Public Health England

Why is surveillance important after introducing vaccines?

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Objectives

- Impact of mass vaccination programmes?
- How are vaccine programmes monitored?
- Case studies

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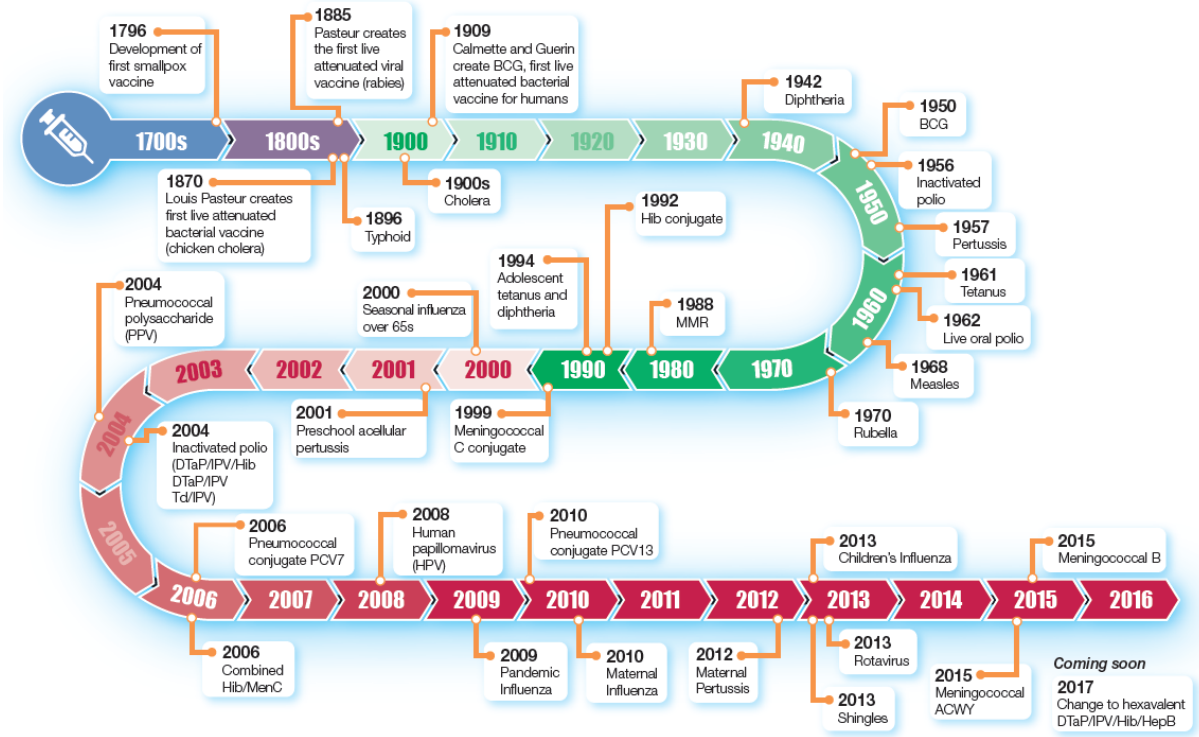
UK Vaccine schedule



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Impact of mass vaccination programmes

- Vaccinate high proportion of population
  - Individual immunity (direct protection) to most of those vaccinated
  - Reduce the risk of infection (including carriage) and disease in those vaccinated

- Also reduce the risk of transmission from those who are vaccinated to
  - Other unvaccinated AND vaccinated individuals
  - indirect protection or herd immunity

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Benefits of first 10 years of measles vaccine in the USA

Cases averted	23,707,000
Lives saved	2,400
Additional normal life years	709,000
School days saved	78,000,000
Physician visits	12,182,000
Hospital days	1,352,000
Net benefits	$1.3 billion

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Surveillance objectives

- Pre-implementation: should vaccine be introduced?
  - Is the disease a public health problem? Assessment of burden (Incidence, mortality…)
  - Is there a safe and effective vaccine? (clinical trials)
- Post implementation: is the vaccine working as intended?
  - Monitor effectiveness, impact
  - Monitor adverse events
- Nearing elimination
  - Identify pockets of susceptibles

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Surveillance of vaccine programmes

- Disease incidence
  - +/- surveillance of infection (e.g. Carriage)
- Vaccine coverage
- Surveillance of immunity
  - Serological surveillance
- Adverse events

