



**Committee on Publication Ethics**

# **How can good publication standards influence research integrity**

Sabine Kleinert

Vice-Chair of COPE

Senior Executive Editor *The Lancet*

**First World Conference on Research Integrity**

**Lisbon, September 2007**

[www.publicationethics.org.uk](http://www.publicationethics.org.uk)

**Hendrik Schön, USA, 2002**



**Jon Sudbø,  
Norway, 2006**



**Hwang Woo-Suk,  
South Korea, 2005**



**Eric T Poehlman,  
Canada, 2005**



## 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**

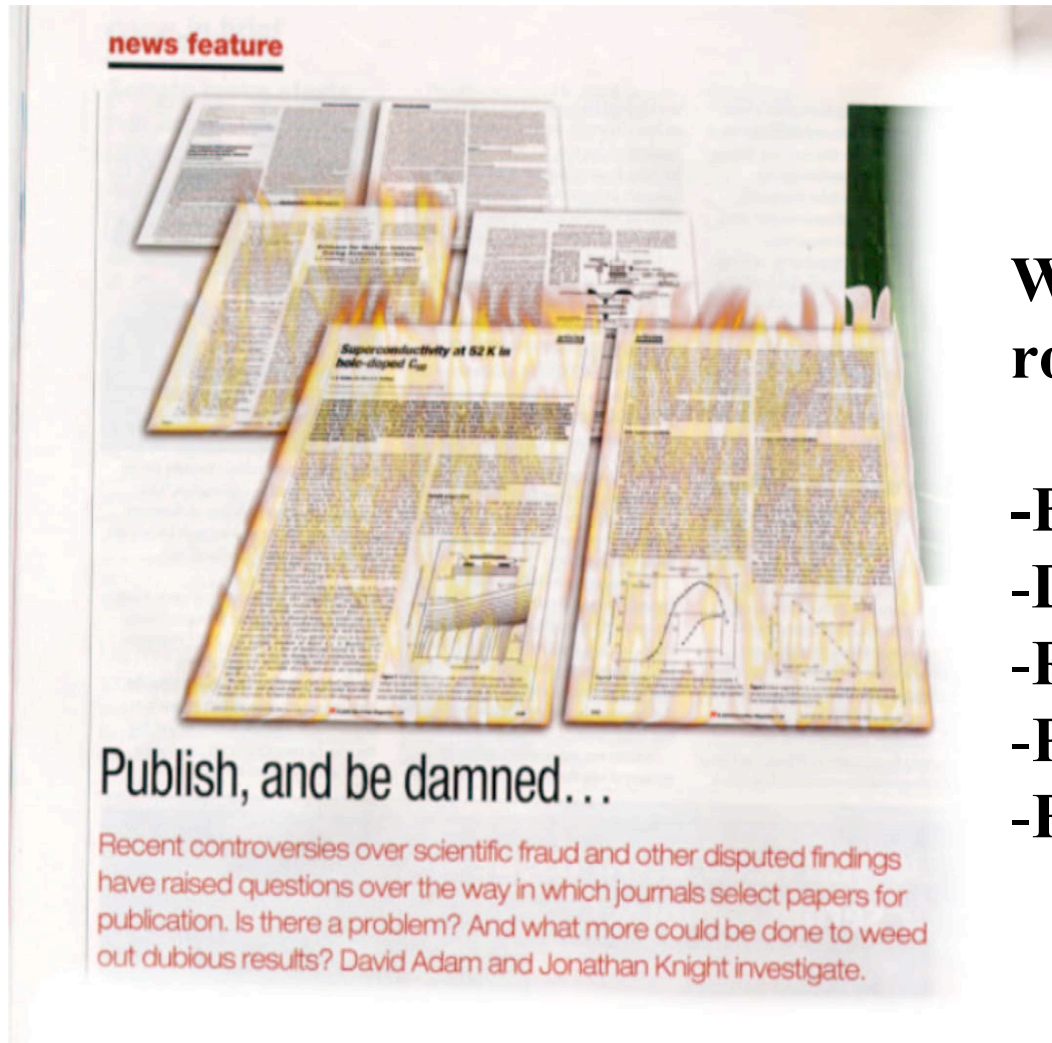
**67 retractions in MEDLINE in 2005**

**97, in 2006**

**What is worse..... many continue to be cited (or included in systematic reviews) after retraction**



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**What is journals' and editors' role in:**

- Being part of the problem**
- Detecting misconduct**
- Reacting to misconduct**
- Preventing misconduct**
- Fostering integrity**

