

ORIGINAL ARTICLE

Do Tuscan people adhere to meningococcal C vaccination during an emergency campaign?

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Keywords

Meningococcal C invasive disease • Vaccination coverage • Emergency immunization campaign • Population adherence • Tuscany

Summary

Objectives. Tuscany region (Italy) recorded a rise in the number of meningococcal disease cases between January 2015 and February 2016, (52 cases) compared to 2014 (16 cases). The aim of this study was to describe the emergency meningococcal C (MenC) vaccination programme in Tuscany and the population's adherence to the activities performed in the Local Health Unit (LHU) of Florence.

Methods. The MenC vaccination programme and the planning of the prevention and communication activities were analysed in the LHU of Florence. As an indicator of population's adherence, the vaccination coverage (VC) during the emergency campaign was investigated and adverse drug reactions (ADR) surveillance was reported.

Results. The communication campaign included a dedicated toll-free telephone number, press releases (newspapers, radio, television, websites), and informative letters addressed to may-

ors, secondary schools, and sports associations. Citizens aged 11-20 years were the primary target of the campaign. Due to the high incidence of cases among older people, the vaccination was extended to subjects over 45 years. The population's adherence to the vaccination campaign was satisfactory: VC reached 47.1% for the primary target. The ADR reporting rate (3.1/10,000) on meningococcal vaccine in our study confirmed the safety of the vaccination.

Conclusions. In 2017, only 10 cases of invasive meningococcal diseases (IMD) were reported, suggesting the effectiveness of the immunization campaign. Similar VC during emergency MenC vaccination programmes have been reached in other Italian regions and other EU countries, too. The achievement of greater vaccination coverage is restricted by a sentiment of hesitancy towards vaccines among the general population.

Introduction

Neisseria meningitidis represents a major cause of meningitis and septicaemia, and it is also a leading cause of morbidity and case fatality rate in all age groups worldwide. Meningococcal disease can lead to permanent sequelae, such as skin scarring, abnormal bone growth, limb loss and multiple amputations, hearing loss, cognitive deficits and visual impairment [1-3]. In Europe, most cases of invasive meningococcal disease (IMD) are caused by serogroups B and C, and the annual notification rate was between 0.55/100,000 population and 1.19/100,000 in the period 2004-2014 [4]. In Italy, the incidence of meningococcal disease was 0.27/100,000 in 2014 [5].

Italian regions can implement different immunization policies and Tuscany was one of the first to recommend meningococcal C vaccination [6]. Since 2005, Tuscany, a central region of Italy with around 3,750,000 inhabitants, has offered the meningococcal C conjugate (MenC) vaccine free of charge at the regional level to all newborns, in the form of a three-dose MenC schedule at three, five, and 13 months of age and a catch-up dose to the children up to six years of age. Since 2008, the MenC vaccine has been of-

ferred to all children in a single-dose schedule at 13 months of age, along with the catch-up strategy. This immunization program has proved to be effective in preventing IMD among the birth cohorts involved in the regional offer. Between 2005 and 2014, the number of IMD cases decreased drastically and no cases occurred among the vaccinated subjects [7]. In addition, since 2014, a catch-up dose of quadrivalent conjugate ACWY vaccine has been offered free of charge to adolescents aged between 11 and 18 years who were never vaccinated [8].

However, an increased number of meningococcal disease cases was observed in Tuscany between 2015 and 2016 compared to the previous years. A total of 38 cases occurred in 2015 (31 serogroup C, 5 serogroup B, 1 serogroup W and 1 unknown) and 41 cases in 2016 (30 serogroup C, 8 serogroup B, 1 serogroup W, 1 serogroup X and 1 unknown), while only 16 cases (9 serogroup B, 3 serogroup Y, 2 serogroup C, 1 serogroup A and 1 unknown) had occurred in 2014 [9]. In most cases, molecular typing identified meningococcal serogroup C clonal complex ST-11: a particularly virulent clone of *N. meningitidis* [10].

The unexpected increase in the number of meningococcal disease cases was reported to the surveillance

system. This called for an appropriate public health intervention, including an emergency immunization campaign, which started from April 2015.