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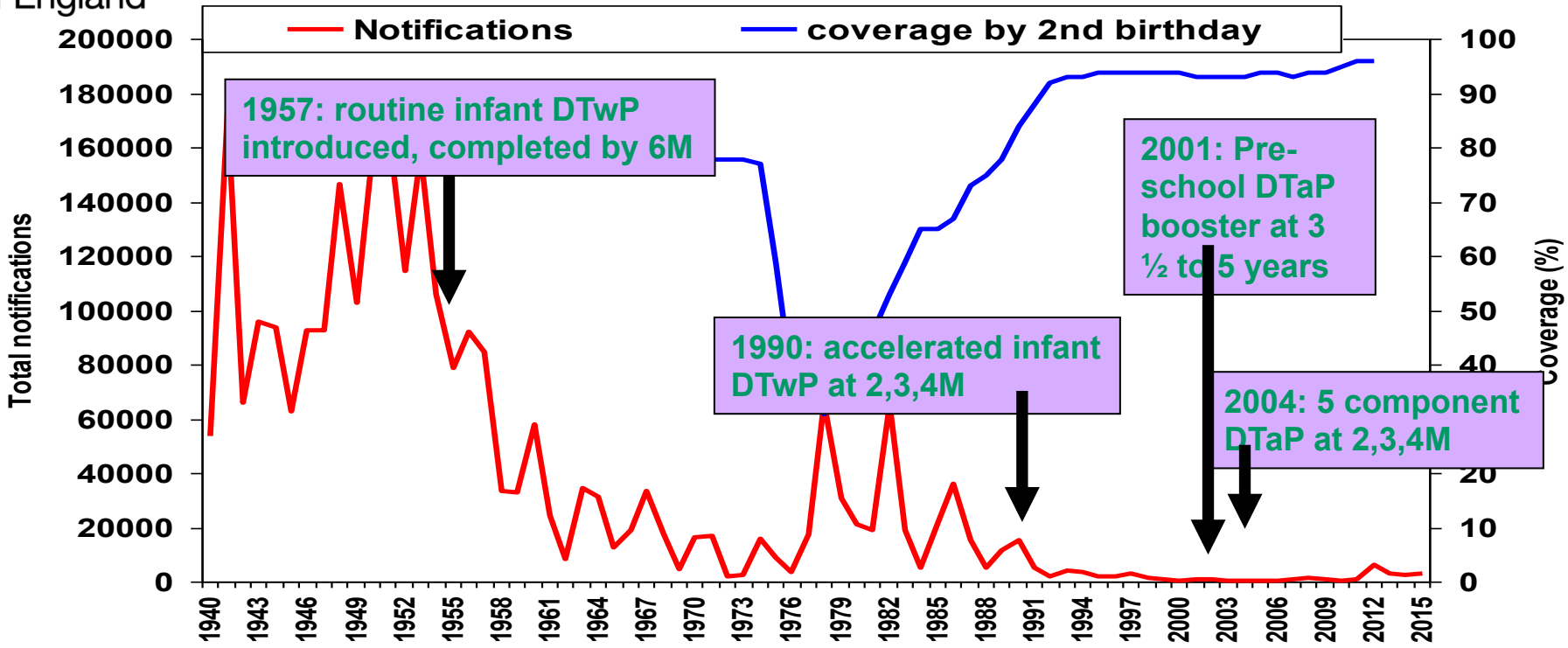
Disease incidence: pertussis



Pertussis notifications & vaccine coverage 1940-2015 (England &Wales)

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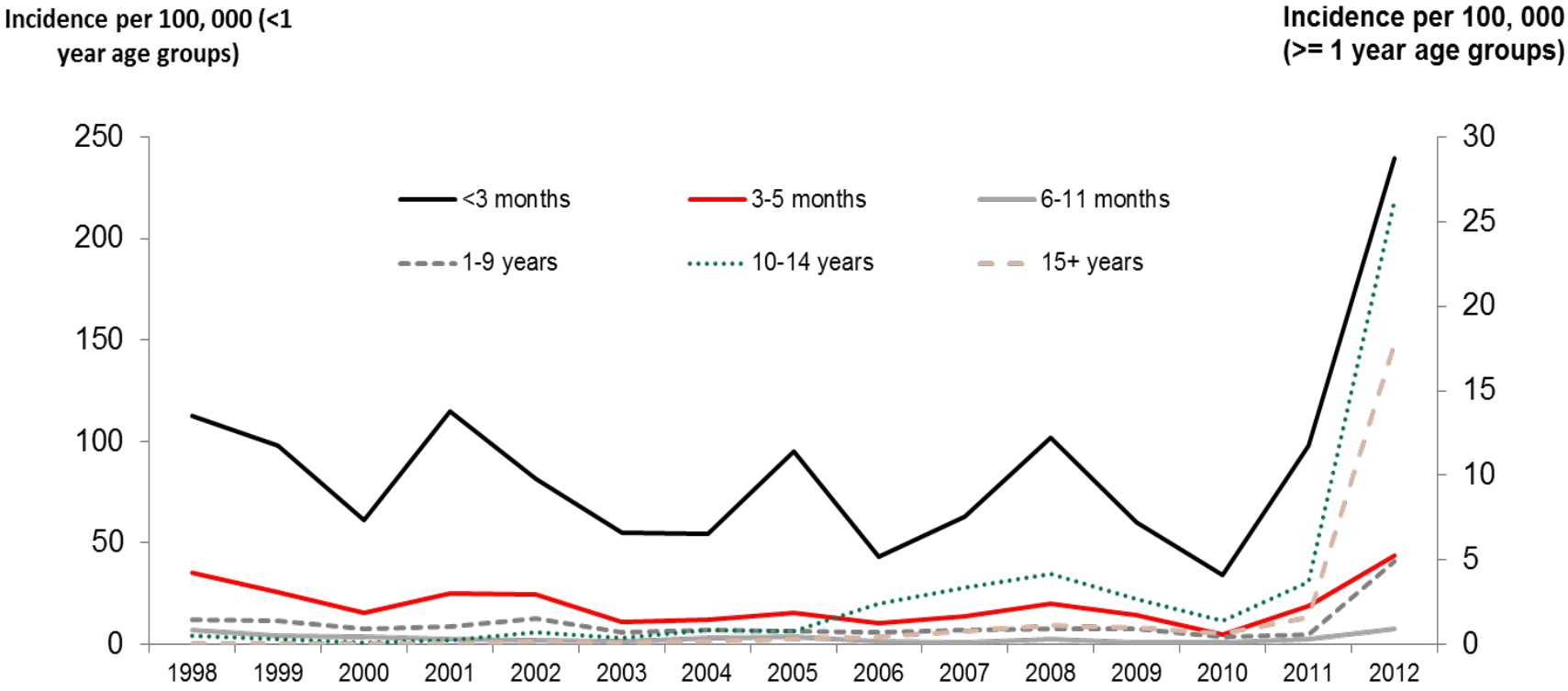
Annual age specific pertussis incidence, England, 1998-2012



