Ankersmit Laboratory

for Diagnosis & Regeneration in Thoracic Diseases & Applied Immunology

MEDIZINISCHE UNIVERSITÄT WIEN

Frauds in science

- The „Jon Sudbø case”-

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MEDIZINISCHE UNIVERSITÄT WIEN

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

The paper

THE LANCET
Volume 366, Issue 9494, 15–21 October 2005, Pages 1359–1366

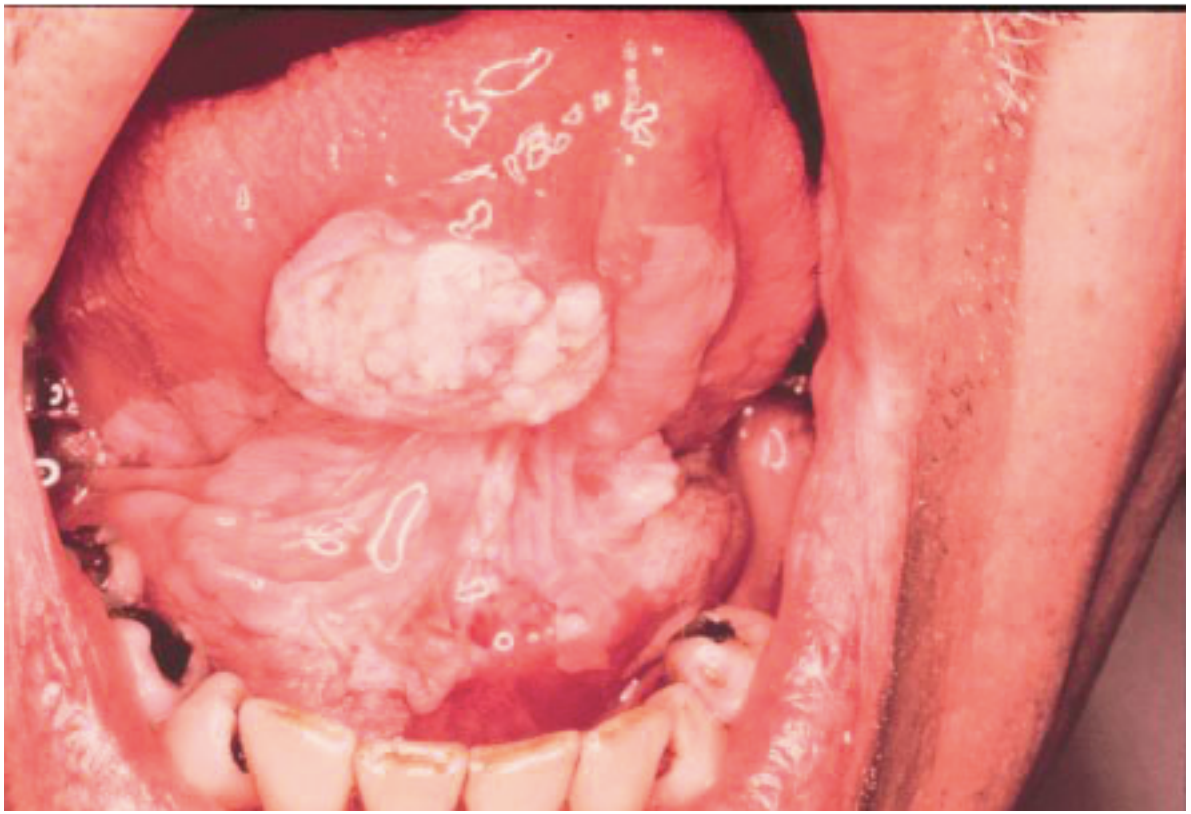
Non-steroidal anti-inflammatory drugs and the risk of oral cancer: a nested case-control study

J Sudbø, J J Lee, S M Lippman, J Mork, S Sagen, N Flatner, A Ristimäki, A Sudbø, L Mao, X Zhou, W Kildal, J F Evensen, A Reith, A J Dannenberg