The current study was aimed at describing the emergency meningococcal C vaccination programme in Tuscany and the population's adherence to the activities performed in the LHU of Florence – with around 815,000 inhabitants – between January 2015 and February 2016.

Methods

EMERGENCY MENINGOCOCCAL C VACCINATION PROGRAMME IN TUSCANY AND THE PLANNING OF PREVENTION ACTIVITIES IN THE LHU OF FLORENCE

Regional deliberations on the meningococcal C vaccination offer were collected for January 2015 - February 2016, and the whole vaccination programme in Tuscany was analysed.

The planning and communication activities of the emergency vaccination programme in the LHU of Florence were deeply analysed and described. In our analyses, we considered the professionals who were involved in the organization and monitoring of the vaccination campaign or in administering the vaccine. Moreover, we also investigated the settings that were selected for the administration of the vaccine.

We also analysed how the need for the vaccine doses to be administered to the target population was estimated and how often the vaccination demand was evaluated to adapt the vaccines supply.

DATA COLLECTION, REPORTING, AND THE ANALYSIS OF COMMUNICATION ACTIVITIES AND THE POPULATION'S ADHERENCE TO THE EMERGENCY CAMPAIGN

We analysed the communication strategies developed to improve population's adherence. We also evaluated how the vaccine was administered and which professionals were involved in it.

The demand for vaccination, the available slots, and the first date available for vaccination were also investigated.

Immunization coverage was calculated for the age groups involved in the vaccination programme among the resident population between April 2015 and February 2016. Immunization coverage was defined as the percentage of vaccinated individuals among the resident population of the target group and was calculated for the age group initially involved in the vaccination campaign (11-45 years). The vaccination coverage was not calculated for the age group of over 45 years because the period of analysis included less than a month after the recommendation to extend the vaccination offer to older age groups. In fact, during the campaign, the meningococcal C vaccination was even extended to the entire population in particular

areas of the region. A filled out consent form was collected from all the vaccines and for those aged more than 55 years additional information were provided: they were informed that no studies were available on the efficacy of the vaccine for people aged over 55 years.

Adverse reactions following vaccine administration were collected and monitored using the adverse drug reaction (ADR) reporting system. ADR records regarding subjects not involved in the target population of the emergency campaign were excluded.

Results

REGIONAL DELIBERATIONS AND WORKING GROUP

To face the increasing incidence of IMD cases starting from 2015 in Tuscany, one dose of meningococcal ACWY quadrivalent vaccine was offered free of charge to adolescents (11-18 years, including previously vaccinated subjects). Subsequently, the offer was extended to people aged 18-20 and 21-45 living in the LHUs, where at least one case of meningococcal C disease had occurred [11, 12]. Due to the high occurrence of cases among people aged over 45 years, in February 2016, the meningococcal vaccination was extended to all people aged over 11 years free of charge in the LHUs where meningococcal cases have been reported. Particularly, the meningococcal quadrivalent ACWY vaccine was offered to people aged between 11 and 20 years and the monovalent meningococcal C vaccine to people aged over 20 years (Fig. 1) [13].

For citizens aged over 45 years living in the other areas of Tuscany, the meningococcal vaccines were available on the basis of co-payment, with a reduced ticket [13].

