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# An outbreak of measles associated with an international dog show in Slovenia, November 2014

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In Slovenia, where measles virus had not been circulating for many years, an outbreak of measles among visitors of an international dog show occurred in November 2014. We identified 23 measles cases plus 21 presumable secondary and tertiary cases. Thirty-nine cases were adults, 27 to 56 years-old, 12 of them vaccinated with two doses. Five were unvaccinated children. Thanks to high vaccination coverage (95.3% in birth cohort 2011) wider transmission is not expected in Slovenia.

On 24 November 2014, the regional epidemiologist from Nova Gorica region notified the Communicable Diseases Centre of the National Institute of Public Health (NIJZ) about two suspected measles cases. Both had visited the international dog show in Vrtojba/Šempeter, close to the Italian border, which took place on 8 and 9 November 2014. Dog owners from 27 (mostly European) countries participated. Around 1,100 persons were present at the exhibition (700 dog owners and ca 400 visitors). As this was the only link between the two cases, we assumed that they were infected there. In both cases, measles infection was laboratory-confirmed on the following two days by positive IgM and positive PCR.

## Outbreak description

On 26 November, NIJZ alerted all primary physicians in the country about the event, to rapidly identify further cases. On the same afternoon, four more suspected cases were reported, and in the next two days, another nine that had all visited the exhibition. The measles case definition used in Slovenia is based on the case definitions of the European Union (EU) [1]. All suspected cases were laboratory-tested and measles was confirmed either by detecting measles-specific IgM antibodies in serum samples by ELISA (Serion Immundiagnostica, Würzburg, Germany) and/or by detecting measles antigen in a throat swab or urine with real-time RT-PCR [2].

In total, 28 suspected measles cases that visited the exhibition were tested for measles antigen and/or measles-specific IgM antibodies. In 18 cases, measles were confirmed according to laboratory criteria, and in five suspected cases measles was excluded. In the remaining five cases (three vaccinated with two doses and two with unknown vaccination status) with clinical presentation of measles, only extremely high IgG of >5,000 mIU/ml was detected (cut-off for positivity: 200 mIU/ml). Although these five cases had negative IgM and negative PCR results, we considered that they, too, fulfilled the case definition and defined them as confirmed cases, which gives a total of 23 confirmed measles cases.

In addition to the 23 measles cases infected at the dog show, we confirmed another 21 measles cases (as of 31 December), which were presumably secondary and tertiary cases. However, we were able to establish an epidemiological link to the primary or secondary cases for only 18 of them.

## Genotyping

As of December 2014, the 450 nt C-terminal end of the nucleoprotein gene of measles virus from seven cases has been sequenced and genotype D8 has been identified in all seven. All sequences are available in the World Health Organization (WHO) measles sequence database MeaNS (MeaNS sequence ID numbers: 61781–61787) [3]. In 2014, exact matching sequences of D8 genotype measles virus were found also in Austria, Bosnia and Herzegovina, Greece, the Russian Federation, and the United Kingdom [3]. Sequencing of measles viruses from further cases is still in progress at the time of publication.

## Epidemiological analysis

As of 31 December, a total of 44 measles cases linked to the dog show have been reported from two of the nine Slovenian regions (Figure 1). For the first generation of

measles cases (the ones that visited the exhibition), the onset of rash started from 21 November, for the second generation from 29 November, and for the third generation from 25 December (Figure 1). Among the 23 cases infected at the exhibition, the majority (n = 16) was from Nova Gorica region and the others (n = 7) were from Ljubljana region. Among the 16 secondary cases, only three were identified in Nova Gorica region, the other 13 were from Ljubljana region, and all five tertiary cases were from Ljubljana region.

Of the 44 measles cases, 19 were male. Five were children between six months and 11 years-old and 39 were adults aged 27 to 56 years, of whom 36 were between 34 and 51 years-old (Figure 2). Among the adults, 12 had been fully vaccinated (with two doses of measles-containing vaccine), nine had received only one dose and 18 were not vaccinated or information was not available (vaccination status unknown or no written proof of vaccination). None of the five children were vaccinated (Figure 2). Only two adult cases required hospitalisation, no fatal outcomes were recorded.

According to our knowledge, only one measles case infected at the exhibition was notified in another country (Belgium). This case is not included in the 44 analysed here.

In addition, six further measles cases were reported in Slovenia in the same period (November to December 2014) which were not linked to the exhibition; five were imported from Bosnia and Herzegovina and one was a secondary case related to one of these imported cases. Also from one of these cases genotype D8 has been identified.

