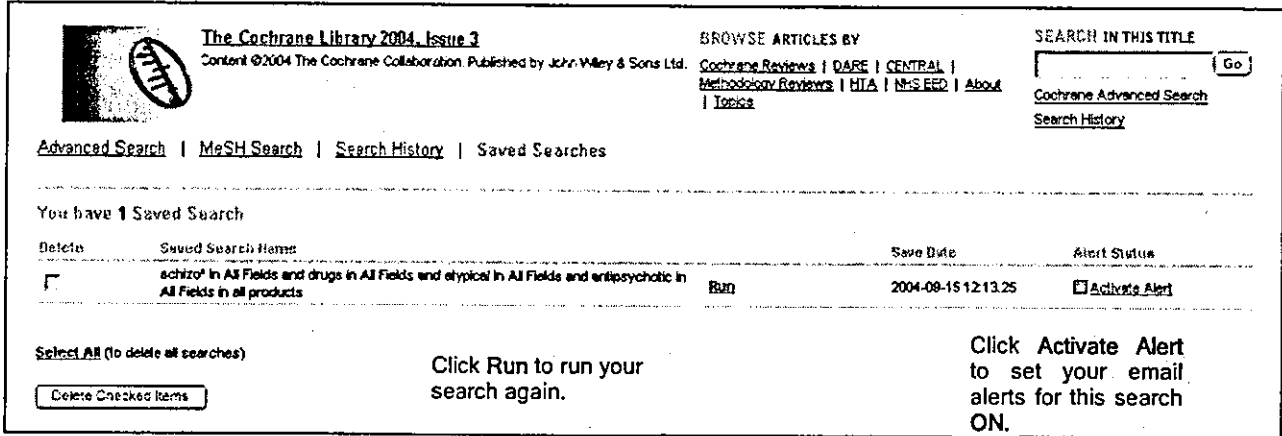


5.2. SAVING YOUR SEARCH

If you want to save your search you can do so by selecting the Save Search button.

Save Search

Your search will be saved ready for you to run it again when desired. You can also activate your alerting service, which will email you each time a new article is published which meets the parameters of your search.



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BROWSE ARTICLES BY
[Cochrane Reviews](#) | [DARE](#) | [CENTRAL](#) | [Methodology Reviews](#) | [HTA](#) | [NHS EED](#) | [About](#) | [Topics](#)

SEARCH IN THIS TITLE

[Cochrane Advanced Search](#)
[Search History](#)

[Advanced Search](#) | [MeSH Search](#) | [Search History](#) | [Saved Searches](#)

You have 1 Saved Search

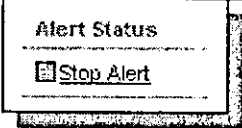
Delete	Saved Search Name	Save Date	Alert Status
<input type="checkbox"/>	schizo* in All Fields and drugs in All Fields and atypical in All Fields and antipsychotic in All Fields in all products	2004-08-15 12:13:25	<input checked="" type="checkbox"/> Activate Alert

Select All (to delete all searches)

Click Run to run your search again.

Click Activate Alert to set your email alerts for this search ON.

Once your alert is on, the alert status icon will change to Stop Alert. If you want to stop receiving alerting emails click on stop alert.

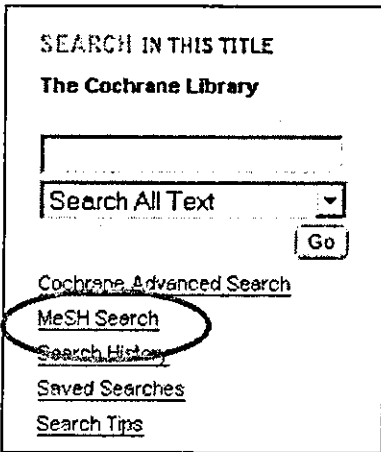


Alert Status
 Stop Alert

5.3. MeSH SEARCH

Keywords drawn from the MeSH Thesaurus published by the US Library of Medicine have been attached to many, but not all, records in The Cochrane Library.

The MeSH Thesaurus is organized hierarchically in 'trees', with the lower levels of the trees containing more specific terms. The MeSH search allows searching of the databases in The Cochrane Library using the MeSH terms and tree structures.



SEARCH IN THIS TITLE
The Cochrane Library

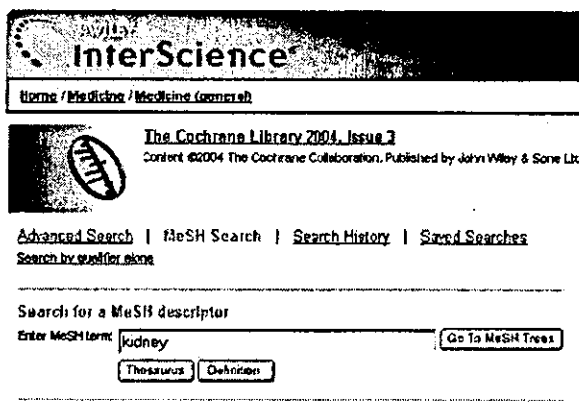
Search All Text

[Cochrane Advanced Search](#)
[MeSH Search](#)
[Search History](#)
[Saved Searches](#)
[Search Tips](#)

To activate a MeSH search click on the MeSH search link in your search box.

