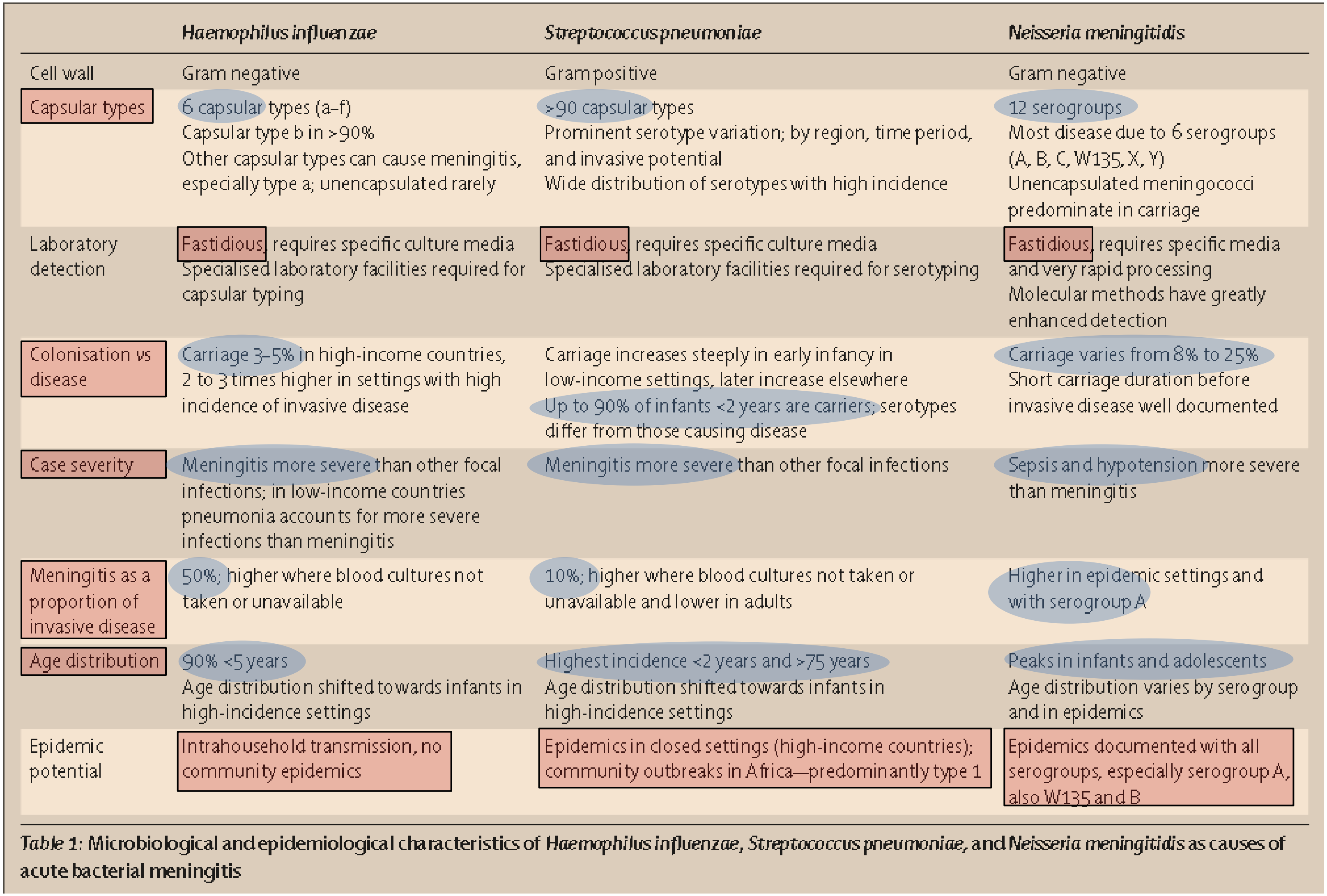
UNIVERSITÀ
DEGLI STUDI
DI PADOVA

UO Igiene e
Sanità Pubblica

Meningiti: la situazione epidemiologica

Vincenzo Baldo

Meningiti batteriche



	Haemophilus influenzae	*Streptococcus pneumoniae*	*Neisseria meningitidis*
Cell wall	Gram negative	Gram positive	Gram negative
Capsular types	6 capsular types (a–f) Capsular type b in >90% Other capsular types can cause meningitis, especially type a; unencapsulated rarely	>90 capsular types Prominent serotype variation; by region, time period, and invasive potential Wide distribution of serotypes with high incidence	12 serogroups Most disease due to 6 serogroups (A, B, C, W135, X, Y) Unencapsulated meningococci predominate in carriage
Laboratory detection	Fastidious, requires specific culture media Specialised laboratory facilities required for capsular typing	Fastidious, requires specific culture media Specialised laboratory facilities required for serotyping	Fastidious, requires specific media and very rapid processing Molecular methods have greatly enhanced detection
Colonisation vs disease	Carriage 3–5% in high-income countries, 2 to 3 times higher in settings with high incidence of invasive disease	Carriage increases steeply in early infancy in low-income settings, later increase elsewhere Up to 90% of infants <2 years are carriers; serotypes differ from those causing disease	Carriage varies from 8% to 25% Short carriage duration before invasive disease well documented
Case severity	Meningitis more severe than other focal infections; in low-income countries pneumonia accounts for more severe infections than meningitis	Meningitis more severe than other focal infections	Sepsis and hypotension more severe than meningitis
Meningitis as a proportion of invasive disease	50%; higher where blood cultures not taken or unavailable	10%; higher where blood cultures not taken or unavailable and lower in adults	Higher in epidemic settings and with serogroup A
Age distribution	90% <5 years Age distribution shifted towards infants in high-incidence settings	Highest incidence <2 years and >75 years Age distribution shifted towards infants in high-incidence settings	Peaks in infants and adolescents Age distribution varies by serogroup and in epidemics
Epidemic potential	Intrahousehold transmission, no community epidemics	Epidemics in closed settings (high-income countries); community outbreaks in Africa—predominantly type 1	Epidemics documented with all serogroups, especially serogroup A, also W135 and B

Table 1: Microbiological and epidemiological characteristics of *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Neisseria meningitidis* as causes of acute bacterial meningitis

Malattie infettive: prevenibilità

Malattia	Tasso di letalità	Note
Ebola[1]	50%−89%	
H5N1 (influenza aviaria)	59%	Casi riportati in Africa e Asia
Vaiolo	≥30%	Considerato eradicato nel1980
Malattia meningococcica invasiva	**9%−12%**	**A dispetto di appropriato trattamento antibiotico**
Difterite[4]	5%−10%	
Pneumococcal pneumonia[4]	5%−7%	
Polio paralitica[4]	2%−5%	
Meningite da Hib [4]	2%−5%	
Varicella[4]	<1%	Bambini e adolescenti
Morbillo[4]	0.2%	United States, 1985−1992
Rotavirus[5]	0.01%	US

1. Rouquet P, et al. *Emerg Infect Dis*. 2005;11:283-290; 2. WHO. http://www.who.int/csr/disease/avian_influenza/country/ cases_table_2010_12_09/en/index.html; 3. WHO. Plague factsheet. http://www.who.int/mediacentre/factsheets/ fs267/en/print.html; 4. Atkinson W et al, eds. *Epi and Prev of Vacc-Prev Dis*. 11th ed. http://www.cdc.gov/vaccines/pubs/pinkbook/pink-chapters.htm; 5. Gerba CP, et al. *Wat Res*. 1996:30;2929-2940.

La rapida progressione della malattia meningococcica

Evoluzione temporale del quadro clinico dall'esordio

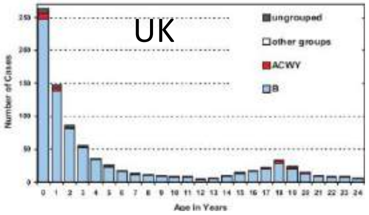
Sintomi precoci (4-8 ore)	**Sintomi classici (12-15 ore)**	**Sintomi terminali (15-~24 ore)**
▪ Irritabilità	▪ Rash emorragico	▪ Confusione/delirio
▪ Inappetenza	▪ Meningismo	▪ Convulsioni
▪ Febbre	▪ Fotofobia	▪ Perdita di coscienza
▪ Nausea		▪ Shock settico
▪ Mal di gola		▪ Possibile decesso

Ricovero in ospedale (tempo medio di ~ 19 ore)

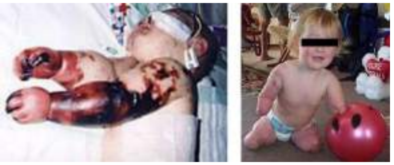
Thompson MJ, et al. *Lancet*. 2006;367:397-403.

Natura della malattia

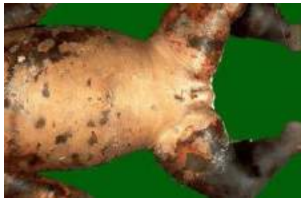
- Colpisce principalmente i bambini e gli adolescenti



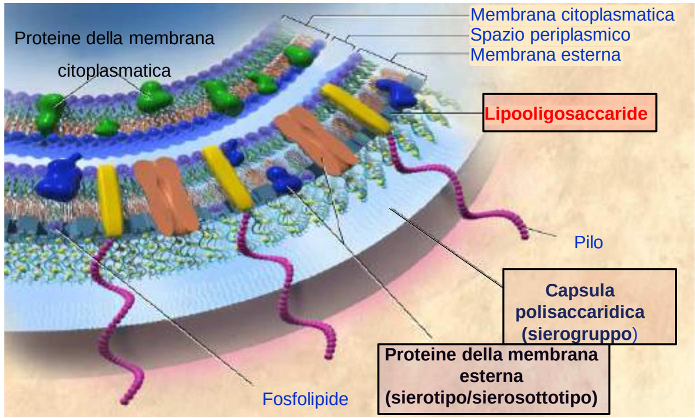
- La malattia **è letale nel 5-10%** dei casi anche con trattamento antibiotico
- Tra gli individui che sopravvivono, **fino al 20% ha sequele** neurologiche permanenti



- La **setticemia meningococcica** è una forma meno comune di malattia meningococcica ed è caratterizzata da un alto tasso di mortalità.



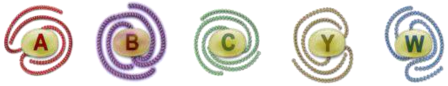
Neisseria meningitidis


Proteine della membrana citoplasmatica
Membrana citoplasmatica
Spazio periplasmico
Membrana esterna
Lipooligosaccaride
Pilo
Capsula polisaccaridica (sierogruppo)
Proteine della membrana esterna (sierotipo/sierosottotipo)
Fosfolipide

Sierogruppo

13 **sierogruppi** identificati sulla base del polisaccaride capsulare

5 **sierogruppi** causano la maggior parte dei casi di malattia



Sierotipo e sierosottotipo

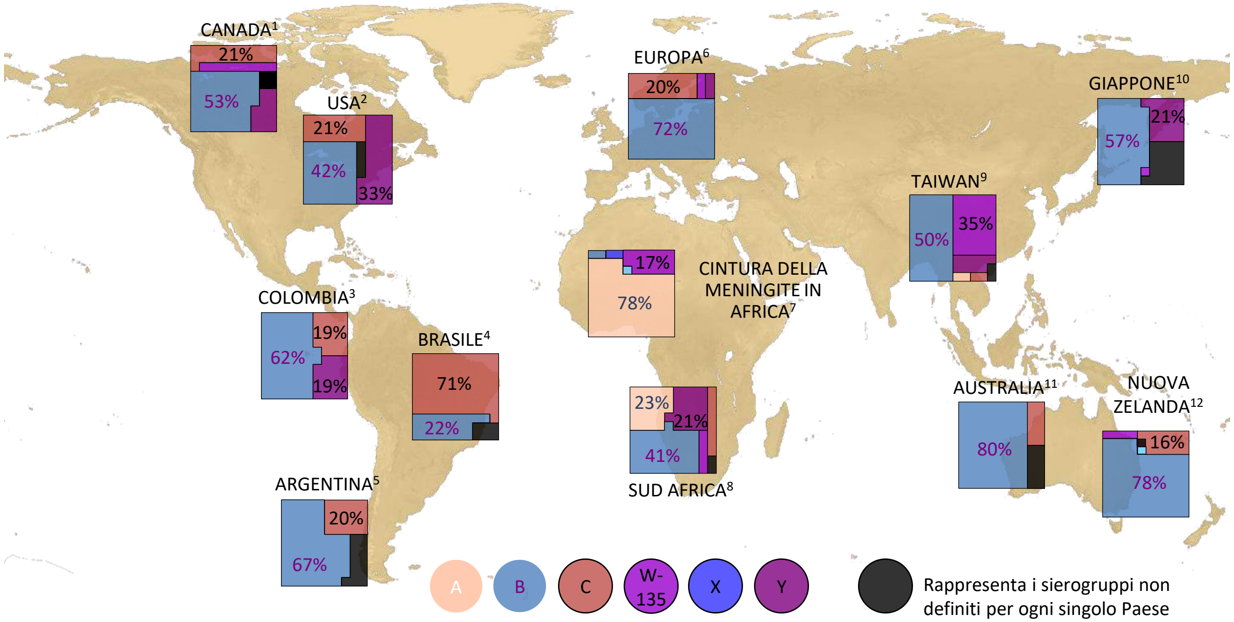
Identificati sulla base delle proteine della membrana esterna incluse le proteine porine di classe 2 e 3 (*porB*) e la proteina porina di classe 1 (*porA*)

Immunotipo

Identificato sulla base dei **lipooligosaccaridi**

Modificato da Rosenstein NE, et al. N Engl J Med. 2001;344:1378-1388.

