COPE COMMITTEE ON PUBLICATION ETHICS

Fraud and Misconduct in Research

Sabine Kleinert,
Senior Executive Editor, *The Lancet*
Vice-Chair of the Committee on Publication Ethics

CHEIA, Annual Conference
Warwick, Sept 2008

- Definitions of Research Misconduct
- How big a problem is it?
- Research Ethics vs Publication Ethics
- How to deal with misconduct
- How to prevent misconduct
- Role of editors, funders, and institutions
- Unsolved issues

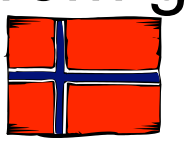
Definitions of Research Misconduct

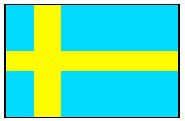
Different bodies/countries, different definitions

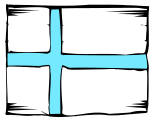
For example, http://ori.dhhs.gov

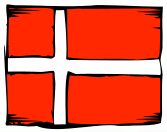
- **"Fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results."**
- **in 2000 added: "serious deviation and intention"**

Definitions of Research Misconduct

"serious deviations from good scientific practice " - Norway 

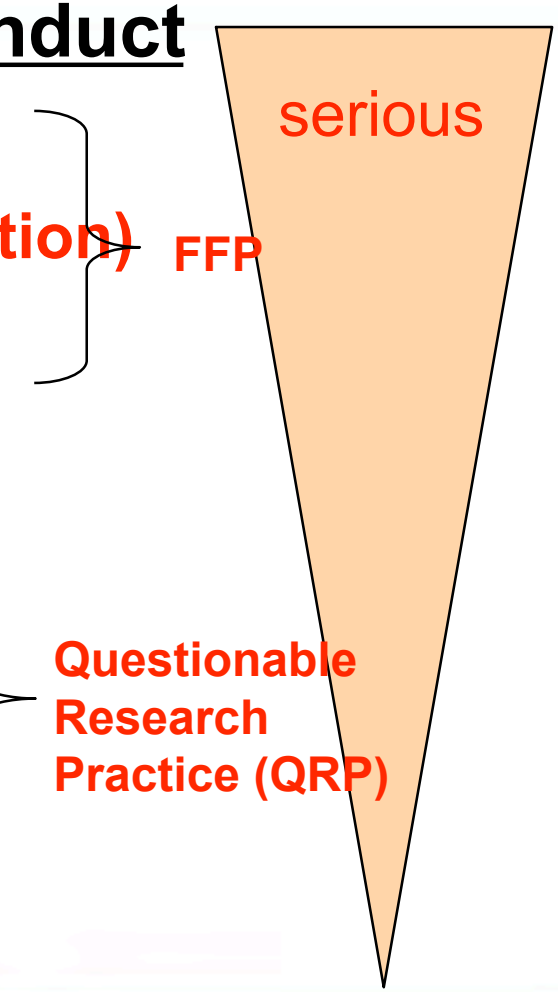
"intentional distortion of the research process" - Sweden 

"violation of good scientific practice" - Finland 

"acts which falsify or distort the scientific message" - Denmark 

Definitions of Research Misconduct

- Fabrication of data or cases
- Wilful distortion of data (Falsification)
- Plagiarism
- No ethics approval
- Not admitting missing data
- Ignoring outliers
- No data on side effects
- Gift authorship
- Redundant publication
- Inadequate literature search



How big a problem is it?

THIS WEEK

NEWS

PAGE 1668 Connecting the senses

1669 Better view for U.K. science

SCIENTIFIC MISCONDUCT

How Prevalent Is Fraud? That's a Million-Dollar Question

Charles Turner still doesn't know whether his experience was like finding a rare bad apple in the barrel. But he is sure that there was something rotten in the survey data going into his federally funded study of sexual behavior. And he knows that it has taken him 2 years to pluck out the spoiled fruit and piece together a clean report for

collection manager who was troubled by the apparent overproductivity of one interviewer. A closer look revealed that the worker was faking results; the address of one interview site, for example, turned out to be an abandoned house. The worker was dismissed, and others came under suspicion.

