

Still feeling the effects: a citation analysis of the highly cited, retracted article on MMR vaccines and autism

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Background

1998 Article
Published¹

2004 Partial
Retraction²

2010 Notice
of Retraction³

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 apthoid ulceration. Histology showed patchy chronic inflammation in the colon in 11 children and reactive ileal lymphoid hyperplasia in seven, but no granulomas. Behavioural disorders included autism (nine), disintegrative psychosis (one), and possible

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 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, including 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 HEMS-4 criteria.⁷ 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

COMMENTARY

Retraction of an interpretation

This statement refers to the Early Report "Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children", published in *The Lancet* in 1998. It is made by 10 of the 12 original authors who could be contacted. It should be noted that this statement does not necessarily reflect the views of the other co-authors.

"The main thrust of this paper" was the first description of an unexpected intestinal lesion in the children reported. Further evidence has been forthcoming in studies from the Royal Free Centre for Paediatric Gastroenterology and other groups to support and extend these findings.^{8,9} While much uncertainty remains about the nature of these changes, we believe it important that such work continues, as autistic children can potentially be helped by recognition and treatment of gastrointestinal problems.

We wish to make it clear that in this paper no causal link was established between MMR vaccine and autism as the data were insufficient. However, the possibility of such a link was raised and consequent events have had major implications for public health. In view of this, we consider now is the appropriate time that we should together formally retract the interpretation placed upon these findings in the paper, according to precedent.⁴

We were unable to contact John Linnell.

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- 1 Wakefield AJ, Murch SH, Anthony A, Linnell J, Casson DM, Malik M, Berelowitz M, Dhillon AP, Thomson MA, Harvey P, Valentine A, Davies SE, Walker-Smith JA. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998; 351: 637-41.
- 2 Murch S. MMR and autism: the debate continues. *Lancet* 2004; 363: 568-69.
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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.

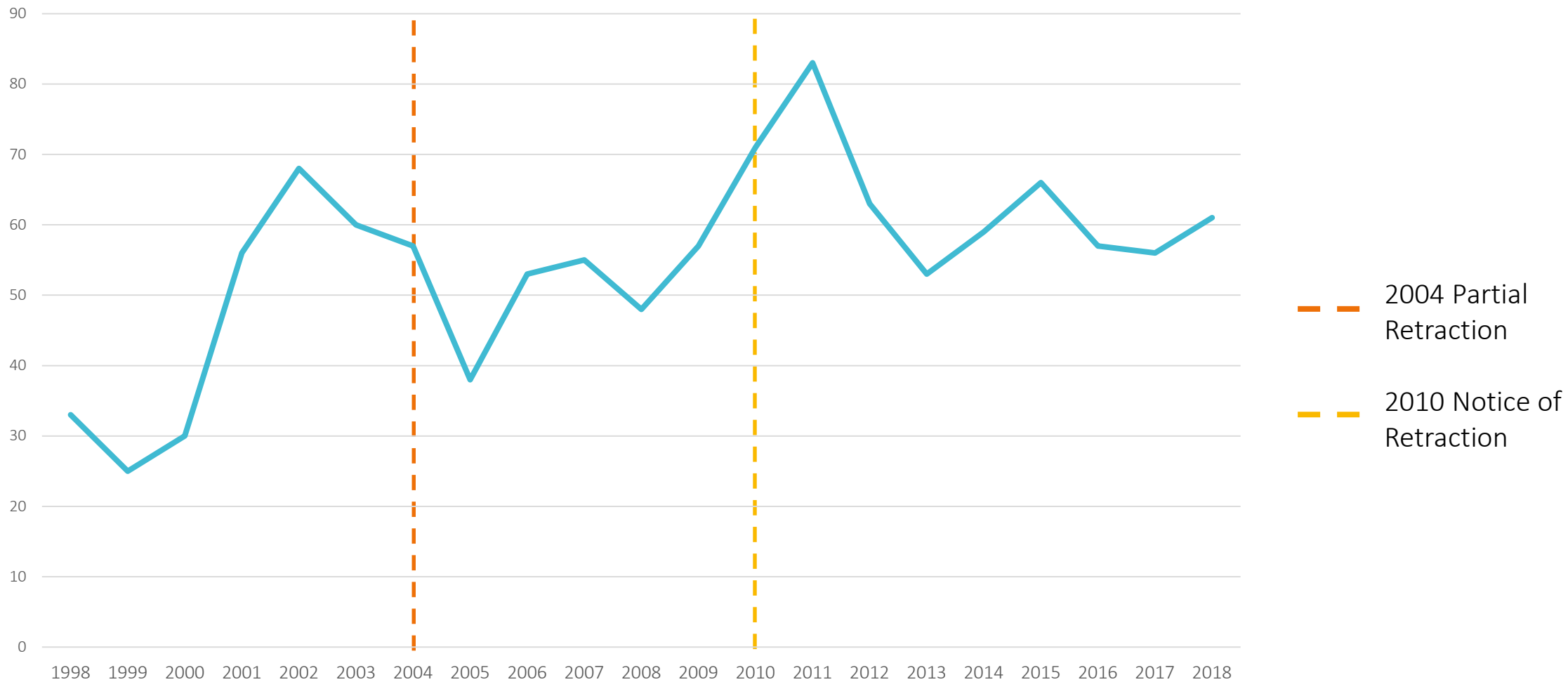
Also under sedation, cerebral magnetic resonance imaging (MRI), electroencephalography (EEG) including visual, brain stem auditory, and sensory evoked potentials (where compliance made this possible), and lumbar puncture were done.