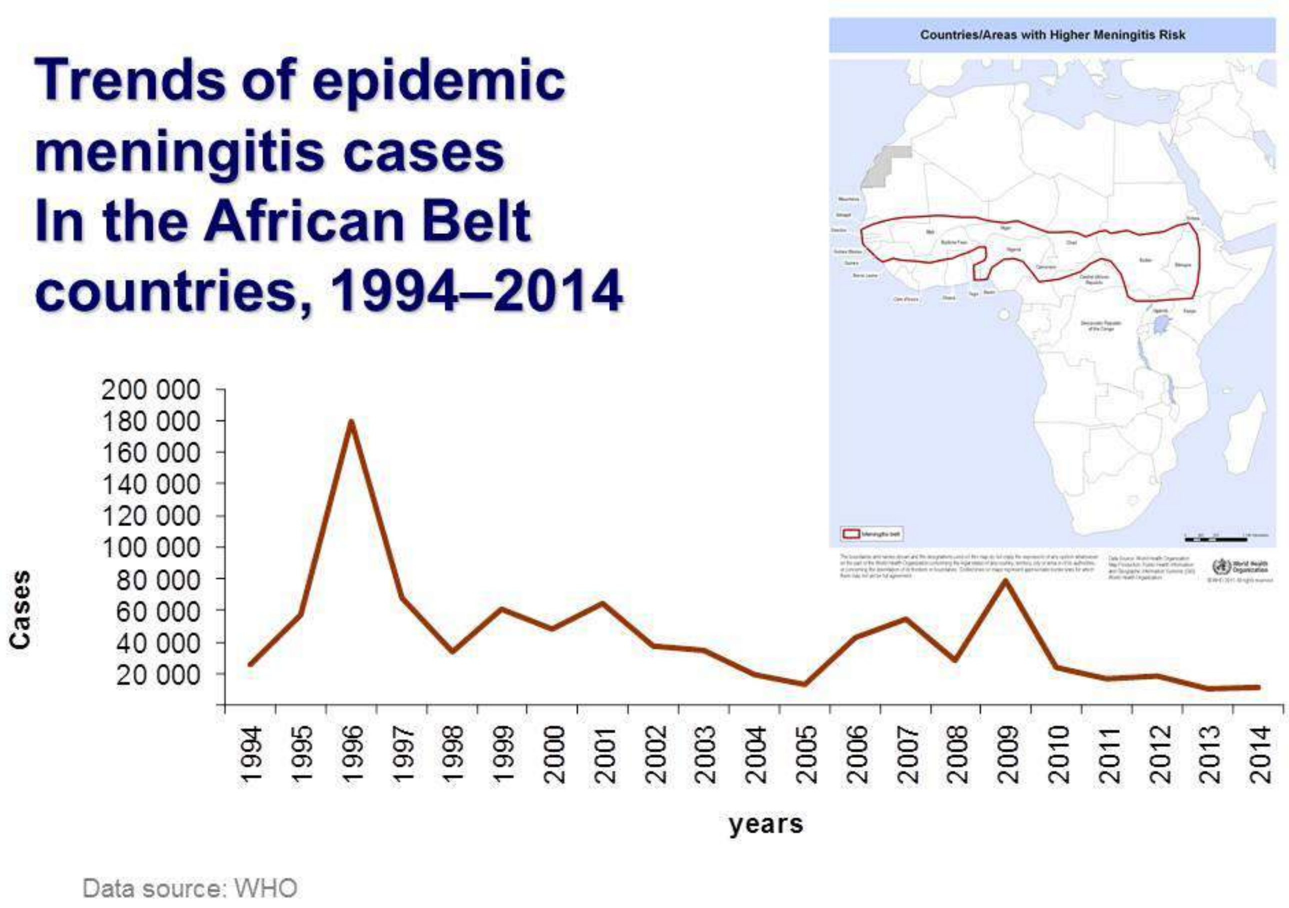
I sierogruppi di Neisseria meningitidis hanno una diversa distribuzione a livello globale



CANADA[1]
21%
53%
USA[2]
21%
42%
33%
EUROPA[6]
20%
72%
GIAPPONE[10]
21%
57%
TAIWAN[9]
50%
35%
17%
78%
CINTURA DELLA MENINGITE IN AFRICA[7]
COLOMBIA[3]
19%
62%
19%
BRASILE[4]
71%
22%
23%
21%
41%
SUD AFRICA[8]
AUSTRALIA[11]
80%
NUOVA ZELANDA[12]
16%
78%
ARGENTINA[5]
20%
67%
A
B
C
W-135
X
Y
Rappresenta i sierogruppi non definiti per ogni singolo Paese

1. Public Health Agency of Canada. *Canada Communicable Disease Report (CCDR)*. June 2007;33:1-15; 2. CDC. Active Bacterial Core Surveillance Report, Emerging Infections Program Network, *Neisseria meningitidis*, 2005; 3. Informe Regional de SIREVA II. Organizacion de Panamericana de la Salud; 2007; 4. Ciccone FH, et al. *BEPA*. 2006;3:7-12; 5. Chiavetta L, et al. *Revista Argentina de Microbiologia*. 2007;39:21-27; 6. EU-IBIS Network. Serogroup analysis: 2006. www.euibis.org; 7. Nicolas P, et al. *J Clin Microbiol*. 2005;43:5129-5135; 8. Coulson GB, et al; Group for Enteric, Respiratory and Meningeal Disease Surveillance in South Africa. *Emerg Infect Dis*. 2007;13:273-281; 9. Chiou CS, et al. *BMC Infect Dis*. 2006;6:25; 10. Takahashi H, et al. *J Med Microbiol*. 2004;53:657-662; 11. Australian Meningococcal Surveillance Programme. *CDI.* 2007;31:185-193; 12. Martin D, et al. Wellington, New Zealand: Ministry of Health; 2006.

Cintura della meningite nell’Africa subsahariana



Trends of epidemic meningitis cases In the African Belt countries, 1994–2014

Data source: WHO

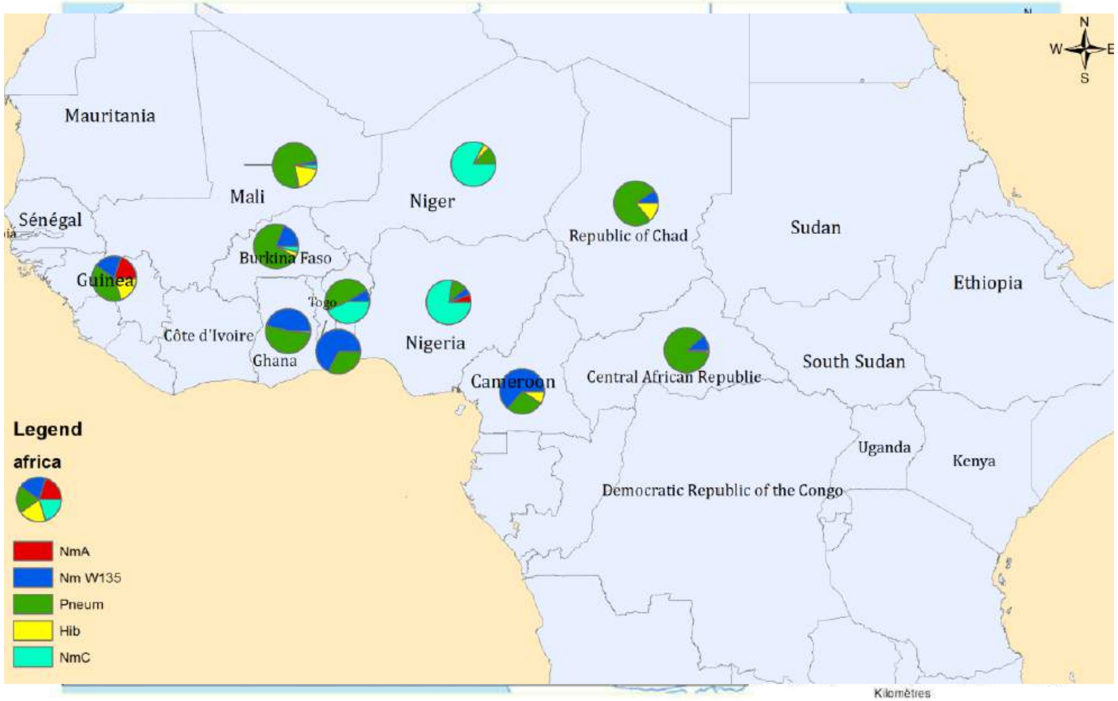
World Health Organization
Regional Office for Africa

Meningitis Weekly Bulletin

Inter country Support Team - West Africa

Semaine/Week 19

2017


Mauritania
Mali
Niger
Sénégal
Guinea
Burkina Faso
Togo
Côte d'Ivoire
Ghana
Nigeria
Republic of Chad
Sudan
Ethiopia
Cameroon
Central African Republic
South Sudan
Uganda
Kenya
Democratic Republic of the Congo
N
W
E
S
Legend
africa
NmA
Nm W135
Pneum
Hib
NmC
Kilomètres

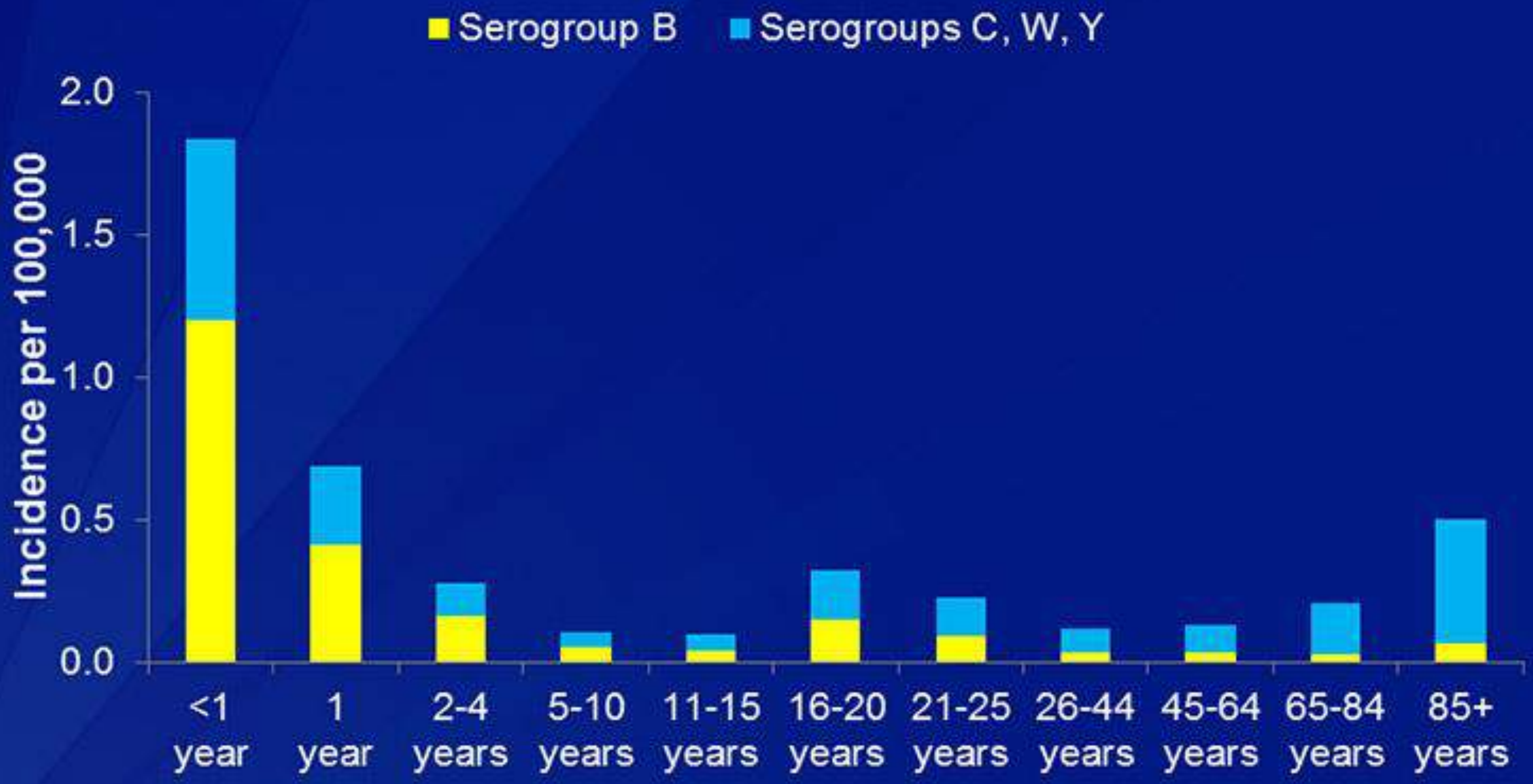
Pays *Country*	Cas *Cases*	Décès *Deaths*	Létalité (%) *CFR (%)*
Benin^{P}	**451**	**42**	**9.3**
Burkina Faso^{T}	**1 607**	**134**	**8.3**
Cameroun^{P}	582	36	6.2
Centrafrique^{P}	**190**	**17**	**8.9**
Côte d'Ivoire^{P}	**83**	**4**	**4.8**
Ethiopia^{T}	**682**	**9**	**1.3**
Ghana^{P}	753	72	9.6
Guinea^{P}	**151**	**4**	**2.6**
Guinée Bissau	0	0	0.0
Gambia^{T}	**27**	**3**	**11.1**
Kenya	**105**	**5**	**4.8**
Mali^{T}	**160**	**1**	**0.6**
Mauritania^{P}	**1**	**0**	**0.0**
Niger^{T}	**3231**	**187**	**5.8**
Nigeria^{P}	**9348**	**592**	**6.3**
RD Congo**	2 775	236	8.5
Senegal^{P}	87	0	0.0
Sierra Leone	0	0	0.0
South Sudan^{P}	23	3	13.0
Sudan^{T}	**47**	**1**	**2.1**
Tanzania	0	0	0.0
Tchad^{T}	**174**	**15**	**8.6**
Togo^{P}	**493**	**34**	**6.9**
Uganda^{P}	81	19	23.5
Total	**21 051**	**1 414**	**6.7**

6,173 samples have been collected out of 21,051 suspected cases (29.3%).
65.3% of these samples tested negative by the laboratory.
The NmC has become the predominant pathogen with 37.3% of positive samples, followed by Sp 26.5%; NmX 14.1% and NmW 9.8% of positive samples.
The proportion of NmX reported by 6 countries is increasing (3rd position)

Comments :

A cumulative total of 21, 051 suspected cases with 1,414 deaths (CFR of 6.7%) have been notified in 2017.
Countries are invited to improve the completeness of data and timeliness of data sharing.