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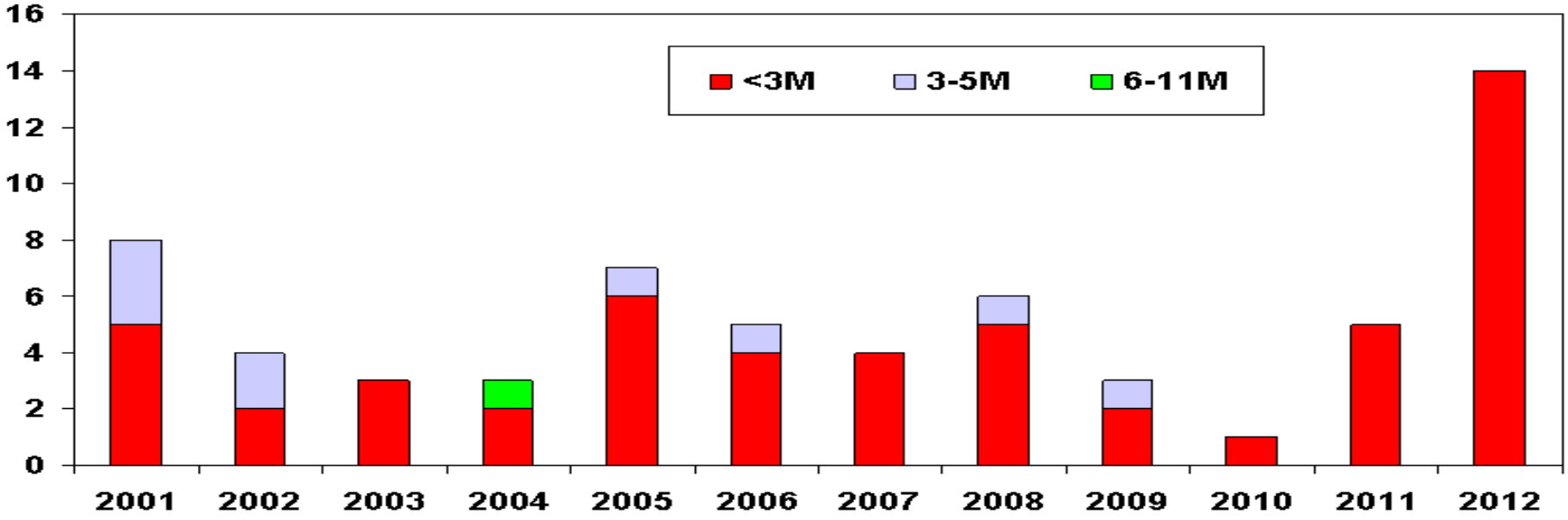
Annual pertussis deaths in infants, England, 1998-2012



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Pertussis Immunisation in pregnancy

- Department of Health recommendation based on JCVI advice: From 1st Oct 2012
- Offer a single dose of vaccine ideally between 28-32 weeks in every pregnancy
  - From 16 weeks since 2016
- Passive immunity until child eligible for primary vaccination