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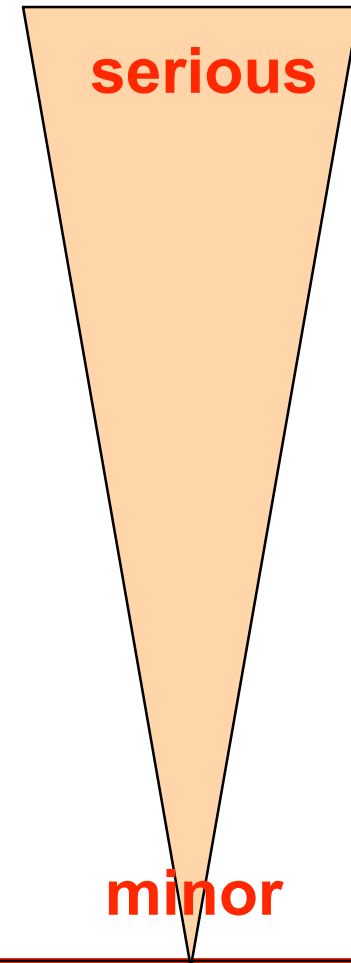
- **What is happening to research integrity (pressure to publish)?**
- **Was there anything journals/editors could have done to prevent publication in these high-profile cases?**
- **Should editors have more stringent rules and be less trusting?**
- **Would it actually help?**

[www.publicationethics.org.uk](http://www.publicationethics.org.uk)



## 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**





# Committee on Publication Ethics

## **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**

[www.publicationethics.org.uk](http://www.publicationethics.org.uk)



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**Summary of COPE cases  
1997- 2006**

[www.publicationethics.org.uk](http://www.publicationethics.org.uk)



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<b>Year</b>	<b>No of cases</b>	<b>“Evidence of misconduct”</b>	<b>“Probably no misconduct”</b>	<b>Not applicable</b>
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
<b>Total</b>	<b>285</b>	<b>219</b>	<b>45</b>	<b>21</b>

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## Problems/dilemmas discussed (n=285)\*



\*More than one possible



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

[www.publicationethics.org.uk](http://www.publicationethics.org.uk)



## 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?**



# Committee on Publication Ethics

- **since 2001 elected Chair, Vice-Chair, Treasurer, and Council (12 members)**
- **2005, Code of Conduct for Editors**

[www.publicationethics.org.uk](http://www.publicationethics.org.uk)



## **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**

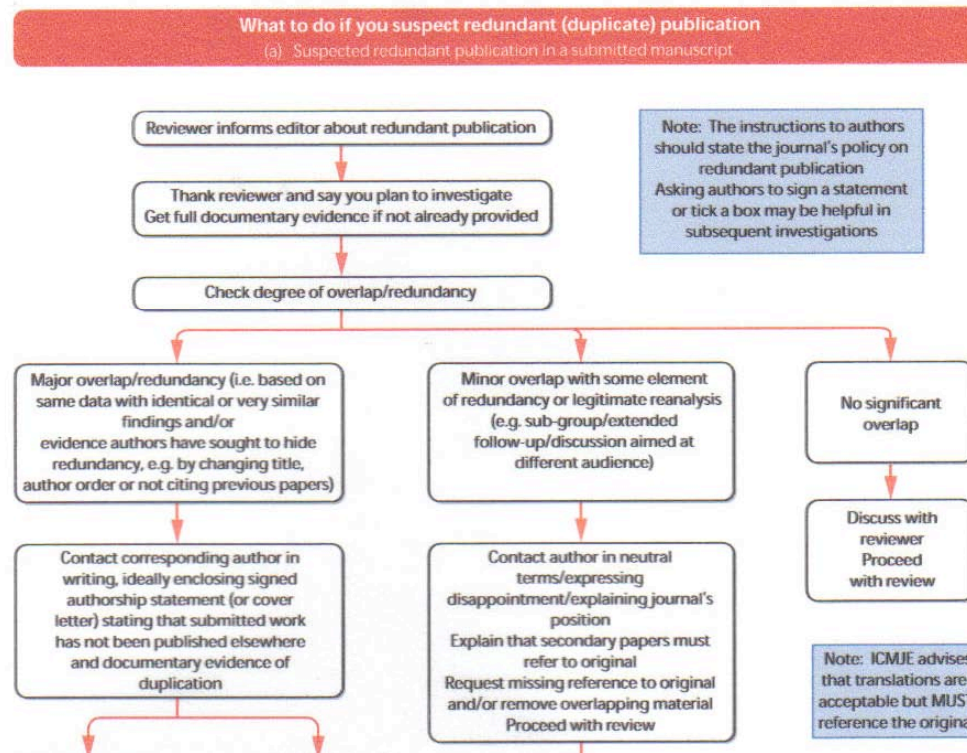


# Committee on Publication Ethics

## 2006, COPE flowcharts as practical guides for editors



### Committee on Publication Ethics Flowchart [www.publicationethics.org.uk](http://www.publicationethics.org.uk)



[www.publicationethics.org.uk](http://www.publicationethics.org.uk)