## Control measures

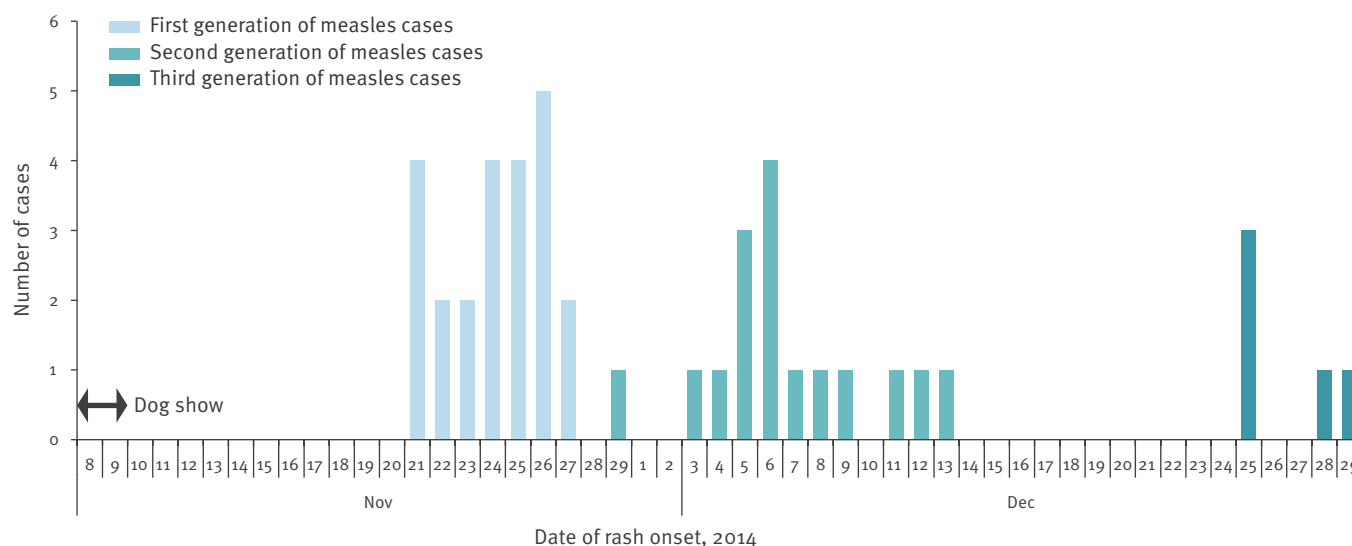
Immediately after confirmation of the first cases, NIJZ alerted all primary physicians about the event. As the contact information for the participants at the dog show was not available, we informed the general public through mass media (radio and television) and regular updates on the NIJZ website. We conducted extensive contact tracing in order to perform prophylactic vaccination where appropriate. As recommended in national guidelines, post-exposure prophylaxis with normal intravenous immunoglobulin (IVIG) was offered to the individuals at high risk of severe disease, including infants younger than six months, pregnant women and immunocompromised persons [4]. We do not have information on how many of those individuals actually received this post-exposure prophylaxis. We also alerted people who intended to travel to Bosnia and Herzegovina or to other countries with ongoing measles outbreaks during the holidays, to update their vaccination status.

## Discussion

Thanks to early introduction of measles vaccination into the Slovenian vaccination programme in 1968 (live measles vaccine prepared from a further-attenuated Edmonston-Zagreb strain was used, replaced by a combined vaccine against measles and mumps in 1979, and from 1990 by trivalent vaccine against measles, mumps and rubella) and to high vaccination coverage in past decades (from 93.9% to 96.1% for birth cohorts 2003 to 2012), Slovenia has been measles-free for many years [5]. No cases were reported from 2000 to 2009. In 2010, a cluster of measles was described in a hospital setting [5]. In 2011, 22 cases of measles were reported, six of whom were imported (from France, Germany, Italy and Romania) with a few single secondary cases, except in one situation that led to nine secondary cases [6]. In 2012, two imported cases (from

**FIGURE 1**

Number of measles cases in an outbreak linked to a dog show, by date of rash onset, Slovenia, notified by 31 December 2014 (n=44)



Cuba and Germany) were reported, whereas in 2013 only one imported case (from London) was reported, with no secondary cases. Before November 2014, two cases imported from Bosnia and Herzegovina were reported in April and July.

This measles outbreak originating in a mass gathering event was the largest in Slovenia after the major outbreak that started in 1994 and peaked in 1995, with a total of 405 cases notified [5]. In contrast to most outbreaks in other European countries, where the majority of cases are seen in unvaccinated children, most cases in the reported outbreak were adults 34 to 51 years of age (birth cohorts 1963 to 1979). These birth cohorts were also the most affected among the cases reported in Slovenia in 2011 (among 22 notified cases, 18 were 31 to 48 years-old, i.e. in birth cohorts 1963 to 1980) [6]. In addition, the serosurveys conducted in Slovenia in the years 1998 and 2000 showed that the same birth cohorts had the highest proportion of measles-seronegative individuals [7].

Nearly half of the cases ( $n = 21$ ) had been vaccinated with one ( $n = 9$ ) or two ( $n = 12$ ) doses of measles-containing vaccine, most of them more than 30 years ago. In an outbreak situation, a substantial proportion of vaccinated cases can usually be expected in a population with very high vaccine coverage [8].

Five cases fulfilled the clinical criteria, had epidemiological links to the dog show, and measles IgG antibodies higher than 5,000 mIU/ml, but negative IgM results and a negative PCR. In these patients, the course of disease was mild. In our experience, such high IgG values are never observed more than three years after

vaccination (three of the five cases were vaccinated with two doses more than 30 years ago), so we considered this too high to be attributed to former immunisation. Presumably, IgG antibodies higher than 5,000 mIU/ml indicate a strong secondary immune response, where the presence of IgM antibodies in the serum and the presence of virus in a throat swab or urine are very short and difficult to detect. The ability to detect IgM and viral RNA in vaccinated cases depends on the individual immune response and the timing of the serum sample collection [9].

