How can good publication standards influence research integrity

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First World Conference on Research Integrity
Lisbon, September 2007
Why does it matter?

- Journal reputation
- **Science and medical journals**: safeguarding the public record – new research builds on published research
- **Medical journals**: patients may be harmed or misinformed! (research misconduct = public health issue)
Why does it matter?

Public trust in research

67 retractions in MEDLINE in 2005
97, in 2006

What is worse..... many continue to be cited (or included in systematic reviews) after retraction
What is journals’ and editors’ role in:

- Being part of the problem
- Detecting misconduct
- Reacting to misconduct
- Preventing misconduct
- Fostering integrity
• What is happening to research integrity (pressure to publish)?

• Was there anything journals/editors could have done to prevent publication in these high-profile cases?

• Should editors have more stringent rules and be less trusting?

• Would it actually help?
Research misconduct - definitions

- 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
- Failure to do adequate literature search
COPE

- started in 1997 as “self-help” group of editors
- 4 meetings a year
- anonymous discussion of suspected misconduct cases
- advice to editors on how to proceed
- cases (and outcomes if available) documented on website
- Guidelines on Good Publication Practice
- annual conferences and reports
Summary of COPE cases
1997-2006
<table>
<thead>
<tr>
<th>Year</th>
<th>No of cases</th>
<th>“Evidence of misconduct”</th>
<th>“Probably no misconduct”</th>
<th>Not applicable</th>
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<tr>
<td>1997-2000</td>
<td>108</td>
<td>87</td>
<td>11</td>
<td>10</td>
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<td>2001</td>
<td>39</td>
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<td>0</td>
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<td>2003</td>
<td>22</td>
<td>15</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>2004</td>
<td>39</td>
<td>26</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
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<tr>
<td>2006</td>
<td>35</td>
<td>26</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>285</strong></td>
<td><strong>219</strong></td>
<td><strong>45</strong></td>
<td><strong>21</strong></td>
</tr>
</tbody>
</table>
Problems/dilemmas discussed (n=285)*

- 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)

*More than one possible
Of 285 cases, 172 (60%) pre-publication, 95 (33%) post-publication.
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?
since 2001 elected Chair, Vice-Chair, Treasurer, and Council (12 members)

2005, Code of Conduct for Editors
**Code of Conduct for Editors**

Calls on editors to take seriously their role as guardians of the research record.

Sets out minimum standards of good editorial conduct.

COPE members must abide by it.
2006, COPE flowcharts as practical guides for editors
COPE future

- Will become a charity (end of 2007)
- Strengthen role in education
  - Distance-learning for editors (COPE-accredited editors)
  - Workshops for editors
- Improved website
  - Publication ethics blog
  - Letter templates for editors
  - Bulletin/newsletter
- PR strategy
COPE members (August 2007)

282 members (with over 300 journals signed up) from 29 countries:

Argentina, Australia, Belgium, Brazil, Canada, China, Croatia, Denmark, Finland, France, Germany, Iceland, India, Iran, Iraq, Ireland, Italy, Japan, New Zealand, Norway, Romania, Serbia, Singapore, Sweden, the Netherlands, Turkey, UK, USA, and Venezuela
Case examples

• Case 1: Plagiarism in foreign-language journal (+authorship issues)

• Case 2: Data fabrication (Jon Sudbø)
Case 1: plagiarism in foreign language
Case 1:

• Paper retracted

• Difficulties:
  – A number of authors very senior respected Norwegian researchers
  – Some on IAB of Norwegian Medical Journal
  – Some clearly not very familiar with content of paper (?authorship)
Case 2: The case of Jon Sudbø

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


Summary
Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are thought to prevent several types of cancer, but could increase the risk of cardiovascular complications. We investigated whether use of NSAIDs was associated with an increase in the incidence of oral cancer as well 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 national 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 (7%) people with oral cancer (279 men, 175 women; mean [SD] age at diagnosis 63 [13] years) and 184 matched controls (n=452). 261 (59%) had used NSAIDs, 83 (37%) had never used NSAIDs, and 10 (4%) had been prescribed (for a minimum of 6 months). 562 (68%) had used nonsteroidal drug. NSAID use (but not nonsteroidal use) was associated with a reduced risk of oral cancer [including in active smokers]: hazard ratio oral cancer = 0.47 (95% CI 0.37-0.60; p=0.0001). Smoking cessation also lowered the risk of oral cancer (4.81; 0.32-0.52; p=0.0001).

