Life and Health Sciences Research Institute
Instituto de Investigação em Ciências da Vida e Saúde

ICVS/3B's
Associate Laboratory
University of Minho

Universidade do Minho
Escola de Ciências da Saúde

Introdução às Revisões Sistemáticas

Sessão 2 e 3

PhD4Moz
Fostering a sustainable platform to support PhD training in Health Sciences in Mozambique

Filipa Pinto Ribeiro

filiparibeiro@med.uminho.pt

Como definir uma pergunta de pesquisa?

COMO DEFINIR E ESTRUTURAR A NECESSIDADE DE INFORMAÇÃO

Em geral a necessidade de informação pode ser de natureza:

Clínica
- Cuidados de saude
- Terapia
- Diagnóstico
- Prevenção
- ...

Epidemiológica
- Prevalência
- Incidência
- Etiologia
- Fatores de risco
- ...

Gestão
- Serviços de saúde
- Recursos humanos
- Recursos materiais
- Avaliação de políticas, programas, serviços ...

Saúde Pública
- Políticas de saúde
- Promoção de saúde
- Programas,
- Planejamento ...

Abordagem – Formulação PICO

1. The **population or participants**	Who are the relevant patients?
2. The **intervention or indicator**	What is the management strategy, diagnostic test or exposure that you are interested in (such as a drug, food, surgical procedure, diagnostic test or exposure to a chemical)?
3.The **comparator or control**	What is the control or alternative management strategy, test or exposure that you will be comparing the one you are interested in with?
4. The **outcome**	What are the patient-relevant consequences of the exposure in which we are interested?

PICO vs. PICo

Paciente/População/Problema

Intervenção

Controlo/Comparador

Outcome/Desfecho

Paciente/População/Problema

Interesse

Contexto

PICO

AUXILIA NA CONSTRUÇÃO DE:

- UMA PERGUNTA DE PESQUISA
- BUSCA DE EVIDÊNCIAS

P	I	C	O
POPULAÇÃO, PACIENTE (IDADE, RAÇA, SEXO, MEDICAÇÃO QUE UTILIZA, STATUS DE SAÚDE) OU PROBLEMA	INTERVENÇÃO, INDICAÇÃO OU INTERESSE	PROCEDIMENTO PADRÃO, INTERVENÇÃO DE COMPARAÇÃO, PLACEBO OU NÃO-INTERVENÇÃO	OUTCOME = DESFECHO, RESULTADO ESPERADO: EFETIVIDADE, MORTALIDADE...

PICO


PERGUNTA DE PESQUISA
PRÉ-ESCOLAR DE 4 ANOS, EM TRATAMENTO COM USO DE ANTIBIÓTICOS
USO DE PROBIÓTICOS
NÃO INTERVENÇÃO
REDUÇÃO DO RISCO DE DIARRÉIA ASSOCIADO AO USO DE ANTIBIÓTICOS
P
I
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O

PICO


PERGUNTA DE PESQUISA
PRÉ-ESCOLAR DE 4 ANOS, EM TRATAMENTO COM USO DE ANTIBIÓTICOS
USO DE PROBIÓTICOS
NÃO INTERVENÇÃO
REDUÇÃO DO RISCO DE DIARRÉIA ASSOCIADO AO USO DE ANTIBIÓTICOS
P I C O
PERGUNTA
HÁ EVIDÊNCIAS DE QUE O USO DE PROBIÓTICOS EM PRÉ-ESCOLAR COM TRATAMENTO DE ANTIBIÓTICOS REDUZ O RISCO DE DIARRÉIA?

PICO


LEVANTAMENTO DOS TERMOS
PRÉ-ESCOLAR
ANTIBIÓTICOS
PROBIÓTICOS
-
DIARRÉIA
P
I
C
O
PERGUNTA
HÁ EVIDÊNCIAS DE QUE O USO DE PROBIÓTICOS EM PRÉ-ESCOLAR COM TRATAMENTO DE ANTIBIÓTICOS REDUZ O RISCO DE DIARRÉIA?

Pesquisa PICO

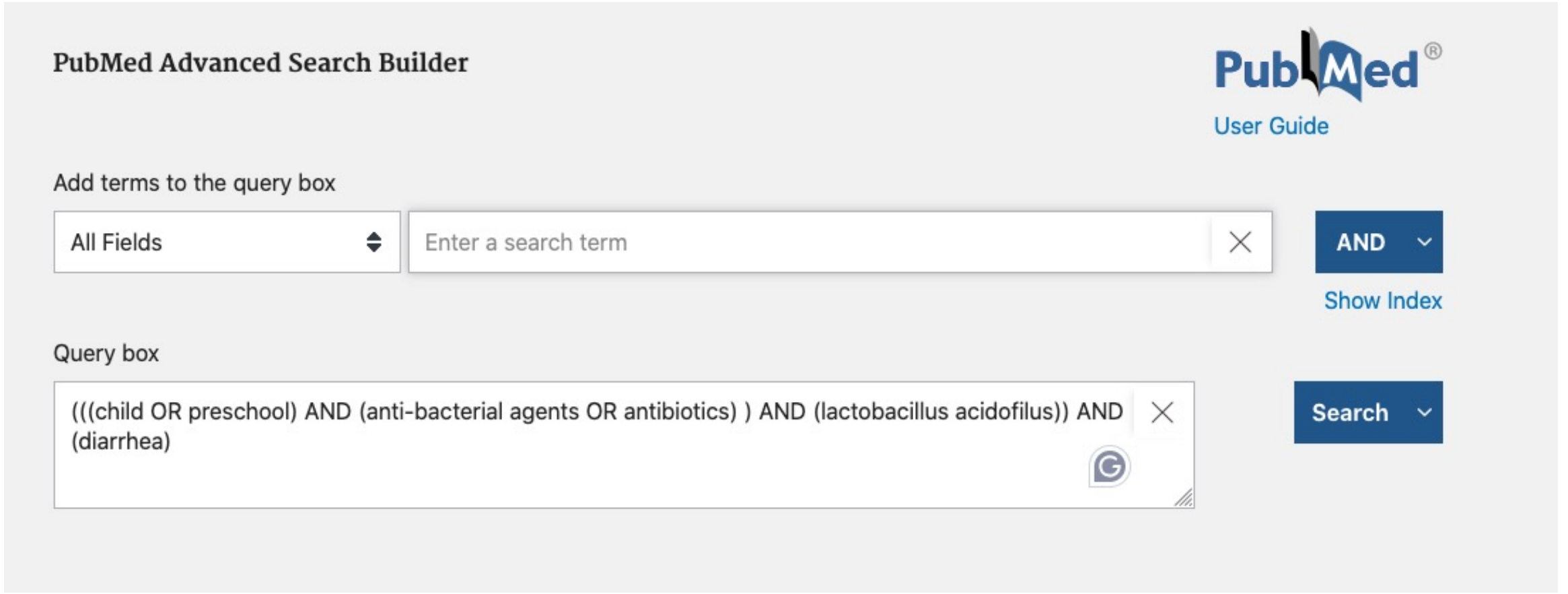
Pesquisa PICO

Pesquisa PICO

UTILIZE OPERADORES BOOLEANOS
(AND, OR, NOT, etc.),
OPERADORES DE TRUNCAMENTO ($ ou *)

pré-escolar **AND** (antibiótic$ **OR** "agentes antibióticos" **OR** "agentes antimicrobiais") **AND** (probiótic$ **OR** lactobacillus acidophilus) **AND** diarréia

Pesquisa PICO - PubMed



Pesquisa PICO - PubMed

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rial agents OR antibiotics)) AND (lactobacillus acidophilus)) AND (diarrhea)

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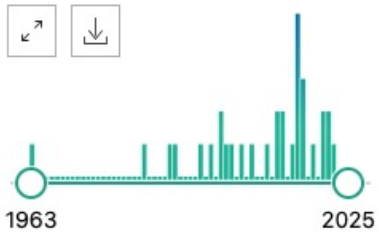

PUBLICATION DATE

- 1 year
- 5 years
- 10 years
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TEXT AVAILABILITY

- Abstract

1 Cite Share

Multispecies Probiotic for the Prevention of **Antibiotic**-Associated **Diarrhea** in **Children**: A Randomized Clinical Trial.

Lukasik J, Dierikx T, Besseling-van der Vaart I, de Meij T, Szajewska H; Multispecies Probiotic in AAD Study Group.

JAMA Pediatr. 2022 Sep 1;176(9):860-866. doi: 10.1001/jamapediatrics.2022.1973.

