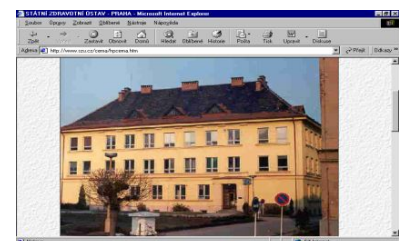


Invazivní meningokokové onemocnění - epidemiologická situace a podklady pro vakcinační doporučení

Pavla Křížová

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Centrum epidemiologie a mikrobiologie
Státní zdravotní ústav
Praha

HVD, říjen 2013



Mění se epidemiologie IMO - celosvětově

[Expert Rev Vaccines](#). 2011 Oct;10(10):1477-86. doi: 10.1586/erv.11.117.

Changing epidemiology of meningococcal disease in Europe from the mid-20th to the early 21st Century.

[Kriz P](#), [Wieffer H](#), [Holl K](#), [Rosenlund M](#), [Budhia S](#), [Vyse A](#).

[Vaccine](#). 2012 May 30;30 Suppl 2:B26-36. doi: 10.1016/j.vaccine.2011.12.032. Epub 2011 Dec 15.

The changing and dynamic epidemiology of meningococcal disease.

[Halperin SA](#), [Bettinger JA](#), [Greenwood B](#), [Harrison LH](#), [Jelfs J](#), [Ladhani SN](#), [McIntyre P](#), [Ramsay ME](#), [Sáfadi MA](#).

[PLoS One](#). 2012;7(11):e50659. doi: 10.1371/journal.pone.0050659. Epub 2012 Nov 29.

The changing epidemiology of meningococcal disease in Quebec, Canada, 1991-2011: potential implications of emergence of new strains.

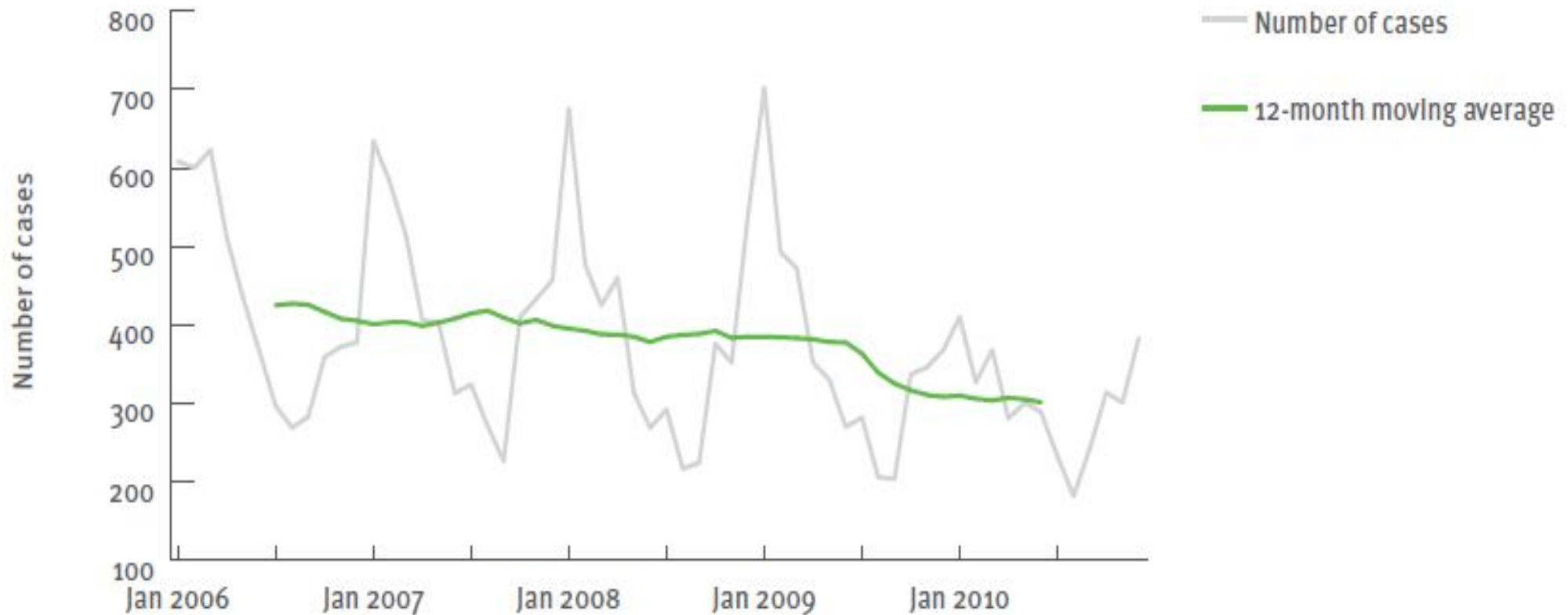
[Gilca R](#), [Deceuninck G](#), [Lefebvre B](#), [Tsang R](#), [Amini R](#), [Gilca V](#), [Douville-Fradet M](#), [Markowski F](#), [De Wals P](#).

[Hum Vaccin Immunother](#). 2013 Jan;9(1):162-71. doi: 10.4161/hv.22302. Epub 2012 Oct 29.

The changing epidemiology of meningococcal disease in North America 1945-2010.

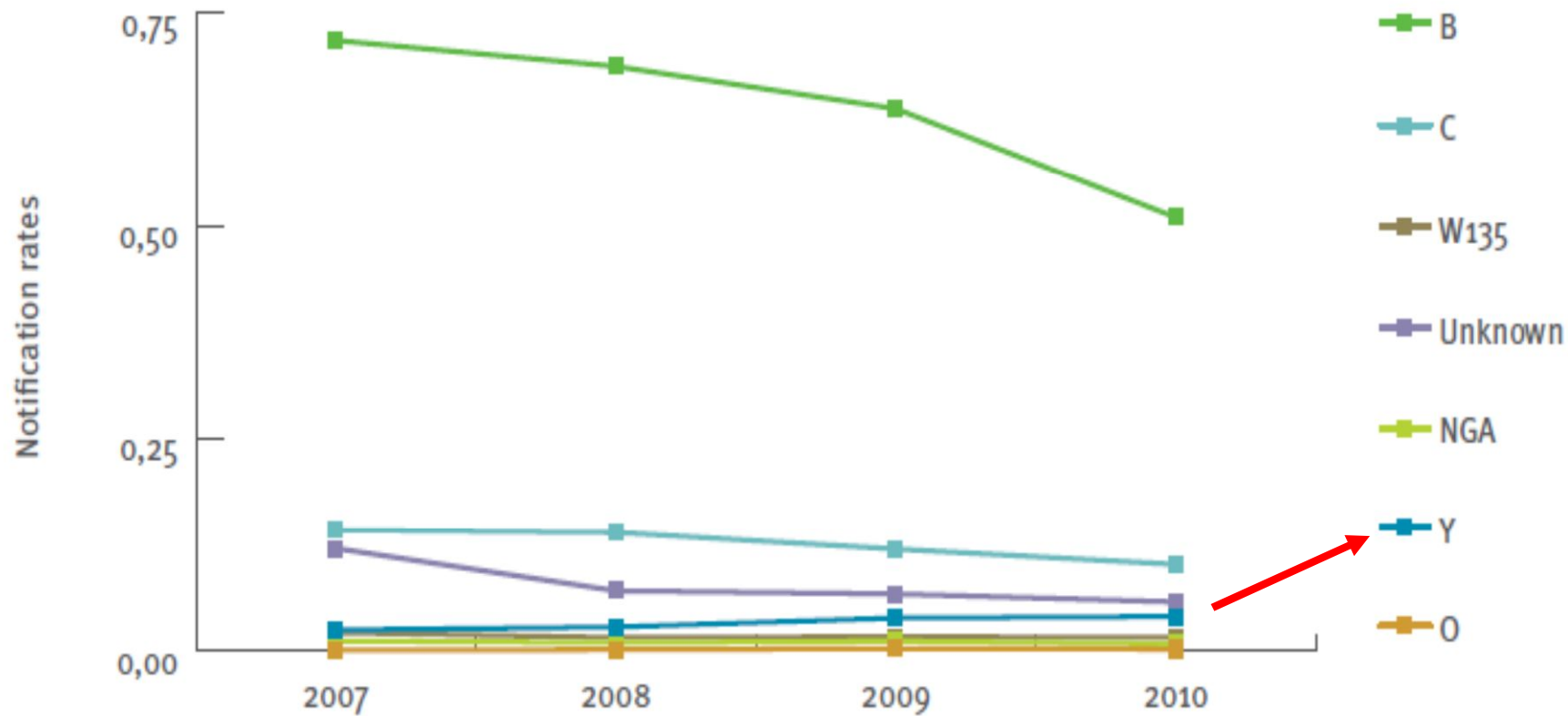
[Baccarini C](#), [Ternouth A](#), [Wieffer H](#), [Vyse A](#).

