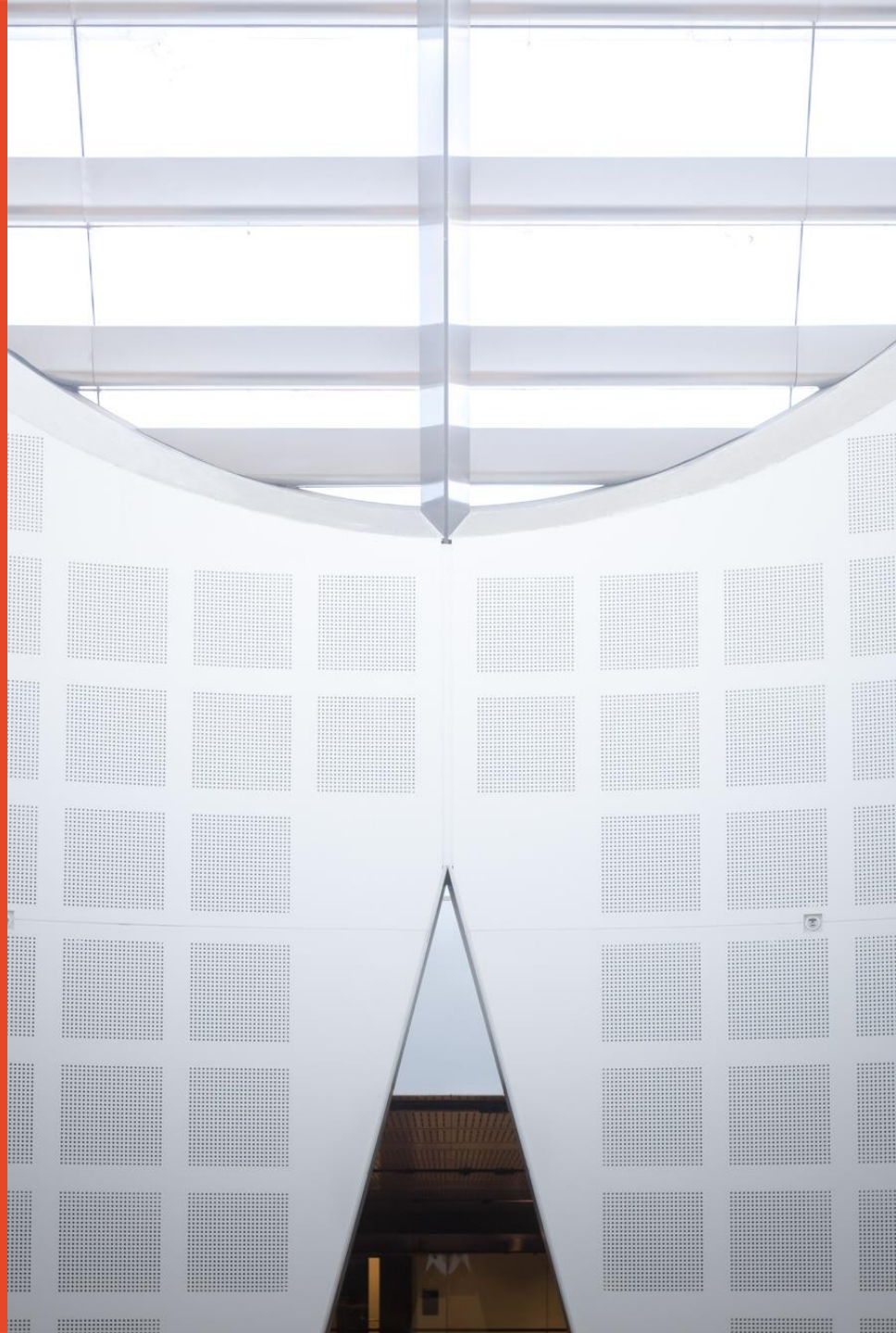
1998 Wakefield MMR Controversy

The Australian Experience

Presented by
Kerrie Wiley
Faculty of Health and Medicine
School of Public Health

THE UNIVERSITY OF SYDNEY



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

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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.