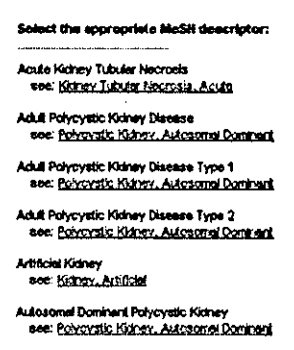
Step 1: Using the MeSH Thesaurus

The Permuted Index is an index of all the words that appear in the MeSH thesaurus. It is used to locate specific MeSH headings:



Open the MeSH search screen by clicking on the MeSH search in your search box

Search the Permuted Index by entering one word and clicking on Thesaurus. For instance if I were to search for the term 'Kidney' - there are 29 descriptors and 44 cross-references returned for that word.

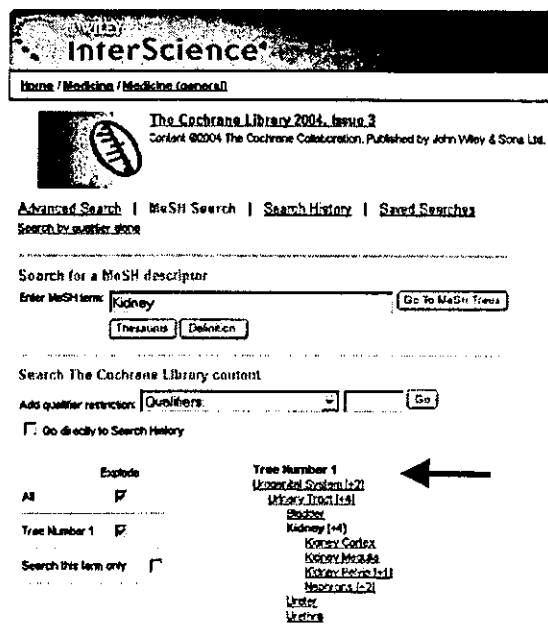


All MeSH headings containing the word 'Kidney' are displayed under the bold entry for that word in alphabetical order.

By browsing these headings, locate the specific MeSH term you are interested in. Some terms are followed by 'see' and the appropriate cross-references for that term. Click on these terms to jump to the cross-referenced section of the Permuted Index.

Click on a MeSH term to display the MeSH tree(s) containing that term. For instance, a click on the MeSH description 'Kidney' will return a screen displaying your MeSH trees:

Step 2: Finding your way around MeSH trees



i. Select your search term

The MeSH tree(s) containing the selected MeSH heading are displayed once a heading has been selected from the Permuted Index. The MeSH trees allow expanding or narrowing the scope of the search, by selection of broader or narrower terms.

To move up to a more general level in a MeSH tree, click on a term that sits higher in the tree.

More specific terms are displayed immediately underneath, and just to the right of your selected term, which appears in red.

Urogenital System is the broadest term in this tree. If you wanted to move up a level in the MeSH tree and expand the range of your search significantly, you could select this term

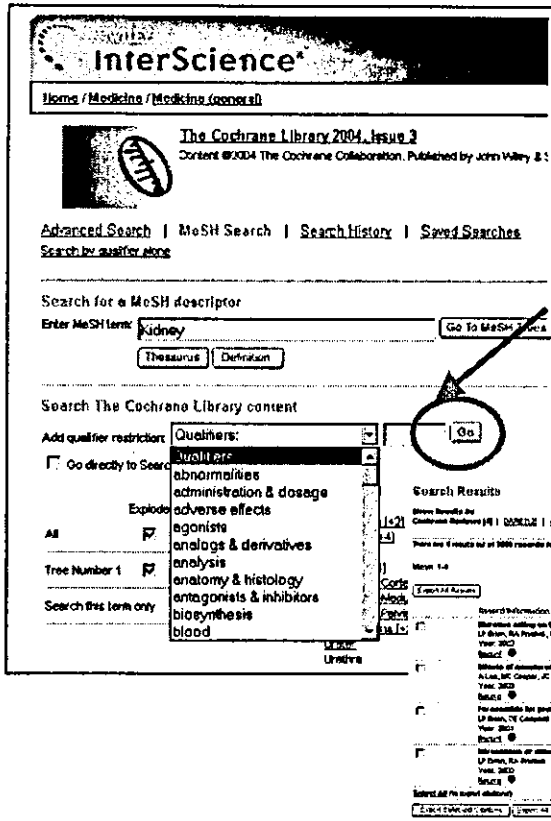
Your search term is highlighted in red. If you wanted to narrow your search down from this term, you could click on one of the narrower terms listed immediately below and slightly to the right.

ii. Select your search option

Once you have selected the term you want to search under, you can choose one of two options.

