SACRO CUORE DON CALABRIA

ECI CANCER CENTRE

I R C C S

SCUOLA DI METODOLOGIA DELLA RICERCA CLINICA

2025 - 11ª EDIZIONE

MODULI SPECIALISTICI - S1

VENERDÌ 14 - SABATO 15 MARZO 2025

NEGRAR DI VALPOLICELLA (VR)

Centro Formazione IRCCS "Sacro Cuore - Don Calabria"

Tipologia delle Revisioni della Letteratura Scientifica.
Obiettivi di una Revisione Sistematica.

Michela CINQUINI

Revisioni narrative e sistematiche

- Non esiste un definizione ufficiale e riconosciuta né di revisione narrativa né di revisione sistematica
- Systematic reviews: “There is no standard definition of an SR. We counted a report as an SR if the authors’ stated objective was to summarize evidence from multiple studies and the article described explicit methods, regardless of the details provided”. (Moher 2007)

REVISIONI NARRATIVE

Narrative reviews are the traditional approach and usually do not include a section describing the methods used in the review. They are mainly based on the experience and subjectivity of the author, who is often an expert in the area.

(Cipriani. Epidemiologia e Psichiatria sociale 2003)

REVISIONI NARRATIVE

- A narrative review discusses and summarises the literature on a particular topic, without generating any pooled summary figures through meta-analysis. This type of review usually gives a comprehensive overview of a topic, rather than addressing a specific question such as how effective a treatment is for a particular condition. Narrative reviews do not often report on how the search for literature was carried out or how it was decided which studies were relevant to include (Glossary – NHS)

REVISIONI NARRATIVE

Rassegne descrittive di un certo numero di studi, presentazioni dei risultati (spesso senza i dati precisi) e conclusioni circa l'efficacia del trattamento

- La strategia di ricerca bibliografica per recuperare gli articoli non è descritta
- I criteri usati per includere gli studi non sono specificati
- Descrivono studi senza dire che % sono di tutti quelli esistenti su quell'argomento
- Spesso le caratteristiche degli studi primari sono descritte sommariamente: non è riportata la numerosità del campione, né i dati relativi all'efficacia
- Non viene valutata la qualità metodologica degli studi inclusi

- **Articoli non validi per trarre conclusioni affidabili circa l'efficacia di un trattamento**

Cosa è una revisione sistematica (RS)? (1)

Un tentativo di sintetizzare i risultati e le conclusioni di due o più pubblicazioni (articoli primari) su una determinata problematica sanitaria.

Vero e proprio progetto di ricerca

Cosa è una RS? (2)

Una valutazione *complessiva ed esaustiva*

- della *qualità*
- della *rilevanza clinica* e
- *eterogeneità*

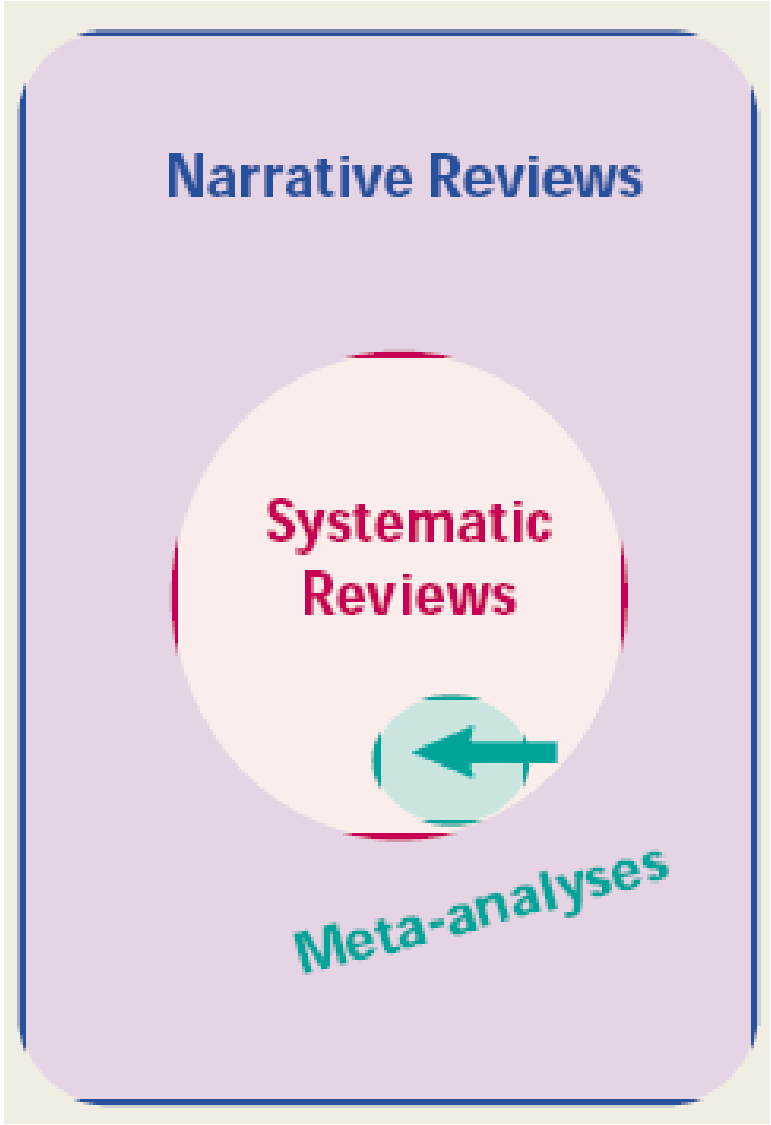
Di tutte le informazioni disponibili su una determinata problematica sanitaria.

- Una revisione che è stata realizzata attraverso un approccio scientifico rigoroso, per ridurre gli errori sistematici e casuali, in un modo documentato nei materiali e metodi.

- Una revisione sistematica può includere, o meno, una metanalisi: un'analisi statistica dei risultati degli studi indipendenti che ha, generalmente, come obiettivo di produrre una singola stima numerica dell'effetto del trattamento.

Chalmers I and Altman DG, 1995

Una visione insiemistica



Principi di una meta-analisi

Una meta-analisi può:

- Combinare i risultati dei singoli studi per ottenere una stima complessiva dell'effetto del trattamento;
- Esplorare l'eterogeneità tra gli studi (e le relative fonti di eterogeneità).

  NB: una revisione sistematica non si conclude forzatamente con una meta-analisi.

Revisioni sistematiche vs Revisioni narrative

Le revisioni tradizionali vs le revisioni sistematiche

CARATTERISTICHE	REVISIONE TRADIZIONALE	REVISIONE SISTEMATICA
Domanda	Ampia	Focalizzata su un unico quesito clinico
Fonti e ricerca	Non specificate	Complete ed esplicita
Selezione	Solitamente non specificata	Basata su criteri specifici
Valutazione critica	Variabile	Rigorosa
Sintesi	Qualitativa	Qualitativa/quantitativa (meta-analisi)

Caratteristiche delle RS (1)

- Chiara definizione del titolo e dell'obiettivo;
- Strategia di ricerca esaustiva che risponda agli obiettivi della RS (studi rilevanti) per includere sia gli studi pubblicati che i non pubblicati;
- Criteri di inclusione/esclusione adottati esplicitati e motivati;
- Lista esaustiva di tutti gli studi identificati;
- Presentazione chiara delle caratteristiche di ogni studio incluso e analisi della loro qualità metodologica;
- Lista degli studi esclusi e motivazione dell'esclusione;
- Analisi trasparente dei risultati degli studi eleggibili utilizzando tecniche di sintesi statistica (meta-analisi) se appropriato e possibile;
- Analisi di sensibilità dei dati se appropriate e possibili;
- Stesura di un rapporto finale che presenti chiaramente l'obiettivo, descriva i materiali e metodi e riporti i risultati.

Perché sono necessarie le revisioni sistematiche?

- Perché il numero di pubblicazioni e di ricerche su un determinato argomento è troppo grande
- Perché considerare solo parte delle informazioni disponibili può determinare errori (publication bias)
- Perché la qualità metodologica degli studi è variabile
- Perché i risultati di studi diversi condotti sullo stesso argomento spesso differiscono tra loro

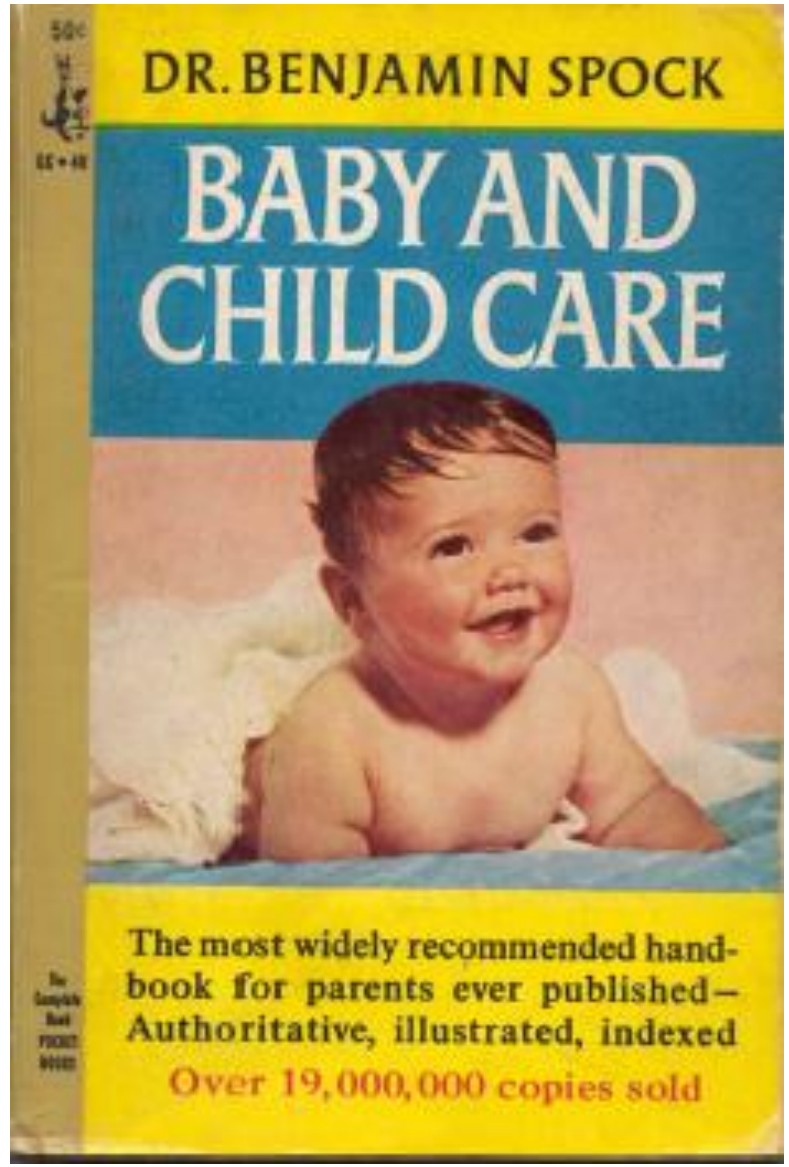
Perché sono utili le revisioni sistematiche?

‘In God we trust, all others (must) bring data’

W Edwards Deming

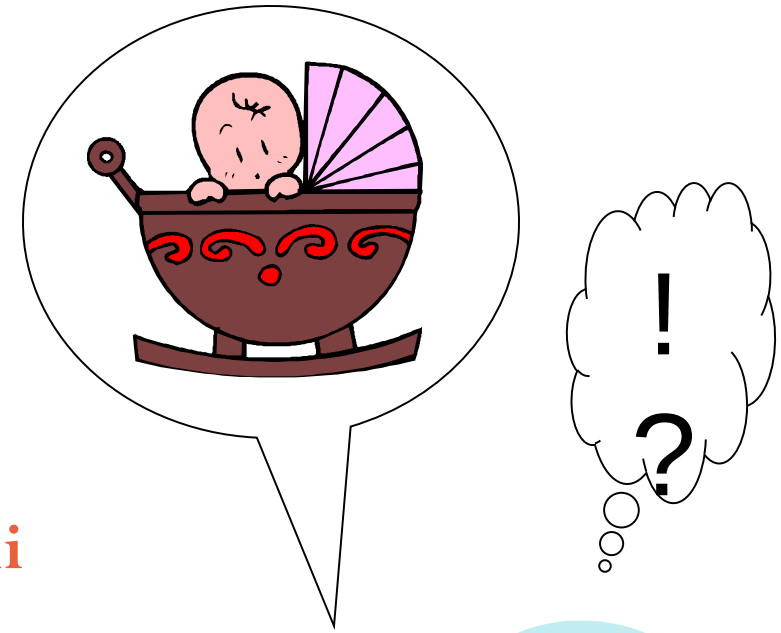
Situazioni di particolare utilità

- Quando risultati conflittuali si accumulano rapidamente con risultati incerti
- Quando una patologia è percepita in modo “drammatico” dalla popolazione
- Quando un trattamento potenzialmente efficace rischia di essere abbandonato
- Quando la ricerca clinica deve essere “ri-orientata”
- Quando bisogna esplicitare la limitazione delle informazioni scientifiche disponibili per le decisioni sanitarie
- Ogni volta che si deve costruire un progetto di ricerca


DR. BENJAMIN SPOCK
BABY AND CHILD CARE
The most widely recommended handbook for parents ever published—Authoritative, illustrated, indexed
Over 19,000,000 copies sold

Benjamin McLane Spock (New Haven, 2 maggio 1903 – La Jolla, 15 marzo 1998) - pediatra statunitense
- fama con la pubblicazione del libro: ***Common Sense Book of Baby and Child Care*.**
Il libro venne **pubblicato** per la prima volta nel **1946** e fu tradotto in tutte le principali lingue del mondo; fu uno dei maggiori successi editoriali dell'immediato dopoguerra, vendendo per circa un decennio un milione di copie all'anno e raggiungendo, nel 2011, un volume complessivo di vendite di circa **50 milioni** di copie. Spock aveva avuto l'abilità di trattare temi molto popolari (soprattutto presso le donne), come la gravidanza, il parto, l'alimentazione e le cure del bambino, con un linguaggio semplice e brillante, spregiudicato e anticonformista, presentando progressi e orientamenti della ginecologia e della pediatria come novità rivoluzionarie derivanti anche dalla sua esperienza professionale.

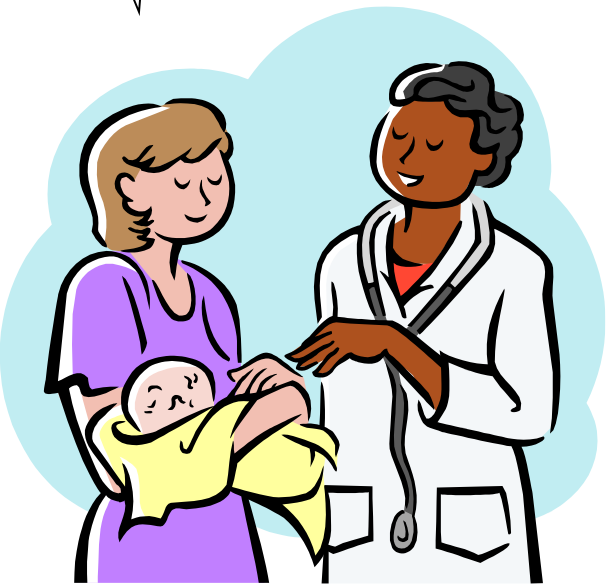
Scenario: 1970 – reparto di ostetricia



Madre primipara, spaventata dalla “**morte in culla”**, alla dimissione dal reparto dopo il parto, **chiede**:

Qual è la posizione migliore in cui porre il neonato durante il sonno ?

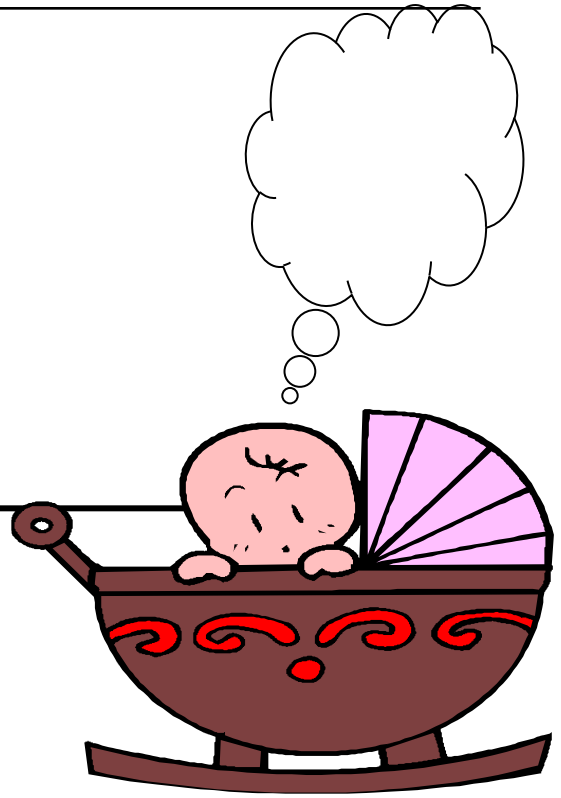
Il medico di stanza scrupoloso commissiona allo specializzando una **ricerca bibliografica …**



Scenario: 1970 – reparto di ostetricia

Ricerca Bibliografica:

Testo	Posizione consigliata
Mollon 1967 1° ed.	Supina
Potts 1967 1° ed.	Prona o fianco
Illingworth & Illingworth 1968 4° ed.	Indifferente
Illingworth 1968 4° ed.	Prona
Mollon 1968 2° ed.	Supina
Spock 1969 3° ed.	Prona

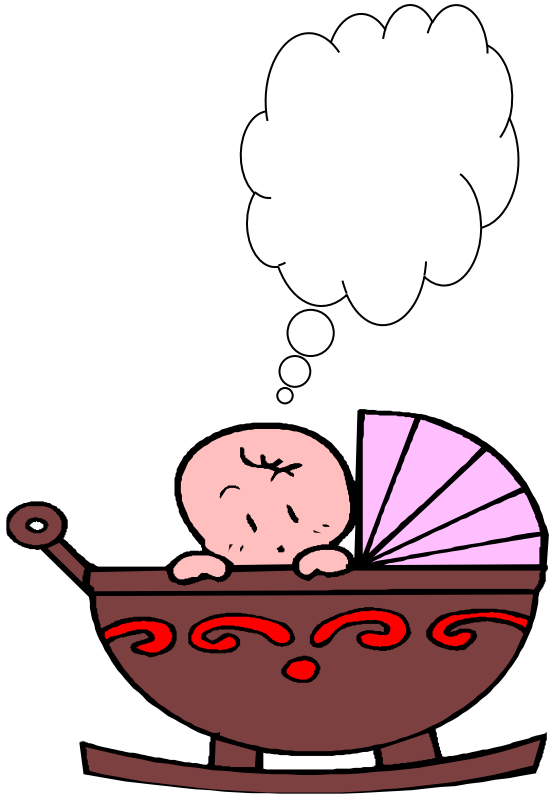


… nella lettera di dimissione, tra le raccomandazioni, viene riportato che *la posizione migliore del neonato nella culla, durante il sonno, è quella* ***prona (pancia in giù)***

...ancora sulla posizione del lattante:

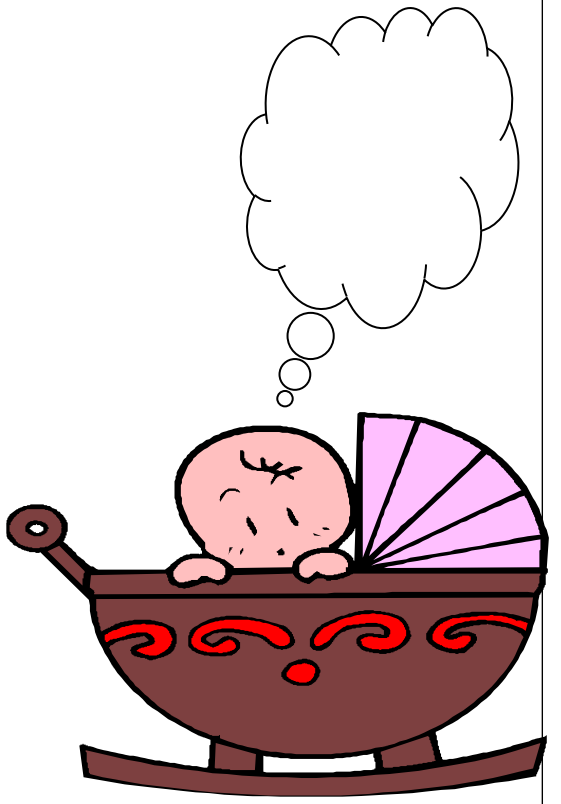
Facoltà di Medicina

Anni 90



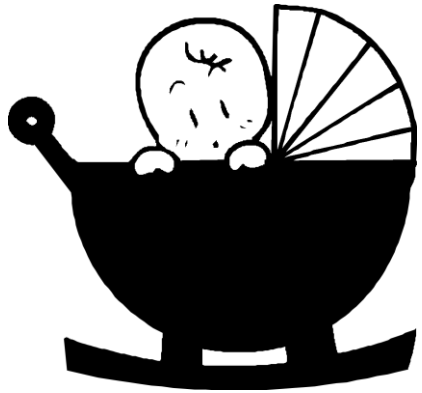
Dal testo consigliato per l'esame di pediatria

- Dalla edizione 1990 e dalla edizione 1997:
  - Sulla morte in culla: 5 (cinque) righe
    - Possibile causa: shock anafilattico da latte vaccino
    - 1-2 casi per 1000 nati vivi
    - Prima causa di morte tra 1 e 12 mesi
  - Sulla posizione dei lattanti nel sonno, riportata per terapia del reflusso gastro-esofageo:
    - "Corretta posizione: prona e su un letto tenuto leggermente inclinato"



Alcune possibili conseguenze di questo modo di procedere:

una strage silenziosa



Int. J. Epidemiol. Advance Access published April 20, 2005

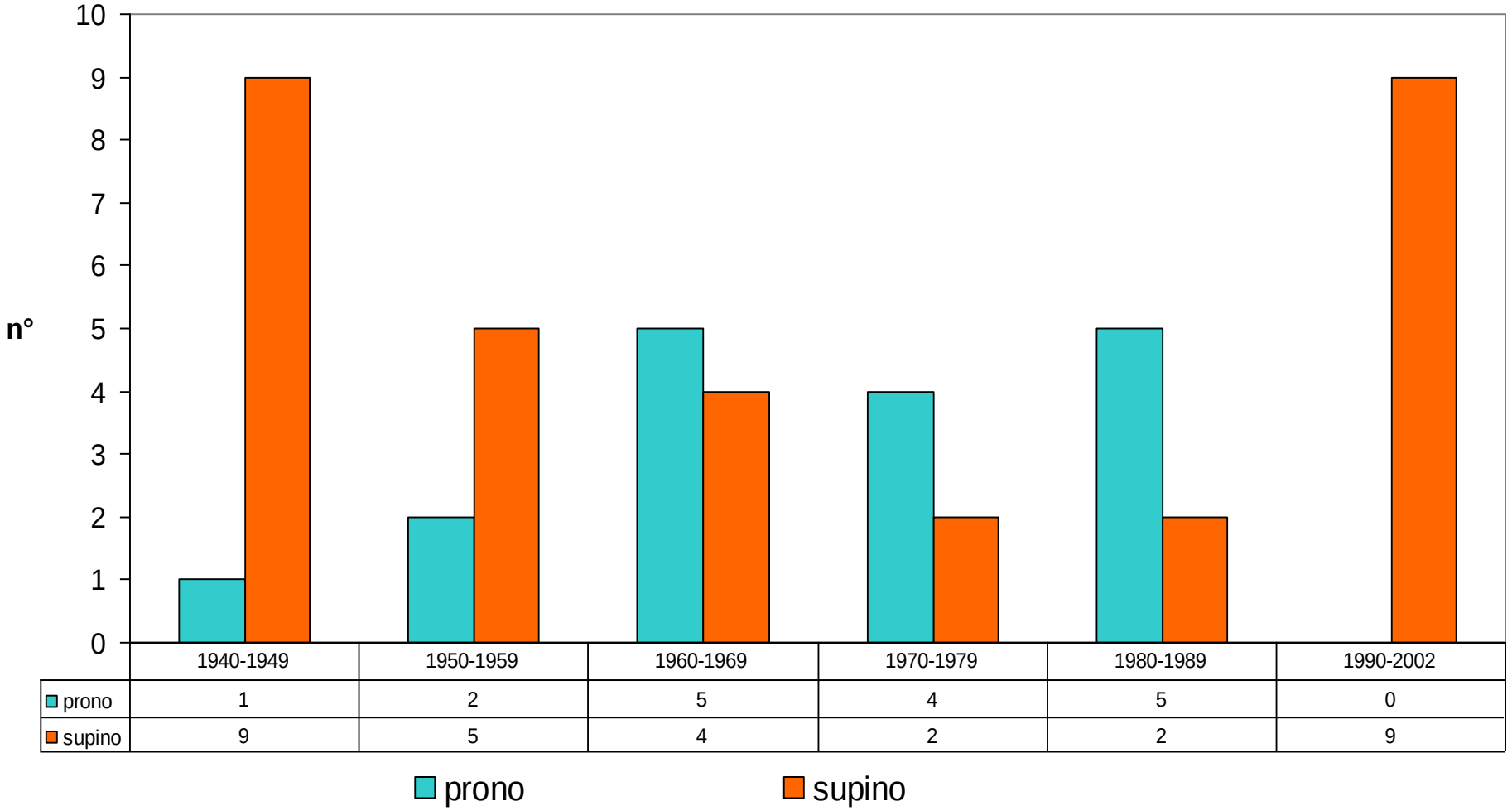
Published by Oxford University Press on behalf of the International Epidemiological Association

International Journal of Epidemiology
doi:10.1093/ije/dyi088

Infant sleeping position and the sudden infant death syndrome: systematic review of observational studies and historical review of recommendations from 1940 to 2002

Ruth Gilbert,[1]* Georgia Salanti,[2] Melissa Harden[1] and Sarah See[1,3]

Raccomandazioni sulle posizioni del sonno nel lattante: letteratura inglese

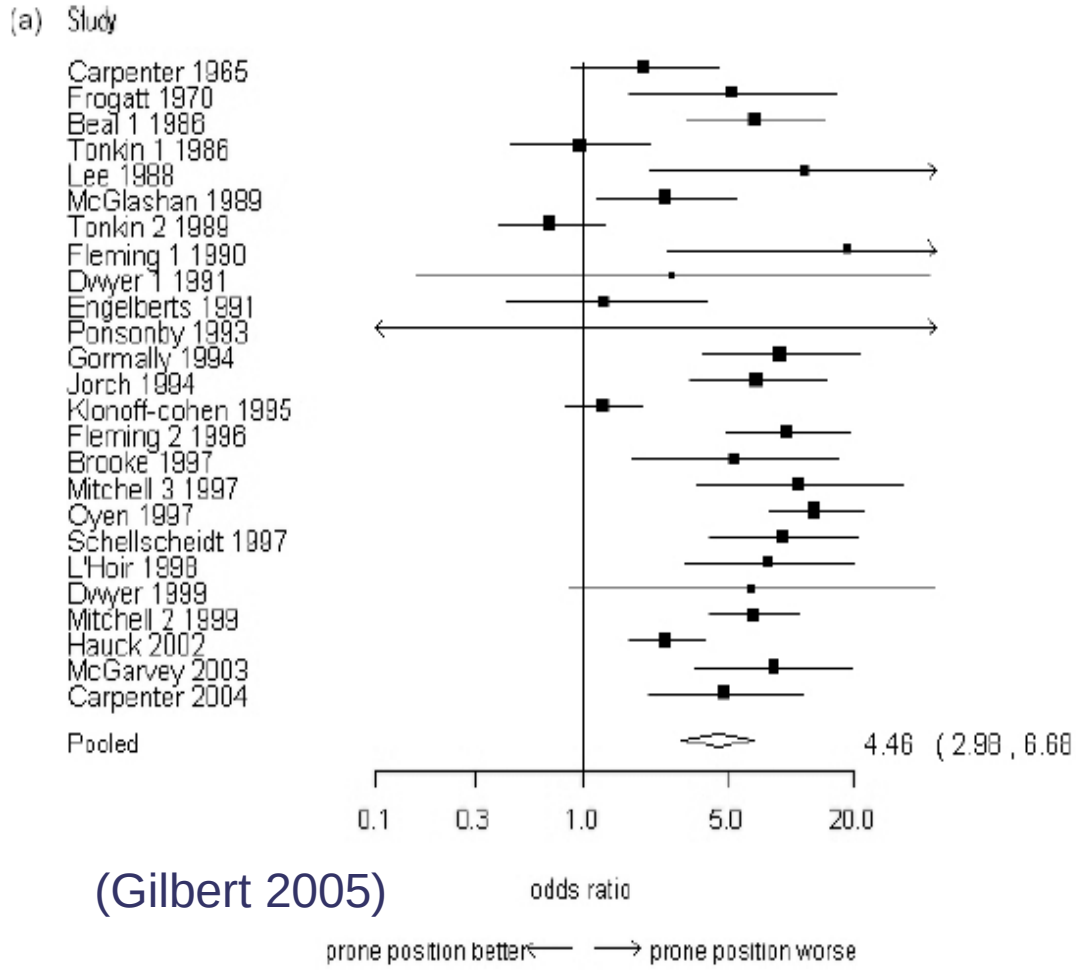


	1940-1949	1950-1959	1960-1969	1970-1979	1980-1989	1990-2002
prono	1	2	5	4	5	0
supino	9	5	4	2	2	9

(Gilbert 2005)

Morte in culla

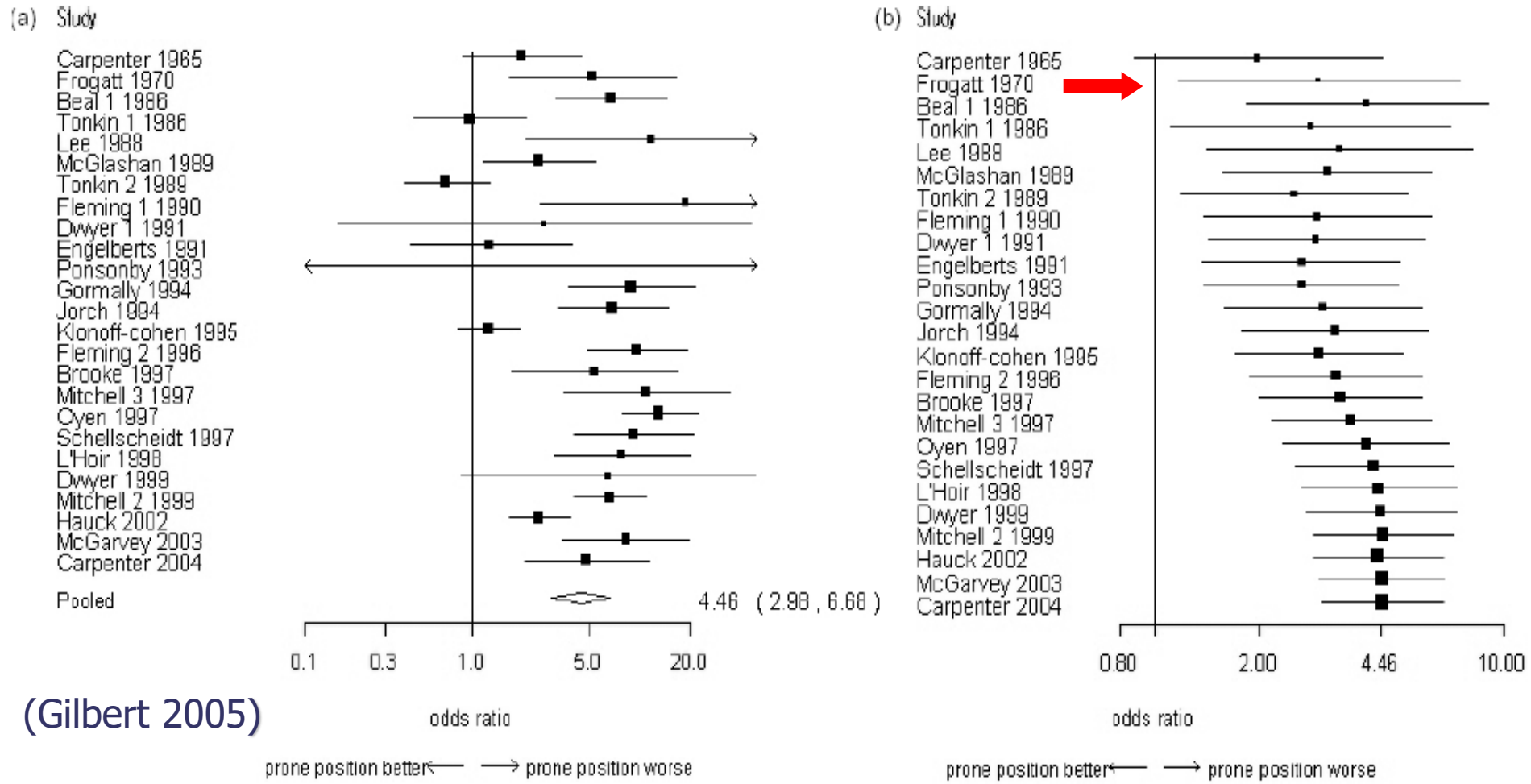
Metanalisi degli studi epidemiologici sulla posizione prona e rischio di morte del lattante nel sonno



(Gilbert 2005)

Morte in culla

Meta analisi CUMULATIVA



(Gilbert 2005)

Morte in culla

Gilbert 2005:

- La raccomandazione di **tenere il neonato in culla in posizione prona è proseguita per circa 50 anni** senza tener conto dell'**evidenza disponibile** già dal **1970** che la posizione prona era dannosa

- **Una revisione sistematica** dei fattori di rischio prevenibili per evitare la morte in culla avrebbe permesso a partire **dal 1970** di **conoscere** che la posizione prona era dannosa e avrebbe **evitato** più di **10.000 morti in Gran Bretagna e almeno 50.000 tra Europa**, Stati Uniti e Australia.

CON CHI?

- Non da soli!
- Multidisciplinare
- Esperti dell'argomento bilanciati da 'ignari'
- Metodologi, epidemiologi clinici o statistici
- Un po' di esperienza e un po' di training non guastano (ecco perché siete qui)
- Coinvolgere pazienti/users (molto Cochrane)

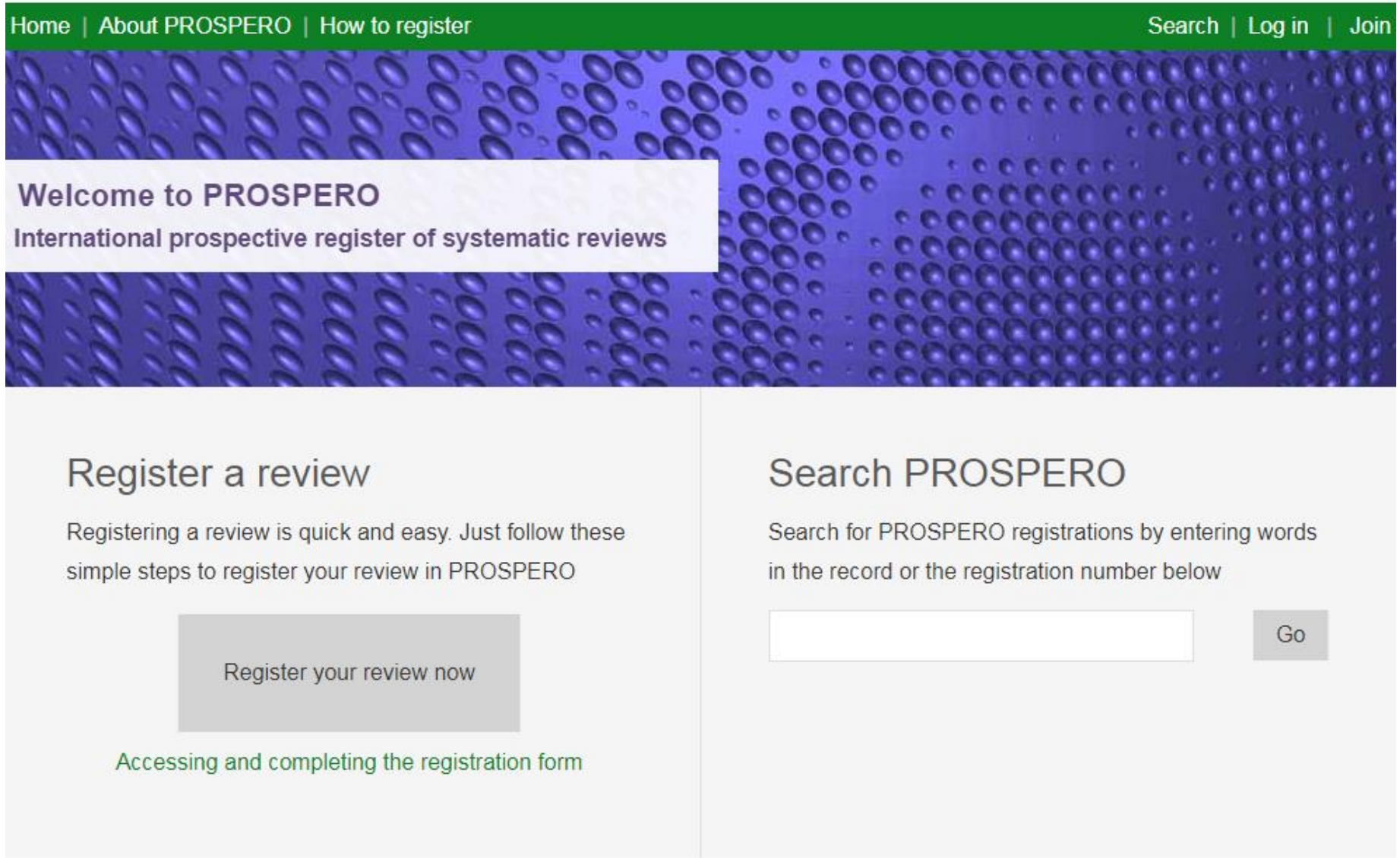
Il protocollo di una revisione sistematica

Protocollo -contenuti

- Background
- Obiettivi della revisione
- Metodi
  - ✓ I criteri di inclusione degli studi
  - ✓ La strategia di ricerca bibliografica
  - ✓ I metodi con cui verranno estratti i dati
  - ✓ I criteri di valutazione di qualità metodologica degli studi che verranno usati
  - ✓ Il metodo usato per l'eventuale sintesi statistica
  - ✓ Eventuali analisi per sottogruppi
  - ✓ Metodo per valutare la qualità dell'evidenza (GRADE)

Protocollo

- Scriverlo: fondamentale
  - ✓più revisori
  - ✓avere idee chiare di quello che si vuole fare
  - ✓evitare il reporting bias (solo i risultati significativi)
- Pubblicarlo: raccomandato



What you will find in PROSPERO

http://www.crd.york.ac.uk/prospero/aboutreg.php?reg=help

Help with registration

Download the guidance notes for registering a systematic review on PROSPERO.

COSA VOGLIAMO FARE?

Il Quesito/obiettivo della vostra revisione sistematica detta titolo e criteri di inclusione/esclusione (i.e. PICO)

A clearly defined, focused review begins with a well framed question

SACRO CUORE DON CALABRIA

ECI CANCER CENTRE

I R C C S

SCUOLA DI METODOLOGIA DELLA RICERCA CLINICA

2025 - 11ª EDIZIONE

MODULI SPECIALISTICI - S1

VENERDÌ 14 - SABATO 15 MARZO 2025

NEGRAR DI VALPOLICELLA (VR)

Centro Formazione IRCCS "Sacro Cuore - Don Calabria"

Strutturazione del Quesito e Misure di Associazione

Giovanni L. PAPPAGALLO

Defining the review question

A clearly defined, focused review begins with a well framed question.

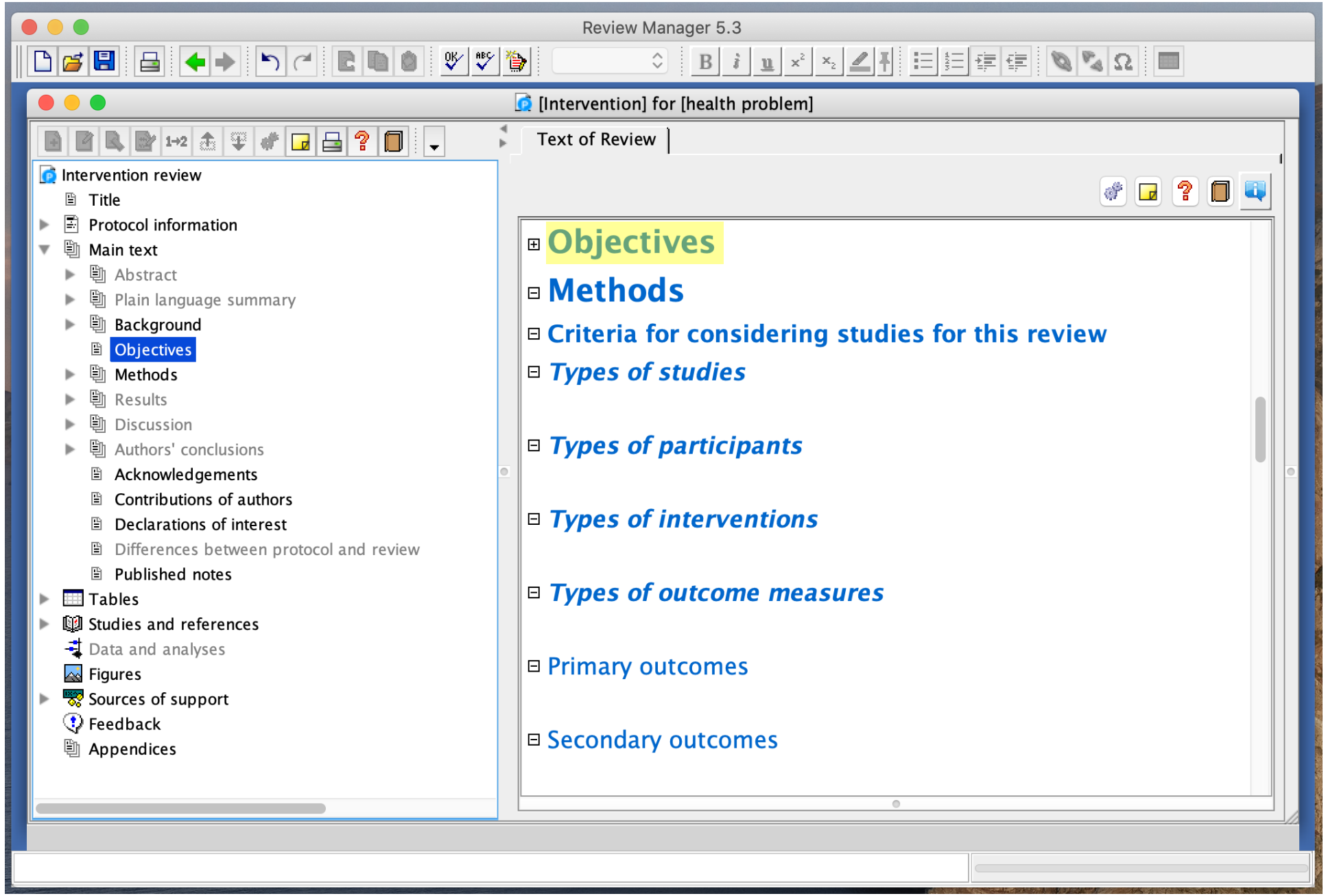
The review question should specify:

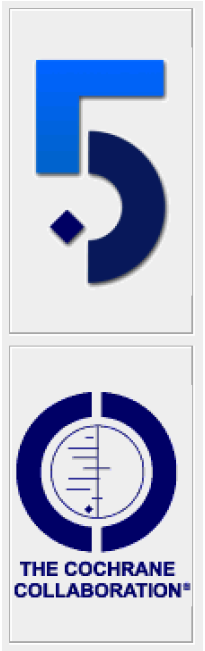
- **types of population** (participants),
- **types of interventions** (and comparisons),
- **types of outcomes** that are of interest.

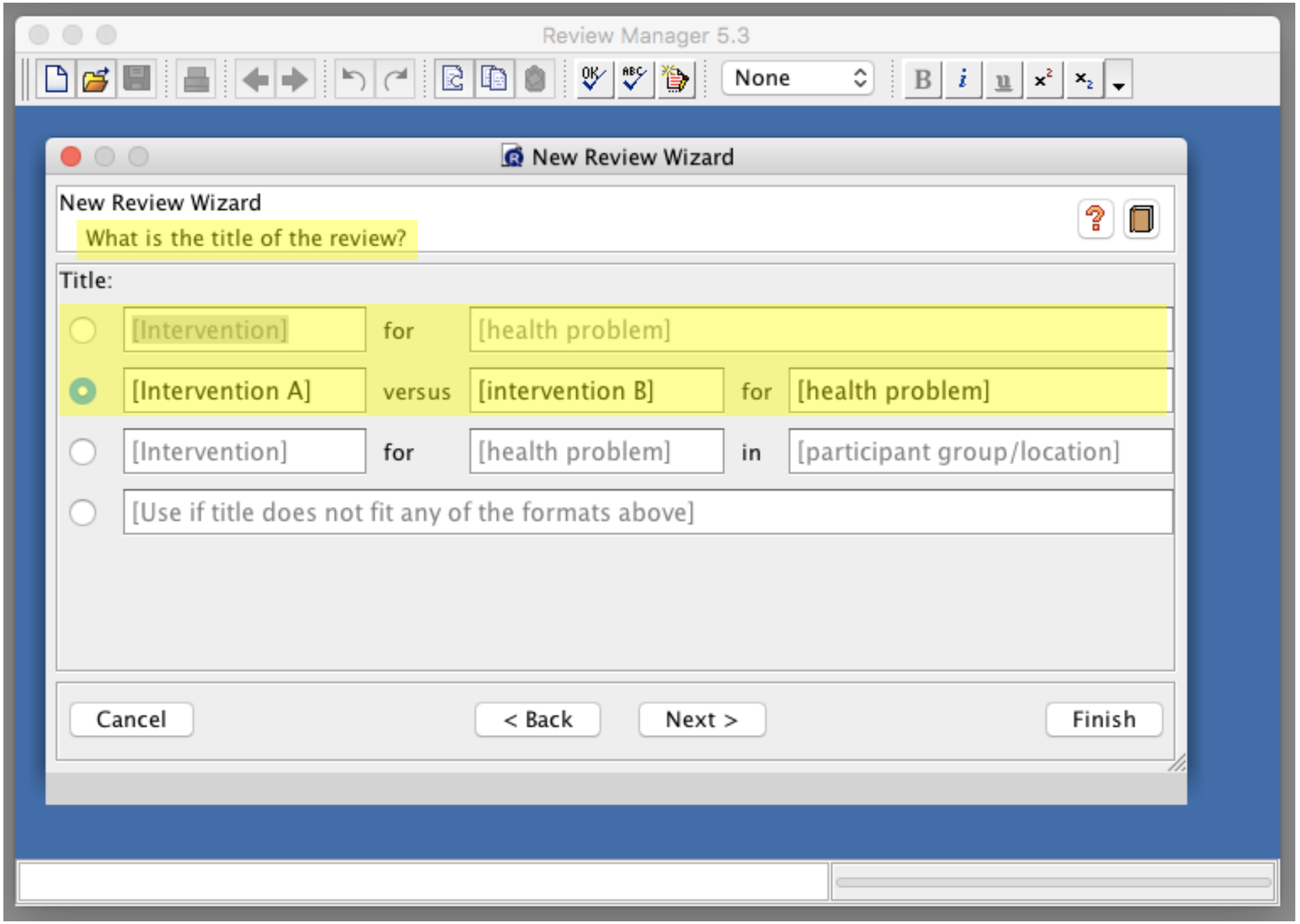
These components of the question, with the additional specification of types of study that will be included, form the basis of the pre-specified eligibility criteria for the review.

Review Manager (RevMan)

There are two versions of Cochrane RevMan: RevMan Web (online) and RevMan 5 (desktop)


Review Manager 5.3
[Intervention] for [health problem]
Text of Review
Intervention review
Title
Protocol information
Main text
Abstract
Plain language summary
Background
Objectives
Methods
Results
Discussion
Authors' conclusions
Acknowledgements
Contributions of authors
Declarations of interest
Differences between protocol and review
Published notes
Tables
Studies and references
Data and analyses
Figures
Sources of support
Feedback
Appendices
Objectives
Methods
Criteria for considering studies for this review
Types of studies
Types of participants
Types of interventions
Types of outcome measures
Primary outcomes
Secondary outcomes


THE COCHRANE
COLLABORATION®


Review Manager 5.3
None
New Review Wizard
New Review Wizard
What is the title of the review?
Title:
[Intervention] for [health problem]
[Intervention A] versus [intervention B] for [health problem]
[Intervention] for [health problem] in [participant group/location]
[Use if title does not fit any of the formats above]
Cancel
< Back
Next >
Finish

Screening for prostate cancer (Review)

Ilic D, Neuberger MM, Djulbegovic M, Dahm P

Cochrane Database of Systematic Reviews 2013, Issue 1.

OBJECTIVES

The primary objective of this review was to determine the efficacy of screening men for prostate cancer in reducing prostate cancer-specific and all-cause mortality.

The secondary objectives of this review were to:

- determine the impact of prostate cancer screening on quality of life and adverse effects; and
- document the costs of screening for prostate cancer.

Defining the review question

A clearly defined, focused review begins with a well framed question.

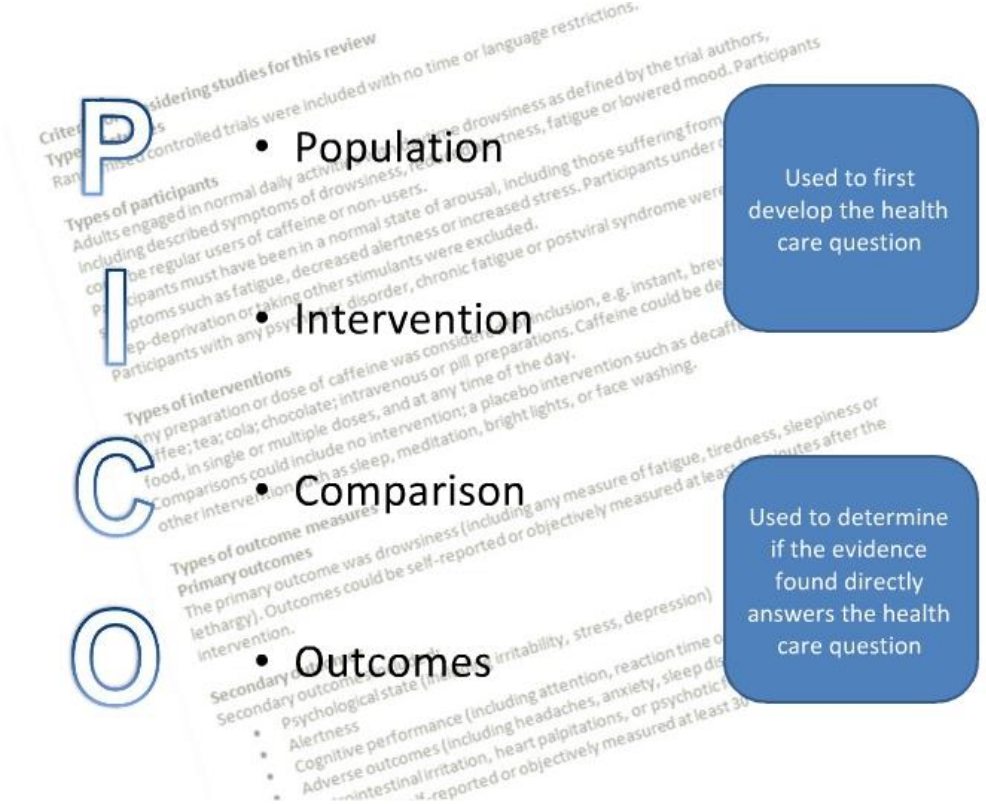
The review question should specify:

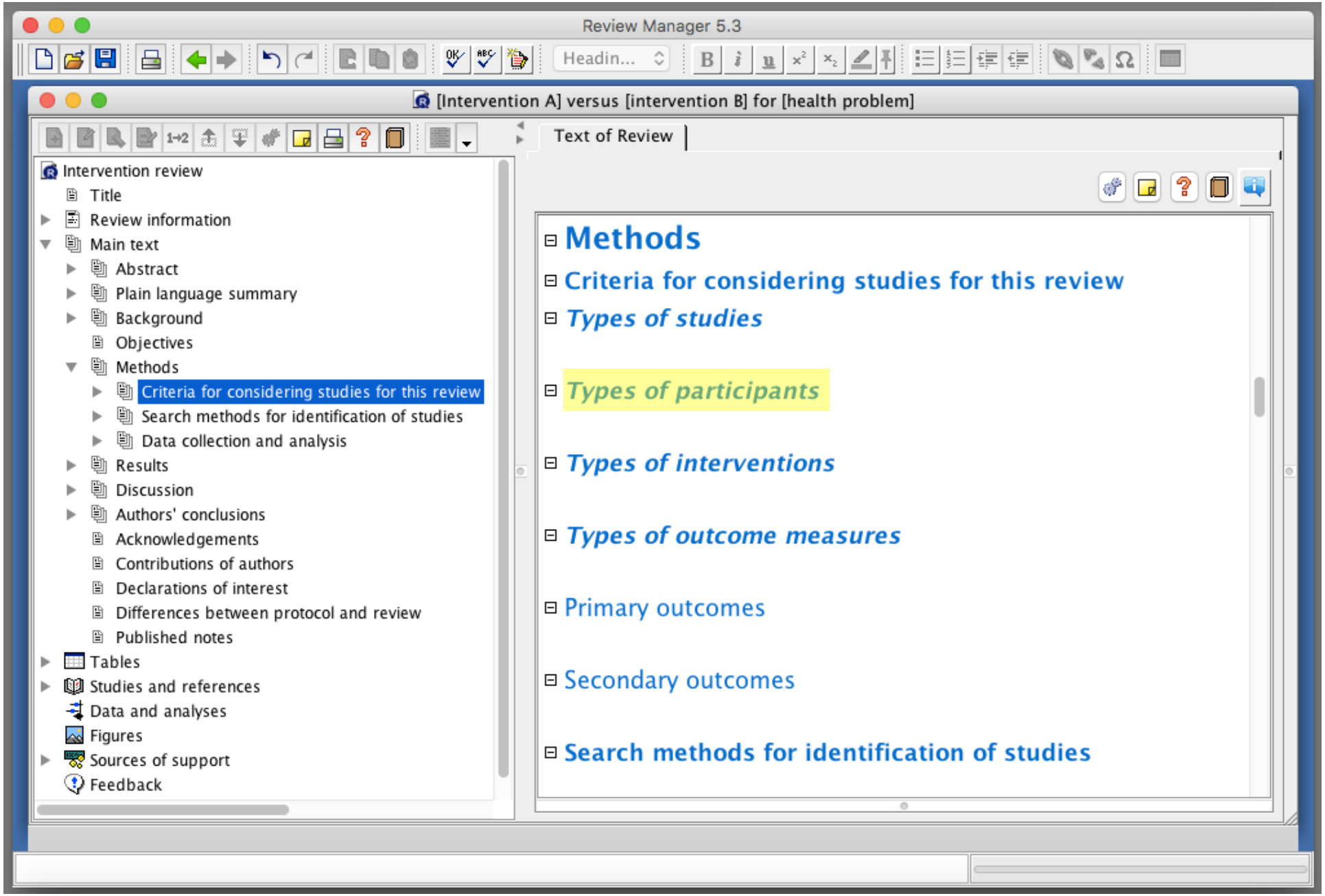
- **types of population** (participants),
- **types of interventions** (and comparisons),
- **types of outcomes** that are of interest.

These components of the question, with the additional specification of types of study that will be included, form the basis of the pre-specified eligibility criteria for the review.

The ‘clinical question’ should specify the types of population (participants), types of interventions (and comparisons), and the types of outcomes that are of interest.

The acronym PICO (**P**articipants, **I**nterventions, **C**omparisons and **O**utcomes) helps to serve as a reminder of these.

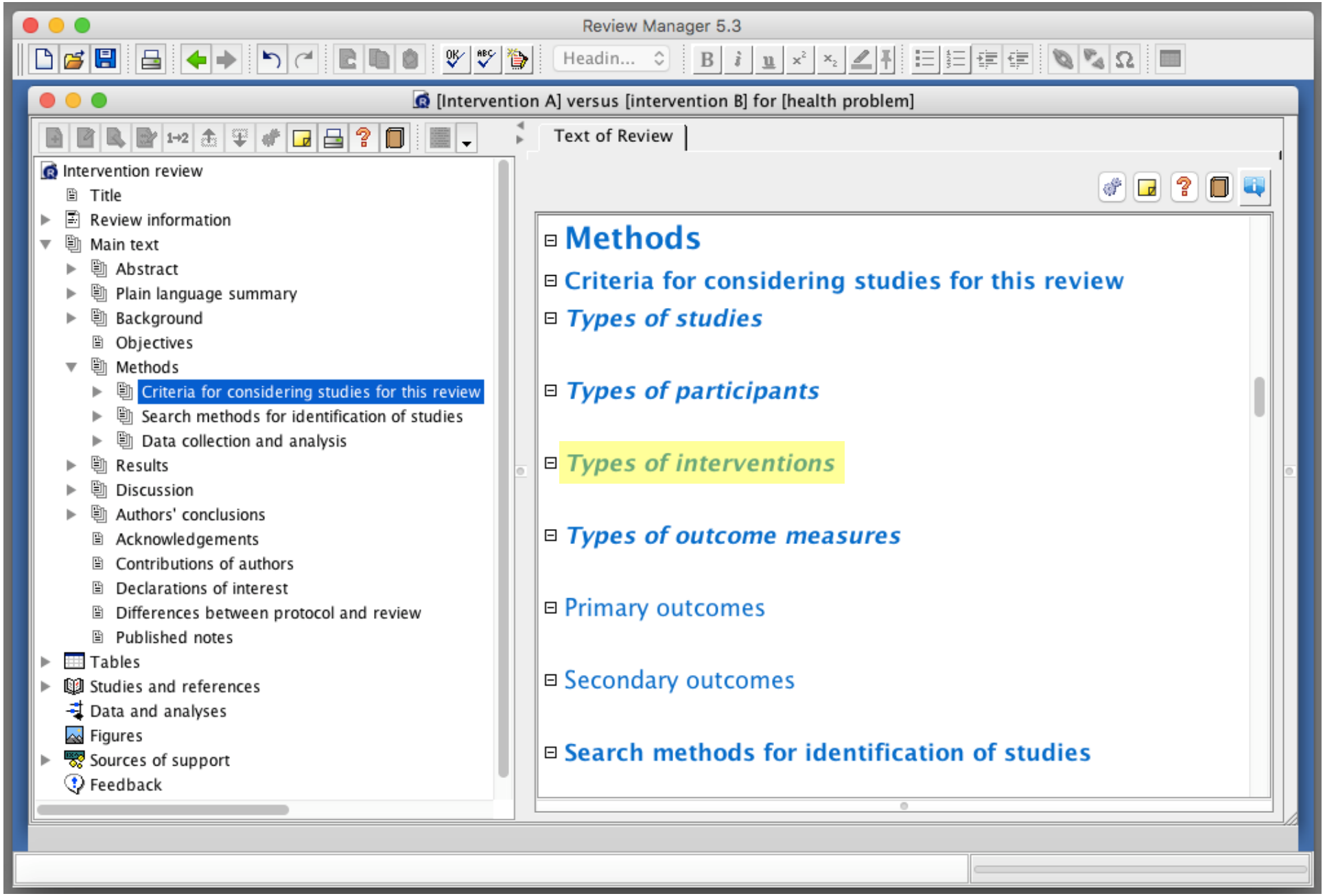



Review Manager 5.3
[Intervention A] versus [intervention B] for [health problem]
Text of Review
Intervention review
Title
Review information
Main text
Abstract
Plain language summary
Background
Objectives
Methods
Criteria for considering studies for this review
Search methods for identification of studies
Data collection and analysis
Results
Discussion
Authors' conclusions
Acknowledgements
Contributions of authors
Declarations of interest
Differences between protocol and review
Published notes
Tables
Studies and references
Data and analyses
Figures
Sources of support
Feedback
Methods
Criteria for considering studies for this review
Types of studies
Types of participants
Types of interventions
Types of outcome measures
Primary outcomes
Secondary outcomes
Search methods for identification of studies

Screening for prostate cancer (Review)
Ilic D, Neuberger MM, Djulbegovic M, Dahm P
Cochrane Database of Systematic Reviews 2013, Issue 1.

Types of participants

All men enrolled in studies of prostate cancer screening were eligible for this review, with no exclusions based on ethnicity, age, or presence of lower urinary tract symptoms. Studies including men with a previous diagnosis and treatment of prostate cancer were excluded.

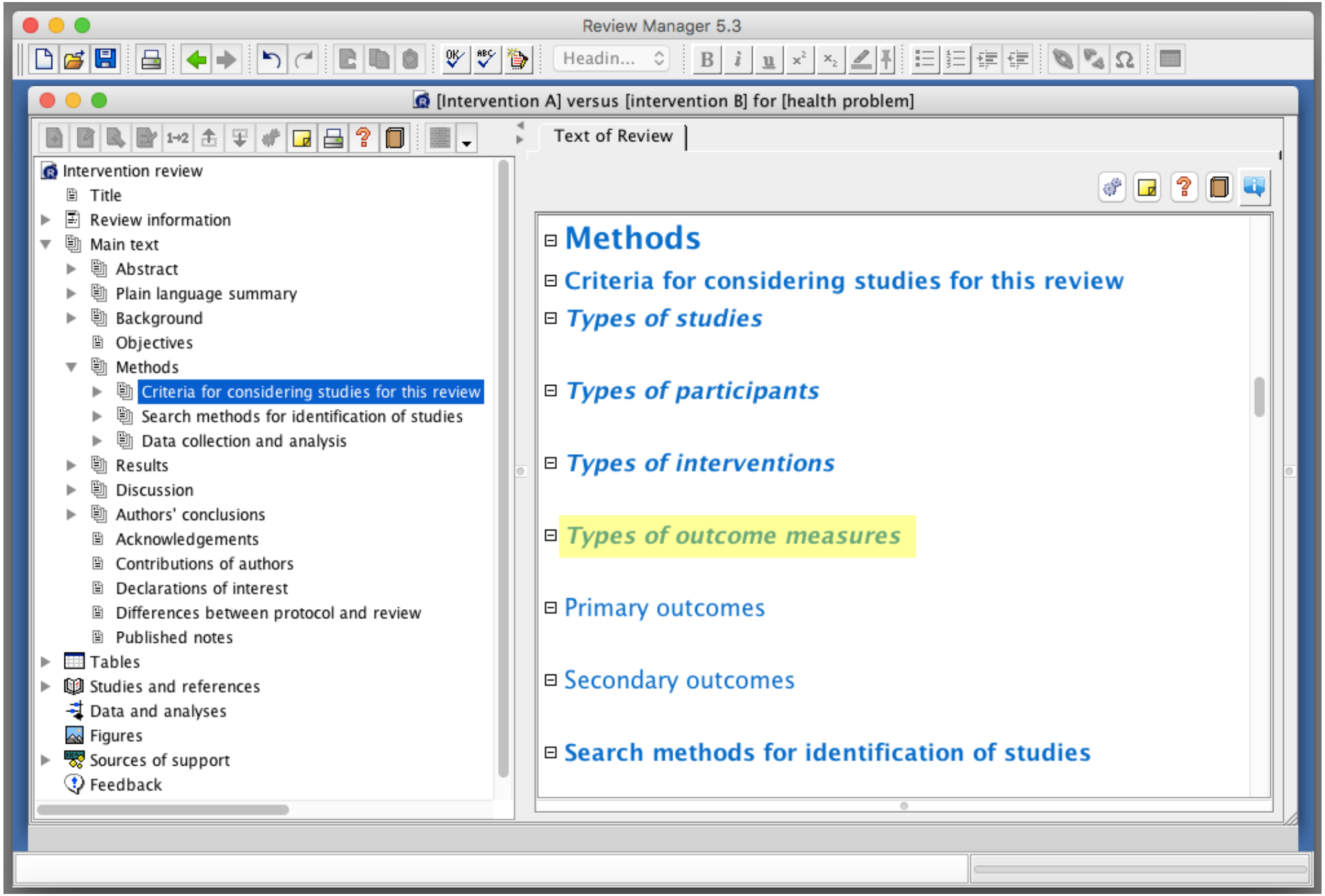

Review Manager 5.3
[Intervention A] versus [intervention B] for [health problem]
Text of Review
Intervention review
Title
Review information
Main text
Abstract
Plain language summary
Background
Objectives
Methods
Criteria for considering studies for this review
Search methods for identification of studies
Data collection and analysis
Results
Discussion
Authors' conclusions
Acknowledgements
Contributions of authors
Declarations of interest
Differences between protocol and review
Published notes
Tables
Studies and references
Data and analyses
Figures
Sources of support
Feedback
Methods
Criteria for considering studies for this review
Types of studies
Types of participants
Types of interventions
Types of outcome measures
Primary outcomes
Secondary outcomes
Search methods for identification of studies

Screening for prostate cancer (Review)
Ilic D, Neuberger MM, Djulbegovic M, Dahm P
Cochrane Database of Systematic Reviews 2013, Issue 1.

