expanded since its inception and people in the later stages of HCV disease may have been over-represented in its earlier years. Statistical analyses were carried out using R version 2.4.0 [11].

To estimate the extent of underreporting of HCV on the death certificate, we computed the proportion of death records that were linked to the HCV Diagnosis database, but failed to list an HCV code as either the underlying or a contributing cause of death. This analysis was also conducted separately for the year range 2000-2006, as the change in cause-of-death coding to the ICD-10 classification in 2000 overcomes the imprecision in the ICD-9 codes for HCV. The main data analysis was based on the linked data only.

Results

Overall description

Between 1 January 1991 and 30 June 2006, a total of 26,861 people died in Scotland whose death record specified a liver-related condition as the underlying or a contributing cause of death (Table 1). The majority of liver-related deaths occurred in males (62%; 16,660/26,861), and the median age at death was

Table 3

Deaths from a liver-related condition by period of death, mention of hepatitis C virus (HCV) in the death record, and linkage to the HCV Diagnosis database, Scotland, 1 January 1991 to 30 June 2006

		Linked to HCV Diagnosis database		
Period	**Mention of HCV in death record[a]**	**Yes (%)**	**No**	**Total (%)**
1991-1999	HCV mentioned HCV not mentioned **Total**	158 (51) 150 (49) **308**	45 12,617 **12,662**	**203 (%)**
2000-2006	HCV mentioned HCV not mentioned **Total**	292 (52) 271 (48) **563**	48 13,280 **13,328**	**340 (%)**
1991-2006	HCV mentioned HCV not mentioned **Total**	450 (52) 421 (48) **871**	93 25,897 **25,990**	**543 (%)**

HCV: hepatitis.

[a]Unlinked per cent gives the percentage of death records not linked to the HCV Diagnosis database.

Table 4

Numbers of deaths from liver-related conditions, proportions of those diagnosed hepatitis C virus-positive, by age at death and year of death, Scotland, 1995–1997 and January 2004–June 2006

	1995-1997		1998-2000		2001-2003		2004-June 2006		Total	
Age at death (%)	**n**	**HCV[a] (%)**	**n**	**HCV[a] (%)**	**n**	**HCV[a] (%)**	**n**	**HCV[a] (%)**	**n**	**HCV[a] (%)**
<25	32	4 (13)	29	2 (7)	17	0 (0)	17	0 (0)	**95**	**6 (6)**
25-34	107	20 (19)	143	27 (19)	138	25 (18)	117	20 (17)	**505**	**92 (18)**
35-44	432	30 (7)	544	66 (12)	691	86 (12)	478	80 (17)	**2,145**	**262 (12.2)**
45-54	972	23 (2.4)	1,196	46 (3.8)	1,444	76 (5.3)	1,180	75 (6.4)	**4,792**	**220 (4.6)**
55+	3,114	55 (1.8)	3,607	55 (1.5)	4,302	70 (1.6)	3,604	60 (1.7)	**14,627**	**240 (1.6)**
All ages	4,657	132 (2.8)	5,519	196 (3.6)	6,592	257 (3.9)	5,396	235 (4.4)	**22,164**	**820 (3.7)**

HCV: hepatitis.

[a]Numbers of deaths diagnosed HCV-positive, determined through linkage to HCV Diagnosis database.

61 years (interquartile range (IQR): 51–71) (Table 2). The overall proportion of deaths linked to the HCV Diagnosis database was 3.2% (871/26,861). The median age at death for individuals identified as diagnosed HCV-positive was 47 years (IQR: 39–58).

We report on deaths from underlying or contributing liver-related causes (n = 26,861), but note that distributions of baseline characteristics and annual trends were similar if the data were restricted to deaths from underlying liver-related causes only (n=16,767; data not shown).

Mention of HCV in death records

Viral hepatitis C was listed as the underlying or a contributing cause of death in 1.6% (543/26,861) of all liver-related deaths, and in 52% (450/871) of liver-related deaths linked to the HCV Diagnosis database. This proportion remained the same: 292/563 (52%) when liver-related deaths occurring from 2000 onwards only (n=13,891) were considered (Table 3).

Alcohol (ICD-10 K70, ICD-9 571.0-3) was mentioned in 45% (12,018/26,861) of all liver-related death records (Table 1), but in 51% of the group aged 25–34 years at death (308/600). People on the HCV Diagnosis database accounted for 17% of the liver-related deaths (17%) in the 25–34 age group (Table 2) and 69% of these deaths mentioned an alcohol-related ICD code (data not shown).

