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Meningococcal C conjugate vaccine effectiveness before and during an outbreak of invasive meningococcal disease due to *Neisseria meningitidis* serogroup C/cc11, Tuscany, Italy

Patrizio Pezzotti [a,1], Alessandro Miglietta [b,c,1], Arianna Neri [a], Cecilia Fazio [a], Paola Vacca [a], Fabio Voller [b], Giovanni Rezza [a], Paola Stefanelli [a,*]

[a] Department of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy
[b] Regional Health Agency of Tuscany, Epidemiologic Observatory, Florence, Italy
[c] Units of Epidemiology and Preventive Medicine, Central Tuscany Health Authority, Florence, Italy

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ABSTRACT

Introduction: In Tuscany, Italy, where a universal immunization program with monovalent meningococcal C conjugate vaccine (MCC) was introduced in 2005, an outbreak of invasive meningococcal disease (IMD) due to the hypervirulent strain of *Neisseria meningitidis* C/cc11 occurred in 2015–2016, leading to an immunization reactive campaign using either the tetravalent (ACWY) meningococcal conjugate or the MCC vaccine. During the outbreak, IMD serogroup C (MenC) cases were also reported among vaccinated individuals. This study aimed to characterize meningococcal C conjugate vaccines (MenC-vaccines) failures and to estimate their effectiveness since the introduction (2005–2016) and during the outbreak (2015–2016).

Methods: MenC cases and related vaccine-failures were drawn from the National Surveillance System of Invasive Bacterial Disease (IBD) for the period 2006–2016. A retrospective cohort-study, including the Tuscany' population of the birth-cohorts 1994–2014, was carried out. Based on annual reports of vaccination, person-years of MenC-vaccines exposed and unexposed individuals were calculated by calendar-year, birth-cohort, and local health unit. Adjusted (by birth-cohort, local health unit, and calendar-year) risk-ratios (ARR) of MenC invasive disease for vaccinated vs unvaccinated were estimated by the Poisson model. Vaccine-effectiveness (VE) was estimated as: VE = 1-ARR.

Results: In the period 2006–2016, 85 MenC-invasive disease cases were reported; 61 (71.8%) from 2015 to 2016. Twelve vaccine failures occurred, all of them during the outbreak. The time-interval from immunization to IMD onset was 20 days in one case, from 9 months to 3 years in six cases, and ≥7 years in five cases. VE was, 100% (95%CI not estimable, p = 0.03) before the outbreak (2006–2014) and 77% (95%CI 36–92, p < 0.01) during the outbreak; VE was 80% (95%CI 54–92, p < 0.01) during the overall period.

Conclusions: In Tuscany, MenC-vaccine failures occurred exclusively during the 2015–2016 outbreak. Most of them occurred several years after vaccination. VE during the outbreak-period was rather high supporting an effective protection induced by MenC-vaccines.

1. Introduction

Meningococcal vaccines impede key steps in the pathogenesis of invasive meningococcal disease (IMD), and reduce the transmission of vaccine serogroup to unvaccinated individuals by preventing the acquisition of carriage of *Neisseria meningitidis*. The introduction of meningococcal conjugate vaccines against *N. meningitidis* serogroup C (MenC-vaccines) determined a positive impact on the epidemiology of IMD due to serogroup C (MenC) meningococci [1]. In the United Kingdom (UK), the first country that introduced a national immunization program with the monovalent meningococcal C conjugate vaccine (MCC) among infants and adolescents at the end of 1999 [2], MenC-cases almost disappeared, providing evidence of the strong population effect of the vaccine [3–5]. A sharp decline in the incidence rate (IR) of MenC was also observed in Italy, as well as in other countries, after the introduction of MCC [6–9]. Herd protection was also confirmed

* Corresponding author at: Dept. of Infectious Diseases, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy.
E-mail address: paola.stefanelli@iss.it (P. Stefanelli).
[1] These authors contributed equally to the work.

