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

Vol. 16 | Weekly issue 20 | 19 May 2011

Rapid communications

Research articles

News

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

www.eurosurveillance.org

A cluster of *Listeria monocytogenes* infections in hospitalised adults, Midlands, England, February 2011

N Coetzee (nic.cotzee@hpa.org.uk)[1], V Laza-Stanca[2], J M Orendi[2], S Harvey[3], N C Elviss[4], K A Grant[5]
1. Health Protection Agency, West Midlands North, Stafford, United Kingdom
2. Department of Microbiology and Infection Control, University Hospital of North Staffordshire NHS Trust, Stoke-on-Trent, United Kingdom
3. Public Protection Division, Stoke on Trent City Council, Stoke-on-Trent, United Kingdom
4. Health Protection Agency, Food, Water and Environmental Microbiology Laboratory, Birmingham, United Kingdom
5. Health Protection Agency, Foodborne Pathogen Reference Unit, London, United Kingdom

Citation style for this article:
Coetzee N, Laza-Stanca V, Orendi JM, Harvey S, Elviss NC, Grant KA. A cluster of Listeria monocytogenes infections in hospitalised adults, Midlands, England, February 2011.
Euro Surveill. 2011;16(20):pii=19869. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19869

Article published on 19 May 2011

Hospital-acquired listeriosis cases are not commonly reported but remain a significant public health problem. We report on three cases in patients with underlying conditions occurring during one week in February 2011. The cases had common exposure to pre-packed sandwiches and salads manufactured in compliance with regulations. Breaches in cold chain and shelf life controls at hospital level were identified as key contributing factors. Rigorous hospital food management systems remain important for patient safety.

Case description and clinical diagnosis

Listeria monocytogenes bacteraemia was confirmed in three patients admitted on 4, 5, and 6 February 2011 to a hospital in the Midlands region of England. Two were male and one was female. All lived in the same city served by the hospital but did not have any social links. Two cases were in the age range 50-59 years and one was older, over 80 years. All the three cases had underlying conditions which included malignancies and inflammatory bowel disease.

Cases were admitted in February 2011 to the same hospital where they had been hospitalised previously between 22 and 31 January 2011. Onset of symptoms leading to readmission of all three patients, ranged from 29 January to 3 February 2011, and these included fever, headache, confusion, abdominal pain and vomiting and *L. monocytogenes* was diagnosed in blood cultures three to four days after admission. All cases responded to antibiotic therapy with full recovery from infection.

Investigation and control measures

The 1,200-bed hospital is the only acute care facility in a district with approximately 500,000 inhabitants. A review of laboratory records for the preceding 12 months identified four unrelated (sporadic) community-acquired listeriosis cases. This background incidence rate is in keeping with national surveillance data, with 162, 180, and 139 non-pregnancy associated cases reported in 2008, 2009, and 2010 across England and Wales [1].

Following the identification of the three cases described above, an outbreak control team convened on 11 February 2011 to investigate the suspected outbreak and to advise on control measures.

Medical staff and management at the hospital were informed of the listeriosis cluster and the possibility of further cases. The hospital infection control team reinforced standard food avoidance advice for ready-to-eat foods commonly associated with listeriosis (such as pâté, smoked fish and mould ripened soft cheeses, or pre-packed sandwiches and salads) to patients with severe underlying conditions and/or on immunomodulating therapy, or pregnancy, and their families [2]. In addition, ward level food storage, distribution, and disposal practices were reviewed and staff reminded to follow existing protocols.

Food history of patients

Interviews with the three cases and their close relatives excluded animal contact and travel as relevant exposures. Food histories of the preceding four months did not identify common food preferences, consumption or purchasing while living at home. None had preference for ready-to-eat foods commonly associated with *L. monocytogenes*, nor were these present in their home refrigerators. The cases had attended the hospital outpatient department on various occasions between the two admissions, prior to disease onset, but had not eaten ready-to-eat foods from on-site shops. Hospital food was not served to patients attending the outpatient department.

The patients reported that during their hospital stays they had not eaten food (including ready-to-eat foods and sandwiches) from home or any of the eight privately-owned on-site visitor/staff canteens and shops. They had all consumed food provided by the hospital, and this had not been kept at room temperature but consumed immediately. The food histories were supplemented by a review of patient menu choice records

kept by the hospital. The only risk factors (common food exposure) identified were pre-packed sandwiches and salads provided by the hospital during the common period of hospitalisation (22 to 31 January 2011). A wide variety of sandwiches and salads were eaten by all the cases, with no single sandwich or salad type being identified as unique common exposure. Salad types consumed included turkey, ham, cheese and coleslaw, and sandwich fillings included cheese, egg, ham, salmon, tuna, turkey, and tomato.

Isolates of *L. monocytogenes* from blood cultures of the three cases were identified as serogroup 4, and fluorescent amplified fragment length polymorphism (fAFLP) type V21. The isolates were thus indistinguishable by molecular typing, supporting a point source outbreak. In the absence of a common food exposure or source (no identified home-based common food exposure and no common food source that they used prior to the first hospital admission) the three cases were most likely exposed to contaminated food during their overlapping admission episode in January 2011. Based on this assumption, incubation periods were estimated to range from one-four days (minimum) to eight-13 days (maximum).

Investigation of food suppliers

An environmental health investigation confirmed that a single manufacturer supplied pre-packed sandwiches to the hospital for inpatient meals. Salad was prepared at the hospital central kitchen. At the hospital, samples for microbiological analysis were taken from ready-to-eat foods (pre-packed sandwiches, pre-packed meats, cheddar cheese, cottage cheese used in on-site salad preparation, and completed salads), and kitchen drains. No *L. monocytogenes* was isolated from a total of 27 samples taken from this hospital between 10 and 24 February 2011.

A review of ready-to-eat food management practices at the hospital revealed that storage temperatures generally did not exceed 5°C, but gaps in recordkeeping were found during evenings and weekends. Some instances were observed of ready-to-eat foods being accepted from the supplier at temperatures above 5°C. Salad preparation in the hospital kitchens revealed lapses of the procedure for washing and disinfecting vegetables using chlorine. In addition, prepared salads were commonly given a two- or three-day shelf life rather than the recommended one day. Measures were taken to rectify these issues and food safety procedures are being updated at this hospital.

The eight privately owned on-site visitor/staff canteens and shops were inspected. Each was found to have different suppliers, and none of them supplied the same food as that given to inpatients in the hospital. Despite the fact that the three cases reported not to have obtained food from these eight outlets, 15 samples were taken of pre-packed sandwiches and salads as a precaution. *L. monocytogenes* serotype 4 (<20 cfu/g) was isolated from one ham and cheddar cheese sandwich but the fAFLP type differed from the isolates of the three cases.

A full production hygiene investigation (focused on sandwich and salad component production) of the manufacturer supplying food for hospital inpatients was undertaken by local environmental officers. There was a fully documented hazard analysis and control system in place and the quality assurance programme included daily microbiological testing of sandwiches for indicator organisms at three days after production (end of shelf life), with enumeration testing for *Listeria* spp., including *L. monocytogenes*, approximately every ten days.

For the five months prior to 20 December 2010, none of 38 samples exceeded 10 cfu/g for *Listeria* spp. Due to adverse winter weather conditions routine sampling had ceased from 21 December 2010, to be resumed only after the detection of the three listeriosis cases early in February 2011. Based on hazard analysis control system documentation, no breach of production quality processes was detected during this period. Further independent sampling by environmental health officers on 23 February 2011 did not detect *L. monocytogenes* in ten sandwich samples and 15 environmental (food production sites and drains) samples. From March 2011, the company revised their microbiological sampling plan (including sampling sandwiches on day of production) and are now using both enumeration and enrichment techniques in *L. monocytogenes* detection. To date, no further *L. monocytogenes* isolates in sandwich samples have been detected from the supplier.

Discussion and conclusion

Detailed investigations identified the consumption of hospital supplied sandwiches and/or salads during the last ten days in January 2011 to be a likely risk factor for infection with *L. monocytogenes*. The cluster is unlikely to be due to a chance occurrence, as cases occurred close together in excess of background incidence, had overlapping hospital stay, and isolates were indistinguishable by fAFLP typing. Microbiological evidence that hospital supplied food was the source of infection could not be established.

The sandwich producer follows the British Sandwich Association target microbiological standard in finished products (at end of shelf life) of *Listeria* spp. at <10 cfu/g which is compliant with European Commission (EC) regulations [3,4]. Whilst the detection of <10 cfu/g of *L. monocytogenes* in sandwiches and salads supplied to patients provides some assurance, sample numbers were low and taken more than ten days after cases were likely to have been exposed. In addition, the break in sampling by the producer before and during the case exposure period coupled with significant cold chain breaches and extended salad shelf life at the hospital preceded the cases. Two extensive United Kingdom (UK)-wide microbiological surveys of

sandwich quality served at hospitals and healthcare institutions reported 2.7 - 3.1% of samples containing *L. monocytogenes* [5]. In both studies, the presence of *Listeria* spp. and *L. monocytogenes* was associated with sandwiches produced outside the hospital, and where storage above 8°C had occurred.

In our experience sandwiches are commonly consumed by all patients in the study hospital, as well as most hospitals across the UK [6,7]. Even low levels of *L. monocytogenes* in sandwiches and ready-to-eat foods pose a risk to certain immunocompromised patients and pregnant women. The vast majority of sandwiches are safe, and hospital incidents and outbreaks of listeriosis are relatively infrequent, with six outbreaks reported in England and Wales from 1999 to 2008 [7]. However, listeriosis is a serious disease in compromised patients, and despite low numbers it remains a significant patient safety concern. Leading investigators have therefore recommended that food served to hospital patients to be free from potential pathogens, including *L. monocytogenes* [5-7].

Although this hospital food manufacturer supplies food to many other hospitals in the UK, no further laboratory confirmed cases of listeriosis of the same fAFLP type (V21) were identified in the UK more than 10 weeks after the cluster was detected and there were no other outbreaks of listeriosis or sporadic cases of this unique fAFLP type. Even though the ready-to-eat foods in this study were manufactured in accordance with the European Union regulations [4], it is possible that lack of temperature and shelf-life controls at the study hospital were key factors leading to increases in listeriosis and infection in vulnerable patients.