Odds of being diagnosed HCV-positive

Of those whose cause of death included a liver-related condition (either underlying or contributing), the odds of being diagnosed HCV-positive were significantly higher for males than for females, and for those who died before the age of 55 years than those who died aged 55 or older. Compared with deaths occurring 1995-1997, the odds of being HCV-diagnosed were higher for deaths occurring in 2001. People who lived in the more deprived regions had significantly higher odds of being HCV-diagnosed than people who lived in the two least deprived quintiles (Table 2). Of the HCV-diagnosed individuals, 32% (278/871) were born between 1960 and 1979. The median interval between HCV diagnosis and death was 2.1 years (range -0.4 to 14.5 years).

Table 4 compares the number and proportion of HCV-linked deaths by age at death and year of death categories, between 1995-1997 and 2004-June 2006. A trend test showed that HCV-linked deaths formed an increasing proportion of liver-related deaths over time, from 2.8% in 1995–1997 to 4.4% in 2004–June 2006 ($p=0.012$). The largest proportional increases over this time-span occurred in people who died aged 35-44 years (from 7% to 17%) and aged 45-54 years (from 2% to 6%). A significant difference in the rate of change in the proportion of HCV-linked deaths over time across age groups was confirmed by an interaction test ($p<0.0001$).

Discussion

Over the past 15 years, we have observed an increasing contribution from HCV infection to mortality due to liver-related causes in Scotland. Deaths increased steadily with time among the 35–54 years age group, and the largest percentage of deaths linked to the HCV Diagnosis database (31%) were of people born from 1950 to 1959. This is consistent with infection of young people in the 1970s and 1980s – before HCV was identified – and the natural history of chronic HCV infection [12]. HCV plays a much smaller role in liver-related deaths in older age groups mainly because relatively few individuals acquired infection at a late enough age.

A relatively high percentage of the liver-related deaths (17%) in the 25–34 age group were HCV-diagnosed individuals; the majority (69%) of these death records mentioned an alcohol-related ICD code. High liver-related mortality in this group may reflect more rapid development of liver disease associated with combined HCV infection and excessive alcohol use [13].

This study is the first to our knowledge that links national HCV diagnosis data to national mortality data to chart the contribution, over time, of HCV to all liver-related deaths [14]. Recent modelling initiatives have predicted substantial rises in HCV-related mortality in the next decade – for example, it is predicted that deaths will increase 2.8-fold between 2000 and 2020 in the United States (US) [15], and increase 1.7-fold between 2005 and 2020 (78 increasing to 129) in current/former injecting drug users (IDUs) in Scotland [16]. In this study, we observed a 1.3-fold rise in the number of liver-related deaths of people diagnosed with HCV infection (71 to 92) from 2000 to 2005, a rate which, if maintained over a further 10 years, would be even steeper than the 2005–2020 projections for IDUs in Scotland. With mortality from liver disease becoming increasingly associated with HCV infection, the importance of offering tests to individuals (particularly those under 55 years of age) presenting to hospital with an unexplained liver-related condition cannot be overemphasised.

It is notable that 48% of the records for liver-related deaths that linked to the HCV Diagnosis database did not mention HCV as either the underlying or a contributing cause of death. This finding has strong implications for public health decision making regarding the HCV epidemic. Underreporting of HCV on death certificates is a problem for many countries, such as England [17] and the US [3,18,19], undermining studies that aim to determine HCV infection's contribution to mortality from liver disease by using cause-of-death coding on death certificates.

Using record-linkage to HCV diagnosis data, we determined that 3.2% of all liver-related deaths were related to HCV infection. This proportion is substantially lower than in previous reports that have considered the role of hepatitis C in mortality from chronic liver disease

– for example, 15% (of 30,933 deaths in 1998) [18] and 16% (56/233 deaths in 2000) [19] in two studies from the US. This difference may be due to a higher prevalence of problem alcohol use in the Scottish population [20], particularly for death at a relatively young age: we note that 45% of all liver-related deaths and 69% of liver-related deaths in the 25-34 years age group mentioned one or more alcohol-related ICD codes.

