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factor **5.49**

# Eurosurveillance

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

**Vol. 18 | Weekly issue 33 | 15 August 2013**

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# A surge of MDR and XDR tuberculosis in France among patients born in the Former Soviet Union

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## Citation style for this article:

Bernard C, Brossier F, Sougakoff W, Veziris N, Frechet-Jachym M, Metivier N, Renvoisé A, Robert J, Jarlier V, on behalf of the MDR-TB Management group of the NRC. A surge of MDR and XDR tuberculosis in France among patients born in the Former Soviet Union. *Euro Surveill.* 2013;18(33):pii=20555. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20555>

Article submitted on 12 August 2013 / published on 15 August 2013

**A marked increase in the number of multidrug-resistant (MDR) tuberculosis (TB) cases entirely related to patients born in the Former Soviet Union was observed in France in the last two years. Very few cases were clustered, suggesting it is a consequence of recent immigration of patients already infected in their country of origin. This major increase challenges the existing structures for management of MDR and extensively drug-resistant TB (XDR-TB).**

We report herein a drastic surge in the number of multidrug-resistant tuberculosis (MDR-TB) cases diagnosed in France in the last two years. MDR-TB, defined as TB with *Mycobacterium tuberculosis* strains resistant to isoniazid (INH) and rifampicin (RMP), is a threat to public health in some parts of the world, notably in Eastern Europe and Central Asia [1-4]. In these regions, and particularly in Former Soviet Union (FSU) countries, nearly one third of new cases and two thirds of previously treated cases are MDR-TB cases [2,5]. In France, which is a low TB incidence country [6], MDR-TB represented 0.7% of new cases and 6.9% of previously treated cases up to 2004 [7].

Surveillance of resistant tuberculosis

All MDR-TB strains sent to the French National Reference Center for Mycobacteria (NRC-MyRMA) between 2006 and 2012 for MDR confirmation and second-line drug susceptibility testing against ofloxacin (OFX), amikacin (AMK), kanamycin (KAN), and capreomycin (CAP) were included. Susceptibility tests were performed on Lowenstein-Jensen medium following the proportion method [8], by using the critical proportion of 1% and the following concentrations: RMP 40 mg/L, INH 0.2 and 1 mg/L, OFX 2 mg/L, AMK and CAP 40 mg/L, KAN 30 mg/L. Detection of mutations involved in the resistance to the above antibiotics was performed by using the line probe assays *MTBDRplus* and *MTBDRsl* (HAIN Lifescience) and by *gyrA* and *gyrB* sequencing.

Extensively drug-resistant TB (XDR-TB) was defined as MDR-TB with additional resistance to any of the fluoroquinolones and to at least one of the three injectable drugs, KAN, AMK or CAP, and pre-XDR-TB was defined as MDR-TB with additional resistance to either fluoroquinolones or one of the three injectable drugs. Genotyping was performed using the 24-loci mycobacterial interspersed repetitive-unit variable-number tandem repeat (MIRU-VNTR) method. A cluster was defined as two or more patients whose strains had identical genotype pattern.

## Results

The NRC-MyRMA received 409 MDR strains from distinct patients between 2006 and 2012. The annual number of MDR-TB strains remained stable around 50 between 2006 and 2010, but increased to 69 in 2011 and 92 in 2012. The surge was related to an increase in patients born in the FSU, from an annual average of nine in 2006 to 2010 to 21 in 2011, and 47 in 2012 (Figure 1).

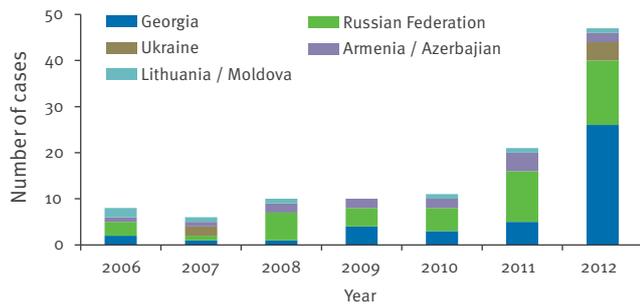
**FIGURE 1**

Distribution by country of birth of patients with multidrug-resistant tuberculosis identified in France, 2006–12 (n=409)



**FIGURE 2**

Distribution by country of birth of patients with multidrug-resistant tuberculosis born in the former Soviet Union, France, 2006–12 (n=113)



The annual number of patients born in Georgia rose from ca. two cases in 2006 to 2010 to five in 2011 and 26 in 2012 (Figure 2); for those born in the Russian Federation from ca. four in 2006 to 14 in 2012; and for those born in Ukraine from two cases in 2007 to four cases in 2012. The number of patients who originated from other parts of the world remained stable, except for those born in Eastern Europe outside the FSU, who doubled from an annual average of four in 2006 to 2008 to eight in 2009 to 2012.

Furthermore, the annual number of XDR-TB cases increased from two in 2006 to 2008 (5% of MDR-TB) to four in 2009 (7% of MDR-TB), six in 2010 (13% of MDR-TB), seven in 2011 (10% of MDR-TB) and suddenly 17 in 2012 (18% of MDR-TB) (Figure 3).

Almost three quarters of the 40 XDR-TB strains (n=31) were isolated from patients born in FSU, the remaining being born in other European countries (n=4) and in Africa (n=5). All 17 XDR strains identified in 2012 were from patients born in FSU, including 14 born in Georgia. Among all 113 MDR strains identified in FSU-born patients during the seven-year period, 31 (27%) were XDR, compared to nine of 296 (3%;  $p < 0.001$ ) among strains isolated from patients born in other countries. Among the 92 MDR strains in 2012, the proportion of XDR and pre-XDR strains was higher for patients born in Georgia (89%) than for other FSU countries (52%;  $p < 0.01$ ), and for non-FSU countries (9%;  $p < 0.001$ ) (Table).

Among the 47 FSU-born patients harbouring MDR strains isolated in 2012 with a mean age of 33 years, 36 were male (28 for other countries;  $p = 0.13$ ), 31 smear-positive (21 for other countries;  $p = 0.05$ ), and 28 previously treated (15 for others countries;  $p = 0.01$ ) (Table). The date of arrival in France was known for 29 of the 47 FSU-born MDR-TB patients identified in 2012: 27 arrived within one year before hospitalisation, including 10 that arrived within one month. The two remaining patients were in France for two and 10 years, respectively.

The MIRU-VNTR patterns of the 47 strains isolated in 2012 from FSU-born patients revealed that 32 (68%) belonged to the Beijing lineage, 10 (21%) to the LAM lineage, one to the Haarlem and one to the Ural lineages. Three isolates had MIRU-VNTR patterns referred as non-typable. Three clusters of five, nine and 10 strains were identified among the 32 Beijing strains, and three clusters of two, two and three strains among the 10 LAM strains. The combination of phenotypic and genotypic antibiotic patterns with MIRU-VNTR patterns decreased the clustering to only one pair in the Beijing lineage and one pair in the LAM lineage, each related to individuals within one household. All other strains had distinct genotypic and phenotypic susceptibility profiles ruling out transmission. Of note, only six (two patients born in China, one in Mongolia, one in France and two in Africa) of the MDR strains from non-FSU patients belonged to the Beijing lineage.

## Discussion

In France, the sudden increase in the number of MDR-TB strains isolated since 2011 was almost entirely related to the surge of MDR strains from FSU-born patients, who accounted for more than 50% of MDR-TB cases in 2012. Specifically, the increase was related to patients born in Ukraine, the Russian Federation and above all in Georgia.

In these three countries, TB incidence was estimated to be between 90 and 125 per 100,000 population in 2011 and the percentages of MDR-TB cases are estimated to be 10–20% in new TB cases and ca. 45% in retreatment cases [9–12]. Because Ukraine and the Russian Federation are countries with high numbers of inhabitants (45 and 143 million, respectively) in contrast to Georgia (4.3 million inhabitants), it is to be expected that more MDR-TB patients are observed originating from Ukraine and the Russian Federation than from Georgia. This is in contrast with what we observed in 2012, when Georgian patients accounted for more than half of MDR-TB cases from the FSU. This suggests that Georgian patients with MDR-TB may be more likely to emigrate to France and that MDR-TB rates in emigrates

**FIGURE 3**

Distribution by country of birth of patients with extensively drug-resistant tuberculosis, France, 2006–12 (n=40)



**TABLE**

Characteristics of patients with multidrug-resistant tuberculosis identified in 2012, by region of birth, France (n=92)

Characteristic	Georgia (n=26)	FSU except Georgia (n=21)	Total FSU (n=47)	Other countries (n=45)	p value <sup>a</sup>
Mean age (years)	36	30	33	28	0.01
Male n (%)	23 (89)	14 (65)	36 (77)	28 (62)	0.13
Smear positive n (%)	19 (73)	12 (62)	31 (66)	21 (46)	0.05
Previous treatment n (%)	18 (67)	10 (50)	28 (60)	15 (33)	0.01
XDR-TB n (%)	14 (54)	3 (14)	17 (36)	0	<0.01
Pre-XDR-TB n (%)	9 (35)	8 (38)	17 (36)	4 (9)	<0.01
Pre-XDR and XDR-TB n (%)	23 (89)	11 (52)	34 (72)	4 (9)	<0.01
Beijing lineage n (%)	16 (62)	16 (76)	32 (68)	6 (13)	<0.01

FSU: Former Soviet Union; XDR-TB: extensively drug-resistant tuberculosis.

<sup>a</sup> Comparison between total FSU and other countries.

cannot be deduced from rates observed in their countries of origin [13].

Previous TB treatment history is known to be a risk factor for resistance [14-16], and this is confirmed in France where two thirds of the FSU-born MDR-TB patients have been previously treated. In addition, more than one third of the FSU-born MDR-TB patients from 2012 had in fact XDR-TB, and all of the XDR-TB patients were FSU-born. Consequently, the important surge in MDR-TB observed recently in France is compounded by a problematic management of antibiotic treatment regimens before the availability of comprehensive susceptibility tests results, reinforcing the importance of universal use of genotypic susceptibility tests in this population. While it is possible that an increase in immigration from the FSU overall could in part explain the observed increase in cases, it is worth mentioning that nine in 10 FSU-born MDR-TB patients are recent immigrants and that one in three arrived only a few days before hospitalisation. Therefore, the possibility needs to be considered that immigration to France may be driven by health reasons and clinicians should be aware of it when such patients arrive in the healthcare system.

In the present study, the genotyping analysis revealed four lineages (Beijing, LAM, Haarlem and Ural) already reported in the FSU [17-19], although the Beijing family was more frequent (68%) in our study. Of interest, the combination of MIRU-VNTR and antibiotic resistance genotypes and phenotypes suggested that almost all strains defined as clustered by MIRU-VNTR were in fact distinct. Thus, the recent increase in France in the number of FSU-born MDR-TB patients is more likely to be a result of recent immigration of patients infected in their country of birth where multiple MDR strains are circulating, than from cross-transmission in France among a closed group.

In conclusion, this increase challenges the existing structures for management of MDR and XDR-TB especially in a low-endemic country for TB.

#### The members of the MDR-TB Management group of the NRC were:

Claire Andrejak, , Amiens; Emmanuelle Cambau, Paris; Katarina Chadelat, Paris; Bertrand Dautzenberg, Paris; Benoit Henry, Paris; Damien Le Dû, Briis sous Forges, Laurent Raskine, Paris; Benedicte Rivoire, Paris; Guillaume Thouvenin, Paris.