Figure 2.5.6. Trend and number of reported confirmed invasive meningococcal disease cases in EU/EEA countries, 2006–10



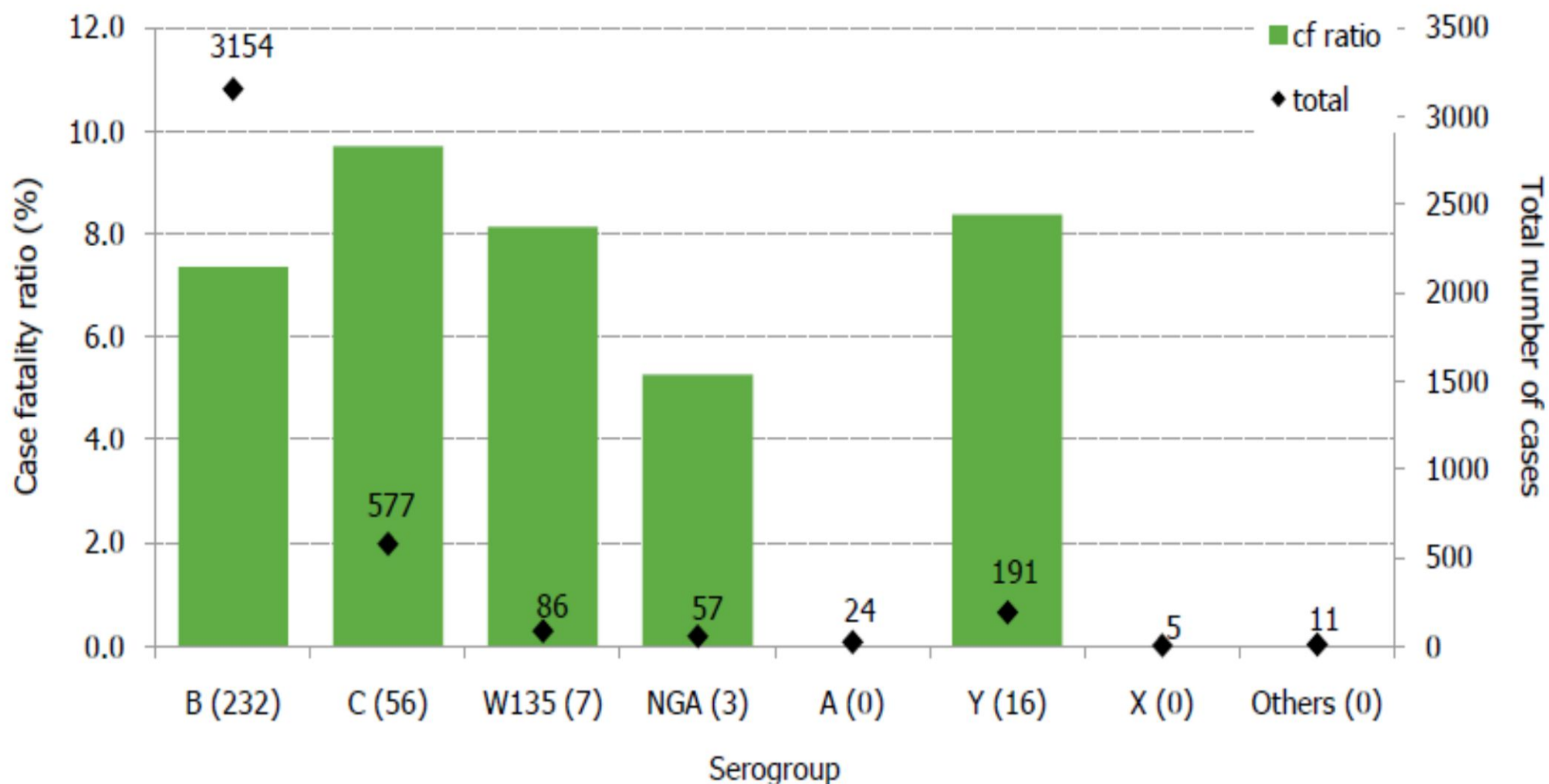
<http://www.ecdc.europa.eu/en/publications/Publications/Annual-Epidemiological-Report-2012.pdf>

Figure 2.5.9. Trend of reported confirmed invasive meningococcal disease cases by year of reporting and by serogroup, EU/EEA countries, 2007–10



Source: Country reports from Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom.
 B, C, W135, NGA, Y, O: serogroups.

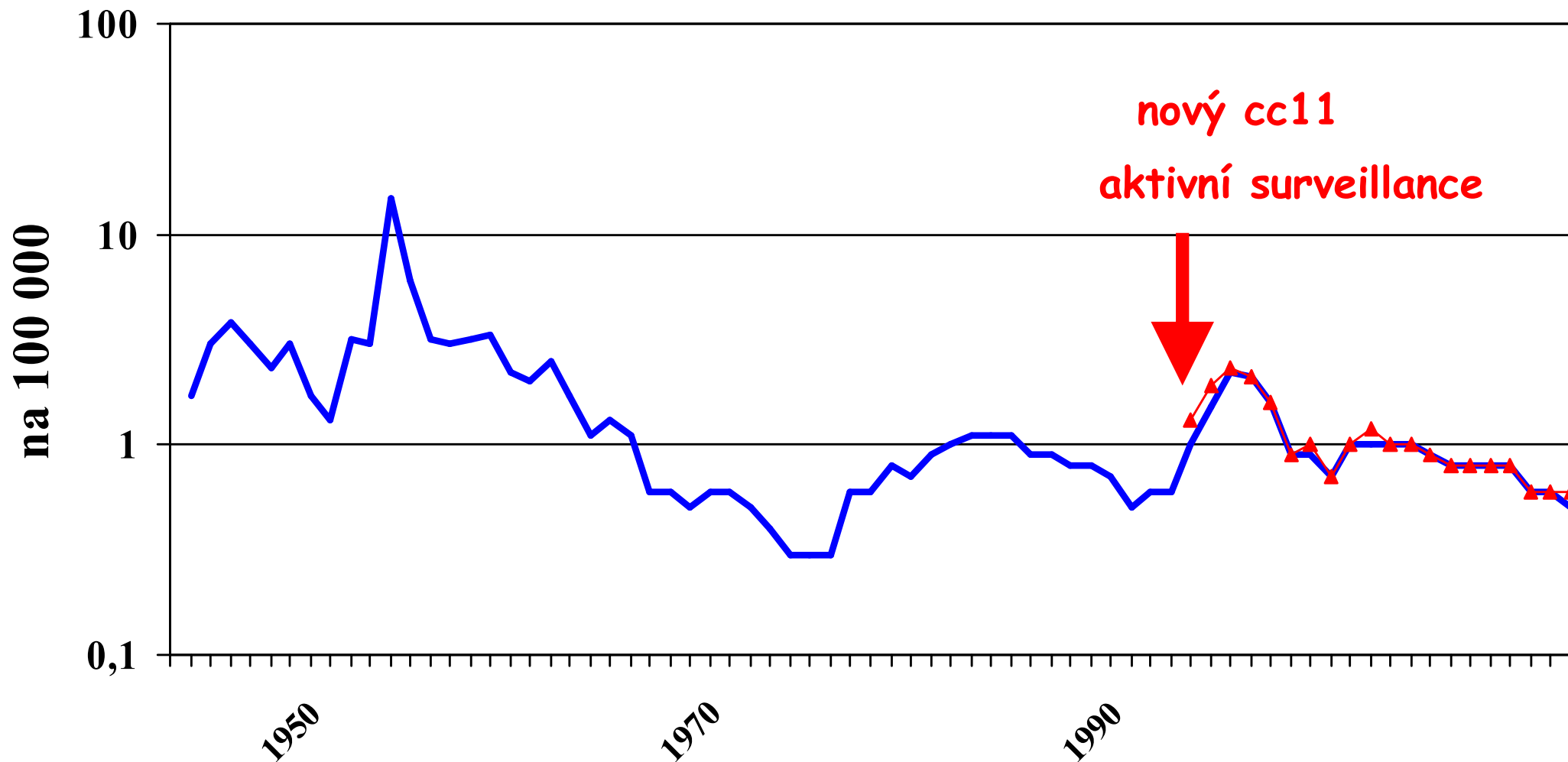
Figure 44 Serogroup-specific case fatality ratio of confirmed invasive meningococcal disease cases in EU/EEA countries, 2009 (n=4 105)