'Search this term only' will search just for the selected term (the one in red)

The explode option will automatically include all narrower terms below the term highlighted in your search as well. This will maximize the number of records retrieved. For some terms you will have more than one tree. You can select whether you want to explode your search to include all trees, or just those selected by checking the box next to them.



iii. Choose search restrictions (if any)

Once you have selected your search option, decide whether you want to restrict your search by additional qualifiers that can be selected from the drop down box provided, or typed into the search box to the right of the drop down box.

iv. Search

Hit 'Go' to conduct your search.

v. Results

Results are presented (see p.9 for more details on search results screen)

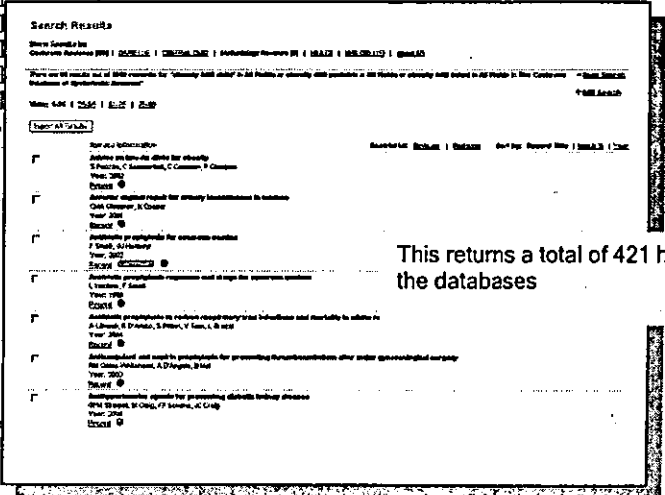
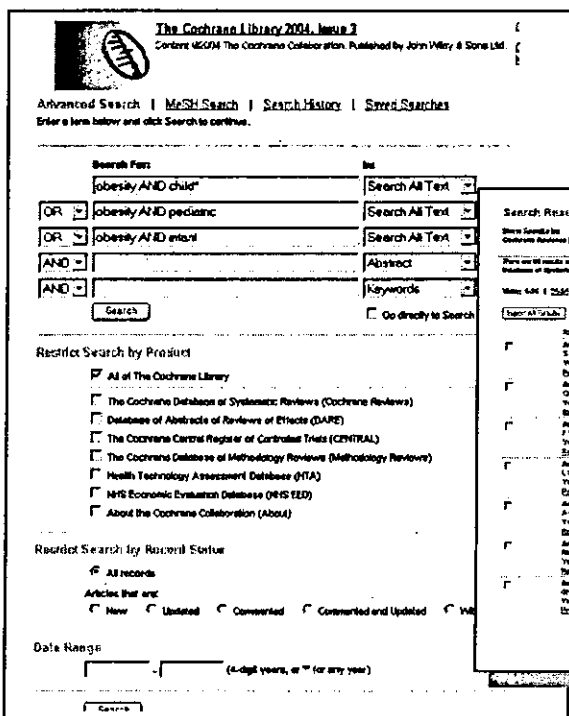
5.4. Search History

Search history provides a history of your searches in your current session on Cochrane. If you want to save your searches for future use in other sessions you can either use the *Save Search* function described on page 11, or you can use the *Save Search Strategy* function in search history (see p. 15).

The search history function is a good way of combining different searches to maximize your search efficiency.

For instance if you were seeking information on childhood obesity, you could run the following search on the Search the Cochrane Library function:

(obesity AND child*) OR (obesity AND pediatric) OR (obesity AND infant)



This returns a total of 421 hits across all the databases

You can then run a MeSH search using the descriptor 'Obesity'.

Search for a MeSH descriptor

Enter MeSH term: [Go To MeSH Trees](#)

[Thesaurus](#) [Definition](#)

Search Cochrane content

Add qualifier restriction: [Qualifiers:](#) [Go](#)

Go directly to Search History

Explosive Tree Number 1 [C18.854.621] **Metabolic and Hormonal Disorders [L2]**

- Malnutrition [L2]
 - Endocrine Disorders [L1]
 - Deficiency Diseases [L2]
 - Obesity [L4]

Tree Number 2 **Obesity in Diseases**

- Obesity, Morbid
- Pickwickian Syndrome
- Prader-Willi Syndrome

Tree Number 3 **Stomatitis**

- Mouth Syndrome [L1]

Tree Number 2 [C23.808.109.621] **Pathological Conditions, Signs and Symptoms [L3]**

- Sore and Swollen [L20]
 - Body Weight Changes [L3]
 - Emaciation [L1]
 - Obesity
 - Thinness

Tree Number 3 [G07.553.481.398.571] **Physiological Processes [L1]**

- Growth and Embryonic Development [L10]
 - Growth [L2]
 - Body Weight [L5]
 - Birth Weight
 - Fetal Weight
 - Obesity
 - Thinness
 - Weight Gain
 - Weight Loss

Search - exploding all trees.

