XI International Symposium for Latin American experts

Meningococcal vaccines

VACCINOLOGY 2018

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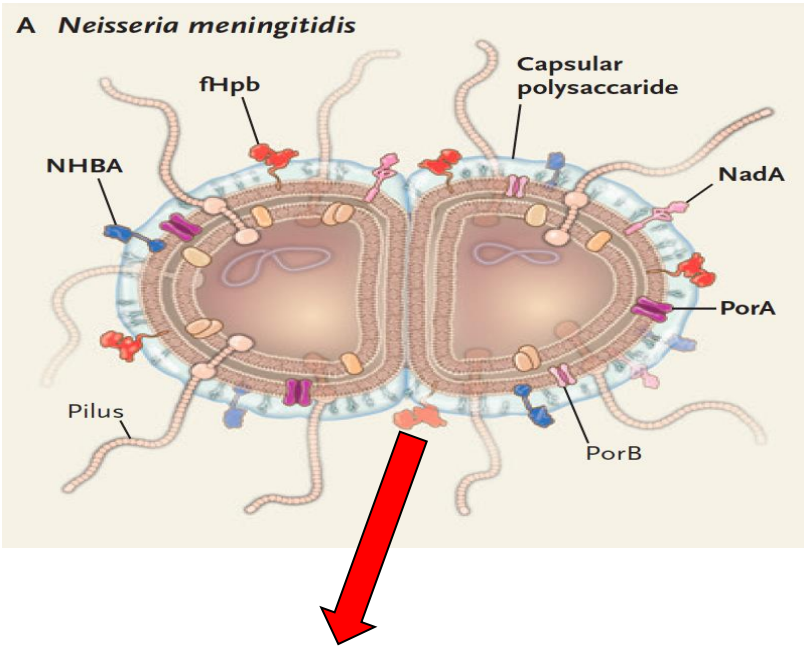
Disclosures

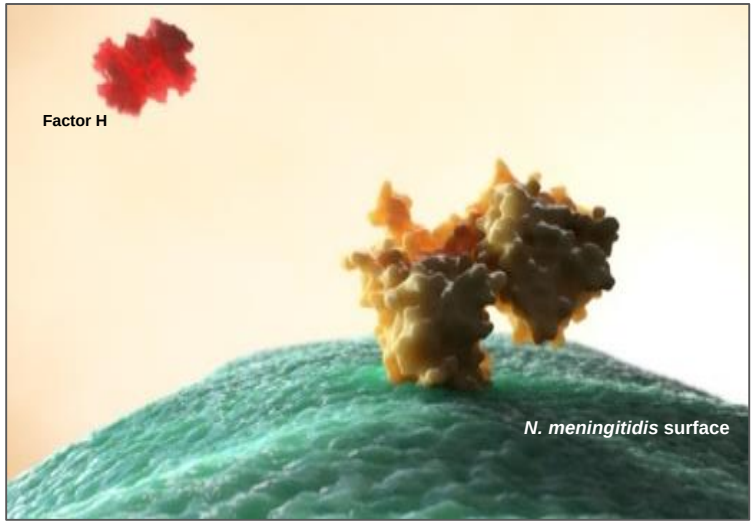
- Speaker at sponsored training sessions/meetings for healthcare workers
  - MSD, Pfizer
- Sponsored attendance to scientific conferences
  - Pfizer

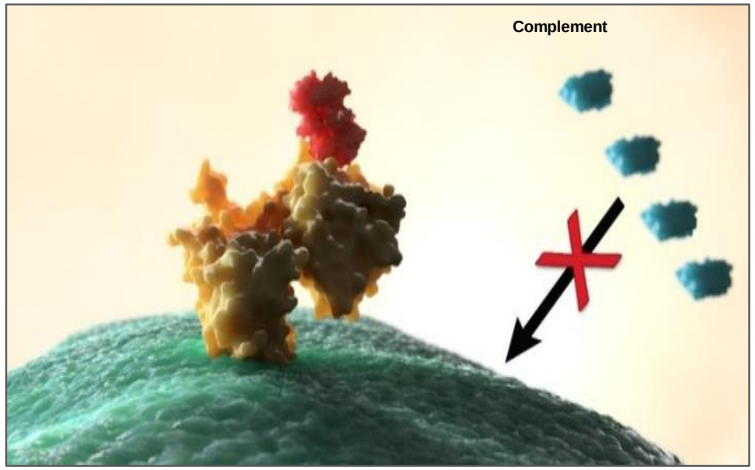
Outline

- Microbiology
- Epidemiology
- Vaccines
  - Polysacharide
  - Conjugate
  - OMP
- Impact of meningococcal vaccines
- Conclusions

Meningococcal disease is a major cause of meningitis and sepsis in infants and adolescents worldwide







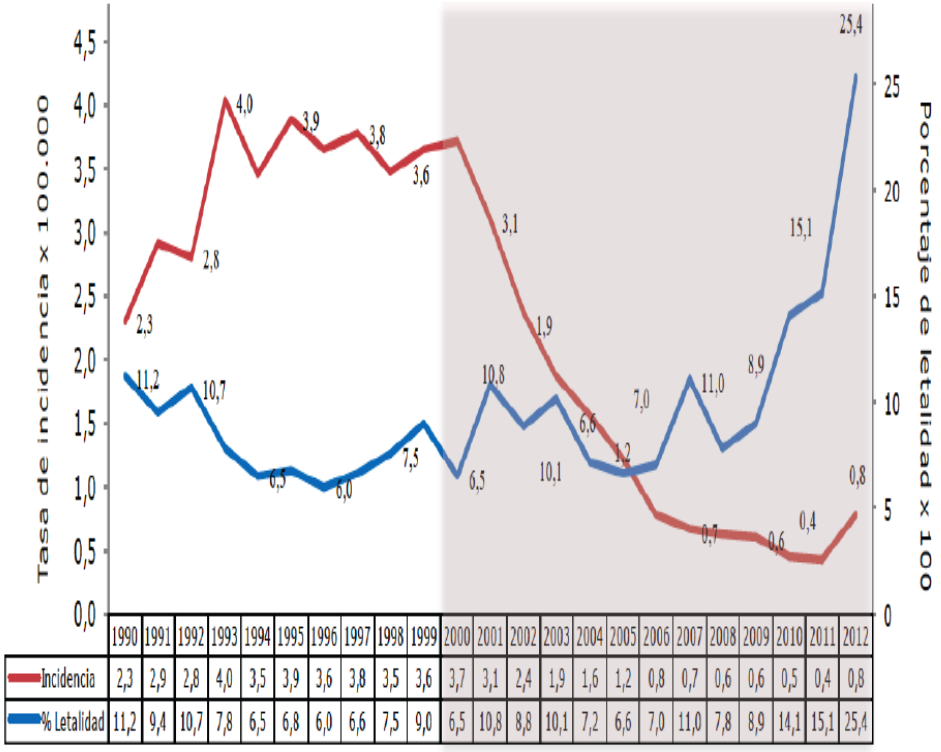
- Serogroups:
  - A, B, C, W, Y, X
- High CFR
- Sequelae: up to 36%

Kim J., n engl j med 375;3 July 21, 2016 Kaplan SL, et al. *Pediatrics.* 2006;118:e979-e984; Viner, Lancet neurology Agosto 2012

Ever changing and unpredictable epidemiology

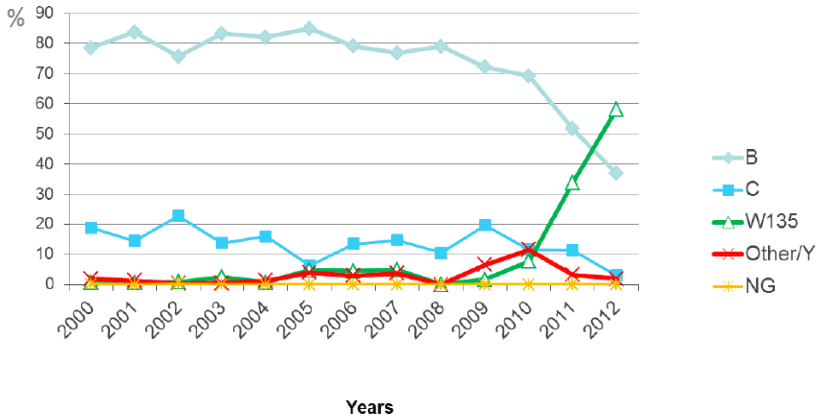
Outbreaks: significant health, social and economic impact

Incidence and CFR of Invasive Meningococcal Disease Chile 1990 to 2012



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Incidencia	2,3	2,9	2,8	4,0	3,5	3,9	3,6	3,8	3,5	3,6	3,7	3,1	2,4	1,9	1,6	1,2	0,8	0,7	0,6	0,6	0,5	0,4	0,8
% Letalidad	11,2	9,4	10,7	7,8	6,5	6,8	6,0	6,6	7,5	9,0	6,5	10,8	8,8	10,1	7,2	6,6	7,0	11,0	7,8	8,9	14,1	15,1	25,4

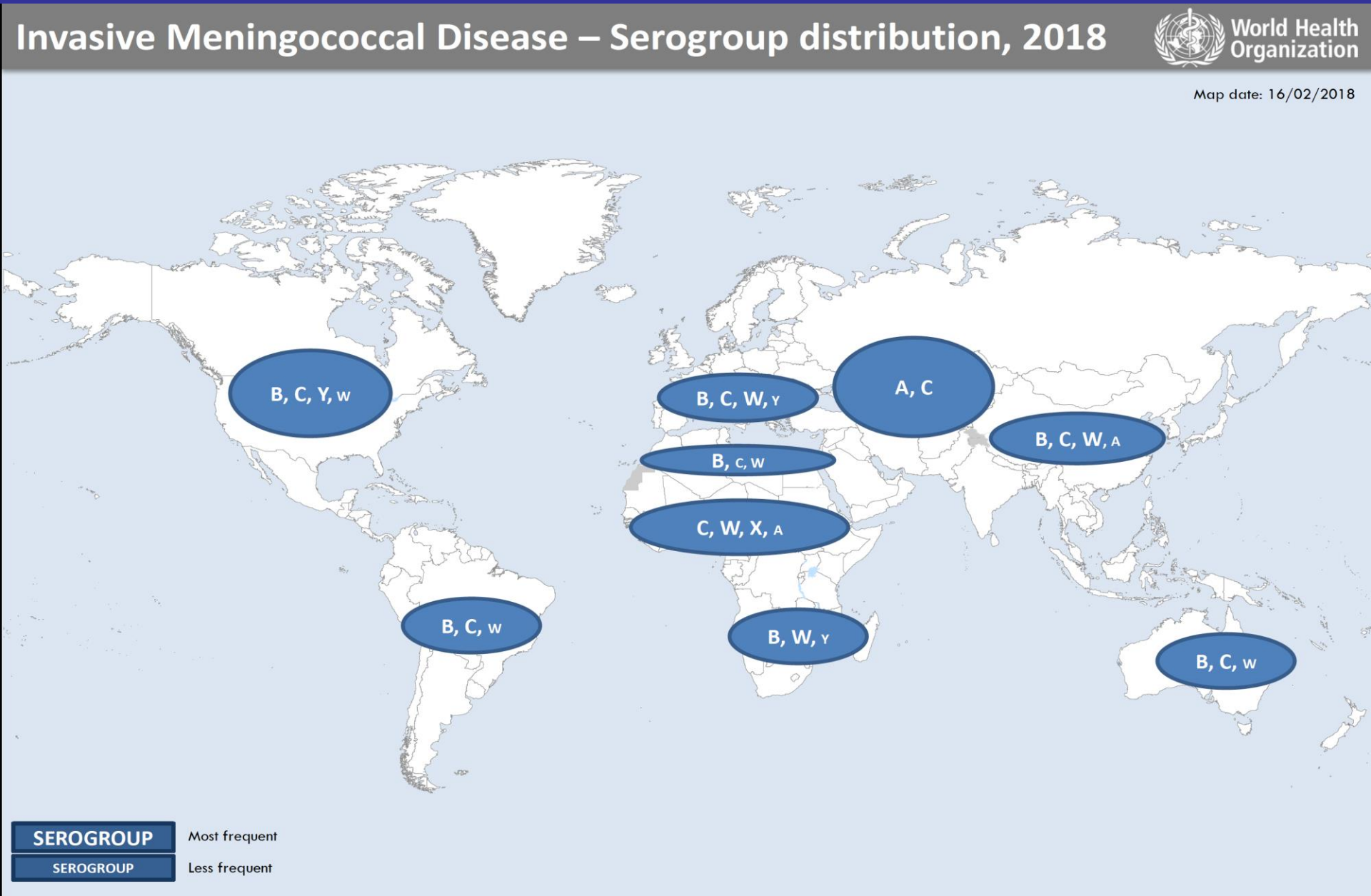
IMD serogroups distribution by year (%), Chile 2000 – 2012



- 2012: Switch from MenB to MenW

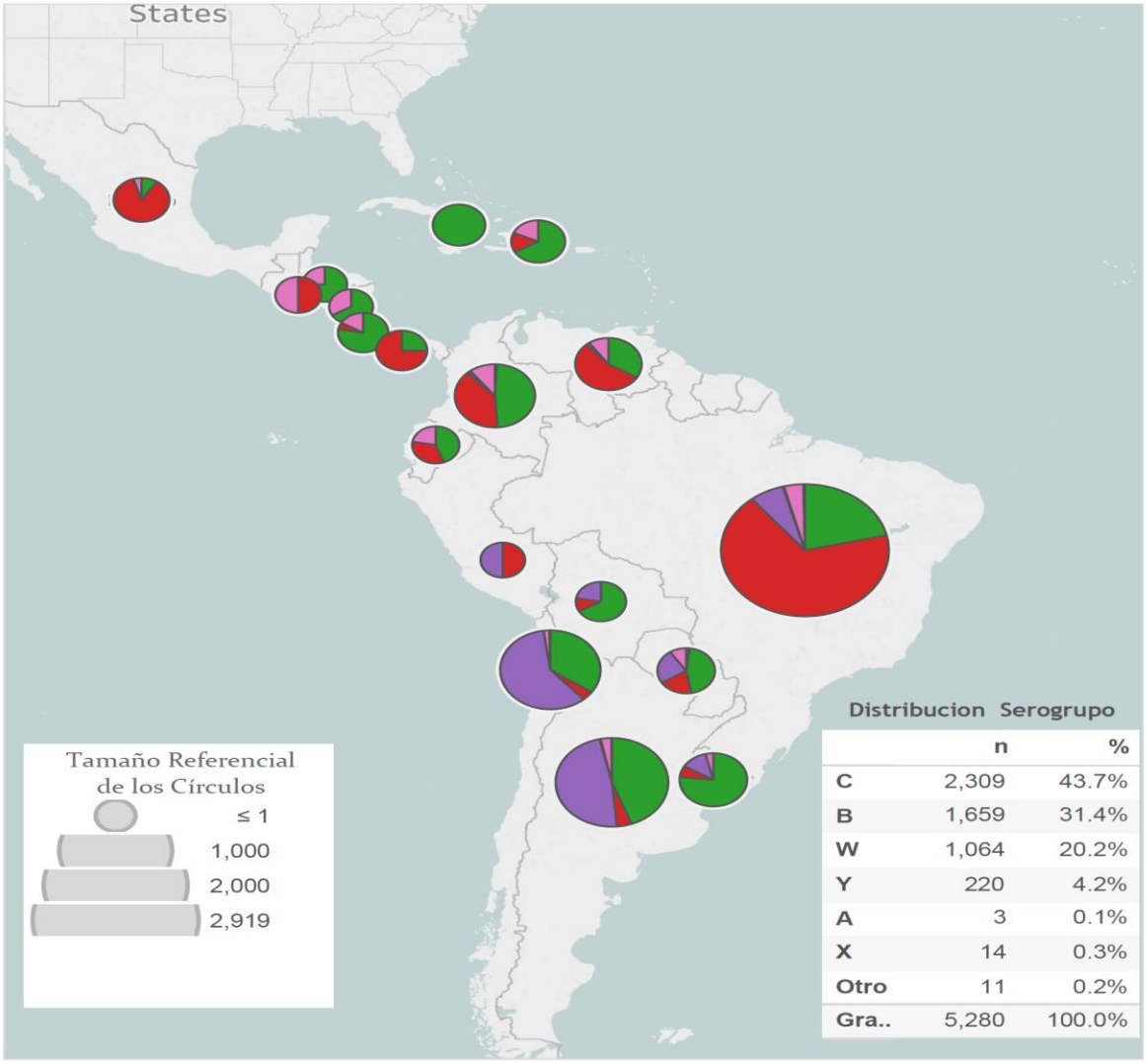
Wilhelm J, Villena R. Rev Chil Pediatr. 2012;83(6):533–9;