As pointed out by some authors, with improved measles control over time (high coverage) and in the absence of circulating virus, boosting by exposure to wild type virus becomes rare and the rate of non-classical infection (mild measles) is likely to increase [10,11].

## Conclusion

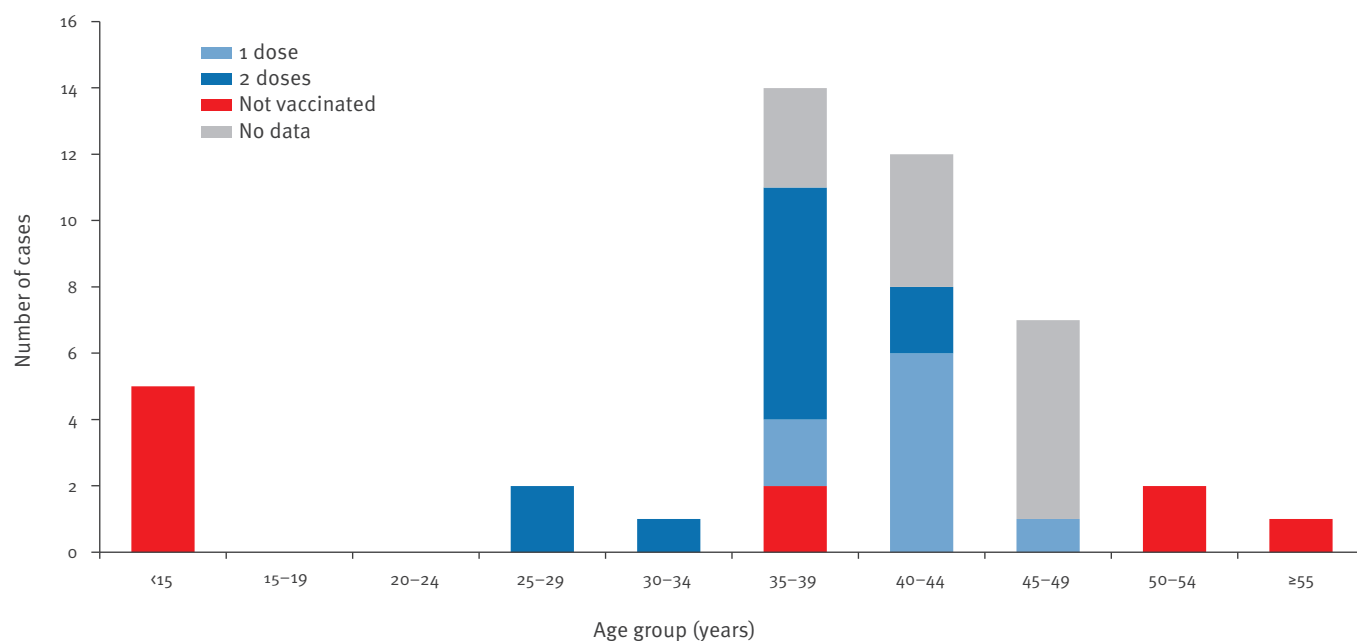
Although two incubation periods have not yet passed since the last case, further widespread transmission is not expected due to high vaccination coverage in Slovenia. As the majority of measles cases occurred in birth cohorts 1963 to 1979, and a third of them were fully vaccinated, it remains necessary to closely follow any measles breakthrough cases and conduct a seroepidemiological study to assess the proportion of susceptibles in these cohorts. This would inform a discussion on the need for an additional (third) dose of measles vaccine in these birth cohorts in Slovenia.

## Conflict of interest

None declared.

## FIGURE 2

Reported measles cases in an outbreak linked to a dog show, by age group and vaccination status, Slovenia, notified by 31 December 2014 ( $n=44$ )



## Authors' contributions

Mario Fafangel, Ondina Jordan Markočič and Katarina Prosenc contributed to acquisition of data. Marta Grgič Vitek and Tatjana Frelj analysed and interpreted the data, and also drafted the manuscript. Mario Fafangel, Veronika Učakar, Katarina Prosenc and Alenka Kraigher critically revised the manuscript. All authors approved the final version of the manuscript.

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# Serogroup C invasive meningococcal disease among men who have sex with men and in gay-oriented social venues in the Paris region: July 2013 to December 2014

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In November 2014, French public health authorities renewed the recommendation to target for vaccination against invasive meningococcal disease men who have sex with men (MSM) and all individuals  $\geq 25$  years attending social venues associated with the gay community. This policy was extended beyond the Paris region as a reaction to the continuing spread of serogroup C isolates belonging to a new lineage within clonal complex cc11 since the recommendation was first issued in July 2013.

In this report, we describe, based on combined epidemiological surveillance data and genetic typing of serogroup C meningococcal isolates, the spread of a specific invasive strain of meningococcus C (MenC) in the Paris region that had started as an outbreak among men who have sex with men (MSM) in June 2013.