Our study has important strengths and limitations. The use of a national deaths register to identify liver-related deaths has provided considerable statistical precision. The main limitations relate to a lack of information about chronic, versus resolved, infection on the HCV Diagnosis database, and to record-linkage errors. We assumed that all individuals who died from a liver-related cause and were diagnosed with HCV were chronically infected. Given that about 26% of those ever diagnosed antibody-positive appear to achieve spontaneous viral clearance [21], we may have overestimated the proportion of liver-related deaths associated with chronic HCV infection, although this is likely to be offset by underestimation due to unrecovered linkages – for example, if critical identifiers were erroneous or missing.

A larger problem of underestimation exists because 60% to 70% of the chronically HCV-infected population in Scotland are estimated to remain undiagnosed [12]. Because these 'missing' HCV-related deaths have not been added to the known HCV-related deaths reported here, we have quantified only the lower bound of the true contribution of HCV infection to liver-related mortality. It is likely, however, that more than 60%-70% of people with HCV infection presenting with fatal liver disease will be tested and diagnosed. Related to this issue, we note that if, say, postmortem HCV testing increased over the study period this would account for part of the increasing trend in the proportion of HCV-diagnosed liver-related deaths. Similarly, if the majority of the 6% of HCV Diagnosis records that were excluded from analysis (because of insufficient identifiers) were from the early part of the database period, then the increasing trend observed in the proportion of deaths that were HCV-diagnosed might be overestimated. No indication of such a distribution was found, however.

Because injecting drugs is the commonest risk factor for acquiring HCV infection in Scotland, the adjusted odds ratios reported here for sex and social deprivation are partly capturing differences in IDU prevalence: a higher proportion of males than females are IDUs, and IDU prevalence is greatest for people who live in the most deprived areas [22].

As we lacked data regarding problem alcohol use, we have not been able to estimate the relative contributions of HCV infection and alcohol consumption to liver-related mortality in people diagnosed with HCV infection; this is of particular interest for cases in whom alcoholic liver disease was specified as the underlying cause of death. High levels of alcohol consumption have been implicated as contributing to premature death in people with chronic HCV infection [23], consistent with a synergistic effect of alcohol and chronic HCV infection on the development of liver disease [13]. IDUs – who comprise the majority of the chronically-infected HCV population in Scotland – have been reported to have a relatively high prevalence (37%–53%) of heavy alcohol consumption (defined as a score of eight or more on the Alcohol Use Disorders Identification Test [AUDIT] scale [24,25], or as two positive responses in the CAGE questionnaire [26]). Consequently, the increase over time in the proportion of liver-related deaths linked to the HCV Diagnosis database that we observed may be partly attributed to a rise in problem alcohol use, if alcohol consumption has increased in the HCV-diagnosed population over the study period.

In conclusion, HCV infection constitutes a significant, growing, public health burden in Scotland in terms of mortality from liver disease. Mortality from HCV-related liver disease is anticipated to increase as the population infected in the 1970s and 80s ages, those infected in the 1990s enter their second or third decade after HCV infection, and the size of the chronically-infected population grows. A better understanding of the risk factors associated with developing HCV-related liver disease will improve treatment and survival.

Acknowledgements

Funding was provided by a grant from the Chief Scientist Office of the Scottish Executive. Sheila M Bird was funded by Medical Research Council, WBS number U.1052.00.002.00001.01. The authors thank Information Services Division for performing the probabilistic record-linkage work, and the following virologists for their support with the HCV Diagnosis database: Dr Sheila Burns, East of Scotland Specialist Virology Centre, Royal Infirmary of Edinburgh, Edinburgh; Dr Sheila Cameron, West of Scotland Specialist Virology Centre, Gartnavel General Hospital, Glasgow; Dr Paul McIntyre, Department of Medical Microbiology, Ninewells Hospital and Medical School, Dundee; Dr Pamela Molyneaux, Department of Medical Microbiology, University Medical School, Foresterhill, Aberdeen.