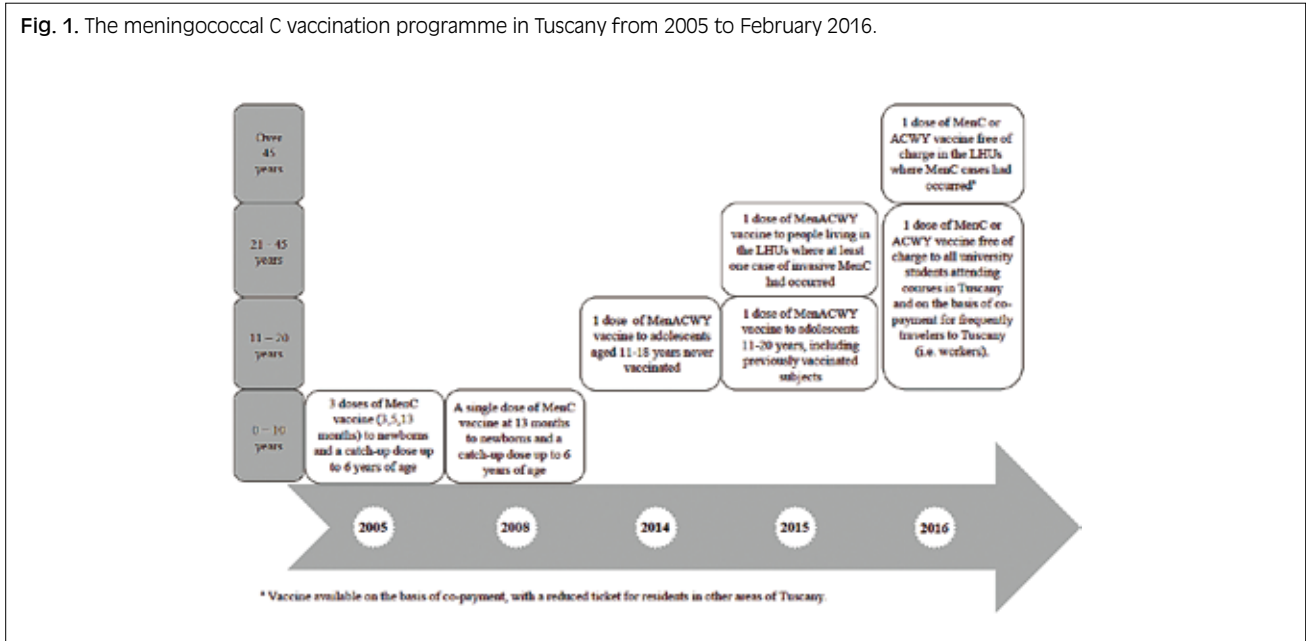
To reach the objectives established by the regional health authorities, a multidisciplinary working group was constituted in the LHU of Florence to plan and organize the emergency campaign. In particular, the following professionals were involved: the Health Directorate of the LHU, the Hygiene and Public Health Service Operative Unit (OU), the Responsibles of the Health Service Booking Centre, and the Health Care Assistance OU.

PLANNING OF THE CAMPAIGN: IDENTIFICATION OF TARGET POPULATION, VACCINATION SETTINGS AND HEALTHCARE PROFESSIONALS INVOLVED

The first step was to quantify the target population of the vaccination programme and the available places for administering the vaccine, both in a hospital setting and in the public health districts.

At the beginning of the campaign, the target population of the vaccination programme consisted of 310,410 people aged between 11 and 45 years in the LHU of Florence. After the extension of the vaccina-

Fig. 1. The meningococcal C vaccination programme in Tuscany from 2005 to February 2016.



tion offer to people aged over 45 years, the number increased to 743,128.

The vaccine was administered at 19 vaccination sites: five in hospitals and 14 in health districts over an area of 2,779 km².

Healthcare professionals working in the public health services administered the vaccines. Each vaccination centre was assigned to a responsible physician, and one or more healthcare assistants were simultaneously involved in the administration of vaccinations.

To guarantee the vaccination offer, additional employees – doctors, nurses, and healthcare assistants – were hired during the monitoring period. Based on shared guidelines, people with a history of allergy or anaphylactic reactions were referred to the Allergy and Clinical Immunology Unit in a hospital care setting, where personnel with expertise in the management of allergic conditions could guarantee additional safety measures.

Moreover, to improve the administration of vaccines, the LHU Health Directorate entered into an agreement with General Practitioners (GPs) and Primary Care Paediatricians. Each physician involved in the campaign had to confirm his/her participation on a voluntary basis via email to a dedicated address. The list of the paediatricians and GPs participating in the vaccination campaign was available on the LHU website. The LHU operators provided the list of unvaccinated patients of the primary target age group (11-20 years) to each GP or paediatrician to increase the immunization coverage of their patients.

As far as primary care was concerned, 88 among 109 primary care paediatricians (80.7%) and 412 among 606 GPs (68%) participated in the emergency vaccination programme.