Types of interventions

Studies that used any of the following screening procedures, individually or in combination, were included:

- digital rectal examination (DRE);
- prostate-specific antigen (PSA) test (including total, velocity, density, and percentage free and complex); and
- transrectal ultrasound (TRUS)-guided biopsy.


Review Manager 5.3
[Intervention A] versus [intervention B] for [health problem]
Text of Review
Intervention review
Title
Review information
Main text
Abstract
Plain language summary
Background
Objectives
Methods
Criteria for considering studies for this review
Search methods for identification of studies
Data collection and analysis
Results
Discussion
Authors' conclusions
Acknowledgements
Contributions of authors
Declarations of interest
Differences between protocol and review
Published notes
Tables
Studies and references
Data and analyses
Figures
Sources of support
Feedback
Methods
Criteria for considering studies for this review
Types of studies
Types of participants
Types of interventions
Types of outcome measures
Primary outcomes
Secondary outcomes
Search methods for identification of studies

Primary outcomes

Primary outcome measures for this review were prostate cancer-specific and all-cause mortality.

Secondary outcomes

Secondary outcome measures included:

- incident prostate cancers by stage and grade at diagnosis;
- metastatic disease at follow-up;
- quality of life;
- harms of screening (including both adverse outcomes from false-positive or false-negative results and their impact upon resulting treatment procedures); and
- costs associated with screening programs.

Outcomes

Should be importance driven NOT evidence driven

Journal of Clinical Epidemiology 64 (2011) 395–400

GRADE guidelines: 2. Framing the question and deciding on important outcomes

Gordon H. Guyatt[a,*], Andrew D. Oxman[b], Regina Kunz[c], David Atkins[d], Jan Brozek[a], Gunn Vist[b], Philip Alderson[e], Paul Glasziou[f], Yngve Falck-Ytter[g], Holger J. Schünemann[a]

If evidence is lacking for an important outcome, this should be acknowledged, rather than ignoring the outcome - that uncertainty may have a bearing on the ultimate recommendation.

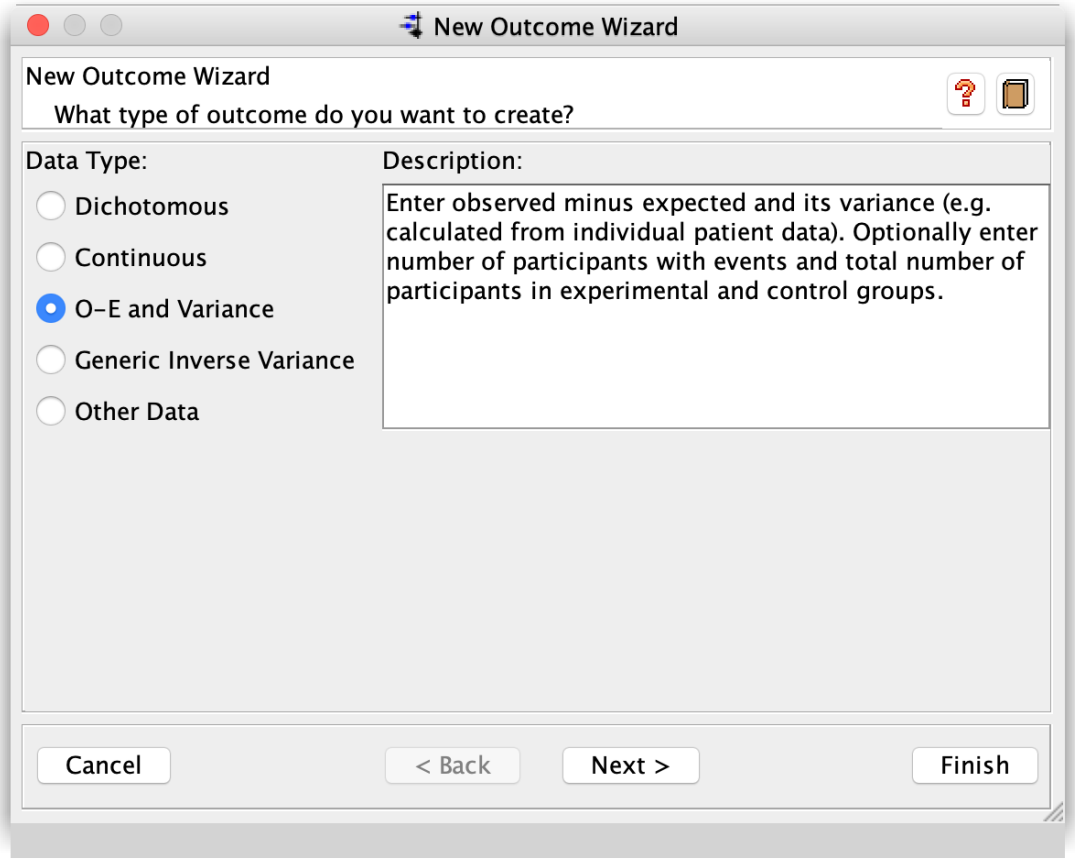
Defining the review question

A clearly defined, focused review begins with a well framed question.

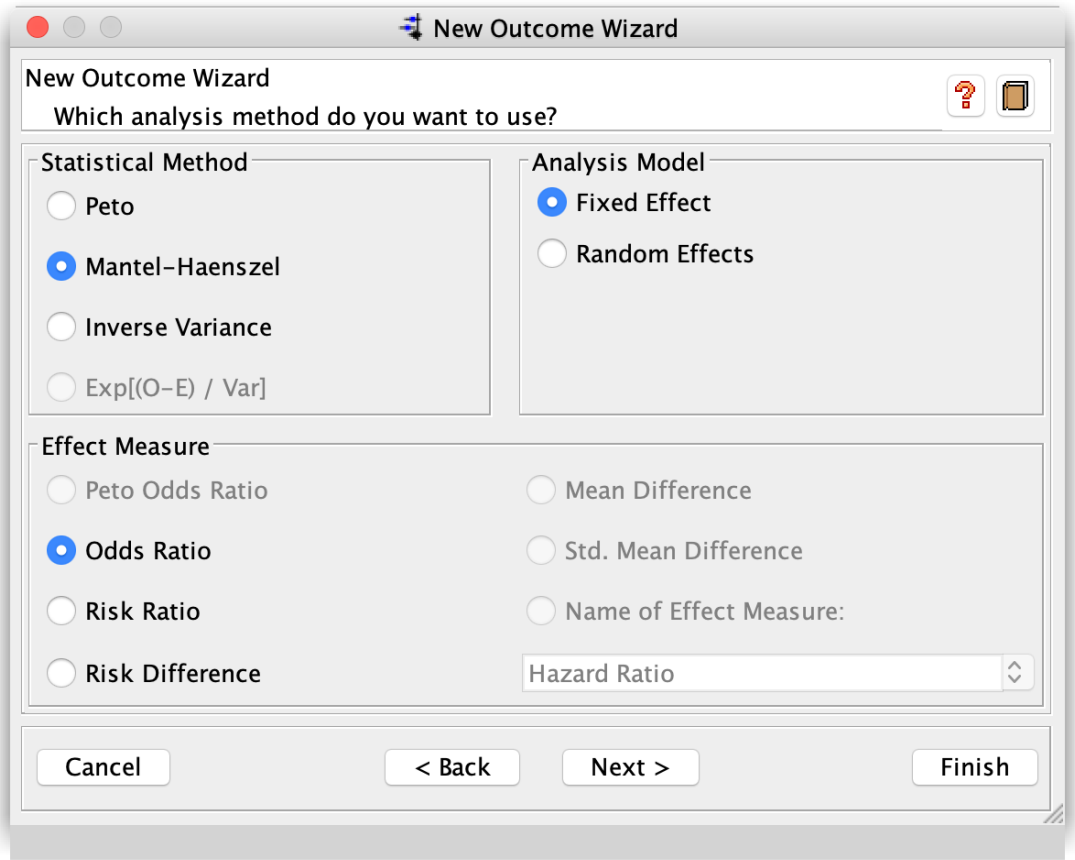
The review question should specify:

- **types of population** (participants),
- **types of interventions** (and comparisons),
- **types of outcomes** that are of interest.

These components of the question, with the additional specification of types of study that will be included, form the basis of the pre-specified eligibility criteria for the review.



variabili di risposta



misure riassuntive di effetto

VARIABILE DI RISPOSTA

- di tipo **qualitativo (nominale)**
  - esprime categorie di risposta del tipo successo / insuccesso (di un trattamento somministrato).
- di tipo **quantitativo**
  - assume uno spettro continuo di valori e viene misurata in riferimento a una scala a intervalli costanti.
- del tipo **“tempo a evento”**
  - rappresenta il tempo trascorso fino al verificarsi (o meno) di un evento.

Risk and Odds

- **Risk** (proportion of persons with disease = cumulative incidence)
  - **Risk Ratio** = ratio of 2 cumulative incidence estimates = Relat[illegible] Risk
  - [illegible] ute difference of 2 cumulative
- Odd[illegible] ent will or will not be observed)
  - [illegible] s

$$\frac{\text{Risk of event within experimental arm}}{\text{Risk of event within control arm}}$$

Sintesi degli indicatori di effetto per variabili qualitative (nominali)…

Misure di effetto relativo

Risk — 70 risposte / 100 pazienti = 0.70

Risk Ratio

$$\frac{\text{70 risposte / 100 pazienti (braccio A)}}{\text{30 risposte / 100 pazienti (braccio B)}} = \frac{0.70}{0.30} = 2.33$$

Odds — 65 risposte / 35 non risposte = 1.86

Odds Ratio

$$\frac{\text{65 risposte / 35 non risposte (braccio A)}}{\text{25 risposte / 75 non risposte (braccio B)}} = \frac{1.86}{0.33} = 5.63$$

Misura di effetto assoluto

Risk Difference 0.70 – 0.30 = 0.40, ovvero: 40 risposte *in più* ogni 100 pazienti trattati

NNT 1 / 0.40 = 2.5, ovvero: una risposta *in più* ogni 2.5 pazienti trattati

Risk and Odds

- **Risk** (proportion of persons with disease = cumulative incidence)
  - R… …umulative incidence estimates =
    R…
  - R… …te difference of 2 cumulative
    i…

$$\frac{\text{Odds of event within experimental arm}}{\text{Odds of event within control arm}}$$

- **Odds** (th… …kelihood that an event will or will not be observed)
  - **Odds Ratio** = ratio of 2 odds

Sintesi degli indicatori di effetto per variabili qualitative (nominali)…

Misure di effetto relativo

Risk 70 risposte / 100 pazienti = 0.70

Risk Ratio $\frac{\text{70 risposte / 100 pazienti (braccio A)}}{\text{30 risposte / 100 pazienti (braccio B)}} = \frac{0.70}{0.30} = 2.33$

Odds 65 risposte / 35 non risposte = 1.86

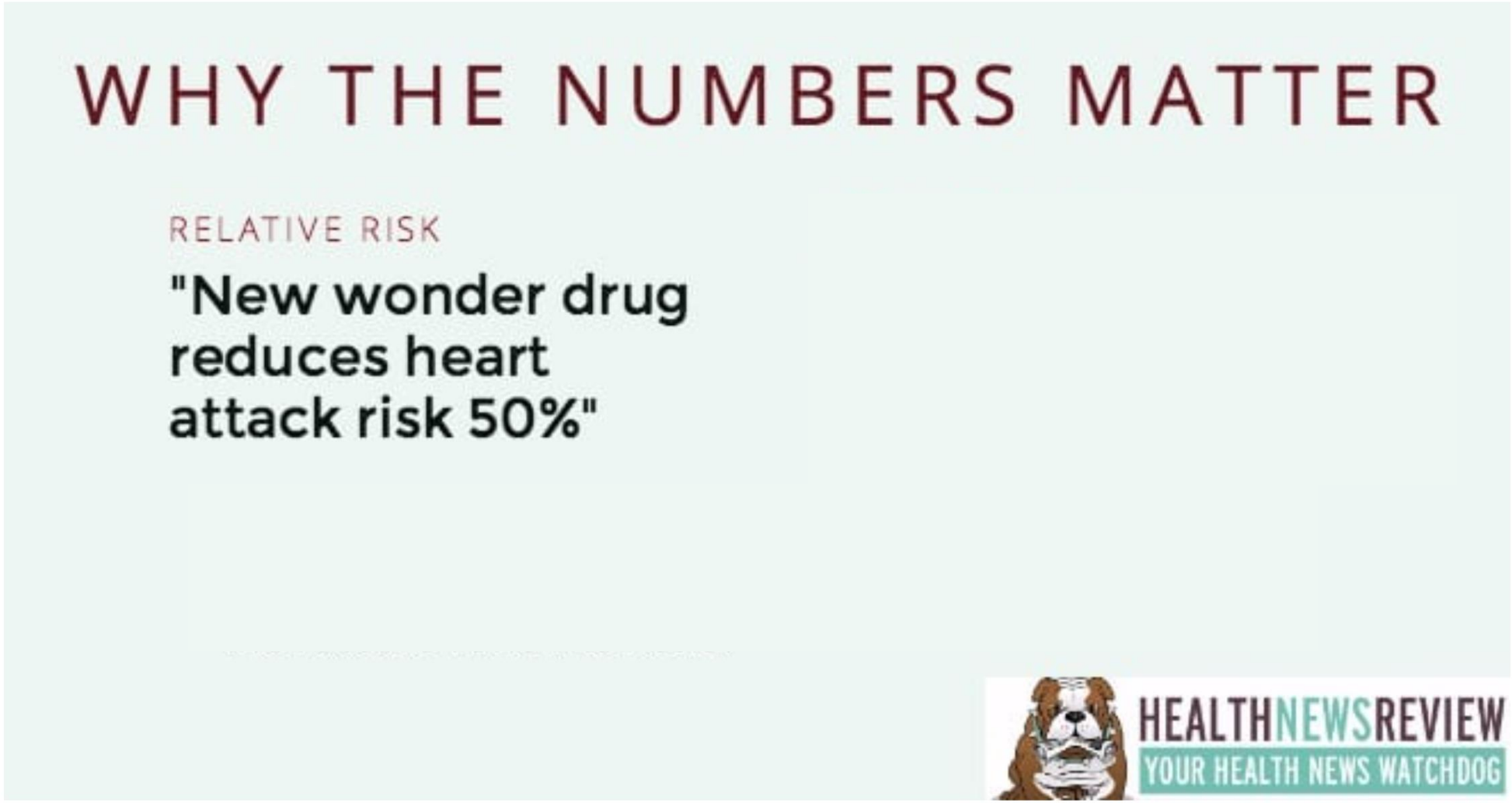
Odds Ratio $\frac{\text{65 risposte / 35 non risposte (braccio A)}}{\text{25 risposte / 75 non risposte (braccio B)}} = \frac{1.86}{0.33} = 5.63$

Misura di effetto assoluto

Risk Difference 0.70 – 0.30 = 0.40, ovvero: 40 risposte *in più* ogni 100 pazienti trattati

NNT 1 / 0.40 = 2.5, ovvero: una risposta *in più* ogni 2.5 pazienti trattati

Beneficio RELATIVO (RR, OR , HR) o ASSOLUTO (RD)?



Beneficio RELATIVO (RR, OR , HR) o ASSOLUTO (RD)?

WHY THE NUMBERS MATTER

RELATIVE RISK

"New wonder drug reduces heart attack risk 50%"

ABSOLUTE RISK

"New wonder drug reduced heart attacks from from 2 per 100 to 1 per 100"

The **absolute risk** is more useful at conveying the true impact of an intervention, yet is often under-reported in the research and the news.

HEALTHNEWSREVIEW
YOUR HEALTH NEWS WATCHDOG

Sintesi degli indicatori di effetto per variabili qualitative (nominali)…

Misure di effetto relativo

- **Risk**: 70 risposte / 100 pazienti = 0.70
- **Risk Ratio**: $\frac{\text{70 risposte / 100 pazienti (braccio A)}}{\text{30 risposte / 100 pazienti (braccio B)}} = \frac{0.70}{0.30} = 2.33$
- **Odds**: 65 risposte / 35 non risposte = 1.86
- **Odds Ratio**: $\frac{\text{65 risposte / 35 non risposte (braccio A)}}{\text{25 risposte / 75 non risposte (braccio B)}} = \frac{1.86}{0.33} = 5.63$

Misura di effetto assoluto

- **Risk Difference**: 0.70 – 0.30 = 0.40, ovvero: 40 risposte *in più* ogni 100 pazienti trattati
- **NNT**: 1 / 0.40 = 2.5, ovvero: una risposta *in più* ogni 2.5 pazienti trattati

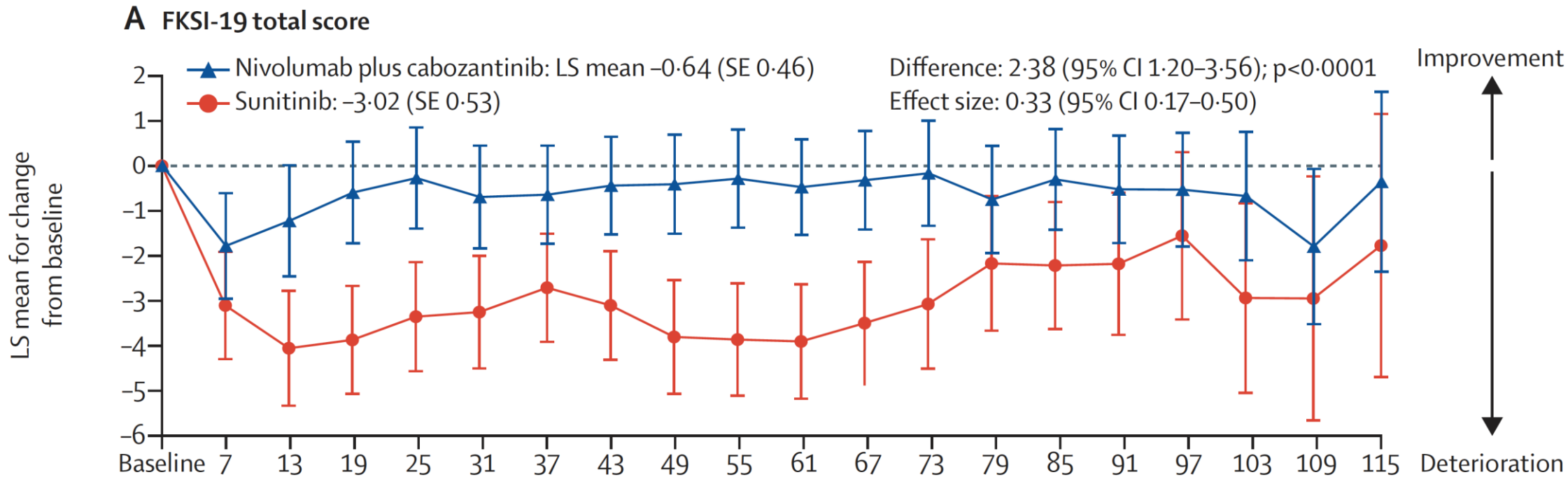
VARIABILE DI RISPOSTA

- di tipo **qualitativo (nominale)**
  - esprime categorie di risposta del tipo successo / insuccesso (di un trattamento somministrato).
- di tipo **quantitativo (intervallare)**
  - assume uno spettro continuo di valori e viene misurata in riferimento a una scala a intervalli costanti.
- del tipo **“tempo a evento”**
  - rappresenta il tempo trascorso fino al verificarsi (o meno) di un evento.

Patient-reported outcomes with first-line nivolumab plus cabozantinib versus sunitinib in patients with advanced renal cell carcinoma treated in CheckMate 9ER: an open-label, randomised, phase 3 trial

David Cella, Robert J Motzer*, Cristina Suarez, Steven I Blum, Flavia Ejzykowicz, Melissa Hamilton, Joel F Wallace, Burcin Simsek, Joshua Zhang, Cristina Ivanescu, Andrea B Apolo, Toni K Choueiri*

Lancet Oncol **2022; 23: 292–303**



VARIABILE DI RISPOSTA

- di tipo **qualitativo (nominale)**
  - esprime categorie di risposta del tipo successo / insuccesso (di un trattamento somministrato).
- di tipo **quantitativo (intervallare)**
  - assume uno spettro continuo di valori e viene misurata in riferimento a una scala a intervalli costanti.
- del tipo “**tempo a evento**”
  - rappresenta il tempo trascorso fino al verificarsi (o meno) di un evento.

Modificato da
un originale di
R. D'Amico, 2008

Hazard Rate

Rappresenta la probabilità che si verifichi l'evento (ricaduta, morte, etc) nell'unità di tempo considerata (giorni, mesi, anni).

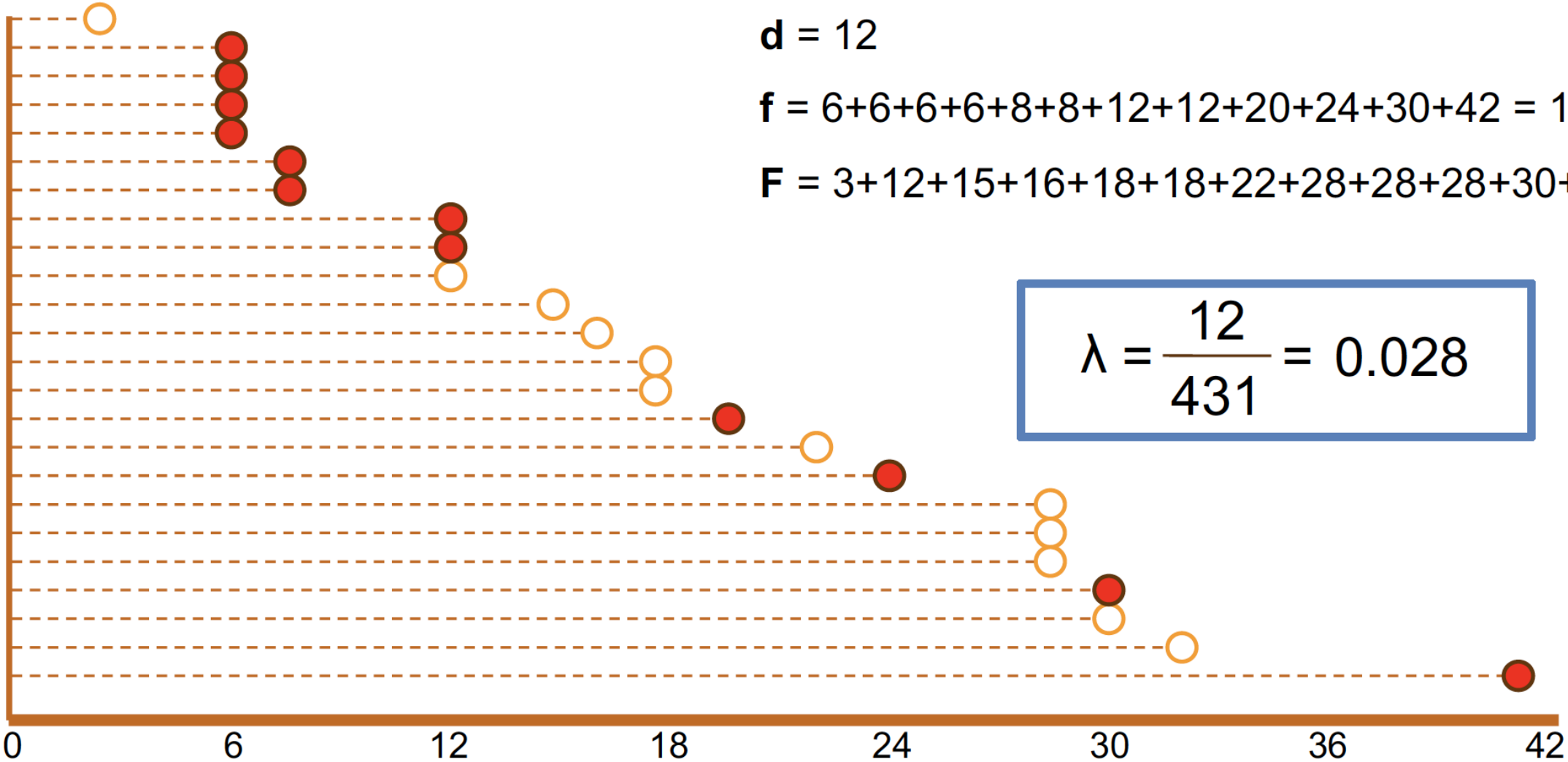
La stima dell'hazard rate λ è data dal rapporto tra il numero persone con l'evento e la lunghezza del follow-up nell'intervallo di tempo considerato

$$\lambda = \frac{d}{f + F}$$

Dove
d = numero di eventi (ad esempio decessi)
f = somma della lunghezza dei follow-up nei pazienti con l'evento
F = somma della lunghezza dei follow-up nei pazienti senza l'evento

Modificato da
un originale di
R. D'Amico, 2008

Hazard Rate



d = 12

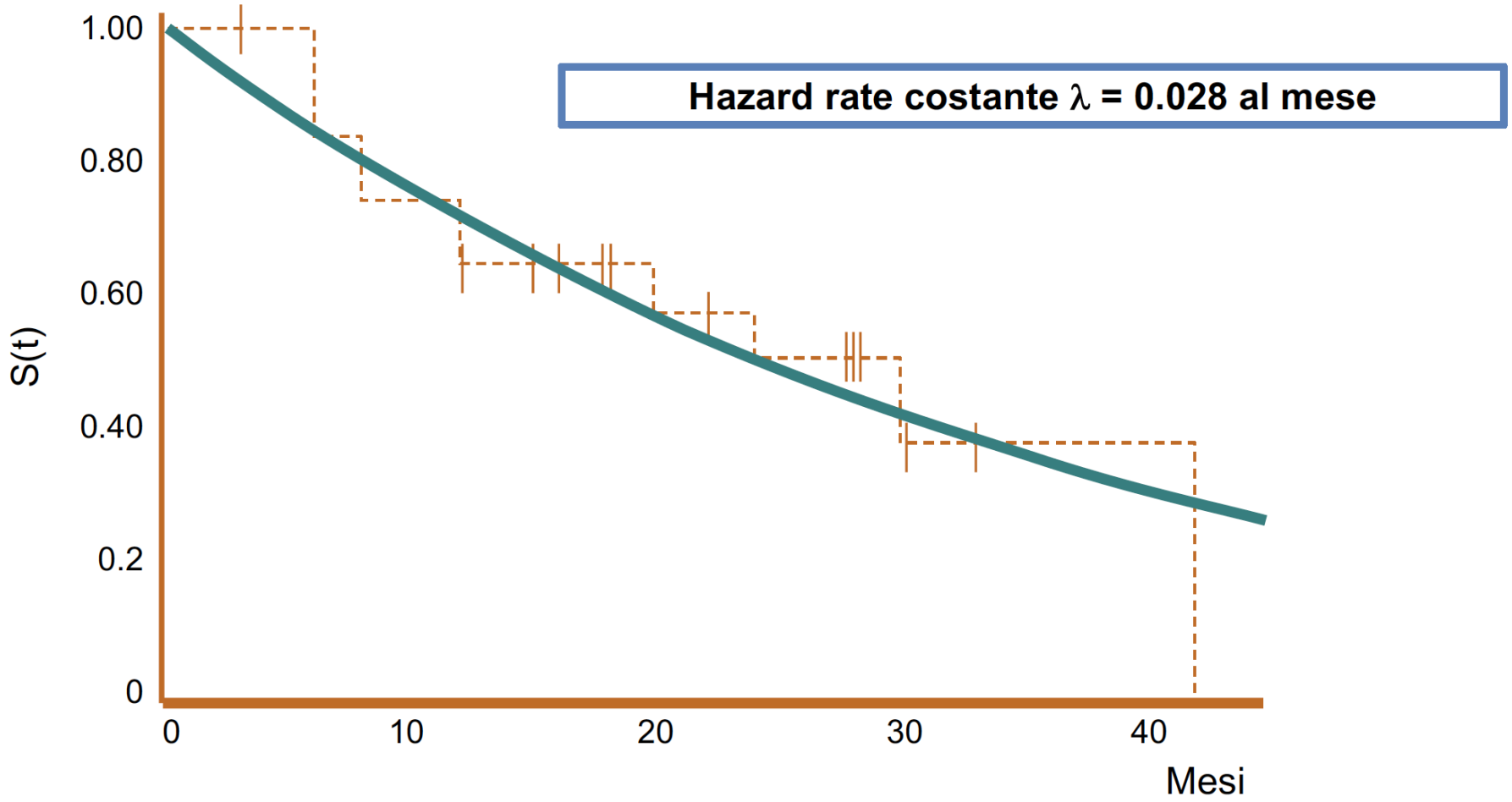
f = 6+6+6+6+8+8+12+12+20+24+30+42 = 180

F = 3+12+15+16+18+18+22+28+28+28+30+33 = 251

$$\lambda = \frac{12}{431} = 0.028$$

Modificato da
un originale di
R. D'Amico, 2008

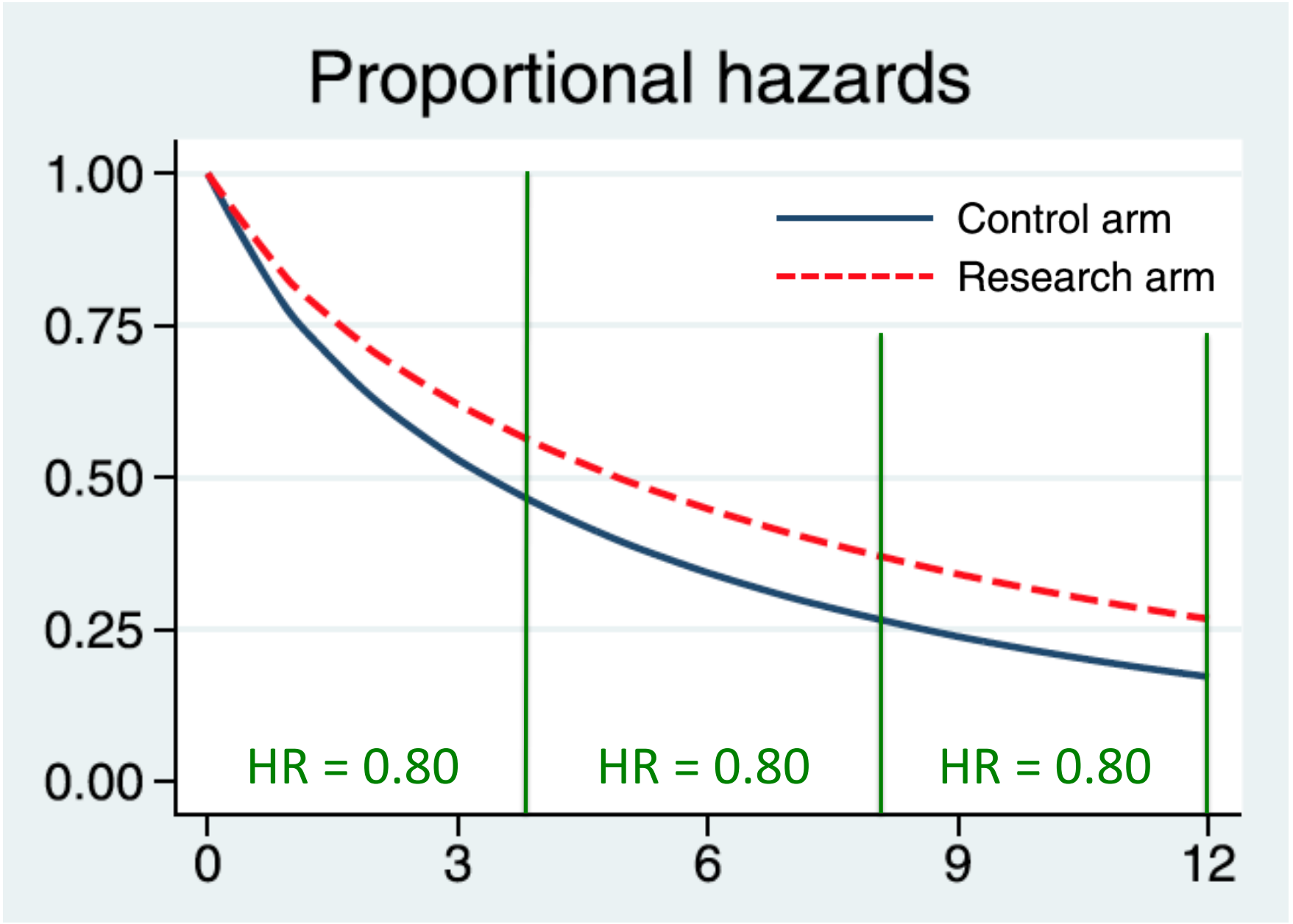
Hazard Rate



L'hazard rate rappresenta il parametro della curva $S(t)=e^{-\lambda t}$ che ne influenza la pendenza (sotto l'ipotesi di *hazard rate* costante)

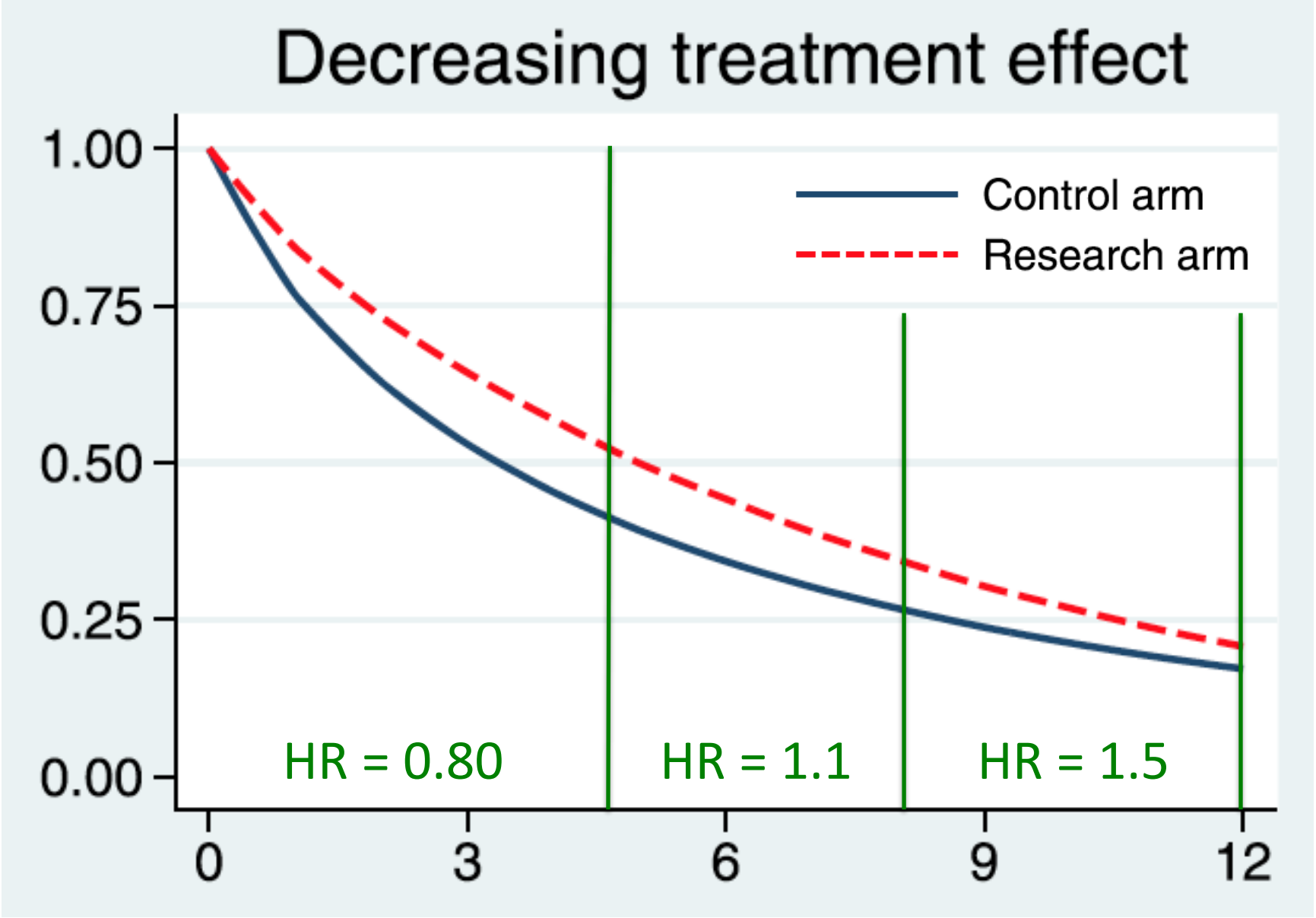
Hazard Ratio (HR)

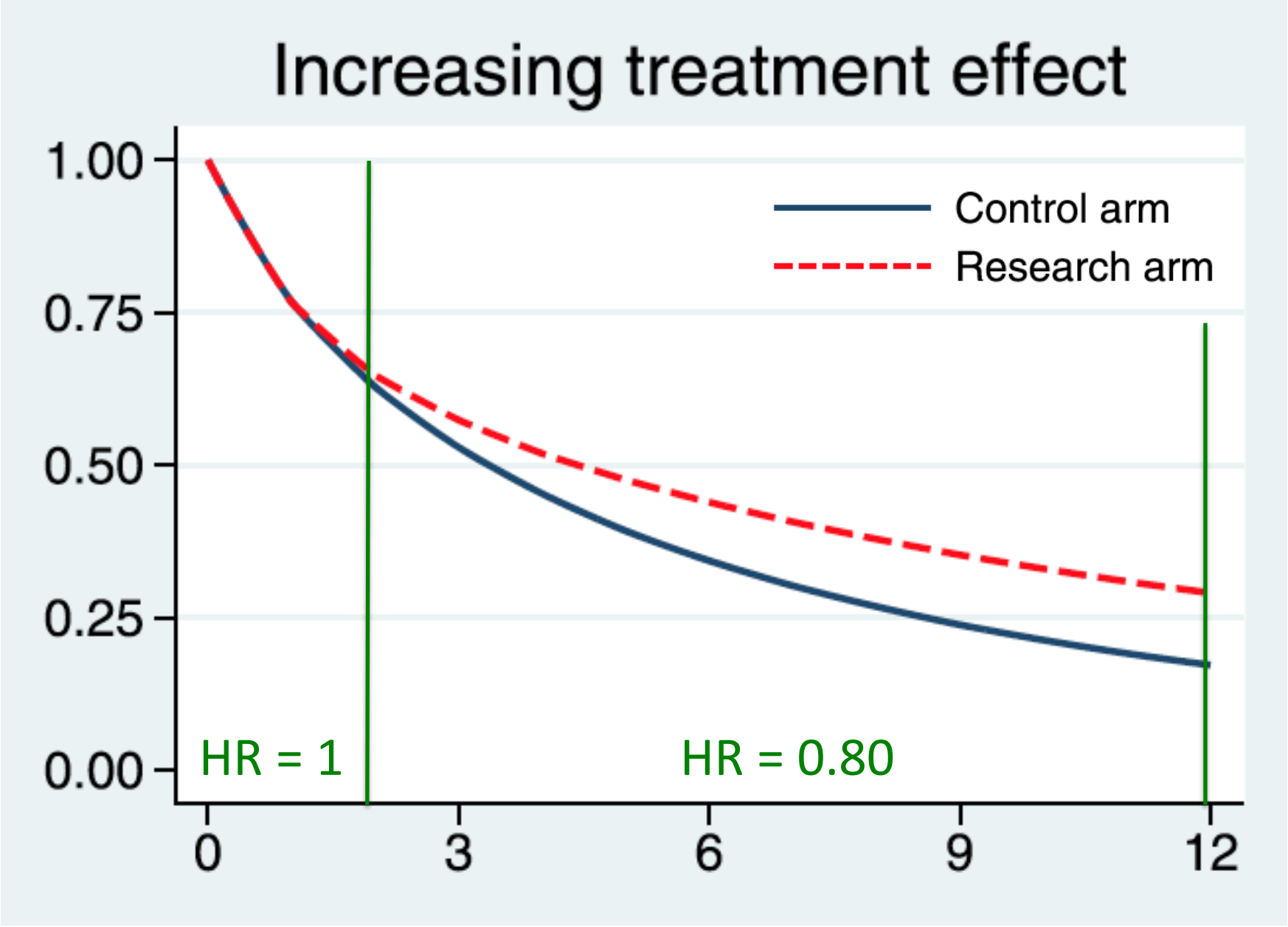
- Compares risk of event in two populations or samples
- The ratio of risk (*hazard rate*) in experimental group to risk (*hazard rate*) in control group
- Assumption: *proportional hazards (PH),* i.e. the risk does not depend on time, that is, "risk is constant over time"
  - If non PH is present, the HR is actually time-dependent and the estimated HR that is obtained is some type of average over the event times


Proportional hazards
1.00
0.75
0.50
0.25
0.00
0
3
6
9
12
Control arm
Research arm
HR = 0.80
HR = 0.80
HR = 0.80

Hazard Ratio (HR)

- Compares risk of event in two populations or samples
- The ratio of risk (*hazard rate*) in experimental group to risk (*hazard rate*) in control group
- Assumption: *proportional hazards (PH),* i.e. the risk does not depend on time, that is, "risk is constant over time"
  - If non PH is present, the HR is actually time-dependent and the estimated HR that is obtained is some type of average over the event times

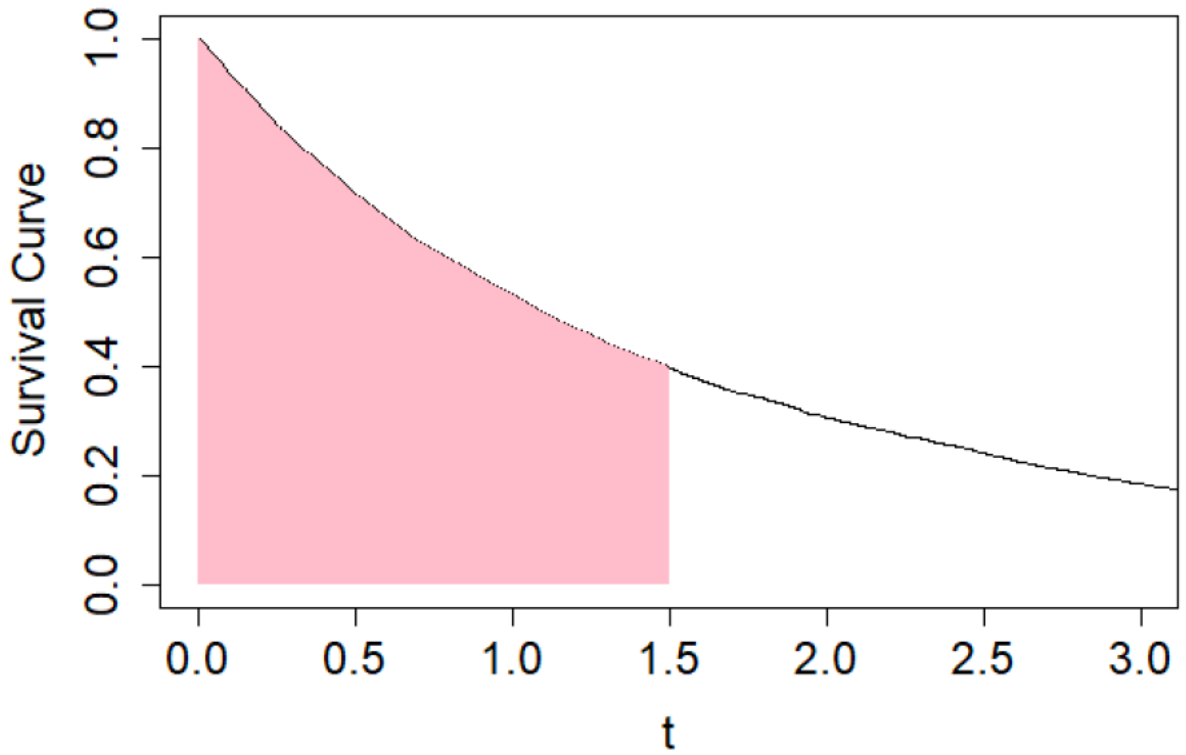

Decreasing treatment effect
1.00
0.75
0.50
0.25
0.00
Control arm
Research arm
HR = 0.80
HR = 1.1
HR = 1.5
0
3
6
9
12


Increasing treatment effect
1.00
0.75
0.50
0.25
0.00
Control arm
Research arm
HR = 1
HR = 0.80
0
3
6
9
12

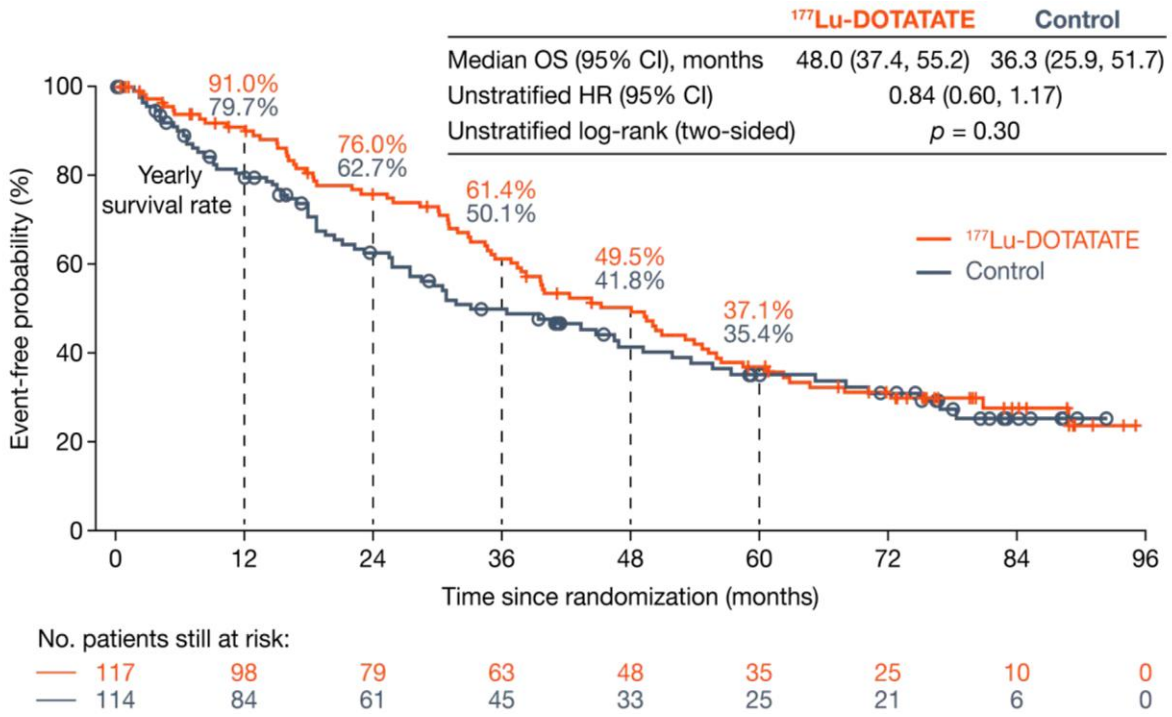
Restricted mean survival time: an alternative to the hazard ratio for the design and analysis of randomized trials with a time-to-event outcome

Patrick Royston* and Mahesh KB Parmar

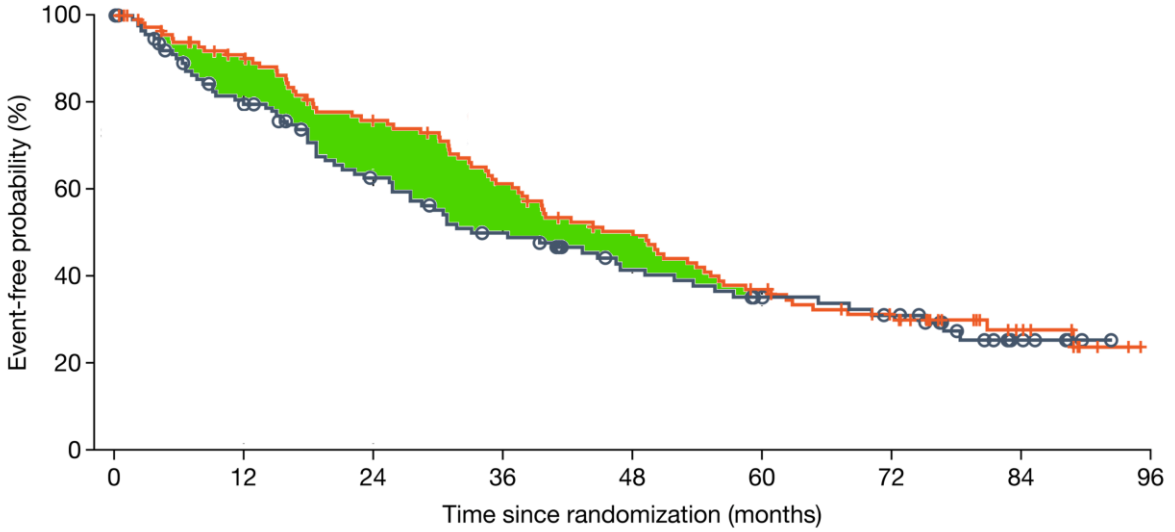
BMC Medical Research Methodology 2013, **13**:152



The phase 3 NETTER-1 study of 177Lu-DOTATATE in patients with midgut neuroendocrine tumours: further survival analyses



Deaths, n (%)	65 (55.6)	63 (55.3)
RMST, months (95% CI)	41.2 (37.6, 44.9)	36.1 (31.9, 40.4)
Difference, months (95% CI)	**5.1 (–0.5, 10.7)**	



Ruszniewski PB, et al. ESMO 2021

Journal of Clinical Epidemiology 118 (2020) 124–131

GRADE guidelines 27: how to calculate absolute effects for time-to-event outcomes in summary of findings tables and Evidence Profiles

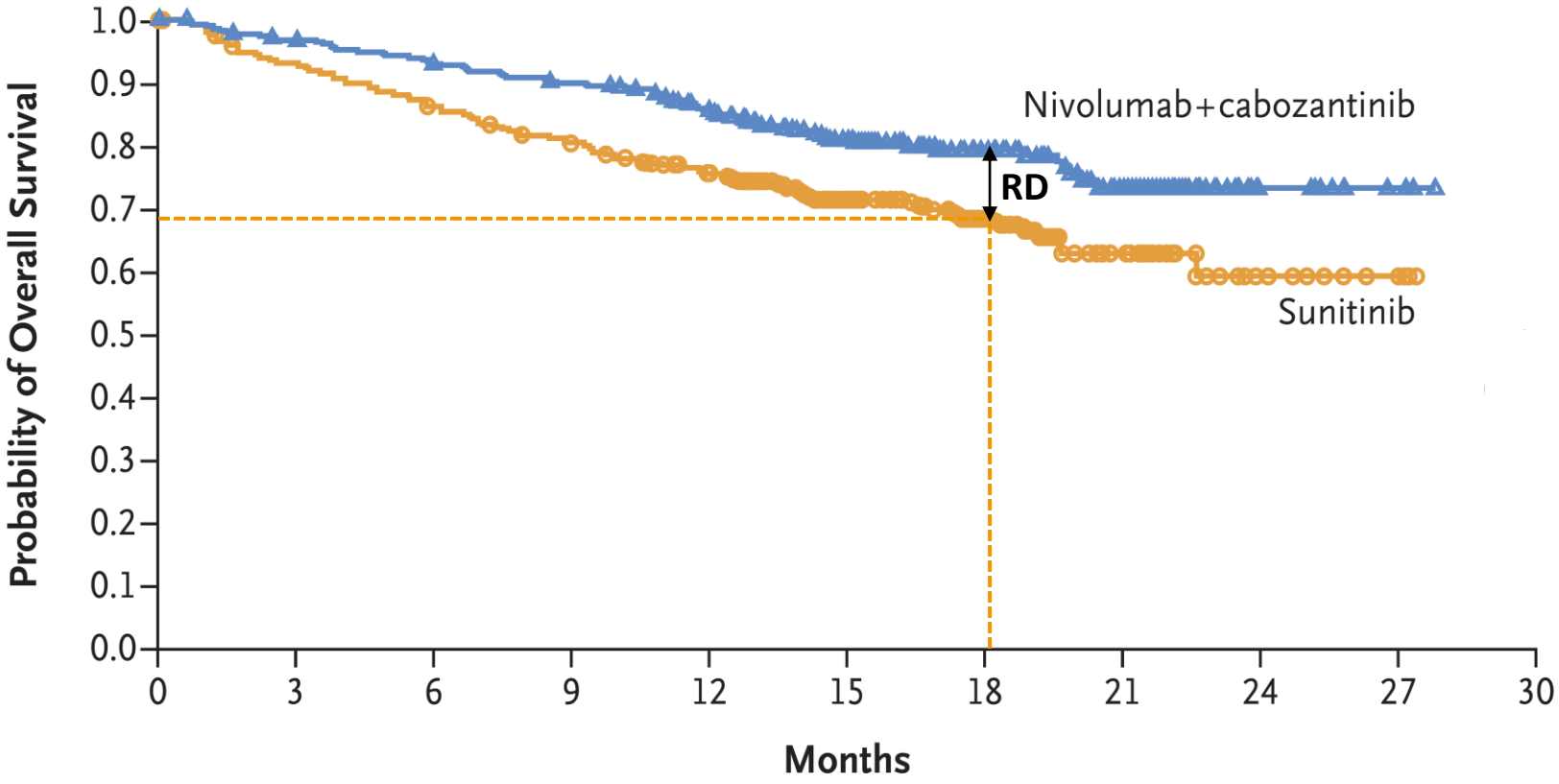
Nicole Skoetz[a,*], Marius Goldkuhle[a], Elvira C. van Dalen[b], Elie A. Akl[c], Marialena Trivella[d], Reem A. Mustafa[e], Artur Nowak[f], Philipp Dahm[g], Holger Schünemann [h], Ralf Bender[i], GRADE Working Group

Absolute effect estimates (i.e., risk difference, the number needed to treat) provide important supplementary information to relative effect estimates by considering the control event rate over a given time period. As they take into account the underlying baseline risk for the event of interest in the study groups, absolute effect estimates are less vulnerable to exaggerated effect interpretation than relative effect estimates and allow a more appropriate assessment of the clinical relevance of effects.

…

Data from Kaplan-Meier survival curves from the control groups of the trials included in the analysis may be used to estimate the baseline risk.

Risk Difference (RD)



Hazard ratio for death, 0.60
(98.89% CI, 0.40–0.89)

- Median f.u.: 18.1 months
  Baseline risk* at median f.u.: 31%
- **Risk Difference**: **11 events lower / 100 pts** (95%CI: 15 lower to 5 lower)

N Engl J Med 2021;384:829-41.

** J Clin Epidemiol 118 (2020) 124-131*

SACRO CUORE DON CALABRIA

ECI CANCER CENTRE

I R C C S

SCUOLA DI METODOLOGIA DELLA RICERCA CLINICA

2025 - 11ª EDIZIONE

MODULI SPECIALISTICI - S1

VENERDÌ 14 - SABATO 15 MARZO 2025

NEGRAR DI VALPOLICELLA (VR)

Centro Formazione IRCCS "Sacro Cuore - Don Calabria"

Database bibliografici e ricerca delle informazioni

Michela CINQUINI

Ricerca sistematica della letteratura scientifica
Obiettivo Generale

Prendere decisioni nella pratica clinica
rispondendo a quesiti attraverso il reperimento
delle evidenze disponibili

Impostare una strategia di ricerca
Quesito clinico

Capitolo 9: Glioblastoma di nuova diagnosi

Q2: Nei pazienti con meno di 70 anni alla radioterapia (60 Gy/30 frazioni) dovrebbe essere associato un trattamento con temozolomide concomitante (75 mg/m2/die) ed adiuvante (150-200 mg/m2per 5 giorni, ogni 28)?

https://snlg.iss.it/wp-content/uploads/2021/10/LG_266_neoplasie_cerebrali_agg2021.pdf

Elaborazione del modello PICO

Articolare il quesito clinico col modello PICO risulta molto efficace per ritrovare evidenze clinicamente rilevanti in letteratura

Elaborazione del modello PICO

P = paziente o popolazione

I = intervento

C = confronto

O = outcome (esito)

Nei pazienti con meno di 70 anni alla radioterapia (60 Gy/30 frazioni) dovrebbe essere associato un trattamento con temozolomide concomitante (75 mg/m2/die) ed adiuvante (150-200 mg/m2per 5 giorni, ogni 28)?

Linee guida «Neoplasie cerebrali». AIOM (Associazione Italiana Oncologia Medica) Edizione 2021.

Elaborazione del modello PICO

P = soggetti affetti di glioblastoma <70anni

I = radioterapia

C = temozolamide

Nei ***pazienti affetti da glioblastoma di nuova diagnosi, con meno di 70 anni,*** alla ***radioterapia*** deve essere associato un trattamento con ***temozolomide*** concomitante o adiuvante?

Linee guida «Neoplasie cerebrali». AIOM (Associazione Italiana Oncologia Medica) Edizione 2021.

Sensibilità

30 records utili su 3000 ritrovati su PubMed

- ✓ Ricerca completa
- X Alto numero di records non rilevanti alla nostra ricerca

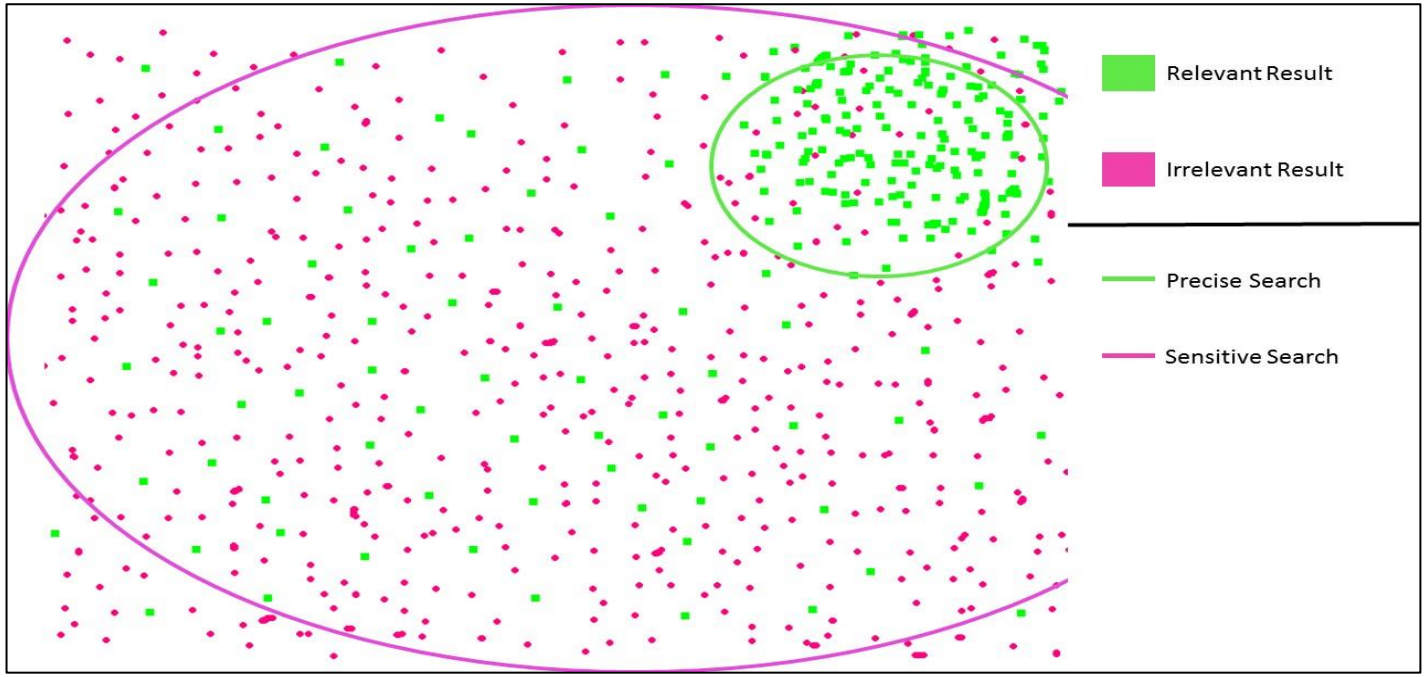
Precisione

10 records utili su 30 ritrovati su PubMed

- ✓ Trova i records rilevanti
- X Pericolo di perdere records, ricerca incompleta

Quindi … sensibilità o precisione?

