

Systematiske oversikter  
Meta-analyser  
Cochrane collaboration  
Internettressurser

**Plan**

0900	Forelesning
1000	Øvelse + pause
1115	Gjennomgang
1200	Lunsj

Presentasjonen blir lagt ut etter forelesningen



”Kunnskapssenteret fremskaffer og formidler forskningsbasert kunnskap om effekt av metoder, virkemidler og tiltak og om kvalitet innen alle deler av helsetjenesten”.



“The medical literature can be compared to a jungle. It is fast growing, full of dead wood, sprinkled with hidden treasure and infested with spiders and snakes.”

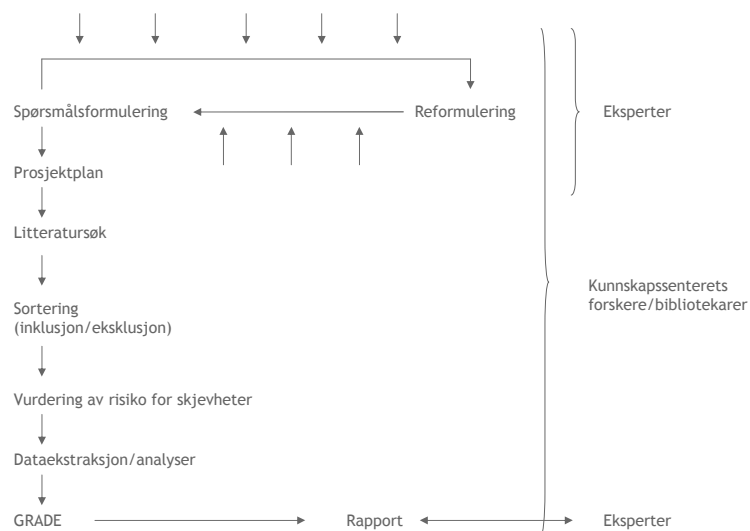
*Peter Morgan, Scientific Editor,  
Canadian Medical Association*

## Oversiktsartikkel versus systematisk oversikt

- Oversiktsartikkel
  - Flere spørsmål
  - Ingen søkestrategi
  - Ingen inklusjonskriterier
  - Ingen sammenstilling av resultater
- Systematisk oversikt
  - Ett spørsmål
  - Eksplisitt søkestrategi
  - Eksplisitte inklusjonskriterier
  - Sammenstilte resultater (metaanalyse)



## Trinn i systematiske oversikter



## Komponenter i en klart formulert problemstilling: PICO



- P** Hvordan kan man beskrive **pasientgruppen**?
- I** Hvilken type **intervensjon** skal vurderes?
- C** Hva er den viktigste sammenlikningen (**comparison**)?
- O** Hvilke utfall (**outcomes**) er viktige?

### Using Pedometers to Increase Physical Activity and Improve Health A Systematic Review

Dena M. Bravata, MD, MS  
Crystal Smith-Spangler, MD  
Vandana Sundaram, MPH  
Allison L. Gienger, BA

**Context** Without detailed evidence of their effectiveness, pedometers have recently become popular as a tool for motivating physical activity.  
**Objective** To evaluate the association of pedometer use with physical activity and health outcomes among outpatient adults.

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## Den beste tilgjengelige kunnskap for forskjellige typer spørsmål