Search Results

More Searches by: [Cochrane Reviews](#) | [DARE](#) | [CENTRAL](#) | [HIA](#) | [HISSED](#)

There are 2470 records for 'Obesity' explorer across in This Cochrane Database of Systematic Reviews [View](#) [Full Search](#)

View: All Full

[Show 10 records](#)

Advanced search options: [Expand](#) [Collapse](#) [Reset](#) [Save](#) [Print](#) [View](#) [Home](#)

1 [Effect on breast size for obesity](#)
S Pardo, C Lumbroso, C Casanova, F Obici
Year: 2007

2 [Efficacy of treatment for high weight-for-height or weight gain during pregnancy](#)
M Hogue
Year: 1998

3 [Social interventions](#)
B Hery, A-H Oakley, W-L Sun, G Lumbroso
Year: 2005

4 [Improving health professionals' management and the organization of care for overweight and obese people](#)
M Hogue
Year: 2001

5 [Interventions for preventing obesity in children](#)
B Lumbroso, A Hery, G Lumbroso, B Oakley, C Lumbroso
Year: 2005

6 [Interventions for treating obesity in children](#)
G Lumbroso, A Hery, W-L Sun, B Oakley, B Hery, G Lumbroso
Year: 2005

7 [Long-term pharmacotherapy for obesity and overweight](#)
B Lumbroso, G Lumbroso
Year: 2005

8 [Surgery for morbid obesity](#)
C Lumbroso, A Oakley, W-L Sun, F Hery
Year: 2005

9 [Efficacy of...](#)

This returns a total of 2470 hits across all the databases

Then, by going to Search History, you can combine these searches. Firstly, your searches will be numbered, #1, #2 and so on.

The Cochrane Library 2004, Issue 3

Advanced Search | [MeSH Search](#) | [Search History](#) | [Saved Searches](#)

Search For: [Go](#)

Date Range (4-digit year): -

Restrict by record status: [All records](#)

Restrict by text: [Search All Text](#)

Current Search History

ID	Search	Hits	Edit	Delete
#1	obesity AND child in ALL fields or obesity AND pediatric in ALL fields or obesity AND infant in ALL fields in all products	421	edit	delete
#2	MeSH descriptor Obesity explode all trees in MeSH products	2470	edit	delete

[Save Search Strategy](#) [Clear History](#)

Your combined search will then come up in your Search History.

The Cochrane Library 2004, Issue 3

Advanced Search | [MeSH Search](#) | [Search History](#) | [Saved Searches](#)

Search For:

Date Range (4-digit year): -

Restrict by record status: [All records](#)

Restrict by text: [Search All Text](#)

Current Search History

ID	Search	Hits	Edit	Delete
#1	obesity AND child in ALL fields or obesity AND pediatric in ALL fields or obesity AND infant in ALL fields in all products	421	edit	delete
#2	MeSH descriptor Obesity explode all trees in MeSH products	2470	edit	delete
#3	Obesity	246	edit	delete

[Save Search Strategy](#) [Clear History](#)

Your combined search history is now listed and you just need to click on it to run it.



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BROWSE ARTICLES BY
Cochrane Reviews | DARE | CENTRAL |
Methodology Reviews | HTA | MESHED | About
| Topics

SEARCH IN THIS TITLE
[Input Field] [Go]
Cochrane Advanced Search
Search History

Search Results

Show Results in:
Cochrane Reviews (7) | DARE (0) | CENTRAL (0) | Methodology Reviews (0) | HTA (0) | MESHED (0) | About (0)

There are 7 results out of 3569 records for: 'UP AND #2) in The Cochrane Database of Systematic Reviews'

View: 1-7

[Export All Results](#)

Restrict by: [Evidence](#) | [Protocol](#) | Sort by: [Record Title](#) | [Match %](#) | [Year](#)

<input type="checkbox"/>	<p>Recent information Adolescent low-fat diets for obesity S Pizzoc, C Summerbell, C Gnanani, P Ouzzar Year: 2002 Details</p>
<input type="checkbox"/>	<p>Energy/protein restriction for high weight for height or weight gain during pregnancy MS Kwan Year: 1996 Details</p>
<input type="checkbox"/>	<p>Improving health of obese people: management and the organization of care for overweight and obese people E. Hevner, A M Ostry, SFL Kirs, CD Summerbell Year: 2001 Details</p>
<input type="checkbox"/>	<p>Interventions for preventing obesity in children K Campbell, E Waters, S O'Meara, S Kelly, C Summerbell Year: 2002 Details</p>
<input type="checkbox"/>	<p>Interventions for treating obesity in children CD Summerbell, V Ashton, KJ Campbell, L Edmunds, S Kelly, E Waters Year: 2003 Details</p>
<input type="checkbox"/>	<p>Long-term pharmacotherapy for obesity and overweight R Pothuizen, GK U, DOW Lau Year: 2003 Details</p>
<input type="checkbox"/>	<p>Surgery for morbid obesity J Colautri, A Ogo, M Sidhu, P Royce Year: 2003 Details</p>

The combined search (#1 AND #2) returns 236 results across all the databases.