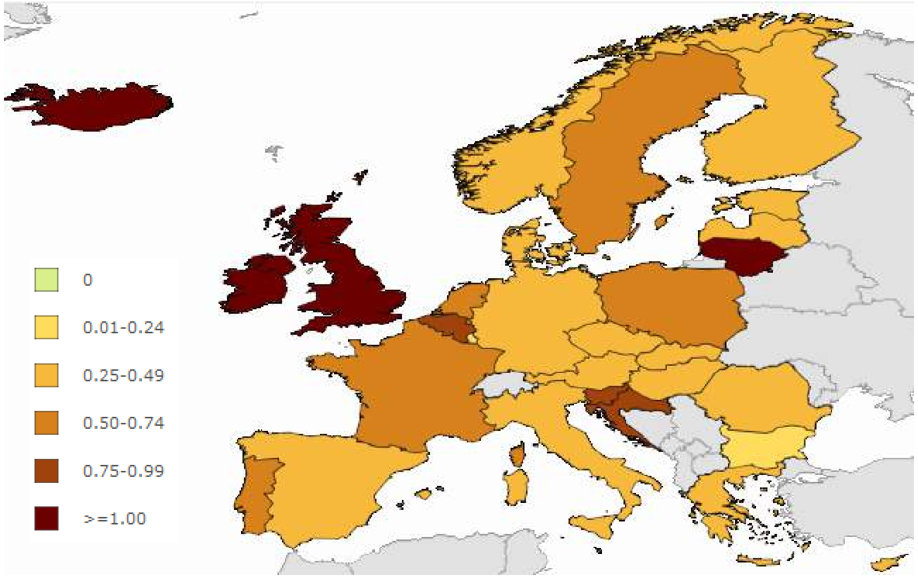
Meningococcal Incidence by Serogroup and Age-Group, 2006-2015



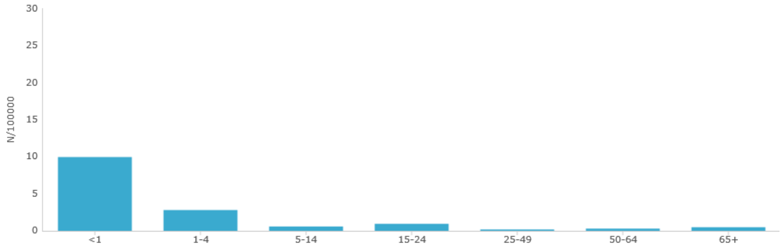
SOURCE: CDC; National Notifiable Diseases Surveillance System with additional serogroup data from Active Bacterial Core surveillance and state health departments.

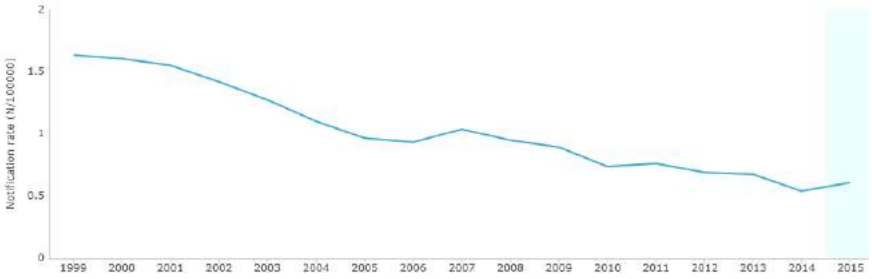
Unknown serogroup (20%) and other serogroups (5%) excluded

In Europa dati 2015 (ECDC modificato)



Serogroup	Cases	%
B	1682	53,9
C	403	12,9
Y	290	9,3
W	317	10,2
Other /not identified	429	13,7
Total	**3121**	**100**





- In 2015, **3121 invasive meningococcal disease were reported**
- The notification rate was **0.6 cases per 100 000 population**
- Age-specific rates were highest in infants **(9,95 cases per 100 000)**
- The majority of cases were **caused by serogroup B**

Meningococco B in Inghilterra

Recommended immunisation schedule

2, 4 and 12 months (2+1)

If second routine primary immunisation appointment due on or after 1st September then follow this schedule:

3, 4 and 12 months (2+1)

If third routine primary immunisation appointment due on or after 1st September then follow this schedule:

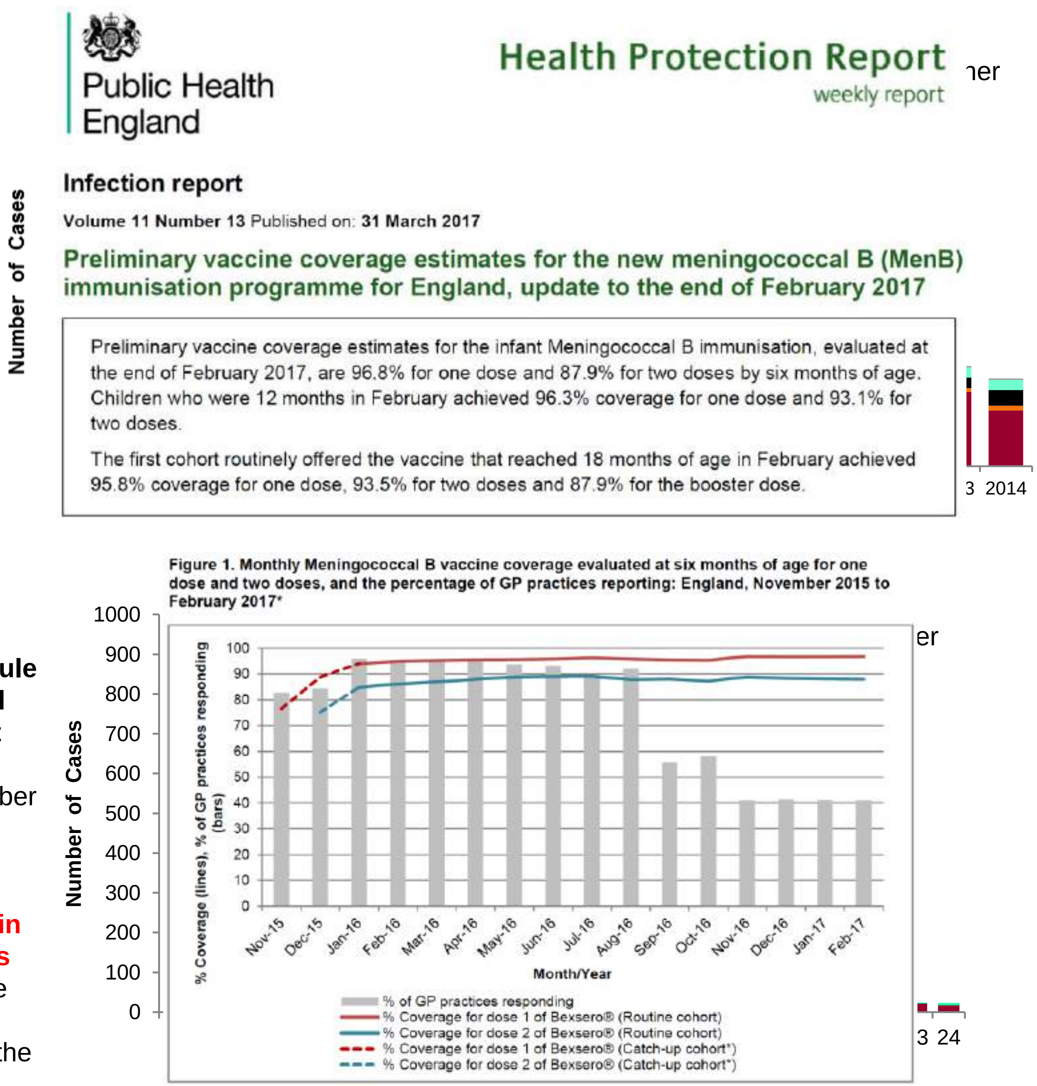
4 and 12 months (1+1)

Effectiveness and impact of a reduced infant schedule of 4CMenB vaccine against group B meningococcal disease in England: a national observational cohort study

[Lancet Volume 388, No. 10061](), p2775–2782, 3 December 2016

Interpretation

The two-dose 4CMenB priming schedule was highly effective in preventing MenB disease in infants. **Cases in vaccine-eligible infants halved in the first 10 months of the programme.** While ongoing national surveillance will continue to monitor the longer-term impact of the programme, these findings represent a step forward in the battle against meningococcal disease and will help reassure that the vaccine protects against this deadly infection.



Public Health England

Health Protection Report

weekly report

Infection report

Volume 11 Number 13 Published on: **31 March 2017**

Preliminary vaccine coverage estimates for the new meningococcal B (MenB) immunisation programme for England, update to the end of February 2017

Preliminary vaccine coverage estimates for the infant Meningococcal B immunisation, evaluated at the end of February 2017, are 96.8% for one dose and 87.9% for two doses by six months of age. Children who were 12 months in February achieved 96.3% coverage for one dose and 93.1% for two doses.

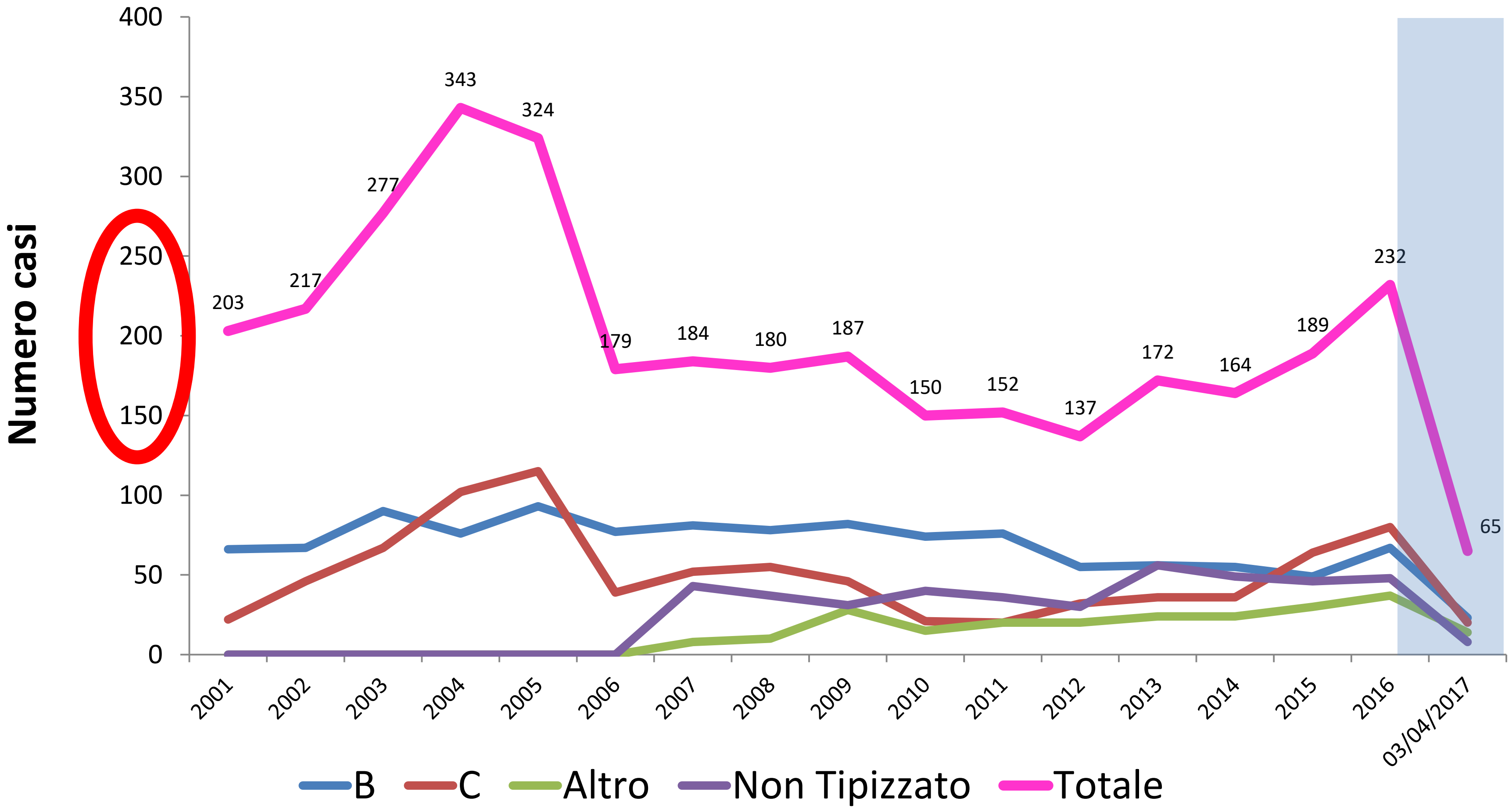
The first cohort routinely offered the vaccine that reached 18 months of age in February achieved 95.8% coverage for one dose, 93.5% for two doses and 87.9% for the booster dose.

Figure 1. Monthly Meningococcal B vaccine coverage evaluated at six months of age for one dose and two doses, and the percentage of GP practices reporting: England, November 2015 to February 2017*

Number of Cases
ner
3 2014
Number of Cases
1000
900
800
700
600
500
400
300
200
100
0
er
3 24
% Coverage (lines), % of GP practices responding (bars)
100
90
80
70
60
50
40
30
20
10
0
Nov-15
Dec-15
Jan-16
Feb-16
Mar-16
Apr-16
May-16
Jun-16
Jul-16
Aug-16
Sep-16
Oct-16
Nov-16
Dec-16
Jan-17
Feb-17
Month/Year
% of GP practices responding
% Coverage for dose 1 of Bexsero® (Routine cohort)
% Coverage for dose 2 of Bexsero® (Routine cohort)
% Coverage for dose 1 of Bexsero® (Catch-up cohort*)
% Coverage for dose 2 of Bexsero® (Catch-up cohort*)

