Finansielle interessekonflikter og lægers adfærd

Fyraftensmøde ved Læger Uden Sponsor

6. maj 2021

Andreas Lundh
Center for Evidensbaseret Medicin Odense (CEBMO) &
Cochrane Danmark
OUH og SDU

Infektionsmedicinsk Afdeling
Hvidovre Hospital

Interessekonflikter

Forsker i interessekonflikter

Medlem af læger uden sponsor

Program

- Lægemiddelreklamer
- Seeding trials
- Honorar og sponsorering

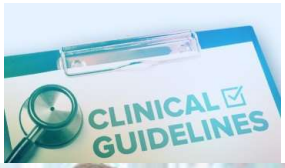
Påvirkning af læger

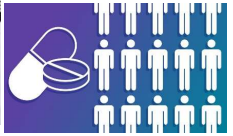
Abbott · ALLERGAN · Baxter · BD · Boots · élan · Lilly · GE Healthcare · GlaxoSmithKline · JANSSEN PHARMACEUTICAL LTD · MERCK SHARP & DOHME · NOVARTIS · Pfizer · Schering-Plough · SOLVAY · Roche · sanofi aventis · SCHWARZ PHARMA · Bristol-Myers Squibb · Wyeth

Forskning

Anbefalinger

Adfærd





The NEW ENGLAND JOURNAL of MEDICINE

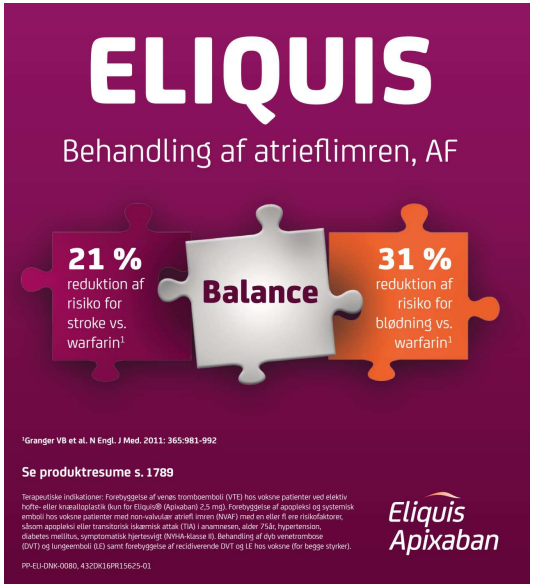
THE LANCET

Volume 385 · Number 9970 · Pages 745–828 · February 28–March 6, 2015 · www.thelancet.com

