Public Health England

Invasive Meningococcal Disease

- prevention through vaccination

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Public Health England

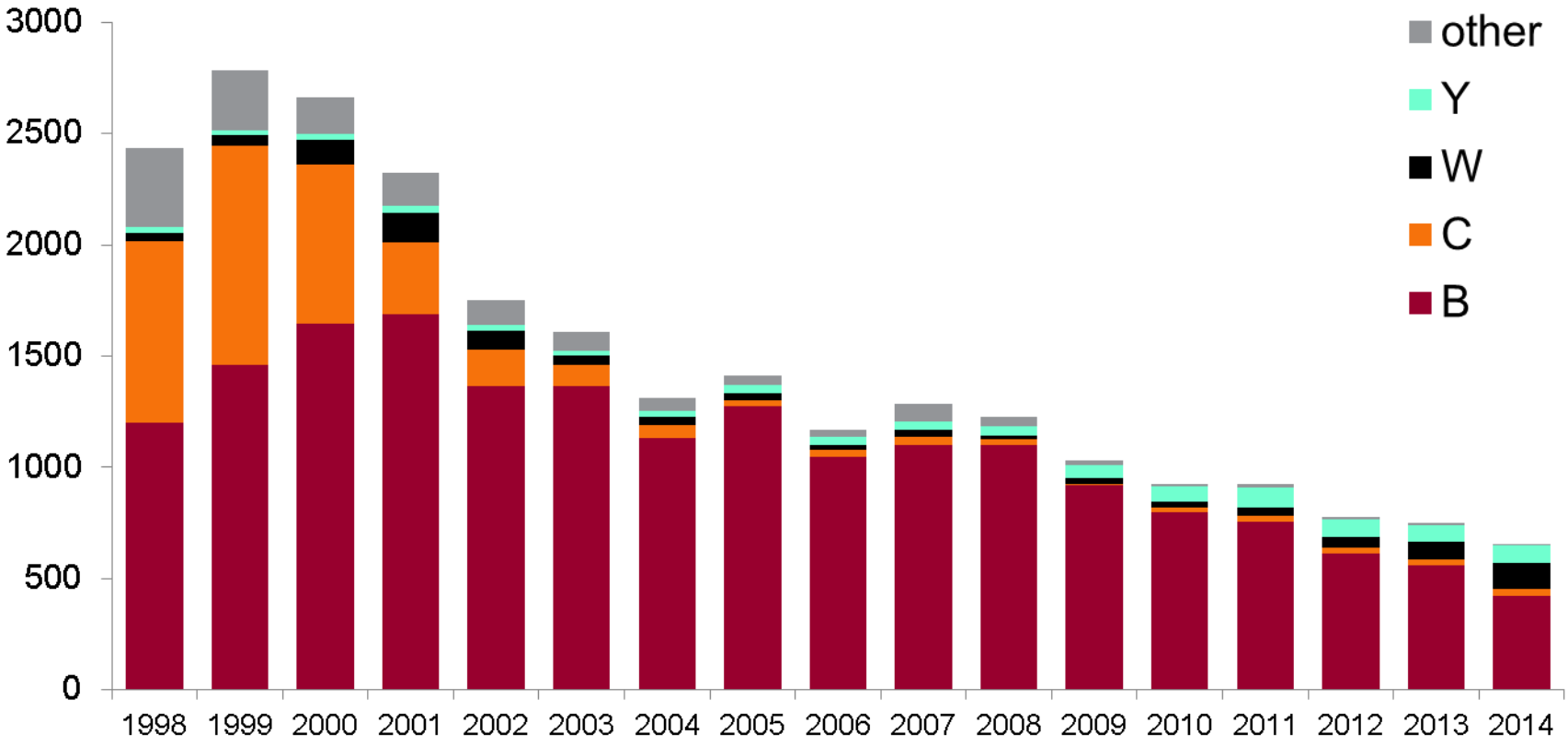
“a pain you cannot describe”

Public Health England

Invasive meningococcal disease

laboratory-confirmed cases

England and Wales



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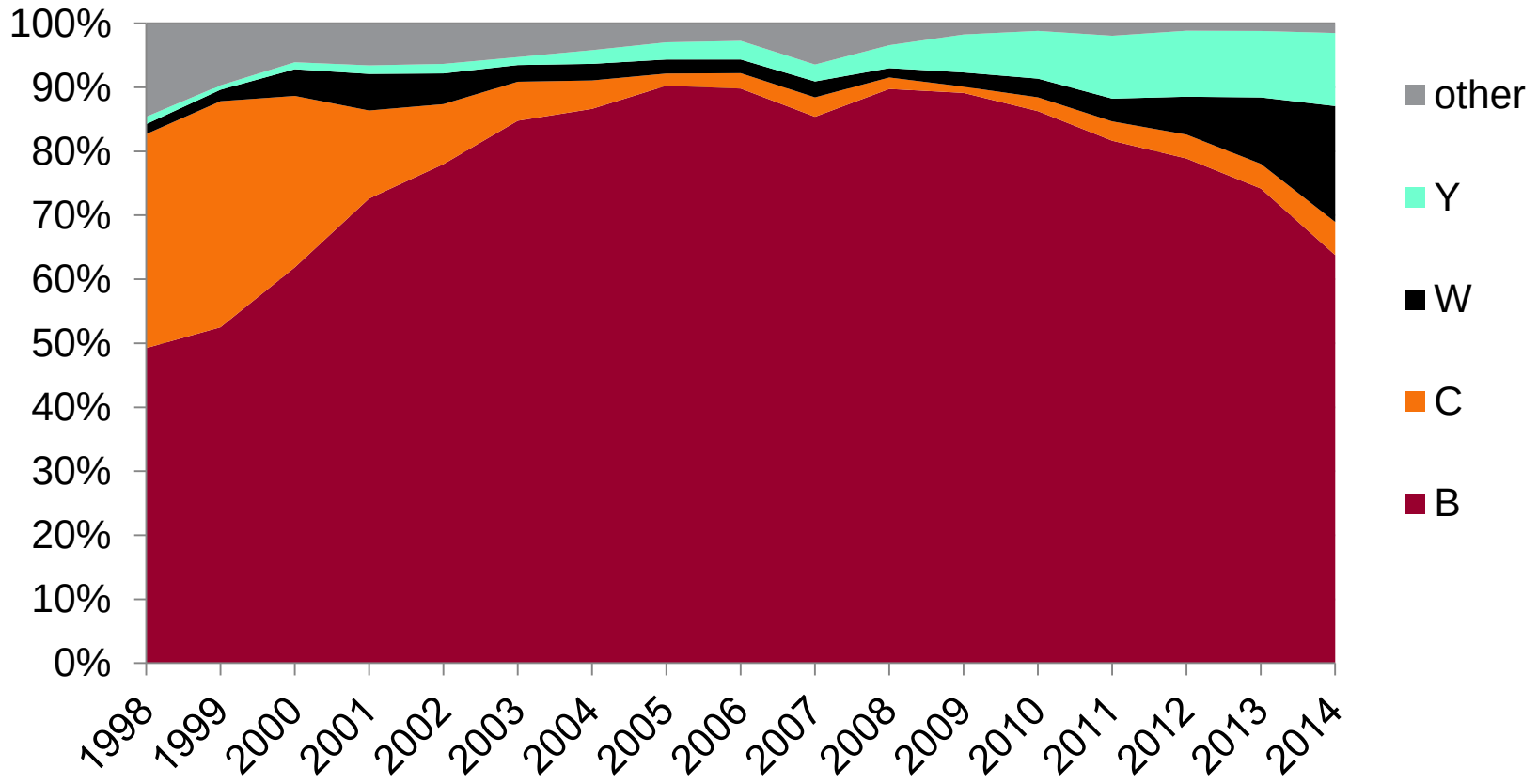
Invasive Meningococcal Disease

England & Wales, 2008-14



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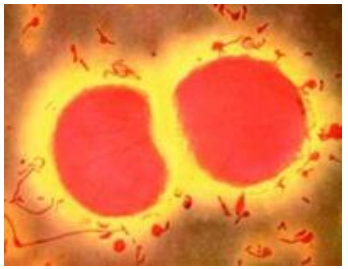
Vaccines against MenB

- MenC and MenACWY conjugate vaccines target the polysaccharide capsules – no cross-protection
- MenB polysaccharide is a polysialic acid - identical to that found on surface of human foetal neuronal cells.
- Consequently;

  (i) Poorly immunogenic.

  (ii) Potential to induce an autoimmune response

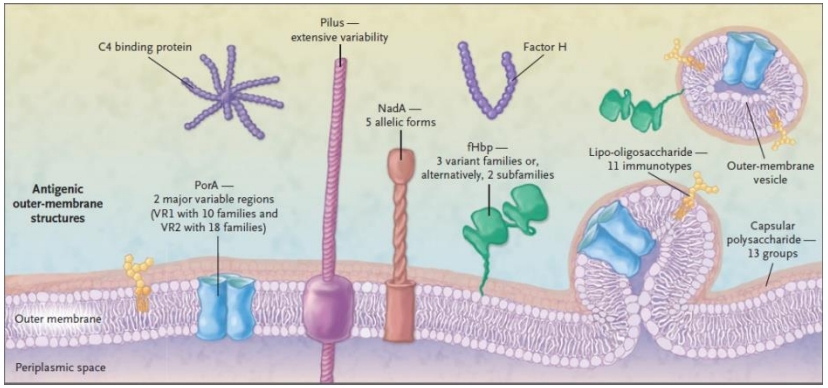


- Use subcapsular antigens, which:

  (i) are Surface-exposed

  (ii) are Conserved

  (iii) induce Bactericidal activity



BEXSERO® Consists of 4 Antigenic Components Chosen to Achieve Broad Protection

fHbp: factor H binding protein

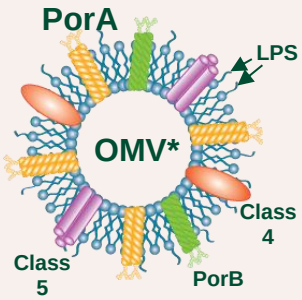
Binds factor H, which enables bacterial survival in the blood[1,2]

NHBA: neisseria heparin-binding antigen

- Binds heparin, which may promote bacterial survival in the blood[7]
- Present in virtually all strains[6,7]

NadA: neisserial adhesin A

- Promotes adherence to and invasion of human epithelial cells[3-5]
- May be important for colonisation[4]



NZ PorA P1.4: porin A

- Major outer membrane vesicle protein—induces strain-specific bactericidal response[8]

Combining antigens that target different steps of meningococcal pathogenesis is likely to help optimize MenB vaccine effectiveness

1. Madico G, et al. *J Immunol*. 2006;177:501-510; 2. Schneider MC, et al. *Nature*. 2009;458:890-893; 3. Comanducci M, et al. *J Exp Med*. 2002;195:1445-1454; 4. Capecchi B, et al. *Mol Microbiol*. 2005;55:687-698; 5. Mazzon C, et al. *J Immunol*. 2007;179:3904-3916; 6. Serruto D, et al. *Proc Natl Acad Sci U S A*. 2010;107:3770-3775; 7. Bambini S, et al. *Vaccine*. 2009;27:1794-2803; 8. Martin DR, et al. *Clin Vaccine Immunol*. 2006;13:486-491.