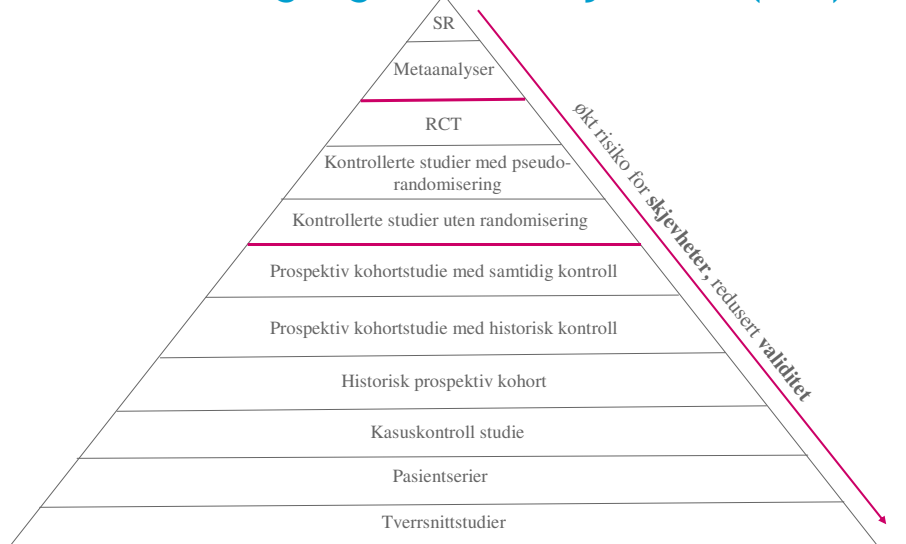
Nivå	Behandling	Prognose	Diagnose
I	<i>Systematisk oversikt over ...</i>	<i>Systematisk oversikt over ...</i>	<i>Systematisk oversikt over ...</i>
II	Randomisert kontrollert forsøk (RCT)	Kohortstudie	Tverrsnittsstudie
III	...	...	...

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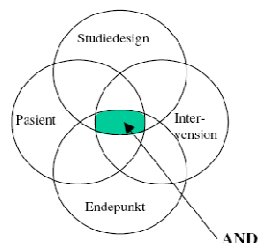
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## Studiedesign og risiko for skjevheter (bias)



## Litteratursøk - en spesialistoppgave

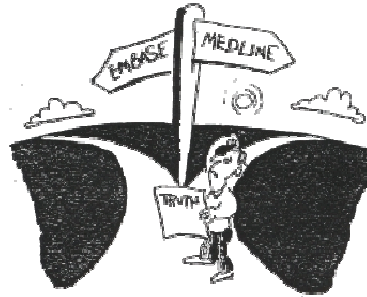


### Draft MEDLINE search strategy

- 1 methadone.mp.
- 2 buprenorphine.mp.
- 3 or/1-2
- 4 Exp Opioid-Related Disorders/  
5 Substance Withdrawal Syndrome/  
6 Substance related disorders/  
7 Heroin dependence/  
8 (substance abuse OR substance misuse OR substance dependen\$).mp.
- 9 (opiod abuse OR opiod misuse OR opiod dependen\$).mp.
- 10 (heroin abuse OR heroin misuse OR heroin dependen\$).mp.
- 11 (opiate abuse OR opiate misuse OR opiod dependen\$).mp.
- 12 or/4-11
- 13 3 and 12

## Søkestrategi

- Søkeord
  - Tekst
  - Emne (MeSH)
- Databaser
  - MEDLINE
  - EMBASE
  - Cochrane Library
  - ISI Web of Knowledge
  - CINAHL
  - ...
- Andre kilder
  - Referanselister
  - Ekspertter
  - Register



## Publikasjonsbias

- Mindre sannsynlig at negative studier publiseres
- Eksempel
  - 737 studier ved Johns Hopkins fulgt opp (Dickersin, JAMA, 1992)
  - 2,5 ganger flere positive studier enn negative INNSENDT for publisering



## Hvilke studier har publikasjonsskjevheter? Hvilke er OK?

1. Alle positive studier?
2. Alle studier med > 100 pasienter
3. Alle studier publisert i BMJ, Lancet, JAMA eller NEJM?
4. Alle registrerte studier?



**World Health Organization**

INTERNATIONAL CLINICAL TRIALS REGISTRY PLATFORM SEARCH PORTAL

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**International Clinical Trials Registry Platform**

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Why register trials?

International Search Portal

Register network

Universal Trial Reference Number

Results reporting

News and events

Resources

**Welcome to the WHO International Clinical Trials Registry Platform**

The mission of the WHO Registry Platform is to ensure that a complete view of research is accessible to all those involved in health care decision making. This will improve research transparency and will ultimately strengthen the validity and value of the scientific evidence base.