#### Conflict of interest

None declared

#### Authors' contributions

Christine Bernard, Florence Brossier, Nicolas Veziris, Vincent Jarlier, Wladimir Sougakoff, Jerome Robert, Aurélie Renvoisé: collected, analysed and interpreted data. Christine Bernard, Vincent Jarlier, Jérôme Robert: wrote the manuscript. All authors provided contribution with comments and reviewed the manuscript.

#### \* Erratum:

The name of A Renvoisé was erroneously left out of the list of authors at the time of publication of this article. This mistake was corrected on 16 August 2013 and we apologise to the authors.

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# Increased incidence of invasive group A streptococcal disease in Ireland, 2012 to 2013

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## Citation style for this article:

Meehan M, Murchan S, Bergin S, O'Flanagan D, Cunney R. Increased incidence of invasive group A streptococcal disease in Ireland, 2012 to 2013. *Euro Surveill.* 2013;18(33):pii=20556. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20556>

Article submitted on 06 August 2013 / published on 15 August 2013

**Invasive group A streptococcal (iGAS) infections have been notifiable in Ireland since 2004. Incidence rates (2004–2011) have ranged from 0.8 to 1.65 per 100,000. In 2012, the iGAS rate rose to 2.66 per 100,000 and was associated with a high proportion of *emm1* isolates. A further increase in January to June 2013 has been associated with increased prevalence of *emm3*. Public health departments and clinicians have been alerted to this increase.**

In this communication, we report the increased incidence of severe *Streptococcus pyogenes* (group A streptococcus; GAS) infection in Ireland and a predominance of *emm1* in 2012. In the first six months of 2013, we observed a further increase in iGAS and the emergence of *emm3*.

## Background

*S. pyogenes* is a major human pathogen that causes a wide spectrum of clinical manifestations. These range from common superficial skin infections and pharyngitis to invasive infections such as bacteraemia, meningitis, cellulitis, pneumonia, and the more severe necrotising fasciitis (NF) and streptococcal toxic shock syndrome (STSS). Invasive GAS (iGAS) infections, though relatively uncommon compared to highly prevalent non-invasive GAS infections, remains a significant global cause of morbidity and mortality. Seven-day case fatality rates range from 8% to 16%, with high rates approaching 50% often associated with STSS [1].

The M protein, encoded by the *emm* gene, is the major virulence factor and an important epidemiological typing tool. In excess of 200 *emm* types have been documented to date [2]. Whereas all types may be associated with invasive GAS (iGAS), *emm1* and *emm3* have been particularly associated with severe iGAS infections and the resurgence of these infections that has occurred since the 1980s [3]. The incidence of iGAS disease exhibits seasonal patterns in addition to periodic upsurges [4]. Moreover, the prevalence of *emm* types has been shown to exhibit temporal and geographical

variations [5,6]. Several factors are thought to play a role in disease fluctuations, including prominent circulating *emm* types, increased host susceptibility, environmental factors and seasonal viral infections such as influenza [4-9].

iGAS has been notifiable in Ireland since 2004 under the Infectious Diseases Regulations 1981 as amended by S.I. no 707 of 2003. Cases are classified as confirmed, probable or possible, based on nationally-agreed case definitions, combining laboratory and clinical criteria [10]. Since 2005, enhanced surveillance, which includes collection of information on isolate site, clinical presentation, risk factors and patient outcome, has been conducted for iGAS cases on a voluntary basis [11]. In 2012 a laboratory reference service commenced to which isolates are voluntarily submitted for *emm* sequence typing.

## Methods

### Clinical data collection

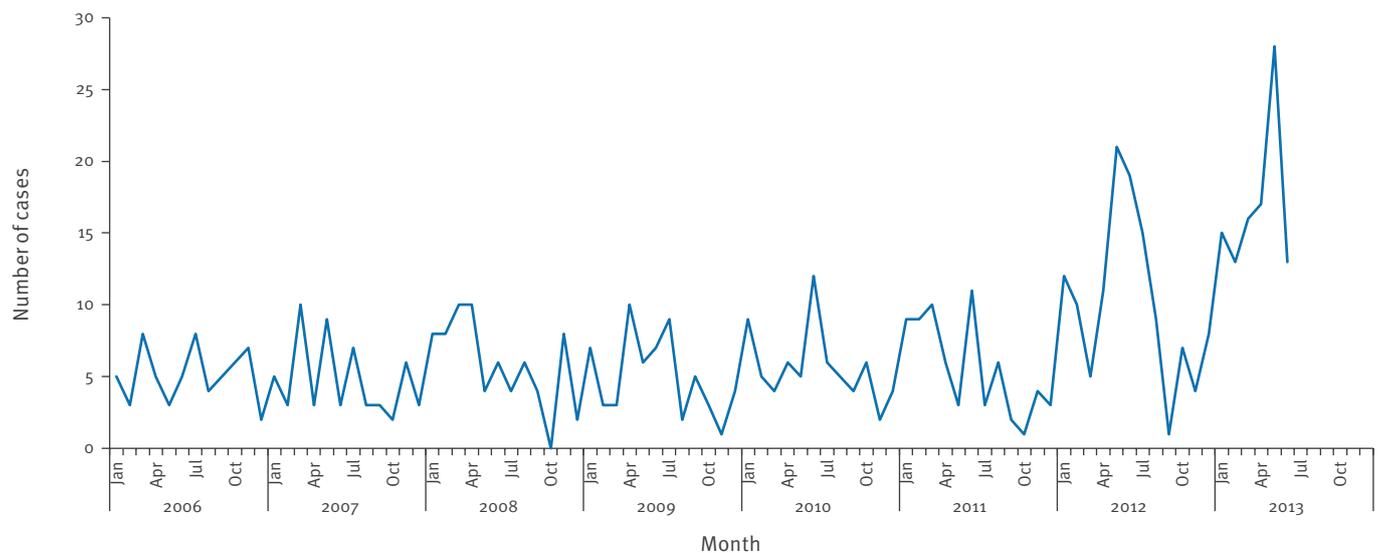
Demographic information on iGAS cases was analysed using data which had been entered in the national electronic infectious disease reporting system (Computerised Infectious Diseases Reporting System, CIDR). CIDR allows exchange of information between laboratories, regional departments of public health and the Health Protection Surveillance Centre (HPSC) and is used to notify iGAS and record enhanced surveillance findings.

### Epidemiological typing

From early 2012 onwards, all available iGAS isolates (n=109 in 2012; n=67 in January to June 2013) were submitted by clinical microbiology laboratories to the GAS reference laboratory for *emm* sequence typing. Isolates which had been archived in 2011 (n=28) were sent to be typed retrospectively. Typing was performed by sequencing the hypervariable region of the *emm* gene as previously described [12].

**FIGURE 1**

Invasive group A streptococcal cases notified by month and year in Ireland, January 2006–June 2013 (n=607)



### Statistics

Incidence rates were calculated using the 2011 population census data. Incidence rate ratios were calculated along with their 95% confidence intervals (CI; Fisher's exact test). The year 2005 was excluded from the analysis of enhanced surveillance data as there may not have been complete data reporting for that year. Difference in the *emm* type distribution was calculated using Fisher's exact test.

### Results

#### Epidemiology

In 2012, 117 confirmed cases and five probable cases of iGAS infection were notified. This corresponds to an annual incidence of 2.66 cases per 100,000 (95% CI: 2.21–3.17 per 100,000). This is the highest annual incidence since iGAS became notifiable in 2004. Annual incidences for 2004 to 2011 have ranged from 0.8 per 100,000 in 2004 to 1.65 per 100,000 in 2008, with incidence rates levelling out in 2009 to 2011 (range: 1.31–1.48 cases per 100,000) [11]. In 2012, the highest number of cases occurred in the months May through July, with the lowest in September (Figure 1). A further increase occurred during the first six months of 2013 with a total of 102 cases notified from January to June compared to 78 and 44 cases in the first six months of 2012 and 2011, respectively (Figure 1). The number of iGAS cases in May 2013 (n=28) represents the highest number of notified cases in any month since iGAS became notifiable in 2004.

In 2012, the age-specific incidence of invasive infection increased across most age groups when compared with the average age-specific incidence over the period 2006 to 2011 (Figure 2). The biggest increases and the highest number of cases occurred in older adults

(older than 75 years) followed by children (under the age of four years;  $p=0.053$  and  $p=0.036$ , respectively) (Figure 2). Males and females were represented equally in most age groups with the exception of those in the age range 0–9 years where boys were more affected (8 female:18 male) and those in the age range 30–44 years where women were more affected (21 female:7 male). Overall, slightly more females than males were affected in 2012 (63 compared to 59); however, this was not statistically significant.

There were 26 cases of STSS in 2012 compared to an average of 6.17 cases per year for the period 2006 to 2011 (range: 3–9 cases per year). The proportion of all iGAS cases that presented with STSS increased from 10% (37 of 383) for the period 2006 to 2011 to 21% in 2012 ( $p=0.04$ ). During the first half of 2013, there were 22 cases of STSS accounting for 22% of all iGAS cases, indicating that the increased severity of iGAS infections observed in 2012 is sustained thus far in 2013.

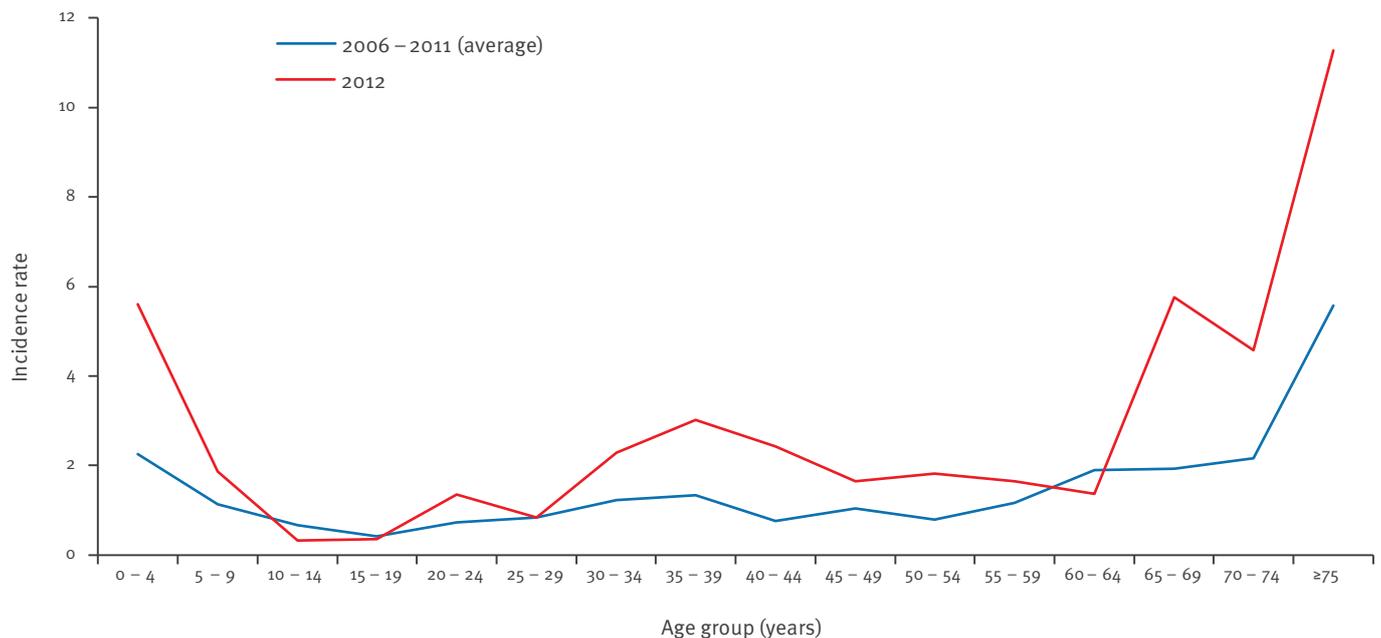
In 2012, eight patients died (12.5% case fatality rate (CFR)) within seven days of onset of the disease for which GAS was identified as the main or contributing cause of death. Of these, six patients presented with STSS. There were five deaths (11.6% CFR) in 2011, of which one case was associated with STSS, and an average of approximately three deaths per year (11% CFR) for the period 2006 to 2011, with approximately one case per year associated with STSS. For the first half of 2013, there have been nine deaths (15.3% CFR) with five cases associated with STSS.

