

Evaluation of a temporary vaccination recommendation in response to an outbreak of invasive meningococcal serogroup C disease in men who have sex with men in Berlin, 2013–2014

J Koch¹, W Hellenbrand¹, S Schink¹, O Wichmann¹, A Carganico², J Drewes³, M Kruspe³, M Suckau⁴, H Claus⁵, U Marcus¹

1. Department for Infectious Disease Epidemiology, Robert Koch Institute, Berlin, Germany

2. AIDS working group of practicing physicians Berlin e.V., Berlin, Germany

3. Free University Berlin, Public Health, Berlin, Germany

4. Infectious Disease Protection Unit, Senate Department for Health and Social Affairs, Berlin, Germany

5. University of Würzburg, Institute for Hygiene and Microbiology and National Reference Laboratory for Meningococci, Würzburg, Germany

Correspondence: Judith Koch (kochj@rki.de)

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Meningococcal serogroup C (MenC) vaccination of men who have sex with men (MSM) was temporarily recommended to control an outbreak of invasive MenC disease among MSM in Berlin in 2012–2013. Vaccination was offered to HIV-infected MSM free of charge; others had to request reimbursement or pay out of pocket. We aimed to assess (i) awareness and acceptance of this recommendation through an online survey of MSM, (ii) implementation through a survey of primary care physicians and analysis of vaccine prescriptions, and (iii) impact through analysis of notified cases. Among online survey respondents, 60% were aware of the recommendation. Of these, 39% had obtained vaccination (70% of HIV-infected, 13% of HIV-negative/non-tested MSM). Awareness of recommendation and vaccination were positively associated with HIV infection, primary care physicians' awareness of respondents' sexual orientation, and exposure to multiple information sources. Most (26/30) physicians informed clients about the recommendation. Physicians considered concerns regarding reimbursement, vaccine safety and lack of perceived disease risk as primary barriers. After the recommendation, no further outbreak-related cases occurred. To reach and motivate target groups, communication of a new outbreak-related vaccination recommendation should address potential concerns through as many information channels as possible and direct reimbursement of costs should be enabled.

Introduction

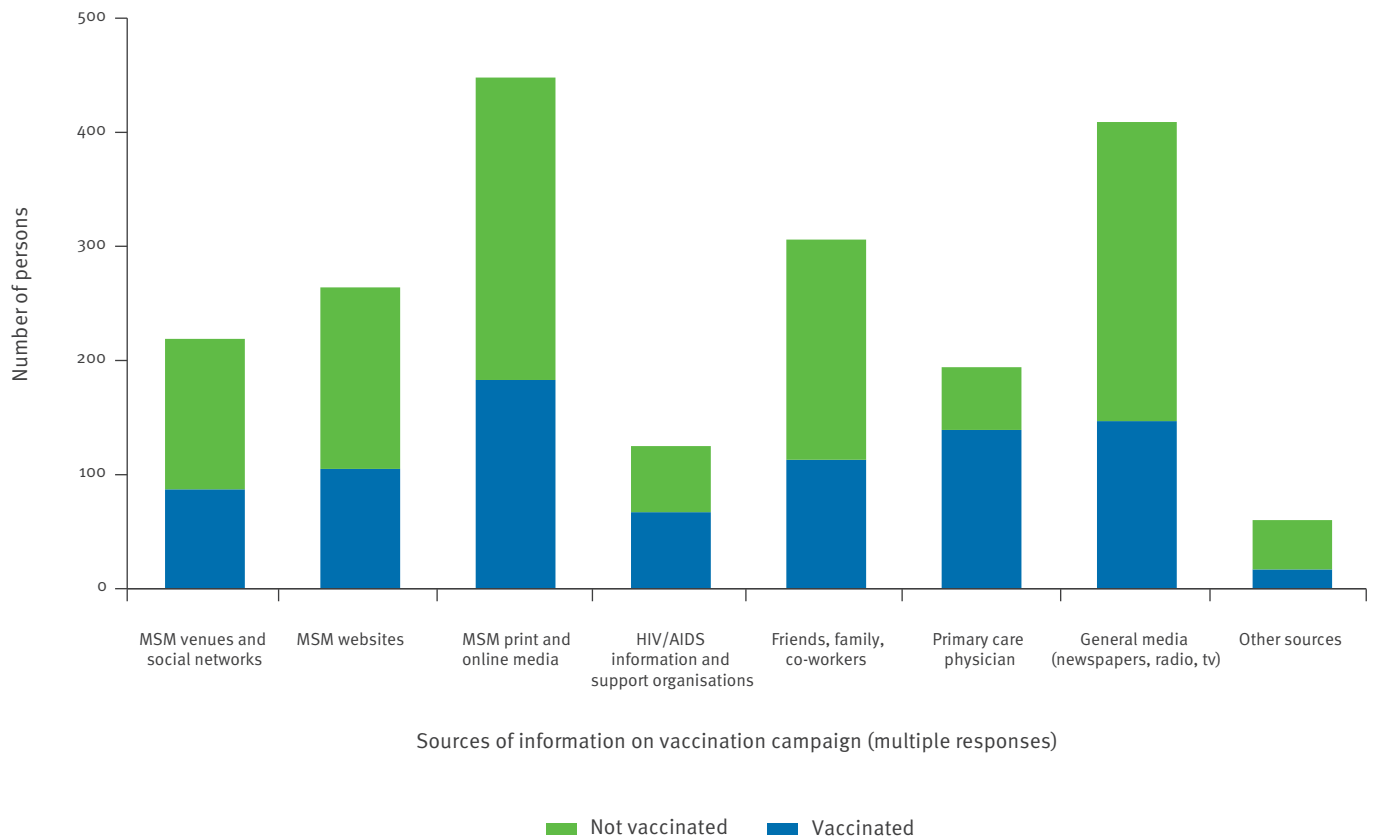
Neisseria meningitidis (Nm) is a gram-negative diplococcus that commonly colonises the human pharynx and respiratory tract [1]. Nm can sometimes cause

invasive meningococcal disease (IMD), presenting as meningitis and/or sepsis. Thus far, 13 serogroups have been identified; of these A, B, C, W, X and Y cause virtually all IMD [2]. Similar to other European and North American countries [3], serogroup B, followed by C, predominate in Germany, with IMD incidence showing a decreasing trend, from 0.95 cases/100,000 inhabitants in 2001 to 0.45/100,000 in 2011 [4]. Overall case fatality from 2009 to 2011 was 7.8%, significantly higher for meningococcal C (MenC) (10.9%) than for meningococcal B (MenB) disease (7.6%). Incidence was highest in infants (8.1 cases/100,000 inhabitants) and toddlers (4.8), with a second, smaller peak in 15–19 year-old adolescents (2.0) [4].