Contributing countries: Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Norway, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

Note: Number of deaths in brackets.

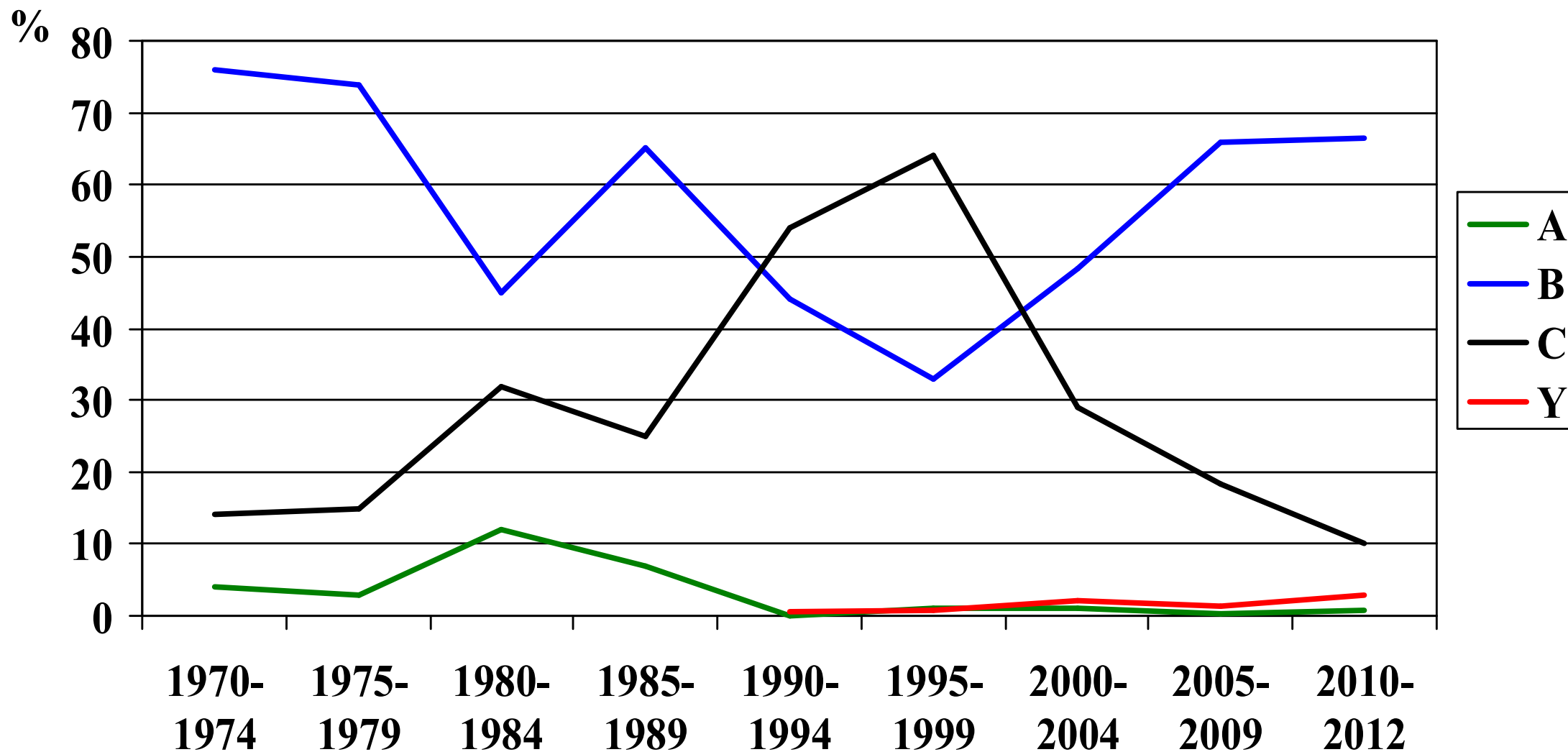
Incidence invazivního meningokokového onemocnění Česká republika, 1943-2012



Rutinní hlášení + surveillance data NRL pro meningokokové nákazy



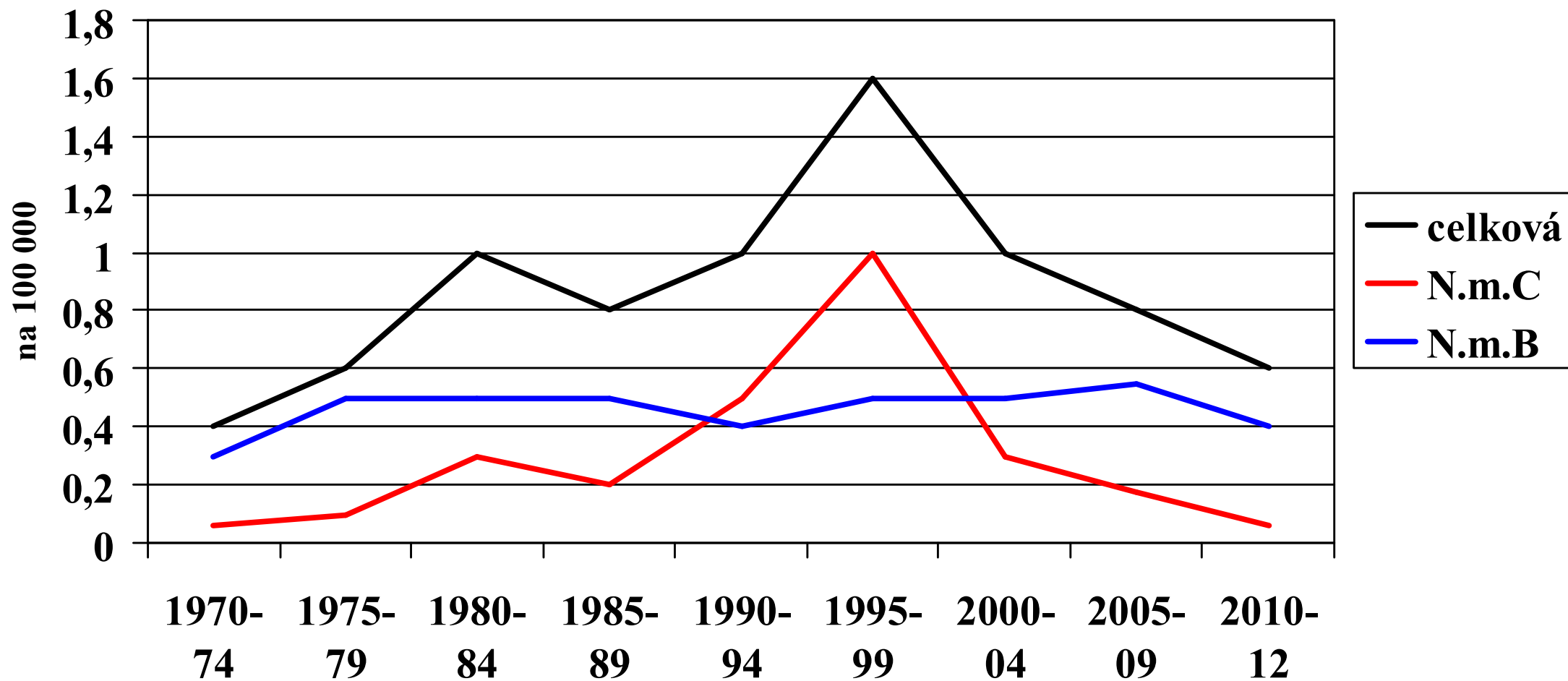
Distribuce séro skupin *Neisseria meningitidis* z IMO Česká republika, 1970-2012