Alta precisione e sensibilità allo stesso tempo … impossibile



Fonte: University of Toronto https://guides.library.utoronto.ca/c.php?g=577919&p=4304403

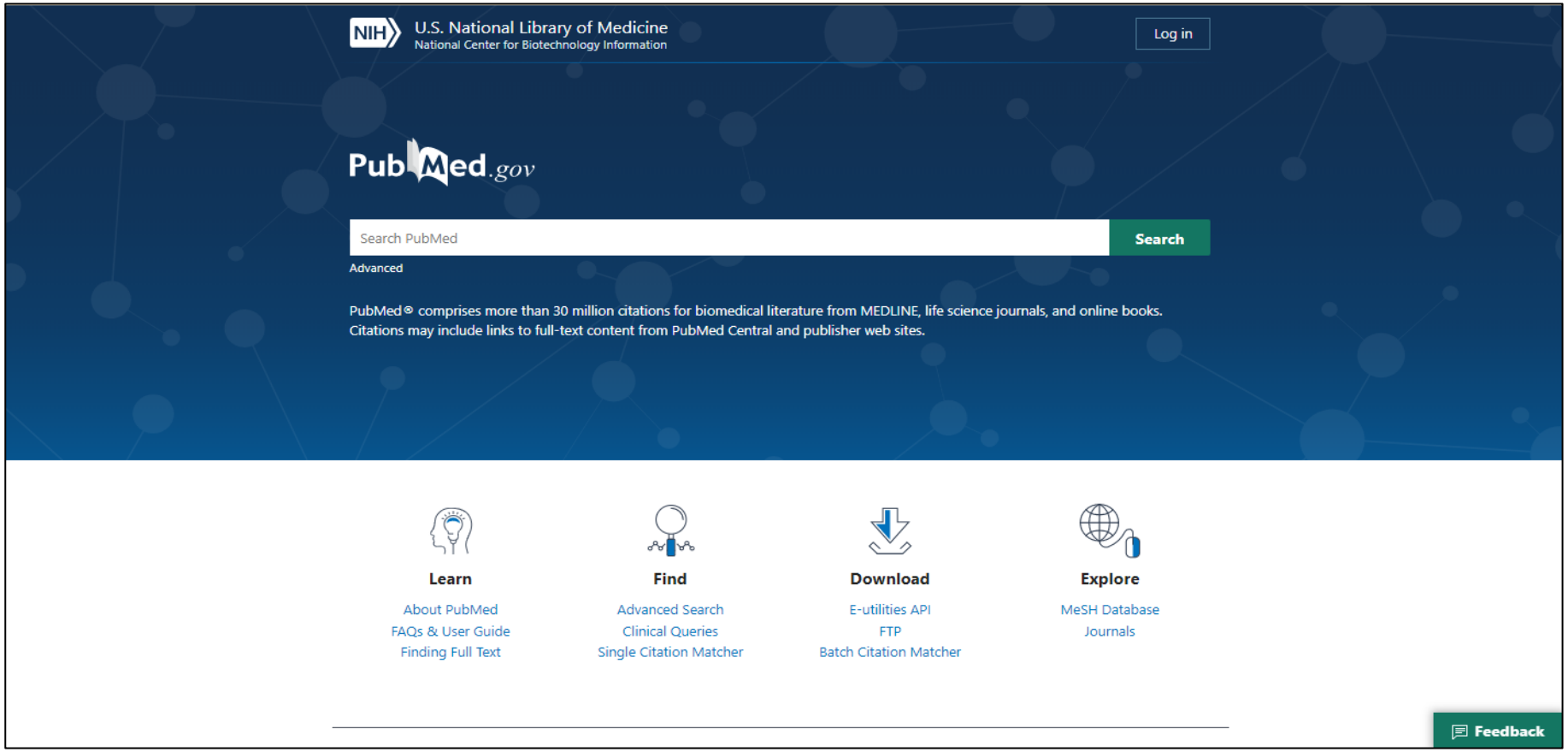
Per fare una revisione sistematica → **sensibilità**

Per il clinico, che deve rispondere ad un quesito clinico → **Precisione**

Creare la stringa di ricerca

Interrogare le diverse banche dati

Trovare gli studi randomizzati (RCT)

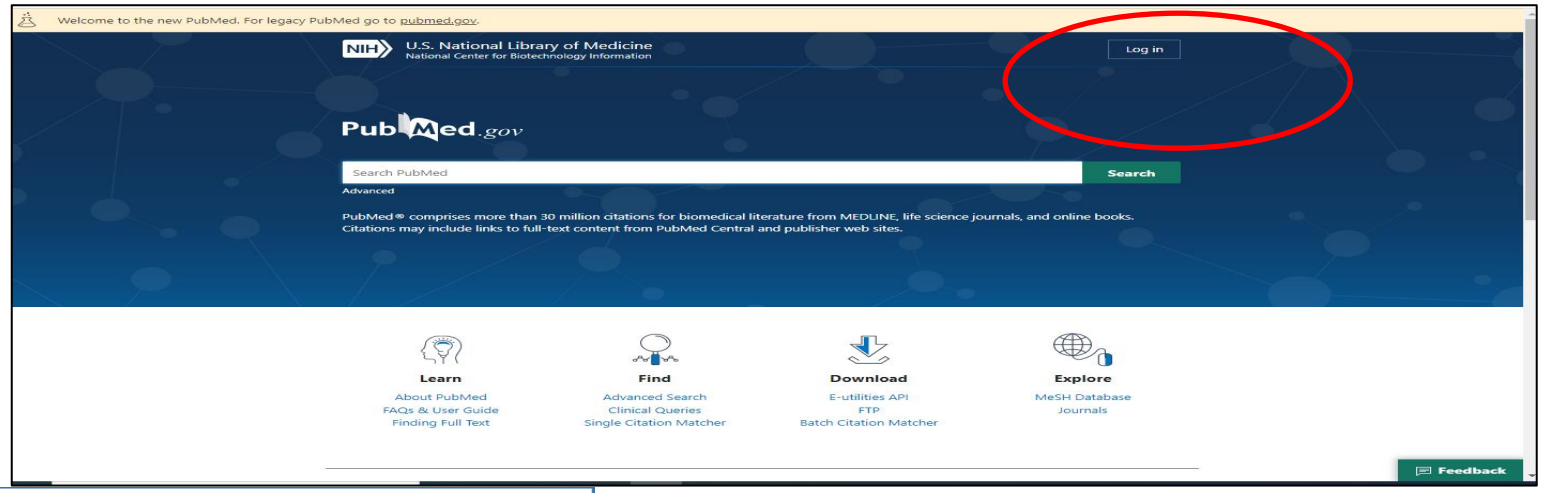


https://www.ncbi.nlm.nih.gov/pubmed/

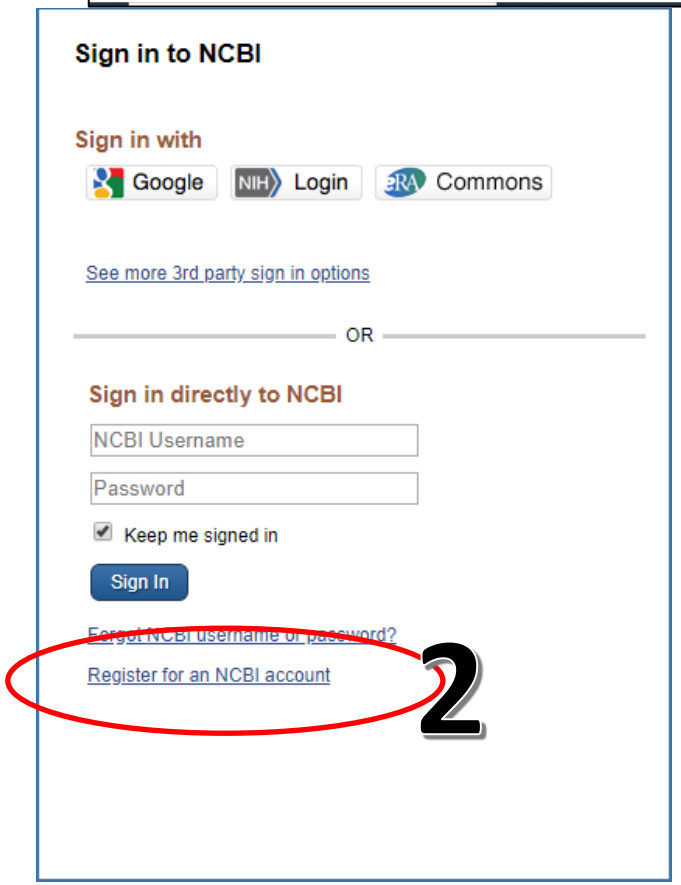
I campi della citazione bibliografica

Guida per una ricerca su PubMed

- Pubmed: Registrarsi e creare un account
- Ricerca libera
- Gli operatori booleani
- Creare una stringa di ricerca
- Mesh: utilizzo
- Risultati: conservazione e rilancio della ricerca
- Scaricare i risultati



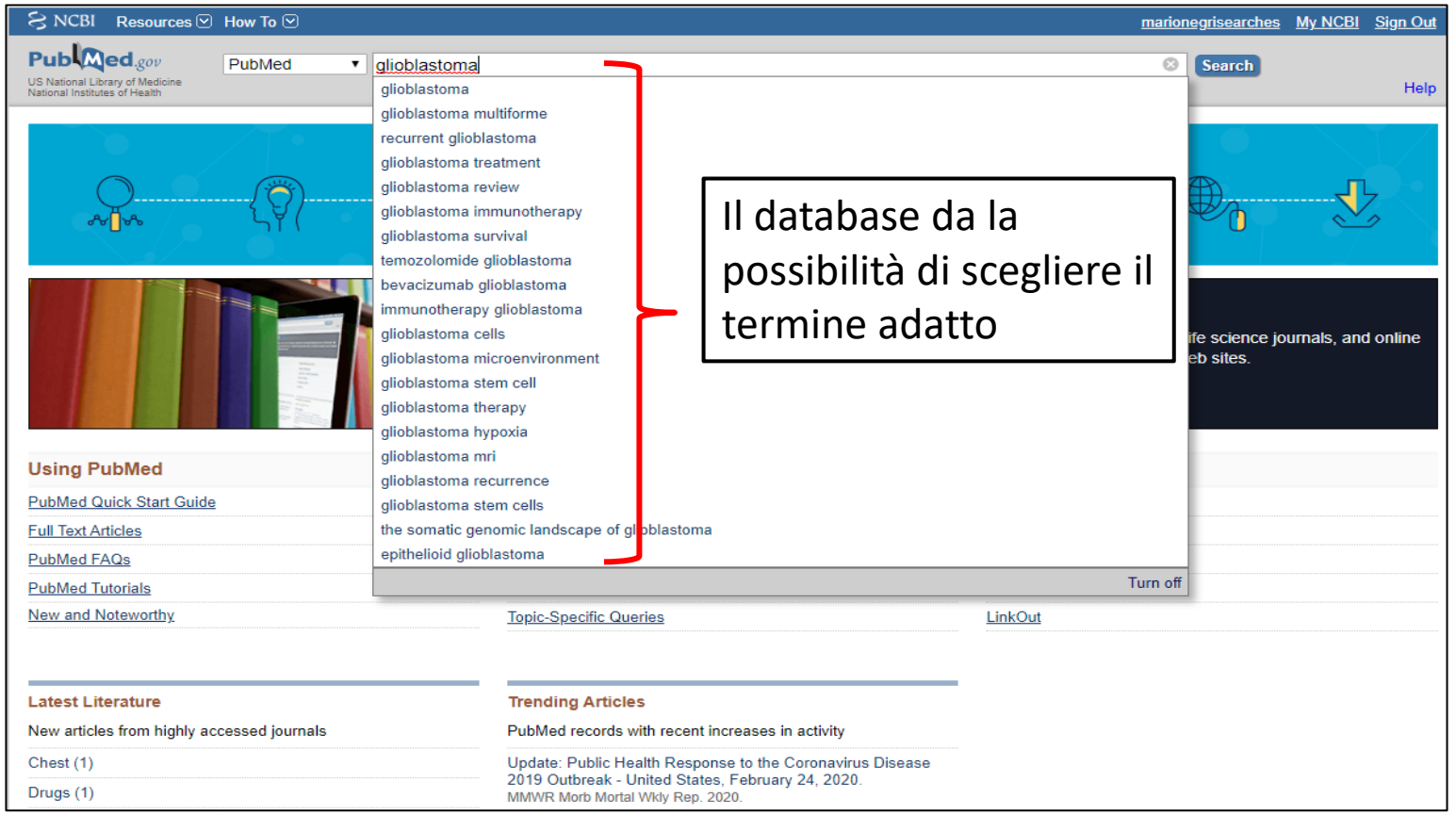
1



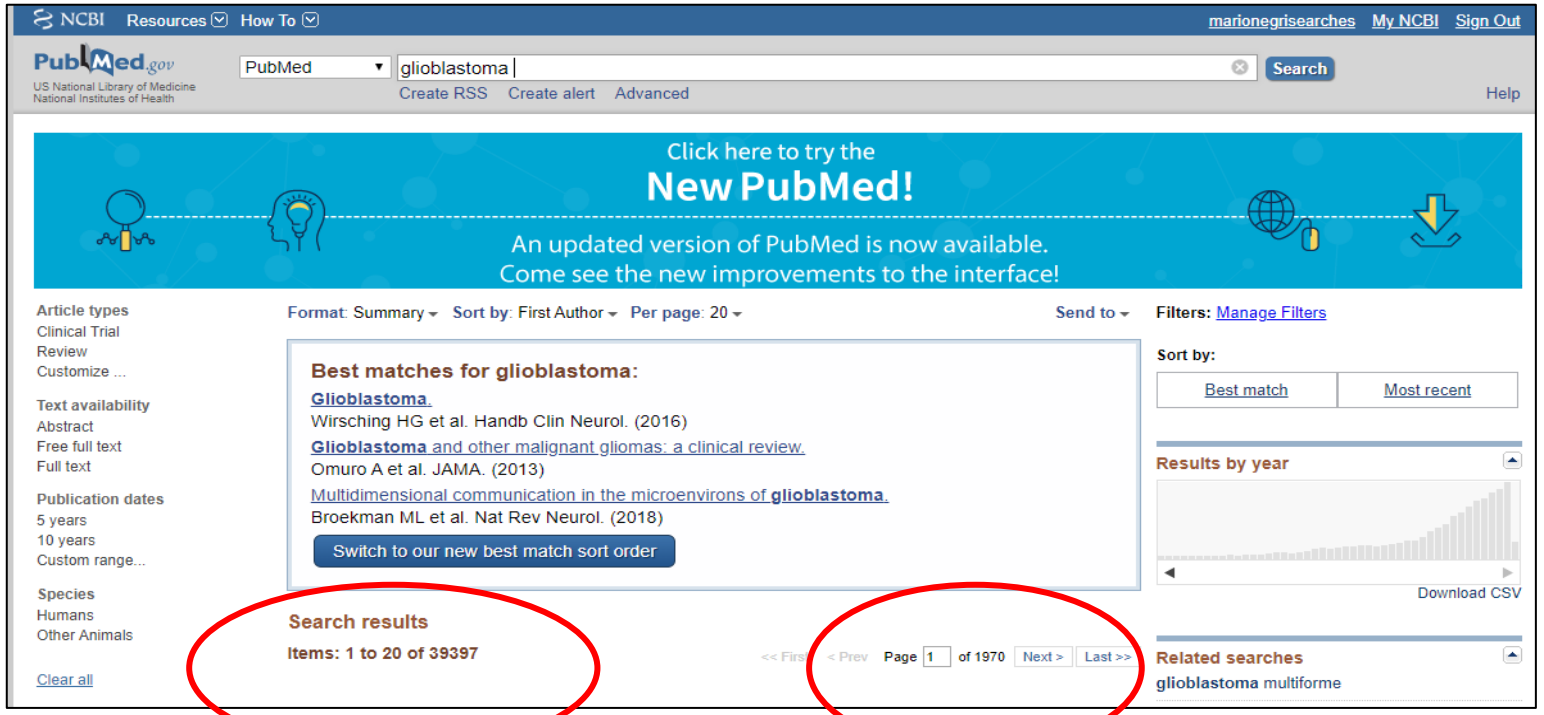
2

Registrarsi sul sito di PubMed e creare una utenza permette di salvare le ricerche e richiamarli per aggiornarli.

Ricerca libera



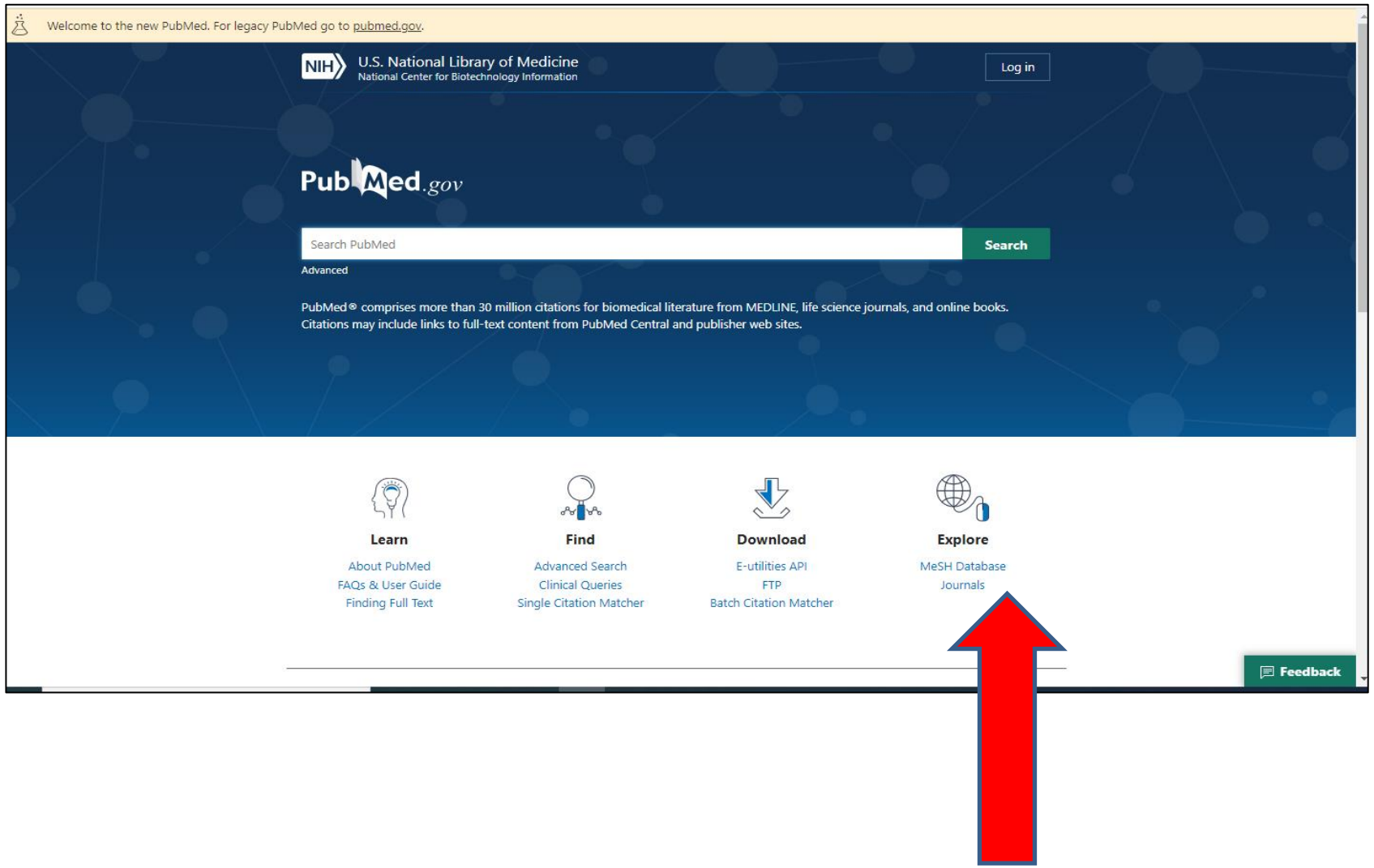
Il database e formato da diversi campi: autore, data, nome del journal, ecc.
Inserendo solo una parola chiave, in questo caso glioblastoma, la ricerca verrà fatta in tutti i campi, la chiamata “ricerca libera”



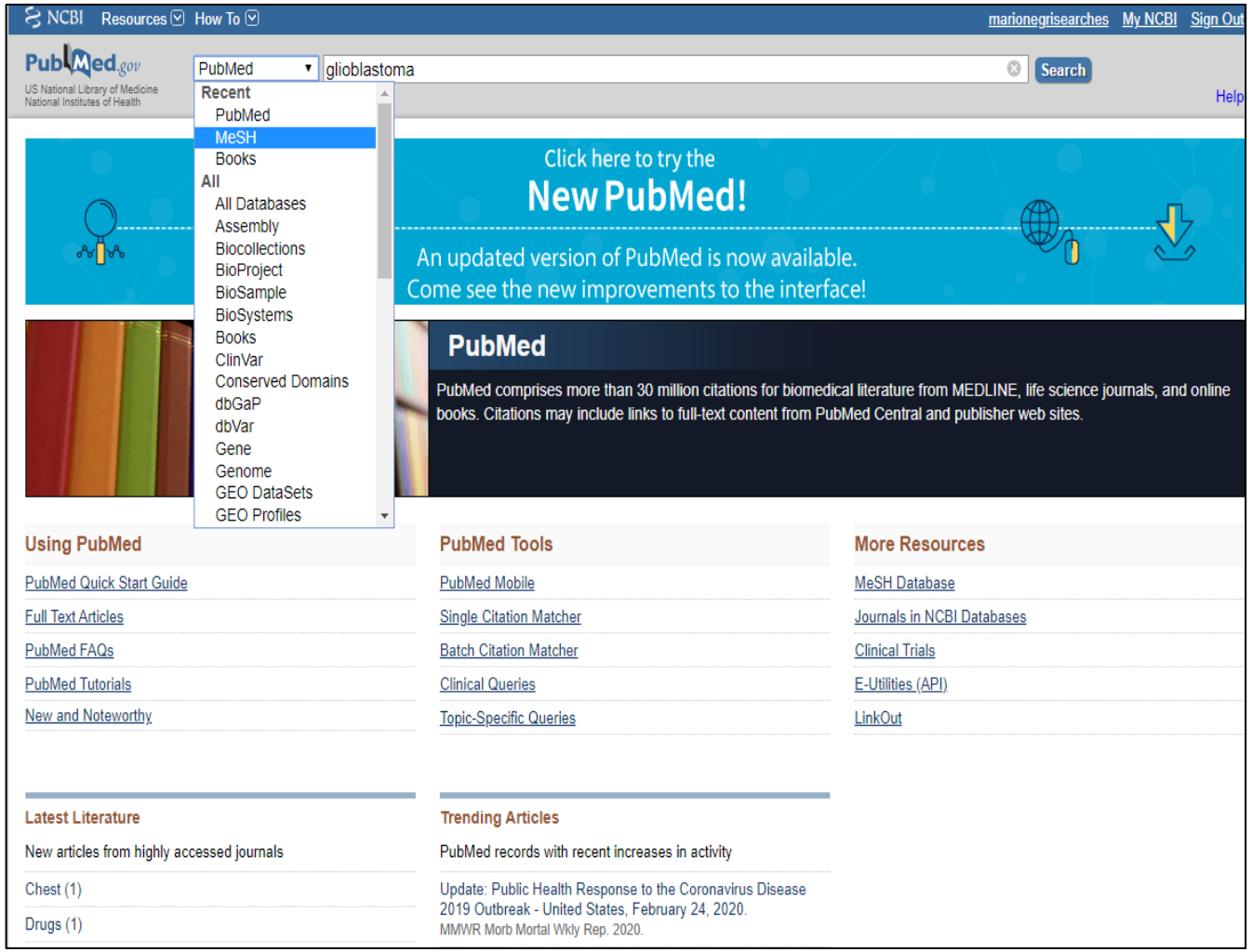
Più di 35.000 risultati e
1.790 pagine da controllare!

La ricerca libera e semplice da fare ma il risultato ritrova un alto numero di records e, nella maggior parte dei casi, poco attinenti alla nostra ricerca.

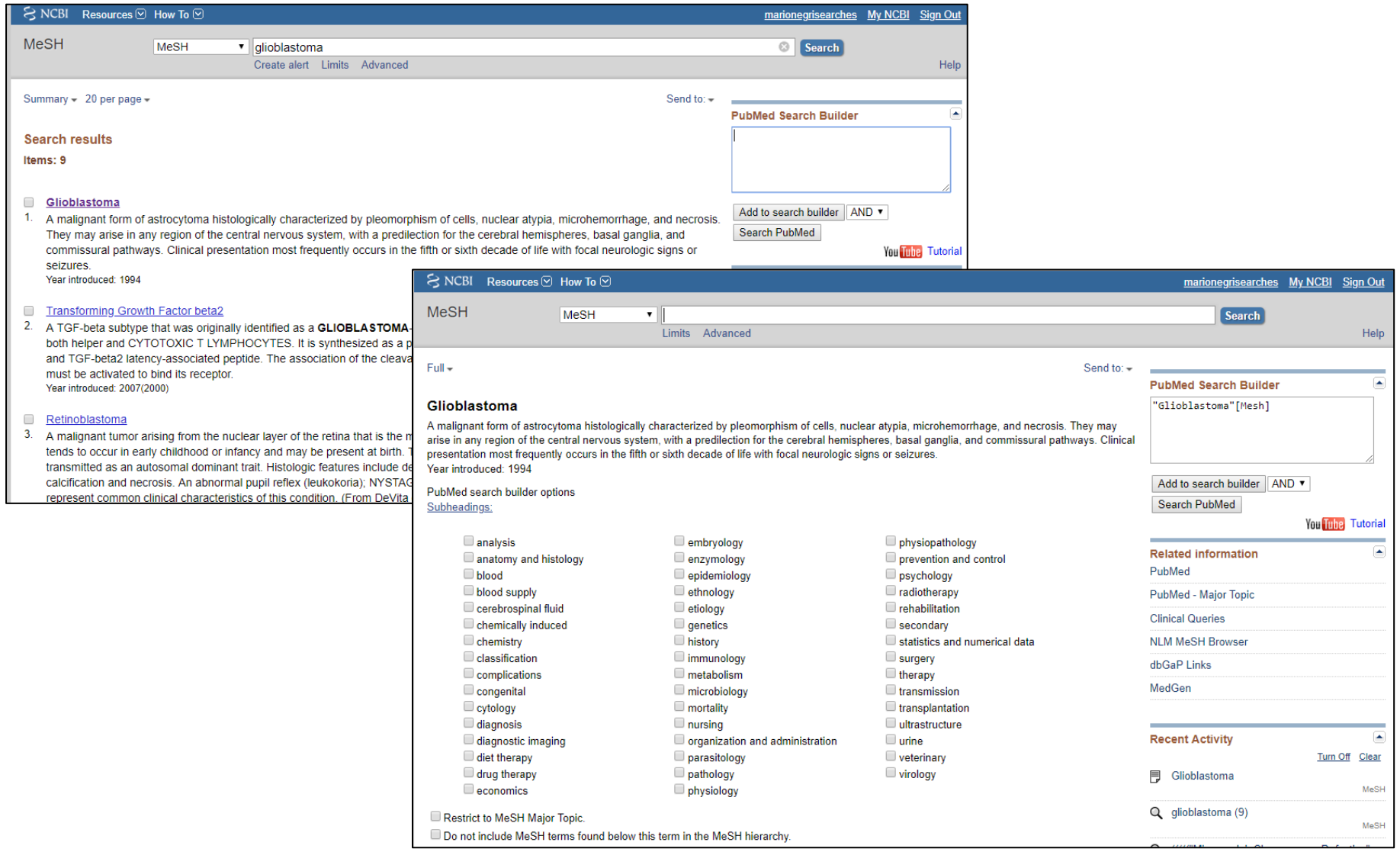
MeSH: Medical Subject Headings



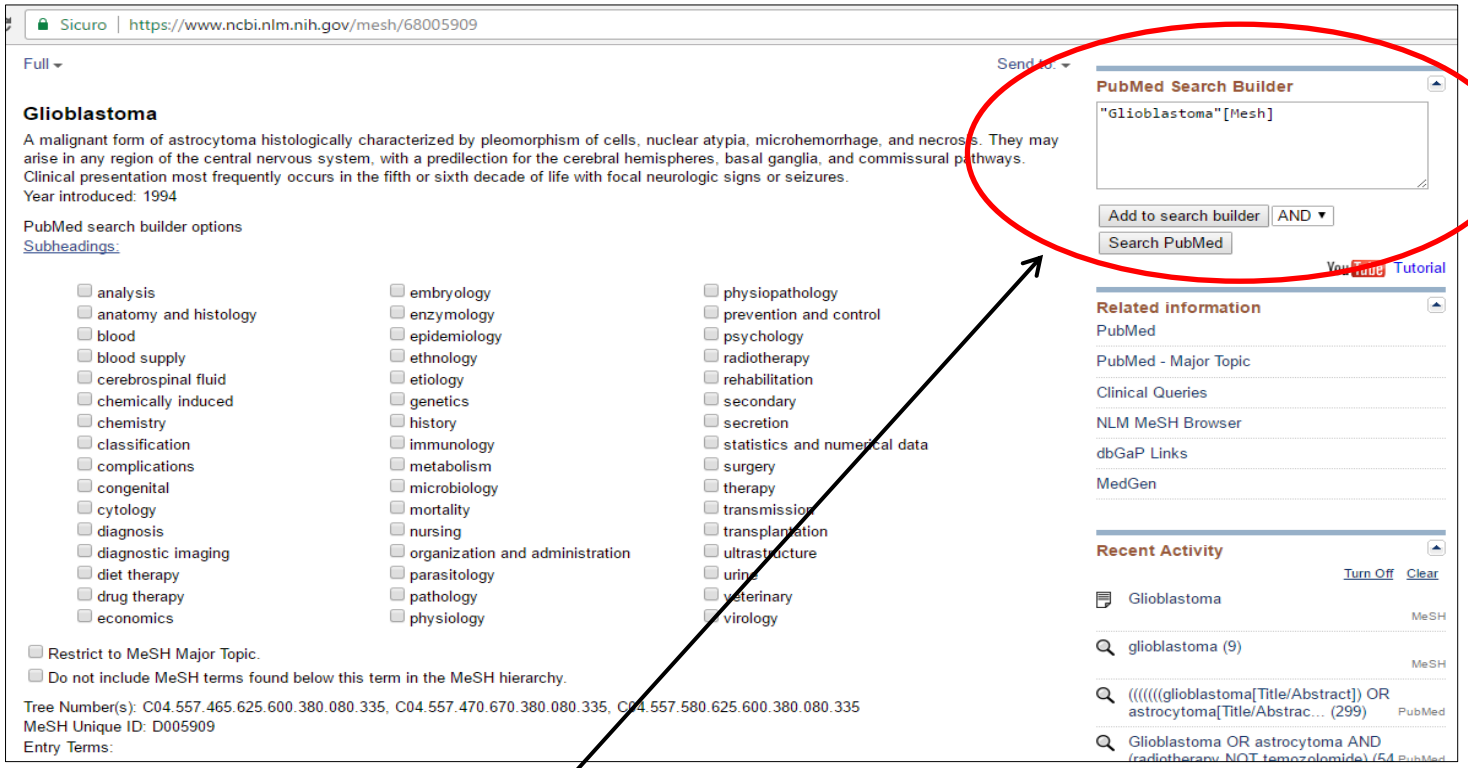
MeSH: Medical Subject Headings



Con il vocabolario controllato possiamo costruire una ricerca più mirata.



Il vocabolario controllato da la possibilità di scegliere
il termine più attinente alla nostra ricerca

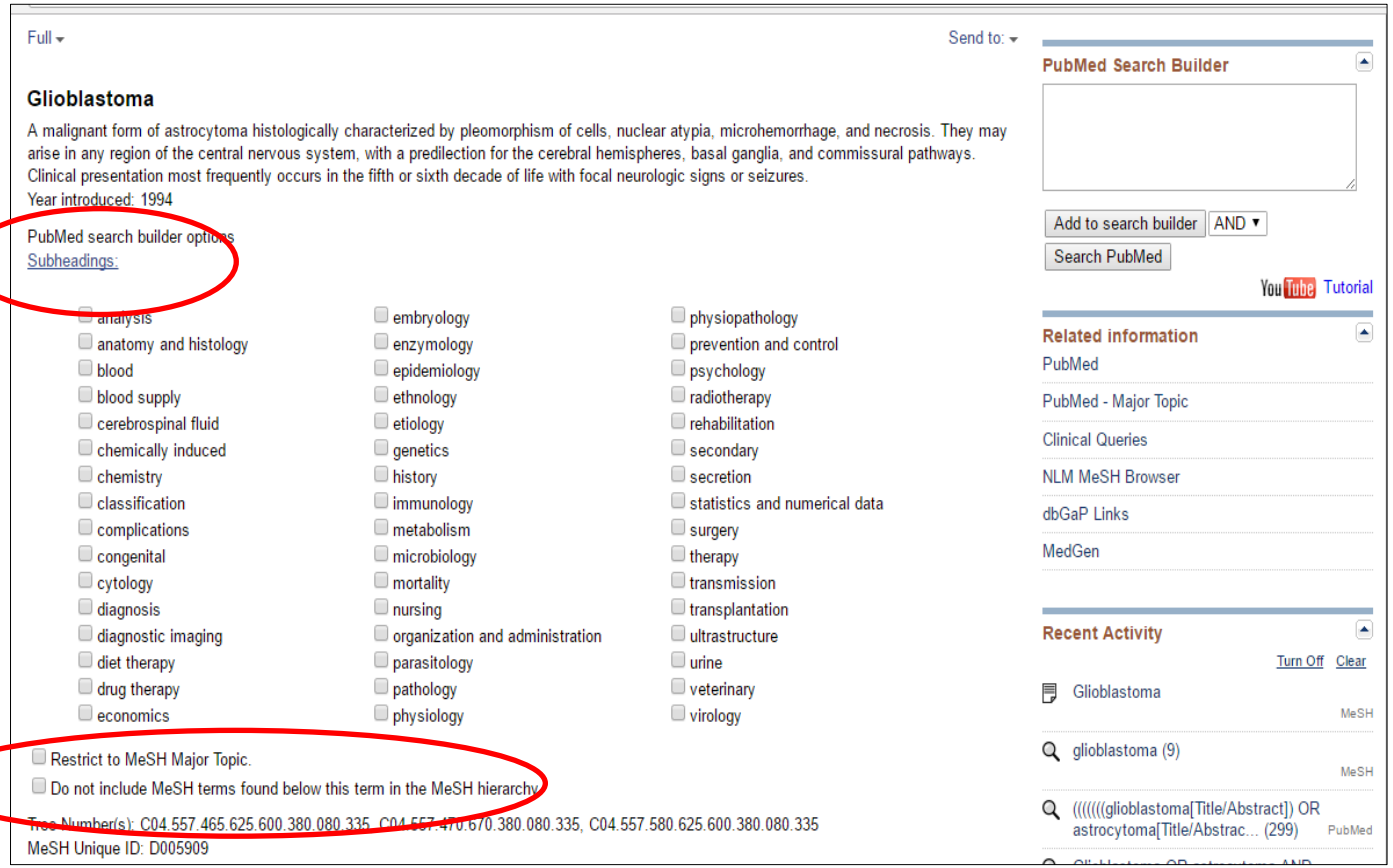


Impostato il termine da cercare se inserisce nella maschera di ricerca

P = soggetti affetti di **glioblastoma** <70anni

I = radioterapia

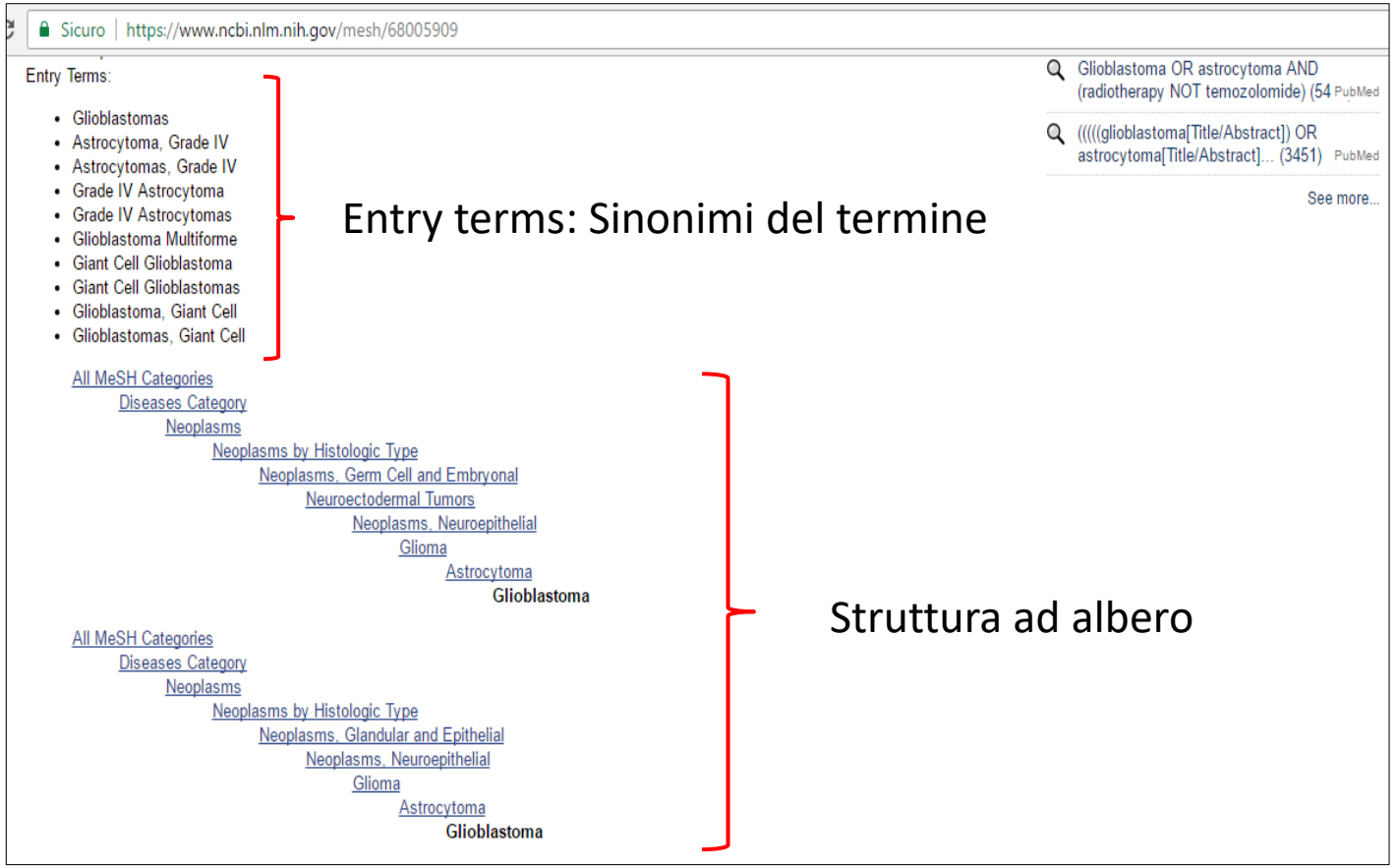
C = temozolamide



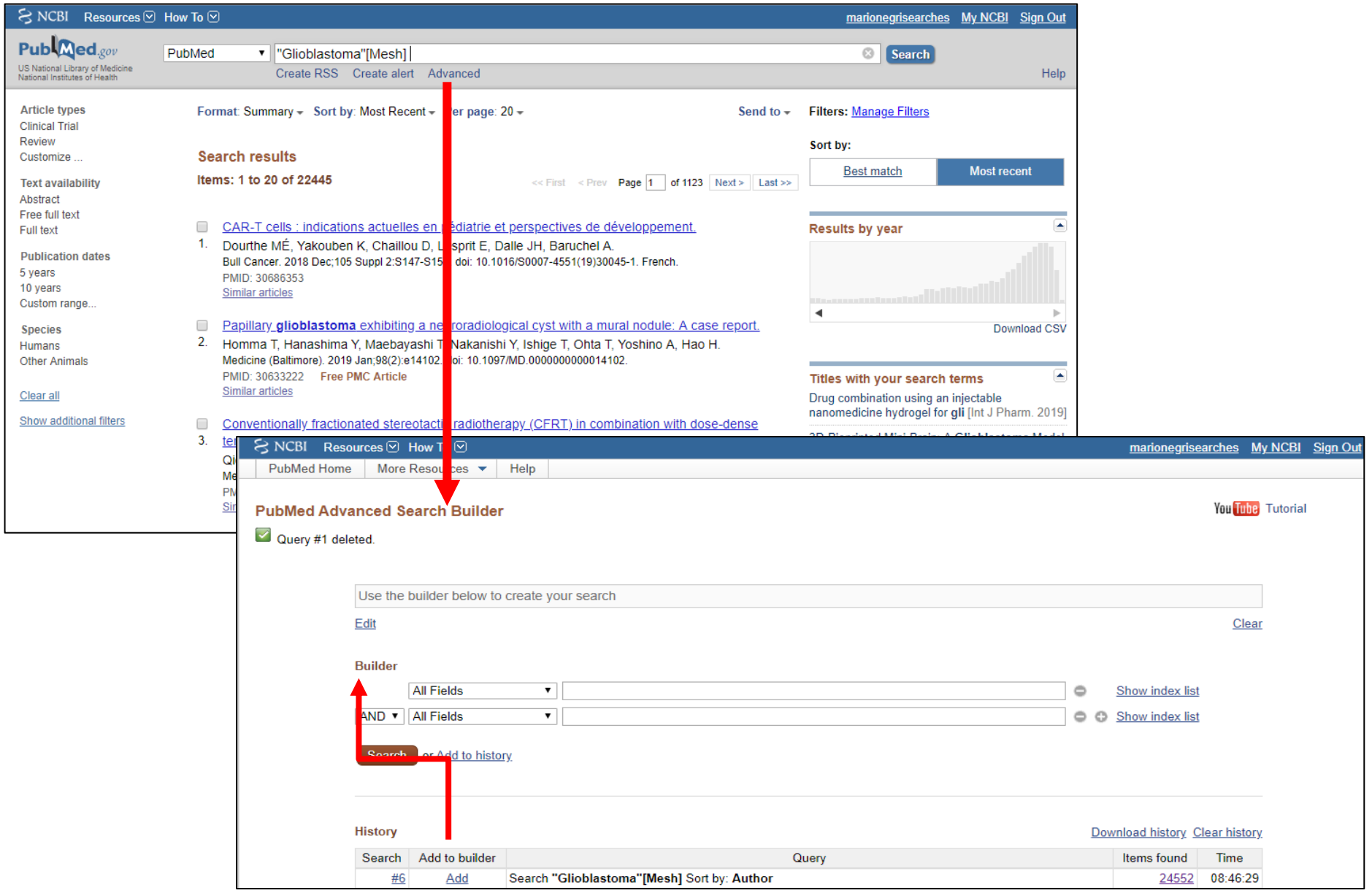
I **subheadings**: restringono il campo ad un aspetto più specifico ed è possibile scegliere più di uno.

Restrict to MeSH Major Topic: con questa opzione i risultati ottenuti ricadranno sul termine MeSH cercato.

Do not include MeSH terms found below this term in the MeSH hierarchy: esplodere o no il termine, I risultati non includeranno i termini al di sotto della nostra parola chiave nella struttura ad albero.

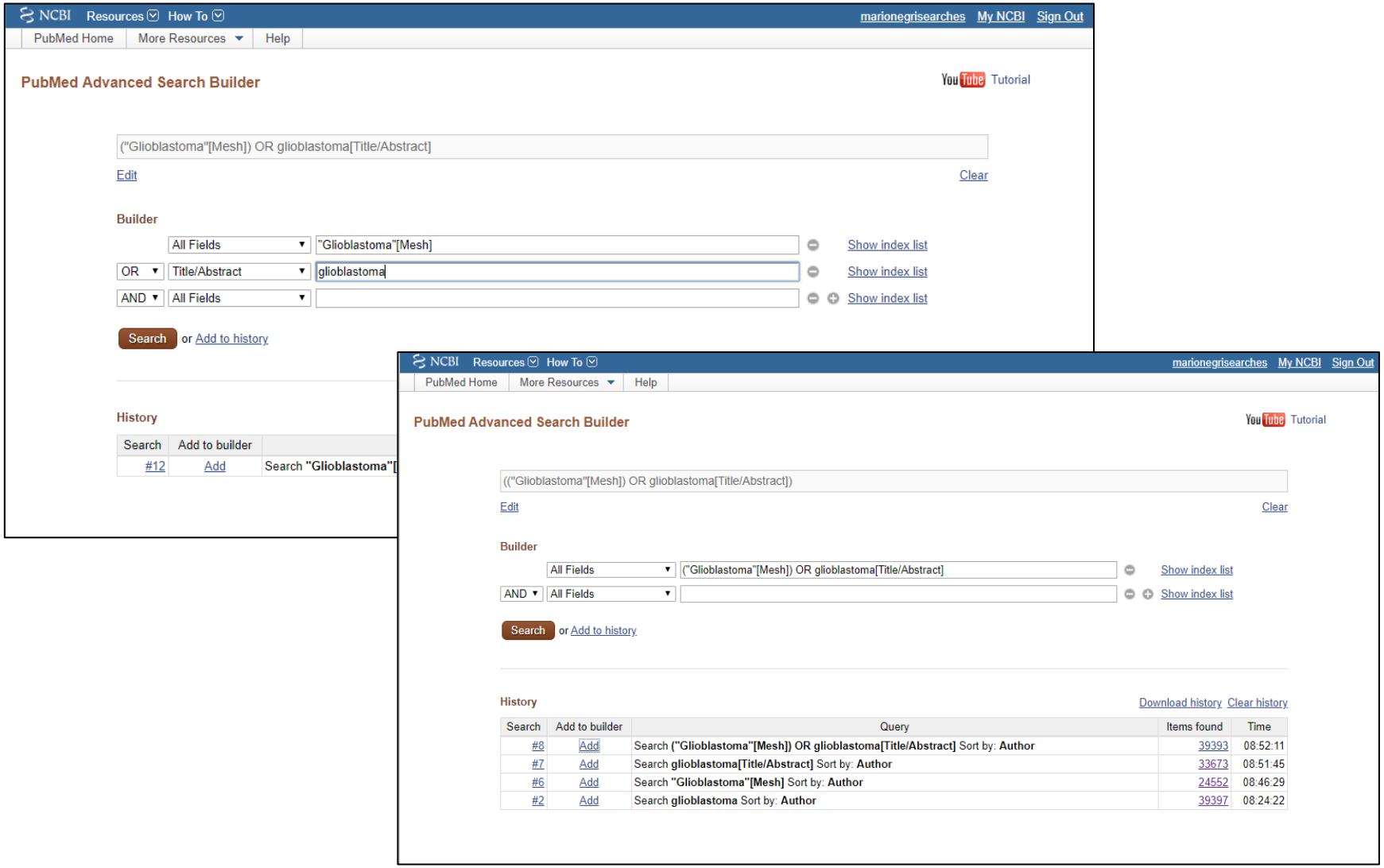


Struttura ad albero: qui si vede a che punto dell'albero è il nostro termine di interesse

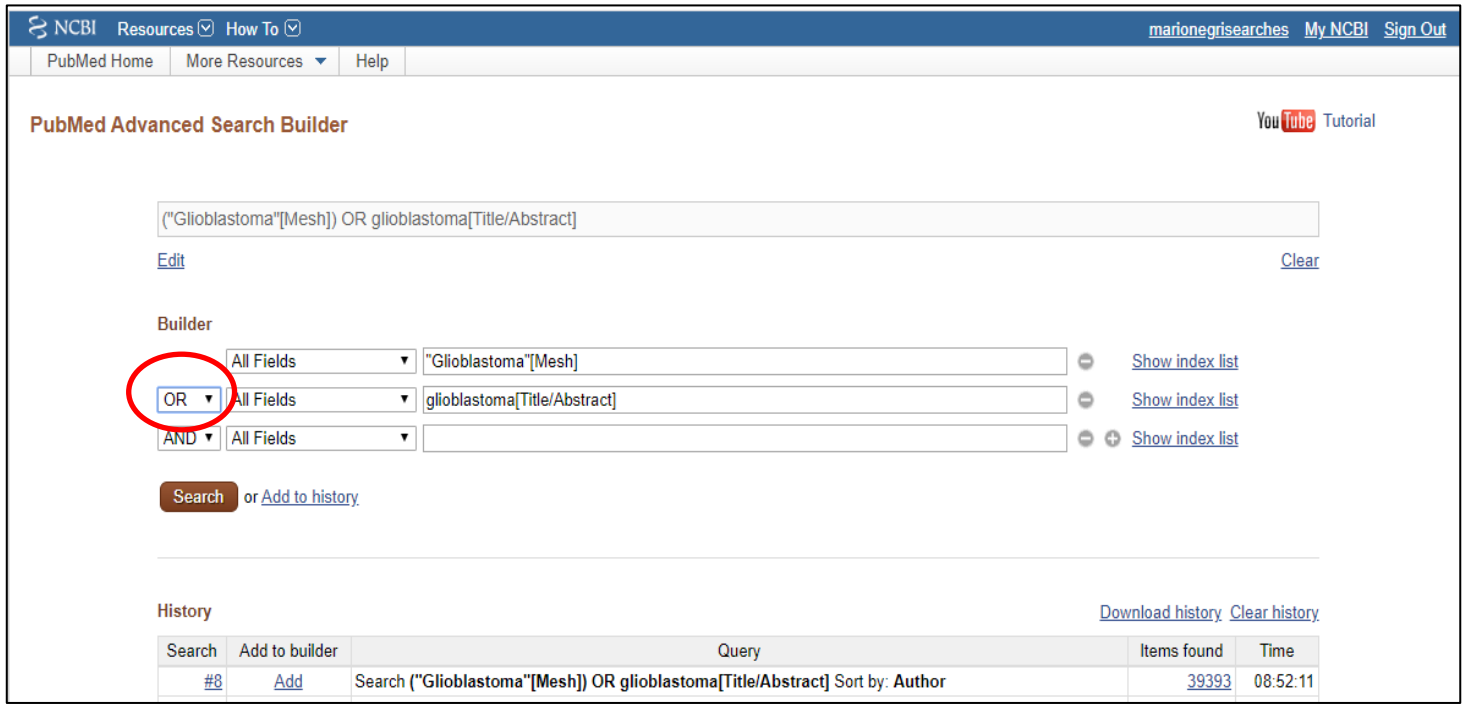


Cliccando su **Advanced** se accede alla pagina che ci permette di costruire una strategia di ricerca.

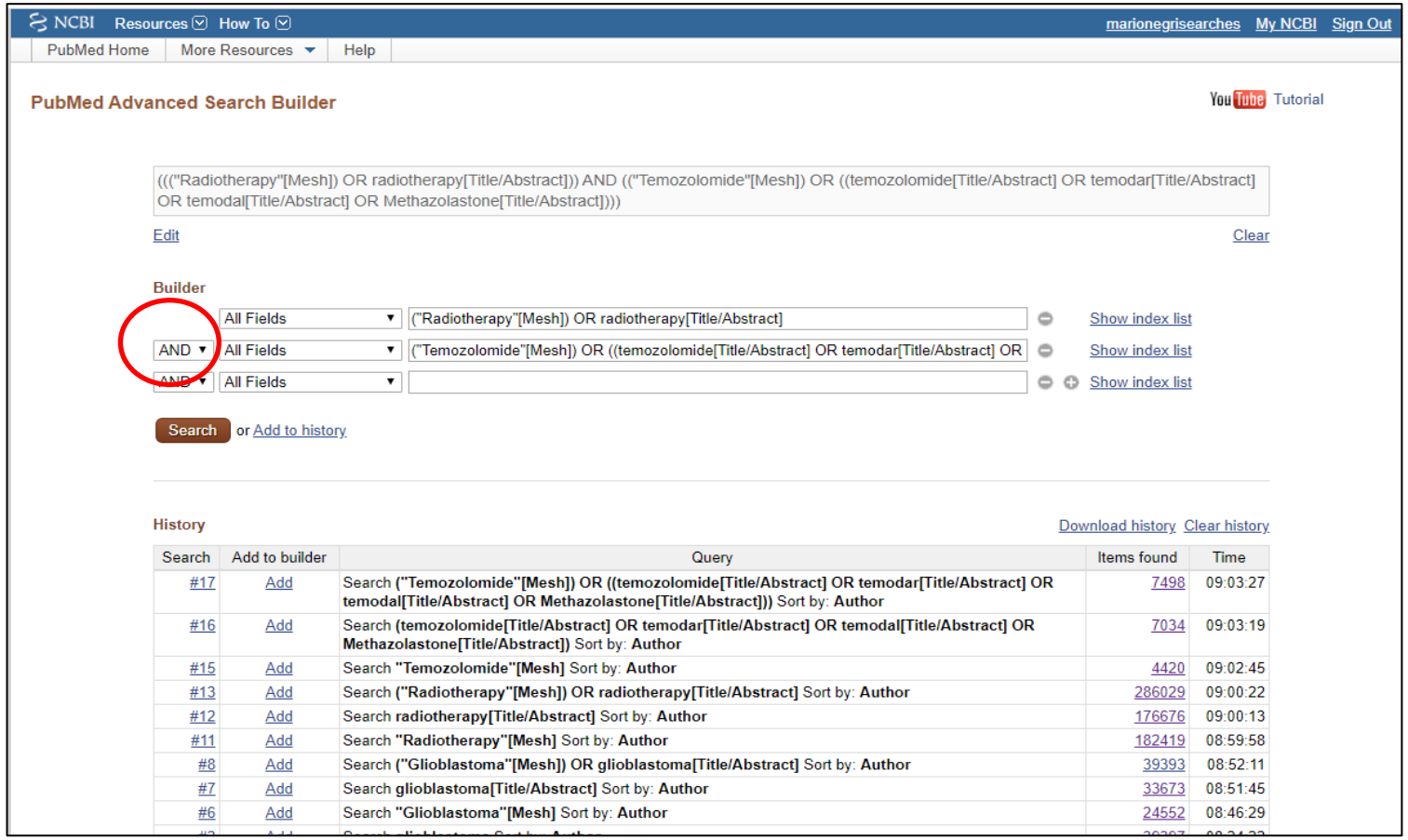
Operatori booleani



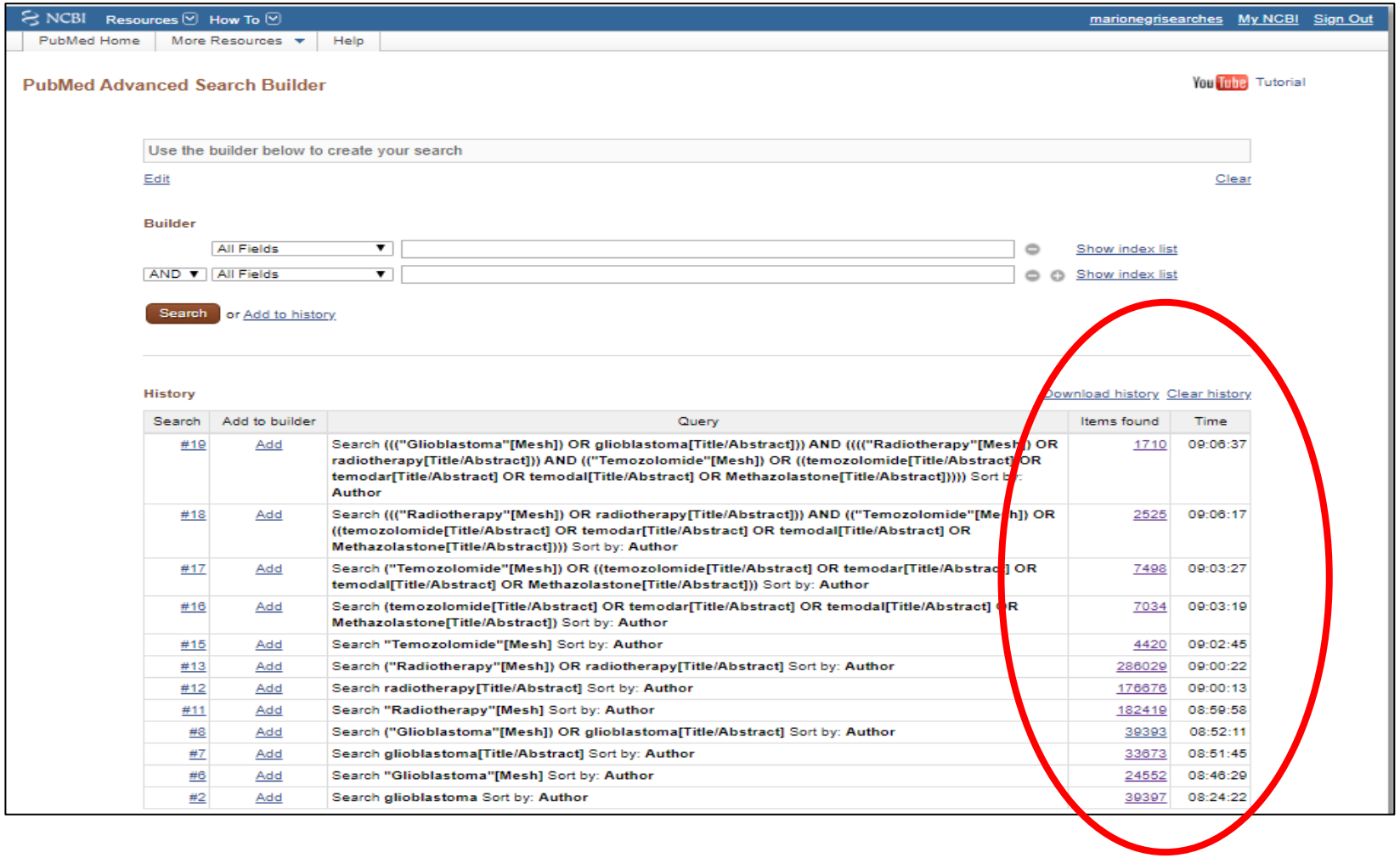
Utilizzando gli operatori logici: OR – AND – NOT
si può stabilire una relazione tra i termini da ricercare.



Con **OR** il database ricercherà i documenti che contengano la parola glioblastoma come termine MeSH o nei titoli e abstract.

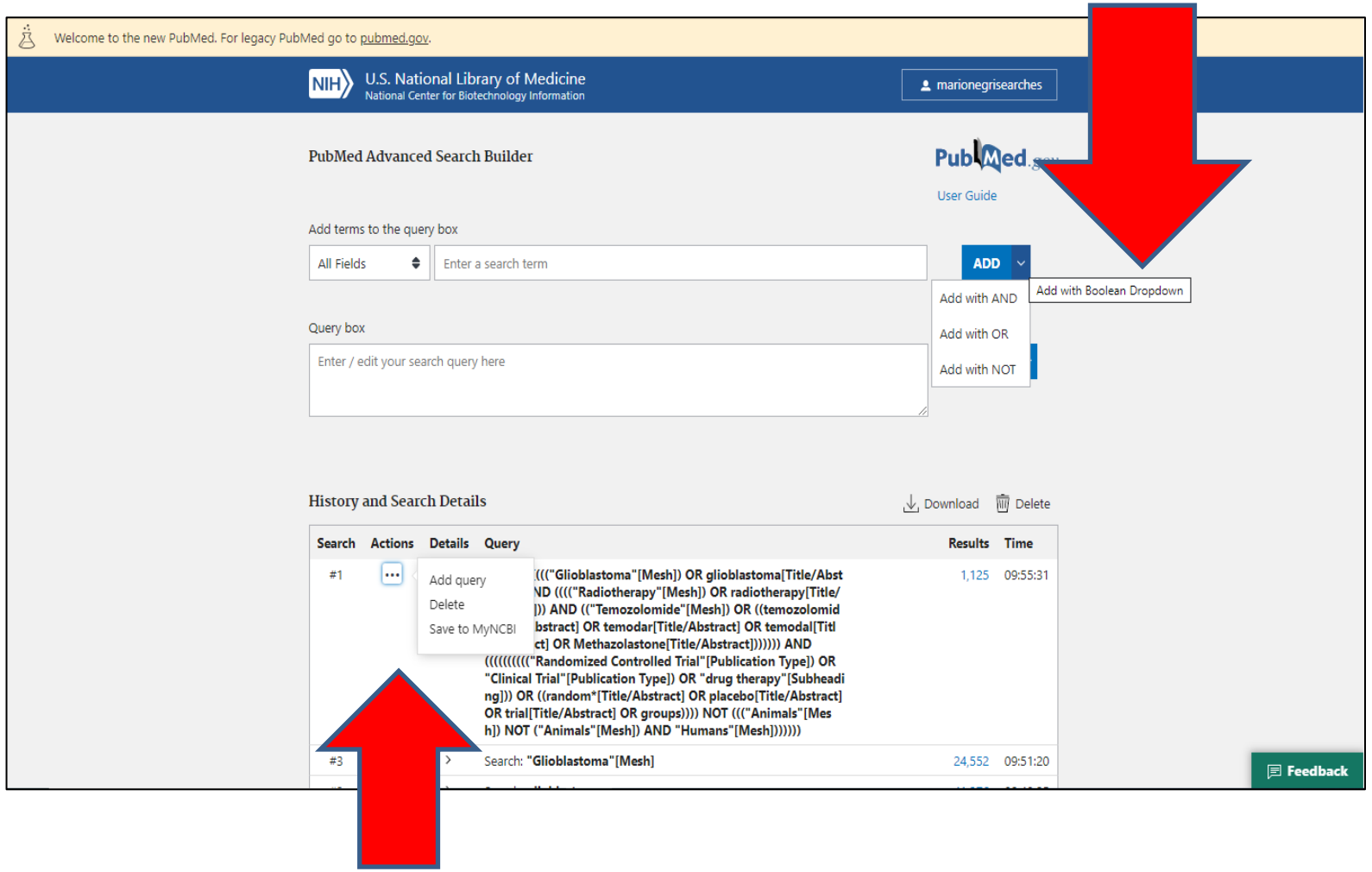


Con **AND** il database ricercherà i documenti che contengano le parole radiotherapy e temozolomide contemporaneamente.



Con una ricerca più elaborata
Il numero dei risultati diminuiscono


Click here to try the
New PubMed!
An updated version of PubMed is now available.
Come see the new improvements to the interface!


Welcome to the new PubMed. For legacy PubMed go to pubmed.gov.
NIH U.S. National Library of Medicine
National Center for Biotechnology Information
marionegrisearches
PubMed Advanced Search Builder
PubMed.gov
User Guide
Add terms to the query box
All Fields
Enter a search term
ADD
Add with Boolean Dropdown
Add with AND
Add with OR
Add with NOT
Query box
Enter / edit your search query here
History and Search Details
Download
Delete
Search Actions Details Query Results Time
#1
Add query
Delete
Save to MyNCBI
(((("Glioblastoma"[Mesh]) OR glioblastoma[Title/Abst
ND ((((("Radiotherapy"[Mesh]) OR radiotherapy[Title/
])) AND (("Temozolomide"[Mesh]) OR ((temozolomid
bstract] OR temodar[Title/Abstract] OR temodal[Titl
ct] OR Methazolastone[Title/Abstract])))))) AND
((((((((("Randomized Controlled Trial"[Publication Type]) OR
"Clinical Trial"[Publication Type]) OR "drug therapy"[Subheadi
ng])) OR ((random*[Title/Abstract] OR placebo[Title/Abstract]
OR trial[Title/Abstract] OR groups)))) NOT ((("Animals"[Mes
h]) NOT ("Animals"[Mesh]) AND "Humans"[Mesh])))))
1,125 09:55:31
#3
Search: "Glioblastoma"[Mesh]
24,552 09:51:20
Feedback

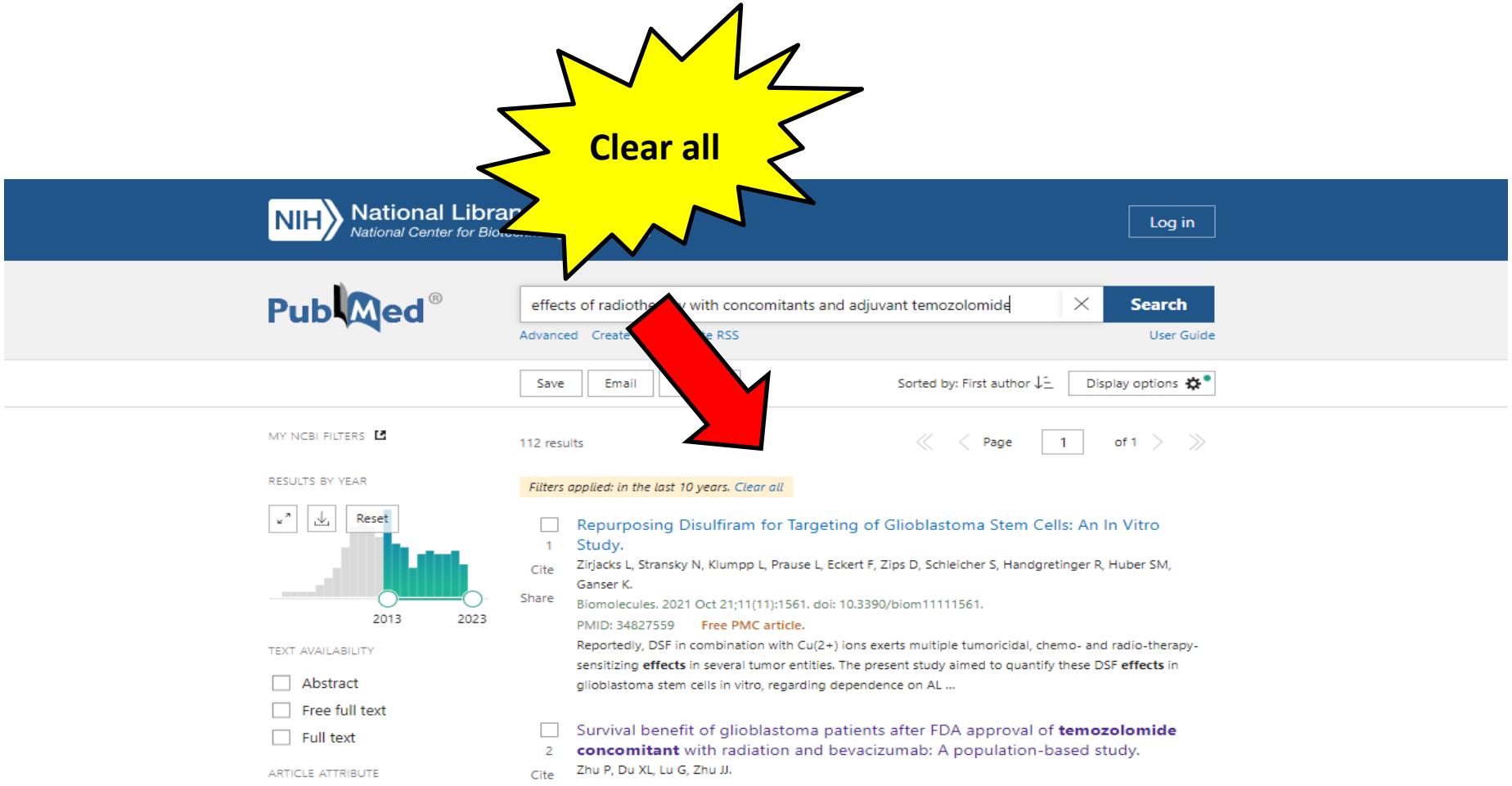
Precisione nella ricerca

P = soggetti affetti di glioblastoma **<70anni**

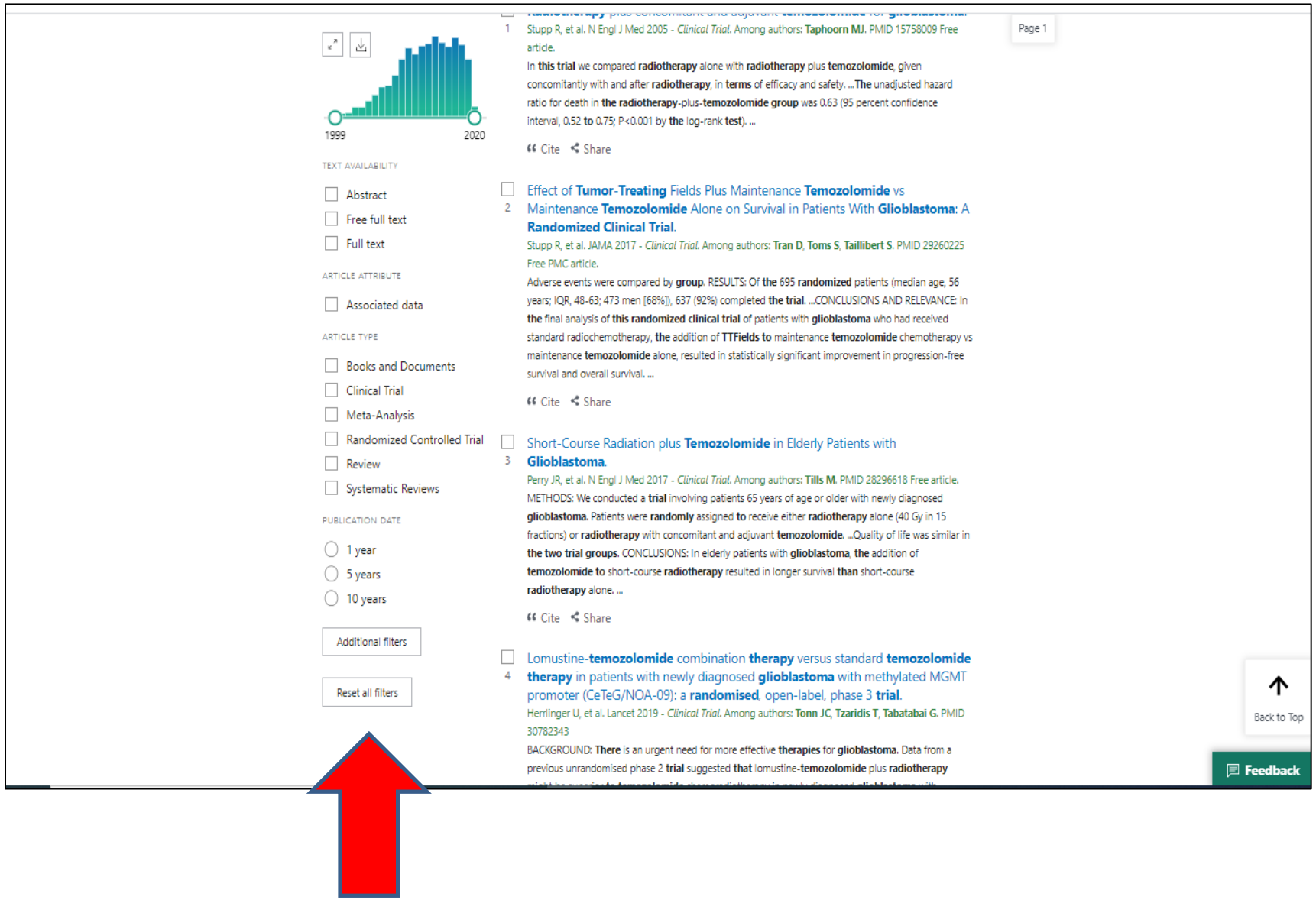
I = radioterapia

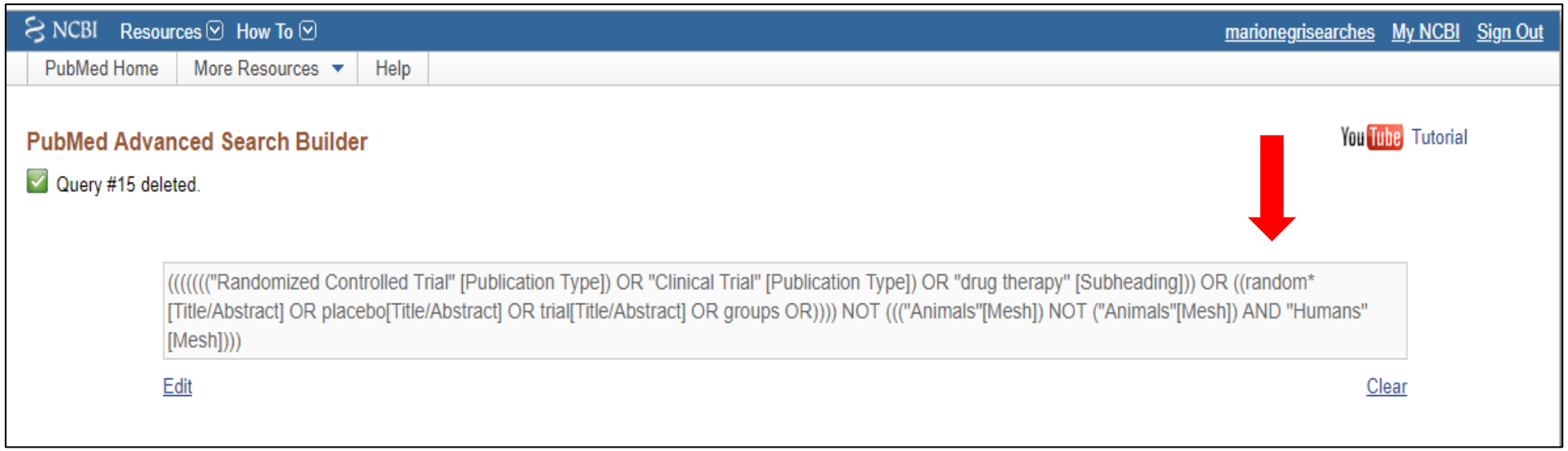
C = temozolamide

I filtri (limits) delimitano la nostra ricerca



E molto importante ricordarci che i limiti impostati vengono mantenuti in memoria nelle ricerche successive, quindi una volta finita la ricerca bisogna disattivarli.