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Predicted meningococcal strain coverage in Europe

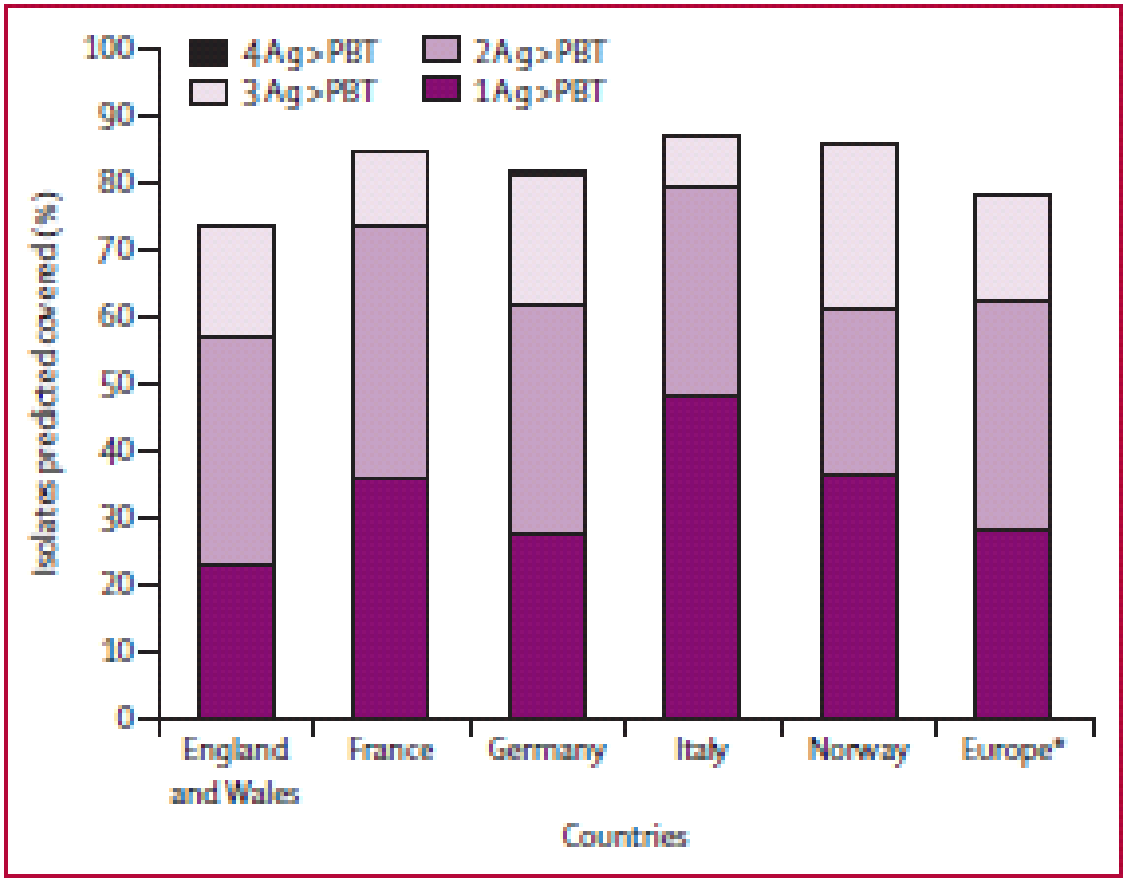

Figure 1: Percentages of isolates predicted by the meningococcal antigen typing system to be covered, and number of antigens, overall and by country

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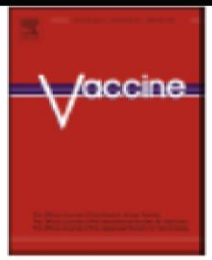
Predicted strain coverage in the UK using hSBA

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine



Bactericidal antibody against a representative epidemiological meningococcal serogroup B panel confirms that MATS underestimates 4CMenB vaccine strain coverage☆

Giacomo Frosi[a,1,3], Alessia Biolchi[a,3], Morena Lo Sapio[a,2], Fabio Rigat[a], Stefanie Gilchrist[b], Jay Lucidarme[b], Jamie Findlow[b], Ray Borrow[b], Mariagrazia Pizza[a], Marzia Monica Giuliani[a], Duccio Medini[a,*]

88% Coverage

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UK MenB programme

Negotiations to procure at cost-effective price were concluded in late March 2015

MenB vaccine given with routine immunisation appointments from 1st September 2015

Routine cohort: infants born on or after the **1 July 2015**

Schedule: 2, 4 and 12 months (2+1)

Catch-up cohort: infants born from **1 May to 30 June 2015**
Schedule: 3, 4 and 12 months (2+1)
Schedule: 4 and 12 months (1+1)

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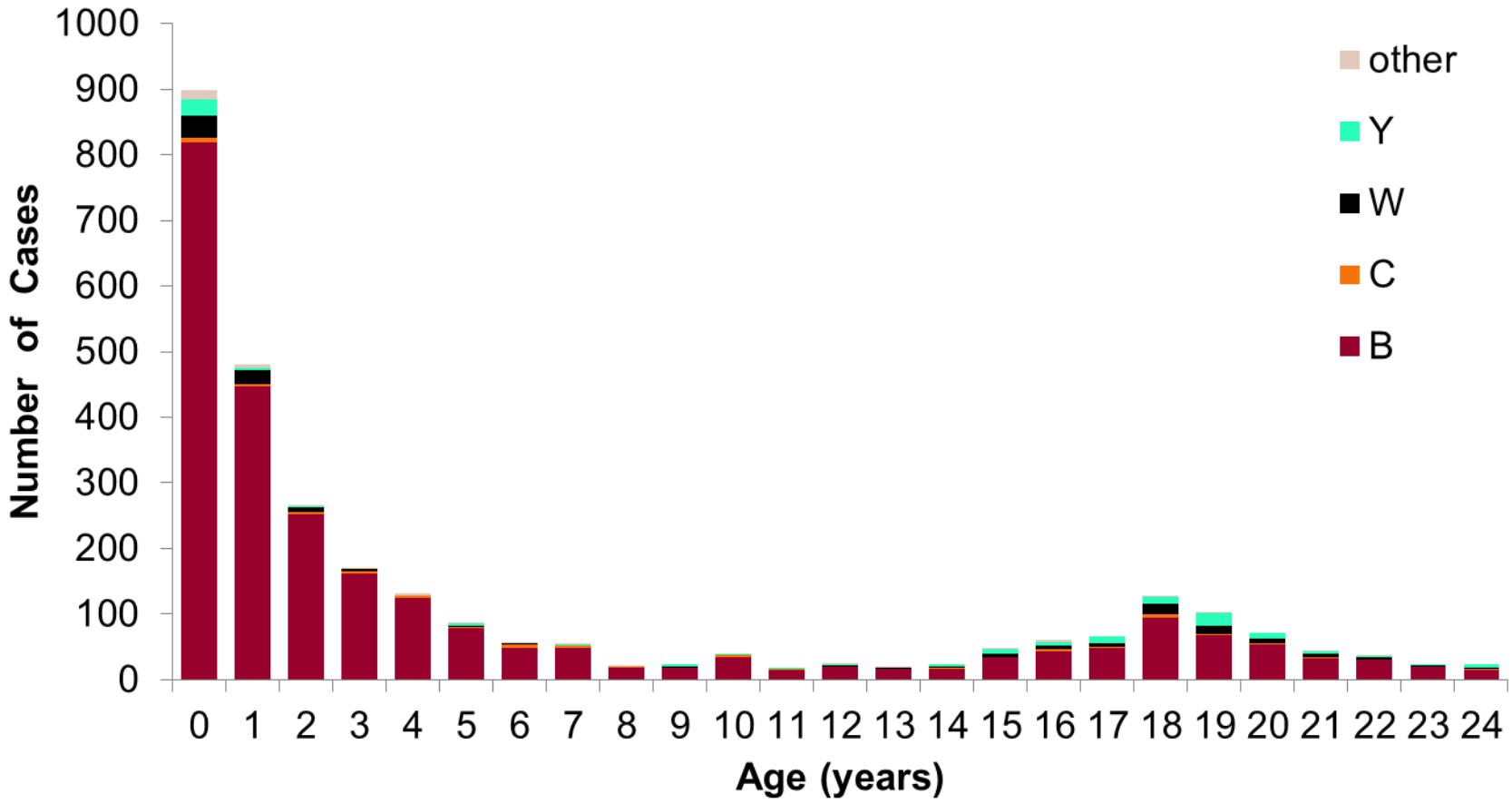
Laboratory confirmed IMD by group and age (2010-2014)



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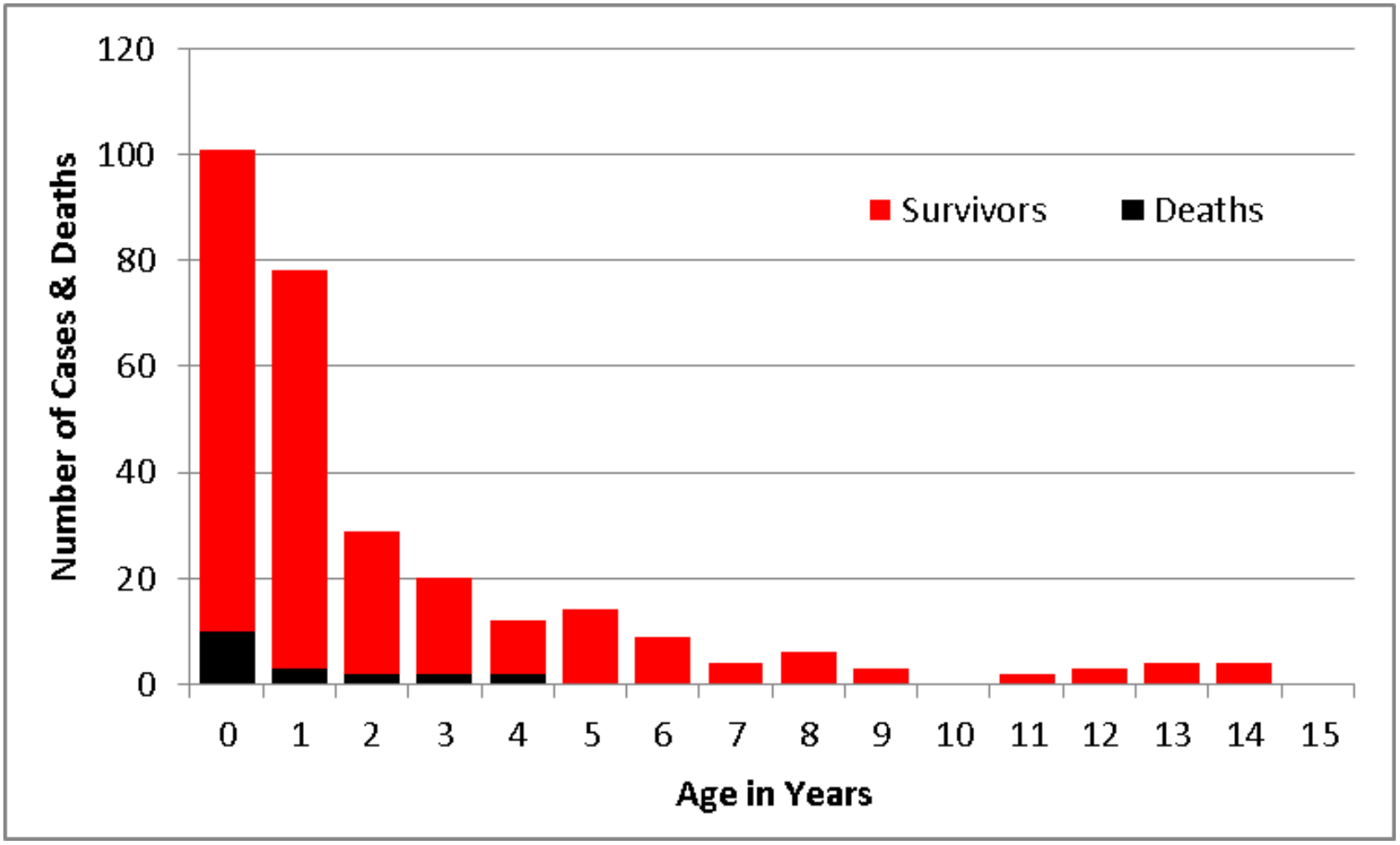
MenB cases/deaths, England 2014/15