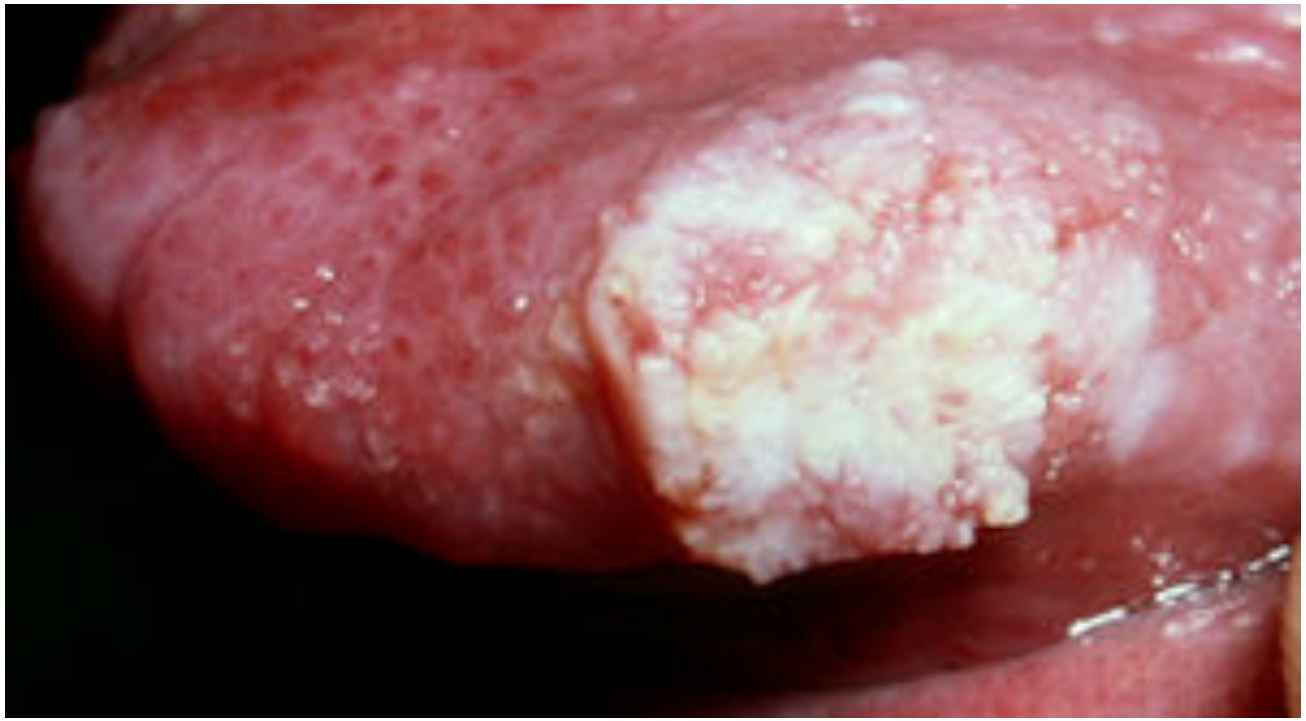
Background

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

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



http://www.merckmanuals.com/professional/ear,-nose,-and-throat-disorders/tumors-of-the-head-and-neck/oral-squamous-cell-carcinoma



http://www.drbicuspid.com/user/images/content_images/nws_rad/2009_05_19_12_22_42_314_2009_05_21_squamous_cell_carcinoma.jpg

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
  - Reducton of risk to develope cancer in animal models
  - Few epidemiological data

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Materials and Methods - Overview -

- „Population-based case-control study“
  - Data from: Cohort of Norway (**CONOR**)

    - Longitudinal health surveys
      - Standardised questionneries, detailed clinical information on participants, ...
    - 123.234 „active“ participants

