Sinteza sistematica si metaanliza ca parte din lucrarea de doctorat

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Ce este o sinteza sistematica (SS)?

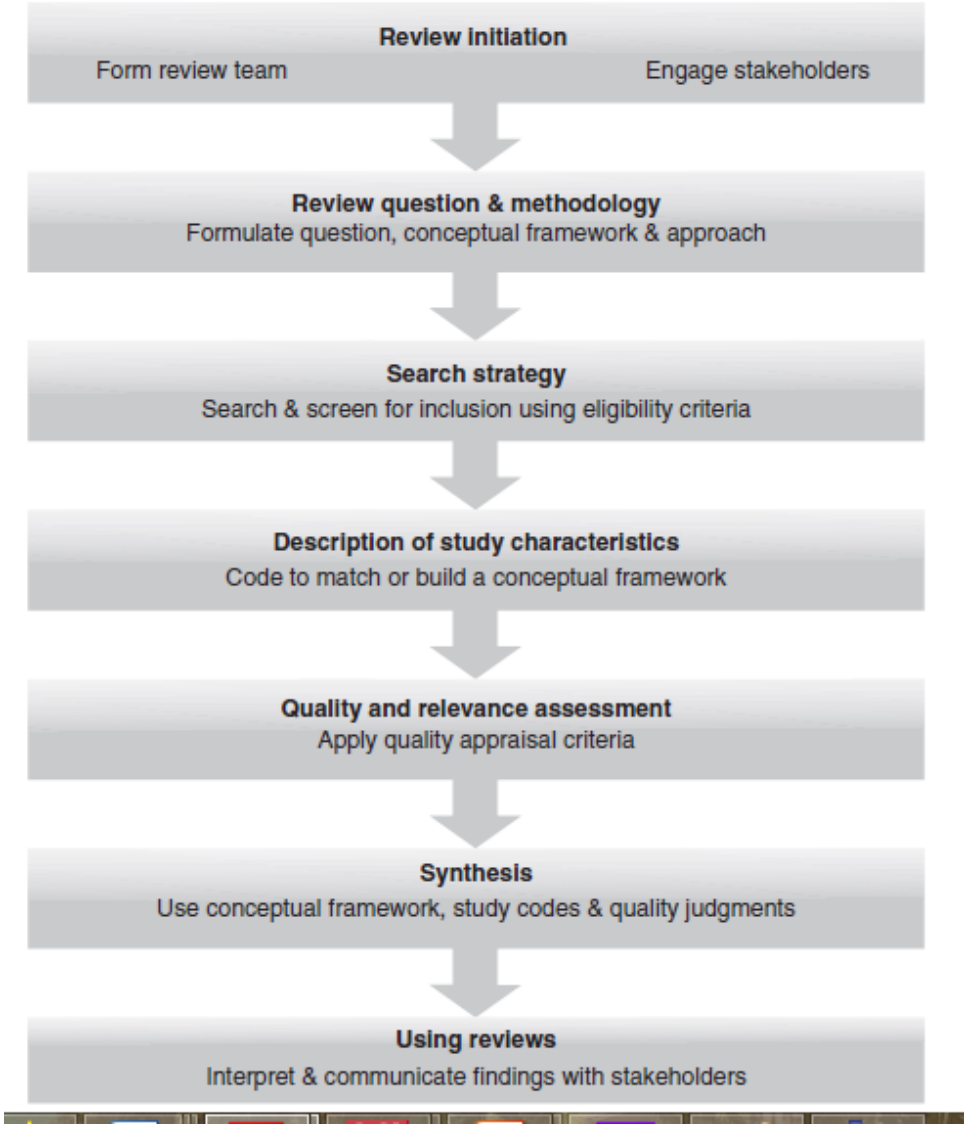
- Scopul este identificarea si sintetizarea **tuturor dovezilor** relevante pentru o intrebare de cercetare
- Sursa importanta pentru cercetare ulterioara

Criteriile PRISMA de raportare a SS

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

Pasi pentru dezvoltarea unei sinteze sistematice



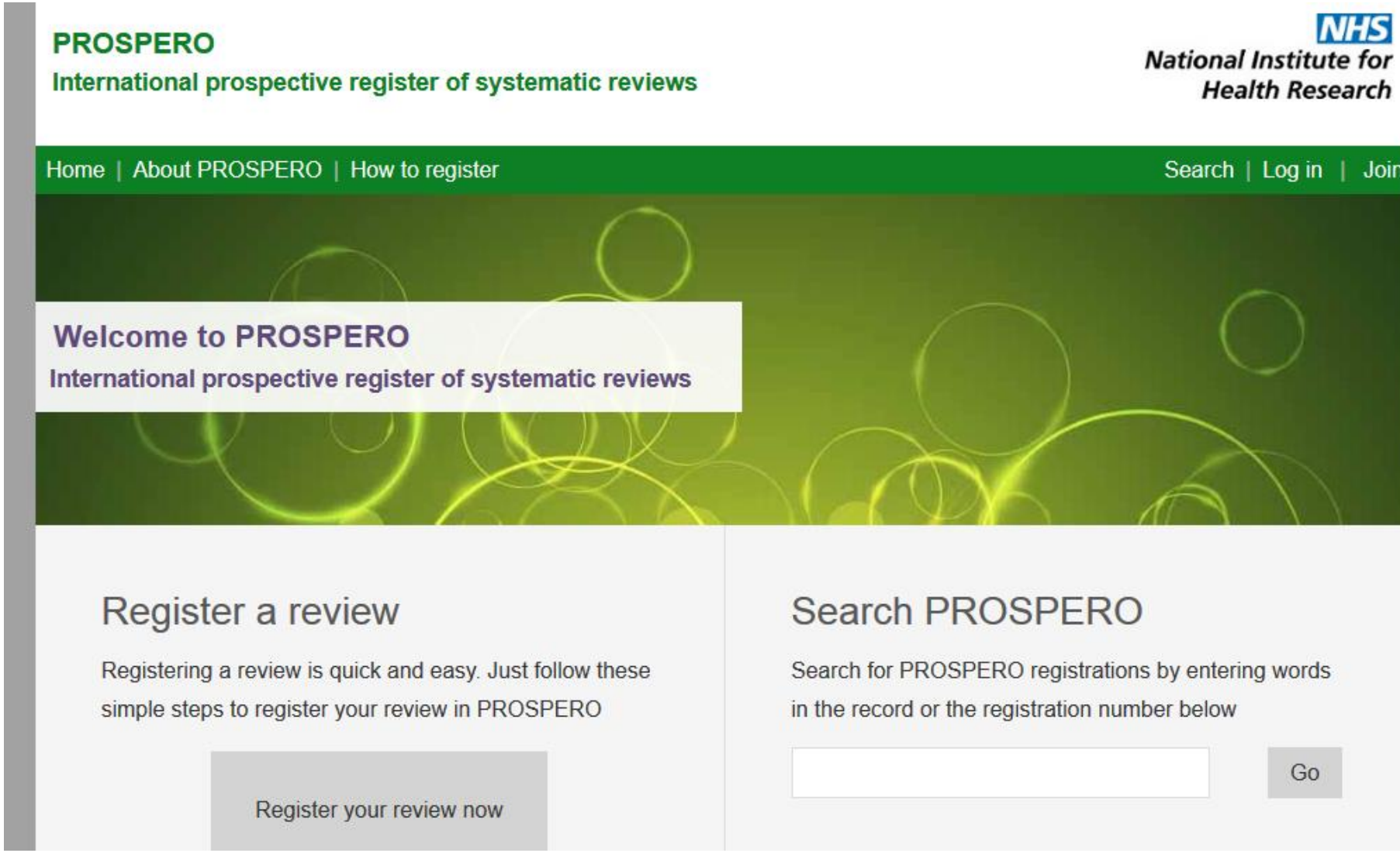
An introduction to systematic reviews. Editor(s) David Gough, Sandy Oliver, James Thomas Date 2017 Publisher SAGE