*The registration of all interventional trials is a scientific, ethical and moral responsibility.*

**What is a clinical trial?**

A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc

**Functions**

[The Register Network](#) | [The International Search Portal](#)

Search

All WHO  This site only

[Search for trials](#)

[The Register Network](#)

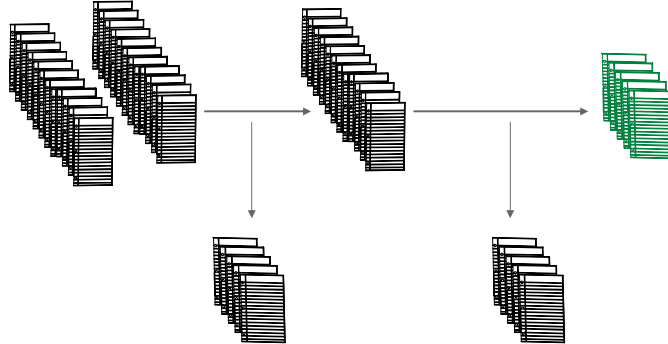
[List of Registers](#)

[Frequently Asked Questions](#)

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## Sortering (inkludasjon/eksklusjon)

- Oppfyller studien alle inkludjonskriteriene?
- Oppfyller studien noen av eksklusjonskriteriene?
- Leseapar



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## Sjekkliste for vurdering av risiko for systematiske feil i RCTer

- **Generering av fordelingssekvens?**
- **Skjult allokering?**
- **Blinding av deltagere, personell og de som målte utfallene?**
- **Ufullstendig oppfølging av utfallsdata?**
- **Selektiv rapportering?**
- **Andre typer systematiske feil?**

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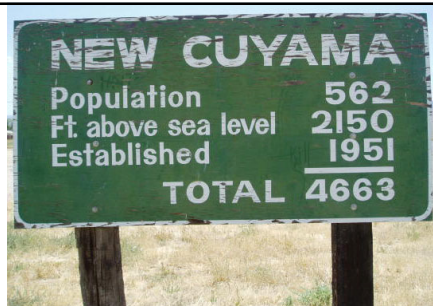


## Dataekstraksjon

Baseline characteristics		[control]	[study drug]
Number randomised			
Number analysed			
Age (wks, mos, yrs) (mean, SD; median, range)			
Male:female n : n			
Duration of dependence (wks, mos, yrs) (mean, SD; median, range)			
Age at diagnosis (wks, mos, yrs) (mean, SD; median, range)			
Newly treated with study intervention, n (%)			
Previously treated with study intervention, n (%)			
Frequency of opioid use (dy, wk, mo) (mean, SD; median, range)			
N <sup>o</sup> (1,2,3,8,9) concomitant drugs, n (%)			
Concomitant non-drug treatments, n (%)			
Previous treatments, n (%) (please specify)			
Alcohol, n (%) / additional illicit drug use, n (%)			
HIV positive n (%) / Hepatitis positive n (%)			

## Sammenstilling av data

- Syntese
  - n
  - PICO
  - Risiko for systematiske feil
  - Hovedfunn
- Metaanalyse
  - Relativ risiko, odds ratio, gjennomsnittsdifferanse
  - Forrest plot
  - Heterogenitet
  - Metaregresjon

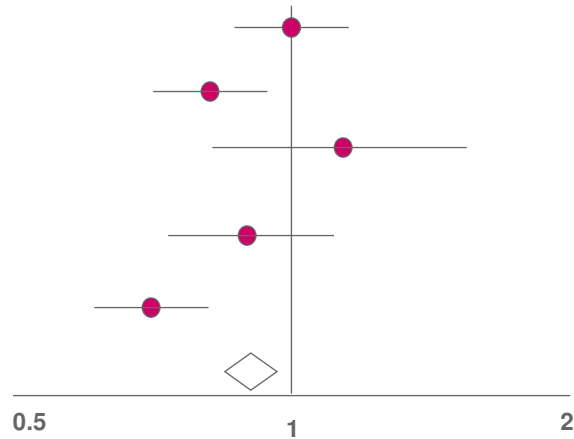


## Relativ risiko vs odd ratio

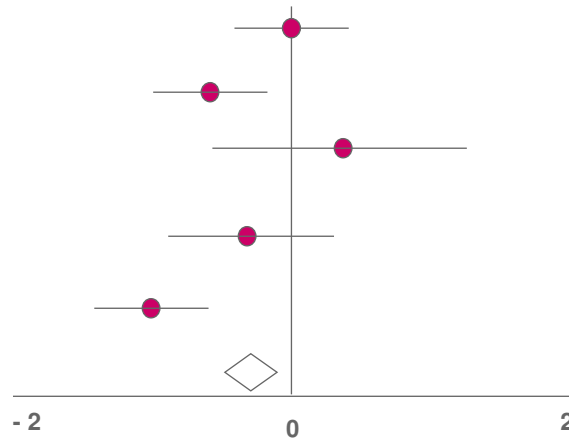
	Syk	Frisk	
Behandling	a	b	<b>a+b</b>
Kontroll	c	d	<b>c+d</b>
	<b>a+c</b>	<b>b+d</b>	n