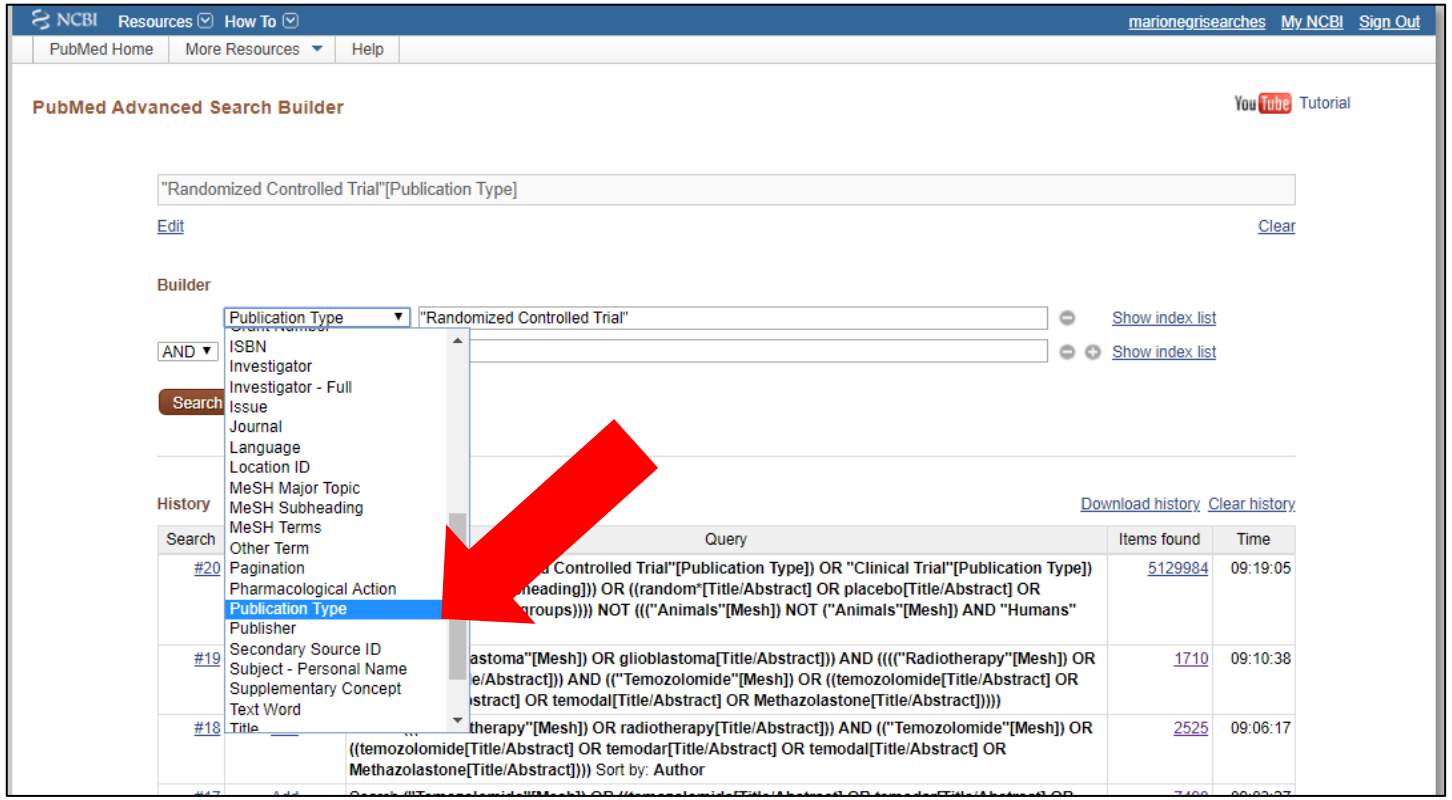

1999
2020
TEXT AVAILABILITY
Abstract
Free full text
Full text
ARTICLE ATTRIBUTE
Associated data
ARTICLE TYPE
Books and Documents
Clinical Trial
Meta-Analysis
Randomized Controlled Trial
Review
Systematic Reviews
PUBLICATION DATE
1 year
5 years
10 years
Additional filters
Reset all filters
1
Stupp R, et al. N Engl J Med 2005 - Clinical Trial. Among authors: Taphoorn MJ. PMID 15758009 Free article.
In this trial we compared radiotherapy alone with radiotherapy plus temozolomide, given concomitantly with and after radiotherapy, in terms of efficacy and safety. ...The unadjusted hazard ratio for death in the radiotherapy-plus-temozolomide group was 0.63 (95 percent confidence interval, 0.52 to 0.75; P<0.001 by the log-rank test). ...
Cite
Share
2
Effect of Tumor-Treating Fields Plus Maintenance Temozolomide vs Maintenance Temozolomide Alone on Survival in Patients With Glioblastoma: A Randomized Clinical Trial.
Stupp R, et al. JAMA 2017 - Clinical Trial. Among authors: Tran D, Toms S, Taillibert S. PMID 29260225 Free PMC article.
Adverse events were compared by group. RESULTS: Of the 695 randomized patients (median age, 56 years; IQR, 48-63; 473 men [68%]), 637 (92%) completed the trial. ...CONCLUSIONS AND RELEVANCE: In the final analysis of this randomized clinical trial of patients with glioblastoma who had received standard radiochemotherapy, the addition of TTFields to maintenance temozolomide chemotherapy vs maintenance temozolomide alone, resulted in statistically significant improvement in progression-free survival and overall survival. ...
Cite
Share
3
Short-Course Radiation plus Temozolomide in Elderly Patients with Glioblastoma.
Perry JR, et al. N Engl J Med 2017 - Clinical Trial. Among authors: Tills M. PMID 28296618 Free article.
METHODS: We conducted a trial involving patients 65 years of age or older with newly diagnosed glioblastoma. Patients were randomly assigned to receive either radiotherapy alone (40 Gy in 15 fractions) or radiotherapy with concomitant and adjuvant temozolomide. ...Quality of life was similar in the two trial groups. CONCLUSIONS: In elderly patients with glioblastoma, the addition of temozolomide to short-course radiotherapy resulted in longer survival than short-course radiotherapy alone. ...
Cite
Share
4
Lomustine-temozolomide combination therapy versus standard temozolomide therapy in patients with newly diagnosed glioblastoma with methylated MGMT promoter (CeTeG/NOA-09): a randomised, open-label, phase 3 trial.
Herrlinger U, et al. Lancet 2019 - Clinical Trial. Among authors: Tonn JC, Tzaridis T, Tabatabai G. PMID 30782343
BACKGROUND: There is an urgent need for more effective therapies for glioblastoma. Data from a previous unrandomised phase 2 trial suggested that lomustine-temozolomide plus radiotherapy
Page 1
Back to Top
Feedback



Troncare le parole con l'asterisco (*): verranno ricercate tutte le varianti che iniziano con la stessa radice.
random* (randomized, randomizes, randomizing, randomization, randomised, randomises, randomising and randomisation)

Le **parentesi** stabiliscono un ordine di priorità nei termini da cercare, in questo caso il database non cercherà gli studi sugli animali e neanche quelli su umani e animali

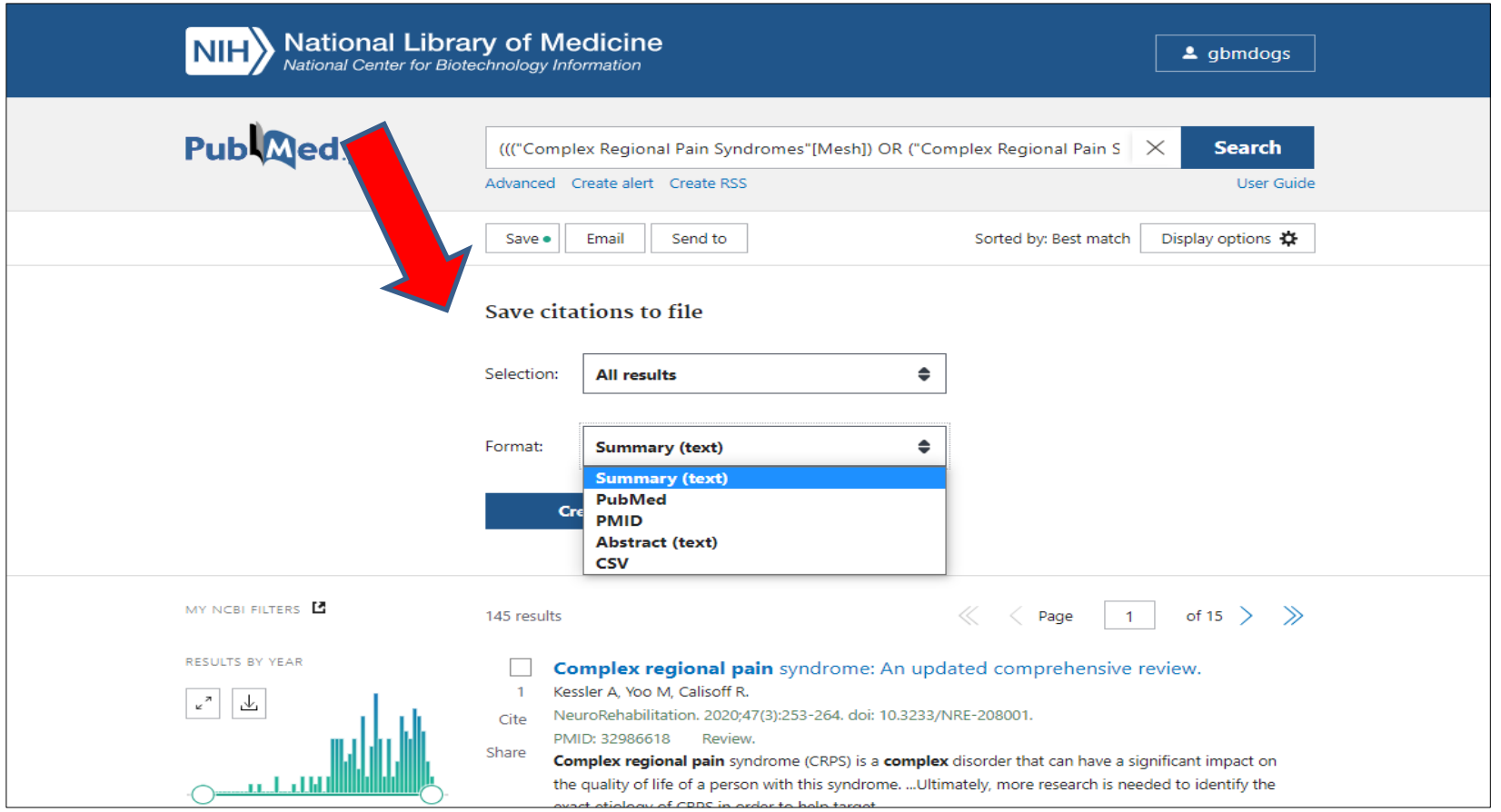
… NOT (("Animals"[Mesh]) NOT ("Animals"[Mesh] AND "Humans"[Mesh]))



"Clinical Trial" [Publication Type] OR "Randomized Controlled Trial" [Publication Type])

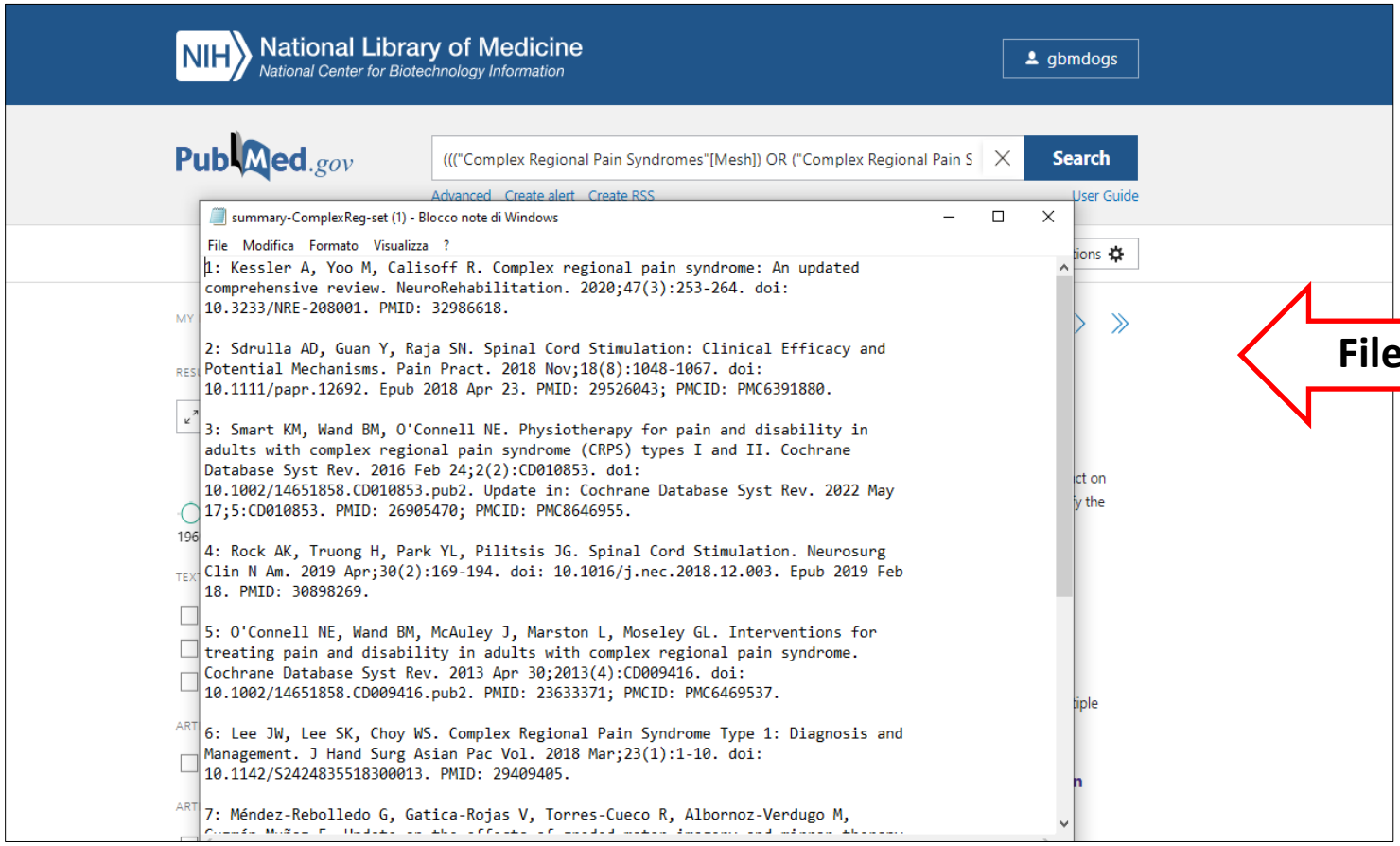
Ricerca per frase: Inserendo più termini nella maschera di ricerca, il database cercherà ogni singolo termine combinandolo con l'operatore AND.
Se invece si vuole trovare un risultato come frase, i termini devono essere racchiusi tra virgolette.

Risultati



Dalle tendine si può scegliere sia il formato che l'ordine da dare all'elenco dei risultati

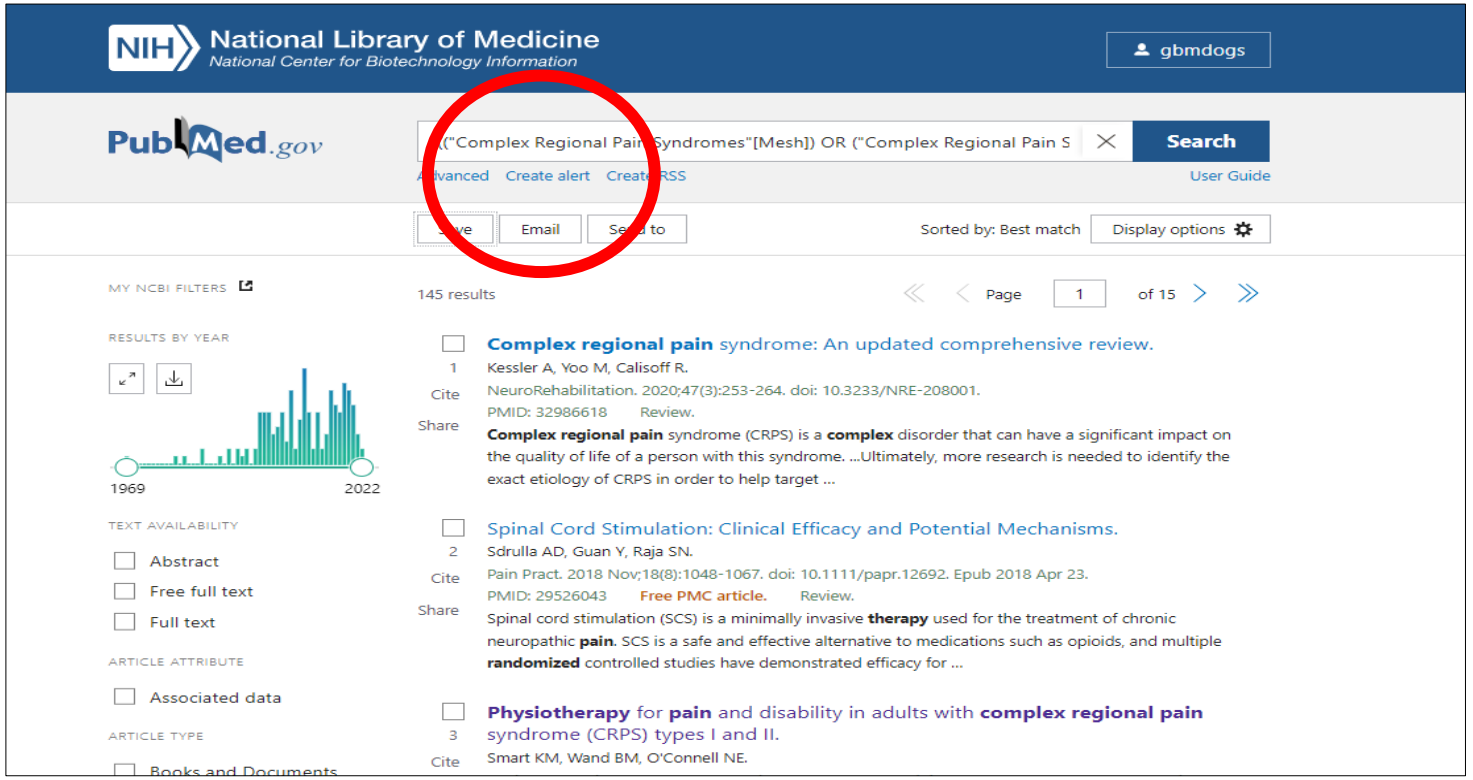
Create file: viene scaricato il file nel formato scelto



File RIS

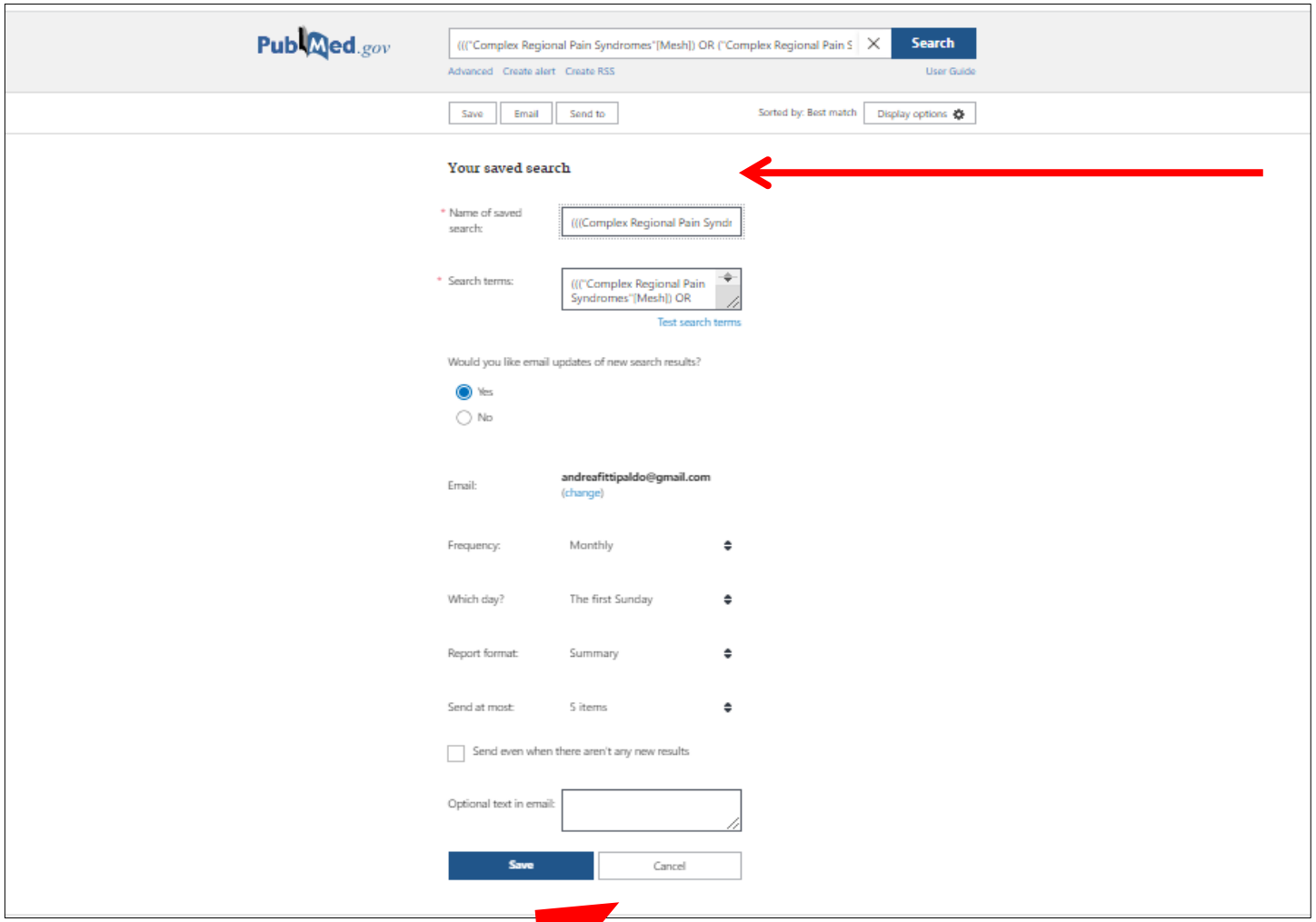
Questo formato di file mi permette di caricarlo in un software che serve alla gestione e condivisione di documenti: **Mendeley e Zotero (gratuiti), Endnote e Refworks (a pagamento)**

Salvare i risultati



1

Create alert: l'elenco dei risultati verranno conservati nell'account Pubmed che abbiamo creato.



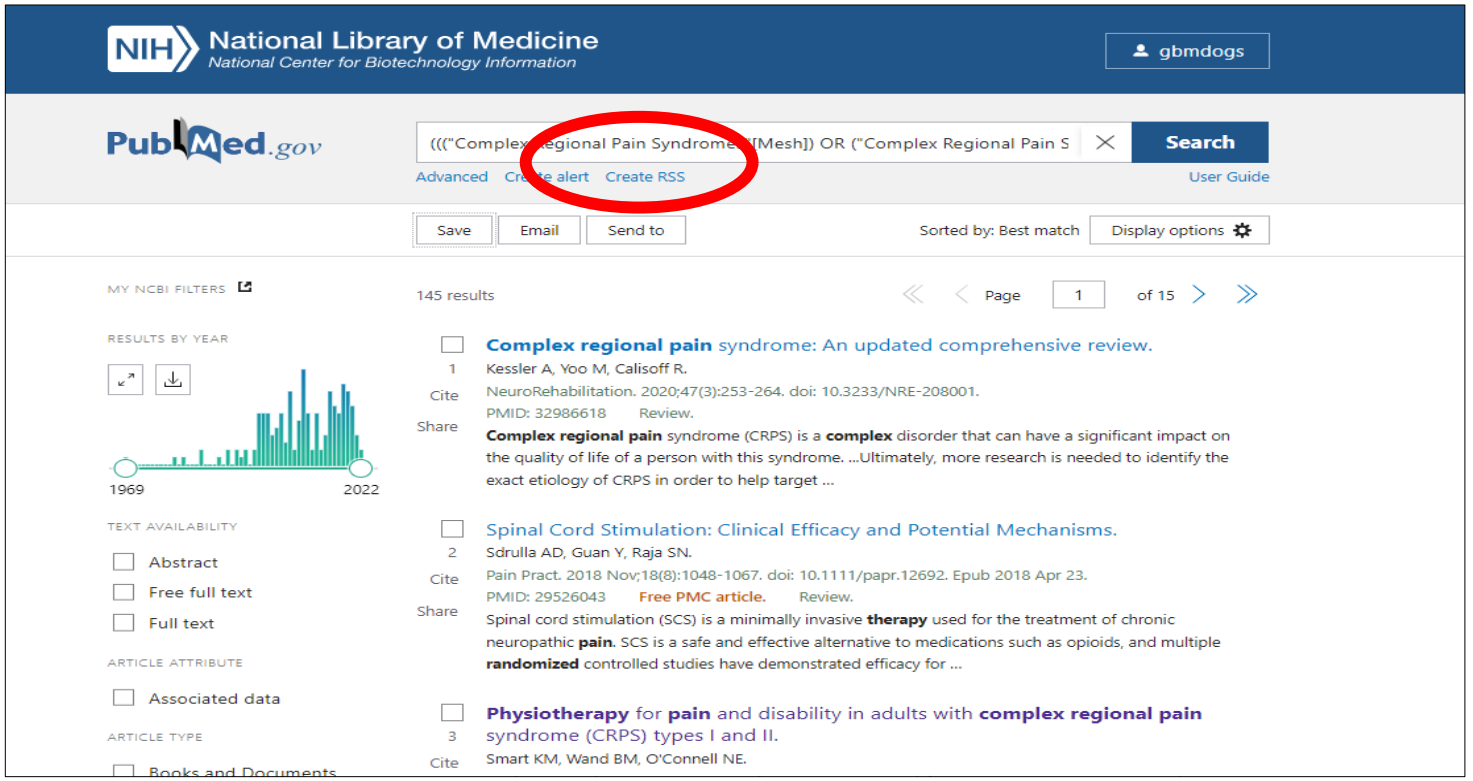
Titolo della nostra Strategia di ricerca

2

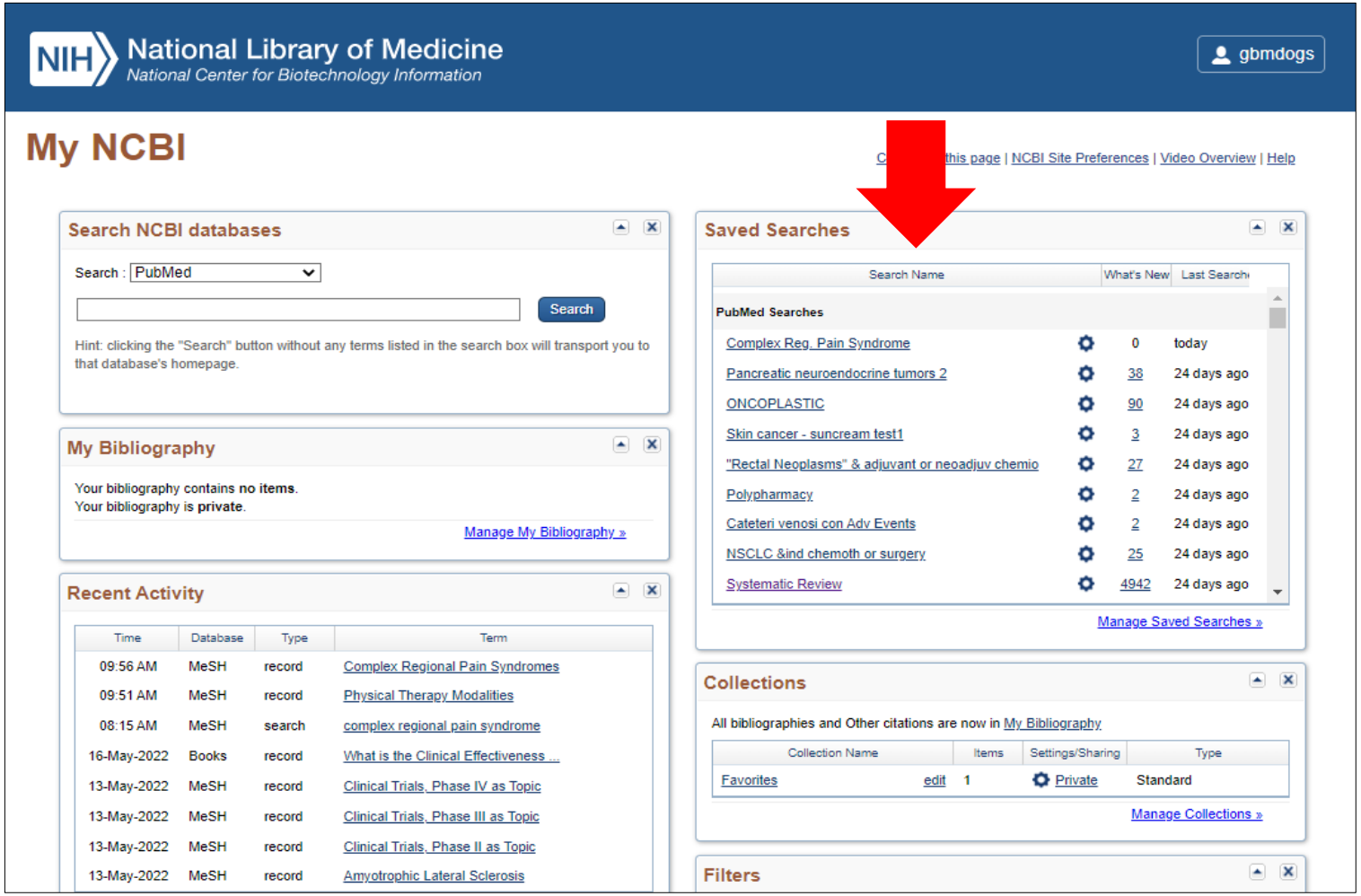
3

Cliccare per salvare

Creare RSS (Really Simple Syndication)



Create RSS: Questa funzione ci permette di ricevere gli aggiornamenti della ricerca.



La ricerca verrà mantenuta nel nostro account per rilanciarla e aggiornare i risultati

Screening

	Zotero	EndNote	Mendeley
Importare records	Plugin	Stringa di ricerca dal database	Plugin
Trovare duplicati	Trova anche quelli non identici	Trova solo quelli identici	Trova anche quelli non identici
Generare citazioni	Cite while you write e trascinamento reference	Cite while you write	Cite while you write e trascinamento reference

rayyan

Rayyan: https://www.rayyan.ai/

RayyanTutorial: https://www.youtube.com/watch?v=yEwbK-EOcp8

SACRO CUORE DON CALABRIA

ECI CANCER CENTRE

I R C C S

SCUOLA DI METODOLOGIA DELLA RICERCA CLINICA

2025 - 11ª EDIZIONE

MODULI SPECIALISTICI - S1

VENERDÌ 14 - SABATO 15 MARZO 2025

NEGRAR DI VALPOLICELLA (VR)

Centro Formazione IRCCS "Sacro Cuore - Don Calabria"

Selezione degli studi; *study flow*

Michela CINQUINI

In pratica..

1. Ottenere una unica lista di referenze

- I risultati della ricerca di ogni database vanno importati su un programma di gestione delle referenze (endnote, excel)
- Eliminare i doppioni (stesso articolo indicizzato su più di una banca dati e quindi trovato più volte)

2. Selezionare gli articoli potenzialmente rilevanti da acquisire in full text

- Scriversi su un foglio i criteri di inclusione sotto forma di PICOS
- Valutare ogni titolo e abstract rispetto al PICOS

3. Obiettivo è non perdere nulla

- Fare il lavoro in due in modo indipendente
- In caso di dubbio, disaccordo o mancanza di abstract il titolo si seleziona lo stesso

4. Procurarsi i full text

5. Rivalutare ogni articolo leggendo il full text rispetto al PICOS

- Fare il lavoro in due in modo indipendente
- Confrontarsi sui risultati
- In questa fase vanno presi solo gli articoli realmente pertinenti In caso di differenze:
  - Risolvere il disaccordo tramite discussione
  - Rivolgersi a terzo revisore

6. Fare lista di studi esclusi

- Indicare ragione dell'esclusione sempre in base al PICOS
- Es: studi esclusi perché partecipanti non nei criteri di inclusione, intervento non nei criteri di inclusione, disegno di studio non nei criteri di inclusione
- Questo lavoro va fatto solo sui full text, non per gli studi esclusi sulla base dell' abstract

7. Fare lista finali di studi inclusi

- Se presenti più record di un articolo tenerli per eventuali dati

  Es: diversi periodi di follow up, analisi di sottogruppi; doppie pubblicazioni (stesso studio pubblicato più volte su riviste diverse con titolo diverso e/o diverso ordine degli autori)

8. Fare flow chart (es: PRISMA)

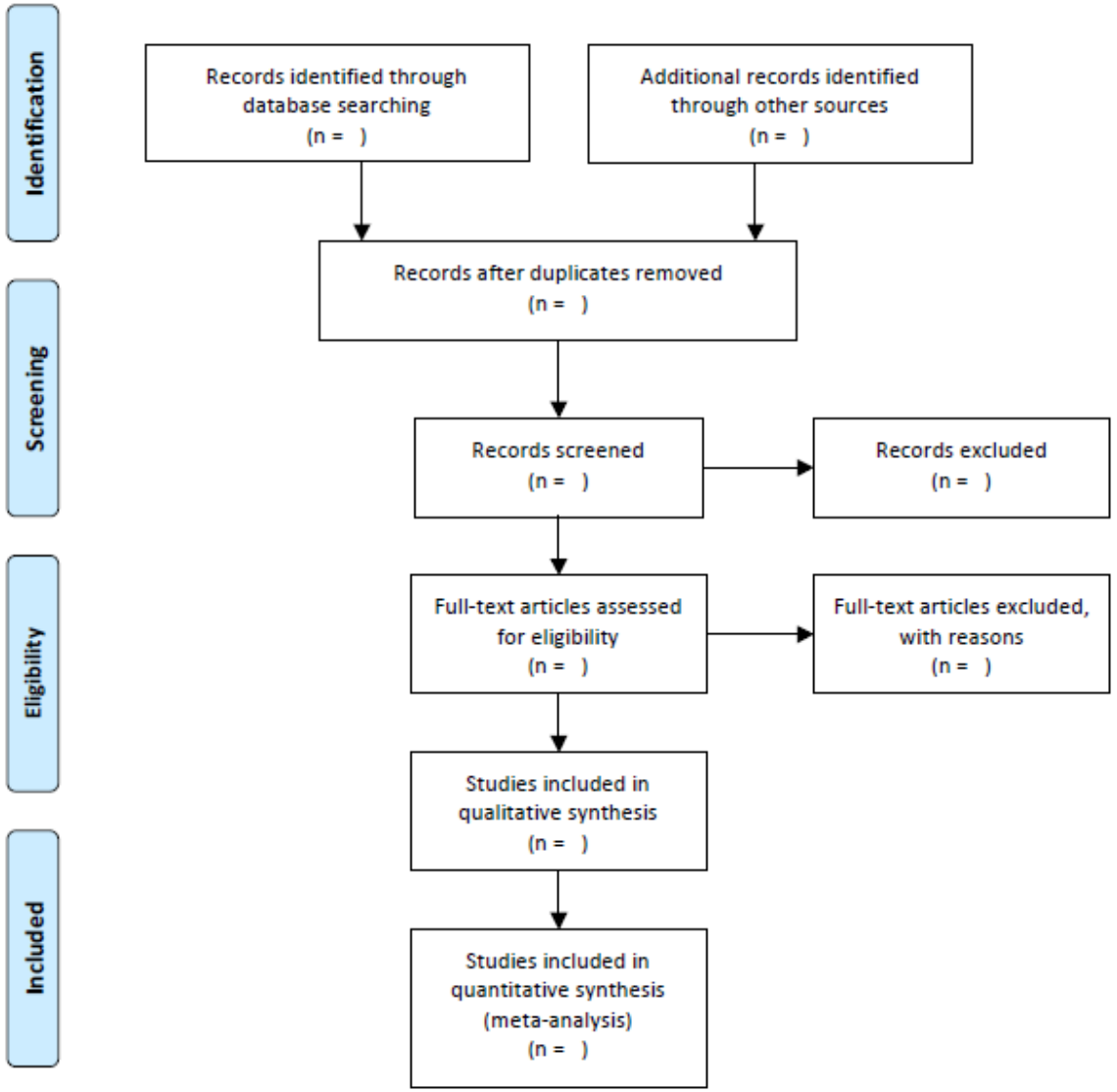
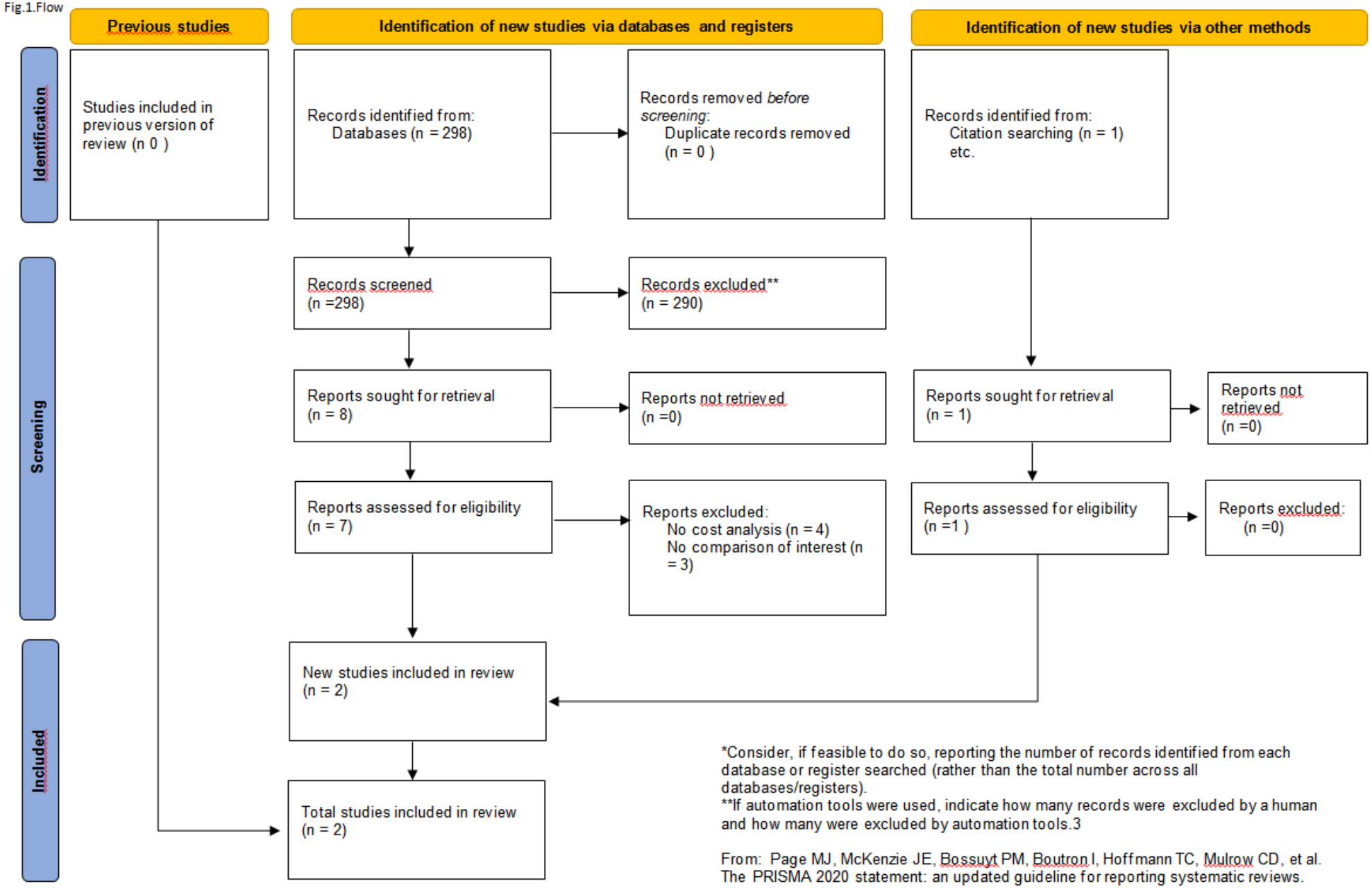


Fig.1.Flow



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.3

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-

9. Estrazione dei dati dai singoli studi

- A seconda del tipo di esito che si sta considerando (RR, OR, HR, medie, mediane, ecc.) bisogerà estrarre tutti gli elementi che servono per effettuare la meta-analisi

- Ad es. se esito dicotomico, sintetizzabile con RR, i dati da estrarre o ricalcolare sono n. eventi exp, N totale exp, n. eventi ctrl, N totale ctrl
- Ad es. se esito continuo: media e SD exp, media e SD ctrl

- **10. Fare le meta-analisi**

SACRO CUORE DON CALABRIA

ECI CANCER CENTRE

I R C C S

SCUOLA DI METODOLOGIA DELLA RICERCA CLINICA

2025 - 11ª EDIZIONE

MODULI SPECIALISTICI - S1

VENERDÌ 14 - SABATO 15 MARZO 2025

NEGRAR DI VALPOLICELLA (VR)

Centro Formazione IRCCS "Sacro Cuore - Don Calabria"

Valutazione del rischio di bias negli studi selezionati

Michela CINQUINI

VALIDITA' INTERNA

La misura in cui uno studio riesce a cogliere la relazione «**vera»** fra due variabili

ERRORE CASUALE

ERRORE SISTEMATICO (BIAS)

ERRORE CASUALE

Errore che si verifica per effetto del caso

Replicazioni multiple della stessa misurazione producono differenti risultati in tutte le direzioni per variazioni casuali ma la media dà il risultato corretto

ERRORE SISTEMATICO

Errore che si verifica per la presenza di un fattore che distorce sistematicamente le osservazioni nella stessa direzione

Es: mancanza di cecità e dati self report; pazienti diversi per fattori prognostici nei due gruppi a confronto

Replicazioni multiple della stessa misurazione producono risultati sempre nella stessa direzione e “sbagliati”

Bias

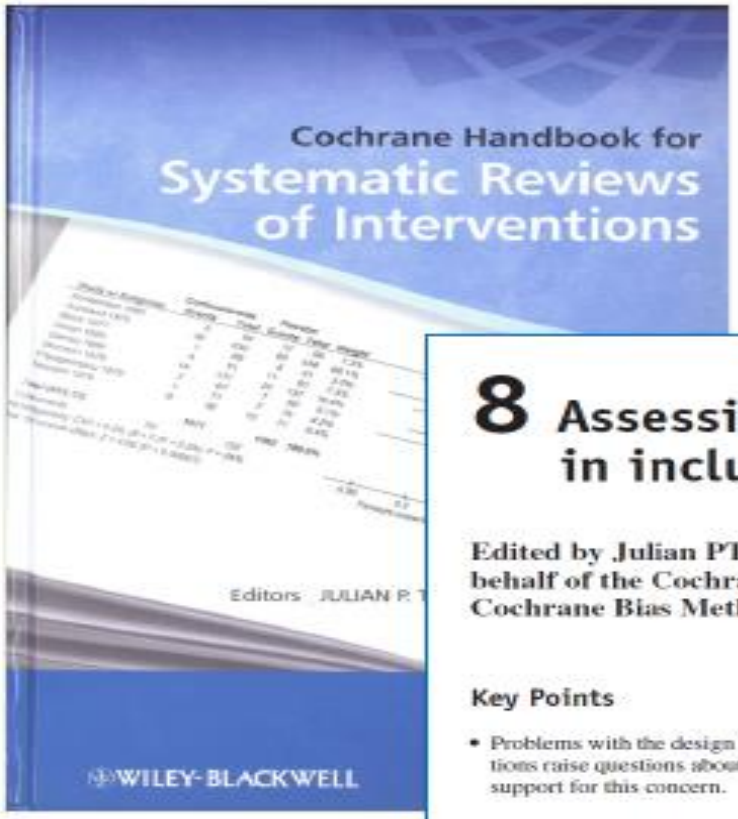
Systematic distortion of the estimated intervention effect away from the truth, caused by **inadequacies** in the **design**, **conduct**, or **analysis** of a trial , or in the **publication of its results**. In other words, in a biased trial, the results observed reflect other factors in addition to (or, in extreme cases, instead of) the effect of the tested therapeutic procedure alone.

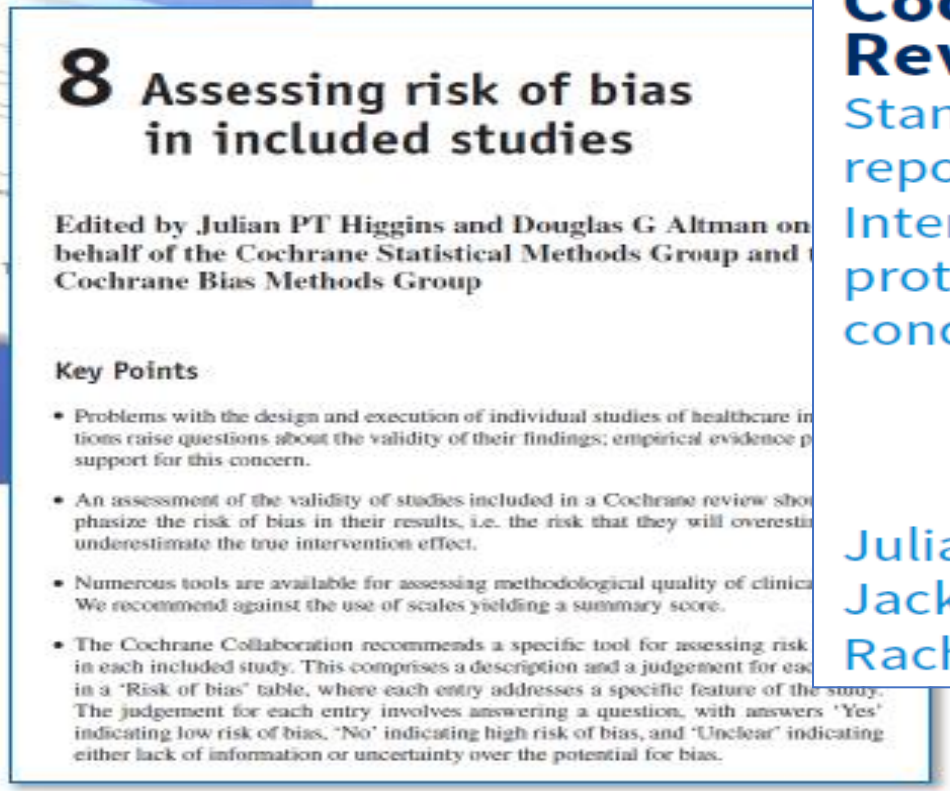
Altman DG, Schulz KF, Moher D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. Ann Intern Med 2001;134:663–94

Errore sistematico e validità interna di uno studio

- I risultati di uno studio sono tanto più validi (probabilmente veri) quanto meno esso è affetto da errori sistematici
- Gli errori sistematici vanno previsti ed evitati o ridotti in fase di disegno dello studio

Dove approfondire



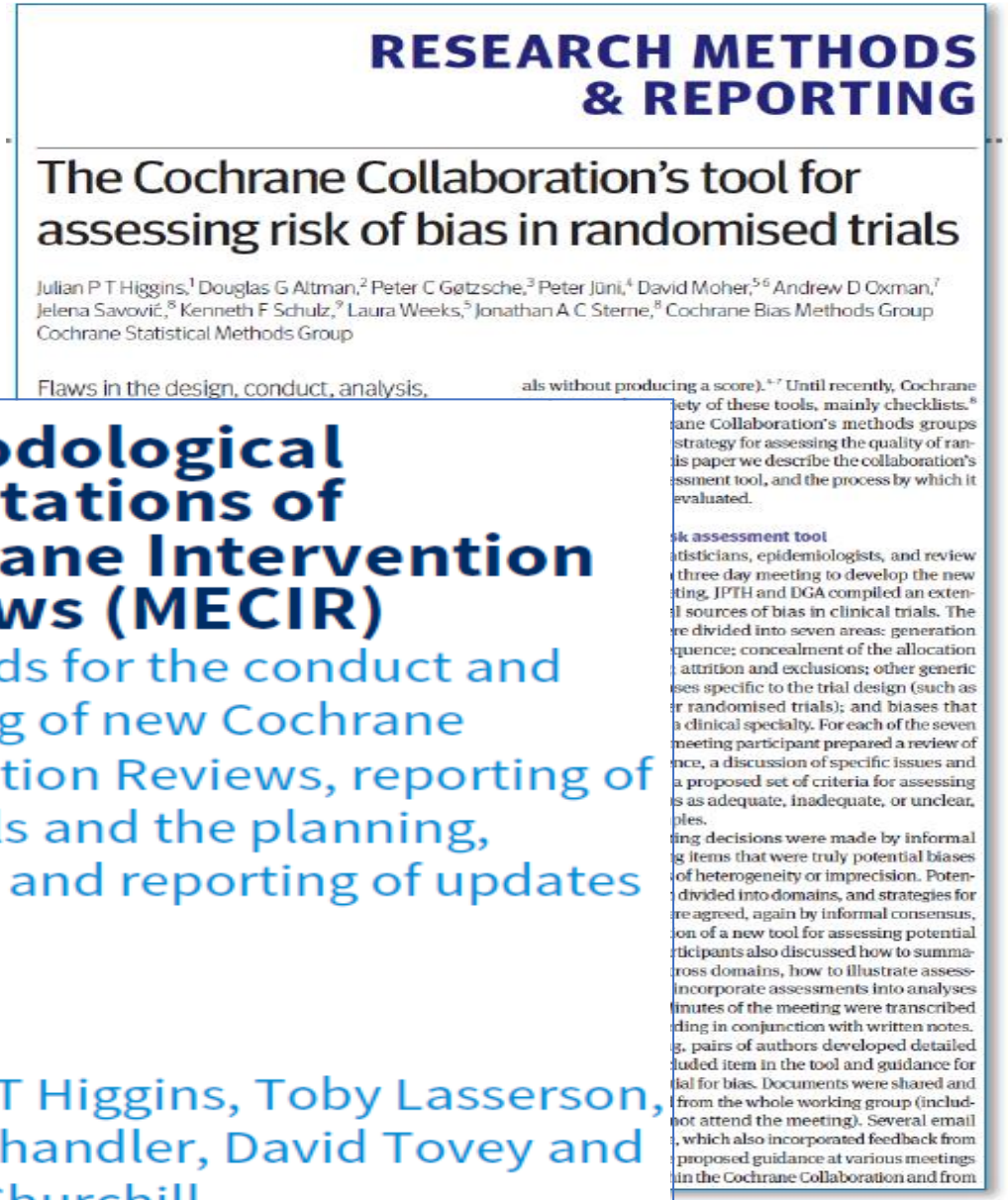


8 Assessing risk of bias in included studies

Edited by Julian PT Higgins and Douglas G Altman on behalf of the Cochrane Statistical Methods Group and the Cochrane Bias Methods Group

Key Points

- Problems with the design and execution of individual studies of healthcare interventions raise questions about the validity of their findings; empirical evidence provides support for this concern.
- An assessment of the validity of studies included in a Cochrane review should emphasize the risk of bias in their results, i.e. the risk that they will overestimate or underestimate the true intervention effect.
- Numerous tools are available for assessing methodological quality of clinical trials. We recommend against the use of scales yielding a summary score.
- The Cochrane Collaboration recommends a specific tool for assessing risk of bias in each included study. This comprises a description and a judgement for each entry in a 'Risk of bias' table, where each entry addresses a specific feature of the study. The judgement for each entry involves answering a question, with answers 'Yes' indicating low risk of bias, 'No' indicating high risk of bias, and 'Unclear' indicating either lack of information or uncertainty over the potential for bias.



RESEARCH METHODS & REPORTING

The Cochrane Collaboration's tool for assessing risk of bias in randomised trials

Julian P T Higgins,[1] Douglas G Altman,[2] Peter C Gøtzsche,[3] Peter Jüni,[4] David Moher,[5 6] Andrew D Oxman,[7] Jelena Savović,[8] Kenneth F Schulz,[9] Laura Weeks,[5] Jonathan A C Sterne,[8] Cochrane Bias Methods Group Cochrane Statistical Methods Group

Flaws in the design, conduct, analysis,

als without producing a score).[4-7] Until recently, Cochrane
ety of these tools, mainly checklists.[8]
ane Collaboration's methods groups
strategy for assessing the quality of ran-
is paper we describe the collaboration's
ssment tool, and the process by which it
evaluated.

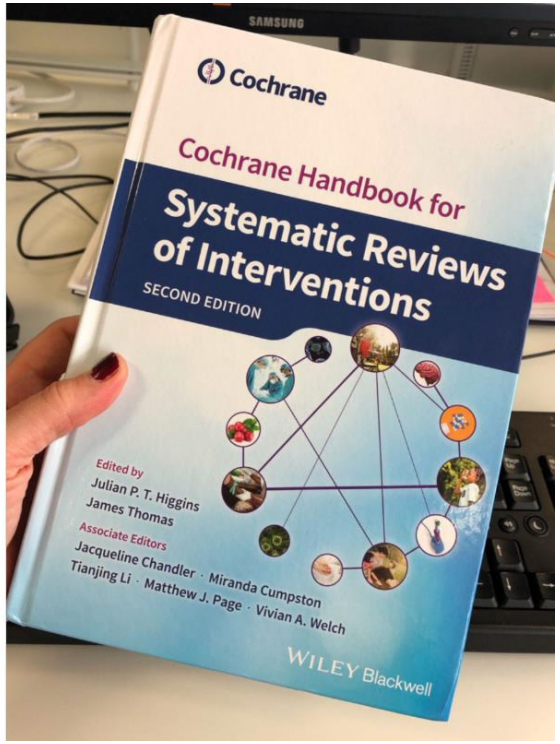
sk assessment tool
atisticians, epidemiologists, and review
three day meeting to develop the new
ting. JPTH and DGA compiled an exten-
l sources of bias in clinical trials. The
re divided into seven areas: generation
quence; concealment of the allocation
attrition and exclusions; other generic
ses specific to the trial design (such as
r randomised trials); and biases that
a clinical specialty. For each of the seven
meeting participant prepared a review of
nce, a discussion of specific issues and
a proposed set of criteria for assessing
s as adequate, inadequate, or unclear.
ples.
ing decisions were made by informal
g items that were truly potential biases
of heterogeneity or imprecision. Poten-
divided into domains, and strategies for
re agreed, again by informal consensus,
on of a new tool for assessing potential
rticipants also discussed how to summa-
ross domains, how to illustrate assess-
incorporate assessments into analyses
inutes of the meeting were transcribed
ding in conjunction with written notes.
g, pairs of authors developed detailed
luded item in the tool and guidance for
ial for bias. Documents were shared and
from the whole working group (includ-
ot attend the meeting). Several email
, which also incorporated feedback from
proposed guidance at various meetings
in the Cochrane Collaboration and from

Methodological Expectations of Cochrane Intervention Reviews (MECIR)

Standards for the conduct and reporting of new Cochrane Intervention Reviews, reporting of protocols and the planning, conduct and reporting of updates

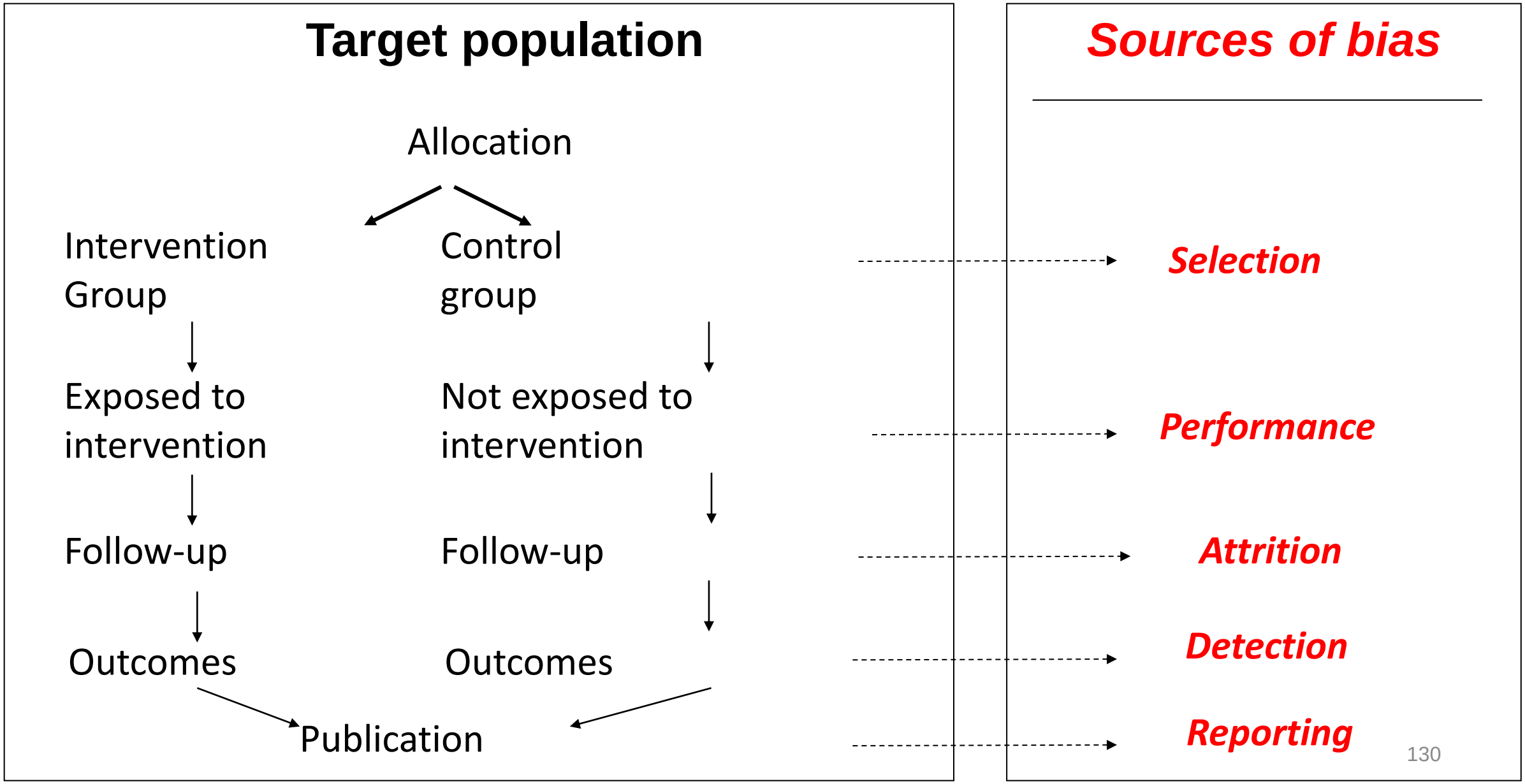
Julian PT Higgins, Toby Lasserson, Jackie Chandler, David Tovey and Rachel Churchill

New Cochrane Handbook for Systematic Reviews of Interventions



Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y / PY / PN / N / NI	[Description]
	1.2 Was the allocation sequence concealed until participants were recruited and assigned to interventions?	Y / PY / PN / N / NI	[Description]
	1.3 Were there baseline imbalances that suggest a problem with the randomization process?	Y / PY / PN / N / NI	[Description]
	Risk of bias judgement	Low / High / Some concerns	[Support]
	Optional: What is the predicted direction of bias arising from the randomization process?		[Rationale]
Bias due to deviations from intended interventions	2.1. Were participants aware of their assigned intervention during the trial?	Y / PY / PN / N / NI	[Description]
	2.2. Were carers and trial personnel aware of participants' assigned intervention during the trial?	Y / PY / PN / N / NI	[Description]
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice?	NA / Y / PY / PN / N / NI	[Description]
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention unbalanced between groups *and* likely to have affected the outcome?	NA / Y / PY / PN / N / NI	[Description]
	2.5 Were any participants analysed in a group different from the one to which they were assigned?	Y / PY / PN / N / NI	[Description]
	2.6 If Y/PY/NI to 2.5: Was there potential for a substantial impact (on the estimated effect of intervention) of analysing participants in the wrong group?	NA / Y / PY / PN / N / NI	[Description]
	Risk of bias judgement	Low / High / Some concerns	[Support]
	Optional: What is the predicted direction of bias due to deviations from intended interventions?		[Rationale]
Bias due to missing outcome data	3.1 Were outcome data available for all, or nearly all, participants randomized?	Y / PY / PN / N / NI	[Description]
	3.2 If N/PN/NI to 3.1: Are the proportions of missing outcome data and reasons for missing outcome data similar across intervention groups?	NA / Y / PY / PN / N / NI	[Description]
	3.3 If N/PN/NI to 3.1: Is there evidence that results were robust to the presence of missing outcome data?	NA / Y / PY / PN / N / NI	[Description]
	Risk of bias judgement	Low / High / Some concerns	[Support]
	Optional: What is the predicted direction of bias due to missing outcome data?		[Rationale]
Bias in measurement of the outcome	4.1 Were outcome assessors aware of the intervention received by study participants?	Y / PY / PN / N / NI	[Description]
	4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received?	NA / Y / PY / PN / N / NI	[Description]
	Risk of bias judgement	Low / High / Some concerns	[Support]
	Optional: What is the predicted direction of bias due to measurement of the outcome?		[Rationale]
Bias in selection of the reported result	Are the reported outcome data likely to have been selected, on the basis of the results, from...		
	5.1. ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	Y / PY / PN / N / NI	[Description]
	5.2 ... multiple analyses of the data?	Y / PY / PN / N / NI	[Description]
	Risk of bias judgement	Low / High / Some concerns	[Support]
	Optional: What is the predicted direction of bias due to selection of the reported result?		[Rationale]
Overall bias	**Risk of bias judgement**	Low / High / Some concerns	[Support]
	Optional: What is the overall predicted direction of bias for this outcome?		[Rationale]

Trial as a flow



randomizzazione

- attribuzione casuale di ogni paziente al gruppo in trattamento sperimentale oppure al gruppo di controllo
- Se è affettutata correttamente, ogni soggetto ha la stessa probabilità di essere assegnato al gruppo sperimentale o al gruppo di controllo
- assicura che tutti i fattori prognostici - **sia noti che sconosciuti** - si distribuiscano omogeneamente nel gruppo sperimentale e in quello di controllo.