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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 611

Inflammatory Bowel Disease Study Group, University Departments of Medicine and Histopathology (A J Wakefield FRCS, A Anthony MB, J Linnell PhD, 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

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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 bloating 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 (diarrhoea, abdominal pain, bloating and food intolerance), were investigated. All children were admitted to the ward for 1 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.[1] Developmental histories 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.[2] 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 antiendomyseal antibodies and boys were screened for fragile-X if this had not been done

AUSTRALIAN STANDARD VACCINATION SCHEDULE
(November 1996)

Age	Disease	Vaccine	Milestones
2 months	Diphtheria, tetanus, pertussis Poliomyelitis Hib	DTPw* OPV-Sabin vaccine Hib vaccine (HbOC or PRP-OMP)**	
4 months	Diphtheria, tetanus, pertussis Poliomyelitis Hib	DTPw* OPV-Sabin vaccine Hib vaccine (HbOC or PRP-OMP)**	
6 months	Diphtheria, tetanus, pertussis Poliomyelitis Hib (HbOC schedule only)	DTPw* OPV-Sabin vaccine Hib vaccine (HbOC)	first 6 months
12 months	Measles, mumps, rubell Hib (PRP-OMP schedule only)	MMR Hib vaccine (PRP-OMP)	second 12 months
18 months	Diphtheria, tetanus, pertussis Hib (HbOC schedule only)	DTPa or DTPw Hib vaccine (HbOC)	third 18 months
Prior to school entry- 4-5 years	Diphtheria, tetanus, pertussis Poliomyelitis	DTPa or DTPw OPV-Sabin vaccine	
10-16 years	Measles, mumps, rubell Hepatitis B (1st dose)	MMR HBV	
1 month later	Hepatitis B (2nd dose)	HBV	
6 months after 1st dose	Hepatitis B (3rd dose)	HBV	
Prior to leaving school- 15-19 years	Diphtheria, tetanus Poliomyelitis	Td (ADT)*** OPV-Sabin vaccine	

Age	Disease	Vaccine
Every 10 years	Diphtheria, tetanus	Td (ADT)***
Post-partum for non-immune women	Rubella	Rubella vaccine or MMR
Over 50 years (Aboriginal and Torres Strait Islander people)	Pneumococcal infections Influenza	Pneumococcal vaccine (every 5 years) Influenza vaccine (annual)
Over 65 years	Pneumococcal infections Influenza	Pneumococcal vaccine (every 5 years) Influenza vaccine (annual)

* DTP is the abbreviation for Diphtheria-Tetanus-Pertussis vaccine.

** Abbreviations for Hib vaccines - HbOC is 'HibTITER'; PRP-OMP is 'PedvaxHIB'. HbOC (HibTITER) is given at 2, 4, 6, and 18 months. PRP-OMP (PedvaxHIB) is given at 2,4, and 12 months.

*** Td is combined Diphtheria-Tetanus vaccine. The DT formulation for children is often referred to by the trade name 'CDT'. The Td formulation for adults is often referred to by the trade name 'ADT'.

Hepatitis B schedule for adolescents - give the 1st dose at the same time as MMR (10-16 yrs), the 2nd dose about 1 month later, and the 3rd dose 6 months after the 1st dose.