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by the dramatic reduction of MenC cases observed in unvaccinated cohorts in the Netherlands [10,11], while it was not as good as expected in Spain, where vaccination coverage among adolescents was suboptimal to trigger the herd immunity in the population [12]. According to a systematic review, MenC-vaccines effectiveness is estimated to be approximately 90% or more in all age groups within the first year after vaccination [13].

The meningococcal serogroup C oligosaccharide is also contained in the tetravalent (ACWY) meningococcal conjugate vaccine [14] that was introduced in USA and Europe for the catch-up vaccination programmes among adolescents [15,16]. The effectiveness of ACWY in preventing MenC has been estimated about 80-to-85% within 3–4 years after vaccination [13]; however, the impact of this vaccine on the epidemiology of MenC has not yet been assessed.

Although most studies reported above show positive results, MenC-vaccines failure has been also described. Firstly, the protection induced by the vaccine may fall to pre-vaccination levels after 4–5 years in children vaccinated with three doses within one year of life, or with a single dose at 13-to-15 months of life [5,17]; in this case, a booster dose and catch-up campaigns among adolescents are required to maintain herd protection [18]. Secondly, the protection declines also in teenagers and adults after some years from the vaccination [19].

Of note, in vaccinated people, the immunological response may not be sufficiently rapid to prevent the invasion of hyperinvasive MenC/cc11 strain, which usually occurs within a few days after colonization [20]. Finally, in a relatively small proportion of cases, primary vaccine-failure may occur as result of the lack of initial response to the vaccine [21,22].

For all the above reasons, the US Advisory Committee on Immunization Practices (ACIP) recently recommended a booster shot of ACWY at 16 years for all those vaccinated at 11–12 years of age [23].

Since March 2015, in response to a MenC-outbreak due to the hypervirulent C/cc11 strain with the finetype P1.5-1,10-8:F3-6, occurred in Tuscany region (Italy), where routine MCC vaccination was introduced in 2006, the Regional Health Authority of Tuscany (RHAT) implemented a reactive vaccination programme with MCC/ACWY targeting adolescents and adults [24].

However, during the outbreak, several MenC cases were reported among vaccinated individuals.

The objectives of this study were: (i) to estimate the overall effectiveness of the MenC-vaccine since its introduction in Tuscany (2006–2016) and during the 2015–2016 outbreak; (ii) to describe the characteristics of the individuals vaccinated with MCC/ACWY affected by MenC invasive disease.

2. Material and methods

2.1. Setting

Tuscany is a region of central Italy, with about 3.75 million of inhabitants (around 6.2% of the Italian population) at the beginning of 2016 (around 3.57 million in 2006); the capital city is Florence [25]. In accordance with the Italian National Health Service (NHS, established on 1978, Italian law 833/78), the Regional system is based on the principles of universal coverage and social financing through the use of general taxation and non-discriminatory access to the health care services; private providers can also operate within the NHS. The territory of Tuscany is subdivided, since 1992, in 12 Local Health Units (LHU) (grouped in 3 with the regional law 84/2015 in 2015) which are responsible for the management of all health services in their area, under the regional control.

2.2. Meningococcal C vaccination strategies

MCC vaccine use was recommended for the first time in the 2005' Italian National Immunization Plan, with a single dose at 13–15 months of age. After its introduction in 2006, some Italian Regions also implemented a catch-up strategy among those aged 11–20 years using ACWY [26]; both vaccination strategies are implemented free of charge.

Tuscany was the first Italian region to introduce a single dose of MCC at 13–15 months of age in 2006 and to implement a catch-up program since 2007 among those aged 11–20 years with ACWY. Vaccines are usually administered by the vaccination centers located in the districts of the local health authorities. Primary care pediatricians may sometimes perform vaccinations. In both cases, for each vaccinated child, information on type of vaccine performed and date of vaccination is registered at local health unit level.