Global distribution of meningococcal serogroups



MD in LATAM, 2010-2016
Variability among Latam countries

Distribución de Serogrupos por País



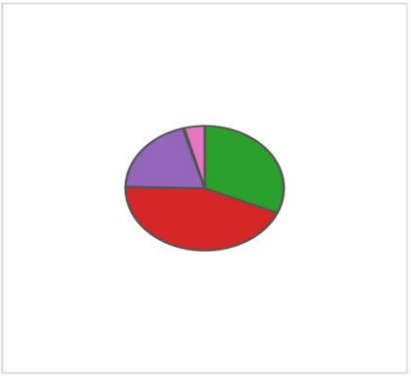
Distribucion Serogrupo

	n	%
C	2,309	43.7%
B	1,659	31.4%
W	1,064	20.2%
Y	220	4.2%
A	3	0.1%
X	14	0.3%
Otro	11	0.2%
Gra..	5,280	100.0%

Número de casos detectados/reportados por País

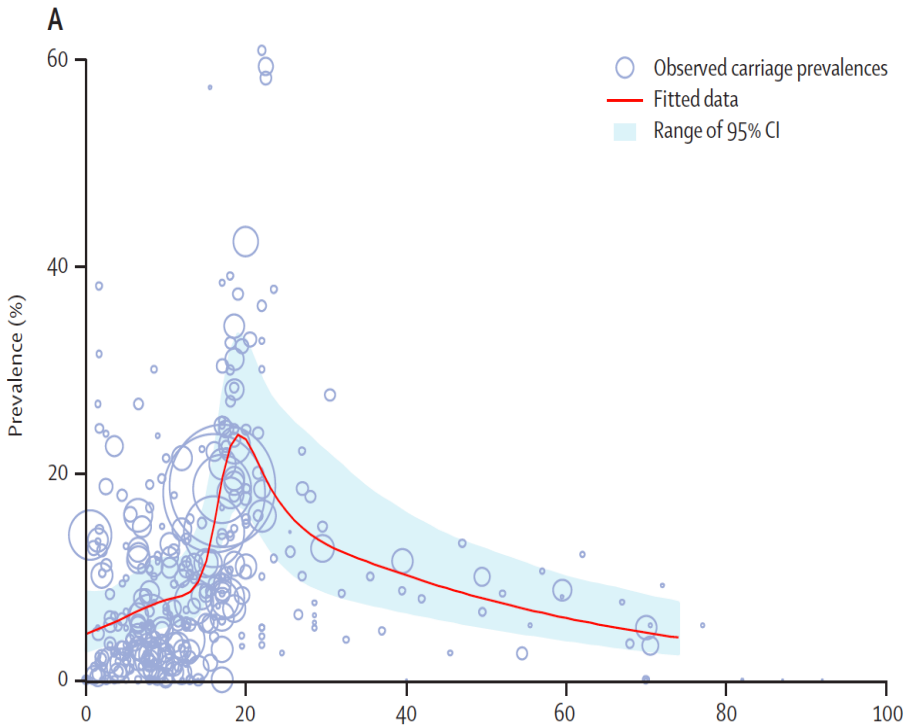
America Central y Mexico	MEX	43
	COR	18
	ELS	6
	GUT	0
	HON	4
	NIC	3
	PAN	20
Caribe	CUB	26
	DOR	33
Andinos	BOL	18
	COL	286
	ECU	9
	PER	4
	VEN	122
Cono Sur y Brasil	BRA	2,919
	ARG	938
	CHI	648
	PAR	53
	URU	133

Serogrupo
- A
- B
- C
- W
- X
- Y
- Otro



http://ais.paho.org/phip/viz/ed_meningo_esp.asp

Nasopharyngeal carriage of *N. meningitidis*



Chile: 2012 - 2013

- 18 - 24 yoa: 4%
  - MenB: 20%; MenW: 15%
- 10 – 19 yoa: 6,5%

Brazil

- Highest carriage prevalence in adolescents from 10–19 yoa
- MenC: 18.4%, MenB: 12.6%

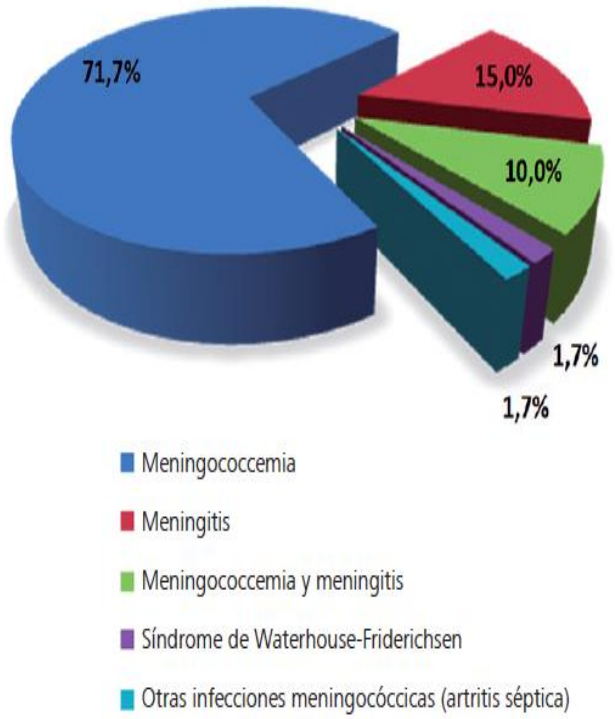
MenAfriCar consortium

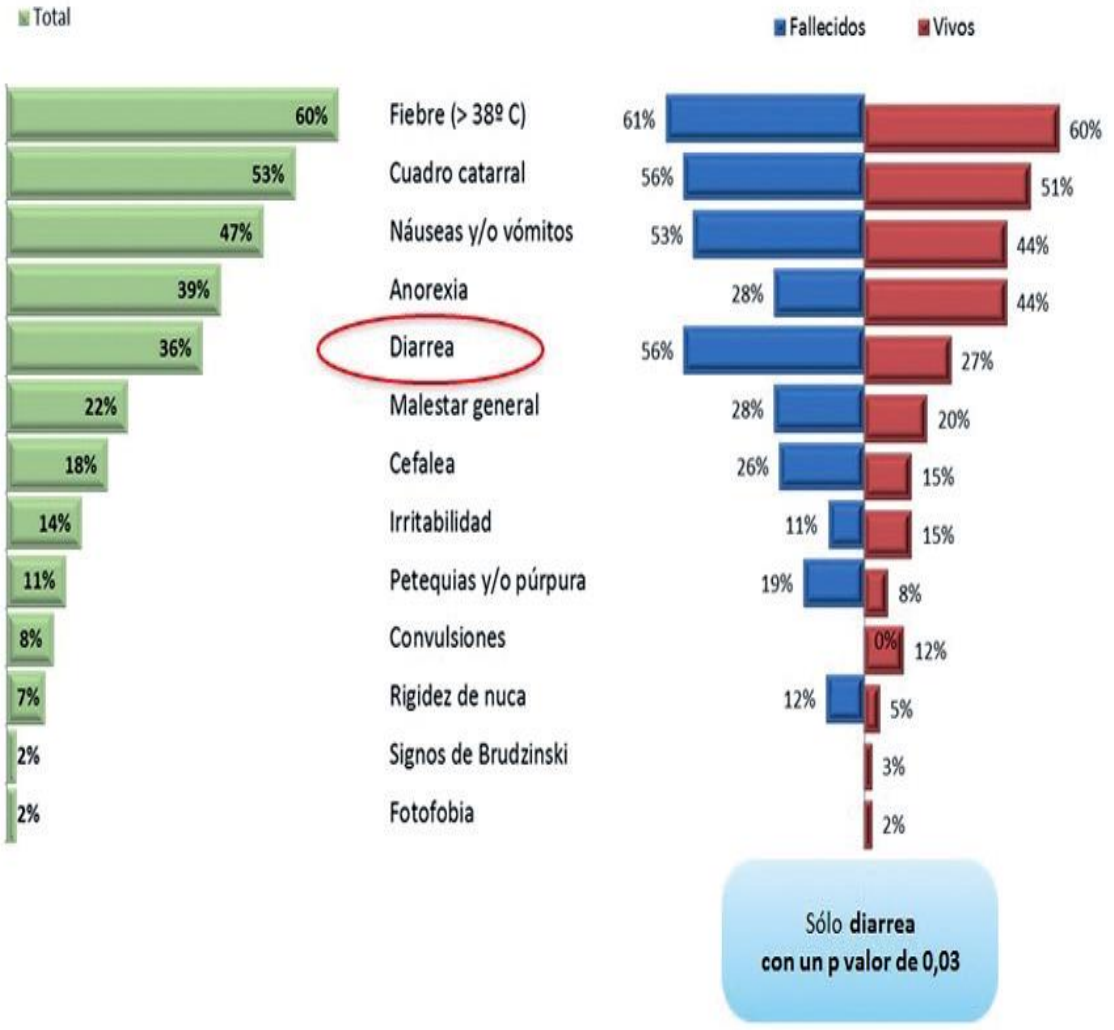
- NP carriage 3,4%
- Subjects 5–14 años OR 1.41
- Men: aOR 1.17
- Rural: aOR 1.44
- Dry season: aOR 1.54
- MenW predominance

Christensen H., et al Lancet Infect Dis 2010; 10: 853–61; Rodriguez P. et al. Vaccine 32 (2014) 5677–5680; Díaz J. et al J Infect Public Health. 2016 Jul-Aug;9(4):506-15. Greenwood JID 2015 Oct 15;212(8):1298-307. Weckx LY, et al Braz J Infect Dis. 2017 Nov - Dec;21(6):587-595

MD: Early diagnosis is difficult; rapid disease course from unspecific signs and symptoms to shock

MenW clinical manifestations at first clinical visit Chile 2012

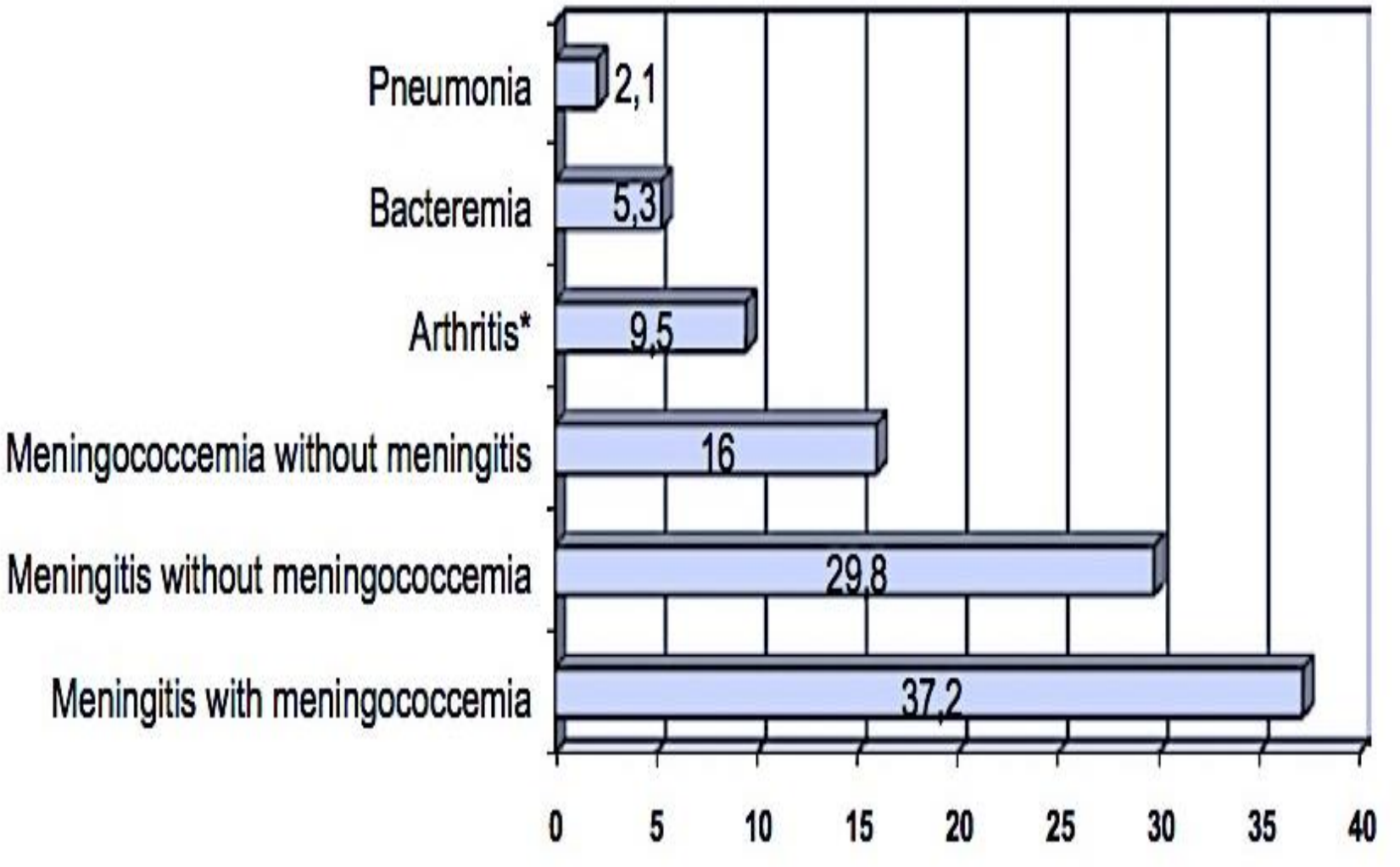




Moreno G, Rev Chilena Infectol 2013; 30 (4): 350-360

Clinical manifestations of MD in children

Hospital-based surveillance, Argentina, 2012 - 2015



Gentile et al. PIDJ 2017;36: 296

Case definition variability

- Latin America
  - Lack of uniform criteria across PAHO countries
  - Confirmed: detection of bacterial antigen(s) in CSF or positive culture laboratory
  - Probable: suspected case plus turbid CSF or link to a confirmed case)
  - Suspected cases: sudden onset of fever plus meningeal sign or petechial or purpuric rash

http://epi.minsal.cl/wp-content/uploads/2017/11/Circular_EM2017.pdf

PCR improves MD diagnostic performance

Underestimation of disease burden?