MSD
INVENTING FOR LIFE

Fyraftensmøde - Mikrobiologiens ABC for klinikere

Lægemiddelreklamer



SDU University of Southern Denmark

Cochrane Denmark

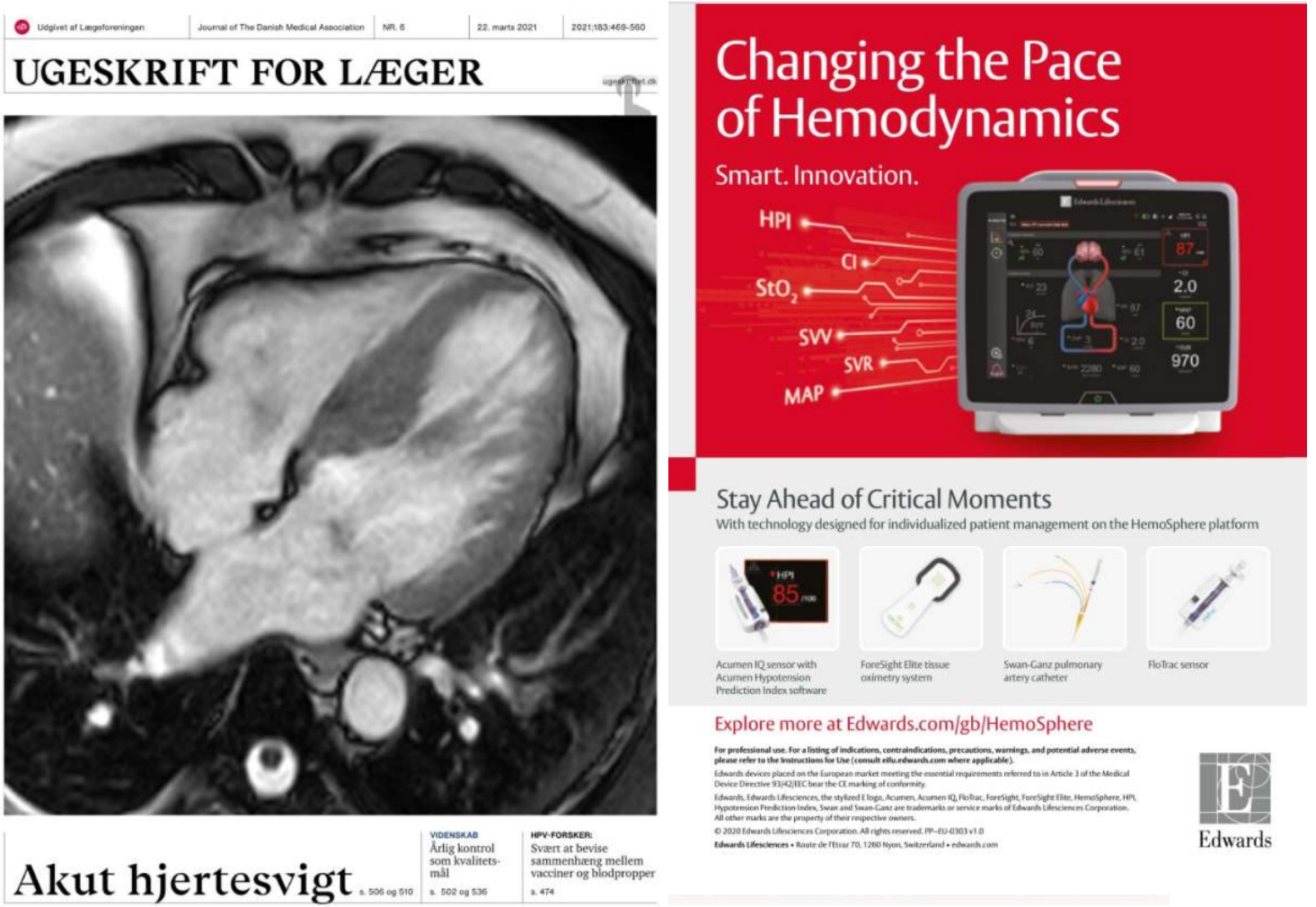
Evidens for budskaber

	Total	Number of claims not supported	95% CI
Drugs			
Antihypertensive	51	35 (69%)	54·1–80·9
Lipid-lowering	51	10 (20%)	9·8–33·1
Journal*			
At Primaria	61	29 (48%)	34·6–60·7
Form Med Cont	18	11 (61%)	35·7–82·7
Jano	34	17 (50%)	32·4–67·6
Med Clin (Barc)	19	12 (63%)	38·6–83·7
Hipertension	38	25 (66%)	48·6–80·4
Rev Esp Cardiol	25	15 (60%)	38·7–78·9
Promotional slogan			
Efficacy	84	36 (43%)	32·1–54·1
Safety	15	6 (40%)	16·3–67·7
Convenience	3	3 (100%)	29·2–100·0
Total	102	45 (44%)	34·3–54·3

*The totals add up to more than 102 because some claims appeared in more than one journal.