The investigation of hospital-based *L. monocytogenes* outbreaks is notoriously difficult due to low attack rates, incomplete case ascertainment, food histories spanning long periods, and food samples often being negative or taken long after the exposure time [7]. Such outbreaks are likely to be underreported, with publication bias towards larger outbreaks confirming microbiological food exposures. In order to develop appropriate future control strategies for this ongoing public health problem, we recommend that investigators make every effort to report and publish the full spectrum of hospital associated *L. monocytogenes* clusters and outbreaks.

Acknowledgments

We would like to thank the hospital infection control team, environmental health officers (Newcastle-under-Lyme Borough Council, Stoke-on-Trent City Council, and City & County of Swansea), Jeremy Hawker (HPA West Midlands), Public Health Wales, and Corinne Amar (HPA Foodborne Pathogen Reference Unit London) for fAFLP analysis of Listeria monocytogenes isolates.

References

1. Health Protection Agency (HPA). Listeria monocytogenes. Human cases in England and Wales reported to the HPA Centre for Infections, 1983-2010. London:HPA. 10 Mar 2011. Available from: http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Listeria/EpidemiologicalData/listeCaseReports19832010/
2. NHS choices. Listeriosis. [Accessed 10 May 2011]. Available from: http://www.nhs.uk/Conditions/Listeriosis/Pages/Introduction.aspx
3. British Sandwich Association. Code of Practice and Minimum Standards for Sandwich Manufacturers (Producers) (updated August 2007). [Accessed 9 May 2011]. Available from: http://www.sandwichesonline.org.uk/about_the_bsa/manufacturer_code_of_practice.shtml
4. European Commission (EC). Commission Regulation (EC) No 1441/2007 of 5 December 2007 amending Regulation (EC) No 2073/2005 on microbiological criteria for foodstuffs. EC. 7 Dec 2007. Available from: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:322:0012:0029:EN:PDF
5. Little CL, Barrett NJ, Grant K, McLauchlin J. Microbiological safety of sandwiches from hospitals and other health care establishments in the United Kingdom with a focus on Listeria monocytogenes and other Listeria species. J Food Prot. 2008;71(2):309-18.
6. Shetty A, McLauchlin J, Grant K, O'Brien D, Howard T, Davies EM. Outbreak of Listeria monocytogenes in an oncology unit associated with sandwiches consumed in hospital. J Hospt Infect. 2009;72(4):332-6.
7. Health Protection Agency (HPA). Human listeriosis linked to hospital sandwiches: implications for procurement and storage. London:HPA. Health Protection Report. 2008;2(35). Available from: http://www.hpa.org.uk/hpr/archives/2008/news3508.htm.

Influenza A(H1N1)2009 antibody seroprevalence in Scotland following the 2010/11 influenza season

W E Adamson (Walt.Adamson@ggc.scot.nhs.uk)[1], E C McGregor[1], K Kavanagh[2], J McMenamin[3], S McDonagh[4], P J Molyneaux[5], K E Templeton[6], W F Carman[1]

1. West of Scotland Specialist Virology Centre, Glasgow, Scotland
2. University of Strathclyde, Glasgow, Scotland
3. Health Protection Scotland, Glasgow, Scotland
4. Microbiology Department, Raigmore Hospital, Inverness, Scotland
5. Department of Medical Microbiology, Aberdeen Royal Infirmary, Aberdeen, Scotland
6. Edinburgh Specialist Virology Centre, Edinburgh, Scotland

Citation style for this article:
Adamson WE, McGregor EC, Kavanagh K, McMenamin J, McDonagh S, Molyneaux PJ, Templeton KE, Carman WF. Influenza A(H1N1)2009 antibody seroprevalence in Scotland following the 2010/11 influenza season.
Euro Surveill. 2011;16(20):pii=19871. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19871

Article published on 19 May 2011

Following the 2010/11 influenza season, we determined the age- and location-specific seroprevalence of antibodies against the influenza A(H1N1)2009 virus in Scotland. Samples were analysed by microneutralisation assay. Age/seropositivity profiles varied significantly between cities. The increases in seroprevalence relative to the previous influenza season (2009/10) were similar across age groups and geographic locations. However, the increased seropositivity in older adults appeared to be driven by exposure to vaccination, indicating significantly lower levels of infection than in younger age groups.

In 2010 we determined the age and location-specific seroprevalence of antibodies against the influenza A(H1N1)2009 virus in Scotland after the second wave of the pandemic [1]. Following the 2010/11 influenza season, we have carried out a similar study to identify the changes in seroprevalence in Scotland from the previous season. Although population demographics and contact patterns may vary between countries, this information can assist European public health policy makers in planning for the 2011/12 influenza season.

Methods

The collection of samples and the materials and methods utilised were identical to those described in our 2010 study [1]. Briefly, anonymised serum and plasma from leftover diagnostic samples taken in February 2011 (subsequently referred to as hospital/general practice (GP) samples) were obtained from biochemistry laboratories in four cities in Scotland: Aberdeen, Edinburgh, Glasgow and Inverness. For each site, samples were categorised by patients' age groups (20–29, 30–39, 40–49 and ≥50 years) and 100 samples of each age group at each site were analysed. In addition, 100 anonymised samples were collected from leftover diagnostic samples taken in February 2011 in genito-urinary medicine (GUM) clinics in each of the four cities. Antibody responses were detected by microneutralisation assays, according to standard methods [2] using the NYMC X-179A reassortant virus strain derived from A/California/7/2009 (supplied by the National Institute for Biological Standards and Control, Potters Bar). It has previously been demonstrated that serum and plasma samples are equally applicable to influenza A(H1N1)2009 microneutralisation assays [3]. Each sample was tested at a dilution of 1:40, since positivity at this dilution has previously been taken to indicate a significant antibody response [4]. Logistic regression analysis was used to estimate the effects of age group, location, sample type, and potential vaccine exposure on seroprevalence. We did not have information on the vaccination status of patients whose samples were tested in this study. However, data on vaccine uptake has been collected from a cohort of approximately 93,000 individuals from 17 general practices (GP) across Scotland [5]. The geographic spread of the cohort does not allow separate uptake calculations for each of the four locations; nevertheless, vaccine uptake can be derived for each age group.

Results

The table shows the percentage of samples that were found to be positive for antibodies against the influenza A(H1N1)2009 virus by age, location, and time point, and how these percentages have increased between March 2010 and February 2011.

The age/seropositivity profile is complex and varies with location (Figure 1A).

Positivity was found to vary significantly with age in Aberdeen ($p=0.014$), Edinburgh ($p=0.003$), and Inverness ($p<0.001$), but not in Glasgow ($p=0.94$). In Aberdeen, seropositivity in the 40–49 year-old age group was lower than in the 20–29 year-old age group ($p=0.007$). In Edinburgh, the three older age groups had significantly lower seropositivity than the 20–29

year-old age group (p=0.037, p<0.001, p=0.015 respectively). In Inverness the 20–29 year-old age group had higher seropositivity than all other age groups (p<0.001 in each case).

Location was found to have a significant effect in all age groups except the 40–49 year-old group (p=0.67). Among 20–29 year-olds, Glasgow showed a significantly lower seroprevalence than Aberdeen (p<0.001), while Edinburgh and Inverness did not. Among 30–39 year-olds, Edinburgh was similar to Aberdeen, with Glasgow (p=0.016) and Inverness (p=0.007) having significantly lower seroprevalence. In the ≥50 year-old age group, all locations had significantly lower seroprevalence than Aberdeen (Edinburgh: p=0.03; Glasgow: p<0.001; Inverness: p<0.001).

The samples obtained from GPs and hospital departments cannot be considered a random sample from the general population as they are likely to have an over-representation among patients in groups more likely to receive an influenza vaccination. It is not likely that patients attending GUM clinics are over-represented in such groups. Figure 1B shows the seropositivity among 20–29 year-old hospital/GP patients and 20–29 year-old GUM clinic attendees for each location. In Glasgow (p=0.013) and Inverness (p=0.014), seropositivity in hospital/GP samples was lower than in GUM samples. No such differences were observed in Aberdeen and Edinburgh.

Despite the differences in age/seropositivity profiles in each location, overall levels of seropositivity in each location increased by similar amounts (p=0.59) between 2010 and 2011 (Figure 2A).

The same is true for all age groups, with similar increases in seropositivity observed (p=0.65) (Figure 2B). An overall increase in seroprevalence was observed between 2010 and 2011 (p<0.001). These interactions indicate that between 2010 and 2011, there was no overall change in the relationship between seropositivity, age and location.

Figure 3 shows the relationship between seroprevalence and vaccine exposure in each age group for 2010 and 2011.

As expected, in all age groups, the proportion of individuals who have received the vaccine increases from 2010 to 2011. However, the increase in those aged ≥50 is much greater than in any other group (a consequence of people aged over 65 being routinely targeted for the seasonal vaccination in season 2010/11, but not for the influenza A(H1N1)2009 vaccination in season 2009/10).