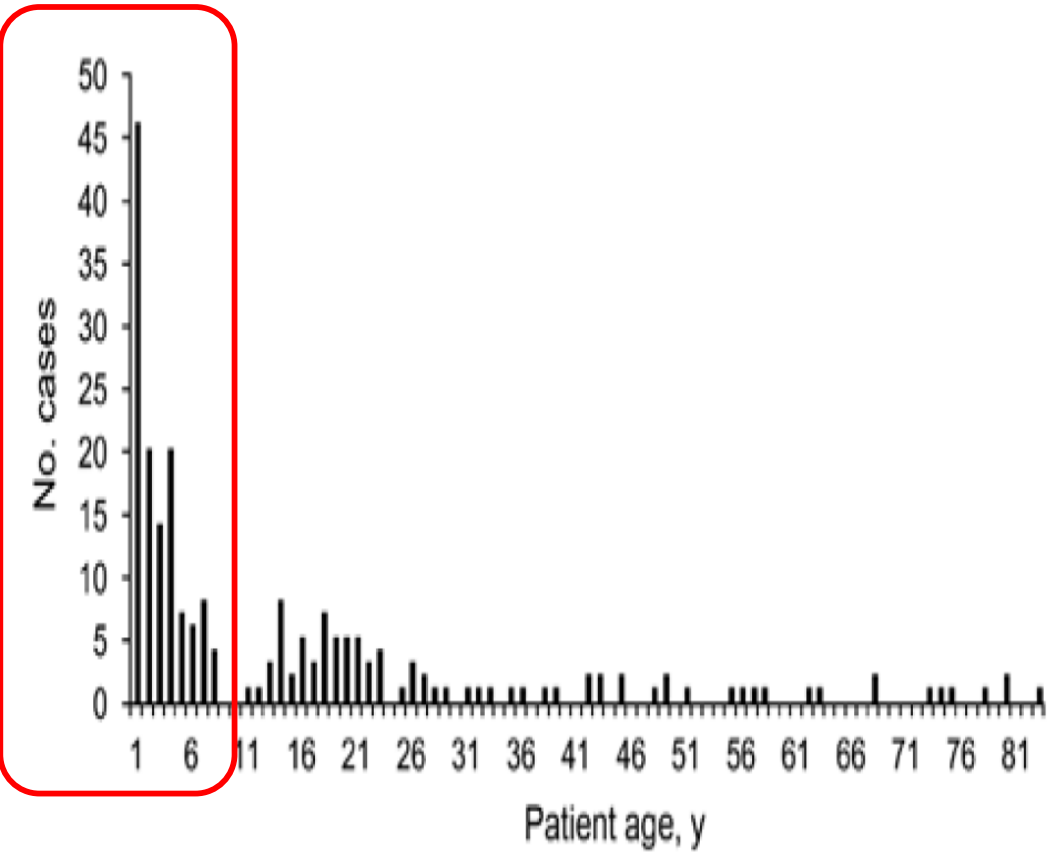


Figure 1 Number of patients PCR-tested for *Neisseria meningitidis* and proportion positive by age group, 2009–2010.

PCR (+) only:

UK: 57,1%

Italia: 58%

Ireland: 63%

Brazil: 85% (CSF)

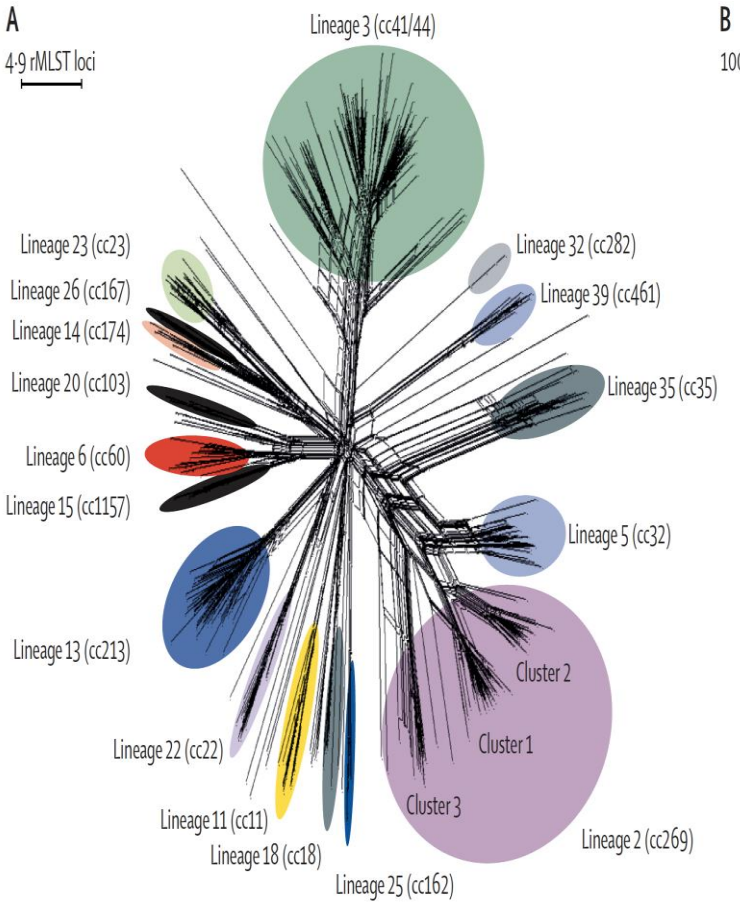
Chile: 15% (based on meningitis definition)

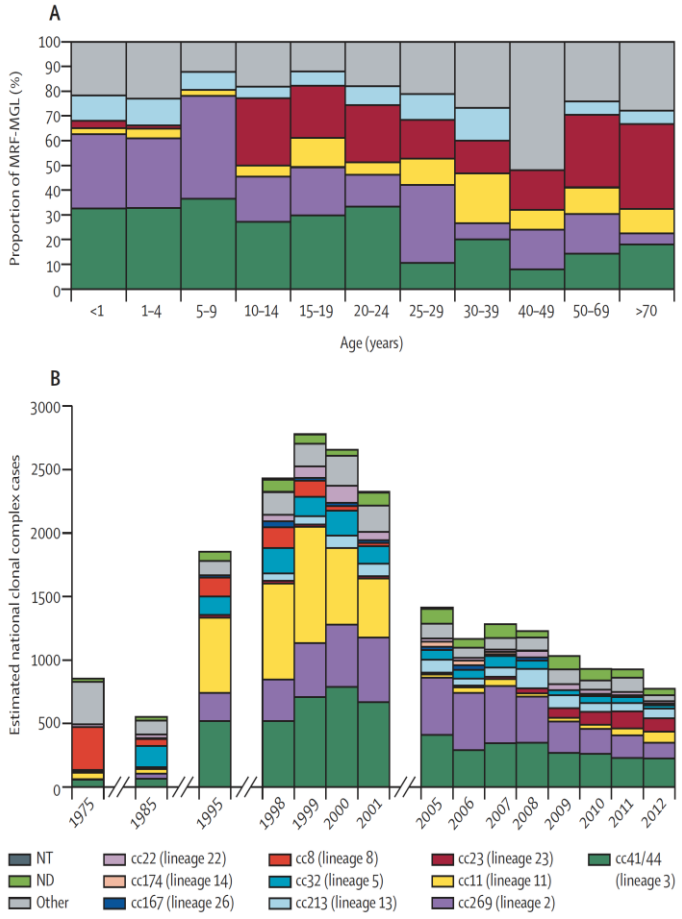
Argentina: 25% (conventional PCR)

http://www.ispch.cl/sites/default/files/Informe%20_Neisseria_meningitidis_SE41.pdf, Sacchi CT, et al PLoS One. 2011;6(6):e20675
Azzari et al, EID Vol. 22, No. 3, March 2016; Ellen Heinsbroek, Journal Infect (2013) 67, 385e390; Gentile A. et al PIDJ 2017;36: 296

Genomic epidemiology of age-associated meningococcal lineages in national surveillance: an observational cohort study

Dorothea M C Hill, Jay Lucidarme*, Stephen J Gray, Lynne S Newbold, Roisin Ure, Carina Brehony, Odile B Harrison, James E Bray, Keith A Jolley, Holly B Bratcher, Julian Parkhill, Christoph M Tang, Ray Borrow, Martin C J Maiden*





Hill DC, et al Lancet 2015;15:1420

N. meningitidis hypervirulent strains

clinical signs and symptoms in children

Santiago, Chile 2008 - 2015

Tabla III: Comparación de casos según complejo clonal.

Variable[a]	ST11 (n=48)		ST41/44 (n=14)		ST32 (n=5)		Valor-p[b]
Manifestaciones clínicas							
Fiebre	48	(100,0%)	14	(100,0%)	5	(100,0%)	-
Vómitos	27	(56,3%)	7	(50,0%)	4	(80,0%)	0,550
Diarrea	10	(20,8%)	2	(14,3%)	0	(0,0%)	0,656
Cefalea	3	(6,3%)	2	(14,3%)	1	(20,0%)	0,237
CEG	21	(43,8%)	3	(21,4%)	4	(80,0%)	0,067
Signos meníngeos	5	(10,4%)	2	(14,3%)	0	(0,0%)	0,802
Déficit neurológico	13	(27,1%)	1	(7,1%)	2	(40,0%)	0,199
Somnolencia	7	(14,6%)	3	(21,4%)	2	(40,0%)	0,246
Petequias	6	(12,5%)	8	(57,1%)	4	(80,0%)	<0,001

Allele 22 of the fHbp gene: 73% → petechiae (15%) vs others allele (61%)

Rivacoba C., et al, en prensa

Meningococcal vaccines

Meningococcal vaccines

- Polysacharide vaccines
  - *Neisseria meningitidis* capsule
- Conjugate vaccines
  - Capsular polysaccharide linked to highly immunogenic proteins
- Outer membrane vaccines (OMV)
  - Non capsular focus

WHO recommendations

- WHO
  - If incidence > 2–10/100,000
    - Massive vaccination and NIP introduction
  - If incidence < 2/100.000
    - Focus in high risk groups
- Latam GMI recommendations
  - Risk groups vaccination:
    - Complement component deficit
    - Immunodeficient (HIV, Asplenia)
    - Occupational risk
    - Travelers to endemic areas

WER, 2011, 86, 521–540; Safadi et al. Vaccine 2015;33: 6529-36

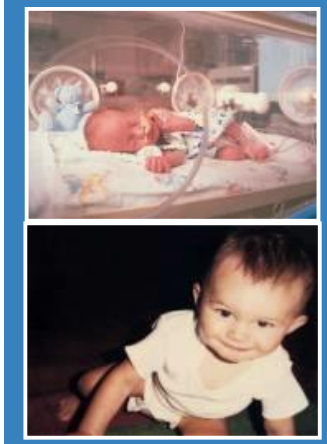
Conjugate vaccines advantages over polysaccharide vaccines

Property	Polysaccharide	Conjugate
Immune memory/ Booster effect	–	✓
Hyporesponsiveness with repeated dosing	✓	–
Reduction of carriage*	–	✓
Contributes to herd effect*	–	✓
Effective in infants	–	✓

*As evidenced by meningococcal serogroup C conjugate vaccines

Harrison LH. *Clin Microbiol Rev.* 2006;19:142-164, Granoff DM, et al. In: *Vaccines*. 4th ed. 2004

Several factors put different populations at risk of meningococcal disease

Naive and immature immune system	Impairment of immune system[2]	Nasopharyngeal irritation	Social factors	Travelers
▪ Infants 	▪ Complement deficiency ▪ Humoral immune impairment ▪ Asplenia ▪ HIV 	▪ Smoking ▪ Respiratory tract infection 	▪ Highest carriage rates ▪ Exposure to and carriage of diverse serogroups ▪ Crowded living conditions 	▪ Exposure to and carriage of diverse serogroups ▪ Overcrowdin ▪ Travelers to endemic regions/Pilgrims 

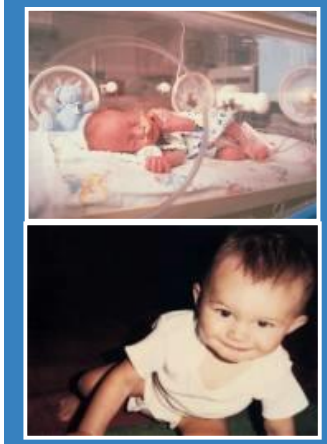
Most cases of meningococcal disease occur in previously healthy people without identified risk factors

Rosenstein NE, et al. *N Eng J Med*. 2001;344:1378-1388; 2. Figueroa JE, et al. *Clin Microbiol Rev.* 1991;4:359-395; 3. Bilukha OO, et al. *MWR Recomm Rep.* 2005;54:1-21; 4. Imrey PB, et al. *J Clin Microbiol*. 1995; 33:3133-3137. CDC. *MMWR* 2007;56(48):1265-1266.

Several factors put different populations at risk of meningococcal disease

Naive and immature immune system

- Infants



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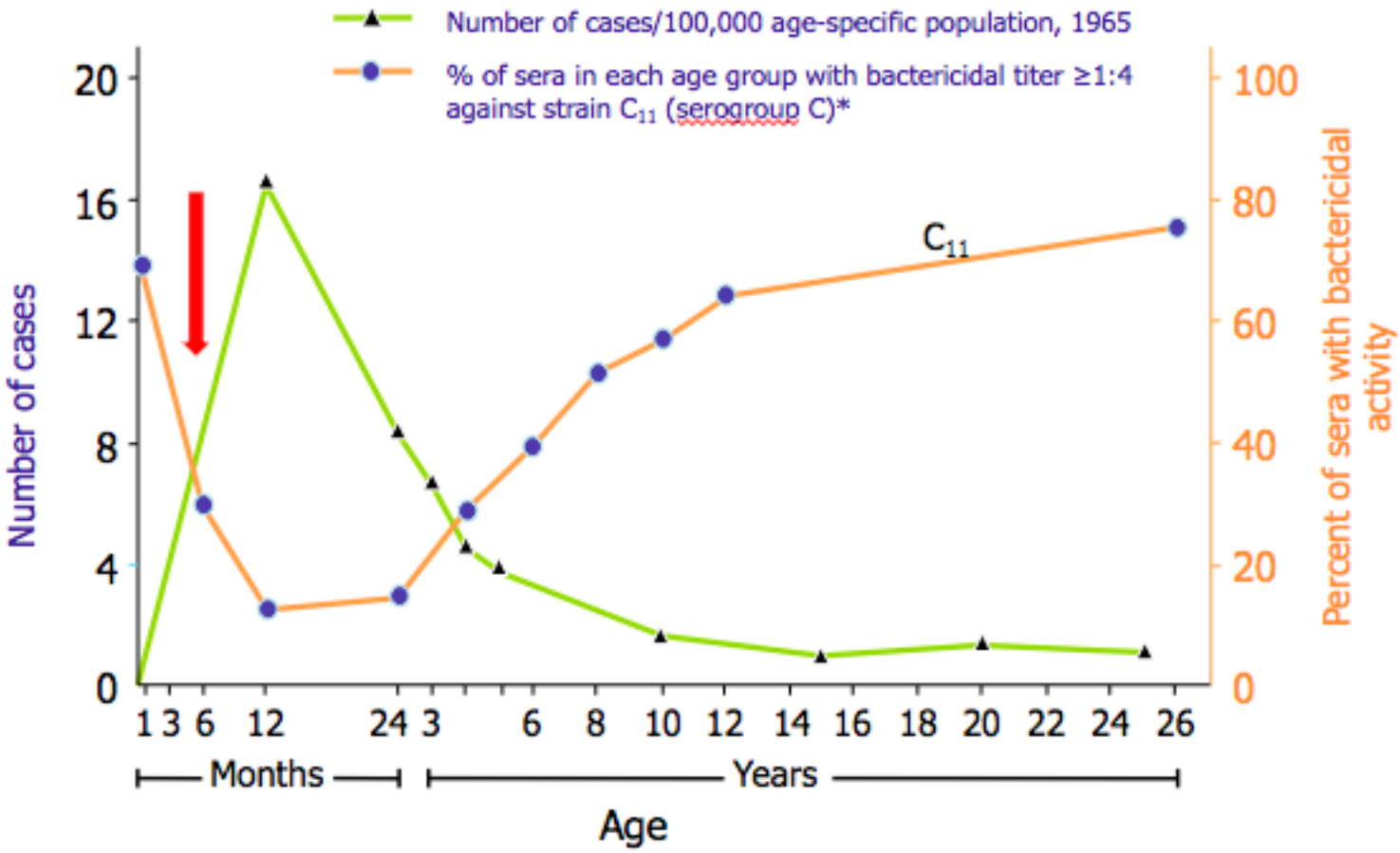
Infants remain susceptible to meningococcal disease due to reduced protective maternal antibody levels