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Pathways to clean hands: highlights of successful hand hygiene implementation strategies in Europe

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Citation style for this article:
Citation style for this article: Magiorakos AP, Leens E, Drouvot V, May-Michelangeli L, Reichardt C, Gastmeier P, Wilson K, Tannahill M, McFarlane E, Simon A. Pathways to clean hands: highlights of successful hand hygiene implementation strategies in Europe. Euro Surveill. 2010;15(18):pii=19560. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19560

This article has been published on 6 May 2010

Hand hygiene is the most effective way to stop the spread of microorganisms and to prevent healthcare-associated infections (HAI). The World Health Organization launched the First Global Patient Safety Challenge - Clean Care is Safer Care - in 2005 with the goal to prevent HAI globally. This year, on 5 May, the WHO's initiative SAVE LIVES: Clean Your Hands, which focuses on increasing awareness of and improving compliance with hand hygiene practices, celebrated its second global day. In this article, four Member States of the European Union describe strategies that were implemented as part of their national hand hygiene campaigns and were found to be noteworthy. The strategies were: governmental support, the use of indicators for hand hygiene benchmarking, developing national surveillance systems for auditing alcohol-based hand rub consumption, ensuring seamless coordination of processes between health regions in countries with regionalised healthcare systems, implementing the WHO's My Five Moments for Hand Hygiene, and auditing of hand hygiene compliance.

Introduction

Ignaz Semmelweis first demonstrated in 1847 that good hand disinfection was able to prevent puerperal fever [1-2] and evidence continues to show that hand hygiene is the simplest, most effective way to prevent cross-transmission of microorganisms and healthcare-associated infections (HAI) [3-5]. Despite all the data that are available supporting the benefits of performing hand hygiene, strict compliance of healthcare workers (HCW) with recommended hand hygiene practices is very difficult to achieve and even when it is achieved, it is very difficult to sustain. Factors found to be associated with poor hand hygiene practices include, among others: being an assistant physician or assistant nurse rather than a physician or a nurse, working on a weekday, having many hand hygiene opportunities per hour of patient care, performing activities with high risk of cross-transmission of microorganisms, working in high-risk areas and wearing gloves and gowns [4,6,7].

No single intervention is adequate enough to bring about change in behaviour, and in fact, for hand hygiene practices to be changed and results to be sustainable, multimodal approaches and complex interventions have been shown to be necessary [7-9].

In 2005, the World Health Organization's (WHO) World Alliance for Patient Safety, launched the First Global Patient Safety Challenge, Clean Care is Safer Care (http://www.who.int/gpsc/background/en/index.html) [10], which targeted the prevention of HAI. Subsequently, in 2009, it launched the SAVE LIVES: Clean Your Hands (http://www.who.int/gpsc/5may/en) initiative, highlighting the importance of hand hygiene and providing guidelines and toolkits for the best implementation of hand hygiene [9,11,12]

The purpose of this article is to highlight one important aspect of the national hand hygiene campaigns from four Member States of the European Union (EU) that we felt to be noteworthy and successful in changing HCW's hand hygiene practices.

Belgium: governmental support as a key factor for success

In Belgium three multimodal, country-wide hand hygiene campaigns were organised from 2005 to 2009 [13]. The purpose of these campaigns was to raise the awareness of HCW in all hospitals and, in doing so, to increase their adherence to good hand hygiene practices. The main foci of the campaigns were to improve the use of alcohol-based hand rubs (ABHR) by HCW and to measure their compliance with hand hygiene before and after each patient intervention. In order to increase adherence, performance feedback, education, workplace reminders and patient empowerment were used.

Government support, one of the WHO's key recommendations for planning national hand hygiene campaigns, was one of the most important reasons for success of the Belgian national campaigns [9]. The Federal Public Service (FPS) for Public Health, Food Chain Safety and Environment gave a strong political commitment during all three campaigns. The Belgian Antibiotic Policy Coordination Committee (BAPCOC), together with the FPS, were the core groups supporting the campaigns. The FPS had a dual role: it funded the campaigns and was part of the national task force that was responsible for their organisation. In addition, the FPS supported the campaigns by sending a written invitation to all Belgian hospitals, requesting voluntary participation in Belgium's national hand hygiene campaigns. In order to solidify the engagement of hospitals at an institutional level, positive replies indicating the intention to participate in the national hand hygiene campaigns, had to be returned to the FPS with signatures from the hospital directors and infection control teams.

Other governmental activities included press conferences at the launch of each hand hygiene campaign by the Belgian Minister of Social Security and Public Health and campaign materials in French and Dutch, made available on the Federal platform for hospital hygiene website (www.hicplatform.be).