1. **Identificarea necesitatii pentru o SS**

-cautarea in literature de specialitate (PubMed)

-cautarea in baze de date – PROSPERO-International Prospective Register of Systematic Reviews

(https://www.crd.york.ac.uk/prospero/)


PROSPERO
International prospective register of systematic reviews
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Welcome to PROSPERO
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- 2. Dezvoltarea protocolului

2A. Definirea **intrebarii de cercetare**

(cursul 1, va amintiti?) o intrebare generala/ mai multe intrebari (“split questions”)

2B Dezvoltarea **criteriilor de includere**

-Lotul/populatia de interes

- Variabila independenta

- Efecte, rezultate (Outcomes)

-Designul studiului

-Locatia/contextul (setting)

-Limba

-Tipul de publicatii

- 2C –CUM
- Vom efectua extragerea datelor?
- Evalua riscul de bias?
- Vom face sinteza datelor?

3. Strategii cautare baze de date: unde cautam?

1. **Baze de date internationale**

- MEDLINE, EMBASE, OVID
- Baze date regionale (Africa, Rusia, China, India..)
- Baze de date ce inregistreaza citarile articolelor (SCI-ISI, ESCI, Scopus)-indici bibliografici
- Baze de date cu teze de doctorat/masterat/licenta (ProQuest Dissertation&Thesis database)
- Cochrane Register of Controlled Trials (CENTRAL)
  - include si studii neindexate MEDLINE, EMBASE
  - Include studii in alte limbi decat engleza
  - Include studii prezentate la conferinte

N.B Nu uitati de “literatura gri” (grey literature)

Informatie care NU este publicata in carti/articole stiintifice

RCT publicate in articole stiintifice au aratat mai mult efect decat cele care sunt prezentate in literatura gri!

10% din referintele S.S. Cochrane sunt din literatura gri

Baze de date:

OpenSIGLE (System for Information on Grey Literature)-Europa

National Technical Information Service (NTIS)-SUA

2. Rezumate conferinte

-partial sunt acoperite de unele baze de date (EMBASE de ex)

-marea majoritate sunt indexate in BIOSIS (www.biosis.org), ISI-proceedings, etc.

?mai mult de 50% din RCT prezentate la conferinte nu sunt publicate sub forma de articol

?Chiar si cele publicate sunt publicate diferit fata de prezentarea anterioara (alte endpointuri, lot largit, etc)

- **3. Alte articole**
- Review-uri similare (nesistematice/sistematice anterioare)-inclusiv referintele acestora

- Ghiduri, consens etc – inclusiv referintele acestora

- Lista de referinta articole incluse in analiza full-text! – ***atentie la "citation bias": citare rezultate pozitive!***

- 4. Studii nepublicate sau nefinalizate

www.ClinicalTrials.gov

De ce studii nefinalizate?

De ce este important sa cautam din mai multe surse?

Unde cautam?-concluzii

- Cel putin 2 baze de date internationale
- Cele mai importante baze: MEDLINE, EMBASE, OVID, CENTRAL
- Atentie la literatura gri!
- Atentia la studiile prezentate la conferinte!
- Intotdeauna cautati si in referintele altor articole review/ghiduri/articole originale incluse!

Cum planificam strategia de cautare?

-vom include numai RCT sau si observationale?

-care este interventia?

-includem si efecte adverse?

- avem o arie geografica de interes?

- avem limitare in timp?

-includem si date nepublicate?

Structura cautarii: P.I.C.O.

- P-populatie (LA CINE?)
- I-interventie (CU CE?)
- C-comparatie (FATA DE CE?)
- O-efect (outcome) (CE URMARESC CU I?)