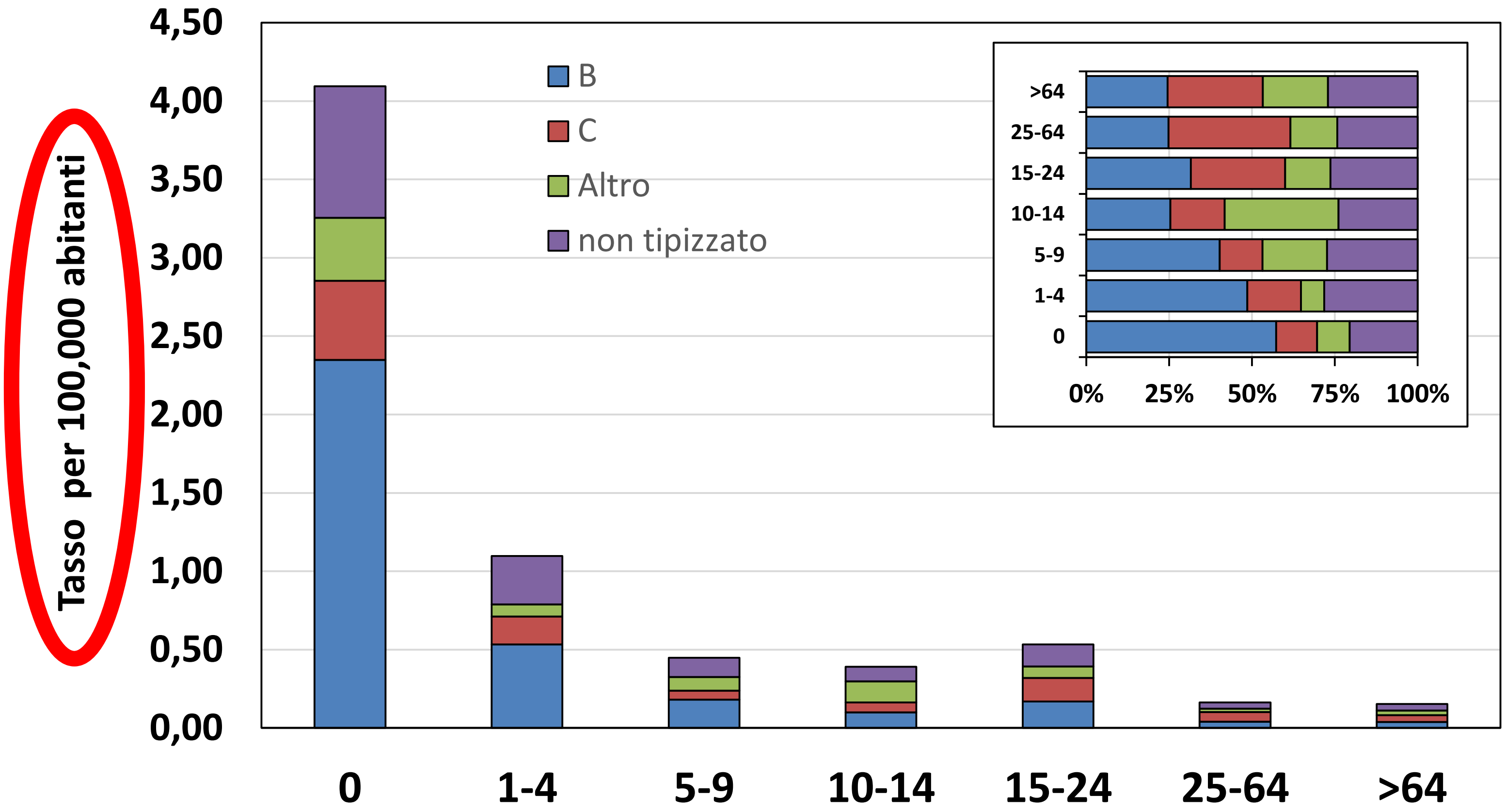
Epidemiologia in Italia: Casi di meningococco 2001-2016

Complessivamente circa il 35% delle Neisserie è di tipo C



Fonte dati: ISS-Dati di sorveglianza delle malattie batteriche invasive

Incidenza e distribuzione N. meningitidis nelle diverse fasce di età (2011-2016)

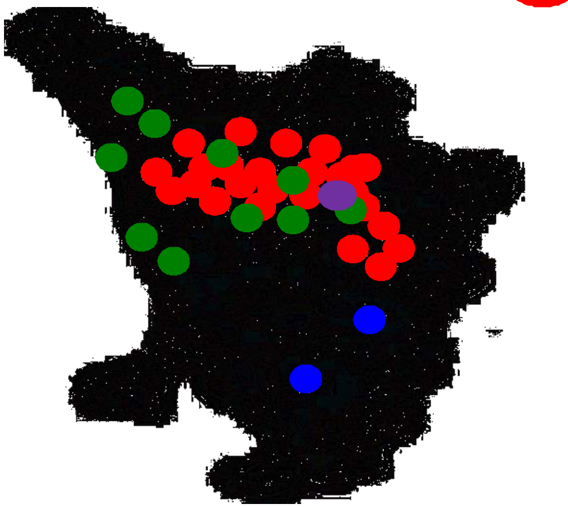


Fonte dati: ISS-Dati di sorveglianza delle malattie batteriche invasive

Il cluster di meningiti in Toscana anno 2015-17

82 casi

Età media: 35 anni



🔴 **Sierogruppo C**
62 casi
13 decessi

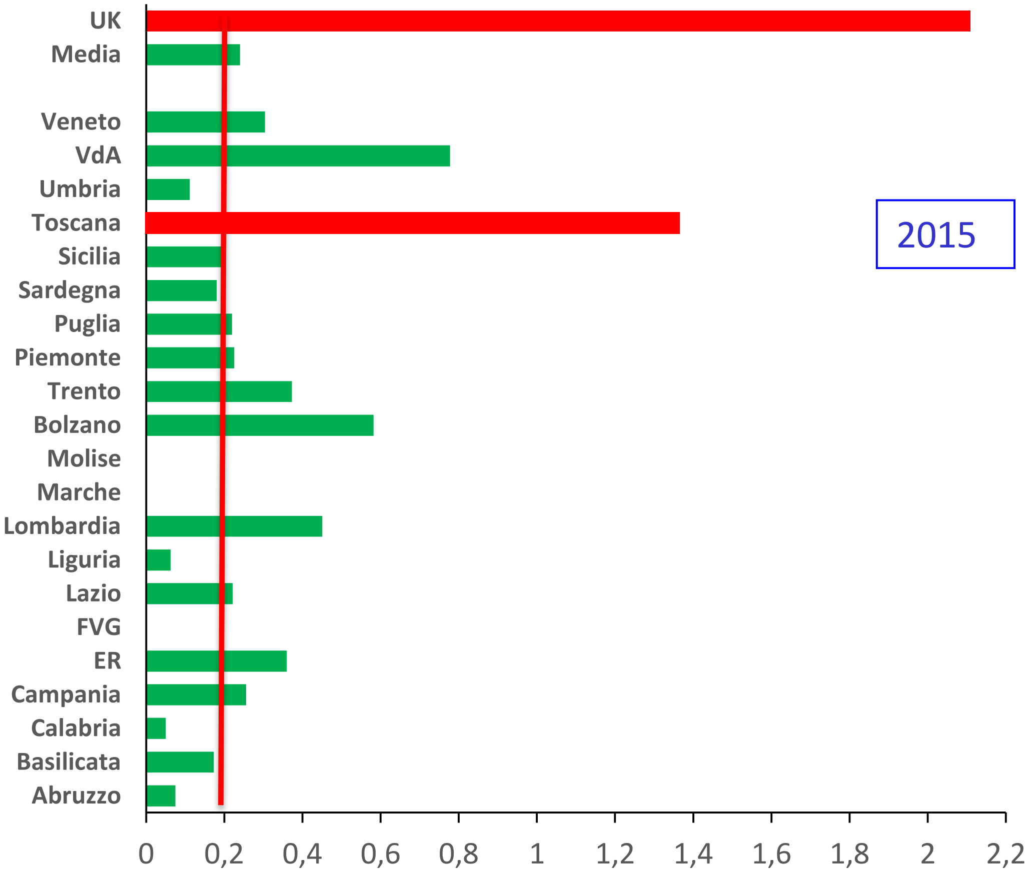
🟢 **Sierogruppo B**
15 casi
1 decesso

🔵 **Sierogruppo W**
2 casi

🟣 **Sierogruppo X**
1 caso

2 casi non tipizzati

Incidenza di infezione meningococcica nelle diverse regioni Italiane (casi x 100.000) anno 2014



2015

Pensiamoci prima di dire che in Toscana c'è un'epidemia…..
La Toscana non è dissimile dalle altre regioni

I casi si trovano….se si cercano!

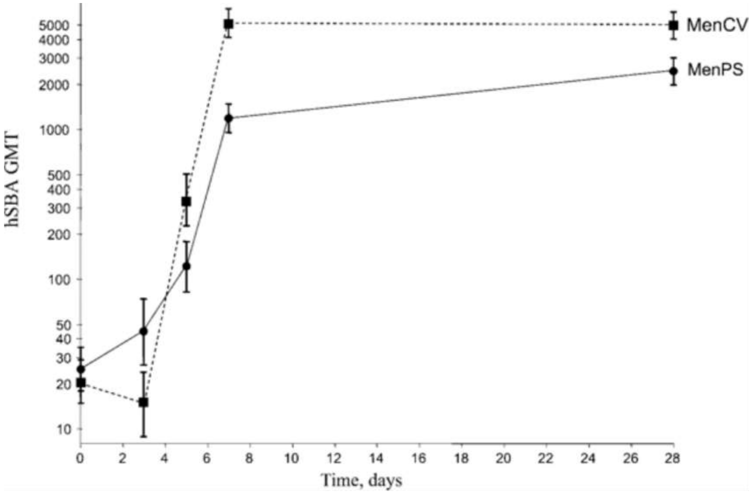
IlFattoQuotidiano.it / Scienza

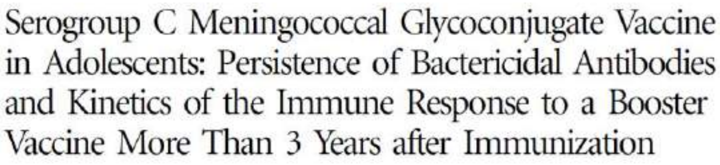
Partecipa alla serata per la Costituzione
LA COSTITUZIONE È NOSTRA

Meningite in Toscana, eccessi di casi di meningococco C. Rezza (Iss): "Ceppo particolarmente virulento"

Complesso clonale ST-11

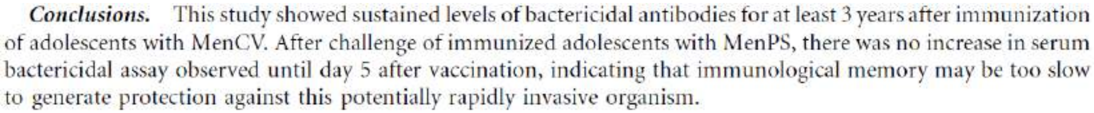
- Utilizzando l'analisi delle sequenze mediante multilocus sequence typing (MLST) é stato, inoltre, tipizzato il complesso clonale ST-11 del meningococco C nella maggior parte dei campioni inviati, che presenta particolare virulenza e contagiosità ed é associato ad una patologia precocemente generalizzata e con un'elevata frequenza di complicanze.
- Clusters di malattia invasiva causati da N. meningitidis di gruppo C con complesso ST-11 sono stati rilevati in Germania e Francia. In Nord Italia tra dicembre 2007 e luglio 2008, sono stati riportati 2 clusters dovuti a meningococco C ST- 11, con alto tasso di letalità e complicanze.





Serogroup C Meningococcal Glycoconjugate Vaccine in Adolescents: Persistence of Bactericidal Antibodies and Kinetics of the Immune Response to a Booster Vaccine More Than 3 Years after Immunization

Snape MD et al. Clinical Infectious Diseases 2006; 43:1387–94



Conclusions. This study showed sustained levels of bactericidal antibodies for at least 3 years after immunization of adolescents with MenCV. After challenge of immunized adolescents with MenPS, there was no increase in serum bactericidal assay observed until day 5 after vaccination, indicating that immunological memory may be too slow to generate protection against this potentially rapidly invasive organism.

La memoria immunologica è presente.

La risposta booster si verifica nel tempo previsto (5-8 gg)

La risposta al MenPS mima l'infezione naturale

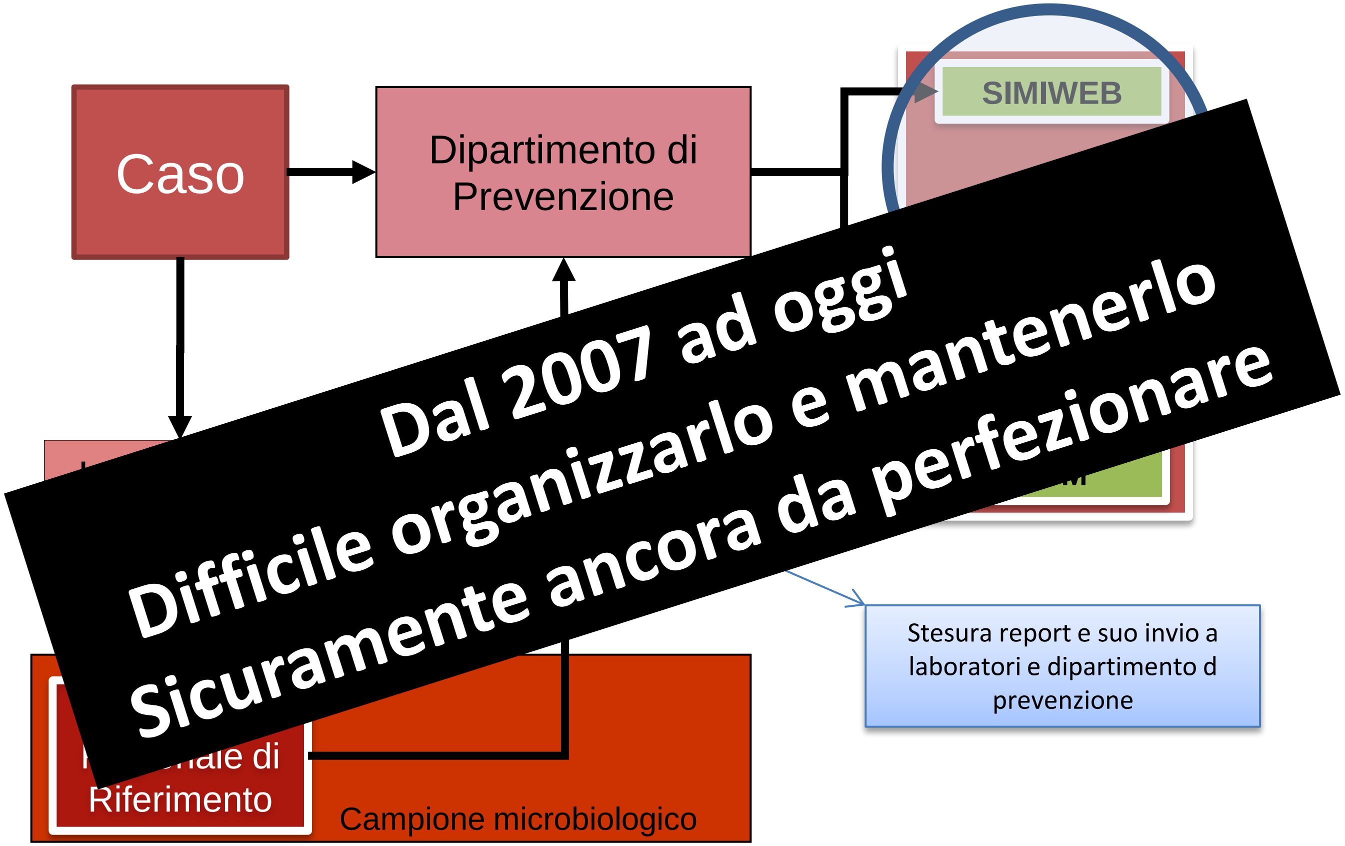
La meningite/sepsi meningococcica non ci consente di aspettare 5 giorni !!!