The overall prevalence of nasopharyngeal meningococcal carriage is about 10%, but varies markedly in different age and population groups [5–8]. Very high Nm carriage rates of over 40% have been reported in men who have sex with men (MSM) [9–10], and one study reported higher carriage rates in MSM (23.8%) than in heterosexual men (11.6%) [11]. Further known risk factors for meningococcal disease, such as exposure to tobacco smoke and crowding [12, 13], may also be more prevalent in venues where MSM meet. Since 2001, IMD clusters in MSM have been reported in Toronto (2001) [14], Chicago (2003) [15] and New York City (2010–2013) [16–17]. All outbreaks were caused by MenC and were of the multilocus sequence type (MLST) 11 (ST-11) [18]. The outbreaks in Toronto and Chicago (six cases each) ended rapidly after carrying out targeted MenC vaccination campaigns in the gay communities affected.

FIGURE 1

Number of men who have sex with men reached by various information sources and vaccination status after meningococcal serogroup C vaccination recommendation, Berlin, November 2013–January 2014



MSM: men who have sex with men.

However, the New York outbreak (22 cases) was more protracted despite intensive efforts to vaccinate MSM.

From October 2012 to May 2013, five IMD cases in MSM living in Berlin were notified to local health authorities (LHA). The patients were between 22 and 28 years old; none were HIV-positive. All cases were caused by MenC strains belonging to ST-11 of the fine type PorA(P)1.5-1.10-8:FetA(F)3-6 [19]. In addition, four of the five strains from these patients had fHbp allele 766, that had not been described previously. All five cases presented with severe sepsis; four died. Only two of the cases had a definite epidemiological link, having spent a night together shortly before illness onset [19]. In this time period MenC clusters among MSM were also reported from New York, Los Angeles and Paris and a single case from Belgium. All European strains showed similar characteristics [20].

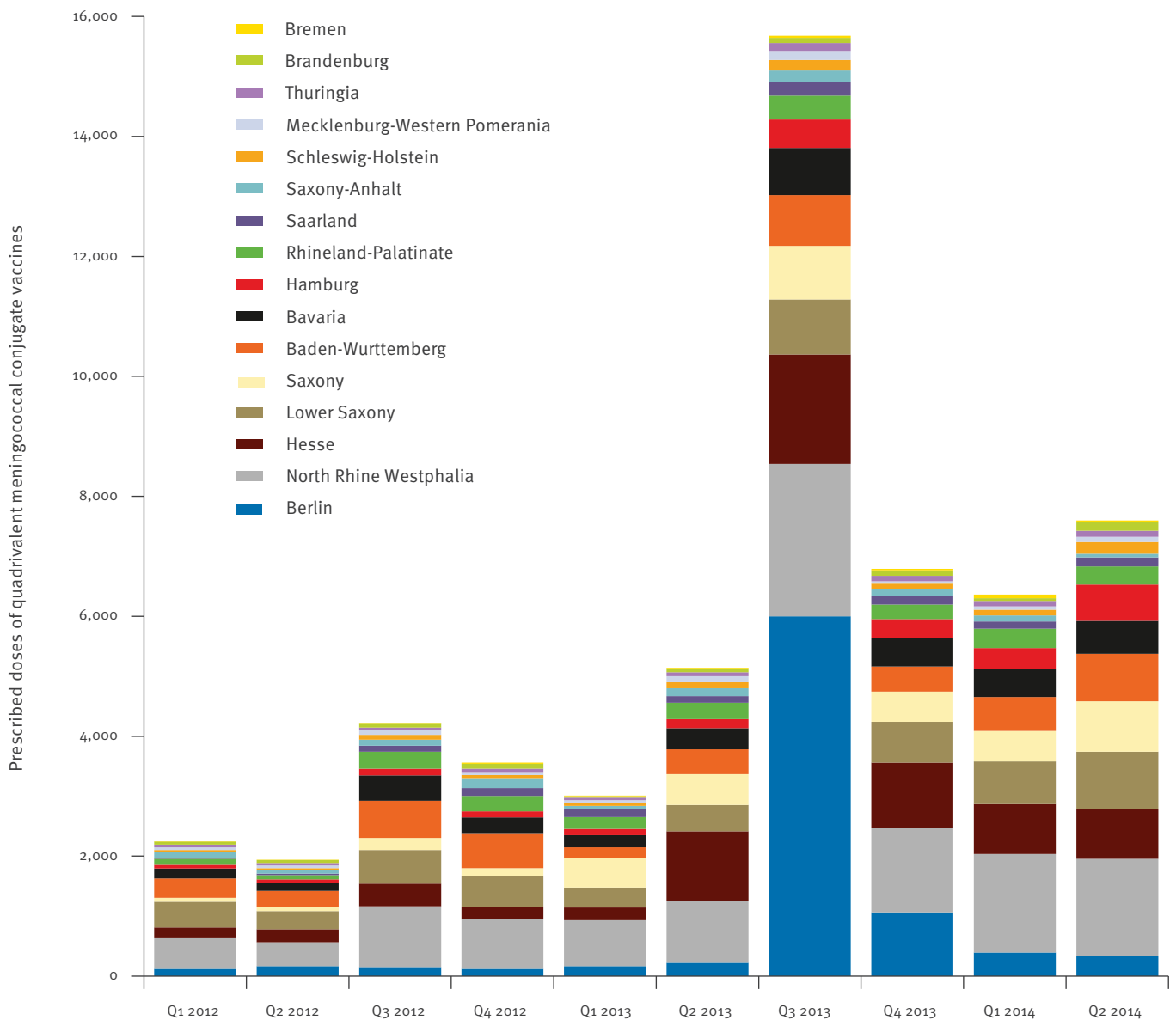
It has been estimated that 80,000 MSM (95%CI 74,000–104,000) aged 20–59 years live in Berlin [21–22]. Among these, an estimated 10,800 MSM had been diagnosed with HIV as of the end of 2013 [22]. Assuming the age distribution among MSM is similar to that of men in the general population, an estimated 18,000 MSM aged 20–29 years live in Berlin, among

whom four MenC IMD cases occurred in the first half of 2013. The resulting incidence of 11 cases/100,000 inhabitants [23] was markedly higher than the nationwide incidence of 0.7/100,000 in 20–29 year old men in 2012 [24].