#### Typing results

A total of 109 isolates (89%) collected from reported iGAS cases in 2012 were typed by *emm* sequence typing (Figure 3). The most prominent types were *emm*<sub>1</sub>,

**FIGURE 2**

Age-specific incidence rate of invasive group A streptococcal infections per 100,000 population by five-year age groups, Ireland, 2012 and averaged over the period 2006–11



which accounted for 48.6% of isolates, followed by *emm12* (9.2%) and *emm28* (7.3%). Whereas, *emm1* was equally distributed between males and females, *emm12* and *emm28* were more predominant in males (65%) and females (87.5%), respectively, although neither value was significant ( $p=0.34$  and  $0.065$ , respectively). The *emm1* type accounted for 17 of 25 STSS cases that were typed and for seven of eight deaths. Only two isolates of *emm1* were detected from October to December 2012, when no cases of STSS were reported (Figure 3). Sixty-seven isolates (66%) have so far been typed from all iGAS cases reported in January to June 2013. The number of *emm1* isolates has declined somewhat, accounting for 40% of typed isolates compared to 54% of typed isolates for the same period in 2012 (January–June). However, there has been a notable increase in *emm3* in the first half of 2013 with 22% ( $n=15$ ) of typed isolates belonging to this *emm* type contrasting with 1.5% ( $n=1$ ) for the same period in 2012 ( $p=0.0001$ ) and 4% ( $n=4$ ) in total for 2012. There is limited information regarding the type distribution of iGAS in Ireland prior to 2012. However, 28 iGAS isolates (42% of total) from 2011 were retrospectively typed and showed a lower prevalence of *emm1* (25%; eight of 28) and a higher prevalence of *emm12* (32%; nine of 28) compared to 2012 and 2013.

## Discussion

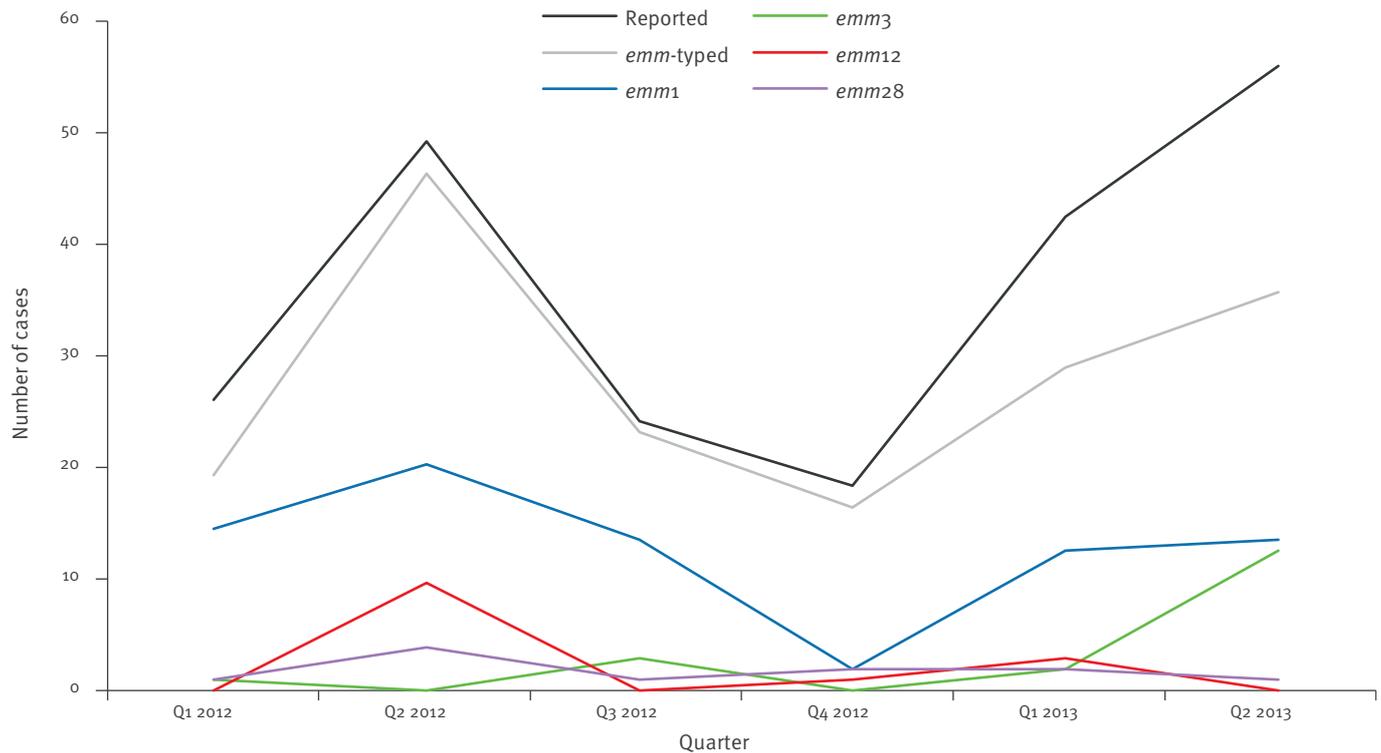
A marked increase in notifications of iGAS occurred in Ireland in 2012 with a further increase observed in 2013. Increased incidences of iGAS have also been reported in 2012/13 in Finland, Norway, Sweden, and England, suggesting an increase in iGAS infections in Northern Europe [13,14]. Public Health England reported 1,038

iGAS cases for weeks 37/2012 to 16/2013 compared to 691 for 2011/12 and 907 for 2008/09, the last peak season for iGAS infection [14], indicating that the upsurge in Ireland (April–July 2012) pre-dated that in neighbouring England. iGAS has been notifiable in Ireland since 2004. It is therefore unlikely that the initiation of iGAS typing in 2012 and alerts issued on iGAS in July 2012 and April 2013 would have had a significant effect on the overall notification rate. There is evidence to suggest that viral infections such as influenza can contribute to an increased risk of invasive bacterial infections such as iGAS [8,9]. The short and mild 2011/12 influenza season in Ireland is unlikely to have had an impact on the increased incidence of iGAS in 2012. However, in 2013, the influenza season was more prolonged and may have been a contributing factor to increased rates of iGAS [15].

The high prevalence of *emm1* is likely to have played a significant role in the increased incidence of iGAS in 2012. The lower prevalence of *emm1* and higher prevalence of *emm12* in 2011 compared to the incidence of these types in 2012 suggests a possible change in the epidemiology of GAS between 2011 and 2012. However, no major conclusions can be drawn due to the small number of isolates which were typed in 2011. Significantly, England, Norway and Sweden have also reported a high prevalence of *emm1* in 2012/13 [13,14]. The increased incidence of *emm3* in 2013 is of concern given its association with a higher case fatality rate compared to other *emm* types [16]. Significantly, in 2013, *emm3* accounted for five of eight fatal cases in Ireland for which typing data was available. An increased prevalence (11%) of *emm3* was also reported

**FIGURE 3**

Quarterly reported invasive group A streptococcal cases (n=224), proportion of typed isolates (n=176) and most prevalent emm types, Ireland, January 2012–June 2013



in Sweden in 2012 [13]. Continued typing of isolates will be required to confirm this trend in 2013 and to monitor any further changes in epidemiology.

The incidence of iGAS infections in Ireland, although increased in 2012, was lower than the 2012 upsurge rate reported in Sweden (6.1 per 100,000 population) [13]. Moreover, the overall annual incidence rates (0.8–1.65 in 2004–11) in Ireland prior to the upsurge were lower than that reported in the United Kingdom (UK), the Nordic countries and North America, which have in general higher reported incidence rates in the range 2.5–5.0 per 100,000 [4,11,13]. The reason(s) for the lower incidence rate of iGAS in Ireland is unclear [11]. A relatively high empiric antibiotic consumption has previously been suggested as a likely explanation [11]. For example, in 2010, outpatient penicillin use was higher in Ireland at 10.70 defined daily doses (DDD) per 1,000 inhabitants per day than in Finland at 6.6 DDD, Sweden at 7.1 DDD and the UK at 8.6 DDD per 1,000 inhabitants per day [17]. A small number of cases may also have gone unreported due to differences in case definitions between Ireland and other countries as previously reviewed [11]. Temporal and geographical fluctuations in iGAS infections may also be due in part to *emm* type distribution, population susceptibility, prevalence of certain risk factors, and environmental factors such as climate and population density [4,11,18].

Similar to other European countries, seasonal variation in iGAS infections was observed in Ireland, with lowest incidence rates in late summer/autumn as reported elsewhere [4,13,19]. The peak rate of iGAS infections in Ireland in May 2012 and 2013 occurred later than in Sweden and other Nordic countries which generally exhibit peak incidences in the first quarter of each year [13,19]. However, occasional peaks in summer can also occur in these countries [13,19]. Noteworthy is the rising incidence of iGAS infections reported in April 2013 in England, possibly indicating a late upsurge similar to that observed in Ireland [14]. Seasonal variations in iGAS may reflect climatic differences such as daylight/sunlight hours, rainfall/humidity, temperatures and seasonal behavioural patterns [4,19]. Certainly, spring 2012 and 2013 exhibited below average temperatures throughout Ireland.

Given the severity and rapid progression of iGAS, prompt detection and medical intervention are the only preventative and control measures available to reduce morbidity and mortality. In response to the increase in iGAS notifications, alerts and guidance have been issued to public health departments and clinicians (particularly general practitioners, emergency physicians, paediatricians, infection specialists and intensive care specialists), and iGAS recognition and management have been highlighted in surveillance bulletins. Laboratories are encouraged to send iGAS

isolates for typing and to submit enhanced surveillance data to monitor the continuing trends in iGAS epidemiology, to investigate any suspected outbreaks and improve our understanding of iGAS epidemiology in Ireland. Moreover, in light of the reported increase in iGAS in several other European countries and the changing epidemiology of iGAS detected here in Ireland, public health institutions in Europe should be alert to any changes in epidemiology for the forthcoming 2013/14 iGAS season. Consideration should also be given to expanding the European Invasive Bacterial Disease Surveillance Network (EU-IBD) to include iGAS.

## Acknowledgements

The authors would like to thank microbiology laboratories and departments of public health for reporting iGAS cases and submission of enhanced surveillance data. Special thanks also to microbiology laboratories for sending iGAS isolates for typing.

## Conflict of interest

None declared.

## Authors' contributions

Mary Meehan and Stephen Murchan performed the analyses and wrote the manuscript. Mary Meehan had overall responsibility for epidemiological typing and collating iGAS isolate data. Stephen Murchan had overall responsibility for collating enhanced clinical data of iGAS cases. Sarah Bergin provided clinical advice. Robert Cunney is the clinical lead for iGAS surveillance at the Health Protection Surveillance Centre, and director of Epidemiology and Molecular Biology Unit and, Irish Meningococcal and Meningitis Reference Laboratory. Darina O'Flanagan is director of the Health Protection Surveillance Centre. All authors supported the analyses, critically read the manuscript and approved the final submitted draft.