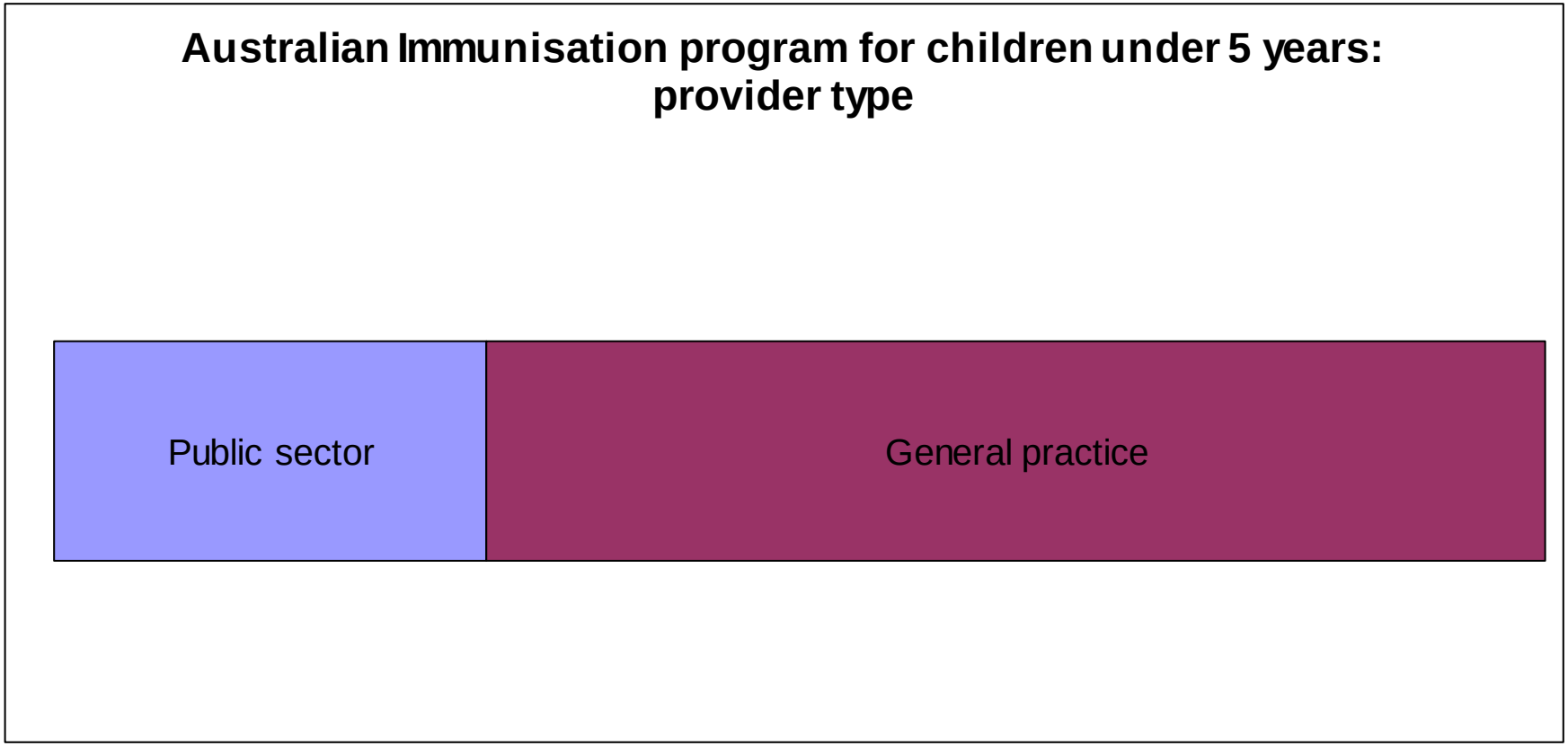
All of the vaccines in the standard schedule, except OPV, are given by intramuscular injection. MMR can also be given by deep subcutaneous injection. OPV is given orally. OPV must never be injected.

INTERIM HEPATITIS B SCHEDULE FOR INFANTS

The NHMRC has endorsed the use of hepatitis B vaccine (HBV) for all infants. HBV should be administered at birth, I month, and 6-12 months of age. Hepatitis B vaccine has not yet been included in the standard infant schedule because it is only available as an additional injection. Parents who express an interest in infant HBV should be encouraged to have their children vaccinated, as long as compliance with schedule vaccines is not jeopardised.

The NHMRC strongly recommends that HBV be offered to all infants born to HBsAg+ mothers and to all infants and young children from groups with a hepatitis B carrier rate of over 2% (see Section 3.8).

