Publication Misconduct and Retraction: Crime and Punishment

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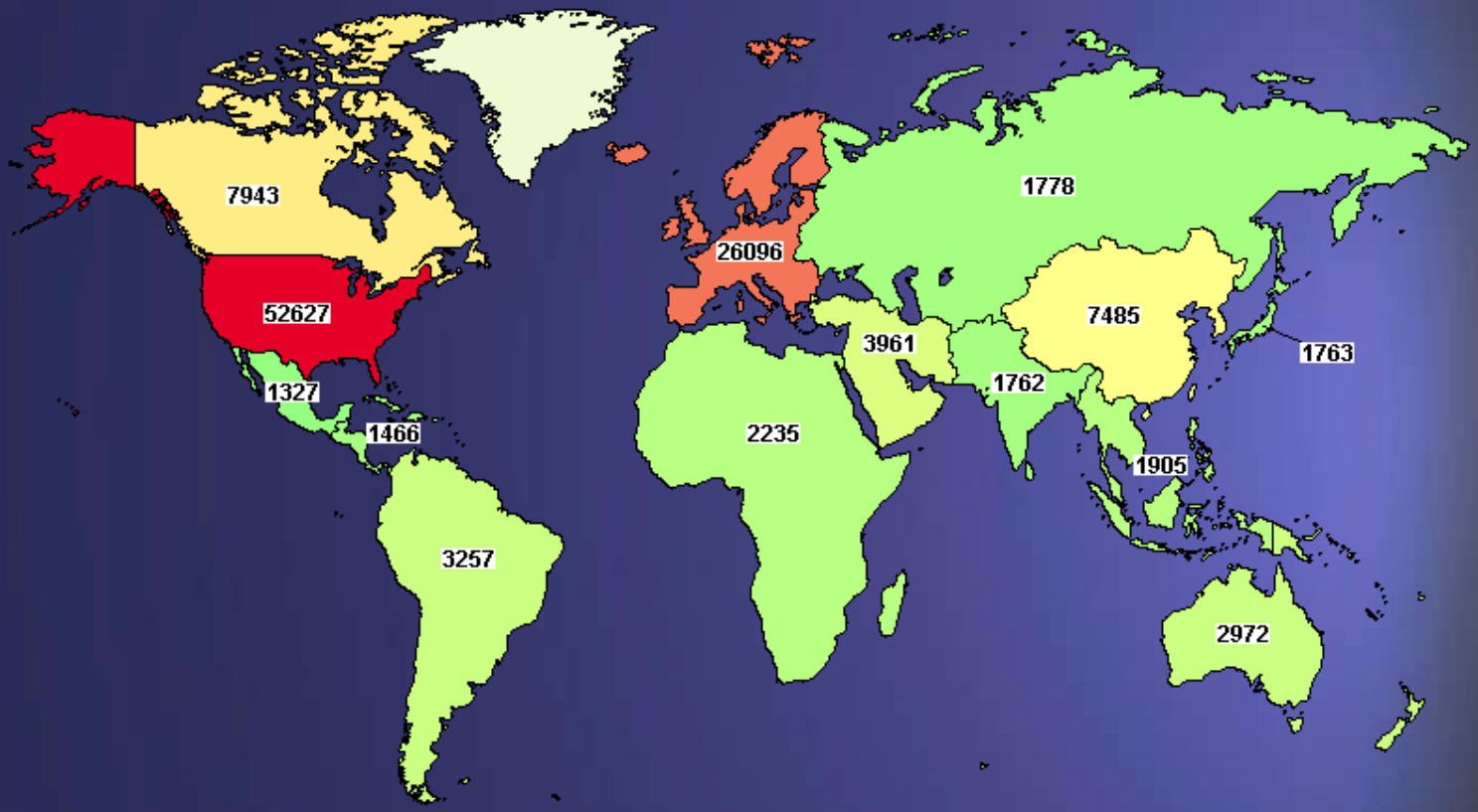
Funded in part by a research grant from ARCS Australia, a professional development organization for the therapeutics industry

ISMPP International Society for Medical Publication Professionals

Globalization of Clinical Research



www.clinicaltrials.gov

7th Annual Meeting ISMPP 2011

Globalization of Authorship

Science Citation Index 2000-2010

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Outline

- Crime
- Punishment
- Characteristics of retracted misconduct publications
- Prevention - what can publication professionals do?