Table 3: **Characteristics of non-supported claims**

Villanueva Lancet 2003



Udgivet af Lægeforeningen | Journal of The Danish Medical Association | NR. 6 | 22. marts 2021 | 2021;183:469-560

UGESKRIFT FOR LÆGER

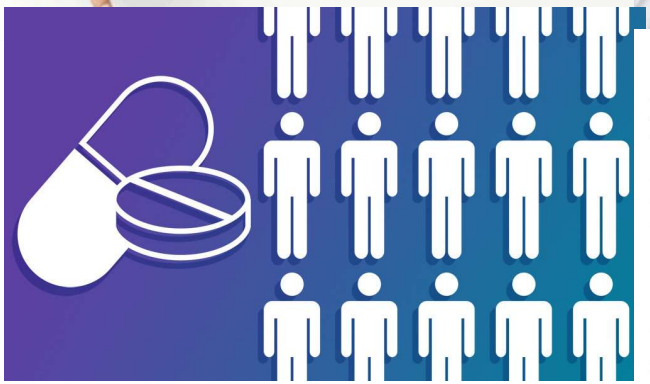
ugeskrift.dk

Akut hjertesvigt s. 506 og 510

VIDENSKAB
Årlig kontrol som kvalitetsmål
s. 502 og 536

HPV-FORSKER:
Svært at bevise sammenhæng mellem vacciner og blodpropper
s. 474

Seeding trials



Gastrointestinal Tolerability and Effectiveness of Rofecoxib versus Naproxen in the Treatment of Osteoarthritis

A Randomized, Controlled Trial

Jeffrey R. Lisse, MD; Monica Perlman, MD, MPH; Gunnar Johansson, MD; James R. Shoemaker, DO; Joy Schechtman, DO; Carol S. Skalky, BA; Mary E. Dixon, BS; Adam B. Polis, MA; Arthur J. Mollen, DO; and Gregory P. Geba, MD, MPH, for the ADVANTAGE Study Group*

Background: Gastrointestinal (GI) toxicity mediated by dual cyclooxygenase (COX)-1 and COX-2 inhibition of nonsteroidal anti-inflammatory drugs (NSAIDs) can cause serious alterations of mucosal integrity or, more commonly, intolerable GI symptoms that may necessitate discontinuation of therapy. Unlike NSAIDs, rofecoxib targets only the COX-2 isoform.

Objective: To assess the tolerability of rofecoxib compared with naproxen for treatment of osteoarthritis.

Design: Randomized, controlled trial.

Setting: 600 office and clinical research sites.

Patients: 5557 patients (mean age, 63 years) with a baseline diagnosis of osteoarthritis of the knee, hip, hand, or spine.

Intervention: Rofecoxib, 25 mg/d, or naproxen, 500 mg twice daily. Use of routine medications, including aspirin, was permitted.

Results: Rates of cumulative discontinuation due to GI adverse events were statistically significantly lower in the rofecoxib group than in the naproxen group (5.9% vs. 8.1%; relative risk, 0.74 [95% CI, 0.60 to 0.92]; $P = 0.005$), as were rates of cumulative use of medication to treat GI symptoms (9.1% vs. 11.2%; relative risk, 0.79 [CI, 0.66 to 0.96]; $P = 0.014$]). Subgroup analysis of patients who used low-dose aspirin (13%) and those who previously discontinued using arthritis medication because of GI symptoms (15%) demonstrated a relative risk similar to the overall sample for discontinuation due to GI adverse events (relative risk, 0.56 [CI, 0.31 to 1.01] and 0.53 [CI, 0.34 to 0.84], respectively). No statistically significant difference was observed between treatments for efficacy in treating osteoarthritis or for occurrence of other adverse events.

