

# 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

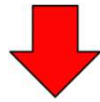
# Program

- Lægemiddelreklamer
- Seeding trials
- Honorar og sponsorering

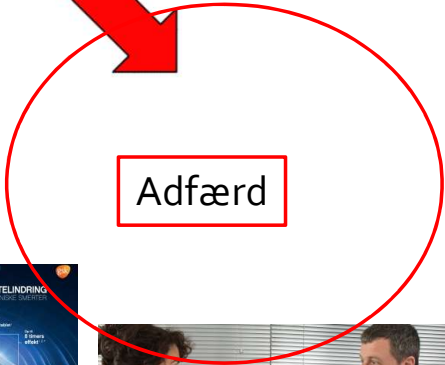
# Påvirkning af læger



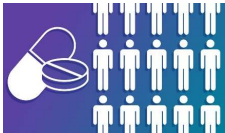
Forskning



Anbefalinger



Adfærd



# Lægemiddelreklamer



**NY BEHANDLINGS-MULIGHED TIL KOL<sup>1</sup>**



**DOKUMENTERET SYMPTOMLINDRING Gennem Helt Døgn<sup>2</sup> MED 2 DAGLIGE DOSERINGER<sup>1,2</sup>**

Duaklir® Genuair<sup>®</sup> (aclidinium bromid/formoterol) er et inhalationsbronkodialatorende vedligeholdelsesmiddel til lindring af symptomer hos voksne patienter med kronisk obstruktiv lungesygdom (KOL).

**AstraZeneca** **Duaklir® Genuair<sup>®</sup>** aclidinium bromid / formoterol

1. Granger VB et al. N Engl J Med. 2011; 365:981-992  
2. D'Amico G et al. Respiratory Research 2014; 15:122 <http://respiratory-research.com/content/15/1/122>  
3. <http://duaklir.com>

**MEDA**



**Acnatac<sup>®</sup>** (clindamycin, tretinoin)  
Ny hudvenlig gel mod acne vulgaris

Start

- Lav hudirritation<sup>1</sup>
- Ingen afblegning af hår og tekstiler

**Acnatac<sup>®</sup>** (clindamycin, tretinoin)  
clindamycin 1% og tretinoin 0,025%

**Valdoxan<sup>®</sup>**  
**Agomelatin**

Til patienter med moderat til svær depression<sup>1</sup>

25 mg  
1 x dagligt  
ved sengetid



**HUSK at markere "Tilskud" på recepten**

- Antidepressiv virkning - uanset sværhedsgrad<sup>1</sup>
- Forbedrer den daglige funktionsevne<sup>2,3</sup>
- Bevarer seksualfunktionen<sup>1,4</sup>

1. Medicinske Valdoxan<sup>®</sup> • 2. Gurev SB et al. Psychopharmacology 2011; 216:202-202 • 3. Linnik K et al. Clinical Psychiatry 2007; 68:172-173  
4. Se påklæbet på k. 204

**ELIQUIS**

Behandling af atrieflimren, AF

**Balance**

21% reduktion af risiko for stroke vs. warfarin<sup>1</sup>

31% reduktion af risiko for blødning vs. warfarin<sup>1</sup>

Se produktresumé s. 1789

**Eliquis Apixaban**

1. Granger VB et al. N Engl J Med. 2011; 365:981-992

Terapeutiske indikationer: Forebyggelse af vrede tromboemboli (VTE) hos voksne patienter ved elektiv hofte- eller knæoperation samt for Eliquis® (Apixaban) 2,5 mg. Forebyggelse af arytmi og systemisk emboli hos voksne patienter med non-valvulær atrieflimren (NAFL) med eller uden risikofaktorer. Symtomatisk eller transitorisk isæmisk attack (TIA) i sammenhæng med NAFL, hypertension, diabetes mellitus, symptomatisk hjertesvigt (NYH-klasse II), behandling af dyb venetrombose (DVT) og lungeemboli (LE) samt forebyggelse af recidiverende DVT og LE hos voksne (for begge stykker).