Prevention of IMD with meningococcal conjugate vaccines is highly effective [25]. In Germany, MenC vaccination was recommended for all one year-old children in 2006; older children can obtain the vaccine on an individual basis free-of-charge. Vaccination coverage of adolescents increased gradually, reaching 59% among 15–17 year-olds in 2013 based on statutory health insurance (SHI) claims data (Thorsten Rieck, personal communication, January 2015). In addition, vaccination against serogroups ACWY (MenACWY) is recommended for persons with congenital or acquired immunodeficiencies with residual T- and/or B-cell function, especially complement/properdin deficiencies, hypogammaglobulinaemia, and asplenia. While HIV infection is not explicitly listed, it is considered to be an indication for meningococcal vaccination under this rubric. Quadrivalent meningococcal vaccination is also recommended for travellers to endemic areas. Finally, vaccination is recommended to control regional IMD outbreaks when three or more cases of an identical

FIGURE 2

Number of prescribed doses of quadrivalent meningococcal serogroups ACWY conjugate vaccines according to quarter and federal state, Germany, 1 January 2012–30 June 2014



Q: quarter.

For information on the prescribed doses, see Text.

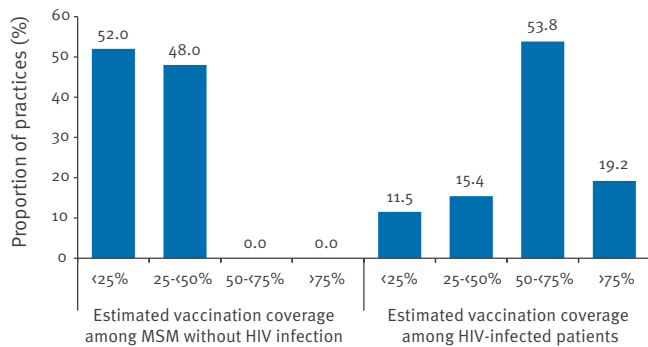
serogroup occur in a specific age group in a particular region within three months in conjunction with an attack rate of 10 or more cases per 100,000 inhabitants in the respective population [26].

Thus, in response to this outbreak, the competent authorities of the federal state of Berlin recommended meningococcal vaccination for all MSM with a vaccine licensed for adults to protect against serogroup C as of 27 July 2013, following advice from the Berlin Advisory Board for Immunisation and announced in a press release on 18 July 2013 [27]. Female partners of MSM were not targeted in this recommendation. The recommendation was to remain in effect until 31 January

2014, but was subsequently extended to 31 December 2014, pending an evaluation of its impact. The recommendation did not entail reimbursement of the vaccine by SHI. However, most insurance companies adopted a policy of individual evaluation and reimbursement upon request. The gay community and physicians were informed via internet forums as well as by radio, TV and the print media. The recommendation was promoted in counselling centres of the gay and lesbian community in Berlin, by the German and Berlin AIDS service organisations (DAH and BAH, respectively), the AIDS working group of practising physicians in Berlin (AK AIDS), the German association of practising physicians treating

FIGURE 3

Vaccination coverage for meningococcal serogroups C and ACWY vaccination as estimated by physicians at the time of the survey in participating practices for men who have sex with men without HIV-infection and HIV-infected patients



MSM: men who have sex with men.

HIV-infected patients (DAGNÄ) and via regional and national gay Internet portals.

Our goal was to evaluate the awareness and implementation of the temporary MenC vaccination recommendation for MSM in Berlin by surveying MSM and physicians. In addition, we analysed IMD cases notified in Berlin after implementation of the recommendation, including the molecular epidemiology of MenC cases, to confirm that the outbreak had been interrupted.

Methods

Internet-based survey among men who have sex with men

Starting in the late 1980s, anonymous knowledge, attitude and behaviour (KAB) surveys on HIV/AIDS were conducted every two to four years among MSM in Germany [28]; from 2007 onwards these were carried out online exclusively. Questions on the Berlin vaccination recommendation were included in the nationwide survey made available online from November 2013 until mid-January 2014. Participants living in Berlin were asked how they obtained information on the MenC vaccination campaign and whether they obtained vaccination. They were recruited by personalised instant messages and banners on social networking and dating websites for MSM. Two multivariable logistic regression models were constructed to analyse factors potentially associated with awareness of the recommendation and with MenC vaccine uptake, respectively. The following factors were investigated: demographic and behavioural characteristics such as age, educational status, income, reported sexual orientation, openness regarding sexual orientation towards colleagues and their physician, affinity to gay subculture (visiting gay venues), information seeking pertaining to HIV, HIV testing, and HIV status, number of sexual partners in the previous year, and sources used to obtain information on the Berlin vaccination

recommendation. Respondents who reported MenC vaccination before the recommendation was issued were excluded from this analysis.

The online survey protocol was evaluated and approved by the ethical review board of the Charité University Clinic in Berlin (EA1/266/13).

Prescription of meningococcal conjugate vaccines

The number of monovalent MenC or quadrivalent MenACWY conjugate vaccine doses prescribed within SHI from July 2013 to March 2014 was analysed based on data from Insight Health (<http://insight-health.de/>). This database contains data from pharmaceutical data-processing centres on all directly reimbursed prescriptions for > 99% of persons insured by SHI (85% of the population) in Germany. However, data on recipients' age and sex are not available. SHI reimburses all prescriptions for vaccinations recommended by the German Standing Committee for Vaccination (STIKO). Thus, prescriptions for meningococcal vaccination of people living with HIV (PLWHIV) were included in the Insight Health database, since vaccination was already recommended by STIKO for this group before the outbreak. However, meningococcal vaccination for non-HIV-infected, otherwise-healthy MSM living in Berlin as recommended by the Berlin authorities was not covered directly by SHI and thus not registered in this database. Rather, patients had to fill individual private prescriptions that SHI reimbursed on a voluntary basis.

Survey of primary care physicians

In February 2014 we conducted a cross-sectional survey among privately practicing physicians belonging to AK AIDS, who represent almost all primary HIV care providers and are known as MSM-friendly. We assumed that most MSM would seek vaccination from one of these practices, which covered a range of relevant medical specialties. The study was presented in January 2014 at the AK AIDS working group meeting to motivate members to participate. Since most members worked in group practices, we conducted the survey per practice. We used a written anonymous questionnaire eliciting participants' demographics (age, sex, physician specialty, location and type of practice), the number of MSM clients and HIV-infected patients in the practice population, information channels used to inform patients, vaccination practices in general and MenC vaccination practices in particular, including type of vaccine used, possible obstacles to immunisation and vaccine uptake by MSM. After pre-testing, the questionnaire was distributed on 14 January 2014 to all 45 practices, with a total of about 70 practicing physicians. Returned questionnaires were entered electronically using Microsoft Excel 2010. We conducted a descriptive analysis, including calculation of proportions and 95% confidence intervals (CI).