Each of the three national hand hygiene campaigns resulted in a significant increase in hand hygiene compliance in HCW and also a higher consumption of ABHR [14-16]. Compliance with hand hygiene, measured by direct observation, increased significantly from 49% to 69% during the first campaign, from 53% to 69% during the second campaign and from 58% to 69% during the third campaign. Hospital participation and commitment, which was voluntary, was 95% for acute care hospitals, 65% for long-term care hospitals and 60% for psychiatric hospitals, for all campaigns.

High hospital participation rate and the improvement of hand hygiene compliance in all types of HCW are indications that behaviour is changing. In view of these positive outcomes, hand hygiene campaigns have now become a priority for the Belgian government, and a separate budget for a new campaign will be allocated every two years. The next campaign will be held in November, 2010.

France: indicators and governmental involvement as key elements for the successful implementation of hand hygiene

Infection control in France began when infection control committees were created in public and private hospitals in 1988 and 1999, respectively, following a ministerial decree from the Ministry of Health in 1988 [17,18].

The first phase of the French national programme for infection control, was created in 1993 and has been responsible for strengthening infection control practices locally and nationally, for the creation of surveillance networks to monitor and prevent HAI, and preventing the emergence and spread of antimicrobial resistance in micro-organisms [19,20]. The French Institute for Public Health Surveillance (Institut de Veille Sanitaire (InVS)) has developed the Réseau d'alerte, d'investigation et de surveillance des infections nosocomiales (RAISIN) (http://www.invs.sante.fr/surveillance/raisin/), which is an early warning surveillance system [19,21].

The second phase of the French national infection control programme, from 2005 to 2008, promoted the implementation of five national quality indicators which are used to benchmark hospital performance in infection control. These indicators were a breakthrough in the field of infection control practices, and through benchmarking and public reporting, 89% of healthcare facilities in France attained the highest rates of performance. The indicators can be found on the website of the Ministry of Health [20] and are listed below:

- Global indicator of infection control (ICALIN) (http://www.icalin.sante.gouv.fr/);
- Surgical site infection surveillance indicator (SURVISO) (http://www.sante-sports.gouv.fr/surviso-indicateur-de-realisation-d-une-surveillance-des-infections-du-site-operatoire-iso.html);
- Alcohol-based hand rub consumption indicator (ICSHA) (http://www.sante-sports.gouv.fr/l-indicateur-icsha.html);

Table

Use of alcohol-based hand rubs from 4,076 hospital units in 2008 in Germany

Type of unit	Number of hospitals	Number of units	Patient days	L/year	mL/PD				
					P10[a]	P25[b]	Median	P75[c]	P90[d]
ICU	303	556	1,223,229	94,744	33	53	73	95	126
Non-ICU	343	3,520	28,065,590	496,824	8	13	14	23	33

ICU: intensive care unit; PD: patient days.

[a]10% Percentile.

[b]25% Percentile.

[c]75% Percentile.

[d]90% Percentile.

- Incidence of meticillin-resistant Staphylococcus aureus (MRSA) indicator (SARM) (http://www.sante-sports.gouv.fr/sarm-staphylococcus-aureus-resistant-a-la-meticilline-dans-les-prelevements-a-visee-diagnostique-en-2005-et-2006-pour-1000-journees-d-hospitalisation.html), measuring incidence of MRSA infections per 1,000 patient-days;
- Antibiotic stewardship and consumption indicator (ICATB) (http://www.sante-sports.gouv.fr/icatb-indice-composite-de-bon-usage-des-antibiotiques.html).

In 2008, France organised a national hand hygiene campaign, available on a dedicated space on the Ministry of Health's website Mission mains propres (http://www.sante-sports.gouv.fr/mission-mains-propres.html) (Mission clean hands) [13], for which there was strong governmental support, mostly by providing finances for auditing of hand hygiene compliance.

Germany: the key to success: standardising the audit of ABHR as part of the national surveillance system

The German national hand hygiene campaign AKTION Saubere Hände (http://www.praxis-page.de/ash/index2.htm) was launched in January 2008 and is supported by the German Ministry of Health. The basic premise of this campaign is the implementation of multimodal interventions to improve hand hygiene compliance. The five key intervention tools it uses are: mandatory educational lectures for HCW, increased availability of ABHR in hospitals, administrative support of the hand hygiene campaign, implementation of the WHO's My Five Moments of Hand Hygiene and the evaluation of compliance by measuring ABHR consumption.