THE CRIME

Altering instrumentation or processes

Non-replicable findi… …ing flawed analyses

Inadequate recor… …disputes

Copying ideas …g data points

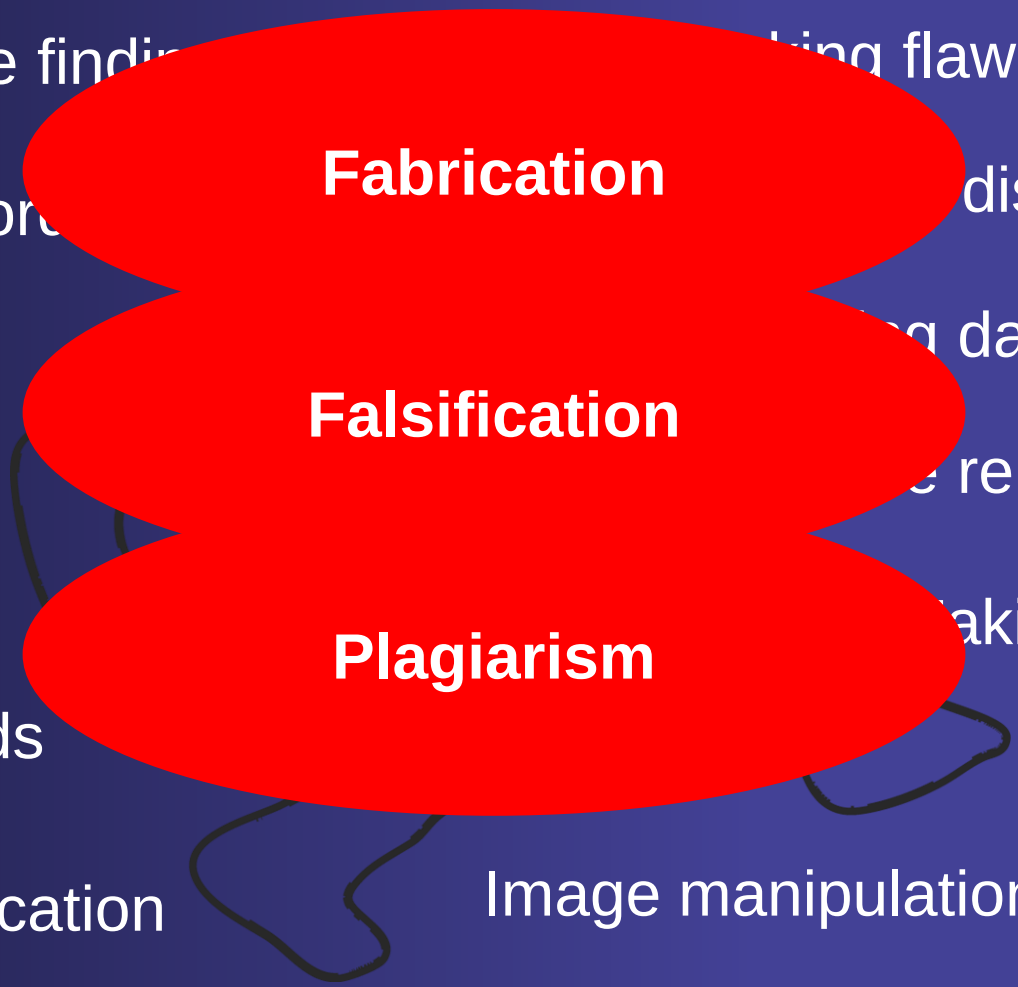
…e reporting

Copying results …aking data

Copying words False study design

Duplicate publication Image manipulation

Falsifying ethics approval / informed consent

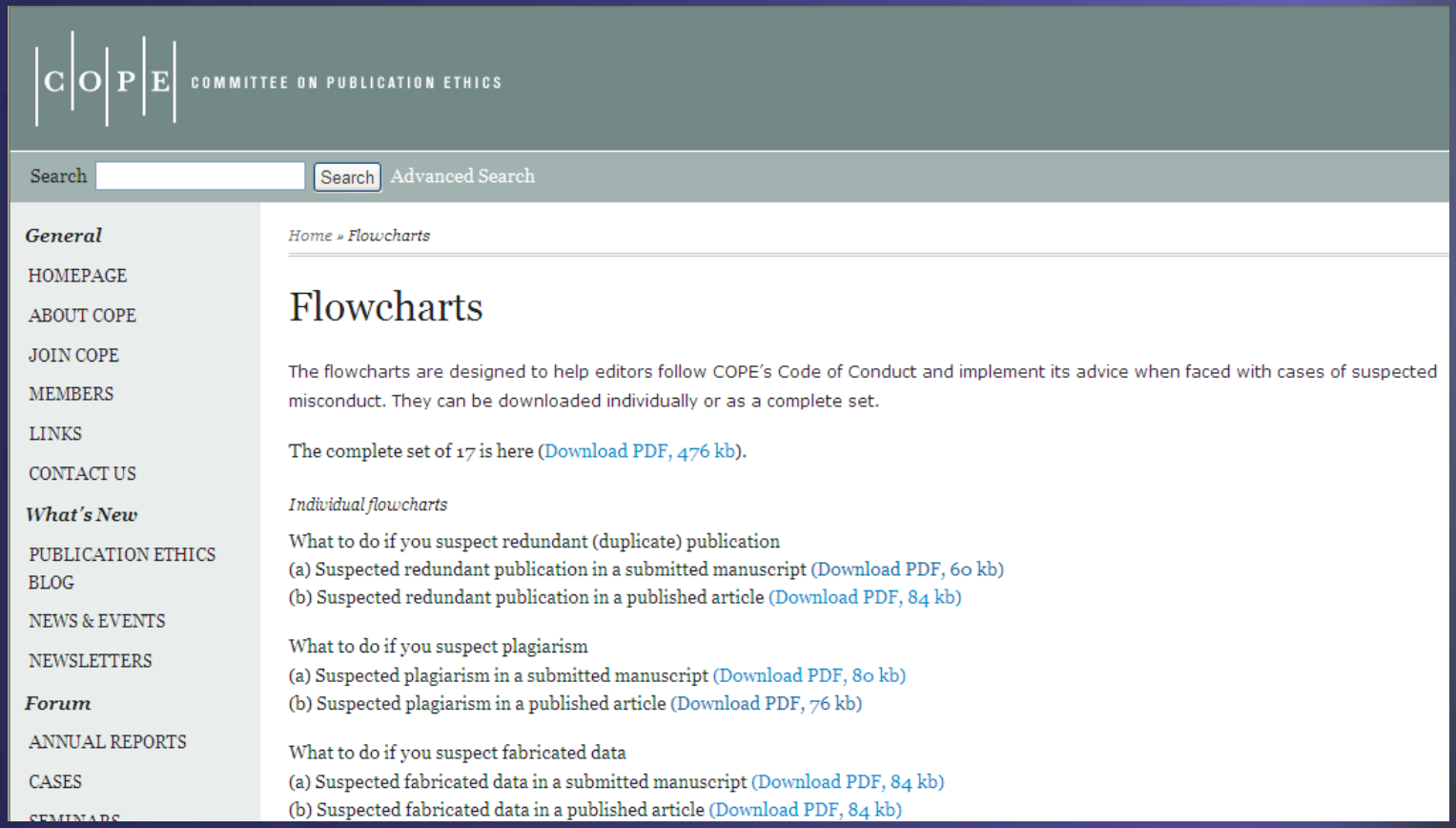


THE PUNISHMENT
National Library of Medicine

- To be retracted from MEDLINE
  - Clear statement of retraction
  - Signed by authors or legal counsel, head of institution, or journal editor
  - Must appear on a numbered page in an issue of the journal

THE PUNISHMENT
Journal practice

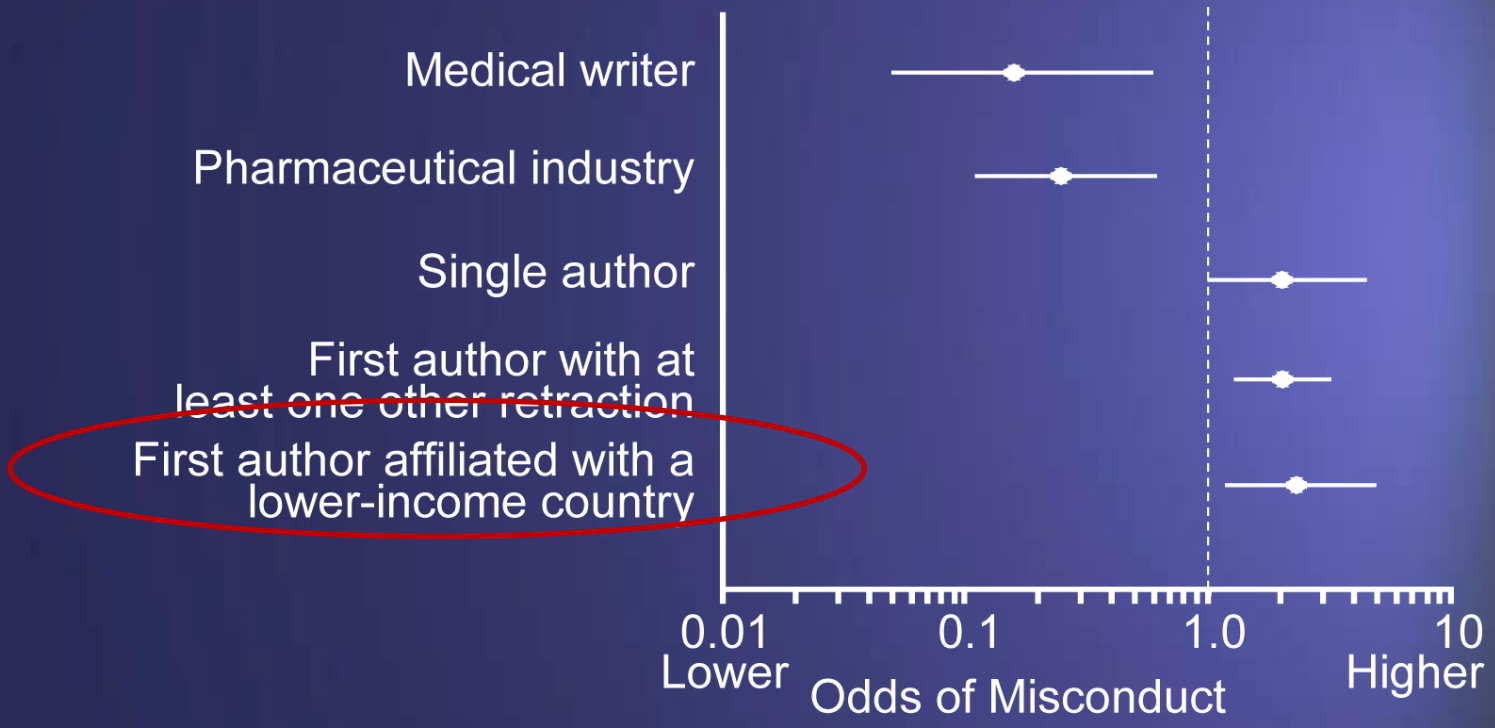
Committee on Publication Ethics



http://publicationethics.org/flowcharts

Lack of involvement of medical writers and the pharmaceutical industry in publications retracted for misconduct[1]

Odds ratio (95% CI)
Misconduct retraction (n = 213) vs Mistake retraction (n = 220)



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[1] Woolley K et al. Curr Med Res Opin 2011; In press.