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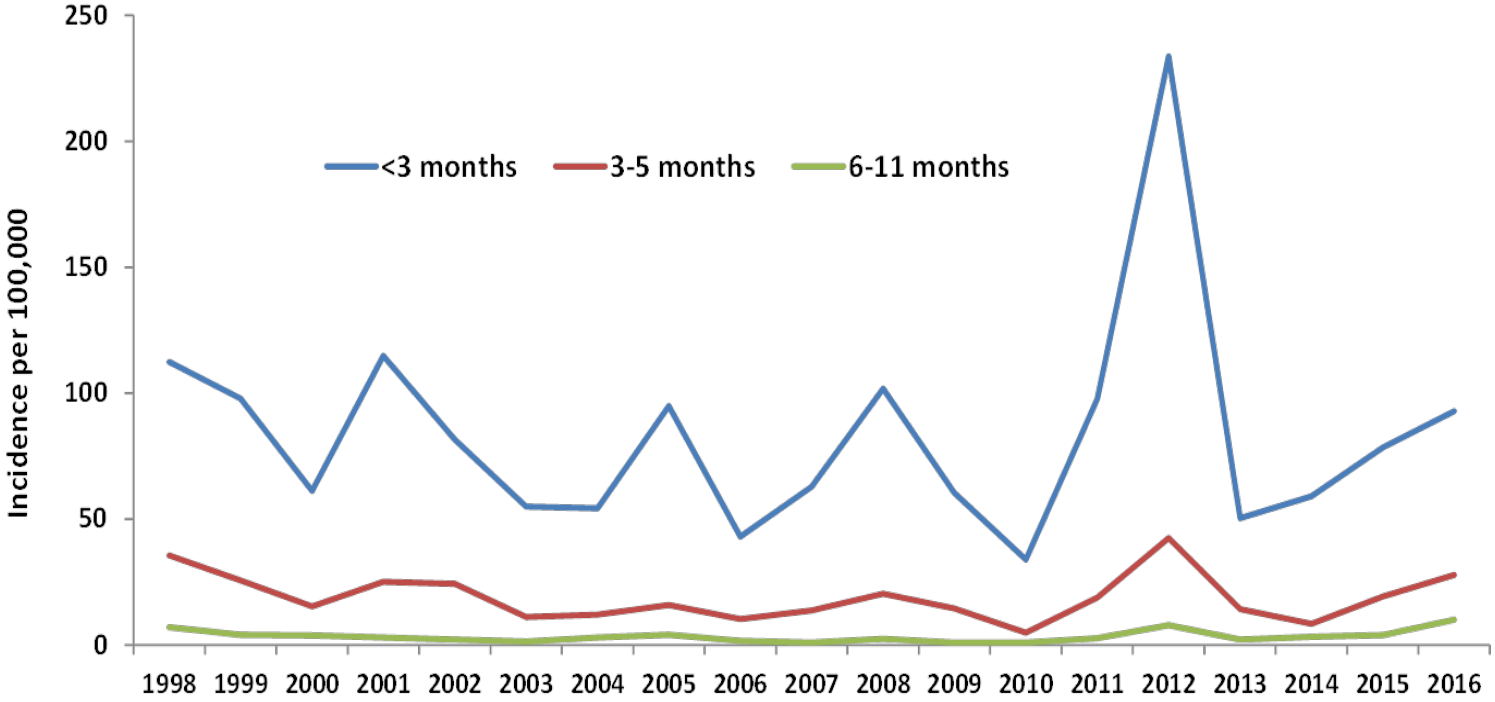
Annual pertussis incidence, England, 1998-2016



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Serotype surveillance: pneumococcal disease

- Over 90 known serotypes of *Streptococcus pneumoniae*
- Around 30-50 serotypes cause IPD in humans
- 2 conjugated vaccines used in children in the UK:
  - The 7-valent conjugate vaccine (Prevnar™)
  - PCV13: 6 additional serotypes

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Serotype surveillance: pneumococcal disease

- Mass vaccination with effective vaccine
  - High level of population immunity
  - Increase pressure on organism to change
  - Eradication of one type leaving an ecological niche for other organisms