The German Krankenhaus-Infektions-Surveillance-System (KISS) (http://www.nrz-hygiene.de/) is a surveillance system of HAI. Within this surveillance system, KISS established a new module named HAND-KISS (http://www.nrz-hygiene.de/surveillance/hand.htm), a surveillance system that measures the ABHR usage as a surrogate measure of compliance with hand hygiene.

To date, 660 healthcare institutions, such as hospitals, senior care centres, rehabilitation centres, ambulatory dialysis centres and emergency services, feed their ABHR consumption data on a mandatory basis into HAND-KISS. These data are reported annually in millilitre (mL), by number of annual patient days (PD) per hospital unit type (intensive care unit or not), and by hospital. HAND-KISS calculates the ABHR in mL per PD for each unit and provides reference data, stratified according to each unit's specialty.

The HAND-KISS consecutive data from 2007 and 2008 and AHBR consumption data from hospitals participating in the AKTION Saubere Hände are presented in the Table. From 2007 to 2008, there was a statistically significant increase of 13% in ABHR consumption in all hospital units participating in HAND-KISS and AKTION Saubere Hände.

Measuring consumption of ABHR is a good way to assess compliance with hand hygiene, as it is difficult to obtain precise data on compliance by auditing the number of hand hygiene observations. Satisfactory inter-rater reliability is hard to achieve when measuring hand hygiene observations and in fact, inter-rater reliability ranged between 30% and 60% when it was assessed during the German national hand hygiene campaign (Reichardt, unpublished data). Due to this variability, hand hygiene compliance rates cannot be used to accurately allow a comparison of rates between hospitals, and quantitative interpretation of data should be done with caution. Measurement of ABHR consumption provides a practical and potentially more reliable system to assess quantitative changes in hand hygiene behaviour and provides a benchmarking system to compare between hospitals. HAND-KISS is the first surveillance system to provide crude data of the distribution of ABHR for benchmarking between hospitals.

United Kingdom - England: My Five Moments for Hand Hygiene and beyond

From 2009 to 2010, the clean**your**hands (http://www.npsa.nhs.uk/cleanyourhands) campaign in England and Wales embraced the WHO's My Five Moments for Hand Hygiene aiming to integrate hand hygiene into every aspect of patient care and to emphasise to HCW that the point of patient care is the critical moment to stop cross-transmission of micro-organisms and thus preventing HAI.

Although My Five Moments for Hand Hygiene was initially developed for the inpatient hospital setting by the University of Geneva Hospitals [12], clean**your**hands has attempted to expand this approach in England and Wales across all types of National Health System (NHS) trust, from the acute inpatient setting to ambulances and mental health institutions.

In order to implement the elements of My Five Moments for Hand Hygiene, educational material and practical tools for training were developed for infection control practitioners to use, but also to train and educate other staff. A key resource that was developed was a film based on one patient's journey through the NHS, from ambulance to hospital and back home, illustrating the multitude of opportunities that were available for hand hygiene and how the Five Moments for Hand Hygiene can be applied in different care settings.

Other activities included a series of regional one-day workshops introducing My Five Moments for Hand Hygiene for infection control staff and those responsible for infection control training in England and Wales. Feedback from the workshops has been

overwhelmingly positive with 95% of respondents considering them good or excellent. Subsequently, the clean**your**hands campaign also facilitated a dedicated workshop for infection control and training representatives from the ambulance service.

To further highlight the Five Moments for Hand Hygiene, an online game called Wi Five? (http://www.npsa.nhs.uk/cleanyourhands/resource-area/wi-five-game) was created and launched for the WHO's Save Lives: Clean Your Hands initiative on 5 May 2009, as a tool for infection control teams to educate and engage staff in this WHO initiative. In the approximately four months following its launch, the Wi Five? game was played 37,362 times. Work is now underway to develop the game further, adding other scenarios to represent more care settings.