You can save this whole record of Search History, which with sophisticated search technique can add up to hundreds of lines of search, by clicking on the button 'Save Search Strategy'

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BROWSE ARTICLES BY
Cochrane Reviews | DARE | CENTRAL |
Methodology Reviews | HTA | MESHED | About
| Topics

[Advanced Search](#) | [MeSH Search](#) | [Search History](#) | [Saved Searches](#)

Search For:
[Input Field] [Go]

Date Range (4-digit year): [Input Field] - [Input Field]

Restrict by record status: [All records](#)

Restrict by field: [Search All Text](#)

Current Search History

#1	obesity AND child	All Fields or obesity AND no diet in All Fields or obesity AND intent in All Fields in all products	421	edit	delete
#2	MeSH descriptor Obesity exclude all trees in MeSH products		2470	edit	delete
#3	(#1 AND #2)		236	edit	delete

[Save Search Strategy](#) [Clear History](#)

Wiley InterScience: Cochrane Search Strategy

Strategy Name:
[Input Field: Childhood Obesity]

Comments:
[Input Field: Advanced Search and MeSH search combined]

[Save Search Strategy](#) [Cancel](#)

Save your Search history by clicking this button

A pop-up box will appear, prompting you to name and add comments to your search.

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BROWSE ARTICLES BY
Cochrane Reviews | DARE | CENTRAL |
Methodology Reviews | HTA | MESHED | About
| Topics

SEARCH IN THIS TITLE
[Input Field] [Go]
Cochrane Advanced Search
Search History

[Advanced Search](#) | [MeSH Search](#) | [Search History](#) | [Saved Searches](#)

Your strategy was successfully saved

You have 2 Saved Searches

Delete	Saved Search Item	Run	Save Date	Alert Status
<input type="checkbox"/>	Childhood Obesity: Advanced Search and MeSH search combined	Run	2004-09-15 13:51:34	no
<input type="checkbox"/>	schizor in All Fields and drugs in All Fields and atypical in All Fields and antipsychotic in All Fields in all products	Run	2004-09-15 12:13:25	<input type="checkbox"/> Alerts Alert

[Select All \(to delete all searches\)](#)

[Delete Checked Items](#)

Now, when you return to your saved searches you will see your saved search history. Click run located to the right of your search name to return to that search strategy.

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SEARCH ARTICLES BY
[Cochrane Reviews](#) | [DARE](#) | [CENTRAL](#) | [Methodology Reviews](#) | [HTA](#) | [NHS RPD](#) | [About](#) | [Links](#)

[Advanced Search](#) | [MeSH Search](#) | [Search History](#) | [Saved Searches](#)

Search For:

Date Range (4-digit year): -

Restrict by record status:

Restrict by field:

Childhood Obesity:
 Advanced Search and MeSH search combined

#	Search	Hits	EdM	Delete
#1	obesity AND child* in All Fields or obesity AND pediatric in All Fields or obesity AND infant in All Fields in all products	421	edit	delete
#2	MeSH descriptor Obesity exclude all trees in MeSH products	2470	edit	delete
#3	#1 AND #2	236	edit	delete

When you run your Saved Search Strategy, you will be returned to the saved search history.

HINT - you don't receive email alerts for saved search histories - but you can for individual searches (with the exclusion of your combined searches e.g. #1 AND #2). If you haven't already saved them, simply run them from your Search History and then click on Save Search on their results page.

6.0. EXPORTING CITATIONS

To export citations for your reference databases (e.g. EndNote), select which records you would like citations exported from by clicking on the boxes next to them. If you want to export all on that page, click the 'Select All' option at the bottom of the page. To export those selected, click the 'Export Selected Citations' button.

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BROWSE ARTICLES BY
[Cochrane Reviews](#) | [DARE](#) | [CENTRAL](#) | [Methodology Reviews](#) | [HTA](#) | [NHS RPD](#) | [About](#) | [Links](#)

SEARCH IN THIS TITLE

[Cochrane Advanced Search](#)
[Search History](#)

Search Results

Show Results In:
[Cochrane Reviews](#) (7) | [DARE](#) (10) | [CENTRAL](#) (20) | [Methodology Reviews](#) (0) | [HTA](#) (0) | [NHS RPD](#) (0) | [About](#) (0)

There are 7 results out of 3689 records for: "(#1) AND (#2)" in The Cochrane Database of Systematic Reviews

View: 1-7

Record Information Restrict to: [Reviews](#) | [Protocols](#) Sort by: [Record Title](#) | [Hits](#) | [Year](#)

<input type="checkbox"/>	Advice on low-fat diets for obesity S Prozzo, C Sumarso, C Cameron, P Oleszko Year: 2002 Record
<input type="checkbox"/>	Energy-protein restriction for high weights-for-height or weight gain during pregnancy MS Nezer Year: 1998 Record
<input type="checkbox"/>	Improving health professionals' management and the organization of care for overweight and obese people E Harvey, A-M O'Leary, SFL Kirk, CD Sumarso Year: 2001 Record
<input checked="" type="checkbox"/>	Interventions for preventing obesity in children K Campbell, E Waters, S O'Leary, S Kelly, C Sumarso Year: 2002 Record
<input checked="" type="checkbox"/>	Interventions for treating obesity in children CD Sumarso, V Ashton, KJ Campbell, L Edmunds, S Kelly, E Waters Year: 2003 Record
<input type="checkbox"/>	Long-term pharmacotherapy for obesity and overweight R Pothuizen, SK LL, DOW Lau Year: 2003 Record
<input type="checkbox"/>	Surgery for morbid obesity J Olszewski, A Chopp, M Sidhu, P Royce Year: 2003 Record