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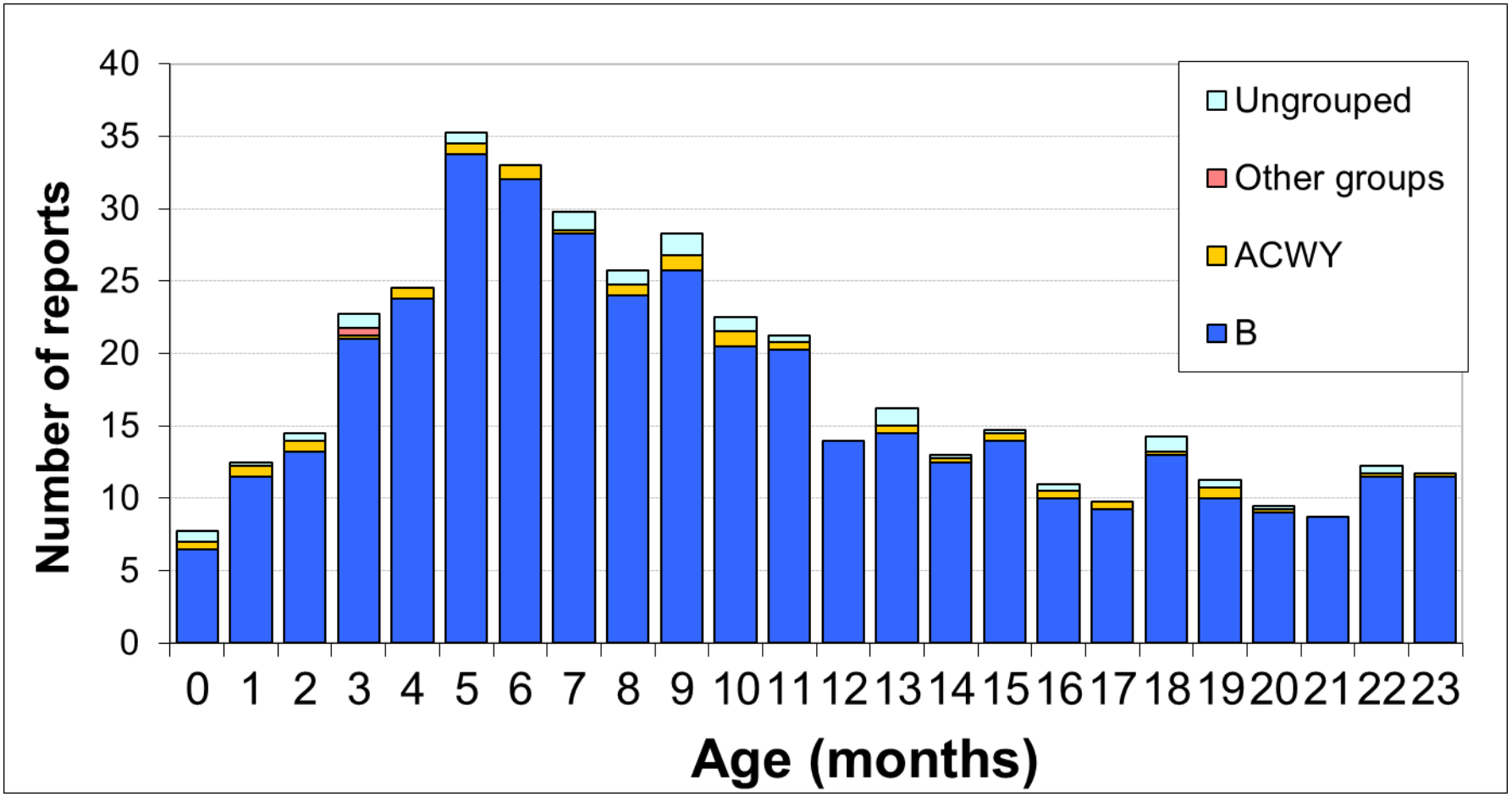
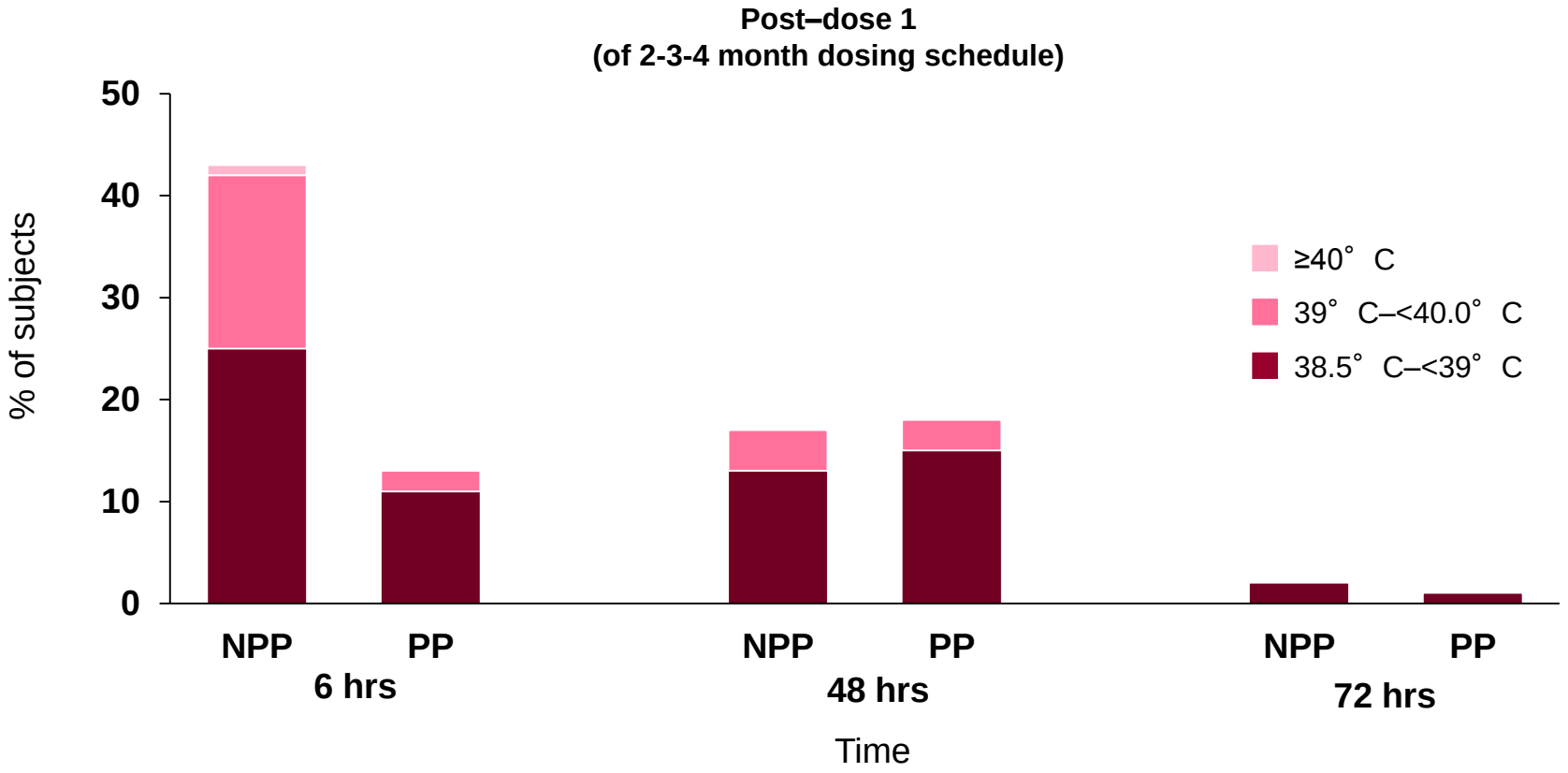
IMD in <2 year-olds

England & Wales (2006/07-2010/11)



Prophylactic Paracetamol at the Time of and Closely After Vaccination Reduced Fever

When BEXSERO® is given concomitantly with routine infant vaccines



NPP: no prophylactic paracetamol (N=182); PP: with prophylactic paracetamol (N=178-179).
Routine vaccines: PCV7 and DTaP-HBV-IPV/Hib.

1. Prymula R, et al. Presented at: 29th Annual Meeting of the European Society for Paediatric Infectious Disease (ESPID); June 7-10, 2011; The Hague, The Netherlands. Poster #631; 2. Data on file, Novartis Vaccines and Diagnostics; 3. BEXSERO [summary of product characteristics]. Siena, Italy: Novartis Vaccines and Diagnostics S.r.l.; January 14, 2013.

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Enhanced surveillance of IMD, England

- September 2015
  - Public Health England (PHE) conducts enhanced IMD surveillance
- PHE Meningococcal Reference Unit (MRU)
  - Confirmation & characterisation of invasive isolates
  - Free national PCR-testing service (20,000 samples, 6% positive)
- High case ascertainment (>95% of cases captured)
- All confirmed cases followed up by PHE Imms
  - Vaccine history
  - Risk factors
  - Clinical course
  - Outcome

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Vaccine Effectiveness

Doses	Cases vaccinated / total	Average matched coverage	VE* (95 %CI)
2+0	9/13 (69%)	92.9%	82.9% (24.1% to 95.2%)

Assuming 88% of MenB strains covered by 4CMenB, then VE against vaccine-preventable strains **~94%**

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Vaccine Effectiveness

Doses	Cases vaccinated / total	Average matched coverage	VE* (95 %CI)
2+0	9/13 (69%)	92.9%	82.9% (24.1% to 95.2%)
1+0	20/28 (71%)	76.2%	22.0% (-105% to 67.1%)

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Vaccine Impact

Analysis	Group	Cases (Sep15-June 16)	Equivalent cohorts (2011/12-2014/15) mean per year	IRR (95% CI) p-value
Compare to past 4 years	Catch-up (Born 1st May -30th June 2015)	9	25	0.36 (0.18-0.72), p=0.004
	Routine (Born on or after 1st July 2015 aged ≥18w)	18	34	0.53 (0.33-0.87), p=0.012
	Routine (Born on or after 1st July 2015 aged 10-17w)	10	15	0.66 (0.34-1.28), p=0.216
	All combined	37	74	0.50 (0.36-0.71), p<0.001
	CONTROLS (<10 weeks old or born before 01 May 2015 and aged <5 years)	173	201	0.86 (0.73-1.01), p=0.073

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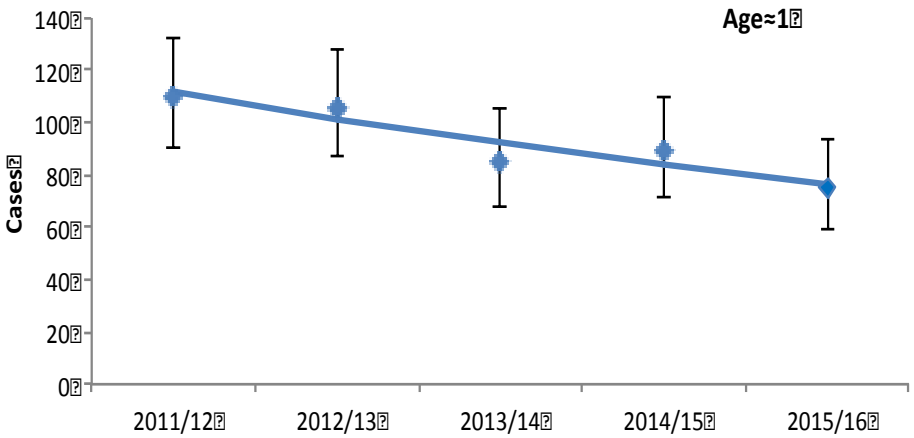
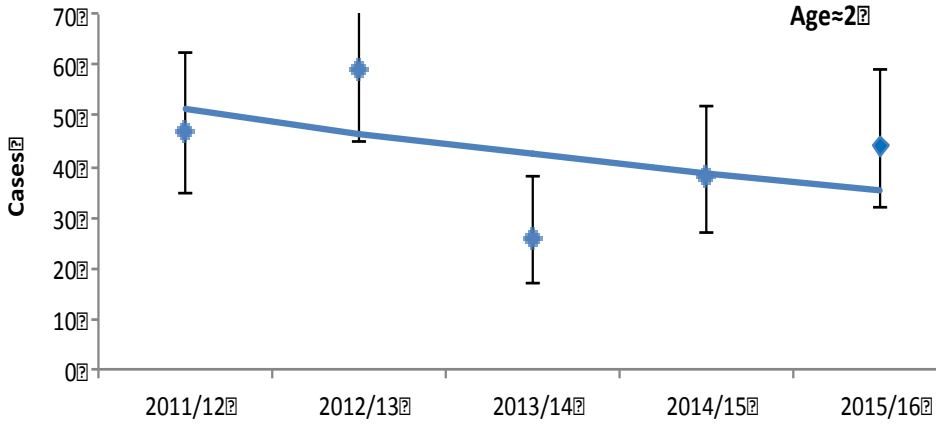
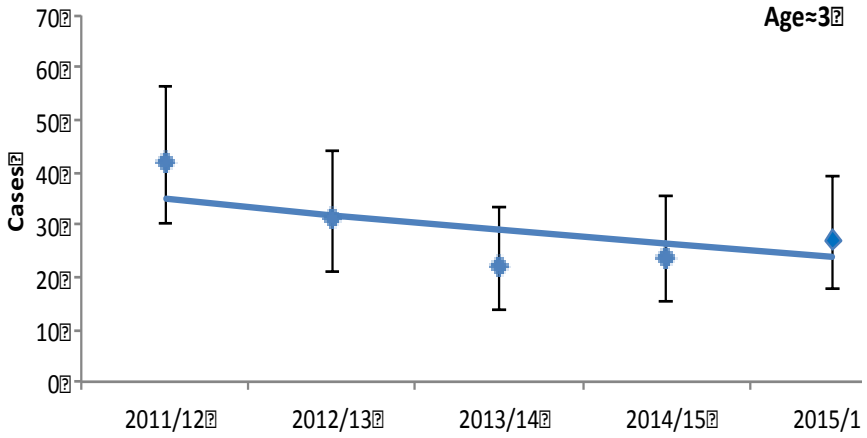
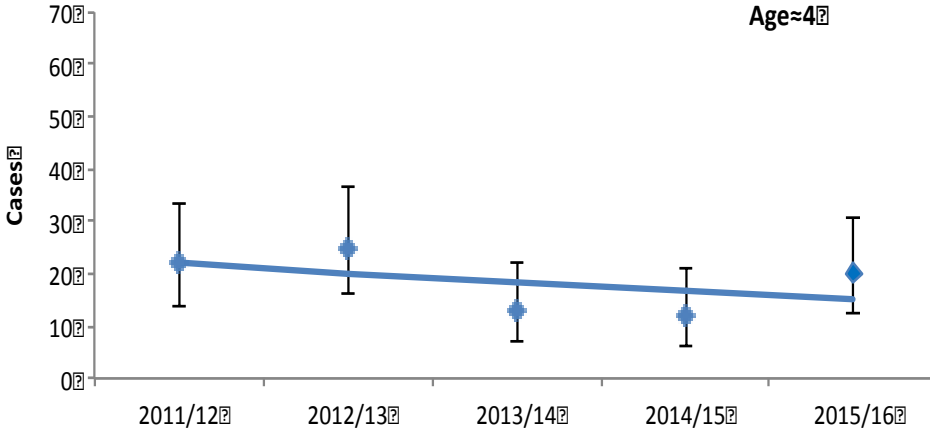
Trends in ineligible children