Flussi informativi presenti nella regione Veneto

- Flusso di **sorveglianza nazionale** delle malattie batteriche invasive
- Flusso afferente al sistema informatizzato malattie infettive **SIMI-WEB**
- Flusso basato sulle **microbiologie** (avviato all'inizio del **2007**)
- [Schede di dimissione ospedaliere (**SDO**)]

Periodo in studio 2007-2016

Sistema Sorveglianza Regione Veneto
MIB - Flussi informativi presenti


Caso

Dipartimento di Prevenzione

SIMIWEB

Stesura report e suo invio a laboratori e dipartimento d prevenzione

ale di Riferimento

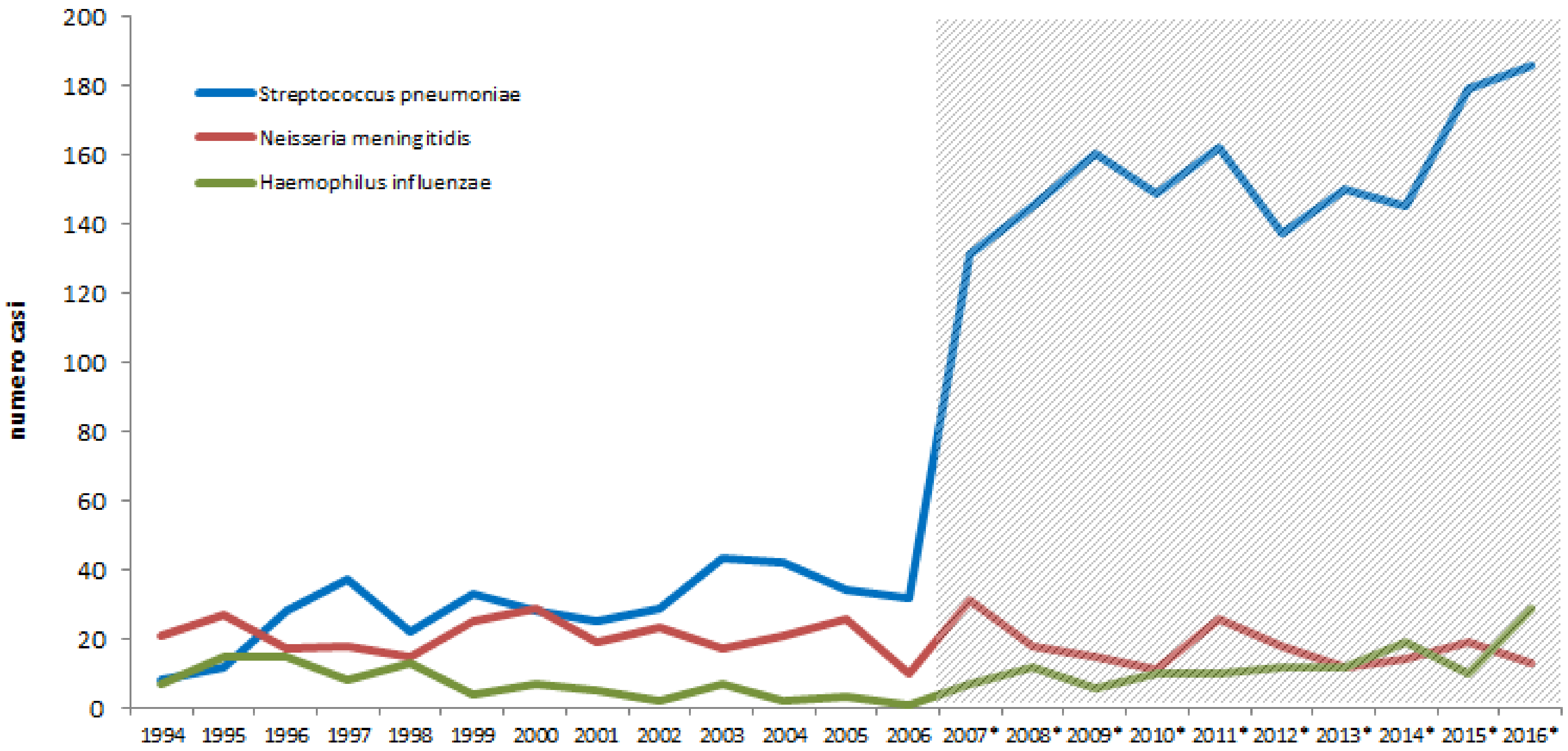
Campione microbiologico

Dal 2007 ad oggi

Difficile organizzarlo e mantenerlo

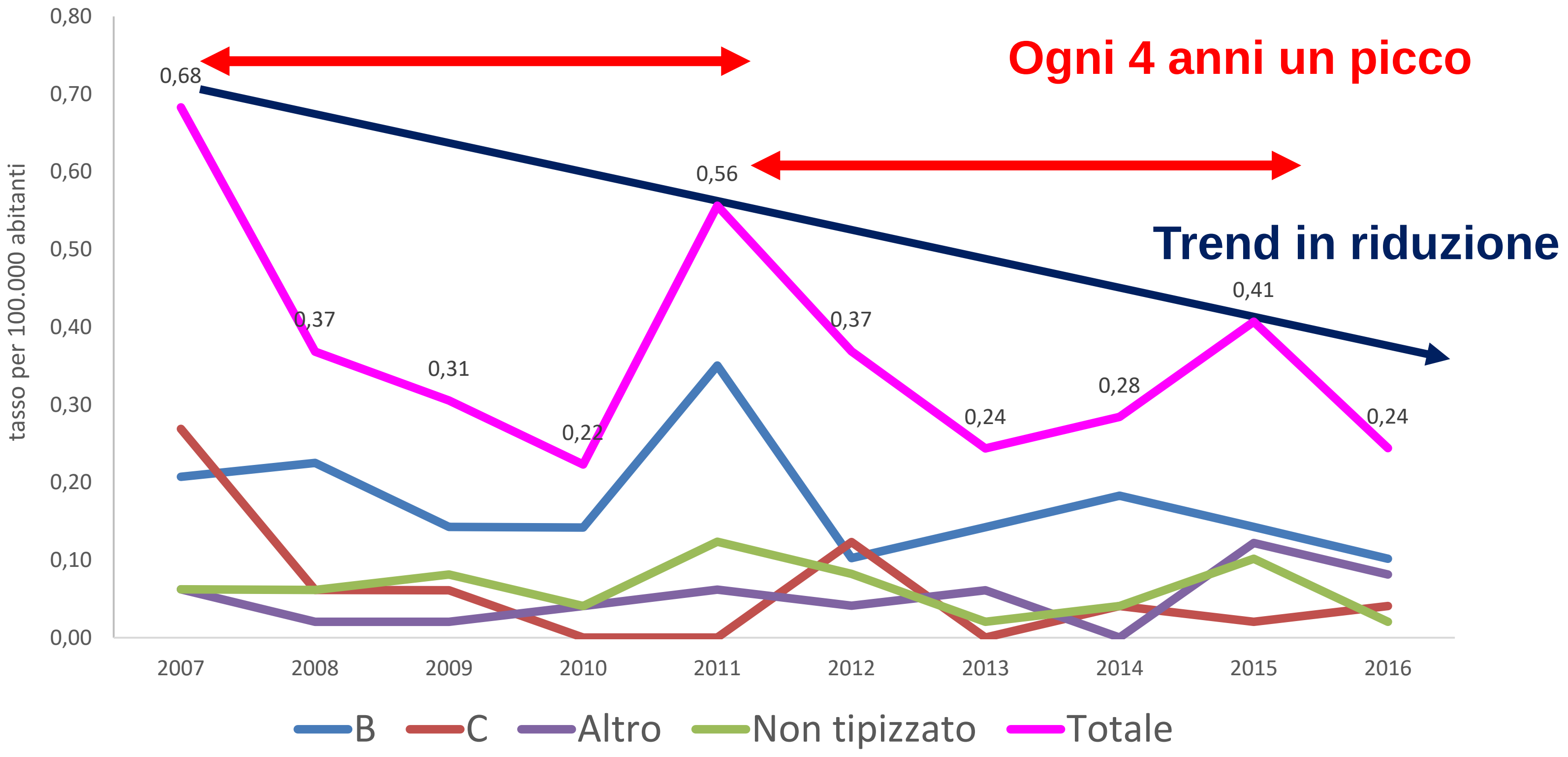
Sicuramente ancora da perfezionare

Numero assoluto notifiche per malattie batteriche invasive nella Regione Veneto 1994-2016



* dall'anno 2007 è attiva la sorveglianza basata sui Laboratori di Microbiologia.

Distribuzione assoluta dei casi notificati per *Neisseria meningitidis* per classe di età, Regione Veneto (2007-2016)

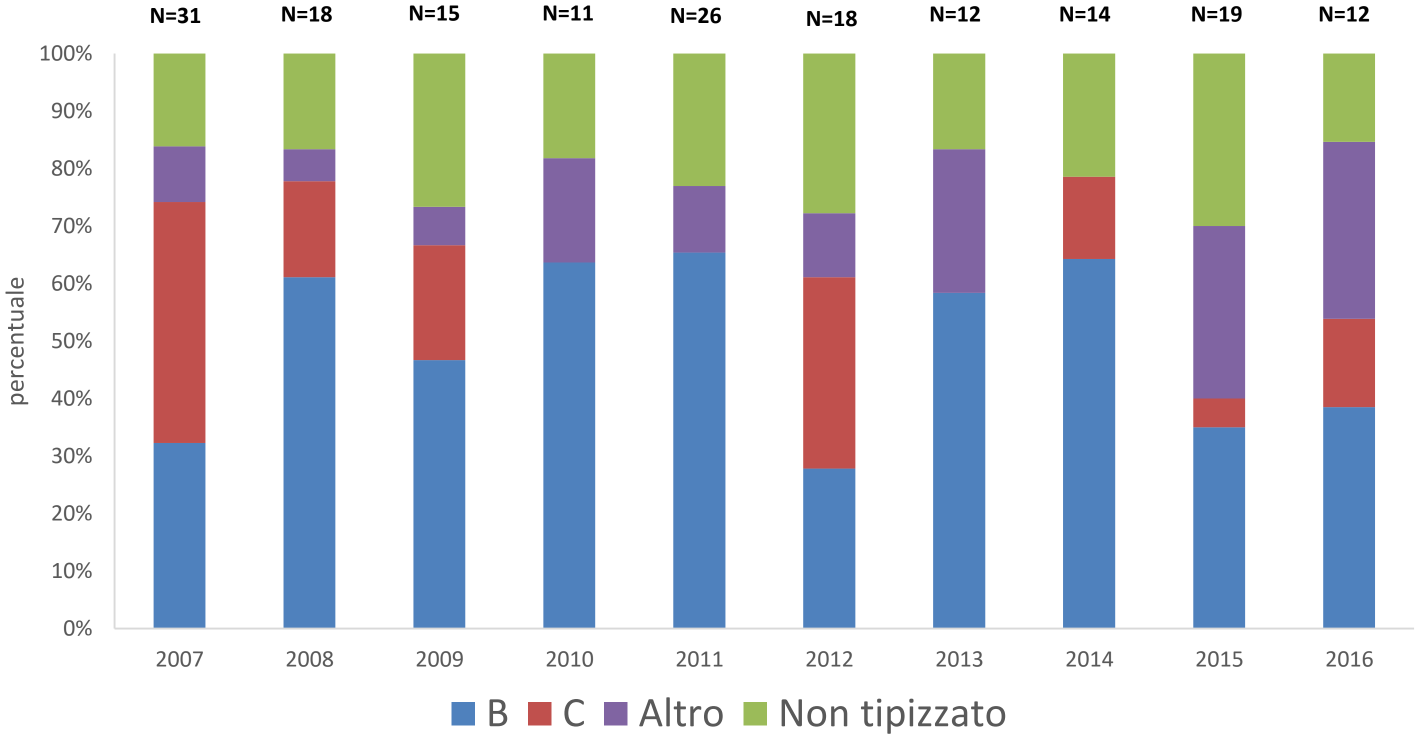


Ogni 4 anni un picco

Trend in riduzione

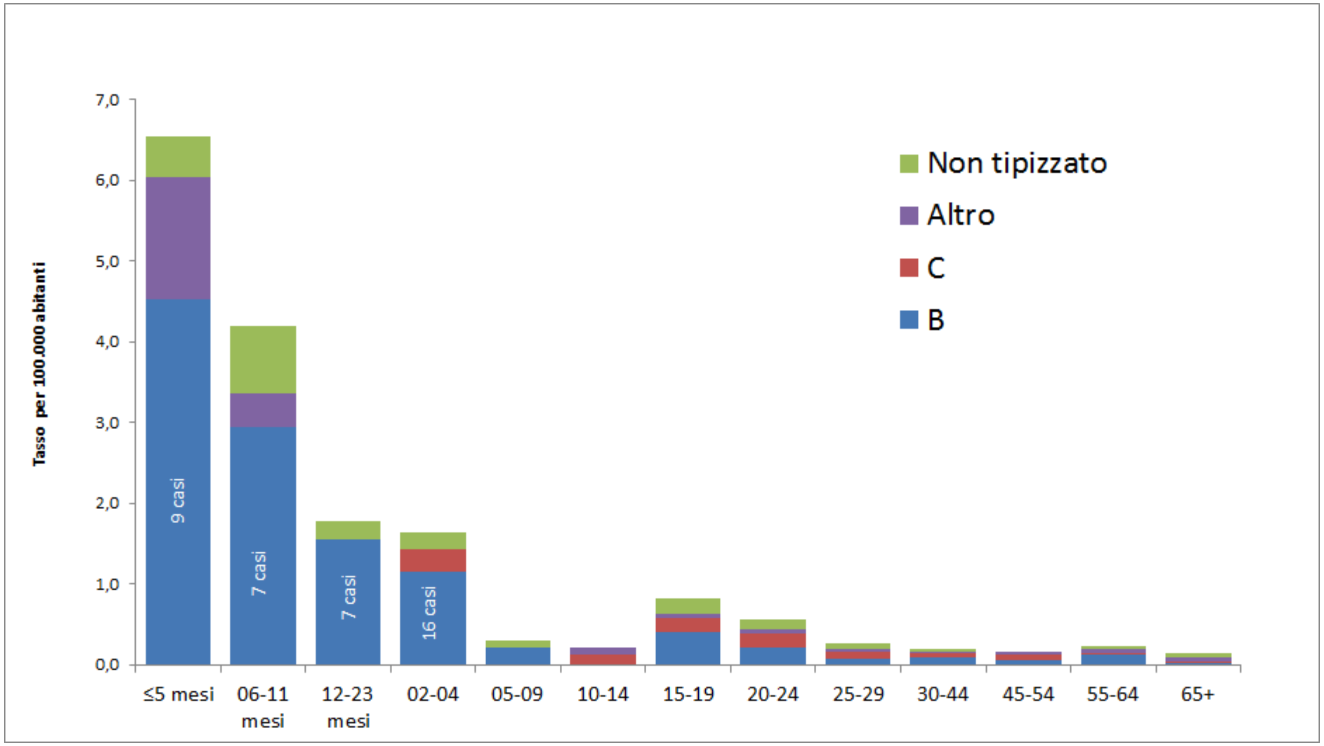
- Nel periodo 2007-2016 **(10 anni di osservazione)** attraverso tutti i flussi di sorveglianza, sono stati notificati complessivamente **176** **(circa 18 casi all’anno)** casi di patologia correlata ad infezione da *Neisseria meningitidis*
- Tasso di notifica medio **0,4 per 100.000 abitanti**

