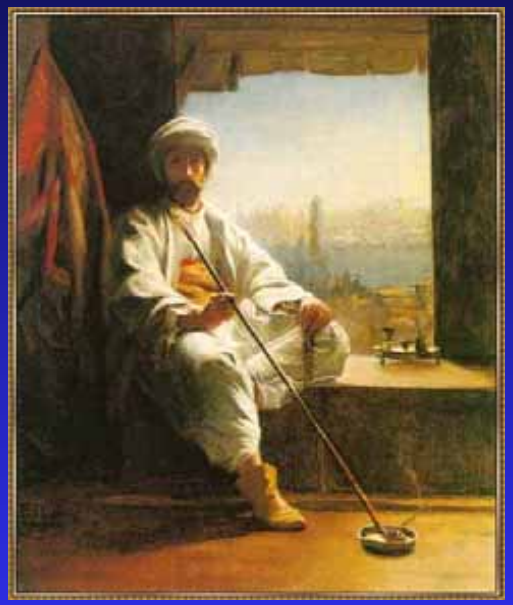
Impact of industrial marketing on decision making



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The physician-industry relationships

”The debate about these relationships revolves around the question of whether drug companies influence physicians` behavior and, if they do, whether the results are, on balance, positive or negative for the quality and cost of health care and for the profession of medicine itself”

Blumenthal. NEJM 2004

The physician-industry relationships

Physicians decision making may be influenced by:

- Grant support
- Consultants or advisory board membership
- Speaker at symposia
- Gifts or trips
- Patent or royalty agreements
- Equity interests

The physician-industry relationships

”Physicians should be sensitive to the possibility that the influence of the relationships may consciously, subconsciously or unconsciously affect their decision making”

Choudhry et al., JAMA 2002

The physician-industry relationships

A classic study has shown that most physicians (61%) believe that they are not influenced by detailers` gifts; however, they believe the same is true for only 16% of their colleagues

Chren. Am J Med 1999

Potential negative consequences of the relationship

- Influence on the prescribing pattern
- Influence on hospital formulary additions
- Influence on costs of drugs and medical device
- Diversion of drugs
- Publication of favorable articles
- Lack of publication of unfavorable articles
- Guest and ghost authorship
- Phase IV ”seeding” trials: Trials designed to promote the prescription of new drugs rather than to generate scientific data. Common trials in a therapeutic crowded field like the opioid market (”me-too drugs”)

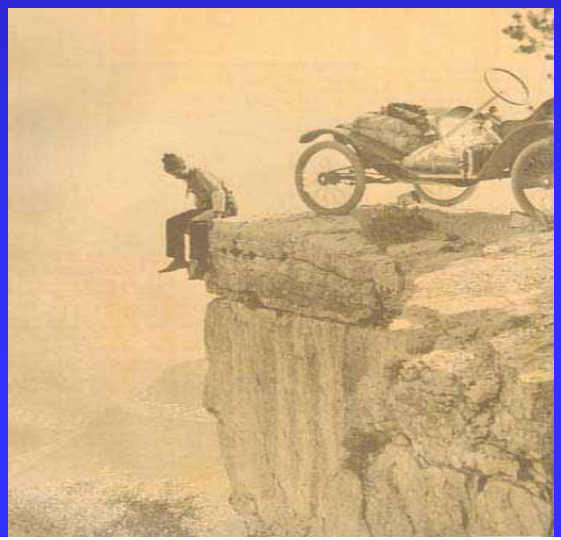
Chren. JAMA 1994
Stelfox et al. NEJM 1998

Friedberg et al. JAMA 1999
Warzana. JAMA 2000

Ghost authorship

”Ghost authorship has been defined as the failure to name, as an author, an individual who has made substantial contributions to the research or writing of the article”

Flanagin et al., JAMA 1998



Potential positive consequences of the relationship

- Financial support to research that is difficult to get from other sources
- Financial support to education that is difficult to get from other sources
- Financial support to scientific congresses
- Technical and knowledge support
- Physicians` influence on drug development
- Increase the dispensing of drugs that physicians underprescribe

Problems with the physician-industry relationships

- Undermine patient-centered medical ethics
- Undermine patients`confidence in the medical profession
- Jeopardize the physician-patient relationship
- Undermine public confidence in medical profession

General marketing figures from the U.S.