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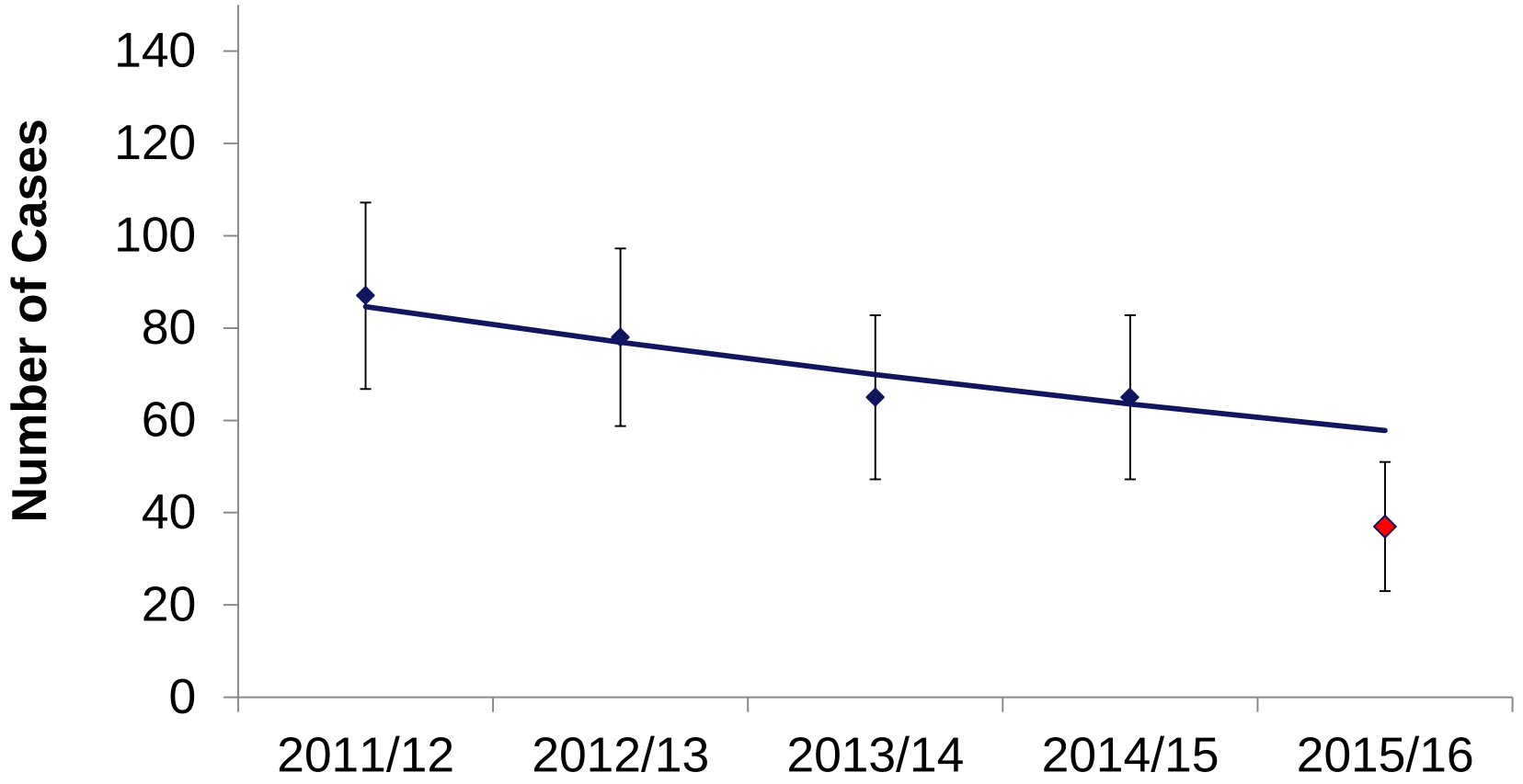
Vaccine-eligible Cohort



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Where are we now?

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Vaccine eligible cohort update

Data until 30th June 2017

- 138 laboratory-confirmed IMD cases in infants eligible for the MenB vaccine – 21 months surveillance (*born on or after 01/05/ 2015*)

92 MenB	4 MenC	32 MenW	7MenY	3 Ungroupable

- In the process of ascertaining vaccination histories for all cases.
- So far → 3 cases of MenB disease in children who received 3 doses of Bexsero®
- 30 deaths in individuals with confirmed MenB disease
  - Only one death occurred in those eligible for vaccine
  - One child received one dose of Bexsero®

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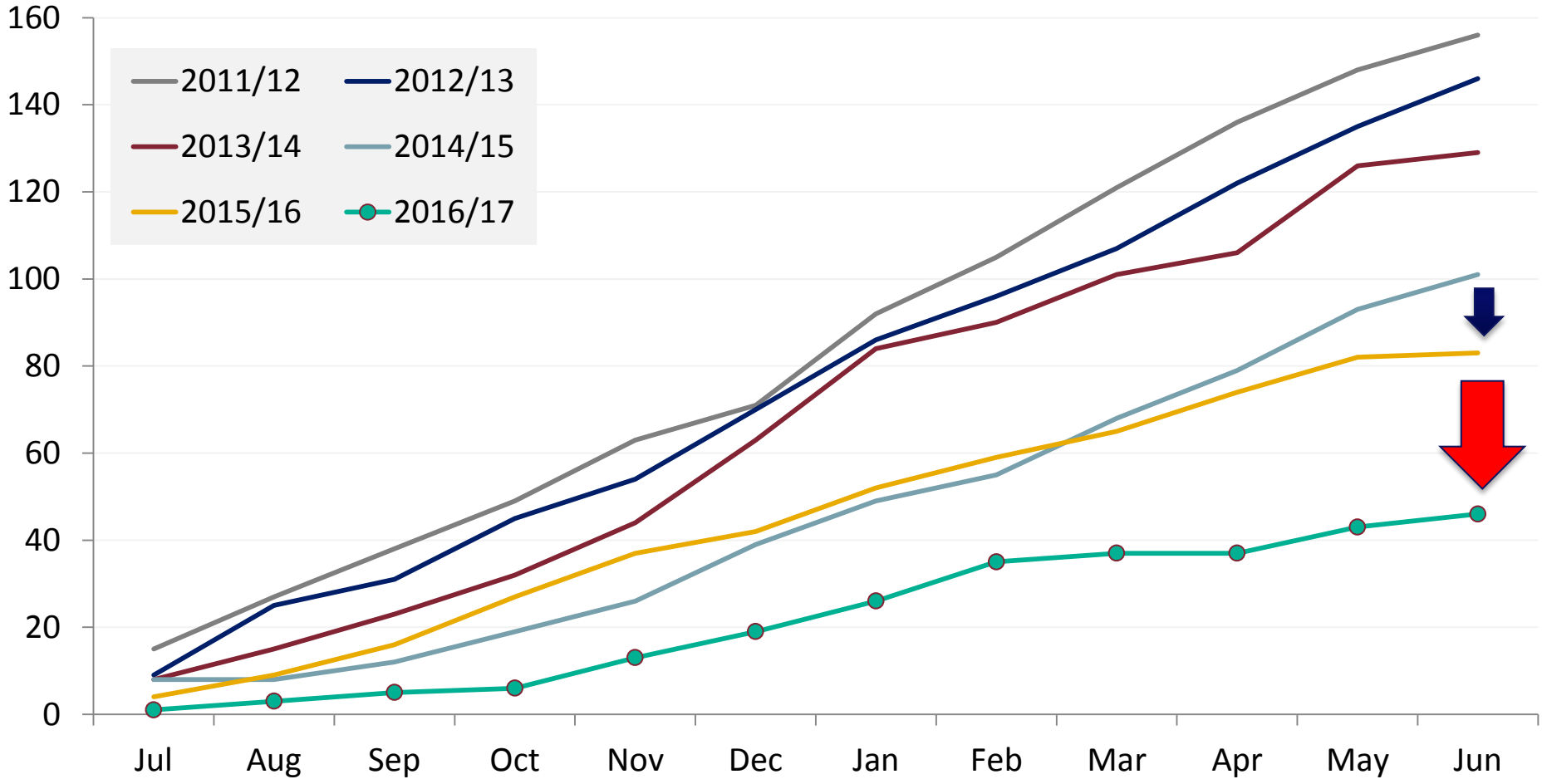
Cases in <1 year-olds



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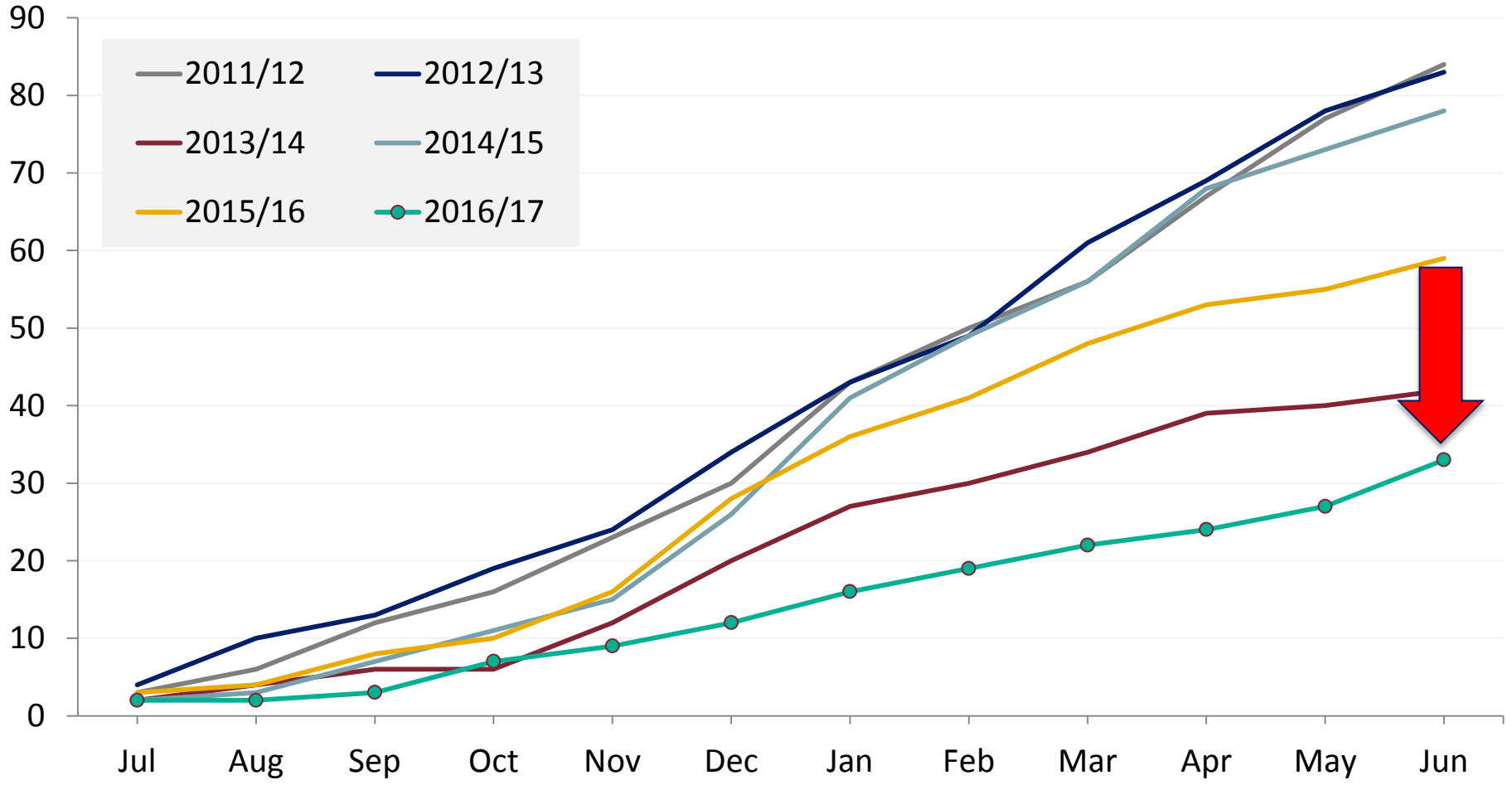
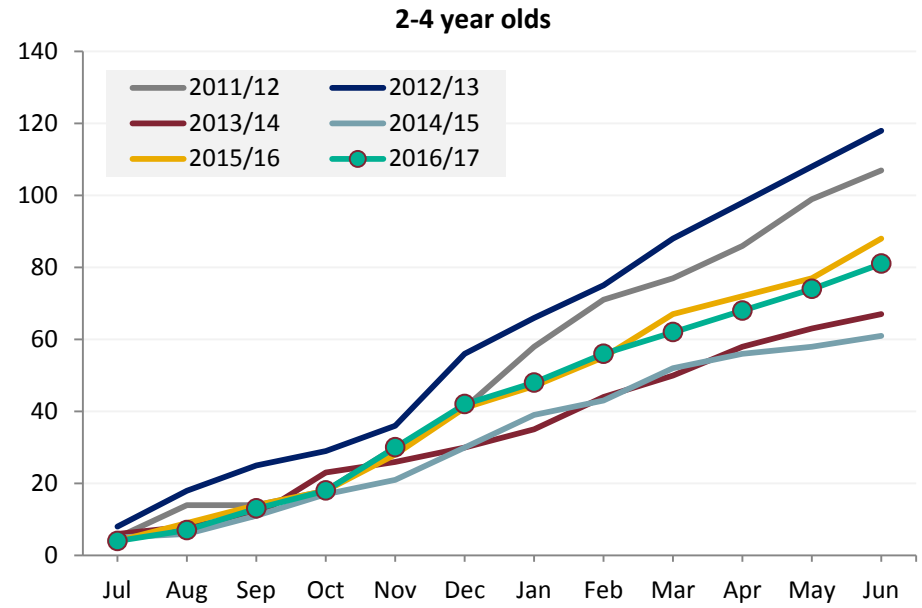
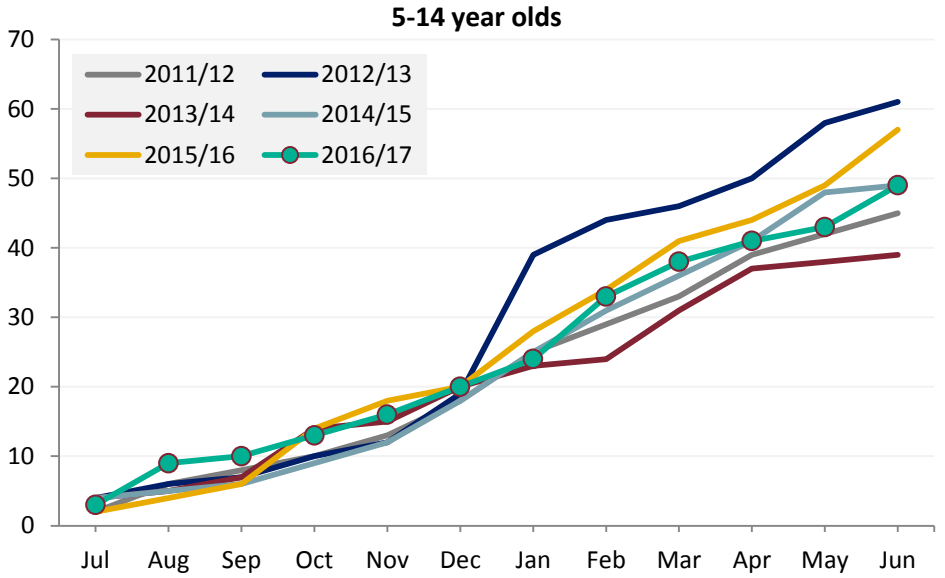
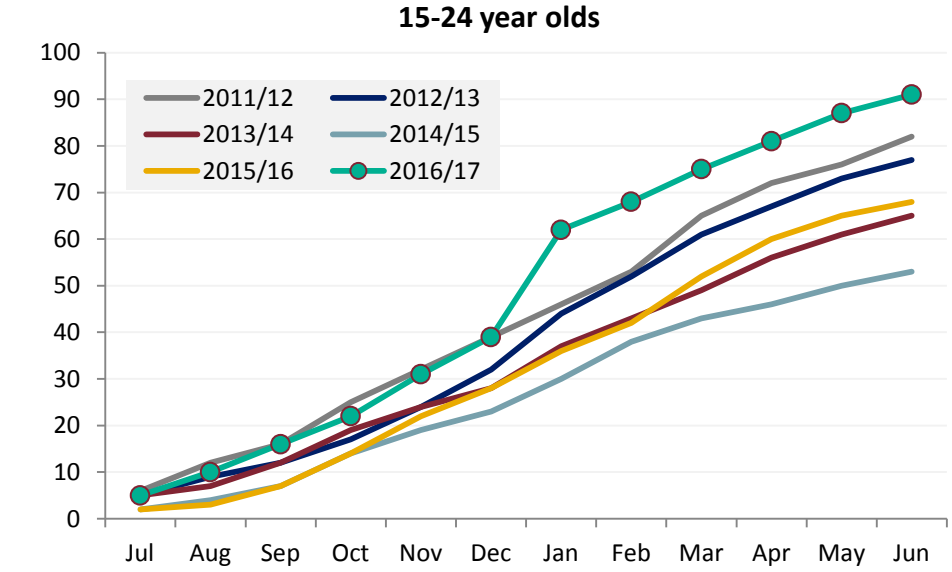
Cases in 1 year-olds