Objectives

- To determine whether the proportion of plagiarism retractions differed between authors affiliated with lower-income and higher-income countries
- To determine other author, journal, and publication factors associated with plagiarism retractions

Methods

Search

MEDLINE: Publications retracted for misconduct
Limits: Human, English, Jan 1966 to Feb 2008

Data Extraction

Original publication and retraction notices
Data extracted using standard definitions and a standardized data collection tool[1]
Lower-income countries comprised low and middle income countries, based on World Bank classifications

Statistical Analysis

Odds ratio (OR), 95% confidence interval (CI), Chi-square test
Primary outcome = plagiarism retractions
Reference group = other misconduct retractions
Independent academic statistician reviewed and approved the study design, and conducted all analyses

[1] Woolley K et al. Curr Med Res Opin 2011; In press.

What were the main reasons for misconduct retractions?

- Plagiarism accounted for almost half of all misconduct retractions

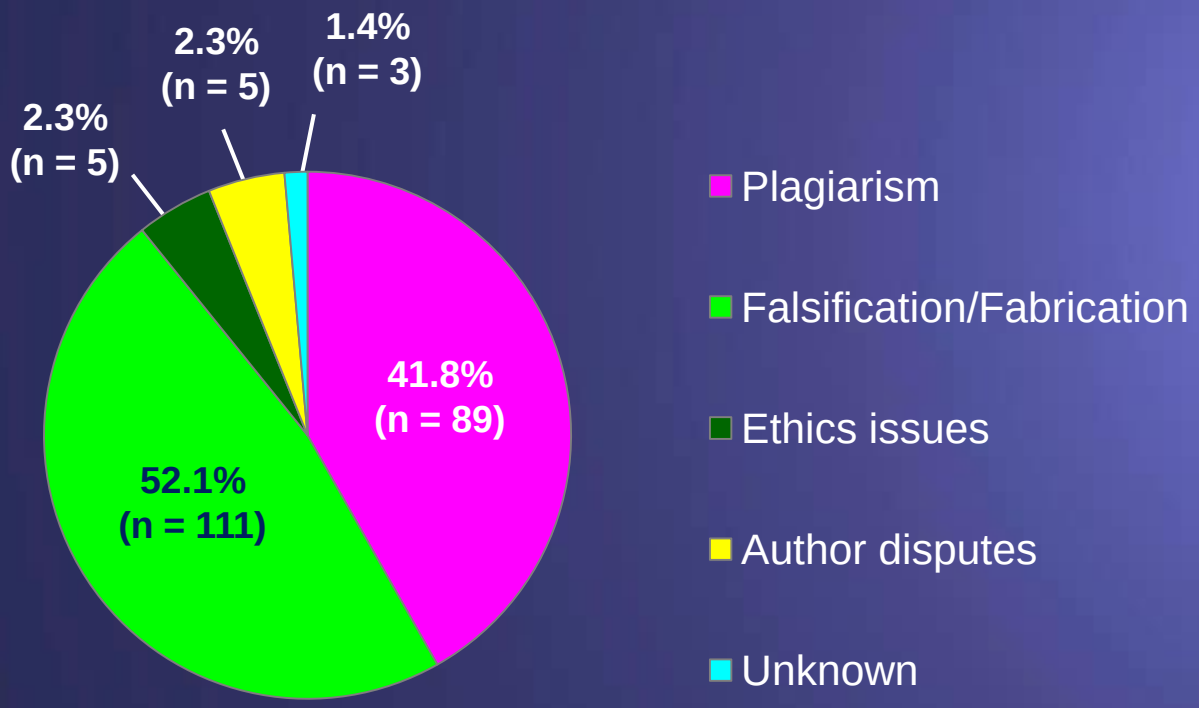
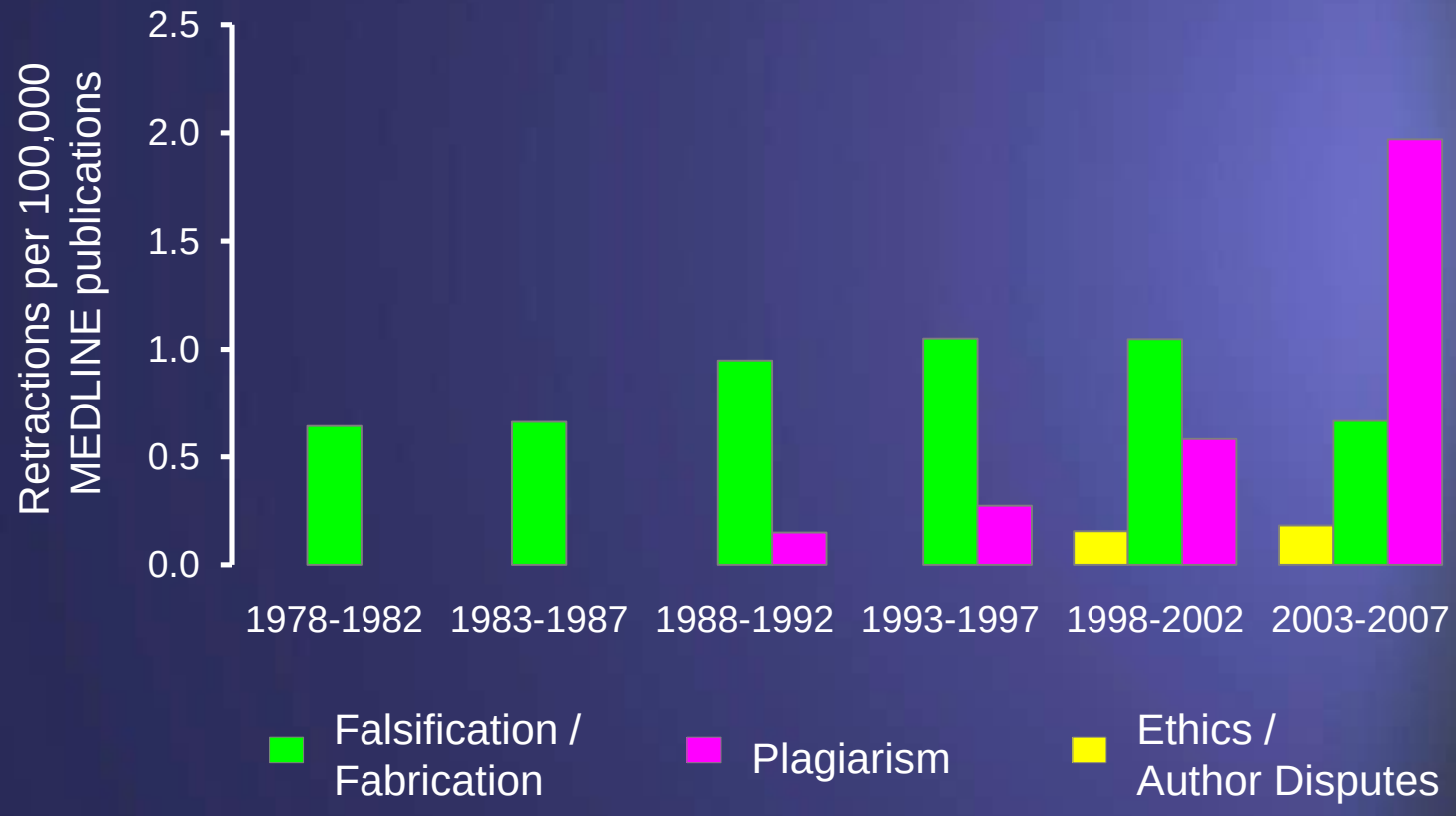