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# Increase in gonorrhoea among very young adolescents, Catalonia, Spain, January 2012 to June 2013

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## Citation style for this article:

Vives N, Lugo R, López E, Garcia de Olalla P, Minguell S, Barrabeig I, Pons P, Lopez-Grado E, Ferré I, Escriche R, Armengol P, Vall M, Soler P, Leon I, Gascon I, Vicente AM, Falguera G, Avecilla-Palau A, Martínez C, Barberá MJ, González V, Caylà J, Casabona J. Increase in gonorrhoea among very young adolescents, Catalonia, Spain, January 2012 to June 2013. *Euro Surveill.* 2013;18(33):pii=20560. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20560>

Article submitted on 05 August 2013 / published on 15 August 2013

Between January 2012 and June 2013, 27 sexually transmitted infections were reported in adolescents aged 13–15 years in Catalonia, Spain. In the first half of 2013, there were nine cases of gonorrhoea, while in the same period of 2012, there was one. In June 2013, two gonorrhoea cases aged 13–14 years, linked to a common source through a social network, were reported. The public health response should be adapted to this vulnerable population.

On 21 June 2013, the Public Health Agency of Catalonia received an alert from the Public Health Agency of Barcelona about the occurrence of gonorrhoea in two boys aged 13 and 14 years. The boys were coinfecting with *Chlamydia* and probably linked to a common exposure source, through an online social network. After case investigation, these two cases were linked to a third adolescent, a girl aged 14 years. As of 30 June, the Centre for Epidemiological Studies on STI/HIV/AIDS of Catalonia – responsible for the surveillance of sexually transmitted infections (STIs), including HIV/AIDS, for the Public Health Agency of Catalonia – observed a steady increase over the previous six months in the number of gonorrhoea cases reported among very young adolescents (13–15 years), which had not been identified as clusters.

We report here on the emergence of STIs among very young adolescents in Catalonia and draw attention

to the potential risk of a gonorrhoea outbreak and transmission of other STIs. We present a preliminary descriptive analysis of epidemiological and microbiological characteristics of cases from 1 January 2012 to 30 June 2013. We also compare the number of cases reported during first six months of 2012 and of 2013.

## Surveillance of sexually transmitted infections in Catalonia

Three institutional information systems are used for STI surveillance in Catalonia: a name-based mandatory disease notification registry (MDI), STI sentinel surveillance registry (RITS) and microbiological notification system (SNMC), as described elsewhere [1]. Infectious syphilis, gonorrhoea and lymphogranuloma venereum (LGV) have been included in the MDI since 2007 [2]. Other STIs, such as genital *Chlamydia* infection, trichomoniasis, genital herpes and genital warts due to human papilloma virus infection, are monitored through the RITS and SNMC.

STI case-report data from the three surveillance systems are entered into the Public Health Agency of Catalonia's Epidemiological Repository System, allowing complementarity of variables and capture of cases. Confidentiality and data protection are assured [3].

STI case definitions used for surveillance reporting are standardised, as the European Union definitions

**TABLE 1**

Epidemiological and behavioural characteristics of adolescents aged 13–15 years with sexually transmitted infections, Catalonia, Spain, January 2012–June 2013 (n=27)

Characteristic	Number of cases		
	Gonorrhoea	Other STIs	Total
Demographic	n=10	n=17	n=27
Sex			
Male	7	1	8
Female	3	16	19
Age (years)			
13	1	0	1
14	1	5	6
15	8	12	20
Country of birth <sup>a</sup>			
Spain	2	11	13
Outside Spain	7	4	11
Health provider reporting the case			
Paediatric service	4	0	4
Sexually Transmitted Infection Unit	0	2	2
Sexual and reproductive health service	1	6	7
Family/general practitioner team	1	6	7
Hospital emergency department	4	3	7
History of STIs and behaviour	n=7	n=8	n=15
Sexual orientation			
Heterosexual	4	7	11
Homosexual	0	1	1
Unknown	3	0	3
Previous STI in the last 12 months			
Yes	0	1	1
No/unknown	7	7	14
HIV positive			
Yes	0	0	0
No	1	3	4
Unknown status	6	5	11
Condom use at last sex			
Yes	0	3	3
No/Unknown	7	5	12
New sex partner in the last three months			
Yes	0	2	2
No/Unknown	7	6	13
Number of sex partners in the last 12 months			
≤2	0	7	7
>2	0	1	1
Unknown	7	0	7
Contact tracing initiated			
Yes	2	5	7
No/unknown	5	3	8

HIV: human immunodeficiency virus; STI: sexually transmitted infection.

<sup>a</sup> Information on country of birth was not available for all cases.

are used [4]. Very young adolescence was defined as a recorded age at STI diagnosis of between 13 and 15 years. A case reported from more than one of the three surveillance systems was counted only once in the analysis. When duplicates were detected, cases in the microbiological notification system were excluded from the analysis.

### Sexually transmitted infections among adolescents aged 13–15 years

Epidemiological and behavioural characteristics of STIs among adolescents aged 13–15 years in Catalonia are shown in Table 1 and the reported STIs in Table 2.

A total of 27 STI cases were reported during the study period (January 2012 to June 2013). Of these, 13 were reported during the first six months of 2013; in the first half of 2012, nine cases were reported (Table 2). This increase was due mainly to the increased number of cases of gonorrhoea. The number of cases with other STIs was very low, making comparisons between the years difficult. Overall, during 2007 to 2012, three syphilis cases (one in 2007, 2011 and 2012) and one gonorrhoea case in 2011 were reported among very young adolescents aged 13–15 years.

#### Gonorrhoea

A total of 10 very young adolescents (13–15 years) with gonorrhoea were reported to the Public Health Agency of Catalonia during January 2012 to June 2013. Seven were boys and seven were born outside of Spain, in Latin America and the Caribbean. Sexual orientation (heterosexual) was known for only four of the cases. Paediatricians notified four of the 10 cases.

Gonorrhoea was the second most frequently reported STI during the study period: nine cases were reported in the first half of 2013 whereas in the same period of 2012, there was only one (Table 2).

#### Other sexually transmitted infections

From January 2012 to June 2013, a total of 17 cases of other STIs were reported among adolescents aged 14–15 years. All except one were girls; one 15 year-old homosexual boy with syphilis was reported. Unlike the situation for the gonorrhoea cases, only four of the 17 cases with other STIs were born outside of Spain.

*Chlamydia trachomatis* infection was the most common STI (11 of the 27 cases) and *Gardnerella vaginalis* infection ranked third (3/27). When comparing January to June of 2012 versus 2013, no increase was observed (Table 2).

#### History of sexually transmitted infections

Most of the cases did not know their HIV status, one had a previous STI in the past year and only three reported condom use at last sex. One case aged 14 years reported having three sexual partners during the last 12 months and two cases reported having a new sexual partner during last three months.

**TABLE 2**

Sexually transmitted infections reported among adolescents aged 13–15 years, Catalonia, Spain, January 2012–June 2013

Infection	Number of cases		
	January 2012–June 2013	January–June 2012	January–June 2013
Infectious syphilis	1	1	0
Gonorrhoea	10	1	9
Lymphogranuloma venereum	0	0	0
<i>Chlamydia trachomatis</i>	11	4	4
Herpes simplex virus	1	0	0
<i>Trichomonas vaginalis</i>	0	0	0
Genital warts due to human papilloma virus infection	1	1	0
<i>Gardnerella vaginalis</i>	3	2	0
<b>Total</b>	<b>27</b>	<b>9</b>	<b>13</b>

Most of these very young adolescents (7/27) were diagnosed in a sexual and reproductive health service or by a family/general practitioner team (n=7). Four cases were diagnosed by paediatricians and two were diagnosed at the Sexually Transmitted Infection Unit. Contact tracing investigations, initiated by the health-care provider who diagnosed the patient, were carried out for seven of the 15 cases for whom epidemiological information was available (initiation of contact tracing following diagnosis is obligatory in Catalonia). No information on use of a newly introduced partner notification card was reported. Active contact tracing follow-up was carried out by the Barcelona city epidemiological surveillance unit for the cluster of three gonorrhoea cases.

#### Microbiological detection

The microbiological notification system detected *C. trachomatis* (n=8), *Neisseria gonorrhoeae* (n=3) and herpes simplex virus (n=1). Polymerase chain reaction (PCR) was used to detection of *C. trachomatis* and no further molecular serovar typing was performed. The three *N. gonorrhoeae* detections were confirmed by culture, all of which were sensitive to ceftriaxone. No molecular typing was carried out.

#### Background

Sexual activity in early adolescence contributes to an increased burden of unplanned pregnancy, abortion, transmission of STIs, including exposure to HIV and can have an impact on a young person's general health [5,6].

Spain has the lowest legal age of consent for sexual activity (13 years) in the European Union [7]. According to the last National Sexual Health and Reproduction Survey, 34% of those interviewed declared starting sexual intercourse before 16 years of age – two-fold higher than in the previous survey (12% in 2003) [8,9]. In contrast, the legal age for use of health services without parental consent is 16 years [10].

In Catalonia, epidemiological data from individualised mandatory STI reporting, introduced in 2007 [2], showed an increase between years 2007 and 2012 for gonorrhoea and syphilis and two outbreaks of lymphogranuloma venereum (LGV). Resistance of *N. gonorrhoeae* to ceftriaxone was documented in Catalonia in 2011 [1].

Approximately 40% of persons with STIs in all age groups in Catalonia are born outside Spain [1]. Sex between men who have sex with men is the route of exposure in about 30% of gonorrhoea cases, 60% of syphilis cases and 100% of LGV cases. Data by age group have only been available since 2007. Young people aged 15–24 years represent about 24% of all reported gonorrhoea cases and 11% of syphilis cases, with no change over time (2007–2012).

#### Discussion

The increase seen in the number of gonorrhoea cases and the occurrence of other STIs in these very young adolescents raises issues regarding the health and vulnerability of this population [11]. In addition, the data indicate a special vulnerability of foreign-born minors diagnosed with gonorrhoea, as the proportion of those born outside Spain is higher than that seen for other STIs and in other age groups [1]. Rapid public health responses are needed to address these issues in very young adolescents (Box).

The reporting of two gonorrhoea cases linked to a common third adolescent and exposure through a social network points towards a potential risk for gonorrhoea to spread among a young population with access to new technologies. In addition, the occurrence of non-congenital syphilis in a homosexual boy (born outside Spain) highlights the potential transmission of this infection and potential for increased exposure to HIV due to unprotected sexual intercourse. In Catalonia, syphilis is mostly observed among men who have sex with men, with 37% HIV coinfection [1].

## Box

### Public health response required to prevent sexually transmitted infections in very young adolescents (aged 13–15 years)

- Communicate to public health agencies and scientific societies the increased vulnerability of this population for STI/HIV transmission.
- Alert paediatricians, family/general practitioners and contraception and sexuality youth centres about the potential transmission of gonorrhoea and other STIs in minors aged under 16 years.
- Review STI surveillance procedures and STI clinical management guidelines regarding minors aged under 16 years.
- Reinforce youth-sensitive counselling, screening and partner notification among very young adolescents.
- Reinforce sexual health education at an early age, as well as training of primary care health professionals and counsellors about sexual health issues in very young adolescents.
- Bring to the attention of the multisector entities (governmental commissions, public health-epidemiological commissions, maternal-child health commissions and non-governmental and community-based organisations) about these emerging health issues.

HIV: human immunodeficiency virus; STI: sexually transmitted infection.

Sex-related behaviour within the very young adolescents showed a low condom use at last sexual intercourse; one case had had more than two sexual partners in the last 12 months. During early puberty, most minors enter into a rapid increase in cognitive and emotional development and face a period influenced by peers and other adults [5,6]. Further analysis of sexual behaviour and STI/HIV exposure should be carried out in this population.