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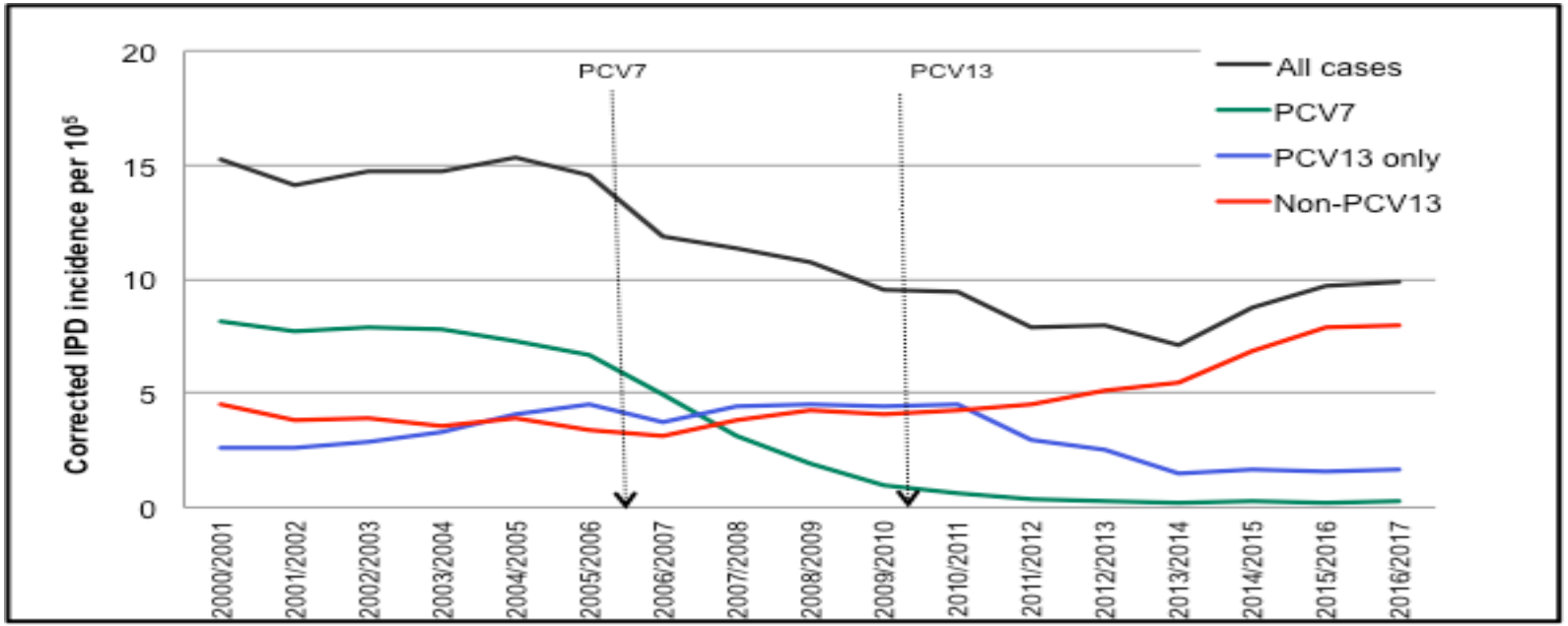
Adjusted annual IPD incidence, 2000-2017



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IPD serotypes in 2016/17

	<5 years	5-64 years	65+ years	All ages
8	33 (10.0%)	621 (27.2%)	463 (15.7%)	1120 (20.1%)
12F	47 (14.2%)	408 (17.9%)	275 (9.3%)	730 (13.1%)
3	23 (6.9%)	159 (7.0%)	340 (11.5%)	525 (9.4%)
9N	9 (2.7%)	159 (7.0%)	207 (7.0%)	375 (6.7%)
22F	17 (5.1%)	141 (6.2%)	216 (7.3%)	375 (6.7%)
19A	13 (3.9%)	119 (5.2%)	178 (6.0%)	310 (5.6%)
15A	18 (5.4%)	63 (2.8%)	152 (5.2%)	234 (4.2%)
33F	17 (5.1%)	57 (2.5%)	106 (3.6%)	180 (3.2%)
10A	27 (8.2%)	58 (2.5%)	90 (3.1%)	176 (3.2%)
23B	21 (6.3%)	43 (1.9%)	71 (2.4%)	135 (2.4%)
23A	3 (0.9%)	30 (1.3%)	89 (3.0%)	122 (2.2%)
11A	5 (1.5%)	36 (1.6%)	71 (2.4%)	112 (2.0%)
15B/C	26 (7.9%)	28 (1.2%)	45 (1.5%)	99 (1.8%)
16F	2 (0.6%)	32 (1.4%)	57 (1.9%)	91 (1.6%)
24F	11 (3.3%)	24 (1.1%)	55 (1.9%)	91 (1.6%)
7F	4 (1.2%)	45 (2.0%)	40 (1.4%)	89 (1.6%)
35B	9 (2.7%)	19 (0.8%)	59 (2.0%)	87 (1.6%)
Other	46 (13.9%)	241 (10.6%)	433 (14.7%)	720 (12.9%)
Total	331	2,283	2,947	5,571

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Coverage: MMR

- MMR Coverage late 1990s >90%

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Coverage: MMR

- MMR Coverage late 1990s >90%

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Coverage: MMR

EARLY REPORT

Early report

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

Summary

Background We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods 12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

Findings Onset of behavioural symptoms was associated by the parents, with measles, mumps, and rubella vaccination in eight of the 12 children, with measles infection in one child, and otitis media in another. All 12 children had intestinal abnormalities ranging from lymphoid nodular hyperplasia to aphthoid ulceration. Histology showed patchy chronic inflammation in 11 children and reactive ileal lymphoid hyperplasia in seven, but no granulomas. Behavioural disorders included autism (nine), disintegrative psychosis (one), and possible postviral or vaccinal encephalitis (two). There were no focal neurological abnormalities and MRI and EEG tests were normal. Abnormal laboratory results were significantly raised urinary methylmalonic acid compared with age-matched controls ($p<0.003$), low haemoglobin in four children, and low serum IgA in four children.