2-4 year olds
2011/12
2012/13
2013/14
2014/15
2015/16
2016/17
140
120
100
80
60
40
20
0
Jul
Aug
Sep
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun


5-14 year olds
2011/12
2012/13
2013/14
2014/15
2015/16
2016/17
70
60
50
40
30
20
10
0
Jul
Aug
Sep
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun


15-24 year olds
2011/12
2012/13
2013/14
2014/15
2015/16
2016/17
100
90
80
70
60
50
40
30
20
10
0
Jul
Aug
Sep
Oct
Nov
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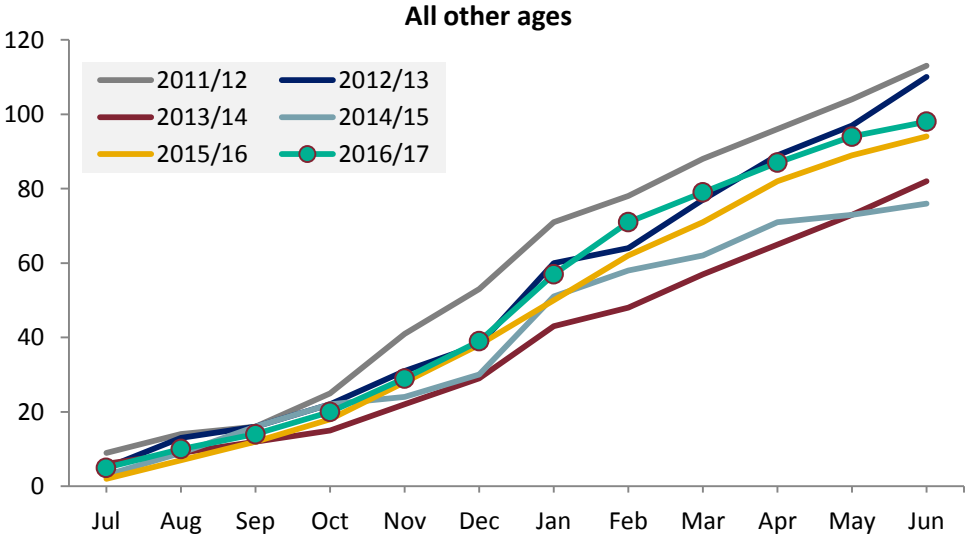
Mar
Apr
May
Jun


All other ages
2011/12
2012/13
2013/14
2014/15
2015/16
2016/17
120
100
80
60
40
20
0
Jul
Aug
Sep
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun

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Vaccine Safety

- So far, 3 million doses given to children so far
- Concerns before vaccine introduction
  - Kawasaki Disease – very rare in <6m, no evidence of increase
  - Seizures – no evidence of increase in any kind of seizure
  - Less likely to have subsequent vaccination – no evidence (97-98% return for their subsequent vaccines)
- Primary Care consultations for fever
  - 2-fold increase in infants attending GP for fever post-vaccination with Bexsero
- Secondary care consultations for fever
  - 3-4 fold increase in infants attending the ED for fever post-vaccinatio
- Hospitalisations for fever
  - Around half the infants attending the ED have septic screens +/- antibiotics
  - ? Did the parents give prophylactic paracetamol as recommended?

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Summary

- The UK introduced 4CMenB (Bexsero®) for infants in September 2015
- MenB cases declined from 349 in 2015/6 to 277 in 2016/17
- After 10 months, MenB cases declined by **50%** in vaccine-eligible infants, irrespective of
    - Vaccine coverage in the population
    - Number of vaccines doses received by the infants
    - MATS coverage of the MenB strains causing IMD cases
    - Vaccine effectiveness against invasive MenB disease
- **VE for 2-dose infant priming schedule was 83%,** equivalent to 94% VE against 88% MenB strain coverage predicted by hSBA
- **In 2016/17, significant reductions are also seen in** 1 year-olds who were eligible for the 12-month booster
- Surveillance on-going … 3 million doses ...No safety concerns so far …

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Controlling the increase in group W meningococcal disease in the UK

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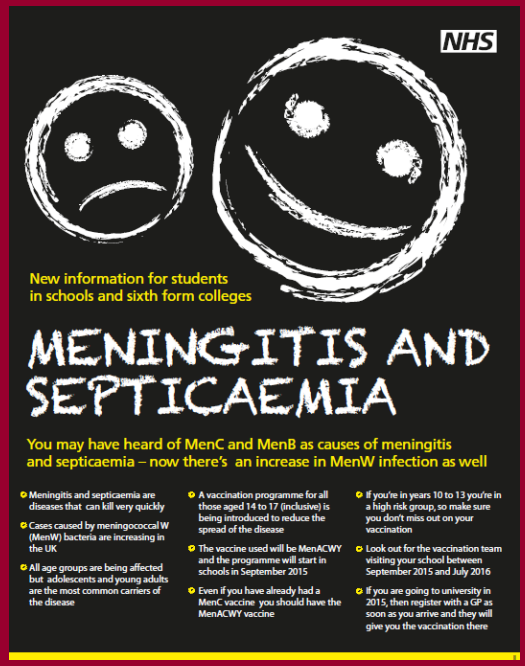

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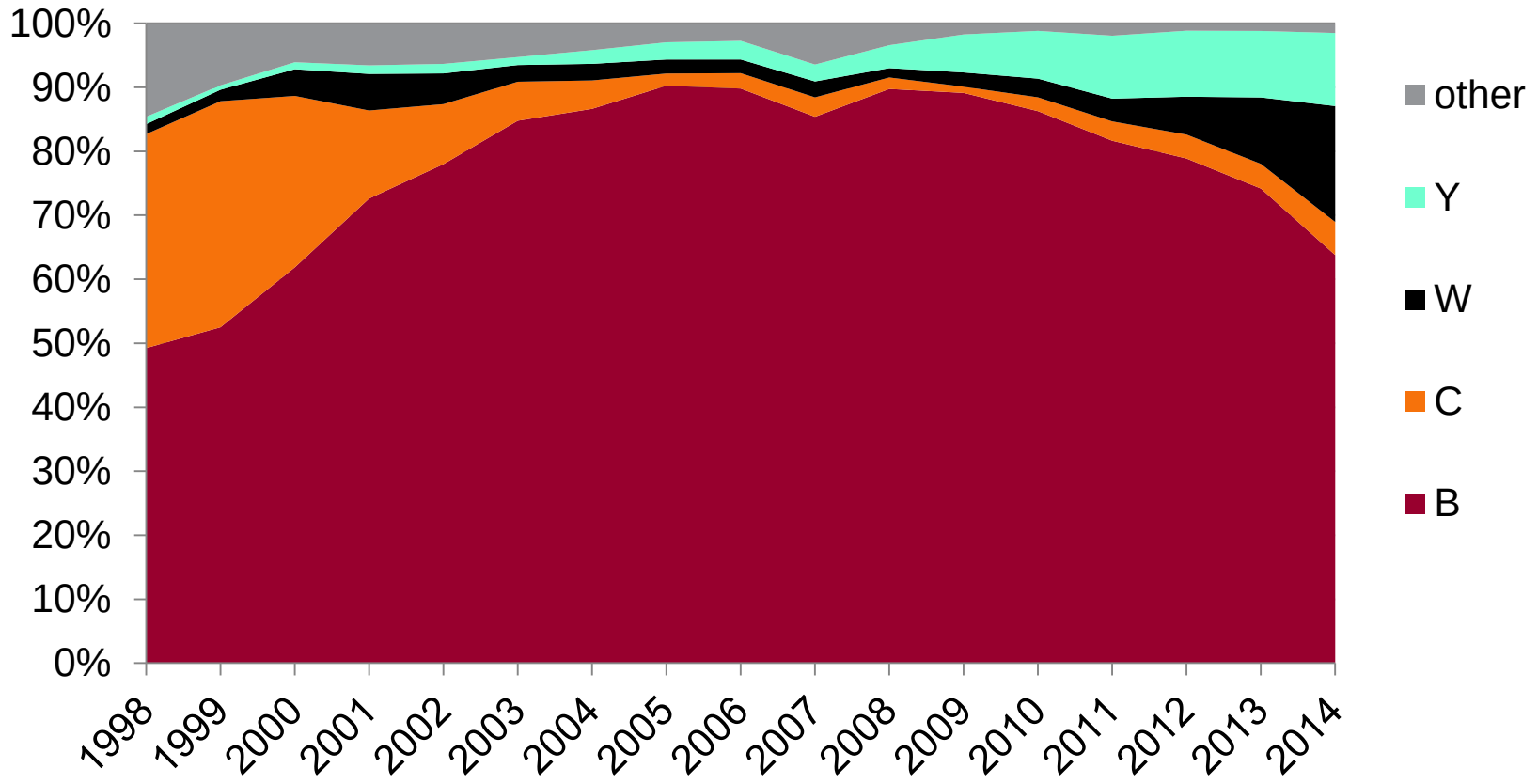
Invasive Meningococcal Disease