<u>Crosslinked</u> with

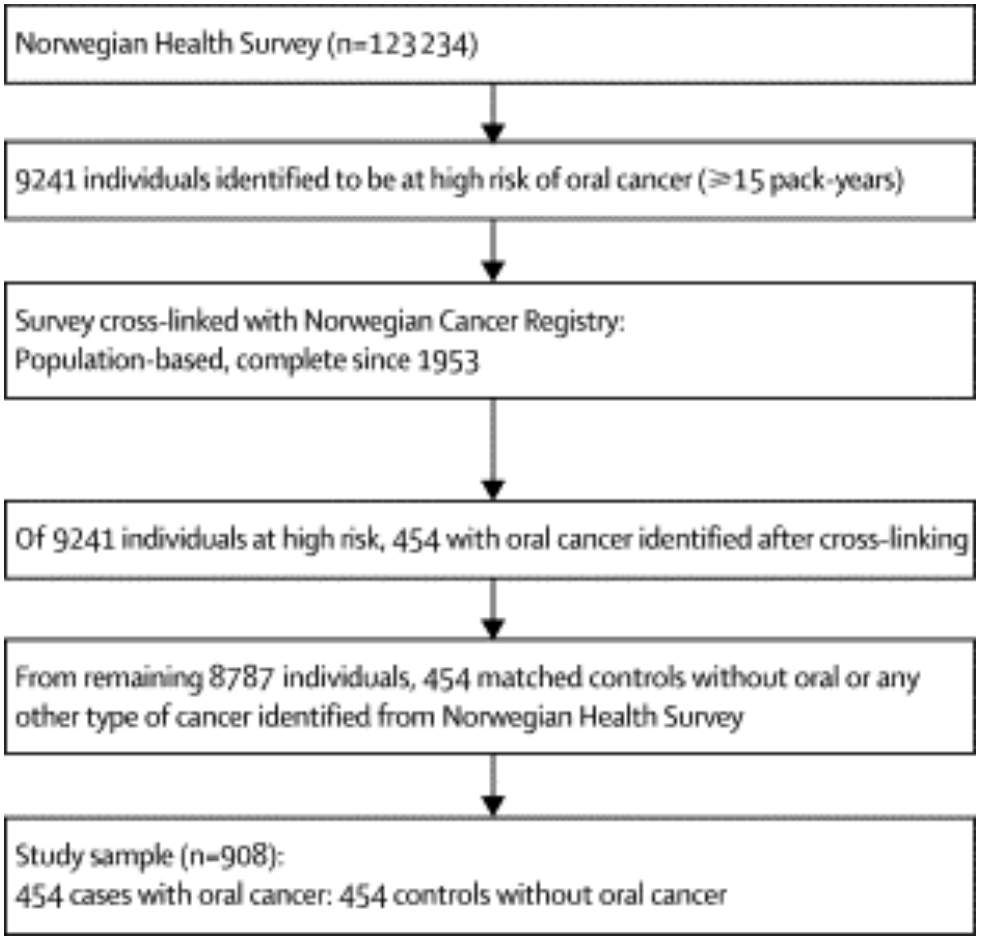
  - Data from disease registries, e.g. Norwegian Cancer Registy

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 → „National death certificate registry“
  - Detailed information on prescriptions → „central registry“
  - etc.

Materials and Methods



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)

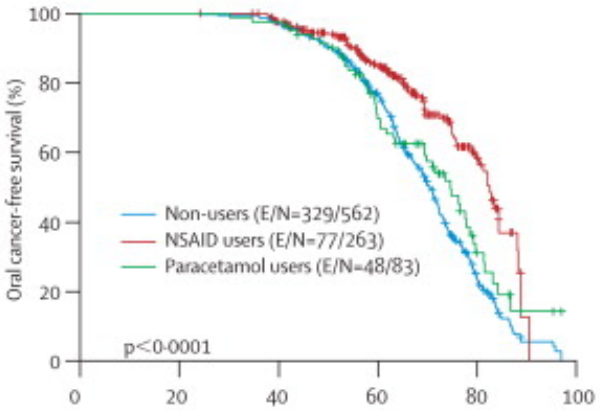
Results

	Cases (n=454)	Controls (n=454)*	Total (n=908)
Age (years)†			
At time of oral cancer or last follow-up	63·3 (13·2)	63·3 (13·2), 73·6 (10·1)‡	63·3 (13·2), 68·4 (12·8)‡
At death or last follow-up	70·4 (10·7), 71·9 (10·9)‡	70·4 (10·7), 73·6 (10·1)‡	70·4 (10·7), 72·8 (10·5)‡
Sex			
Male	279 (61%)	279 (61%)	558 (61%)
Female	175 (39%)	175 (39%)	350 (39%)
Tobacco smoking			
Number of cigarettes			
15–20 cigarettes/day	186 (41%)	189 (42%)	375 (41%)
21–30 cigarettes/day	166 (37%)	153 (34%)	319 (35%)
31–40 cigarettes/day	76 (17%)	81 (18%)	157 (17%)
>40 cigarettes/day	26 (6%)	31 (7%)	57 (6%)
Pack-years	43·0 (14·6)	39·0 (14·7)	41·0 (14·8)
Alcohol			
Never	24 (5%)	30 (7%)	54 (6%)
1–5 units/week	164 (36%)	165 (36%)	329 (36%)
>5 units/week	194 (43%)	199 (44%)	393 (43%)
No information	72 (16%)	60 (13%)	132 (15%)
Drug type used			
NSAID	77 (17%)	186 (41%)	263 (29%)
Aspirin	5	9	14
Ibuprofen	13	39	52
Naproxen	16	39	55
Indometacin	15	47	62
Piroxicam	17	35	52
Ketoprofen	11	17	28
Paracetamol	48 (11%)	35 (8%)	83 (9%)
Length of NSAID use (years)			
<5	10	21	31 (12%)
5–10	22	25	47 (18%)
10–15	26	61	87 (33%)
⩾15–26	19	79	98 (37%)