Interpretation We identified associated gastrointestinal disease and developmental regression in a group of previously normal children, which was generally associated in time with possible environmental triggers.

Lancet 1998; **351**: 637–41
See Commentary page

Inflammatory Bowel Disease Study Group, University Departments of Medicine and Histopathology (A J Wakefield FRCS, A Anthony MB, J Linnell FRCS, A P Dhillon MRCPath, S E Davies MRCPath) **and the University Departments of Paediatric Gastroenterology** (S H Murch MB, D M Casson MRCP, M Malik MRCP, M A Thomson FRCP, J A Walker-Smith FRCP), **Child and Adolescent Psychiatry** (M Berelowitz FRCPsych), **Neurology** (P Harvey FRCP), **and Radiology** (A Valentine FRCR), **Royal Free Hospital and School of Medicine, London NW3 2QG, UK**
Correspondence to: Dr A J Wakefield

Introduction

We saw several children who, after a period of apparent normality, lost acquired skills, including communication. They all had gastrointestinal symptoms, including abdominal pain, diarrhoea, and vomiting and, in some cases, food intolerance. We describe the clinical findings, and gastrointestinal features of these children.

Patients and methods

12 children, consecutively referred to the department of paediatric gastroenterology with a history of a pervasive developmental disorder with loss of acquired skills and intestinal symptoms, mainly abdominal pain, bloating and food intolerance, were investigated. All children were admitted to the ward for a week, accompanied by their parents.

Clinical investigations

We took histories including details of immunisations and exposure to infectious diseases, and assessed the children. In 11 cases the history was obtained by the senior clinician (JW-S). Neurological and psychiatric assessments were done by consultant staff (PH, MB) with 'HMS-4 criteria.' Developmental history included a review of prospective developmental records from parents, health visitors, and general practitioners. Four children did not undergo psychiatric assessment in hospital; all had been assessed professionally elsewhere, so these assessments were used as the basis for their behavioural diagnosis.

After bowel preparation, ileocolonoscopy was performed by SHM or MAT under sedation with midazolam and pethidine. Paired frozen and formalin-fixed mucosal biopsy samples were taken from the terminal ileum; ascending, transverse, descending, and sigmoid colons, and from the rectum. The procedure was recorded by video or still images, and were compared with images of the previous seven consecutive paediatric colonoscopies (four normal colonoscopies and three on children with ulcerative colitis), in which the physician reported normal appearances in the terminal ileum. Barium follow-through radiography was possible in some cases.

Also under sedation, cerebral magnetic-resonance imaging (MRI), electroencephalography (EEG) including visual, brain stem auditory, and sensory evoked potentials (where compliance made these possible), and lumbar puncture were done.

Laboratory investigations

Thyroid function, serum long-chain fatty acids, and cerebrospinal-fluid lactate were measured to exclude known causes of childhood neurodegenerative disease. Urinary methylmalonic acid was measured in random urine samples from eight of the 12 children and 14 age-matched and sex-matched normal controls, by a modification of a technique described previously.[3] Chromatograms were scanned digitally on computer, to analyse the methylmalonic-acid zones from cases and controls. Urinary methylmalonic-acid concentrations in patients and controls were compared by a two-sample t test. Urinary creatinine was estimated by routine spectrophotometric assay.

Children were screened for antiendomysial antibodies and boys were screened for fragile-X if this had not been done

RETRACTED

Andrew Wakefield struck off register by General Medical Council

MMR-autism controversy doctor portrays himself as a victim of British establishment pragmatism