England & Wales, 2008-14



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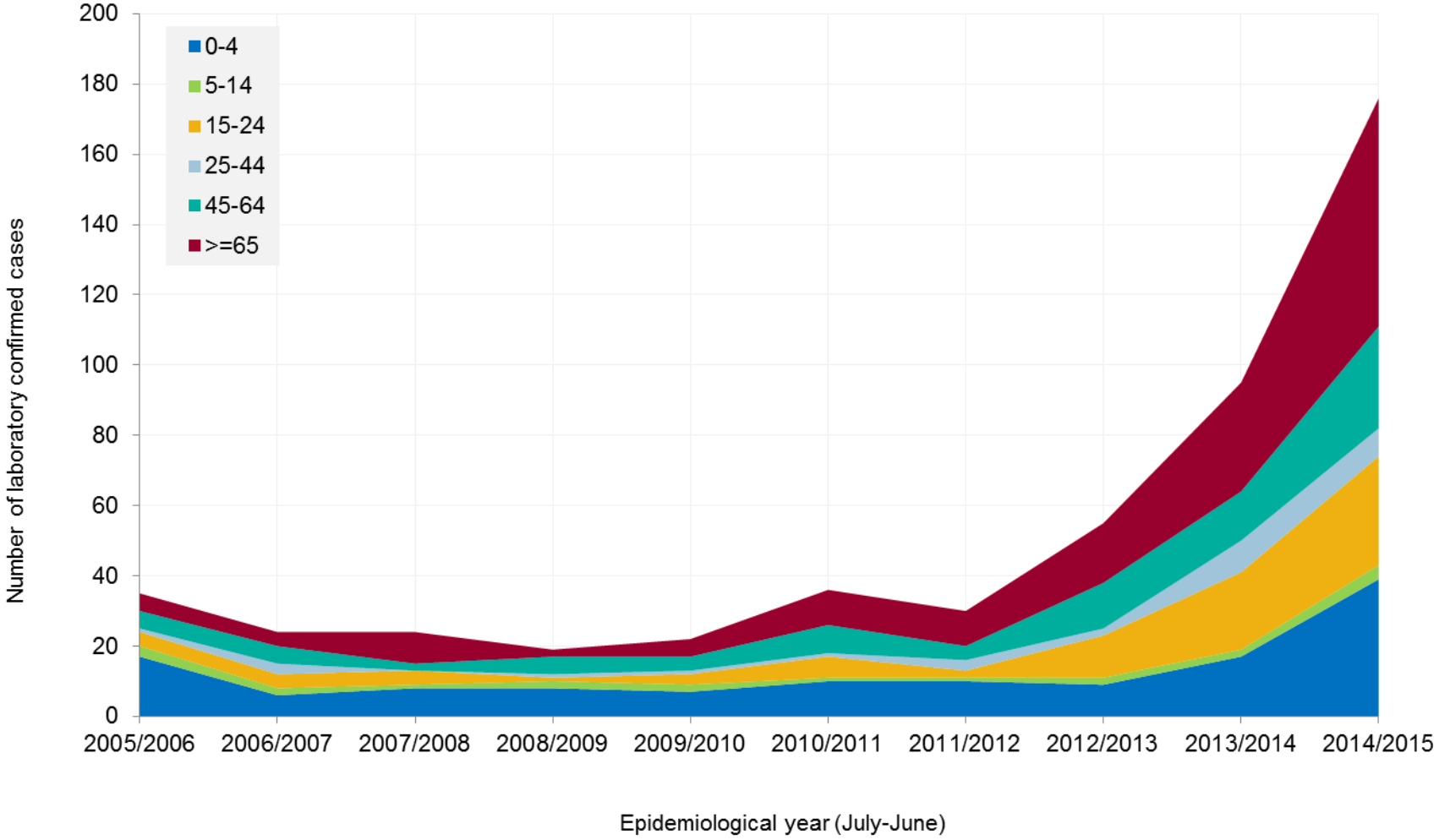
MenW cases in England, 2005/06-2014/15



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MenW Clinical Presentation

RAPID COMMUNICATIONS

Presentation with gastrointestinal symptoms and high case fatality associated with group W meningococcal disease (MenW) in teenagers, England, July 2015 to January 2016

H Campbell [1], SR Parikh [1], R Borrow [2], E Kaczmarski [2], ME Ramsay [1], SN Ladhani [1,3]

1. Immunisation Department, Public Health England, London United Kingdom
2. Meningococcal Reference Unit, Public Health England, Manchester United Kingdom
3. St. George's University of London, United Kingdom

Correspondence: Sydel R. Parikh (sydel.parikh@phe.gov.uk)

Citation style for this article:
Campbell H, Parikh SR, Borrow R, Kaczmarski E, Ramsay ME, Ladhani SN. Presentation with gastrointestinal symptoms and high case fatality associated with group W meningococcal disease (MenW) in teenagers, England, July 2015 to January 2016. Euro Surveill. 2016;21(12):pii=30175. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2016.21.12.30175

Article submitted on 04 March 2016 / accepted on 24 March 2016 / published on 24 March 2016

Caracterización clínica de los casos de enfermedad meningocóccica por serogrupo W135 confirmados durante el año 2012 en Chile

Gabriela Moreno, Darío López, Natalia Vergara, Doris Gallegos, María F. Advis y Sergio Loayza

Clinical characterization of cases with meningococcal disease by W135 group in Chile, 2012

Background: During 2012 in Chile, there were 60 cases of serogroup W135 meningococcal disease, which accounts for 57.7% of identified serogroup cases. *Aim:* To describe main clinical features of patients with serogroup W135 meningococcal disease confirmed in 2012. *Material and Methods:* Descriptive study of case series based on retrospective review of medical records. *Results:* Male patients represented 61.7% and 46.7% were children under 5 years. At first clinical attention, 3.4% of patients were suspected of meningococcal disease, while 83.3% had meningococcemia as final diagnosis. Also at first attention, the most common symptoms or clinical signs were fever ≥ 38.0° C (60.3%), cold symptoms (52.5%), and nausea or vomiting (46.7%). Meningeal signs had a low frequency (8.7%). Diarrhea was the second most common symptom found among deceased patients (55.6%) and statistically higher than survivors (26.8%; p = 0.034). Six cases reported with sequelae: limb amputation, hearing loss or neurological damage, and mortality was 31.7%. *Discussion:* In 2012, serogroup W135 meningococcal disease reported high mortality, atypical clinical presentation, low initial meningococcal disease diagnosis, and a high number of cases with poor clinical course.

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Strategies to control the MenW outbreak

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Timelines for MenACWY programme

- Regular monitoring of MenW cumulative curve
- Reporting to the JCVI every 6 months
- **Oct 2014**: Concerns about doubling number of cases reported to the JCVI

  → Plan made to consider replacing teenage MenC at 13/14 years with MenACWY at next national tender
- **Feb 2015**: JCVI informed of accelerating number of cases

  →Modelling to estimate 2x & 4x increase in cases

  →Model using MenC trajectory from the late 1990's

  →A programme to vaccinate all14-18 years of age (school years 10-13) with MenACWY should be undertaken as soon as practicable

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JCVI recommendations: February 2015

- Even though the number of cases is low, JCVI considered this situation a public health emergency
  - rapid increase in virulent MenW
  - international experience (e.g. South America)

- The MenACWY programme will have direct impact on vaccinated teenage cohorts (2nd highest incidence group)
  - Excellent protection expected after a single dose

- Importance of completing catch-up quickly: to generate herd protection across age range & slow the rate of increase
  - Important to balance supply and demand, offering the vaccine first to those at highest risk

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Strategy to control MenW

Wide age range affected

- Incidence highest in infants and adolescents
- Still high number of cases in older adults

Strategy in Chile of vaccinating children, only impacted on vaccinated age group

- Failed to control overall disease rates

Only feasible strategy is to target carriers with conjugate ACWY vaccine

- Plan to immunise adolescents
- Vaccinating adolescent cohorts simultaneously in catch up will accelerate control: ~4x faster

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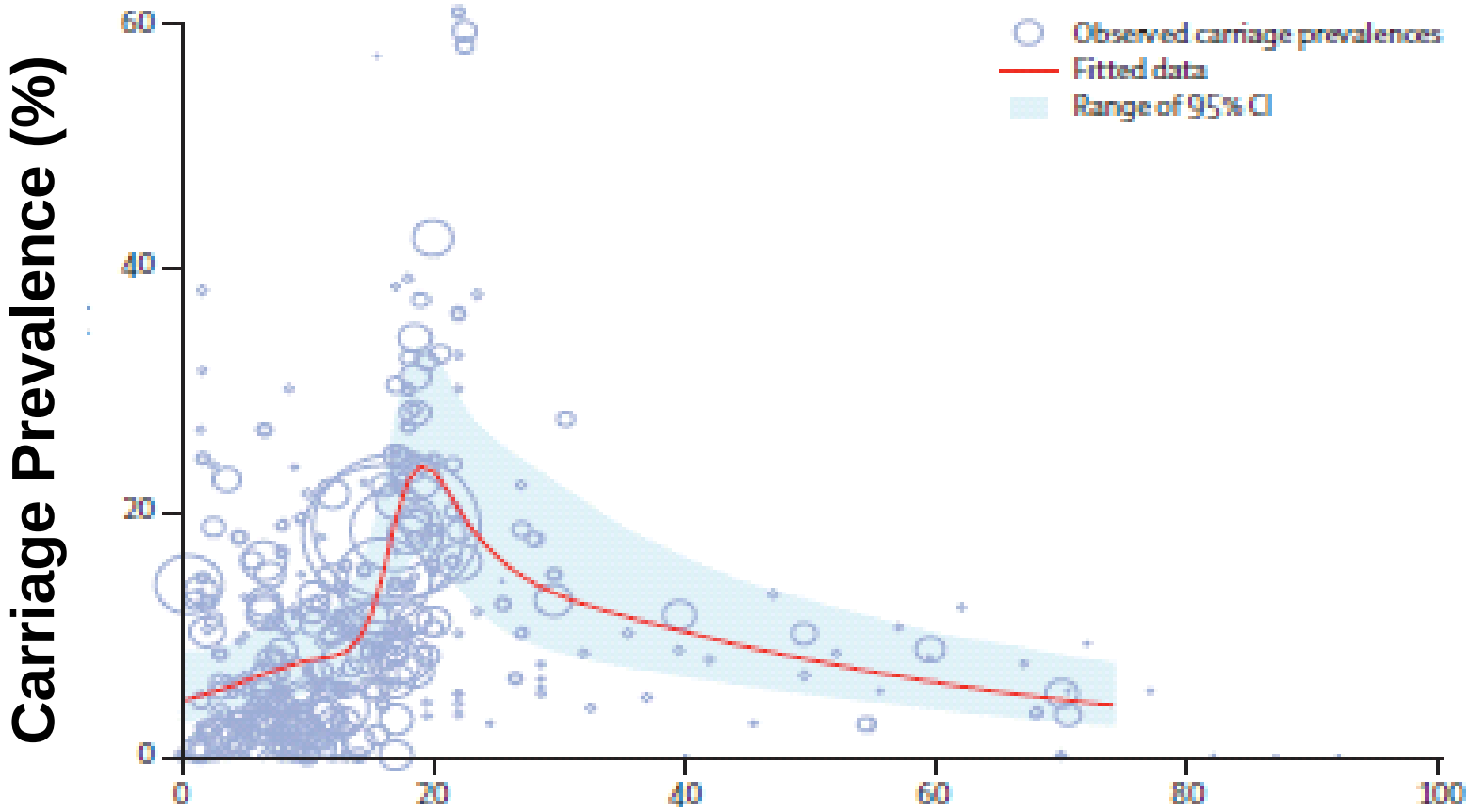
Meningococcal carriage by age: a systematic review and meta-analysis

Hannah Christensen, Margaret May, Leah Bowen, Matthew Hickman, Caroline L Trotter

Lancet Infect Dis 2010; 10: 853-61



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ACWY programme – planned roll-out

Birth cohort	2014/15 year - age	Academic year				
		2014/15	2015/16	2016/17	2017/18	2018/19
01/09/2003-31/08/2004	Y6 – 10/11				Y9 ACWY	
01/09/2002-31/08/2003	Y7 - 11/12			Y9 ACWY		
01/09/2001-31/08/2002	Y8 - 12/13		Y9 ACWY			
01/09/2000-31/08/2001	Y9 - 13/14		Y10 ACWY			
01/09/1999-31/08/2000	Y10 - 14/15	Y10 MenC		Y12 ACWY		
01/09/1998-31/08/1999	Y11 - 15/16			Y13 ACWY		
01/09/1997-31/08/1998	Y12 - 16/17		Y13 ACWY			
01/09/1996-31/08/1997	Y13 – 17/18	Y13 ACWY				

Key

- Routine schedule MenC
- Routine schedule ACWY
- School based catch-up ACWY
- Primary care catch-up cohorts
- Delivery mechanism to be decided
- Completed

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Recommended vaccines

- Menveo® is supplied in 5 dose pack (powder in a vial and solution in a vial = 10 vials per pack), no needles.