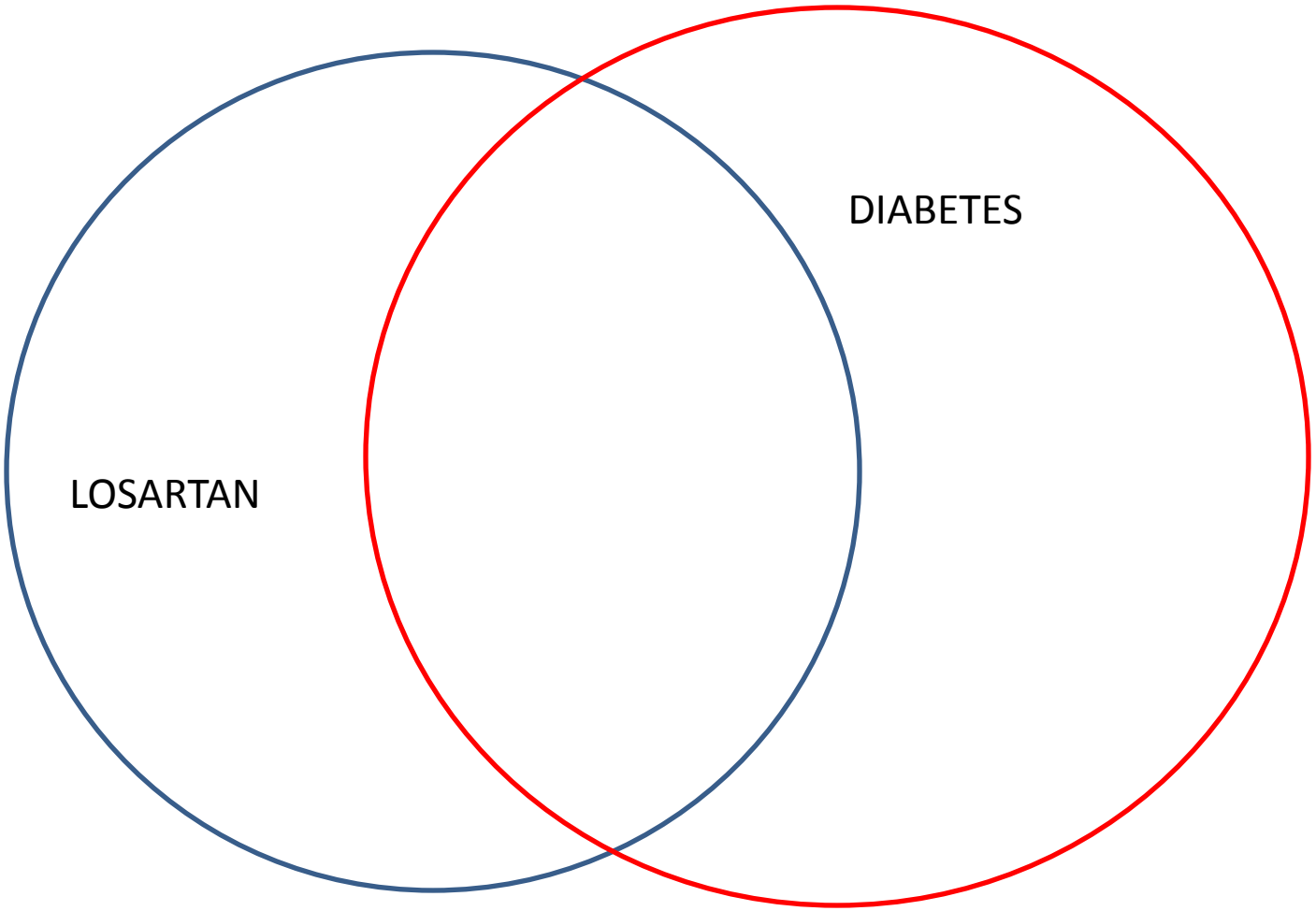
Cum cautam eficient?
Termenii cautarii

- Termeni legati de:

1. Tip studiu - RCT? Cohorta?
2. Populatia de interes
3. Interventia pe care o evaluam

Operatori logici (Boolean)

- OR AND NOT



Aplicatie practica

- Intrebare de cautare

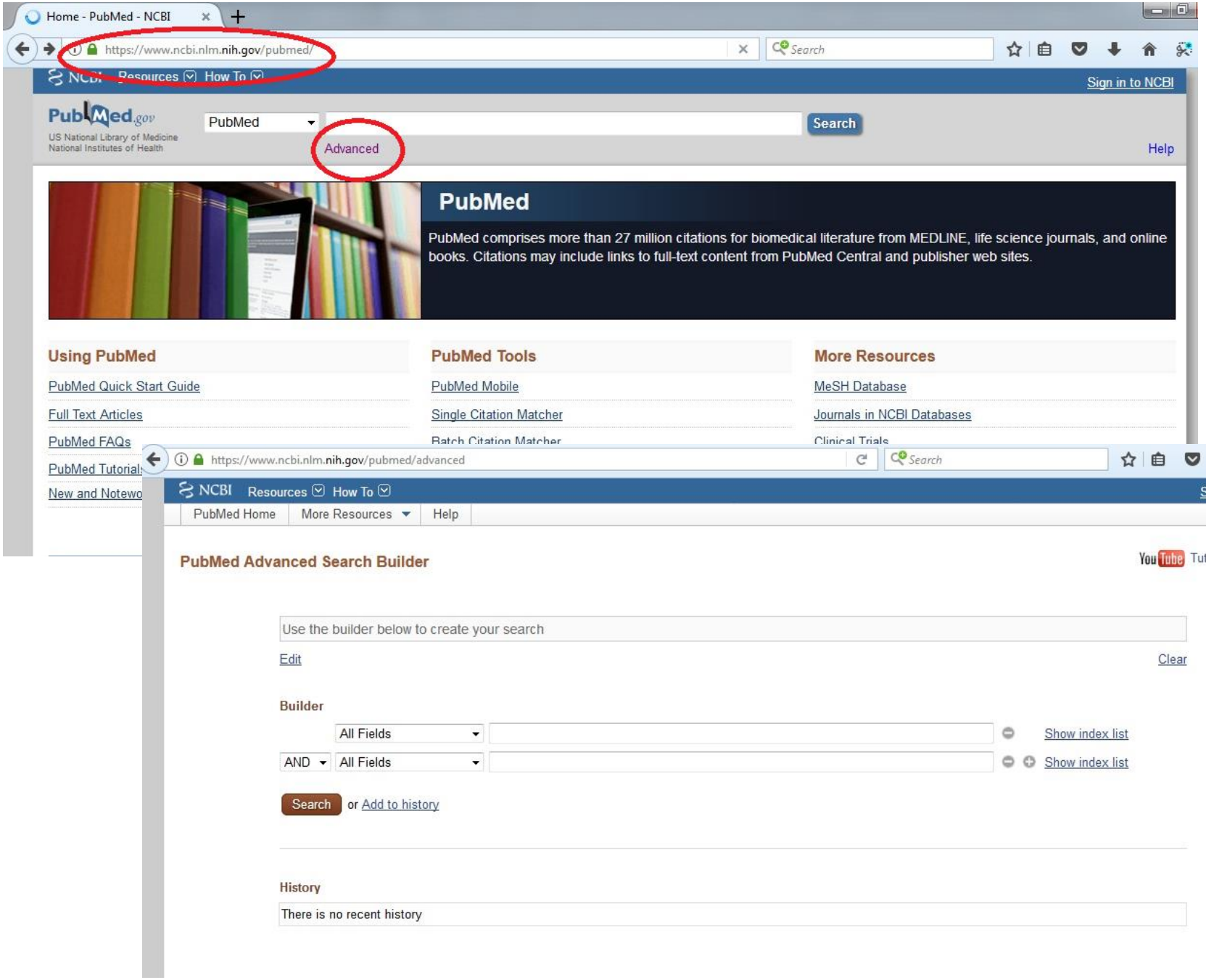
  ARE EFECT ACIDUL ALFA-LIPOIC in NEUROPATIA DIABETICA?

P- Neuropatie diabetica

I- Acidul alfa-lipoic

C- Placebo

Studii clinice randomizate


Home - PubMed - NCBI
https://www.ncbi.nlm.nih.gov/pubmed/
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PubMed.gov
US National Library of Medicine
National Institutes of Health
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Help
PubMed
PubMed comprises more than 27 million citations for biomedical literature from MEDLINE, life science journals, and online books. Citations may include links to full-text content from PubMed Central and publisher web sites.
Using PubMed
PubMed Quick Start Guide
Full Text Articles
PubMed FAQs
PubMed Tutorials
New and Notewo
PubMed Tools
PubMed Mobile
Single Citation Matcher
Batch Citation Matcher
More Resources
MeSH Database
Journals in NCBI Databases
Clinical Trials
https://www.ncbi.nlm.nih.gov/pubmed/advanced
Search
NCBI Resources How To
Sign in to NCBI
PubMed Home
More Resources
Help
PubMed Advanced Search Builder
YouTube Tutorial
Use the builder below to create your search
Edit
Clear
Builder
All Fields
Show index list
AND
All Fields
Show index list
Search
or Add to history
History
There is no recent history

Abrevieri

[tiab]- titlu sau abstract

[sh]- subheading “floating subheading”

[pt]- publication type

[tw]-text word

[mesh]- Termenul din MeSh “explodat”