$$RR(\text{syk}) = \frac{a/a+b}{c/c+d} \quad OR(\text{syk}) = \frac{a/b}{c/d}$$

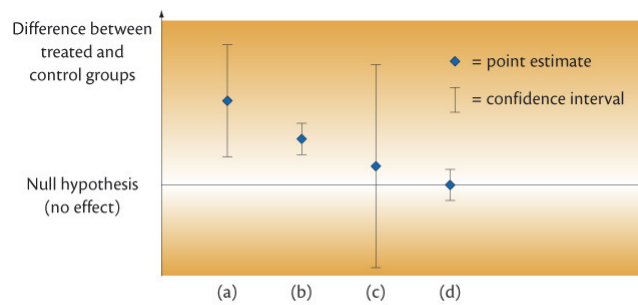
## Forrest plot: RR, OR



## Forrest plot: gjennomsnittsdifferanse



## Reading confidence intervals



- (a) Statistically significant result ( $P < 0.05$ ) but low precision
- (b) Statistically significant result ( $P < 0.05$ ) with high precision
- (c) Not statistically significant result ( $P > 0.05$ ) with low precision
- (d) Not statistically significant result (no effect) with high precision

## Heterogenitet

- For studier
  - sammenliknbare utvalg, intervensjoner og utfall
  - bruk skjønn!
- For resultater
  - sammenliknbare effektmål
  - Test for heterogenitet:  $\chi^2/I^2$  (lav p-verdi/ $I^2 \geq 75\%$  betyr heterogene resultater)

## Er disse resultatene forskjellige?

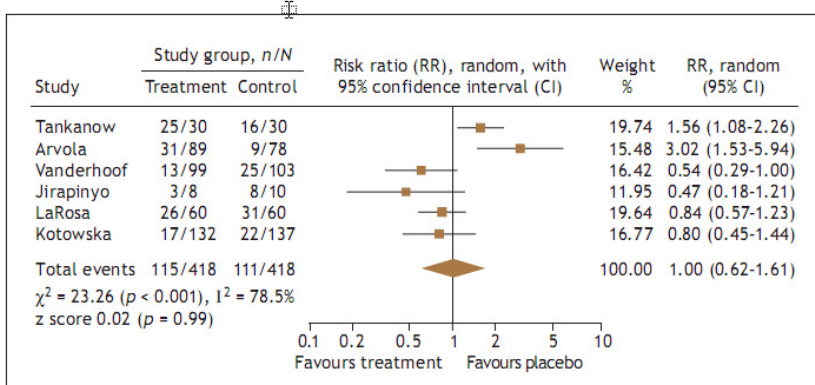


Fig 3: Incid showed a r cally signifi  $\chi^2 = 23.26$  ( $p < 0.001$ ),  $I^2 = 78.5\%$  analysis. The analysis score) and statisti-  $z$  score 0.02 ( $p = 0.99$ )

GRADEpro [Raykefyllt Hegegrd] ver 3.2.2.20090501

File Add View Options Help  
 New Open Print Save Undo all changes Add profile group Add profile Add outcome Import from RevMan Preview SoF table