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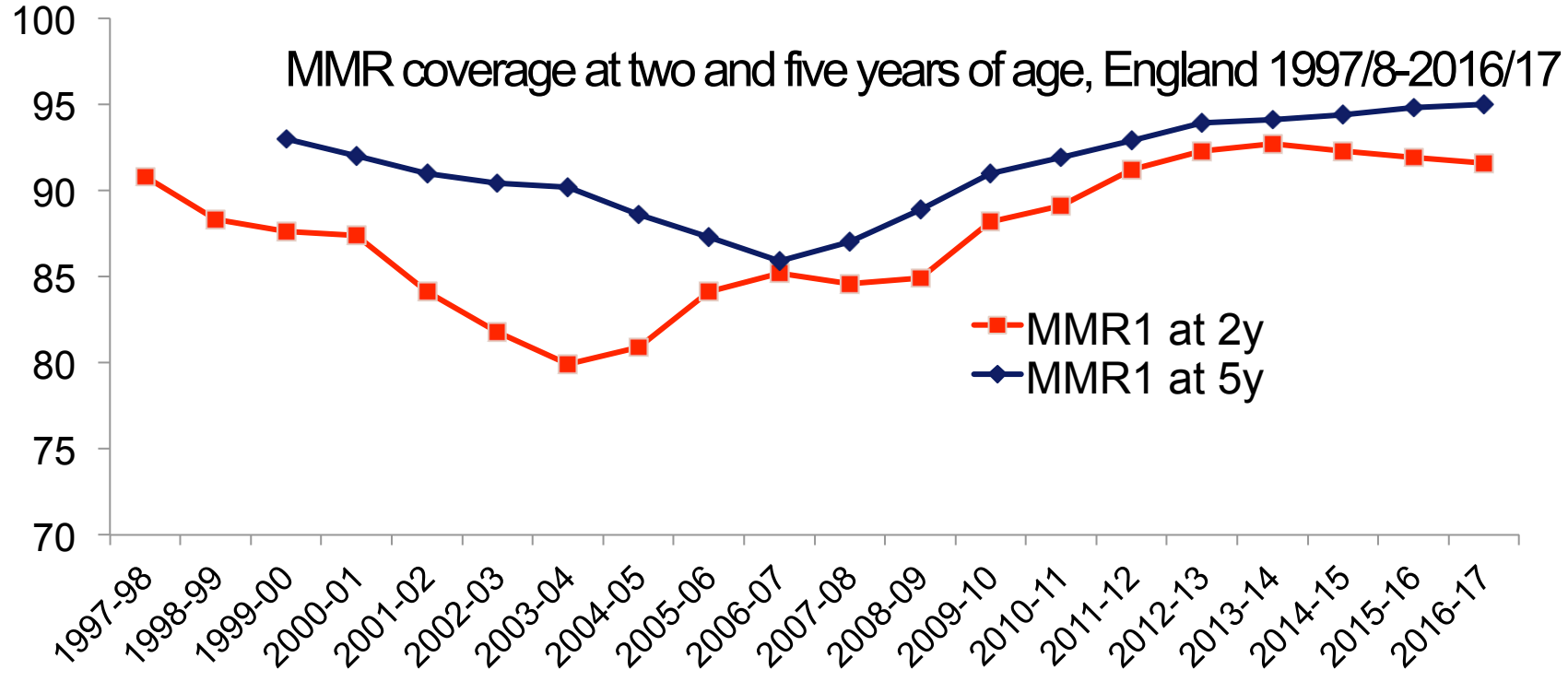
Coverage: MMR



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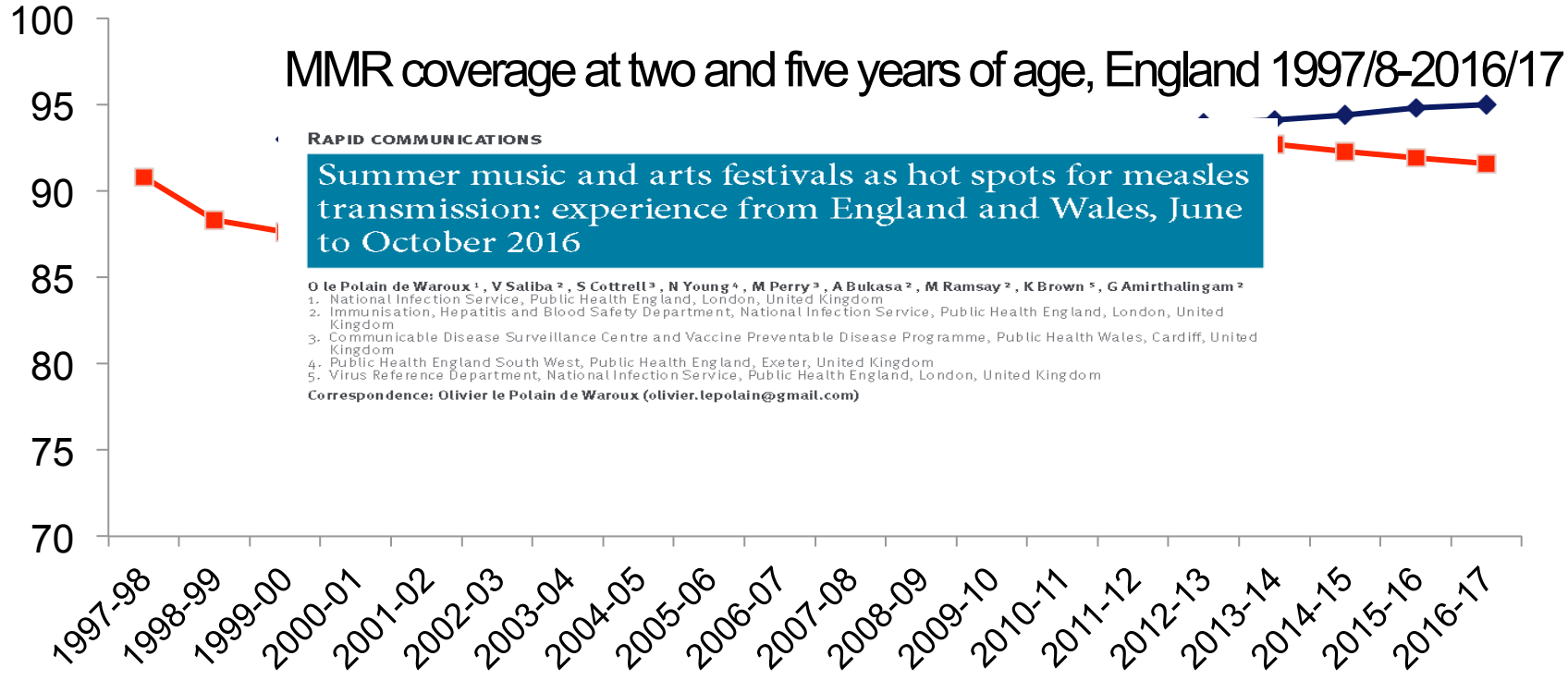
Coverage: MMR