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: Squamous cell carcinoma of the oral cavity is associated with disease-related and treatment-related mortality and a poor prognosis that has not improved greatly over the past three decades. Tobacco smoking is the major cause of this disease. Patients who have oral leukoplakia with the genetic immunosuppression virus have an 80% risk of developing oral cancer with a 5 year relative risk and a 70% risk of death in 5 years. Complete surgical excision does not reduce the high risk of aggressive, lethal oral cancer associated with oral leukoplakia. Smoking cessation could offer some protection in this setting, but is often difficult to achieve or sustain. Therefore, there is an urgent need for new treatment strategies, such as chemoprevention with non-steroidal anti-inflammatory drugs (NSAIDs), to reduce the risk of cancer in patients with atypical oral leukoplakia.

NSAIDs inhibit cyclooxygenase (Cox) activity and thereby suppress the synthesis of prostaglandins E. Increased concentrations of prostaglandin E2, the inflammatory factor of the COX, several lines of evidence, beyond the finding of elevated amounts of prostaglandins E, in tumours, suggest that Cox enzymes contribute to the development of oral cancer. COX can convert polystyrene

- 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)
January 13, 2006: the story broke

A chance discovery: how many people truly read the paper?
Committee on Publication Ethics

The Lancet’s sJefredaktør etter forskersvindelen
Krever svar fra alle forskerne

Is The Lancet more interested in great headlines than correct science?

How often are you being warned about flawed research?

Why didn’t you listen to your peer reviewers?
Dear Dr. Horton,

On behalf of the commission appointed by the University of Oslo and Rikshospitalet to investigate possible scientific misconduct by dr Jon Sudbo, I have the sad duty to inform you that the commission has concluded that the paper “Sudbo J, Lee JJ, Lippman SM, Mork J, Sagen S, Flaten N, Ristimäki A, Sudbo A. Non-steroidal anti-inflammatory drugs and the risk of oral cancer: a nested case-control study. Lancet, 2005 Oct 15-21;366(9494):1359-66” contains fabricated data and should in our opinion be retracted.

Yours sincerely,

Anders Ekbohm
Professor of Clinical Epidemiology

Expression of concern: January 21, 2006

Retraction: February 4, 2006
Summary of Sudbø case

From the left Mr. Sheldon Kozin, Dr. Richard Horton, Prof. Magne Nylenna, Prof. Anders Ekbom and Dr. Harvey Marcovitch (photo: Kfell Tjensvoll).

Michael
Publication Series of The Norwegian Medical Society

Research misconduct: learning the lessons
Magne Nylenna, Richard Horton (eds.)

www.publicationethics.org.uk
What can editors do?

• COPE – pursue misconduct, adhere to good publication standards
  COPE support for editors might facilitate response from authors/institutions

• Heightened vigilance, especially high-risk papers (public impact, collaborations, unexpected results, commercial interest, reviewers’ suspicion)
What can editors do?

- Insist on prospective trial registration
- Check protocol with submission
What can editors do?

- Ensure adherence to best reporting standards (CONSORT, STARD, STROBE.......etc) – oddities may be more apparent
What can editors do?

- Screening for:
  - Plagiarism (CrossCheck or similar)
  - Figure manipulation (J Cell Biol)

BUT: time-consuming and not fool-proof
What can editors do?

- Declared transparent policies on conflict of interest and role of sponsor (prior to peer review)

- Ask questions at submission stage (authors’ contributions, involvement of medical writer....etc)
What can editors do?

• Demand independent data monitoring for all studies

• Emphasise responsibility of ALL authors for data integrity!!
the future: hope or delusion?

If ALL journals, editors, and publishers were to declare openly and insist on good publication policies and standards combining vigilance with swift actions, we would have achieved a large step towards fostering research integrity.