- In 2002 the industry expended 1/3 of its revenues on ”selling and administration”
- In 2001 there was one salesperson for every 4.7 physicians
- Ninety % of the effort aimed at physicians
- Direct-to-consumer advertising of prescription drugs increases dramatically in several countries
- Promotional meetings increased from 120,000 (1998) to 371,000 (2004)
- In 2004 pharmaceutical companies expended US$ 29.6 billion on research and development (RD) as compared to US$ 27.7 billion for all promotional activities
- In 2004 US$ 4.9 billion of RD activities was spent on phase IV trials. 75% of these were considered promotional trials

Blumenthal. NEJM 2004
Donohue et al., NEJM 2007
Gagnon and Lexchin. PloS Med 2008

General marketing figures from the U.S.

- The industry invests relatively little in new drugs
- 65% of new drugs introduced between 1989 and 2000 used active ingredients already on the market and 76% offered no significant benefit over already available products
- Much drug development involves new dosage forms or combinations of existing drugs

National Institute for Health Care Management. 2002

Cancer patients` share in a population`s use of opioids

Jarlbæk et al., J Pain Symptom Manage 2004

- Data on opioid prescriptions and cancer diagnoses from a Danish county (n=470.000) were retrieved from a prescription database and The Danish Cancer Registry (1993-1997)
- In a given year, 14% of the population`s opioid users were cancer patients
- Cancer patients used 23% of the total opioid consumption

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www.elsevier.com/locate/pain

Critical issues on opioids in chronic non-cancer pain: An epidemiological study

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Abstract

The aim of the study was epidemiologically to evaluate the long-term effects of opioids on pain relief, quality of life and functional capacity in long-term/chronic non-cancer pain. The study was based on data from the 2000 Danish Health and Morbidity Survey. As part of a representative National random sample of 16,684 individuals (>16 years of age), 10,066 took part in an interview and completed a self-administered questionnaire. Cancer patients were excluded. The interview and the self-administered questionnaire included questions on chronic/long-lasting pain (>6 months), health-related quality of life (SF-36), use of the health care system, functional capabilities, satisfaction with medical pain treatment and regular or continuous use of medications. Participants reporting pain were divided into opioid and non-opioid users. The analyses were adjusted for age, gender, concomitant use of anxiolytics and antidepressants and pain intensity. Pain relief, quality of life and functional capacity among opioid users were compared with non-opioid users. Opioid usage was significantly associated with reporting of moderate/severe or very severe pain, poor self-rated health, not being engaged in employment, higher use of the health care system, and a negative influence on quality of life as registered in all items in SF-36. Because of the cross-sectional nature causative relationships cannot be ascertained. However, it is remarkable that opioid treatment of long-term/chronic non-cancer pain does not seem to fulfil any of the key outcome opioid treatment goals: pain relief, improved quality of life and improved functional capacity.

Keywords: Epidemiology; Chronic non-cancer pain; Opioids; Quality of life; Functional capacity

Critical issues on opioids

Regular use of medicine	2000 Survey		
Variables	**Study population N = 10,666**	**Pain Group N = 1,871**	**Control Group N = 8,019**
Analgesics	**9%**	**30%**	**4%**
Non-opioids	**9%**	**30%**	**4%**
Opioids	**3%**	**12%**	**1%**
Weak	**2%**	**9%**	**1%**
Strong	**1%**	**3%**	**0%**
Anxiolytics	**1%**	**3%**	**1%**
Antidepressants	**2%**	**4%**	**2%**
No analgesics	**91%**	**70%**	**96%**

Opioid consumption in Denmark: The top five ”strong” and ”weak” opioids (1.000 DDD)