Conclusions: In patients with osteoarthritis treated for 12 weeks, rofecoxib, 25 mg/d, was as effective as naproxen, 500 mg twice daily, but had statistically significantly superior GI tolerability and led to less use of concomitant GI medications. Benefits of

ADVANTAGE forsøget

Annals of Internal Medicine | ARTICLE

Gastrointestinal Tolerability and Effectiveness of Rofecoxib versus Naproxen in the Treatment of Osteoarthritis

Study Sample

Physicians predominantly at primary care practices associated with investigational sites recruited patients from their existing practices or recruited new patients presenting with osteoarthritis who were screened for study participation. Patients were at least 40 years of age and had osteo-

We enrolled 5557 patients at 600 study sites, 581 in the United States and 19 in Sweden. At the baseline visit,

Lisse Ann Intern Med 2003

Marketing forklædt som forskning?

- Adgang til data fra retssag
- Forsøg initieret 2 måneder før FDA godkendt Vioxx (27. marts 1999)
- Forsøget var designet, udført og rapporterret af Merck's marketingsafdeling

First, the trial was targeted to a select group of critical customers. The clinical trial program for VIOXX focused primarily on specialists. While they would be critical to the early uptake and advocacy for VIOXX, the large majority of prescriptions in the A&A [arthritis and analgesia] market (~60%) come from primary care physicians. The ADVANTAGE trial utilized this important group of prescribers as investigators. In addition to gaining experience with VIOXX, many of these physicians gained a highly coveted introduction to clinical research. Second, the design of the trial focused on demonstrating the value of VIOXX to this important audience.

Merck designed the trial, paid for the trial, ran the trial. Merck came to me after the study was completed and said, "We want your help to work on the paper." The initial paper was written at Merck, and then it was sent to me for editing.

The objectives were to provide [a] product trial among a key physician group to accelerate uptake of VIOXX as the second entrant in a highly competitive new class and gather data important to this customer group.

Hill Ann Intern Med 2008

Seeding trials

- 194 randomiserede lægemiddelforsøg publiceret i 'the big six' i 2011
  - 41 (21%) havde tegn på 'marketing' forsøg
  - 14 (7%) havde måske tegn på 'marketing' forsøg