Se la randomizzazione non è eseguita in maniera corretta è possibile introdurre un bias di selezione anche negli studi randomizzati

Selection bias: due componenti

Generazione lista di randomizzazione

- **Basso rischio di bias**. Uso di metodi realmente casuali come ad esempio: tavole di numeri random, sistemi computerizzati, lancio di una moneta o di un dado, sorteggio.
- **Alto rischio di bias.** Uso di metodi **NON** realmente casuali come ad esempio: giorno di nascita o di ammissione in ospedale, giudizio del medico, preferenze del paziente, risultati di test di laboratorio, disponibilità del trattamento, alternanza
- **Rischio incerto**. Quando non sono disponibili sufficienti informazioni per definire il rischio (bassa qualità del reporting)

Nascondimento della sequenza di randomizzazione*

- **Basso rischio di bias**. Sperimentatori che arruolano i pazienti non possono prevedere in quale gruppo verrà inserito il paziente perché si usa uno dei seguenti metodi: randomizzazione centralizzata (telefonica, via web, o gestita da personale esterno alla sperimentazione - farmacista, statistico); buste chiuse e opache.
- **Alto rischio di bias.** Sperimentatori che arruolano i pazienti possono prevedere in quale gruppo verrà inserito il paziente perché si usa uno dei seguenti metodi: liste di randomizzazione, buste aperte o non opache, alternanza, data di nascita, numero di cartella, ect.
- **Rischio incerto**. Non sono disponibili sufficienti informazioni per definire il rischio (bassa qualità del reporting)

*allocation concealment

Blinding

- Sperimentatori e partecipanti non conoscono gruppo di allocazione (*performance bias*)

- Valutatori degli esiti non conoscono gruppo di allocazione (*detection bias*)

Singolo cieco
i pazienti inclusi nello studio non conoscono il gruppo al quale sono stati assegnati

Doppio cieco
i pazienti e gli sperimentatori non conoscono il gruppo al quale (i pazienti) sono stati assegnati

Triplo cieco
i pazienti, gli sperimentatori e i valutatori degli esiti non conoscono il gruppo di allocazione

…

Non sempre il significato è questo … è sempre bene valutare chi è davvero in cieco!

Performance bias

Si verifica quando i partecipanti allo studio (sperimentatori o pazienti) modificano i loro comportamenti perché sanno a quale gruppo è assegnato un dato paziente

Esempi:

Lo sperimentatore controlla la presenza di effetti avversi più frequentemente nei pazienti assegnati al gruppo di trattamento.

Un paziente nel gruppo placebo assume altri farmaci, fa più (o meno) visite di controllo.

Detection bias

Si verifica quando la valutazione degli esiti dello studio viene influenzata dalla conoscenza del gruppo al quale è assegnato un dato paziente

Esempi:

Interpretazione di esiti radiologici, risoluzione dei sintomi, valutazione delle ricadute di malattia diversa nei pazienti assegnati al trattamento e al controllo

Performance&Detection bias

- Derivano da comportamenti consci o non consci
- Sovrastimano/sottostimano l'effetto dell'intervento
- La distorsione potenziale è tanto maggiore quanto più soggettivo è l'esito misurato
- Si limitano se pazienti, sperimentatori, valutatori degli esiti dello studio non sono a conoscenza del trattamento che il paziente sta effettivamente ricevendo

Performance bias

Cecità di pazienti e sperimentatori

- **Basso rischio di bias.** Pazienti e sperimentatori non conoscono l'assegnazione dei pazienti al gruppo di controllo o di trattamento oppure è poco probabile che la mancanza di cecità influenzi la performance di pazienti e sperimentatori
- **Alto rischio di bias.** Pazienti e sperimentatori conoscono l'assegnazione dei pazienti o, durante lo studio, diventa chiaro a quale gruppo di trattamento sono allocati (rottura del cieco). Studi definiti come "open label"
- **Rischio incerto**. Quando non sono disponibili sufficienti informazioni per definire il rischio (bassa qualità del reporting)

Conduzione dello studio in cieco

Trattamento sperimentale = controllo (ad esempio, capsule identiche nell'aspetto, forma, colore, sapore).

Non sempre si può fare (ad esempio confronto tra farmaci con profili di tossicità specifici, interventi fisioterapici, educativi, chirurgici, ecc).

Non basta pianificarlo. E' importante garantire che, durante lo studio, sperimentatori e pazienti non "scoprano" il gruppo di allocazione (ad esempio perché un trattamento ha effetti collaterali particolari).

Detection bias

Cecità del valutatore degli esiti dello studio (outcome)

- **Basso rischio di bias.** L'esito dello studio è valutato senza conoscere l'assegnazione dei pazienti al gruppo di controllo o di intervento; oppure è poco probabile che la mancanza di cecità influenzi la valutazione
- **Alto rischio di bias.** L'esito dello studio è valutato conoscendo l'assegnazione dei pazienti al gruppo di controllo o di intervento ed è probabile che la mancanza di cecità influenzi la valutazione
- **Rischio incerto**. Quando non sono disponibili sufficienti informazioni per definire il rischio (bassa qualità del reporting)

Valutazione esiti in cieco

- Gli esiti di uno studio possono essere valutati dai pazienti stessi (diari, questionari), dagli sperimentatori, oppure da valutatori indipendenti
- Visite di follow up effettuate da uno sperimentatore diverso
- Non sempre si può fare (ad esempio esiti riferiti dal paziente in uno studio in aperto)
- Tanto più l'esito è soggettivo (dolore, qualità della vita, ecc.) tanto più il rischio di detection bias è alto se la valutazione non avviene in cieco.
- Anche esiti apparentemente oggettivi, non sempre lo sono (imaging, morte/causa)

Performance and detection bias

- Impatto diverso su outcome **soggettivi** e **oggettivi** (quindi la valutazione va fatta separatamente)
- Se studio su **farmaco in doppio cieco** e dice che tutti gli operatori erano all'oscuro dell'assegnazione è probabile che sia in cieco anche l'outcome assessor, anche se non espressamente detto
- Se studio su **interventi che non possono essere in doppio cieco** (psicosociali, educativi, chirurgici, riabilitativi) importante che sia in cieco l'outcome assessor e deve essere specificato
  - Performance: high risk per outcomes soggettivi sempre
  - Detection: low risk se c'è blinding of outcome assessor anche per outcomes soggettivi

Allocation concealment

- It prevents **selection bias** in intervention assignment by protecting the allocation sequence **before and until** assignment
- It can always be successfully implemented regardless of the study topic

≠

Blinding

- It seeks to prevent **performance and detection bias** by protecting the sequence **after** assignment
- Not always feasible – for example, in trials comparing surgical with medical interventions

Attrition bias

- Quando non tutti i soggetti randomizzati completano lo studio
- i soggetti non escono a caso dallo studio: è possibile che quelli che escono siano sistematicamente diversi da quelli che non escono: i gruppi non sono più randomizzati
- **Validità esterna** : es: escono tutti i più giovani, o i meno gravi, o i maschi: posso trarre conclusioni solo su quelli che rimangono
- **Validità interna (Bias):** se la probabilità di uscire dallo studio è legata all'intervento o all'outcome, cioè se quelli che escono hanno sistematicamente probabilità più alte o più basse di avere l'outcome di quelli che restano

Attrition bias

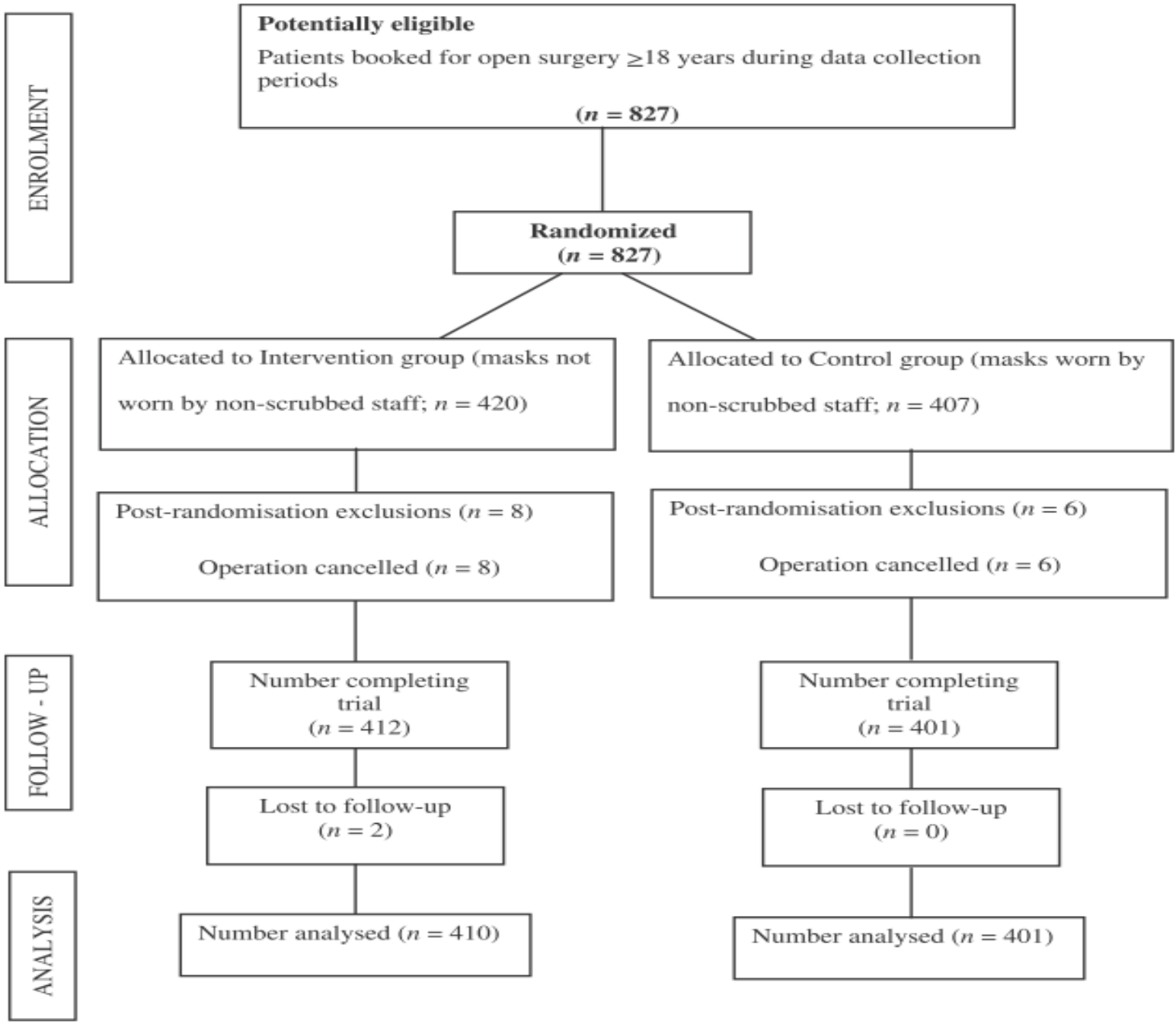
Low risk of bias

- No missing outcome data;
- the proportion of missing outcomes compared with observed event risk not enough to have a relevant impact on the intervention effect;
- Missing outcome data balanced in numbers across intervention groups, with similar reasons across groups;
- Missing data imputed using appropriate methods
- All patients analysed in the group they were allocated to by randomisation irrespective of non-compliance and co-interventions (intention to treat)

High risk of bias:

- the proportion of missing outcomes compared with observed event risk enough to induce relevant bias in intervention effect estimate
- Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups;

A tota
enrolled and 811 (98.1%) patients complete
group and 410 No Mask group (Fig. 1).



What is publication bias (1)?

- Definition

"Publication bias refers to the greater likelihood that studies with positive results will be published"

JAMA 2002;287:2825-2828

What is publication bias (2)?

- An alternative definition:

Publication bias is the selective or *multiple* publication *or suppression* of trial results so that the scientific record is distorted

Extension: applied to trial parts - outcomes, subgroups, adverse events
REPORTING BIAS

The likelihood of finding studies is related to the results of those studies (positive vs negative/detrimental)

Why does it matter?

- Distorts the scientific record
- Hides the “truth”
- Influences doctors’ decision making
- Misleads policy makers
- Causes harm to patients
- Costly for the health service
- A form of scientific and research misconduct

- TO U: It will matter if the studies you don’t find differ systematically from the ones you have found
- You might arrive at different answers, or even THE WRONG ANSWER

Reporting bias is selection bias

- Reporting bias is perhaps the greatest source of selection bias
- Originally defined as the publication or non-publication of studies depending on the direction and statistical significance of the results
- Is a complex phenomenon

Full — n and effect size, plus precision / *p*-value for continuous data

Partial — Effect size or precision (± n or *p*-value)

Qualitative — *p*-value

Unreported

Incompletely reported outcomes

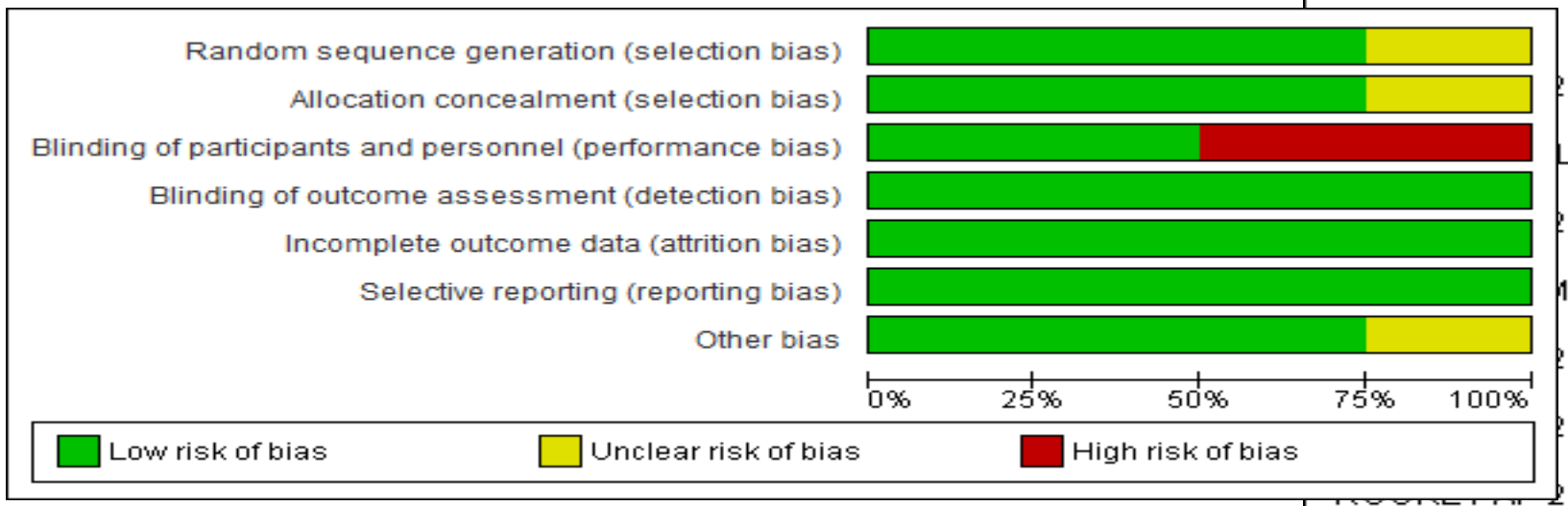
(Chan, 2004)

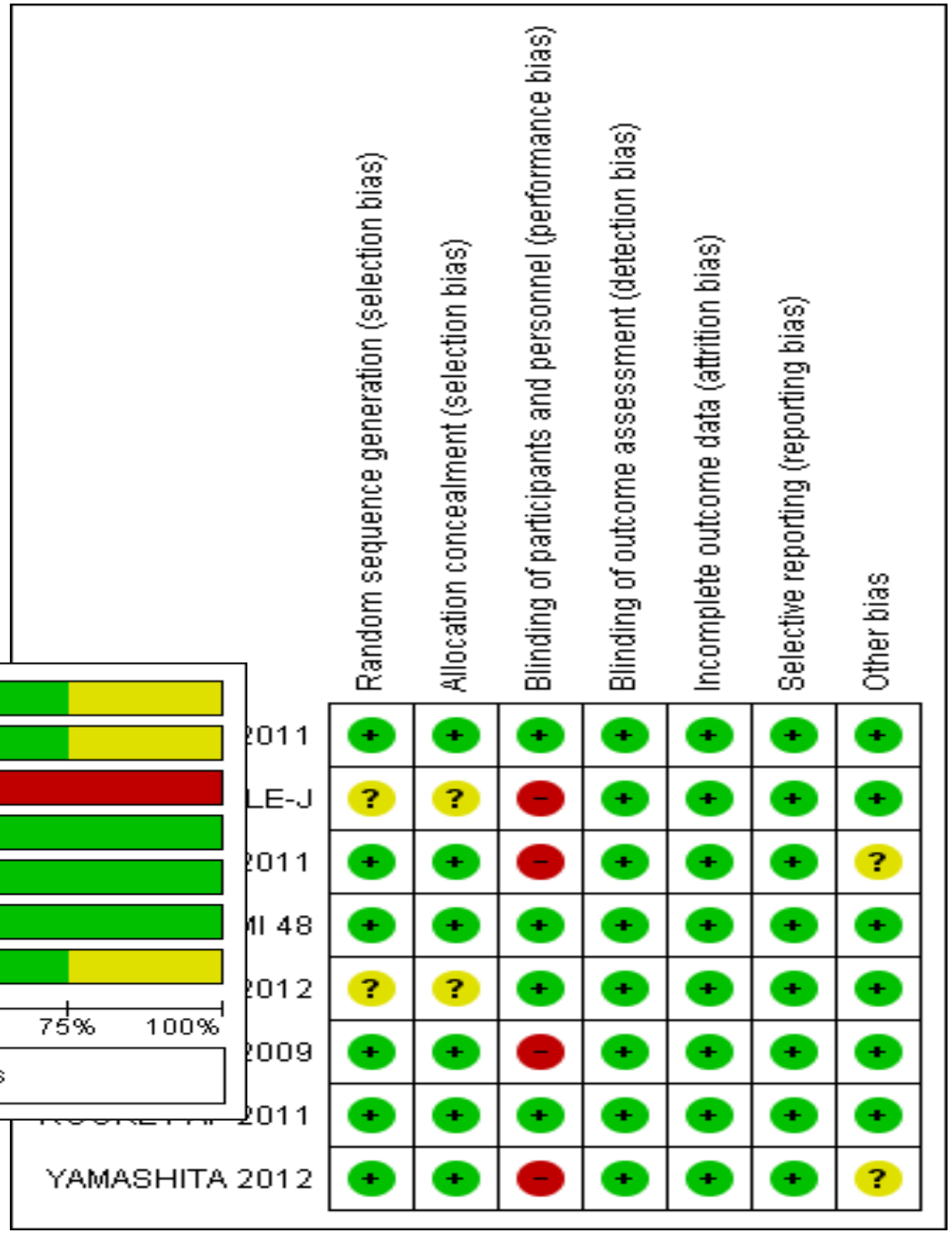
Risk of bias in one study

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	NR
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias)	High risk	open label
Blinding of outcome assessment (detection bias)	Low risk	An independent blinded endpoint committee adjudicated all reported bleeding and efficacy events
Incomplete outcome data (attrition bias)	Low risk	ITT. all patients followed up
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	

Risk of bias across studies/domains





SACRO CUORE DON CALABRIA

ECI CANCER CENTRE

I R C C S

SCUOLA DI METODOLOGIA DELLA RICERCA CLINICA

2025 - 11ª EDIZIONE

MODULI SPECIALISTICI - S1

VENERDÌ 14 - SABATO 15 MARZO 2025

NEGRAR DI VALPOLICELLA (VR)

Centro Formazione IRCCS "Sacro Cuore - Don Calabria"

Metanalisi: eterogeneità e analisi di sottogruppo

Michela CINQUINI

Principi di una meta-analisi

Una **meta-analisi** può:

•Combinare i risultati dei singoli studi per ottenere una stima complessiva dell'effetto del trattamento;

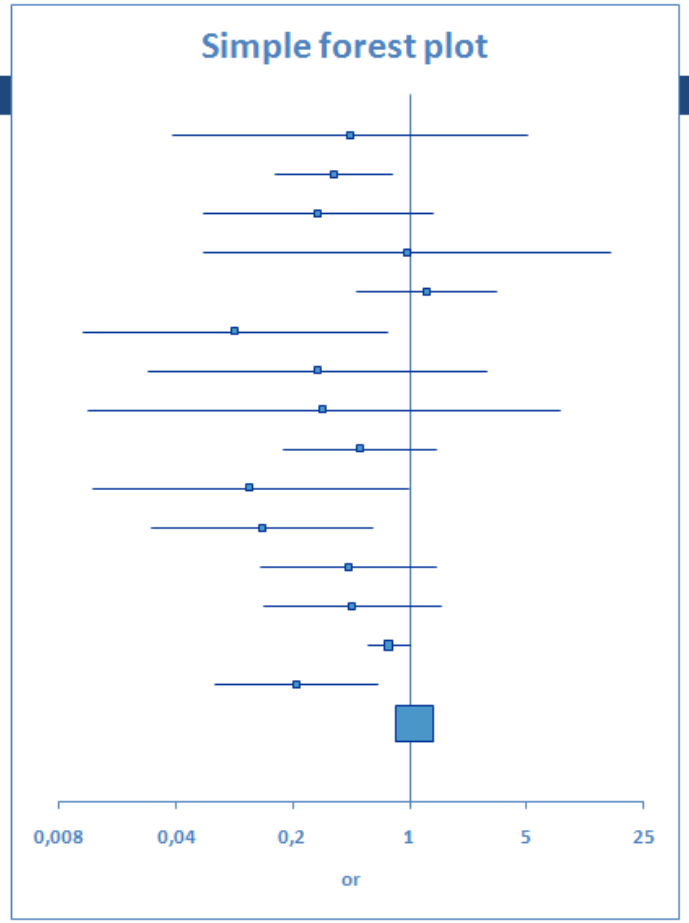
•Esplorare l'eterogeneità tra gli studi (e le relative fonti di eterogeneità).

E' efficace?

Author(s)		Reference					
Teo et al.		Effects of intravenous magnesium in suspected acute myocardial infarction. BMJ 1991;303:1499–501					
Outcome object	Unit	Intervention (e)		Control (c)			
Mortality	Event	Intravenous magnesium		Control			
Study ID	Ref #	n[e]	n[e](E=1)	n[c]	n[c](E=1)	Study date	-
Morton	1	40	1	36	2	1984	
Rasmussen	2	135	9	135	23	1986	
Smith	3	200	2	200	7	1986	
Abraham	4	48	1	46	1	1987	
Feldstedt	5	150	10	148	8	1988	
Schechter	6	59	1	56	9	1989	
Ceremuzynski	7	25	1	23	3	1989	
Bertschat	8	22	0	21	1	1989	
Singh	9	76	6	75	11	1990	
Pereira	10	27	1	27	7	1990	
Schechter 1	11	89	2	80	12	1991	
Golf	12	23	5	33	13	1991	
Thogersen	13	130	4	122	8	1991	
LIMIT-2	14	1159	90	1157	118	1992	
Schechter 2	15	107	4	108	17	1995	
ISIS-4	16	29011	2216	29039	2103	1995	

Forest plot (meta-graph) analitico

author	year	n[I]	N[I]	n[C]	N[C]	Weight	or	ci-	ci+	p
Morton	1984	1	40	2	36	0,06%	0,44	0,04	5,02	0,51
Rasmussen	1986	9	135	23	135	0,54%	0,35	0,15	0,78	0,01
Smith	1986	2	200	7	200	0,14%	0,28	0,06	1,36	0,11
Abraham	1987	1	48	1	46	0,05%	0,96	0,06	15,77	0,98
Feldstedt	1988	10	150	8	148	0,39%	1,25	0,48	3,26	0,65
Schechter	1989	1	59	9	56	0,08%	0,09	0,01	0,74	0,02
Ceremuzynsk	1989	1	25	3	23	0,07%	0,28	0,03	2,88	0,28
Bertschat	1989	0	22	1	21	0,03%	0,30	0,01	7,88	0,47
Singh	1990	6	76	11	75	0,32%	0,50	0,17	1,43	0,19
Pereira	1990	1	27	7	27	0,08%	0,11	0,01	0,97	0,05
Schechter 1	1991	2	89	12	80	0,15%	0,13	0,03	0,60	0,01
Golf	1991	5	23	13	33	0,24%	0,43	0,13	1,44	0,17
Thogersen	1991	4	130	8	122	0,24%	0,45	0,13	1,54	0,21
LIMIT-2	1992	90	1159	118	1157	4,33%	0,74	0,56	0,99	0,04
Schechter 2	1995	4	107	17	108	0,28%	0,21	0,07	0,64	0,01
ISIS-4	1995	2216	29011	2103	29039	92,99%	1,06	1,00	1,13	0,07



META-ANALYSIS

General

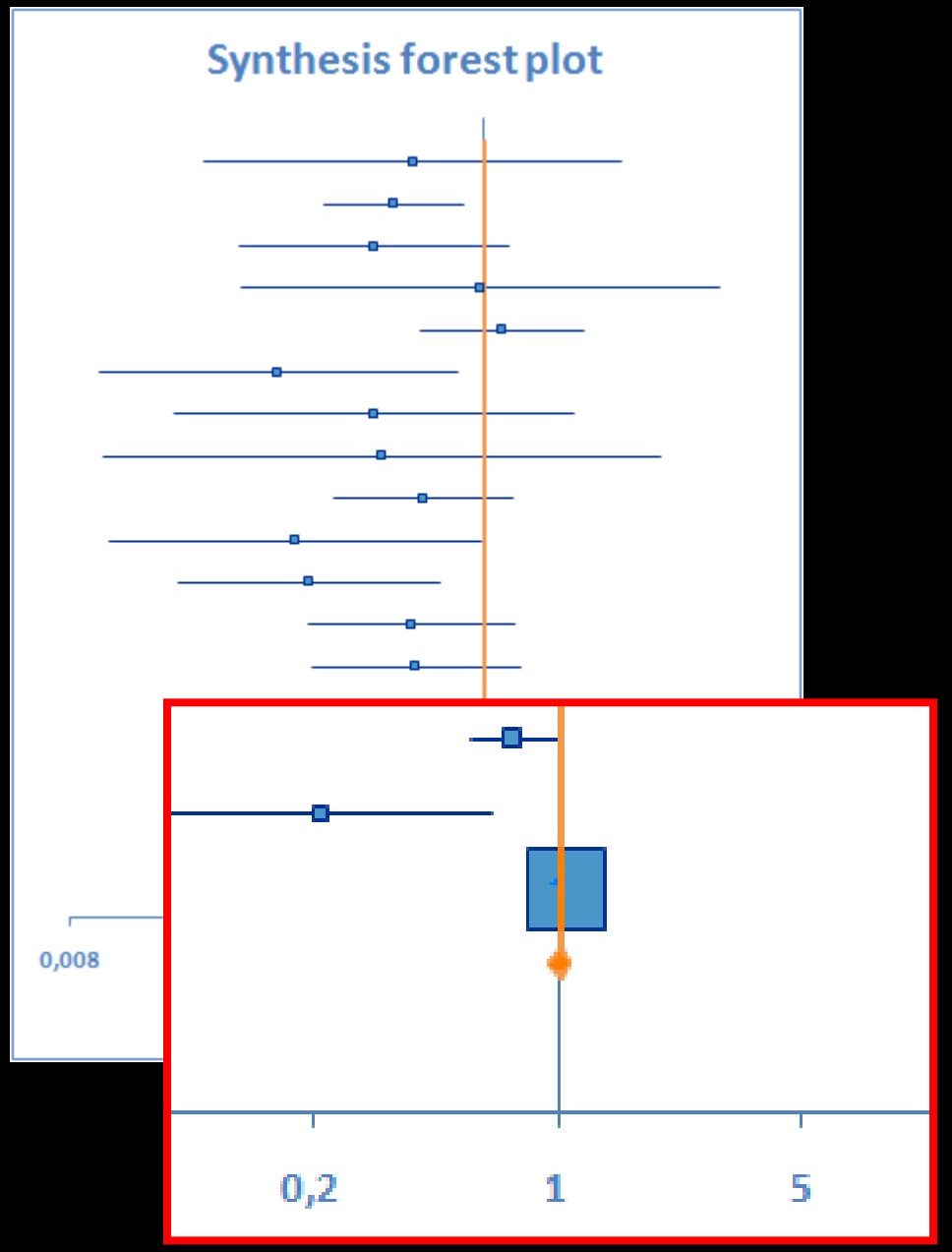
Number of studies	16
Number of participants	62607 (62607)

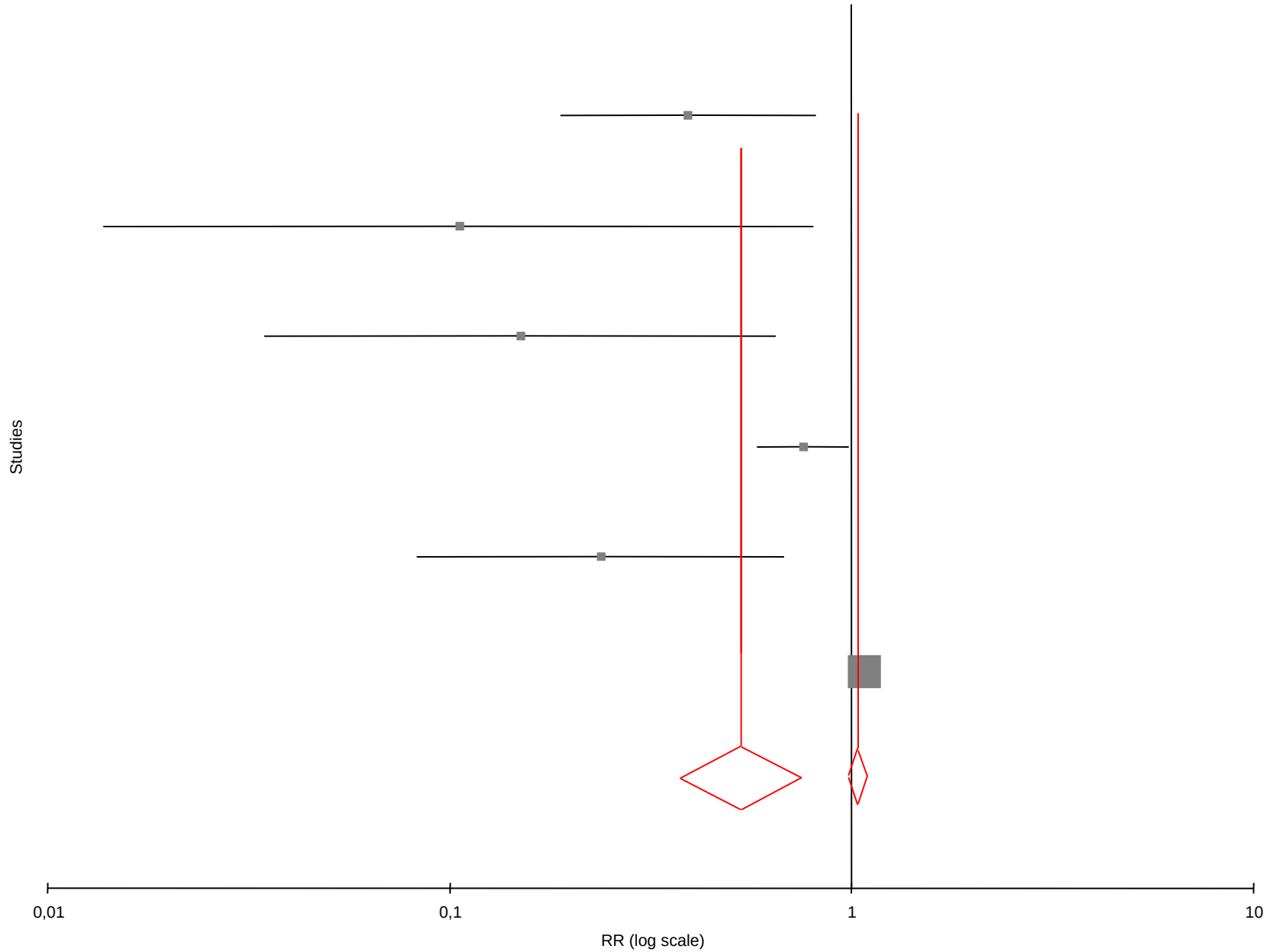
OR (MH) - Fixed effect model

Meta-analysis outcome	1,0063
95% CI lower limit	0,9482
95% CI upper limit	1,068
z	0,2073
p-value (two-tailed)	0,8358

Heterogeneity

Q	47,1363
p-value (two-tailed)	< 0,0001
I^2	68,18%
95% CI lower limit	46,53%
95% CI upper limit	81,06%




Studies
0,01
0,1
1
10
RR (log scale)

Come si decide quanto pesa uno studio?

- Il peso è proporzionale al contributo informativo dello studio alla capacità di effettuare una stima
- Studi di ampie dimensione e/o con molti eventi potrebbero contribuire di più
- In gergo sono quelli più precisi

- Ma tutto è relativo … tutti gli studi stanno misurando lo stesso effetto?

What is heterogeneity?

- Heterogeneity is variation between the studies' results

What is heterogeneity?

Differences between studies with respect to:

Clinical heterogeneity (clinical diversity)

- *Participants*
  - e.g. conditions under investigation, eligibility criteria for trials, geographical variation
- *Interventions*
  - e.g. intensity / dose / duration, sub-type of drug, mode of administration, experience of practitioners, nature of the control (placebo/none/standard care)
- *Outcomes*
  - e.g. definition of an event, follow-up duration, ways of measuring outcomes, cut-off points on scales

What is heterogeneity?

Differences between studies with respect to:

Methodological heterogeneity (methodological diversity)

- *Design*
  - e.g. randomised vs non-randomised, crossover vs parallel group vs cluster randomised, pre-test and long follow up
- *Conduct*
  - e.g. allocation concealment, blinding etc, approach to analysis, imputation methods for missing data

What is heterogeneity?

What do we do if there ***is*** statistical heterogeneity?

- Variation in the *true effects* underlying the studies
- ...which may manifest itself in more observed variation than expected by chance alone

- May be due to clinical diversity (different treatment effects) or methodological diversity (different biases)

Come si misura questa eterogeneità?


KEEP
CALM
e fà
BALA'
L'OEUCC!

- Confidence interval overlapping Eyeball test

- Cochran's Q: to assess whether observed differences in results are compatible with change alone

χ^2 distribution; low power (small number of studies, small sample size)

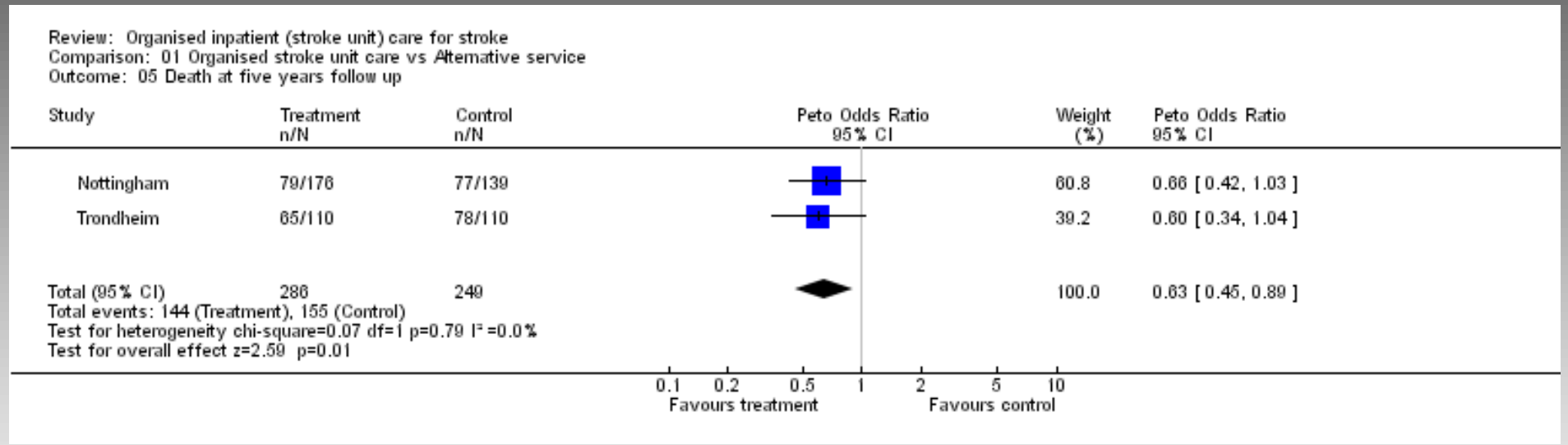
p=<0.10 (heterogeneity)

- I^2 quantifing heterogeneity (describes the percentage of variation across studies that is due to heterogeneity rather than chance)

0-40% might not be important
30-60% may represent moderate heterogeneity
50-90% may represent substantial heterogeneity
75-100% considerable heterogeneity

- Tau….

Esempio di Metaview



How to deal with heterogeneity

1. Do not pool at all
2. Ignore heterogeneity: use ***fixed effect model***
3. Allow for heterogeneity: use ***random effects model***
4. Explore heterogeneity: subgroups analysis or meta-regression (tricky)

Fixed and random effects

Fixed effect

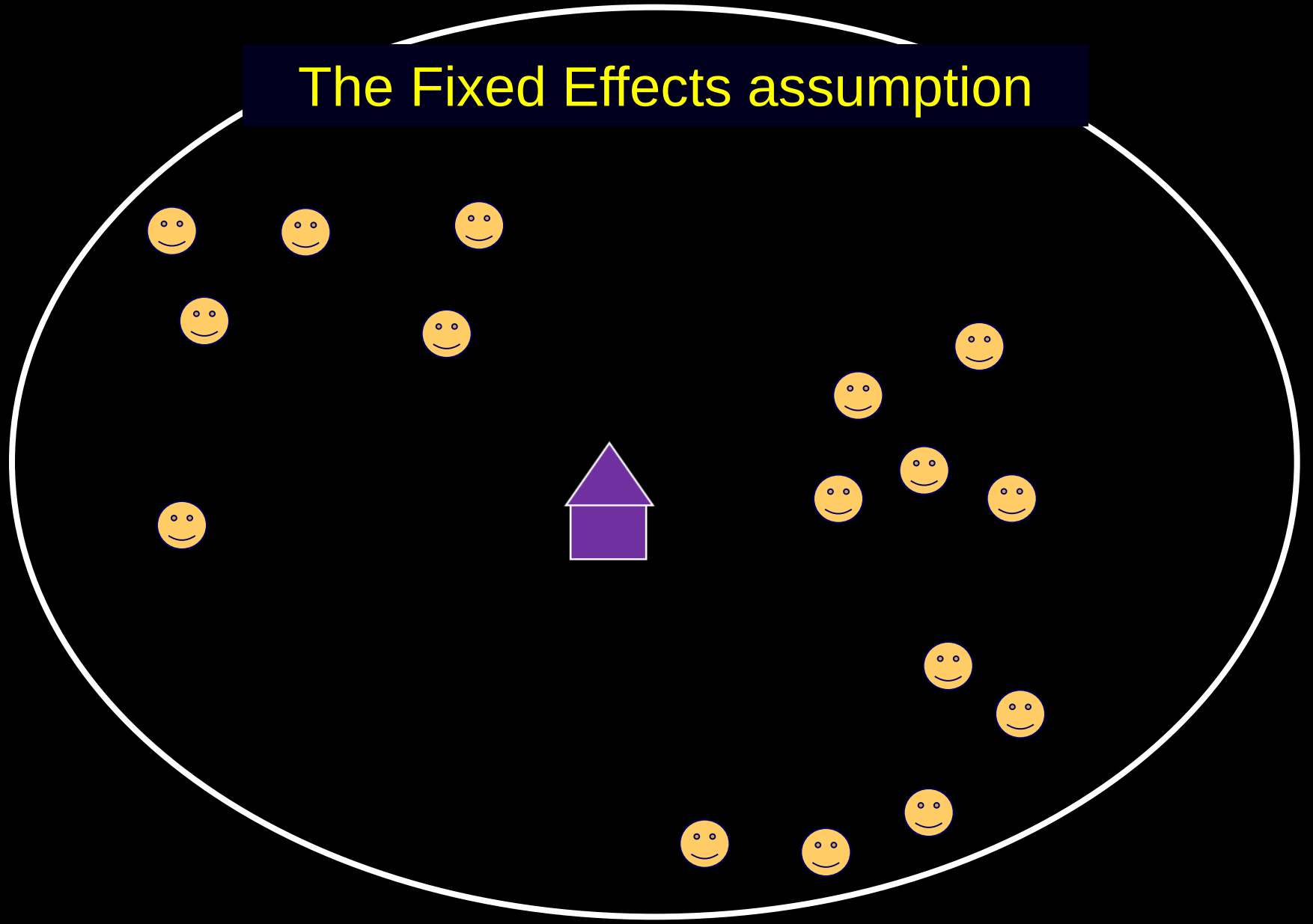
Philosophy behind ***fixed effect model***

- there is one real value for the treatment effect
- all trials estimate this one value

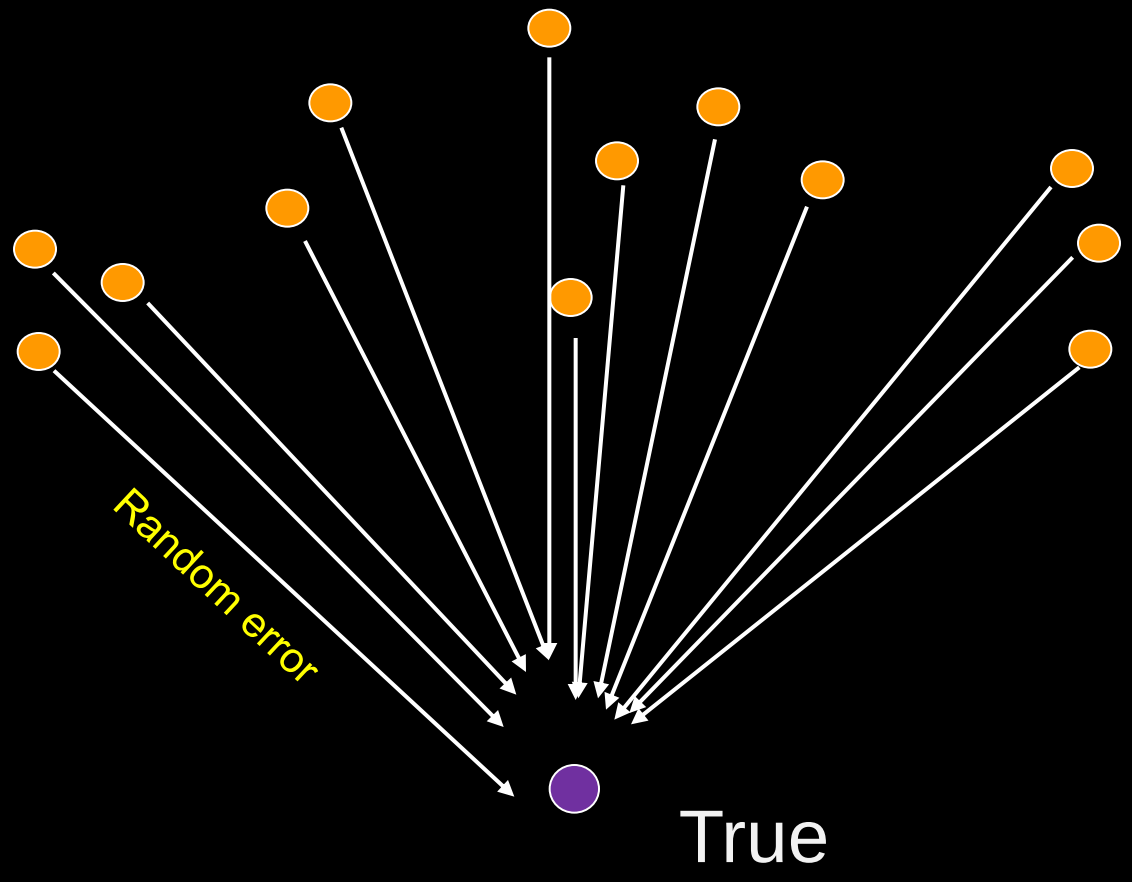
Problems with ignoring heterogeneity:

- confidence intervals too narrow

The Fixed Effects assumption



The Fixed Effects assumption

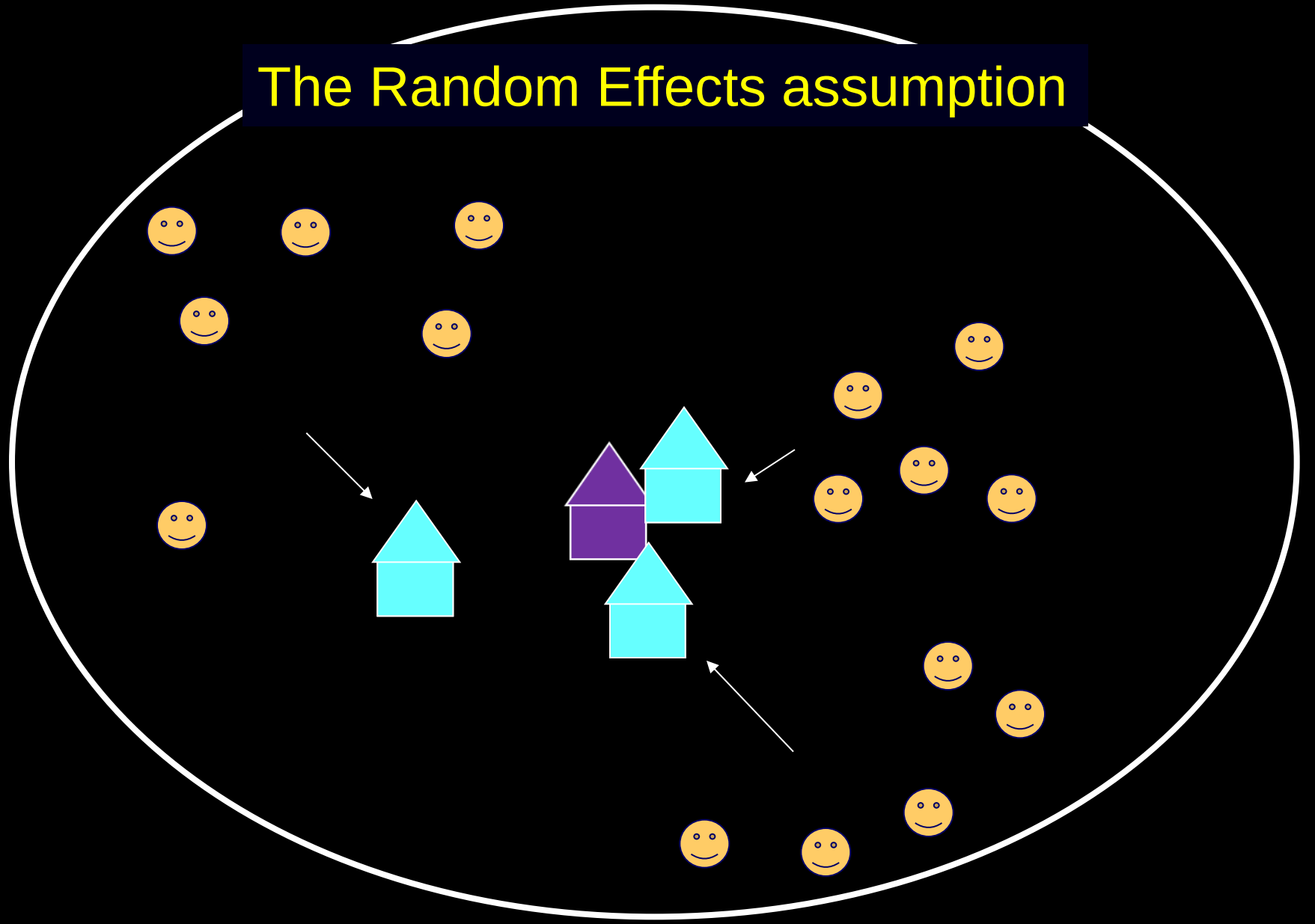


Random effects

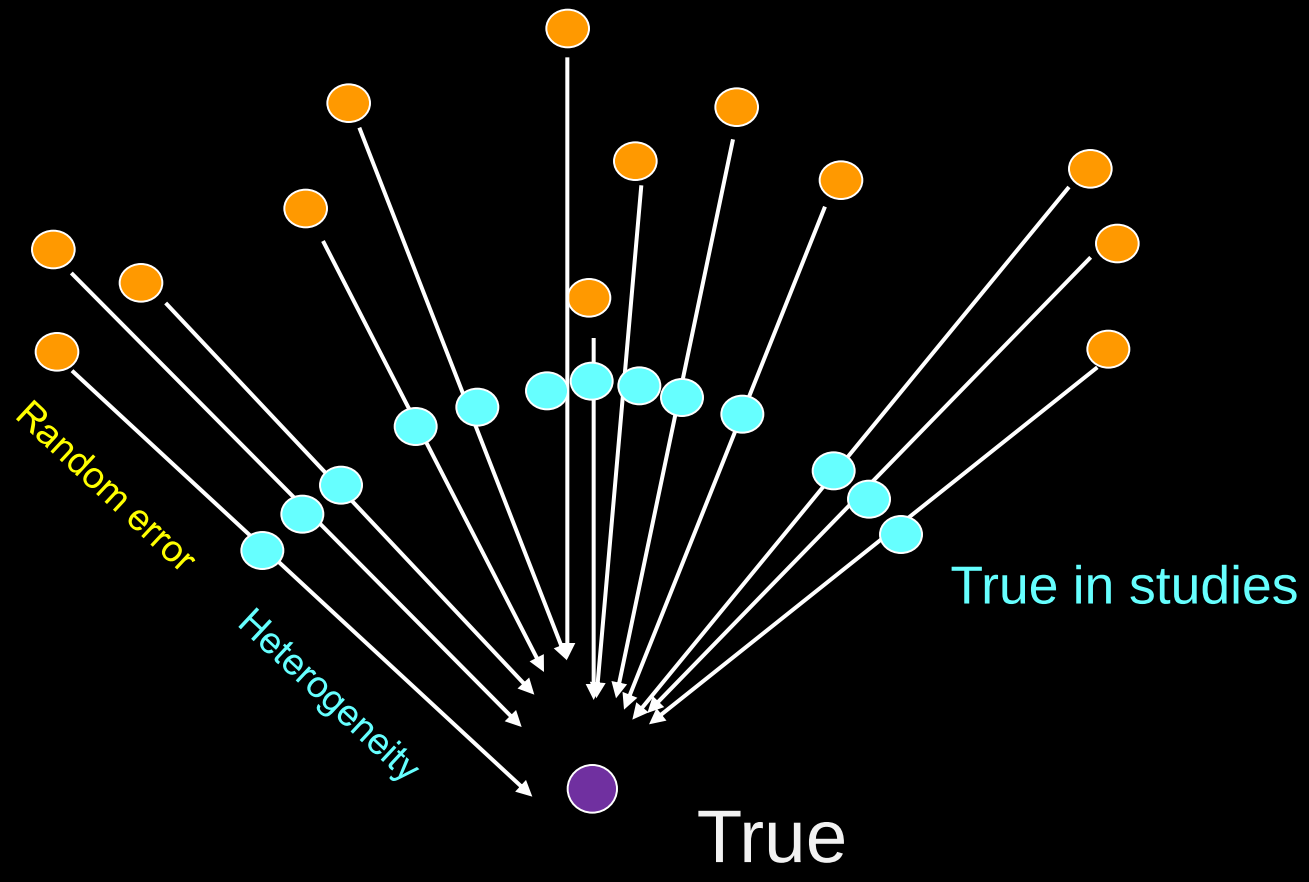
Philosophy behind ***random effects model***

- there are many possible real values for the treatment effect (depending on dose, duration, etc etc).
- each trial estimates its own real value

The Random Effects assumption

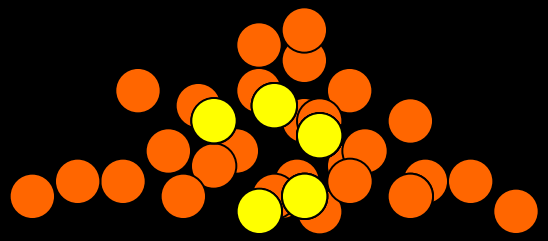


The Random Effects assumption

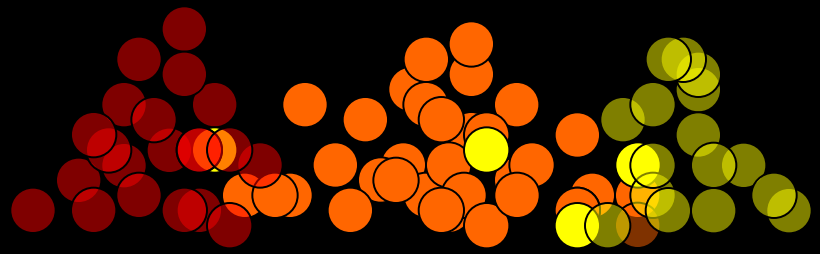


Quale modello?