Health professionals, in particular paediatricians, should be aware of the recent cases and be prepared to test for these infections in their very young adolescent patients. There should also be adequate follow-up, which respects privacy and confidentiality issues and the cognitive maturity of these very young adolescents concerning their own sexual health.

The three surveillance systems have been shown to be useful, allowing us to identify and describe the epidemiology of this vulnerable population. Nevertheless, the coverage and case-finding capacity of these systems needs to be improved.

The data presented show that important STIs such as syphilis, *chlamydia* and gonorrhoea are appearing in very young adolescents. These findings are consistent with data from European countries, where an increase in the proportion of STI in the age group 15–19 years is being observed [12]. This observation raises important public health issues regarding age at first sexual intercourse, unprotected sex and other high-risk behaviours, including the use of social networks for sex and contact with high-risk populations in urban areas. Further analysis should be carried out to identify risk

determinants, in order to design specific public health programmes and interventions that potentiate a comprehensive approach to young people's sexual health.

## Acknowledgements

We are grateful to all colleagues from the local epidemiology surveillance units (UVE), STI sentinel surveillance network (RITS) and local laboratories (SNMC) for the provided data to the Integrated STI/HIV/AIDS Surveillance System. We also acknowledge the work of our colleagues from the CEEISCAT, specifically Noemi Romero and Rafael Muñoz for their timely and quality of the data entered. Finally, the authors would like to thank: The Catalan Public Health Agency, Catalan Government (Agència de Salut Pública de Catalunya, Generalitat de Catalunya), and the CIBER Epidemiología y Salud Pública (CIBERESP), Spain.

## Conflict of interest

None declared.

## Authors' contributions

Designed the study: NV, RL and EL; Wrote the first draft: NV; Collected, synthesised and analysed the data: NV, RL, EL, PGO, SM, IB, PP, ELG, IF, RE, PA, MV, PS, IL, IG, AMV, GF, AAP, CM, MJB, VG, JAC, JC; Interpreted the results critically and revised the article to ensure important intellectual content: NV, RL, EL and JC; All authors read and approved the final manuscript.

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# Mumps epidemiology in Germany 2007-11

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## Citation style for this article:

Takla A, Wichmann O, Klinc C, Hautmann W, Rieck T, Koch J. Mumps epidemiology in Germany 2007-11. *Euro Surveill.* 2013;18(33):pii=20557. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20557>

Article submitted on 22 January 2013 / published on 15 August 2013

In Germany, mumps has been notifiable until 2013 only in the five Eastern federal states (EFS) of former East Germany. Due to different immunisation policies until 1990 and varying vaccination coverages thereafter, mumps incidences cannot be extrapolated to the 11 Western federal states (WFS). We studied mumps-related International Classification of Diseases (ICD-10) code diagnoses claimed through statutory health insurances between 2007 and 2011 to estimate countrywide mumps incidences in the outpatient sector, and compared them with case numbers from ambulatory notification data. Overall, 32,330 outpatient mumps cases were claimed. Annual incidence ranged between 9.3/100,000 and 11.8/100,000 and showed a significant decreasing trend. Compared with EFS, mumps incidence in WFS was higher and indicated a shift towards older age groups. Notified outpatient case numbers in EFS were 13-fold lower and from voluntary surveillance during an outbreak in the WFS Bavaria 8-fold lower than from insurance data ( $n=316$  versus  $n=4,217$  and  $n=238$  versus 1,995, respectively). Of all notified cases with available information, 75.4% (EFS) and 57.6% (Bavaria) were unvaccinated; 6.8% (EFS) and 19.3% (Bavaria) required hospitalisation. In Germany, mumps is still endemic despite decades of vaccination, with considerable underreporting in the established notification systems.

## Introduction

Mumps is a vaccine-preventable viral disease, typically characterised by swelling of the parotid glands, but can also cause severe complications like orchitis, meningitis, encephalitis or pancreatitis [1,2]. The disease usually occurs among children and in the pre-vaccine era, the annual reported mumps incidences in Western European countries ranged between 100 and 600 per 100,000 inhabitants [3]. With the availability of a live-attenuated mumps vaccine since the 1960s [4], disease incidence dramatically decreased in countries with mumps vaccination programmes [5,6]. Over the past years, however, numerous reports from different countries with long-established vaccination programmes have been published about extensive mumps

outbreaks that occurred predominantly among vaccinated children, adolescents, and young adults [7-15].

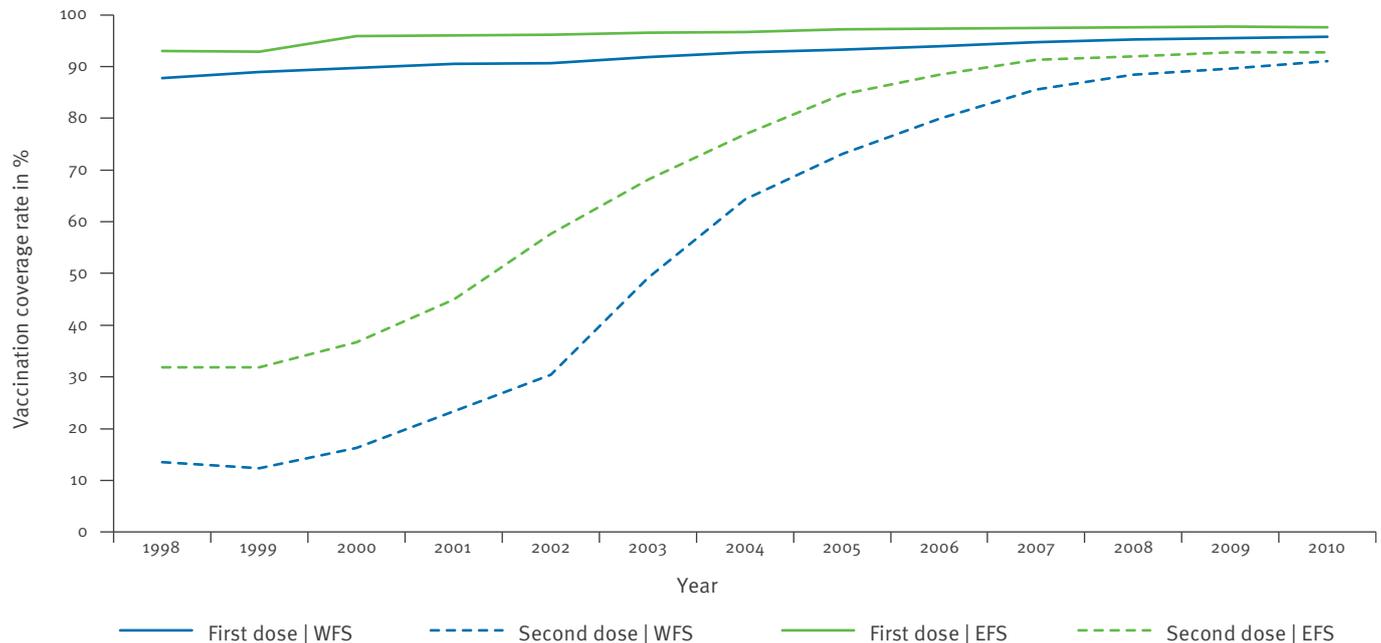
Until 2013, mumps has been notifiable in Germany only in the five Eastern federal states (EFS) of former East Germany. During the years 2001 to 2011, annually reported incidence for all EFS ranged between 0.26 and 0.78/100,000 [16]. There was no mandatory notification system in place in the remaining 11 Western federal states (WFS) of former West Germany. However, if an outbreak occurs in an institutional setting, the ‘German Infection Protection Act’ requires the institution to immediately inform the district health authority. A recent comprehensive survey suggested an increase in the number of mumps outbreaks over the past 10 years [17]. The largest recorded outbreak occurred in the WFS of Bavaria in 2010/11. Voluntary (ad-hoc) reporting was set up during the outbreak period and identified 295 cases.

Although mumps incidences have been available for EFS for the past 10 years, incidences cannot be extrapolated to the 11 WFS due to historical differences in vaccination schedules and coverage rates. While West Germany had recommended one dose of mumps vaccine as part of the routine childhood vaccination schedule from 1976 onwards, East Germany had no mumps vaccination programme in place until reunification in 1990. Since 1991, two doses (in the second and sixth year of life) have been recommended throughout the reunified Germany, since 2001 with the first dose given at 11–14 months and the second dose at 15–23 months of age [18]; the vaccine strain predominantly used is Jeryl Lynn. Although routine mumps vaccination was adopted in EFS 15 years later than in WFS, vaccination coverage rates at school entry have been substantially higher in EFS since introduction of coverage monitoring in 1998 (Figure 1) [19].

In the absence of a countrywide mandatory mumps notification requirement until March 2013 we used billing data of the Associations of Statutory Health Insurance Physicians (ASHIP) for outpatients as an alternative data source. Approximately 85% of the

**FIGURE 1**

Mumps vaccination coverage rates for first and second dose at school entry (age 5–7 years) in Western and Eastern federal states, Germany, 1998–2010



EFS: Eastern federal states; WFS: Western federal states.

population living in Germany is covered by statutory health insurances (total population in Germany in 2011: 81.8 million; WFS: 69.0 million, EFS: 12.8 million), and mumps is a disease usually treated on an outpatient basis (in EFS 2001–11: 94%). The aim of our study was to use countrywide ASHIP data (i) to estimate ambulatory mumps incidences and describe mumps-related demographics countrywide and separately for EFS and WFS, (ii) to estimate incidence and describe demographics for the outbreak in Bavaria 2010/11, and (iii) to compare the number of cases and demographics identified in the ambulatory ASHIP dataset with corresponding figures from the mandatory notification system in EFS and ad-hoc notification during the 2010/11 outbreak in Bavaria.

## Methods

### Definitions

For ASHIP data, a mumps case was defined as a person diagnosed with a mumps-related International Classification of Diseases (ICD-10) code (B26.0-orchitis, B26.1-meningitis, B26.2-encephalitis, B26.3-pancreatitis, B26.8-‘other complication’, B26.9-‘no complication’), and for notification data as a person fulfilling the mumps case definition (clinical case, i.e. more than two days of one- or two-sided parotid swelling without any other apparent cause, and/or clinical case with epidemiological link and/or clinical case with laboratory confirmation) [20]. Incidence based on

ASHIP data was defined as number of outpatient cases per 100,000 statutory health-insured [21], whereas incidence based on the mandatory notification system was defined as number of outpatient cases per 100,000 inhabitants in Germany [22]. The German federal states of Brandenburg, Mecklenburg-Western Pomerania, Saxony, Saxony-Anhalt, and Thuringia were classified as EFS; Baden-Württemberg, Bavaria, Berlin (comprising of the former Eastern and Western part of the city), Bremen, Hamburg, Hesse, Lower Saxony, North Rhine-Westphalia, Rhineland-Palatinate, Saarland, Schleswig-Holstein as WFS. The Bavarian outbreak period ranged from the third quarter of 2010 to the second quarter of 2011, the non-outbreak period were the remaining quarters in the years 2007 to 2011.

### ASHIP data structure and data included in the analysis

Statutory health insurance physicians send their reimbursement claims for provided ambulatory medical services, based on the ICD-10 code, to their corresponding regional ASHIP on a quarterly basis. Our dataset included the patient’s anonymous unique identifier (ID), sex, month/year of birth, district/state of residence, state of billing physician’s practice, ICD-10 code, quarter/year of diagnosis, reliability of diagnosis (suspected, confirmed, excluded or recovered), and type of diagnosis (current state, previous state, unknown or not provided).