After "a horrible 6 months" pulling apart

don't discuss the issue. And the incident never became public, he says, because no one was ever publicly accused of wrongdoing and the institute chose to avoid the risk of litigation.

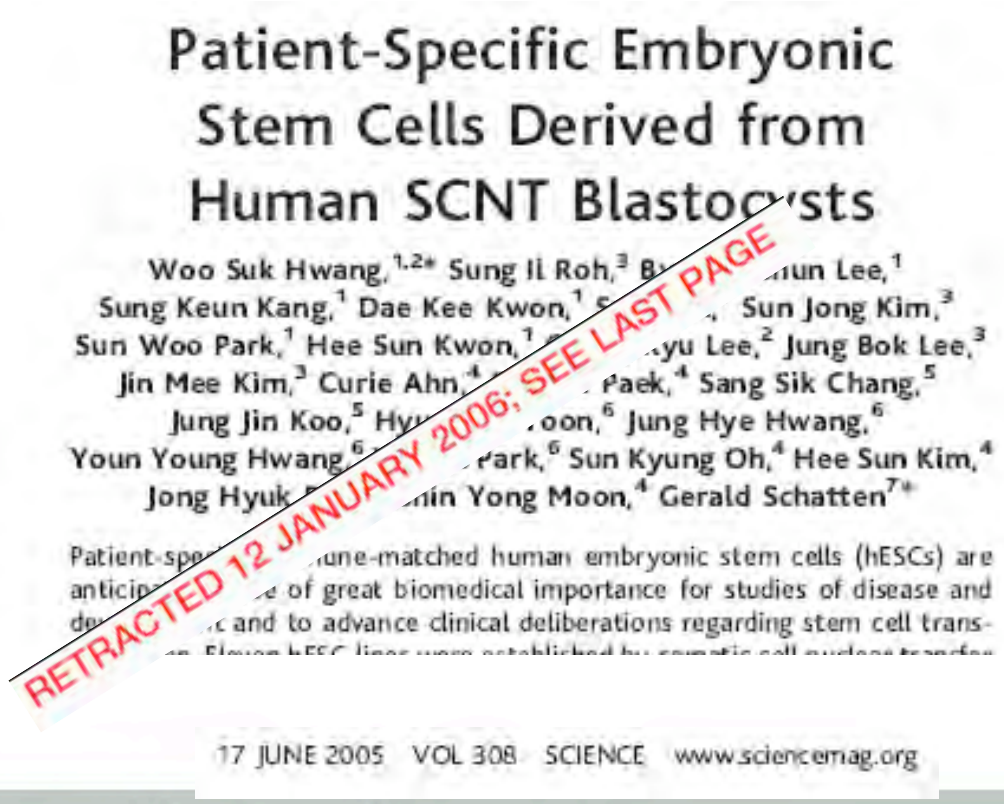
How often does misconduct like this occur? There appears to be no consensus on the answer, although science historian Nicholas Steneck of the University of Michigan, Ann Arbor, co-chair of the conference, has drawn up a range of estimates. At the low end is an estimate of 1 fraud per 100,000 scientists per year. That's based on 200 official federal cases that fit a narrow definition that counts only fraud, data fabrication, and plagiarism, out of a community

ZABETH W. DAVIDSON ET AL.

How big a problem is it? –

a few high-profile rogue cases?

Hwang Woo-Suk,
South Korea, 2005



Patient-Specific Embryonic Stem Cells Derived from Human SCNT Blastocysts

Woo Suk Hwang,[1,2*] Sung Il Roh,[3] B... ...un Lee,[1]
Sung Keun Kang,[1] Dae Kee Kwon,[1] S... Sun Jong Kim,[3]
Sun Woo Park,[1] Hee Sun Kwon,[1] ...yu Lee,[2] Jung Bok Lee,[3]
Jin Mee Kim,[3] Curie Ahn,[4] ... Paek,[4] Sang Sik Chang,[5]
Jung Jin Koo,[5] Hy... ...oon,[6] Jung Hye Hwang,[6]
Youn Young Hwang,[6] ... Park,[6] Sun Kyung Oh,[4] Hee Sun Kim,[4]
Jong Hyuk ... ...in Yong Moon,[4] Gerald Schatten[7*]

Patient-spe... ...une-matched human embryonic stem cells (hESCs) are anticip... ...e of great biomedical importance for studies of disease and de... ...c and to advance clinical deliberations regarding stem cell trans-

RETRACTED 12 JANUARY 2006; SEE LAST PAGE

17 JUNE 2005 VOL 308 SCIENCE www.sciencemag.org

How big a problem is it? –

How big a problem is it?