Moreover, an agreement was established with some voluntary associations to organize vaccination clinics

for the volunteers themselves and it was subsequently extended to all citizens.

In addition, the LHU involved their occupational physicians to provide meningococcal C vaccine doses to private companies interested in getting their workers vaccinated.

COMMUNICATION ACTIVITIES

The communication campaign with the population included different strategies to improve population's adherence.

Firstly, a dedicated toll-free telephone number, managed by healthcare assistants, was activated to offer information regarding the vaccination programme. If the line was busy, people could leave a voice message with their name and telephone number, to be called later by a healthcare assistant.

During the whole immunization campaign, several press releases – in newspapers and on the radio, television, and websites – were issued at the regional and local levels [14, 15].

Letters containing information regarding the disease and the vaccination campaign were sent to mayors, to secondary schools, local education agencies, and sports associations.

Moreover, vaccine promotion days for voluntary associations were also organized. In particular, the vaccine days were promoted with the support of the Italian Red Cross.

Since October 2015, about 8,000 informative SMSs were sent to people aged between 18 and 20 years who had previously accessed the Booking Centre number. The SMS text was as follows: "LHU of Florence reminds free meningococcal C vaccination for citizens aged 11-45 years". In the same period, an informative voice message on the meningococcal C campaign was

relayed during the waiting time before speaking to the operator at the LHU Booking Centre. Reminders for vaccination appointments were sent via SMS the week before the scheduled date. Public health and primary care services also played an important role in the communication strategy. They informed people about the disease, its prevention through vaccination, and the way to access immunization services (Fig. 2).

MONITORING OF VACCINATION DEMAND, COVERAGE AND ADR

The working group for the evaluation of the vaccine campaign monitored the vaccination demand continuously, on a daily basis. The weekly average trend of vaccination demand from April 22, 2015 to February 29, 2016 and the day of the onset of the IMD symptoms have been shown in Figure 3.

Following the first IMD cases, the weekly demand for vaccination increased twofold from the first to the second week of monitoring. The values increased from 538 to over 1,000 weekly contacts.

During summer, the average weekly demand for vaccination reached its lowest level.

The highest values were recorded in February 2016. In week 45, 3,280 daily contacts were registered on an average, with more than 4,000 requests being received on workdays and a peak of 5,334 contacts.

During the monitoring period, the demand for vaccination was zero or very low on weekends or national holidays. Only in the last month of the observation period, even during the weekends, an average of more than 400 contacts was registered.

Public health service professionals recorded vaccinations in a computerized immunization register or in paper forms, while the GPs and Primary Care Paediatricians emailed periodic reports to the LHU staff. During the evaluation period (April 2015 - February 2016) 64,998 subjects aged between 11 and 45 years

(32,053 in the 11-20 age group and 32,945 in the 21-45 age group) were vaccinated, reaching the coverage of 21%. The vaccination coverage obtained in the LHU of Florence and in Tuscany has been reported in Table I.

In the LHU of Florence, 20 adverse reactions in the target population were notified to the reporting system in that period. Among the about 65,000 administered doses, 18 mild reactions (fever, swelling, redness and pain at the injection site, general feeling of discomfort, and headache) were reported. Only two severe reactions, both with complete recovery, were reported to the monitoring system. One case was of convulsion and bradycardia and another of hyperpyrexia and delirium.

The ADR reporting rate in the overall period was 3.1/10,000. The mean age of the people with an adverse reaction was 28 years (range: 11-43 years).

Discussion

The regional emergency meningococcal C vaccination campaign was planned and implemented in an extremely short time. Moreover, it was continuously adjusted to the evolution of the epidemiological situation.

The main goal of the vaccination programme was to protect adolescents and young adults – the most susceptible subgroups of the population – and to reduce the bacterial circulation among the general population, by means of the herd immunity effect, through the vaccination of people aged 11-20 years with a single dose of meningococcal ACWY vaccine.

The achievement of high coverage rates among adolescents is an important public health issue, in order to reduce the nasopharyngeal carriage [16]. Conversely, the vaccination offer to older people mostly represents an individual preventive measure.