PMID: 35727573 **Free PMC article.** Clinical Trial.

IMPORTANCE: The efficacy of multispecies probiotic formulations in the prevention of **antibiotic**-associated **diarrhea** (AAD) remains unclear. OBJECTIVE: To assess the effect of a multispecies probiotic on the risk of AAD in **children**. ...INTERVENTIONS: A multispe ...

2 Cite Share

Effect of Simulated Gastrointestinal Tract Conditions on Survivability of Probiotic Bacteria Present in Commercial Preparations.

Stasiak-Różańska L, Berthold-Pluta A, Pluta AS, Dasiewicz K, Garbowska M.

Int J Environ Res Public Health. 2021 Jan 27;18(3):1108. doi: 10.3390/ijerph18031108.

PMID: 33513771 **Free PMC article.**

Probiotics are recommended, among others, in the diet of **children** who are under **antibiotic** therapy, or that suffer from food allergies or travel **diarrhea**, etc. ...Five probiotics (each including one of these strains: Bifidobacterium BB-12, **Lactobacillus** ...

Pesquisa PICO - PubMed

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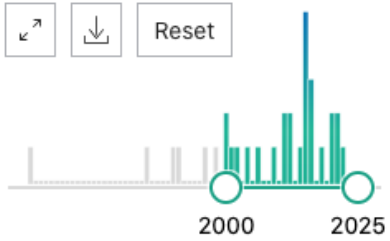
24 results Page 1 of 3

RESULTS BY YEAR

Reset



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RESULTS BY YEAR

PUBLICATION DATE

- ○ 1 year
- ○ 5 years
- ○ 10 years
- ○ Custom Range

TEXT AVAILABILITY

- ☐ Abstract
- ☐ Free full text
- ☐ Full text

ARTICLE TYPE

- ☐ Books and Documents
- ☑ Clinical Trial
- ☐ Meta-Analysis
- ☐ Randomized Controlled Trial
- ☐ Review
- ☐ Systematic Review

See all article type filters

7 results

Page 1 of 1

Filters applied: Clinical Trial. Clear all

1 ☐ Cite Share

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2 ☐ Cite Share

Can probiotic yogurt prevent **diarrhoea** in **children** on **antibiotics**? A double-blind, randomised, placebo-controlled study.

Fox MJ, Ahuja KD, Robertson IK, Ball MJ, Eri RD.

BMJ Open. 2015 Jan 14;5(1):e006474. doi: 10.1136/bmjopen-2014-006474.

PMID: 25588782 **Free PMC article.** Clinical Trial.

The study was conducted through general practices and pharmacies in Launceston, Tasmania, Australia. PARTICIPANTS AND INTERVENTIONS: **Children** (aged 1-12 years) prescribed **antibiotics**, were randomised to receive 200 g/day of either yogurt (probiotic) containing **La** ...

Pesquisa PICO - PubMed

ARTICLE TYPE

- [ ] Books and Documents
- [ ] Clinical Trial
- [ ] Meta-Analysis
- [ ] Randomized Controlled Trial
- [ ] Review
- [x] Systematic Review

PubMed®

rial agents OR antibiotics)) AND (lactobacillus acidophilus)) AND (diarrhea) Search

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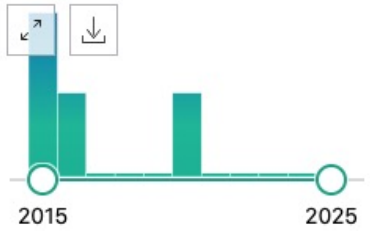
RESULTS BY YEAR



PUBLICATION DATE

- 1 year
- 5 years
- 10 years
- Custom Range

TEXT AVAILABILITY

3 results

Page 1 of 1

Filters applied: Systematic Review. Clear all

1 Cite Share

Postbiotics for Preventing and Treating Common Infectious Diseases in **Children**: A Systematic Review.

Malagón-Rojas JN, Mantziari A, Salminen S, Szajewska H.

Nutrients. 2020 Jan 31;12(2):389. doi: 10.3390/nu12020389.

PMID: 32024037 **Free PMC article.**

Seven RCTs involving 1740 **children** met the inclusion criteria. For therapeutic trials, supplementation with heat-killed **Lactobacillus acidophilus** LB reduced the duration of **diarrhea** (4 RCTs, n = 224, mean difference, MD, -20.31 h, 95% CI -27.06 to -13. ...

2 Cite Share

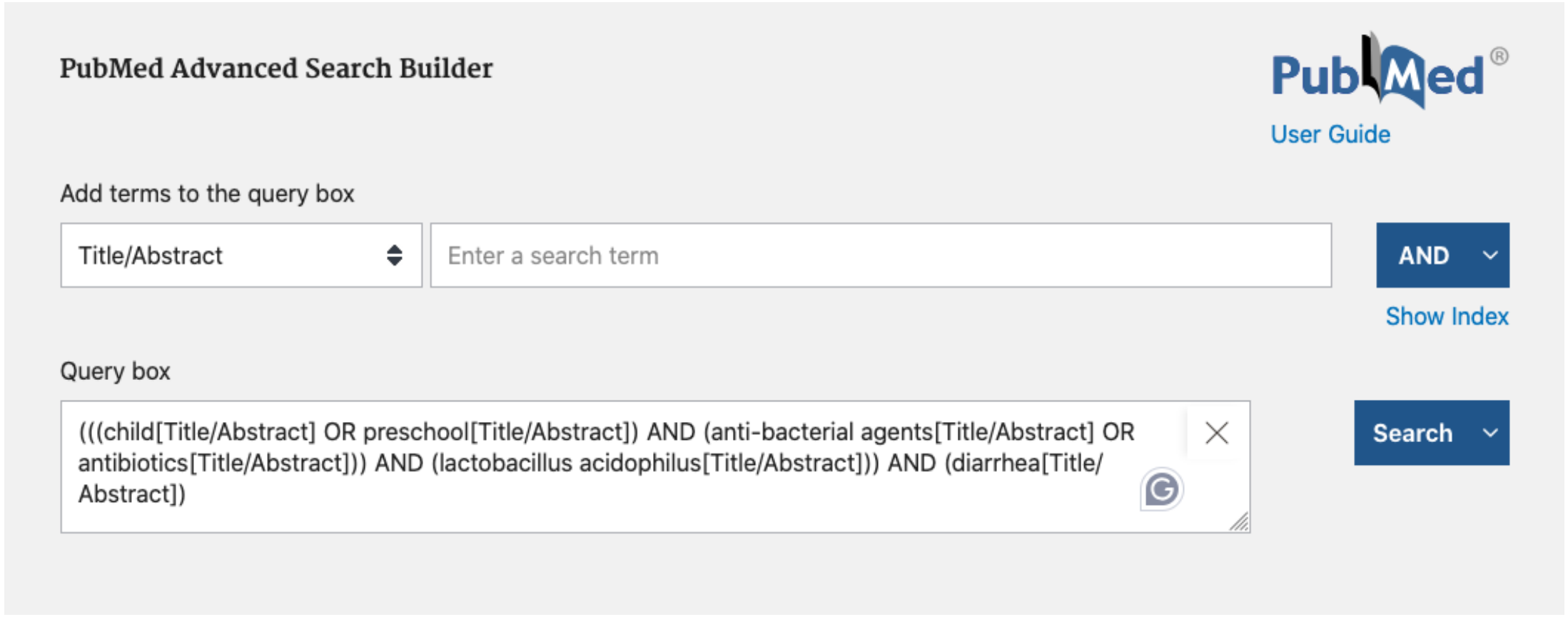
Systematic review and meta-analysis: Multi-strain probiotics as adjunct therapy for Helicobacter pylori eradication and prevention of adverse events.

McFarland LV, Huang Y, Wang L, Malfertheiner P.

United European Gastroenterol J. 2016 Aug;4(4):546-61. doi: 10.1177/2050640615617358. Epub 2015 Nov 13.

PMID: 27536365 **Free PMC article.**

Pesquisa PICO - PubMed



Pesquisa PICO - PubMed

> Rev Colomb Pediatr Pueric. 1963 Apr:21:71-9.