Documented cases	**1 in 10 000**
Know of an undisclosed case	**1-13 in 100**
Major deviation found in audit	**1 in 10**
Misrepresentations in fellowship applications	**1 in 5**
Students willing to fake data	**1 in 2**

First ORI research conference, Nov 18-20, 2000

How big a problem is it?

Sandra Titus, James A Wells, Lawrence J Rhoades
Repairing research integrity

Nature **453:** 980-2

Of 2212 researchers, 192 (8.7%) described that they had observed or had direct evidence of research misconduct in a total of 265 incidents (64 did not meet the ORI definition).

120 fabrication or falsification, 73 plagiarism, 8 unknown.

Amounts to 3 incidents per 100 researchers per year, or more than 2300 observations of potential misconduct by DHHS-funded researchers per year (ORI deals with only about 24)

How big a problem is it? –

Research misconduct vs Publication misconduct

→ big overlap

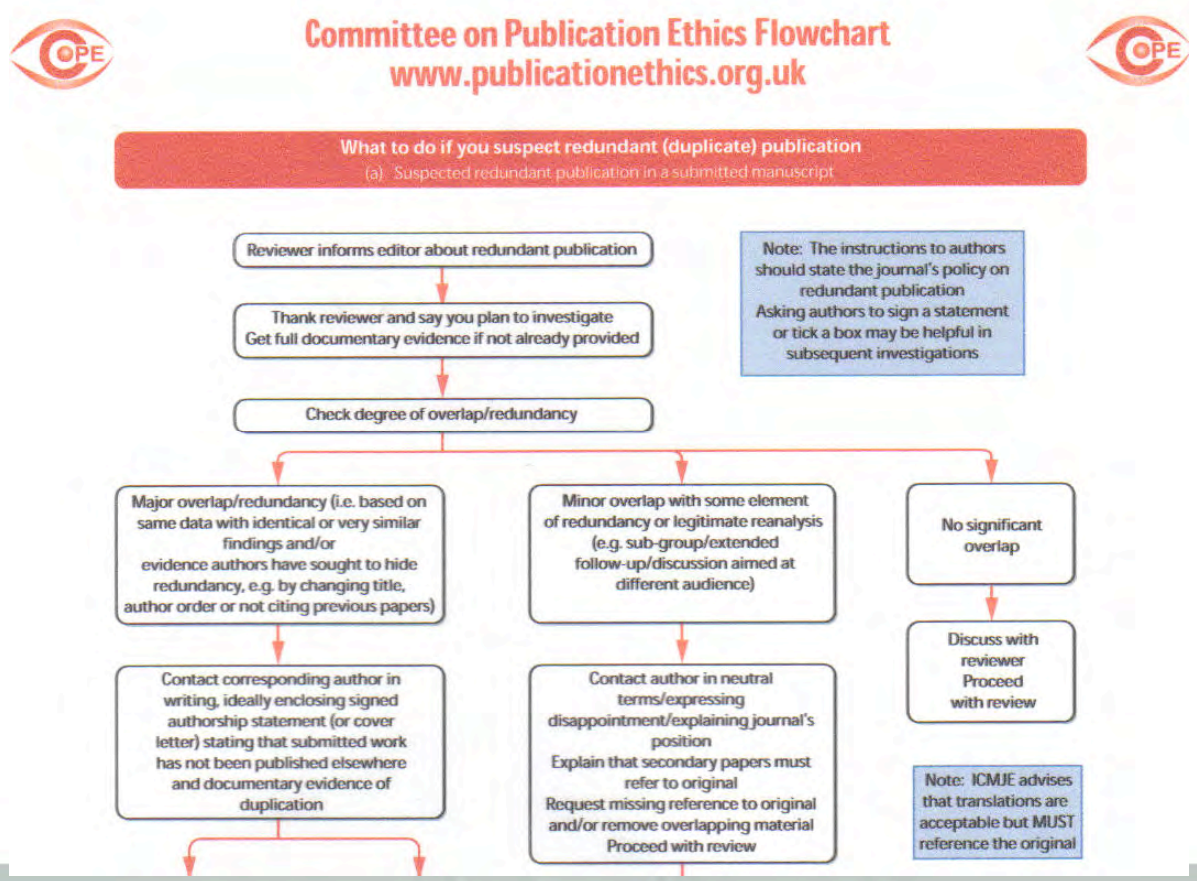
Any research misconduct once published becomes publication misconduct