Table

Increase in percentages of samples positive for antibodies against the influenza A(H1N1)2009 virus by age, location, and time point, Scotland, March 2010 and February 2011

Location	Age group [1, 2] (years)	March 2010 [1]	February 2011	Increase
		Percentage of positive samples (95% confidence interval)	Percentage of positive samples (95% confidence interval)	Percentage of positive samples (95% confidence interval)
Aberdeen	20–29	47 (39.8 to 53.6)	69 (62.6 to 75.4)	22 (9.0 to 35.6)
	30–39	51 (41.2 to 60.8)	63 (53.5 to 72.5)	12 (-7.3 to 11.7)
	40–49	39 (29.4 to 48.6)	53 (43.2 to 62.8)	14 (-5.4 to 33.4)
	≥50	39 (29.4 to 48.6)	73 (64.3 to 81.7)	24 (15.7 to 52.3)
Edinburgh	20–29	43 (36.1 to 50.1)	72 (65.8 to 78.2)	29 (15.7 to 42.1)
	30–39	35 (25.7 to 44.3)	60 (50.4 to 69.6)	25 (6.1 to 43.9)
	40–49	28 (19.2 to 36.8)	52 (42.2 to 61.8)	24 (5.4 to 42.6)
	≥50	45 (35.2 to 54.8)	58 (48.3 to 67.7)	13 (-6.5 to 32.5)
Glasgow	20–29	26 (20.0 to 32.2)	44 (36.6 to 50.4)	17 (4.4 to 30.4)
	30–39	18 (10.5 to 25.5)	46 (36.2 to 55.8)	28 (10.7 to 45.3)
	40–49	26 (17.4 to 34.6)	45 (35.2 to 54.8)	19 (0.6 to 37.4)
	≥50	33 (23.8 to 42.2)	42 (32.3 to 51.7)	9 (-9.9 to 27.9)
Inverness	20–29	50 (43.1 to 56.9)	71 (64.7 to 77.3)	21 (7.8 to 34.2)
	30–39	29 (20.1 to 37.9)	44 (34.3 to 53.7)	15 (-3.6 to 33.6)
	40–49	28 (19.2 to 36.8)	49 (39.2 to 58.8)	21 (2.4 to 39.6)
	≥50	19 (11.3 to 26.7)	30 (21.0 – 39.0)	11 (-5.7 to 27.7)

[1] In the 20–29 year-old groups, hospital/general practice and genito-urinary medicine clinic samples are combined (n=200 samples in each location for 2011, while in 2010 n=199 samples in Aberdeen, 195 in Edinburgh, 199 in Glasgow, 200 in Inverness).

[2] In the 30–39, 40–49, and ≥50 year-old groups, n=100 samples per age group in each location at each time point.

Increases in vaccine exposure are strongly related to increased seroprevalence ($p<0.001$), but the increase in seropositivity among those aged ≥50 is significantly less than would have been expected relative to those aged less than 50 ($p<0.001$). This implies that in the ≥50 year-old age group a higher proportion of the increase in seropositivity is due to vaccination than in any other age group.

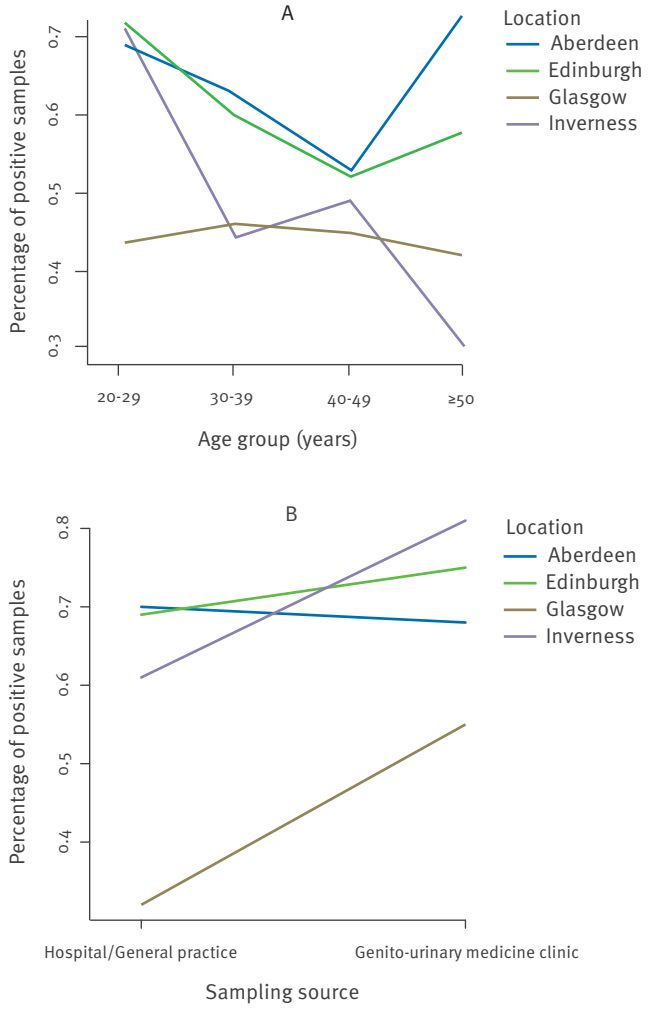
Discussion

Since the outbreak of influenza A(H1N1)2009, several studies have been undertaken to measure the frequency of antibodies against the virus [1, 6–10]. Taken together, these studies illustrate the spread of the virus at different time points and geographic locations since it began to spread in spring 2009. The work described here represents one of the earliest assessments of antibody seroprevalence following the 2010/11 influenza season in the northern hemisphere. In addition, due to the consistencies in sampling, materials, and methods with the study that we carried out following the 2009/10 influenza season [1], it has been possible to estimate increases in antibody seroprevalence in Scotland during the third wave of infection. While hospital/GP samples cannot be considered to be a random sample from the general population, such samples have previously been used to estimate seroprevalence [4].

In our previous study, we speculated that Glasgow and Inverness might experience higher levels of influenza activity than Aberdeen and Edinburgh during the 2010/11 influenza season [1]. However the results described here indicate that similar levels of influenza activity occurred in each of the four locations (although geographical variations in vaccine uptake are not known). Overall, age/seroprevalence graphs for each city have essentially shifted upwards in relation to 2010: Aberdeen and Edinburgh still show higher levels of seropositivity than Glasgow, with seropositivity in Inverness still decreasing with increased patient age.

Figure 1

Samples positive for antibodies against the influenza A(H1N1) 2009 virus by age, and sampling source for each location, Scotland, February 2011

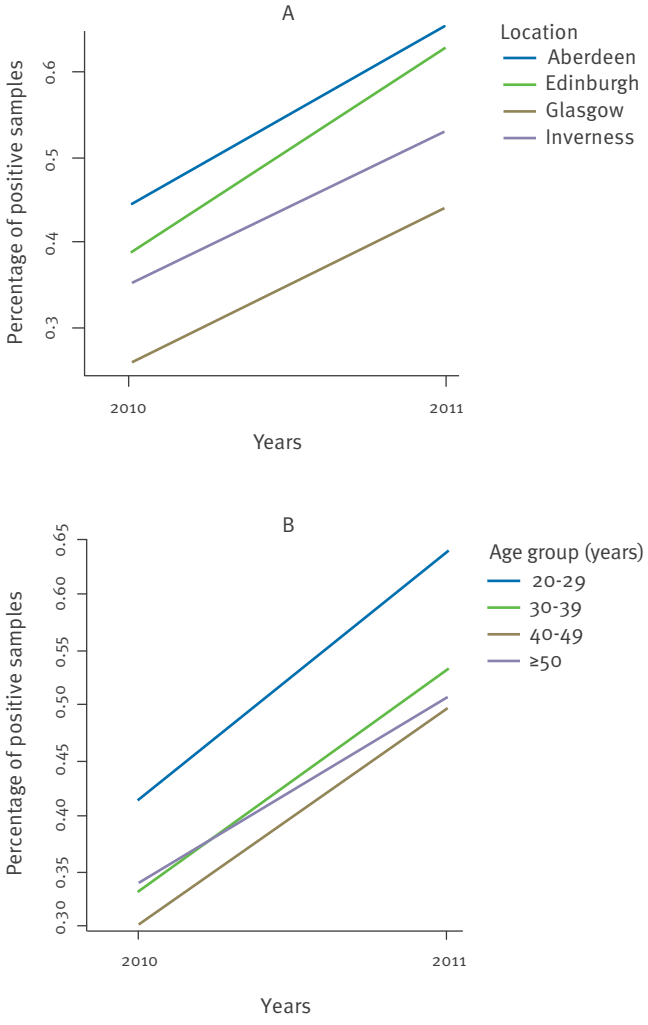


A: Variations in age/seropositivity profile by location.

B: Seropositivity among 20–29 year-olds attending hospital/general practice and genito-urinary medicine clinics for each location.

Figure 2

Seropositivity for the influenza A(H1N1)2009 virus by year and location (A) and year and age (B), Scotland, March 2010 and February 2011



In contrast to 2010, we observed higher levels of seropositivity in GUM samples than in hospital/GP samples in Glasgow and Inverness. The reason for this is unclear; however, a possible explanation might involve differences in social interactions between the two patient groups, with GUM patients mixing with other individuals more than those in the hospital/GP group. In Aberdeen and Edinburgh, seropositivity levels were higher, with less opportunity for the virus to be transmitted to susceptible individuals regardless of social mixing.

A weakness of this study is that we do not have any information on the risk group and vaccination status of the patients as only aggregate data could be used, which could not be linked to any patient characteristics. This means that we are unable to separate the effect of vaccination from infection, or to adjust seroprevalence among hospital samples for possible selection bias associated with risk groups.

The observation that increased seropositivity in the ≥50 age group between 2010 and 2011 is strongly correlated with vaccination may suggest that compared to younger individuals that the force of infection is weaker in the older age group. This hypothesis assumes that the cohort of 93,000 individuals is representative of the influenza vaccine profile in samples taken from hospital/GP and GUM sites. This might be due to older individuals being protected from influenza A(H1N1)2009 as a result of previous exposure. If this is the case then it indicates that testing samples in the microneutralisation assay at a dilution of 1:40 might represent too conservative an estimate of levels of protection against influenza A(H1N1)2009. To examine this in more detail, we have tested the samples described in this study at lower dilution levels. Initial findings indicate that low levels of antibodies that are reactive against influenza A(H1N1)2009 can be detected in a significant proportion of patients who are seronegative at 1:40, and that this observation is particularly true for patients in the ≥50 age group. These data are currently being collated for publication.

There remains significant variation in antibodies by age and location to influenza A(H1N1)2009 virus among the Scottish population with between 27% and 70% of any age group or location being susceptible to infection. These observations support the World Health Organization recommendation of the inclusion influenza A(H1N1)2009 in the trivalent seasonal influenza vaccine for the northern hemisphere this coming season [11]. However, these overall figures may be revised following the analysis of samples at other dilutions in the microneutralisation assay.