PR-ELI-DNK-0080, 432DK16PR15625-01

**Panodil<sup>®</sup>** (paracetamol) 665 mg **esk**

**24 TIMERS SMERTELINDRING**  
TIL PATIENTER MED KRONISKE SMERTER

Unik dobbeltlags-tablet<sup>1</sup>

Hurtig udløsning af paracetamol

Op til 8 timers effekt<sup>1,2\*</sup>

24 timers smertelindring med kun 2 tabletter, 3 gange dagligt

Formuleret til at opnå maksimal anbefalet daglig dosis på 4 g paracetamol<sup>1</sup>



\*Hvis smerte kun forekommer ved at tage 2 tabletter Panodil<sup>®</sup> (paracetamol) 665 mg x 6 tabletter x 300 g

LDL-C BEHANDLING FORSTÆRKET VIA VIRKNING I BÅDE LEVER OG TARM<sup>1</sup>

**EZETROL<sup>®</sup>** (EZETIMIBE) + STATIN

KOMPLEMENTÆR virkning



**EZETROL<sup>®</sup>** (EZETIMIBE)

1. Ezetimibe (EZETIMIBE) MSD

TIL BEHANDLING AF PATIENTER MED TYPE 2-DIABETES

**JANUMET<sup>®</sup>**  
(SITAGLIPTIN/METFORMIN)

MARKANT REDUKTION AF HbA1c<sup>1</sup>

NÅR DU IKKE KOMMER I MÅL MED METFORMIN ALENE



**JANUMET<sup>®</sup>** (SITAGLIPTIN/METFORMIN)

Hvis et enkelt tablet ikke er nok, er her et tilfælde af hypoglykæmi vs metformin + SJ<sup>2</sup>

Se vejligt EMA godkendt produktresumé inden receptudstedelse.

MSB, Læstuevej 4, 2750 Ballerup

**Janumet** (sitagliptin/metformin, MSD)



# Evidens for budskaber

	Total	Number of claims not supported	95% CI
<b>Drugs</b>			
Antihypertensive	51	35 (69%)	54.1–80.9
Lipid-lowering	51	10 (20%)	9.8–33.1
<b>Journal*</b>			
<i>At Primaria</i>	61	29 (48%)	34.6–60.7
<i>Form Med Cont</i>	18	11 (61%)	35.7–82.7
<i>Jano</i>	34	17 (50%)	32.4–67.6
<i>Med Clin (Barc)</i>	19	12 (63%)	38.6–83.7
<i>Hipertension</i>	38	25 (66%)	48.6–80.4
<i>Rev Esp Cardiol</i>	25	15 (60%)	38.7–78.9
<b>Promotional slogan</b>			
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

# UGESKRIFT FOR LÆGER



## Akut hjertesvigt

**VIDENSKAB**  
Årlig kontrol som kvalitetsmål  
s. 506 og 510

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

# Changing the Pace of Hemodynamics

Smart. Innovation.

**Stay Ahead of Critical Moments**  
With technology designed for individualized patient management on the HemoSphere platform

Acumen IQ sensor with Acumen Hypotension Prediction Index software

ForeSight Elite tissue oximetry system

Swan-Ganz pulmonary artery catheter

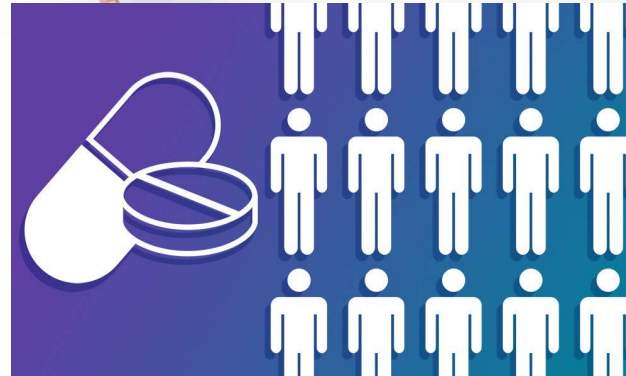
FloTrac sensor

[Explore more at Edwards.com/gb/HemoSphere](https://www.edwards.com/gb/HemoSphere)