Australian National Immunisation Programme in 1998



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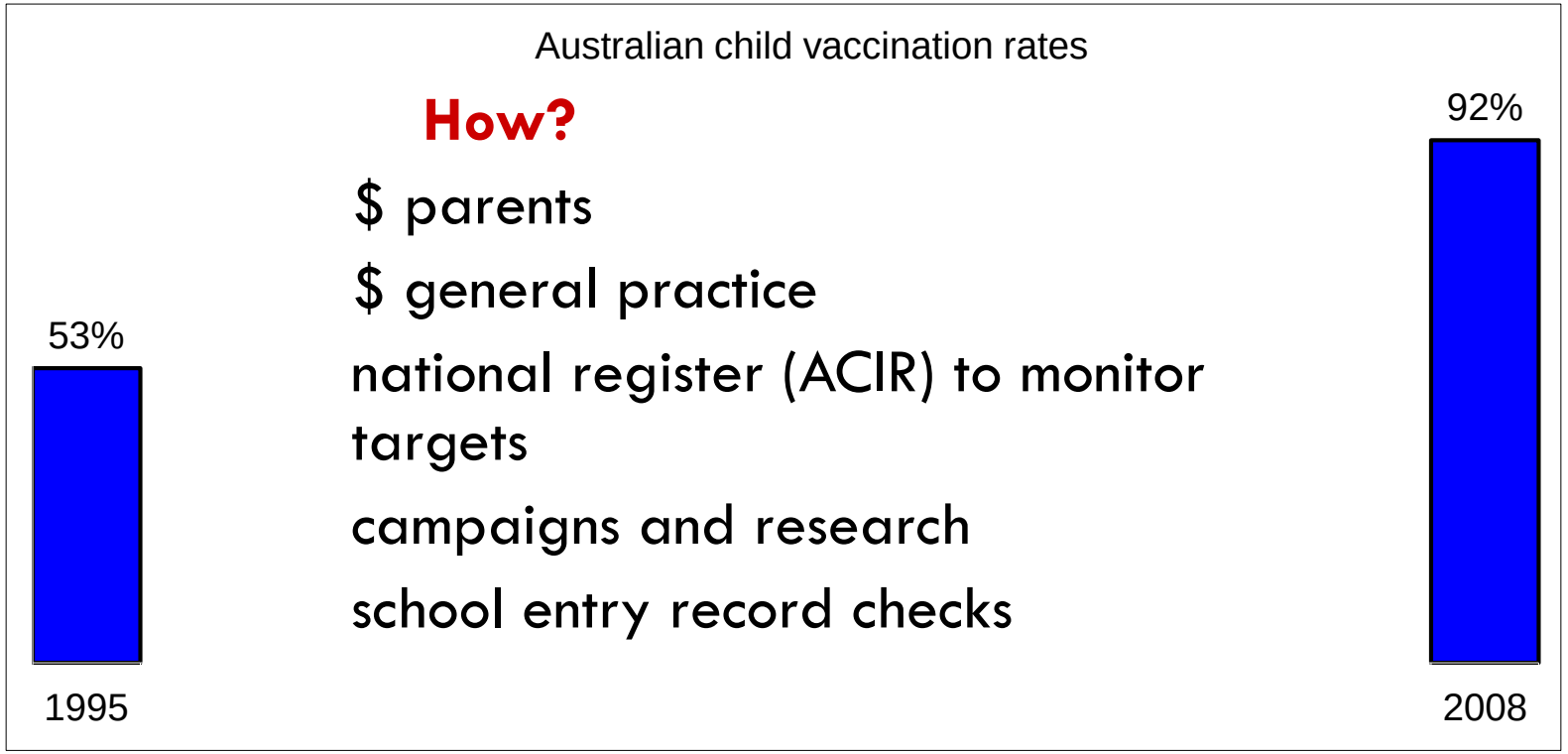

IMMUNISE AUSTRALIA PROGRAM

An Australian, State and Territory Governments initiative

What happened in the UK?

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"…I have to say that there is sufficient anxiety in my own mind of the safety, the long term safety of the polyvalent, that is the MMR vaccination in combination, that I think that it should be suspended in favour of the single vaccines…."- Andrew Wakefield, New Release Video, 1998

Feb 1998
Wakefield paper published describing new enterocolitis "syndrome" in autistic children, linked to Measles vaccine by parental recall

monovalent vaccine) is implicated in Autism

1998 onwards
Wide UK media coverage

theguardian

Scientists go public with doubts over MMR vaccine.