Acknowledgments

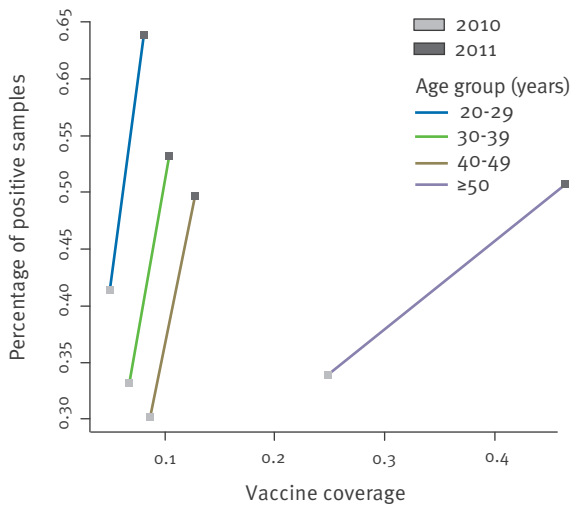
We thank Diane Major, National Institute for Biological Standards and Control; Potters Bar, for supplying the influenza virus and control serum used in microneutralisation assays; Ian Collacott, Department of Medical Microbiology, Aberdeen; Matt Noel, Specialist Virology Centre, Edinburgh; Richard Spooner, Biochemistry, Gartnavel Hospital; Anne Pollock, Head of Biochemistry, Raigmore Hospital.

References

1. Adamson WE, Maddi S, Robertson C, McDonagh S, Molyneaux PJ, Templeton KE, et al. 2009 pandemic influenza A(H1N1) virus in Scotland: geographically variable immunity in Spring 2010, following the winter outbreak. Euro Surveill. 2010;15(24):pii=19590. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19590
2. Rowe T, Abernathy RA, Hu-Primmer J, Thompson WW, Lu X, Lim W, et al. Detection of antibody to avian influenza A (H5N1) virus in human serum by using a combination of serologic assays. J. Clin. Microbiol. 1999;37(4):937-43.
3. Adamson WE, Carman WF. Microneutralisation assays for the detection of 2009 pandemic influenza A(H1N1) antibodies: a comparative test of serum and plasma. J Clin Virol. 2010;49(4):303.
4. Miller E, Hoschler K, Hardelid P, Stanford E, Andrews N, Zambon M. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. Lancet. 2010;375(9720):1100-8.

Figure 3

The relationship between seroprevalence, vaccine coverage, age, and year, Scotland, March 2010 and February 2011



Age group (years)	Number vaccinated against influenza A(H1N1)-2009 in 2009/10	Number vaccinated against seasonal influenza in 2010/11	Number receiving at least one vaccine against influenza A(H1N1)-2009 in 2009/10 or 2010/11	Denominator	Cumulative vaccine coverage in February 2011 (%)
20–29	696	654	1,119	13,722	8.1
30–39	884	823	1,353	12,931	10.5
40–49	1,271	1,373	1,866	14,562	12.8
≥50	8,267	14,117	15,432	33,214	46.5
All age groups	**11,118**	**16,967**	**19,770**	**74,429**	**26.6**

5. Health Protection Scotland (HPS). Influenza season. Glasgow: HPS. [Accessed 10 May 2011]. Available from: http://www.hps.scot.nhs.uk/resp/influenzaseason.aspx#background
6. Baguelin M, Hoschler K, Stanford E, Waight P, Hardelid P, Andrews N, et al. Age-Specific Incidence of A/H1N1 2009 Influenza Infection in England from Sequential Antibody Prevalence Data Using Likelihood-Based Estimation. PLoS ONE. 2011;6(2): e17074.
7. Gilbert GL, Cretikos MA, Hueston L, Doukas G, O'Toole B, Dwyer DE. Influenza A (H1N1) 2009 antibodies in residents of New South Wales, Australia, after the first pandemic wave in the 2009 southern hemisphere winter. PLoS One. 5(9): e12562.
8. Hardelid P, Andrews NJ, Hoschler K, Stanford E, Baguelin M, Waight PA, et al. Assessment of baseline age-specific antibody prevalence and incidence of infection to novel influenza AH1N1 2009. Health Technol Assess. 2010;14(55):115–92.
9. McVernon J, Laurie K, Nolan T, Owen R, Irving D, Capper H, et al. Seroprevalence of 2009 pandemic influenza A(H1N1) virus in Australian blood donors, October – December 2009. Euro Surveill. 2010;15(40):pii=19678. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19678
10. Waalen K, Kilander A, Dudman SG, Krogh GH, Aune T, Hungnes O. High prevalence of antibodies to the 2009 pandemic influenza A(H1N1) virus in the Norwegian population following a major epidemic and a large vaccination campaign in autumn 2009. Euro Surveill. 2010;15(31):pii=19633. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19633
11. World Health Organization (WHO). Recommended composition of influenza virus vaccines for use in the 2011-2012 northern hemisphere influenza season. Geneva:WHO. 17 Feb 2011. Available from: http://www.who.int/csr/disease/influenza/2011_02_recommendation.pdf.

Toxin producing *Vibrio cholerae* O75 outbreak, United States, March to April 2011

TJ M Onifade[1,2], R Hutchinson[1,2], K Van Zile[1,2], D Bodager[1,2], R Baker[3], C Blackmore (Carina.Blackmore@doh.state.fl.us)[1]
1. Florida Department of Health Bureau of Environmental Health Medicine, United States
2. Food and Waterborne Disease Program, United States
3. Florida Department of Health Bureau of Laboratories, United States

Citation style for this article:
Onifade TM, Hutchinson R, Van Zile K, Bodager D, Baker R, Blackmore C. Toxin producing Vibrio cholerae O75 outbreak, United States, March to April 2011. Euro Surveill. 2011;16(20):pii=19870. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19870

Article published on 19 May 2011

The Florida Department of Health, Florida, United States, is investigating a *Vibrio cholerae* O75 outbreak. Ten cases with disease onsets from 23 March to 13 April 2011, presented with gastrointestinal symptoms of diarrhoea, nausea, vomiting, cramps, chills, and/or fever, after consuming raw or lightly cooked oysters harvested from Apalachicola Bay, Florida. Symptoms were milder than those during outbreaks of epidemic (serogroup O1 and O139) *Vibrio cholerae*; no case required rehydration treatment or hospitalisation.

Outbreak report

On Friday 15 April, 2011 the epidemiology team of the Escambia County Health Department (CHD), Florida, United States (US), notified the Florida Department of Health's Food and Waterborne Disease Program (FWDP) of a case of *Vibrio cholerae* non-O1/non-O139. The man in his early 20s had fallen ill with cramps, fever, watery diarrhoea, and nausea on 12 April after consuming raw oysters on 6 April in a restaurant. The bacterial isolate was sent to the Florida Department of Health's Bureau of Laboratories (BOL) in Jacksonville for typing and toxin testing. The suspect toxin-producing *V. cholerae* O75 specimen was forwarded to the Centers for Disease Control and Prevention (CDC) and confirmed positive on 19 April.

In the US, the intra- and interstate regulation of oysters is performed by state (Florida Department of Agriculture and Consumer Services, Division of Aquaculture (DOACS)) and federal agencies (US Food and Drug Administration (FDA)), respectively. These agencies require the tracking of oysters through tags that note the harvest date and area. Attempts were made to collect the oyster tags but they were unavailable from the restaurant.

On 18 April, Nassau CHD reported two cases in their late 40s and late 20s respectively, who developed a gastrointestinal illness the day after having purchased live shell stock oysters and consuming them steamed on 10 April. Symptoms included nausea, vomiting, diarrhoea, and chills. One of the patients provided a stool sample that tested positive for toxigenic *V. cholerae* O75.The other, who had presented with the same symptoms, did not provide samples. This patient was included in our case count as a probable case. The tag for the oysters had been discarded but records at the seafood dealer indicated that they had been harvested from Apalachicola Bay area 1642.

The FWDP was notified of a Louisiana, US *V. cholerae* non-O1/non-O139 case on Monday 19 April. The case became ill on 9 April after consuming raw oysters at a restaurant in Okaloosa, Florida, on 7 April. Tags for oysters likely eaten by the case were retrieved from the restaurant on Tuesday 20 April. The oysters had been harvested from the Apalachicola Bay area 1642 on 3 and 6 April. The toxin status for that case is still unconfirmed by CDC so this remains a suspected case.

On Wednesday 20 April, the FWDP investigators contacted the Florida DOACS, the agency with oversight over the Florida oyster industry, notifying them of the *V. cholerae* non-O1/non-O139 cluster investigation.

On 21 April, the FWDP coordinator and investigators issued a state-wide alert to the Florida EpiCom system, a state-wide epidemiology electronic alert system, notifying public health officials of the toxigenic *V. cholerae* oyster related case investigation. A similar notification was posted nationally on the CDC EpiX notification system, the federal epidemiology alert system, on 28 April.

Ten cases (eight confirmed, one probable, and one suspect) were identified in this outbreak (Figure 1). Seven were Florida residents, the three other cases were from Indiana, Georgia and Louisiana (Figure 2). The cases ranged from 22 to 74 years of age; six of the ten cases were males. Most cases were in good health, with only one reporting to have pre-existing conditions (kidney problems and a coronary artery stent). Cases reported gastrointestinal symptoms of nausea (n=7), vomiting (n=4), diarrhoea (n=9), chills (n= 8), cramps (n=1) and/

or fever (n=1) and none required hospitalisation. Dates of exposure ranged from 21 March to 11 April and onset of symptoms occurred between 23 March and 13 April. The average time from exposure to onset of symptoms was 2 days (range: 1 to 6 days). Information gathered during the investigation, which was derived from three sets of oyster tags, implicated one single harvest area in the Apalachicola Bay, Gulf of Mexico, as the source of the contaminated oysters. No additional cases of *V. cholerae* have been reported since 13 April and no oysters harvested later than 6 April have been implicated in any related illnesses.