Our analysis contained mumps diagnoses billed between 1 January 2007 and 31 December 2011. Data from the states of Baden-Württemberg (2007 only) and Hesse (2007–11) had to be excluded due to incomplete information. After the exclusion, the data set covered 79% of the population living in Germany during 2008 to 2011 and 68% during 2007.

### ASHIP data cleaning

We only included confirmed diagnoses that were labelled as ‘current state’ for the calculation of incidences. To limit the dataset to a single diagnosis per unique ID, we used the following algorithm:

1. Exclusion of incompatible or implausible coding combinations of ‘reliability of diagnosis’ (e.g. all four options coded in the same quarter);
2. Exclusion of observations coded as suspected, excluded or recovered (‘reliability of diagnosis’);
3. Exclusion of observations coded as previous state, unknown or not provided (‘type of diagnosis’);
4. Limitation to the most severe ICD-10 code diagnosed at the earliest point in time (one observation per unique ID), using the following ranking (from most to least severe): encephalitis>meningitis>orchitis>pancreatitis>other complication>no complication.

For data from Bavaria, Rhineland-Palatinate (2007–11) and regional parts of North Rhine-Westphalia (2008–11), step 3 had to be omitted as the transmitted data did not routinely contain information on ‘type of diagnosis’.

### Mandatory and ad-hoc notification data

We retrieved mandatory mumps notification data reported from EFS through the German electronic surveillance system ‘SurvNet’ [23] that is routinely used by public health authorities to anonymously report information on inpatient and outpatient cases with notifiable diseases to the national level. The ‘SurvNet’ system was also used by district health authorities for the voluntary ad-hoc mumps reporting during the outbreak in Bavaria 2010/11. Notification datasets contained information on age, sex, date of disease onset, notification week, district/state of residence, vaccination status, and whether the case required hospitalisation.

### Statistical analysis

We used chi-square test to test differences in incidences and proportions and Poisson regression to determine trends in incidence rate ratios (IRR). P values were defined as statistically significant if  $<0.05$ . Statistical analysis was performed by using Stata version 12.1 (StataCorp, Texas, US).

## Results

### Cleaning of ASHIP data

A total of 137,087 mumps diagnoses were billed during 2007 to 2011 (Bavaria, Rhineland-Palatinate and parts

of North Rhine-Westphalia: 47,165; remaining included states: 89,922). In data cleaning step 1, the number of diagnoses decreased to 136,142 (46,728 and 89,414), in step 2 to 49,746 (16,516 and 33,230), and in step 3 to 40,819 (16,516 (not applicable) and 24,303). Step 4 limited the dataset to 32,330 confirmed mumps cases (11,330 and 21,000). Among the 86,396 diagnoses excluded in step 2, 36,957 (42.8%) observations were coded as suspected diagnoses that would, if included in the dataset, have accounted for an additional 29,514 suspected mumps cases after steps 3 and 4 (10,406 and 19,108).

### Estimation of countrywide and regional incidences based on ASHIP data

Of the 32,330 confirmed cases, 15,000 (46.4%) were male; for 212 (0.7%) no sex was specified. For the years 2007 to 2011, overall countrywide mumps incidence was 10.3/100,000 and ranged between 9.3/100,000 in 2010 and 11.8/100,000 in 2008, corresponding to an IRR of 0.95 (95% confidence interval (CI): 0.95–0.96;  $p<0.005$ ). The most affected age groups in 2007 to 2011 were children aged five to nine years (mean annual incidence: 20.7/100,000) and adolescents aged 15 to 19 years (17.9/100,000). The most common complication was orchitis ( $n=933$ ; 6.2% of male cases), followed by ‘other complication’ ( $n=581$ ; 1.8%), meningitis ( $n=141$ ; 0.4%), pancreatitis ( $n=92$ ; 0.3%), and encephalitis ( $n=61$ ; 0.2%). Except for orchitis, proportions of complications showed no statistically significant difference between sexes. The proportion of complications among cases 15 years and older was significantly higher for all entities than among cases younger than 15 years (orchitis: 7.9% versus 1.8% among male cases; ‘other complication’: 1.9% versus 1.3%; meningitis: 0.5% versus 0.2%; pancreatitis: 0.3% versus 0.1%; encephalitis: 0.2% versus 0.0%;  $p<0.005$  for all).

Mean annual mumps incidence in 2007 to 2011 was significantly higher in WFS than in EFS (10.9/100,000 versus 7.5/100,000;  $p<0.005$ ). Incidences ranged between 7.0 and 8.4/100,000 in EFS, with a significant declining trend over the five years under observation (IRR=0.95; 95% CI: 0.93–0.97;  $p<0.005$ ), and between 9.8 and 12.6/100,000 in WFS (IRR=0.96; 95% CI: 0.95–0.96;  $p<0.005$ ). Stratification by age group showed a significant decreasing trend for incidences in the under 20 year-olds in EFS. In the WFS, incidences significantly decreased in the age groups of under 20 year-olds and of those aged 40 years and older, but significantly increased in the 20 to 29 year-olds (Table). The mean annual incidence of orchitis was higher in WFS than in EFS (0.72/100,000 versus 0.12/100,000 male cases;  $p<0.005$ ). The proportion of orchitis complications among male cases by age group and geographic region is displayed in Figure 2.

### Description of the 2010/11 outbreak in Bavaria based on ASHIP data

Between 2007 and 2011, Bavarian physicians billed 6,111 confirmed outpatient mumps cases to the

**TABLE**

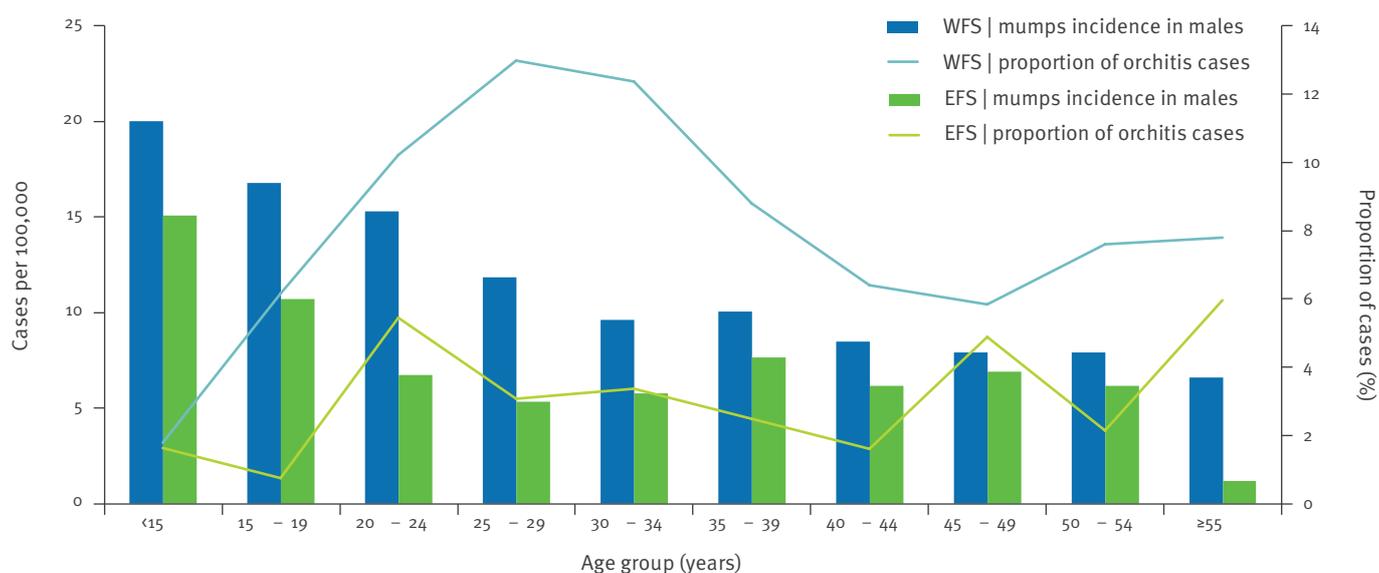
Annual mumps incidence, incidence rate ratio and p value, by age group, based on ambulatory statutory health insurance claims data, Germany, 2007–2011 (n=32,330)

Age group (years)	2007	2008	2009	2010	2011	IRR	95% CI	p value
Western federal states								
<10	<b>22.7</b>	<b>23.3</b>	<b>16.8</b>	<b>15.4</b>	<b>14.7</b>	<b>0.87</b>	<b>0.86–0.90</b>	<b>&lt;0.005</b>
10–19	<b>19.3</b>	<b>20.7</b>	<b>15.2</b>	<b>15.3</b>	<b>18.4</b>	<b>0.96</b>	<b>0.94–0.98</b>	<b>&lt;0.005</b>
20–29	<b>12.6</b>	<b>16.8</b>	<b>12.3</b>	<b>16.0</b>	<b>17.2</b>	<b>1.06</b>	<b>1.03–1.08</b>	<b>&lt;0.005</b>
30–39	9.9	11.9	9.8	9.4	11.0	1.00	0.97–1.02	0.707
40–49	<b>8.8</b>	<b>9.7</b>	<b>8.4</b>	<b>7.1</b>	<b>8.3</b>	<b>0.96</b>	<b>0.93–0.98</b>	<b>&lt;0.005</b>
≥50	<b>8.3</b>	<b>7.9</b>	<b>7.5</b>	<b>6.4</b>	<b>6.6</b>	<b>0.93</b>	<b>0.92–0.95</b>	<b>&lt;0.005</b>
Eastern federal states								
<10	<b>19.4</b>	<b>17.1</b>	<b>13.6</b>	<b>13.0</b>	<b>9.9</b>	<b>0.85</b>	<b>0.81–0.90</b>	<b>&lt;0.005</b>
10–19	<b>15.9</b>	<b>18.1</b>	<b>12.5</b>	<b>11.4</b>	<b>10.1</b>	<b>0.88</b>	<b>0.83–0.93</b>	<b>&lt;0.005</b>
20–29	9.1	9.7	8.6	7.4	8.7	0.96	0.91–1.02	0.208
30–39	6.6	9.2	7.7	7.5	8.3	1.02	0.96–1.09	0.486
40–49	7.0	7.7	6.6	6.9	7.5	1.00	0.95–1.06	0.867
≥50	5.5	5.2	4.9	5.2	5.2	0.99	0.95–1.03	0.527

CI: confidence interval; IRR: incidence rate ratios.  
Significant IRR, 95%CI and p values are shown in bold.