## The alert in June 2013

In the first half of 2013, 14 serogroup C IMD cases were reported in France in 25 to 59 year-old men, while six cases were reported in women. Of the adult male cases, six affected residents of the Paris region and three occurred within one week in early June in MSM. The variable regions 1 and 2 of PorA, the variable region of FetA and the clonal complex (cc) of the three isolates were characterised. These isolates showed the genotype C:P1.5-1,10-8:F3-6:cc11 and belonged to the electrophoretic type (ET) 15 of the cc11 (cc11 harbours several lineages). Between October 2012 and May 2013, five serogroup C IMD cases in MSM were also reported in Germany [1], caused by isolates sharing the same characteristics as the ones in France. Further genetic analysis showed that the German and the French isolates shared additional markers that also differed from other lineages of the cc11 isolates (data not shown). These findings raised the question of the emergence of a new clone of serogroup C *Neisseria meningitidis* in the European MSM community [2]. Considering that serogroup C outbreaks occurred also

among MSM in Canada in 2001 and in the United States in 2003 (Chicago) and in 2011–13 (New York City), a rapid risk assessment was prepared by the European Centre for Disease Prevention and Control (ECDC) in July 2013 [3,4].

We established a national enhanced surveillance and prompted the regional public health officers to assess a possible link to the MSM community for all cases infected by C:P1.5-1,10-8:F3-6:cc11 isolates.

## Serogroup C invasive meningococcal disease cases in the Paris region from July 2013 to December 2014

Since July 2013, 34 cases of serogroup C IMD have been notified in the Paris region and two other cases have been diagnosed in other countries but were very likely to be linked to a source of exposure in the Paris region. Among these 36 cases, 17 were 25 to 59 years-old and five were aged 60 years and older. The case fatality rate was 17% (6/36). The male/female ratio was 1.6 (22/14) (Table1). None of the cases had been vaccinated against MenC disease.

Isolates from 29 of the 36 cases were subjected to a complete molecular analysis and 14 were related to the genotype C:P1.5-1,10-8:F3-6:cc11. Among those 14, nine isolates showed the above-mentioned additional specific markers (Figure1). They corresponded to seven men (one aged 15–24 years and six aged 25–59 years) and two women (one aged 25–59 years and one in the age group 60 years and older). One additional male case (15–24 years-old) was epidemiologically linked to one of them (family cluster). These 10 cases were directly or indirectly linked to the MSM community (four cases aged 25–59 years who self-identified as MSM and six who did not identify as MSM but attended social venues associated with the gay community in the Paris region).



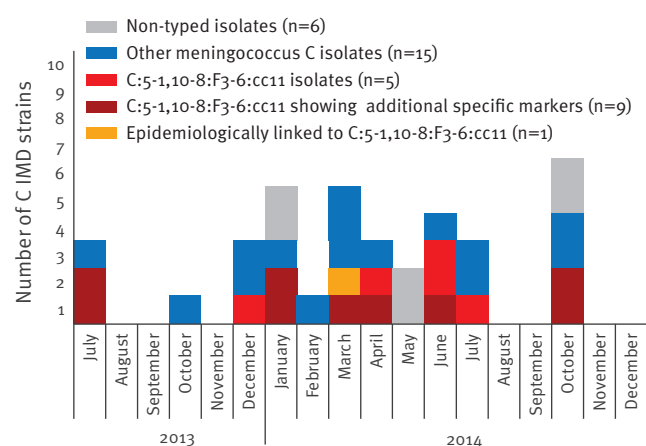
## Incidence rates and risk evaluation

When considering all reported serogroup C IMD cases for all age-groups and both women and men, no excess of cases was observed in the Paris region compared with the general population of France since July 2013. In contrast, we observed a gradual increase in the incidence of serogroup C IMD in the Paris region since 2013, a trend that was less marked elsewhere in France (Figure 2).

Moreover, IMD caused by C:P1.5-1,10-8:F3-6:cc11 isolates have increased since 2011 particularly in the Paris region where it represented about half (11/22) of the notified meningococcus C IMD cases in 2014 (vs 12% elsewhere in France,  $p < 10^{-3}$ ). During the period from 2011 to 2014, the mean annual reporting rate for these isolates was estimated at 0.05 cases per 100,000 inhabitants in the Paris region (vs 0.02 elsewhere in France,  $p < 10^{-3}$ ).

**FIGURE 1**

Cases of serogroup C invasive meningococcal disease by month of hospitalisation and genotypic combination, Paris region, France, 1 July 2013–31 December 2014 (n=36)



IMD: invasive meningococcal disease.

**TABLE 1**

Incidence and case fatality rates of serogroup C invasive meningococcal disease cases by age and sex, 1 July 2013–31 December 2014, Paris region (n = 36)

Age group	Female		Male		Total		CFR
	Number	Incidence <sup>a</sup>	Number	Incidence <sup>a</sup>	Number	Incidence <sup>a</sup>	
<1 year	1	1.17	0	-	1	0.57	0%
1–4 years	0	-	1	0.30	1	0.15	0%
5–14 years	1	0.13	1	0.13	2	0.13	0%
15–24 years	3	0.38	7	0.91	10	0.64	11%
25–59 years	6	0.20	11	0.39	17	0.29	12%
≥60 years	3	0.24	2	0.20	5	0.22	60%
<b>Total</b>	<b>14</b>	<b>0.23</b>	<b>22</b>	<b>0.38</b>	<b>36</b>	<b>0.30</b>	<b>17%</b>

CFR: case fatality rate.