In response to the outbreak, DOACS conducted an investigation into the implicated oyster harvesting area, Apalachicola Bay area 1642 (Figure 2). The area was closed on 30 April and all dealers and retailers were asked to recall any implicated product still in commerce. The area was reopened to harvesting on 11 May 2011 after DOACS had 15 oyster samples from 10 different sections of the implicated harvest area tested for *V. cholerae* O75 at the FDA laboratory in Dauphin Island, Louisiana. All samples were negative.

Background

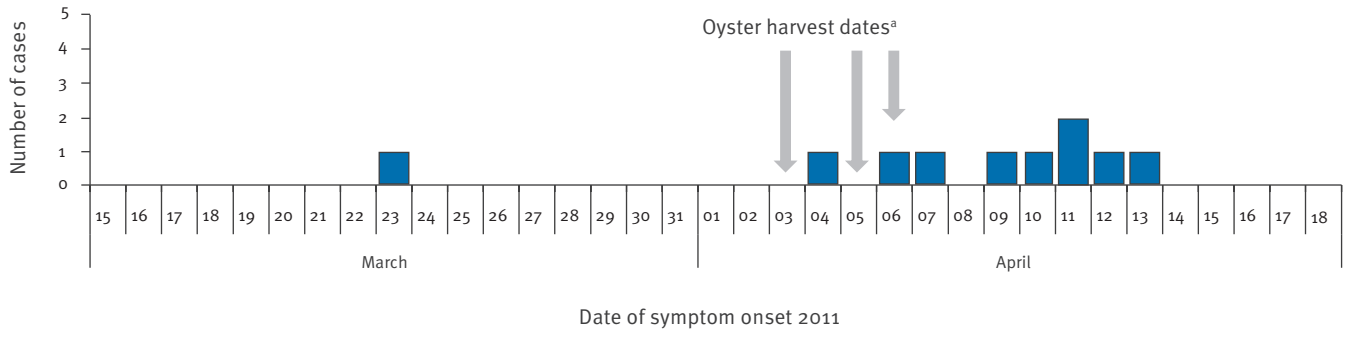
Vibrio spp. bacteria are common in the warm coastal waters of the state of Florida and are also found in local shell fish. *Vibrio vulnificus* is an important cause of gastrointestinal illness and wound infection in the state, causing 24 cases of illness and six deaths in 2009 [1]. Human illness from native, nontoxigenic non-O1 and non-O139 serogroups of *V. cholerae* are reported regularly [2] and all *Vibrio* diseases are notifiable in Florida. However, despite the favourable ecological conditions, and the fact that Florida receives many travellers from cholera endemic countries, toxigenic *V. cholerae* infections are uncommon. After the 2010 cholera outbreak in Haiti, ten cases of imported *V. cholerae* O1 serotype Ogawa were confirmed in state residents, with no secondary transmission detected (Ann Schmitz, personal communication, 16 April 2011) [3]. The subsequent heightened awareness of cholera has increased the number of human samples submitted to Florida Department of Health's BOL for *V. cholerae* testing, with more than 40 isolates having been evaluated since November 2010 [4]. At the same time, the turnaround time for test results has also been improved by adding capacity for the detection of cholera toxin. For *V. cholerae* testing, isolates or stools from ill persons, which were previously screened by hospital or private laboratories and suspected *V. cholerae* positive, are referred to the BOL as "suspect *V. cholerae*". Stools are tested by direct thiosulfate citrate bile sucrose agar (TCBS) and enrichment (alkaline peptone water 35°C incubation for 8 hours and 18 hours), then subculture to TCBS. Suspect colonies are checked biochemically for the matching *V. cholerae* pattern of reactions and then serology is performed with O1 and O139 antisera. All *V. cholerae* isolates are also checked for cholera toxin. When isolates do not agglutinate in O1 or O139 antisera but do produce cholera toxin, isolates are referred to CDC and serology for *V. cholerae* O75 is performed. This process takes from 10 to 14 days.

Discussion and conclusions

Toxigenic *V. cholerae* infections are highly unusual in Florida. This report describes the first *V. cholerae* O75 outbreak detected in the state, between 23 March and 13 April 2011. In Florida, the first isolate of toxigenic *V. cholerae* O75 to be identified was reported in November 2010, and originated from an immunocompromised Florida resident with a history of oyster consumption. Previously, the serogroup had been associated with sporadic cases of gastrointestinal disease after oyster and other seafood consumption in the south-eastern US [5]. Tobin-D'Angelo et al. [5] describe eight cases with a similar diarrhoeal disease to the ones reported here, who were identified in Georgia, Louisiana, Alabama and South Carolina between 2003 and 2007. These sporadic cases differ from the cases in the outbreak in question here. Four of five cases described in detail had underlying health conditions, whereas only one of the cases in this outbreak had underlying conditions. Two of the eight cases were hospitalised in the analysis of the sporadic cases whereas cases associated with this outbreak experienced milder symptoms

Figure 1

Cases of cholera O75 outbreak from oyster consumption, United States, March–April 2011 (n=10)



[a] When these dates were available from the oyster tags.

and did not require hospitalisation. Some of these differences may be explained by the increases in testing, which were also the result of recent concerns of imported cholera from Haiti. Persons displaying gastrointestinal symptoms are more likely to have cholera testing done than in the past. Historically, cases with severe illness may have been more likely tested than those with milder symptoms, resulting mainly in severe cases being reported. These factors may have allowed the current detection of this rare serotype of cholera in a relatively healthy population.

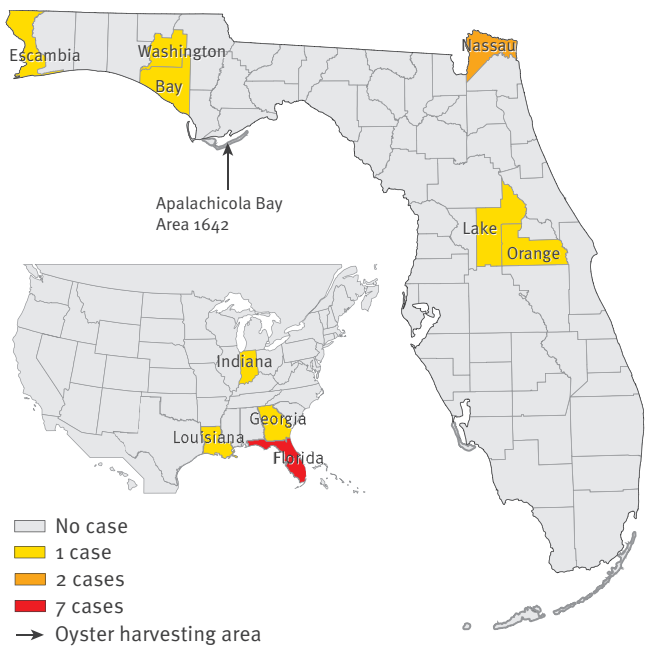
Epidemic cholera is an important cause of morbidity and mortality worldwide [6]. Outbreaks generally occur when there are significant deficits in the water sanitation and hygiene infrastructure in the communities, allowing for rapid spread of disease via food and/or water consumption. Gastrointestinal symptoms are generally mild, however about 20% of affected individuals develop acute, severe, dehydrating watery diarrhoea which can be fatal if left untreated. The *V. cholerae* O75 appears to cause a milder disease than infection with *V. cholerae* serogroups O1 and O139 and outbreaks in countries with universal access to health care are likely to have limited public health impact. The outbreak reported here is a reminder of the conductive environmental conditions for *V. cholerae* growth in Florida waters and the importance of maintaining sanitary and food safety practices to avoid future outbreaks.

This is the first recorded outbreak related to *V. cholerae* O75 and oyster consumption. The identification of the outbreak could be the result of an increase in testing for *V. cholerae* in human stool isolates, allowing unprecedented detection of a phenomenon that may have recurrently occurred in the past. Alternatively, the outbreak could be due to some change in the environment, acute or longer term, which has allowed this pathogen to establish or emerge in the oyster population. In the wake of this outbreak, there is concern around the oyster harvesting environment and the regulatory agency, DOACS, is continuing to look into incidents that could have influenced the presence or load of this pathogen in the oyster harvest areas.

Florida is a state of international significance given the large numbers of tourist that visit the state annually and this may raise concern internationally. Here we report preliminary results of the investigation to raise awareness among public health professionals worldwide about this rare oyster related *V. cholerae* outbreak. We will be monitoring for future cases of *V. cholerae* O75, and will continue our investigation into other factors associated with this outbreak.

Figure 2

Geographical distribution by state or county of residence of cholera O75 cases from oyster consumption, and oyster harvesting area, United States, March–April 2011 (n=10)



Acknowledgments

The authors of this outbreak report would like to thank the Florida Department of Health's Bureaus of Laboratories and Epidemiology, the epidemiology and environmental health staff of Nassau, Lake, Bay, Escambia, Orange, and Washington County Health Departments, the Florida Department of Agriculture and Consumer Services Division of Aquaculture and the Waterborne Disease Prevention Branch at Centers for Disease Control and Prevention.

