Frauds in science

- The „Jon Sudbø case”-
Jon Sudbø
Jon Sudbø

- born on May 3, 1961
- Norwegian dentist / physician / oral surgeon
- renowned researcher in the field of oncology
  - articles in NEJM, Journal of Clinical Oncology (IF=18.4), The Lancet, Journal of Pathology, etc.
- associate professor @ University of Oslo
  - until 2006
- consultant oncologist @ Radium Hospital
  - until 2006
Non-steroidal anti-inflammatory drugs and the risk of oral cancer: a nested case-control study

Background

• Squamous cell carcinoma
  – Poor prognosis
  – Major cause: tobacco smoking (and alcohol)
  – High risk for patients with oral leucoplakia & aneuploidy
    • 5-years survival $\rightarrow$ 30%
    • Surgical resection $\rightarrow$ no reduction of high risk

(...), “NEED FOR NEW TREATMENT STRATEGIES“(...)

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Background

• Cyclooxygenase-2 and prostaglandin-E2
  – Biological role:
    • cell proliferation
    • Angiogenesis
    • Immune stimulation
  – involved in various malignacities
    • E.g. squamous cell carcinoma

• NSAIDs → inhibition of Cyclooxygenase-2 & prostaglandin-E2
  – Reduction of risk to develop cancer in animal models
  – Few epidemiological data
Materials and Methods
- Overview -

• „Population-based case-control study“

  – Data from: Cohort of Norway (CONOR)
    • Longitudinal health surveys
      – Standardised questionnaires, detailed clinical information on participants, ...
    • 123,345 „active“ participants

Crosslinked with

  – Data from disease registries, e.g. Norwegian Cancer Registry

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Materials and methods

• Detailed information on
  – age
  – sex
  – risk factors for head and neck cancer
  – Treatment drug use
    • Type and duration of NSAID use
  – Survival
  – etc.

• All data obtained from „central registers“
  – Participants from CONOR and Norwegian Cancer Registry
  – Survival data \(\rightarrow\) „National death certificate registry“
  – Detailed information on prescriptions \(\rightarrow\) „central registry“
  – etc.
Materials and Methods

- Norwegian Health Survey (n=123,234)

- 9,241 individuals identified to be at high risk of oral cancer (≥15 pack-years)

- Survey cross-linked with Norwegian Cancer Registry: Population-based, complete since 1953

- Of 9,241 individuals at high risk, 454 with oral cancer identified after cross-linking

- From remaining 8,787 individuals, 454 matched controls without oral or any other type of cancer identified from Norwegian Health Survey

- Study sample (n=908): 454 cases with oral cancer; 454 controls without oral cancer
Materials and methods

“(…)The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication. (…)“
Results

• total: n=908
  – oral cancer cases: n=454
    • tongue: n=157
    • floor or mouth: n=149
    • other: n=148
  – high risk controls: n=454
    • without oral SCC