Laboratory investigations

Thyroid function, serum long-chain fatty acids, and cerebrospinal fluid lactate were measured to exclude known

Background

Number of Citing References per Year



Objectives

- › Determine the characteristics of citations from scholarly literature that reference the 1998 Wakefield study
- › Investigate if authors are accurately citing retracted references.

Methodology

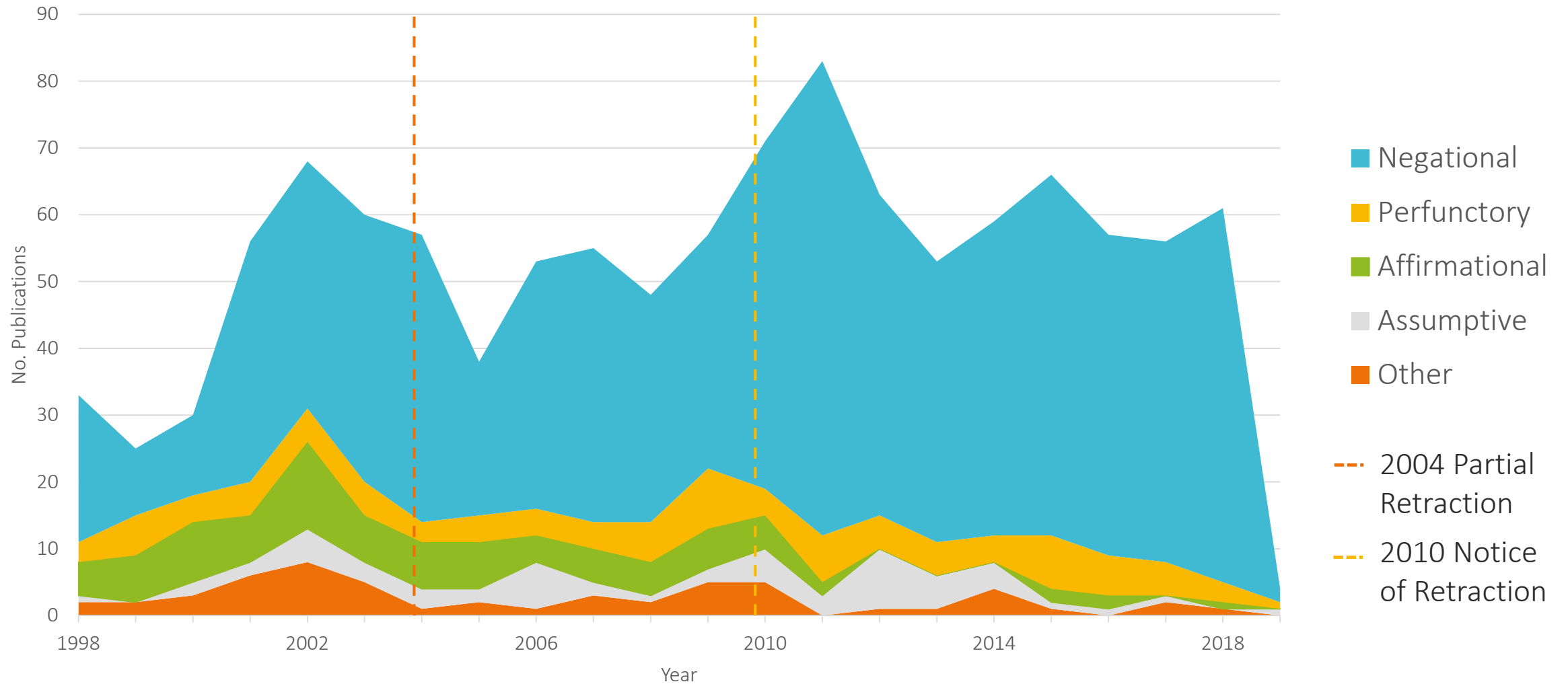
- I. Cited reference search was run in Web of Science on March 11,2019
 - a. 1211 works retrieved
 - b. Excluded Non-English language works, works that could not be verified
- II. 1153 publications underwent blinded screening in Covidence
 - a. Characteristics were assigned to each citation
 - b. Mentions of retractions were documented
- III. Qualitative data analysis was conducted using Excel

Methodology

Characteristic	Definition
Affirmational	Citing work confirms, is supported by, depends on agrees with, or is strongly influenced by cited work.
Assumptive	Citing work refers to assumed knowledge that is general/specific background or an historical account or acknowledges cited work pioneers.
Negational	Citing work disputes, corrects/questions or negatively evaluates cited work.
Perfunctory	Citing work makes a perfunctory reference, is cited without additional comment, makes a redundant reference to cited work, or is not apparently strictly relevant to the author's immediate concerns.