United Kingdom – Scotland: auditing as a key factor for successful implementation of hand hygiene campaigns

In 2005, the Scottish Minister for Health and Community Care participated in the First Global Patient Safety Challenge, Clean Care is Safer Care [22,23] and pledged to develop and fund a national hand hygiene campaign in Scotland. Consequently, in January 2007, Scotland's campaign Germs. Wash your hands of them (http://www.washyourhandsofthem.com/) was launched by Health Protection Scotland (HPS). The campaign is funded until March 2011 and includes both professional and public elements. Campaign activities include educational posters for staff and visitors in acute and community healthcare settings, public media campaigns, information for children, leaflets for the public and for healthcare staff, credit card-sized fliers depicting My Five Moments for Hand Hygiene [12], research activities, presentation of national hand hygiene compliance data, a dedicated enquiry service (including telephone and email inbox enquiry service) and a campaign website.

Auditing hand hygiene compliance is a key method to monitor hand hygiene compliance in the Scottish hand hygiene campaign and is in accordance with the recommendations in the WHO's My Five Moments for Hand Hygiene. An audit tool and a supporting protocol were developed by HPS to ensure a standard methodology for data collection [24] and were adopted in Scotland for use in acute healthcare settings. The Scottish hand hygiene compliance data that are collected are published by HPS [25].

Local campaign activities at each National Health Service (NHS) board in Scotland are implented by the Local Health Board Coordinators for hand hygiene (LHBCs). The LHBCs are employed to perform audits of hand hygiene compliance, to promote hand hygiene practice among HCW and to raise awareness of campaign materials. Initial training for the LHBCs in the use of the audit protocol is provided by HPS and training updates are offered regularly. These are necessary because auditors can report different hand hygiene rates depending on their training [26] and any observation method will be susceptible to an inherent observer bias [27]. For this reason, a quality assurance exercise for LHBCs was undertaken and results indicated good inter-rater reliability for observed hand hygiene behaviour.

Local Health Board Coordinators for hand hygiene perform audits in acute healthcare settings during mandatory national audit periods. They measure compliance of HCWs by observing 20 opportunities for hand hygiene during the course of one working day. Fifteen one-day audits are conducted during each mandatory audit period, which equates to 300 opportunities per NHS board. After every audit period, the data are submitted to HPS for quality assurance and analysis.

The campaign has helped the NHS boards to meet, and even exceed, the hand hygiene compliance target of 90% set by the Scottish Government for November 2008. In February 2007, the first audit period, hand hygiene compliance across NHS Scotland for acute healthcare settings was 68%, and in the latest report published in January 2010, national hand hygiene compliance was 94% [25]. In fact, national hand hygiene compliance has remained above 90% since August 2008. The next phase of the campaign will focus on sustainability of hand hygiene improvements as well as extension into the non-NHS healthcare sector.

Conclusions and perspectives

Adherence of HCW to good hand hygiene practices is necessary during all aspects of patient care. Despite all the evidence supporting the benefits of hand hygiene, compliance with hand hygiene among HCW is low, and there is still much room for improvement to ensure that patients remain free from HAI. Only complex, multimodal interventions have been shown to change HCW behaviour and to achieve high rates of compliance and sustainability.

Although compliance with good hand hygiene practices represents an important part of infection control and prevention of HAI, other important practices, for instance the prudent use of antibiotics, must be strongly reinforced and used in parallel with hand hygiene. Preventing healthcare-associated infections, such as catheter-associated blood-stream infections and *Clostridium difficile* colitis, also require multimodal strategies, examples of which are education, feedback and guidance for HCW.

Hand hygiene campaigns in the EU Member States can range from local hospital-based hand hygiene activities to national campaigns [13]. Important factors in the support and success of national campaigns include governmental support, use of indicators for benchmarking, national surveillance systems for auditing AHBR consumption, coordination of processes between health regions, implementation of hand hygiene

toolkits and guidelines, and auditing and feedback of hand hygiene compliance.

In accordance with the Council Recommendation of the European Commission of 9 June 2009 on patient safety [28], which includes the prevention and control of HAI, the implementation of best practices and infection prevention and control programmes are important issues for the EU Member States . The benefits of complying with good practices of hand hygiene in the EU are now being recognised and many Member States are making hand hygiene a priority, frequently within the framework of patient safety, and are developing strategies or adapting or adopting those already used by others.

In order to further highlight the importance of hand hygiene and to increase the awareness and communication between the EU Member States, Belgium, as part of the Belgian EU Presidency celebration, will organise a conference in November 2010, during which a hand hygiene workshop will be held. This will be arranged in collaboration with the WHO and the European Centre for Disease Prevention and Control (ECDC), to provide a further platform and tools for raising awareness and implementing best hand hygiene practice in Europe.

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