Figure. Type and percentage of misconduct retractions (N = 213)

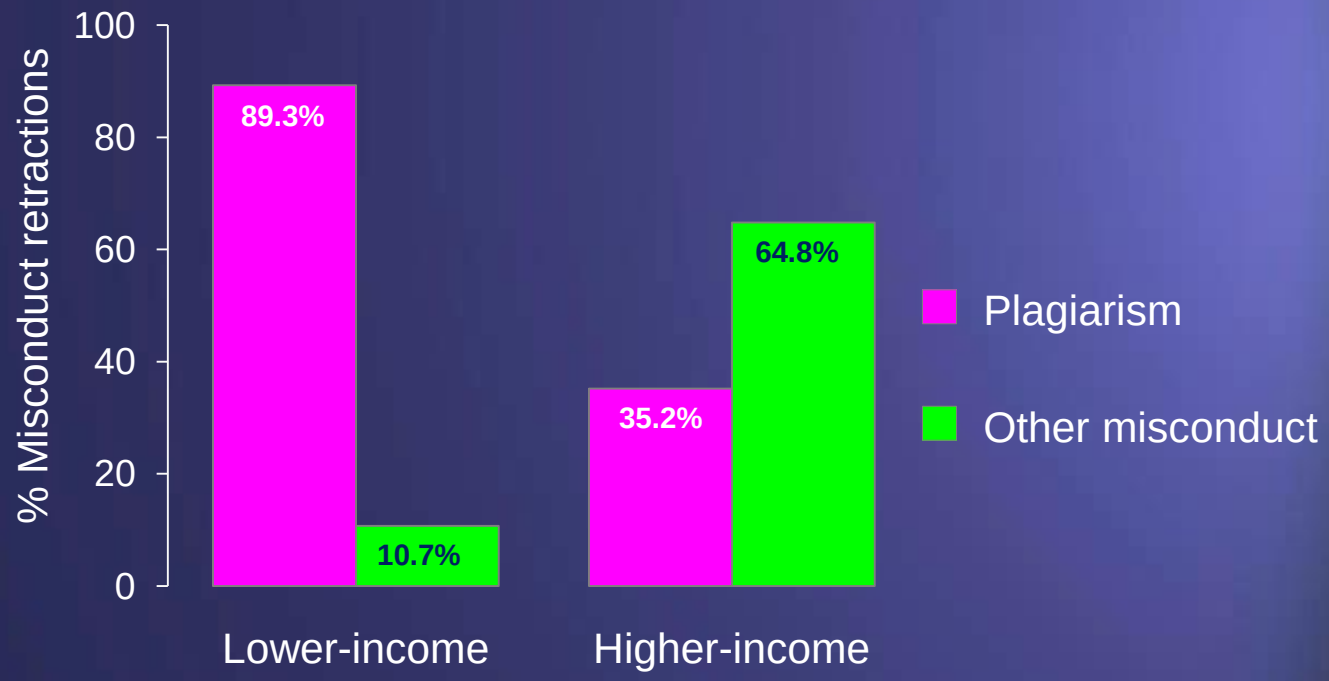
Have misconduct retractions changed over time?

- Plagiarism retractions have increased over the past decade

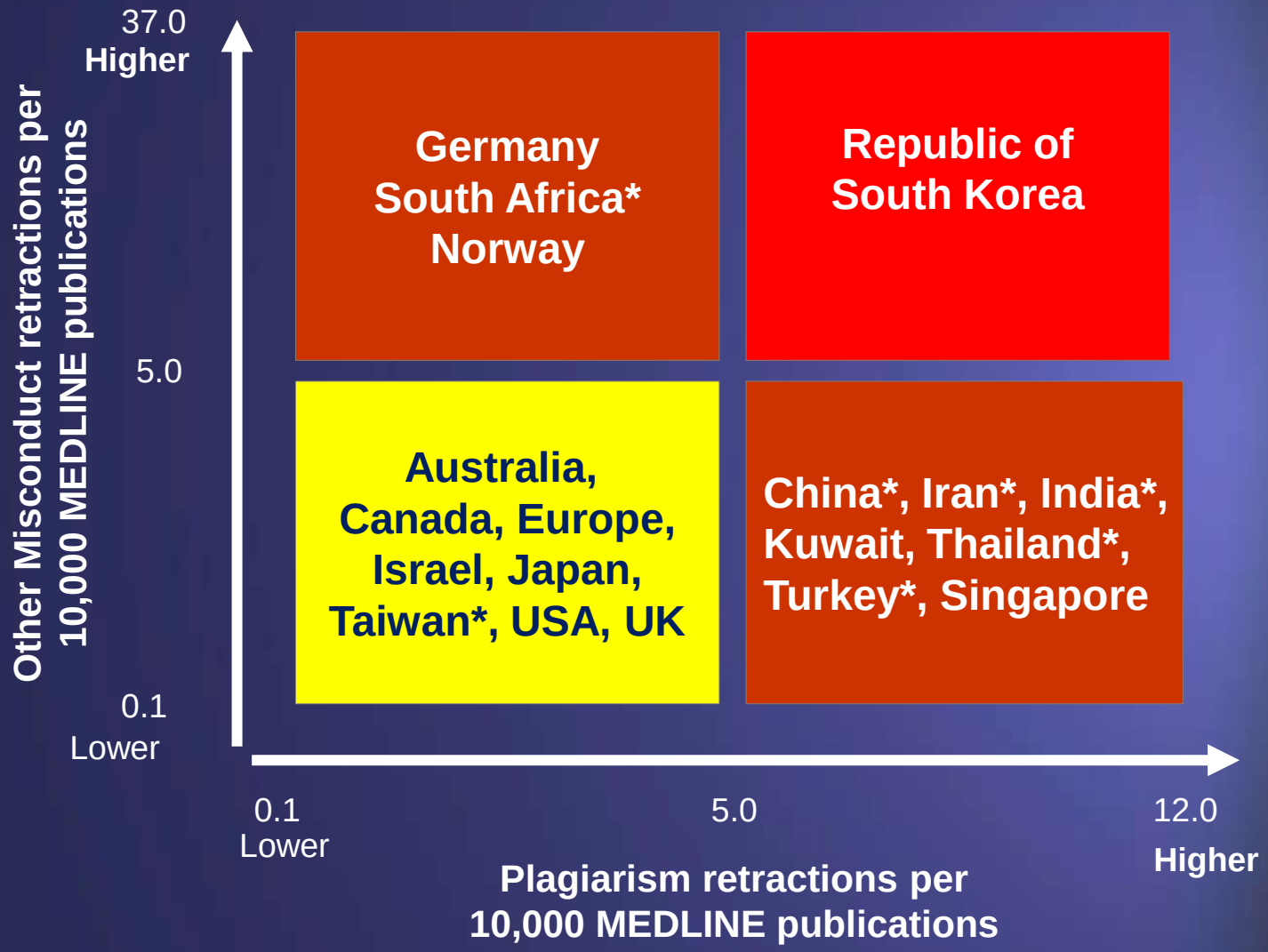


Did misconduct retractions differ between countries?