By Sarah Boseley
649 words
27 February 1998
The Guardian
GRDN
5
English
(c) 1998

London Evening Standard

OUTCRY over autism began

SCIENTISTS WARNING PROMPTS FEARS OVER MEASLES VACCINE

JO REVILL
291 words
26 February 1998
The Evening Standard
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1
English
(c) 1998 Associated Newspapers. All rights reserved

Andrew Wakefi scientists and (

They are damn

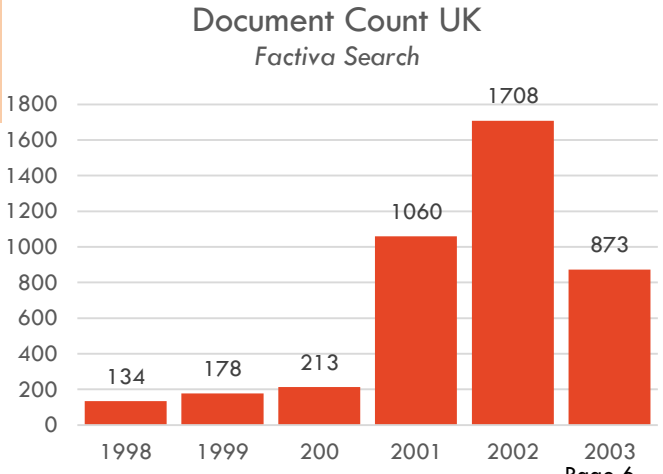
News of the wc passionate abc

"One of our prc began to leak (

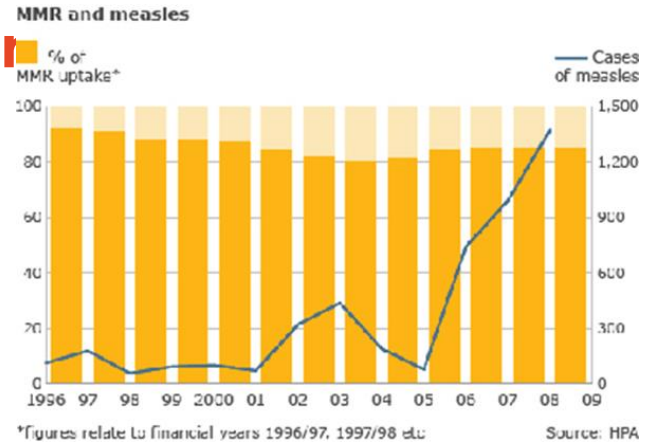
Their findings (

MEASLES vaccinations may be triggering the onset of **autism** and bowel disease in children, scientists in London announced today.

Although it is thought to be a very rare occurrence, the news will come as a huge shock to parents whose children have had, or are about to have, the measles, mumps and rubella (**MMR**) vaccine at around 15 months of age.



What happened in



1998 – 2000's
Becomes a political issue in UK

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2000 onward
MMR coverage in UK drops to 80% in 2003-04, 1144 cases in UK 2009

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2004 - 2010
Brian Deer Investigation

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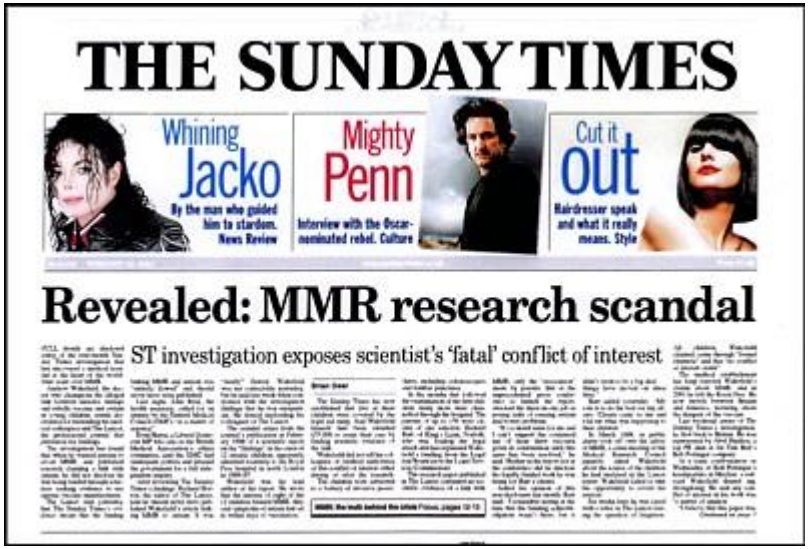
THE SUNDAY TIMES