**FIGURE 2**

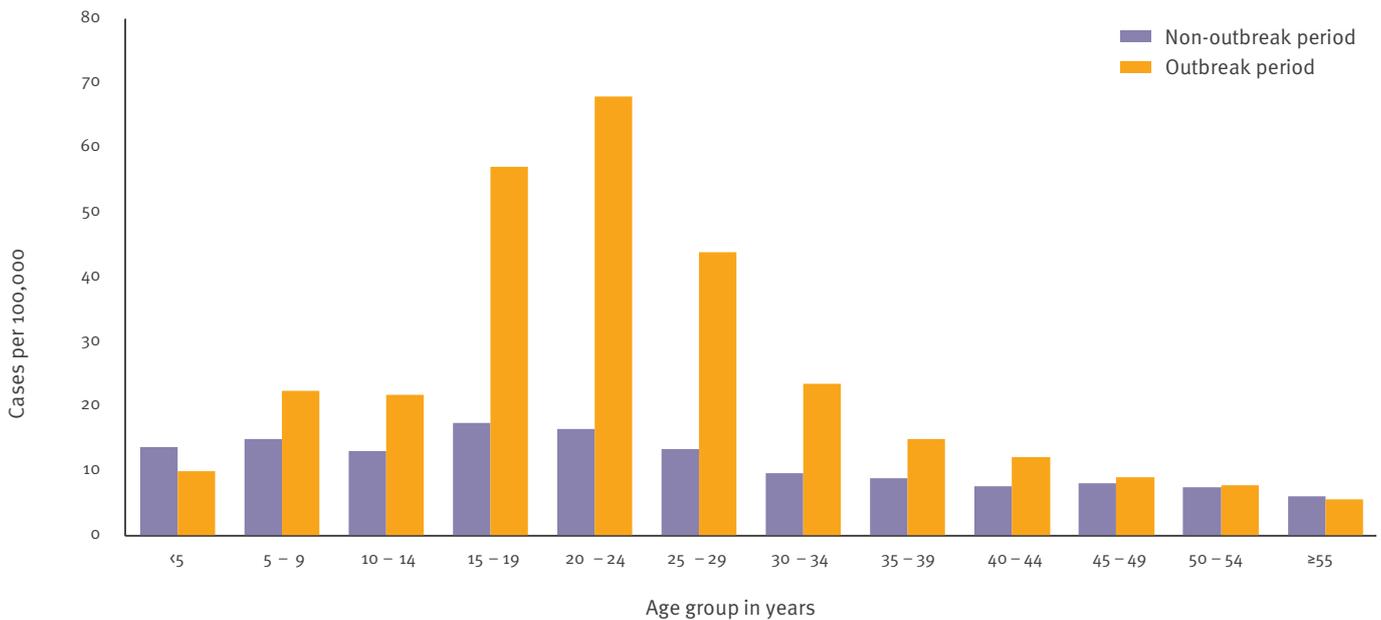
Mean annual mumps incidence among males and proportion of mumps-associated orchitis among all male mumps cases per age group, based on ambulatory statutory health insurance claims data, Germany 2007–2011



EFS: Eastern federal states; WFS: Western federal states.  
Point estimates for incidences showed 95% confidence intervals spanning a range of less than 0.05 (not shown in figure).

### FIGURE 3

Title: Mumps incidence per age group based on ambulatory statutory health insurance claims data during the 2010/11 outbreak period (n=1,995) and non-outbreak period (n=4,116), Bavaria, 2007–2011



Point estimates showed 95% confidence intervals spanning a range of less than 0.05 (not shown in figure).

statutory health insurances. Of those, 1,995 (32.6%) were claimed during the outbreak period with the peak occurring in the first quarter of 2011 (n=752; 37.7%). The proportion of claimed male cases was higher during the outbreak period than in the non-outbreak period (52.0% versus 47.5%;  $p < 0.005$ ), and a comparison of age-specific incidences indicated that the outbreak affected mainly the age group of 15–34 year-olds (Figure 3). Furthermore, the proportion of orchitis complications was significantly higher during the outbreak period compared to the non-outbreak period (17.7% versus 11.7%;  $p < 0.005$ ); all other proportions of complications showed no significant differences (data not shown).

#### EFS: Comparison of ASHIP data with mandatory notification data

In EFS, physicians claimed 4,217 confirmed outpatient mumps cases during 2007 to 2011 through the statutory health insurances. The median age of claimed cases was 38 years, and 1,825 (43.3%) were male. In the same time period, 316 ambulatory and 23 cases that required hospitalisation were reported via the mandatory notification system. The median age of the reported 316 outpatient cases was 12 years, and 148 (46.8%) were male. In total, 13.3 times more insurance cases were claimed than reported via the mandatory notification system. Stratified by age, 3,048 claimed ambulatory cases were adults ( $\geq 20$  years) compared to 113 notified ambulatory cases (27.0-fold difference); among persons younger than 20 years, the difference was 5.8-fold (1,169 claimed versus 203 notified cases).

Vaccination status was available for 284 (83.8%) of the 339 cases from the notification system: 214 (75.4%) were unvaccinated, whereas 70 (24.6%) had received at least one vaccination (33 received one dose, 36 received two doses, and one received four doses). Vaccination status by age group is shown in Figure 4.

#### Bavarian outbreak 2010/11: Comparison of ASHIP data with ad-hoc notification data

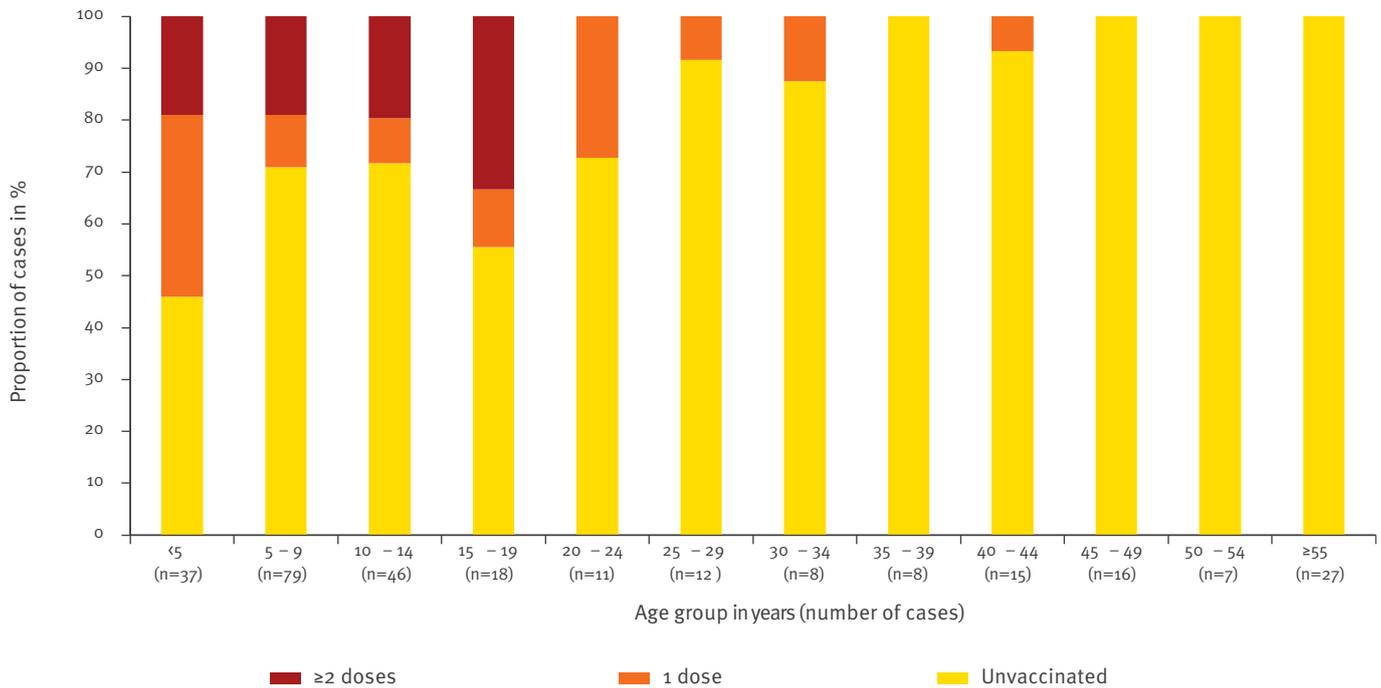
Temporary voluntary notification during the mumps outbreak in Bavaria identified 238 ambulatory cases and 57 cases requiring hospitalisation. Of the ambulatory cases, 124 (52.1%) were male. The median age was 21 years versus 24 years in ASHIP data. In comparison to ASHIP data (n=1,995), there was an 8.3-fold difference to ad-hoc reporting. Stratified by age, 107 reported ambulatory cases were younger than 20 years, compared with 594 outpatient cases claimed in insurance data (a 5.6-fold difference); in the group 20 years and older, 131 cases were reported, in contrast to 1,401 cases from ASHIP data (a 10.7-fold difference). Vaccination status was available for 217 of 295 (73.6%) reported cases: 125 (57.6%) were unvaccinated and 92 (42.4%) had received at least one vaccination (38 received one dose, 53 received two doses and one received three doses); for vaccination status per age group see Figure 5.

#### Discussion

Because countrywide mandatory mumps notification was not in place until 2013, we used mumps-related ICD-10 code diagnoses claimed through statutory

**FIGURE 4**

Vaccination status per age group among mumps cases with known status, reported via the mandatory notification system, Eastern federal states, 2007–2011 (n=284)



health insurances to estimate the magnitude of mumps incidence in Germany. Our results demonstrate that mumps is still endemic in Germany despite long-established vaccination programmes. However, overall incidences have dramatically declined from an estimated 100 to 1,000 cases per 100,000 in the pre-vaccine era [24] to 10.3 per 100,000 in the time period from 2007 to 2011. Moreover, incidences showed a further slight but statistically significant decreasing trend during the five-year study period, although incidence patterns across age groups differed in WFS and EFS. This discrepancy can be explained by different dates of mumps vaccine introduction and different vaccination coverages in the following years.

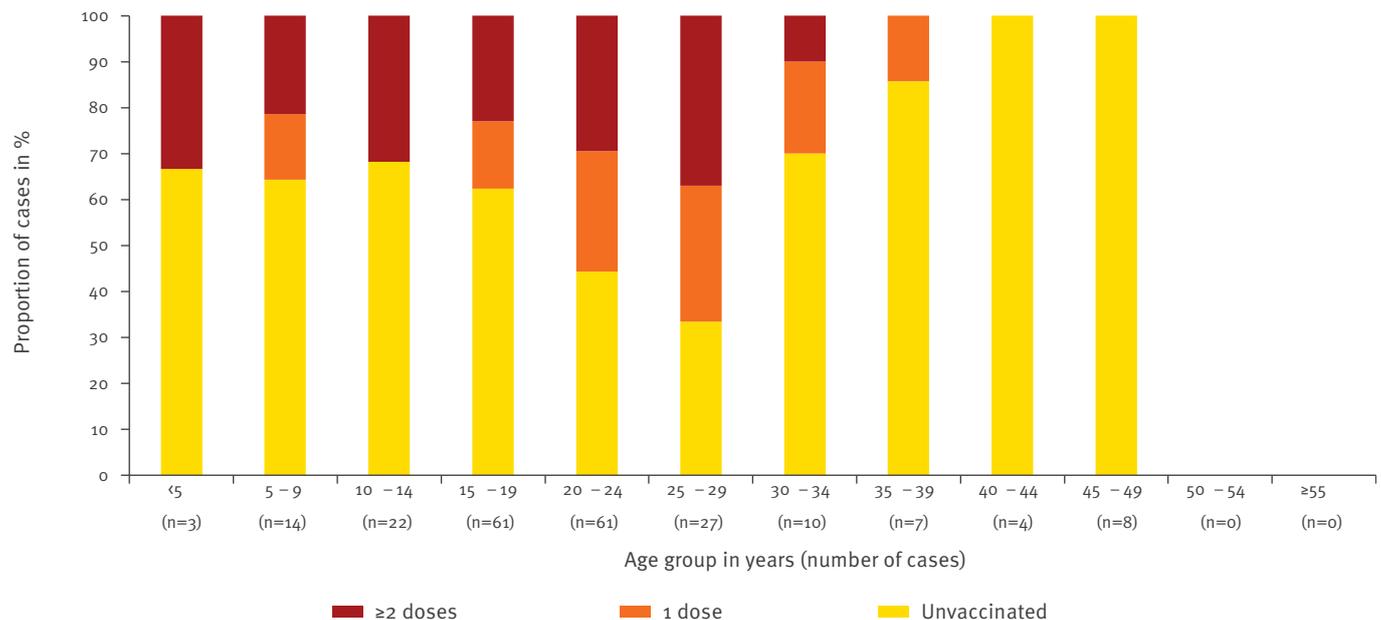
In the absence of a mumps vaccination programme in EFS until 1991, a great proportion of the EFS-population born before 1990 is likely to have been exposed to the wild virus and to have acquired natural immunity during childhood, consistent with the considerably lower incidences in adults in EFS compared with WFS, especially in the age group of 20 to 29 year-olds. Serosurveys from European countries in the pre-vaccine era have shown that 90% of the population was seropositive by the age of 14 to 15 years [4]. Because routine mumps vaccination was introduced in the WFS in 1976, high prevalence rates of naturally acquired immunity are only found in those who were born in 1975 and later (in our dataset 32 to 36 years and older). During 1976–90, the WFS recommended one mumps vaccine dose, but comprehensive data on coverage rates from that period are not available. The

two-dose mumps recommendation, introduced in WFS and EFS in 1991, has only targeted children born after 1990 (in our dataset 17 to 21 years and younger). The significant incidence differences in individuals younger than 20 years as well as the significant decreasing trend over the study period correspond to increasing vaccination coverages seen at school entry in both EFS and WFS. However, two-dose coverage in EFS has been substantially higher since beginning of monitoring. Although two-dose vaccination coverage rates are approaching levels to reach herd immunity of at least 92% [25] in both parts of the country, previous lower rates and a lack of catch-up vaccination activities may have left a pool of susceptibles that account for the high incidences in children and young adults. A representative seroprevalence study, conducted in 2003 to 2006 among more than 13,000 individuals aged 0 to 17 years in Germany, revealed approximately 20–22% to be mumps IgG-negative or borderline-positive, with higher proportions in the WFS [26]. However, if the present high vaccination coverage at school entry can be sustained, incidences among children can be expected to further decrease.