- Nimenrix® is supplied in single pack as a powder in a vial (MenACWY) and 0.5ml solvent in a pre-filled syringe. Two needles are included.

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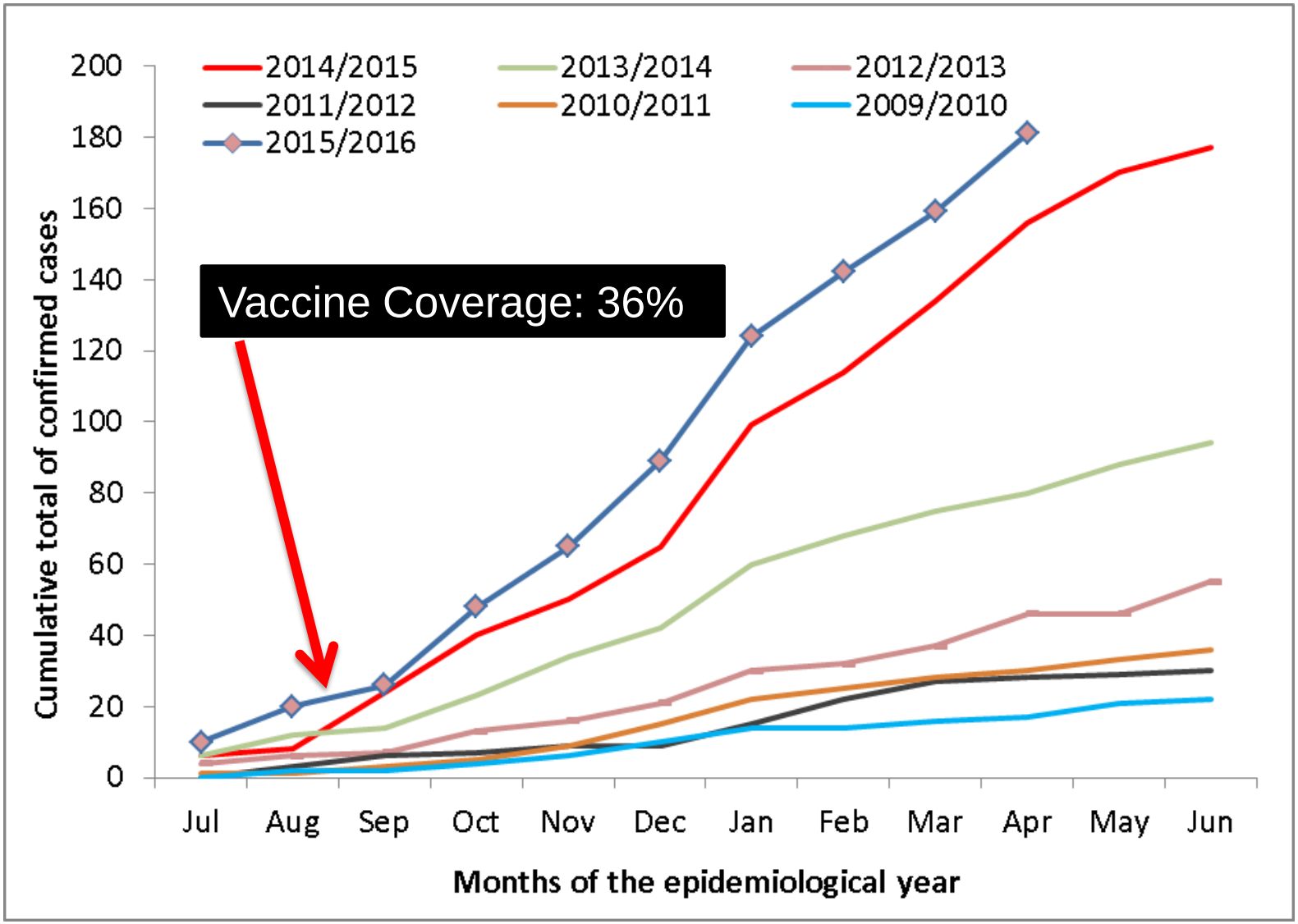
Serum bactericidal antibody killing of UK W cc11 strains by serum from infants immunised with Bexsero®

Lab number	Site	Type	Pre-	Pool1	Pool2	Pool3	Pool4 Post 4th
							>128
							64
							>64
							128
M11-240798	Blood	W:NT:P1.5,2 cc11	<2	>64	>64	>64	>64
M12-240754	Blood	W:NTP1.5,2 cc11	<2	64	64	>64	>64

This work suggests that children immunised with Bexsero may have some protection against the emerging strain of MenW

Public Health England

Confirmed MenW cases in England



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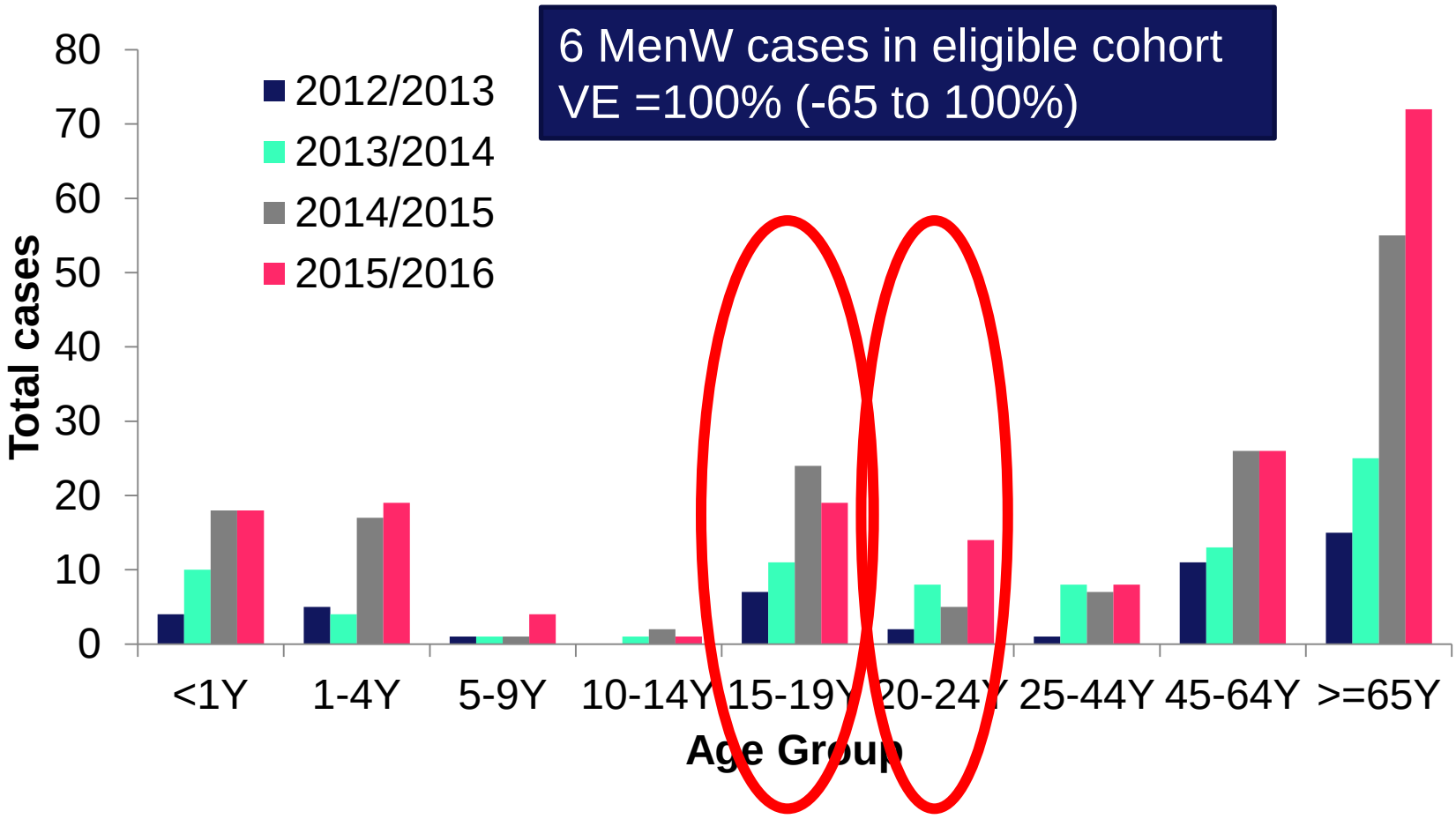
Confirmed MenW cases
by epidemiological year, England



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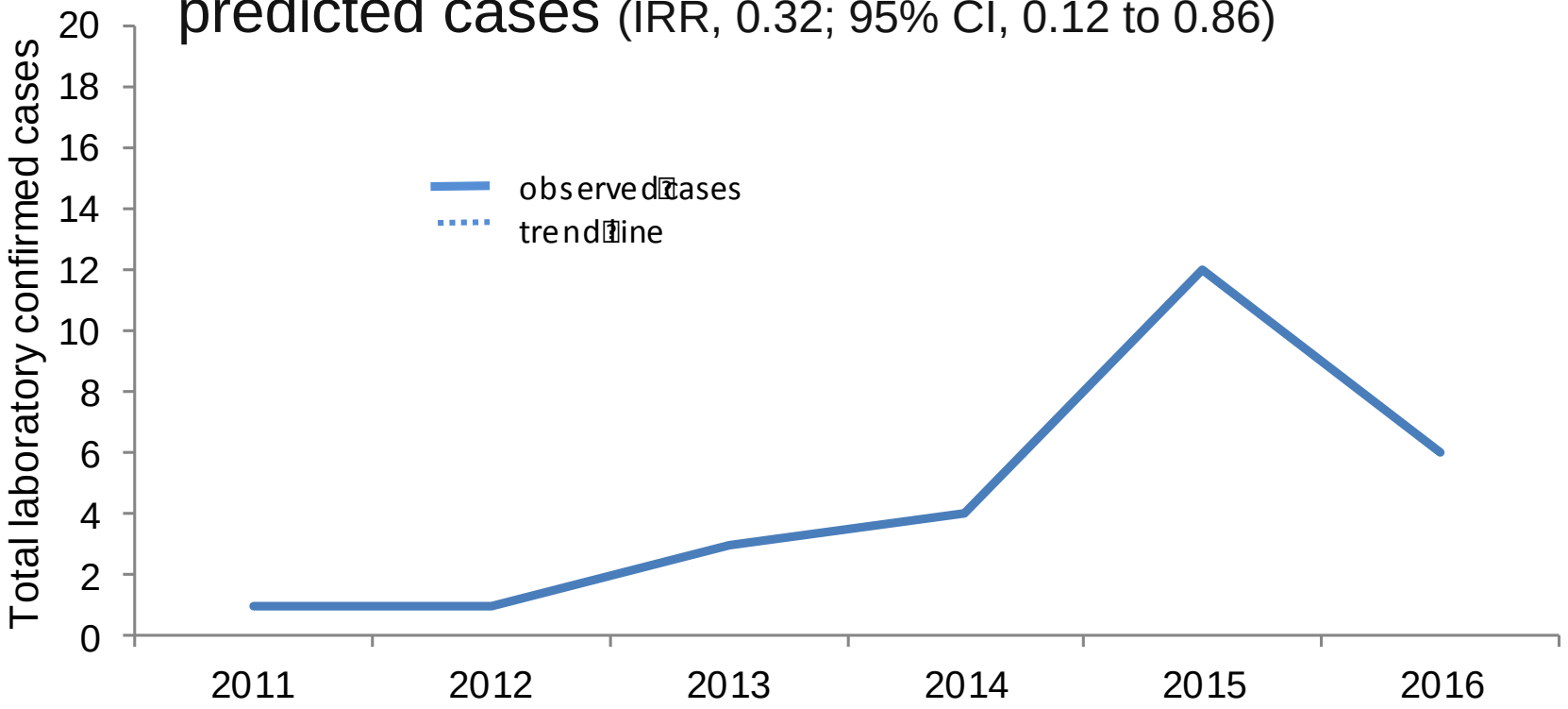
Preliminary Impact Data

Trend Analysis: 68% reduction compared to predicted cases (IRR, 0.32; 95% CI, 0.12 to 0.86)