<sup>a</sup> Incidence per 100,000 inhabitants.

In order to estimate the incidence among MSM in the Paris region, we used as the denominator the estimated figures from the 2006 national survey on sexual behaviour [5]. About 175,000 men living in the Paris region and aged 25 to 59 years reported sexual encounters with men at least once during their life.

Taking into account the four cases notified in MSM since July 2013, the incidence of serogroup C IMD among 25 to 59 year-old MSM (individuals older than 25 years are not targeted by the national vaccination programme) in the Paris region was 2.28 per 100,000 person-years. The observed number of cases was 10 times greater than the expected number among men in this age group, if the incidence rate of C IMD cases was the same in Paris region than in all regions in France. No excess risk was demonstrated among men living in the Paris region who did not identify as MSM (Table 2).

## Public health response and discussion

Surveillance of invasive meningococcal disease (IMD) in France relies on the mandatory reporting of cases to the French Institute for Public Health Surveillance (InVS) and the characterisation of invasive strains at the National Reference Centre (NRC) for Meningococci. Combined epidemiological surveillance and genetic typing of meningococcal isolates highlighted an increase of invasive meningococcal disease among MSM. These data suggested that the excess of serogroup C IMD cases among MSM living in the Paris region was linked to the circulation since mid-2013 of C:P1.5-1,10-8:F3-6:cc11 isolates with additional specific markers, not only in MSM but also among individuals (women, as well as those men who do not identify as MSM) who attend social venues associated with the gay community. Following the first outbreak reported in June 2013, the French Council of Public Health (HCSP) issued a recommendation for a three-month period of vaccination, with a meningococcal conjugate C vaccine offered to all MSM aged 25 years and older, living in the Paris region and attending social venues associated with the gay community. This recommendation also included all individuals attending gay festivals

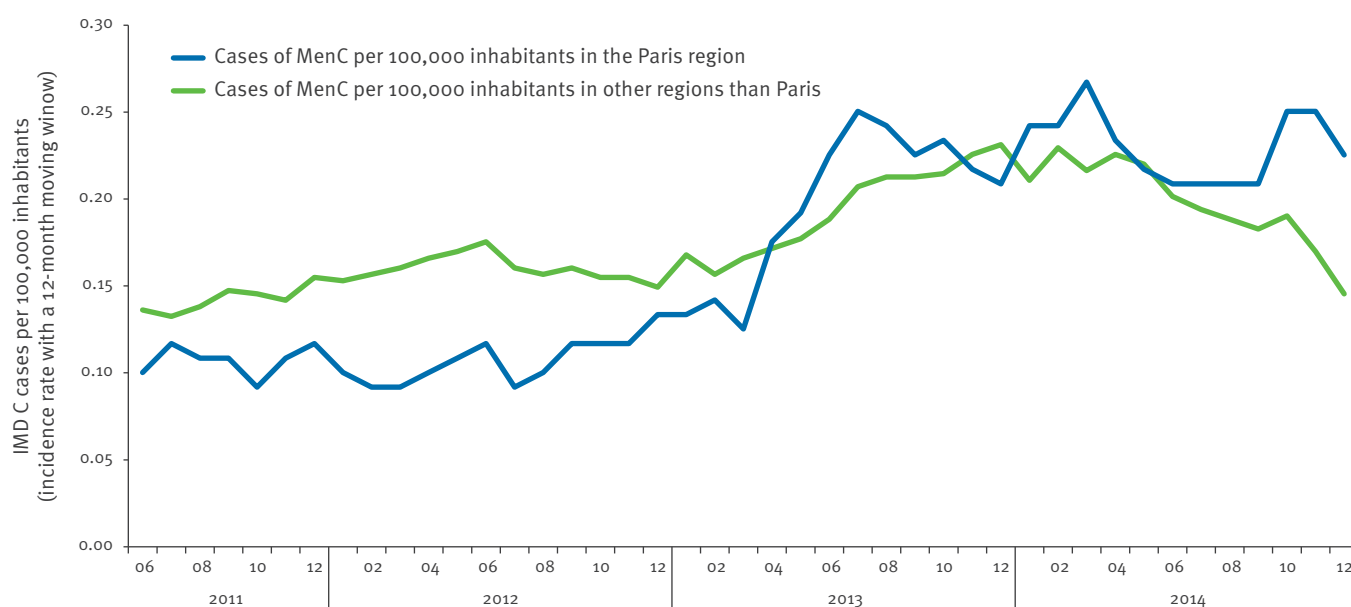
during summer 2013 in France [6]. Several health promotion activities were carried out during that summer by associations well-known in the gay community in France, but no vaccination campaign was officially performed. No data are available on the vaccine coverage reached in the targeted population.