• 29% NSAIDs and 9 % paracetamol intake (>6 months)
## Results

<table>
<thead>
<tr>
<th></th>
<th>Cases (n=454)</th>
<th>Controls (n=454)</th>
<th>Total (n=908)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At time of oral cancer or last follow-up</td>
<td>63.3 (13.2)</td>
<td>63.3 (13.2)</td>
<td>63.3 (13.2)</td>
</tr>
<tr>
<td></td>
<td>(10.1)²</td>
<td>(10.1)²</td>
<td>(10.1)²</td>
</tr>
<tr>
<td>At death or last follow-up</td>
<td>70.4 (10.7)</td>
<td>70.4 (10.7)</td>
<td>70.4 (10.7)</td>
</tr>
<tr>
<td></td>
<td>(10.9)²</td>
<td>(10.9)²</td>
<td>(10.9)²</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>279 (61%)</td>
<td>279 (61%)</td>
<td>558 (61%)</td>
</tr>
<tr>
<td>Female</td>
<td>175 (39%)</td>
<td>175 (39%)</td>
<td>350 (39%)</td>
</tr>
<tr>
<td><strong>Tobacco smoking</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of cigarettes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–20 cigarettes/day</td>
<td>186 (41%)</td>
<td>189 (42%)</td>
<td>375 (41%)</td>
</tr>
<tr>
<td></td>
<td>(10.7)²</td>
<td>(10.9)²</td>
<td>(10.7)²</td>
</tr>
<tr>
<td>21–30 cigarettes/day</td>
<td>166 (37%)</td>
<td>153 (34%)</td>
<td>319 (35%)</td>
</tr>
<tr>
<td></td>
<td>(10.1)²</td>
<td>(10.1)²</td>
<td>(10.1)²</td>
</tr>
<tr>
<td>31–40 cigarettes/day</td>
<td>76 (17%)</td>
<td>81 (18%)</td>
<td>157 (17%)</td>
</tr>
<tr>
<td></td>
<td>(10.8)²</td>
<td>(10.8)²</td>
<td>(10.8)²</td>
</tr>
<tr>
<td>&gt;40 cigarettes/day</td>
<td>26 (6%)</td>
<td>31 (7%)</td>
<td>57 (6%)</td>
</tr>
<tr>
<td></td>
<td>(9.8)²</td>
<td>(9.8)²</td>
<td>(9.8)²</td>
</tr>
<tr>
<td><strong>Pack-years</strong></td>
<td>43.0 (14.8)</td>
<td>39.0 (14.7)</td>
<td>41.0 (14.8)</td>
</tr>
<tr>
<td><strong>Alcohol</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>24 (5%)</td>
<td>30 (7%)</td>
<td>54 (6%)</td>
</tr>
<tr>
<td>1–5 units/week</td>
<td>154 (38%)</td>
<td>166 (36%)</td>
<td>320 (36%)</td>
</tr>
<tr>
<td>&gt;5 units/week</td>
<td>194 (43%)</td>
<td>199 (44%)</td>
<td>393 (43%)</td>
</tr>
<tr>
<td>No information</td>
<td>72 (16%)</td>
<td>60 (13%)</td>
<td>132 (15%)</td>
</tr>
<tr>
<td><strong>Drug type used</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>5 (17%)</td>
<td>9 (41%)</td>
<td>26 (12%)</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>13 (38%)</td>
<td>39 (38%)</td>
<td>52 (37%)</td>
</tr>
<tr>
<td>Naproxen</td>
<td>16 (43%)</td>
<td>39 (44%)</td>
<td>55 (37%)</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>15 (41%)</td>
<td>47 (41%)</td>
<td>62 (37%)</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>17 (38%)</td>
<td>36 (39%)</td>
<td>53 (39%)</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>11 (38%)</td>
<td>17 (38%)</td>
<td>28 (39%)</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>48 (11%)</td>
<td>35 (5%)</td>
<td>83 (9%)</td>
</tr>
<tr>
<td><strong>Length of NSAID use (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>10 (41%)</td>
<td>21 (42%)</td>
<td>31 (12%)</td>
</tr>
<tr>
<td>5–10</td>
<td>22 (44%)</td>
<td>25 (42%)</td>
<td>47 (18%)</td>
</tr>
<tr>
<td>10–15</td>
<td>26 (38%)</td>
<td>61 (37%)</td>
<td>87 (33%)</td>
</tr>
<tr>
<td>&gt;15–26</td>
<td>19 (37%)</td>
<td>79 (37%)</td>
<td>98 (37%)</td>
</tr>
</tbody>
</table>

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• Use of NSAIDs & paracetamol

  – reduced risk of oral cancer
    • NSAIDs → reduced risk even for heavy smokers (>40 pack years)

  – no association with overall survival

  – some NSAIDs → increased risk for cardiovascular-disease-related death
„non-NSAID users”
### Univariate analysis

<table>
<thead>
<tr>
<th></th>
<th>Number (%) of cardiovascular-disease-related deaths</th>
<th>Total number of people</th>
<th>HR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals who had not used NSAIDs</td>
<td>41 (7%)</td>
<td>562</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Individuals who had used NSAIDs</td>
<td>42 (16%)</td>
<td>263</td>
<td>2.06 (1.34–3.18)</td>
<td>0.001</td>
</tr>
<tr>
<td>Aspirin</td>
<td>2 (14%)</td>
<td>14</td>
<td>1.16 (0.28–4.80)</td>
<td>0.84</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>12 (23%)</td>
<td>52</td>
<td>2.86 (1.50–5.45)</td>
<td>0.001</td>
</tr>
<tr>
<td>Naproxen</td>
<td>7 (13%)</td>
<td>55</td>
<td>1.70 (0.76–3.79)</td>
<td>0.20</td>
</tr>
<tr>
<td>Indometacin</td>
<td>10 (16%)</td>
<td>62</td>
<td>2.26 (1.13–4.52)</td>
<td>0.02</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>7 (13%)</td>
<td>52</td>
<td>1.84 (0.82–4.11)</td>
<td>0.14</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>4 (14%)</td>
<td>28</td>
<td>1.90 (0.68–5.31)</td>
<td>0.22</td>
</tr>
<tr>
<td>Individuals who had used paracetamol</td>
<td>4 (5%)</td>
<td>83</td>
<td>0.51 (0.18–1.42)</td>
<td>0.20</td>
</tr>
</tbody>
</table>