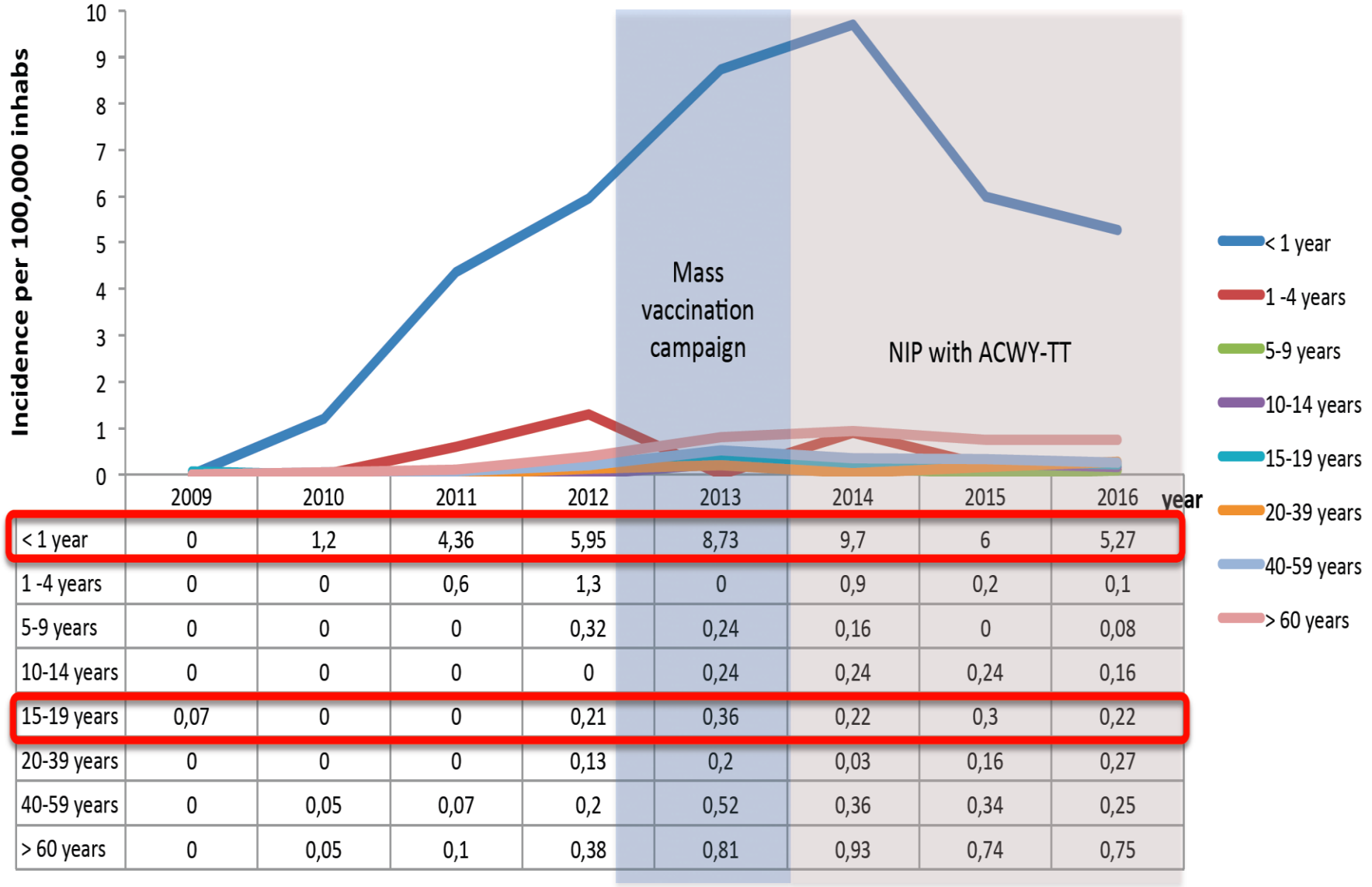


*Similar results were observed for strains A_1 (serogroup A) and B (serogroup B).

Goldschneider I, et al. *J Exp Med.* 1969;129:1307-1326

MenW incidence by age group

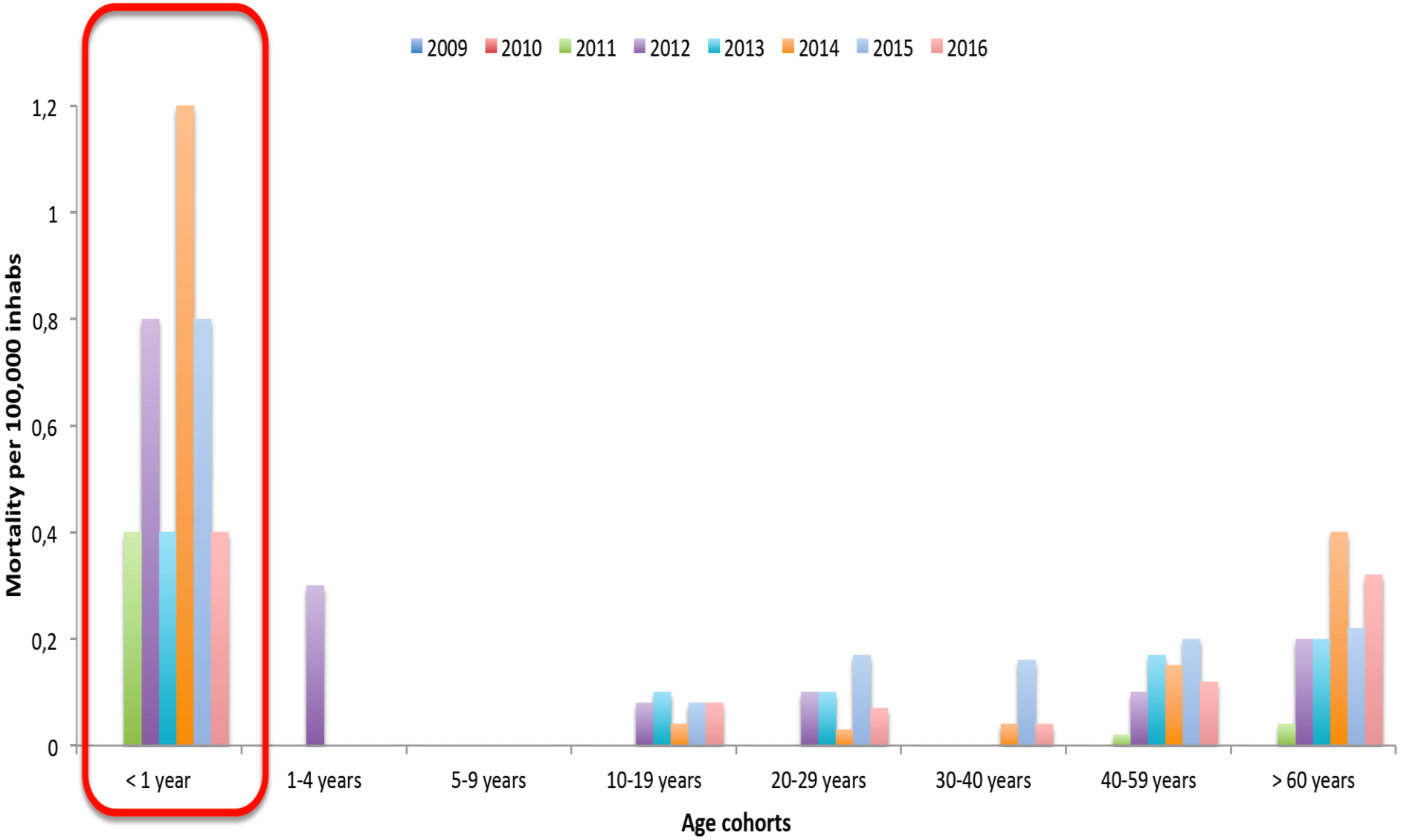
Chile 2009–2016



year	2009	2010	2011	2012	2013	2014	2015	2016
< 1 year	0	1,2	4,36	5,95	8,73	9,7	6	5,27
1 -4 years	0	0	0,6	1,3	0	0,9	0,2	0,1
5-9 years	0	0	0	0,32	0,24	0,16	0	0,08
10-14 years	0	0	0	0	0,24	0,24	0,24	0,16
15-19 years	0,07	0	0	0,21	0,36	0,22	0,3	0,22
20-39 years	0	0	0	0,13	0,2	0,03	0,16	0,27
40-59 years	0	0,05	0,07	0,2	0,52	0,36	0,34	0,25
> 60 years	0	0,05	0,1	0,38	0,81	0,93	0,74	0,75

Villena R; 14th EMGM, Prague, Czech Republic, 2017

Men W mortality rate per 100,000 inhabs by age and year, Chile 2009 - 2016



Villena R; 14th EMGM, Prague, Czech Republic, 2017

Hospital-based surveillance of MD in children
Argentina, 2012 - 2015

- 94 cases: median age: 12.5 moa
- 48% in <1 yoa, 60% in <2 yoa
- Argentina incidence: 0.7/100,000
  - < 1 yoa: 14/100,000
- Study incidence: 5.1/10,000 hospitalized patients
- MenW in <1 yoa (OR 3,28, 95% CI: 1,14-8,89)

TABLE 3. *Neisseria meningitides* Serogroups by Age

Serogroup	Age (mo) Median (range)	Age Groups (mo) <12 n	<12 %	12–23 n	12–23 %	24–59 n	24–59 %	≥60 n	≥60 %	n
B	45.0 (1–180)	17	38.6	7	15.9	9	20.5	11	25.0	44
W	9.5 (1–171)	24	66.7	6	16.7	3	8.3	3	8.3	36

C: 2; Y: 1; nontypeable: 1.

Gentile et al. PIDJ 2017;36: 296

Several factors put different populations at risk of meningococcal disease

Impairment of immune system[2]

- Complement deficiency
- Humoral immune impairment
- Asplenia
- HIV

Most cases of meningococcal disease occur in previously healthy people without identified risk factors

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Complement component deficit or impairment

- **Deficit of C3, C5-9, Properdin, Factor D and Factor H**
- Risk 5000 folds higher
- Recurring MD
- Preserved response to capsular antigens
  - Similar to controls
- Require booster doses
  - 1st booster: 3 years after primary
  - Next boosters every 5 years

Platonov A., et al Clin Exp immunoi 1995; 100:32 39; MMWR June 20, 2014 Vol. 63 No. 24

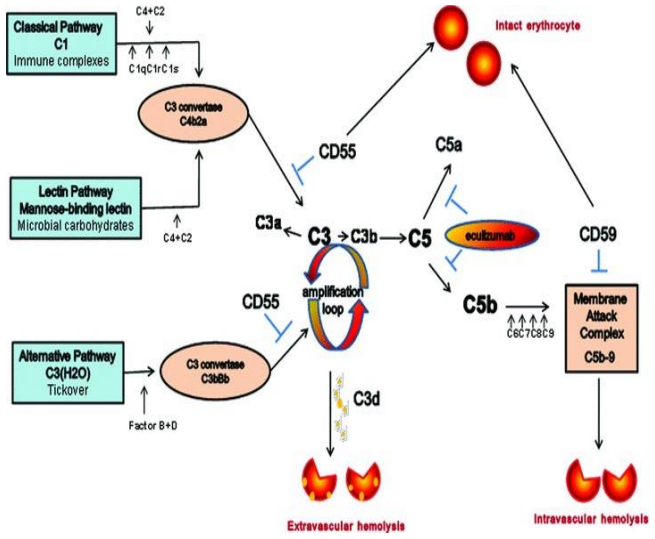
Biological therapies
blocked activation of the complement cascade

- **Eculizumab:** monoclonal antibody used in atypical HUS and paroxysmal hemoglobinuria
  - Blocks activation of C5
  - Increases risk for MD in 1000 to 2000 folds
    - Non-typeable meningococci
  - Must receive complete immunization against meningococcus

SOLIRIS®
(eculizumab)
Injection for Intravenous Use

- ACIP
  - Administrate Men vaccines at least 2 weeks before starting therapy
  - Boosters MenACWY: c / 5 years

- Consider chemoprophylaxis



Hentgen V., Archives de Pediatrie 2015;22(HS2):41-42

Functional or anatomic asplenia

- Risk 10-50 folds higher
- In planned splenectomy: vaccinate 2 weeks before
- Coverages: 7.8% – 22.8%
- Improve adherence

Vaccine	Age of primary vaccination	Booster doses*	Indicated for infants who:	Not indicated for:
MenACWY-CRM (Menveo)	2, 4, 6, and 12 months	• 1st booster 3 years after primary series • Additional boosters every 5 years	• Have complement component deficiencies • Have functional or anatomic asplenia (including sickle cell disease) • Are in the risk group for an outbreak for which vaccination is recommended • Are traveling to or residing in regions where meningitis is epidemic or hyperendemic	
MenACWY-D (Menactra)	9 and 12 months†	• 1st booster 3 years after primary series • Additional boosters every 5 years	• Have complement component deficiencies • Are in the risk group for an outbreak for which vaccination is recommended • Are traveling to or residing in regions where meningitis is epidemic or hyperendemic	• Infants with functional or anatomic asplenia (including sickle cell disease)§

R Lopez Almaraz BSCP Can Ped 2004; 28-nº1; Castagnola et al. Eur. Jour. Haem. 2003; MMWR / March 22, 2013 / Vol. 62 / No. 2
Martino C., et al Hum Vaccin Immunother. 2016 May 3;12(5):1277-9; Nived . Et al Vaccine. 2015 Mar 30;33(14):1688-94: MMWR June 20, 2014 Vol. 63 No. 24

People living with HIV are at increased risk for MD

- High nasopharyngeal carriage: 43%
- Rectal (2%) and urethral (1%) colonization rates in MSM
- Increased risk of 10-60 folds
  - Independent of serogroup
- Subjects with CD4 ≤ 200/mm^3 → high risk of MBA
- CFR: 20% vs 11% (OR: 2.1, 95% CI 1.1-3.9]
- Multivariate analysis
  - CFR in bacteremia: 35%; Meningitis: 7%
- HAART decreases MD risk

Domingo P,Suarez-Lozano I, J Acquir Immune Defic Syndr. 2009; 51(5): 582-7; available at<http://www.researchgate.net/publication/26279285>.; Cohen C IDS. 2010 Jun 1;24(9):1351-60

Waning immunity after chemotherapy

- Protective titers wane for Men C: 87%
- Subjects previously vaccinated against Men C:
  - 17% protective titers → 12% > 1:8
- Revaccination: significant increase in titers
  - 96% 1:128

Table 6. Geometric mean titer (GMT) of meningococcus C serum bactericidal antibody, before and after receipt of 1 dose of meningococcus C conjugate vaccine.