For professional use. For a listing of indications, contraindications, precautions, warnings, and potential adverse events, please refer to the Instructions for Use (consult [edwards.com](https://www.edwards.com) where applicable).  
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# 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. Polls, 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,

# 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 rapporteret 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.

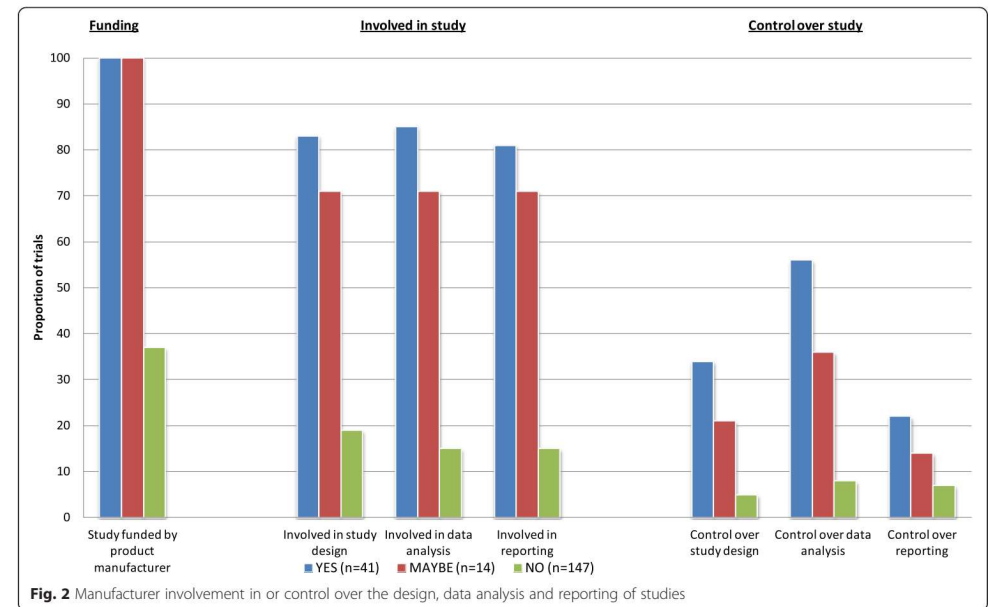
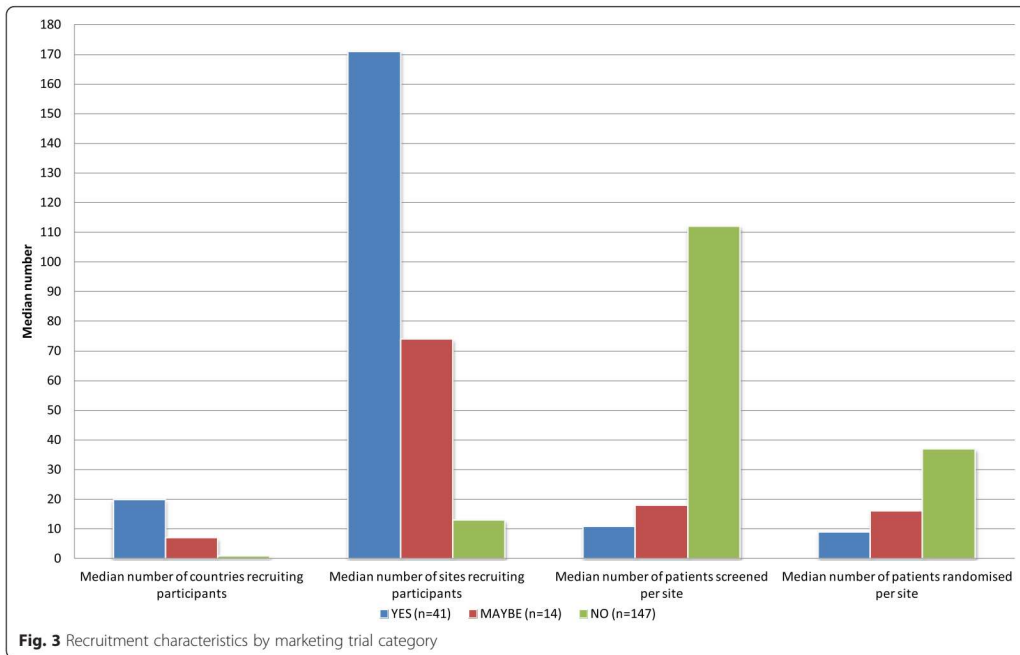
The objectives were to provide [a] product trial among a key physician group to accelerate uptake of VIOXX as the second entrant in a highly competitive new class and gather data important to this customer group.