### Multicovariate analysis

<table>
<thead>
<tr>
<th></th>
<th>...</th>
<th>...</th>
<th>2.05 (1.33–3.16)</th>
<th>0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAID use</td>
<td>...</td>
<td>...</td>
<td>0.50 (0.18–1.40)</td>
<td>0.18</td>
</tr>
<tr>
<td>Paracetamol use</td>
<td>...</td>
<td>...</td>
<td>1.02 (0.65–1.60)</td>
<td>0.93</td>
</tr>
<tr>
<td>Smoking pack-years (&lt;40 or ≥40)</td>
<td>...</td>
<td>...</td>
<td>1.13 (0.72–1.77)</td>
<td>0.60</td>
</tr>
<tr>
<td>Quit smoking (yes or no)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>
Discussion

• advantages vs. disadvantages by long-term NSAIDs and paracetamol intake
  – cancer risk vs. cardiovascular risk

  – promising results especially in high-risk groups
    • more acceptable than in low-risk groups?
    • tantamount to cancer therapy?
„Bad luck“

Christmas 2005

- Camilla Stoltenberg (head of Norwegian Institute of Public Health AND sister of Prime Minister of Norway)

  - found it suspicious that

  the database - mentioned in the article - was supposed to open at the beginning of 2006
„Bad luck“

• C.S. started „digging“ and found out that

250 of the patients had birthday on the same day

Report in "Dagbladet"
The fraud

Stein Vaaler, director of strategy @ Radium Hospital:

(...)“He faked everything: names, diagnosis, gender, weight, age, drug use. There is no real data whatsoever, just figures he made up himself. Every patient in this paper is a fake“ (...)
The fraud

• some days later, Sudbo has acknowledged that:

“he has faked at least two more papers”
(published in NEJM and Journal of Clinical Oncology)

an independent Commission of Inquiry led by Prof. Anders Ekbom, started further investigation
The fraud

30 June of 2006
report of the commission:

15 of his articles were fraudulent,
incl. his doctoral dissertation
Consequences

- Retraction of several fraudulent articles
Consequences

• Resigned from all university-based positions in 2006
• Revocation of the license to practice medicine and dentistry 2006
• Revocation of the doctoral thesis in 2006
Effects of fraud

• massive critics on University of Oslo & Radium hospital
  – lack of control → faked dissertation(!)

• Norway’s scientific reputation
  – some projects granted by U.S. National Cancer Institute

• effects on co-authors
  – although not involved, massive effects on reputation
Today

• 2009 → grant of restricted authorizations to practice dentistry
  – Head of Seljord Dental Clinic
    (Telemark fylkeskommune, Norway)

• prohibition of involvement in research
Interesting

• wife and brother → co-authors

• no knowledge of the fabrication!
Interesting

• key-role of sister of Norwegian Prime Minister

• two weeks after announcement

new law: medical fraud as criminal act, „Norway as first country“
Questions?
References

• **Case Summary: Sudbo, Jon:** DEPARTMENT OF HEALTH AND HUMAN SERVICES, Office of the Secretary, Findings of Scientific Misconduct, [http://ori.hhs.gov/content/case-summary-sudbo-jon](http://ori.hhs.gov/content/case-summary-sudbo-jon)


• https://www.timeshighereducation.com/features/cleaning-up-the-act/403288.article

• [http://www.naturalnews.com/019353_medical_ethics_stem_cell_research.html](http://www.naturalnews.com/019353_medical_ethics_stem_cell_research.html)

• **Research misconduct: lessons to be learned?** by Magne Nylenna, **Professor of community medicine**
  Department of Public Health and General Practice Norwegian University of Science and Technology