[INTESTINAL DYSBACTERIOSIS, A GRAVE PEDIATRIC PROBLEM]

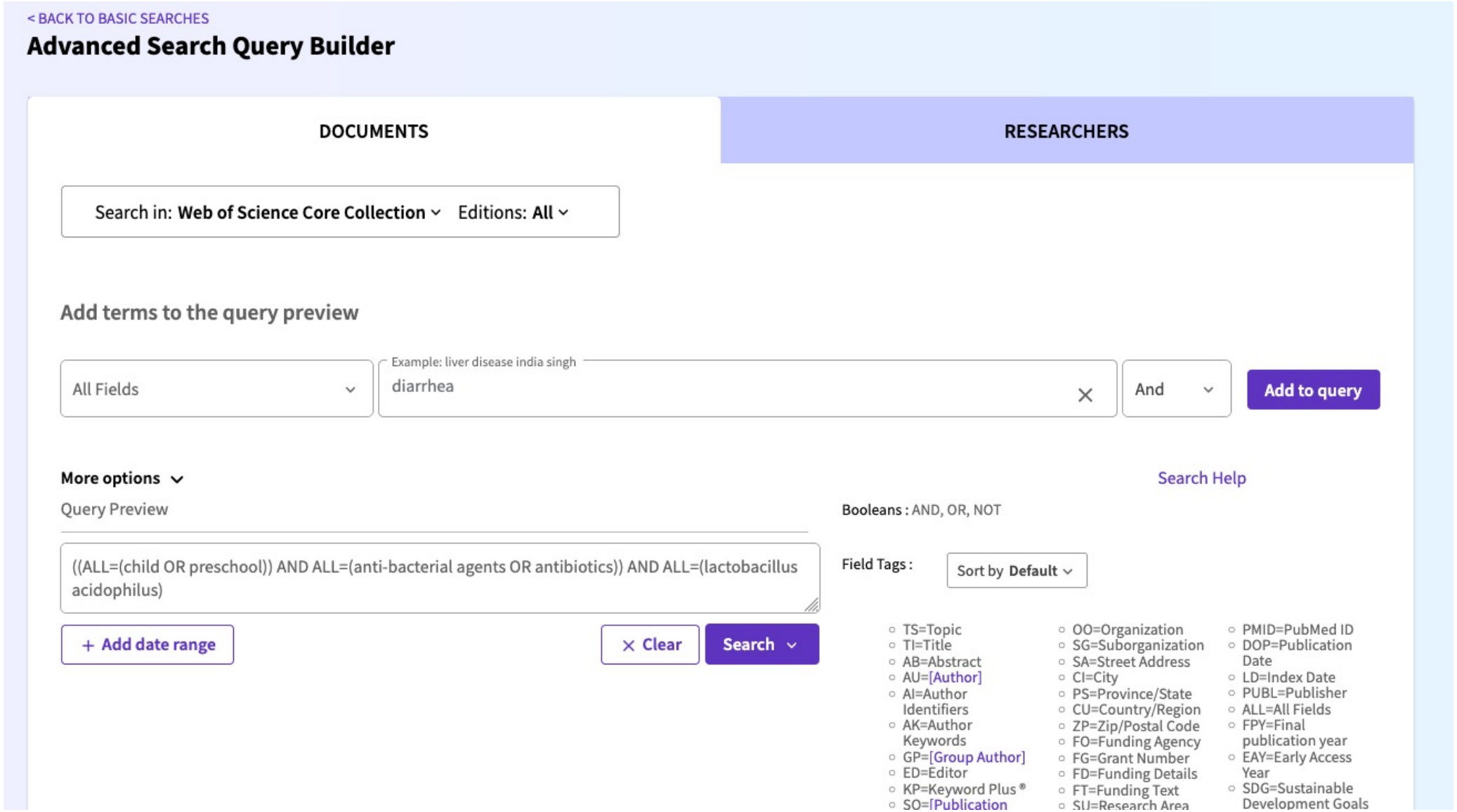
[Article in Spanish]

M A CARIA, F ESCARDO, I DECESAREDEWEBER

PMID: 14086303

No abstract available

Pesquisa PICO - WoS



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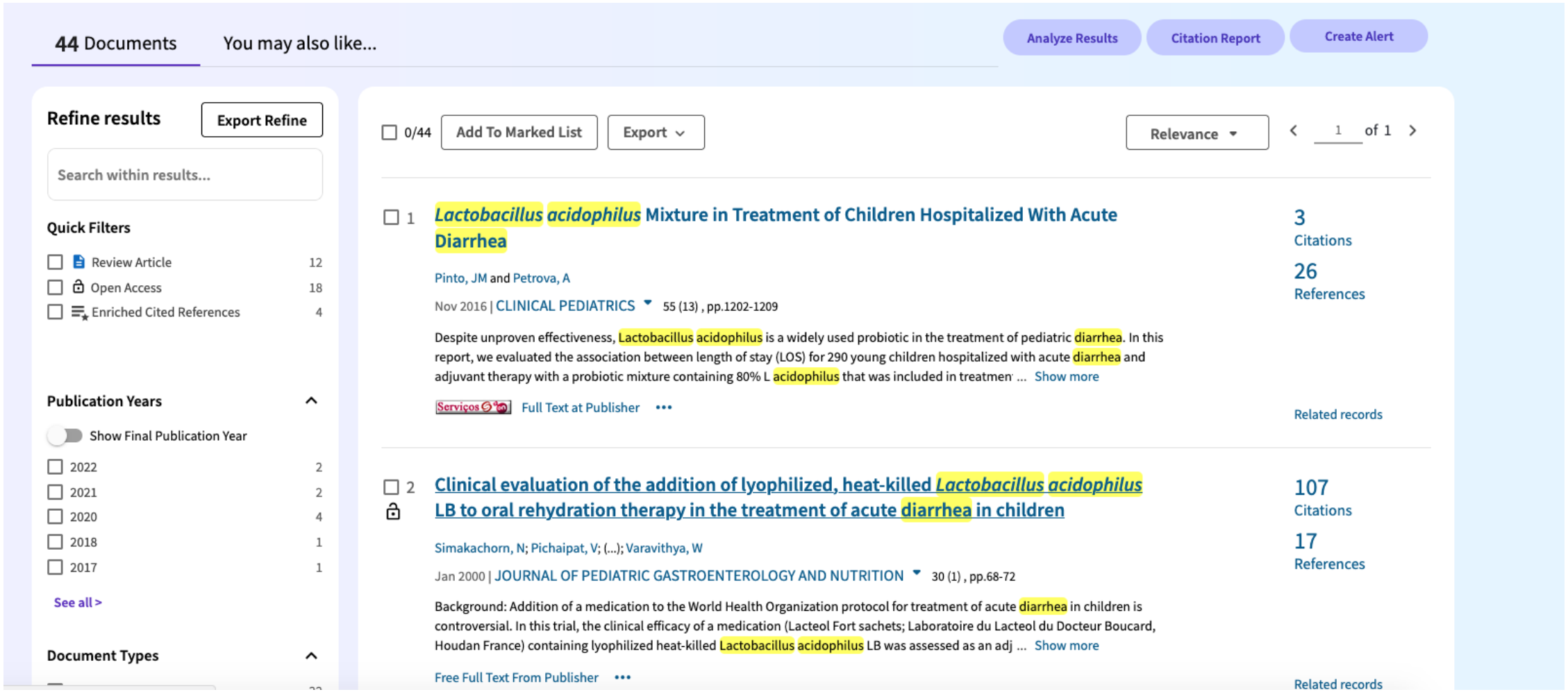