Tipizzazione *Neisseria meningitidis* per anno, Regione Veneto (2007-2015)



- **176 soggetti totali**
- riduzione dei ceppi isolati con **sierogruppo C**
- **aumento percentuale nel tempo** dei ceppi A, **Y, W**

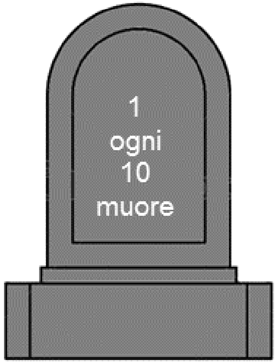
Tasso di notifica per *Neisseria meningitidis* per classe di età e per sierogruppo Regione Veneto (2007-2016)

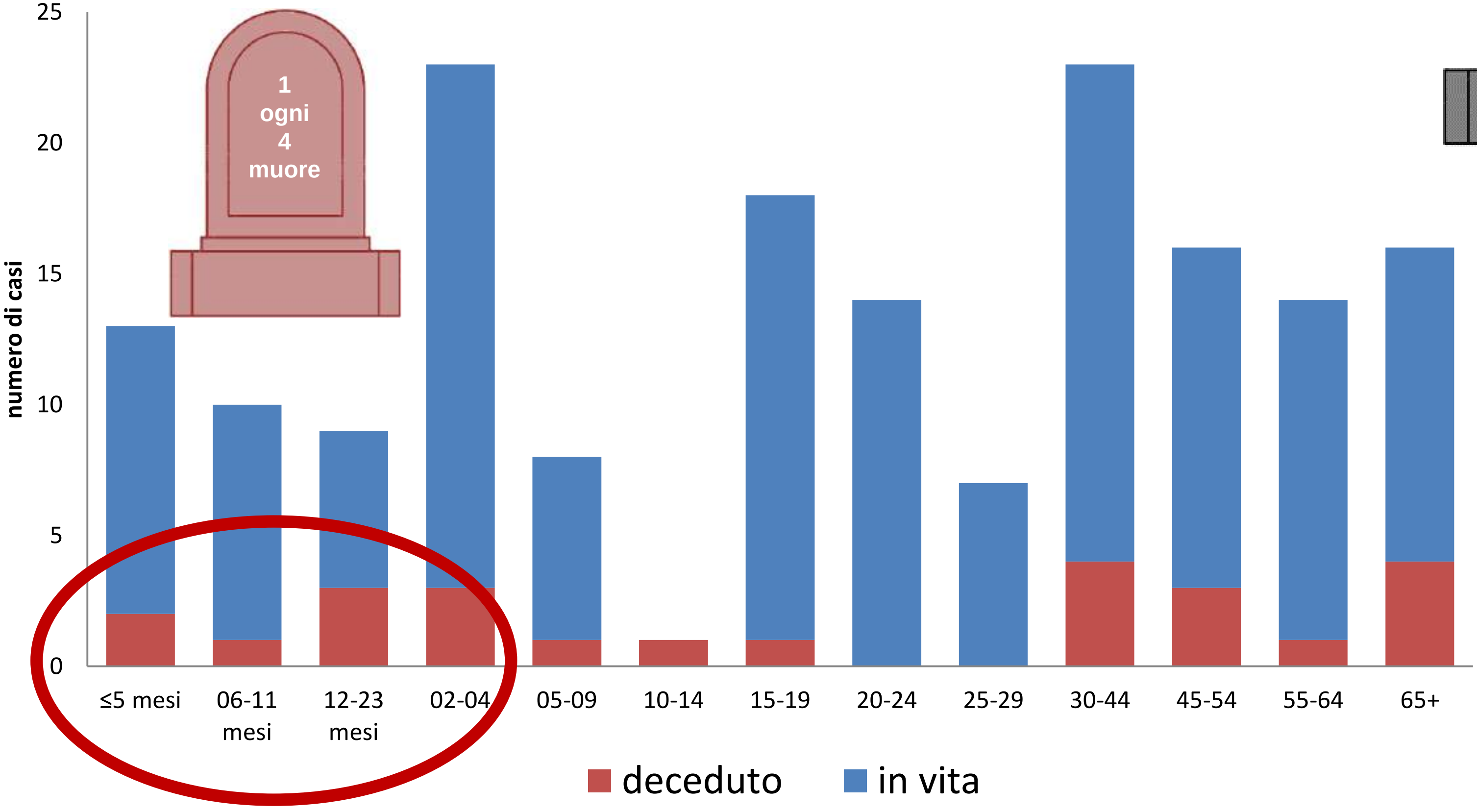


- Maggiore incidenza **nei soggetti con età inferiore** all'anno di età (6,5 per 100.000 abitanti).
- Sotto l'anno di età **il 72,7% dei casi sono attribuibili al meningococco tipo B** (16 casi su 23 totali) tasso specifico per il **ceppo B pari a 3,7 per 100.000 abitanti**;
- **Nella classe di età 01-04 anni** (2,4 casi per 100.000 con un tasso specifico per **meningococco B di 1,7 per 100.000 abitanti**)

Casi notificati per *Neisseria meningitidis* tipo B per classe di età e esito, Regione Veneto (2007-2016)

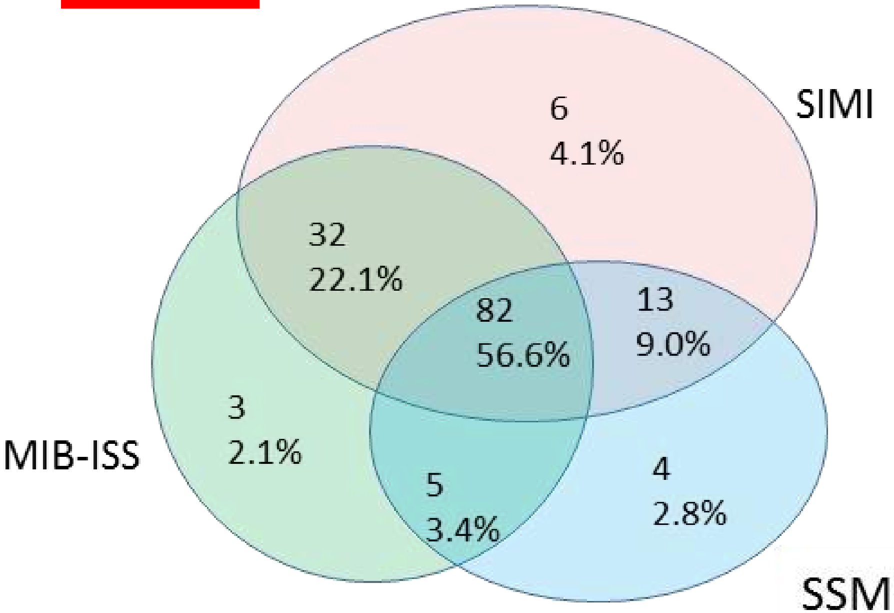
24 decessi nel periodo, letalità pari a 13,5%, di cui 12 casi da MenB





Numero assoluto e percentuale delle notifiche e concordanza tra i tre flussi (**2007-2014**)

145 casi



Analisi cattura-ricattura

[(criteri Akaike (AIC) e sul criterio di Bayes (BIC)]

Modello	DoF	G2	p-value	AIC	BIC	X^	N^	95%CI
A B C	3	4,43	0,22	-1,57	-1,41	0	145	145-148
A B C (AB) (AC)	5	0,1	0,76	-1,9	-1,85	2	147	145-159
A B C (AB) (BC)	5	0,31	0,58	-1,69	-1,64	1	146	145-154
A B C (AC) (BC)	5	4,42	0,04	2,42	2,48	0	145	145-149
A B C (AB) (AC) (BC)	6	0	1	0	0	2	147	145-167

Il modello stima 146 casi totali (95%CI: 145-152)

A: Mandatory Notification System; B: National Surveillance System ; C= Laboratories Surveillance System; G2: likelihood ratio statistic; AIC: Akaike Information Criterion; BIC: Bayesian Information Criterion; x^: estimated total cases not reported; N^: estimated total cases.

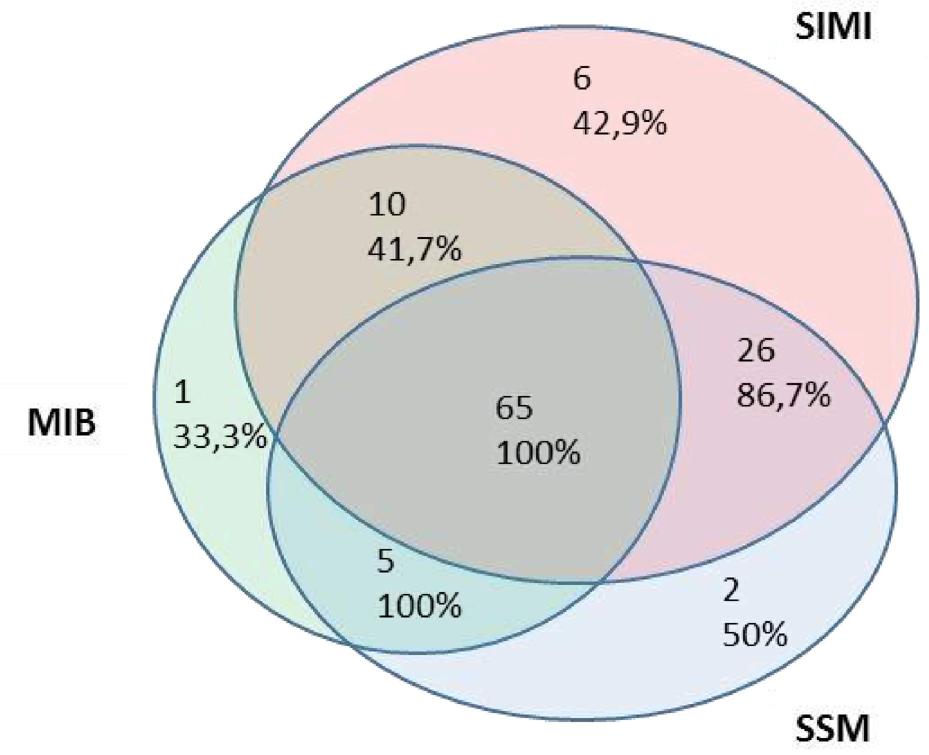
La sensibilità è del **99,3%** (95%CI: 95,4%-100%).

La completezza

- **SIMI è del 91,1%** (95%CI: 87,6%-91,7%).
- **MIB è del 83,5%** (95%CI: 80,3%-84,1%).
- **SSM è del 71,2%** (95%CI: 68,43%-71,7%).

Baldovin T, et al. BMJ Open 2017;7:e012478. doi:10.1136/bmjopen-2016-012478

Tipizzati: 79,3% del totale degli isolati (2007-2014)

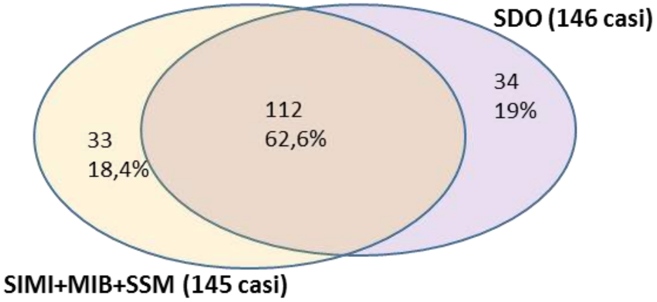

SIMI
6
42,9%
10
41,7%
26
86,7%
MIB
1
33,3%
65
100%
5
100%
2
50%
SSM

- tipizzati dall’SSM è il **94,2%**;
- altri due flussi (SIMI, MIB) è il **41,4%**

Baldovin T, et al. BMJ Open 2017;7:e012478. doi:10.1136/bmjopen-2016-012478

Linkage dati flusso delle SDO

- Ricerca codice ICD 9-CM 036.xx
  - Il numero di casi estratti: **146**



Analisi cattura-ricattura (Chao)

Il modello stima 189 casi (95%CI: 181-197)

La sensibilità è del **94,7%** (95%CI: 90,8%-98,8%)