## 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

REVIEW

Review

### Management of acute optic neuritis

S J Hickman, C M Dalton, D H Miller, G T Plant

**Optic neuritis is a common condition that causes reversible loss of vision. It can be clinically isolated or can arise as one of the manifestations of multiple sclerosis. Occasional cases are due to other causes, and in these instances management can differ radically. The treatment of optic neuritis has been investigated in several trials, the results of which have shown that corticosteroids speed up the recovery of vision without affecting the final visual outcome. Other aspects of management, however, are controversial, and there is uncertainty about when to investigate and when to treat the condition. Here we review the diagnostic features of optic neuritis, its differential diagnosis, and give practical guidance about management of patients. The condition's association with multiple sclerosis will be considered in the light of studies that define the risk for development of multiple sclerosis and with respect to results of trials of disease-modifying drugs in these individuals.**

Optic neuritis is common, having an incidence of 1–5 per 100 000 per year.<sup>1–3</sup> The incidence is highest in caucasians,<sup>1</sup> in countries at high latitudes,<sup>2</sup> and in spring.<sup>3</sup> Individuals aged 20–49 years are most at risk, with women more often affected than men.<sup>2</sup> The condition usually presents as subacute unilateral loss of vision, although loss of vision in both eyes can arise, either simultaneously or sequentially. Most instances of optic neuritis are due to idiopathic inflammatory demyelination, which can arise in isolation, or as a manifestation of multiple sclerosis.<sup>4</sup>

Despite some major studies there are still many controversial areas in the management of optic neuritis, with differences of opinion expressed in surveys done to investigate the way the condition is managed.<sup>5,6</sup> In this Review, we discuss the diagnosis and management of optic

might be seen by the patient on eye movement.<sup>11</sup> Clearly, subclinical cases are frequent, since some patients present with Uhthoff's phenomenon (visual deterioration on getting warm, or during exercise),<sup>12</sup> and delayed visual evoked potentials are not uncommon in early multiple sclerosis, even without a previous history of optic neuritis.<sup>13</sup>

The maximum visual loss varies from minor blurring to no perception of light in the affected eye. Abnormal colour vision, reduced contrast sensitivity, visual field loss, and a relative afferent pupillary defect (RAPD) are usually present in the affected eye.<sup>4,10,14</sup> The presence of an RAPD is a useful objective sign of a unilateral optic neuropathy, although it is not specific for optic neuritis. The absence of an RAPD can indicate mild clinical involvement in the affected eye, previous optic neuritis in the contralateral

TRUKKET TILBAKE

ie Tidsskr Nor Lægeforen 2005; 125: 2056

Øversiktsartikkel MEDISIN OG VITENSKAP

### Optikusnevritt – diagnose, behandling og oppfølging

#### Sammendrag

**Bakgrunn.** Optikusnevritt er en vanlig tilstand som kan opptre isolert eller som en manifestasjon av multipel sklerose. Tilstanden er godt klinisk karakterisert, men differensialdiagnostisk vil mange tilstander måtte overveies. Behandling av optikusnevritt har vært undersøkt i flere studier. Disse viser at kortikosteroider bidrar til raskere restitusjon av synstyrken uten at den endelige synstyrken påvirkes vesentlig. Både diagnose og behandlingsmuligheter har endret seg i de senere år. Aspekter ved utredning, behandling og oppfølging er kontroversielle.

**Materiale og metode.** En nasjonal gruppe av nevrologer og øyeleger har vurdert retningslinjer for diagnose, behandling og oppfølging av optikusnevritt basert på egen klinisk erfaring og gjennomgåelse av relevante bokkapitler samt literatursøk i PubMed.

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#### Klinikk og sykdomsforløp

I ramme 1 skisseres de typiske symptomer og tegn ved optikusnevritt (11). Tilstanden viser seg som regel som en subakutt ensidig synsreduksjon med moderate smerter som aksentueres ved øybevegelser og progredierer i løpet av få dager til to uker (12). Smerteintensiteten er varierende, nattesøvn forstyrres vanligvis ikke, og en tidel rapporterer ingen smerte. Enkelte pasienter observerer lysglimt (fotopsier) ved øybevegelser. Noen pasienter fremviser Uhthoff's fenomen (synsreduksjon ved økt kroppstemperatur eller i tilknytning til fysisk anstrengelse). Forsinket visuelt fremkalt respons er heller ikke uvanlig å finne ved debut av multipel sklerose, noe som kan tyde på en tilsynelatende asymptomatisk optikusnevritt (13).