Moreover, data from national surveillance highlighted that two family clusters of two cases each were also reported outside the Paris region in 2014, indicating that such isolates may spread all over the country and not only in the Paris region. Because of the high serogroup C IMD incidence due to the C:P1.5-1,10-8:F3-6:cc11 isolates and the persistence of cases linked to the MSM community, the recommendation was

renewed in November 2014 for one year and extended beyond the Paris region to the whole country, targeting MSM and all individuals aged 25 years and older attending social venues associated with the gay community [7]. Vaccination against serogroup C meningococci had been recommended in France since 2010 at the age of 12 months, with a catch-up in children and young adults (13 months to 24 years-old). However, the incidence of serogroup C IMD gradually increased between 2010 and 2013, mostly in infants younger than one year and in adults [8]. This increase suggested a lack of vaccine-induced herd immunity to reduce circulation of serogroup C meningococci, caused by low vaccine uptake (56% at the age of two years and 17% among the 15 to 19 year-olds in 2013).

**FIGURE 2**

Incidence rates<sup>a</sup> of serogroup C invasive meningococcal disease cases France, 2010–14 (n=409)



IMD: invasive meningococcal disease; MenC: meningococcus C.

<sup>a</sup> Moving averages calculated over the last 12 months moving window.

**TABLE 2**

Risk analysis of excess cases of serogroup C invasive meningococcal disease in 25–59 year-old MSM and men not identifying as MSM, Paris region, France, 1 July 2013–31 December 2014 (n=11)

Population of 25–59 year-old men	Number of C IMD cases	Incidence per 100,000	Expected cases	Estimation of the risk excess of serogroup C IMD cases			
				SIR <sup>a</sup>	p value <sup>b</sup>	Lower CI	Upper CI
MSM	4	2.28	0,39	10.16	0.001	2.73	26.02
Not MSM	7	0.24	6,37	1.10	0.454	0.44	2.26
<b>Total</b>	<b>11</b>	<b>0.35</b>	<b>6,77</b>	<b>1.63</b>	<b>0.083</b>	<b>0.81</b>	<b>2.91</b>

CI: confidence interval; IMD: invasive meningococcal disease; MSM: men who have sex with men; SIR: standardised incidence ratios.

<sup>a</sup> Indirect standardisation method: These ratios were calculated by dividing the observed number of cases in the Paris region by the expected number of cases derived from the incidence rates observed in France among men aged 25 to 59 years. The expected number was calculated by multiplying the number of the population of 25 to 59 year-old MSM living in Paris and exposed between July 2013 and December 2014 by the incidence rate of C IMD in all men of that age living in France and exposed in that period (person-years).

<sup>b</sup> p values were calculated by unilateral exact test based on a Poisson distribution; p < 0.025 was defined as a significant excess of cases.

The Table shows that MSM living in the Paris region and aged for 25–59 years have a 10 times higher risk to contract a serogroup C IMD than the same population living in other regions in France.



Vaccine policy for targeting 1 to 24 year-olds should be strengthened more efficiently in France. In addition, enhanced microbiological and epidemiological surveillance should be currently maintained for the isolates responsible of continuous spread of invasive MenC among MSM and adults older than 25 years attending social venues associated with the gay community.

### Acknowledgements

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### Conflict of interest

None declared.

### Authors' contributions

L. Aubert drafted the manuscript, analysed data from epidemiological and molecular surveillance and conducted to risk analysis in Paris region. M-K Taha supervised molecular typing of the bacterial isolates from IMD cases on the territory, initiated retrospective molecular typing of strains with a similar combination of genotypic characteristics as the initial cluster of C IMD cases detected in June 2013, initiated enhanced surveillance of these isolates in France and largely contributed to the manuscript. N. Boo coordinated the outbreak investigation in Paris region, collected cases' information about a possible link with the MSM community and contributed to the manuscript. Y. Le Strat contributed to risk analysis and to the manuscript. A-E Deghmane contributed to molecular typing of the bacterial isolates received at the National Reference Centre for Meningococci and contributed to the manuscript. A. Sanna contributed to the risk analysis and to the manuscript. AS Barret participated in the initial three-case cluster investigation in June 2013 and contributed to the manuscript. D. Levy Bruhl was involved in the establishment by the French Council of Public Health (HCSP) of the recommendation targeting MSM in 2013 and the renewal of this recommendation in November 2014 and contributed to the manuscript. S Vandentorren contributed to the analysis of epidemiological situation in Paris region and to the manuscript. I. Parent du Châtelet coordinated outbreak investigation in the initial three-case cluster, coordinated epidemiological surveillance and outbreak investigation of IMD cases in France, participated at the recommendations established in 2013 and 2014 by the HCSP, supervised this analysis and contributed actively to the manuscript.

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# Lactating mothers infected with Ebola virus: EBOV RT-PCR of blood only may be insufficient

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**We describe two Ebola virus (EBOV) RT-PCR discordant mother–child pairs. In the first, blood from the breast-feeding mother, recovering from EBOV infection, tested negative twice but her urine tested positive. Her child became infected by EBOV and died. In the second, the breastfed child remained EBOV-negative, although the mother’s blood tested positive. We highlight possible benefits of EBOV RT-PCR testing in urine and breast milk and the need for hygiene counselling when those fluids are EBOV-positive.**

We report two Ebola virus (EBOV) RT-PCR discordant mother-child pairs that illustrate that EBOV RT-PCR testing of relevant fluids in addition to blood, such as urine and breast milk, may be useful, in certain instances.