MMR coverage at two and five years of age, England 1997/8-2016/17

RAPID COMMUNICATIONS

Summer music and arts festivals as hot spots for measles transmission: experience from England and Wales, June to October 2016

O le Polain de Waroux [1], V Saliba [2], S Cottrell [3], N Young [4], M Perry [3], A Bukasa [2], M Ramsay [2], K Brown [5], G Amirthalingam [2]
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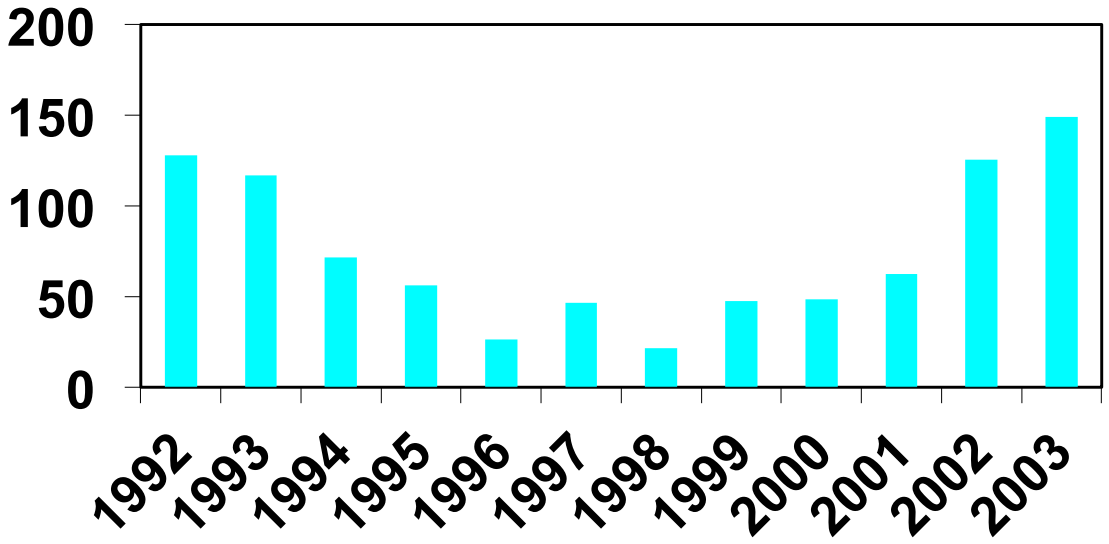
Immunity: Hib

Invasive Hib infections in adults, 1992-2003

England and Wales, PHE reconciled data, adjusted for untyped cases



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Immunity: Hib

- Reduced boosting of older children and adults
- Decline in population immunity
- Waning of natural and vaccine related immunity
  - Hib antibody in adults in UK:
    - 1.29 µg/ml (95% CI 0.90, 1.64) in 1991
    - 0.70 µg/ml (0.57, 0.89) in 1994 (p=0.006)
- Booster introduced in 2006

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Adverse events: rotavirus

- Intussusception: prolapsing of part of the intestine into another
- Background rate (US): 18-43 per 100,000/year per year for unvaccinated children aged 6–35 weeks
- Rotashield pre-licensing trial (1998): 5 intussusception cases among 10,054 vaccinated infants vs 1/4,633 placebo group(0.05% vs 0.02%, p >0.45)
- 1999: Vaccine Adverse Event Reporting Systems (VAERS) reported 15 cases of intussusception among: strong relationship between RotaShield and intussusception- product withdrawn
- New product developped (Rotarix) : large scale safety trial, indicated no increased risk of intussusception compared with placebo

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Surveillance in an elimination context

- Epidemiological patterns associated with nearing elimination
  - Outbreaks concentrated in “hard to reach” groups
  - Many cases associated with importation from endemic countries
  - Mainly sporadic cases or small clusters
- Test attributes (sensitivity/specificity) become more important
  - Incidence decreases
  - Every case matters
- Molecular typing of cases important (identify clusters, importations, vaccine escape)

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Summary- role of surveillance post implementation

- Impact of mass vaccination can be dramatic (due to added impact of indirect protection)
- Vaccine schedule is dynamic
  - New vaccines, more/less doses, timing
- Surveillance of disease, coverage, immunity and safety influences vaccine policy
  - Importance of quality data