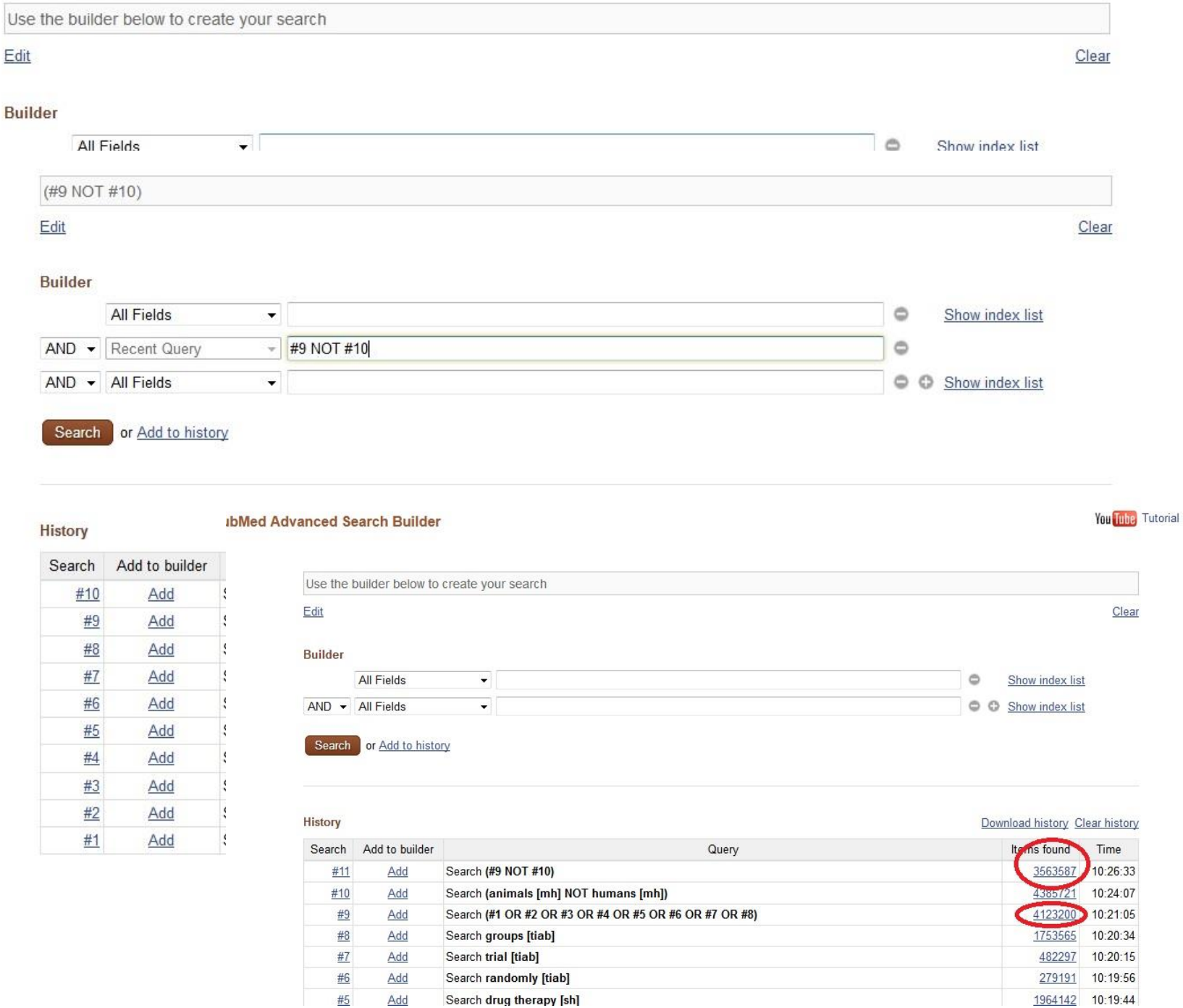
[mesh:noexp]- Termenul din MeSh “neexplodat”

*

Cum definim RCT?

- Cautare standard Cochrane

#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	4132320
#8	groups [tiab]	1747952
#7	trial [tiab]	480263
#6	randomly [tiab]	278254
#5	drug therapy [sh]	1959634
#4	placebo [tiab]	187932
#3	randomized [tiab]	421447
#2	controlled clinical trial [pt]	531074
#1	randomized controlled trial [pt]	445386


Use the builder below to create your search
Edit
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Use the builder below to create your search
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Items found
Time
#11 Add Search (#9 NOT #10) 3563587 10:26:33
#10 Add Search (animals [mh] NOT humans [mh]) 4385721 10:24:07
#9 Add Search (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8) 4123200 10:21:05
#8 Add Search groups [tiab] 1753565 10:20:34
#7 Add Search trial [tiab] 482297 10:20:15
#6 Add Search randomly [tiab] 279191 10:19:56
#5 Add Search drug therapy [sh] 1964142 10:19:44

Cum definim neuropatia diabetica

- - Diabetes mellitus[mesh] OR diabet*[tw]**=DIABET**

  - Peripheral Nervous System Diseases [mesh] OR neuropath*[tw] OR polyneuropath*[tw]

  =POLINEUROPATIE

INTERSECTIA CELOR DOUA MULTIMI OR diabetic neuropathies [mesh:noexp]

Use the builder below to create your search

Edit Clear

Use the builder below to create your search

Edit Clear

Builder

All Fields Show index list

AND All Fields Show index list

Search or Add to history

History Download history Clear history

Search	Add to builder	Query	Items found	Time
#19	Add	Search **(#17 OR #18)**	24863	10:40:53
#18	Add	Search **diabetic neuropathies [mesh:noexp]**	13422	10:39:54
#17	Add	Search **(#14 AND #16)** POLINEUROPATIE DIABETICA	24863	10:36:12
#16	Add	Search **((#15 OR neuropath*[tw] OR polyneuropath*[tw]))**	213809	10:31:35
#15	Add	Search **Peripheral Nervous System Diseases [mesh]**	133332	10:31:13
#14	Add	Search **(#12 OR #13)**	588280	10:29:22

Cum definim acid alfa-lipoic?

thioctic acid [mesh:noexp] OR lipoic acid[tw] OR alpha lipoic[tw] or thioc*[tw]

Builder

All Fields | Show index list

AND | All Fields | Show index list

Search or Add to history

History

Download history Clear history

Search	Add to builder	Query	Items found	Time
#22	Add	Search **(#20 OR #21)**	24665	10:45:12
#21	Add	Search **(lipoic acid[tw] OR alpha lipoic[tw] OR thioc*[tw])**	24665	10:44:44
#20	Add	Search **thioctic acid [mesh:noexp]**	3668	10:44:20
#19	Add	Search **(#17 OR #18)**	24863	10:40:53
#18	Add	Search **diabetic neuropathies [mesh:noexp]**	13422	10:39:54
#17	Add	Search **(#14 AND #16)**	24863	10:36:12
#16	Add	Search **((#15 OR neuropath*[tw] OR polyneuropath*[tw]))**	213809	10:31:35
#15	Add	Search **Peripheral Nervous System Diseases [mesh]**	133332	10:31:13
#14	Add	Search **(#12 OR #13)**	588280	10:29:22
#13	Add	Search **diabet*[tw]**	586578	10:28:56
#12	Add	Search **Diabetes Mellitus [mesh]**	370143	10:28:44
#11	Add	Search **(#9 NOT #10)**	3563587	10:26:33
#10	Add	Search **(animals [mh] NOT humans [mh])**	4385721	10:24:07