Results

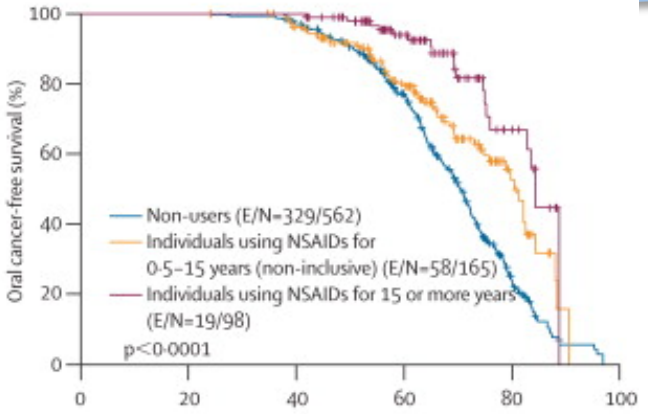
- Use of NSAIDs & paracetamol
  - reduced risk of oral cancer
    - NSAIDs → reduced risk even for heavy smokers (>40 pack years)
  - no association with overall survival
  - some NSAIDs → increased risk for cardiovascular-disease-related death

A



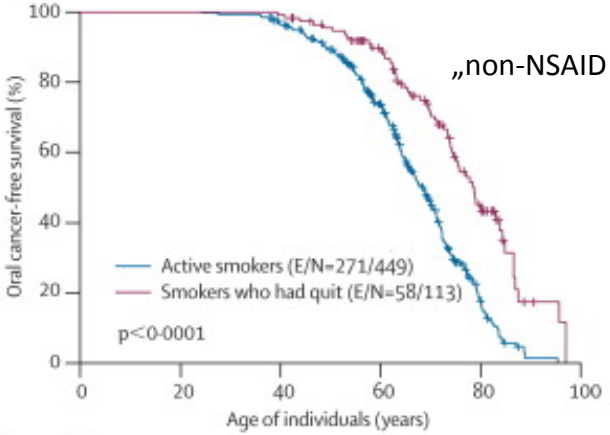
Numbers at risk				
Non-users	562	531	351	50
NSAID users	263	249	162	33
Paracetamol users	83	80	49	11

B



Numbers at risk				
Non-users	562	531	351	50
Individuals using NSAIDs for 0·5–15 years (non-inclusive)	165	151	98	18
Individuals using NSAIDs for 15 or more years	98	98	64	15

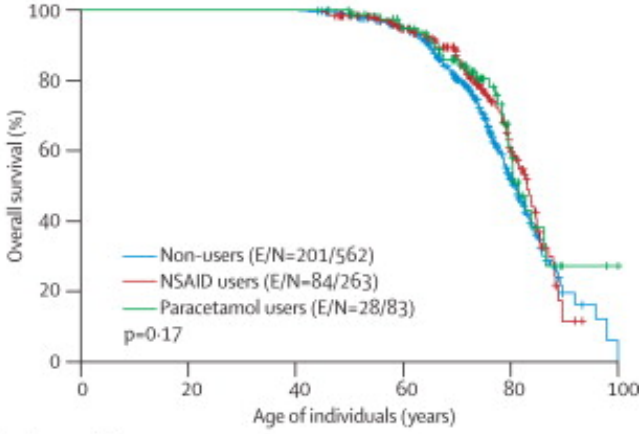
C



„non-NSAID users“

Numbers at risk				
Active smokers	449	419	263	26
Smokers who had quit	113	112	88	24