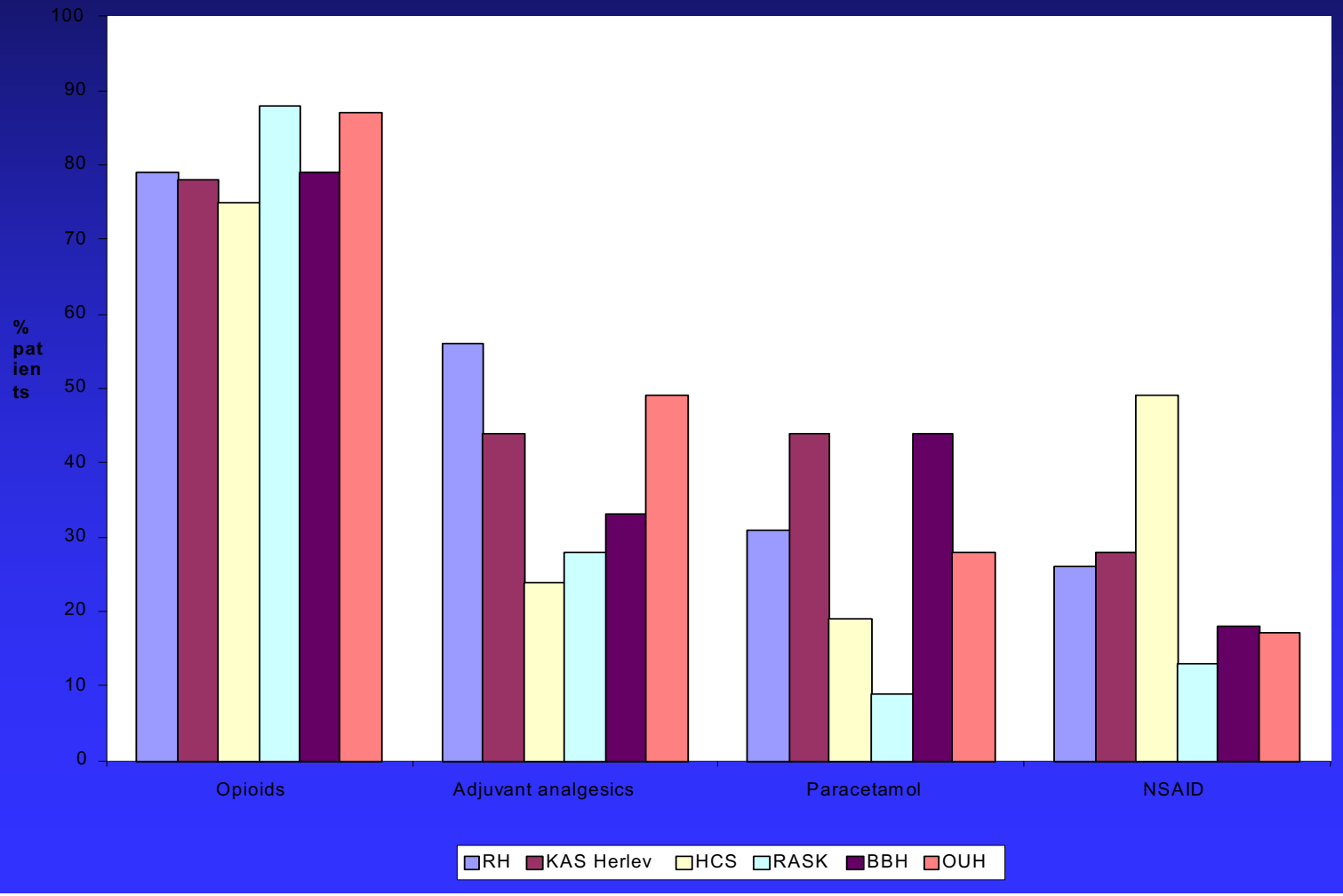
	2003	2004	2005	2006	2007
Total DDD	33.500	34.889	36.424	37.888	39.107
Morphine	4.598	4.454	4.193	4.042	3.905
Oxycodone	1.994	2.549	3.345	3.994	4.646
Fentanyl	2.533	2.650	2.916	3.213	3.389
Tramadol	12.931	13.951	14.869	15.683	16.370
Codeine	5.401	5.460	5.700	5.858	5.836