Surveillance of invasive meningococcal disease cases in men who have sex with men after meningococcal C vaccine recommendation

In Germany, surveillance of IMD is based on statutory notification by physicians and laboratories to LHAs [29]. LHAs transmit laboratory-confirmed and epidemiologically linked IMD cases to the Robert Koch Institute (RKI) via the federal state authorities according to a standardised case definition. These data are routinely matched to data of invasive meningococcal strains that undergo molecular genetic typing at the national reference laboratory for meningococci and *Haemophilus influenzae* (NRLMHi) as described previously [30]. During the outbreak, all LHA in Berlin were requested to elicit sexual orientation of IMD cases in men which is otherwise not routinely done. Ethical approval was not necessary since according to the Protection against Infection Act, local health authorities are authorised to request information on any risk factors relevant to outbreak control in patients and forward this information anonymously to the Robert Koch Institute. Possible outbreak-related cases were defined as follows: All MenC IMD in MSM aged 20-49 years, living in Berlin with illness onset from 1 July 2013 to 31 August 2014.

Results

Internet-based survey among men who have sex with men

MenC-related questions were answered by 1,471 online survey participants. Of these, 42 (2.9%) reported MenC vaccination before the recommendation was published and were excluded from further analysis, leaving a study sample of 1,429 men.

The median age of respondents was 40 years (range: 16–78 years); 72% had at least a high school diploma. The majority (78%) reported exclusively male sexual partners in the previous 12 months, but only 37% reported regularly visiting gay venues. About half (52%) stated that they were single, 44% reported having a steady male partner, and 4% a steady female partner. Most (81.5%) had been tested for HIV at least once; among those tested ($n = 1,199$), 23% were HIV-positive. Table 1 presents demographic, behavioural and information-seeking characteristics stratified according to awareness of the recommendation and vaccine uptake.

Of all participants, 852 (59.6%) were aware of the recommendation and 333 (23.3%) obtained MenC vaccination. Positive HIV status, the primary healthcare provider being aware of the respondent's sexual orientation, having received information about the recommendation from a larger number of different information channels, higher educational level, and > 10 sexual partners in the past year were independently associated with both awareness of the recommendation and obtaining vaccination (Table 2). Frequent visits to gay venues were also significantly associated with awareness, while men who reported having mainly female partners were less likely to have

heard of the recommendation (Table 2). Over two-thirds (69.6% (183/263) of HIV-infected MSM, but only 12.9% (150/1,166) of non-tested or HIV-negative participants reported obtaining MenC vaccination.

MSM whose physicians personally recommended MenC vaccination during a healthcare visit had the highest vaccine uptake, followed by those who learned of the recommendation through HIV/AIDS information and support organisations. However, only 18.8% (268/1,429) of all survey participants and 31.5% of survey participants aware of the vaccination recommendation (268/852) were exposed to these sources. The highest number of MSM was reached through MSM online and print media, followed by general print and broadcast media, but vaccine uptake among these MSM was lower (Figure 1).

Prescription of meningococcal conjugate vaccines

From Q1 2012 to Q2 2014, the number of monovalent conjugate MenC vaccine doses (Menjugate Kit, NeisVac-C and Meningitec) prescribed and directly reimbursed by SHI fluctuated between 159,000 and 213,000, with peak values in Q3 2012 as well as Q3 2013 in all federal states and the lowest number in Q1 2013. In contrast, the number of prescribed and directly reimbursed doses of quadrivalent conjugate ACWY vaccines (Nimenrix and Menveo) increased markedly in Q3 of 2013 (Figure 2). By far the largest increase (ca 37-fold, from a mean of 159 doses per quarter in Q1 2012 to Q2 2013 to 6,001 in Q3 2013) was seen in Berlin, but increases were also seen in other states. Thereafter, the number of prescriptions for MenACWY vaccines decreased rapidly, but remained two- to three-fold higher in most federal states than prior to Q3 2013. In Berlin, 7,798 doses of quadrivalent vaccine were prescribed in Q3 2013 to Q2 2014, compared with 635 expected doses based on the mean of 159 per quarter in Q1 2012 to Q2 2013. If we assume the 7,163 excess doses were mainly used to vaccinate MSM known to be HIV-positive, this implies up to 66% of the estimated 10,800 MSM with HIV diagnoses living in Berlin received meningococcal vaccination.

Survey of primary care physicians

Of 45 distributed questionnaires, 30 (66.7%) were returned completed. The respondents' median age was 50 years (range: 41–64 years), 22 were male and six female. The two most common disciplines of the surveyed practices were family ($n=12$) and internal medicine ($n=13$), followed by dermatology ($n=4$). This was similar to the distribution of disciplines among all contacted practices. Of responding physicians, 22 worked in group practices and eight in solo practices. Practice size was highly variable, and thus also the number of patients with an existing or new indication for MenC vaccination. Based on the participants' estimates, an average of 480 HIV-infected patients (median: 425; range 1–2,000) and 530 MSM without HIV-infection

TABLE 1

Demographic and behavioural characteristics of Internet survey respondents resident in Berlin stratified according to awareness of vaccine recommendation and vaccine uptake, November 2013–January 2014 (n=1,429)

		Unaware of campaign n=577		Aware, not vaccinated n=519		Aware, vaccinated n=333		Row totals N = 1,429	Pearson's chi-squared test
		n	%	n	%	n	%		
Age group (years old)	<25	89	15.4%	68	13.1%	14	4.2%	171	<0.001
	≥25	488	84.6%	451	86.9%	319	95.8%	1,258	
Education	<High school diploma	176	31.2%	131	25.5%	84	25.7%	391	0.075
	≥High school diploma	389	68.8%	382	74.5%	243	74.3%	1,014	
Monthly income	<€1,000	125	23.2%	89	18.2%	56	17.7%	270	0.062
	≥€1,000	413	76.8%	401	81.8%	260	82.3%	1,074	
Openness regarding sexual orientation towards co-workers	≥50% know	275	50.3%	369	73.8%	252	79.5%	896	<0.001
	<50% know	272	49.7%	131	26.2%	65	20.5%	468	
Openness regarding sexual orientation towards primary care provider	Is informed	211	36.6%	285	54.9%	294	88.3%	790	<0.001
	Does not know/unsure	366	63.4%	234	45.1%	39	11.7%	639	
Visiting gay venues	Infrequent	435	75.5%	212	34.2%	153	45.9%	894	<0.001
	Frequent	141	24.5%	306	59.1%	180	54.1%	533	
Sexual orientation	Exclusively male sex partners	401	69.5%	424	81.7%	291	87.4%	1,116	<0.001
	Predominantly male sex partners	101	17.5%	77	14.8%	41	12.3%	219	
	Predominantly female sex partners	75	13.0%	18	3.5%	1	0.3%	94	
HIV test status	HIV-positive	38	6.7%	42	8.1%	183	55.0%	263	<0.001
	HIV-negative recent test ≤12 months	216	37.4%	229	44.1%	112	33.6%	557	
	HIV negative test >12 months ago	152	26.3%	157	30.3%	29	8.7%	338	
	Never tested	171	29.6%	91	17.5%	9	2.7%	271	
Number of information sources on MenC recommendation	None, unaware of vaccination recommendation	577	100.0%	0	0.0%	0	0.0% ^a	577	<0,001
	1–2	NA	NA	342	66.3%	187	56.3%	529	
	3–4	NA	NA	141	27.3%	99	29.8%	240	
	≥5	NA	NA	33	6.4%	46	13.9%	79	
Number of sexual partners in previous 12 months	≤1	159	27.9%	102	19.8%	32	9.7%	293	<0.001
	2–5	221	38.8%	159	30.8%	64	19.3%	444	
	6–10	85	14.9%	96	18.6%	56	16.9%	237	
	>10	105	18.4%	159	30.8%	179	54.1%	443	

MenC: meningococcal C; NA: not applicable.