Period	No. of patients with data		GMT of meningococcus C serum bactericidal antibody (95% CI)		
	Patients with ALL	Patients with AML	All patients	Patients with ALL	Patients with AML
Before vaccination (n = 49)	36	13	2.9 (2.2–3.9)[a]	2.3 (1.8–2.85)[a]	2.5 (1.73–3.7)[b]
After vaccination (n = 28)	23	5	1000 (483–2064)	1120 (496–2532)	588 (54–6408)

Patel S., et al CID 2007: 44, 1 March, 635; Zignol M., Cancer 2004; 101:635-41; Von der Hardt K. *Vaccine. 2000:18;2999-3004;* Ek T, et al. J Pediatr Hematol Oncol 2004; 26:727–34;

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Social factors

- Highest carriage rates
- Exposure to and carriage of diverse serogroups
- Crowded living conditions

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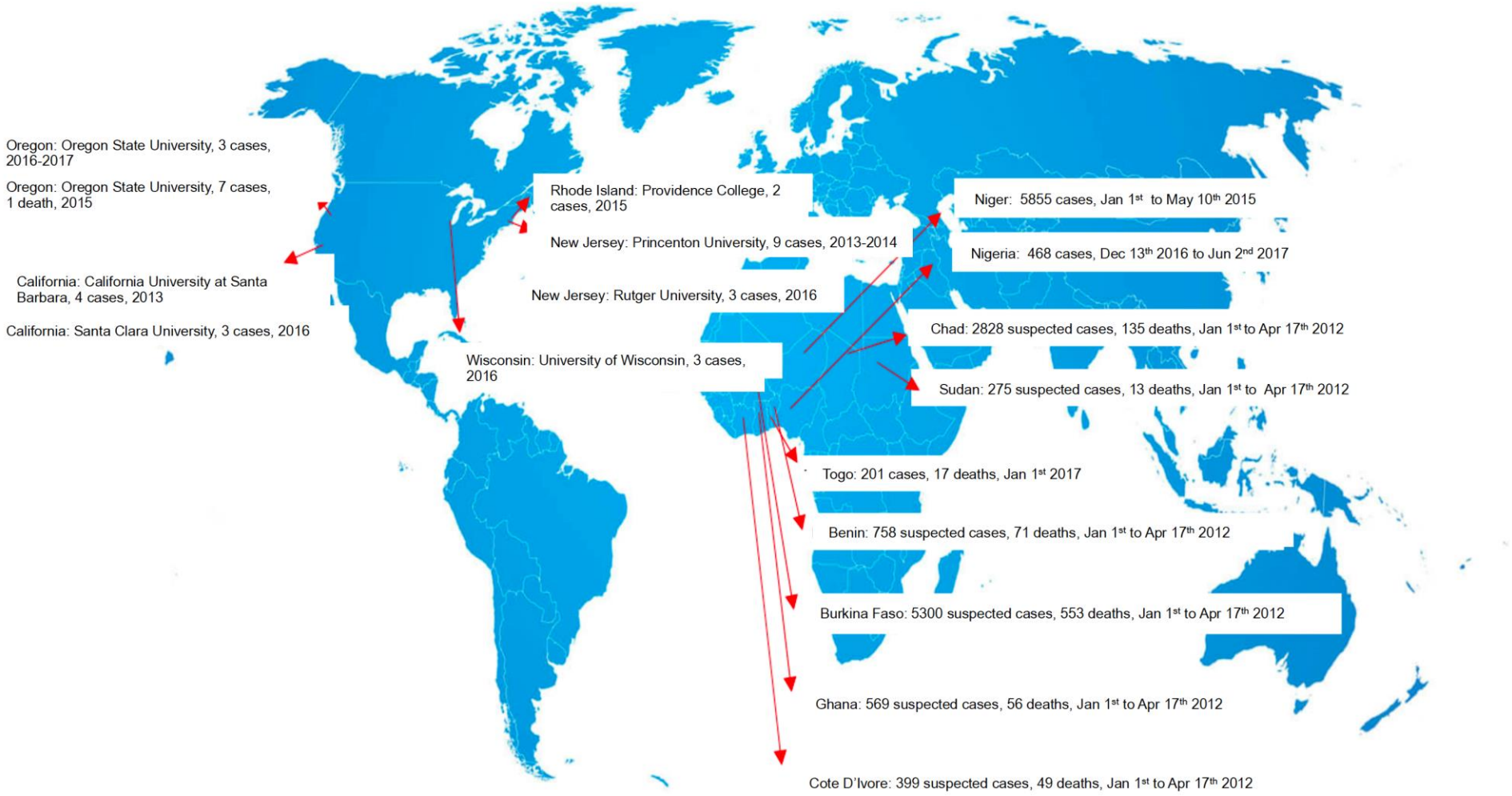
Rosenstein NE, et al. *N Eng J Med*. 2001;344:1378-1388; 2. Figueroa JE, et al. *Clin Microbiol Rev.* 1991;4:359-395; 3. Bilukha OO, et al. *MWR Recomm Rep.* 2005;54:1-21; 4. Imrey PB, et al. *J Clin Microbiol*. 1995; 33:3133-3137. CDC. *MMWR 2*007;56(48):1265-1266.

Meningococcal outbreaks reported to the WHO 2012–2017



Villena R., et al Hum Vaccin Immunother. 2018 Apr 18:1-16

BMJ 2015;350:h1486 doi: 10.1136/bmj.h1486 (Published 16 March 2015)

NEWS

Teenagers in England to be vaccinated against meningitis group W

Jacqui Wise

- England: low incidence of MD by serogroup W
- Increase in annual report of cases
- 2009: 22 → 2014: 117
- JCVI: vaccination adolescents from 14 to 18 yoa
- MenACWY conjugate vaccine: 1 dose
- March 2015

http://www.nitag-resource.org/uploads/media/default/0001/03/5c7ce952ec60f9f20ae4d307822b1de6d9ae3d57.pdf

Recommended meningococcal vaccines for adolescents in the US

TABLE 6. Recommended meningococcal vaccines for use in children and adults — Advisory Committee on Immunization Practices (ACIP), United States, 2012

Age group	Vaccine	Status
11–21 yrs	MenACWY-D or MenACWY-CRM	Primary: • Age 11–12 yrs, 1 dose • Age 13–18 yrs, 1 dose if not vaccinated previously • Age 19–21 yrs, not routinely recommended but may be administered as catch-up vaccination for those who have not received a dose after their 16th birthday Booster: • 1 dose recommended if first dose administered before 16th birthday

Several factors put different populations at risk of meningococcal disease

Travelers

- Exposure to and carriage of diverse serogroups
- Overcrowdin
- Travelers to endemic regions/Pilgrims

Most cases of meningococcal disease occur in previously healthy people without identified risk factors

Rosenstein NE, et al. *N Eng J Med*. 2001;344:1378-1388; 2. Figueroa JE, et al. *Clin Microbiol Rev.* 1991;4:359-395; 3. Bilukha OO, et al. *MWR Recomm Rep.* 2005;54:1-21; 4. Imrey PB, et al. *J Clin Microbiol*. 1995; 33:3133-3137. CDC. *MMWR* 2007;56(48):1265-1266.

Travelers or residents in hyperendemic areas

- Travelers or residents in hyperendemic areas
- Contact with locals
- Sub-Saharan meningitis belt (Dec - Jun)
- Pilgrims to Hajj, Saudi Arabia
  - Required Men ACWY
  - Booster doses if vaccination 5 or more years ago
- Adherence to immunizations in pediatric travelers: 6.5 - 77%

Smith W., Travel Med Infect Dis. 2008 Jul;6(4):182-6; MMWR / March 22, 2013 / Vol. 62 / No. 2
Caillet-Gossot S., Journal of Travel Medicine 2013; Volume 20 (Issue 3): 171–176

Men vaccines indications in countries <2 cases/100,000 inhabs

	Australia	Canada	UK	EEUU
Infants	12	12	2, 3, 4 and 12, 13m	No
Adolescents	15-19 yoa	12 yoa	14 – 18 yoa	11-12yoa; 16yoa; 16-18yoa
Dorms	yes	No	yes	yes
Asplenia	yes	yes	yes	yes
CPD	yes	yes	yes	yes
VIH	yes	yes	yes	yes
Transplants	yes	yes	No	No
Lab workers	yes	yes	yes	yes
Travellers	yes	yes	yes	yes

Crum-Cianflone N., Infect Dis Ther (2016) 5:89–112

Men vaccines into NIPs in Latam countries

	Vaccine	Schedule	Adolescents	Comments
Argentina	MenACWY	3, 5 and 15moa	11 yoa	Infants and adolescents started simultaneously in 2017 without catch up
Brazil	MenC	3, 5 and 12-15 moa	11-13yoa	Infants: 2010 Adolescents: 2017 2020: 9 – 10 yoa
Chile	MenACWY	12 moa	No	Campaign: 9 moa – 4 yoa 2012-2013 NIP: 2014 Infants: 2019? Adolescents: 2020?
Cuba	Men BC	3, 5 moa	No	1989: massive campaign: 3 moa – 24 yoa Infants: 1991 Efficacy: 93 - 98% in children < 5 yoa

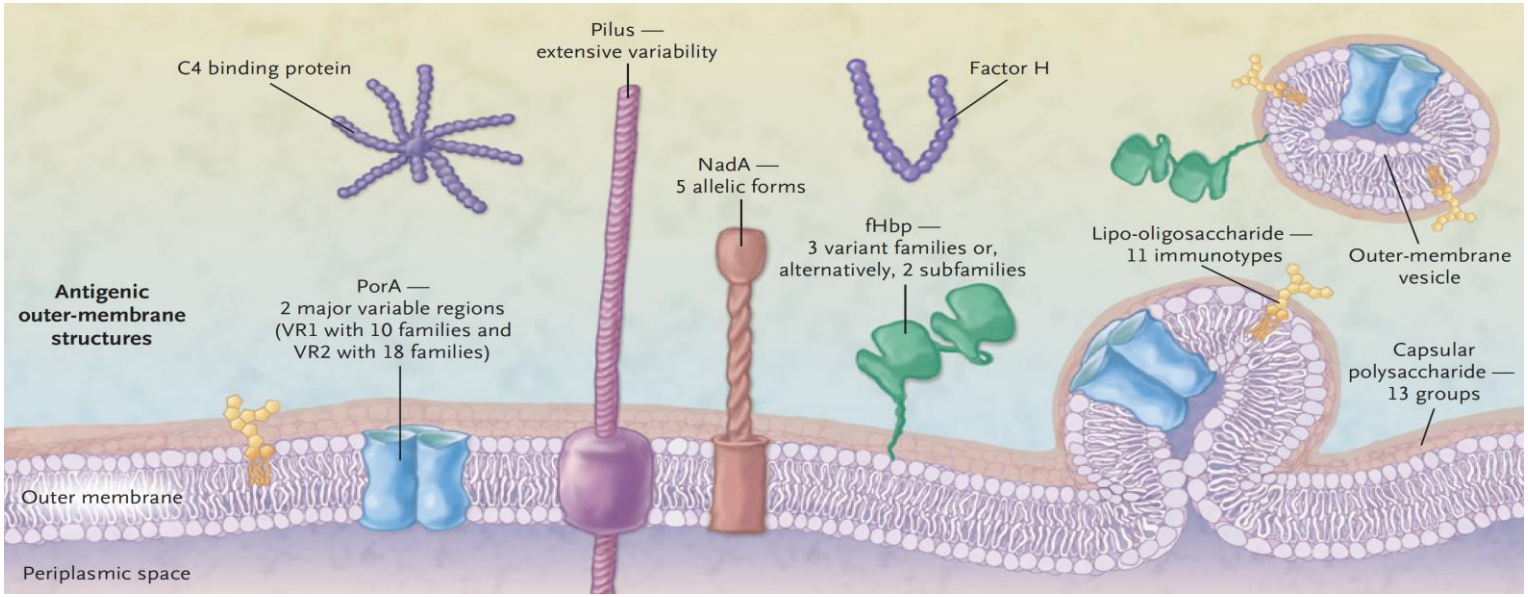
MenACWY conjugate vaccines

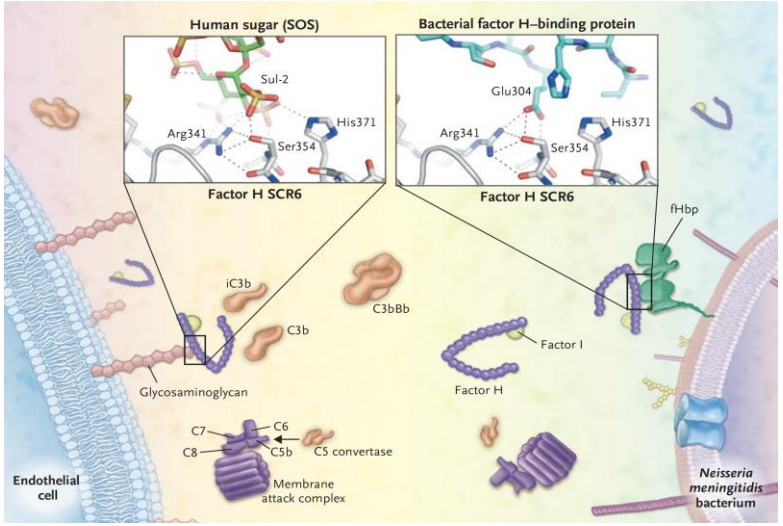
MenACWY conjugate vaccines

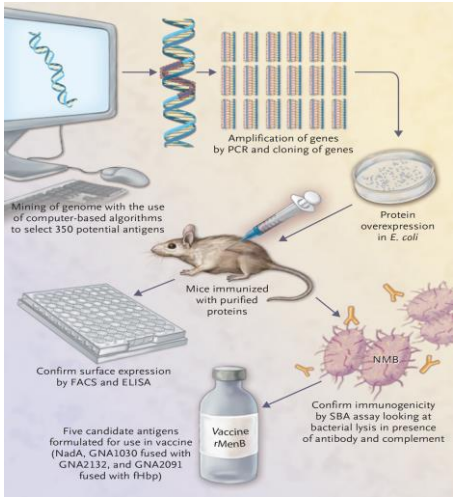
Characteristics	Menactra	Menveo	Nimenrix
Conjugate with ...	DT	CRM_{197}	TT
Thimerosal/Adjuvants	No	No	No
Age to start	9 moa	2 moa	6 woa
Age up to ...	55 yoa	55 yoa/None	None
Schedule < 1 yoa	2	2+1/ 3+1	2+1/3+1
Doses 1 – 2 yoa	2	2	1
Doses > 2 yoa	1	1	1
Simultaneous administration	PCV-7, HAV, MMR, MMRV, TF	PCV-7, PCV-13, RV5, HAV, Hexavalent, MMR, MMRV, YF, TF, Rabies	PCV-10, PCV-13 Hexavalent, HAV, MMR, MMRV
Persistence	5 years	4 − 5 years	5 years