In contrast to EFS, we observed in WFS a significant increasing incidence trend among 20 to 29 year-olds, suggesting an age-shift over time. This observation is mirrored by the Bavarian outbreak 2010/11 where highest incidences were seen among 15 to 29 year-olds; the finding is further in line with recent outbreak reports from other countries with long-established vaccination programmes [10–13,15]. One reason could be that

**FIGURE 5**

Vaccination status per age group among mumps cases with known status, reported via the voluntary ad-hoc notification system, Bavarian outbreak 2010/2011 (n=217)



suboptimal vaccination coverage rates combined with low circulation of wild virus have caused an accumulation of susceptibles in those age groups. This theory is supported by the German serosurvey [26], but also by 86,098 immunisation records from 10 to 12 year-olds in Bavaria in 1988 (born one to three years after adoption of mumps vaccination) that revealed mumps coverage rates of only 55% [27]. Another relevant factor could be waning immunity. In the same serosurvey, authors identified significant waning effects already in 0 to 17 year-old immunised children [26], and those effects could be even more dominant in older age groups with longer time spans since last vaccination and/or only one vaccination dose. Furthermore, the proportion of vaccinated cases in the Bavarian outbreak increased with age in the group of 15 to 29 year-olds. Although we only had vaccination status information for 217 reported cases, age and sex distribution were comparable with findings from ASHIP data. The results could therefore be a hint that waning immunity may indeed play a role in those age groups in Germany. In contrast, breakthrough infections were not observed among young adult cases in EFS; all breakthrough infections occurred among children and adolescents and could therefore reflect the expected proportion of vaccine failure in populations with high vaccination coverage.

Mumps incidences for Germany based on ASHIP data are substantially higher than incidences for Europe published by the European Centre for Disease Prevention and Control: 3.5 per 100,000 in 2010 [28] and 3.2 per 100,000 in 2009 [29]. However, the 27 countries differ in their mumps surveillance systems, case definitions

and time points of routine mumps vaccine introduction [30,31], and comparisons are therefore difficult.

Comparison of the mandatory notification data with ASHIP data in EFS indicated severe underreporting, especially among adults. Underreporting could even be higher, as we only included cases coded as confirmed and diagnosed in an ambulatory practice. Our findings suggest that in EFS, where mandatory mumps surveillance has been in place since 1964 [24], physicians diagnose mumps, but fail to report cases to public health authorities. This has important implications as Germany has introduced nationwide mandatory reporting of mumps as of March 2013. To retain reliable mumps notification data, it is crucial not only to (re)inform physicians about their reporting duty, but to think of new strategies to ease reporting. One approach could be to develop computer tools that directly link the ICD coding of notifiable infectious diseases with a report to the health authorities.

There is an increasing use of electronic health records or claims data to estimate disease trends or disease burden, especially for admission or discharge ICD codes from hospitals, e.g. for rotavirus, gonorrhoea, or varicella [32-34]. In Germany, ICD-10 codes have previously been used to assess the herpes zoster disease burden also in the outpatient sector [35], and to assess reporting completeness of notifiable disease surveillance systems [36,37]. However, electronic health records or claims data cannot and should not replace a surveillance system, as the data are usually only available with a time lag of several months, precluding rapid containment actions in the event of an outbreak, and

are primarily intended for documentation or reimbursement, not surveillance purposes. In the case of ASHIP data, important information such as vaccination status at diagnosis or required hospitalisation is lacking. Nevertheless, such data can be an important source to assess the magnitude of incidences, disease trends and underreporting, and their reliability to determine communicable disease trends and burden should be further explored, also for the outpatient sector.

Using ASHIP data to estimate mumps incidences had several limitations related to data structure. There are no standardised guidelines for physicians of when to code a case as suspected or confirmed. Aiming at a conservative estimate, we decided to only include confirmed diagnoses. This restriction, as well as limiting the dataset to one observation per patient (who may have had several physician consultations during one disease episode), reduced the initial dataset considerably during the cleaning process. Therefore, the extent of the reduction cannot be interpreted as an indicator for the ASHIP data quality per se. As laboratory confirmation is not required to code a case as confirmed, the proportion of laboratory confirmations is unknown. Moreover, ASHIP data only cover ambulatory cases. However, since mumps has a very distinct clinical presentation and the vast majority of mumps patients remain outpatients or have consulted their ambulatory physician before complications may require hospitalisation, it can be assumed that our incidence estimates are a good reflection of the true disease incidence.

Our dataset did not include the ca. 15% of the population with private health insurance. However, we used the ASHIP population as denominator to calculate incidences and do not expect that mumps vaccination coverage differs substantially between privately and statutory insured. Finally, as information on 'type of diagnosis' is routinely missing for Bavaria, Rhineland-Palatinate and parts of North Rhine-Westphalia, we could not exclude diagnoses coded as 'previous state', 'unknown' or 'not provided' in the data cleaning process. However, if proportions of reduction had been applied to these federal states as observed for the others (step 3: 26.9%; step 4: 13.6%), the total number of cases would have been reduced by only 899 (2.7%).

## Conclusions

ASHIP data proved a valuable alternative data source to estimate mumps incidences. The identified shift in age distribution, the vaccination status of reported cases, and serosurveys indicate that inadequate coverage (with less than two mumps vaccine doses) is the main reason for outbreaks and sustained mumps virus circulation in Germany. In 2010, the German Standing Committee on Vaccination (STIKO) recommended an additional MMR vaccination for persons born after 1970 with less than two measles vaccinations in their childhood [18], a recommendation that may simultaneously close some of the existing mumps vaccination gaps in adults. However, no catch-up vaccination activities

for mumps have been initiated so far. In view of recent mumps outbreaks among adolescents and young adults and indications of waning immunity, the option of a third routine mumps vaccine dose is being discussed in the scientific literature [10,14,38]. However, comprehensive data on the long-term effectiveness of two-dose mumps vaccination (e.g. measured during outbreaks among adolescents and young adults) and on the additional benefits of a third dose are lacking. For the youngest age groups, efforts should focus on sustaining and even increasing the existing high vaccination coverage. In this respect, Finland has set an important example of how to successfully eliminate mumps by reaching and maintaining vaccination coverages of more than 95% [39].

## Acknowledgements

We thank all Associations of Statutory Health Insurance Physicians for providing claims data; the district and state health authorities of Brandenburg, Mecklenburg-Western Pomerania, Saxony, Saxony-Anhalt, and Thuringia as well as the Bavarian district health authorities for collecting and transmitting mumps case notification data; Marcel Feig for initial preparation of ASHIP data, Kristin Tolksdorf for her statistical support, and Katharina Alpers for her helpful comments on the manuscript draft (all Robert Koch Institute).

The project was funded by the Robert Koch Institute and the German Federal Ministry of Health.

## Conflict of interest

None declared.

## Authors' contributions

JK, AT and OW developed the design for the study; CK and WH coordinated the collection of the Bavarian surveillance data; TR and AT were involved in ASHIP data management and analyses; AT drafted the manuscript; all co-authors reviewed and assisted in the editing of the final version of the manuscript.

## \* Erratum:

The names of C Klinc and J Koch were erroneously left out of the list of authors at the time of publication of this article. This mistake was corrected on 16 August 2013 and we apologise to the authors.

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# Journal of Open Public Health Data launched

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**Citation style for this article:**

Eurosurveillance editorial team. Journal of Open Public Health Data launched. Euro Surveill. 2013;18(33):pii=20558. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20558>

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Article published on 15 August 2013

The Journal of Open Public Health Data (JOPHD) was launched in July this year. It aims to incentivise the publication of openly available public health datasets according to community standards [1]. JOPHD publishes data papers, which do not contain research results but rather a description of a dataset, and where to find it. The journal accepts only papers for datasets that authors agree to make freely available in a public repository. This means that they have been deposited in a data repository under an open licence, such as a Creative Commons Zero licence [2], and are therefore freely available to anyone with an Internet connection, anywhere in the world.

A data paper is a publication that is designed to make other researchers aware of data that are of potential use to them for scientific and educational purposes. Data papers can describe deposited data from studies that have not been published elsewhere (including replication research) but also from studies that have previously been published in another journal. As such, the data paper describes the methods used to create the dataset, its structure, its reuse potential, and a link

to its location in a repository. It is important to note that a data paper does not replace a research article, but complements it. The data paper should contain references to any research papers associated with the dataset and when referring to the data behind a study, a research paper should reference any existing data paper for further details.

JOPHD accepts any kind of public health data, including for example: epidemiology, ecology, environmental, and genotype data, geographic information system (GIS) data and maps, image and video data, quantitative and qualitative survey data.

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# WHO launches World health report 2013

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**Citation style for this article:**

Eurosurveillance editorial team. WHO launches World health report 2013. Euro Surveill. 2013;18(33):pii=20559. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20559>

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Article published on 15 August 2013

On 15 August 2013, the World Health Organization (WHO) launched the 'World health report 2013: Research for universal health coverage' [1]. The report addresses funding organisations, researchers (active and in the future) and policy makers. It shows how countries, when developing a system for universal health coverage, can use research to determine what health issues should be addressed, how a system should be structured and how to measure progress according to their specific health situation.

The report is divided in five chapters: Chapter 1 deals with the role of research for universal health coverage, for the provision of, and access to, high-quality health services; and financial risk protection for people who need to use these services. Chapter 2 gives an overview of the changing landscape of research while Chapter 3 presents examples of studies that show how research can address some of the major questions about achieving universal health coverage, and can deliver results that have influenced, or could influence, policy and health outcomes.

Chapter 4 describes the essential functions of national health research systems, namely: to set research priorities, to develop research capacity, to define norms and standards for research, and to translate evidence into practice. It presents mechanisms to stimulate and facilitate research for universal health coverage – monitoring (national and international observatories), coordination (information-sharing, collaborative research studies) and financing (raising and distributing funds to support global and national research priorities).

Chapter 5 proposes a set of actions by which the research community, national governments, donors, civil society and international organisations can support the research that is needed to reach universal health coverage.

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