^a Men already vaccinated before the vaccination recommendation targeting men who have sex with men were excluded from this analysis

(median: 200; range 1-3,000) attended each practice annually.

As summarised in table 3, surveyed physicians learned of the vaccination recommendation most frequently through the Berlin Senate press release (n=30) or HIV-specific medical networks (n=14). Of the 30 practices, 26 actively informed their patients about the new MenC vaccination recommendation, usually during routine consultations. Before the recommendation was issued, 20 practices regularly vaccinated certain patient groups against MenC. International travel was the most common indication (19/20), with only 5/20 reporting HIV-related immunodeficiency as being an indication.

Responding physicians estimated MenC vaccine uptake to be markedly higher among HIV-infected patients than HIV-non-infected patients in February 2014, ca 6 months after implementation of the recommendation (Figure 3). They administered quadrivalent MenACWY vaccine almost exclusively (28/29) rather than a monovalent vaccine. Twenty-two practices reported that MSM patients sometimes declined MenC vaccination despite the recommendation, most commonly due to a lack of perceived risk, a negative attitude towards vaccination, or fear of side effects (Table 3). Half the responding physicians believed that concerns regarding reimbursement of vaccination costs by SHI led to refusal of the recommended vaccination in approximately one-third of eligible patients in these practices.

TABLE 2

Results of two multivariable logistic regression models analysing factors associated with awareness of the vaccination recommendation and uptake of the MenC vaccine, Berlin, November 2013–January 2014

Factors	Awareness of vaccination campaign (n=1,346)				Vaccine uptake (n=786)			
	Number of individuals	OR	95% CI	p	Number of individuals	OR	95% CI	p
Primary care physician								
Unaware of patient's sexual preference(s)	766	Ref.	NA	NA	542	Ref.	NA	NA
Aware of patient's sexual preference(s)	580	2.1	1.6–2.8	<0.000	244	2.6	1.7–4.2	<0.000
HIV status								
HIV-positive	257	Ref.	NA	NA	209	Ref.	NA	NA
HIV-negative ≤12 months	532	0.4	0.3–0.6	<0.000	316	0.1	0.1–0.2	<0.000
HIV-negative >12 months	315	0.4	0.3–0.7	<0.000	172	0.1	0.03–0.1	<0.000
Never tested for HIV (status unknown)	242	0.3	0.2–0.4	<0.000	89	0.1	0.02–0.1	<0.000
Number of partners within past 12 months								
2–5 partners	410	Ref.	NA	NA	202	Ref.	NA	NA
≤1 partner	278	0.8	0.6–1.2	0.294	129	0.5	0.3–1.0	0.044
6–10 partners	229	1.3	0.9–1.8	0.226	138	1.0	0.6–1.7	0.978
>10 partners	429	1.8	1.3–2.5	0.001	317	1.6	1.0–2.5	0.057
Number of information sources on the vaccination campaign								
1–2 sources	NA	NA	NA	NA	482	Ref.	NA	NA
3–4 sources	NA	NA	NA	NA	226	1.3	0.9–1.9	0.214
≥5 sources	NA	NA	NA	NA	78	2.5	1.4–4.5	0.003
Level of education								
≤Secondary school	376	Ref.	NA	NA	199	Ref.	NA	NA
≥High-school diploma	970	1.6	1.2–2.1	0.001	587	1.7	1.1–2.7	0.012
MSM venues: infrequent or no visits								
Infrequent or no visits	837	Ref.	NA	NA	421	NS	NS	NS
Regular visits	509	1.7	1.3–2.2	<0.000	365	NS	NS	NS
Sexual partner(s)								
Male only	1,057	Ref.	NA	NA	665	NS	NS	NS
Majority male	201	0.8	0.6–1.1	0.138	104	NS	NS	NS
Majority female or female only	88	0.3	0.2–0.5	<0.000	17	NS	NS	NS

NA: not applicable; NS: not significant; OR: odds ratio; 95%CI: 95% confidence interval; Ref: reference group.

Factors excluded from the model as non-significant: income (≤ EUR1,000 /month vs > EUR 1,000/month); age (≤25 years-old vs >25 years-old).

Invasive meningococcal disease cases in men who have sex with men after meningococcal C vaccine recommendation

No further outbreak-related cases occurred in Berlin from July 2013 to August 2014. Only four men with MenC IMD were notified in Berlin from July 2013 to August 2014, aged 37–48 years. None were MSM. While strains from two of these cases had the fine type P1.5-1,10-8:F3-6, the other two did not. None had fHbp allele 766. MenC incidence in 20–29-year old men in Berlin decreased from 1.58 cases/100,000 inhabitants in the first half of 2013 (four cases) to none in the second half of 2013, and none in the first half of 2014. From 2008 to 2012, annual MenC incidence in this age group in Berlin ranged from 0 to 0.79 (1–2 cases/year). The outbreak strain with fHbp 766 was not identified in any female cases.

Discussion

We evaluated the implementation, acceptance and impact of a temporary MenC vaccination recommendation issued in response to a MenC outbreak among MSM in Berlin in 2013. In the 13 months following endorsement of the recommendation, no further outbreak-related cases were reported among MSM. As LHA elicited sexual orientation of all reported IMD cases, it is unlikely that cases in MSM were missed. The recommendation led to enhanced meningococcal vaccination activities among MSM, but primarily among those with an HIV diagnosis. It seems plausible that the targeted vaccination campaign reduced meningococcal transmission in the population at risk. However, due to the rare and sporadic nature of IMD occurrence, it is possible that the outbreak would have also ended without enhanced vaccination activities.