In response to the sharp increase of MenC-cases since January 2015, the RHAT implemented a mass vaccination campaign targeting individuals between 11 and 45 years old with MCC/ACWY vaccines, and extended this campaign also to people over 45 years in January 2016. After the outbreak, in 2017, the Region introduced an additional booster dose of MCC at 6–9 years of age [27].

2.3. Surveillance system, vaccine coverage data and definition of vaccine failure

In Italy, all cases of IMD are notified in the frame of the National Surveillance System of Invasive Bacterial Diseases (IBD), coordinated by the Istituto Superiore di Sanità (ISS). The case definition of IMD in Italy is based on the EU Commission Decision 2012/506/EU, 8 August 2012 [28]. Confirmed cases are reported to regional and national authorities through the LHUs. For each IMD case, epidemiological information (including the vaccination status) and samples (isolate, blood and/or cerebrospinal fluid, when available) are sent to the ISS for further confirmation and characterization. The immunization status of IMD cases is collected by LHUs during the epidemiological investigation using LHUs vaccination registries; then it is reported into the IBD reporting form, which mandatorily requires this information within the frame of the enhanced IBD surveillance. Serogroup by slide agglutination and/or by Polymerase chain reaction (PCR) and the genomic profile of meningococcal DNA were defined by ISS. Multilocus sequence typing (MLST), PorA and FetA typing, Bexsero antigen genes are also identified referring to http://neisseria.org/. The finetype is identified as follows: capsular group: *porA* (P1). VR1, VR2: *fetA* VR: ST (cc). Moreover, the alleles Neis0430, *penA*, *porB*, and the *fHbp* variant are determined (http://neisseria.org/platform), as well as the electrophoretic type (ET) [29].

To the purpose of this study, data on confirmed MenC-cases occurred in Tuscany were drawn from the IBD database for the period 2006–2016. MCC/ACWY coverage data related to the Tuscany Region population were collected by the regional annual reports. These reports contain the number of all vaccinations (stratified by vaccine preventable disease) performed by birth cohort. These numbers are obtained summing all documented vaccinations performed by both the public vaccination centers and primary care paediatricians within each LHU. Aggregated annual MCC/ACWY coverage data (i.e., number of vaccinated individuals by year (2006–2016) were available, stratified by birth-cohort (1994–2014) and LHU (n = 12). Information on the type of vaccine administered (i.e., MCC or ACWY), time of administration, and booster doses was not available.

Annual population data of Tuscany stratified by LHU and birth cohort was obtained from the Italian National Institute of Statistics (ISTAT, www.demo.istat.it).

We used the definition of MenC related vaccine-failure reported in the World Health Organization (WHO) Position Paper on Meningococcal Vaccines: a laboratory confirmed MenC-case occurring ≥10 days after vaccination with a meningococcal serogroup C vaccine [30].

2.4. Statistical analyses

Descriptive characteristics of MenC-cases and related vaccine-failures occurred during the years 2006–2016 were provided. The case fatality rate (CFR) was calculated as the proportion of those died within one week after symptoms onset. The CFR stratified by vaccination status was also estimated. The Chi-square test was calculated to evaluate the statistical significance of the associations. The association of CFR with vaccination status (i.e., vaccinated vs. unvaccinated) was evaluated after adjusting by age at MenC symptoms onset by a logistic model.

MenC IRs per 100,000 population by year were calculated to evaluate the time trend.