- Significantly higher odds of plagiarism retractions for first authors affiliated with lower-income than higher-income countries (OR, 95% CI: 5.4, 4.5 - 52.9; *P* < 0.001)



Should we be concerned?



* Lower-income country

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Research conclusions

- Almost half of all misconduct retractions were because of plagiarism
- The number of plagiarism retractions as a proportion of MEDLINE publications has increased in the past decade
- The type of misconduct retraction differed between authors affiliated with lower- and higher-income countries

“When a thing has been said well, have no scruple. Take it and copy it.”

http://en.wikipedia.org/wiki/Anatole_France

Anatole France
(Nobel Prize for Literature 1921)

- Publication professionals should
  - Challenge perceptions
  - Know the risk factors
  - Inform / educate their authors

Publication Misconduct: What Publication Professionals Need to Know

John C. Galland, Ph.D., Director
Division of Education and Integrity
Office of Research Integrity
United States Department of Health and Human Services

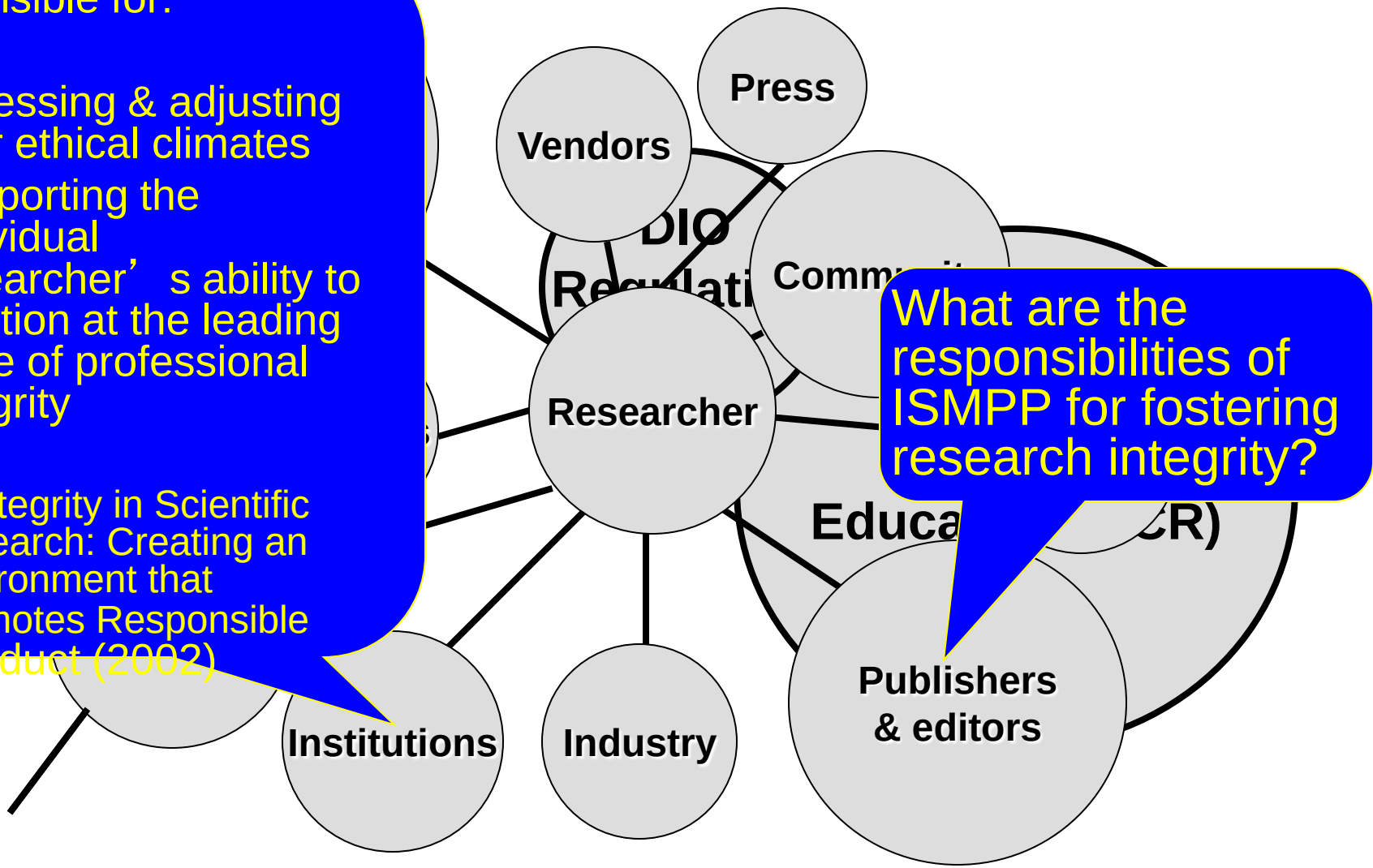
ISMPP International Society for Medical Publication Professionals

Guardians of the Trust

Responsible for:

1. Assessing & adjusting their ethical climates
2. Supporting the individual researcher's ability to function at the leading edge of professional integrity

NAS -Integrity in Scientific Research: Creating an Environment that Promotes Responsible Conduct (2002)



What are the responsibilities of ISMPP for fostering research integrity?

Partnerships for Success

RCR Instructional Areas

1. Research misconduct
2. Human Subjects
3. Animal Welfare
4. Mentor/ Trainee Responsibilities
5. Data Acquisition, Management, Sharing, & Ownership
6. Publication Practices & Responsible Authorship
7. Peer Review
8. Conflict of Interest and Commitment
9. Collaborative Science

RCR Instructional Areas

10 Management

11 Advocacy

12 Leadership

13 Security (Dual Use)

14 Ethics

15 Communication

16 Safety

17 Green (Sustainable) Labs

18 ?