References

1. State of Florida Department of Health. Florida Morbidity Statistics Report 2009. Tallahassee (FL): 2010 Dec. Available from: http://www.doh.state.fl.us/disease_ctrl/epi/Morbidity_Report/2009/AMR_%202009.pdf
2. Weis KE, Hammond RM, Hutchinson R, Blackmore CG. Vibrio illness in Florida 1998-2007. Epidemiol Infect. 2011:139(4):591-8.
3. Jenkins PH, Montejano HJ, Abbasi MJ, Crowley MS, O'Brien MG; Conte V, et al. Update on Cholera — Haiti, Dominican Republic, and Florida, 2010, MMWR Morb Mortal Wkly Rep. 2010;59(50):1637-41.
4. Florida Department of Health. Guidance for Haiti-related Toxigenic Vibrio cholerae Type O1, Case Reporting for County Health Departments. [Accessed 15 May 2011]. Available from: http://www.doh.state.fl.us/disease_ctrl/epi/acute/haiti_cholera_impact_surv_guidance_chds_v1.1.pdf
5. Tobin-D'Angelo M, Smith AR, Bulens SN, Thomas S, Hodel M, Izumiya H et al. Severe diarrhea caused by cholera toxin–producing vibrio cholerae serogroup O75 infections acquired in the southeastern United States. Clin Infect Dis. 2008;47(8):1035-40.
6. World Health Organization (WHO). Cholera. Fact sheet No 107. June 2010. [Accessed 16 May 2011]. Available from: http://www.who.int/mediacentre/factsheets/fs107/en/

Long term trends introduce a potential bias when evaluating the impact of the pneumococcal conjugate vaccination programme in England and Wales

S Flasche (Stefan.Flasche@hpa.org.uk)[1,2], M Slack[3], E Miller[1]
1. Immunisation, Hepatitis and Blood Safety Department, Health Protection Agency, London, United Kingdom
2. Department of Mathematics and Statistics, Strathclyde University, Glasgow, United Kingdom
3. Respiratory and Systemic Infection Laboratory (RSIL), Health Protection Agency, London, United Kingdom

Citation style for this article:
Flasche S, Slack M, Miller E. Long term trends introduce a potential bias when evaluating the impact of the pneumococcal conjugate vaccination programme in England and Wales.
Euro Surveill. 2011;16(20):pii=19868. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19868

Article published on 19 May 2011

A pneumococcal conjugate vaccine (PCV7) was introduced into the United Kingdom's childhood immunisation schedule in September 2006. Evaluation of its impact on the incidence of invasive pneumococcal disease (IPD) as assessed by routine reports of laboratory-confirmed cases should take into account possible long-term trends due to factors like changes in case ascertainment. To this end, we compared pre-PCV7 trends in reported IPD incidence in England and Wales identified by blood culture with those for two other bacteraemias, *Escherichia coli* and non -pyogenic streptococci, for which there has not been any public health intervention. While no trend was detected in the age group 65 years and older, there was an annual increase of 3% and 11% in those aged under five years and between five and 64 years, respectively, which was similar for IPD and the other two pathogens. After PCV7 introduction, a continuing trend was only found for non-pyogenic streptococci in under five year-olds. These trends in the incidence for bacteraemias for which there has been no intervention could suggest that there have been changes in case ascertainment because of increased reporting or blood culturing. Accounting for them will improve the evaluation of the impact of PCV7 on IPD.

Introduction

Streptococcus pneumoniae, also called pneumococcus, is a common cause of mortality and morbidity worldwide. It causes a variety of disease presentations, the most serious, invasive pneumococcal disease (IPD), associated with spread via the blood stream resulting in septicaemia, meningitis, bacteraemic pneumonia or invasion of other normally sterile sites such as pleural or synovial fluid. A seven-valent pneumococcal conjugate vaccine (PCV7) became available in the United States in 2000 offering protection against both carriage [1,2] and disease [3] from the seven most common serotypes causing IPD in children in developed countries. In September 2006 PCV7 was introduced into the immunisation schedule in the United Kingdom as a 2/4/13 month routine schedule (one dose at two and four months plus a booster dose at 13 months of age) with a catch-up for children up to two years of age.

Most pneumococcal surveillance systems focus on IPD and have shown large reductions in the numbers of cases infected with vaccine-type strains (VT cases) in the targeted age groups, irrespective of vaccine schedule [4,5]. However differences have been reported between countries in the percentage reduction of VT disease and the induced herd effect in older age groups as well as in non-vaccine-type (NVT) replacement disease. Comparison of the incidences of VT and NVT IPD cases before and after the introduction of PCV7 implicitly assumes that the reported disease incidence in the absence of vaccination has not changed, that a similar level of ascertainment has been maintained, and that there were no secular trends in individual serotypes. A recent World Health Organization (WHO) meeting that reviewed the post-PCV7 experience in different countries identified changes in the sensitivity of the surveillance systems due to alterations in clinical awareness, reporting techniques and blood culturing practice as

Figure 1

Age distribution of invasive pneumococcal disease and control infections, England and Wales, 2001/02 to 2005/06

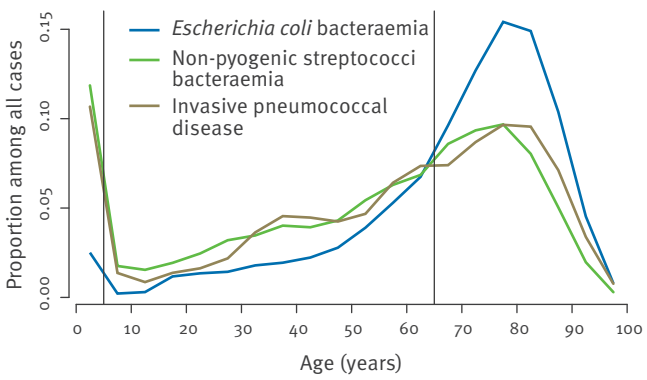
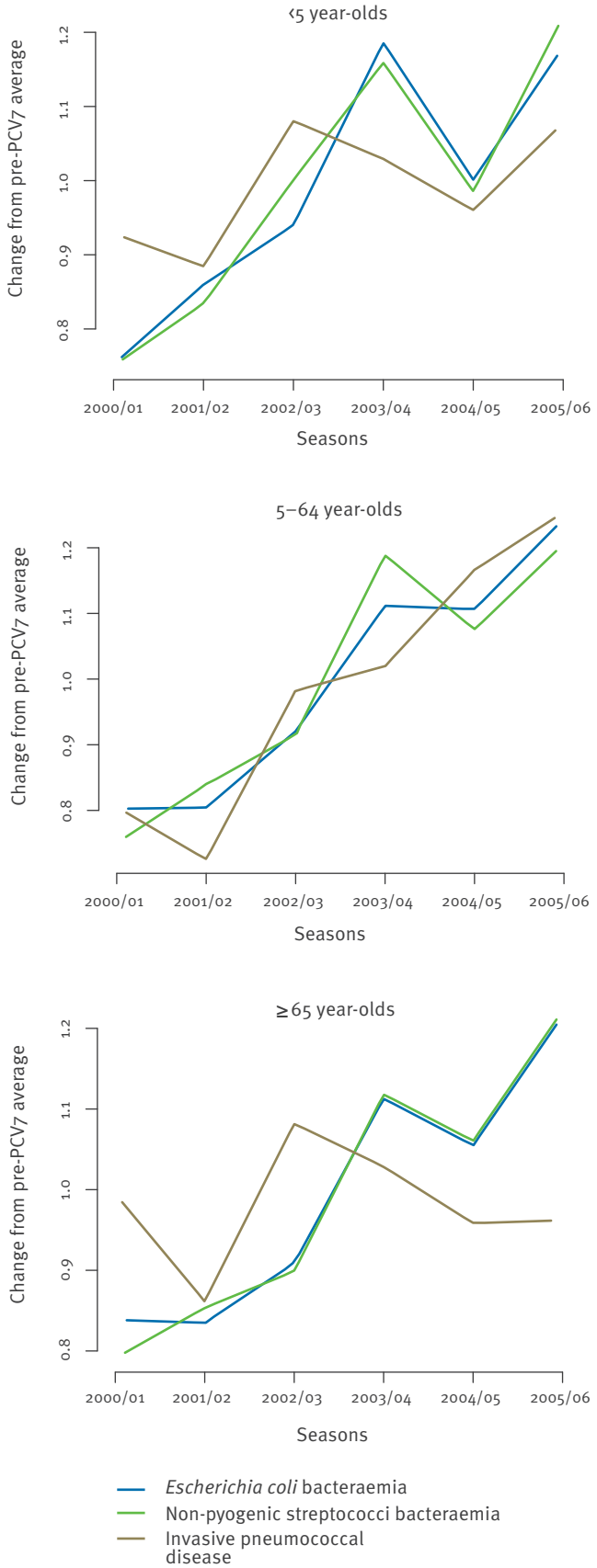


Figure 2

Pre-PCV7 trends in invasive pneumococcal disease and control infections stratified by age groups, England and Wales, 2000/01–2005/06



PCV7: seven-valent pneumococcal vaccine.

For the ease of comparison trends for all pathogens are plotted after scaling by the respective average incidence.

potential important confounders when making such comparisons over time and between countries [6].

Given the severity of IPD and the continuing universal access to the National Health System (NHS) it is reasonable to assume that care seeking behaviour of IPD patients in England and Wales has remained constant in recent years. However, this might not be the case for laboratory investigation or reporting behaviour which may have been subject to changes in practice over time. Reporting rates for IPD in hospitalised cases have been shown to vary with blood culturing rates which may have changed as clinical practice has evolved [7], while recent technical developments may have improved reporting of laboratory-confirmed cases [8].

In order to interpret changes in the incidence of IPD after the introduction of PCV7 into the routine childhood vaccination scheme in England and Wales we assessed trends in reported IPD cases before introduction of PCV7 and related them to changes observed before and after that date in a control group of pathogens that similarly depend on blood culturing practice and reporting, but for which there have been no public health or other interventions. Our findings are relevant to the evaluation of the impact of PCV7 in England and Wales.

Methods

Pathogens

Control pathogens selected for the comparison with IPD were those of the most commonly reported bacteraemias that fulfilled the following inclusion criteria: (i) endemic in England and Wales and not solely outbreak-related, (ii) not influenced by vaccination or any other interventions during the time period of the comparison, (iii) sufficiently common to provide statistically robust numbers in each age group, (iv) mainly diagnosed through blood culture. The two pathogens identified that fulfilled these criteria were *Escherichia coli* and non-pyogenic streptococci (*Streptococcus acidominimus, S. bovis, S. gordonii, S. intermedius, S. mitis, S. mutans, S. oralis, S. parasanguinis, S. salivarius*, and not further typable: alpha-haemolytic Streptococcus *sp.*, non-haemolytic *Streptococcus sp.*, *S. anginosus* group, *S. milleri* group, *S. mitis* group, *S. sanguinis* group).

Data on all infections reported between July 2000 and June 2010 (between 2000 and 2007 for pneumococcus) and identified by blood culture were obtained from the national routine laboratory surveillance system of England and Wales (LabBase) [8]. Only one isolate per disease episode was included in the analysis. More than one isolate from the same person where the interval between specimens was less than 14 days and the same pathogen was isolated were assumed to represent the same illness episode. As part of the enhanced surveillance [9] episodes of IPD were checked for duplicates using personal identifiers.