Whining Jacko
By the man who guided him to stardom. News Review

Mighty Penn
Interview with the Oscar-nominated rebel. Culture

Cut it out
Hairdresser speak and what it really means. Style

Revealed: MMR research scandal

ST investigation exposes scientist's 'fatal' conflict of interest

What happened

COMMENTARY

Retraction of an interpretation

This statement refers to the Early Report "Ileal-l
nodular hyperplasia, non-specific colitis, and
developmental disorder in children",[1] pub
The Lancet in 1998. It is made by 10 of the 1
authors who could be contacted. It should be r
this statement does not necessarily reflect the vi
other co-authors.

The main thrust of this paper[1] was the first d
of an unexpected intestinal lesion in the children
Further evidence has been forthcoming in stu

General Medical Council

Regulating doctors
Ensuring good medical practice

FITNESS TO PRACTISE PANEL HEARING
28 JANUARY 2010

On 16 July 2007 a Fitness to Practise Panel considered the case of:

A. **Dr Andrew Jeremy WAKEFIELD**
GMC reference number: 2733564

B. **Professor John Angus WALKER-SMITH**
GMC reference number: 1700583

C. **Professor Simon Harry MURCH**
GMC reference number: 2540201

This case was considered by a Fitness to Practise Panel applying the General Medical Council's Preliminary Proceedings Committee and Professional Conduct Committee (Procedure) Rules 1988

Panel Members: Dr S Kumar, Chairman (Medical)
Mrs S Dean (Lay)
Ms W Golding (Lay)
Dr P Moodley (Medical)
Dr S Webster (Medical)

Legal Assessor: Mr Nigel Seed QC

EARLY REPORT

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THE LANCET • Vol 351 • February 28, 1998 637

RETRACTED

2004
10 of original paper authors issues partial retraction of paper in Lancet

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2007-2010
GMC found Wakefield found guilty of "dishonesty and irresponsibility" and banned from practice due to the "serious and wide-ranging findings against him"

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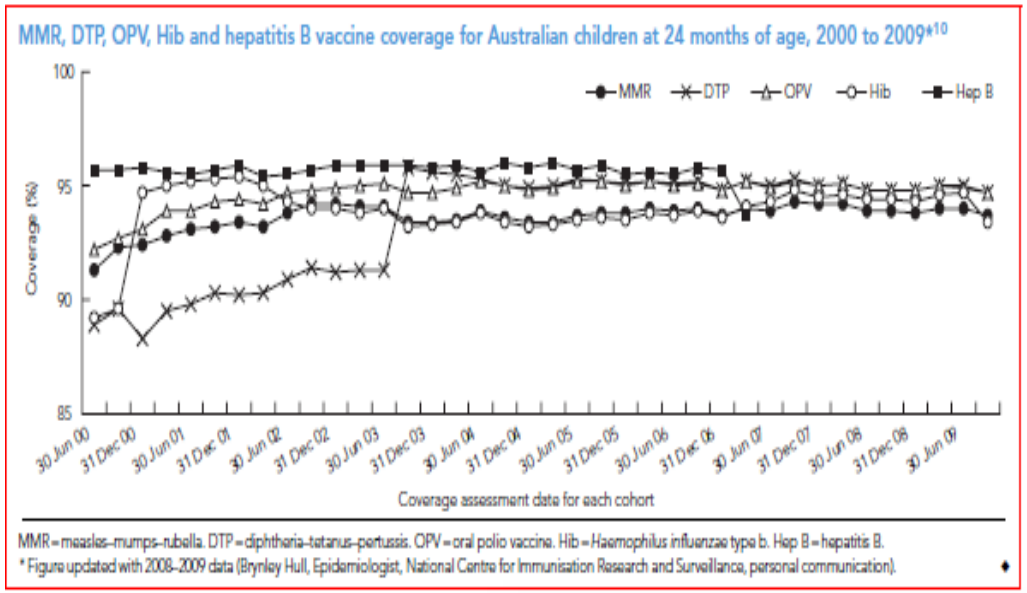
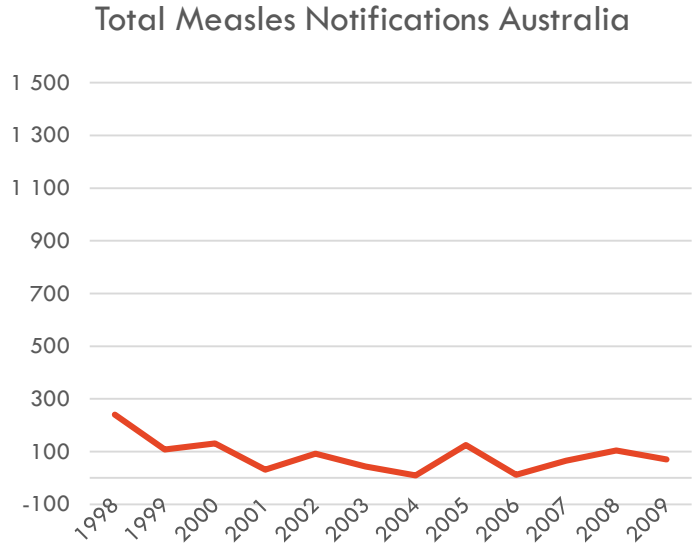
2010
Lancet fully retracts 1998 article