La completezza

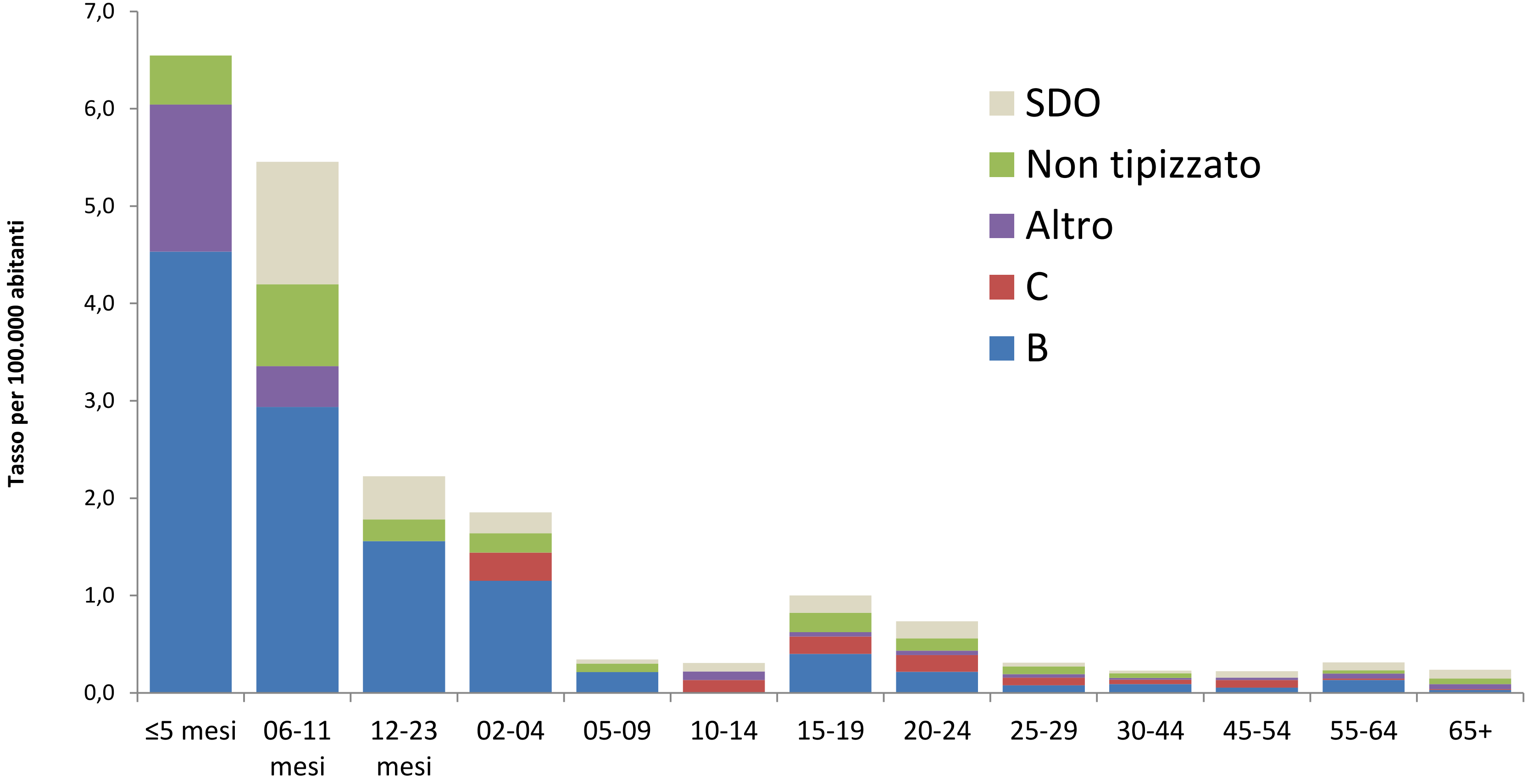
- **SIMI+MIB+SSM: 76,7%** (95%CI: 73,6%-80,1%)
- **SDO: 77,2%** (95%CI: 74,1%-80,6%).

179 casi totali nel periodo 2007-2014

I casi notificati esclusivamente nel sistema SIMIWEB-MIB-SSM incrociano con SDO con diagnosi di dimissione
NON per meningite meningococcica

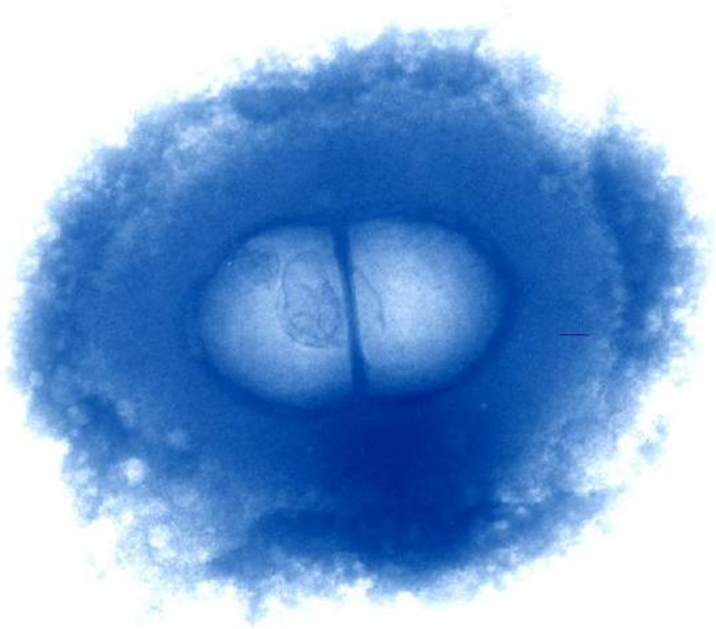
Baldovin T, et al. BMJ Open 2017;7:e012478. doi:10.1136/bmjopen-2016-012478

Tasso di notifica per malattie batteriche invasive da meningococco nella Regione Veneto (1994-2016)



42 casi in più nel periodo 2007-2016

Streptococcus pneumoniae

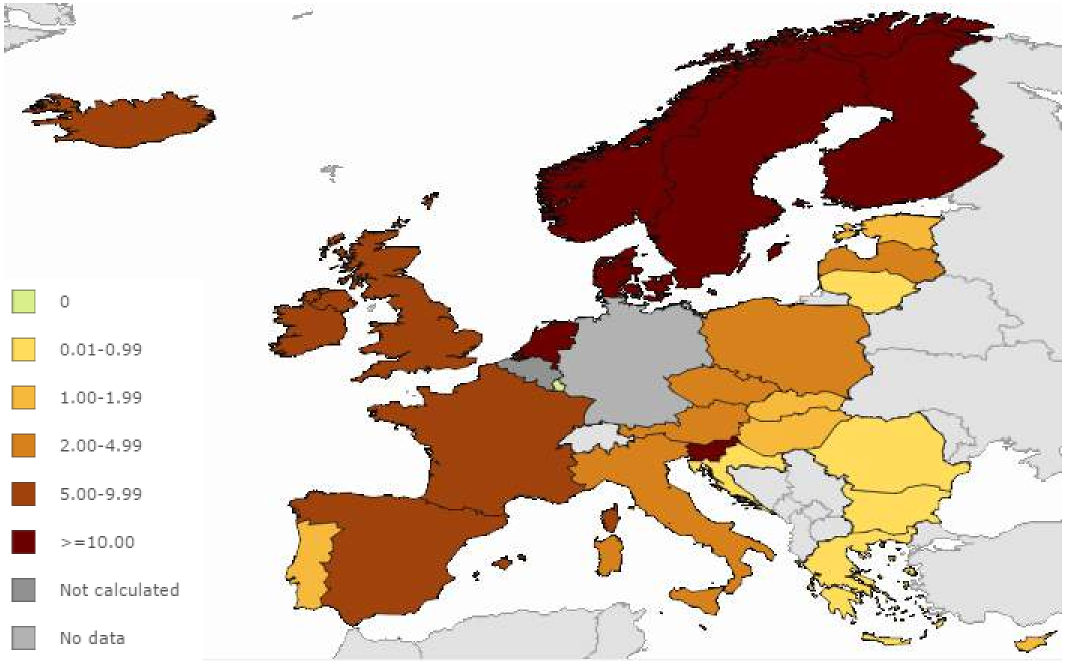


Serotype 19F; Photograph by Rob Smith (Wyeth)

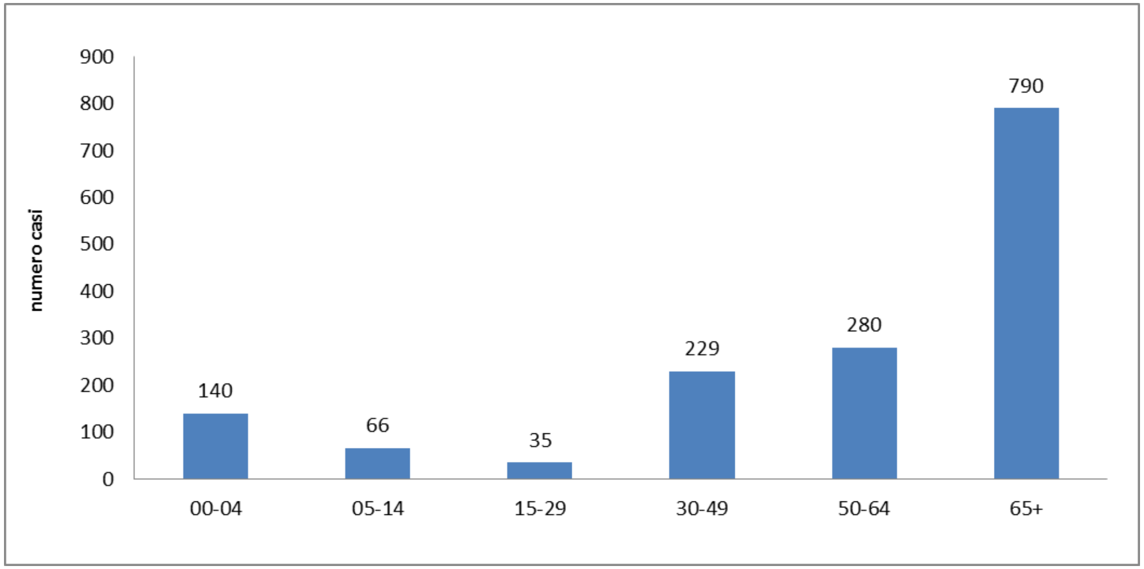
- Si osserva in coppie (diplococchi) o in piccole catene
- L'identificazione tipo-specifico è basata sulla capsula polisaccaridica che circonda la parete cellulare
- 91 (siero)tipi finora identificati sulla base della loro reazione a specifici anti sieri
- Anticorpi opsonizzanti
  - sono protettivi
  - tipo-specifici
- I 10 più comuni sierotipi sono responsabili di circa il 62% delle patologie invasive

Tasso di IPD (per 100.000) in Europa

- **21.118** casi in Europa nel 2015
- Tasso del **5,58 per 100,000** abitanti
- **Range 0,27-16,9** per 100,000 della popolazione europea, con oscillazioni significative da regione a regione
- CFR del **14,9%**
- **Sistemi di sorveglianza eterogenei**

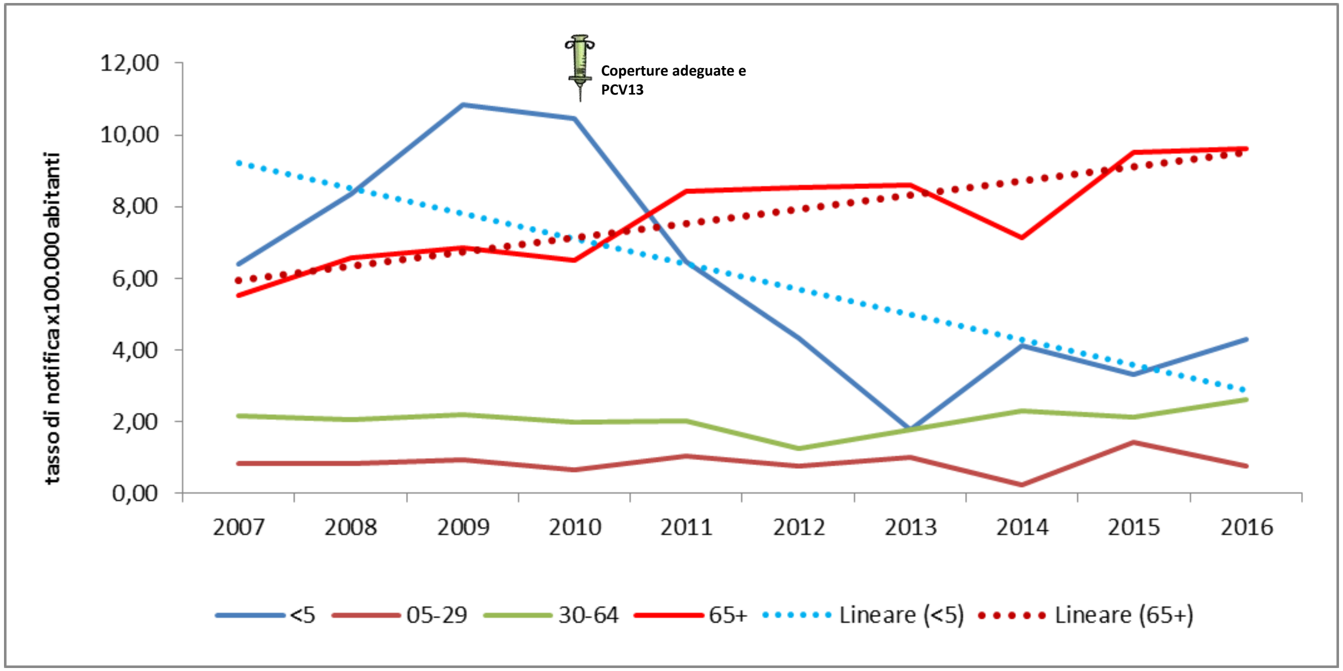

0
0.01-0.99
1.00-1.99
2.00-4.99
5.00-9.99
>=10.00
Not calculated
No data

Distribuzione del numero di casi di Streptococcus pneumoniae per classe di età, Regione Veneto 2007-2016



Nel periodo 2007-2016, attraverso i tre flussi di sorveglianza, sono stati notificati complessivamente 1.554 casi di patologia correlata ad infezione da *Streptococcus pneumoniae*.