Fixed effect



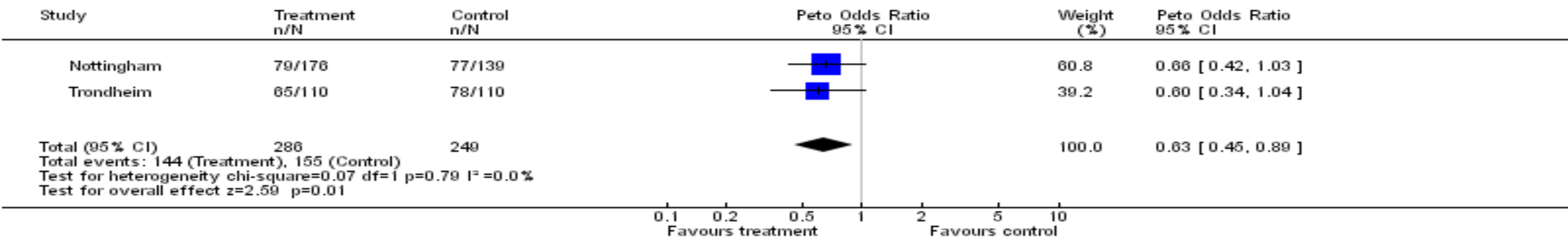
Random effect



Un diamante è «per sempre» ma dipende ma molti aspetti

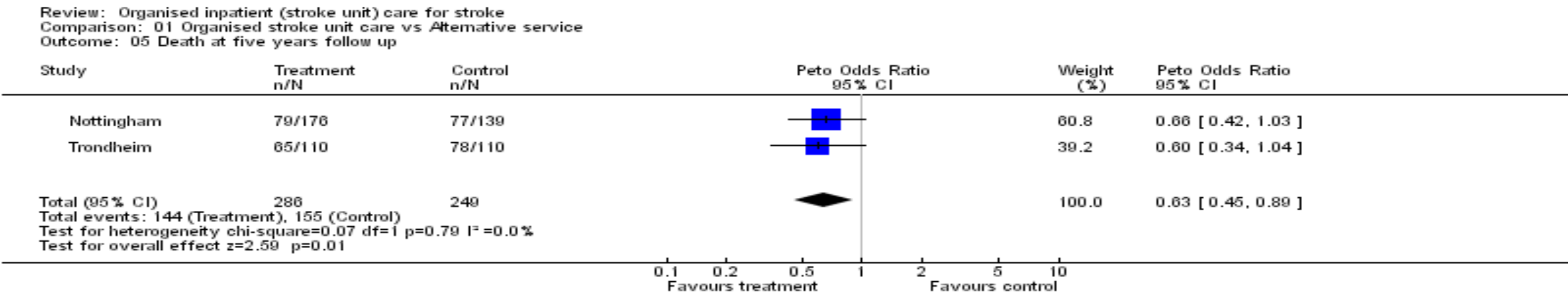
- *P.I.C.O.*
- *Disegno di studio*
- *Esito considerato*
- *Misura di effetto (RR,OR, HR, MD, SMD)*
- *Peso degli studi inclusi (modello effetti fissi o random)*
- *Eterogeneità e sue fonti (sottogruppi)*
- *Bias*

Review: Organised inpatient (stroke unit) care for stroke
Comparison: 01 Organised stroke unit care vs Alternative service
Outcome: 05 Death at five years follow up



Miti da sfatare (1)

Se combino studi con risultati non statisticamente significativi, il risultato della meta-analisi sarà non significativo



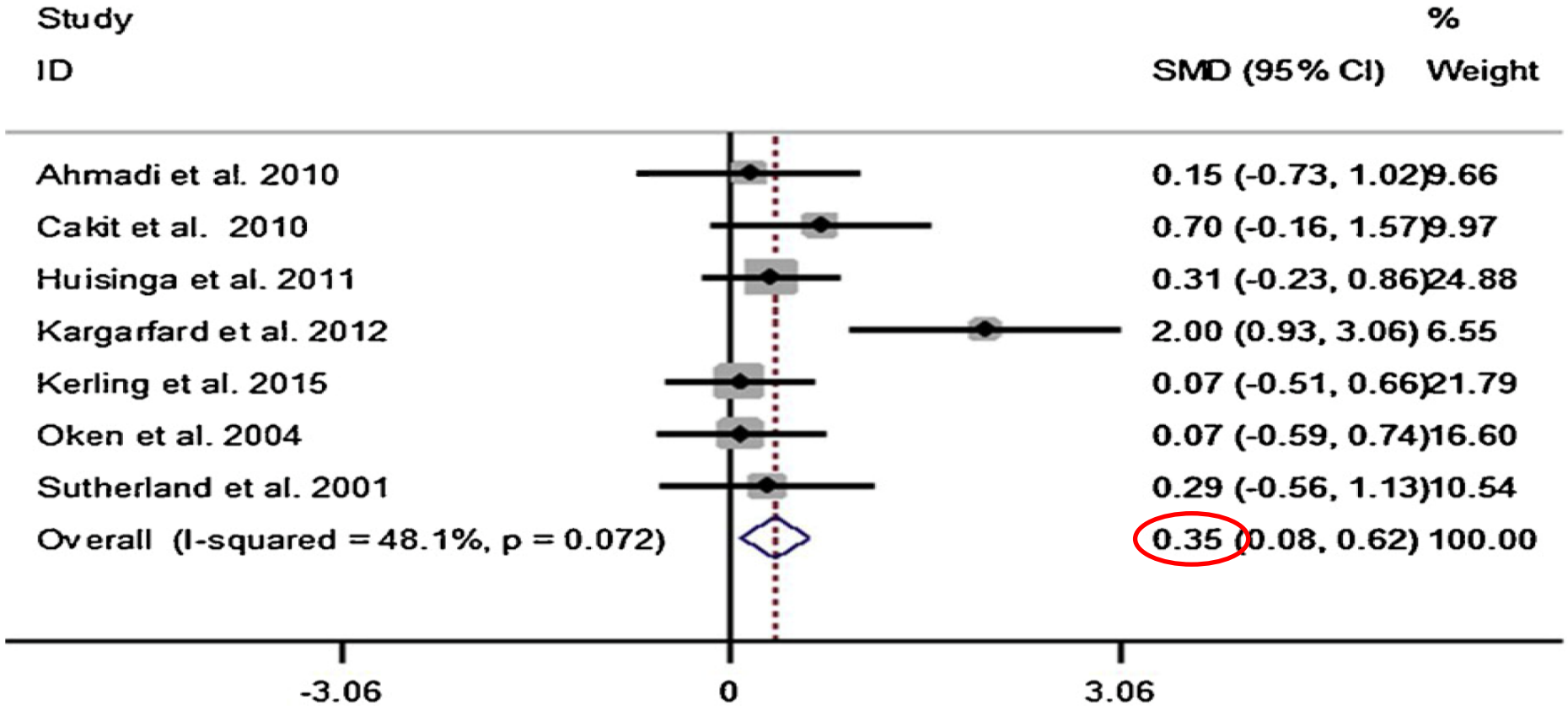
Miti da sfatare (2)

Se il risultato della meta-analisi è statisticamente significativo, allora il risultato è clinicamente rilevante

The effect of exercise, yoga and physiotherapy on the quality of life of people with multiple sclerosis: Systematic review and meta-analysis

Khrisha B. Alphonsus[a,*], Yingying Su[a], Carl D'Arcy[a,b]

Complementary Therapies in Medicine 43 (2019) 188–195

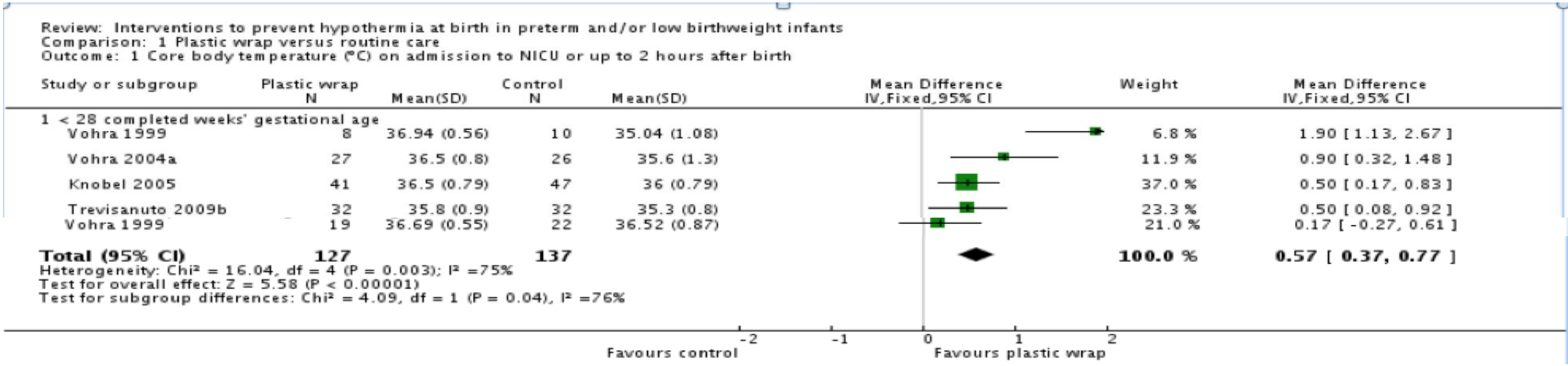


Cohen effect size 0.2 small effect
0.5 medium effect
0.8 large effect

Miti da sfatare (3)

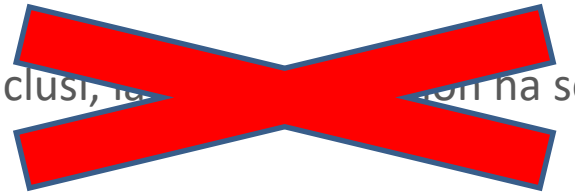
Se trovo elevata eterogeneità tra gli studi inclusi, la meta-analisi non ha senso (si mettono insieme mele e pere)

Esito: Temperatura corporea



Miti da sfatare (3)

Se trovo elevata eterogeneità tra gli studi inclusi, la [illegible] non ha senso (si mettono insieme mele e pere)



- Dipende dal quesito: se il quesito fosse sulla frutta?
- Dipende dal peso degli studi che «creano» eterogeneità
- Dipende dalla direzione e non dalla magnitudo dell'effetto dei singoli studi
- Dipende dal fatto di poterla spiegare (analisi per sottogruppi)

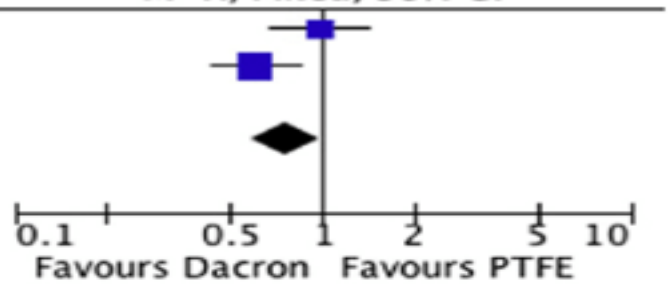
Un diamante è per sempre ma dipende ma molti aspetti

a

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Abbott,Green et al	36	112	39	119	40.3%	0.98 [0.68, 1.42]
van Det et al	34	114	56	114	59.7%	0.61 [0.43, 0.85]
Total (95% CI)		**226**		**233**	**100.0%**	**0.76 [0.59, 0.97]**
Total events	70		95			

Heterogeneity: $Chi^2 = 3.50$, $df = 1$ ($P = 0.06$); $I^2 = 71\%$

Test for overall effect: $Z = 2.19$ ($P = 0.03$)

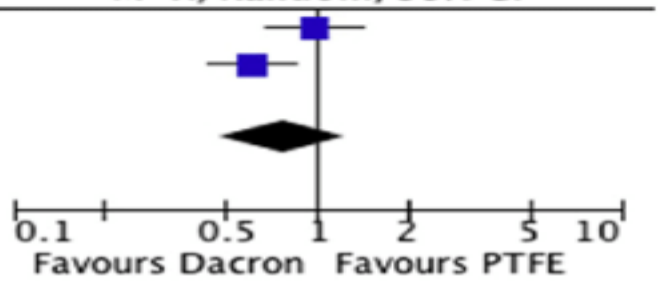


b

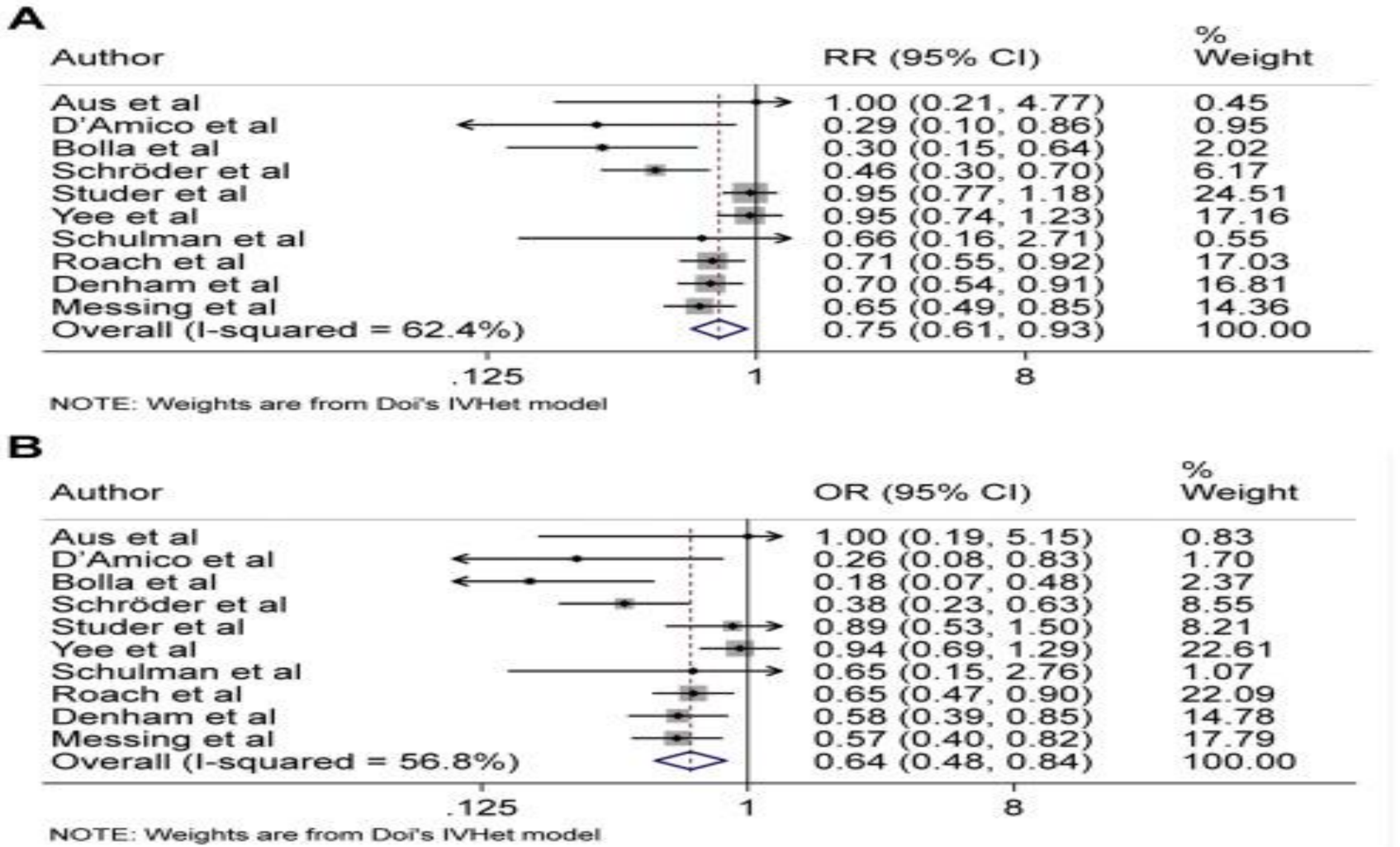
Study or Subgroup	Dacron Events	Dacron Total	PTFE Events	PTFE Total	Weight	Risk Ratio M-H, Random, 95% CI
Abbott,Green et al	36	112	39	119	48.6%	0.98 [0.68, 1.42]
van Det et al	34	114	56	114	51.4%	0.61 [0.43, 0.85]
Total (95% CI)		**226**		**233**	**100.0%**	**0.77 [0.48, 1.23]**
Total events	70		95			

Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 3.50$, $df = 1$ ($P = 0.06$); $I^2 = 71\%$

Test for overall effect: $Z = 1.11$ ($P = 0.27$)



Un diamante è per sempre ma dipende ma molti aspetti



Miti da sfatare (4)

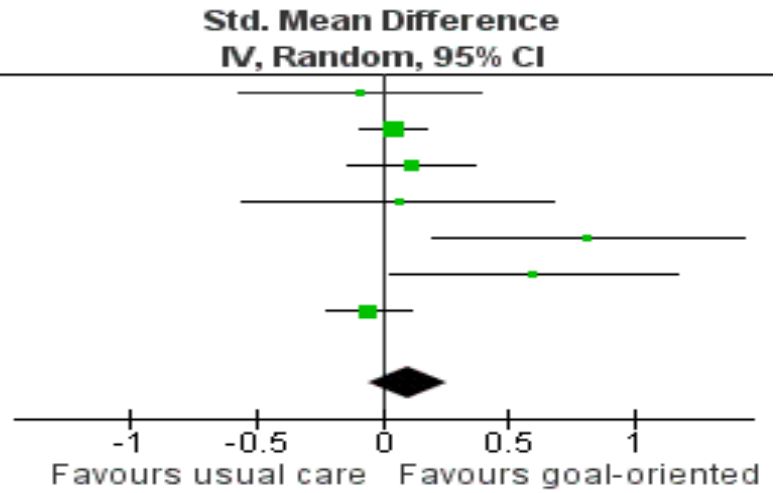
Garbage in, garbage out

Esito: QoL

	goal-oriented care			usual care				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Barley 2014	32.4	10.7	32	33.3	9.2	37	8.5%	-0.09 [-0.56, 0.38]
Blom 2016	6.82	1.34	276	6.76	1.39	1044	29.2%	0.04 [-0.09, 0.18]
Ell 2017	38.3	0.8	122	38.2	0.9	122	19.0%	0.12 [-0.13, 0.37]
Ford 2019	0.56	0.25	18	0.54	0.34	23	5.6%	0.06 [-0.55, 0.68]
Garvey 2015	65.7	20.2	22	50.5	16.3	22	5.5%	0.81 [0.20, 1.43]
Park 2014	-2.8	0.6	25	-3.3	1	25	6.4%	0.60 [0.03, 1.16]
Verdoorn 2019	0.73	0.2	266	0.74	0.18	261	25.7%	-0.05 [-0.22, 0.12]
Total (95% CI)			**761**			**1534**	**100.0%**	**0.10 [-0.06, 0.26]**

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 11.44$, $df = 6$ ($P = 0.08$); $I^2 = 48\%$

Test for overall effect: $Z = 1.25$ ($P = 0.21$)



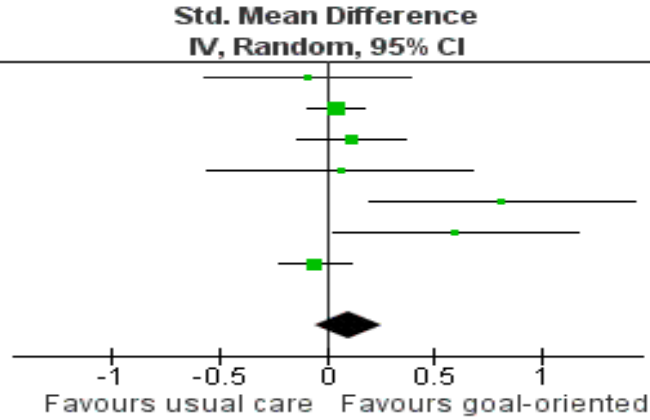
Miti da sfatare (4)

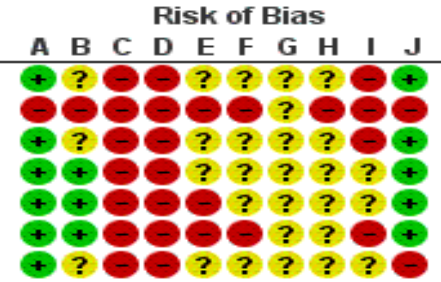
Garbage in, garbage out

Esito: QoL

Study or Subgroup	goal-oriented care Mean	SD	Total	usual care Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Barley 2014	32.4	10.7	32	33.3	9.2	37	8.5%	-0.09 [-0.56, 0.38]
Blom 2016	6.82	1.34	276	6.76	1.39	1044	29.2%	0.04 [-0.09, 0.18]
Ell 2017	38.3	0.8	122	38.2	0.9	122	19.0%	0.12 [-0.13, 0.37]
Ford 2019	0.56	0.25	18	0.54	0.34	23	5.6%	0.06 [-0.55, 0.68]
Garvey 2015	65.7	20.2	22	50.5	16.3	22	5.5%	0.81 [0.20, 1.43]
Park 2014	-2.8	0.6	25	-3.3	1	25	6.4%	0.60 [0.03, 1.16]
Verdoorn 2019	0.73	0.2	266	0.74	0.18	261	25.7%	-0.05 [-0.22, 0.12]
Total (95% CI)			**761**			**1534**	**100.0%**	**0.10 [-0.06, 0.26]**

Heterogeneity: Tau² = 0.02; Chi² = 11.44, df = 6 (P = 0.08); I² = 48%
Test for overall effect: Z = 1.25 (P = 0.21)





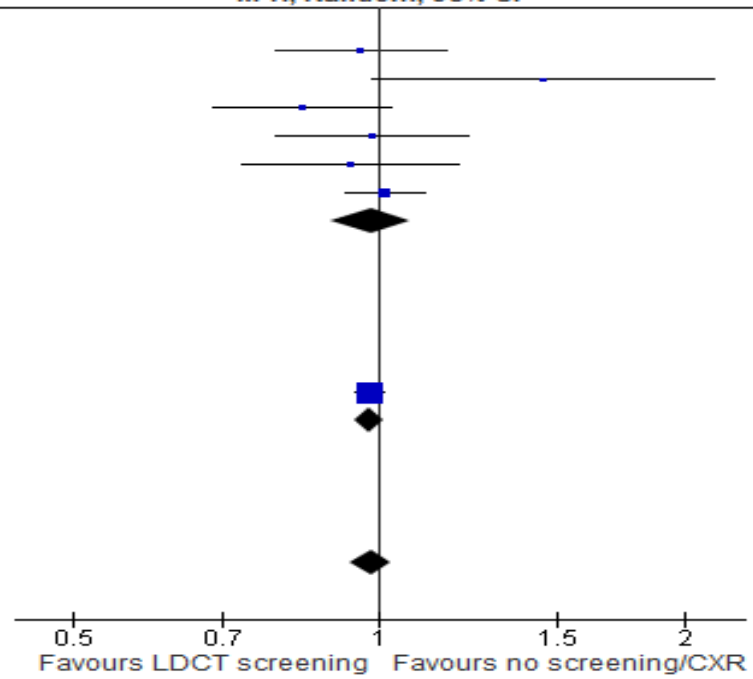
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (Quality of life)
(**E**) Blinding of outcome assessment (Social Functioning)
(**F**) Blinding of outcome assessment (patient's satisfaction)
(**G**) Blinding of outcome assessment (Hospital admission)
(**H**) Blinding of outcome assessment (Caregiver burden)
(**I**) Incomplete outcome data (attrition bias)
(**J**) Selective reporting (reporting bias)

Miti da sfatare (4)

Garbage in, garbage out

Esito: Overall mortality

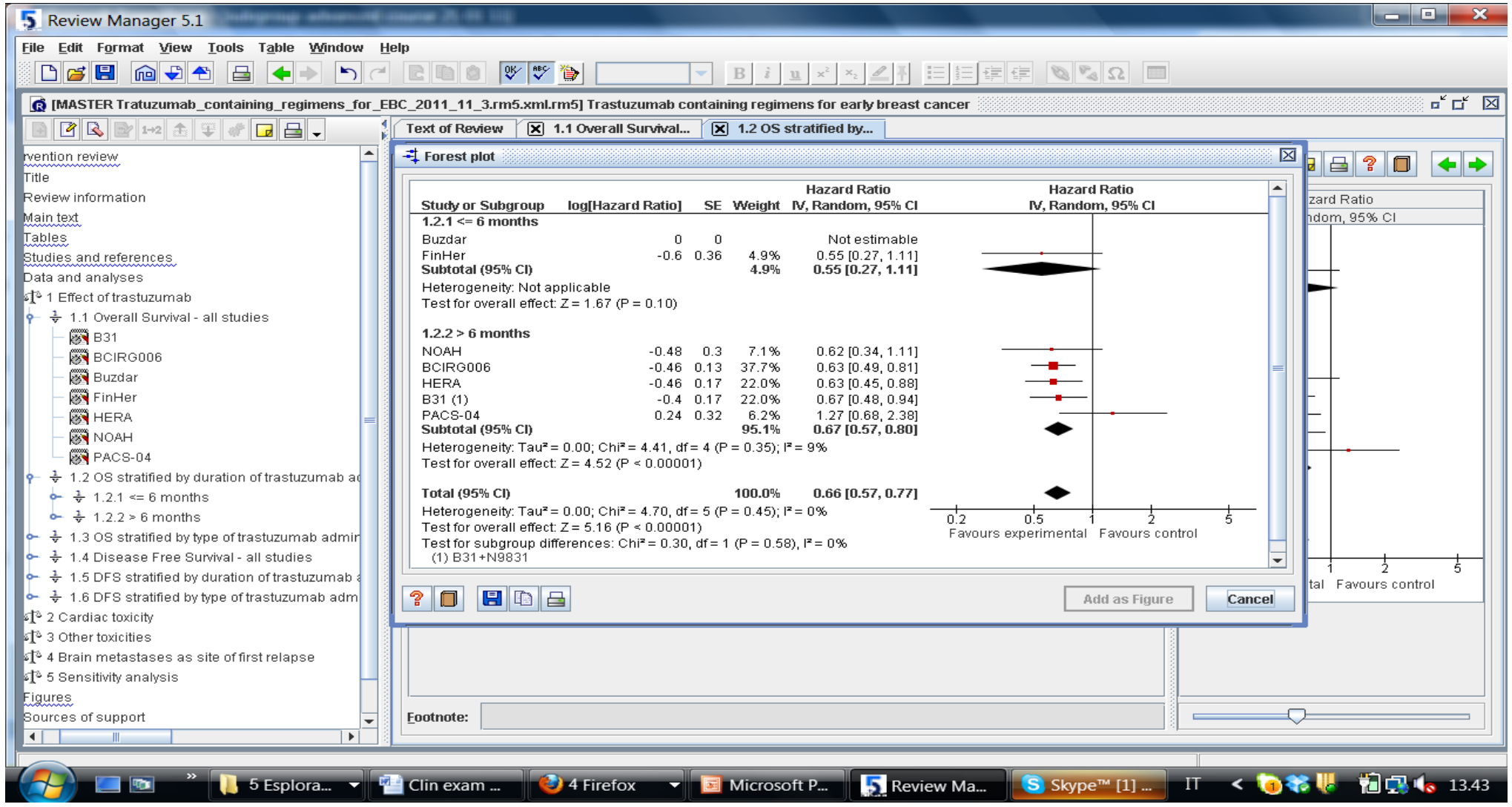
Study or Subgroup	LDCT screening Events	Total	no screening/CXR Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 LDCT vs no screening						
DANTE	180	1264	176	1186	5.3%	0.96 [0.79, 1.16]
DLCST	61	2052	42	2052	1.4%	1.45 [0.99, 2.14]
ITALUNG	154	1613	181	1593	4.8%	0.84 [0.69, 1.03]
LUSI	148	2029	150	2023	4.2%	0.98 [0.79, 1.22]
MILD	137	2376	106	1723	3.3%	0.94 [0.73, 1.20]
NELSON	868	6583	860	6612	20.8%	1.01 [0.93, 1.11]
Subtotal (95% CI)		**15917**		**15189**	**39.7%**	**0.98 [0.90, 1.07]**
Total events	1548		1515			
Heterogeneity: Tau² = 0.00; Chi² = 6.81, df = 5 (P = 0.23); I² = 27%						
Test for overall effect: Z = 0.40 (P = 0.69)						
1.2.2 LDCT vs CXR						
NLST	5253	26722	5366	26730	60.3%	0.98 [0.95, 1.01]
Subtotal (95% CI)		**26722**		**26730**	**60.3%**	**0.98 [0.95, 1.01]**
Total events	5253		5366			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.21 (P = 0.23)						
Total (95% CI)		**42639**		**41919**	**100.0%**	**0.98 [0.94, 1.03]**
Total events	6801		6881			
Heterogeneity: Tau² = 0.00; Chi² = 6.88, df = 6 (P = 0.33); I² = 13%						
Test for overall effect: Z = 0.78 (P = 0.44)						
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.95), I² = 0%						



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)

Miti da sfatare (5)

La lettura dei sottogruppi



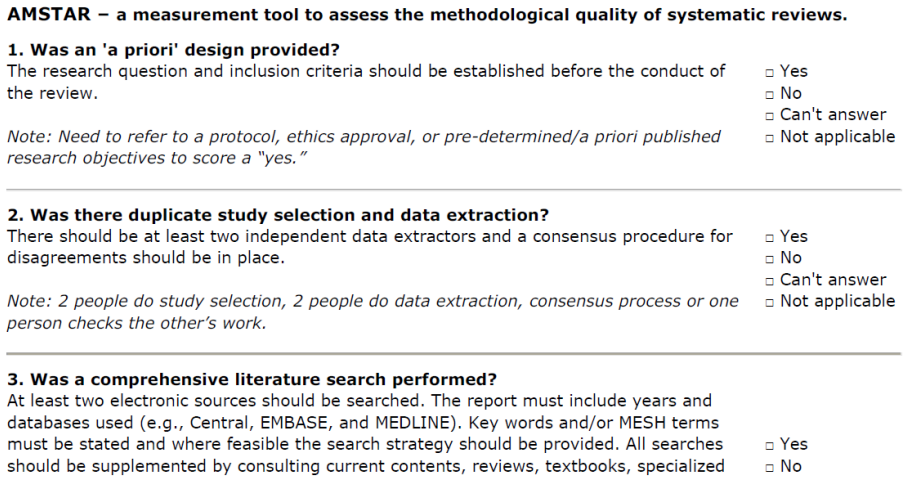
General Assumptions in Subgroup Analysis

- Hypotheses tested usually address an overall or ‘average’ treatment effect in the study population
- No assumption of homogeneity of effect across subgroups - interaction
- Direction, not magnitude, of the treatment effect is expected be the same in subgroups

•*Only one thing is worse than doing subgroup analyses---believing the results* R. Peto

AMSTAR CHECKLIST

- Valuta il ***QUALITY OF CONDUCT***: la misura in cui la revisione è esente da errori sistematici
- Per aiutare chi legge a capire se la SR è affidabile e valida
- Composta di 11 items
- Shea BJ et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol. 2007 Feb 15;7:10.



AMSTAR – a measurement tool to assess the methodological quality of systematic reviews.

1. Was an 'a priori' design provided?
The research question and inclusion criteria should be established before the conduct of the review.

Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."

□ Yes
□ No
□ Can't answer
□ Not applicable

2. Was there duplicate study selection and data extraction?
There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.

Note: 2 people do study selection, 2 people do data extraction, consensus process or one person checks the other's work.

□ Yes
□ No
□ Can't answer
□ Not applicable

3. Was a comprehensive literature search performed?
At least two electronic sources should be searched. The report must include years and databases used (e.g., Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized

□ Yes
□ No

AMSTAR CHECKLIST II

- *"… The original AMSTAR instrument did not include an assessment of the risk of bias in non-randomised studies included in a review, which is a key issue given the diversity of designs that such studies may use and the biases that may affect them".*
- Shea BJ et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017 Sep 21;358:j4008
- 16 items

ELSEVIER

CrossMark

Journal of Clinical Epidemiology 69 (2016) 225–234

Journal of Clinical Epidemiology

ROBIS: A new tool to assess risk of bias in systematic reviews was developed

Penny Whiting[a,b,c,*], Jelena Savović[a,b], Julian P.T. Higgins[a,d], Deborah M. Caldwell[a], Barnaby C. Reeves[e], Beverley Shea[f], Philippa Davies[a,b], Jos Kleijnen[c,g], Rachel Churchill[a], the ROBIS group

[a]School of Social and Community Medicine, University of Bristol, Canynge Hall, 39 Whatley Road, Bristol BS8 2PS, UK
[b]The National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care West at University Hospitals Bristol NHS Foundation Trust, 9th Floor, Whitefriars, Lewins Mead, Bristol BS1 2NT
[c]Kleijnen Systematic Reviews Ltd, Unit 6, Escrick Busin
[d]Centre for Reviews and Dissemination, U
[e]School of Clinical Sciences, University of Bristol, Bristol Royal Infirma
[f]Community Information and Epidemiological Technologies Institute of Popula
[g]School for Public Health and Primary Care (CAPHRI), Maastrich

Accepted 5 June 2015; Publ

Abstract

Objective: To develop ROBIS, a new tool for assessing the risk
Study Design and Setting: We used four-stage approach to develc face meeting, and refine the tool through piloting.

ROBIS
QUALITY OF CONDUCT
Checklist

Phase 2: Identifying concerns with the review process

DOMAIN 1: STUDY ELIGIBILITY CRITERIA	
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:	
1.1 Did the review adhere to pre-defined objectives and eligibility criteria?	Y/PY/PN/N/NI
1.2 Were the eligibility criteria appropriate for the review question?	Y/PY/PN/N/NI
1.3 Were eligibility criteria unambiguous?	Y/PY/PN/N/NI
1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	Y/PY/PN/N/NI
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)?	Y/PY/PN/N/NI
Concerns regarding specification of study eligibility criteria	LOW/HIGH/UNCLEAR
Rationale for concern:	

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES	
Describe methods of study identification and selection (e.g. number of reviewers involved):	
2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y/PY/PN/N/NI
2.2 Were methods additional to database searching used to identify	Y/PY/PN/N/NI

QUALITY OF REPORTING

PRISMA Statement

OPEN ACCESS Freely available online

PLoS MEDICINE

Guidelines and Guidance

Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement

David Moher[1,2]*, Alessandro Liberati[3,4], Jennifer Tetzlaff[1], Douglas G. Altman[5], The PRISMA Group[¶]

1 Ottawa Methods Centre, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada, **2** Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada, **3** Università di Modena e Reggio Emilia, Modena, Italy, **4** Centro Cochrane Italiano, Istituto Ricerche Farmacologiche Mario Negri, Milan, Italy, **5** Centre for Statistics in Medicine, University of Oxford, Oxford, United Kingdom

http://www.prisma-statement.org/

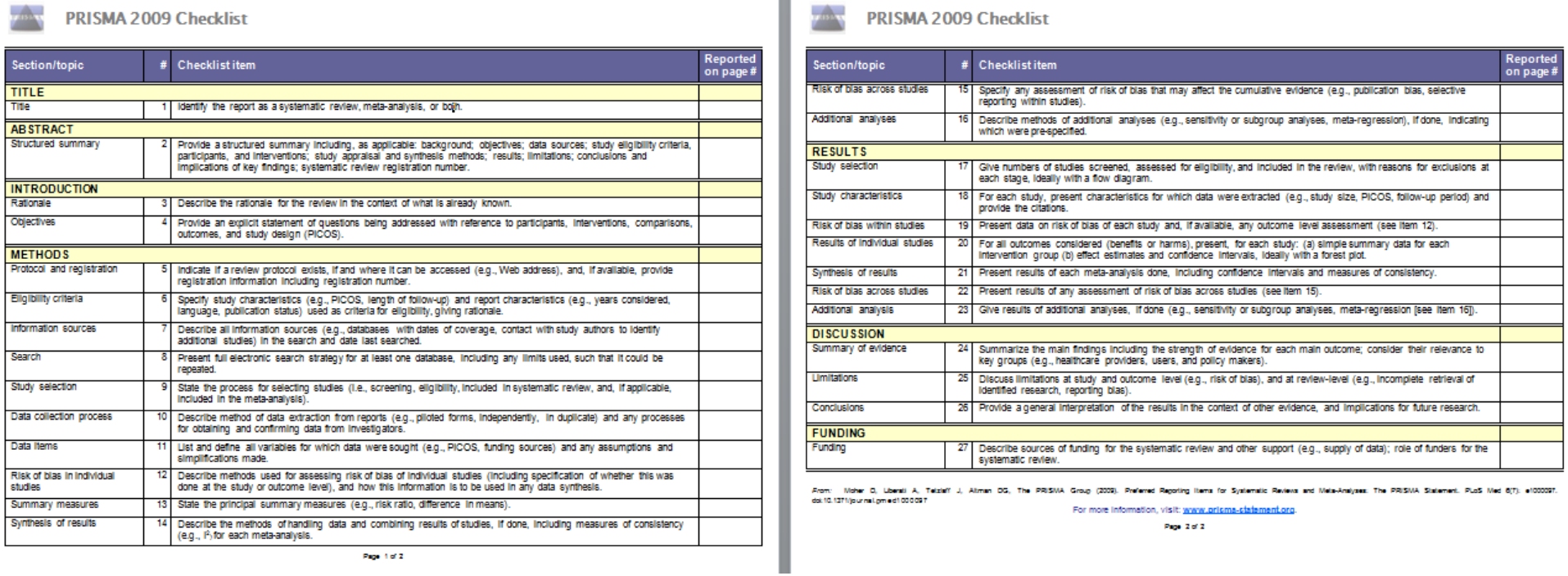
PRISMA

- Pubblicato nel 2009, evoluzione del QUOROM statement (guida, pubblicata nel 1999, per migliorare il reporting di meta-analisi di RCT).
- Valuta il ***QUALITY OF REPORTING***
- Pubblicato in Annals of Internal Medicine, PLoS Medicine, Open Medicine, the British Medical Journal and the Journal of Clinical Epidemiology.

KEY DOCUMENTS

- PRISMA Statement
- PRISMA Checklist
- PRISMA flow diagram
- PRISMA E&E

PRISMA Checklist



PRISMA 2009 Checklist

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.	

PRISMA 2009 Checklist

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.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7). e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Submission Guidelines

PLOS Medicine publishes original research articles of outstanding medical importance. We will consider manuscripts of any length; we encourage the submission of both substantial full-length bodies of work and shorter manuscripts that report novel findings that might be based on a more limited range of experiments.

The writing style should be concise and accessible, avoiding jargon so that the paper is understandable for readers outside a specialty or those whose first language is not English. Editors will make suggestions for how to achieve this, as well as suggestions for deletions or additions that could be made to the article to strengthen the argument. Our aim is to make the editorial process rigorous and consistent, but not intrusive or overbearing. Authors are encouraged to use their own voice and to decide how best to present their ideas, results, and conclusions.

Systematic reviews and meta-analyses

Reports of systematic reviews and meta-analyses must adhere to the PRISMA Statement or alternative guidelines appropriate to the study design, and include the completed checklist and flow diagram to accompany the main text. Authors must complete the appropriate reporting checklist not only with page references, but also with sufficient text excerpted from the manuscript to explain how they accomplished all applicable items.

Download blank templates of the checklist and flow diagram from the EQUATOR web site.

Abstracts should follow PRISMA for Abstracts, using the PLOS abstract format. Authors must also state within the Methods section of their paper whether a protocol exists for their systematic review, and if so, provide a copy of the protocol as supporting information.

Esempio

PLOS ONE

Efficacy of muscle exercise in patients with muscular dystrophy: a systematic review showing a missed opportunity to improve outcomes

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	done
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.	Structured abstract done
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Page #2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Page #2
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.	None
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.	Page #2-3
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.	Page #3
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Page #3
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).	Page #3
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	Page #4

http://www.equator-network.org/

Example of bad reporting

Hip Int. 2012 Jul-Aug;22 Suppl 8:S19-24. doi: 10.5301/HIP.2012.9566.

Value of debridement and irrigation for the treatment of peri-prosthetic infections. A systematic review.

Abstract

Debridement and irrigation has been proposed as a salvage procedure for early post-operative and late acute haematogenous periprosthetic hip and knee infections, however the effective ability of this procedure to avoid recurrent infection is still debated. In this systematic review of the literature we reviewed full-text papers published from 1970 through 2011, that reported the success rate of infection eradication after debridement and irrigation with prosthesis retention for the treatment of early septic complications (within six weeks from surgery) or late acute haematogenous infections after hip or knee prosthesis. In all, 14 original articles, reporting the results of 710 patients were retrieved. The average success rate has been, respectively, 45.9% and 52% after a single or repeated debridement and irrigation procedures, at a mean follow-up of 53.3 months. The methodological limitations of this study and the heterogeneous material in the reviewed papers notwithstanding, this systematic review shows that debridement and irrigation procedure is associated with a rather poor outcome, even in a population of patients selected on the basis of symptoms' duration and patients should be adequately informed prior to undergo this salvage procedure.

- ✓ **ABSTRACT NON STRUTTURATO IN INTRODUZIONE, OBIETTIVI, RISORSE RICERCA, CRITERI DI ELIGIBILITA', INTERVENTI, CRITICAL APPRISAL, SINTESI DEI METODI, RISULTATI, LIMITAZIONI CONCLUSIONI, IMPLICAZIONI**
- ✓ **SYSTEMATIC REVIEW REGISTRATION NUMBER**
- ✓ **MANCANO BANCHE DATI**

Example of good reporting

Virtual Reality Therapy for Adults Post-Stroke: A Systematic Review and Meta-Analysis Exploring Virtual Environments and Commercial Games in Therapy

Abstract

Background: The objective of this analysis was to systematically review the evidence for virtual reality (VR) therapy in an adult post-stroke population in both custom built virtual environments (VE) and commercially available gaming systems (CG).

Methods: MEDLINE, CINAHL, EMBASE, ERIC, PSYCInfo, DARE, PEDro, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews were systematically searched from the earliest available date until April 4, 2013. Controlled trials that compared VR to conventional therapy were included. Population criteria included adults (>18) post-stroke, excluding children, cerebral palsy, and other neurological disorders. Included studies were reported in English. Quality of studies was assessed with the Physiotherapy Evidence Database Scale (PEDro).

Resu VR thera VE and C 32, 0.85], rall effect

ABSTRACT STRUTTURATO IN INTRODUZIONE, OBIETTIVI, RISORSE RICERCA, CRITERI DI ELIGIBILITA', INTERVENTI, CRITICAL APPRISAL, SINTESI DEI METODI, RISULTATI, LIMITAZIONI CONCLUSIONI, IMPLICAZIONI, SYSTEMATIC REVIEW REGISTRATION NUMBER

Discussion: VR rehabilitation moderately improves outcomes compared to conventional therapy in adults post-stroke. Current CG interventions have been too few and too small to assess potential benefits of CG. Future research in this area should aim to clearly define conventional therapy, report on participation measures, consider motivational components of therapy, and investigate commercially available systems in larger RCTs.

Trial Registration: Prospero CRD42013004338

SACRO CUORE DON CALABRIA

ECI CANCER CENTRE

I R C C S

SCUOLA DI METODOLOGIA DELLA RICERCA CLINICA

2025 - 11ª EDIZIONE

MODULI SPECIALISTICI - S1

VENERDÌ 14 - SABATO 15 MARZO 2025

NEGRAR DI VALPOLICELLA (VR)

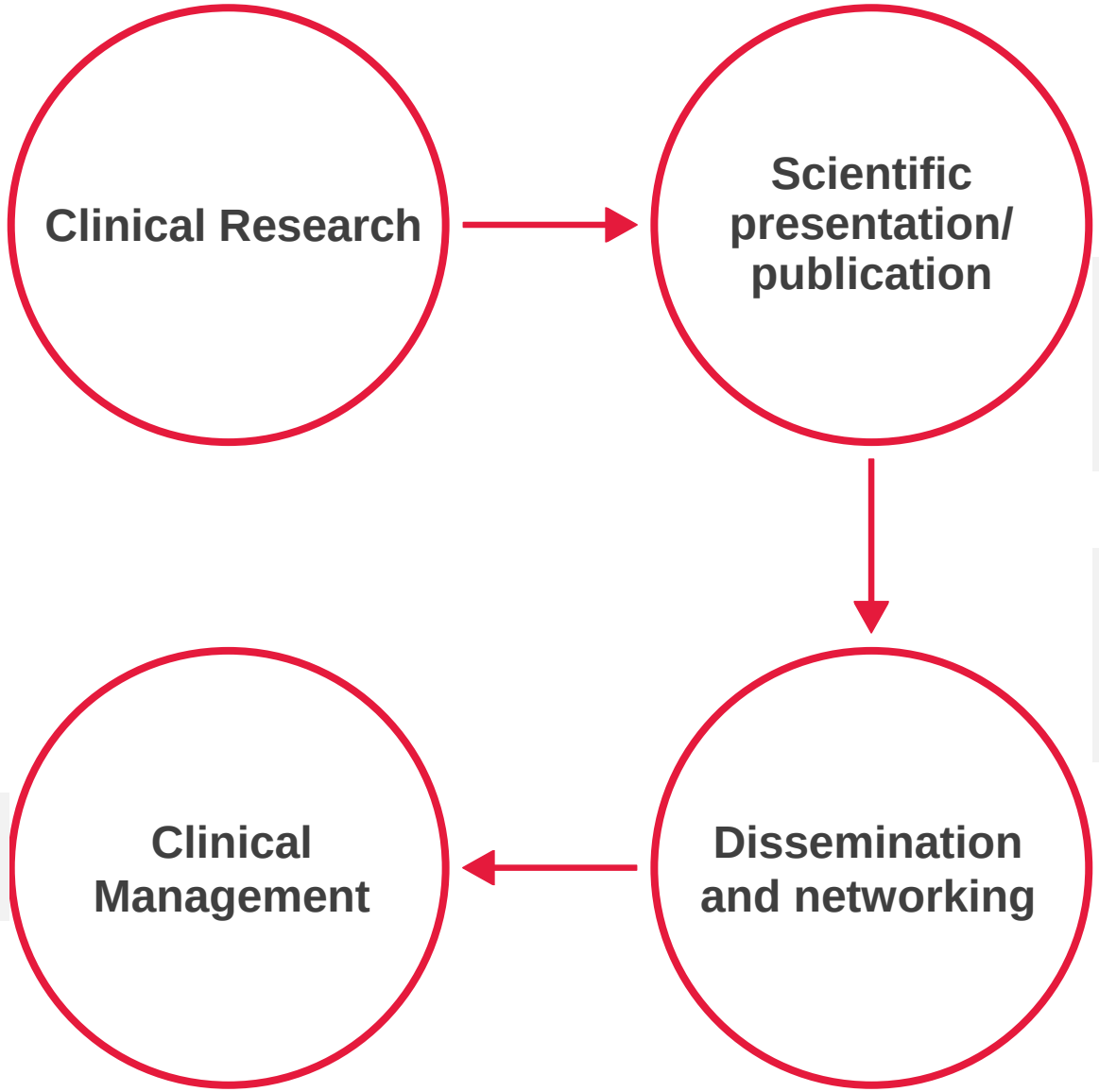
Centro Formazione IRCCS "Sacro Cuore - Don Calabria"

Metodi di valutazione di autori e riviste scientifiche: indici bibliometrici classici e innovativi

Giulio ZUANETTI

Twenty years ago

RCT



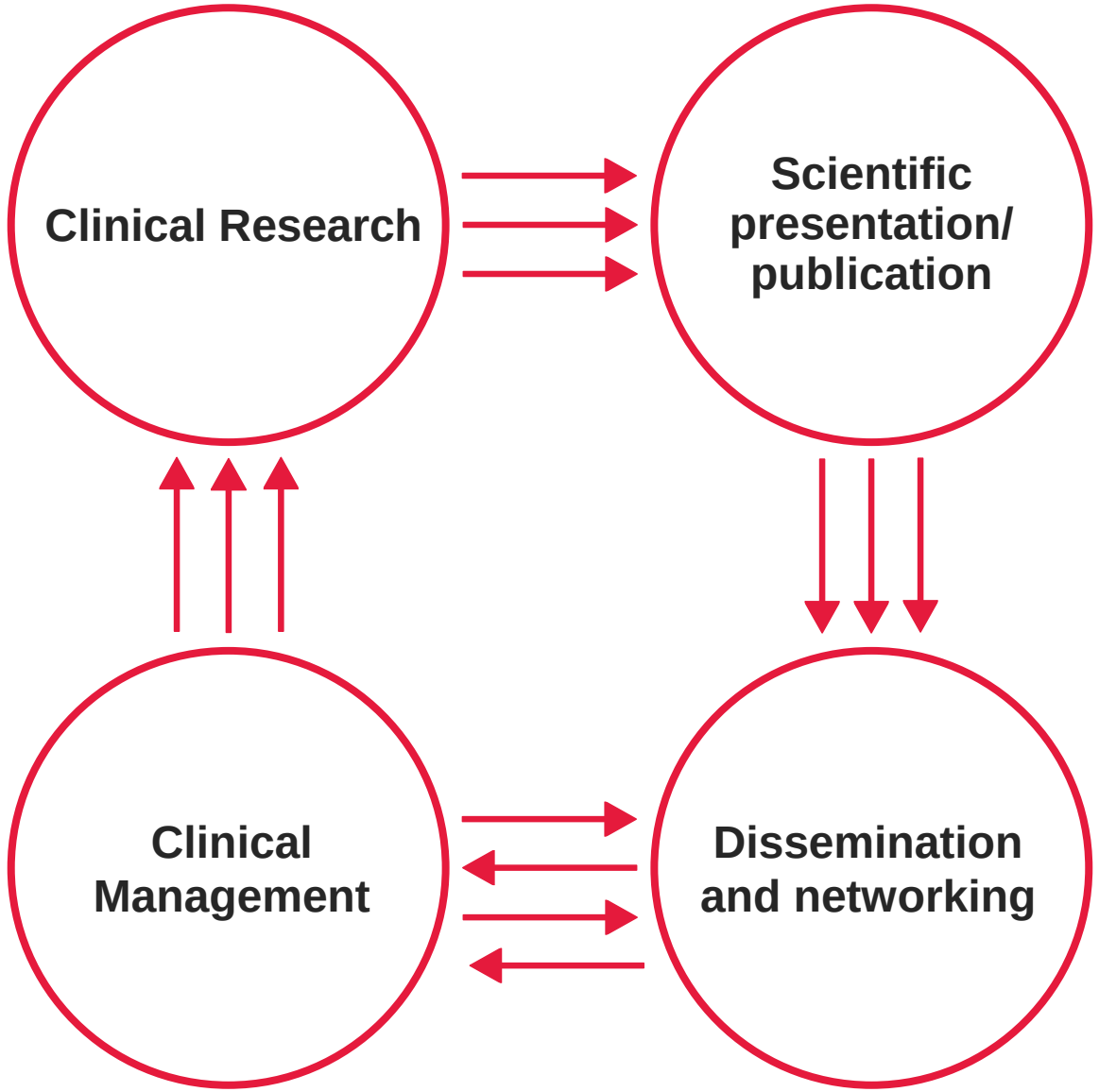
Society Congresses

Peer- reviewed journals

Just do it

Now

RCT,
RWE,
metanalysis,
network met,
etc



Congresses,
PeerRev Journals,
Preprints,
Media & Events,
Forums,
Social networks..

Collect data,
analyze &
tell about it

L’ERA PAYWALLED

~1970 Per la prima volta le riviste scientifiche utilizzano un processo di peer-review simile a quello che abbiamo oggi

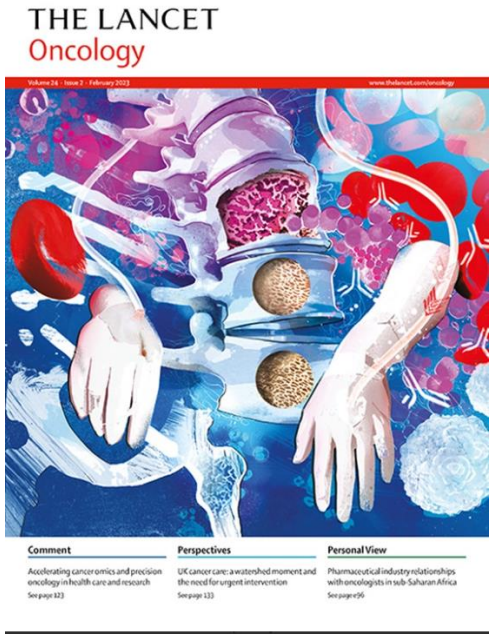
1971 Viene lanciato Medlars, il progenitore d Medline / Pubmed, disponibile a una piccolo gruppo di biblioteche scientifiche.

1975 Viene pubblicato per la prima volta l’Impact Factor delle riviste scientifiche, sulla base del Science Citation Index

1975-2000 …per 25 anni, non succede quasi nulla

Il publishing scientifico rimane chiuso in una fortezza

Il paywall: l’accesso alla letteratura scientifica ristretto a pochi addetti ai lavori



To read this article in full you will need to make a payment

Purchase one-time access:

Academic & Personal: 24 hour online access

Corporate R&D Professionals: 24 hour online access

▶ One-time access price info

Subscribe:

Subscribe to *The Lancet Oncology*

Already a print subscriber? Claim online access

Already an online subscriber? Sign in

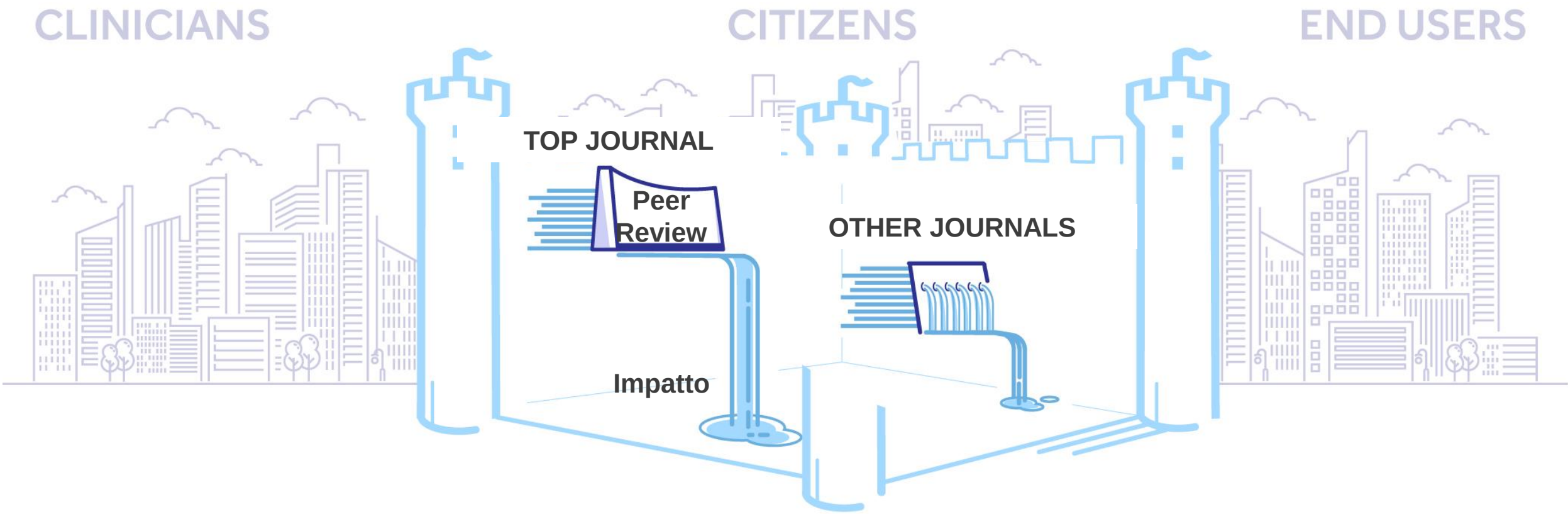
Register: Create an account

Institutional Access: Sign in to ScienceDirect

Or purchase The Lancet Choice

Access any 5 articles from the Lancet Family of journals

I veri beneficiari delle novità scientifiche, clinici e pazienti, rimanevano molto lontani



Tutto era limitato a un mondo accademico “chiuso”

©HPS

L'ERA OPEN SCIENCE

1998

Medline diventa disponibile a tutti, gratis

2000

Vengono lanciate le riviste Fully Open Access

2004

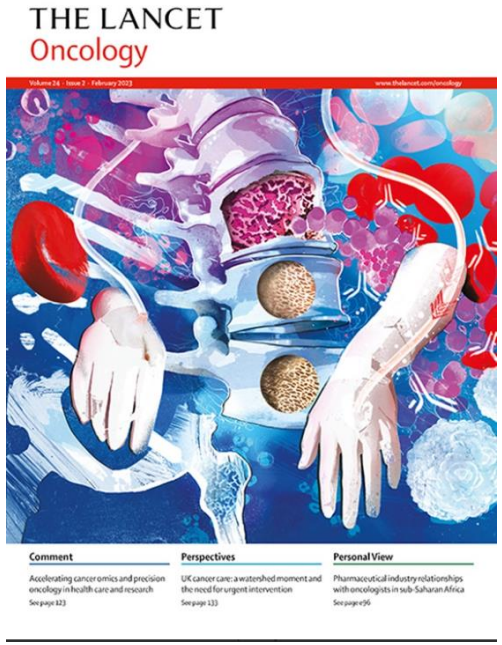
Nascono Twitter, LinkedIn e Google Scholar

2011

Viene coniato il termine Altmetrics

2012

Anche i Top Journal diventano Ibridi e pubblicano in OA



Open access and funding

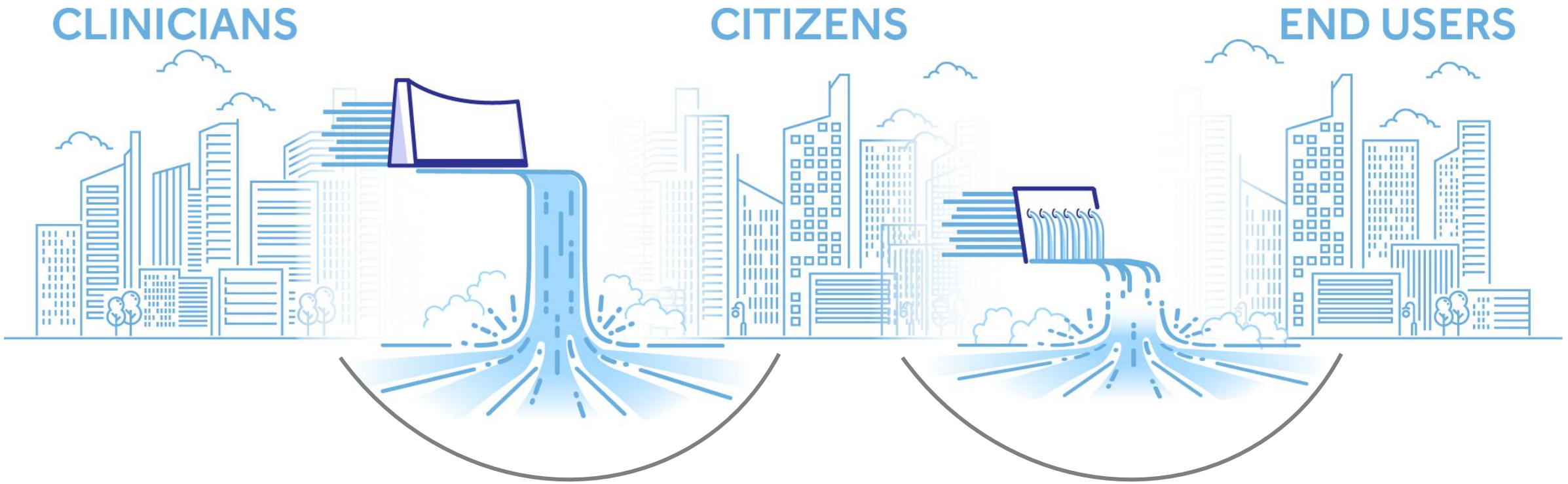
Open access

- *The Lancet Oncology* is committed to support authors in making their research publicly and freely available. The editors encourage all authors to post their peer-reviewed, accepted article on their personal or institutional websites any time after publication in print or online. Your document should indicate the article's citation and a link to the published article on *The Lancet* website.
- *The Lancet Oncology* is a hybrid journal. In this journal, we offer authors of research Articles with funding that requires open access publication either a gold open access or a subscription green open access solution for their submission. Open access publication in our hybrid journals is available for authors whose research is funded by specific funders. Find out more about open access at https://www.thelancet.com/open-access.
- For the gold open access solution, we offer a choice of creative commons licences (CC BY or CC BY-NC-ND). Please check with your funder whether a specific creative commons license is preferred. Information on the article processing charge (APC) for *The Lancet Oncology* can be found at https://www.thelancet.com/open-access

Il full text degli articoli è liberamente disponibile, a tutti.
I clinici e i pazienti hanno più facile accesso alle fonti primarie dei dati.

Nell’era Open Access i muri della fortezza sono crollati

L’Open Access, Google e i Social Network hanno aperto grandi opportunità



Si può aumentare l’impatto dei propri lavori grazie a un buon lavoro di disseminazione….

…anche quando non si pubblica su un top journal

©HPS

Questa è oggi un’importante opportunità da cogliere, come studiosi e come autori, ma…

Ricordatevi di controllare la tipologia di Open Access del vostro articolo!

Traditional Publishing

Non Open Access articles
©Publisher
Any commercial reuse must come through publisher

CC BY NC

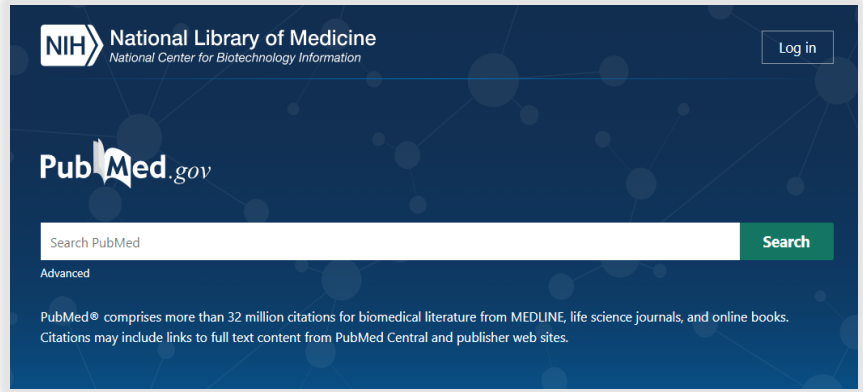
Open Access articles
©Author
Personal use and sharing permitted
Commercial reuse must come through publisher

CC BY

Open access articles
©Author
All use permitted including commercial reuse

In un mondo sempre più Open Access come avviene la ricerca dei lavori scientifici?

…oggi i ricercatori, in particolare i giovani, non cercano solo su PubMed…



https://pubmed.ncbi.nlm.nih.gov/

Google Scholar

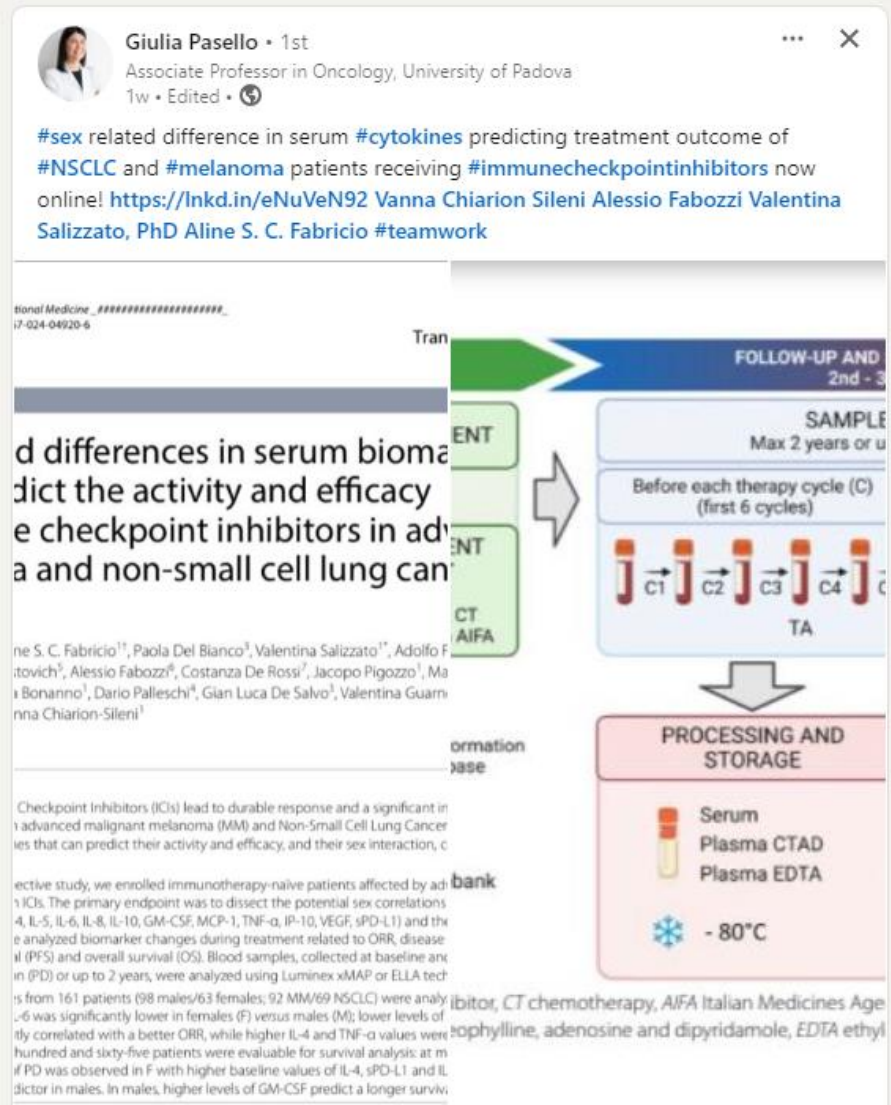
Articles Case law

Stand on the shoulders of giants

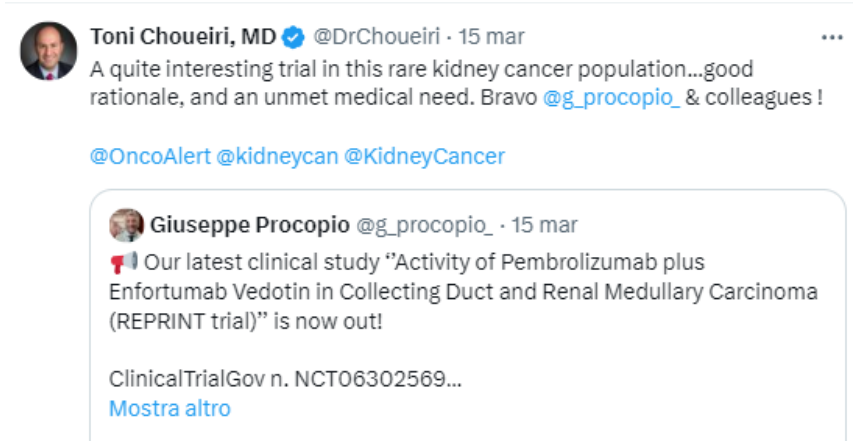
..ma sempre più utilizzano I motori di ricerca che si basano su algoritmi propri dei motori di ricerca generalisti…

In realtà sempre più spesso si scoprono i nuovi lavori sui social network, sia generalisti che professionali

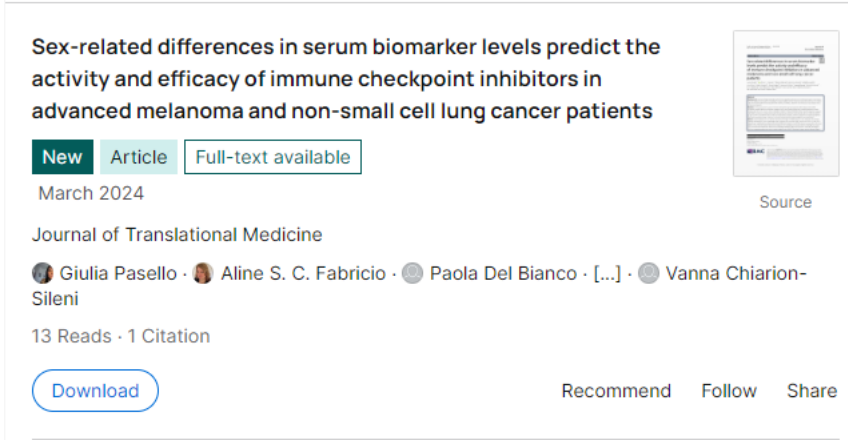
LinkedIn



X (ex-Twitter)



ResearchGate



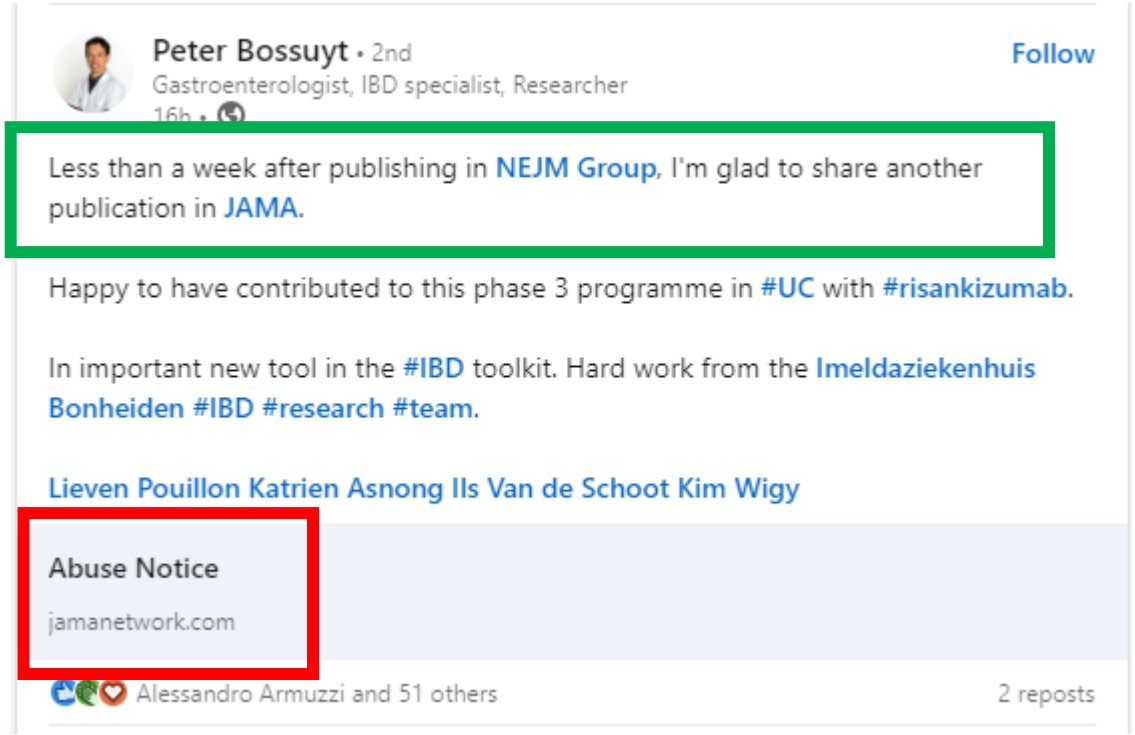
Spesso le ricerche non partono più dai database classici

Spesso si scoprono i nuovi lavori sui social

La linea di demarcazione tra riviste “top” e le altre diventa meno netta.

Conta moltissimo cosa l’autore/autrice del lavoro fa prima, durante e dopo la pubblicazione per ottimizzarne la visibilità.

Non condividete i Full Text se non siete sicuri di poterlo fare



An "abuse notice" on LinkedIn typically refers to a report filed by a user regarding inappropriate or harassing behavior by another member.

When such a report is submitted, LinkedIn reviews the content through its processes to assess its validity and take appropriate actions, which may include removing content, restricting account access, or notifying law enforcement if necessary

Per aumentare la visibilità conviene anticipare la pubblicazione depositando un preprint?

Sapete cosa sono i preprint?