A cross-sectional study on the prescription on opioids in six specialised units for pain management and palliative care

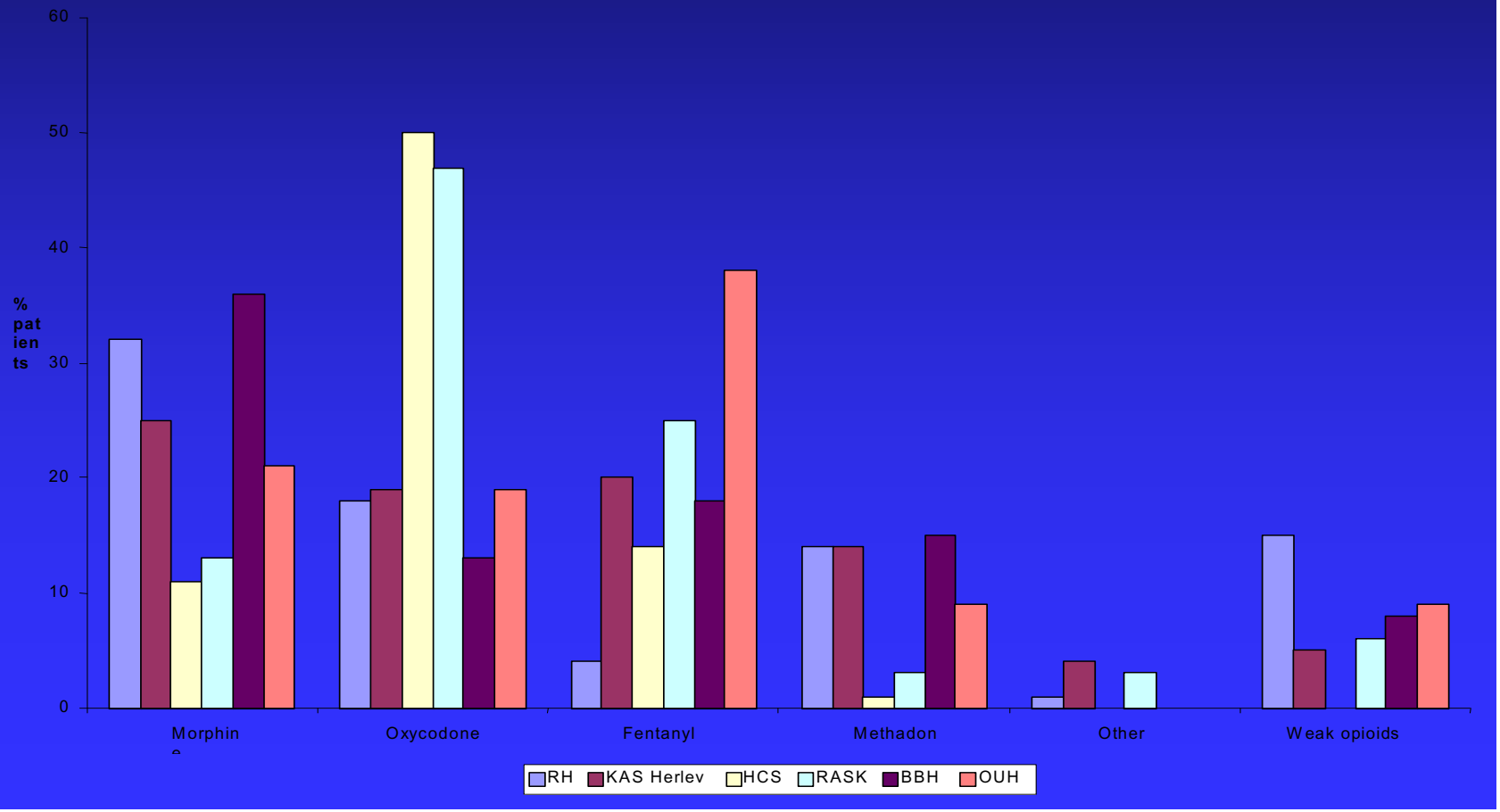
Olesen et al., Ugeskr Læg 2007

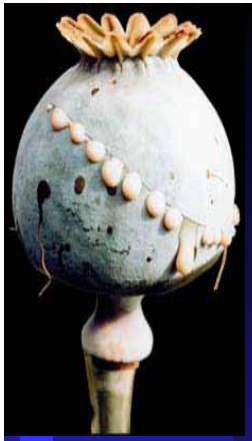
- The study was performed in 2004 and included the files of 347 cancer patients treated six specialised treatment units
- Eigthy % were treated with opioids for background pain
- Of those 73% received short-acting opioids on demand for breakthrough pain

Use of analgesics in the units



Use of opioids in the units





Morphine: ”the gold standard”

- The most widely used and thoroughly investigated opioid
- A classical μ-receptor agonist
- The reference drug
- A cheap drug
- Can be administered orally, rectally, parenterally, spinally and topically
- Recommended by WHO, EAPC and IASP (EFIC) as the opioid of first choice

Zech et al., Pain 1995
Grond et al., Pain 1999

Meuser et al., Pain 2001
Hanks et al., Br J Cancer 2001

The physician-industry relationships

”Clinical practice guidelines are intended to present a synthesis of current evidence and recommendations preformed by expert clinicians and may affect the practice of large numbers of physicians”

Choudhry et al., JAMA 2002

Relations between authors of clinical practice guidelines (CPG) and the pharmaceutical industry

Choudhry et al. JAMA 2002

AIM: to quantify the extent and nature of interactions between authors of CPG and the industry

Methods: Cross-sectional survey of 192 authors of 44 CPG`s on common adult diseases. Data collection: Declarations (industry and non-industry sources) and questionnaire (the nature of support and how conflict of interest were managed)

Results: Response rate 52%

78% had interactions with the industry

59% with companies whose drugs were considered in the guideline

58% received financial support

38% served as employees or consultants for the industry

7% thought that their relationship influenced the guideline; 19% thought that their co-authors were influenced by such a relationship

Relations between authors of clinical practice guidelines (CPG) and the pharmaceutical industry

Choudhry et al. JAMA 2002

A semi-structured in depth interview diclosed other biases and aspects of the relationships:

- Multiple small relationships with different sponsors vs large relationship with few sponsors
- Funding from govermental agencies (including this research in the CPGs)
- Individual academic promotion (self-citation)

Relations between authors of clinical practice guidelines (CPG) and the pharmaceutical industry

Choudhry et al. JAMA 2002

The authors recommendations:

1. Formal disclose of potential conflicts of interest
2. A full discussion about relationships among the authors before the start of the writing proces
3. What level of conflict is significant? (the only treshold that is not arbitrary is zero!)

A new code of conduct governing physician-industry relationships

(PhRMA 2002 and NSL 2007)

The code states that the interactions between company representatives and physicians should primarily benefit patients and enhance the practice of medicine

A national survey of physician-industry relationships

Campell et al., NEJM 2007

Aim: Financial associations of U.S. physicians (2003-2004)

Methods: A questionnaire survey of 3167 physicians in 6 specialities (anesthesiology, cardiology, family practice, general surgery, internal medicine, and pediatrics)

Results: Response rate 52%
94% had some relationship during the previous year
83% received food at their workplace
78% received drug samples
35% received reimbursement (meetings, education, advisory boards ect)
28% received payments (consulting, lectures, enrolling patients in trials)

Cardiologists were more than twice as likely as family practioners to receive payments. Family practioners met more frequently with industry representatives (16 meetings /month) than did physicians from other specialities (anesthesiologists 2 meetings/month)

A national survey of physician-industry relationships

Campell et al., NEJM 2007

Conclusion: The variations in the nature and frequency of the physician-industry relationships suggest that involved parties need to develop guidelines and recommendations that are specific to the context of each speciality and practice setting

The physician-industry relationships

”The parties involved will face constant temptations to test the limits of professionel and industry codes and government regulations. One can predict, therefore, that there will be ongoing cycles of scandal and reform for foreseeable future”

Blumenthal. NEJM 2004