Statistical analysis

For each of the pathogens a negative binomial regression model was fitted to the observed number of cases per 100,000 population. We regressed the number of cases with a linear trend and a five-level factor to indicate the period before and the four seasons after PCV7 introduction, 2006/07, 2007/08, 2008/09, 2009/10 and included a population offset. The (anti-logged) slope of this model indicates the pre-PCV7 trend, i.e. a slope >1 indicates a positive trend and a slope <1 a negative trend in a negative binomial model. To test for differences in slopes we tested their confidence intervals for overlap which provides conservative estimates [10]. Each of the post-PCV7 factors indicates the deviation of the post-2005/06 data from the extrapolated pre-2005/06 trend. No adjustment for multiple comparisons was made.

Data for all analyses were stratified into three age groups (<5, 5–64, ≥65 years) with missing age information being imputed from the age distribution observed for the pathogens, and were performed in R version 2.11 [11].

Results

More than 150,000 disease episodes before PCV7 introduction were considered. They were differently distributed amongst the age groups (Figure1). While IPD and non-pyogenic streptococci showed similar patterns, most of the *E. coli* episodes were reported in the elderly population. In the population under five years of age 27% of disease episodes were due to *E. coli*, 49% to IPD and 25% to non-pyogenic streptococci. In the 5–64 year-olds the respective distribution was 50%, 34% and 16%, and for those 65 years and older it was 70%, 21% and 9%.

The regression model found a positive trend in IPD incidence prior to the introduction of PCV7 in the age groups under five years and between five and 64 years. The trend was most pronounced in the 5–64 year-olds with an average yearly increase of about 11% (p<0.001). In the under five year-olds reports of IPD increased about 3% per year (p=0.031). In the over 65 year-olds we estimated this trend to be not significantly different from zero (p=0.91) (Table 1).

Table 1

Estimated slopes in models of the pre-PCV7 trend in invasive pneumococcal disease and control infections, England and Wales, 2000/01–2005/06

Age group	Invasive pneumococcal disease slope [95% CI]	*Escherichia coli* slope [95% CI]	Non-pyogenic streptococci slope [95% CI]
<5 years	1.030 [1.002–1.058]	1.091 [1.052–1.132]	1.093[1.051–1.138]
5-64 years	1.106 [1.075–1.138]	1.095 [1.075–1.114]	1.097 [1.061–1.134]
≥65 years	0.999 [0.972–1.027]	1.074 [1.055–1.193]	1.087 [1.063–1.111]

CI: confidence interval; PCV7: seven-valent pneumococcal vaccine.

Table 2

Percentage difference between the incidence of control infections and the incidence predicted by two different models, England and Wales, 2000/01–2008/09

Age group	Season	*Escherichia coli*		Non-pyogenic streptococci	
		Model A[a]	Model B	Model A	Model B
<5 years	2006/07	-15.5% [-27.2 to -2.0]	-8.1%	-16.7% [-27.2 to -2.0]	-9.2%
	2007/08	-13.8% [-26.8 to 1.6]	5.1%	-5.2% [-19.6 to 11.8]	15.9%
	2008/09	-19.5% [-33 to -3.2]	8.7%	-8.3% [-23.9 to 10.4]	24.3%
	2009/10	-25.5% [-39.4 to -8.4]	9.5%	-17.3% [-32.9 to 2.0]	22.3%
5-64 years	2006/07	-7.4% [-14.1 to -0.2]	4.4%	-10.9% [-22.5to 2.6]	0.7%
	2007/08	-5.9% [-13.4 to 2.4]	15.9%	-15.8% [-28.0 to -1.5]	4.0%
	2008/09	-12.3% [-20.1 to -3.6]	18.0%	-23.1% [-35.6 to -8.3]	3.9%
	2009/10	-16.1% [-24.4 to -6.8]	23.3%	-31.9% [-44.1 to -17.1]	-0.8%
≥65 years	2006/07	-8.6% [-15.4 to -1.3]	2.3%	-11.1% [-18.7 to -2.8]	0.7%
	2007/08	-8.3% [-15.9 to 0.0]	10.8%	-7.5% [-16.2 to 2.1]	14.3%
	2008/09	-12.2% [-20.3 to -3.3]	15.0%	-18.0% [-26.7 to -8.3]	11.0%
	2009/10	-11.9% [-20.9 to -1.9]	25.2%	-25.0% [-33.8 to -15.0]	11.5%

PCV7: seven-valent pneumococcal vaccine.

Model A: extrapolation of the trend in the period before introduction of PCV7.

Model B: assuming the trend to discontinue from the season 2005/06 onwards.

[a] For model A 95% confidence intervals are presented.

For *E. coli* and non-pyogenic streptococci the trends were significantly positive in all age groups (all p<0.001). Pre-PCV7 trends in IPD were not significantly different from those in *E. coli* and non-pyogenic streptococci (Table 1) in the under 65 year-olds, although in the children trends in IPD were slightly smaller than in the other pathogens (Table 1, Figure 2). However, in the age group 65 years and older no significantly positive trend was found for IPD, while reports for *E. coli* and non-pyogenic streptococci increased by 7–9% per year.

In the youngest age group (under five years of age) the reported incidence of non-pyogenic streptococci closely followed the prediction extrapolated from the trend before the season 2006/07 (Figure 3). However, the prediction for *E. coli* significantly overestimated the actual incidence (Table 2) although the reported incidences were still higher then before the date of PCV7 introduction. In the 5–64 year-olds the pre-PCV7 trend of non-pyogenic streptococci diminished in the seasons after introduction of PCV7 and the incidence remained at the level of the incidence observed in the season 2005/06. Again *E. coli* differed: the observed incidences were in between the predictions that assumed the pre-PCV7 to continue and those assuming no trend after introduction of PCV7. In the oldest age group the reports for both *E. coli* and non-pyogenic streptococci were in between these two prediction scenarios.

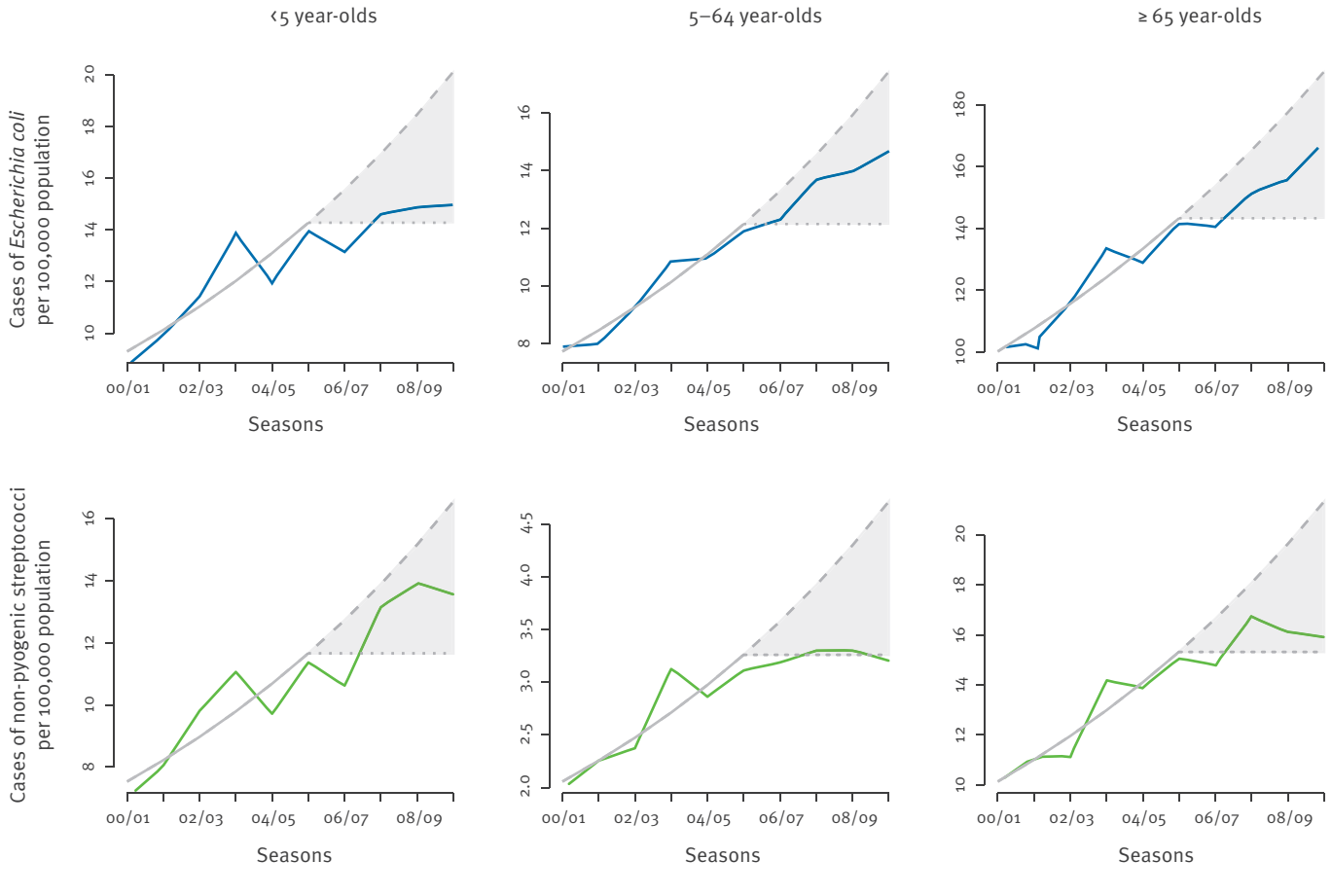
Discussion and conclusion

Upward trends in the annual numbers of some bacteraemias have been reported previously [12]. The similarity of the trends for IPD and the two control pathogens in the age groups under 65 years before 2005/06 suggests that the sensitivity of the national surveillance system in England and Wales was increasing prior to introduction of PCV7. While the trends for the control pathogens extrapolated from the period before PCV7 introduction were not entirely consistent with the observed incidence in the period after 2005/06, they may nevertheless provide an equally likely indication of the expected numbers of bacteraemia reports in the post-PCV7 period compared to those assuming the trend to discontinue after 2005/06.