To analyze the effectiveness of MenC-vaccines we used the routine annual report on vaccinated individuals by birth-cohort and LHU of residence. Then, after subtracting the number of vaccinated from the population of Tuscany (by year, birth-cohort, and LHU), the population was subdivided every year (from 2006 to 2016) in vaccinated and not vaccinated, stratifying by LHU and birth-cohort. Given that population size and number of vaccinated people referred to the end of each year, annual person-years (PY) by vaccination status, birth cohort, and LHU were calculated as the arithmetic mean of two consecutive years. We included in the vaccine effectiveness (VE) analysis only birth-cohorts 1994–2015 (people aged 1–22 years at the end of the study period), because vaccination data were available only for these cohorts. MenC IRs per 100,000 PY were estimated as the ratio between cases multiplied by 1,000,000 and the PY. IRs were stratified by vaccination status, calendar-period (2006–2014 and 2015–2016), LHU, and birth-cohort. The incidence rate ratio (IRR) was then calculated by vaccination status and stratified by calendar-period. Multiple regression models for count (i.e., Poisson, negative binomial and zero inflated Poisson) were performed to evaluate the IRR between vaccinated and non-vaccinated individuals, adjusting by birth-cohort, calendar-period (2006–2014, 2015–2016), and LHU. We also performed a multilevel Poisson regression model using the calendar-period and vaccination-status as covariates, and the LHU as grouping variable.

Because all these models estimated similar adjusted IRR for vaccination-status and calendar-period, and, furthermore, birth-cohort and LHU did not provide a significant increase in terms of goodness to fit for each class of model, the latter two variables were not included in the final model.

Due to the similarity of the estimates, only the results of the Poisson model without the multilevel effect due to LHU were shown in the results section.

VE was calculated with the formula: (1 − IRR (or adjusted IRR [AIRR]) * 100 [31]. We reported 95% confidence intervals (95% CI) to measure the uncertainty; a p-value <0.05 was defined as statistically significant. All analyses were performed by Stata software (version 13.0).

2.5. Ethical consideration

The study was carried out in accordance with the Helsinki Declaration of 1975. Ethical approval was not required because the study was based on data routinely collected.

3. Results

3.1. Surveillance data

In the period 2006–2016, 85 MenC cases were reported to the IBD surveillance system; of them, 61 (71.8%) occurred in the years 2015–2016 (31 cases in 2015 and 30 in 2016) (Table 1). In the period 2006–2014, 24 MenC-cases were reported, ranging from zero in 2010 to five in 2008, with an overall IR of 0.07 per 100,000 PY and no significant changes by calendar year (p = 0.26). The IR significantly increased during 2015–2016 (0.81 per 100,000 PY; p < 0.01) compared to the period 2006–2014. Overall, vaccine-coverage increased during the study period, reaching the highest value at the end of 2016 (83.6%).

No vaccine failures occurred in the pre-outbreak period (2006–2014), while 12 (21% of 61) vaccine failures were reported in 2015–2016.

Of the 12 cases among vaccinated individuals, 3 (25.0%) occurred in 2015 and 9 (75.0%) in 2016. Of them, 3 (25.0%) were vaccinated with ACWY and 9 (75.0%) with MCC; none received two doses of MCC and/or ACWY (Table 2). The time interval from vaccination to symptoms onset was >7 years for five cases (cases: 1, 2, 4, 9, 10), ≤3 years for six cases (cases: 3, 6, 7, 8, 11, 12), and 20 days in one case (case 5).

The median age of MenC-cases classified as vaccine failures was 14.5 years (range: 4–58) compared with a median age of 28 years (range: 2 months–84 years) of the unvaccinated cases (p < 0.01).

The case fatality rate (CFR) was 18.8% in the period 2005–2016; during the outbreak period (i.e., 2015–2016) the CFR was 21.3% compared to 12.5% in the previous period (p = 0.35). Older patients had a significantly higher CFR (OR = 1.47 per ten-years increase, 95%CI: 1.15–1.88, p < 0.01). The CFR was lower in vaccinated (only one died) than in unvaccinated MenC-cases, but the difference was not statistically significant (8.3% vs. 20.5%, p = 0.32). Similar results were observed when restricting this comparison to MenC-cases occurred during the outbreak period (8.3% vs. 24.5%, p = 0.22) and further restricting to those born between 1994 and 2015 (11.1% vs 18.2%, p = 0.66) (data not shown). No pre-existing clinical condition emerged among the 12 vaccinated cases; the vaccinated person who died had received a vaccine dose 8 years before symptoms onset with a documented transitory immunosuppression at the time of immunization.