*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*





# 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



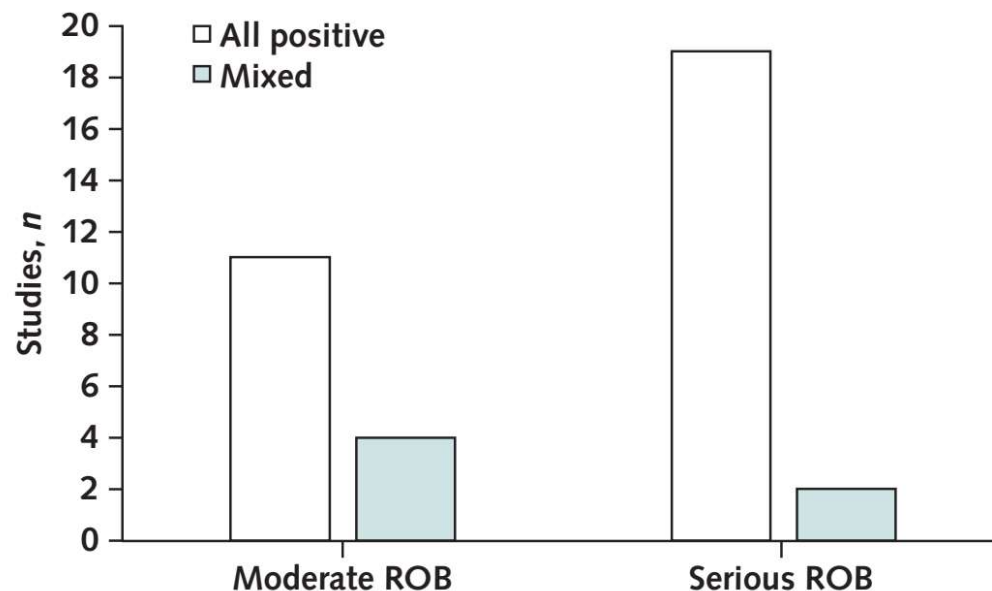
# Industrihonorar og ordinationsmønstre

## Geographic region

Entire United States	32 (88.9)
U.S. state, municipality, or hospital	3 (8.3)
France	1 (2.8)