## Background

The current West African Ebola virus disease (EVD) epidemic is different from all previous EVD outbreaks [1]. Because of its regional and international distribution, the massive strain on the local health systems in the affected countries and the very large number of persons infected, the current outbreak has evolved into a major humanitarian crisis [2].

Offering patient care to breastfeeding Ebola virus (EBOV) infected women and their children in such a setting can be particularly challenging because evidence-based guidelines about breastfeeding are lacking. This

report of two EBOV RT-PCR discordant mother-child pairs illustrates possible benefits of EBOV RT-PCR testing in urine and breast milk, not just in blood.

## Case 1: mother-child pair

In early October 2014, a woman in her late 30s was referred to the Ebola Treatment Centre (ETC) of Médecins Sans Frontières (MSF) in Guéckédou, Guinea because of general malaise and myalgia. She was accompanied by her asymptomatic, almost exclusively breastfed, six-month-old infant.

The patient had taken care of a relative who had developed symptoms compatible with EBOV in early September and had died 12 days after symptom onset. The patient had also organised the funeral. Two days after the relative’s death, she developed high fever, intense fatigue, headache, muscle and abdominal pain, vomiting and diarrhoea. She was admitted to a local hospital where she received oral and intravenous empirical anti-malaria treatment and antibiotics for three days. The diagnosis was unclear. Although she had symptoms compatible with EBOV infection, she was not tested for EVD as EBOV RT-PCR tests were not available.

After three days in hospital, 13 days after the onset of her symptoms, the patient was referred to the ETC of MSF for persistent malaise and myalgia. Upon admission, she was afebrile. Given the clinical history and

the high-risk contact, the patient was admitted to the ETC in the 'suspect' zone of the 'high-risk' area. Her asymptomatic child was housed in a nursery next to the ETC and breastfeeding was stopped. On day 14 of illness, the patient's EBOV RT-PCR blood test (Realstar Filovirus Screen, RT-PCR Kit 1.0, Altona Diagnostics, Hamburg) as well as a rapid malaria test (SD BIOLINE Malaria Ag P.f, Standard Diagnostics Inc.) were negative.

On the same day (day 14 of illness of the mother), the child developed fever (39.1°C), diarrhoea and severe weakness; a malaria rapid test was negative but EBOV RT-PCR test was positive (cycle threshold (CT) value 19.80; CT values <20 are highly positive whereas >35 are weakly positive).

A second EBOV RT-PCR blood test of the mother, 16 days after symptom onset, remained negative but the urine EBOV RT-PCR test from the same day was positive (CT value 29.09). EBOV RT-PCR test of breast milk performed on day 17 after symptom onset was negative and breastfeeding was restarted. The patient had recovered well and was discharged on the same day but the child passed away three days later.

## Case 2: mother-child pair

A woman in her mid-20s developed a febrile syndrome four days after having given birth to a healthy baby and was admitted to an MSF ETC in Guéckédou five days later. We note that a close relative of the patient who was present during the delivery, developed symptoms compatible with EVD on the day following the delivery and died one week later. The patient had taken care of this relative.

Upon admission, the patient's temperature was 39°C and she had severe weakness, myalgia, arthralgia, anorexia, dysphagia, hiccups, abdominal pain and diarrhoea. Minor bloody vaginal discharge was noted. An oral antibiotic (cefixime) and anti-malaria treatment were started empirically. On day 6 after onset of illness, a rapid malaria test was negative but an EBOV RT-PCR blood test was positive (CT value 23.92). The clinical course of the patient was favourable and she was declared cured 12 days later (day 18 after onset of illness). After two negative EBOV RT-PCR blood tests, 24 hours apart, she was discharged from hospital. No EBOV RT-PCR of the breast milk was performed.

Upon admission, her infant was 10 days old and had been breastfed since birth. The child was immediately separated from the mother and breastfeeding was stopped. Six days later, the child developed fever (38.9°C). Ceftriaxone and gentamicin were started. Artesunate was also given but stopped after a negative malaria test. EBOV RT-PCR blood tests were negative on day 1 and 3 after onset of fever. Gentamicin was stopped after two days but ceftriaxone continued for eight days with a favourable clinical outcome. The infant rapidly became asymptomatic and was followed

up for 21 days after the last contact with the sick mother. The child did not develop EVD.

## Discussion

We describe two EBOV RT-PCR discordant mother-child pairs that illustrate the complexity of taking care of patients with EBOV infection.

If a lactating mother's blood is EBOV RT-PCR negative and has an EBOV-positive breastfed child (Case 1), healthcare workers should investigate whether the mother recently recovered from a confirmed or suspected EBOV infection. The mother's urine and breast milk should be tested by EBOV RT-PCR for shedding of EBOV even after the virus becomes undetectable in the blood [3,4]. The child in Case 1 described, was most likely infected by the mother, however, whether the child became infected through breast milk or through contact with another bodily fluid, remains unknown. We cannot fully rule out the possibility that the source of the child's infection was the relative who was taken care of by the child's mother but this would mean the incubation period of the child was at least 16 days which is long given the average incubation period of 8 to 10 days [5].