Meanwhile in Australia……

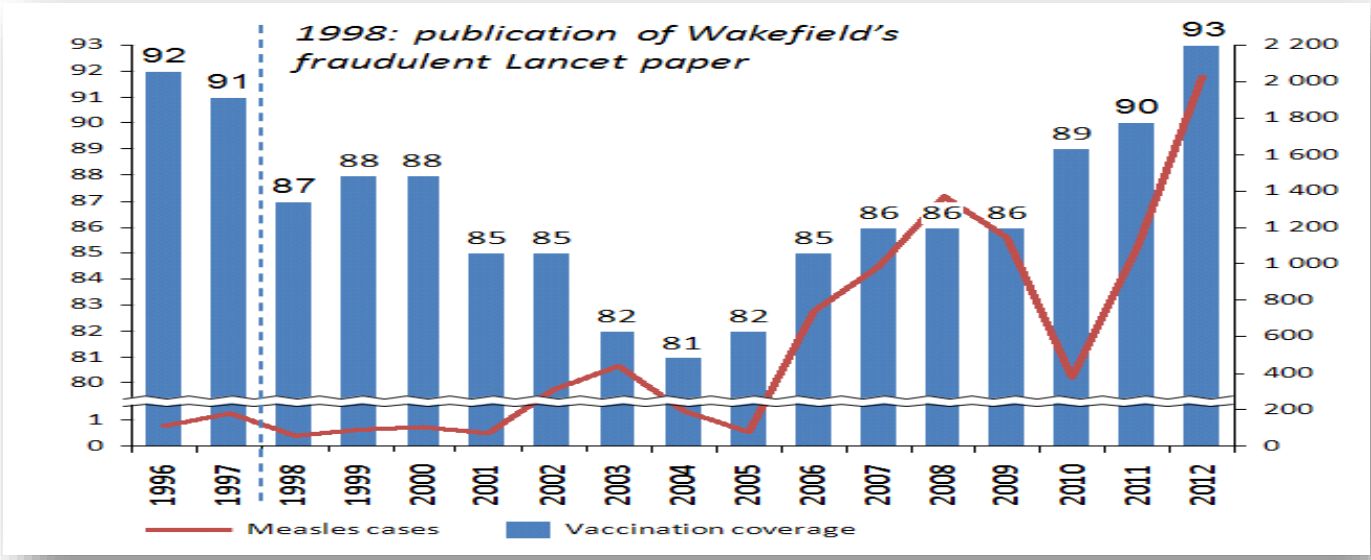
- MMR coverage remained stable and disease low





From Leask, J., Booy, R. & McIntyre, P; *MMR, Wakefield and The Lancet: What can we learn?* MJA 193(1) 5-7.