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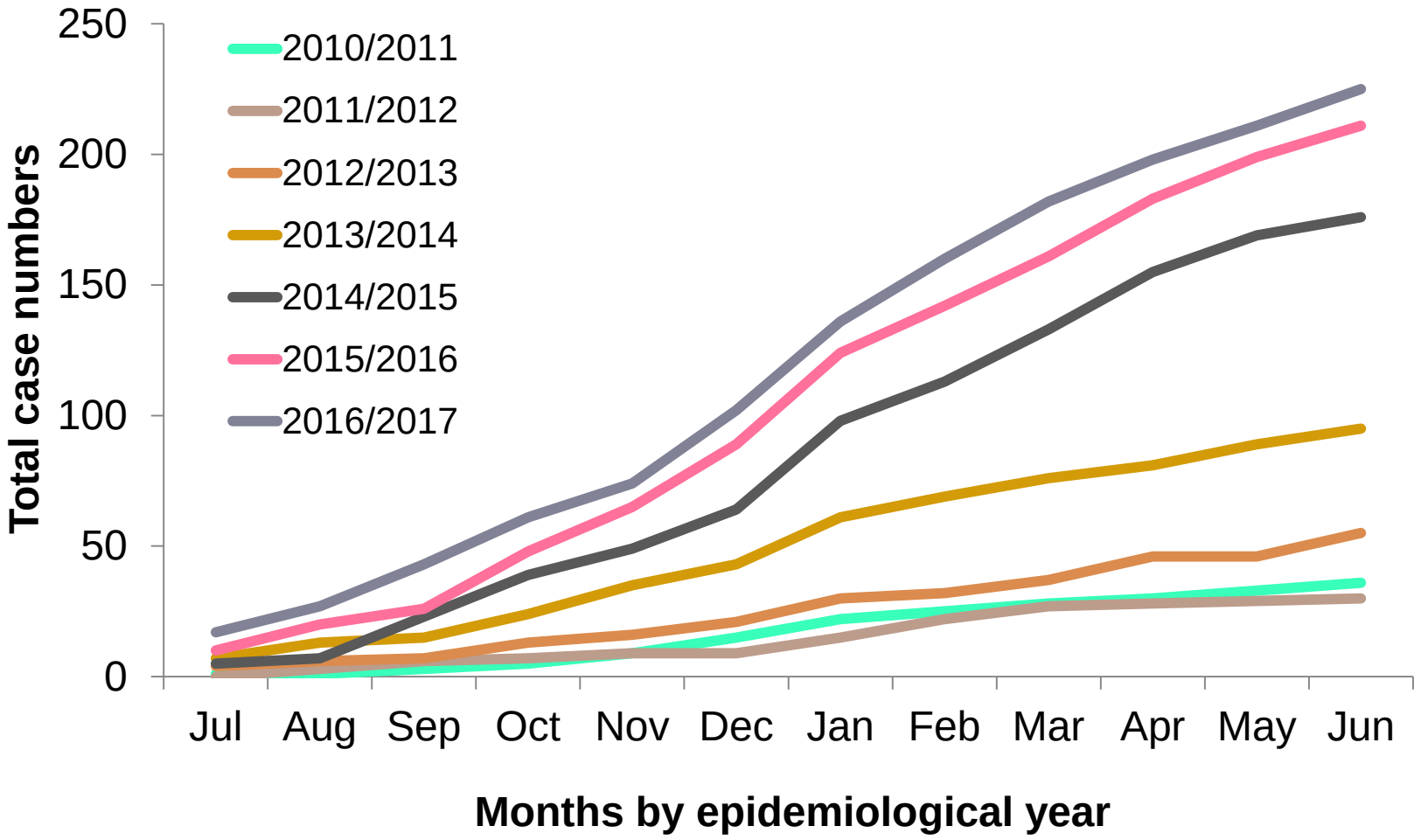
Cumulative curve: Men W cases, England



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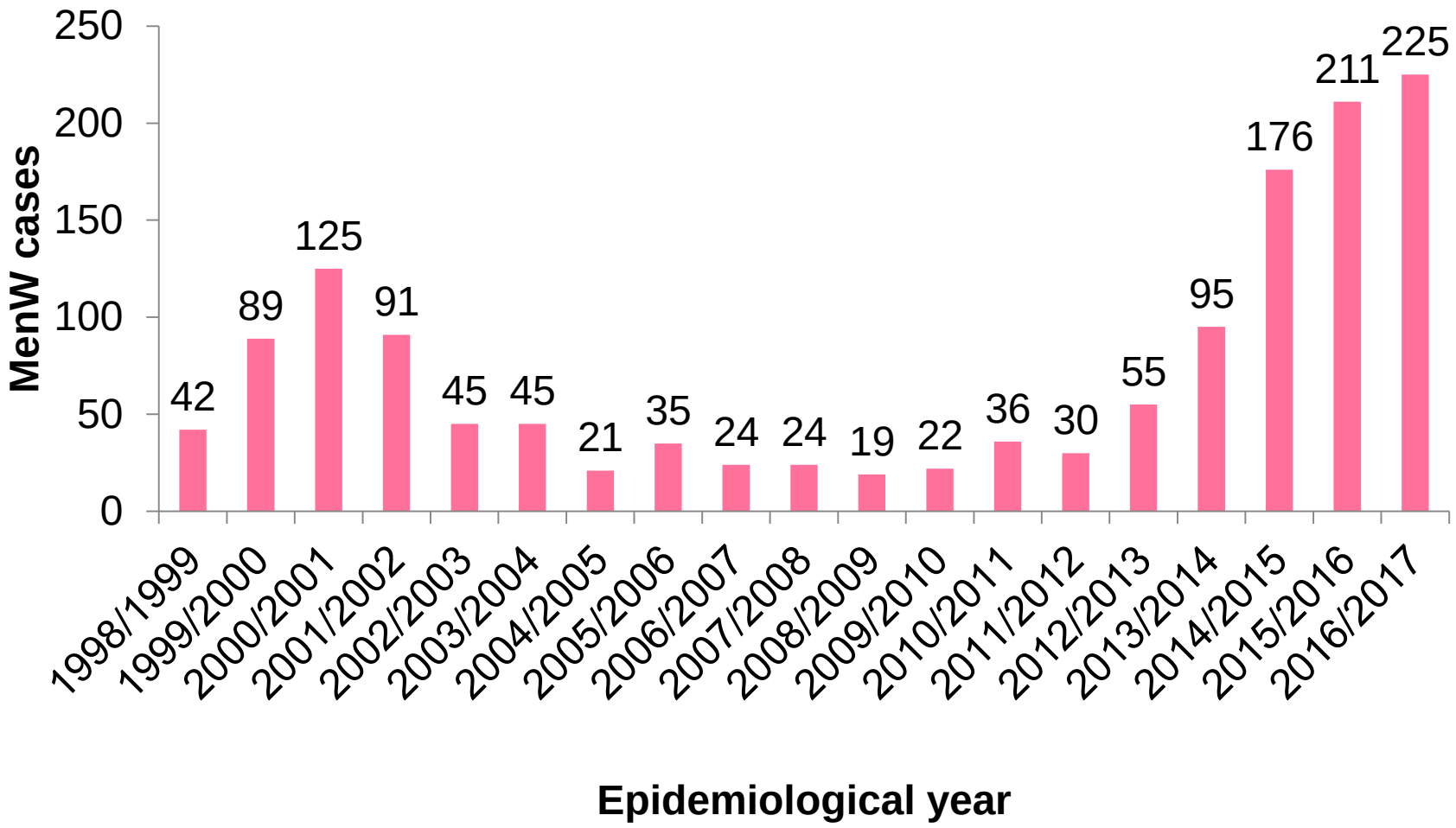
MenW IMD by epidemiological year



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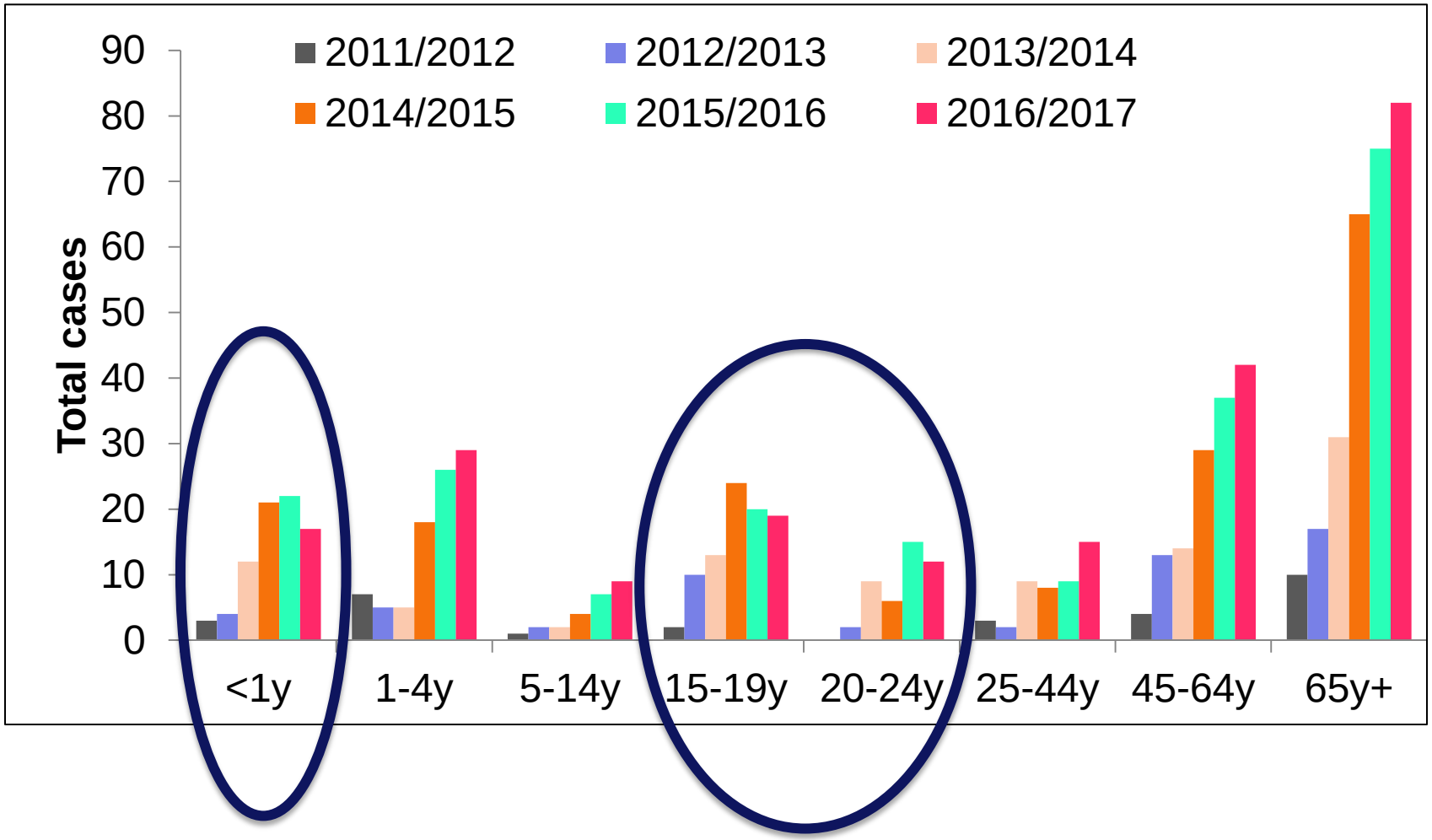
Current Trends (up to 2016/17)



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SUMMARY

1. The UK has been experiencing an national MenW outbreak since 2009.
2. Cases increases initially in older adults → all age groups, including teenagers, toddlers and infant
3. MenACWY vaccine programme started August 2015: plan to vaccinate all 13-18 year-olds over 24 months + university entrants
4. Impact in school leavers (17-18 year-olds) seen within 12 months, despite 36% vaccine coverage
5. Herd protection likely to take several years – 4 x faster because of catch-up programme for 13-18 year-olds

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Resources for health professionals and patients

- PHE MenB Health Care Worker Q+A
- PHE MenB vaccine leaflet (long version)
- PHE MenB vaccine leaflet: 3 minute guide
- PHE MenACWY vaccination programme patient information leaflet and posters
- PHE MenACWY Health Care Worker Q+A
- PHE Paracetamol Patient Information Leaflet
- Training the trainer slide sets and animated voice over
- OVG video on parent consultation

- Meningitis Research Foundation: http://www.meningitis.org/
- Meningitis Now. https://www.meningitisnow.org/
- NHS Choices. http://www.nhs.uk/conditions/Meningitis/Pages/Introduction.aspx

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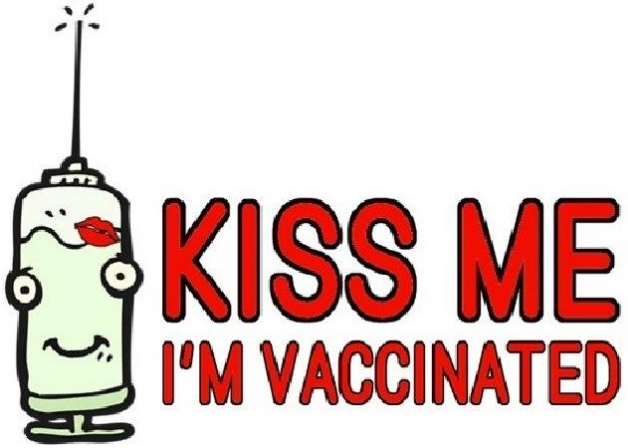


Thank you