TABLE 3

Survey results of physicians of the working group on AIDS regarding the temporary implementation of meningococcal serogroup C vaccine recommendation for men who have sex with men in Berlin Berlin, Germany, February 2014 (n=30)

Question	n	%	95% CI
How did you learn of the MenC vaccination recommendation for MSM in Berlin? (n=30)			
Press release by the Senate of Berlin	20	66.7	50.2–83.8
German association of practising physicians treating HIV-infected patients (DAGNÄ)	14	46.7	29.1–64.9
German AIDS service organisation (DAH)	10	33.3	16.2–49.8
Berlin AIDS service organisation (BAH)	9	30.0	13.6–46.4
From patients	6	20.0	7.9–38.1
Gay community counselling centres in Berlin	7	23.3	5.7–34.3
Gay community Internet portals	4	13.3	1.0–25.0
Have you informed your MSM patients of the temporary MenC vaccination recommendation? (n=30)			
Yes	26	86.7	75.0–99.9
No	4	23.3	1.0–25.0
If yes, how did you inform your patients? (n=26)			
During routine consultation	24	92.3	81.6–102.4
Information sheets and/or poster	7	26.9	9.9–44.1
Patient letter	3	11.5	-0.5–24.5
Did you regularly vaccinate certain groups of patients against meningococcal disease prior to the announcement of the recommendation? (n=29)			
Yes	20	69.0	52.2–85.8
No	9	31.0	14.2–47.8
What were the indications for vaccination against meningococcal disease?(n=20)			
Travel vaccination	19	95.0	95.4–104.6
HIV infection independent of a immunodeficiency	5	25.0	6.0–44.0
Immunodeficiency due to HIV infection	4	20.0	2.5–37.5
Routine childhood immunisation	3	15.0	-0.6–30.6
General immunisation of MSM	0	0.0	-
What vaccine did you use for the MenC vaccination? (n=29)			
Quadrivalent MenACWY conjugate vaccine	28	96.6	90.8–96.6
Monovalent MenC conjugate vaccine	1	3.4	-3.2–9.2
Did any patients decline the recommended MenC vaccination? (n=28)			
Yes	22	78.6	63.9–94.1
No	6	21.4	5.9–36.1
If yes, why? (n=22)			
Patient considered themselves to be not at risk	20	90.9	79.0–103.0
General refusal of vaccinations	17	77.3	59.4–94.6
Fear of side effects	16	72.7	54.4–91.6
Concerns that cost of vaccine would not be reimbursed	14	63.6	43.9–84.1
MenC disease not perceived as dangerous	8	36.4	15.9–56.1
Feared stigmatisation	4	18.2	1.9–34.1
Others advised against vaccination	4	18.2	1.9–34.1
Doubts about the effectiveness of the vaccine	3	13.6	-0.5–28.5

CI: confidence interval; MenC: meningococcal serogroup C; MSM: men who have sex with men.

As IMD clusters in the MSM community seem to be a recurring problem [14-16,18], heightened awareness should be upheld during routine surveillance to ensure early detection of and response to outbreaks in this group. All IMD cases should be reported promptly to responsible LHA and sexual orientation elicited during epidemiological case investigation.

The results of the surveys among MSM and physicians and vaccine prescription data showed both directly

and indirectly that targeting information to the relevant groups was effective, reaching an estimated 60% of MSM according to the internet-based survey. Preventive measures such as pneumococcal and influenza vaccination were well established in the everyday practice of physician members of the working group on AIDS, likely facilitating the prompt response to the new recommendation. Almost all responding practices reported offering the recommended MenC vaccine during patient visits. The conditions for the

implementation of a new vaccination recommendation were particularly favourable in this network of competent and dedicated physicians with an interest in treatment of HIV-infected patients. For MSM who did not routinely consult such practices, the situation might be different. Their doctors may not have offered meningococcal vaccination due to a lower level of awareness of the recommendation. Nonetheless, estimated vaccination coverage according to participating physicians was similar to that based on analysis of prescription data and the online survey.

The majority of meningococcal vaccinations were administered to HIV-positive MSM, over two thirds of whom were vaccinated based on the internet survey and prescription data, versus only 13% of the HIV-negative or untested internet survey participants. This may reflect less frequent physician contacts in the latter group. In addition, primary care providers also faced healthcare system- and patient-related barriers to vaccine delivery, including uncertainty regarding reimbursement of vaccination costs, fear of side effects and scepticism towards vaccination in general. Being required to at least indirectly reveal their sexual orientation to SHI to receive reimbursement for MenC vaccination may have been a further barrier for patients. In future similar situations, it might be helpful to communicate more detailed information on vaccine safety and requirements for reimbursement during the initial promotion of the campaign. Convincing SHI companies to directly reimburse vaccination costs in the case of outbreak-related vaccination recommendations and/or to provide funding for anonymous and free community-based vaccination sites would likely increase willingness to receive vaccination in similar situations.

In agreement with other studies, our survey among MSM showed that personal advice from the physician is pivotal in influencing willingness to be vaccinated [31-32]. In this case of a vaccination recommendation being limited to MSM, the physicians' recommendation had an even greater impact when the sexual orientation of the patient was known, emphasising the importance of a trusting doctor-patient relationship. In addition, vaccination could be conveniently obtained at routine healthcare visits, at least in HIV-positive MSM. In the implementation of a preventive measure such as a vaccination campaign, it is a particular challenge to reach the population most at risk. Our results show that repeated information via different sources led to higher vaccination uptake, similar to the findings of Friedman et al. during a community-wide hepatitis A vaccination campaign [33]. Nonetheless, 40% of MSM who participated in the online survey were unaware of the campaign. These men tended to be less open about their sexual orientation, reported less risky sexual behavior and visited gay venues less often. It would still be important to reach this group for targeted prevention measures, and for this, other channels of information must be identified.

Despite the long-standing STIKO recommendation to vaccinate immunocompromised patients against IMD, the majority of HIV-positive online survey participants (96%) were not vaccinated prior to the Berlin MenC vaccination recommendation. Only 20% of physicians in the practice-based survey stated that HIV-related immunodeficiency was an indication for meningococcal vaccination prior to the recommendation. Rather, travel abroad was the most common indication for meningococcal vaccination of MSM. The prescription data showed that MenC vaccine uptake increased in states other than Berlin as well. While this suggests that the Berlin MenC vaccination recommendation increased awareness for the pre-existing STIKO recommendation to immunise HIV-infected persons, more widespread education of physicians is required.

Our study has several limitations. Firstly, the impact of the vaccination campaign could only be determined indirectly through an observed decrease in the number of cases. Due to the sporadic nature of meningococcal clusters, we cannot say definitively that no further cases would have occurred even without vaccination. Studies to investigate the direct impact of vaccination on circulation of the pathogen in the gay community would be extremely difficult to perform since colonisation with MenC is very rare compared to other serogroups [5]. In addition, for population groups such as MSM it is impossible to determine the representativeness of an online sample. It is likely that MSM participants in the survey were more socially and sexually active, as well as more open about their sexual orientation, than MSM who did not participate. Such MSM may be more easily reachable by a vaccination campaign promoted through gay media [34-35]. However, the remarkable agreement in the estimated proportion of HIV-positive MSM vaccinated after the Berlin recommendation based on the internet survey with prescription data and physicians' estimates suggests that at least HIV-positive MSM were well represented in the survey.