Select All (to export citations)

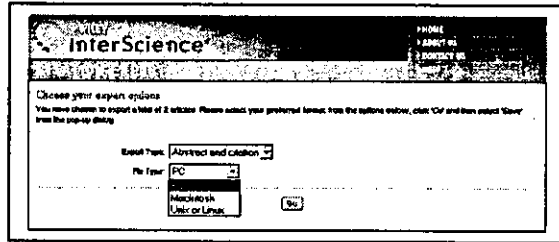
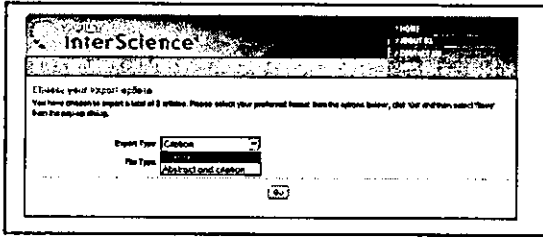
MULTIPLE RESULTS PAGES

The number of citations you export is not restricted. For multiple results pages, check items you want to export, then continue process for all page displays.

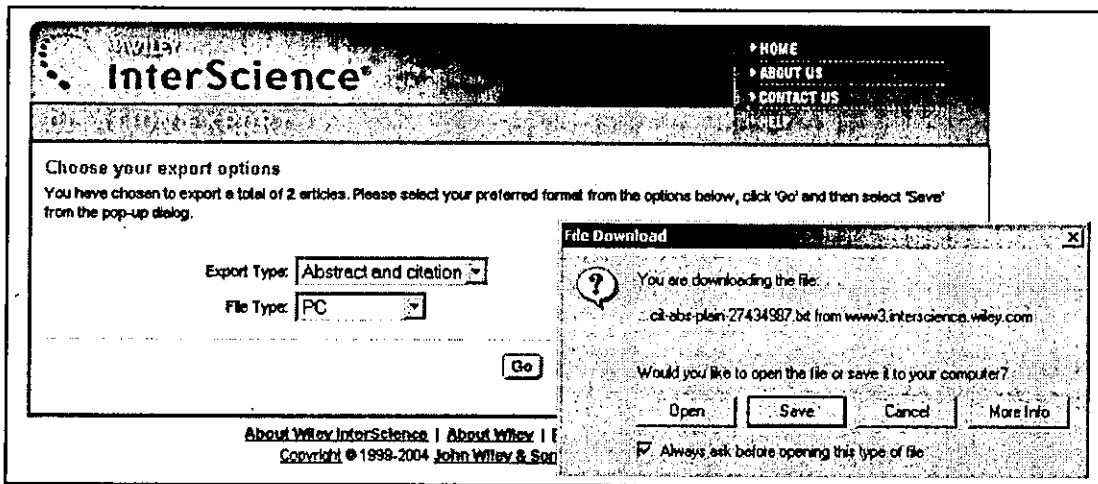
A pop up box will appear prompting you to select your Export Type and File Type from the drop down boxes:

Select your Export Type - choose between Citation only, or abstract and citation.

Select your File Type, depending on whether you are working on a PC, Mac or Unix/Linux



You will be prompted to either open or save the file:



7.0 NAVIGATING YOUR WAY AROUND A REVIEW

When you open a review in The Cochrane Library, it is displayed in frames. Below is an example of a Complete Review from the Cochrane Database of Systematic Reviews.

A Table of Contents for the article appears on the left of your screen. You can link directly to the section of the article that interests you using these links.

- [Review] Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries in children and adolescents
- PDF (Size 824K)
- Abstract
- Synopsis
- Background
- Objectives
- Criteria for considering studies for this review
- Search strategy for identification of studies
- Methods of the review
- Description of studies
- Methodological quality
- Results
- Discussion
- Reviewers' conclusions
- Potential conflict of interest
- Acknowledgements
- Characteristics of included studies
- Characteristics of excluded studies
- Characteristics of ongoing studies

You can choose to export the citation for this article from this TOC:

- References
- Export Citation

Figures (full size)
Tables

You can also link to figures and tables associated with the article.