All Fields — Show index list

AND — All Fields — Show index list

Search or Add to history

History

Download history Clear history

Search	Add to builder	Query		Items found	Time
#23	Add	Search **(#11 AND #19 AND #22)**	rezultat final	178	10:48:23
#22	Add	Search **(#20 OR #21)**		24665	10:45:12
#21	Add	Search **(lipoic acid[tw] OR alpha lipoic[tw] OR thioc*[tw])**		24665	10:44:44
#20	Add	Search **thioctic acid [mesh:noexp]**		3668	10:44:20
#19	Add	Search **(#17 OR #18)**		24863	10:40:53
#18	Add	Search **diabetic neuropathies [mesh:noexp]**		13422	10:39:54
#17	Add	Search **(#14 AND #16)**		24863	10:36:12

History

Download history Clear history

Search	Add to builder	Query		Items found	Time
#22	Add	Search **(#20 OR #21)**	ACID ALFA LIPOIC	24665	10:45:12
#21	Add	Search **(lipoic acid[tw] OR alpha lipoic[tw] OR thioc*[tw])**		24665	10:44:44
#20	Add	Search **thioctic acid [mesh:noexp]**		3668	10:44:20
#19	Add	Search **(#17 OR #18)**	POLINEUROPATIE DIABETICA	24863	10:40:53
#18	Add	Search **diabetic neuropathies [mesh:noexp]**		13422	10:39:54
#17	Add	Search **(#14 AND #16)**		24863	10:36:12
#16	Add	Search **((#15 OR neuropath*[tw] OR polyneuropath*[tw]))**		213809	10:31:35
#15	Add	Search **Peripheral Nervous System Diseases [mesh]**		133332	10:31:13
#14	Add	Search **(#12 OR #13)**		588280	10:29:22
#13	Add	Search **diabet*[tw]**		586578	10:28:56
#12	Add	Search **Diabetes Mellitus [mesh]**		370143	10:28:44
#11	Add	Search **(#9 NOT #10)**	STUDIU CLINIC RADNDOMIZAT	3563587	10:26:33
#10	Add	Search **(animals [mh] NOT humans [mh])**		4385721	10:24:07

NCBI Resources How To Sign in to NCBI

PubMed.gov
National Library of Medicine
National Institutes of Health

PubMed (#11 AND #19 AND #22) Search

Create RSS Create alert Advanced Help

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how additional filters

Format: Summary Sort by: Most Recent Per page: 20 Send to

Filters: Manage Filters

Search results

Items: 1 to 20 of 178

<< First < Prev Page 1 of 9 Next > Last >>

1. α-Lipoic Acid as Adjunctive Treatment for Schizophrenia: An Open-Label Trial.
Sanders LLO, Menezes CES, Chaves Filho AJM, Viana GA, Fechine FV, de Queiroz MGR, Fonseca SGDC, Vasconcelos SMM, de Moraes MEA, Gama CS, Seybolt S, Campos EM, Macêdo D, de Lucena DF.
J Clin Psychopharmacol. 2017 Oct 19. doi: 10.1097/JCP.0000000000000800. [Epub ahead of print]
PMID: 29053478
Similar articles

2. Effects of High-Dose α-Lipoic Acid on Heart Rate Variability of Type 2 Diabetes Mellitus Patients with Cardiac Autonomic Neuropathy in Korea.
Lee SJ, Jeong SJ, Lee YC, Lee YH, Lee JE, Kim CH, Min KW, Cha BY.
Diabetes Metab J. 2017 Aug;41(4):275-283. doi: 10.4093/dmj.2017.41.4.275.
PMID: 28868825 Free PMC Article
Similar articles

3. Preventing Complications and Treating Symptoms of Diabetic Peripheral Neuropathy [Internet].
Dy SM, Bennett WL, Sharma R, Zhang A, Waldfogel JM, Nesbit SA, Yeh HC, Chelladurai Y, Feldman D, Wilson LM, Robinson KA.
Rockville (MD): Agency for Healthcare Research and Quality (US); 2017 Mar.
PMID: 28749633 Free Books & Documents
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Search details

#11 AND #19 AND #22

Search See more...

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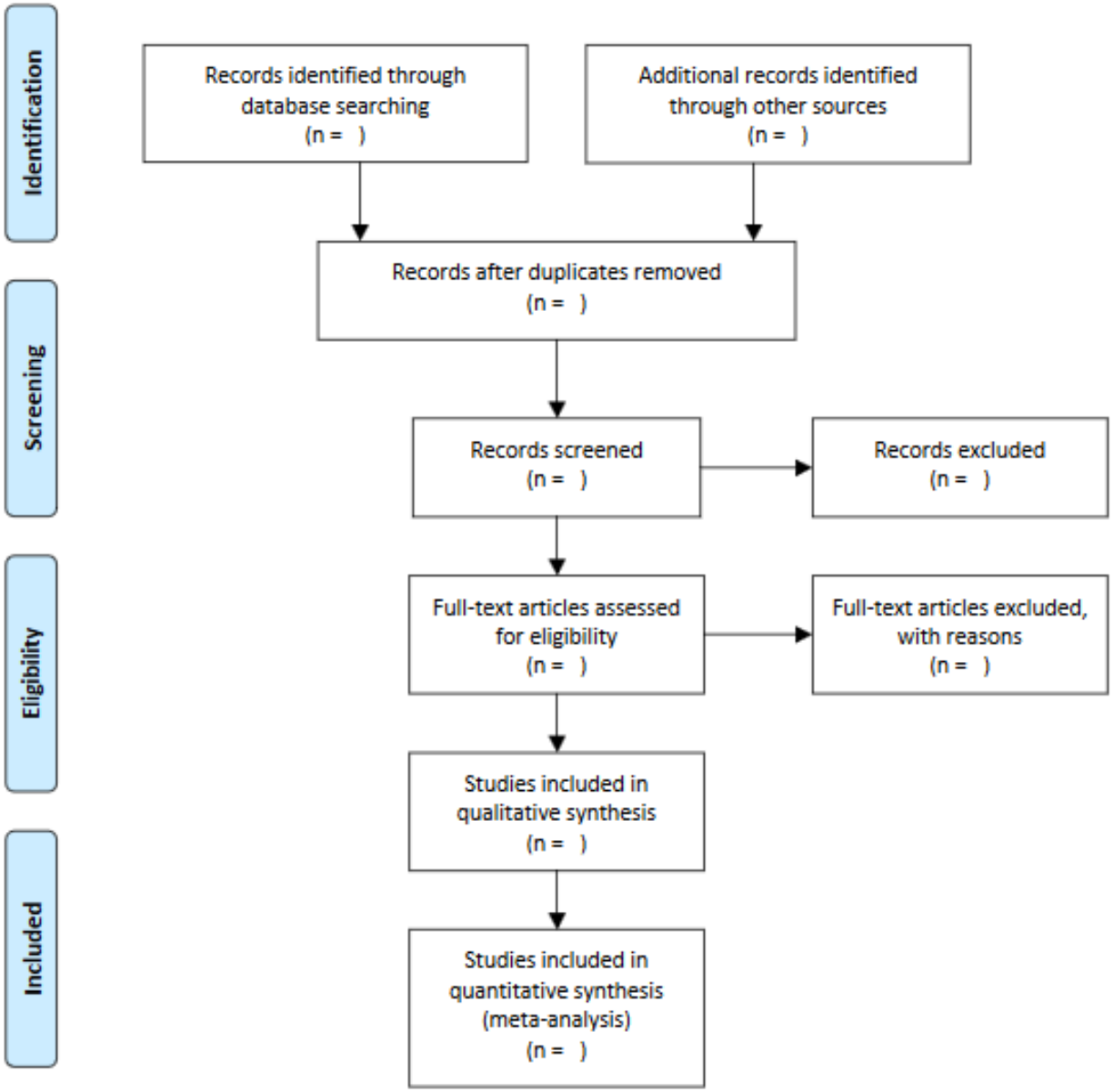
(((randomized controlled trial[pt]) OR (controlled clinical trial... (178) PubMed