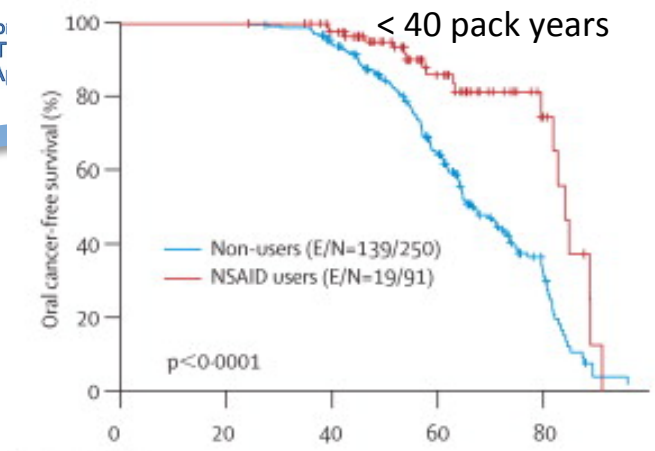
D



Numbers at risk				
Non-users	562	562	460	98
NSAID users	263	263	213	53
Paracetamol users	83	83	71	19

A

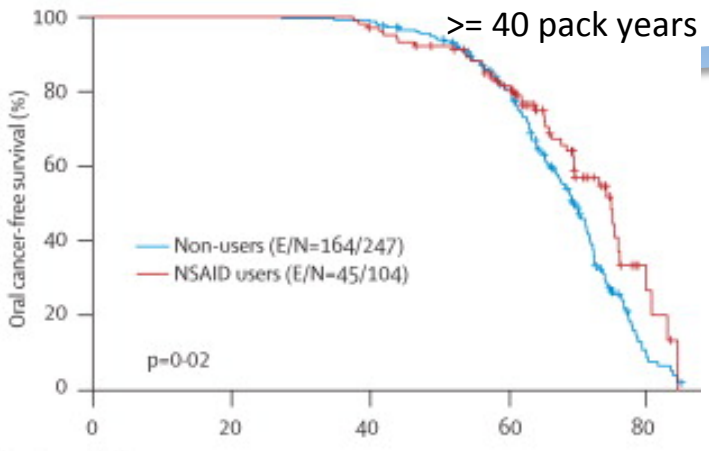
< 40 pack years



Numbers at risk				
Non-users	250	220	114	24
NSAID users	91	82	40	9

B

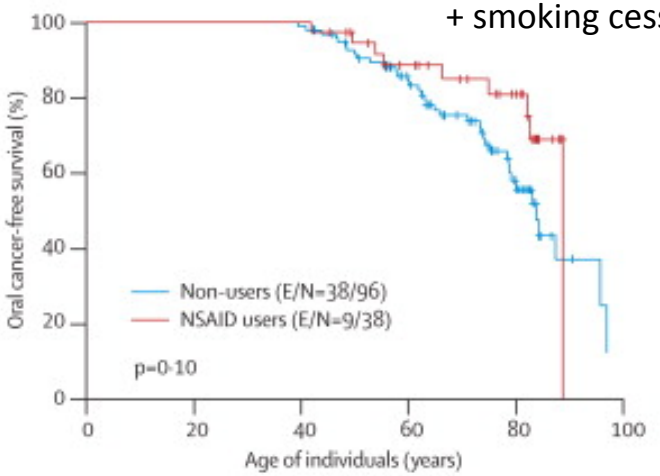
>= 40 pack years



Numbers at risk				
Non-users	247	244	174	8
NSAID users	104	100	69	4

C

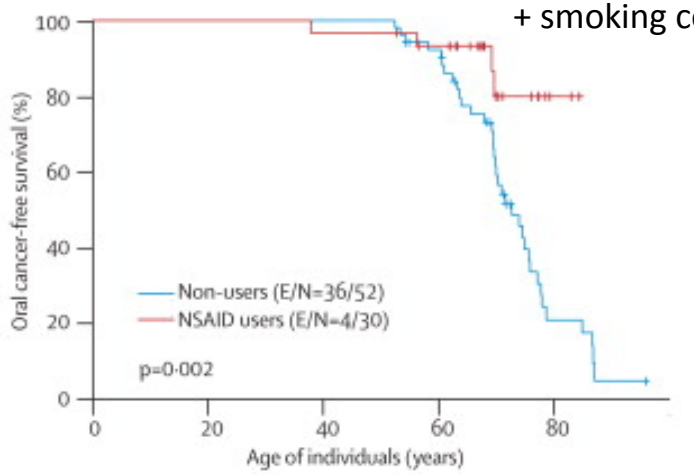
< 40 pack years
+ smoking cessation



Numbers at risk				
Non-users	96	95	67	23
NSAID users	38	38	27	17

D

>= 40 pack years
+ smoking cessation



Numbers at risk				
Non-users	52	52	45	6
NSAID users	30	29	26	3

	Number (%) of cardiovascular-disease-related deaths	Total number of people	HR (95% CI)	p
Univariate analysis				
Individuals who had not used NSAIDs	41 (7%)	562	..	..
Individuals who had used NSAIDs	42 (16%)	263	2·06 (1·34–3·18)	0·001
Aspirin	2 (14%)	14	1·16 (0·28–4·80)	0·84
Ibuprofen	12 (23%)	52	2·86 (1·50–5·45)	0·001
Naproxen	7 (13%)	55	1·70 (0·76–3·79)	0·20
Indometacin	10 (16%)	62	2·26 (1·13–4·52)	0·02
Piroxicam	7 (13%)	52	1·84 (0·82–4·11)	0·14
Ketoprofen	4 (14%)	28	1·90 (0·68–5·31)	0·22
Individuals who had used paracetamol	4 (5%)	83	0·51 (0·18–1·42)	0·20
Multicovariate analysis				
NSAID use	..	..	2·05 (1·33–3·16)	0·001
Paracetamol use	..	..	0·50 (0·18–1·40)	0·18
Smoking pack-years (<40 or ⩾40)	..	..	1·02 (0·65–1·60)	0·93
Quit smoking (yes or no)	..	..	1·13 (0·72–1·77)	0·60

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 whatsever, 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 <u>further investigation</u>