Novel rMenB vaccines

Re-searching for new vaccines against MenB







Tan L, et al N Engl J Med 2010;362:1511-20

rMenB vaccines

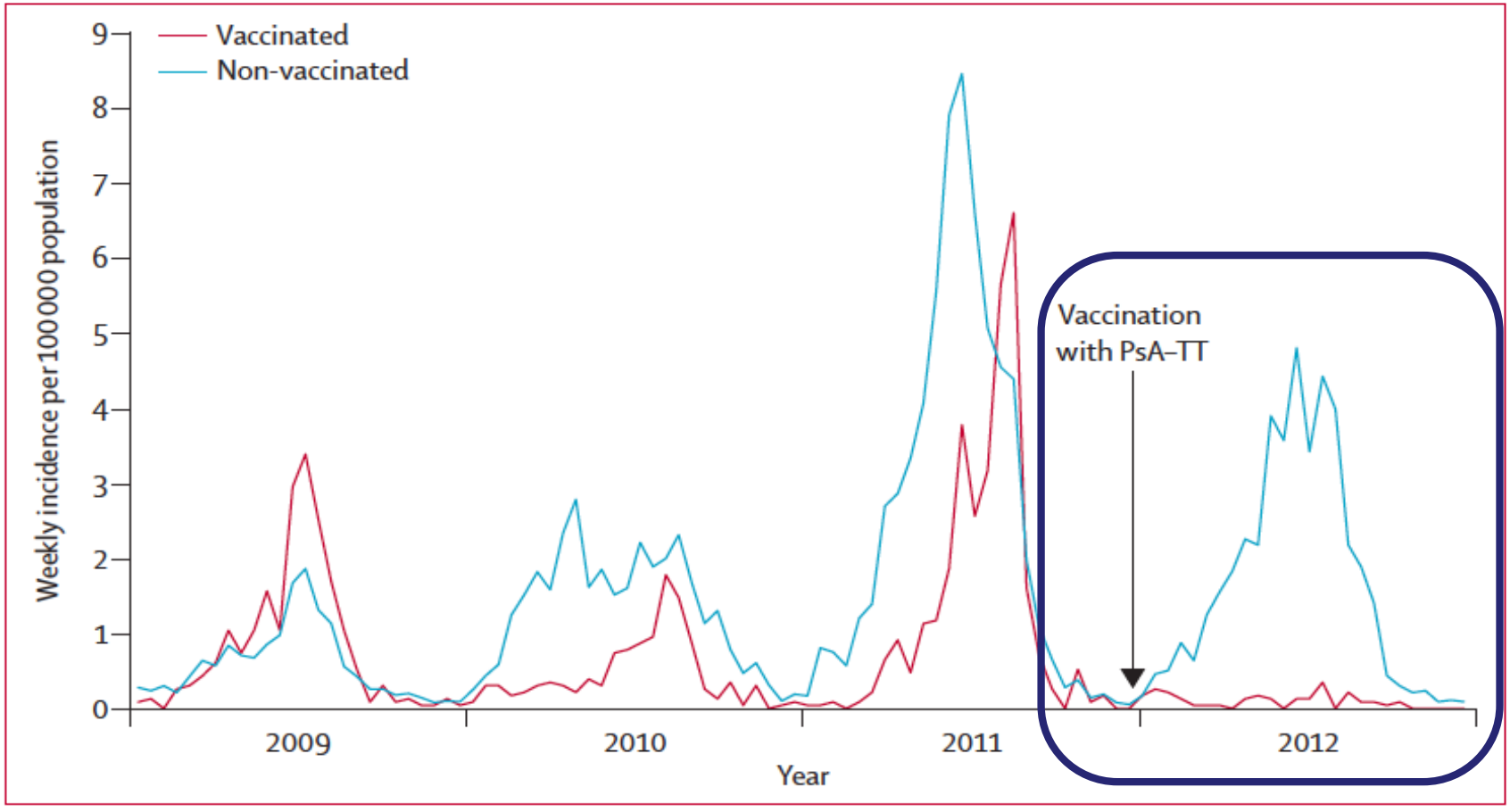
Characteristics	Bexsero (4CMenB)	Trumenba (rLP2086)
Proteins included	NadA; NHBP; fHbp; OMV	fHbp A and B subfamilies
Age to start	2 moa	10 yoa
Infants schedule	3+1 / 2+1	NA
Doses in children	2	NA
Doses in adolescents	2 doses: 0 y 6 months	2 or 3 doses: 0,1-2 y 6 months; 0 y 6 months
Simultaneous administration	MenC, DTaP-IPV, Hib, HBV, MMRV, PCV-7	HPV 4v; TdaP-IPV; MenACWY; Tdap
Safety	Fever in infants and pain in injection site in adolescents	Headache and fatigue
Cross protection	MenCWYX	MenCWYX
Reduction in NP carriage	BCWY…?	?
Persistence	4 years ?	4 years ?
Real world experience	NIP + outbreaks	Outbreaks

Impact of Men vaccines

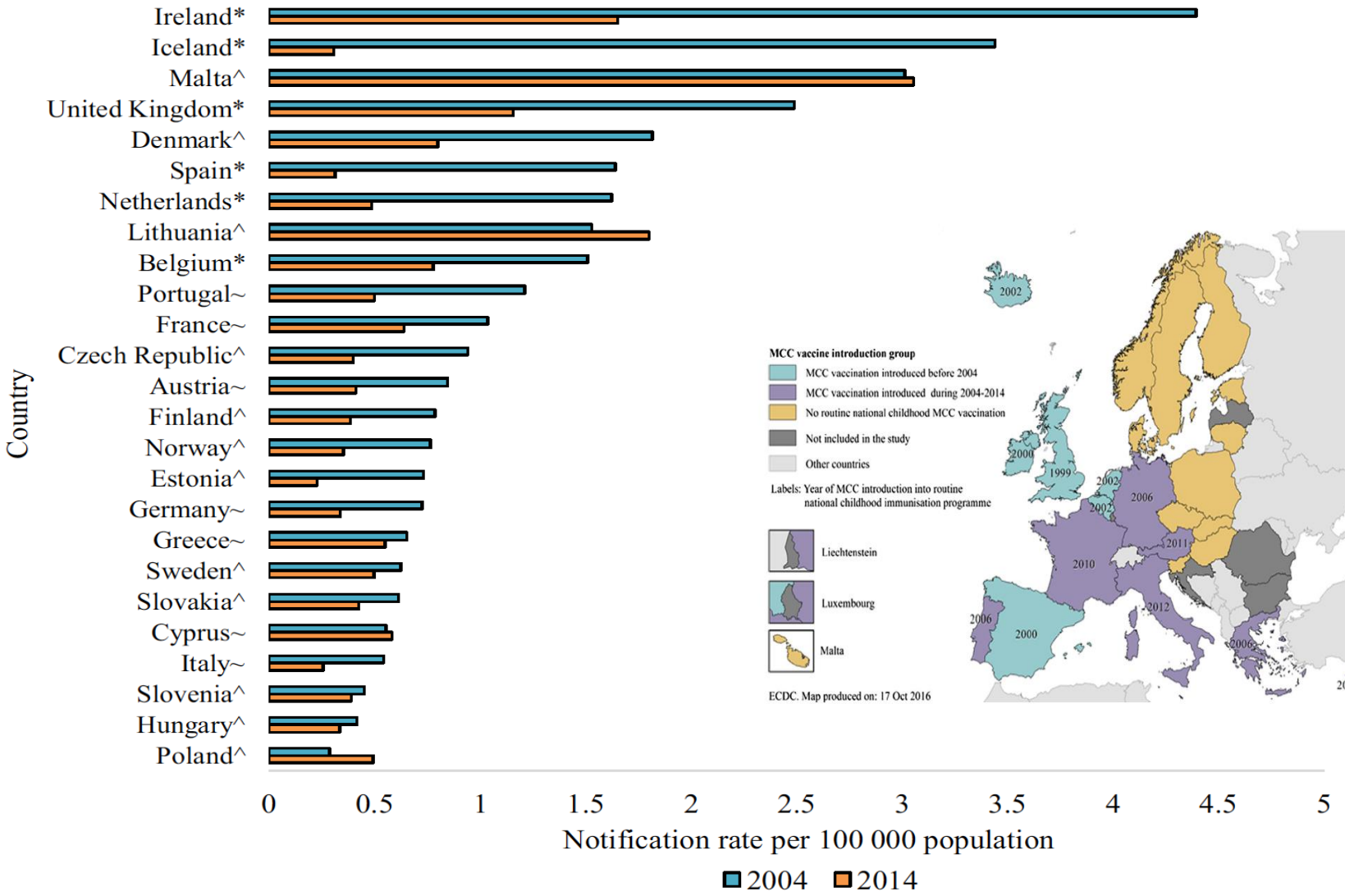
Effect of a serogroup A meningococcal conjugate vaccine (PsA–TT) on serogroup A meningococcal meningitis and carriage in Chad: a community trial

D M Daugla, J P Gami, K Gamougam, N Naibei, L Mbainadji, M Narbé, J Toralta, B Kodbesse, C Ngadoua, M E Coldiron, F Fermon, A-L Page, M H Djingarey, S Hugonnet, O B Harrison, L S Rebbetts, Y Tekletsion, E R Watkins, D Hill, D A Caugant, D Chandramohan, M Hassan-King, O Manigart, M Nascimento, A Woukeu, C Trotter, J M Stuart, M C J Maiden, B M Greenwood

Greenwood, Lancet, Sept 12, 2013

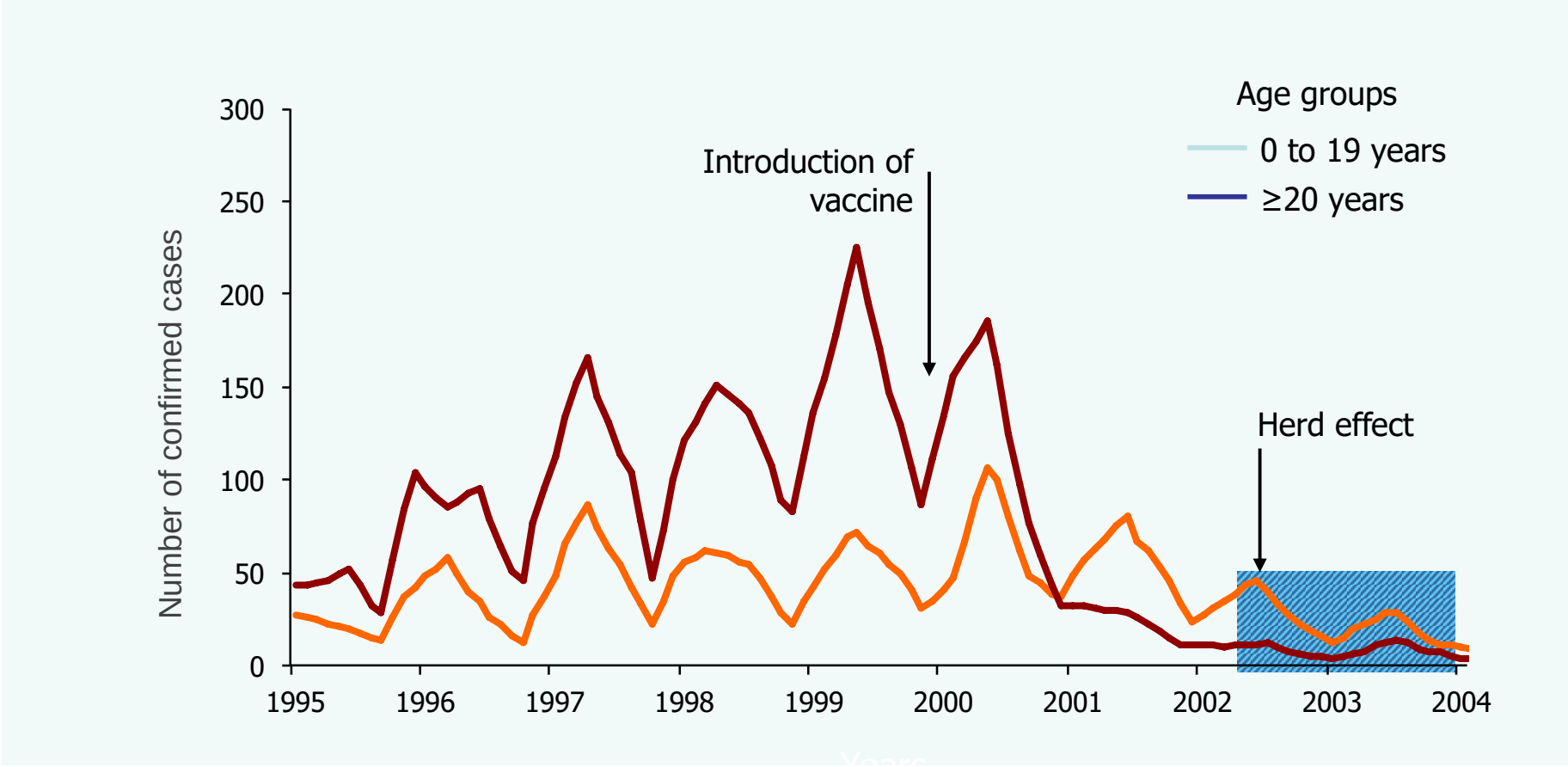


Impact according to incidence and local strategies against MenC in Europe, 2004 - 2014



R. Whittaker et al. Vaccine 35 (2017) 2034–2041

MenC Immunization reduced disease burden in vaccinated and unvaccinated population (UK)

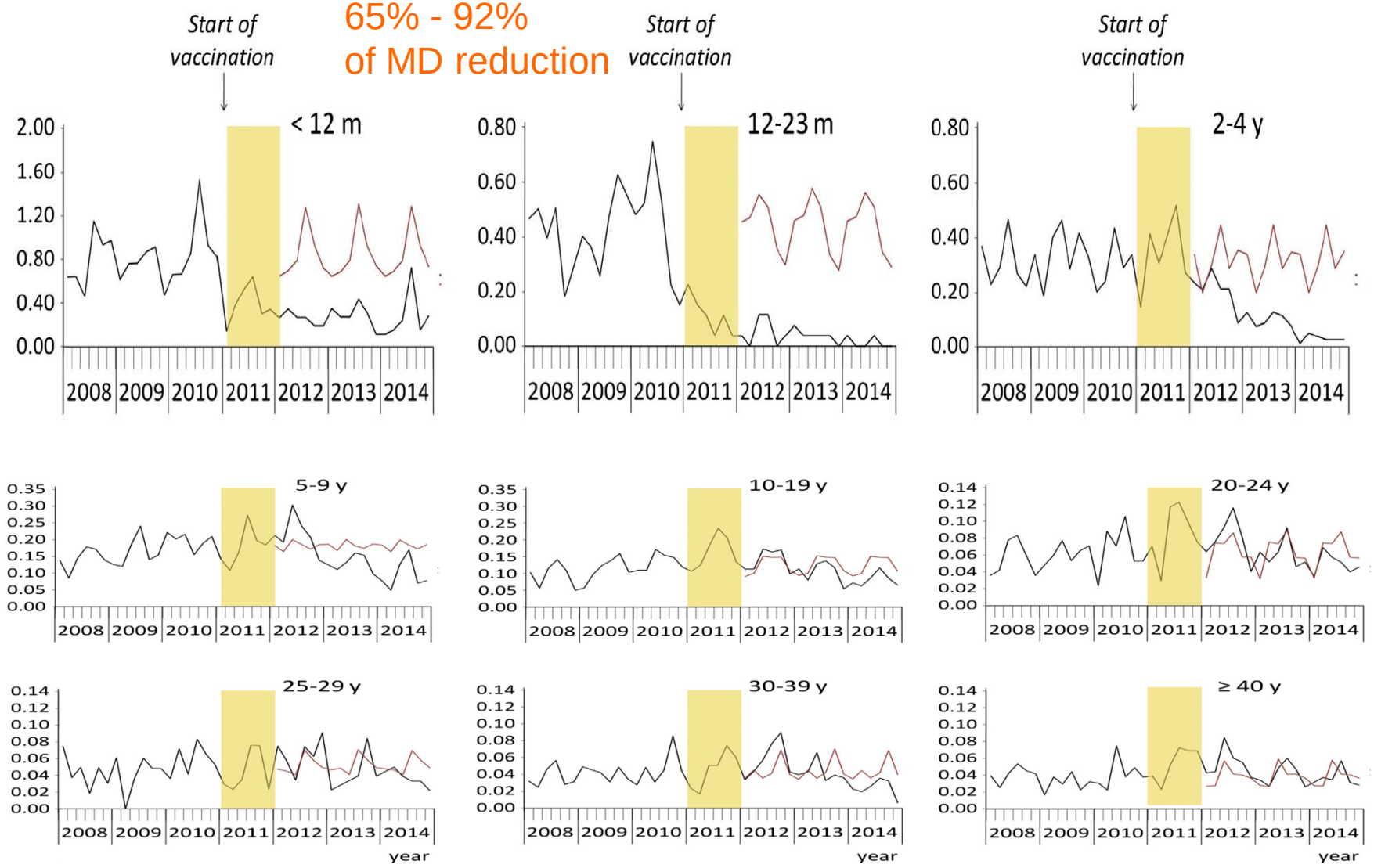


Rapid, sustained and marked decline in the number of MenC cases, with evidence of herd immunity

Trotter CL, et al. *Lancet*. 2004;364:365-367; 2. Maiden MC, et al. *J Infect Dis*. 2008;197:737-743.