Barbour Trials 2016

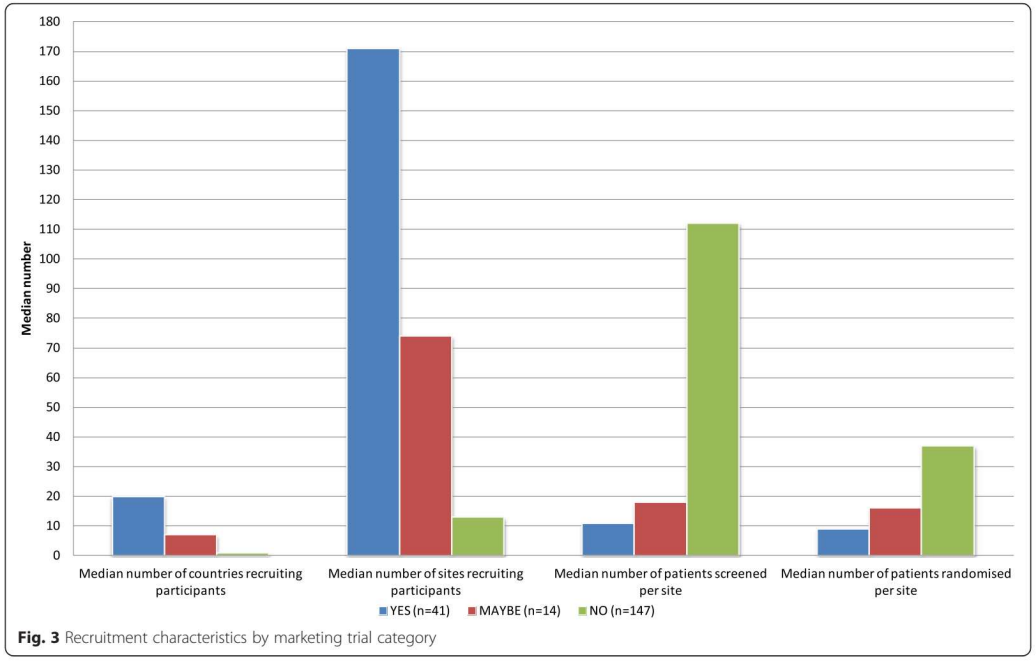


Fig. 3 Recruitment characteristics by marketing trial category

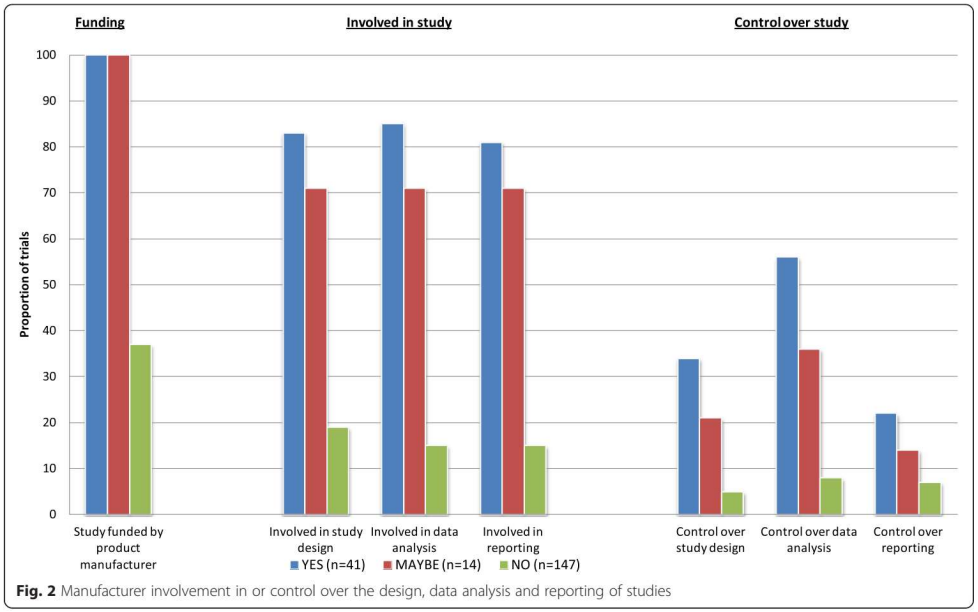


Fig. 2 Manufacturer involvement in or control over the design, data analysis and reporting of studies

Seeding trials

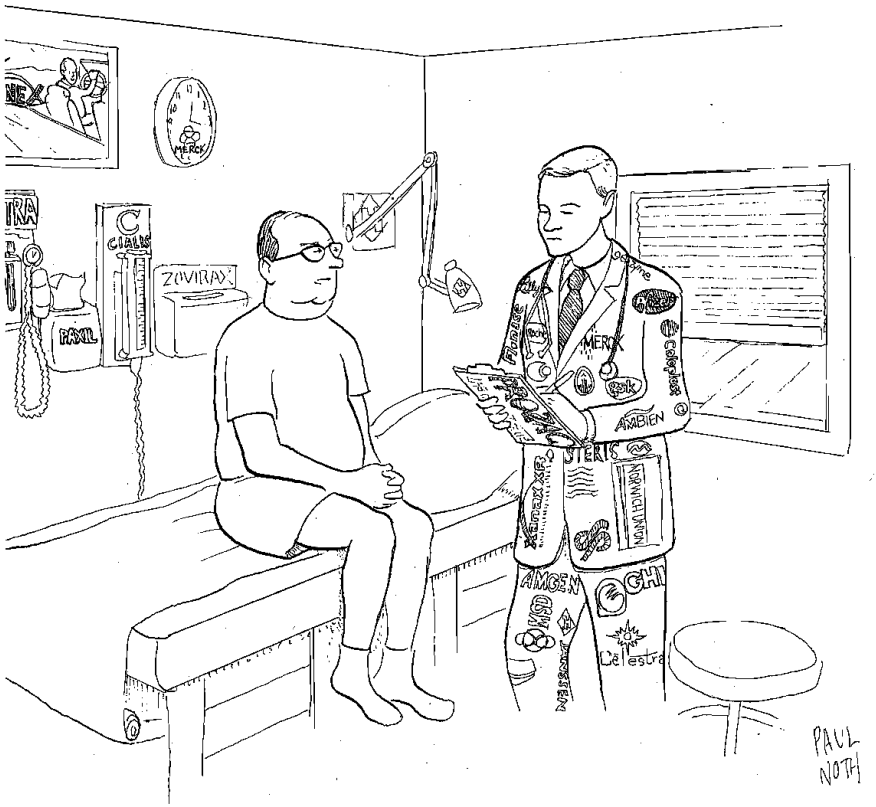
How Conducting a Clinical Trial Affects Physicians' Guideline Adherence and Drug Preferences