Data on how long infective EBOV can be present in other body fluids such as saliva, tears, urine, stool, breast milk, vaginal and amniotic fluid and seminal fluids, are still limited [4]. We do know that in the 36-year-old patient with EVD who was evacuated in August 2014 to an isolation facility in Hamburg, Germany, infective EBOV was still isolated from urine samples on day 26 of his illness, nine days after the clearance of EBOV from plasma [3]. We also know that EBOV can be isolated from convalescent patients in semen up to 82 days after disease onset [6]. However, in a study by Bausch et al., EBOV could not be cultured from the urine in 11 cases, but this might have been caused by virus degradation from breaks in the cold chain during sample collection, storage and shipping [4].

Detection for long periods of time in urine is known for other viruses, such as the West Nile virus [7] but poorly documented for EVD. The added value of EBOV testing of the urine of convalescent patients remains to be determined. Indeed, a positive PCR test does not mean the urine is still infectious and it would be impossible to keep patients with positive EBOV RT-PCR urine or semen tests for months in isolation.

EBOV has been detected in breast milk previously [4] but the timing of EBOV appearance, how long it remains in breast milk in an EBOV-infected lactating mother and the exact risk for a child to become infected through breastfeeding, remain poorly understood. EBOV was isolated from the breast milk of one lactating woman 15 days after disease onset, and after EBOV was already cleared from the blood [4]. We will need prospective studies of mother and child pairs, combining PCR testing with virus culture of breast milk to finally come

up with evidence-based recommendations regarding breastfeeding in cases of lactating mothers with EVD. Although high levels of actively produced IgA in breast milk have been shown to provide limited local mucosal protection for breastfed children against influenza virus infection [8], further studies are needed to determine the cellular and immunologic effects of breast milk-secreted antibodies in EVD patients.

These two cases demonstrate that when caring for mother-child pairs, healthcare workers should consider the potential role of testing relevant body fluids in addition to blood, such as urine and breast milk.

In case of discordant RT-PCR results between an EBOV-positive mother and her EBOV-negative breastfed child, ideally, breastfeeding should be stopped if safe replacement for breastfeeding is available [9]. Otherwise, feeding the child with heat-treated expressed breast milk [10] could be considered. Where a mother has survived EVD, ideally, her breast milk should be confirmed negative for EBOV before resuming breastfeeding. If EBOV RT-PCR diagnostic is not available, it is advised to avoid breastfeeding by EVD-surviving mothers [9].

The possibility of prolonged EBOV shedding in urine and breast milk means that counselling about hygiene in handling those fluids should be an important component of health promotion at the time of discharge from the ETC.

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## Conflicts of interest

None declared.

## Authors' contributions

Michel Moreau, Craig Spencer, Julia Garcia Gozalbes, Alseny Modey Camara were involved in the care of patients at the ETC in Guéckédou. Sophie Gryseels and Benny Borremans performed the PCR testing. Michel Moreau and Robert Colebunders wrote the first draft. Michel Van Herp, Tom Decroo, Annabelle Lefevre, Antonino Di Caro, Roman Wölfel, Dirk Becker, Stephan Günther, Joseph Bore, Raymond Koundouno, Leentje Peetermans, all reviewed the paper, and their comments were incorporated.

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# First Innovative Medicines Initiative Ebola projects launched

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The first eight projects on Ebola, selected from proposals submitted in the framework of the Innovative Medicines Initiative (IMI) first Ebola+ programme Call for proposals [1], are being launched. The projects aim to accelerate all aspects of Ebola vaccine development and manufacturing as well as deployment and compliance with vaccine regimens and diagnostics.

With a total budget of € 215 million, the eight projects cover the following fields: (i) development of Ebola vaccines, (ii) the scaling up of vaccine manufacture, (iii) compliance with vaccine regimens, and (iv) the development of rapid diagnostic tests.

The IMI Ebola+ programme was created in response to the ongoing Ebola outbreak in western Africa. The projects bring together partners from the pharmaceutical and diagnostics industries, public health bodies, academia, aid organisations, and small biotech companies in Europe, Africa and the United States. Previous experience at IMI has shown that consortia of this kind, which bring together diverse groups from different parts of the world, can make progress in even very challenging disease areas.

Further Calls for proposals are planned for the coming months. These could address issues such as the development of a vaccine that offers broad protection against both Ebola and other, related viruses such as Marburg.

The budget is partly funded by the European Union Horizon 2020 programme [2], and partly in the form of in-kind contributions from the European Federation of Pharmaceutical Industries and Associations.

For more information, see:  
<http://www.imi.europa.eu/content/ebola-programme>

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# European Food Safety Authority organises second scientific conference in October 2015

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On 14–16 October the European Food Safety Authority (EFSA) is organising a conference with the title ‘Shaping the future of food safety, together’. The objectives of the conference are to take stock of challenges and opportunities for risk assessment to contribute to policy development and the assessment in the area of food safety.

The conference consists of two plenary sessions, one asking ‘What does the future hold for Assessment Science?’ and a second titled ‘Science, Innovation & Society’, each of which is followed by five breakout sessions. Keynote lectures follow each plenary session, reflecting on developments affecting the role and the conduct of assessment science and areas of biology including the role of gut flora, neural science, reproductive endocrinology and epigenetics.

EFSA is organising the conference in collaboration with national organisations, European Union agencies, the European Commission and international risk assessment bodies.

Read more about the conference here:  
<http://www.efsaexpo2015.eu/conference/>