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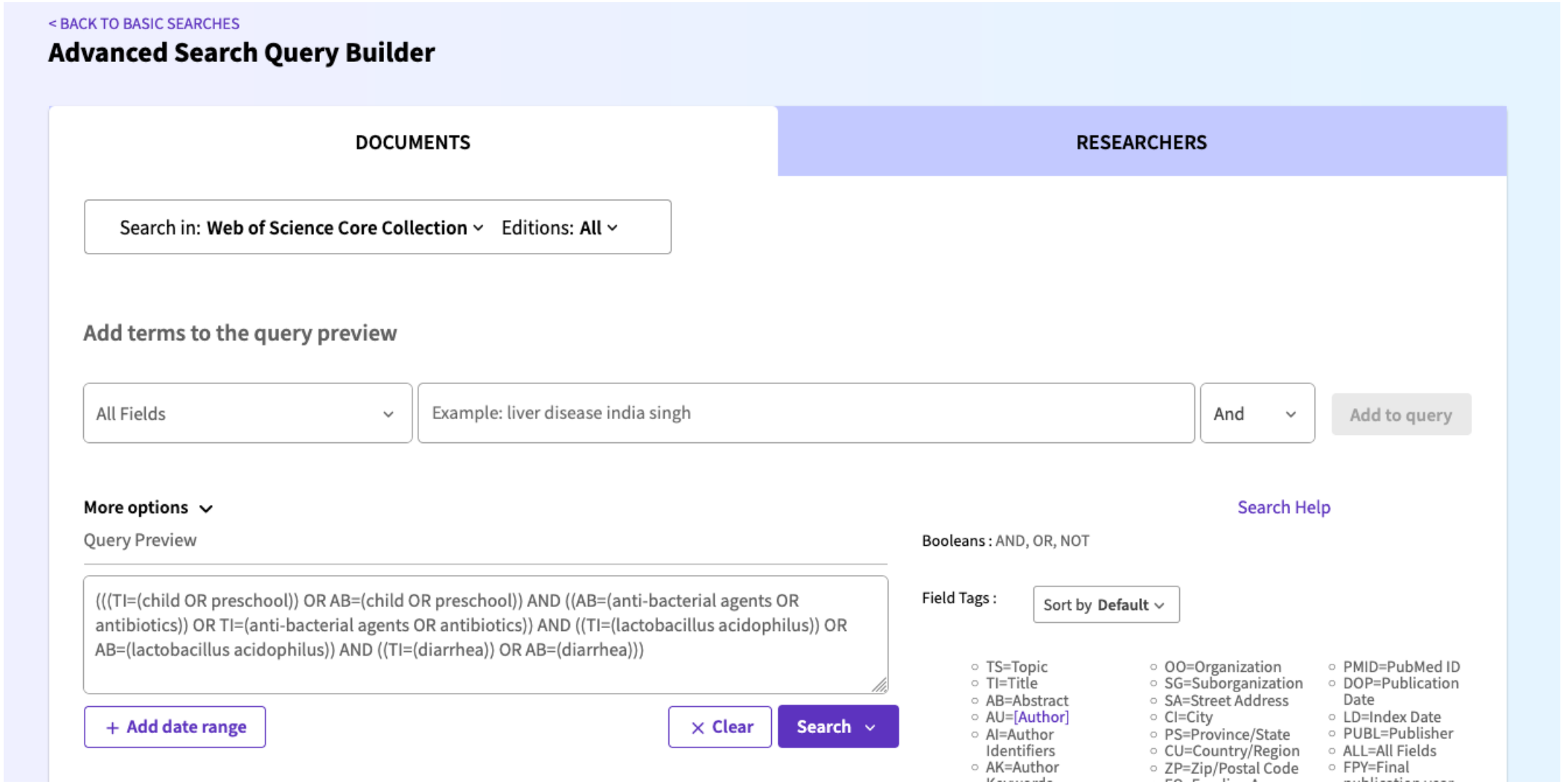


Pesquisa PICO - WoS

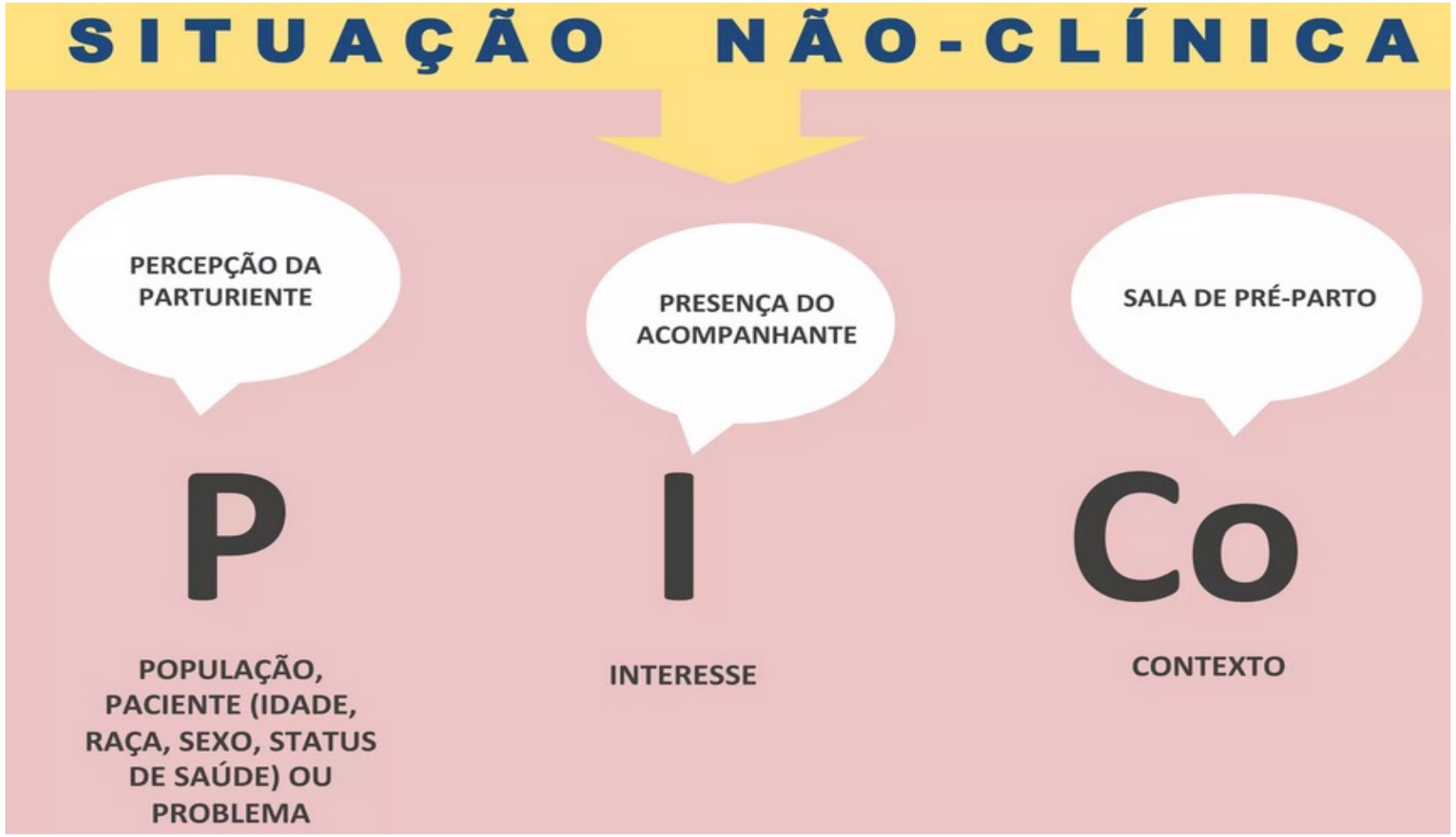
PICo

PICo

METODOLOGIA VOLTADA PARA PESQUISA NÃO-CLÍNICA

- Paciente/População/Problema
- Interesse
- Contexto

PICo


SITUAÇÃO NÃO-CLÍNICA
PERCEPÇÃO DA PARTURIENTE
PRESENÇA DO ACOMPANHANTE
SALA DE PRÉ-PARTO
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POPULAÇÃO, PACIENTE (IDADE, RAÇA, SEXO, STATUS DE SAÚDE) OU PROBLEMA
INTERESSE
CONTEXTO