Profiles tree  
 - Effekt, sikkerhet og kostnadseffektivitet  
 - varenline og bupropion for smok  
 - Raykefyllt (7 day point prevalen  
 - Raykefyllt (7 day point prevalen  
 - Raykefyllt (continuous quit rate)  
 - Raykefyllt (continuous quit rate)  
 - Alvorlige bivirkninger - alle som  
 - Kvalme - alle som mottok beh  
 - Vektkning - alle som fullførte  
 - Søvnløshet - alle som mottok t  
 - Hodpine - alle som mottok b  
 - Unormale diamaner - alle som  
 - Tretthet - alle som mottok beh  
 - Psykiatriske symptomer - alle  
 - Angst - alle som mottok behar  
 - Svimmelhet - alle som mottok  
 - Varenline vs NRT for  
 - Nikotinplaster og Nikotin nesep  
 - Nikotinplaster og Kombinason av  
 - Nikotin nesepay vs Kombinason  
 - Nikotin byggegunn og Nikotin pl  
 - Nikotin byggegunn og Nikotin ve  
 - Nikotin byggegunn og Nikotin inn  
 - Nikotin plaster vs Nikotin inn  
 - Nikotin nesepay vs Nikotin inn  
 - Kombinason av Nikotin byggegun  
 - Adferde gruppe rådgivning og Nik  
 - Nikotin plaster vs kombinason av  
 - Nikotin innandingsapparat vs kon  
 - Kombinason av Nikotin byggegun  
 - Bupropion vs NRT for  
 - NRT vs Kombinason av Bupropi  
 - Bupropion vs Kombinason av B  
 - Bupropion tillegg til Kognitiv adf  
 - Kombinason av Bupropion og N  
 - Nikotin byggegunn og Nikotin pa  
 - Nikotin plaster vs Nikotin bygge  
 - NRT vs Kombinason av Bupropi  
 - Bupropion tillegg til Kognitiv adf  
 - NRT vs Kombinason av Bupropi

Edit  
 Outcome: - alle randomiserte, worst-case - 12 uker  
 dichotomous pooled Importance: 6 IMPORTANT  
 continuous  
 No of studies: 2  
 Study design: randomised trials  
 Quality of evidence: HIGH  
 Decrease quality of evidence  
 Limitations in design: no  
 Inconsistency: no  
 Indirectness: no  
 Imprecision: no  
 Publication bias: unlikely  
 Increase quality of evidence  
 Large effect: no  
 Plausible confounding would change the effect: no  
 Dose-response gradient: no  
 Delete Revert Go to Summary of findings

Profile: varenline vs bupropion for smoking cessation  
 Raykefyllt (7 day point prevalence of abstinence) - alle randomiserte, worst-case - 12 uker (follow-up 12 weeks) | 2 studies

Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Importance
randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	IMPORTANT
Patients (varenline)	Control (Bupropion)	Relative effect	Absolute effect	Quality		
350/696 (50.3%)	242/671 (36.1%)	OR 1.79 (1.44 to 2.23)	142 more per 1000 (from 88 more to 196 more)	⊕⊕⊕⊕ HIGH		

Raykefyllt (7 day point prevalence of abstinence) - alle randomiserte, worst-case - 24 uker (follow-up 24 weeks) | 2 studies

Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Importance
randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	IMPORTANT
Patients (varenline)	Control (Bupropion)	Relative effect	Absolute effect	Quality		
239/696 (34.3%)	172/671 (25.6%)	OR 1.52 (1.2 to 1.92)	87 more per 1000 (from 36 more to 142 more)	⊕⊕⊕⊕ HIGH		

Raykefyllt (7 day point prevalence of abstinence) - alle randomiserte, worst-case - 52 uker (follow-up 52 weeks) | 2 studies

Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Importance
randomised trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	IMPORTANT
Patients (varenline)	Control (Bupropion)	Relative effect	Absolute effect	Quality		
204/696 (29.3%)	155/671 (23.1%)	OR 1.38 (1.08 to 1.76)	62 more per 1000 (from 14 more to 115 more)	⊕⊕⊕⊕ HIGH		

Footnotes  
 1. Large confidence intervals  
 2. Substantial statistical heterogeneity  
 3. Small no of events

Add new Change order Edit Delete

## Snarveier til systematiske oversikter



**NHS**  
 National Institute for  
 Health and Clinical Excellence

**ClinicalEvidence**



**helsebiblioteket.no**



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# The Cochrane Collaboration

The reliable source of evidence in health care



- Grunnlagt 1993, oppkalt etter epidemiolog Archie Cochrane
- Internasjonal not-for-profit organisasjon
- Styringsgruppe, subgrupper og sekretariat
- Enheter: sentre, review groups, methods groups, fields/networks
- Utgiver av bl a the Cochrane database of Systematic Reviews



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The BBC News discusses new Cochrane evidence on acupuncture for headaches.