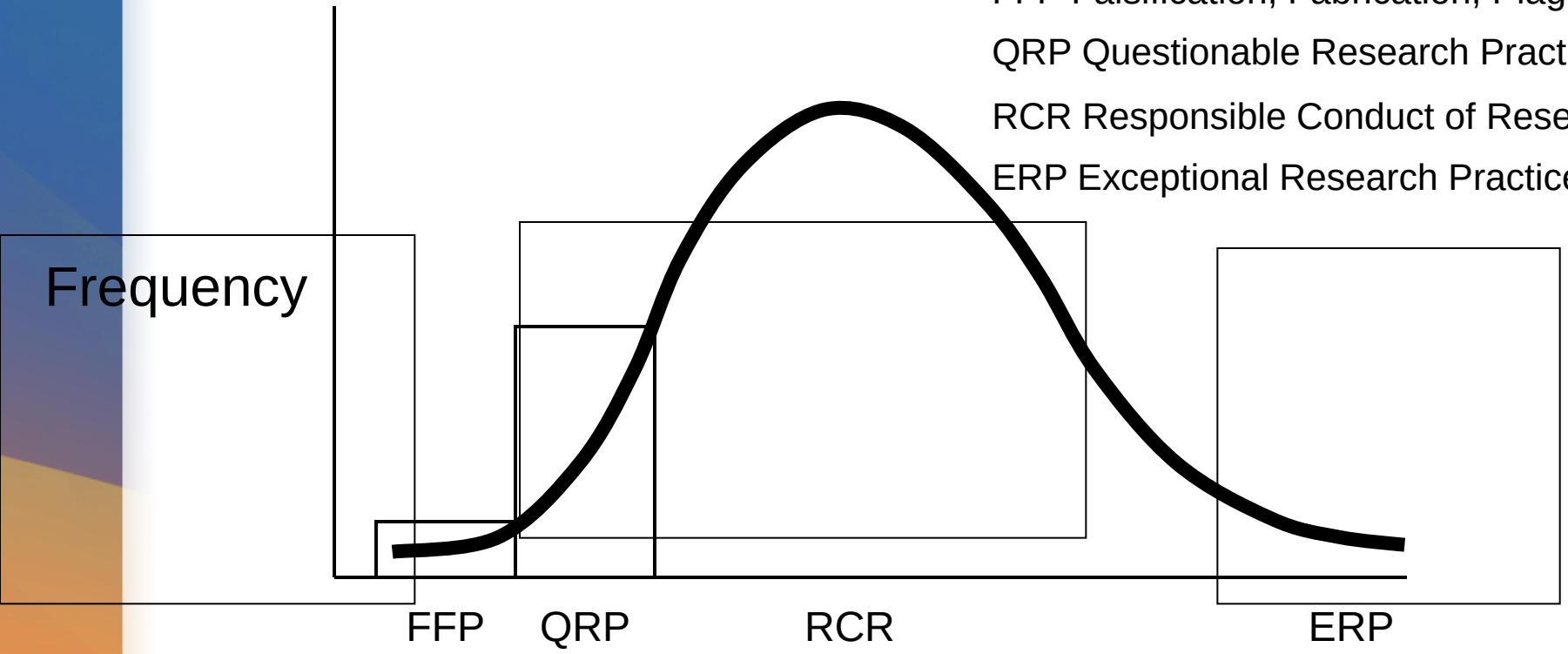
For Whom Does DEI Serve?

FFP Falsification, Fabrication, Plagiarism

QRP Questionable Research Practices

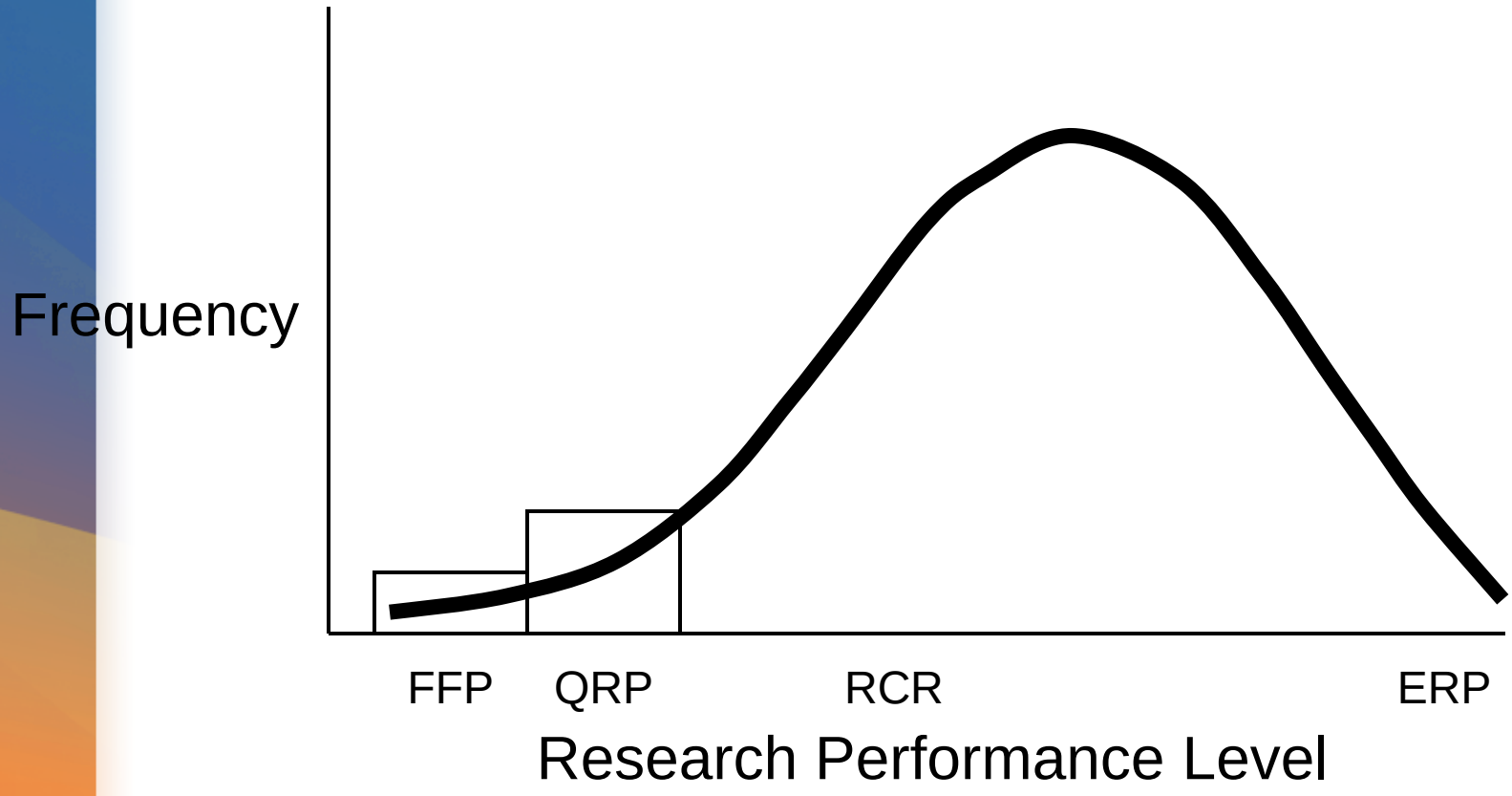
RCR Responsible Conduct of Research

ERP Exceptional Research Practices



Questionable research practices far more common than outright misconduct

For Whom Does DEI Serve?



Scope of RCR Education

- **Information about compliance (i.e., rules, regulations, policies, guidelines)**
- **The ethics of the research itself and of the research process**
- **Abilities that give rise to ethical behavior**
  - **ethical sensitivity, reasoning and judgment, identity formation, habits** (James Rest, 1983)
- **The manner in which the research is conducted** (that reduces uncontrolled variability)
- **The situation** or conditions (location, urgency) under which planning and execution depends

What jeopardizes research integrity?