3. Algoritm cautare in literatura



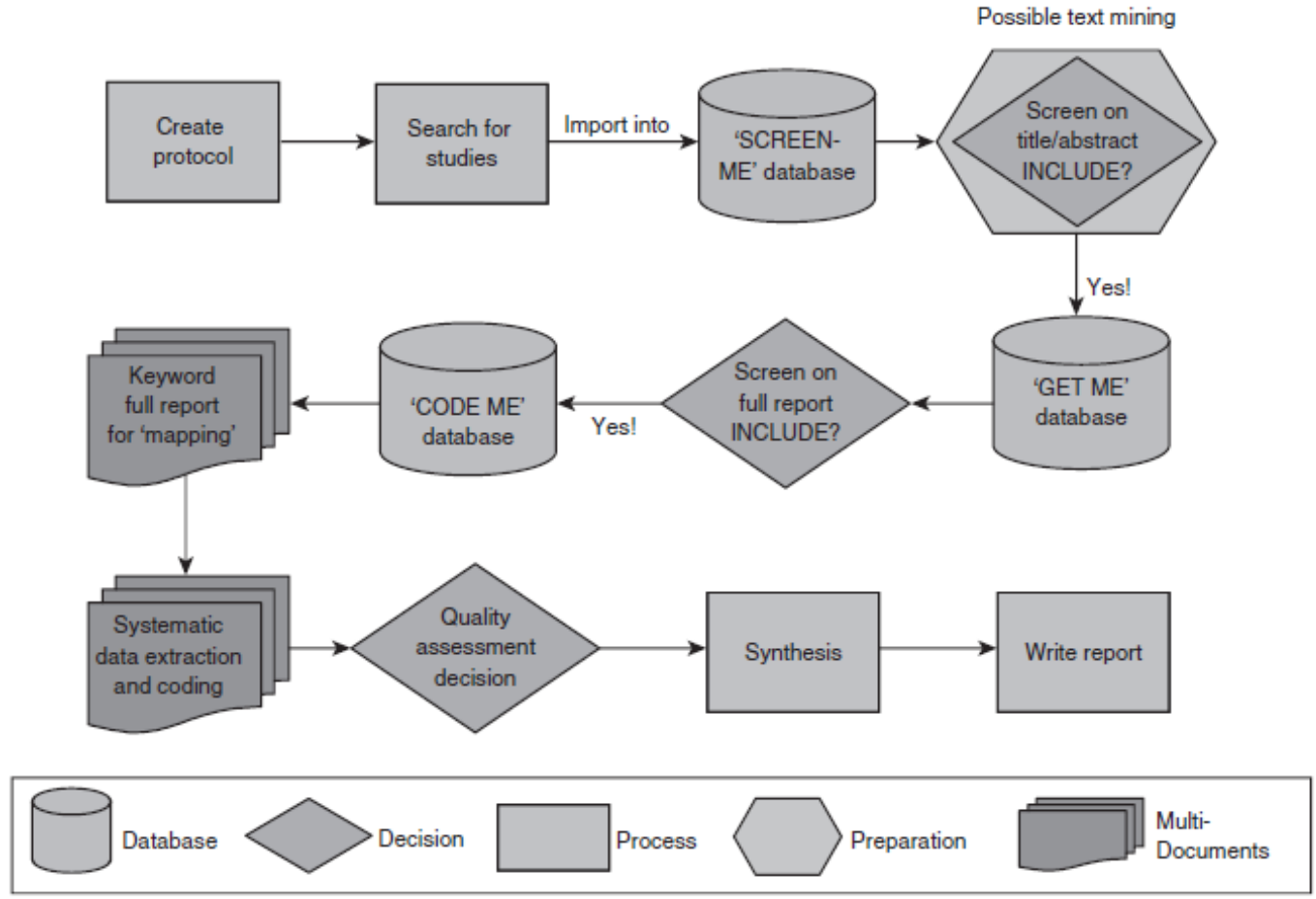


Figure 5.3 Flow of references through a review

4. Extragerea datelor

Baza de date (similara cu cea pt un studiu original)

- Ganditi-va la datele pe care doriti sa le analizati/ datele descriptive pe care doriti sa le prezentati
- Adaptata scopului si obiectivelor sintezei
- Testati o extragere ”pilot” a datelor din primele 2-3 articole – puteti ajusta campurile din baza de date
- **Calitatea si relevanta analizei** – evaluare critica a articolelor? Utilizati toate cunostintele de metodologia cercetarii si cautati **instrumentele de evaluare calitate articole**

Study description

Aims and objectives of the study

Study setting (e.g. geographical location, time period)

Study design (e.g. cohort or case-control)

Recruitment procedures used

Inclusion and exclusion criteria

Length of follow-up

Participant description

Baseline characteristics

Follow-up characteristics

Target population and final number of subjects studied for outcome

Description of exposure (or intervention) and outcome measurements

Description of measurement of exposure and outcome (e.g. instrument, protocol, reliability)

Description of intervention, randomization and blinding (if applicable)

Statistical data/results

Statistical techniques used (e.g. regression, t-tests)

Confounding factors adjusted for

Results of study analysis (e.g. direction and magnitude of association, precision)

Conclusions of study

doi: 10.1186/0778-7367-71-21.