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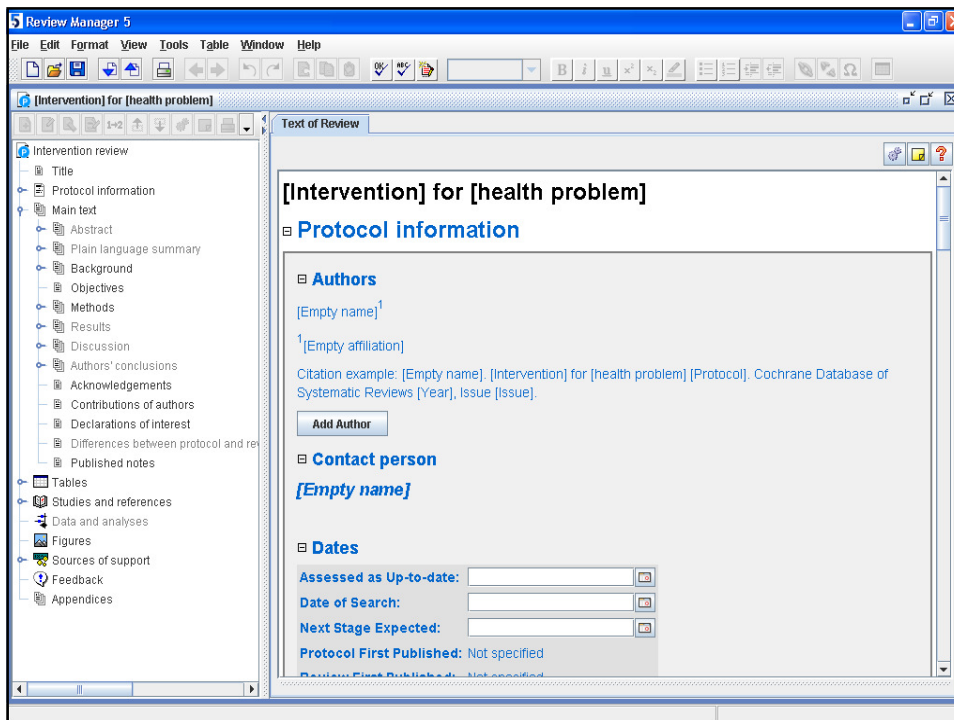
### Browse by topic:

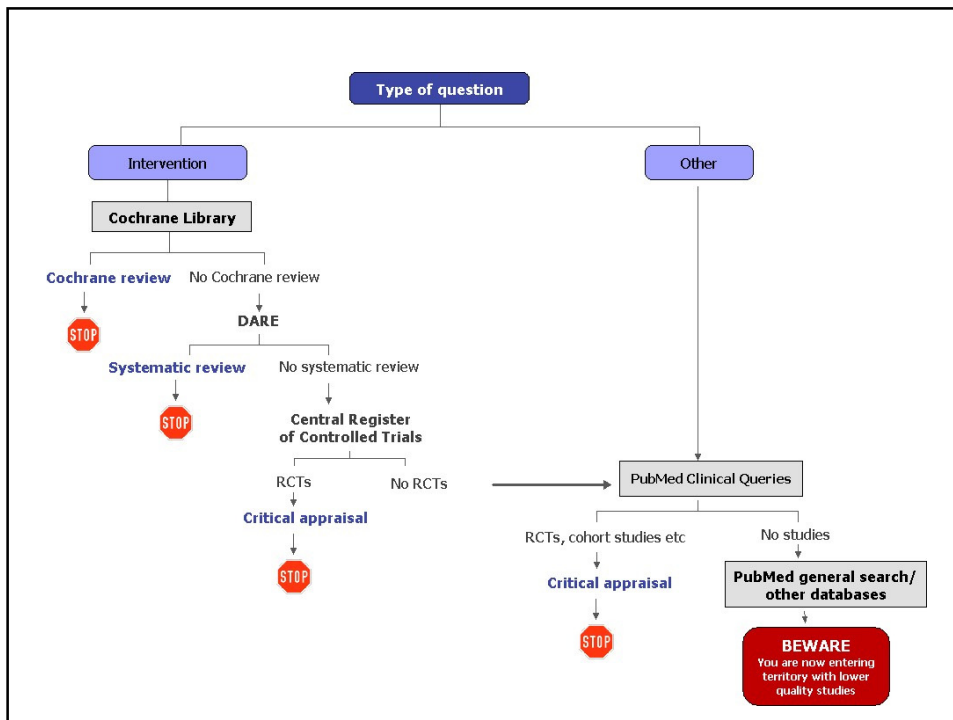
--Select topic (Review Group)--

deutsch espanol

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[Acupuncture for tension-type](#)





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## PubMed Clinical Queries

This page provides the following specialized PubMed searches for clinicians:

- Search by Clinical Study Category
- Find Systematic Reviews
- Medical Genetics Searches

Results of searches on these pages are limited to specific clinical research areas. For comprehensive searches, use PubMed directly.