Results

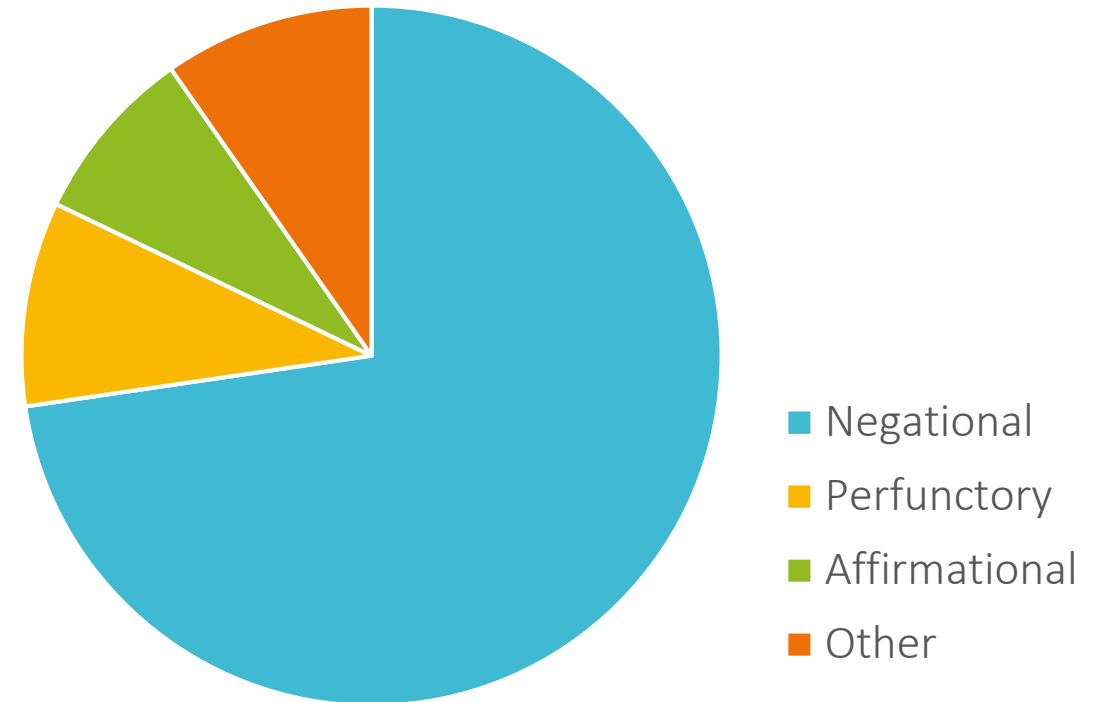
Characteristics of References to the Wakefield Article by Year Published