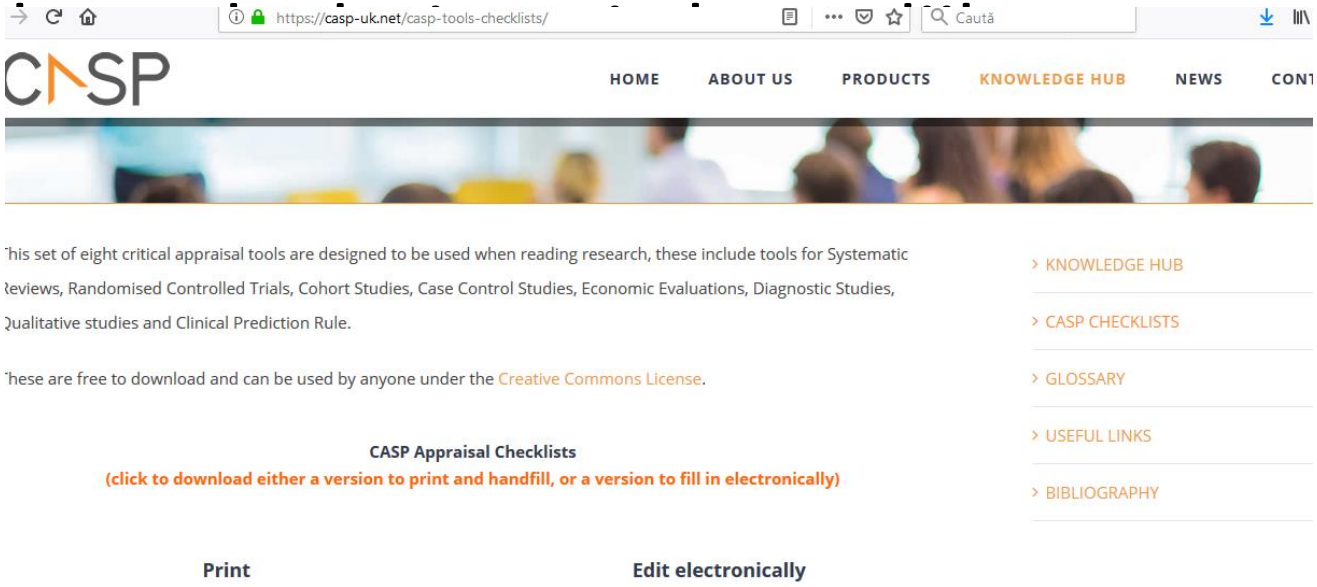
An	Autor	Tip studiu	Nr pacienti	Grup martor	Analiza vitamina D	Masurare despresie	Concluzie
2018	Jennings	transversal	123	N/A	ELISA	PHQ9	vitamina D mai mare la pacientii cu scor PH

Instrumente pentru analiza calitativa a articolelor incluse

- Cochrane Collaboration handbook (RCT)

RISK OF BIAS ASSESSMENT TOOL

- Critical Appraisal Skills Programme (CASP) pt o varietate



Skills Programme

9. Do you believe the results?

Yes ☐

No ☐

HINT: Consider

- big effect is hard to ignore!
- Can it be due to chance, bias, or confounding
- are the design and methods of this study sufficiently flawed to make the results unreliable
- consider Bradford Hills criteria (e.g. time sequence, does-response gradient, strength, biological plausibility)

Comments:

- Nu uitati de instrumentele specifice pentru analiza calitatii pe care le puteti folosi in functie de scopul sintezei sistematice

(Ex: Sinteza sistematica a biomarkerilor proteomici identificati prin spectrometrie de masa: criterii de raportare / systematic review of proteomic biomarkers identified in mass spectrometry: criteria for reporting e.g Mischak H, Allmaier G, Apweiler R, et al. (2010). Recommendations for biomarker identification and qualification in clinical proteomics. Sci Transl Med 2:46ps42)

5. Redactarea raportului (rezultate)

- Sinteza narativa a rezultatelor din baza de date
- UTILIZATI TABELE
- Prezentati datele in **sectiunea de rezultate**
- Meta-analiza?

6. Meta-analiza

= Metoda statistica pentru combinarea rezultatelor numerice ale studiilor

MARIMEA EFECTULUI – rezultat al studiului

-intotdeauna asociaza un grad de incertitudine statistica (eroarea standard-> INTERVAL DE INCREDERE)

1. CONTINUE (T.A, valoare Cho, etc)
2. DIHOTOMICE (da/nu: deces, infarct)

Calcularea marimii efectului pentru fiecare studiu este adesea cel mai dificil si cronofag aspect al meta-analizei!!!

Utilizati instrumente software online!RevMan, Meta, MIX2.0 (utilizeaza Excel)

Cautati pe Google daca nu sunteti siguri!

Daca nu aveti datele puteti contacvta autorul corespondent

Standardized mean difference (SMD) – Diferenta medie standardizata

- Studii diferite care masoara acelasi efect au utilizat instrumente diferite pentru a isi masura rezultatele (scale diferite pentru depresie)
- Convertiti rezultatele la o scala comuna pentru a combina efectele (to “pool” effect sizes=> COMBINED (POOLED) EFFECT SIZE)

Standardized mean difference (SMD) – Diferenta medie standardizata

- Exprima marimea efectului interventiei in fiecare studiu in functie de variabilitatea observata in studiul respectiv

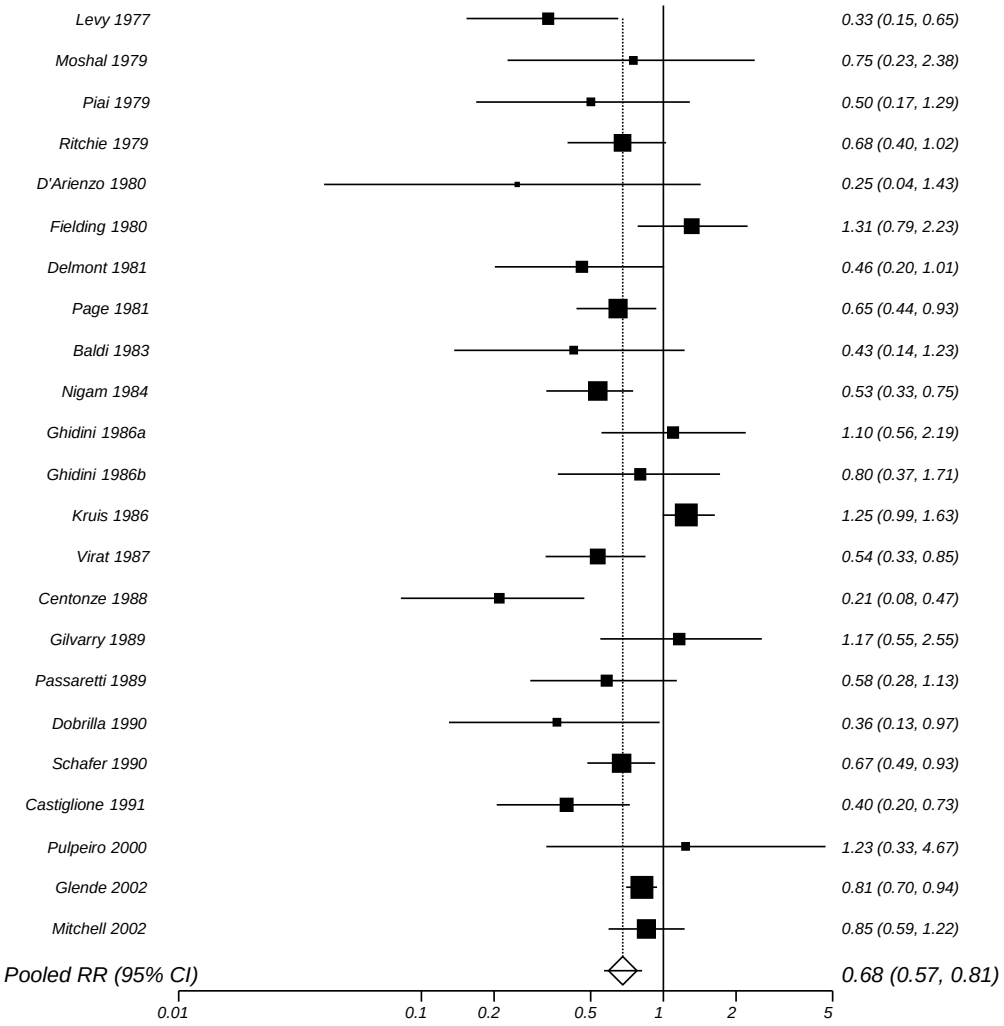
- Calculata prin instrumente online https://www.polyu.edu.hk/mm/effectsizefaqs/calculator/calculator.html
- REVMAN (softul Cochrane)