Publication misconduct (ie duplicate publication, redundant publication) influences research and clinical practice

COPE's experience

- started in 1997 as "self-help" group of editors (Richard Smith, Richard, Horton, Mike Farthing) and about 60 members, now a registered charity with over 6000 members
- 4 meetings a year (Council and Forum)
- anonymous discussion of suspected misconduct cases
- advice to editors on how to proceed
- cases (and outcomes if available) on website
- annual conferences
- Code of Conduct and Best Practice Guidelines for Editors
- flowcharts on how to handle common misconduct scenarios

COPE's flowcharts



COPE's experience

Year	No of cases	"Evidence of misconduct"	"Probably no misconduct"	Not applicable
1997-2000	108	87	11	10
2001	39	30	9	0
2002	18	14	4	0
2003	22	15	5	2
2004	39	26	8	5
2005	24	21	3	0
2006	35	26	5	4
Total	285	219	45	21

COPE's experience

• Duplicate/redundant publication	77
• No ethics approval	34
• Authorship issues	31
• No or inadequate informed consent	30
• Falsification or fabrication	28
• Plagiarism	26
• Unethical research or clinical malpractice	19
• Undeclared conflict of interest	15
• Reviewer misconduct	8
• Editorial misconduct	6
• (miscellaneous	41)

COPE's experience

Of 285 cases, 172 (60%) pre-publication
95 (33%) post-publication

How to deal with misconduct?

Common difficulties for editors

- Time consuming!
- No reply from authors
- No reply from head of institutions
- Inadequate investigation by institution
- No institution
- Managing/analysing raw data
- What to do, if alleged misconduct is unproven

How to deal with misconduct (institutions/investigating body)?

Don't ignore!

Due process

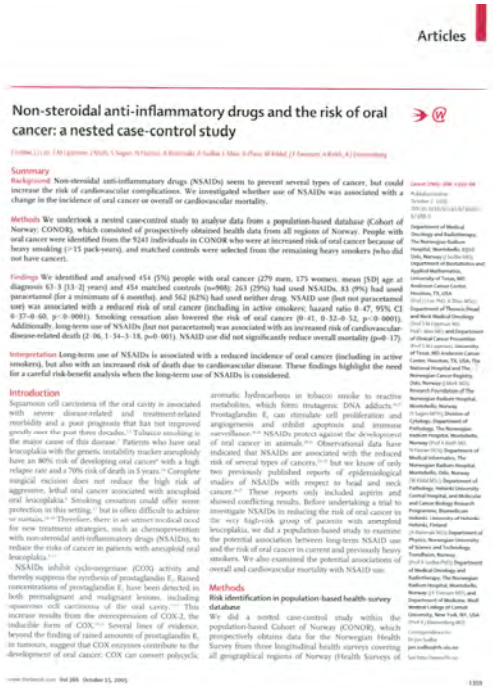
Fair and speedy investigation (publish results), ideally independent

Inform all relevant stakeholders (journals, funders...etc)

Protection of whistleblowers

Appropriate sanctions and consequences

Case: The case of Jon Sudbø



Articles

Non-steroidal anti-inflammatory drugs and the risk of oral cancer: a nested case-control study

Summary

Background Non-steroidal anti-inflammatory drugs (NSAIDs) seem to prevent several types of cancer, but could increase the risk of cardiovascular complications. We investigated whether use of NSAIDs was associated with a change in the incidence of oral cancer or overall or cardiovascular mortality.