Conclusion

In conclusion, the vaccination campaign launched to control the IMD outbreak in Berlin achieved a marked increase in vaccination coverage in MSM with HIV. The much lower coverage achieved in non-tested or HIV-negative MSM reflects known challenges of outbreak control in specific social groups such as MSM compared to in institutional settings [28]. Nonetheless, no further IMD cases occurred in MSM, and ongoing molecular genetic monitoring at the NRLMHi did not detect the outbreak strain in any IMD cases from Germany. A key finding of our study was that receiving information on the campaign from several sources increased vaccination uptake; thus widespread promotion of a new recommendation through all possible venues is crucial to reach target groups. Promotion of such a recommendation should also directly motivate persons in the target group to visit their physician and contact specific support groups, as these measures were associated

with the highest vaccine uptake. In particular, the long-standing and effective network of MSM-friendly physicians was crucial in implementing the vaccination campaign. Since lack of perceived risk for IMD and concerns regarding adverse vaccine effects were identified as important barriers to vaccination uptake, these issues should be more specifically addressed in future vaccination campaigns. Finally, in addition to direct reimbursement of physician-based vaccination, offering free and preferably anonymous vaccination at community-based vaccination sites might improve uptake, especially among those targeted persons who rarely consult a physician.

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Conflict of interest

None declared

Authors' contributions

JK designed and coordinated the survey of the general practitioners, analysed the data and drafted the manuscript. WH contributed to the questionnaire and data analysis of the survey of the general practitioners, and performed the analysis of the statutory health insurance prescription data. UM, JD and MK designed the questions for the MSM internet survey, which was implemented by JD and MK. The survey data were analysed by UM, SS, JD and MK. UM, WH and SS contributed to the manuscript draft. AC supported the execution of the physician's survey and reviewed the physicians' questionnaire. OW and MS critically reviewed the physicians' questionnaire and the manuscript. HC performed molecular genetic analysis of meningococcal strains and critically reviewed the manuscript. All authors read and approved the final manuscript.

References

- Halperin SA, Bettinger JA, Greenwood B, Harrison LH, Jelfs J, Ladhani SN, et al. The changing and dynamic epidemiology of meningococcal disease. *Vaccine*. 2012;30(Suppl 2):B26-36. DOI: 10.1016/j.vaccine.2011.12.032 PMID: 22178525
- Harrison OB, Claus H, Jiang Y, Bennett JS, Bratcher HB, Jolley KA, et al. Description and nomenclature of *Neisseria meningitidis* capsule locus. *Emerg Infect Dis*. 2013;19(4):566-73. DOI: 10.3201/eid1904.111799 PMID: 23628376
- Harrison LH, Trotter CL, Ramsay ME. Global epidemiology of meningococcal disease. *Vaccine*. 2009;27(Suppl 2):B51-63. DOI: 10.1016/j.vaccine.2009.04.063 PMID: 19477562
- Robert Koch Institut (RKI). Invasive Meningokokken-Erkrankungen, 2009 – 2011 [Invasive meningococcal disease, 2009-2011]. *Epidemiologisches Bulletin*. 2012;(39):389-97. German. Available from : http://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2012/Ausgaben/39_12.pdf?__blob=publicationFile.
- Trotter CL, Gay NJ, Edmunds WJ. The natural history of meningococcal carriage and disease. *Epidemiol Infect*. 2006;134(3):556-66. DOI: 10.1017/S0950268805005339 PMID: 16238823
- Christensen H, May M, Bowen L, Hickman M, Trotter CL. Meningococcal carriage by age: a systematic review and meta-analysis. *Lancet Infect Dis*. 2010;10(12):853-61. DOI: 10.1016/S1473-3099(10)70251-6 PMID: 21075057
- Claus H, Maiden MC, Wilson DJ, McCarthy ND, Jolley KA, Urwin R, et al. Genetic analysis of meningococci carried by children and young adults. *J Infect Dis*. 2005;191(8):1263-71. DOI: 10.1086/428590 PMID: 15776372
- Ala'aldein DA, Oldfield NJ, Bidmos FA, Abouseada NM, Ahmed NW, Turner DP, et al. Carriage of meningococci by university students, United Kingdom. *Emerg Infect Dis*. 2011;17(9):1762-3. DOI: 10.3201/eid1709.101762 PMID: 21888817
- Faur YC, Wilson ME, May PS. Isolation of *N. meningitidis* from patients in a gonorrhea screen program: a four-year survey in New York City. *Am J Public Health*. 1981;71(1):53-8. DOI: 10.2105/AJPH.71.1.53 PMID: 6789687
- Janda WM, Bohnhoff M, Morello JA, Lerner SA. Prevalence and site-pathogen studies of *Neisseria meningitidis* and *N. gonorrhoeae* in homosexual men. *JAMA*. 1980;244(18):2060-4. DOI: 10.1001/jama.1980.03310180026026 PMID: 6776296
- Russell JM, Azadian BS, Roberts AP, Talboys CA. Pharyngeal flora in a sexually active population. *Int J STD AIDS*. 1995;6(3):211-5. PMID: 7647127
- Baker M, McNicholas A, Garrett N, Jones N, Stewart J, Koberstein V, et al. Household crowding a major risk factor for epidemic meningococcal disease in Auckland children. *Pediatr Infect Dis J*. 2000;19(10):983-90. DOI: 10.1097/00006454-200010000-00009 PMID: 11055601
- Fischer M, Hedberg K, Cardosi P, Plikaytis BD, Hoesly FC, Steingart KR, et al. Tobacco smoke as a risk factor for meningococcal disease. *Pediatr Infect Dis J*. 1997;16(10):979-83. DOI: 10.1097/00006454-199710000-00015 PMID: 9380476
- Tsang RS, Kiefer L, Law DK, Stoltz J, Shahin R, Brown S, et al. Outbreak of serogroup C meningococcal disease caused by a variant of *Neisseria meningitidis* serotype 2a ET-15 in a community of men who have sex with men. *J Clin Microbiol*. 2003;41(9):4411-4. DOI: 10.1128/JCM.41.9.4411-4.2003 PMID: 12958279
- Schmink S, Watson JT, Coulson GB, Jones RC, Diaz PS, Mayer LW, et al. Molecular epidemiology of *Neisseria meningitidis* isolates from an outbreak of meningococcal disease among men who have sex with men, Chicago, Illinois, 2003. *J Clin Microbiol*. 2007;45(11):3768-70. DOI: 10.1128/JCM.01190-07 PMID: 17728467
- Simon MS, Weiss D, Gulick RM. Invasive meningococcal disease in men who have sex with men. *Ann Intern Med*. 2013;159(4):300-1. DOI: 10.7326/0003-4819-159-4-201308200-00674 PMID: 23778867
- Centers for Disease Control and Prevention (CDC). Notes from the field: serogroup C invasive meningococcal disease among men who have sex with men - New York City, 2010-2012. *MMWR Morb Mortal Wkly Rep*. 2013;61(51-52):1048. PMID: 23282863
- Weiss D, Varma JK. Control of recent community-based outbreaks of invasive meningococcal disease in men who have sex with men in Europe and the United States. *Euro Surveill*. 2013;18(28):20522. DOI: 10.2807/1560-7917.ES2013.18.28.20522 PMID: 23870094
- Marcus U, Vogel U, Schubert A, Claus H, Baetzing-Feigenbaum J, Hellenbrand W, et al. A cluster of invasive meningococcal disease in young men who have sex with men in Berlin, October 2012 to May 2013. *Euro Surveill*. 2013;18(28):20523. DOI: 10.2807/1560-7917.ES2013.18.28.20523 PMID: 23870095
- European Centre for Disease Prevention and Control (ECDC). Invasive meningococcal disease among men who have sex with men. Stockholm: ECDC; 2013. Available from: <http://www.ecdc.europa.eu/en/publications/Publications/rapid-risk-assessment-invasive-meningococcal-disease-among-MSM.pdf>.
- Marcus U, Schmidt AJ, Hamouda O, Bochow M. Estimating the regional distribution of men who have sex with men (MSM) based on Internet surveys. *BMC Public Health*. 2009;9(1):180. DOI: 10.1186/1471-2458-9-180 PMID: 19519888
- Robert Koch Institut. HIV/AIDS in Berlin – Eckdaten der Schätzung [HIV/AIDS in Berlin – Key figures of the estimates]. 2012 [Accessed 24 Oct 2014]. German Available from: http://www.rki.de/DE/Content/InfAZ/H/HIVAIDS/Epidemiologie/Daten_und_Berichte/EckdatenBerlin.pdf?__blob=publicationFile.
- Office for Health and Social Affairs Berlin (LAGeSo). [Cases of invasive meningococcal infection by a particular type of sequence of *N. meningitidis* type C in MSM in Berlin 2012-2013]. *Epi-Info-Wochenbericht*. 2013(28):17-23. German.
- Robert Koch Institut (RKI). Infektionsepidemiologisches Jahrbuch meldepflichtiger Krankheiten für 2013 [Yearbook for notifiable diseases 2013, Invasive meningococcal disease]. Berlin: RKI; 2014:154-9. German. Available from: <http://www.rki.de/DE/Content/Infekt/Jahrbuch/Jahrbuecher/2013.html?nn=2374622>
- Campbell H, Andrews N, Borrow R, Trotter C, Miller E. Updated postlicensure surveillance of the meningococcal C conjugate vaccine in England and Wales: effectiveness, validation of