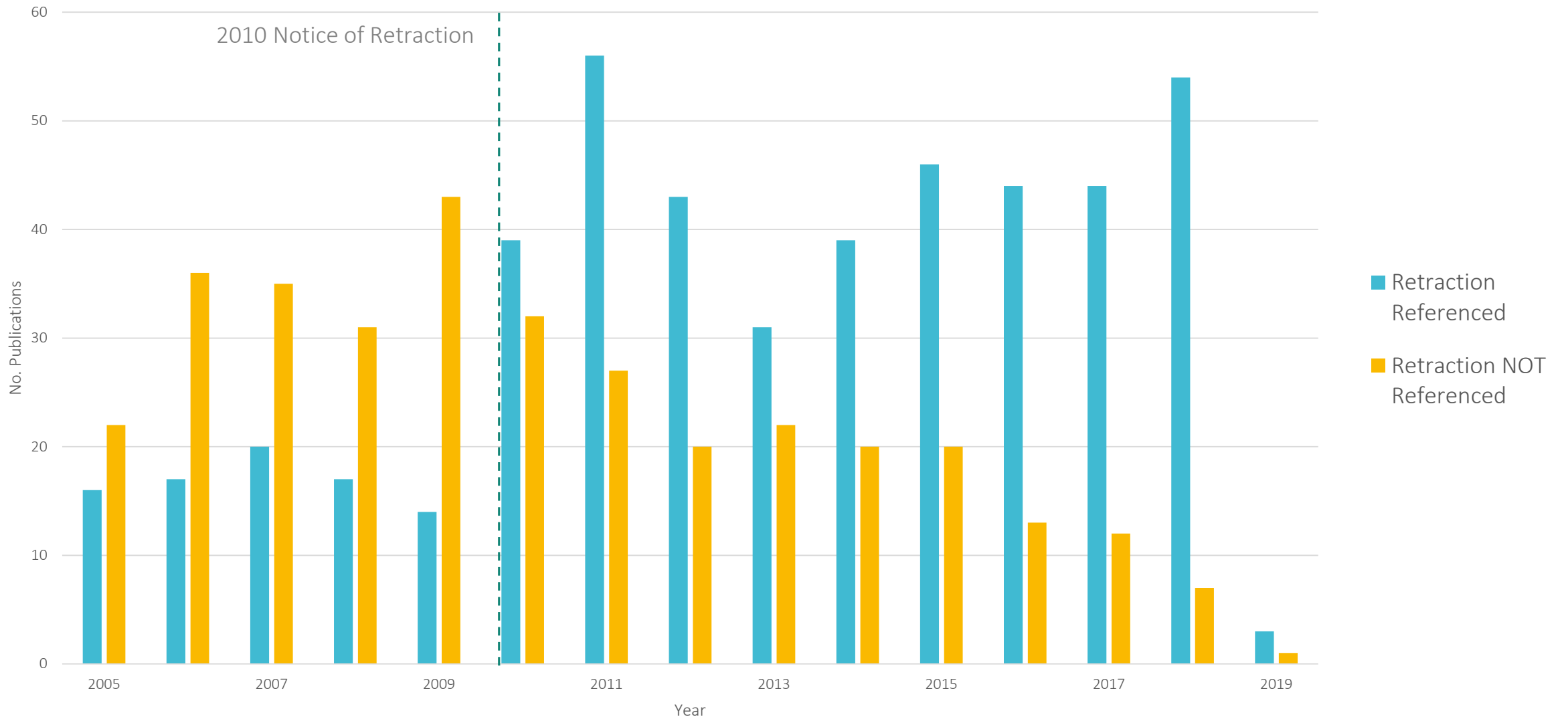
Results

The most common citation characteristics:

- › Negational, 838 of 1153 (72%)
- › Perfunctory, 106 of 1153 (9%)
- › Affirmational, 94 of 1153 (8%)



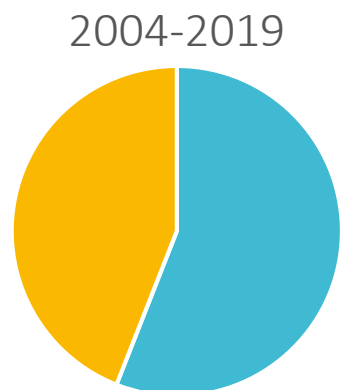
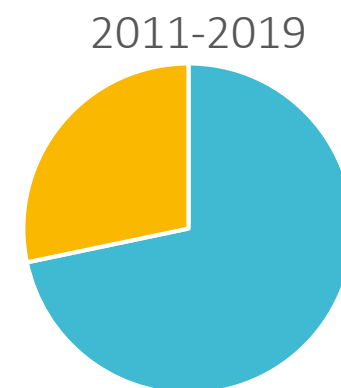
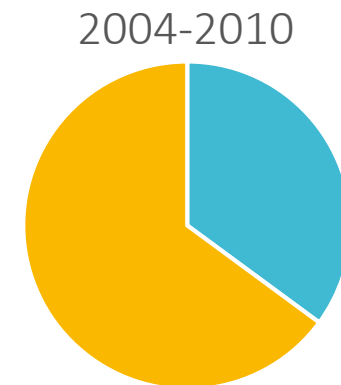
Results



Results

Retractions referenced:

- › 2004-2010, 133 of 379 (35%)
- › 2011-2019, 360 of 502 (72%)
- › 2004-2019, 493 of 881 (56%)



- Retraction Referenced
- Retraction NOT Referenced

Discussion

- › Characteristics were overwhelmingly negative
 - › *Pre-2004 retraction, authors pointed out the methodological flaws of the study and the small sample size*
 - › *After 2005, authors had the opportunity to reference the retracted status of the article*

Discussion

- › A significant number of articles published after the retraction did not cite the retraction
- › *Barriers to citing the retraction include lack of guidelines on how to cited retracted articles from journals, citation managers and citation style guides.*

Conclusions

Scholarly community overwhelmingly negated the findings of the Wakefield article.

There is a need for greater vigilance in ensuring that retracted articles are referenced properly.

Conclusions

This is an example of an infamously retracted study, so readers are probably aware of the retracted status.

For retracted studies that are less well known, can authors assume that their readers will know about the retracted status of the cited work?

Future Research

- › Identify barriers to citing retracted articles properly
- › Provide recommendations for how journals and bibliographic databases handle retracted publications.

References

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