Methods We undertook a nested case-control study to analyse data from a population-based database (Cohort of Norway: CONOR), which consisted of prospectively obtained health data from all regions of Norway. People with oral cancer were identified from the 9241 individuals in CONOR who were at increased risk of oral cancer because of heavy smoking (>15 pack-years), and matched controls were selected from the remaining heavy smokers (who did not have cancer).

Findings We identified and analysed 454 (5%) people with oral cancer (279 men, 175 women; mean (SD) age at diagnosis 63·3 [13·2] years) and 454 matched controls (n=908). 263 (29%) had used NSAIDs, 83 (9%) had used paracetamol (for a minimum of 6 months), and 562 (62%) had used neither drug. NSAID use (but not paracetamol use) was associated with a reduced risk of oral cancer (including in active smokers; hazard ratio 0·47, 95% CI 0·37–0·60, p<0·0001). Smoking cessation also lowered the risk of oral cancer (0·41, 0·32–0·52, p<0·0001). Additionally, long-term use of NSAIDs (but not paracetamol) was associated with an increased risk of cardiovascular-disease-related death (2·06, 1·34–3·18, p=0·001). NSAID use did not significantly reduce overall mortality (p=0·17).

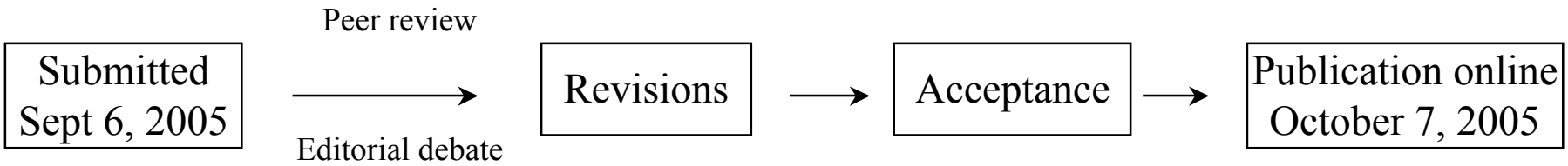
Interpretation Long-term use of NSAIDs is associated with a reduced incidence of oral cancer (including in active smokers), but also with an increased risk of death due to cardiovascular disease. These findings highlight the need for a careful risk-benefit analysis when the long-term use of NSAIDs is considered.

Introduction

Methods

- Nested case-control study
- 454 cases (oral cancer): 454 controls
- NSAID use: Hazard ratio oral cancer = 0.47 (95% CI 0.37-0.60)
- NSAID use: Hazard ratio CV death = 2.06 (95% CI 1.34-3.18)

What happened?



KREFTBLØFFEN

AVSLØ

av statsministere

– Jeg så med en gang at dette måtte være feil.

Meget godt ryktе

Forsker diktet opp data – mottok 70 mill. i støtte

Utorstæig

- January 13, 2006: the story broke

- A chance discovery:

The Ekbom Commission

Expression of concern: Jan 21, 2006

Retraction: February 4, 2006

- Swift, thorough, independent investigation
- Report published
- Lessons learnt

Case: The case of Hannes Strasser

Articles

Autologous myoblasts and fibroblasts versus collagen for treatment of stress urinary incontinence in women: a randomised controlled trial

Hannes Strasser, Rainer Marksteiner, Eva Margreiter, Germar Michael Pinggera, Michael Mitterberger, Ferdinand Frauscher, Hanno Ulmer, Martin Fussenegger, Kurt Kofler, Georg Bartsch

Summary

Background Preclinical studies have suggested that transurethral injections of autologous myoblasts can aid in regeneration of the rhabdosphincter, and fibroblasts in reconstruction of the urethral submucosa. We aimed to compare the effectiveness and tolerability of ultrasonography-guided injections of autologous cells with those of endoscopic injections of collagen for stress incontinence.