The data sources introduced some limitations to our analysis. While we employed the data from the national

Figure 3

Pre-and post-PCV7 trends in control infections stratified by pathogen and age group, England and Wales, 2000/01–2008/09



laboratory-based surveillance for *E. coli* and non-pyogenic streptococci the data on *S. pneumoniae* was further enhanced and controlled for duplicates due to inconsistencies specific to IPD in the national laboratory-based surveillance dataset in the years 2002 and 2003 when duplicates had been included in error; such duplicates were removed from the enhanced IPD dataset (which contains an extra 10–20% of cases identified solely from referral of isolates for serotyping). A further limitation which may have affected the data was the migration in mid-2001 of the national surveillance database to a new platform which could have caused inconsistencies for all pathogens if data deduplication was compromised. Non-pyogenic streptococci are sometimes associated with contamination. This could artificially increase the reported incidence of bacteraemias caused by non-pyogenic streptococci. However, this is unlikely to alter the trend estimates for increasing ascertainment since these would be equally reflected by the contaminated samples.

We assessed the goodness of fit of the regression models in the pre-PCV7 era (goodness of fit is not an issue for the post PCV7 period since the model is saturated there, i.e. the model is set up to exactly fit the data). For all six models (three age groups for both *E. coli* and non-pyogenic streptococci) the root mean square error was between 1.29 and 1.34. Also, considering the logarithm of time rather than time as a linear variable did not improve the Akaike information criterion.

Secular trends in the reports of laboratory-confirmed IPD in the absence of vaccination have been observed for some serotypes [13,14]. These trends are poorly understood, cannot be predicted and are likely to affect the estimates of the vaccine impact. However, in the younger age groups our pre-PCV7 trend estimates for IPD and the other pathogens were similar, which suggest that these trends were more pronounced in that period than any pathogen-specific secular trends.

The similar trends prior to 2005/06 between pneumococcus and the other pathogens in the age groups under five years and between five and 64 years could reveal a common source causing this trend; increasing ascertainment of cases. This could be due to numerous reasons including increasing blood culturing practice and an increasing number of laboratories choosing to report these non-notifiable diseases to the national database. Additional factors might have contributed to the observed trends, such as increasing automation of detection techniques or improved survival of people with underlying conditions, which could have increased the numbers of vulnerable people in the population. However, in the population aged 65 years and older, the trends in IPD were different from the other pathogens. This could possibly be attributed to the step-wise introduction of a vaccination programme with the 23-valent pneumococcal polysaccharide vaccine (PPV) from August 2003 for this age group. A detailed evaluation of the effectiveness of PPV in the elderly and the likely impact of the universal vaccination programme for this age group is currently being undertaken by the Health Protection Agency.

To assess the probable development of reported cases of IPD in the absence of vaccination we compared two predictions, continuing pre-PCV7 trend (Model A) and no trend (Model B), to the actual reports for *E. coli* and non-pyogenic streptococci. Although we have no clear evidence that one of the predictions was more correct than the other, the reported number of cases was in between both predictions in all age groups. While Model A might provide the better prediction for the under five year-olds, Model B seemed to provide more reliable estimates in the age group between five and 64 years.

These findings do have important implications for analysing the effect of the introduction of PCV7 to the childhood immunisation scheme: We find that by ignoring the pre-PCV7 trend, one is likely to underestimate the reduction in IPD and overestimate the degree of replacement disease. However, allowing for trends introduces the risk to overestimate the reduction in VT IPD and underestimate possible replacement especially in the 5–64 year-olds. This analysis helps to estimate the uncertainty introduced by changing ascertainment when analysing the effects of PCV in England and Wales. Similar analyses from other countries would be valuable to improve the comparability of the vaccine effects.

Conflicts of interest

SF and EM have no conflict of interest. MS has received funding from GSK and Pfizer to attend scientific meetings and conferences.

Acknowledgments

The authors would like to thank Theresa Lamagni for her epidemiological input and Nick Andrews for his statistical advice. We also like to thank Doris Otomewo for supplying the data sets for E. coli and non-pyogenic streptococci and Pauline Kaye for supplying the IPD dataset and advising on its interpretation.

References

1. Dagan R, Melamed R, Muallem M, Piglansky L, Greenberg D, Abramson O, et al. Reduction of nasopharyngeal carriage of pneumococci during the second year of life by a heptavalent conjugate pneumococcal vaccine. J Infect Dis. 1996;174(6):1271-8.
2. Dagan R, Givon-Lavi N, Zamir O, Sikuler-Cohen M, Guy L, Janco J, et al. Reduction of nasopharyngeal carriage of Streptococcus pneumoniae after administration of a 9-valent pneumococcal conjugate vaccine to toddlers attending day care centers. J Infect Dis. 2002;185(7):927-36.
3. Black S, Shinefield H, Fireman B, Lewis E, Ray P, Hansen JR, et al. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. Northern California Kaiser Permanente Vaccine Study Center Group. Pediatr Infect Dis J. 2000;19(3):187-95.

4. Pilishvili T, Lexau C, Farley MM, Hadler J, Harrison LH, Bennett NM, et al. Sustained reductions in invasive pneumococcal disease in the era of conjugate vaccine. J Infect Dis. 2010;201(1):32-41.
5. Rodenburg GD, de Greeff SC, Jansen AG, de Melker HE, Schouls LM, Hak E, et al. Effects of pneumococcal conjugate vaccine 2 years after its introduction, the Netherlands. Emerg Infect Dis. 2010;16(5):816-23.
6. Changing epidemiology of pneumococcal serotypes after introduction of conjugate vaccine: July 2010 report. Wkly Epidemio Rec. 2010;85(43):434-6.
7. Ihekweazu CA, Dance DA, Pebody R, George RC, Smith MD, Waight P, et al. Trends in incidence of pneumococcal disease before introduction of conjugate vaccine: South West England, 1996-2005. Epidemiol Infect. 200;136(8):1096-102.
8. Laboratory Reporting to the Health Protection Agency. Guide for Diagnostic Laboratories. Version 3.0. London: Health Protection Agency; August 2010. Available from: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947381307
9. Trotter CL, Waight P, Andrews NJ, Slack M, Efstratiou A, George R, et al. Epidemiology of invasive pneumococcal disease in the pre-conjugate vaccine era: England and Wales, 1996-2006. J Infect. 2010;60(3):200-8.
10. Payton ME, Greenstone MH, Schenker N. Overlapping confidence intervals or standard error intervals: what do they mean in terms of statistical significance? J Insect Sci. 2003;3:34.
11. R Development Core Team. R: A language and environment for statistical computing. Vienna: R Foundation for Statistical Computing; 2008; Available from: http://www.r-project.org/
12. Wilson J, Elgohari S, Livermore DM, Cookson B, Johnson A, Lamagni T, et al. Trends among pathogens reported as causing bacteraemia in England, 2004-2008. Clin Microbiol Infect. 2011;17(3):451-8.
13. Black S. The volatile nature of pneumococcal serotype epidemiology: potential for misinterpretation. Pediatr Infect Dis J. 2010; 29(4):301-3.
14. Harboe ZB, Benfield TL, Valentiner-Branth P, Hjuler T, Lambertsen L, Kaltoft M, et al. Temporal trends in invasive pneumococcal disease and pneumococcal serotypes over 7 decades. Clin Infect Dis. 2010;50(3):329-37.

WHO urges polio-endemic countries to completely halt the transmission of the wild polio virus by 2012

Eurosurveillance editorial team (eurosurveillance@ecdc.europa.eu)[1]
1. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

Citation style for this article:
Eurosurveillance editorial team. WHO urges polio-endemic countries to completely halt the transmission of the wild polio virus by 2012. Euro Surveill. 2011;16(20):pii=19872. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19872

Article published on 19 May 2011

On 17 May 2011, at the ongoing World Health Assembly (WHA) in Geneva, Switzerland (16–25 May), the World Health Organization (WHO) Director-General Dr Margaret Chan and Mr Bill Gates of the the Bill & Melinda Gates Foundation, met with Ministers of Health from countries with ongoing transmission of poliomyelitis to discuss the steps needed to eradicate polio by 2012.

Dr Chan urged the representatives from Afghanistan, Angola, Chad, Democratic Republic of the Congo, India, Nigeria, Pakistan and international development agencies to make concerted efforts to eradicate the disease by next year.

The meeting follows a report by the Independent Monitoring Board (IMB) [1], a body established following a request by the WHA to monitor the progress towards achieving a polio-free world. The IMB held its inaugural meeting on 21–22 December 2010, then met again on 31 March–1 April 2011. The report affirmed the progress made under the new Global Polio Eradication Initiative (GPEI) but at the same time expressed concern that remaining operational gaps in key infected countries and underfunding are hindering progress.

In 2008, the WHA requested the Director-General to develop a new strategy to renew the fight to eradicate poliomyelitis from the remaining affected countries. In order to lay the basis for the new strategy, a special, one-year Programme of Work 2009 of the GPEI (www.polioeradication.org) was undertaken. The 2010 WHA acknowledged the progress made and agreed with the framework for a new strategic plan for 2010–2012 [2], which was then finalised and launched in June 2010.

The IMB will meet quarterly to monitor the implementation and impact of the new strategic plan 2010–2012 [2] against the major milestones and process indicators established for that purpose, and advise countries and partner agencies on corrective actions as appropriate. A WHO Progress Report on polio eradication has been presented at the 2011 WHA [3].

References

1. Monitoring progress towards global polio eradication: poliovirus surveillance, 2009–2010. Wkly Epidemiol Rec. 2011;86(16):153-60.
2. World Health Organization (WHO). WHA63/2010/REC/3, summary record of the eighth meeting of Committee B, section 2A 23 December 2010.
3. World Health Organization (WHO). Progress reports. Sixty-fourth World Health Assembly. Provisional agenda item 13.17. A64/26, 21 April 2011. Available from: http://apps.who.int/gb/ebwha/pdf_files/WHA64/A64_26-en.pdf.