The C:P1.5-1,10-8:F3-6:ST-11 (cc11) (Neis0430/*penA* 398/248) (*porB* 2-2) (fHbp 1.13) (ET-15) strain was isolated in all MenC vaccinated cases (data not shown).

3.2. Vaccine effectiveness analyses

The descriptive characteristics of the IMD cases included in the VE-analyses (i.e., only birth-cohorts 1994–2015 [people aged 1-to-22 years at the end of the study period] are shown in Table 3. Overall, 25 MenC-cases belonging to the births-cohorts 1994–2015 were included, 9 of them (36.0%) were classified as vaccine-failures.

Table 4 shows the results of the effectiveness analysis of MenC-vaccines. VE was 100% (95%CI not estimable; p = 0.03) during 2006–2014 compared with a VE of 77% (95%CI 36–92; p < 0.01) during 2015–2016. Combining the two periods there was an overall reduction in the VE (47%; 95%CI 0–79; p = 0.13) with an apparent non-significant protection of MenC-vaccines. However, this estimate was largely confounded by the impact of the outbreak started in 2015. In fact, in the multiple Poisson regression model adjusted for the effect of the calendar period (grouped as 2006–2014 and 2015–2016), the overall estimated vaccine effectiveness was 80% (95%CI 54–92; p < 0.01).

Table 1
Number and incidence rate (IR) per 100,000 population of serogroup C invasive meningococcal diseases cases by year and vaccination status, Tuscany, Italy, 2006–2016.

Year	Vaccinated (n)	Not vaccinated (n)	Total (n)	IR (per 100,000)	Coverage^
2006	0	2	2	0.06	8.7
2007	0	3	3	0.08	13.0
2008	0	5	5	0.14	17.8
2009	0	4	4	0.11	22.5
2010	0	0	0	0.00	35.5
2011	0	1	1	0.03	45.5
2012	0	4	4	0.11	57.6
2013	0	3	3	0.08	65.0
2014	0	2	2	0.05	68.9
2015	3	28	31	0.83	74.1
2016	9	21	30	0.80	83.6

^ Coverage refers to birth cohorts 1994–2015.

Table 2
Detailed information on the twelve cases of serogroup C invasive meningococcal diseases occurred among vaccinated. Tuscany, Italy.

N	Month/year of vaccination	Age at vaccination	Month/year IMD-C onset	Age at IMD-C onset	Interval vaccination to IMD-C onset	Type of vaccine
1	February 2006	13 months	January 2015	9 years	8 years & 11 months	MCC
2	February 2007	4 years	February 2015	12 years	8 years	MCC
3	March 2013	14 years	May 2015	17 years	2 years & 2 months	MCC
4	January 2008	14 years	January 2016	22 years	8 years	MCC
5	March 2016	58 years	March 2016	58 years	20 days	MCC
6	May 2015	47 years	July 2016	48 years	14 months	ACWY
7	March 2014	13 months	September 2016	3 years	2 years & 6 months	MCC
8	December 2015	19 years	October 2016	20 years	10 months	ACWY
9	October 2008	13 months	November 2016	9 years	8 years & 1 month	MCC
10	September 2009	16 months	November 2016	8 years	7 years & 2 months	MCC
11	December 2013	14 months	December 2016	4 years	3 years	MCC
12	March 2016	20 years	December 2016	20 years	9 months	ACWY

MCC: monovalent meningococcal C conjugate vaccine; ACWY: tetravalent meningococcal conjugate vaccine; IMD-C: invasive meningococcal disease serogroup C.