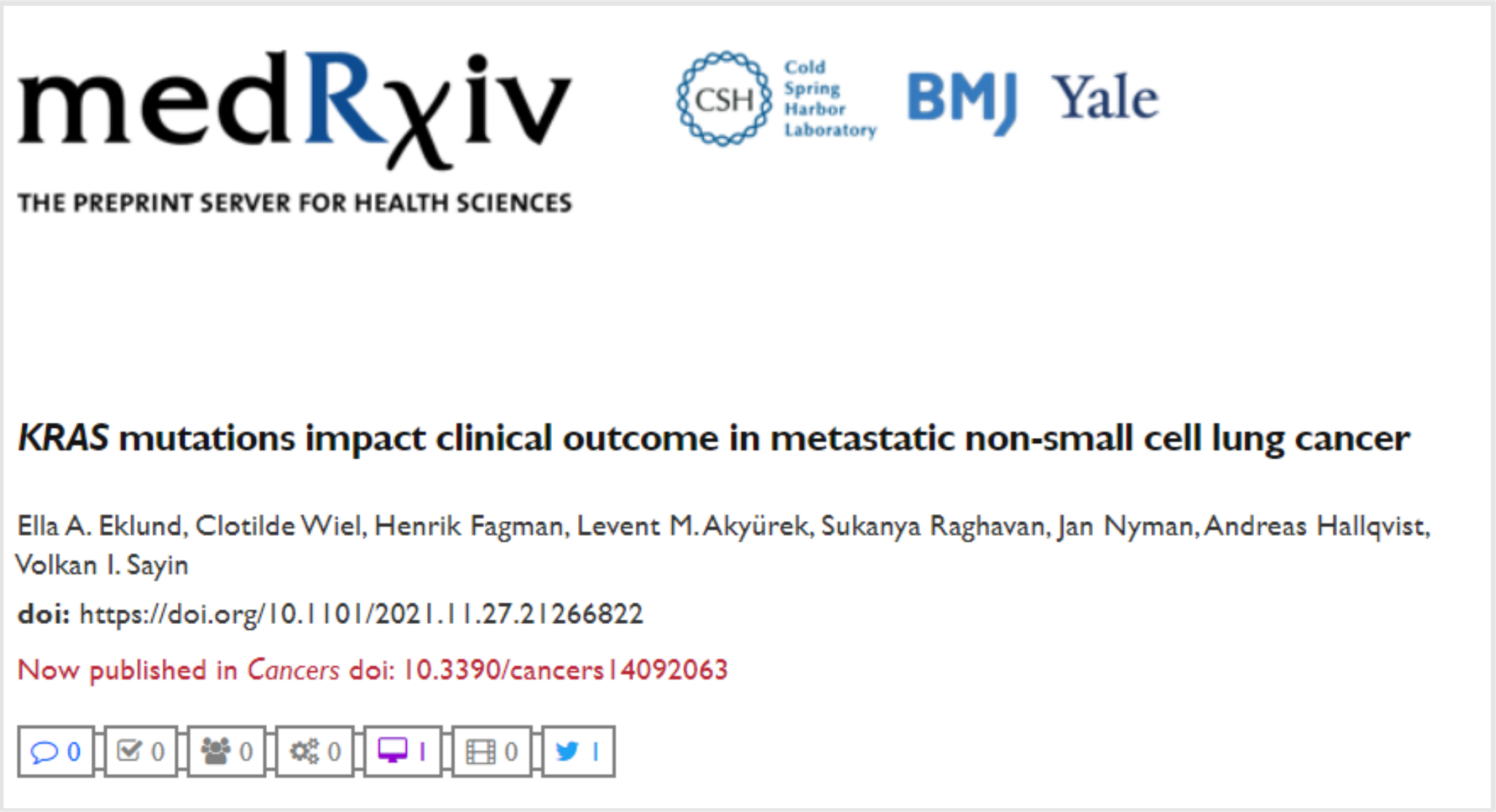
I preprint NON sono preprint.

Infatti NON sono lavori scientifici che devono andare in stampa, come il termine suggerirebbe….

Sono invece manoscritti che gli autori depositano in repositories definiti **“preprint servers”** subito dopo il completamento del lavoro e **che non hanno ancora di fatto superato il processo di peer review.**

Il concetto di preprint è radicato da quasi 30 anni in alcune branche di ricerca come la fisica, ma negli ultimi anni ha preso piede nel mondo medico scientifico.

Esempio di preprint in oncologia…



…e successivo lavoro

cancers

MDPI

Article

KRAS Mutations Impact Clinical Outcome in Metastatic Non-Small Cell Lung Cancer

Ella A. Eklund [1,2,3], Clotilde Wiel [1,2], Henrik Fagman [4,5], Levent M. Akyürek [4,5], Sukanya Raghavan [6], Jan Nyman [3,7], Andreas Hallqvist [3,7] and Volkan I. Sayin [1,2,*]

1 Sahlgrenska Center for Cancer Research, Department of Surgery, Institute of Clinical Sciences, University of Gothenburg, 40530 Gothenburg, Sweden; ella.ang@gu.se (E.A.E.); clotilde.wiel@gu.se (C.W.)
2 Wallenberg Centre for Molecular and Translational Medicine, University of Gothenburg, 40530 Gothenburg, Sweden
3 Department of Oncology, Sahlgrenska University Hospital, 41345 Gothenburg, Sweden; jan.nyman@vgregion.se (J.N.); andreas.hallqvist@vgregion.se (A.H.)
4 Department of Laboratory Medicine, Institute of Biomedicine, University of Gothenburg, 40530 Gothenburg, Sweden; henrik.a.fagman@vgregion.se (H.F.); levent.akyurek@gu.se (L.M.A.)
5 Department of Clinical Pathology, Sahlgrenska University Hospital, 41345 Gothenburg, Sweden
6 Department of Microbiology and Immunology, Institute for Biomedicine, Sahlgrenska Academy, University of Gothenburg, 40530 Gothenburg, Sweden; sukanya.raghavan@microbio.gu.se
7 Department of Oncology, Institute of Clinical Sciences, University of Gothenburg, 40530 Gothenburg, Sweden
* Correspondence: volkan.sayin@wlab.gu.se

Received: 17 March 2022
Accepted: 18 April 2022
Published: 20 April 2022

Confronto tra Abstract: secondo voi qual è il preprint e qual è il lavoro ufficialmente pubblicato?

Abstract – A

Purpose There is an urgent need to identify new predictive biomarkers for treatment response to both platinum doublet chemotherapy (PD) and immune checkpoint blockade (ICB) with pembrolizumab. Here we evaluated whether treatment outcome could be affected by KRAS mutational status in patients with metastatic (stage IV) non-small cell lung cancer (NSCLC).

Methods All consecutive patients molecularly assessed and diagnosed between 2016-2018 with stage IV NSCLC in the region of West Sweden were included in this multi-center retrospective study. Primary study outcome was overall survival (OS).

Results Out of 580 stage IV NSCLC patients, 35.5% harbored an activating mutation in the KRAS gene (KRASMUT). Compared to KRAS wild-type (KRASWT), KRASMUT was a negative factor for OS (p = 0.014). On multivariate analysis, KRASMUT persisted as a negative factor for OS (HR 1.288, 95% CI 1.091-1.521, p = 0.003). When treated with first-line platinum doublet (n = 195), KRASMUT is a negative factor for survival (p = 0.018) with median OS 9 months vs KRASWT 11 months. On multivariate analysis, KRASMUT persisted as a negative factor for OS (HR 1.564, 95%CI 1.124-2.177, p = 0.008). KRASMUT patients with high PD-L1 expression (PD-L1high) had better OS than PD-L1high KRASWT patients (p = 0.036). In response to first-line ICB, KRASMUT patients had a significant (p = 0.006) better outcome than KRASWT with a median OS 23 vs 6 months. On multivariable Cox analysis, KRASMUT status was an independent prognostic factor for better OS (HR 0.349, 95%CI 0.148-0.822, p = 0.016).

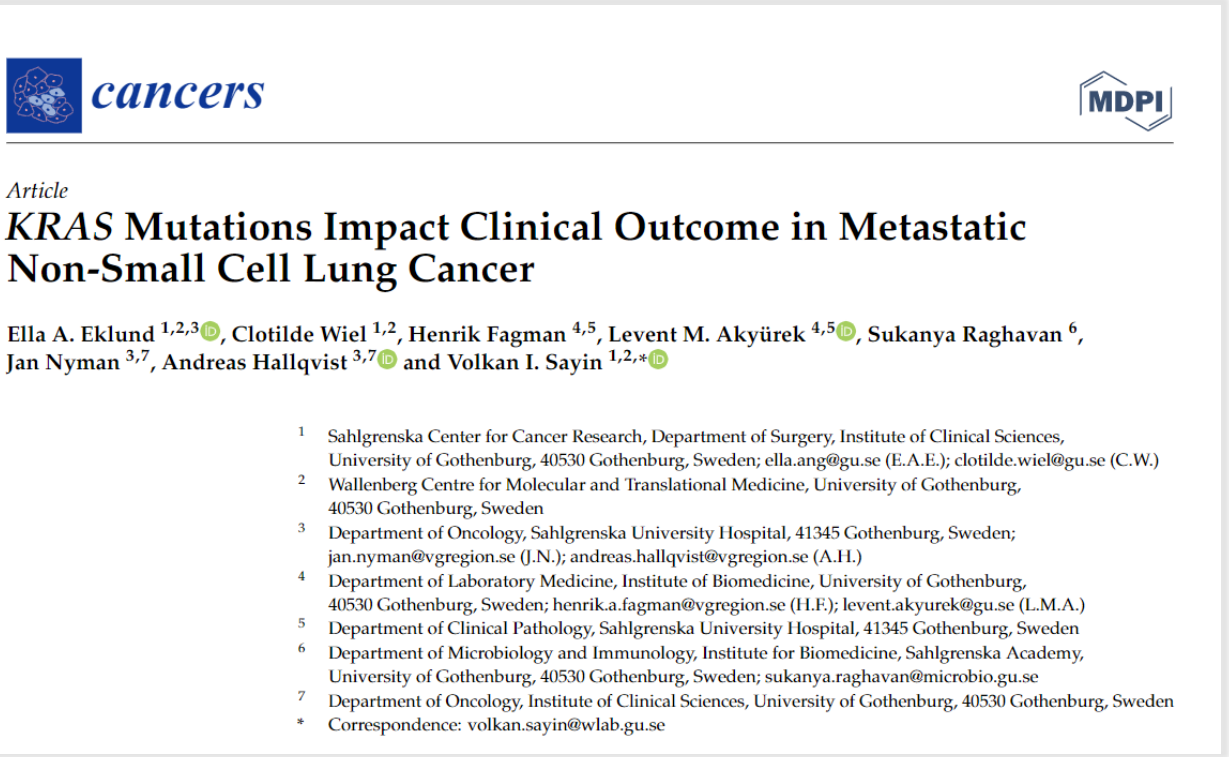
Conclusions KRAS mutations is a positive predictive factor for treatment with pembrolizumab and a negative predictive factor for platinum doublet chemotherapy as well as general OS in stage IV NSCLC.

Abstract – B

There is an urgent need to identify new predictive biomarkers for treatment response to both platinum doublet chemotherapy (PT) and immune checkpoint blockade (ICB). Here, we evaluated whether treatment outcome could be affected by *KRAS* mutational status in patients with metastatic (Stage IV) non-small cell lung cancer (NSCLC). All consecutive patients molecularly assessed and diagnosed between 2016-2018 with Stage IV NSCLC in the region of West Sweden were included in this multi-center retrospective study. The primary study outcome was overall survival (OS). Out of 580 Stage IV NSCLC patients, 35.5% harbored an activating mutation in the *KRAS* gene ($KRAS^{MUT}$). Compared to *KRAS* wild-type ($KRAS^{WT}$), $KRAS^{MUT}$ was a negative factor for OS ($p = 0.014$). On multivariate analysis, $KRAS^{MUT}$ persisted as a negative factor for OS (HR 1.478, 95% CI 1.207-1.709, $p < 0.001$). When treated with first-line platinum doublet ($n = 195$), $KRAS^{MUT}$ was a negative factor for survival ($p = 0.018$), with median OS of 9 months vs. $KRAS^{WT}$ at 11 months. On multivariate analysis, $KRAS^{MUT}$ persisted as a negative factor for OS (HR 1.564, 95% CI 1.124-2.177, $p = 0.008$). $KRAS^{MUT}$ patients with high PD-L1 expression ($PD\text{-}L1^{high}$) had better OS than $PD\text{-}L1^{high}KRAS^{WT}$ patients ($p = 0.036$). In response to first-line ICB, $KRAS^{MUT}$ patients had a significantly ($p = 0.006$) better outcome than $KRAS^{WT}$ patients, with a median OS of 23 vs. 6 months. On multivariable Cox analysis, $KRAS^{MUT}$ status was an independent prognostic factor for better OS (HR 0.349, 95% CI 0.148-0.822, $p = 0.016$). *kRAS* mutations are associated with better response to treatment with immune checkpoint blockade and worse response to platinum doublet chemotherapy as well as shorter general OS in Stage IV NSCLC.

A

B



Anche la linea di demarcazione tra contenuti “grezzi” e contenuti peer reviewed sta diventando meno netta.

Questo sicuramente genera confusione, anche per chi vuole citare un singolo lavoro che però ha due versioni.

Bisogna fare chiarezza sui database e sugli indici

Qui l’avvento del digitale ha rivoluzionato il modo con cui viene giudicato l’impatto dei lavori scientifici in due modi:

Fornendo degli **indici sempre più accurati** e analitici della perfomance degli autori e dei lavori scientifici

Creando **nuovi indici** che misurano l’impatto dei lavori sia all’interno che al di fuori del ristretto cerchio degli addetti ai lavori

Gli indici di valutazione scientifica bibliometrici:

Riviste

Articoli Scientifici

Trastuzumab deruxtecan in patients with solid tumours harbouring specific activating *HER2* mutations (DESTINY-PanTumor01): an international, phase 2 study

*Bob T Li, Funda Meric-Bernstam, Aditya Bardia, Yoichi Naito, Salvatore Siena, Philippe Aftimos, Ian Anderson, Giuseppe Curigliano, Maria de Miguel, Maitri Kalra, Do-Youn Oh, Joon Oh Park, Sophie Postel-Vinay, Sun Young Rha, Taroh Satoh, Iben Spanggaard, Flavia Michelini, Ann Smith, Karime Kalil Machado, Cristina Saura, on behalf of the DESTINY-PanTumor01 study group**

Autori

Summary

Background Trastuzumab deruxtecan is a HER2-directed antibody–drug conjugate approved by the US Food and Drug Administration and the European Medicines Agency for *HER2*-mutant non-small-cell lung cancer. Few treatment options exist for patients with *HER2*-mutant solid tumours beyond lung cancers. We investigated trastuzumab deruxtecan in metastatic solid tumours with specific activating *HER2* mutations.

Methods In this open-label, phase 2, basket study done in 29 centres in Asia, Europe, and North America, we investigated trastuzumab deruxtecan (5·4 mg/kg every 3 weeks by intravenous infusion) in patients aged 18 years or older with unresectable or metastatic solid tumours with specific activating *HER2* mutations, an Eastern Cooperative Oncology Group performance status of 0 or 1, and disease progression following previous treatment (previous HER2-targeted therapy was permitted) or with no satisfactory alternative treatment options. The primary endpoint was confirmed objective response rate by independent central review. Anti-tumour activity and safety were analysed in all patients who received at least one dose of trastuzumab deruxtecan. This trial is registered with ClinicalTrials.gov, NCT04639219, and is active but no longer recruiting.

Findings Between Dec 30, 2020, and Jan 25, 2023, 102 patients (62 [61%] female and 40 [39%] male; median age 66·5 years [IQR 58–72]; 51 [50%] White, two [2%] Black or African American, 38 [37%] Asian, and 11 [11%] did not have race information reported) with solid tumours with activating *HER2* mutations received trastuzumab deruxtecan and were included in the anti-tumour activity and safety analyses sets. Patients had a median of three (IQR 2–4) previous treatment regimens. The median duration of follow-up was 8·61 months (IQR 3·71–12·68). The objective response rate by independent central review was 29·4% (95% CI 20·8–39·3; 30 of 102 patients). 52 (51%) patients had a treatment-emergent adverse event of grade 3 or worse; the most common events (in ≥5% of patients) were anaemia (16 [16%]) and neutrophil count decreased (eight [8%]). Drug-related treatment-emergent serious adverse events occurred in ten (10%) patients. Adjudicated drug-related interstitial lung disease or pneumonitis of any grade occurred in 11 patients (11%; three grade 1, five grade 2, one grade 3, and two grade 5); there were two (2%) cases of fatal adjudicated drug-related interstitial lung disease or pneumonitis.

Interpretation Trastuzumab deruxtecan showed anti-tumour activity and durable responses in heavily pretreated patients across multiple tumour types with activating *HER2* mutations, with no new safety signals. Prespecified *HER2* mutations might be targeted by HER2-directed antibody–drug conjugates and our findings support further investigation of trastuzumab deruxtecan in the pan-tumour setting.

Funding AstraZeneca and Daiichi Sankyo.

Lancet Oncol 2024; 25: 707–19
Published Online
May 3, 2024
https://doi.org/10.1016/S1470-2045(24)00140-2

*Group members listed in the appendix (p 2)

Memorial Sloan Kettering Cancer Center, New York, NY, USA (B T Li MD); Weill Cornell Medicine, Cornell University, New York, NY, USA (B T Li); Department of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA (Prof F Meric-Bernstam MD); Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA (A Bardia MD); Department of General Internal Medicine, National Cancer Center Hospital East, Kashiwa, Chiba, Japan (Y Naito MD); Niguarda Cancer Center, Grande Ospedale Metropolitano Niguarda, Milan, Italy (Prof S Siena MD); Institut Jules Bordet-Université Libre de Bruxelles, Brussels, Belgium (P Aftimos MD); Providence Medical Group, Santa Rosa, CA, USA (I Anderson MD); Istituto Europeo di Oncologia, IRCCS Milan, Italy (Prof G Curigliano MD); Department of Oncology and Hemato-Oncology, Università degli Studi di Milano (La Statale), Milan, Italy

Ci sono pochi database fondamentali dove le riviste sono indicizzate, una di gestione pubblica USA, le altre invece di società private:

Web of Science

Clarivate Analytics

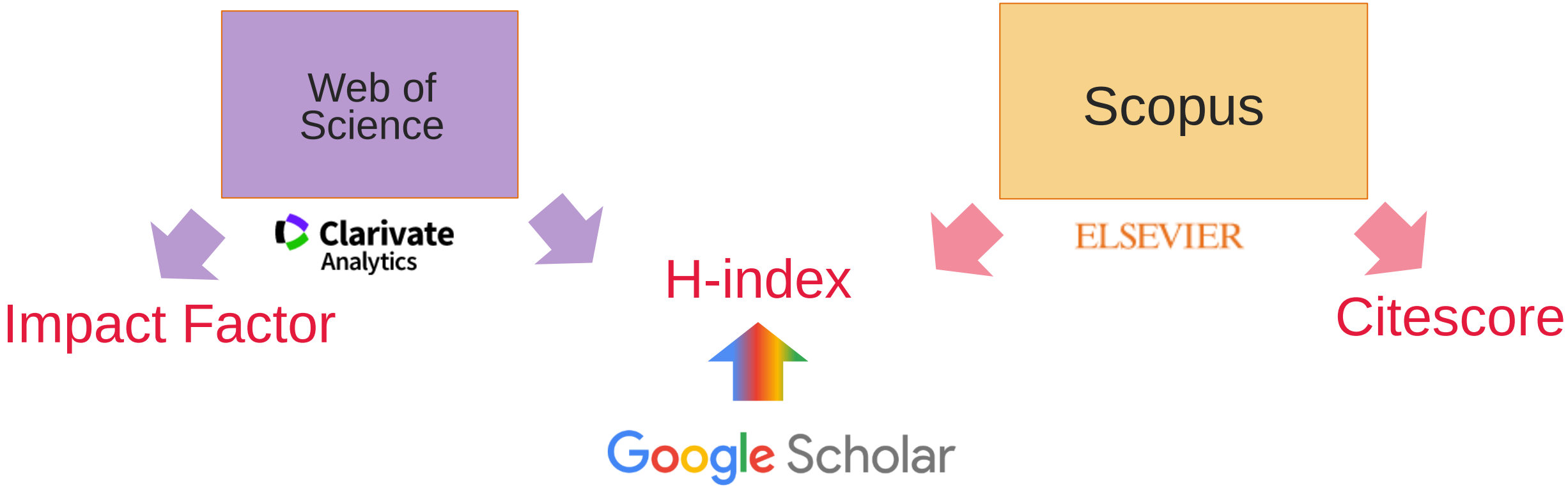
Medline/ Pubmed

Embase, Scopus

ELSEVIER

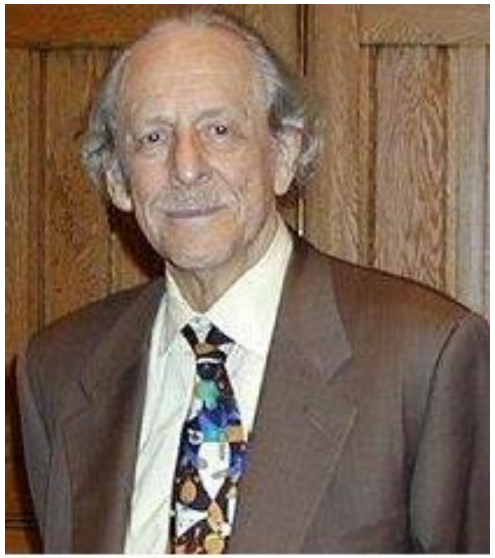
La presenza di un articolo in uno o più di questi database è un elemento di garanzia sulla qualità del lavoro, tuttavia i confini sono ora meno definiti rispetto al passato. Soprattutto….

Le società private hanno sviluppato degli indicatori di performance delle riviste: questi sono indici **bibliometrici** (quindi basati sul numero di citazioni) che vengono ottenuti analizzando i dati da due dei loro databases.



L’Impact Factor non è un indice molto recente

L’anno in cui si è iniziato a calcolare l’Impact Factor è il **1975,** ma il lavoro su cui si basa il calcolo dell’indice è stato pubblicato nel **1955**



Citation Indexes for Science

A New Dimension in Documentation through Association of Ideas

Eugene Garfield

Mr. Garfield is a documentation consultant with offices at 1530 Spring Garden St., Philadelphia 1, Pa.

1955 SCIENCE, VOL. 122

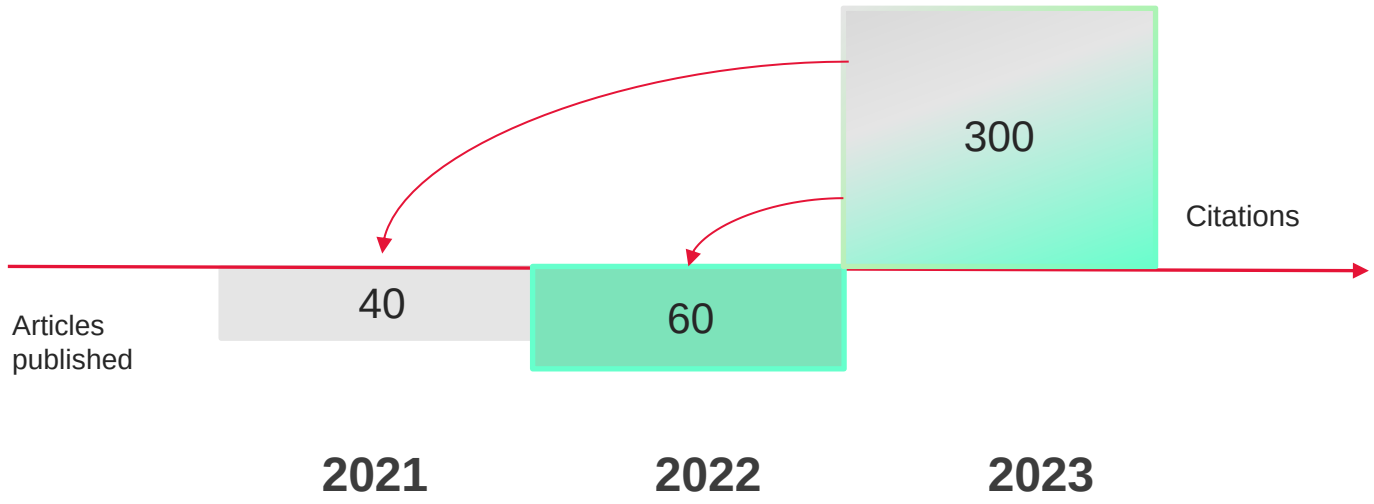
Eugene Garfield è il creatore dell’Impact Factor.

Il calcolo dell'Impact Factor

Alla data del Corso (Marzo 2025), l'ultimo IF è quello pubblicato nel Giugno **2024** che si basa sulle **citazioni** totali nell'anno **2023** dei **lavori** pubblicati nel **2021** e **2022**

È definito come il **rapporto** tra numero complessivo di citazioni da parte di qualsiasi rivista presente in Web of Science, pertinenti ad articoli della rivista in esame pubblicati nei due anni precedenti, **diviso** il numero totale degli articoli della rivista in esame pubblicati sempre nei due anni precedenti.

Esempio



$$\text{2024 IF} = \frac{300}{40 + 60} = 3.0$$

- L’IF è un indicatore (con diversi limiti) della “bontà” di una rivista ma sicuramente NON degli autori che pubblicano sulla stessa.

- Il fatto che l’IF si riferisca sempre ad articoli pubblicati 2 o 3 anni prima della valutazione la rende poco “attuale”

→ Il problema è che non abbiamo comunque niente di veramente meglio dell’IF….

I competitor dell'IF: Citescore di Elsevier

- I dati sono disponibili a tutti, non soltanto agli abbonati come nel caso dell'IF
- Solo gli articoli peer-reviewed sono inclusi nel numeratore e nel denominatore
- Si contano tutti gli articoli e tutte le citazioni presenti andando indietro fino a 4 anni.
- Il CiteScore può essere calcolato anche dopo un solo anno di pubblicazione della rivista

CiteScore non sta riuscendo a scalzare l'IF come indice di riferimento

I falsi IF (e qui cominciano i problemi dell'Open Science)

- Cite Factor
- Cosmos Impact Factor
- Directory of Indexing and Impact Factor
- General Impact Factor
- Global Impact Factor
- Global Science Citation Impact Factor
- Impact Factor Services for International Journals
- International Journal Impact Factor
- Journal Impact Factor
- Journals Impact Factor
- Research Journal Impact Factor
- Science Impact Factor
- Scientific Journal Impact Factor
- Systematic Impact Factor
- Technical Impact Factor
- Universal Impact Factor

Queste sono le fonti dei problemi….

La letteratura scientifica è sempre di più “intossicata” da lavori pseudo-scientifici pubblicati dai cosiddetti “predatory publisher” su riviste con fantomatici impact factor

I predatory publishers

The definition (Nature, dicembre 2019)

"Predatory journals and publishers are entities that prioritize self-interest at the expense of scholarship and are characterized by **false or misleading information**, **deviation from best editorial and publication practices**, a lack of transparency, and/or the **use of aggressive and indiscriminate solicitation practices.**"

Agnes Grudniewicz, David Moher, Kelly D. Cobey and 32 co-authors

SCIVISION PUBLISHERS

International Journal of Research in Oncology

Open Access

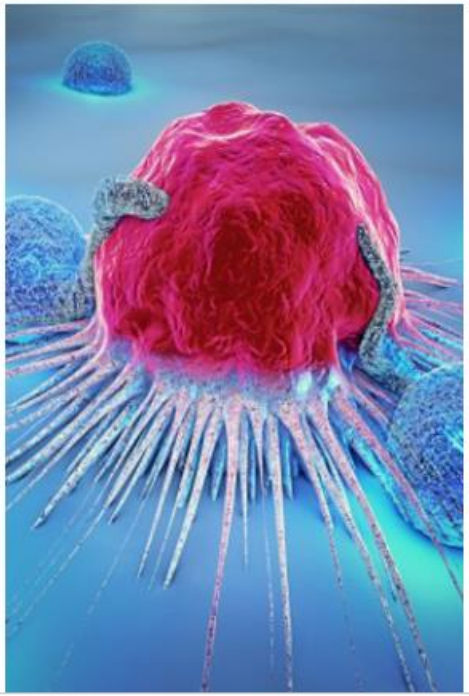
ISSN: 2833-0390

International Journal of Research in Oncology is a rigorously peer-reviewed, Open Access journal which publishes original research articles, review articles and case reports relating to oncology and cancer treatment.

IJRO accepts high quality works on all aspects of oncology research including Carcinogenesis, Breast Cancer, Chemotherapy, Lung Cancer, Gastrointestinal Cancer, Genitourinary Cancer, Head and Neck Cancer, Metastasis, Neuro-oncology, Paediatric Oncology, Skin Cancer, Soft Tissue and Bone Sarcomas, Palliative and Supportive Care, Viral oncology, etc.

Our journal strongly supports the Open Access initiative. All published articles will be assigned DOI provided by Cross Ref. International Journal of Research in Oncology will keep up-to- date with the latest advancements in the field of oncology. Abstracts and Pdfs of all articles published are freely available to everyone immediately after publication.

Authors are requested to submit manuscripts as an e-mail attachment to the Editorial Office at editor@scivisionjournals.com.



Our Articles at PubMed

Recent Articles

Abstracting and Indexing

CiteFactor Academic Scientific Journals

Google scholar

ROAD DIRECTORY OF OPEN ACCESS SCHOLARLY RESOURCES

Academic Resource Index ResearchBib

Scilit

OCLC WorldCat®

SIS Scientific Indexing Services

Metadata from Crossref

ResearchGate

Research Article

ISSN 2833-0390

International Journal of Research in Oncology

Pulsar to Overcome Acquired Resistance (AR) to Immunocheck-Point Inhibitors (ICIs) in Oligometastastic Cancer Progression: A Clinical and Translational Research

Grazia Lazzari[1]*, Angela Solazzo[1], Barbara D'Andrea[1], Ilaria Benevento[1], Antonietta Montagna[1], Alessia Giordano[2], Giovanni Storto[2], Ilaria Laurenzana[3], Antonella Caivano[3], Fiorella D'Auria[3], Giovanni Calice[4], Teodora Statuto[3], Raffaele Tucciariello[5] and Antonella Bianculli[5]

[1]*Radiation Oncology Unit, IRCCS-CROB, Rionero in Vulture (PZ), Italy.*

[2]*Nuclear Medicine Unit, Radiation Oncology Unit, IRCCS-CROB, Rionero in Vulture (PZ), Italy.*

[3]*Translational Research Laboratory, IRCCS-CROB, Rionero in Vulture (PZ), Italy.*

[4]*Biostatistic Unit, IRCCS-CROB, Rionero in Vulture (PZ), Italy.*

[5]*Physics Unit, IRCCS-CROB, Rionero in Vulture (PZ), Italy.*

*Correspondence:
Dr. Grazia Lazzari, Radiation Oncology Unit, IRCCS-CROB, Rionero in Vulture (PZ), Italy.

Received: 18 Jun 2024; **Accepted:** 01 Aug 2024; **Published:** 08 Aug 2024

Citation: Grazia Lazzari, Angela Solazzo, Barbara D'Andrea, et al. Pulsar to Overcome Acquired Resistance (AR) to Immunocheck-Point Inhibitors (ICIs) in Oligometastastic Cancer Progression: A Clinical and Translational Research. Int J Res Oncol. 2024, 3(2): 1-5.

Si trovano spesso lavori di autori italiani su predatory journals

Pubblicare su un predatory journal

- Fa perdere tempo e determina un eventuale danno economico
- Rende impossibile o comunque molto difficile ripubblicare i dati del lavoro su una rivista “seria”
- Aiuta un dark system che contribuisce alla disseminazione di fake-news credibili

Controllate sempre che il dato di Impact Factor e l’indicizzazione su PubMed siano veri!

I publishers Open Access non considerati puri predatory ma problematici:

MDPI, Frontiers, Hindawi (brand ora non più attivo)

MDPI

Viene considerato da alcuni come un predatory publisher

Research Evaluation, 30(3), 2021, 405–419
doi: 10.1093/reseval/rvab020
Advance Access Publication Date: 11 August 2021
Article

OXFORD

Journal citation reports and the definition of a predatory journal: The case of the Multidisciplinary Digital Publishing Institute (MDPI)

M. Ángeles Oviedo-García*

Economics and Business Management Faculty, Business Management and Marketing Department, Univesity of Seville, Avda. Ramón y Cajal, 1, Seville 41018, Spain

*Corresponding author. Email: maoviedo@us.es

ROYAL SOCIETY OF CHEMISTRY

Sanctioning of 50 journals raises concerns over special issues in 'mega-journals'

Il suo mega journal IJERPH ha perso l'Impact Factor

One journal delisted was the *International Journal of Environmental Research and Public Health (IJERPH)*, a so-called mega-journal that published over 9500 papers in 2020 and 17,000 papers in 2022 and had an impact factor of 4.6. In a statement, its publisher

MDPI

Journals Topics Information Author Services Initiatives About Sign In / Sign Up Submit

Search for Articles: Title / Keyword Author / Affiliation / Email Cancers All Article Types Search Advanced

Journals / Cancers

IMPACT FACTOR 6.575 Indexed in: PubMed

Marzo 2023

E-Mail Alert

MDPI

Journals Topics Information Author Services Initiatives About Sign In / Sign Up Submit

Search for Articles: Title / Keyword Author / Affiliation / Email Cancers All Article Types Search Advanced

Journals / Cancers

IMPACT FACTOR 5.2 Indexed in: PubMed CITESCORE 7.4

Marzo 2024

E-Mail Alert

Add your e-mail address to receive forthcoming issues of th

Enter Your E-Mail Ad

Subs

IMPACT FACTOR 4.5 Indexed in: PubMed CITESCORE 8.0

Marzo 2025

cancers

Submit to *Cancers*

Review for *Cancers*

Share

Journal Menu

- *Cancers* Home
- Aims & Scope
- Editorial Board
- Reviewer Board
- Topical Advisory Panel
- Instructions for Authors
- Special Issues
- Topics
- Sections & Collections
- Article Processing Charge

Monitoring and Surveillance of Patients with Gastroenteropancreatic Neuroendocrine Tumors Undergoing Radioligand Therapy

Cancers

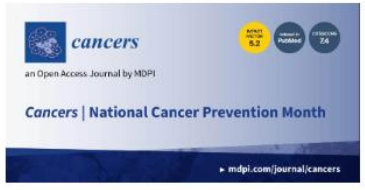
Cancers is a **peer-reviewed**, open access journal of oncology, published semimonthly online by MDPI. The **Irish Association for Cancer Research (IACR)**, **Spanish Association for Cancer Research (ASEICA)**, **Biomedical Research Centre (CIBM)**, **British Neuro-Oncology Society (BNOS)** and **Spanish Group for Cancer Immuno-Biotherapy (GÉTICA)** are affiliated with *Cancers* and their members receive a discount on the article processing charges.

- **Open Access** — free for readers, with **article processing charges (APC)** paid by authors or their institutions.

News

26 February 2024

Cancers **| National Cancer Prevention Month**



Death at MDPI

October 10, 2024 | MDPI

Young employee's death puts workplace culture in spotlight at publisher MDPI

Please stay away from MDPI

Professional Misconduct in Research

Hi everyone! I worked for MDPI for 3 years, left last year on full burnout and depression.

Last friday a colleague, a 27 years old girl from Bucharest died at the office. She collapsed at work and the manager refused to call an ambulance or "allow" her to go home, the reason being that she is ok now. After her second collapse, some colleagues called an ambulance but unfortunately it was too late.

If this post is inappropriate, delete it. I only want to share this with you and maybe you can share with others and together we can raise awareness of the tirany of this company.

Everyone is afraid of the colleagues from China, because they make all the decisions, including an inhumane work environment, full of bullying, micro management, public shaming and so on. The managers from other offices close their eyes and allow this behavior because they are afraid of losing their jobs and this unfortunately leads to the death of their employees.

Hindawi

ha avuto il maggior numero di riviste rimosse dal database di Web of Science

Web of Science de-listed 82 journals, including 15 from Hindawi

March 23, 2023 | Hindawi, Impact Factor, MDPI, Predatory Publishing, Web of

Wiley to stop using “Hindawi” name amid $18 million revenue decline

Nel Dicembre 2023 il marchio Hindawi è stato cancellato da Wiley, che aveva acquistato la società nel Dicembre 2021

THE WALL STREET JOURNAL.

May 14th, 2024

EXCLUSIVE

Flood of Fake Science Forces Multiple Journal Closures

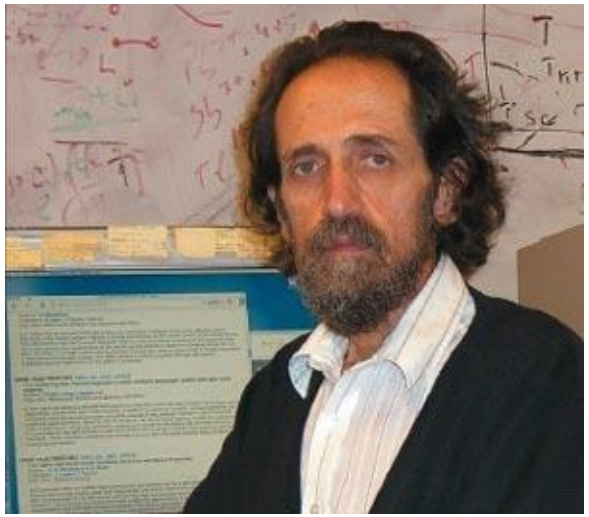
Wiley to shutter 19 more journals, some tainted by fraud

The sources of the fake science are “paper mills”—businesses or individuals that, for a price, will list a scientist as an author of a wholly or partially fabricated paper. The mill then submits the work, generally avoiding the most prestigious journals in favor of publications such as one-off special editions that might not undergo as thorough a review and where they have a better chance of getting bogus work published.

Gli indici di valutazione scientifica bibliometrici per gli autori

H-Index

Indice molto più “giovane” dell’Impact Factor, creato nel 2005



a scientist has an index h if h of their papers have at least h citations each, and their other papers have no more than h citations each

Hirsch, Jorge (2005) PNAS 46: 16569
arXiv:physics/0508025

Un h-index di 10 significa che un ricercatore ha pubblicato almeno 10 lavori che hanno avuto almeno 10 citazioni.

H-Index

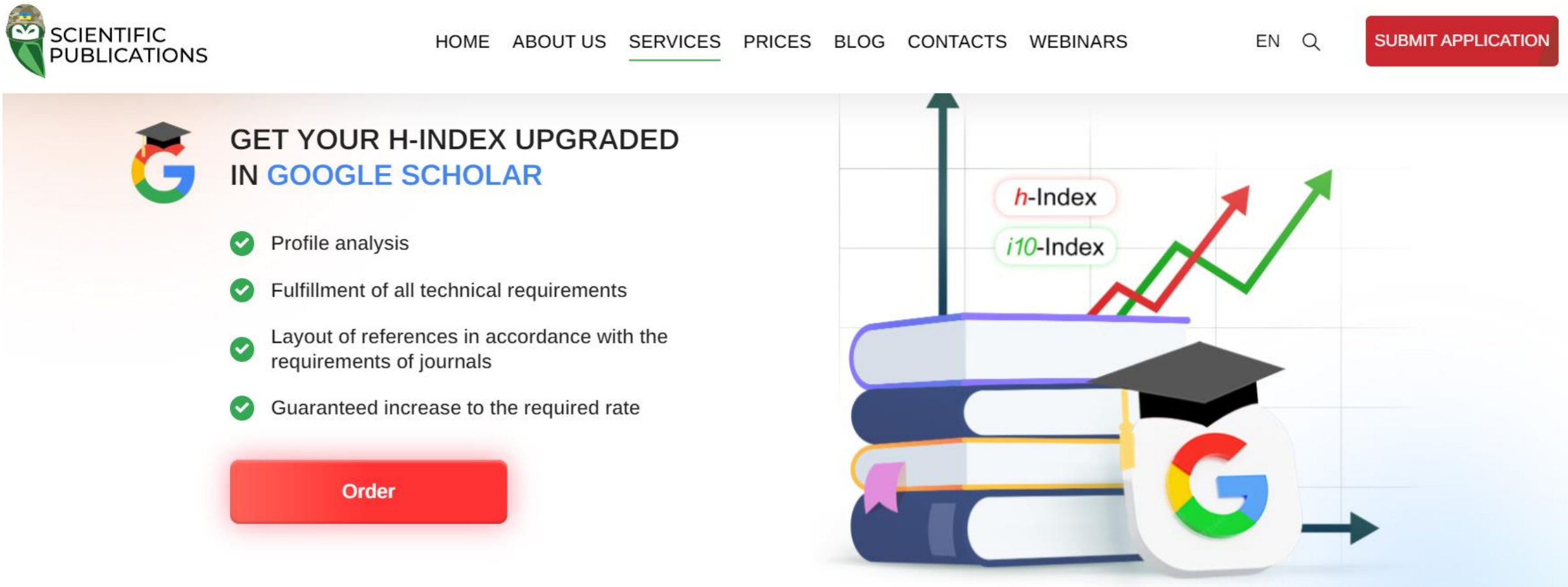
Diversi databases, tra cui Web of Science, Scopus, **Google Scholar** e altri, calcolano automaticamente l'H-index,

→quindi abbiamo DIVERSI H-index

L'H-index è un indicatore sia della quantità che della qualità dei lavori, inteso sempre come numero delle citazioni

Non è un indice per giovani (è evidente che se un autore ha pubblicato pochi articoli non potrà avere un h-index alto)

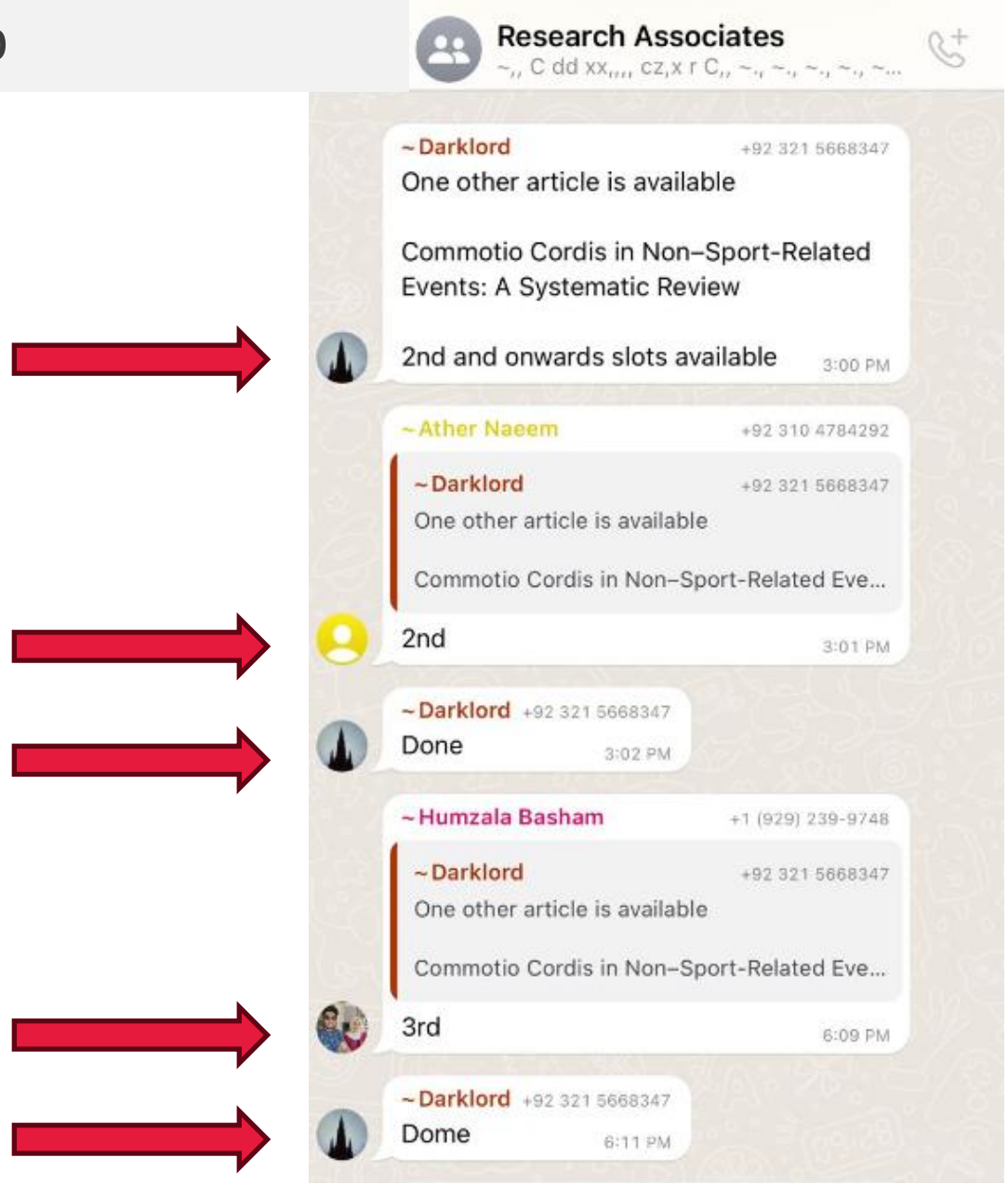
H-index di Google Scholar può essere manipolato e ci sono servizi di upgrade di H-index Google Scholar a pagamento



Ci sono servizi di authorship a pagamento

Jahanzeb Malik

A cardiologist in Pakistan has been selling coauthorship of his research papers to scientists, particularly medical students, who were not involved in the work.



Il nuovo indice di valutazione scientifica bibliometrica per gli autori

Author Beamplots

Sono il nuovo indice alternativo all’H-index, disponibile dal Marzo 2021 e basato sui dati presenti in Web of Science.

Esprimono i dati in termine di percentile rispetto alle altre pubblicazioni dello stesso anno, dello stesso argomento e dello stesso tipo di documento (articolo di ricerca originale oppure review)

Questo consente di ottenere dei dati normalizzati, quindi più confrontabili tra diverse discipline e che non dipendono dall’età accademica.

Author Beamplots

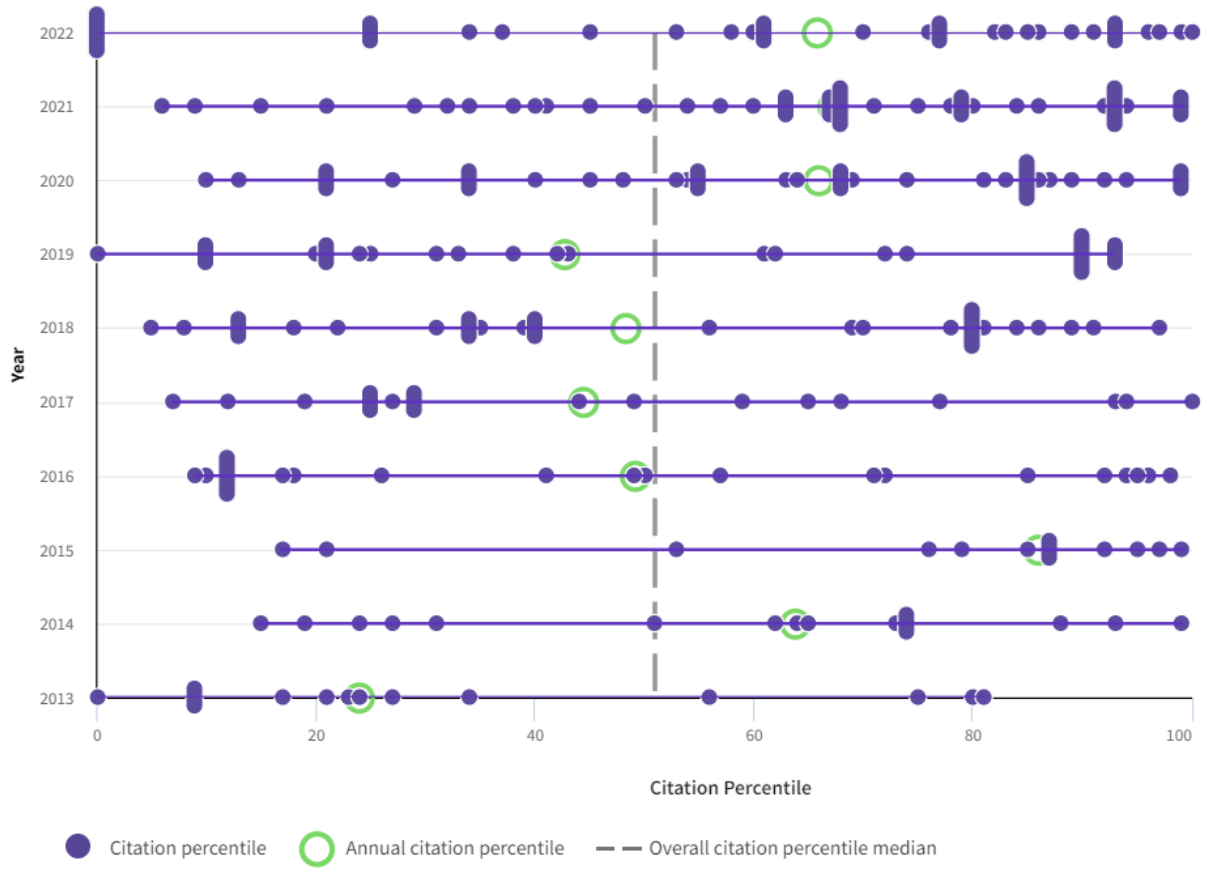
VIEWING 2 COMBINED AUTHOR RECORDS

Di Maio, Massimo *This is an algorithmically generated author record*

(Mai, Massimo Di)

University of Turin

Open Filters ›



Profile summary

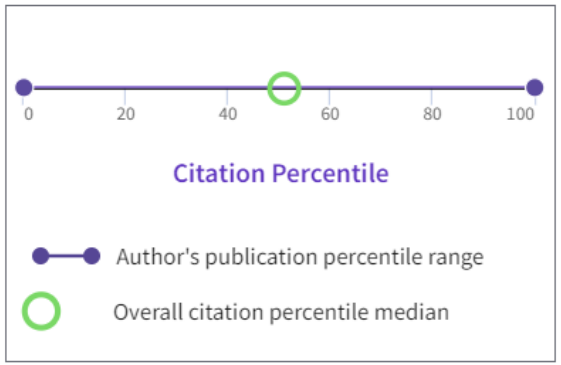
604 Total documents
603 Web of Science Core Collection publications
1 Preprint

Web of Science Core Collection metrics

56 H-Index	**603** Total Publications
11,425 Sum of Times Cited	**10,374** Citing Articles

View citation report

Author Impact Beamplot Summary

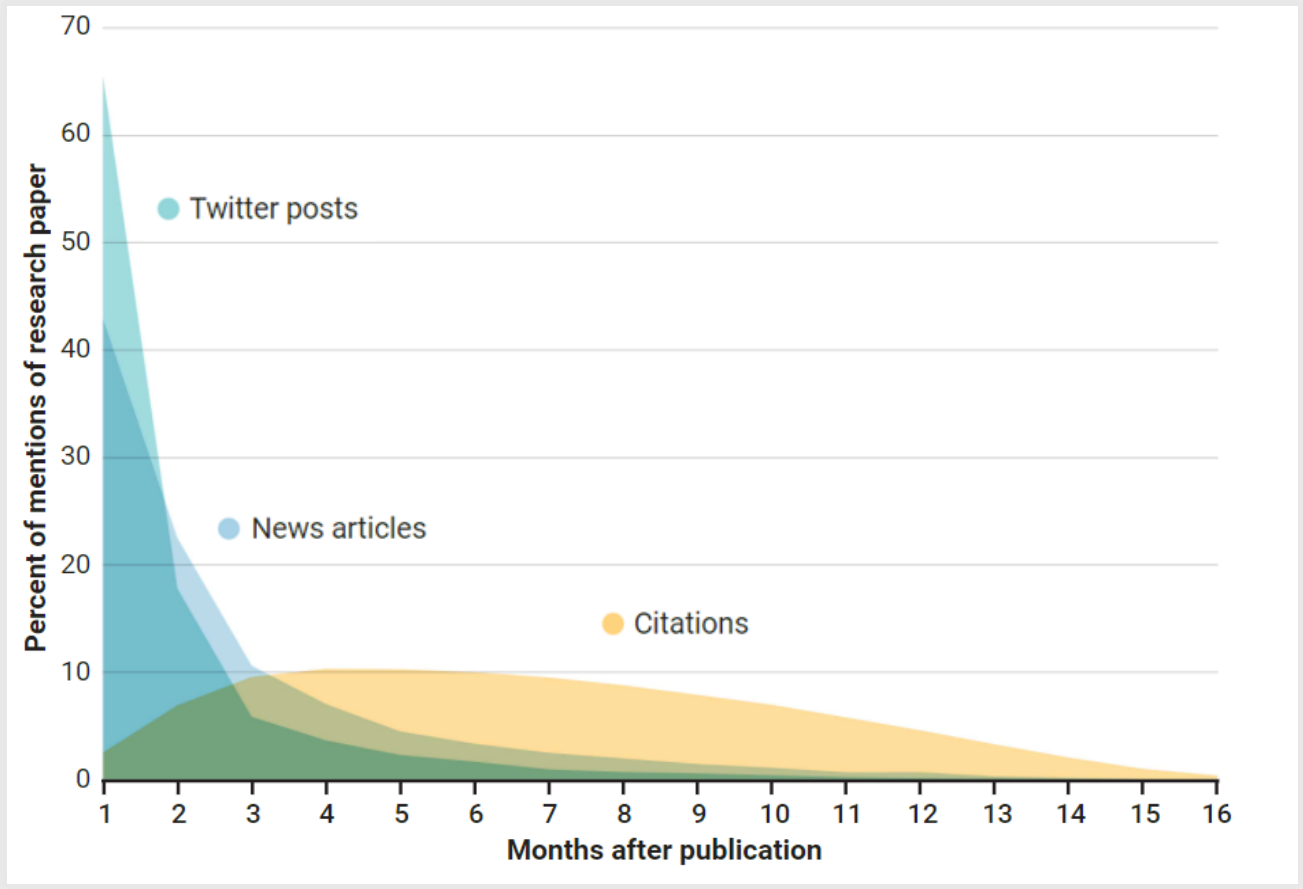


Percentile range displays for authors from 1980 to 2022 . View all publications in full beamplot.

Gli indici di valutazione degli articoli scientifici

Le citazioni sono un fenomeno molto lento, a differenza dell'impatto mediatico

Il numero di citazioni di un singolo articolo rimane un indice fondamentale dell'interesse della comunità scientifica attorno a quel contenuto



Science

24 MAR 2022 • BY JEFFREY BRAINARD

Diversi anni orsono sono stati sviluppati indici chiamati Altmetric che utilizzano i Social e altri Media come indice di “impatto” mediatico dell’articolo

I colori che formano i “donuts” riflettono il mix delle fonti che determinano lo score, azzurro per Twitter (ora X), giallo per i blog etc etc

Rappresenta forse l’elemento più *disruptive* nella misurazione dell’impatto degli articoli scientifici su una audience fatta di addetti ai lavori ma non solo

L'Attention score ha avuto una «bolla» di interesse durante la pandemia

Unexpected detection of SARS-CoV-2 antibodies in the prepandemic period in Italy.

Apolone G[1], Montomoli E[2], Manenti A[3], Boeri M[1], Sabia F[1], Hyseni I[4], Mazzini L[2], Martinuzzi D[4], Cantone L[5], Milanese G[6], Sestini S[1], Suatoni P[1], Marchianò A[1], Bollati V[5], Sozzi G[1], Pastorino U[1]

Author information

Tumori, 11 Nov 2020, 300891620974755
DOI: 10.1177/0300891620974755 PMID: 33176598

Citations & impact

This article has not been cited yet.

Impact metrics

Alternative metrics

Altmetric
Discover the attention surrounding your research
https://www.altmetric.com/details/94264046

Dati al 30 Novembre 2020

About this Attention Score

In the top 5% of all research outputs scored by Altmetric

MORE...

Mentioned by

- **205** news outlets
- **6** blogs
- **3679** tweeters
- **4** Facebook pages
- **1** Wikipedia page
- **19** Redditors

Ora si è tornati alla normalità. Il valore di Attention Score varia moltissimo.

valori di Attention Score
(scala personale)

- >1000: Interesse molto alto
- 100-1000: Interesse alto
- 10-100: Interesse medio
- <10: Interesse basso

Se diventate appassionati di Altmetric potete aggiungere un widget Altmetric nel vostro browser….

Step 1. Look up altmetrics for an article on a topic that interests you

You can find altmetrics using several tools that are free to researchers.

Altmetric bookmarklet

A. **Download** the Altmetric browser bookmarklet: https://www.altmetric.com/products/free-tools/bookmarklet/

B. **Visit** an article on a topic that interests you (or your own article) on a publisher's site

C. **Click** the bookmarklet to see an abbreviated report of the altmetrics for the article

D. "**Click for more details**" to see the Altmetric details page

E. **Move** on to Step 2

ARTICLES · Volume 25, Issue 6, P707-719, June 2024 Download Full Issue

Trastuzumab deruxtecan in patients with solid tumours harbouring specific activating *HER2* mutations (DESTINY-PanTumor01): an international, phase 2 study

Bob T Li, MD [a,b] · Prof Funda Meric-Bernstam, MD [c] · Aditya Bardia, MD [d] · Yoichi Naito, MD [e] · Prof Salvatore Siena, MD [f,j] · Philippe Aftimos, MD [g] · et al. Show more

Affiliations & Notes · Article Info

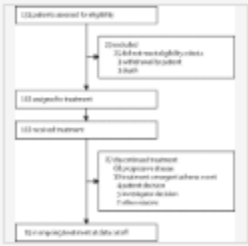
Show Outline

Summary

Background

Trastuzumab deruxtecan is a HER2-directed antibody–drug conjugate approved by the US Food and Drug Administration and the European Medicines Agency for *HER2*-mutant non-small-cell lung cancer. Few treatment options exist for patients with *HER2*-mutant solid tumours beyond lung cancers. We investigated trastuzumab deruxtecan in metastatic solid tumours with specific activating *HER2* mutations.

Figures (3) Figure Viewer



Il potenziale problema di Altmetric…

Altmetric ha iniziato a monitorare altri social networks tra cui BlueSky

Visualizing Impact: Plum Print

- Includes the 5 categories of metrics
- Circles dynamically change size based on metrics in each category

- Citations
- Usage
- Captures
- Mentions
- Social Media

} ALLmetrics

Indici classici

Indici innovativi

Riviste	Articoli Scientifici	Autori
Impact Factor	Numero di citazioni	H-index
	Altmetric	**Author Beamplots**

L’ERA OPEN SCIENCE

1998 

Medline diventa disponibile a tutti, gratis

2000 

Vengono lanciate le riviste Fully Open Access

2004 

Nascono Twitter, LinkedIn e Google Scholar

2011 

Viene coniato il termine Altmetrics

2012 

Anche i Top Journal diventano sempre piu ibridi

2013 

Vengono scoperti i predatory publisher

2020 

Proliferano i preprints

2021 

Vengono scoperti i papermills

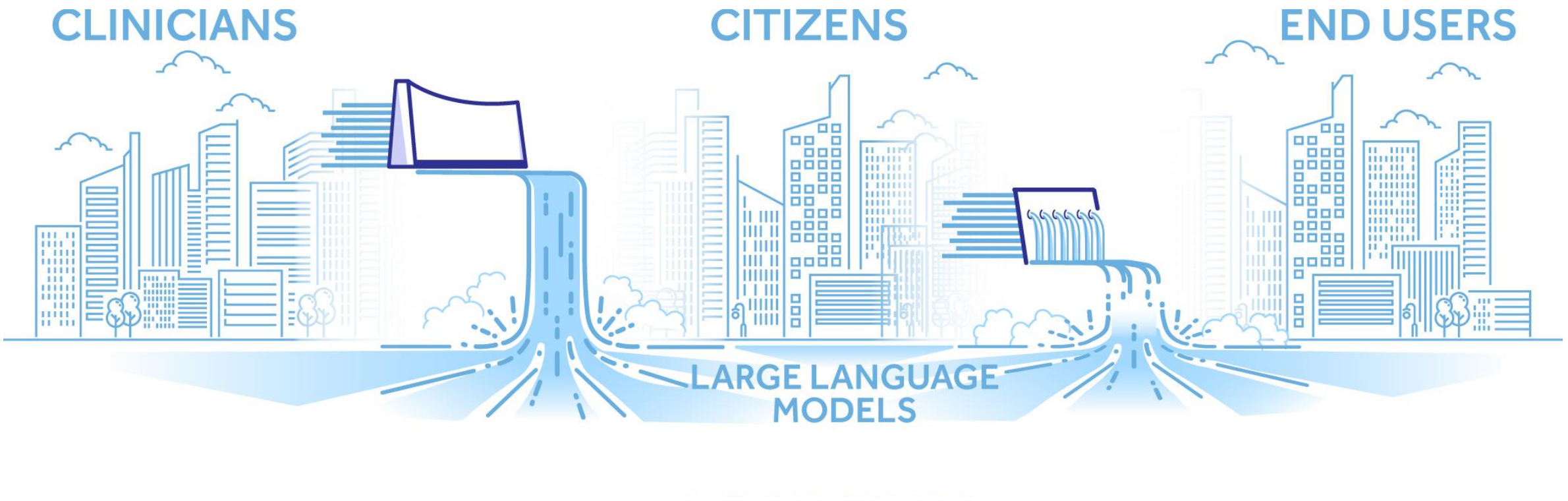
2022 

Twitter diventa X

2023 

L’AI generativa entra prepotentemente nel publishing

L’avvento della intelligenza artificiale generativa rende ancora più complesso lo scenario della letteratura scientifica



Research Letter

ONLINE FIRST

November 9, 2023

JAMA Ophthalmol. Published online November 9, 2023. doi:10.1001/jamaophthalmol.2023.5162

Large Language Model Advanced Data Analysis Abuse to Create a Fake Data Set in Medical Research

Andrea Taloni, MD[1]; Vincenzo Scorcia, MD[1]; Giuseppe Giannaccare, MD, PhD[1,2]

[1]Department of Ophthalmology, University Magna Graecia of Catanzaro, Catanzaro, Italy

[2]Eye Clinic, Department of Surgical Sciences, University of Cagliari, Cagliari, Italy

Gli autori hanno chiesto a ChatGpt di creare dati su 250 “pazienti” con cheratocono e che sarebbero stati sottoposti a due tecniche alternative di cheratoplastica (Dalk e Pk).

Hanno predefinito il range di dati che il database avrebbe dovuto contenere, cosi **che la loro analisi generasse le caratteristiche demografiche e cliniche attese** e che soprattutto **potesse dimostrare un’efficacia significativamente superiore** per la Dalk rispetto alla Pk (l’ipotesi di lavoro da testare nello studio).

A parte alcune piccole incongruenze nella distribuzione dei dati dei “pazienti”, **il database creato ad hoc era del tutto credibile.**

Come «richiesto» dagli autori, riusciva a dimostrare una superiorità statisticamente significativa di una tecnica rispetto all’altra.

Harvard Kennedy School Misinformation Review[1]
September 2024, Volume 5, Issue 5

Reprints and permissions: misinforeview@hks.harvard.edu
DOI: https://doi.org/10.37016/mr-2020-156
Website: https://misinforeview.hks.harvard.edu

Research Note

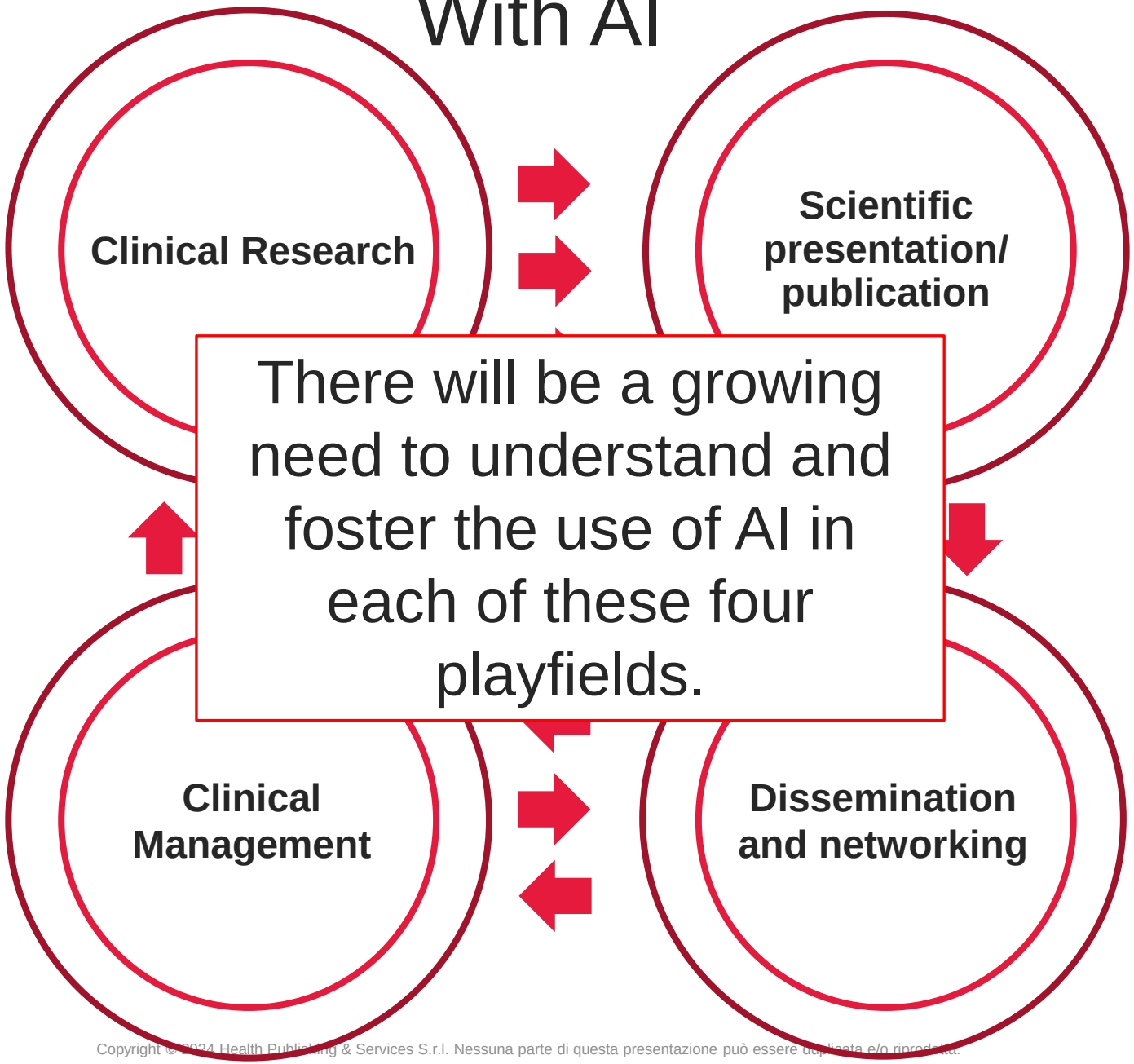
GPT-fabricated scientific papers on Google Scholar: Key features, spread, and implications for preempting evidence manipulation

Academic journals, archives, and repositories are seeing an increasing number of questionable research papers clearly produced using generative AI. They are often created with widely available, general-purpose AI applications, most likely ChatGPT, and mimic scientific writing. Google Scholar easily locates and lists these questionable papers alongside reputable, quality-controlled research. Our analysis of a selection of questionable GPT-fabricated scientific papers found in Google Scholar shows that many are about applied, often controversial topics susceptible to disinformation: the environment, health, and computing. The resulting enhanced potential for malicious manipulation of society's evidence base, particularly in politically divisive domains, is a growing concern.