- Anything that introduces uncontrolled variation into the dataset?
- When self interest replaces truth as the primary goal of research

U.S. Public Funding Agencies

- Health and Human Services (HHS)
  - National Institutes of Health (NIH)
  - Centers for Disease Control (CDC)
  - Food and Drug Administration (FDA)
- National Science Foundation (NSF)
- National Aeronautics and Space Administration (NASA)
- Other Cabinet level funding agencies

Research Integrity
Regulatory Offices in HHS

- Office of the Secretary
  - Office of Research Integrity (**ORI**)
  - Office of Human Research Participants (**OHRP**)
- National Institutes of Health
  - Office of Laboratory Animal Welfare (**OLAW**)
  - Office of Management Assessment

Legal Definition of Research Misconduct

Research misconduct is defined as *fabrication*, *falsification*, or *plagiarism* (FFP) in proposing, performing, or reviewing research, or in reporting research results

Definition of Research Misconduct

- **Fabrication** is making up data or results and recording or reporting them

- **Falsification** is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record

Definition of Research Misconduct

- **Plagiarism** is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit

- Research misconduct does not include honest error or differences of opinion

  (42 CFR Part 93.103)

Proof of Research Misconduct

Requires all the following:

- That there be a significant departure from accepted practices of the relevant research community, and
- The misconduct be committed intentionally, knowingly, or recklessly; and
- The allegation be proven by a preponderance of the evidence. (42 CFR Part 93.104)

Handling Cases of Research Misconduct

Institution

Allegation

↓

Assessment

↓

Inquiry

↓

Investigation

ORI

DIO Review

↓

Recom-
mendation

↓

Settlement
or charge
letter

Judge

Hearing

↓

Appeal

↓

Admin.
action

	Reversed value(s)
	Falsified value
	Fabricated value

Correct TEE values

Dr. Poehlman's TEE values

	BodyComp&EE		RevisedTEE's	
First	TEE-1	TEE-2	TEE1	TEE2
jean		2043.00	2399	2043
ray			3069	2923
beth			3728	3404
seth	2460.00	1838.00	2460	1838
alice		2750.00	2950	2750
thomas	2540.00	2945.00	2945	2540
david			3392	3312
harry		3423.00	3423	2655
frances		1854.00	2377	1854
john		2147.00	3244	2147
anita			2680	2399
carol			2136	2130
anthony	2919.00	3264.00	3264	2919
ron		2950.00	3593	2950
patrick		3221.00	3453	3221
walter			4445	3873
tom		2545.00	3001	2545
john		2723.00	3541	2723
ann		2351.00	2201	2351
mary	2638.00	2227.00	2638	2227
derroll		4056.00	4314	4056
jean		3350.00	3473	3350
lloyd			3593	3410
david		3760.00	3991	3760
berenice		2611.00	2898	2611
david			3837	3471
hild	2328.00	2518.00	2518	2328
elliot		2822.00	3739	2822
ann	2045.00	2359.00	2359	2045

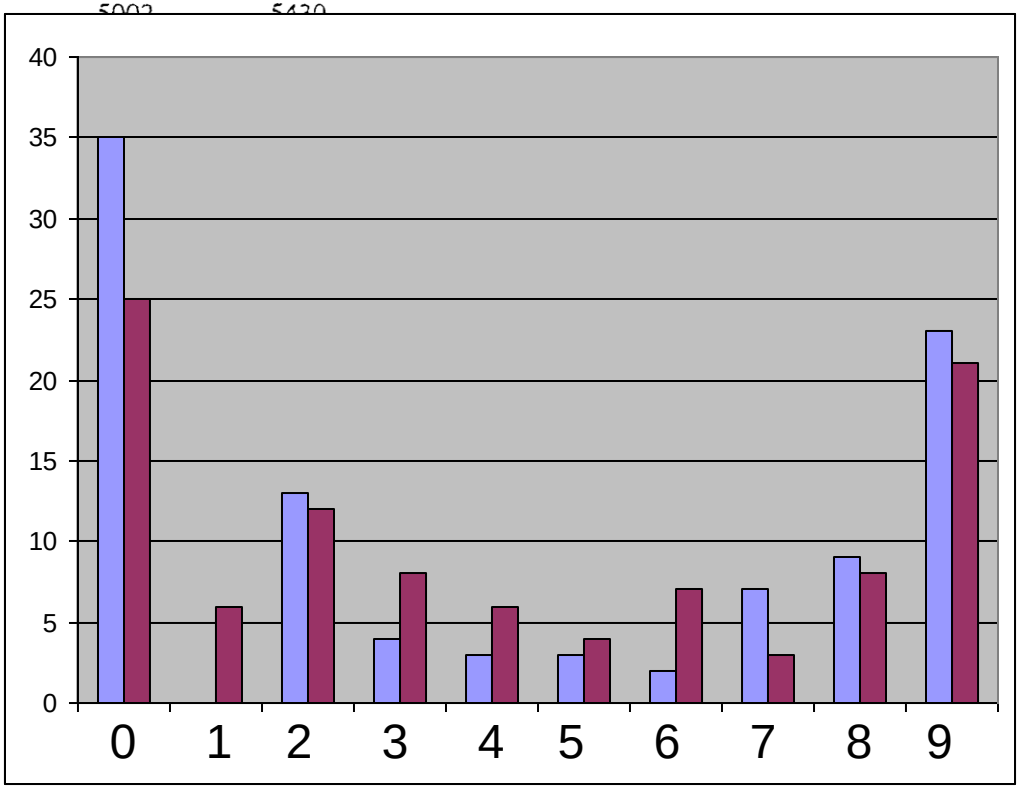
Dr. Poehlman's changes to total energy expenditure values included many fabrications (blue) and reversals of visit one and visit two values (red)

The net effects were to greatly inflate the number of subjects and to reverse the apparent effect of aging.

	BodyComp&EE		RevisedTEE's	
	TEE-1	TEE-2	TEE1	TEE2
Count	55.00	109.00	135	135
Mean	2391.09	2658.07	2925.97037	2624.57037
Std. Dev.	618.53	640.12	645.699389	613.445074

Can you tell if numbers have been fabricated?

	cpms			
[3H]estradiol (2.5 nM)	4600	5098	4900	5534
+ vehicle	4540	5123	[illegible]	[illegible]
+ 0.001 nM estradiol	4230	4798		
+ 0.005	3890	4650		
+ 0.01	2910	3209		
+0.1	2410	2643		
+ 1	1902	2102		
+ 10	1020	1546		
+ 100	720	1029		
+ endosulfan (1 uM)	4709	4908		
+ 5 uM	4500	4845		
+10 uM	4202	4500		
+ 30 uM	4102	4300		
+ dieldrin (1 uM)	4202	4700		
+ 5 uM	4319	4676		
+ 10 uM	4143	4390		
+ 30 uM	4100	4457		
+ toxaphene (1 uM)	4389	4598		
+ 5 uM	4290	4689		
+ 10 uM	4129	4410		
+ 30 uM	4302	4529	4290	4402
+ Chlordane (1 uM)	4700	5192	5320	5469
+ 5 uM	4890	5232	5400	5230
+ 10 uM	5095	5289	5129	5157
+ 30 uM	4799	5167	5329	5439



What do you do when you suspect FFP?

- Reject the manuscript?
- Talk to the primary author?
- Talk to all the authors?
- Talk to the primary reviewer?
- Talk to the primary author’s Dean?
- Talk to the RIO at the primary author’s institution?
- Talk to ORI?