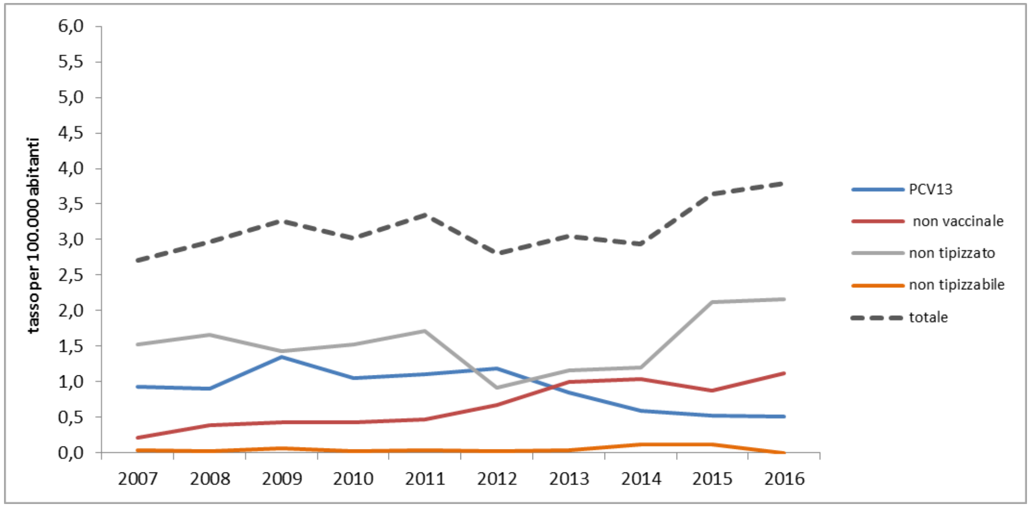
Andamento temporale delle MBI da Streptococco pneumoniae Regione Veneto (2007-2016)



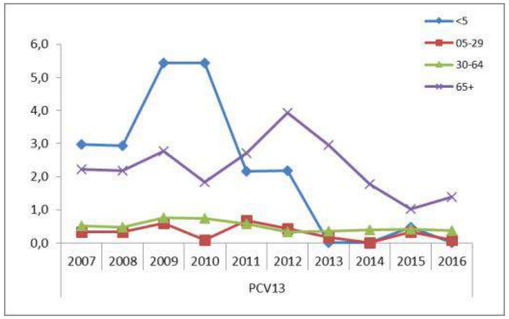
Il tasso di notifica nel periodo è pari complessivamente a 3,2 per 100.000 abitanti

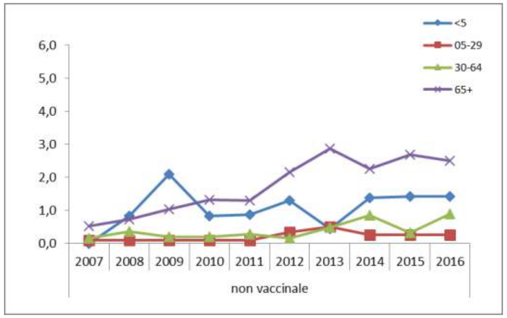
Tasso di notifica (x100.000 abitanti) per MBI da Streptococco pneumoniae per anno e valenza vaccinale, Regione Veneto (2007-2016)

1554
casi notificati



766 **(49,6%)**
ceppi tipizzati

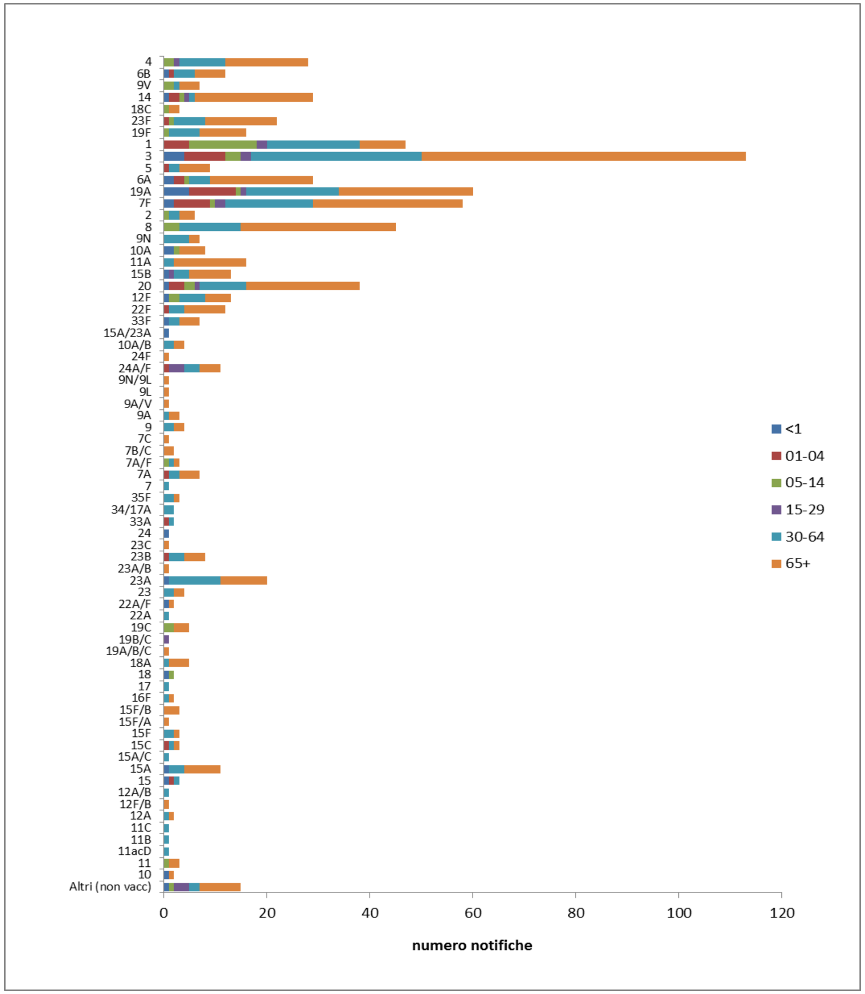




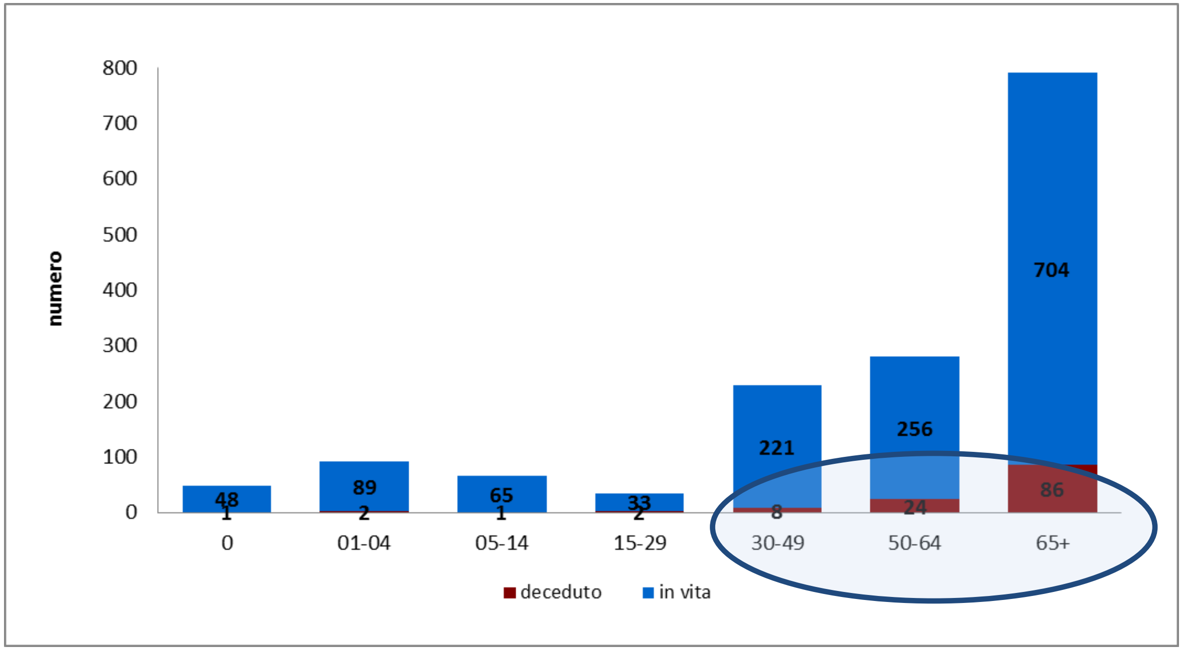
Distribuzione assoluta dei sierotipi di Streptococcus pneumoniae per classe di età, Regione Veneto (2007-2016)

Sierotipi	%
non vaccinali (NO-PCV13)	57,4
sierotipi 13 valente	42,6

sierotipo	%
3	15,0
19A	8,0
1	7,7
7F	6,2
6A	4,3
5	1,2



Casi notificati per Streptococco pneumoniae per classe di età, per esito Regione Veneto (2007-2016)



124 decessi totali, letalità pari a 8,0%, di cui:

Pneumococcal Conjugated Vaccine Reduces the High Mortality for Community-Acquired Pneumonia in the Elderly: an Italian Regional Experience

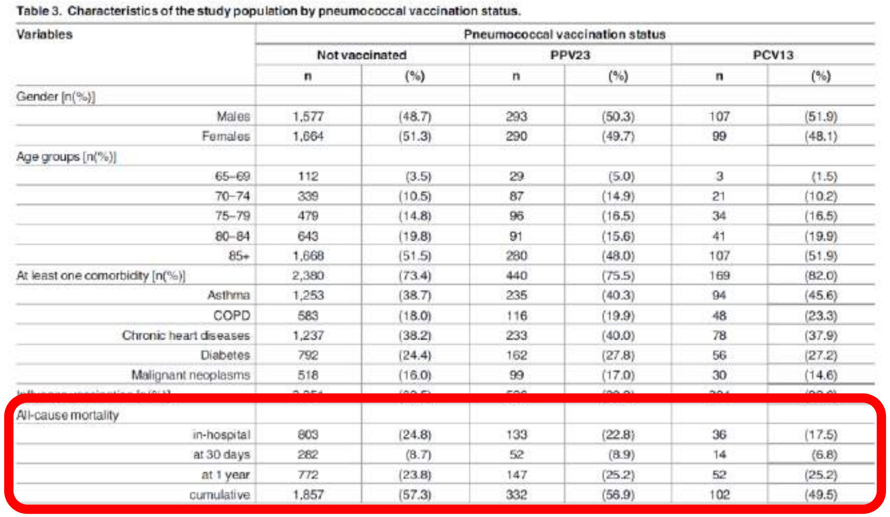
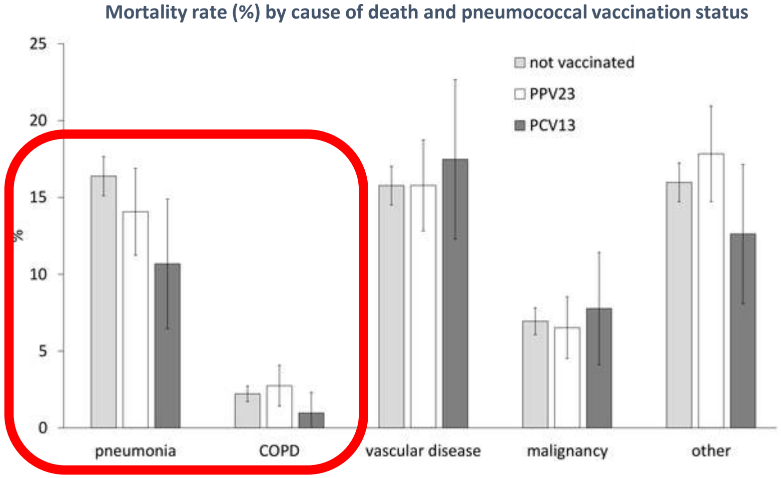


Table 3. Characteristics of the study population by pneumococcal vaccination status.

Variables	Pneumococcal vaccination status					
	Not vaccinated		PPV23		PCV13	
	n	(%)	n	(%)	n	(%)
Gender [n(%)]						
Males	1,577	(48.7)	293	(50.3)	107	(51.9)
Females	1,664	(51.3)	290	(49.7)	99	(48.1)
Age groups [n(%)]						
65–69	112	(3.5)	29	(5.0)	3	(1.5)
70–74	339	(10.5)	87	(14.9)	21	(10.2)
75–79	479	(14.8)	96	(16.5)	34	(16.5)
80–84	643	(19.8)	91	(15.6)	41	(19.9)
85+	1,668	(51.5)	280	(48.0)	107	(51.9)
At least one comorbidity [n(%)]	2,380	(73.4)	440	(75.5)	169	(82.0)
Asthma	1,253	(38.7)	235	(40.3)	94	(45.6)
COPD	583	(18.0)	116	(19.9)	48	(23.3)
Chronic heart diseases	1,237	(38.2)	233	(40.0)	78	(37.9)
Diabetes	792	(24.4)	162	(27.8)	56	(27.2)
Malignant neoplasms	518	(16.0)	99	(17.0)	30	(14.6)
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
All-cause mortality						
in-hospital	803	(24.8)	133	(22.8)	36	(17.5)
at 30 days	282	(8.7)	52	(8.9)	14	(6.8)
at 1 year	772	(23.8)	147	(25.2)	52	(25.2)
cumulative	1,857	(57.3)	332	(56.9)	102	(49.5)



Mortality rate (%) by cause of death and pneumococcal vaccination status

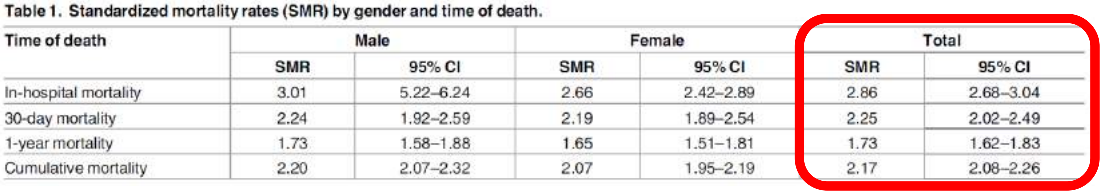
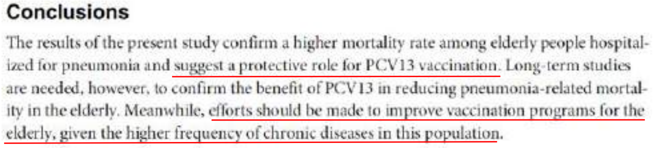


Table 1. Standardized mortality rates (SMR) by gender and time of death.

Time of death	Male		Female		Total	
	SMR	95% CI	SMR	95% CI	SMR	95% CI
In-hospital mortality	3.01	5.22–6.24	2.66	2.42–2.89	2.86	2.68–3.04
30-day mortality	2.24	1.92–2.59	2.19	1.89–2.54	2.25	2.02–2.49
1-year mortality	1.73	1.58–1.88	1.65	1.51–1.81	1.73	1.62–1.83
Cumulative mortality	2.20	2.07–2.32	2.07	1.95–2.19	2.17	2.08–2.26



Conclusions

The results of the present study confirm a higher mortality rate among elderly people hospitalized for pneumonia and suggest a protective role for PCV13 vaccination. Long-term studies are needed, however, to confirm the benefit of PCV13 in reducing pneumonia-related mortality in the elderly. Meanwhile, efforts should be made to improve vaccination programs for the elderly, given the higher frequency of chronic diseases in this population.

Baldo V, Cocchio S, Gallo T, Furlan P, Romor P, et al. (2016). PLOS ONE 11(11): e0166637. doi:10.1371/journal.pone.0166637
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0166637

Grazie per l'attenzione!!!