Authors: Jutta Haider (1), Kristofer Rolf Söderström (2), Björn Ekström (1), Malte Rödl (3)
Affiliations: (1) Swedish School of Library and Information Science, University of Borås, Sweden, (2) Department of Arts and Cultural Sciences, Lund University, Sweden, (3) Division of Environmental Communication, Swedish University of Agricultural Sciences, Sweden
How to cite: Haider, J., Söderström, K. R., Ekström, B., & Rödl, M. (2024). GPT-fabricated scientific papers on Google Scholar: Key features, spread, and implications for preempting evidence manipulation. *Harvard Kennedy School (HKS) Misinformation Review*, 5(5).
Received: May 20th, 2024. Accepted: August 14th, 2024. Published: September 3rd, 2024.

With AI

More data will be generated at a faster rate, collected in the clinics and analyzed in multiple ways, to foster R&D and its application into practice



More data will be translated into manuscripts to be submitted and articles to be published. Information will be disseminated through multiple channels at a faster rate

Q&A

Giulio.Zuanetti@aboutscience.eu

Giulio.Zuanetti@aboutpharma.com

https://www.linkedin.com/in/giuliozuanetti/

SACRO CUORE DON CALABRIA

ECI CANCER CENTRE

I R C C S

SCUOLA DI METODOLOGIA DELLA RICERCA CLINICA

2025 - 11ª EDIZIONE

MODULI SPECIALISTICI - S1

VENERDÌ 14 - SABATO 15 MARZO 2025

NEGRAR DI VALPOLICELLA (VR)

Centro Formazione IRCCS "Sacro Cuore - Don Calabria"

Summary of Findings tables
(S.O.F. / Tabelle Sinottiche dell'Evidenza)

Ivan MOSCHETTI

Cos'è la Summary Of Findings

- **Summary of findings**: tabular presentation of key information about relevant outcomes of alternative health care interventions. It presents information about the body of evidence, key numerical results, and **summary judgment about the certainty of underlying evidence** for each outcome. SoF table has been chosen by the Cochrane Collaboration to present main findings of a systematic review.

Evidence profile: summary of evidence for a given question; it rpesentes relevant information about the body of evidence, key numerical results, and with a **detailed quality assessment** and a explicit judgment of each factor that determines the quality. Used by guideline producers

PICO

Self management for patients with chronic obstructive pulmonary disease

Patient or population: patients with chronic obstructive pulmonary disease
Settings: primary care, community, outpatient
Intervention: self management[1]
Comparision: usual care

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **usual care**	Corresponding risk **self management**				
Quality of Life St George's Respiratory Questionnaire. Scale from: 0 to 100. (follow-up: 3 to 12 months)	The mean quality of life ranged across control groups from **38 to 60 points**	The mean Quality of Life in the intervention groups was **2.58 lower** (5.14 to 0.02 lower)		698 (7)	⊕⊕⊕◯ **moderate**[2]	Lower score indicates better quality of life. A change of less than 4 points is not shown to be important to patients.
Dyspnoea Borg Scale. Scale from: 0 to 10. (follow-up: 3 to 6 months)	The mean dyspnoea ranged across control groups from **1.2 to 4.1 points**	The mean Dyspnoea in the intervention groups was **0.53 lower** (0.96 to 0.1 lower)		144 (2)	⊕⊕◯◯ **low**[3,4]	Lower score indicates improvement
Number and severity of exacerbations[5]	See comment	See comment	Not estimable[5]	591 (3)	See comment	Effect is uncertain
Respiratory-related hospital admissions (follow-up: 3 to 12 months)	**Low risk population**[6] **10 per 100**	**7 per 100** (5 to 9)	**OR 0.64** (0.47 to 0.89)	966 (8)	⊕⊕⊕◯ **moderate**[7]	
	High risk population[6] **50 per 100**	**35 per 100** (27 to 46)				
Emergency department visits for lung diseases (follow-up: 6 to 12 months)	The mean emergency department visits for lung diseases ranged across control groups from **0.2 to 0.7 visits per person per year**	The mean Emergency department visits for lung diseases in the intervention groups was **0.1 higher** (0.2 lower to 0.3 higher)		328 (4)	⊕⊕⊕◯ **moderate**[4]	
Doctor and nurse visits (follow-up: 6 to 12 months)	The mean doctor and nurse visits ranged across control groups from **1 to 5 vists per**	The mean Doctor and nurse visits in the intervention groups was **0.02 higher** (1 lower to 1 higher)		629 (8)	⊕⊕⊕◯ **moderate**[8]	

McMaster University
Inspiring Innovation and Discovery

Primary outcomes – up to 7

Self management for patients with chronic obstructive pulmonary disease

Patient or population: patients with chronic obstructive pulmonary disease
Settings: primary care, community, outpatient
Intervention: self management[1]
Comparision: usual care

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **usual care**	Corresponding risk **self management**				
Quality of Life St George's Respiratory Questionnaire. Scale from: 0 to 100. (follow-up: 3 to 12 months)	The mean quality of life ranged across control groups from **38 to 60 points**	The mean Quality of Life in the intervention groups was **2.58 lower** (5.14 to 0.02 lower)		698 (7)	⊕⊕⊕◯ **moderate**[2]	Lower score indicates better quality of life. A change of less than 4 points is not shown to be important to patients.
Dyspnoea Borg Scale. Scale from: 0 to 10. (follow-up: 3 to 6 months)	The mean dyspnoea ranged across control groups from **1.2 to 4.1 points**	The mean Dyspnoea in the intervention groups was **0.53 lower** (0.96 to 0.1 lower)		144 (2)	⊕⊕◯◯ **low**[3,4]	Lower score indicates improvement
Number and severity of exacerbations[5]	See comment	See comment	Not estimable[5]	591 (3)	See comment	Effect is uncertain
Respiratory-related hospital admissions (follow-up: 3 to 12 months)	**Low risk population**[6]		**OR 0.64** (0.47 to 0.89)	966 (8)	⊕⊕⊕◯ **moderate**[7]	
	10 per 100	**7 per 100** (5 to 9)				
	High risk population[6]					
	50 per 100	**35 per 100** (27 to 46)				
Emergency department visits for lung diseases (follow-up: 6 to 12 months)	The mean emergency department visits for lung diseases ranged across control groups from **0.2 to 0.7 visits per person per year**	The mean Emergency department visits for lung diseases in the intervention groups was **0.1 higher** (0.2 lower to 0.3 higher)		328 (4)	⊕⊕⊕◯ **moderate**[4]	
Doctor and nurse visits (follow-up: 6 to 12 months)	The mean doctor and nurse visits ranged across control groups from **1 to 5 vists per**	The mean Doctor and nurse visits in the intervention groups was **0.02 higher** (1 lower to 1 higher)		629 (8)	⊕⊕⊕◯ **moderate**[8]	

- Choose primary outcomes early – avoid reporting bias
- Choose patient important outcomes
- Include primary outcomes – even if no information
- Describe the outcome – scale, follow-up

McMaster University
Inspiring Innovation and Discovery

Results – Baseline risks (Assumed Risk)

Self management for patients with chronic obstructive pulmonary disease

Patient or population: patients with chronic obstructive pulmonary disease
Settings: primary care, community, outpatient
Intervention: self management[1]
Comparision: usual care

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **usual care**	Corresponding risk **self management**				
Quality of Life St George's Respiratory Questionnaire. Scale from: 0 to 100. (follow-up: 3 to 12 months)	The mean quality of life ranged across control groups from **38 to 60 points**	The mean Quality of Life in the intervention groups was **2.58 lower** (5.14 to 0.02 lower)		698 (7)	⊕⊕⊕◯ **moderate**[2]	Lower score indicates better quality of life. A change of less than 4 points is not shown to be important to patients.
Dyspnoea Borg Scale. Scale from: 0 to 10. (follow-up: 3 to 6 months)	The mean dyspnoea ranged across control groups from **1.2 to 4.1 points**	The mean Dyspnoea in the intervention groups was **0.53 lower** (0.96 to 0.1 lower)		144 (2)	⊕⊕◯◯ **low**[3,4]	Lower score indicates improvement
Number and severity of exacerbations[5]	See comment	See comment	Not estimable[5]	591 (3)	See comment	Effect is uncertain
Respiratory-related hospital admissions (follow-up: 3 to 12 months)	**Low risk population**[6] **10 per 100**	**7 per 100** (5 to 9)	**OR 0.64** (0.47 to 0.89)	966 (8)	⊕⊕⊕◯ **moderate**[7]	
	High risk population[6] **50 per 100**	**35 per 100** (27 to 46)				
Emergency department visits for lung diseases (follow-up: 6 to 12 months)	The mean emergency department visits for lung diseases ranged across control groups from **0.2 to 0.7 visits per person per year**	The mean Emergency department visits for lung diseases in the intervention groups was **0.1 higher** (0.2 lower to 0.3 higher)		328 (4)	⊕⊕⊕◯ **moderate**[4]	
Doctor and nurse visits (follow-up: 6 to 12 months)	The mean doctor and nurse visits ranged across control groups from **1 to 5 vists per**	The mean Doctor and nurse visits in the intervention groups was **0.02 higher** (1 lower to 1 higher)		629 (8)	⊕⊕⊕◯ **moderate**[8]	

- From meta-analysis
- Needs to be representative of population
- Can present mean, range, low risk, moderate risk, high risk

McMaster University
Inspiring Innovation and Discovery

Results – Risk with intervention (Corresponding Risk)

Self management for patients with chronic obstructive pulmonary disease

Patient or population: patients with chronic obstructive pulmonary disease
Settings: primary care, community, outpatient
Intervention: self management[1]
Comparision: usual care

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **usual care**	Corresponding risk **self management**				
Quality of Life St George's Respiratory Questionnaire. Scale from: 0 to 100. (follow-up: 3 to 12 months)	The mean quality of life ranged across control groups from **38 to 60 points**	The mean Quality of Life in the intervention groups was **2.58 lower** (5.14 to 0.02 lower)		698 (7)	⊕⊕⊕◯ **moderate**[2]	Lower score indicates better quality of life. A change of less than 4 points is not shown to be important to patients.
Dyspnoea Borg Scale. Scale from: 0 to 10. (follow-up: 3 to 6 months)	The mean dyspnoea ranged across control groups from **1.2 to 4.1 points**	The mean Dyspnoea in the intervention groups was **0.53 lower** (0.96 to 0.1 lower)		144 (2)	⊕⊕◯◯ **low**[3,4]	Lower score indicates improvement
Number and severity of exacerbations[5]	See comment	See comment	Not estimable[5]	591 (3)	See comment	Effect is uncertain
Respiratory-related hospital admissions (follow-up: 3 to 12 months)	**Low risk population**[6] **10 per 100**	**7 per 100** (5 to 9)	**OR 0.64** (0.47 to 0.89)	966 (8)	⊕⊕⊕◯ **moderate**[7]	
	High risk population[6] **50 per 100**	**35 per 100** (27 to 46)				
Emergency department visits for lung diseases (follow-up: 6 to 12 months)	The mean emergency department visits for lung diseases ranged across control groups from **0.2 to 0.7 visits per person per year**	The mean Emergency department visits for lung diseases in the intervention groups was **0.1 higher** (0.2 lower to 0.3 higher)		328 (4)	⊕⊕⊕◯ **moderate**[4]	
Doctor and nurse visits (follow-up: 6 to 12 months)	The mean doctor and nurse visits ranged across control groups from **1 to 5 vists per**	The mean Doctor and nurse visits in the intervention groups was **0.02 higher** (1 lower to 1 higher)		629 (8)	⊕⊕⊕◯ **moderate**[8]	

- Calculated using the Relative Effect or Mean Differences
- Confidence intervals provided

McMaster University
Inspiring Innovation and Discovery

Results – Relative effects

Self management for patients with chronic obstructive pulmonary disease

Patient or population: patients with chronic obstructive pulmonary disease
Settings: primary care, community, outpatient
Intervention: self management[1]
Comparision: usual care

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **usual care**	Corresponding risk **self management**				
Quality of Life St George's Respiratory Questionnaire. Scale from: 0 to 100. (follow-up: 3 to 12 months)	The mean quality of life ranged across control groups from **38 to 60 points**	The mean Quality of Life in the intervention groups was **2.58 lower** (5.14 to 0.02 lower)		698 (7)	⊕⊕⊕◯ **moderate**[2]	Lower score indicates better quality of life. A change of less than 4 points is not shown to be important to patients.
Dyspnoea Borg Scale. Scale from: 0 to 10. (follow-up: 3 to 6 months)	The mean dyspnoea ranged across control groups from **1.2 to 4.1 points**	The mean Dyspnoea in the intervention groups was **0.53 lower** (0.96 to 0.1 lower)		144 (2)	⊕⊕◯◯ **low**[3,4]	Lower score indicates improvement
Number and severity of exacerbations[5]	See comment	See comment	Not estimable[5]	591 (3)	See comment	Effect is uncertain
Respiratory-related hospital admissions (follow-up: 3 to 12 months)	**Low risk population**[6] **10 per 100**	**7 per 100** (5 to 9) **High risk population**[6] **50 per 100**	**OR 0.64** (0.47 to 0.89)	966 (8)	⊕⊕⊕◯ **moderate**[7]	
Emergency department visits for lung diseases (follow-up: 6 to 12 months)	The mean emergency department visits for lung diseases ranged across control groups from **0.2 to 0.7 visits per person per year**	The mean Emergency department visits for lung diseases in the intervention groups was **0.1 higher** (0.2 lower to 0.3 higher)		328 (4)	⊕⊕⊕◯ **moderate**[4]	
Doctor and nurse visits (follow-up: 6 to 12 months)	The mean doctor and nurse visits ranged across control groups from **1 to 5 vists per**	The mean Doctor and nurse visits in the intervention groups was **0.02 higher** (1 lower to 1 higher)		629 (8)	⊕⊕⊕◯ **moderate**[8]	

- From meta-analysis
- Relative Risks, Odds ratios, Hazard ratios, etc.

McMaster University
Inspiring Innovation and Discovery

Results – Number of Participants/studies

Self management for patients with chronic obstructive pulmonary disease

Patient or population: patients with chronic obstructive pulmonary disease
Settings: primary care, community, outpatient
Intervention: self management[1]
Comparision: usual care

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **usual care**	Corresponding risk **self management**				
Quality of Life St George's Respiratory Questionnaire. Scale from: 0 to 100. (follow-up: 3 to 12 months)	The mean quality of life ranged across control groups from **38 to 60 points**	The mean Quality of Life in the intervention groups was **2.58 lower** (5.14 to 0.02 lower)		698 (7)	⊕⊕⊕◯ **moderate**[2]	Lower score indicates better quality of life. A change of less than 4 points is not shown to be important to patients.
Dyspnoea Borg Scale. Scale from: 0 to 10. (follow-up: 3 to 6 months)	The mean dyspnoea ranged across control groups from **1.2 to 4.1 points**	The mean Dyspnoea in the intervention groups was **0.53 lower** (0.96 to 0.1 lower)		144 (2)	⊕⊕◯◯ **low**[3,4]	Lower score indicates improvement
Number and severity of exacerbations[5]	See comment	See comment	Not estimable[5]	591 (3)	See comment	Effect is uncertain
Respiratory-related hospital admissions (follow-up: 3 to 12 months)	**Low risk population**[6] **10 per 100**	**7 per 100** (5 to 9)	**OR 0.64** (0.47 to 0.89)	966 (8)	⊕⊕⊕◯ **moderate**[7]	
	High risk population[6] **50 per 100**	**35 per 100** (27 to 46)				
Emergency department visits for lung diseases (follow-up: 6 to 12 months)	The mean emergency department visits for lung diseases ranged across control groups from **0.2 to 0.7 visits per person per year**	The mean Emergency department visits for lung diseases in the intervention groups was **0.1 higher** (0.2 lower to 0.3 higher)		328 (4)	⊕⊕⊕◯ **moderate**[4]	
Doctor and nurse visits (follow-up: 6 to 12 months)	The mean doctor and nurse visits ranged across control groups from **1 to 5 vists per**	The mean Doctor and nurse visits in the intervention groups was **0.02 higher** (1 lower to 1 higher)		629 (8)	⊕⊕⊕◯ **moderate**[8]	

- From meta-analysis
- Or when no meta-analysis from individual studies

McMaster University
Inspiring Innovation and Discovery

Results

Self management for patients with chronic obstructive pulmonary disease

Patient or population: patients with chronic obstructive pulmonary disease
Settings: primary care, community, outpatient
Intervention: self management[1]
Comparision: usual care

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **usual care**	Corresponding risk **self management**				
Quality of Life St George's Respiratory Questionnaire. Scale from: 0 to 100. (follow-up: 3 to 12 months)	The mean quality of life ranged across control groups from **38 to 60 points**	The mean Quality of Life in the intervention groups was **2.58 lower** (5.14 to 0.02 lower)		698 (7)	⊕⊕⊕◯ **moderate**[2]	Lower score indicates better quality of life. A change of less than 4 points is not shown to be important to patients.
Dyspnoea Borg Scale. Scale from: 0 to 10. (follow-up: 3 to 6 months)	The mean dyspnoea ranged across control groups from **1.2 to 4.1 points**	The mean Dyspnoea in the intervention groups was **0.53 lower** (0.96 to 0.1 lower)		144 (2)	⊕⊕◯◯ **low**[3,4]	Lower score indicates improvement
Number and severity of exacerbations[5]	See comment	See comment	Not estimable[5]	591 (3)	See comment	Effect is uncertain
Respiratory-related hospital admissions (follow-up: 3 to 12 months)	**Low risk population**[6] **10 per 100**	**7 per 100** (5 to 9)	**OR 0.64** (0.47 to 0.89)	966 (8)	⊕⊕⊕◯ **moderate**[7]	
	High risk population[6] **50 per 100**	**35 per 100** (27 to 46)				
Emergency department visits for lung diseases (follow-up: 6 to 12 months)	The mean emergency department visits for lung diseases ranged across control groups from **0.2 to 0.7 visits per person per year**	The mean Emergency department visits for lung diseases in the intervention groups was **0.1 higher** (0.2 lower to 0.3 higher)		328 (4)	⊕⊕⊕◯ **moderate**[4]	
Doctor and nurse visits (follow-up: 6 to 12 months)	The mean doctor and nurse visits ranged across control groups from **1 to 5 vists per**	The mean Doctor and nurse visits in the intervention groups was **0.02 higher** (1 lower to 1 higher)		629 (8)	⊕⊕⊕◯ **moderate**[8]	

- Describes the score on a scale (38 to 60 points)
- Describes change on the scale with intervention (2.58 points lower)

McMaster University
Inspiring Innovation and Discovery

Results – Outcomes not reported / not measured / not pooled

Self management for patients with chronic obstructive pulmonary disease

Patient or population: patients with chronic obstructive pulmonary disease
Settings: primary care, community, outpatient
Intervention: self management[1]
Comparision: usual care

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **usual care**	Corresponding risk **self management**				
Quality of Life St George's Respiratory Questionnaire. Scale from: 0 to 100. (follow-up: 3 to 12 months)	The mean quality of life ranged across control groups from **38 to 60 points**	The mean Quality of Life in the intervention groups was **2.58 lower** (5.14 to 0.02 lower)		698 (7)	⊕⊕⊕◯ **moderate**[2]	Lower score indicates better quality of life. A change of less than 4 points is not shown to be important to patients.
Dyspnoea Borg Scale. Scale from: 0 to 10. (follow-up: 3 to 6 months)	The mean dyspnoea ranged across control groups from **1.2 to 4.1 points**	The mean Dyspnoea in the intervention groups was **0.53 lower** (0.96 to 0.1 lower)		144 (2)	⊕⊕◯◯ **low**[3,4]	Lower score indicates improvement
Number and severity of exacerbations[5]	See comment	See comment	Not estimable[5]	591 (3)	See comment	Effect is uncertain
Respiratory-related hospital admissions (follow-up: 3 to 12 months)	**Low risk population**[6] **10 per 100**	**7 per 100** (5 to 9)	**OR 0.64** (0.47 to 0.89)	966 (8)	⊕⊕⊕◯ **moderate**[7]	
	High risk population[6] **50 per 100**	**35 per 100** (27 to 46)				
Emergency department visits for lung diseases (follow-up: 6 to 12 months)	The mean emergency department visits for lung diseases ranged across control groups from **0.2 to 0.7 visits per person per year**	The mean Emergency department visits for lung diseases in the intervention groups was **0.1 higher** (0.2 lower to 0.3 higher)		328 (4)	⊕⊕⊕◯ **moderate**[4]	
Doctor and nurse visits (follow-up: 6 to 12 months)	The mean doctor and nurse visits ranged across control groups from **1 to 5 vists per**	The mean Doctor and nurse visits in the intervention groups was **0.02 higher** (1 lower to 1 higher)		629 (8)	⊕⊕⊕◯ **moderate**[8]	

- Outcomes without data are still presented
- Outcomes not pooled are still presented and graded

McMaster University
Inspiring Innovation and Discovery

Comments

Self management for patients with chronic obstructive pulmonary disease

Patient or population: patients with chronic obstructive pulmonary disease
Settings: primary care, community, outpatient
Intervention: self management[1]
Comparision: usual care

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **usual care**	Corresponding risk **self management**				
Quality of Life St George's Respiratory Questionnaire. Scale from: 0 to 100. (follow-up: 3 to 12 months)	The mean quality of life ranged across control groups from **38 to 60 points**	The mean Quality of Life in the intervention groups was **2.58 lower** (5.14 to 0.02 lower)		698 (7)	⊕⊕⊕◯ **moderate**[2]	Lower score indicates better quality of life. A change of less than 4 points is not shown to be important to patients.
Dyspnoea Borg Scale. Scale from: 0 to 10. (follow-up: 3 to 6 months)	The mean dyspnoea ranged across control groups from **1.2 to 4.1 points**	The mean Dyspnoea in the intervention groups was **0.53 lower** (0.96 to 0.1 lower)		144 (2)	⊕⊕◯◯ **low**[3,4]	Lower score indicates improvement
Number and severity of exacerbations[5]	See comment	See comment	Not estimable[5]	591 (3)	See comment	Effect is uncertain
Respiratory-related hospital admissions (follow-up: 3 to 12 months)	**Low risk population**[6]		**OR 0.64** (0.47 to 0.89)	966 (8)	⊕⊕⊕◯ **moderate**[7]	
	10 per 100	**7 per 100** (5 to 9)				
	High risk population[6]					
	50 per 100	**35 per 100** (27 to 46)				
Emergency department visits for lung diseases (follow-up: 6 to 12 months)	The mean emergency department visits for lung diseases ranged across control groups from **0.2 to 0.7 visits per person per year**	The mean Emergency department visits for lung diseases in the intervention groups was **0.1 higher** (0.2 lower to 0.3 higher)		328 (4)	⊕⊕⊕◯ **moderate**[4]	
Doctor and nurse visits (follow-up: 6 to 12 months)	The mean doctor and nurse visits ranged across control groups from **1 to 5 vists per**	The mean Doctor and nurse visits in the intervention groups was **0.02 higher** (1 lower to 1 higher)		629 (8)	⊕⊕⊕◯ **moderate**[8]	

- More description
- E.g. relevance of findings, notes when no data, no meta-analysis, or meta-analysis plus studies not in meta-analysis

McMaster University
Inspiring Innovation and Discovery

SoF: Quando e Perché?

- Nelle revisioni Cochrane è obbligatorio (si parla di *Summary of Findings*)
- Per concludere una revisione sistematica per sintetizzare i risultati e la loro qualità (si parla di *Summary of Findings*)
- Come materiale di base per la elaborazione di Linee Guida per la pratica clinica (si parla di *Evidence Profile*)

2. Scegliere quali *outcomes* per la SoF

Di interesse per i pazienti e decisori

Utili per prendere decisioni cliniche

E’ possibile riportarne al massimo 7 (desiderabili e indesiderabili)

In genere solo gli outcomes primari della revisione

Dovrebbero essere definiti nel protocollo

Outcomes

Should be

importance driven

NOT

evidence driven

QUALITY OF EVIDENCE

Self management for patients with chronic obstructive pulmonary disease

Patient or population: patients with chronic obstructive pulmonary disease
Settings: primary care, community, outpatient
Intervention: self management[1]
Comparision: usual care

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **usual care**	Corresponding risk **self management**				
Quality of Life St George's Respiratory Questionnaire. Scale from: 0 to 100. (follow-up: 3 to 12 months)	The mean quality of life ranged across control groups from **38 to 60 points**	The mean Quality of Life in the intervention groups was **2.58 lower** (5.14 to 0.02 lower)		698 (7)	⊕⊕⊕◯ **moderate**[2]	Lower score indicates better quality of life. A change of less than **4** points is not shown to be important to patients.
Dyspnoea Borg Scale. Scale from: 0 to 10. (follow-up: 3 to 6 months)	The mean dyspnoea ranged across control groups from **1.2 to 4.1 points**	The mean Dyspnoea in the intervention groups was **0.53 lower** (0.96 to 0.1 lower)		144 (2)	⊕⊕◯◯ **low**[3,4]	Lower score indicates improvement
Number and severity of exacerbations[5]	See comment	See comment	Not estimable[5]	591 (3)	See comment	Effect is uncertain
Respiratory-related hospital admissions (follow-up: 3 to 12 months)	**Low risk population**[6] **10 per 100**	**7 per 100** (5 to 9)	**OR 0.64** (0.47 to 0.89)	966 (8)	⊕⊕⊕◯ **moderate**[7]	
	High risk population[6] **50 per 100**	**35 per 100** (27 to 46)				
Emergency department visits for lung diseases (follow-up: 6 to 12 months)	The mean emergency department visits for lung diseases ranged across control groups from **0.2 to 0.7 visits per person per year**	The mean Emergency department visits for lung diseases in the intervention groups was **0.1 higher** (0.2 lower to 0.3 higher)		328 (4)	⊕⊕⊕◯ **moderate**[4]	
Doctor and nurse visits (follow-up: 6 to 12 months)	The mean doctor and nurse visits ranged across control groups from **1 to 5 vists per**	The mean Doctor and nurse visits in the intervention groups was **0.02 higher** (1 lower to 1 higher)		629 (8)	⊕⊕⊕◯ **moderate**[8]	

Formulate question

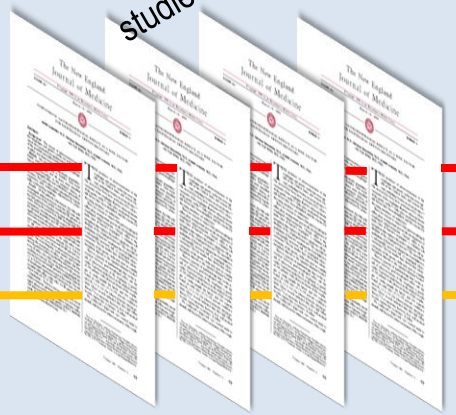
P
I
C
O

Select outcomes

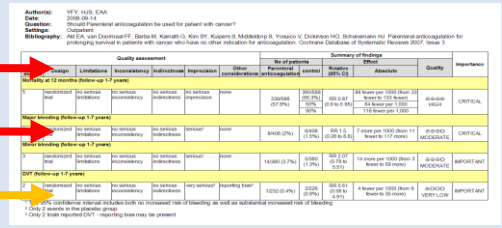
Rate importance

Outcome — Critical
Outcome — Critical
Outcome — Important
Outcome — Not important

Outcomes across studies



Create evidence profile with GDT



Summary of findings & estimate of effect for each outcome

Rate quality of evidence for each outcome

High
Moderate
Low
Very low

Randomization raises initial quality
RCTs: high
Observational: low

Grade down

1. Risk of bias
2. Inconsistency
3. Indirectness
4. Imprecision
5. Publication bias

Grade up

1. Large effect
2. Dose response
3. Opposing bias & Confounders

Grade overall quality of evidence
across outcomes based on lowest quality of ***critical*** outcomes

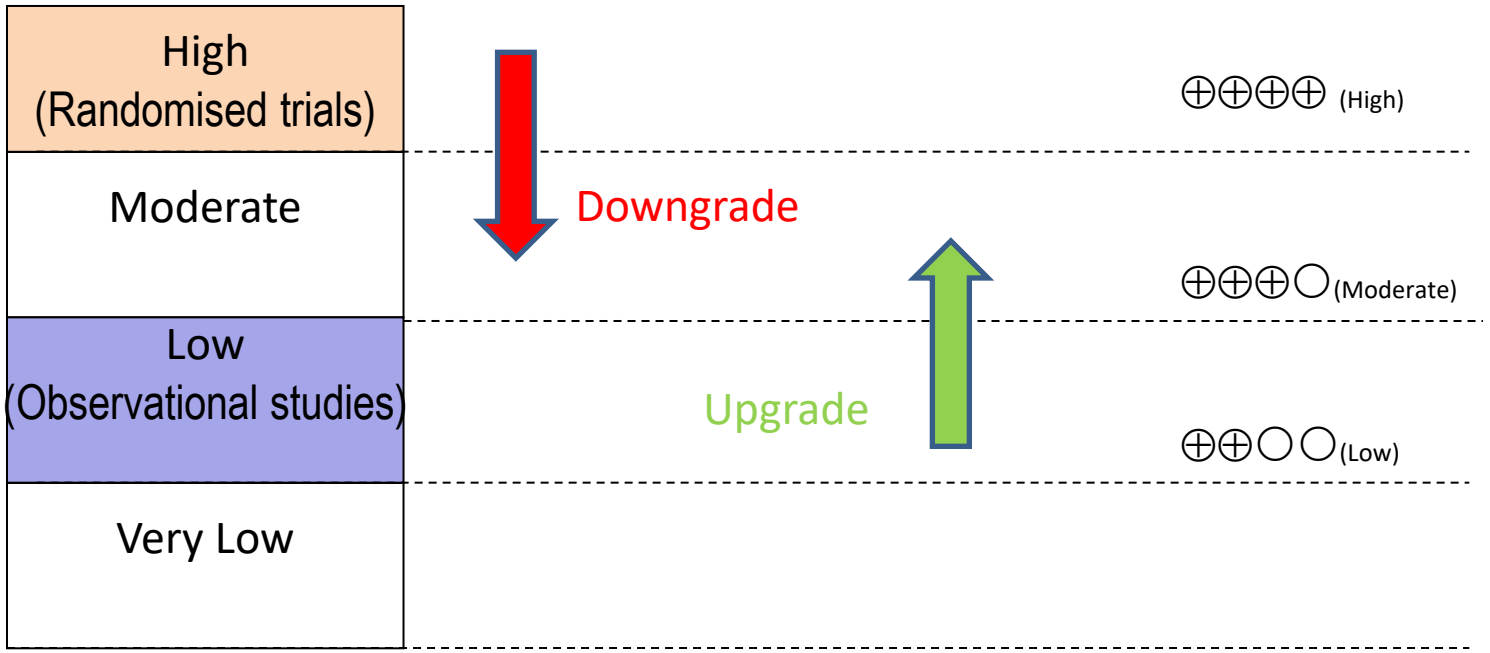
Evidence synthesis (SR, HTA)

Quality of evidence

- GRADE is "**outcome centric**": rating is made for each outcome, and quality may differ -indeed, is likely to differ - from one outcome to another **within a single study** and **across a body of evidence**
- E.g: subjective outcomes are prone to performance and detection bias, while objective outcomes are not
- E.g. one outcome within a review could have imprecision in the pooled estimate of the effect, while another could have not
- E.g. one outcome could have high attrition bias (use of substance) while another could have not (drop out)

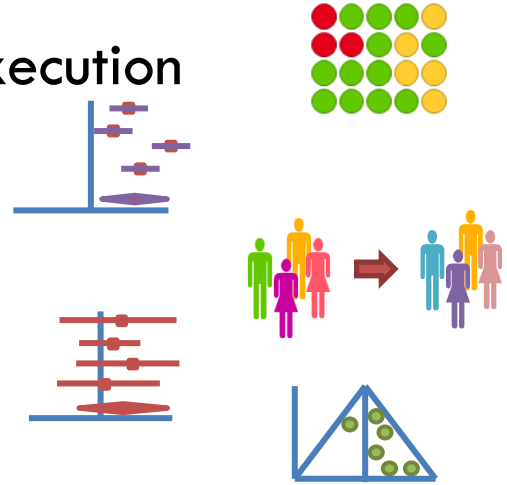
Rating quality of evidence

GRADE's approach begins with the study design. Randomized controlled trials (RCTs) start as high-quality evidence and observational studies as low-quality evidence supporting estimates of intervention effects

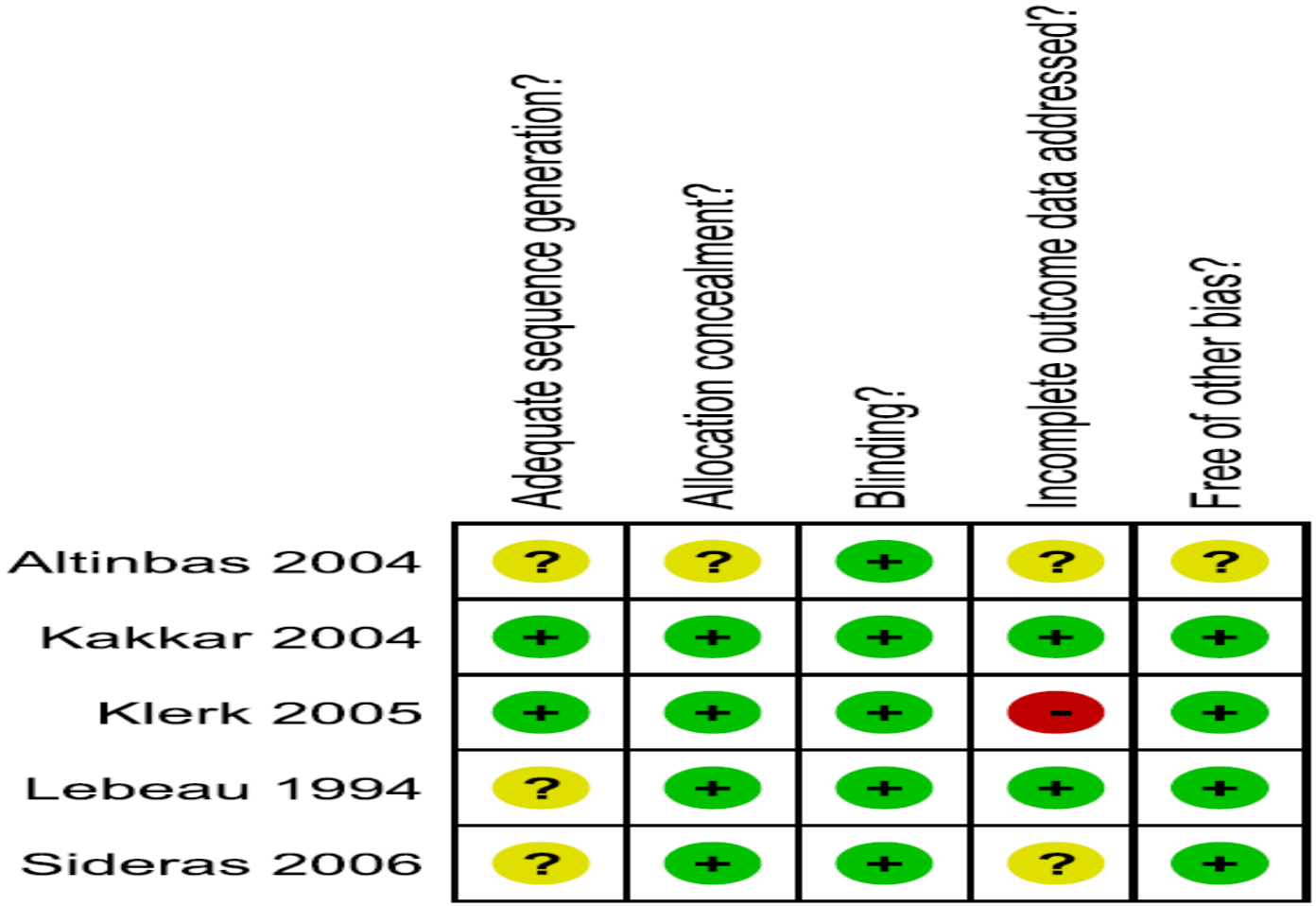


Determinants of quality/certainty of a body of evidence

- **RCTs ⊕⊕⊕⊕**
- **observational studies ⊕⊕◯◯**
- **5 factors that can lower quality**
  1. limitations in detailed study design and execution *(risk of bias criteria)*
  2. Inconsistency *(or heterogeneity)*
  3. Indirectness *(PICO and applicability)*
  4. Imprecision
  5. Publication bias
- **3 factors can increase quality**
  1. large magnitude of effect
  2. opposing plausible residual bias or confounding
  3. dose-response gradient



1. Study limitations (risk of bias)



Akl E, Barba M, Rohilla S, Terrenato I, Sperati F, Schünemann HJ. "*Anticoagulation for the long term treatment of venous thromboembolism in patients with cancer*". Cochrane Database Syst Rev. 2008 Apr 16;(2):CD006650.

Risk of bias

- Outcome specific
- Do not average risk quality across the studies
- Evaluate the extent to which each trial contributes toward the estimate of magnitude of effect. This contribution will usually reflect study sample size and number of outcome events -larger trials with many events will contribute more, much larger trials with many more events will contribute much more (look at the weight of each study in the forest plot)

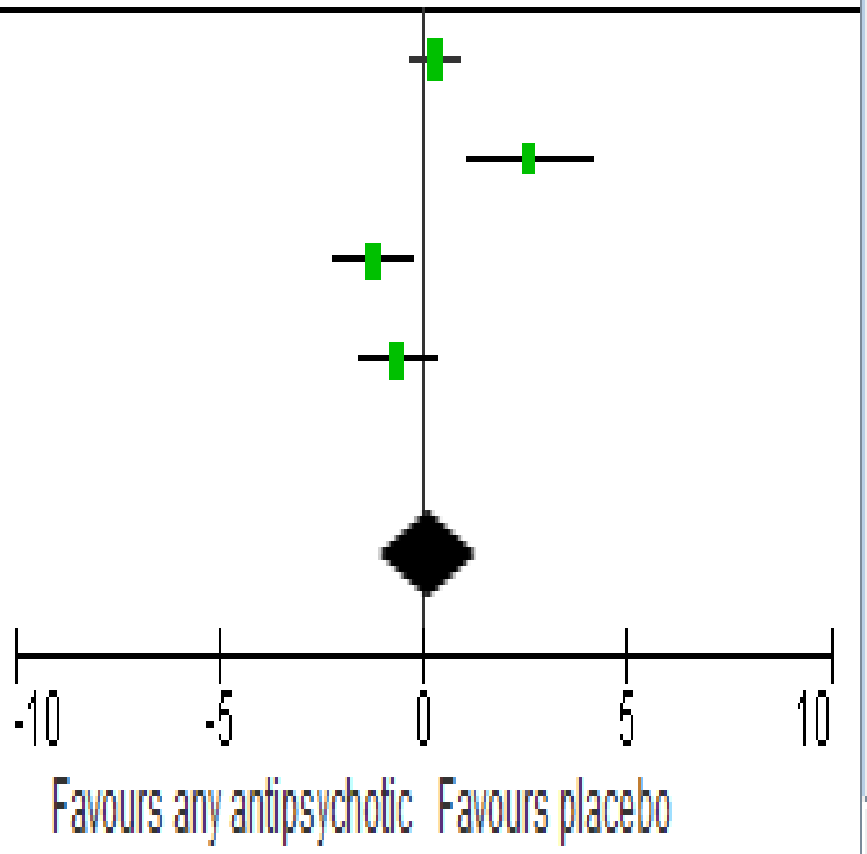
2.Inconsistency (heterogeneity) between studies results

- Variation in size of effect (**Point estimates** vary widely across studies)
- **Confidence intervals** (CIs) show minimal or no overlap
- The statistical test for heterogeneity which tests the null hypothesis that all studies in a meta-analysis have the same underlying magnitude of effect shows a low **P-value** (< 0.05)
- The $\mathbf{I^2}$ which quantifies the proportion of the variation in point estimates due to among-study differences (< 40% : low, 30 e 60% :moderate, 60 e 90% :substantial, 75 e 100% : considerable)
- All statistical approaches have limitations, and their results should be seen in the context of a subjective examination of the variability in point estimates and the overlap in CIs.

Study or Subgroup	Any antispsychotic Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Kampman 2003	1.3	0.8	15	1	0.9	15	28.3%	0.30 [-0.31, 0.91]
Reid 2005	6.1	2.1	16	3.5	2.3	15	20.3%	2.60 [1.05, 4.15]
Tapp 2015	0.4	1.26	29	1.63	2.39	31	25.6%	-1.23 [-2.19, -0.27]
Winhusen 2007	2.8	2.45	60	3.44	2.76	59	25.8%	-0.64 [-1.58, 0.30]
Total (95% CI)			120			120	100.0%	0.13 [-1.08, 1.35]

Heterogeneity: $Tau^2 = 1.26$; $Chi^2 = 19.78$, df = 3 ($P = 0.0002$); $I^2 = 85\%$

Test for overall effect: $Z = 0.22$ ($P = 0.83$)



3. Directness of Evidence generalizability, transferability, applicability

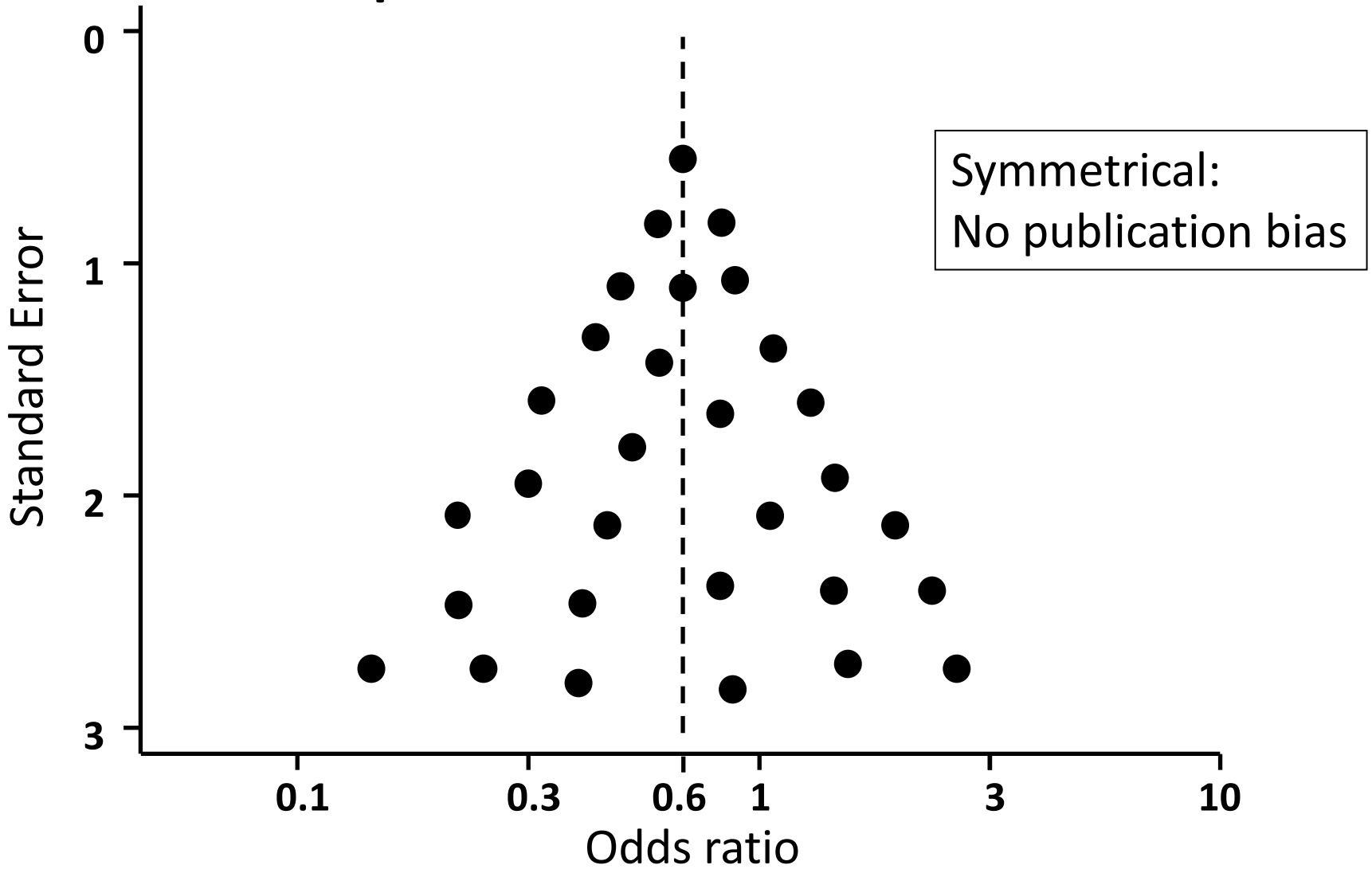
- differences between PICO and available evidence in
  - populations/patients (interested in children but found adults population)
  - interventions (interested in high dosage but found low dosage, interested in long treatment but found short, etc)
  - outcomes (interested in important but we found surrogate; e.g hip fracture vs bone density; interested in long term but found short term results)
- indirect comparisons
  - interested in A versus B
  - found A versus C and B versus C

4. Publication Bias

Consider rating down if:

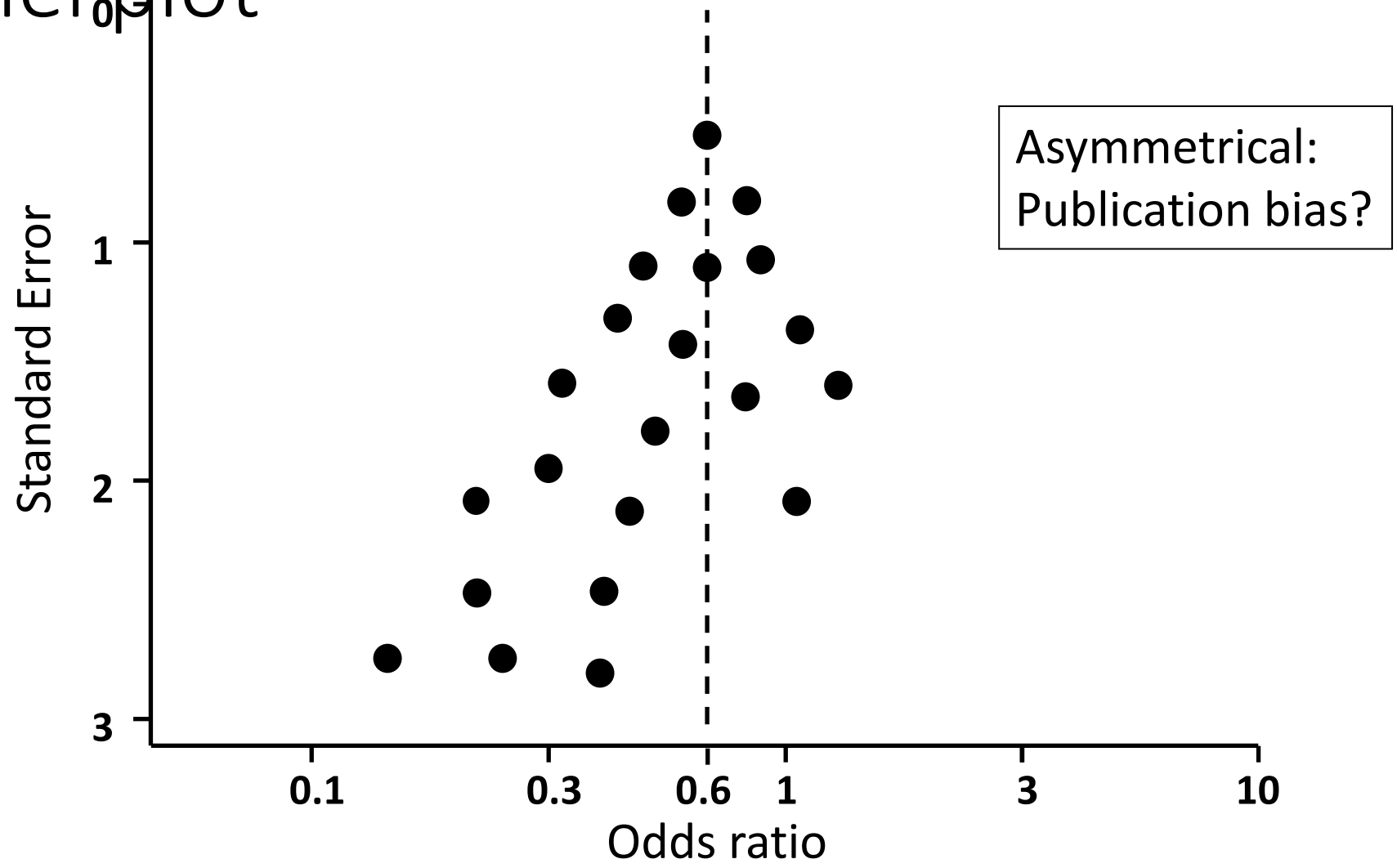
- You find **systematic reviews performed early**, when only few initial studies are available, that will overestimate effects when ‘‘negative’’ studies face delayed publication. Early positive studies, particularly if small in size, are suspect.
- You **find only small “positive” studies, mainly if sponsored by industry**
- **Funnel plot showing asimmetry** but
- Funnel plot should be seen as a generic means of displaying small-study effects – a tendency for the intervention effects estimated in smaller studies to differ from those estimated in larger studies (Sterne 2000). Small-study effects may be due to reasons other than publication bias (low methodological quality, chance, patients characteristics).
- **Funnel plot should be used only when there are at least 10 studies** included in the meta-analysis, because when there are fewer studies the power of the tests is too low to distinguish chance from real asymmetry

Funnel plot



Egger M, Cochrane Colloquium Lyon 2001

Funnel plot



Asymmetrical:
Publication bias?

Egger M, Cochrane Colloquium Lyon 2001

GRADE re-clarification of the construct of certainty of evidence

ELSEVIER

Journal of Clinical Epidemiology 87 (2017) 4–13

Journal of Clinical Epidemiology

GRADE UPDATE OF PAPERS

The GRADE Working Group clarifies the construct of certainty of evidence

Monica Hultcrantz[a,b,*], David Rind[c,d], Elie A. Akl[e,f], Shaun Treweek[g], Reem A. Mustafa[e,h], Alfonso Iorio[e,i], Brian S. Alper[j,k], Joerg J. Meerpohl[l,m], M Hassan Murad[n], Mohammed T. Ansari[o], Srinivasa Vittal Katikireddi[p], Pernilla Östlund[a,q], Sofia Tranæus[a,q,r], Robin Christensen[s], Gerald Gartlehner[t,u], Jan Brozek[e,i], Ariel Izcovich[v], Holger Schünemann[e,i], Gordon Guyatt[e,i]

ELSEVIER

Journal of Clinical Epidemiology 137 (2021) 163–175

Journal of Clinical Epidemiology

ORIGINAL ARTICLE

GRADE guidelines 32: GRADE offers guidance on choosing targets of GRADE certainty of evidence ratings

Linan Zeng[a,b,*], Romina Brignardello-Petersen[b], Monica Hultcrantz[c], Reed A.C. Siemieniuk[b], Nancy Santesso[b], Gregory Traversy[d], Ariel Izcovich[e], Behnam Sadeghirad[b,f], Paul E. Alexander[b], Tahira Devji[b], Bram Rochwerg[b,g], Mohammad H. Murad[h], Rebecca Morgan[b], Robin Christensen[i,j], Holger J. Schünemann[b,g], Gordon H. Guyatt[b,g]

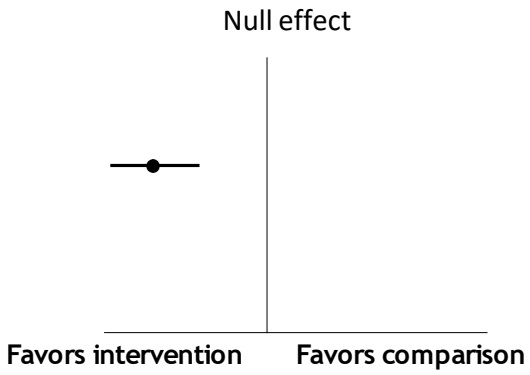
In either guidelines or systematic reviews, when we rate the certainty of evidence, we are assessing our confidence where the point effects lies relative to particular threshold(s) of interest.

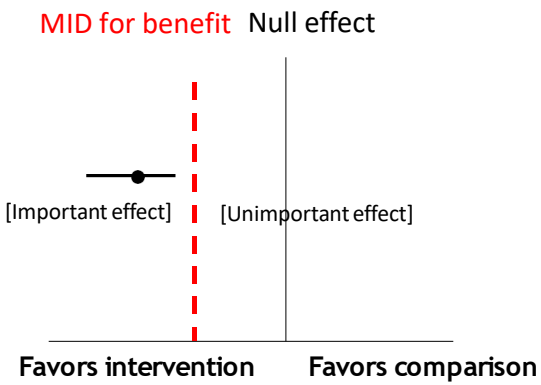
Additional insights regarding imprecision rating

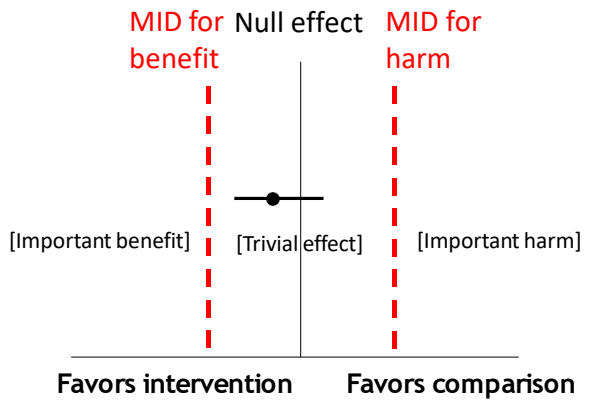
1) In systematic reviews, we are much more likely to use the approach that relies on thresholds and CIs (hereafter that “CI approach”) than optimal information size (OIS) to judge imprecision.
2) We should consider rating down more than one level when the CI appreciably crosses the threshold(s) of interest.

Threshold of interest, target of certainty of evidence rating in minimally contextualized approach

Threshold of interest	(a) Null effect	(b) Minimally important difference (MID)	(c) Range of trivial or no effect
Target of certainty rating	An effect is truly present or not.	An important effect is truly present or not.	A trivial or no effect is truly present or not.








DON'T TRY THIS AT HOME !

What can raise quality?

1. **large magnitude of effect** can upgrade (**RRR 50%/RR 2**)
   - very large two levels **(**RRR 80%/RR 5) ; modeling studies suggests that confounding (from nonrandom allocation) alone is unlikely to explain associations with a relative risk (RR) greater than 2 (or less than 0.5), and very unlikely to explain associations with an RR greater than 5 (or less than 0.2)
   - Es: relationship between infant sleeping position and sudden infant death syndrome (SIDS) found an odds ratio (OR) of 4.1 (95% confidence interval [CI]: 3.1, 5.5) of SIDS occurring with front vs. back sleeping positions

What can raise quality?

2. **dose response relation**
    - higher INR – increased bleeding
    - childhood lymphoblastic leukemia
        - risk for CNS malignancies 15 years after cranial irradiation
        - no radiation: 1% (95% CI 0% to 2.1%)
        - 12 Gy: 1.6% (95% CI 0% to 3.4%)
        - 18 Gy: 3.3% (95% CI 0.9% to 5.6%)

Residual confounding

- 3. all plausible residual confounding may be working to reduce the demonstrated effect or increase the effect if no effect was observed (underestimate of the treatment effect)

- Es: effect of condom use on HIV infection among men who have sex with men RR: 0.34 [0.21, 0.54] (RRR: 66%) in favor of condom use compared with no condom use. Condom users were more likely to have more partners (but studies did not adjust for this confounding factor in their analyses). Considering the number of partners would, if anything, strengthen the effect estimate in favor of condom use.

Assessing Certainty in the Evidence by Outcome

Table: GRADE's approach to rating quality of evidence (aka confidence in effect estimates)

For each outcome based on a systematic review and across outcomes (lowest quality across the outcomes critical for decision making)

1. Establish initial level of confidence		2. Consider lowering or raising level of confidence		3. Final level of confidence rating
Study design	*Initial confidence in an estimate of effect*	*Reasons for considering lowering or raising confidence*		*Confidence in an estimate of effect across those considerations*
		↓ Lower if	↑ Higher if*	
Randomized trials →	High confidence	Risk of Bias Inconsistency Indirectness Imprecision Publication bias	Large effect Dose response All plausible confounding & bias • would reduce a demonstrated effect **or** • would suggest a spurious effect if no effect was observed	High ⊕⊕⊕⊕
				Moderate ⊕⊕⊕◯
Observational studies →	Low confidence			Low ⊕⊕◯◯
				Very low ⊕◯◯◯

*upgrading criteria are usually applicable to observational studies only.

Lowering certainty in RCTs

Table: GRADE's approach to rating quality of evidence (aka confidence in effect estimates)

For each outcome based on a systematic review and across outcomes (lowest quality across the outcomes critical for decision making)

1. Establish initial level of confidence		2. Consider lowering or raising level of confidence		3. Final level of confidence rating
Study design	*Initial confidence in an estimate of effect*	*Reasons for considering lowering or raising confidence*		*Confidence in an estimate of effect across those considerations*
		↓ Lower if	↑ Higher if*	
Randomized trials →	High confidence	Risk of Bias Inconsistency Indirectness Imprecision Publication bias	Large effect Dose response All plausible confounding would reduce a demonstrated effect or • would suggest a spurious effect if no effect was observed	High ⊕⊕⊕⊕
				Moderate ⊕⊕⊕◯
Observational studies →	Low confidence			Low ⊕⊕◯◯
				Very low ⊕◯◯◯

*upgrading criteria are usually applicable to observational studies only.

McMaster University
Inspiring Innovation and Discovery

Altering certainty in observational studies

Table: GRADE's approach to rating quality of evidence (aka confidence in effect estimates)

For each outcome based on a systematic review and across outcomes (lowest quality across the outcomes critical for decision making)

1. Establish initial level of confidence		2. Consider lowering or raising level of confidence		3. Final level of confidence rating
Study design	*Initial confidence in an estimate of effect*	*Reasons for considering lowering or raising confidence*		*Confidence in an estimate of effect across those considerations*
		⬇ Lower if	⬆ Higher if*	
Randomized trials ➔	High confidence	Risk of Bias Inconsistency Indirectness Imprecision Publication bias	Large effect Dose response All plausible confounding & bias • would reduce a demonstrated effect or • would suggest a spurious effect if no effect was observed	High ⊕⊕⊕⊕
				Moderate ⊕⊕⊕◯
Observational studies ➔	Low confidence			Low ⊕⊕◯◯
				Very low ⊕◯◯◯

*upgrading criteria are usually applicable to observational studies only.

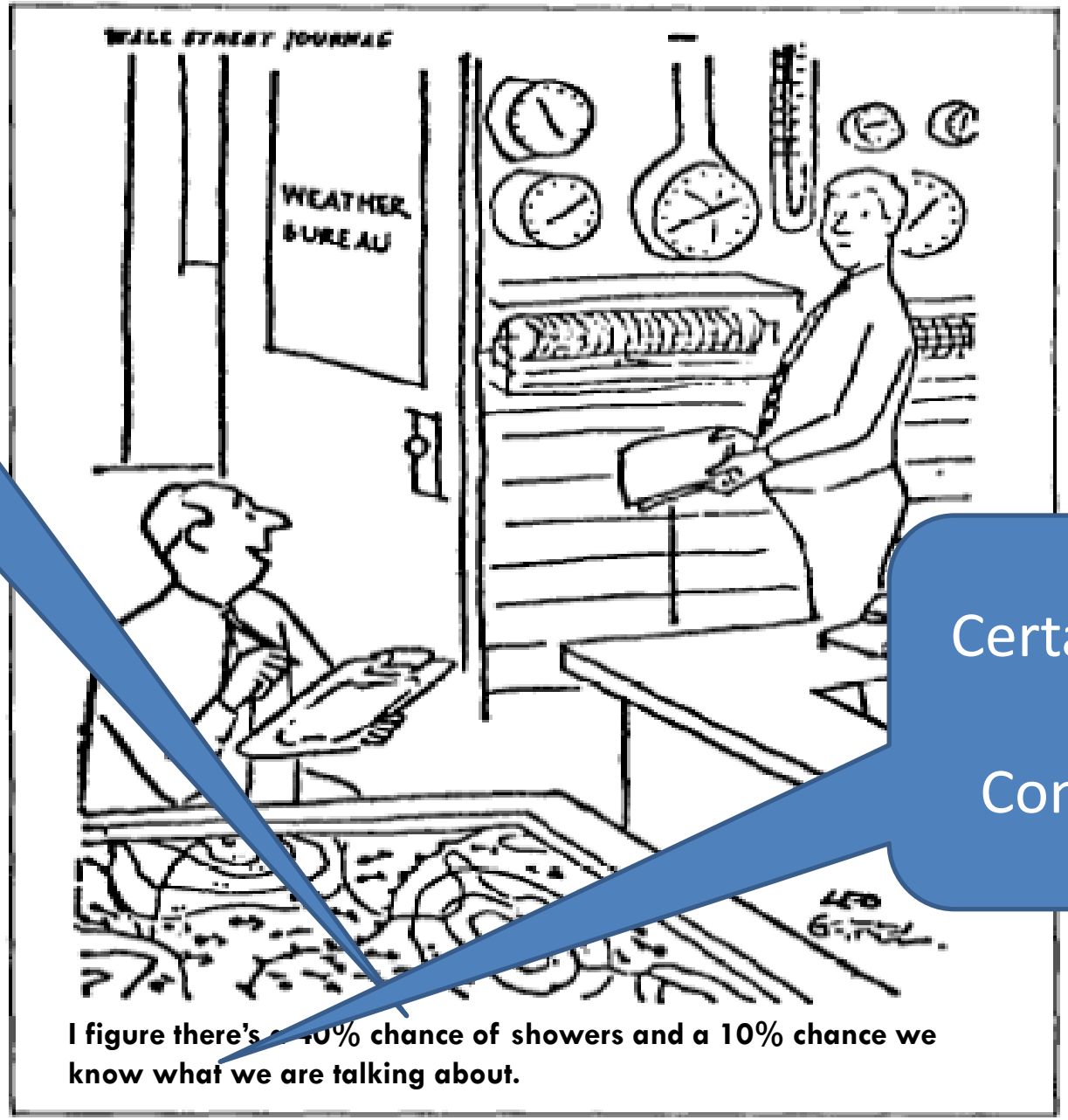
Grades of evidence and Interpretation

Symbol	Quality	Interpretation
⨁⨁⨁⨁	**High**	We are very confident that the true effect lies close to that of the estimate of the effect
⨁⨁⨁◯	**Moderate**	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
⨁⨁◯◯	**Low**	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
⨁◯◯◯	**Very low**	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

grades of evidence and Interpretation

Quality of evidence = certainty of the results

Magnitude of Effect



Likelihood of and certainty in the evidence or effect

Certainty or Quality of evidence
Confidence in effect