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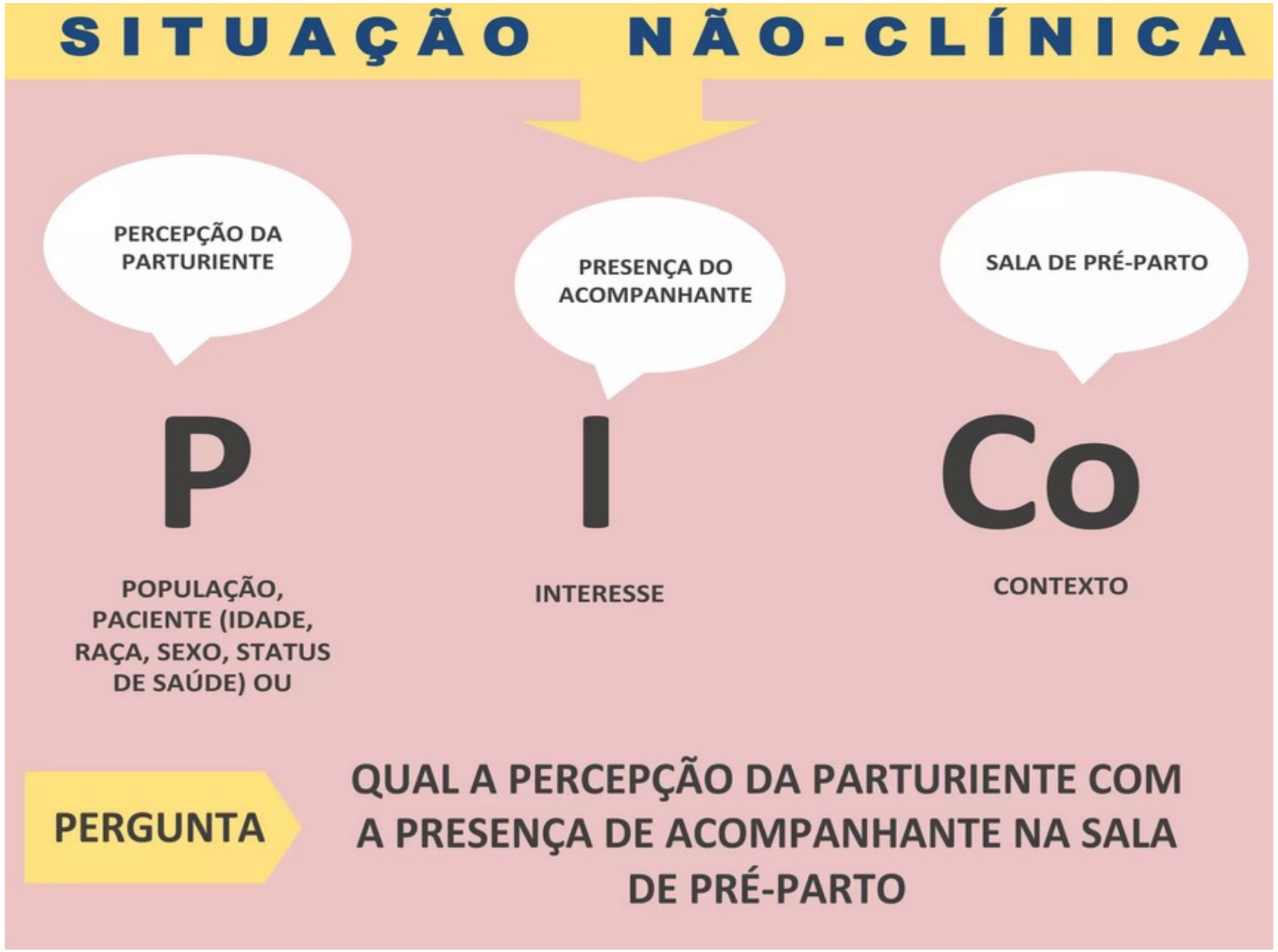
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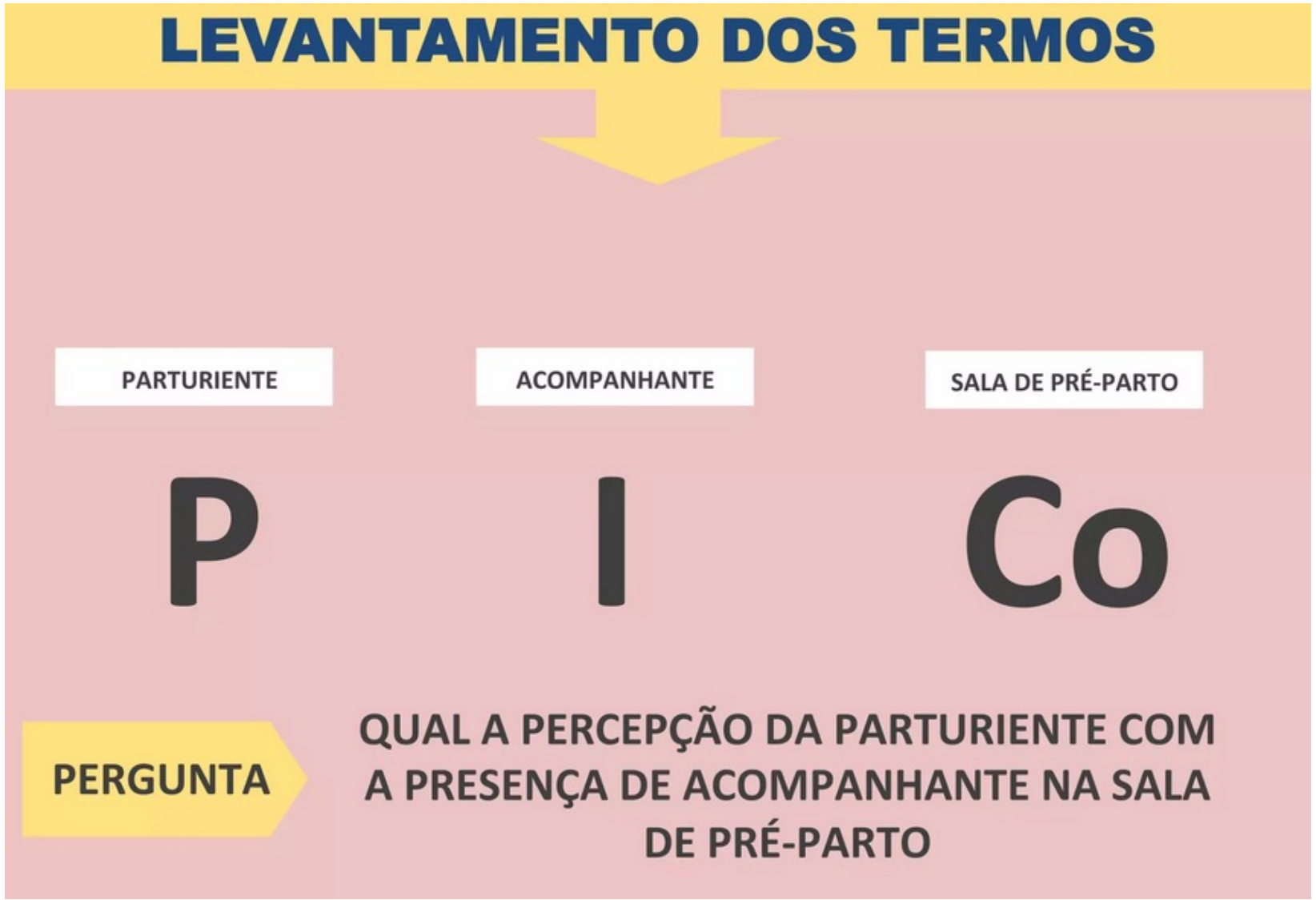
INTERESSE
CONTEXTO
PERGUNTA
QUAL A PERCEPÇÃO DA PARTURIENTE COM A PRESENÇA DE ACOMPANHANTE NA SALA DE PRÉ-PARTO

PICo


LEVANTAMENTO DOS TERMOS
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ACOMPANHANTE
SALA DE PRÉ-PARTO
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PERGUNTA
QUAL A PERCEPÇÃO DA PARTURIENTE COM A PRESENÇA DE ACOMPANHANTE NA SALA DE PRÉ-PARTO

PICo


PERGUNTA
QUAL A PERCEPÇÃO DA PARTURIENTE COM A PRESENÇA DE ACOMPANHANTE NA SALA DE PRÉ-PARTO
1
BASE DE DADOS ESPECIALIZADA
P
GESTANTES
PARTURIENTE
I
ACOMPANHANTES FORMAIS EM EXAMES FÍSICOS
MÃES
CÔNJUGES
AMIGOS
PAI, etc.
Co
SALAS DE PARTO
SALAS DE PRÉ-PARTO
2
BASE DE DADOS MULTIDISCIPLINAR
P
GESTANTES
PARTURIENTE
I
ACOMPANHANTES FORMAIS EM EXAMES FÍSICOS
MÃES
CÔNJUGES
AMIGOS
PAI, etc.
Co
SALAS DE PARTO
SALAS DE PRÉ-PARTO

PICo

UTILIZE OPERADORES BOOLEANOS (AND, OR, NOT, etc.), OPERADORES DE TRUNCAMENTO ($ ou *)

gestantes
OR
parturiente

AND

"acompanhantes formais em exames físicos"
OR "mães"
OR "conjuges"
OR "amigos"
OR "pai"

AND

"salas de parto"
OR
"salas de pré-parto"

Outros Formatos de perguntas de pesquisa

P Population	• Patients suffering from advanced stages of both primary and secondary liver tumors. • Non-responders to chemotherapy or non-surgical candidates
I Intervention	• Combined minimal-invasive intrahepatic treatment using TARE and CT-HDRBT
C Comparison	• Best supportive care as proposed by current guidelines
O Outcome	• Primary: survival rate, OS, TTUP • Secondary: Safety
T Timeframe	• According to institutional SOPs, follow-up intervals were every 3 months in the first year after treatment followed by visits every 6 months afterwards

Outros Formatos de perguntas de pesquisa

Variation: Use CoCoPop.