Table 3. Sponsor's Share of Total Prescribed Asthma Drug Volume in Defined Daily Doses for Trial-Conducting and Non–Trial-Conducting Practices

	Trial-Conducting Practices, %*	Non–Trial-Conducting Practices, %*	Difference, % (95% CI)†
Baseline	52.9	52.8	
1 y	56.3	53.1	3.1 (0.2-5.0)
2 y	58.7	51.9	6.7 (3.0-11.7)

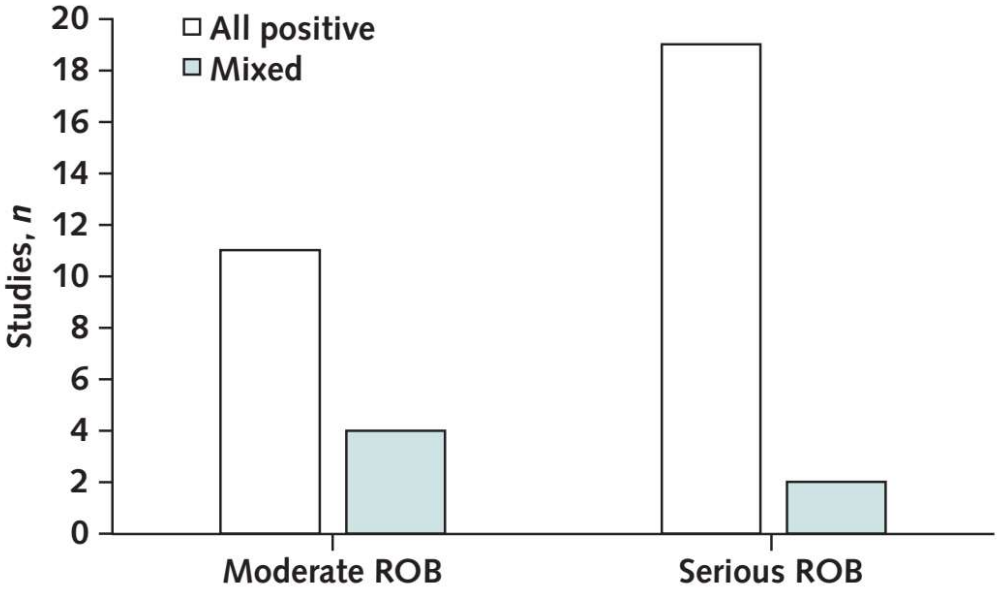
Andersen JAMA 2006

Honorar og sponsorering



Industrihonorar og ordinationsmønster

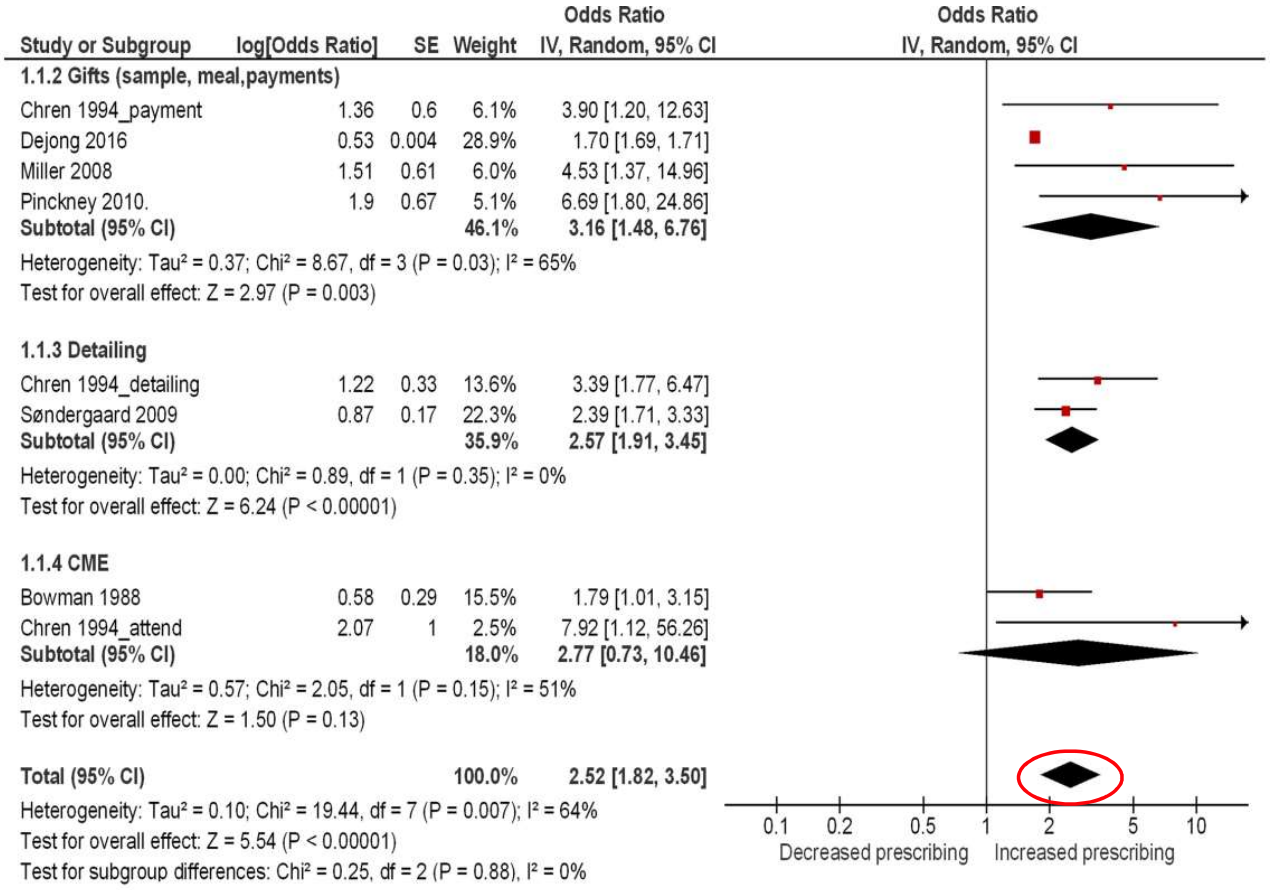
Geographic region	
Entire United States	32 (88.9)
U.S. state, municipality, or hospital	3 (8.3)
France	1 (2.8)
Class of drugs studied	
Multiple drugs from different classes	11 (30.6)
Opioids	7 (19.4)
Antineoplastic	3 (8.3)
Anti-VEGF	3 (8.3)
Biologics for inflammatory bowel disease	1 (2.8)
Erectile dysfunction	1 (2.8)
Gabapentinoids	1 (2.8)
Intranasal corticosteroids	1 (2.8)
Multiple sclerosis drugs	1 (2.8)
α-Blockers and overactive bladder drugs	1 (2.8)
Proton-pump inhibitors	1 (2.8)
Statins	1 (2.8)
Tumor necrosis factor inhibitors	1 (2.8)
Anticoagulant	1 (2.8)
Antipsychotic	1 (2.8)
NMDA receptor antagonist	1 (2.8)