Rutinní hlášení + surveillance data NRL pro meningokokové nákazy



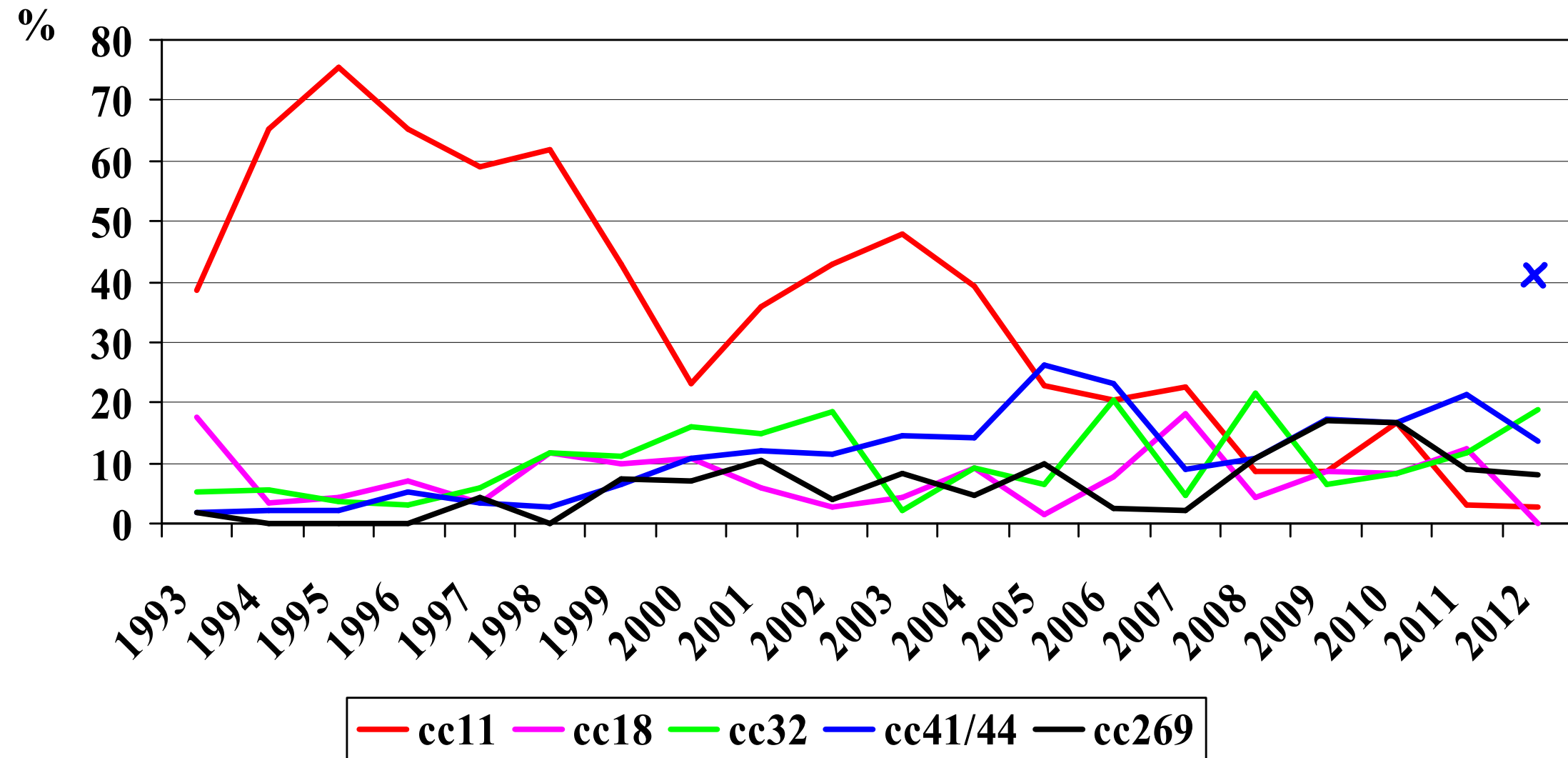
Nemocnost IMO - celková a specifická dle séro skupin Česká republika, 1970-2012



Rutinní hlášení + surveillance data NRL pro meningokokové nákazy

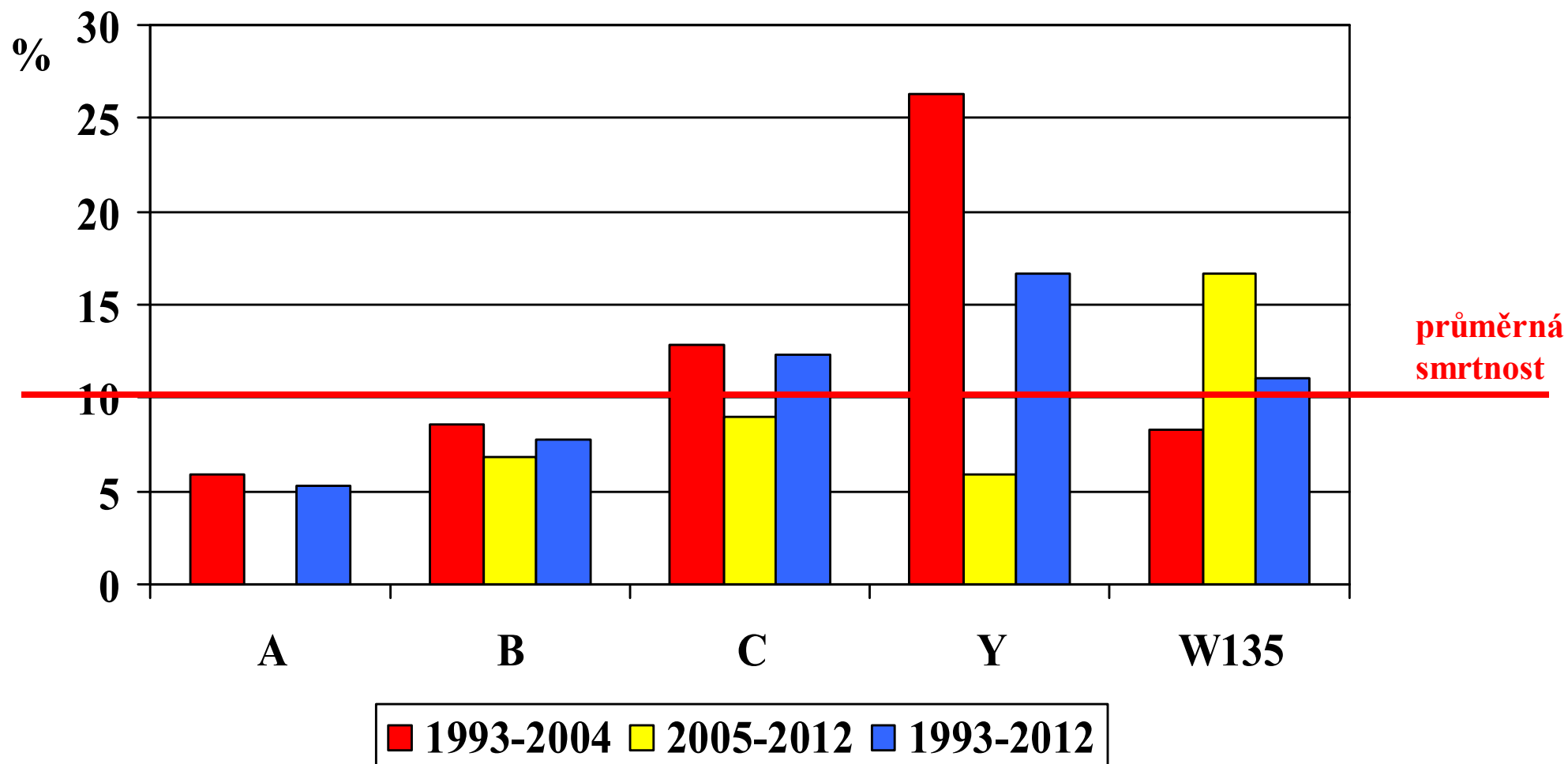


Hlavní hypervirulentní komplexy *N. meningitidis* působící IMO Česká republika, 1993 - 2012