Den maksimale synsreduksjon varierer fra lett tåkesyn til manglende lyssans på affisert øye. Redusert fargesyn, redusert kontrastsensitivitet, synsfeltutfall og relativ afferent pupilldefekt i pupillrefleks ved belysning er vanligvis til stede i det affiserte øyet. Selv om ingen av disse funn isolert sett er spesifikk for optikusnevritt, gir de sammen



## 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

Articles

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

J Sudbø, J Lee, S M Lippman, J Mørk, S Sagen, N Flatner, A Ristimäki, A Sudbø, L Mao, X Zhou, W Kildal, J F Evensen, A Røith, A J Dannerberg

#### 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 ( $\geq 15$  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

Squamous cell carcinoma of the oral cavity is associated with severe disease-related and treatment-related morbidity and a poor prognosis that has not improved greatly over the past three decades.<sup>1,2</sup> Tobacco smoking is the major cause of this disease.<sup>3</sup> Patients who have oral leucoplakia with the genetic instability marker aneuploidy have an 80% risk of developing oral cancer<sup>4</sup> with a high relapse rate and a 70% risk of death in 5 years.<sup>5,6</sup> Complete surgical excision does not reduce the high risk of aggressive, lethal oral cancer associated with aneuploid oral leucoplakia.<sup>7</sup> Smoking cessation could offer some protection in this setting,<sup>8,9</sup> but is often difficult to achieve or sustain.<sup>10–12</sup> Therefore, there is an unmet medical need for new treatment strategies, such as chemoprevention with non-steroidal anti-inflammatory drugs (NSAIDs), to reduce the risks of cancer in patients with aneuploid oral leucoplakia.<sup>13</sup>

NSAIDs inhibit cyclo-oxygenase (COX) activity and thereby suppress the synthesis of prostaglandin E<sub>2</sub>. Raised concentrations of prostaglandin E<sub>2</sub> have been detected in both premalignant and malignant lesions, including squamous cell carcinoma of the oral cavity.<sup>14,15</sup> This increase results from the overexpression of COX-2, the inducible form of COX.<sup>16,17</sup> Several lines of evidence, beyond the finding of raised amounts of prostaglandin E<sub>2</sub> in tumours, suggest that COX enzymes contribute to the development of oral cancer. COX can convert polycyclic

aromatic hydrocarbons in tobacco smoke to reactive metabolites, which form mutagenic DNA adducts.<sup>18,19</sup> Prostaglandin E<sub>2</sub> can stimulate cell proliferation and angiogenesis and inhibit apoptosis and immune surveillance.<sup>20,21</sup> NSAIDs protect against the development of oral cancer in animals.<sup>22</sup> Observational data have indicated that NSAIDs are associated with the reduced risk of several types of cancers,<sup>23–25</sup> but we know of only two previously published reports of epidemiological studies of NSAIDs with respect to head and neck cancer.<sup>26,27</sup> These reports only included aspirin and showed conflicting results. Before undertaking a trial to investigate NSAIDs in reducing the risk of oral cancer in the very high-risk group of patients with aneuploid leucoplakia, we did a population-based study to examine the potential association between long-term NSAID use and the risk of oral cancer in current and previously heavy smokers. We also examined the potential associations of overall and cardiovascular mortality with NSAID use.

#### Methods

##### Risk identification in population-based health-survey database

We did a nested case-control study within the population-based Cohort of Norway (CONOR), which prospectively obtains data for the Norwegian Health Survey from three longitudinal health surveys covering all geographical regions of Norway (Health Surveys of



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See <http://www.thelancet.com>

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- **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)**



# Committee on Publication Ethics



•January 13, 2006:  
the story broke

•A chance discovery:  
how many people  
truly read the paper?

[www.publicationethics.org.uk](http://www.publicationethics.org.uk)



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**Aftenposten** JOBB & UTDANNING

Morgen, Tirsdag 17. januar 2006, Uke 3, Nr. 27, 142. årg. Nr. 75. Trykketross: Nord-Norge Nr. 28.

**- Gi en million pr. gullmedalje**

36 sider med råd, tips og inspirasjon for studenter og jobbsøkere.