Explanation	***Example: What is the prevalence of claustrophobia in adult patients undergoing MRI?***
COndition Which condition, disease, problem or symptom are you looking at?	Claustrophobia
COntext When is this happening? Where is this happening? (Geographical location, e.g. Australia / Service location, e.g. hospital)	MRI
POPulation How is your population defined? (e.g. age, gender, ethnic group …)	Adults

Outros Formatos de perguntas de pesquisa

Situation: I want to investigate attitudes or opinions.

Variation: Use SPICE, a framework for qualitative questions evaluating experiences, meaningfulness etc.

Explanation	***Example: I want to know what caregivers of dementia patients think about reminiscence therapy.***
Setting - where is the study set e.g. in a specific country, community, in a hospital, in a care home etc.	This could be a country, or it could be nursing homes, memory care facilities,
Population or Perspective: from whose perspective is the study done, e.g. the patients, the health professionals., the caregivers, etc.	Caregivers
Intervention - what intervention is being examined?	Reminiscence therapy
Comparison - is the intervention being compared with another?	No comparison
Evaluation - the outcome measures	Attitudes

Outros Formatos de perguntas de pesquisa

The ECLIPSE question format is useful for qualitative research topics investigating the outcomes of a policy or service.

ECLIPSE questions identify six concepts: expectation, client group, location, impact, professionals, and service.

ECLIPSE	Definition	Example
Expectation	What are you looking to improve/change? What is the information going to be used for?	to increase access to wireless internet in the hospital
Client Group	Who is the service/policy aimed at?	patients and families
Location	Where is the service/policy located?	hospitals
Impact	What is the change in service/policy that the researcher is investigating?	clients have easy access to free internet
Professionals	Who is involved in providing/improving the service/policy?	IT, hospital administration
Service	What kind of service/policy is this? What service/policy is seeking the information?	provision of free wireless internet to patients

Research question: How can I increase access to wireless internet for hospital patients?

Outros Formatos de perguntas de pesquisa

The PEO question format is useful for qualitative research topics.

PEO questions identify three concepts: population, exposure, and outcome.

PEO	Definition	Example
Population	Who is my question focused on?	mothers
Exposure	What is the issue I'm interested in?	postnatal depression
Outcome	What, in relation to the issue, do I want to examine?	daily living experiences

Research question: What are the daily living experiences of mothers with postnatal depression?

Outros Formatos de perguntas de pesquisa

The SPIDER question format is useful for qualitative or mixed methods research topics focusing on "samples" rather than populations.

SPIDER questions identify five concepts: sample, phenomenon of interest, design, evaluation, and research type.

SPIDER	Definition	Example
Sample	Who is the group of people being studied?	young parents
Phenomenon of **I**nterest	What are the reasons for behavior and decisions?	attendance at antenatal education classes
Design	How has the research been collected (e.g., interview, survey)?	interviews
Evaluation	What is the outcome being impacted?	experiences
Research Type	What type of research (qualitative or mixed methods)?	qualitative studies

Research question: What are the experiences of young parents in attendance at antenatal education classes?

Pesquisa nas bases de dados de registo de revisões sistemáticas

- Cochrane Library – Base de dados das revisões da Cochrane.
- Database of Abstracts of Reviews of Effects (DARE)
- Joanna Briggs Institute Systematic Review Register – Listagem das RS em desenvolvimento.

Disciplina: Área da Saúde

- Open Science Framework OSF – Base de dados de Registo de RS.
- PROSPERO – Base de dados de Registo de RS.
- Research Registry – Base de dados de registo de todo o tipo de estudos.

- Systematic Reviews – Revista que publica não só RS como os respetivos protocolos.

https://libguides.adelaide.edu.au/c.php?g=901895&p=6912919

Prospero

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PROSPERO
International prospective register of systematic reviews

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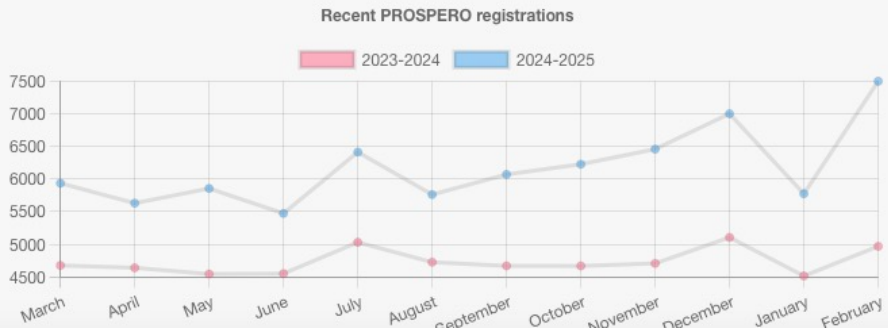
PROSPERO is an international systematic review registry that aims to promote transparency and open science, reduce reporting bias and help prevent unintended duplication and research waste.

The PROSPERO database currently includes records of over **328000** prospectively registered systematic reviews with health related outcomes, providing easy access to key information about planned, in-progress and completed reviews.

PROSPERO is produced by the Centre for Reviews and Dissemination (CRD) and funded by the National Institute for Health and Care Research (NIHR)



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Registering a review is quick and easy and free of charge. You must be logged in to register a review.

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News

We are pleased to launch the new PROSPERO system!

New functionality includes automated system checks for similar already registered systematic reviews, guided completion of fields including using pick lists and type ahead functions and faster searching.

We hope you will enjoy our updated look

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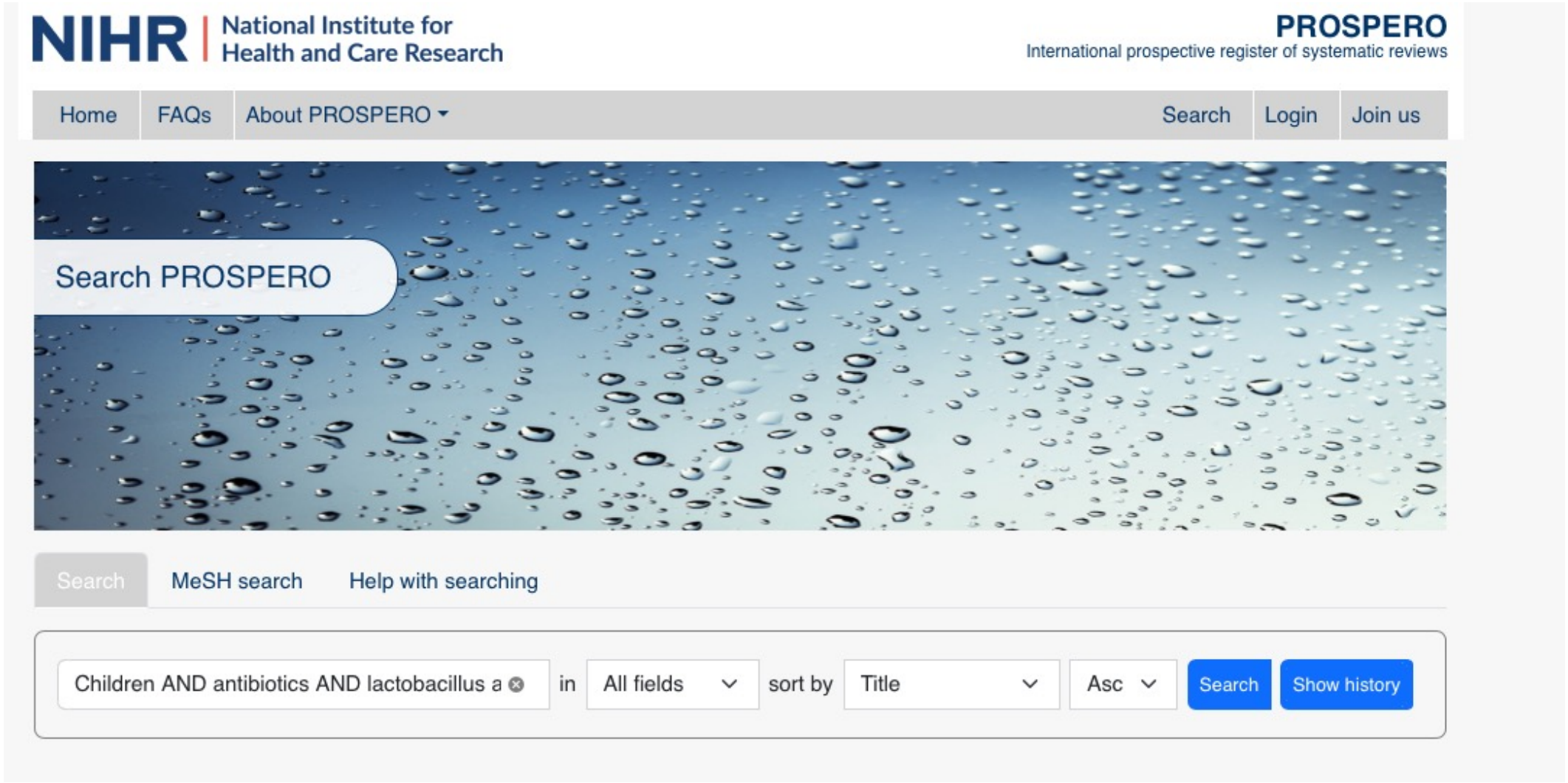
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MeSH search
Help with searching
Children AND antibiotics AND lactobacillus a
in
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sort by
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Search
Show history