Combinarea marimii efectelor in meta-analiza

- Studiilor incluse le trebuie atribuita mai multa sau mai putina semnificatie
- “Greutate” (‘Weight’) atribuita diferitelor studii

- “Greutatea” (‘Weight’) este influentata de marimea esantionului si de varianta (studiile mai mici vor avea o greutate mai mica atribuita)

Cum exprimati rezultatele unei sinteze sistematice - “ Forrest Plot”



Effect of Antispasmodics in IBS

I^2 value = 62.4%, Chi^2 P < 0.001

Testele statistice care se asociaza unui “Forrest plot”

- **Heterogenitatea statistica – Q cu grad de libertate**-> cat de heterogene sunt marimile efectelor si valorea p (gasirea semnificatiei statistice a heterogenitatii)
- **Valoarea I^2 (“eye-squared”)** gradul de heterogenitate secundar diferentelor dintre studii dar nu efectului aleator

Cum sa calculam marimea efectului combinate din studiile incluse

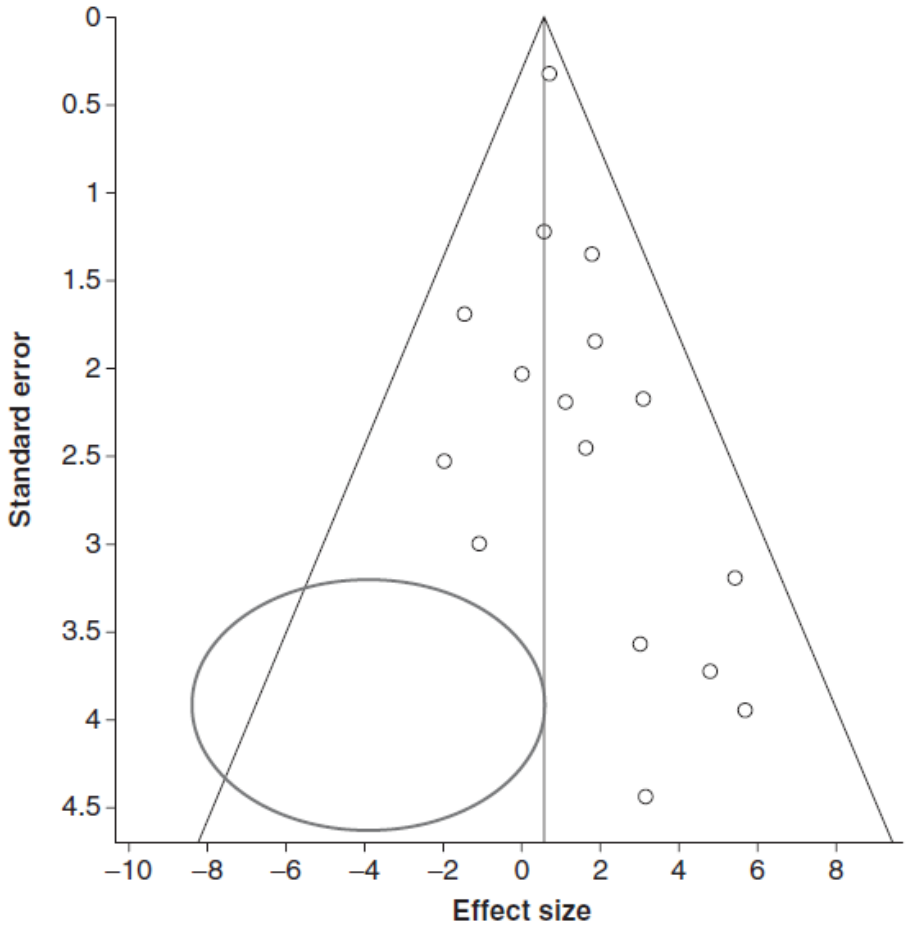
- 2 modele statistice (folositi software-uri-ex.RevMan)

  MODELUL FIX- daca este putina heterogenitate.

  MODELUL EFECTULUI ALEATOR-Daca exista multa heterogenitate dar intervale de incredere largi

PUTETI RAPORTA AMBELE MARIMI ALE EFECTULUI COMBINAT si comentati

Evaluation of **publication bias-** ”Funnel plots”



From Chapter 7 An introduction to systematic reviews. Editor(s) David Gough, Sandy Oliver, James Thomas Date 2017 Publisher SAGE

Transformarea marimii efectului in meta-analiza

- Date Continue : **direct**
- Date Binare: **Pooled ORs, RRs**
- **Util:** incercati sa folositi datele originale continue si diferentele brute (daca e posibil) decat SMD (mai dificil de interpretat)

Concluzii

- Definiti o intrebare de cercetare pentru sinteza
- Dezvoltati o strategie de cautare
- Dezvoltati un protocol
- Includeti articole si extrageti datele relevante in baza de date
- **Evaluati critic** si **analizati calitatea** articolelor incluse (utilizati instrumente care sa va ghideze**)**
- **NU este obligatoriu sa faceti meta-analiza.** Va puteti referi strict la descrierea rezultatelor fara analizarea lor statistica – in cazul in care nu e aplicabil/ adecvat !

Daca faceti meta-analiza

- Calculati Diferenta medie standard = **Standard mean difference** (SMD) daca marimile efectelor sunt exprimate diferit
- Folositi **modele pentru efecte aleatorii (random effect models) sau modele fixe** in functie de **heterogenitatea** studiilor
- Prezentati datele folosind **Forrest plots**
- Analizati eroare sistematica de publicare utilizand **Funnel plots**
- Transformati marimile efectelor astfel incat sa fie usor de inteles

Bibliografie

1. Denison HJ, Dodds RM, Ntani G, Cooper R, Cooper C, Sayer AA, Baird J. How to get started with a systematic review in epidemiology: an introductory guide for early career researchers. Arch Public Health. 2013 Aug 7;71(1):21. doi: 10.1186/0778-7367-71-21.
2. An introduction to systematic reviews. Editor(s) David Gough, Sandy Oliver, James Thomas Date 2017 Publisher SAGE