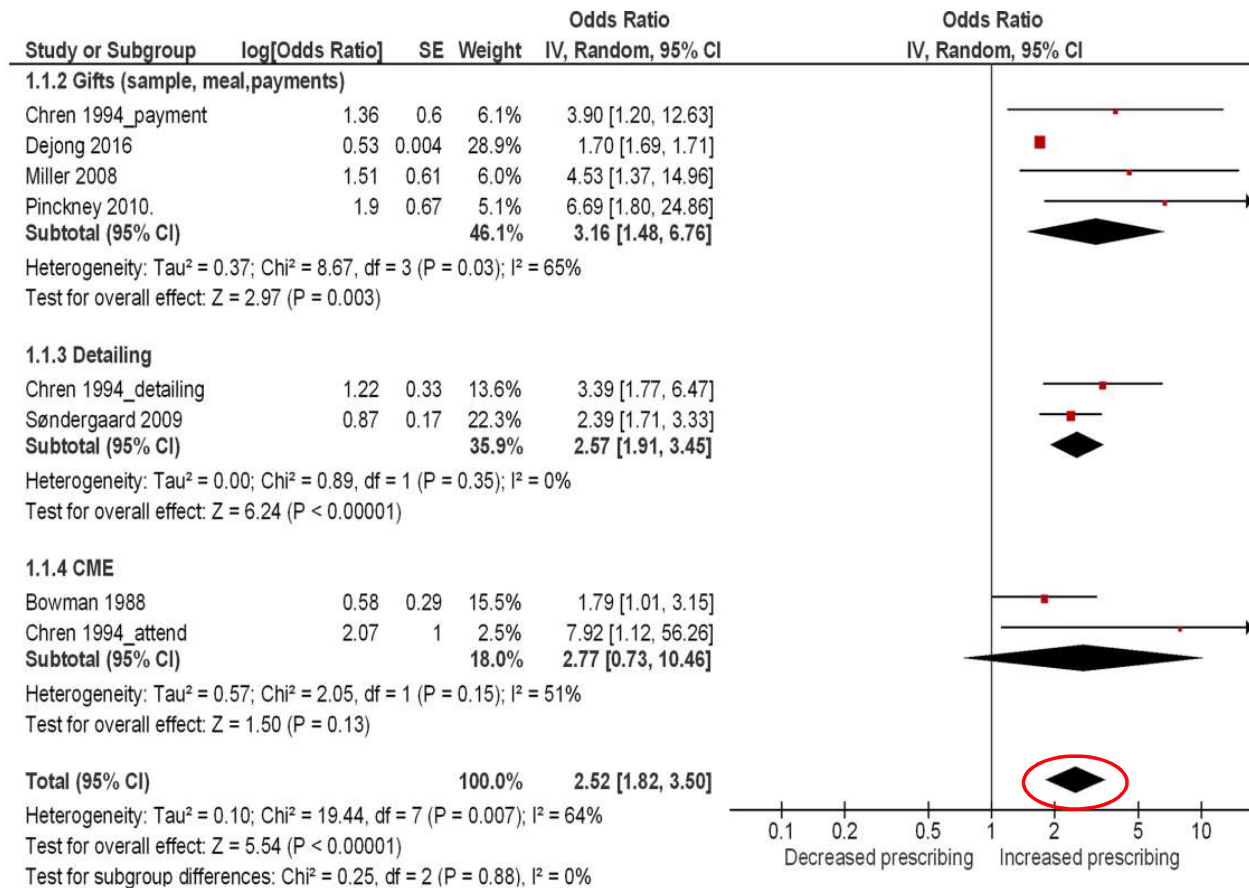
## Class of drugs studied

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*

# Sponsorering og ordinationsmønstre

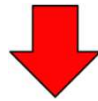


Brax PLoS ONE 2017

# Konklusion



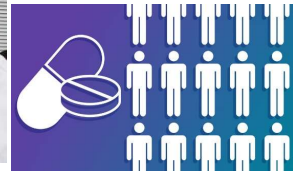
Forskning



Anbefalinger



Adfærd



# Spørgsmål?

**CEBMO**

[www.cebmo.dk](http://www.cebmo.dk)

**Cochrane Denmark**

[www.cochrane.dk](http://www.cochrane.dk)

**Cochrane Denmark på Twitter**

@CochraneDK

**Andreas Lundh på Twitter**

@AndreasLundh2