In 2015, the incidence of meningococcal disease of serogroup C in Tuscany was 0.83/100,000, about three times higher than the previous years. The median age of the cases was 28 years (range 3-82). Most of the cases occurred in people aged 15-20 and 21-30 years, with incidence rates of 3.23/100,000 and 2.83/100,000 respectively [17].

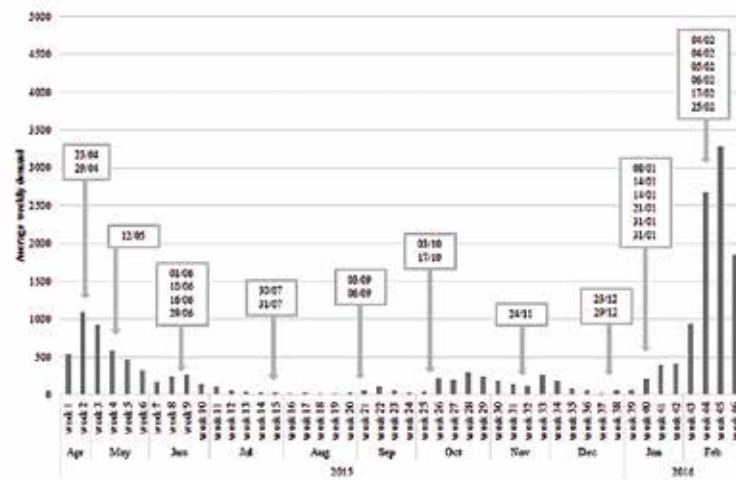
Usually, in the previous years, the highest incidence of IMD was observed in the younger age groups [7, 16]. In Tuscany, a consistent number of cases (28%) has occurred in people older than 50 years since 2015. Of that, 19% has occurred in people aged over 65 years. The increase in the number of IMD cases among adults in Tuscany can be partly explained by the extension of the bio-molecular diagnostic method to adults since 2015 [18].

As expected, the occurrence of each new meningococcal invasive case generated a rise in vaccination demand. In particular, in February 2016, weekly contacts on workdays were almost 3,000 on an average, reaching peaks of over 4,000 requests per day.

Fig. 2. The LHU of Florence vaccination programme. Organization and communication strategies during the emergency meningococcal C campaign in Tuscany.



Fig. 3. The average weekly demand for meningococcal vaccination and the date of invasive meningococcal cases^a (the date of the onset of symptoms in the cases have been reported in the boxes) in Tuscany (April 22, 2015 - February 29, 2016).



The doses supply and vaccination demand were checked daily so as to modulate the offer. The vaccine doses availability was monitored to ensure an adequate response to the vaccination demand for the following days. To meet the increased demand for vaccines, the doses were also obtained from abroad and, starting from February 2016, it was decided that the monovalent C vaccine would be used as an alternative to the tetravalent vaccine for people aged over 20 years.

The VC calculated is the most effective measure of the population’s adherence to the emergency vaccination campaign. Concerning the period investigated in this study, after 11 months of emergency campaign in the LHU of Florence, as well as in Tuscany, around 21% vaccination coverage was achieved among 11- to 45-year-old people, while almost half of the primary target (subjects aged 11-20) in Tuscany were vaccinated in the observation period. This VC was obtained thanks to interventions targeting adolescents through school-based communication activities, involvement of sports associations and SMS with informative text on the vaccination campaign sent to subjects aged 18-20 years.

Similar emergency meningococcal C vaccination programs have also been planned in the last decades in other Italian regions, such as Veneto, as well as in other EU countries, due to the changes in IMD incidence rates [19-21].

In 2007, a cluster of IMD cases, due to the same clonal complex ST-11, was reported among subjects aged between 15 and 33 years in Veneto. A campaign was started to offer meningococcal C vaccination to all inhabitants aged between 15 and 29 years living in the province of Treviso where the cases occurred. The overall vaccination coverage was 60%, but it decreased to 40% in the older age group [20, 21].

Tab. I. The meningococcal C vaccination coverage for people aged 11-20 and 21-45 years in the Local Health Unit of Florence and in Tuscany (April 2015 - February 2016).