**VIL ANMELDE LAKSEMINNENE**  
 Forbrukerklaget ber Mattilsynet om å politianmelde dem som har brukt nitritt i røkelaks. ØKONOMI • side 6

**SV KNEBLER SEG SELV OM OLJE**  
 Den store oljeforbruksgiganten har nektert seg over uønskede "vasspartikkel". Er egentlig 90% sålegrønn i Barentshavet? I et spørsmål der partiet har vært tildrende klart i årevis, er svarne nå uoversiktlige, vage eller ikke-eksisterende. Partisekretæren avviser innmeldt at han har pålegg de tillatte valgte miniskur i saken. DEL 1 • side 8

**MILD JANUAR- UKE HVERT ÅR**  
 Klimaforskere skal undersøke hvorfor det alltid er mildere en de andre måneder i januar. DEL 1 • side 6 og 7

RUBRIKKANNONSER - SE SIDE 2

## Første kvinne på topp i Afrika



Ellen Johnson-Sirleaf ble i går tatt i ed som president i Liberia, til stor jubel fra flere tusen fremmøtte i hovedstaden Monrovia. Landet ligger i vesten etter 34 år med borgerkrig, og statsmagnaten må gjenopbygges. Det er store forventninger til kvinnen, som også vil bekjempe korupsjonen. DEL 1 • side 14 og 15

## The Lancets sjefredaktør etter forskersvindelen

# Krever svar fra alle forskerne



«Vi kan aldri sikre oss helt mot svindel, sier redaktør Richard Horton i «The Lancet».

**KREFTBLØFFEN.** - Dette er den største svindelen fra en forsker verden noen gang har sett, sier Lancet-redaktør Richard Horton. Han mener det er ubegripelig at medforfatterne av den fabrikkerte kreftstudien ikke har visst noe. DEL 1 • side 2, 3, 4 og 5

**Det lønner seg å starte NÅ.** Verdi opp til **800,-**

Mange har allerede beryttet tilbudet. Du har fremdeles muligheten.

**Meldt du deg inn t.o.m 31. januar får du:**

- 12 måneders medlemskap til "gammat pris"
- Halve administrasjonsgebyret inn på din SATSkonto

Sjanger med tips og 12 måned medlemskap. Meld deg inn på SATSkonto. Spørsmål? Kaller oss på telefonnummeret 116 116 eller på nettsiden vår. Trening du har glede av

## Tough questions

- 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?



## **The Ekblom Commission**

**Expression of concern:** January 21, 2006

**Retraction:** February 4, 2006

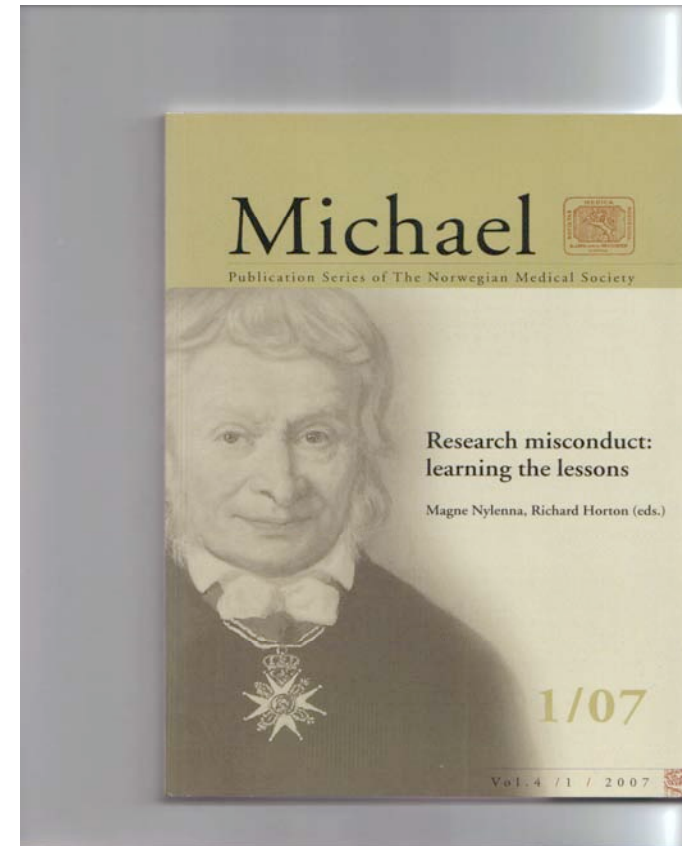


# Committee on Publication Ethics

## Summary of Sudbø case



*From the left Mr. Sheldon Kotzin, Dr. Richard Horton, Prof. Magne Nylenna, Prof. Anders Ekbohm and Dr. Harvey Marcovitch (photo: Kjell Tjensvoll).*





## 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**