The fraud

30 June of 2006
report of the commission:

15 of his articles were **fraduelent**,
incl. his **doctoral dissertation**

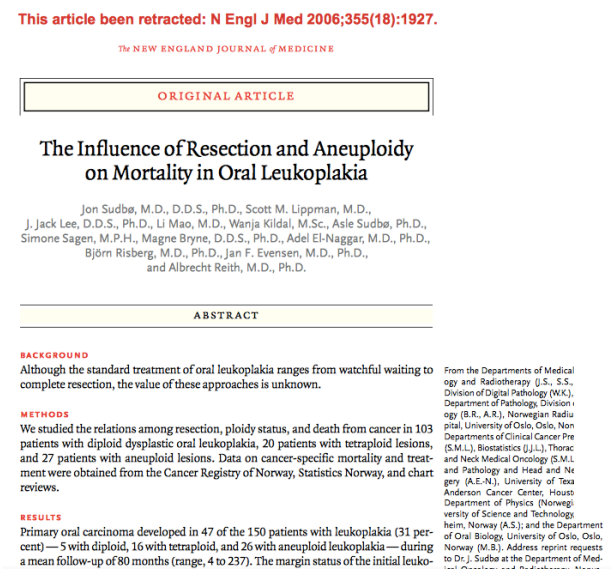
Consequenses

- Retraction of several fraudulent articles

Articles

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

RETRACTED

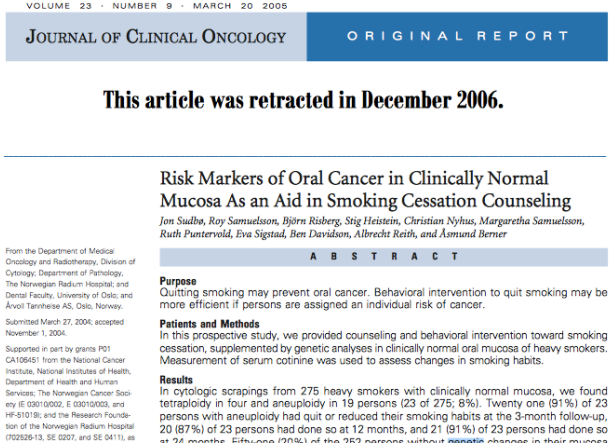


This article been retracted: N Engl J Med 2006;355(18):1927.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

The Influence of Resection and Aneuploidy on Mortality in Oral Leukoplakia



VOLUME 23 · NUMBER 9 · MARCH 20 2005

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

This article was retracted in December 2006.

Risk Markers of Oral Cancer in Clinically Normal Mucosa As an Aid in Smoking Cessation Counseling

Consequenses

- 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 controll → 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 involvation 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 announcment

↓

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://**www.the-scientist.com**/?articles.view/articleNo/25540/title/Norwegian-dentist-falsified-grant/
- https://**www.timeshighereducation.com**/features/cleaning-up-the-act/403288.article
- 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
  http://www.dnms.no/pdf/2007/1-7-9.pdf
- http://**www.hopkinsmedicine.org**/research/synergy/offices/OPC/Research_Integrity/Deans_Lectures_2011_2012/DeansRILecture6_02152012_Hruban.pptx.