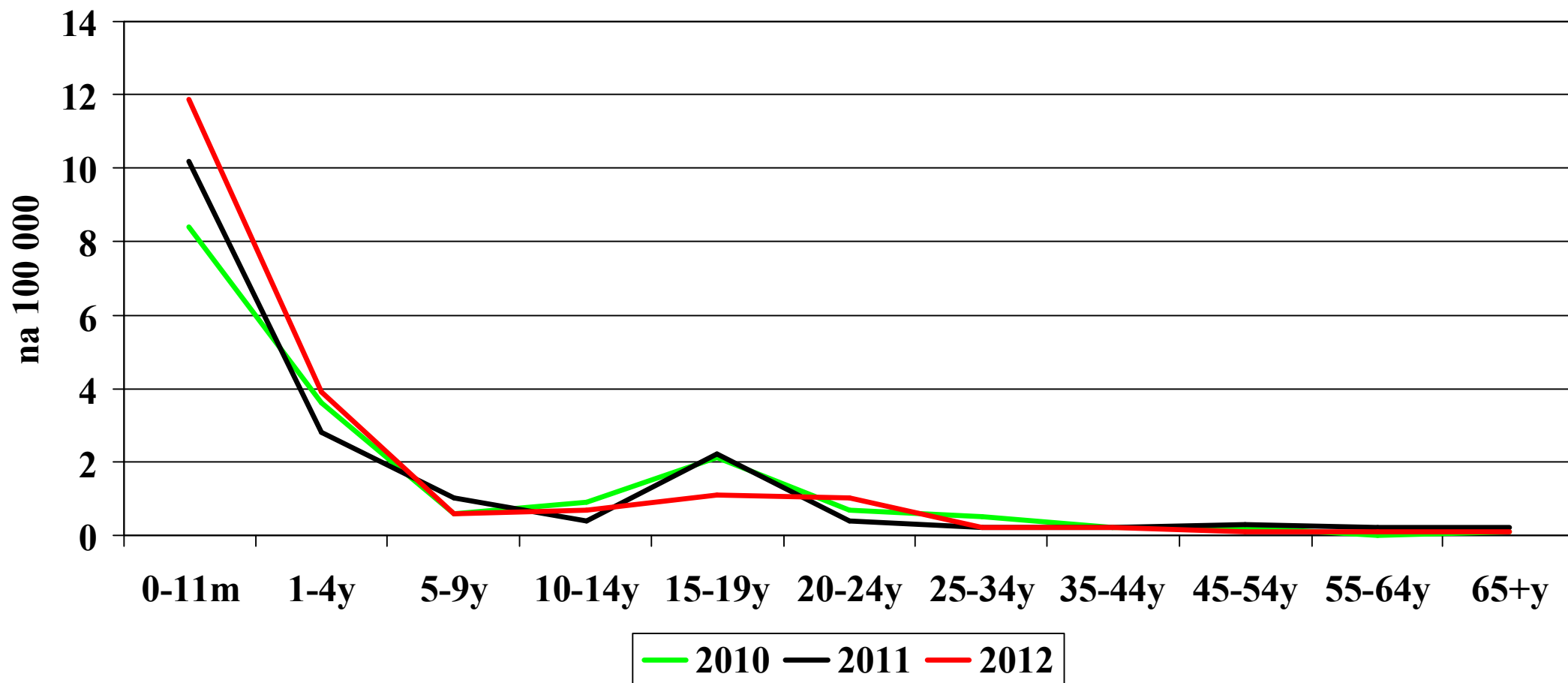


Surveillance data NRL pro meningokokové nákazy

Smrtnost IMO dle séro skupin *Neisseria meningitidis*
Česká republika, 1993-2012
(n = 2283)