Mitchell Ann Intern Med 2021

SDU University of Southern Denmark | Cochrane Denmark | CEBMO Centre for Evidence-Based Medicine Odense

Sponsorering og ordinationsmønster



Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
1.1.2 Gifts (sample, meal,payments)				
Chren 1994_payment	1.36	0.6	6.1%	3.90 [1.20, 12.63]
Dejong 2016	0.53	0.004	28.9%	1.70 [1.69, 1.71]
Miller 2008	1.51	0.61	6.0%	4.53 [1.37, 14.96]
Pinckney 2010.	1.9	0.67	5.1%	6.69 [1.80, 24.86]
Subtotal (95% CI)			**46.1%**	**3.16 [1.48, 6.76]**
Heterogeneity: Tau² = 0.37; Chi² = 8.67, df = 3 (P = 0.03); I² = 65%				
Test for overall effect: Z = 2.97 (P = 0.003)				
1.1.3 Detailing				
Chren 1994_detailing	1.22	0.33	13.6%	3.39 [1.77, 6.47]
Søndergaard 2009	0.87	0.17	22.3%	2.39 [1.71, 3.33]
Subtotal (95% CI)			**35.9%**	**2.57 [1.91, 3.45]**
Heterogeneity: Tau² = 0.00; Chi² = 0.89, df = 1 (P = 0.35); I² = 0%				
Test for overall effect: Z = 6.24 (P < 0.00001)				
1.1.4 CME				
Bowman 1988	0.58	0.29	15.5%	1.79 [1.01, 3.15]
Chren 1994_attend	2.07	1	2.5%	7.92 [1.12, 56.26]
Subtotal (95% CI)			**18.0%**	**2.77 [0.73, 10.46]**
Heterogeneity: Tau² = 0.57; Chi² = 2.05, df = 1 (P = 0.15); I² = 51%				
Test for overall effect: Z = 1.50 (P = 0.13)				
Total (95% CI)			**100.0%**	**2.52 [1.82, 3.50]**
Heterogeneity: Tau² = 0.10; Chi² = 19.44, df = 7 (P = 0.007); I² = 64%				
Test for overall effect: Z = 5.54 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.25, df = 2 (P = 0.88), I² = 0%				

Brax PLoS ONE 2017

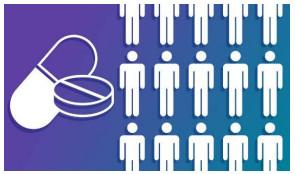
Konklusion

Abbott · ALLERGAN · Baxter · BD · Boots · élan · Lilly · GE Healthcare · GlaxoSmithKline · JANSSEN PHARMACEUTICAL LTD · MERCK SHARP & DOHME · NOVARTIS · Pfizer · Schering-Plough · SOLVAY · Roche · sanofi aventis · SCHWARZ PHARMA · Bristol-Myers Squibb · Wyeth

Forskning

Anbefalinger

Adfærd



The NEW ENGLAND JOURNAL of MEDICINE

THE LANCET

Volume 385 · Number 9970 · Pages 745–828 · February 28–March 6, 2015 · www.thelancet.com

CROI 2019
Conference on Retroviruses and Opportunistic Infections
4-7 March 2019 | Seattle, USA

MSD
INVENTING FOR LIFE

Fyraftensmøde - Mikrobiologiens ABC for klinikere

Spørgsmål?

CEBMO	www.cebmo.dk
Cochrane Denmark	www.cochrane.dk
Cochrane Denmark på Twitter	@CochraneDK
Andreas Lundh på Twitter	@AndreasLundh2