Methods Between 2002 and 2004, we recruited 63 eligible women with urinary stress incontinence. 42 of these women

Lancet 2007; 369: 2179–86

See Comment page 2139

Department of Urology (H Strasser MD, G M Pinggera MD, M Mitterberger MD, K Kofler PhD, Prof G Bartsch MD),

- 42 women randomly assigned to injections of autologous myoblasts and 21 to collagen for stress urinary incontinence
- At 12 months, 38/42 completely continent vs 2/21 in controls

The case of Hannes Strasser

- paper published after peer review on June 30, 2007
- Lancet contacted by University's Rector and members of ethics committee with concerns
- DoE published correcting CoIs, funding source, and affiliations of some authors Feb, 2008
- Lancet is being made aware of investigation by Government Body following a court case and a parliamentary question
- Expression of concern issued by Lancet May 3

The case of Hannes Strasser

- report by Austrian Government Agency for Health and Food Safety concludes in Aug, 2008

- serious irregularities in study conduct including Consent procedure, data documentation, Patient insurance….etc

- doubts as to whether study as described ever existed

The case of Hannes Strasser

Coauthors distance themselves from paper claiming only honorary authorship

Rector of University dismissed by University governing body for allegedly unrelated reasons on Aug 21

Paper retracted by Lancet on Sept 6


nature

Case not closed

Scandalous behaviour

"Austria, is a small country, and networks between power-brokers are small and tight. But something, it seems, is rotten in the state of Austria, and it needs to be faced and dealt with openly."

Lancet Editorial on role and responsibilities of coauthors, accompanying the retraction:

"Coauthors abrogating responsibility is a recurrent theme in serious research misconduct cases…. Requiring signed statements on contributions is not enough to ensure that coauthors take responsibility for a study's integrity as well as basking in the glory of a high-profile publication with all its associated credit."

difficulties

- Took a reasonably long time
- Report is subject to Austria's officials' Secret Act and not made public
- University reacts defensively
- ??whistleblower dismissed

BUT: Austria is now thinking about setting up a national body to deal with research misconduct cases

How to prevent misconduct - journals/editors

- Only indirect influence
- Reporting standards (CONSORT, STROBE...etc)
- Promote honesty and transparency
  - Protocols, ethics approval, trial registration
  - contributor statements/guarantor
  - conflict of interest/role of sponsor
- Editorials/commentaries

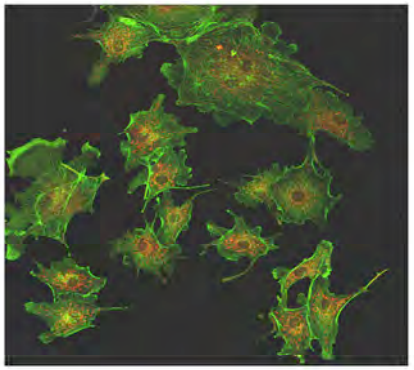
How to prevent misconduct - journals/editors

<u>?? Screening</u>

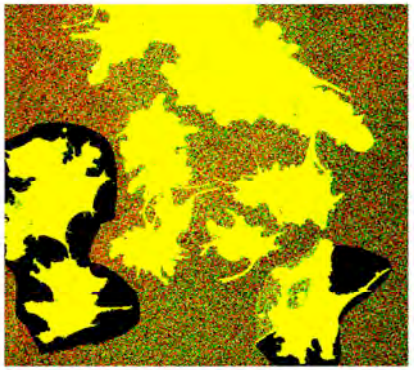
- for plagiarism
- Figure manipulation

Figure 6

Manipulated image



Manipulation revealed by contrast adjustment



Rossner M, Yamada KM *J Cell Biol* 2004: **166: 11-15.**

How to prevent misconduct - institutions

- Guidelines covering ALL aspects of research (but with clear consequences)
- Education (all researchers, including professors and students)
- Central documentation of protocols
- Central documentation/storage of raw data
- Random checks/audit
- Clear and transparent policies (CoI, intellectual property)

COPE COMMITTEE ON PUBLICATION ETHICS

THE LANCET

HIGHER EDUCATION FUNDING COUNCIL FOR ENGLAND hefce

???Role of editors, funders, and institutions

And how can we work together???

National Institutes of Health
The Nation's Medical Research Agency

wellcome trust

MRC Medical Research Council

Leading science for better health

www.publicationethics.org.uk

Unsolved issues

- Collaborative research (disciplines/institutions/countries – who is responsible?
- Does minor misconduct lead to major misconduct
- Is pressure to publish having an influence?
- Are commercially funded studies more or less likely to lead to misconduct?
- Which preventive actions work?
- Are international bodies needed to deal with research integrity?