Prospero

Search term: **Children AND antibiotics AND lactobacillus acidophilus AND diarrhea**

3 results

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- Meta-analysis of single strain probiotics for the eradication of Helicobacter pylori infections and prevention of adverse events **2014** CRD42014012896 (Ongoing)
- The Role of Probiotics in the Prevention and Management of Antibiotic-Associated **Diarrhea**: A Systematic Review and Meta-analysis of Randomized Controlled Trials **2025** CRD420251003761 (Ongoing)
- Which probiotic has the best effect on the prevention of Clostridium difficile-Associated **Diarrhea**? A systematic review and network meta-analysis **2018** CRD42018106115 (Ongoing)

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PROSPERO
International prospective register of systematic reviews

The Role of Probiotics in the Prevention and Management of Antibiotic-Associated Diarrhea: A Systematic Review and Meta-analysis of Randomized Controlled Trials

Najihah Mohd Azri, Nurin Zarifah Rosairie, Ahmad Naoras Bitar, Salah Abdalrazak Alshehade

Citation

Najihah Mohd Azri, Nurin Zarifah Rosairie, Ahmad Naoras Bitar, Salah Abdalrazak Alshehade. The Role of Probiotics in the Prevention and Management of Antibiotic-Associated Diarrhea: A Systematic Review and Meta-analysis of Randomized Controlled Trials. PROSPERO 2025 CRD420251003761. Available from https://www.crd.york.ac.uk/PROSPERO/view/CRD420251003761.

REVIEW TITLE AND BASIC DETAILS

Review title

The Role of Probiotics in the Prevention and Management of Antibiotic-Associated Diarrhea: A Systematic Review and Meta-analysis of Randomized Controlled Trials

Condition or domain being studied

Antibiotic-associated Diarrhea; Intestinal dysbiosis; Lactobacillus; Lactobacillus Rhamnosus Gg; Lactobacillus Acidophilus; Lactobacillus Casei Rhamnosus; Bifidobacterium Infantis; Bifidobacterium Lactis; Bifidobacterium Longum; Saccharomyces Boulardii

This review focuses on antibiotic-associated diarrhea (AAD), a common complication of antibiotic therapy caused by intestinal dysbiosis, where the balance of gut microbiota is disrupted. Probiotic strains such as Lactobacillus rhamnosus GG, Lactobacillus acidophilus, Bifidobacterium infantis, Bifidobacterium lactis, Bifidobacterium longum, and Saccharomyces boulardii are evaluated for their role in restoring microbiota balance and preventing or managing AAD. This review aims to provide insights into strain-specific efficacy and safety.

Rationale for the review

Antibiotic-associated diarrhea (AAD) affects 5–35% of patients receiving antibiotics, resulting in significant health and economic burdens. It arises from gut microbiota disruptions, leading to dysbiosis, impaired gut barrier integrity, and increased susceptibility to pathogens like Clostridioides difficile. Probiotics, live microorganisms that confer health benefits when consumed in adequate amounts, have demonstrated potential in reducing AAD incidence by restoring microbial balance and enhancing gut health.

Existing reviews on probiotics for AAD prevention provide inconsistent findings due to methodological limitations, such as outdated evidence, limited subgroup analyses, and inconsistent risk-of-bias assessments. Some reviews also fail to evaluate the impact of specific probiotic strains, dosages, and treatment durations, leading to gaps in clinical guidance.

This systematic review and meta-analysis address these gaps by synthesizing the latest evidence from randomized controlled trials (RCTs) using rigorous methodologies, including the Cochrane Risk of Bias 2 tool and GRADE framework. The review aims to evaluate the efficacy and safety of probiotics in preventing and managing AAD across diverse populations, with a focus on strain-specific and dosage-specific effects.

The findings will provide updated and robust evidence to guide healthcare practices, inform policy recommendations, and improve patient outcomes, particularly in vulnerable populations such as the elderly and immunocompromised. This review builds on prior work by addressing methodological limitations, incorporating new evidence, and providing more comprehensive insights into the role of probiotics in AAD prevention and management.

Review objectives

1. To evaluate the effectiveness of probiotics in decreasing the occurrence of antibiotic-associated diarrhea (AAD) compared to Placebo, Standard of Care (SoC), or any intervention

2. To assess the impact of probiotics on the composition of gut microbiota, particularly the growth of beneficial bacteria such as Bifidobacterium, in patients undergoing antibiotic therapy.

3. To identify any potential adverse effects associated with probiotic use in patients receiving antibiotics, particularly in vulnerable populations such as the immunocompromised and hospitalized patients.

4. To assess and evaluate the quality of evidence on probiotics in the prevention and management of antibiotic-associated diarrhea (AAD)

Keywords

Antibiotic-associated diarrhea; Probiotics; Gut microbiota; Dysbiosis; Lactobacillus; Lactobacillus rhamnosus GG; Saccharomyces; Saccharomyces boulardii; Bifidobacterium

Country

Malaysia

ELIGIBILITY CRITERIA

Population

Included

- Adults (age ≥18 years and & <70 years)
- Adults clinically diagnosed with AAD defined/diagnosed by the presence of three or more loose or watery stools per day during or following antibiotic use
- Adults with controlled diabetes, hypertension, or mild to moderate heart disease
- Adults with stable condition and do not affect gastrointestinal function or the risk of diarrhea

Excluded

- Adolescents (< 18 years of age) and elderly people (≥ 70 years of age)
- Adults with severe gastrointestinal diseases (e.g., Crohn's disease, ulcerative colitis), severe immunosuppression, or other conditions that directly impact bowel motility or function
- Adults with malignancy, liver disease or HIV

Intervention(s) or exposure(s)

Included
Probiotics; Lactobacillus; Bifidobacterium Longum; Bifidobacterium Infantis; Bifidobacterium Lactis; Saccharomyces Boulardii

Studies evaluating oral probiotics, including Lactobacillus (e.g., L. rhamnosus GG), Bifidobacterium (e.g., B. longum, B. infantis, B. breve), and Saccharomyces boulardii, administered during or after antibiotic therapy, for short-term or long-term use to prevent or manage antibiotic-associated diarrhea (AAD).

Excluded
Studies that do not specify the type of probiotics used, involve non-oral routes of administration, combine probiotics with other interventions without separate analysis, or lack details on dosage, duration, or administration timing.

Comparator(s) or control(s)

Included
PICO tags selected: Placebo

Studies that compare the use of probiotics with placebo, standard care, or no intervention during antibiotic therapy for preventing or managing antibiotic-associated diarrhea (AAD).

Excluded
Studies that do not provide a clearly defined comparator group or use interventions other than probiotics or standard care.

Study design

Only randomized study types will be included.

Included
Randomized controlled trials (RCTs) with parallel or crossover designs that evaluate the efficacy and safety of probiotics in preventing or managing antibiotic-associated diarrhea (AAD). No restrictions on study setting or sample size will be applied.

Excluded
Non-randomized studies, observational studies, case reports, editorials, reviews, conference abstracts, and studies not reporting primary outcome measures or lacking sufficient methodological details.

Context

This review will include studies conducted in diverse healthcare settings, including hospitals, community clinics, and outpatient care. Eligible studies must involve participants receiving antibiotic therapy and experiencing or at risk of antibiotic-associated diarrhea (AAD). There are no geographic restrictions, allowing the inclusion of studies from high-income, low-income, and middle-income countries to ensure broad applicability.