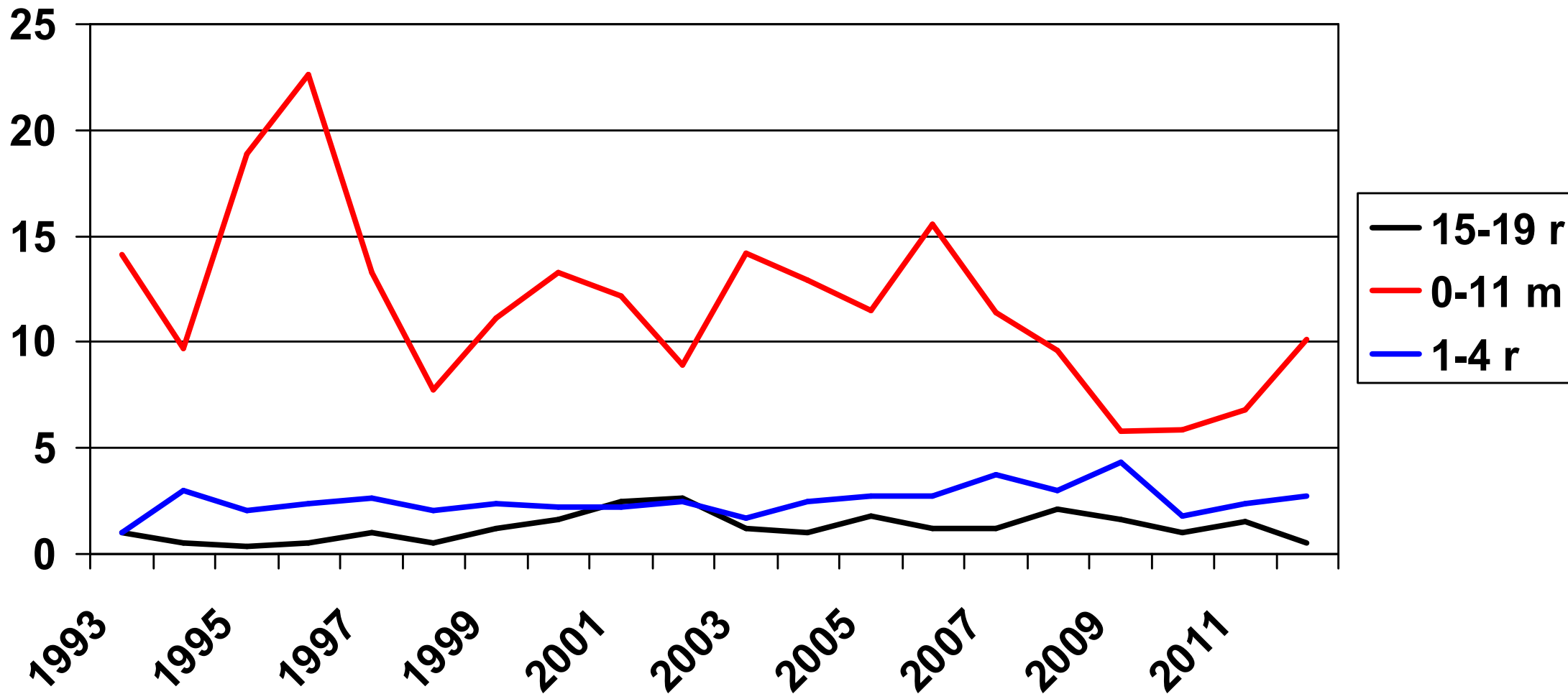


IMO - věkově specifická nemocnost Česká republika, 2010, 2011, 2012



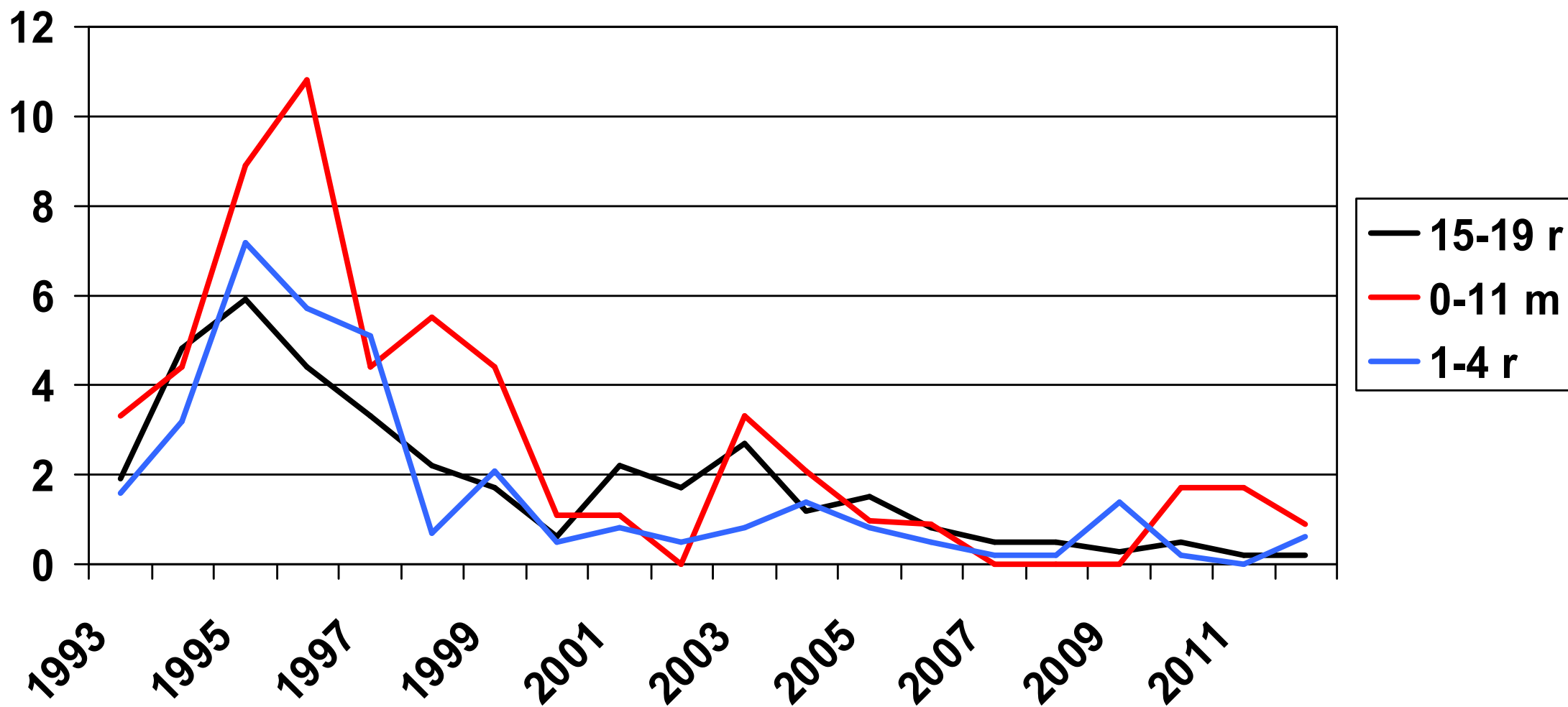
Surveillance data NRL pro meningokokové nákazy