[Review] Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries in children and adolescents

VOC Murrho, JPT Higgins, S Logan, A Sheiham

The Cochrane Database of Systematic Reviews 2004 Issue 3
Copyright © 2004 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
DOI: 10.1002/14651858.CD002782 This version first published online 20 October 2003 in Issue 4, 2003
Date of Most Recent Substantive Amendment: 20 August 2003

This record should be cited as: Murrho VOC, Higgins JPT, Logan S, Sheiham A. Topical fluoride (toothpastes, most dental cements in children and adolescents. *The Cochrane Database of Systematic Reviews* 2003, Issue 4, Art. No.: CD002782. DOI: 10.1002/14651858.CD002782

Background

Dental caries and its consequences pose important and uncomfortable problems in all industrialized societies and in a large number of developing countries. Although the prevalence and severity of dental caries in most industrialized countries have decreased substantially in the past two decades, reaching averages as low as 1.1 decayed, missing and filled teeth (DMFT) in 12 year olds, nearly half of those without any tooth decay or fillings (Marthaler 1996), this largely preventable disease is still common, increases significantly with age, and remains a public health problem for a significant proportion of the world population (Burt 1998). In the United Kingdom, 30% of 3.5 to 4.5 year olds (Moynihan 1996), and 50% of 12 year olds (Downer 1995) had experienced caries in 1993. In 2000, the figures were 40% for 2001 and 38% for 12 year olds in England and Wales (Pitts 2002). These findings demonstrate the consistency of caries prevalence and treatment services for these age groups in a country that has experienced a substantial caries level: vary considerably between and within different countries, but children in the lower socio-economic levels than those in the upper SES groups, and these differences are consistent in industrialized and in un-

Fluoride therapy has been the cornerstone of caries-preventive strategies since the introduction of water fluoridation schemes over five decades ago (Murray 1991). Fluoride controls the initiation and progression of carious lesions. Intensive laboratory and epidemiologic research on the mechanism of action of fluoride in preventing caries indicates that fluoride's predominant effect is topical, which occurs: of remineralization of early caries lesions and by reducing sound tooth enamel demineralization (Featherstone 1988). V. use have evolved, each with its own recommended concentration, frequency of use, and dosage schedule. The use of it in particular, which are much more concentrated than the fluoride in drinking water, has increased over recent decades: toothpastes (dentifrices), combinations. By definition the dentition, at elevated typical methods of professional also been used as a self-applied therapy. The extensive use regarding its cost-effectiveness children. Such procedures widespread form of fluoride been mainly attributed to it

However, there is currently the potential risks (mainly decreased caries prevalence selective professional fluor

SYNOPSIS

The use of fluoride toothpastes, mouthrinses, gels or varnishes reduces tooth decay in children and

Tooth decay (dental caries) is painful, expensive to treat and can seriously damage teeth. Fluoride is a mineral that prevents tooth decay. The review of trials found that children aged 5 to 16 years who applied fluoride in the form of toothpastes, mouthrinses, gels or varnishes had fewer decayed, missing and filled teeth regardless of whether their drinking water was fluoridated. Supervised use of self-applied fluoride increases the benefit. Fluoride varnishes may have a greater effect but more high quality research is needed to be sure of how by a difference these treatments make, and whether they have adverse effects.

BACKGROUND

Dental caries and its consequences pose important and uncomfortable problems in all industrialized societies and in a large number of developing countries. Although the prevalence and severity of dental caries in most industrialized countries have decreased substantially in the past two decades, reaching averages as low as 1.1 decayed, missing and filled teeth (DMFT) in 12 year olds, nearly half of those without any tooth decay or fillings (Marthaler 1996), this largely preventable disease is still common, increases significantly with age, and remains a public health problem for a

and epidemiologic research on the mechanism of action of fluoride in preventing caries indicates that fluoride's predominant effect is topical, which occurs mainly through promotion of remineralization of early caries lesions and by reducing sound tooth enamel demineralization (Featherstone 1988). Various modes of fluoride use have evolved, each with its own recommended concentration, frequency of use, and dosage schedule. The use of topically applied fluoride in particular, which are much more concentrated than the fluoride in drinking water, has increased over recent decades and fluoride containing toothpastes, dentifrices, mouthrinses, gels and varnishes are the modalities most

Header material includes the DOI (Digital Object Identifier), when the article was first published, the date of the most recent substantive amendment, and the correct method of citing the article.

The blue reference links will take you directly to that reference in the article's bibliography.

You can open, print and save PDFs of Reviews using the PDF link at the top of the Table of Contents. This is a good way of determining how many pages a review has before you print - this one has 131!

You can also use the PDF search feature to search the entire document for a particular word or phrase.

7.1 How to link to primary material cited:

The screenshot shows the InterScience interface. On the left is a navigation menu with options like 'Objectives', 'Criteria for considering studies for this review', etc. The main area displays a list of references. One reference is circled in red, and a red arrow points to the word 'Links' next to it. A text box on the right says 'Click on 'Links' next to the cited article you would like to link to.'

Ensure you are in the References section of your review

This will take you to a page with links to Title and Abstract indices for this citation:

The screenshot shows the PubMed search results page. The search query is '[ACTA ODONTOL SCANDINAV] AND 57[1] AND 12'. The search result for 'Gisselsson H, Birkhed D, Emilson CG' is displayed. A red box highlights the 'Links available for this article' section on the left side of the page, which includes links for 'Full Text', 'Abstract', and 'Indexing Services'.

Choose the link to the indexing service you wish to use to link to title, abstract and linking information for the paper.