Table 3
Descriptive characteristics of the 25 cases of serogroup C invasive meningococcal disease included in the vaccine effectiveness analysis (birth-cohorts 1994–2015 & age at onset >1 year). Tuscany, Italy, 2006–2016.

		Not vaccinated		Vaccinated		Total
		N	%	N	%	
Age at onset	1–4	5	71.4	2	28.6	7
	5–9	0	0.0	2	100.0	2
	10–14	2	50.0	2	50.0	4
	15–24	9	75.0	3	25.0	12
Year of birth	1994–1999	9	75.0	3	25.0	12
	2000–2007	7	70.0	3	30.0	10
	2008–2014	0	0.0	3	100.0	3
Year of onset	2006	1	100.0	0	0.0	1
	2007	2	100.0	0	0.0	2
	2008	2	100.0	0	0.0	2
	2009	1	100.0	0	0.0	1
	2011	0	–	0	–	0
	2012	0	–	0	–	0
	2013	0	–	0	–	0
	2014	0	–	0	–	0
	2015	6	66.7	3	33.3	9
	2016	4	40.0	6	60.0	10
Total		16		9		

Note: three vaccinated cases were excluded from this analysis because born before 1994 (1993, 1968, 1957); three non-vaccinated cases were excluded because they were <1 year-old at the date of symptoms onset.

4. Discussion

This study assessed the effectiveness of MenC-vaccines since its introduction in Tuscany, Italy, and during an outbreak of IMD due to *N. meningitidis* serogroup C/cc11 occurred in the Region during 2015–2016.

Since the introduction of MCC in 2005 and ACWY in 2007, no vaccine failures were reported in Tuscany up to the end of 2014. Then, during the 2015–2016 outbreak, twelve cases occurred among vaccinated persons. Vaccine batches investigation found no-vaccine-related issues; in fact, vaccine failures involved 12 different batches from three different brands, which were used also in other Italian Regions where no IMD-C related vaccine-failures were reported (data not shown). This finding suggests that vaccine failures observed during the outbreak were, to some extent, related to the clonal expansion of the C:P1.5-1,10-8:F3-6:ST-11 (cc11)

Table 4
Incidence rates (IR) per 100,000 population, risk ratio (RR) and meningococcal C conjugate vaccine effectiveness Tuscany, Italy, 2006–2016.

Calendar period	Vaccination status	Person-years	IMD-C cases	IR	Crude RR (95%CI)	Effectiveness (95%CI)	p
2006–2014	*Vaccinated*	1,895,597	0	0.00	0.00 (NE)	100% (NE)	0.03
	Not vaccinated	2,516,133	6	0.24	(ref)		
2015–2016	*Vaccinated*	1,044,351	9	0.86	0.23 (0.08–0.64)	77% (36–92)	<0.01
	Not vaccinated	270,504	10	3.70	(ref)		
2006–2016	*Vaccinated*	2,939,948	9	0.31	0.53 (0.21–1.28)	47% (0–79)	0.13
	Not vaccinated	2,786,637	16	0.57	(ref)		
					ARR* (95%CI)		
2006–2016	*Vaccinated*				0.20 (0.08–0.46)		
	Not vaccinated				(ref)	80% (54–92)	<0.01

IR: incidence rates; RR: risk ratio; IMD-C: invasive meningococcal disease serogroup C; NE: not estimable.
* Adjusted risk ratio by calendar period (ARR 2015–2016 vs. 2006–2014: 19.2; 95%CI: 7.4–49.8; p < 0.01).