Nemocnost (na 100000) IMO N.m.B - specifická dle věku Česká republika, 1993-2012

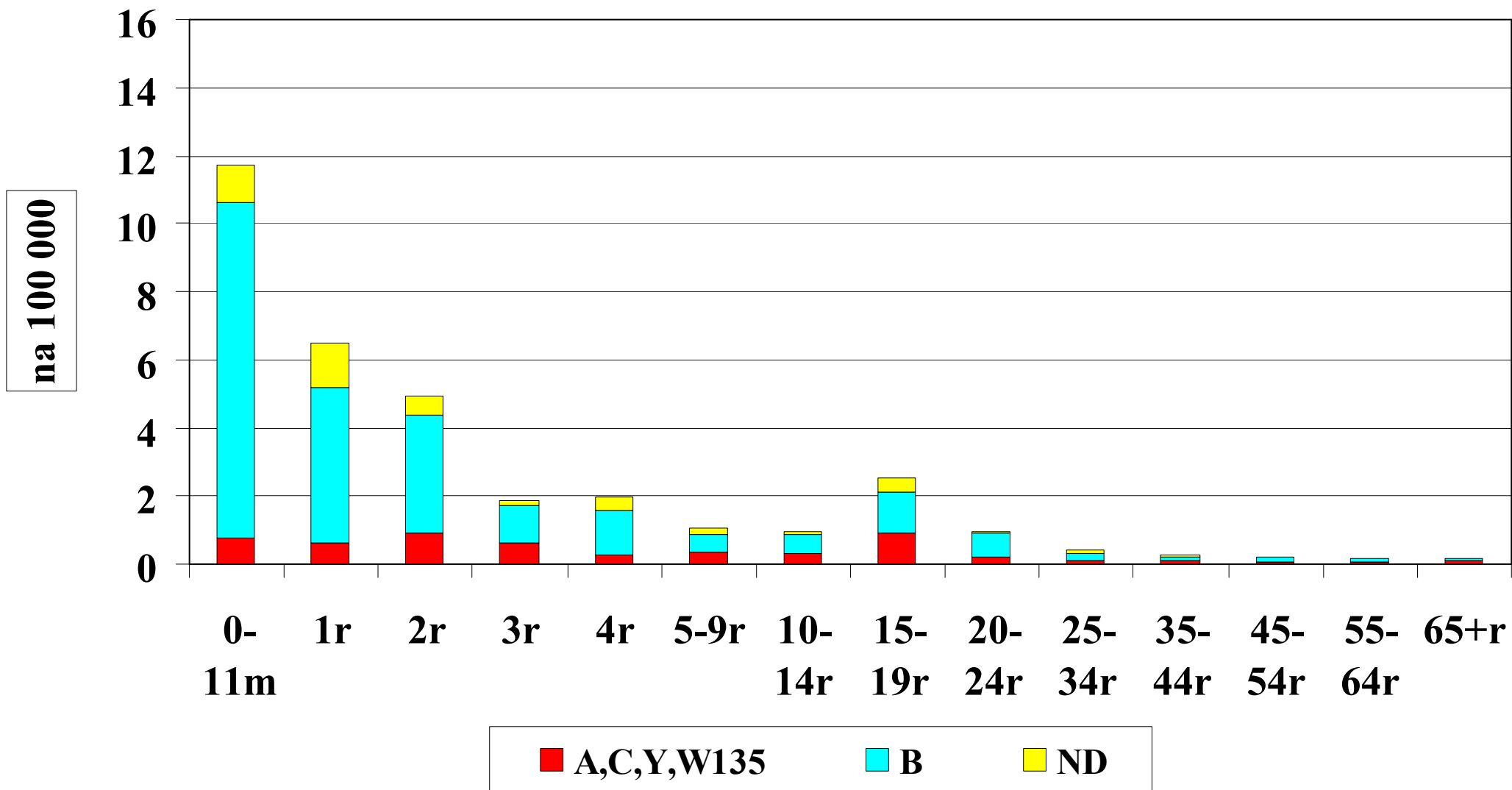


Surveillance data NRL pro meningokokové nákazy

Nemocnost (na 100000) IMO N.m.C - specifická dle věku Česká republika, 1993-2012

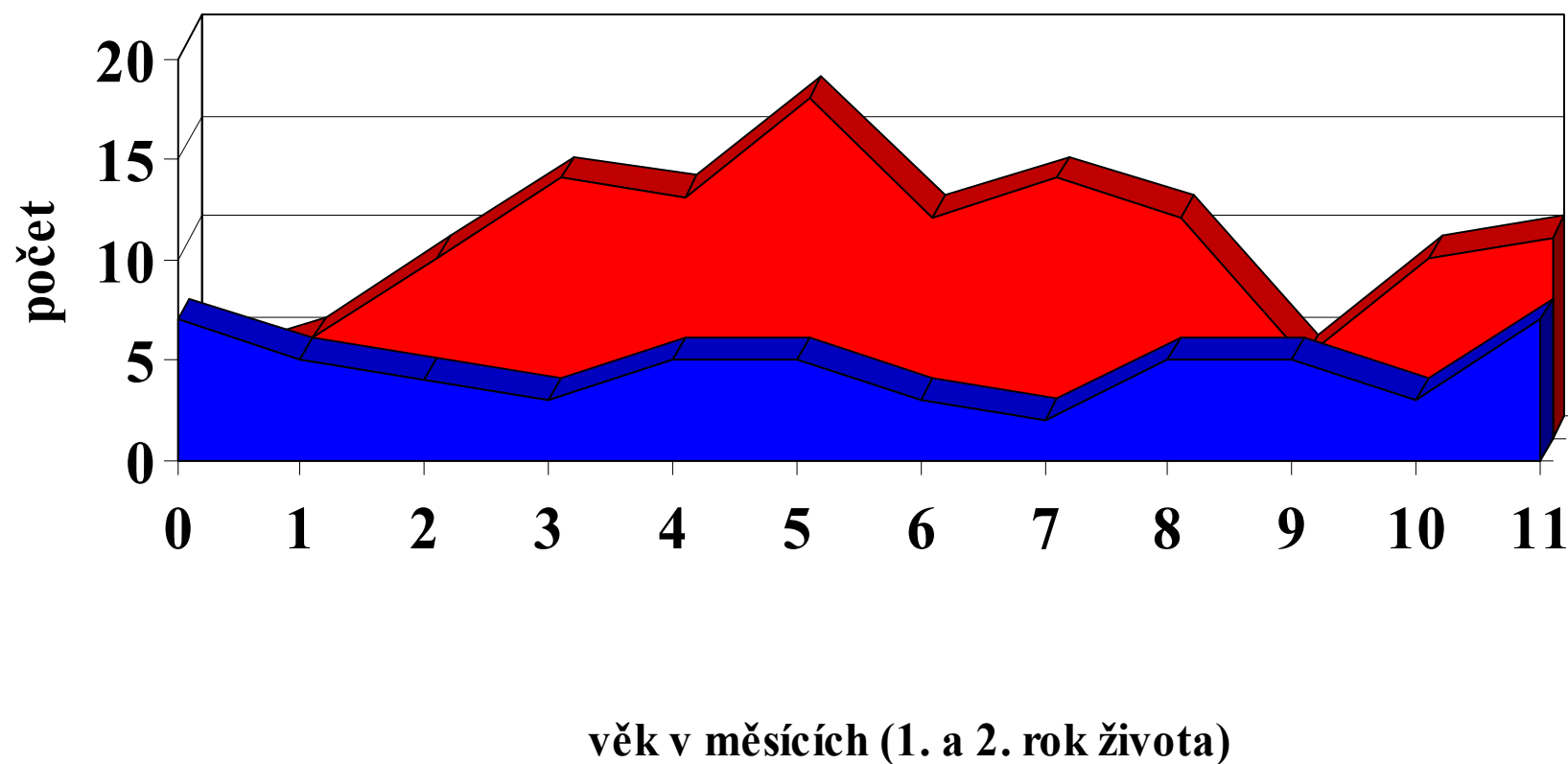


IMO - věkově specifická nemocnost dle séro skupin Česká republika, 2002-2012 A,C,Y,W135 a B a ND



Surveillance data NRL pro meningokokové nákazy
Data NRL pro meningokokové nákazy
Surveillance data NRL pro meningokokové nákazy

Kumulativní počet IMO N.m.B u dětí do 2 let věku v měsíčních intervalech Česká republika, 2003-2013 (25.k.t.)



■ N.m.B - 2. rok věku ■ N.m.B - 1. rok věku



Surveillance data NRL pro meningokokové nákazy

Invazivní meningokokové onemocnění
(včetně úmrtí), Česká republika 2013 (38.k.t.)

Surveillance data NRL pro meningokokové nákazy

Věk	Séroskopina <i>Neisseria meningitidis</i>						Celkem
	B	C	X	Y	W135	ND	
0-11 m	10 (+ 2m)						10
1-4 r	5	3				1	9
5-9 r	1					1	2
10-14 r	1		1				2
15-19 r	5	2 (+ 18r)					7
20-24 r		1		1		1	3
25-34 r	5			1			6
35-44 r	1						1
45-54 r	4					1	5
55-64 r	1						1
65+ r	3						3
Celkem	36	7		2		4	49
%	73,4	14,3		4,1		8,2	100,0

2 úmrtí = 4,1 % smrtnost

díky !

Novinky v mezinárodním vývoji meningokokových vakcín z posledních let

- dostupnost konjugované tetravakcíny **A,C,Y,W135** i pro malé děti
- uznání nutnosti přeočkování konjugovanými vakcínami k dosažení solidní imunity
- dostupnost vakcíny **proti séro skupině B**, vyrobené metodou reverzní vakcinologie

Aktuální doporučení vakcinační strategie NRL pro meningokokové nákazy

- očkování **tetravakcínou A,C,Y,W135** od dětského předškolního věku a přeočkovávání až k dosažení preadolescentního věku, eventuálně mladého dospělého věku;
- očkování **MenB vakcínou** v co nejmladším věku před dosažením jednoho roku - základní očkování sestává ze tří dávek, doporučení k přeočkování jsou diskutována.



EMGM –The European Meningococcal Disease Society

Statement of the EMGM Society on meningococcal disease surveillance after licensure and implementation of vaccination with Bexsero™ in European countries

- 1. Molecular Typing:** To monitor vaccine induced changes in invasive meningococcal strains, molecular typing of vaccine antigen encoding genes must be provided by reference laboratories [1]. Furthermore, to detect potential changes in the bacterial population, the multilocus sequence type of invasive isolates must be determined for a representative sample of strains [2]. Countries planning to introduce the vaccine should provide financial resources to ensure molecular typing for at least five years following broad introduction of the vaccine. Whole genome sequencing is now an option to obtain the necessary data by a single sequencing approach that may be considered [3,4], although it is only available at specialized laboratories to date.
- 2. Antigen Expression Analysis:** The Meningococcal Antigen Typing System (MATS) provided by Novartis is currently the sole validated and reliable instrument to obtain expression data for three antigens (fHbp, NhbA, and NadA), which is of pivotal importance for assessment of vaccine strain coverage [5–7]. Without this tool, harmonized assessment of strain coverage in European countries will not be possible. Therefore, the unrestricted availability of MATS for European countries must be guaranteed. The producer of the kit should be pledged to reliably deliver the assay to national reference laboratories for at least three years after implementation of the vaccine. Due to the fact that the assay is provided by the manufacturer of the vaccine, reference laboratories should develop alternative assays to secure assay supply.
- 3. Serological analyses:** Possible vaccine failures, i.e. vaccinated cases suffering from meningococcal group B disease, may be caused either by insufficient antibody titers due to primary vaccine failure or waning immunity or by disease isolates that do not bind vaccine-induced bactericidal antibodies. Thus vaccine specific antibody titers need to be determined. Only the serum bactericidal assay using human complement can be a surrogate of protection [8]. However, very few laboratories in Europe have the delicate test. Thus countries implementing serogroup B vaccination are strongly advised to establish an operating procedure for testing vaccinated serogroup B cases either in a national laboratory or by shipping to a qualified laboratory in a neighbouring country.

Molekulární typizace
MLST ✓ **NRL**
WGS ✓ **EMGM**

Expresse MenB antigenů
MATS ✓ **EMGM**

Protilátky v séru
SBA ✓ **EMGM**

financování ???