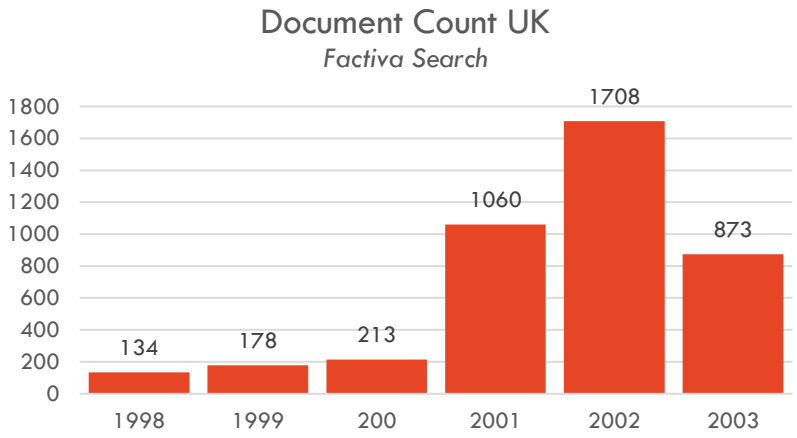
- Unlike in the UK….

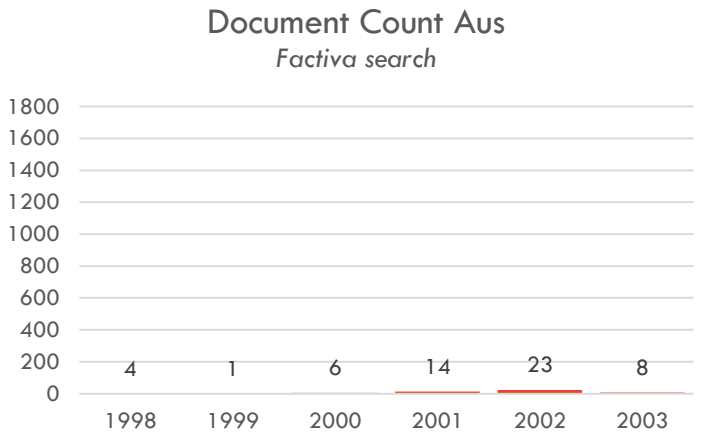


Source: WHO, UNICEF, Public Health England

Meanwhile in Australia……

- Nowhere near the same level of media coverage





- Although some evidence that some providers accepted the MMR / autism link

Table 3: Beliefs about MMR vaccine among NSW regional health professionals.

		%[a]		
		Inflammatory bowel disease	Autism	Idiopathic thrombocytopenic purpura
Beliefs about an association between MMR vaccine and each condition	yes	17	12	7
	unsure	37	29	45
	no	59	59	48

Note:
(a) Weighted percentages

Leask J, Quinn HE, Macartney K, et al. Immunisation attitudes, knowledge and practices of health professionals in regional NSW. Aust N Z J Public Health 2008; 32: 224-229.

MMR scare: UK versus Australia

UK	Australia
Wakefield was a "home grown" champion of MMR / autism theory	No local "champion" of the theory
Media coverage "extensive and sustained"	Media coverage "sporadic"
"Grandstanding" by member of UK conservative opposition party, and then-prime minister refused to divulge whether his son was vaccinated	Consistent strong bipartisan political support for immunisation
Public trust in government assurances already eroded by mis-handling of CJD	No such erosion of public trust

Adapted from Leask, J., Booy, R. & McIntyre, P; *MMR, Wakefield and The Lancet: What can we learn?* MJA 193(1) 5-7.

What were the learnings?

- Vaccine scares are inevitable
  - Should be planned for
  - Involve multiple stakeholders
- Communication
  - should involve interactive engagement with professionals, the public and the media
  - Media should be cautioned against providing “false balance” to unfounded criticisms
- Better vaccine safety surveillance and timely, transparent reporting
- Transparent research integrity