### Search by Clinical Study Category [↑ Top](#)

This search finds citations that correspond to a specific clinical study category. The search may be either broad and sensitive or narrow and specific. The search filters are based on the work of Haynes RB et al. See the [filter table](#) for details.

Search

Category	Scope
<input type="radio"/> etiology	<input checked="" type="radio"/> narrow, specific search
<input type="radio"/> diagnosis	<input type="radio"/> broad, sensitive search
<input checked="" type="radio"/> therapy	
<input type="radio"/> prognosis	
<input type="radio"/> clinical prediction guides	

### Find Systematic Reviews [↑ Top](#)

For your topic(s) of interest, this search finds citations for systematic reviews, meta-analyses, reviews of clinical trials, evidence-based medicine, consensus development conferences, and guidelines.

For more information, see [Help](#). See also [related sources](#) for systematic review searching.

Search

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## Øvelse: kritisk vurdering av systematisk oversikt

**Journal of Experimental & Clinical Cancer Research**

### Sjekkliste for systematiske oversikter

**Research**

**Traditional Chinese medicines in the treatment of hepatocellular cancers: a systematic review and meta-analysis**

Ping Wu<sup>1</sup>, Jean Jacques Dugoua<sup>2</sup>, Oghenowede Eyawo<sup>3</sup> and Edward J Mills<sup>3,4</sup>\*

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Journal of Experimental & Clinical Cancer Research 2009, 28:112      doi:10.1186/1756-9966-28-112      Accepted: 12 August 2009

This article is available from: <http://www.jeccr.com/content/28/1/112>

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**Abstract**

**Background:** Liver cancer is a common malignancy with a high mortality rate. Given the poor prognosis associated with this cancer, many patients seek additional therapies that may improve quality of life or survival. Several Traditional Chinese Medicines (TCM) have been evaluated in clinical trials, but little is known about them outside of China.

**Methods:** We searched independently and in duplicate 8 electronic databases, including 2 Chinese language databases, until February 2009. We included any randomized clinical trials (RCT) evaluating a TCM oral preparation for the treatment of hepatocellular cancers. We abstracted data on survival, tumor response, and performance scores. We conducted a random-effects meta-analysis and applied a meta-regression analysis.

**Results:** We included 45 RCTs (n = 3,236). All studies employed an active control group. In general, the reporting of methodological issues was poor. We analyzed data from 37 trials

Sjekkliste for systematiske oversikter*		Ja	Uklart	Nei
1	Beskriver forfatterne klart hvilke metoder de brukte for å finne primærstudiene?			
<i>Kommentar</i>				
2	Be det utført et tilfredsstillende litteratursøk? (bruk hjelpesporsmål på neste side for å besvare dette spørsmålet)			
<i>Kommentar</i>				
3	Beskriver forfatterne hvilke kriterier som ble brukt for å bestemme hvilke studier som skulle inkluderes (studiedesign, deltakere, tiltak, ev. endepunkter)?			
<i>Kommentar</i>				
4	Be det sikret mot systematiske skjevheter (bias) ved seleksjon av studier (eksplisitte seleksjonskriterier brukt, vurdering gjort av flere personer uavhengig av hverandre)?			
<i>Kommentar</i>				
5	Er det klart beskrevet et sett av kriterier for å vurdere intern validitet?			
<i>Kommentar</i>				
6	Er validiteten til studiene vurdert (enten ved inklusjon av primærstudier eller i analysen av primærstudier) ved bruk av relevante kriterier?			
<i>Kommentar</i>				
7	Er metodene som ble brukt da resultatene ble sammenfattet, klart beskrevet?			
<i>Kommentar</i>				

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