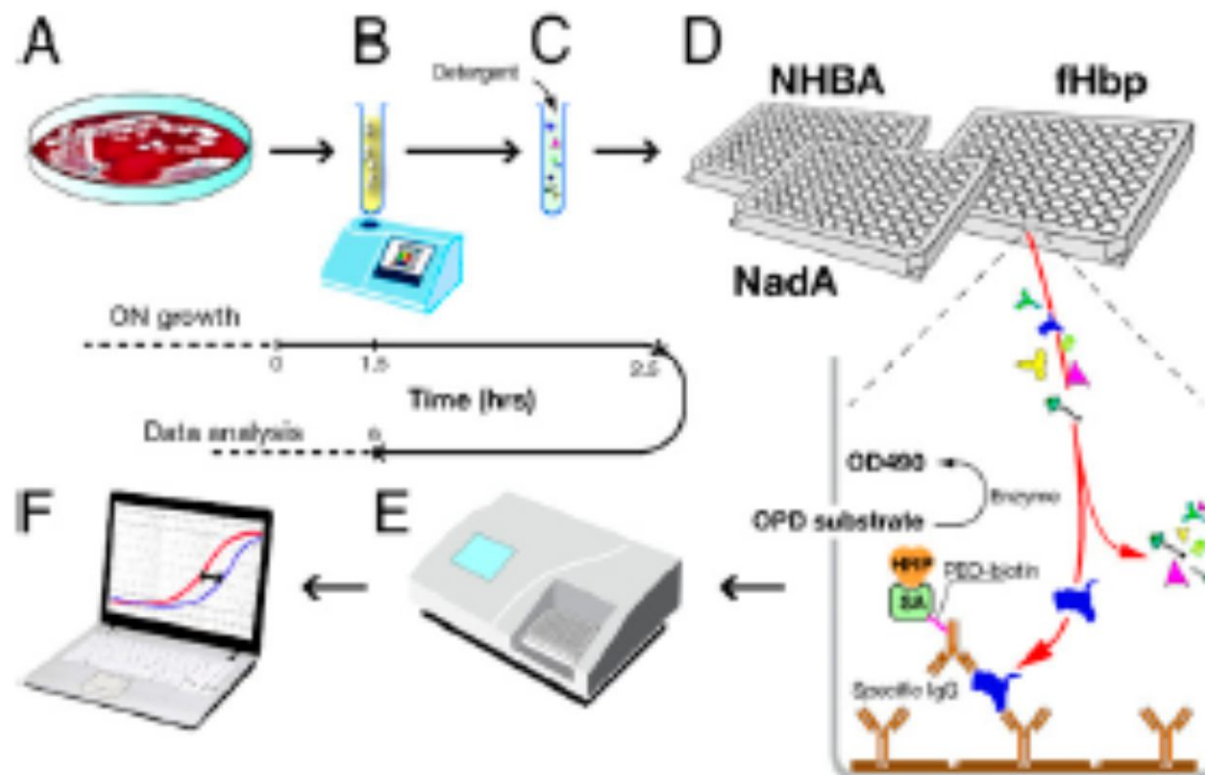
Qualitative and quantitative assessment of meningococcal antigens to evaluate the potential strain coverage of protein-based vaccines

MATS

John Donnelly^{a,1}, Ducdo Medini^a, Giuseppe Boccadifuoco^a, Alessia Biolchi^a, Joel Ward^b, Carl Frasch^c, E. Richard Moxon^d, Maria Stella^a, Maurizio Comanduci^a, Stefania Bambini^a, Alessandro Muzzi^a, William Andrews^e, Jie Chen^e, George Santos^f, Laura Santini^a, Philip Boucher^a, Davide Serruto^a, Mariagrazia Pizza^a, Rino Rappuoli^{a,1}, and Marzia Monica Giuliani^a

19490–19495 | PNAS | November 9, 2010 | vol. 107 | no. 45

www.pnas.org/cgi/doi/10.1073/pnas.1013758107



[Lancet Infect Dis](#). 2013 May;13(5):416-25. doi: 10.1016/S1473-3099(13)70006-9. Epub 2013 Feb 13.

Predicted strain coverage of a meningococcal multicomponent vaccine (4CMenB) in Europe: a qualitative and quantitative assessment.

[Vogel U](#), [Taha MK](#), [Vazquez JA](#), [Findlow J](#), [Claus H](#), [Stefanelli P](#), [Caugant DA](#), [Kriz P](#), [Abad R](#), [Bambini S](#), [Carannante A](#), [Deghmane AE](#), [Fazio C](#), [Frosch M](#), [Frosi G](#), [Gilchrist S](#), [Giuliani MM](#), [Hong E](#), [Ledroit M](#), [Lovaglio PG](#), [Lucidarme J](#), [Musilek M](#), [Muzzi A](#), [Oksnes J](#), [Rigat F](#), [Orlandi L](#), [Stella M](#), [Thompson D](#), [Pizza M](#), [Rappuoli R](#), [Serruto D](#), [Comanducci M](#), [Boccadifuoco G](#), [Donnelly JJ](#), [Medini D](#), [Borrow R](#).

Abstract

BACKGROUND:

A novel multicomponent vaccine against meningococcal capsular group B (MenB) disease contains four major components: factor-H-binding protein, neisserial heparin binding antigen, neisserial adhesin A, and outer-membrane vesicles derived from the strain NZ98/254. **Because the public health effect of the vaccine, 4CMenB (Novartis Vaccines and Diagnostics, Siena, Italy), is unclear, we assessed the predicted strain coverage in Europe.**

METHODS:

We assessed invasive MenB strains isolated mainly in **the most recent full epidemiological year in England and Wales, France, Germany, Italy, and Norway**. Meningococcal antigen typing system (MATS) results were linked to multilocus sequence typing and antigen sequence data. To investigate whether generalisation of coverage applied to the rest of Europe, we also assessed isolates from the **Czech Republic and Spain**.

FINDINGS:

1052 strains collected from July, 2007, to June, 2008, were assessed from England and Wales, France, Germany, Italy, and Norway. All MenB strains contained at least one gene encoding a major antigen in the vaccine. **MATS predicted that 78% of all MenB strains would be killed by postvaccination sera (95% CI 63-90, range of point estimates 73-87% in individual country panels)**. Half of all strains and 64% of covered strains could be targeted by bactericidal antibodies against more than one vaccine antigen. Results for the 108 isolates from the Czech Republic and 300 from Spain were consistent with those for the other countries.

INTERPRETATION:

MATS analysis showed that a multicomponent vaccine could protect against a substantial proportion of invasive MenB strains isolated in Europe. Monitoring of antigen expression, however, will be needed in the future.

ČR 74 %



**MATS - pokrytí N.m.B vakcínou Bexsero
ČR, 2007-2010, 108 izolátů z IMO
NRL meningo Praha + NRL meningo Wurzburg**

antigen	%
fHbp	30
fHbp + NHBA	33
NHBA	6
fHbp + NadA	3
NHBA + NadA	1
fHbp + NHBA + porA	1
žádný antigen	26

ZÁVĚR

- Aktuální incidence IMO v ČR je nízká - není apel na masovou vakcinaci, která navozuje kolektivní imunitu.
- **O to větší je však apel na budování ochrany jednotlivce:**
 - co nejdříve
 - co nejdéle
 - co nejširší
- **Poprvé v historii** máme v rukou vakcíny, jejichž kombinací a vhodným očkovacím schématem lze tyto požadavky na širokou a dlouhodobou antimeningokokovou ochranu jedince splnit.
- Po zavedení MenB vakcíny: **zvýšené nároky na surveillance IMO**, včetně **molekulárních metod + hlášení vakcinačního stavu IMO do EPIDAT**.
- Sledování IMO B očkovaných MenB vakcínou k **odlišení:**
 - selhání vakcíny
 - nepokrytí vakcínou

MATS
SBA



Poděkování

- Velké díky patří všem, kdo pomáhají realizovat kvalitní surveillance IMO v ČR.
- Velké díky pracovníkům NRL pro meningokokové nákazy.
- Sekvenční charakterizace izolátů *N. meningitidis* byla podpořena projektem IGA MZ reg. č. NT/11424-4.