hypervirulent strain [25]. To this regard, Auckland et al. [20] reported that the strain C:ST-11/cc11 was found in 86% of MCC/ACWY vaccine failures observed in the UK; these findings supported the hypothesis that the immune response during the infection with this strain may be not sufficiently rapid to prevent bacterial invasion. Five cases (Table 2, cases 1, 7, 9, 10, 11) received only one dose of MCC at 13–16 months of age, according to the National immunization schedule, and developed IMD from 2 to 8 years after vaccination. The hypothesis that vaccine failures were related to the single dose administered is suggestive even though not consistent with the findings of another study [11] which did not find evidence of a lower efficacy of a single dose schedule compared with a two-doses regimen. On the other hand, three of these five vaccine failures (Table 2 cases 1, 9, 10) occurred after 7–8 years since vaccination, thus they were likely to be associated with a decrease of serum protection (secondary failures) [19,32]. Furthermore, it should be noted that MenC cases in Tuscany dramatically declined after the implementation of the immunization campaign, and only ten cases (all due to the same hypervirulent strain) during the year 2017; among them, only one vaccine-failure was observed (a 41-years-old man vaccinated with ACWY nine months before IMD case). In fact, the estimated VE was high even in the outbreak period, thus we may assume that the vaccine was highly protective also against the epidemic strain. A limited number of cases occurring among vaccinated individuals is expected, then a large proportion of the population is immunized but the herd immunity threshold is not reached, considering that vaccine efficacy, though very high, is likely to be – to some extent – lower than 100%.

Of note, the case fatality rate was higher among unvaccinated than vaccinated patients, suggesting a protective role of the vaccine. However, this effect was not statistically significant perhaps due to the limited number of vaccinated patients. The only vaccinated person who died had been vaccinated 8 years before and was affected by a transitory immunosuppression condition at the time of vaccination.

After the reactive immunization campaign, the number of cases decreased dramatically. Unlike the meningococcal C polysaccharide vaccine, which had no effect on *N. meningitidis* serogroup C carriage, meningococcal C conjugate vaccines appear to provide high levels of protection in the short term [33,34], reducing the prevalence of serogroup C asymptomatic carriage and contributing to herd immunity [35–37]. However, the duration of the protection seems to be age-dependent, being longer in older children compared with infants [38]. Adolescents have both the highest rates of transmission and carriage, thus they are likely to sustain meningococcal circulation in the population. Mathematical models suggest that the elimination of the serogroup C meningococcal disease depends on the degree and the duration of protection conferred by vaccination [39] and that the introduction of a booster dose in adolescents may have both an individual and herd immunity effect. For this reason, teenagers are now considered the main target for large catch-up campaigns [40]. This finding is consistent with our analysis showing that, after reaching high vaccine coverage among adolescents, the outbreak was kept under control.

Possible limits of this study were represented by the unavailability of data by type of vaccine administered (i.e. MCC or ACWY), that did not allow a separate analysis for MCC and ACWY, time of administration, and booster doses. Moreover, the availably of vaccination coverage data only for the birth-cohorts 1994-to-2015, restricted the VE analysis to the 1–22 age-group. Regarding vaccine failures, the small number of vaccine failure cases observed during the 11-year study period (n = 16) prevents any firm conclusion regarding the potential causes of vaccine failures, although they occurred during an outbreak due to a hypervirulent meningococcal strain [25]. Further, we adjusted our vaccine effectiveness estimates only for place of residence (LHU), calendar year, and birth cohorts. Other factors that may be associated both with disease risk and immunization status were not controlled for (i.e. socio-economic status, or day-care nursery attendance). to this regard, it should be mentioned that a case-control study on the effectiveness of meningococcal polysaccharide vaccine in Quebec [41] showed that unadjusted VE estimates were systematically higher than adjusted VE estimates among children, after taking these factors into account.

5. Conclusions

The introduction of MenC-vaccines in children and adolescent immunization programs may dramatically reduce the spread of MenC [39]. Nevertheless, the possible rapid loss of protection suggests that a booster dose might help to maintain herd protection in the population, ensuring the success of immunization programs [40].

The results of our study confirm the high effectiveness of MenC-vaccines even in case of outbreaks sustained by the hypervirulent MenC strain. These data support the adoption of reactive vaccination programs as an outbreak control strategy.

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Conflict of interest

Authors declare no conflict of interest.

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