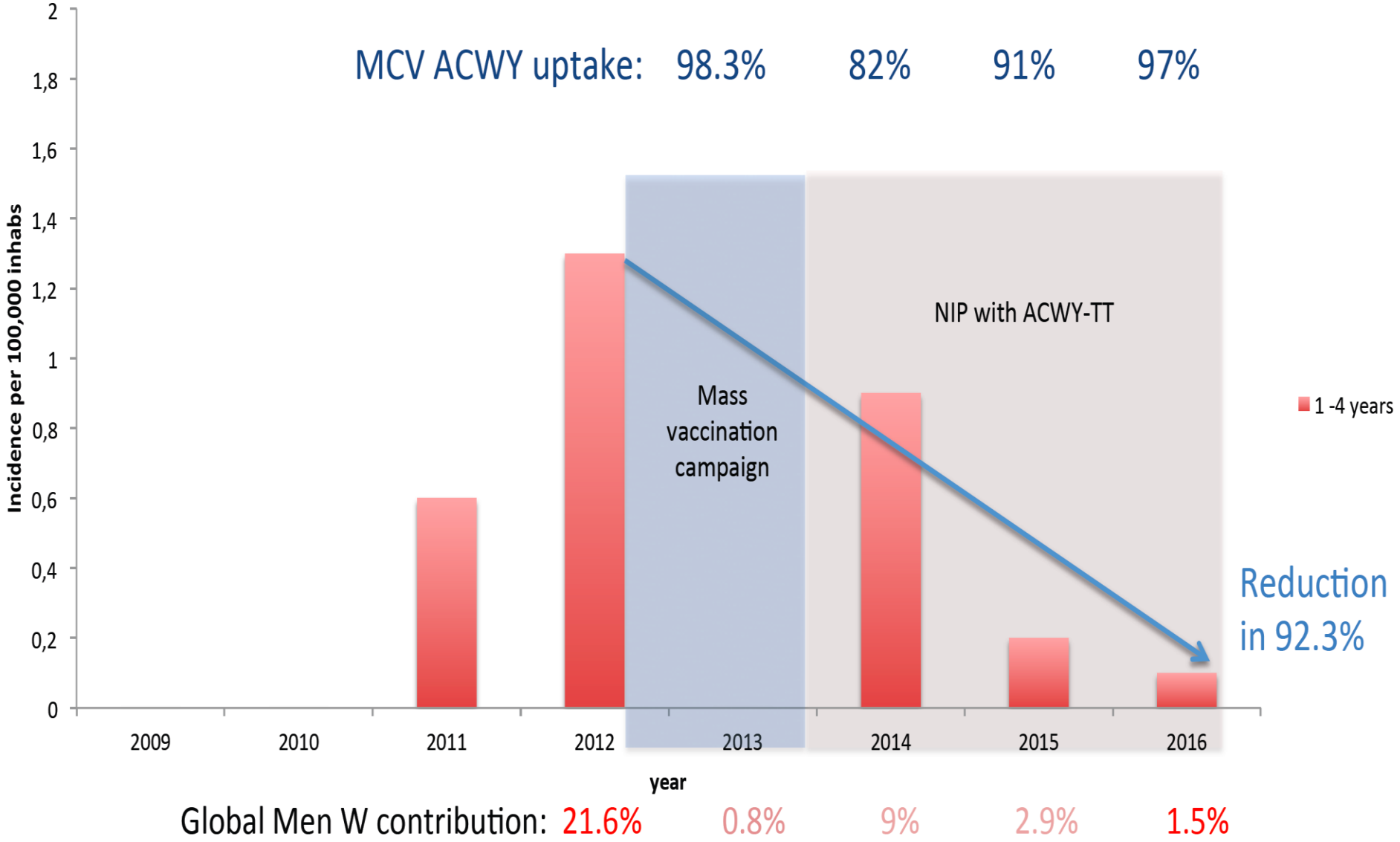
Brazil 2+1 infant schedule since 2010

direct protection over target population



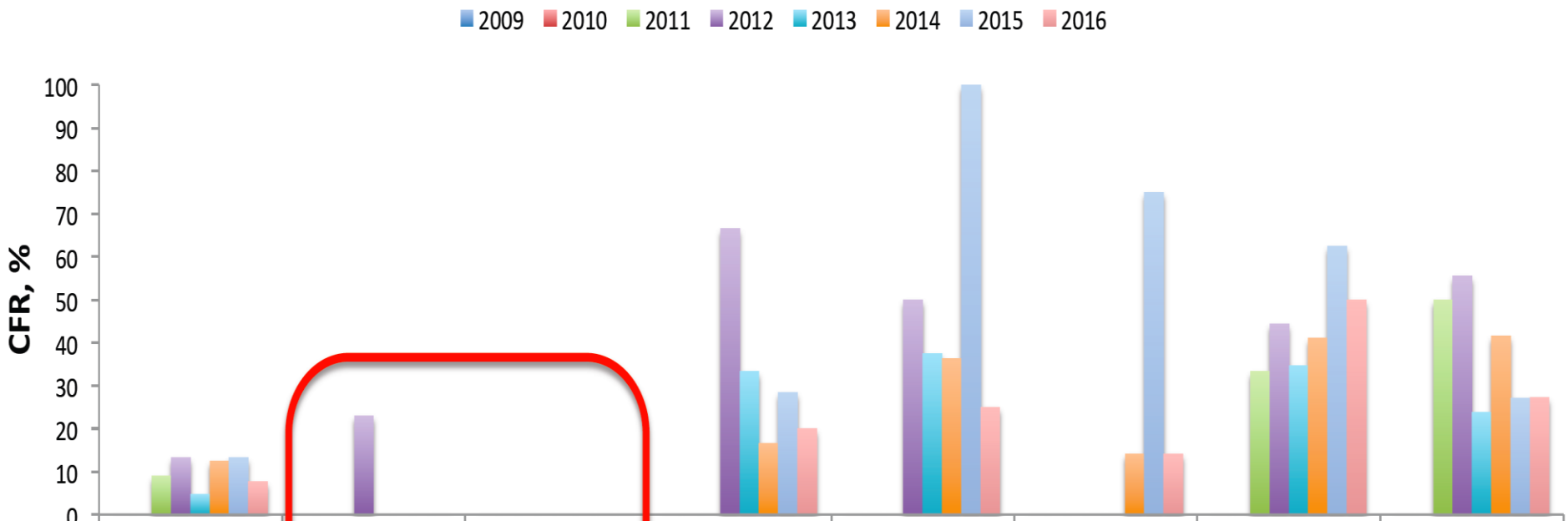
A.L. Andrade et al. Vaccine 35 (2017) 2025–2033

MenW incidence in children 1 – 4 years of age, target cohorts for vaccination campaign, by year Chile 2009 - 2016



Villena R; 14th EMGM, Prague, Czech Republic, 2017

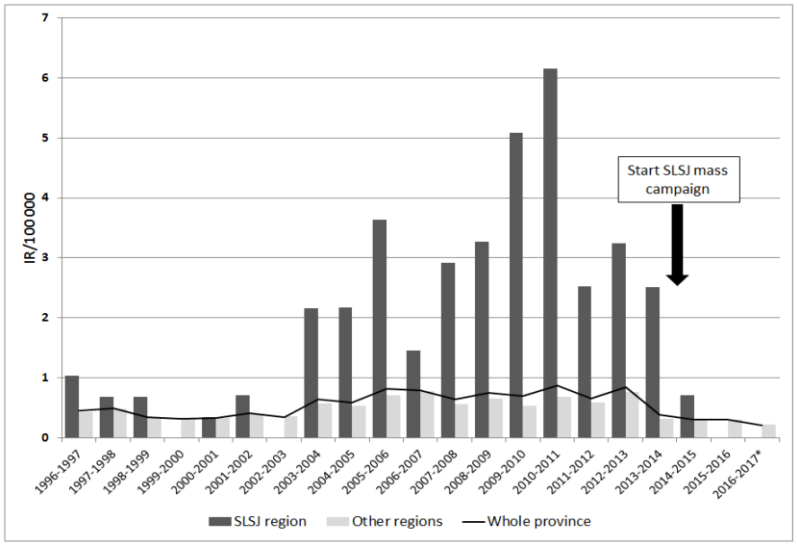
MenW CFR by age and year, Chile 2009-2016



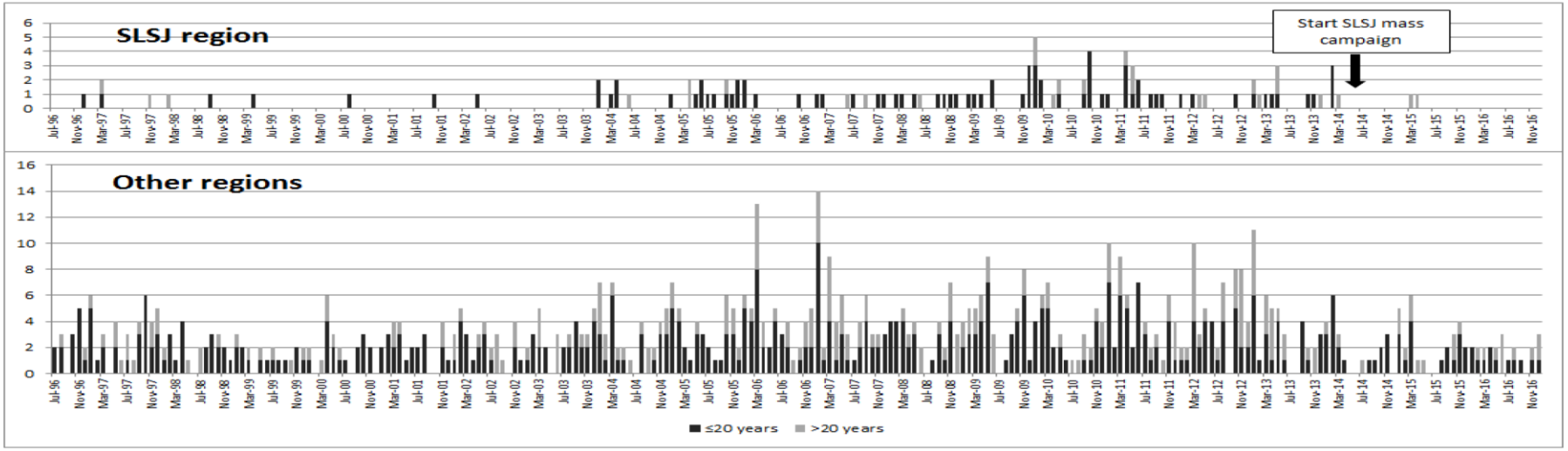
	< 1 year	1-4 years	5-9 years	10-19 years	20-29 years	30-40 years	40-59 years	> 60 years
2009	0	0	0	0	0	0	0	0
2010	0	0	0	0	0	0	0	0
2011	9	0	0	0	0	0	33,3	50
2012	13,3	23	0	66,6	50	0	44,4	55,5
2013	4,7	0	0	33,3	37,5	0	34,7	23,8
2014	12,5	0	0	16,6	36,3	14,2	41,1	41,6
2015	13,3	0	0	28,5	100	75	62,5	27,2
2016	7,7	0	0	20	25	14,2	50	27,3

Villena R; 14th EMGM, Prague, Czech Republic, 2017

Saguenay– Lac-Saint-Jean Region Experience



- 50,000 people between 2 months and 20 years
- 4CMenB
- Vaccine uptake
  - 1 dose: 82%, 2 doses 70%
- MD reduction: 77%
- Non MenB cases among vaccinees



De Wals P, et al Clin Infect Dis. 2017;9(64):1263–7

4CMenB immunogenicity …

ORIGINAL ARTICLE

Immunogenicity of a Meningococcal B Vaccine during a University Outbreak

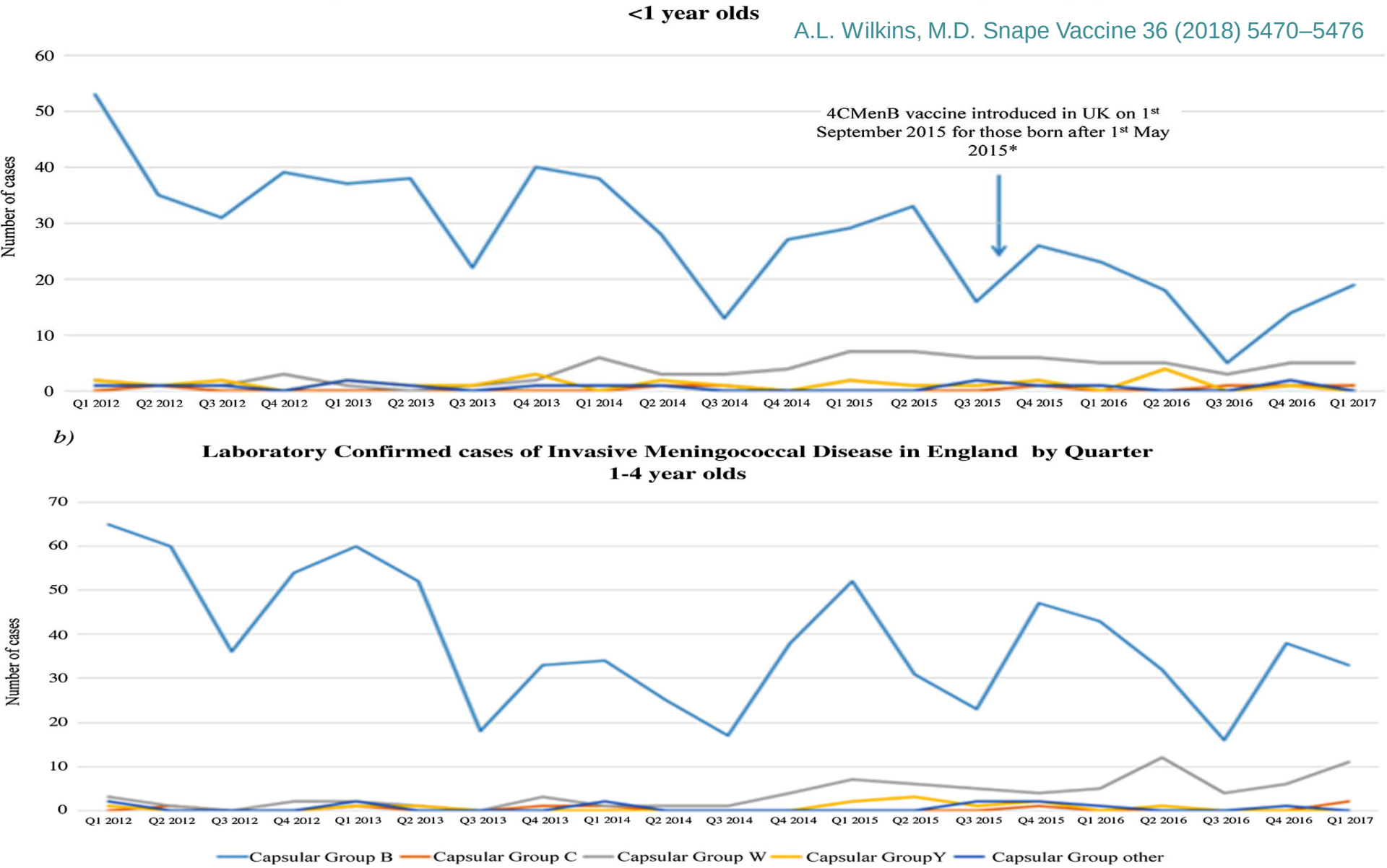
Table 2. Seropositivity and Geometric Mean Titers for the Meningococcal B Outbreak Strain According to Vaccination Status.*

Characteristic	Two Doses (N=499)	One Dose (N=17)	No Vaccination (N=19)
hSBA ≥4			
No. of participants	330	10	4
% (95% CI)	66.1 (61.8–70.3)	58.8 (32.9–81.6)	21.1 (6.1–45.6)
GMT (95% CI)	7.6 (6.7–8.5)	5.4 (2.5–11.7)	2.8 (2.3–3.5)

* Seropositivity is defined as a human serum bactericidal antibody (hSBA) titer of 4 or more. CI denotes confidence interval, and GMT geometric mean titer.