Participants must be clinically stable, without severe underlying gastrointestinal diseases (e.g., Crohn's disease, ulcerative colitis) or systemic conditions that directly impact gut health. Studies involving probiotics administered orally as part of standard or experimental care will be considered. The review excludes studies conducted exclusively in specialized care settings (e.g., intensive care units) or populations with severe immunosuppression, where outcomes may not generalize to broader populations.

TIMELINE OF THE REVIEW

Date of first submission to PROSPERO
11 March 2025

Review timeline
Start date: 5 March 2025. End date: 6 June 2025.

Date of registration in PROSPERO
11 March 2025

AVAILABILITY OF FULL PROTOCOL

Availability of full protocol
A full protocol has been written and uploaded to PROSPERO. The protocol will be made available after the review is completed.

SEARCHING AND SCREENING

Search for unpublished studies
Both published and unpublished studies will be sought.

Main bibliographic databases that will be searched
The main databases to be searched are *CENTRAL - Cochrane Central Register of Controlled Trials*, *CINAHL - Cumulative Index to Nursing and Allied Health Literature*, *Embase.com*, *PubMed* and *Scopus*.

Other important or specialist databases that will be searched

- UpToDate
- ClinicalKey
- ClinicalTrials.gov
- Cochrane Guideline

Search language restrictions
The review will only include studies published in English.

Search date restrictions
Databases will be searched for articles published before 30 May 2025, there are no restrictions on search start date.

Other methods of identifying studies
Other studies will be identified by: *contacting authors or experts*, *looking through all the articles that cite the papers included in the review ("snowballing")*, *reference list checking* and *searching trial or study registers*.

Link to search strategy
A full search strategy is available in the full protocol as described in the *Availability of full protocol* section

Selection process
Studies will be screened independently by at least two people (or person/machine combination) with a process to resolve differences.

Other relevant information about searching and screening
Two reviewers (NND and NZR) will independently screen titles and abstracts for inclusion based on predefined eligibility criteria. Full-text articles of potentially eligible studies will also be reviewed independently by both reviewers. Discrepancies during screening will be resolved through discussion or, if necessary, by consulting a third reviewer (ANB). Manual reference list checking and searches of trial registries (e.g., ClinicalTrials.gov) will also be performed to identify additional relevant studies. The PRISMA flow diagram will be used to document the selection process, ensuring transparency.

DATA COLLECTION PROCESS

Data extraction from published articles and reports

Data will be extracted independently by at least two people (or person/machine combination) with a process to resolve differences.

Authors will be asked to provide any required data not available in published reports.

Study risk of bias or quality assessment

Risk of bias will be assessed using: *Cochrane RoB-2*

Data will be assessed independently by at least two people (or person/machine combination) with a process to resolve differences.

Additional information will be sought from study investigators if required information is unclear or unavailable in the study publications/reports.

Reporting bias assessment

Risk of bias due to missing results will be assessed using funnel plots to detect publication bias. If sufficient studies are available, statistical tests such as Egger's test may be conducted. Missing outcome data will also be evaluated using the Cochrane RoB 2 tool to address reporting biases.

Certainty assessment

Certainty of evidence will be assessed using the GRADE approach, considering factors such as risk of bias, inconsistency, indirectness, imprecision, and publication bias. The GRADEpro GDT software will be used to generate a Summary of Findings table, summarizing the certainty of evidence for primary and secondary outcomes.

OUTCOMES TO BE ANALYSED

Main outcomes

Incidence of antibiotic-associated diarrhea (AAD) among patients receiving probiotics compared to placebo or standard care.

Additional outcomes

- Duration of diarrhea: The mean or median time to resolution of diarrhea in patients receiving probiotics compared to placebo or standard care.
- Quality of life: Assessed using validated scales (e.g., SF-36 or EQ-5D) to compare changes between intervention and control groups.
- Incidence of adverse effects: Frequency and type of adverse events related to probiotic use, including serious or treatment-limiting effects.
- Gastrointestinal symptom severity: Changes in GI symptom scores (e.g., GI symptom rating scale) between probiotic and control groups.

PLANNED DATA SYNTHESIS

Strategy for data synthesis

The data will be synthesized through a meta-analysis using an inverse variance random-effects model to account for variability across studies. A fixed-effects model may also be explored in cases where heterogeneity is minimal to ensure the robustness of findings.

For dichotomous outcomes, such as the incidence of antibiotic-associated diarrhea (AAD), odds ratios (OR) with 95% confidence intervals (CI) will be calculated. For continuous outcomes, such as the duration of diarrhea, mean differences (MD) or standardized mean differences (SMD) with 95% CI will be used.

Heterogeneity will be assessed using the I^2 statistic. An I^2 value greater than 50% will indicate substantial heterogeneity, and sources of heterogeneity will be explored through subgroup analyses and sensitivity analyses. Subgroup analyses will include factors such as probiotic strain, dosage, duration of intervention, patient age group, and geographical location.

Publication bias will be assessed through visual inspection of funnel plots for asymmetry. If asymmetry is observed, it will be noted and considered in the interpretation of findings.

The meta-analysis and data synthesis will be conducted using RevMan 5.4.2 software, with results presented as forest plots and summary statistics. This approach will ensure a rigorous evaluation of the efficacy and safety of probiotics in preventing and managing AAD.

CURRENT REVIEW STAGE

Stage of the review at this submission

Review stage	Started	Completed
Pilot work		
Formal searching/study identification		
Screening search results against inclusion criteria		
Data extraction or receipt of IPD		
Risk of bias/quality assessment		
Data synthesis		

Review status

The review is currently planned or ongoing.

Publication of review results

Results of the review will be published in English.

REVIEW AFFILIATION, FUNDING AND PEER REVIEW

Review team members

Miss Najihah Mohd Azri. Universiti Sultan Zainal Abidin. Malaysia.

No conflict of interest declared.

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No conflict of interest declared.

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No conflict of interest declared.

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No conflict of interest declared.

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Funding source

Review has no specific/external funding but is supported by guarantor/review team (non-commercial) institutions.

Peer review

The review protocol has been peer-reviewed by the lead supervisor, Dr. Ahmad Naoras Bitar, and other academic members of the Faculty of Pharmacy, University Sultan Zainal Abidin. The review process includes oversight during the design, methodology, and implementation phases to ensure academic rigor and adherence to systematic review standards.

ADDITIONAL INFORMATION

Review conflict of interest

Declared individual interests are recorded under team member details.. No additional interests are recorded for this review.

Medical Subject Headings

Anti-Bacterial Agents; Diarrhea; Drug-Related Side Effects and Adverse Reactions; Gastrointestinal Microbiome; Humans; Incidence; Probiotics; Randomized Controlled Trials as Topic; Vulnerable Populations; Bifidobacterium; Bifidobacterium animalis; Bifidobacterium longum subspecies infantis; Dysbiosis; Lacticaseibacillus rhamnosus; Lactobacillus; Lactobacillus acidophilus; Saccharomyces boulardii; Standard of Care

SIMILAR REVIEWS

Check for similar records already in PROSPERO

PROSPERO identified a number of existing PROSPERO records that were similar to this one (last check made on 5 March 2025). These are shown below along with the reasons given by that the review team for the reviews being different and/or proceeding.

- The Effectiveness of Prebiotics and Probiotics in Preventing Antibiotic-Associated Diarrhea (AAD) [published 15 October 2024] [CRD42024597456]. The review was judged **not to be similar**
- Probiotics for the prevention of Antibiotic-Associated Diarrhea in children: a systematic review and meta-analysis [published 13 March 2023] [CRD42023406801]. The review was judged **not to be similar**
- Probiotics for the prevention and treatment of antibiotic-associated diarrhea: an Umbrella review of Meta-analyses of Randomized clinical trials [published 13 October 2023] [CRD42023465792]. The review was judged **not to be similar**

PROSPERO version history

- Version 1.0, published 11 Mar 2025

Disclaimer

Principais passos

Desenvolvimento da pergunta de investigação

Pesquisa preliminar (Registos de RS e artigos)

3. Definição dos critérios de inclusão/exclusão

Definição da estratégia de pesquisa

Pesquisa nas bases de dados

6. Registo do protocolo de investigação
7. Triagem por título e resumo
8. Triagem do texto integral
9. Pesquisa manual das referências bibliográficas
10. Extração dos dados
11. Avaliação da qualidade
12. Verificação de dados e análise estatística
13. Meta-análise
14. Verificação das análises (e dados)
15. Redação do manuscrito
16. Submissão do manuscrito

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Sessão 2 e 3

Questões

PhD4Moz

Fostering a sustainable platform to support
PhD training in Health Sciences in Mozambique

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