Age group	Vaccination coverage in LHU of Florence	Vaccination coverage in Tuscany
11-20 y ^a	47.1%	46.3%
21-45 y ^b	13.6%	14.1%
Total	20.9%	21.2%

^a: LHU of Florence inhabitants - 68,082; Tuscany inhabitants - 317,911; ^b: LHU of Florence inhabitants - 242,328; Tuscany inhabitants - 1,119,990.

In England and Wales, the meningococcal vaccination campaign consisted of a vaccination offer to all newborns and citizens aged between five months and 17 years. GPs administered the vaccine to children up to five years, while the subjects belonging to the 6-17-year-old age group were vaccinated in schools. The overall coverage achieved through the school-based campaign was at least 85%. The highest vaccination coverage was reached among children aged between 8 and 12 years, while it was the lowest (43%) among 15- to 17-year-olds. Adolescents represent a difficult group to reach for vaccination and the results obtained in Tuscany are similar to those in the UK [22].

Nevertheless, IMD cases continued to occur in Tuscany and some cases were also registered among the vaccinated subjects. The occurrence of IMD in the vaccinated subjects has been reported in other EU countries, too [23]. However, in Tuscany, the fatal cases in 2015 occurred only in the subjects who were never vaccinated or who were vaccinated many years before. Following this evidence and in accordance with confirmation from scientific literature, Tuscany region recommended meningococcal vaccination for all adolescents, included the subjects already vaccinated in childhood [24, 25]. Currently, in Tuscany, meningococcal C vaccination consists of a three-dose

schedule: the first dose at 13-15 months (monovalent vaccine), the second dose at six to nine years (monovalent vaccine), and the third dose at 13-20 years (quadrivalent ACWY vaccine). This strategy is supported by the evidence that meningococcal serogroup C antibody levels wane rapidly after meningococcal conjugate vaccination among young children, leaving adolescents with low antibody levels. Booster doses are needed to sustain antibody levels in teens. Moreover, in Tuscany, the second (or the third) dose with meningococcal ACWY vaccine is guaranteed to subjects aged between nine and 20 years already vaccinated more than five years previously. During the transition to the new vaccination schedule with three doses, vaccination is also assured for unvaccinated subjects aged up to 20 years [26].

Our results described about a year of emergency campaign in the LHU of Florence and the population's adherence to the vaccination offer. When this report was being written, the emergency meningococcal C vaccination campaign in Tuscany was still going on and the number of primary care physicians involved in the vaccination campaign had increased [27].

In 2017, only 10 IMD cases were reported, suggesting the effectiveness of the meningococcal immunization campaign among adolescents and the general population [28]. The achievement of greater vaccination coverage is restricted by a sentiment of hesitancy towards vaccines among the general population, especially as far as the safety issues of vaccinations are concerned. However, the ADR reporting rate on meningococcal vaccine for our study confirms the safety of the meningococcal vaccination, even for adolescents and adults.

Conclusions

IMD cases in Tuscany sparked alarm among the general population and prompted the health authorities to plan an emergency vaccination and communication program. The preventive activities provided by the LHU of Florence, in agreement with the regional health authorities, represented an example of good practice in the surveillance and control of this particularly frightening disease.

Moreover, the involvement of public health professionals and primary care physicians made possible the widest distribution of vaccinations in the Florentine area, even to the subjects who were the most difficult to reach, such as adolescents and young adults, with satisfactory adherence to the vaccination campaign.

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Conflict of interest statement

None declared.

Authors' contributions

AB, DP, FP, make substantial contributions to conception and design, and/or acquisition of data (DP, FP, LB, GM, MGS, TB, SG, EG), and/or analysis and interpretation of data (AB, DP, LB). SB, PB, GB participate in drafting the article or revising it critically for important intellectual content. All authors give final approval of the version to be submitted and any revised version.

Ethical approval: ethical approval was not required for this study, because the vaccination coverage, the demand for vaccination and the ADR data were collected in an aggregated way and properly anonymized. Moreover, information on the onset of Meningococcal C cases were in the public domain (newspaper accounts).

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