Basta N., n engl j med 375;3 July 21, 2016

rMenB effectiveness in the United Kingdom
82.9% → 94.2%



Safety of multicomponent meningococcal group B vaccine (4CMenB) in routine infant immunisation in the UK: a prospective surveillance study

Philip Bryan, Suzie Seabroke, Jenny Wong, Katherine Donegan, Elizabeth Webb, Charlotte Goldsmith, Caroline Vipond, Ian Feavers

Research in context

Evidence before this study

We considered published reports of pre-licensure pivotal clinical trials and post-licensure use in Canada of the multicomponent meningococcal group B vaccine (4CMenB). In these reports, 4CMenB was associated with high rates of local reactions and fever when given at the same time as other routine infant vaccines. However, very rare adverse reactions and the potential effect of the increased reactogenicity can only be identified and characterised during use in large population cohorts.

Added value of this study

Following widespread use of 4CMenB in UK infants, the safety profile appears consistent with that seen in clinical trials, with local reactions and fever being the most commonly reported adverse reactions. Additionally, our study showed no significant new safety concerns arising and high compliance with the second and third 4CMenB doses, and the addition of 4CMenB to the routine infant immunisation schedule did not seem to have had an adverse effect on compliance with other vaccinations.

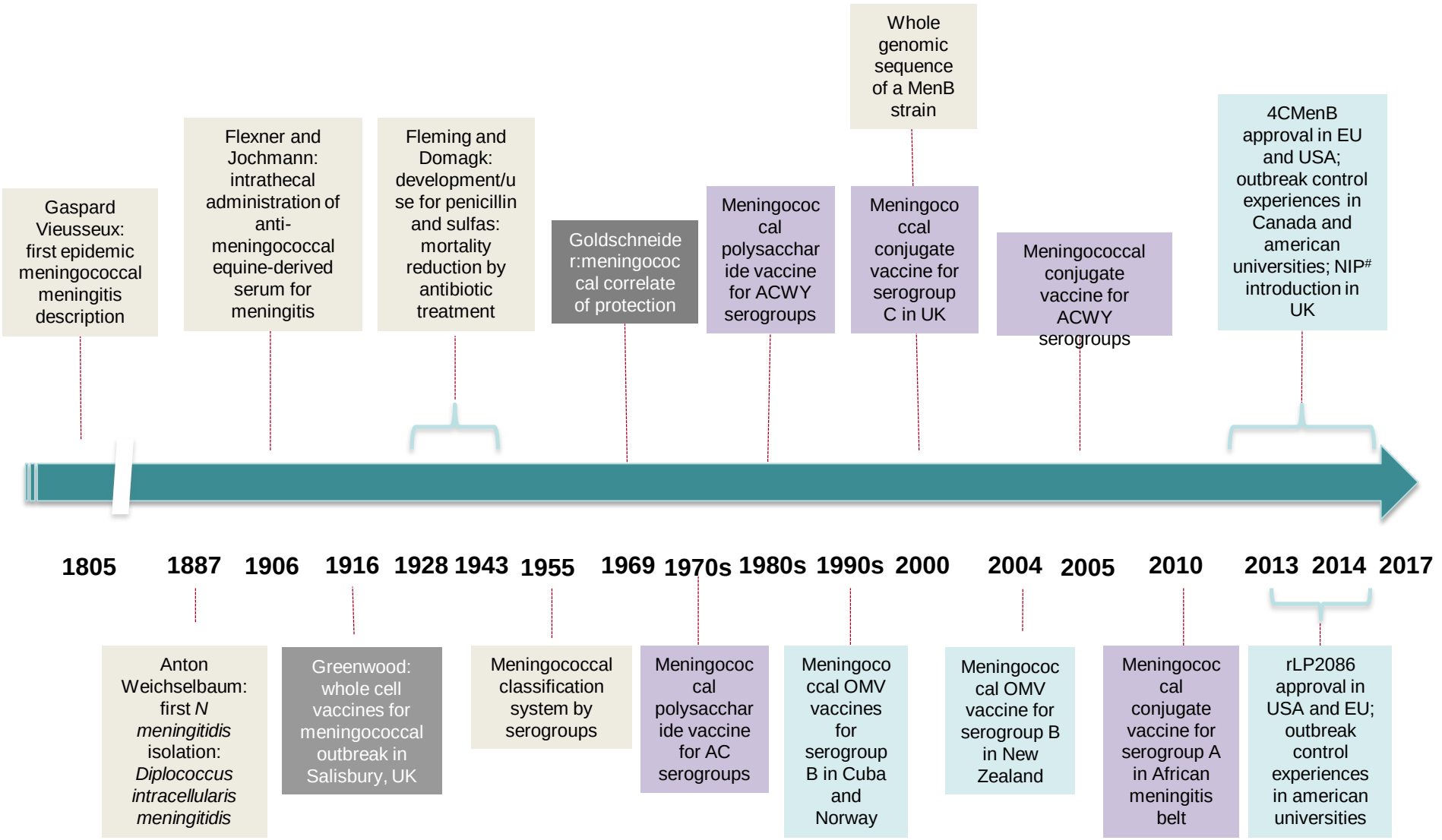
Implications of all the available evidence

Alongside the emerging data for vaccine effectiveness, the experience so far from the UK routine immunisation programme shows that 4CMenB has a favourable benefit–risk profile. It is important that safety remains under continual review to further characterise the reported suspected adverse reactions.

Bryan P., et al Lancet Child Adolesc Health 2018April 24, 2018 http://dx.doi.org/10.1016/S2352-4642(18)30103-2

Meningococcal disease control and prevention

Timeline

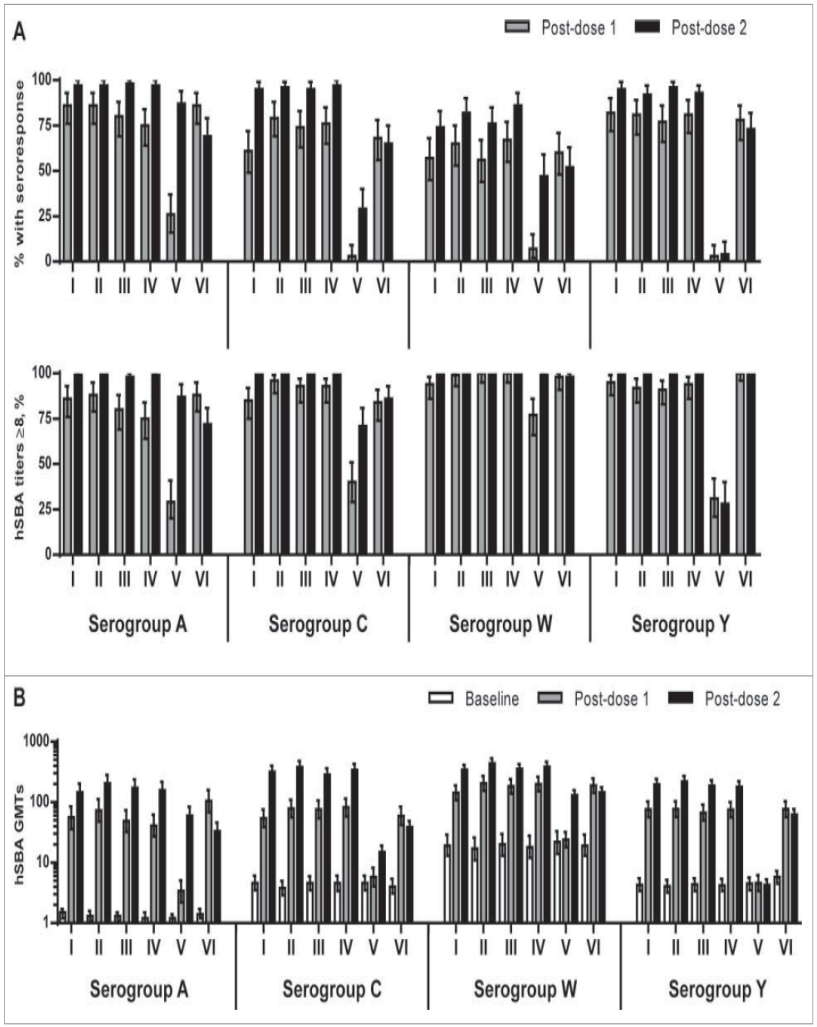


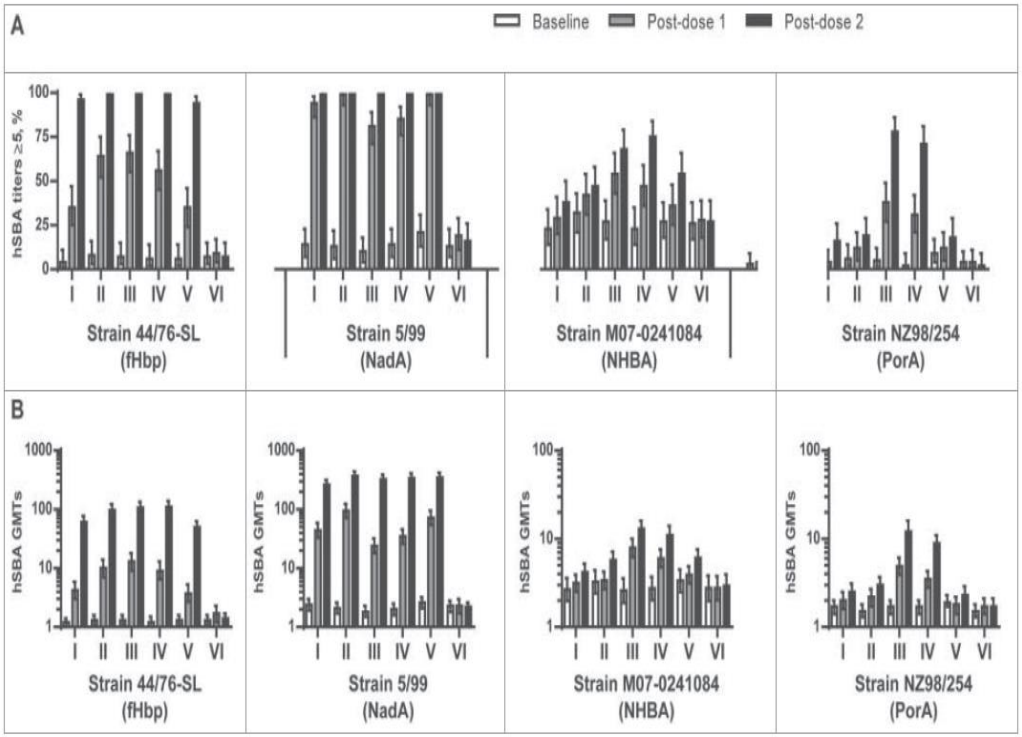
Villena R., et al Hum Vaccin Immunother. 2018 Apr 18:1-16

RESEARCH PAPER
Human Vaccines & Immunotherapeutics 11:6, 1507–1517; June 2015; © 2015 Taylor & Francis Group, LLC

Immunogenicity and safety of investigational vaccine formulations against meningococcal serogroups A, B, C, W, and Y in healthy adolescents

Xavier Saez-Llorens[1], Diana Catalina Aguilera Vaca[2], Katia Abarca[3], Emmanuelle Maho[4], Maria Gabriela Graña[5], Esther Heijnen[4], Igor Smolenov[4,*], and Peter M Dull[6]





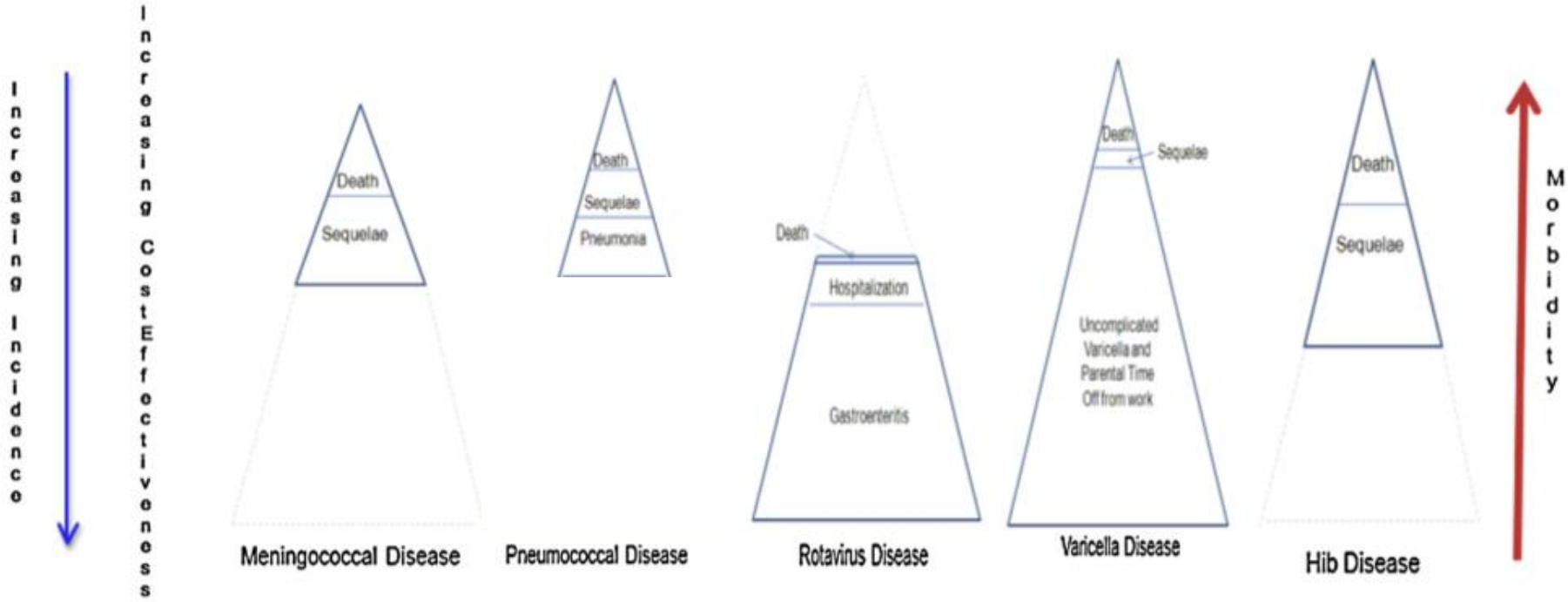
- 2 doses (0 and 2 months) of any combination → high immunogenicity against serogroups ACWY
- Similar to the immune response with rMenB vaccine alone

Review

The role of health economic analyses in vaccine decision making☆

Steven Black*

Center for Global Health, Cincinnati Children's Hospital, 3333 Burnett Avenue, Cincinnati, OH 45229, USA



- Disease burden; Financial-costs and efficiency
- Vaccine efficacy; Vaccine safety
- Feasibility for vaccine delivery and supply

Vaccine 31 (2013) 6046–6049

Conclusions

Take home messages

- MD epidemiology is constantly changing
  - Case criteria definition consensus …
  - Local and consistent surveillance across the time
- Molecular epidemiology contribution
  - Hypervirulent strains
- MCV ACWY are safe, immunogenic and effective
  - Persistence
- Novel rMenB vaccines real world experience promisory data
  - NP carriage – Cross protection – Persistence

XI International Symposium for Latin American experts

Meningococcal vaccines

GRACIAS!!

OBRIGADO!!

THANK YOU!!

MERCI!!