- serological correlates of protection, and modeling predictions of the duration of herd immunity. *Clin Vaccine Immunol.* 2010;17(5):840-7. DOI: 10.1128/CVI.00529-09 PMID: 20219881
26. German Standing Committee on Vaccination (STIKO),. (Recommendations of the Standing Committee on Vaccination (STIKO) at the Robert Koch Institute). *Epidemiol Bull.* 2013;(34):313-44.
 27. Senatsverwaltung für Gesundheit und Soziales. Empfehlung des Berliner Impfbeirates zur Impfung gegen Meningokokken-Erkrankungen [Recommendation of vaccination against meningococcal disease by the Berlin Advisory Board for Immunisation] [press release]. Berlin: Senatsverwaltung für Gesundheit und Soziales; 18 Jul 2013. German. Available from: <http://www.berlin.de/sen/gessoz/presse/pressemitteilungen/2013/pressemitteilung.150750.php>
 28. Bochow M, Lenuweit S, Sekuler T, Schmidt AJ. Schwule Männer und HIV/AIDS: Lebensstile, Sex, Schutz- und Risikoverhalten [Gay Men and HIV/AIDS: lifestyles, sex, protection and risk behavior 2010], AIDS Forum DAH Berlin: Deutsche AIDS-Hilfe; 2011. German Available from: http://www.emis-project.eu/sites/default/files/public/publications/emis_nationalreport_germany.pdf
 29. Krause G, Altmann D, Faensen D, Porten K, Benzler J, Pfoch T, et al. SurvNet electronic surveillance system for infectious disease outbreaks, Germany. *Emerg Infect Dis.* 2007;13(10):1548-55. DOI: 10.3201/eid1310.070253 PMID: 18258005
 30. Hellenbrand W, Elias J, Wichmann O, Dehnert M, Frosch M, Vogel U. Epidemiology of invasive meningococcal disease in Germany, 2002-2010, and impact of vaccination with meningococcal C conjugate vaccine. *J Infect.* 2013;66(1):48-56. DOI: 10.1016/j.jinf.2012.09.008 PMID: 23043893
 31. Böhmer MM, Walter D, Krause G, Müters S, Gösswald A, Wichmann O. Determinants of tetanus and seasonal influenza vaccine uptake in adults living in Germany. *Hum Vaccin.* 2011;7(12):1317-25. DOI: 10.4161/hv.7.12.18130 PMID: 22108034
 32. Weigel M, Weitmann K, Rautmann C, Schmidt J, Bruns R, Hoffmann W. Impact of physicians' attitude to vaccination on local vaccination coverage for pertussis and measles in Germany. *Eur J Public Health.* 2014;24(6):1009-16. DOI: 10.1093/eurpub/cku013 PMID: 24599940
 33. Friedman MS, Blake PA, Koehler JE, Hutwagner LC, Toomey KE. Factors influencing a communitywide campaign to administer hepatitis A vaccine to men who have sex with men. *Am J Public Health.* 2000;90(12):1942-6. DOI: 10.2105/AJPH.90.12.1942 PMID: 11111274
 34. EMIS network, Marcus U, Hickson F, Weatherburn P, Schmidt AJ. Age biases in a large HIV and sexual behaviour-related internet survey among MSM. *BMC Public Health.* 2013;13(1):826. DOI: 10.1186/1471-2458-13-826 PMID: 24020518
 35. EMIS Network, Marcus U, Hickson F, Weatherburn P, Schmidt AJ. Prevalence of HIV among MSM in Europe: comparison of self-reported diagnoses from a large scale internet survey and existing national estimates. *BMC Public Health.* 2012;12(1):978. DOI: 10.1186/1471-2458-12-978 PMID: 23151263