Some ORI Statistics

1992 to July 2007

• Total misconduct findings	189
• Findings leading to debarment	119
• Total cases opened from 1992	501
• Total cases closed from 1992	531
• Total cases pending	43
• Misconduct findings involving clinical research	27%
Total allegations (≈225/year)	3,084

Statistics (Journal Articles)

• Retracted papers	114
• Corrected papers	31
• Withdrawn papers	4
– Total	149

PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE:

I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE:

I ... that the statements herein are true, complete and accurate to the ... knowledge and accept the obligation to comply with Public ...rvice terms and conditions if a grant is awarded as a result of this application ... aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

398 (Rev. 4/98)

Advancing Values:
It's about character

Shared Values in the Culture of Science

- **Honesty**
- **Accuracy**
- **Efficiency**
- **Objectivity**

Values: ORI Introduction to the Responsible Conduct of Research, Nicholas H. Steneck; http://ori.dhhs.gov/documents/rcrintro.pdf

Welcome to….

The 7th Annual Meeting of ISMPP

Anticipating Change in Medical Publications: Leading Now for the Future

International Society for Medical Publication Professionals

Publication Misconduct: What Publication Professionals Need to Know

Cindy W. Hamilton, PharmD

John C. Galland, PhD

Serina Stretton, PhD

ISMPP International Society for Medical Publication Professionals

Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst

Woo Suk Hwang,[1,2]* Young June Ryu,[1] Jong Hyuk Park,[3] Eul Soon Park,[1] Eu Gene Lee,[1] Ja Min Koo,[4] Hyun Yong Jeon,[1] Byeong Chun Lee,[1] Sung Keun Kang,[1] Sun Jong Kim,[3] Curie Ahn,[5] Jung Hye Hwang,[6] Ky Young Park,[7] Jose B. Cibelli,[8] Shin Yong Moon[5]*

Retracted

Somatic cell nuclear transfer (SCNT) technology has recently been used to generate animals with a common genetic composition. In this study we report the derivation of a pluripotent embryonic stem (ES) cell line (SCNT-hES-1) from a cloned human blastocyst. The SCNT-hES-1 cells displayed typical ES cell morphology and cell surface markers and were capable of differentiating into embryoid bodies in vitro and of forming teratomas in vivo containing cell derivatives from all three embryonic germ layers in severe combined immunodeficient mice. After continuous proliferation for more than 70 passages, SCNT-hES-1 cells maintained normal karyotypes and were genetically identical to the somatic nuclear donor cells. Although we cannot completely exclude the possibility that the cells had a parthenogenetic origin, imprinting analyses support a SCNT origin of the derived human ES cells.

Science 2004;303:1699-74.

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

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 (diarrhoea, 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.[1] Developmental data 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

Wakefield et al.
Lancet 1998;
351:637-41.

What is publication misconduct?

- Research misconduct
  - Fabrication (making up data or results)
  - Falsification (manipulating research materials, or changing or omitting data or results)
  - Plagiarism (appropriation of another's ideas)
  - *Not* honest error or differences of opinion
- Other types of publication misconduct (duplicate publication, self-plagiarism, faked author approval, and other ethical violations)

Office of Research Integrity
http://ori.hhs.gov/misconduct/definition_misconduct.shtml

What's the harm?

- Distraction from truth
- Adoption of ineffective or harmful interventions
- Damaged reputations
- Sensationalism in news media
- Erosion of trust in research

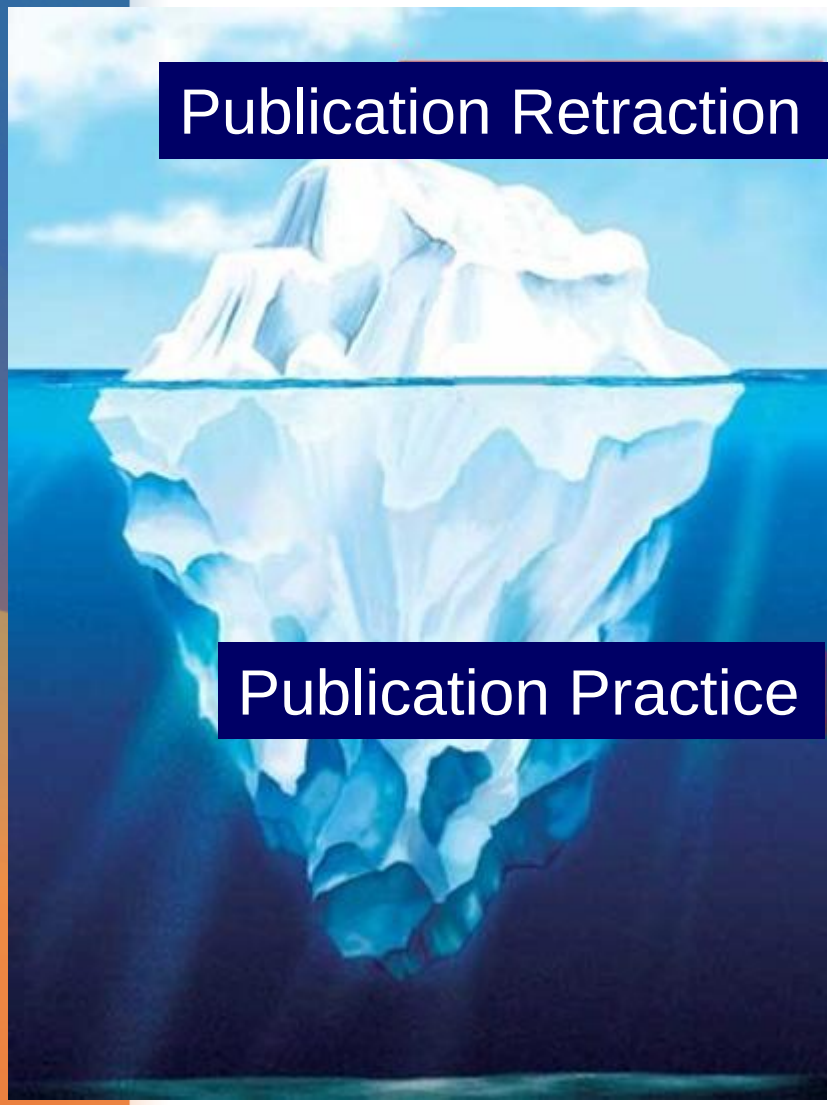
Trikalinos et al. *J Clin Epidemiol* 2008

What can be done?

- Identify every tainted article.[1]
- Retract fraudulent articles.[1]
  - Time to retraction: >28 months[2]
  - Awareness of retraction: <5% of citing papers[3]
- Prevent citation of fraudulent research.[1]

1. Sox and Rennie. *Ann Intern Med* 2006;144:609-13.
2. Trikalinos et al. *J Clin Epidemiol* 2008;61:464-70.
3. Neale et al. *Sci Eng Ethics* 2010;16:251-61.

Tip of the iceberg?



- 0.3 misconduct retractions per 10,000 MEDLINE publications[1]
- 41 highly similar publications per 10,000 MEDLINE publications in 2008[2]
- 2% of scientists admitted to fabricating, falsifying, or modifying data at least once[3]
- 34% of scientists admitted to questionable research practice[3]

1. Stretton et al. Unpublished data
2. Garner. *Urol Oncol* 2011;29:95-99
3. Fanelli. *PLoS ONE* 2009;4(5): e5738

Déjà vu?

- Creutz. Manuscript Originality Checking in the Scientific, Technical & Medical Information Sector. ISMPP 4th Annual Meeting, 2008
- Garner. Combating unethical publications with plagiarism detection services. *Urol Oncol* 2011;29:95-9