7.2. Displaying the CDSR Odds-Ratio diagrams and tables

An integral feature of The Cochrane Database of Systematic Reviews is the odds-ratio figures provided for each review. These diagrams provide a clear and concise visual representation of the analyses of results for each trial included in a review, each outcome considered and any meta analysis of trials data.

The screenshot shows the Cochrane Review interface. On the left is a navigation menu with links: Abstract, Synopsis, Background, Objectives, Criteria for considering studies for this review, Search strategy for identification of studies, Methods of the review, Description of studies, Methodological quality, Results, Discussion, Reviewers' contribution, Potential conflict of interest, Acknowledgements, Characteristics of included studies, Characteristics of excluded studies, Characteristics of ongoing studies, Additional tables, Graphs, Sources of support, Index team, Cover sheet, References, and Support Contact. The main content area displays the review title: "Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries in children and adolescents" by YCC M ulaha, PPT Higgins, S Logan, A Shalton. Below the title is a "Background" section. A callout box with the text "Figures (full size) Tables" is overlaid on the page, with an arrow pointing from the "Tables" link in the callout to the "Tables" link in the left-hand menu.

Use the links to Figures and Tables to display pop-up screens of these features.

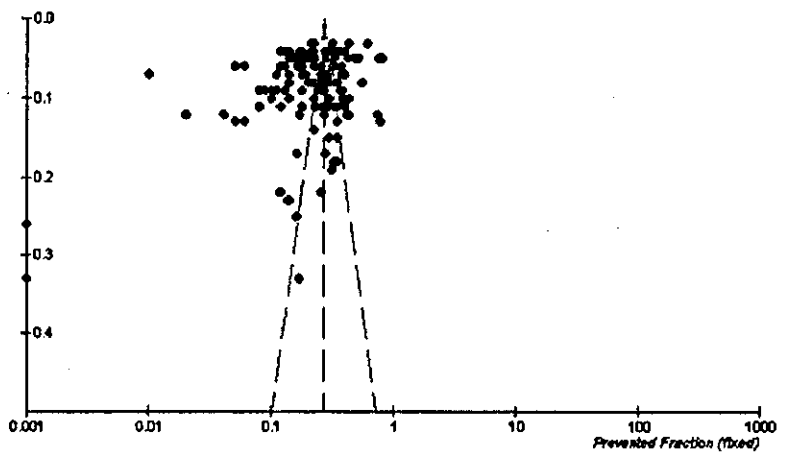
A screen containing Odds-Ratio diagrams will appear. The 'Tables' link will take you to associated tables. The Odds-Ratio diagrams are a very convenient tool - at first they may appear complicated, but as you become familiar with them and what they represent you will find that they are an invaluable means of providing a reliable overview of the evidence. A very useful training guide on interpreting these diagrams is available at: <http://www.york.ac.uk/inst/crd/clibsec3.pdf>



Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries in children and adolescents

Funnel Plot of D(M)FS PFs according to standard errors of the studies included in the meta-analysis

Review: Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries in children and adolescents
Comparator: 01 Topical Fluoride versus Placebo/No-treatment
Outcome: 01 D(M)FS increment (PF) - nearest to 3 years (133 trials)



To view an interactive version of this diagram, click on the 'Show Statistical Analysis' link.

D(M)FS increment (PF) - nearest to 3 years (133 trials) Show Statistical Analysis

Review: Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries in children and adolescents
Comparator: 01 Topical Fluoride versus Placebo/No-treatment
Outcome: 01 D(M)FS increment (PF) - nearest to 3 years (133 trials)

Study	TFT N	PLANT N	Prevented Fraction (SE)
01 Fluoride Toothpaste versus Placebo			
Abrams 1980	701	380	0.12 (0.04)
Andise 1975	984	376	0.21 (0.04)
Ashley 1977a	248	121	0.21 (0.08)
Blinkhorn 1983a	184	92	0.28 (0.09)
Brudevold 1986	906	223	0.21 (0.05)
Bube 1984	850	427	0.22 (0.03)
Cohen 1982	1200	708	0.13 (0.04)
Di Iagnello 1980	22	20	0.81 (0.03)
Dolles 1988	24	23	0.17 (0.32)

Hide Statistical Analysis

Statistic: Inv. Var. Row data Extra columns on graph

Effect: Random Year

Scale: Linear: -1 to 1 O-E and Variance (Peto and Hazard only)

CI Study: 95% Allocation Concealment

Overall CI: 95% User Defined

Review: Topical fluoride (toothpastes, mouthrinses, gels or varnishes) for preventing dental caries in children and adolescents
Comparator: 01 Topical Fluoride versus Placebo/No-treatment
Outcome: 01 D(M)FS increment (PF) - nearest to 3 years (133 trials)

Study	TFT N	PLANT N	Prevented Fraction (SE)	Prevented Fraction (Random) 95% CI	Weight (I)	Prevented Fraction (Random) 95% CI
01 Fluoride Toothpaste versus Placebo						
Abrams 1980	701	380	0.12 (0.04)	0.12 (0.04, 0.20)	1.0	0.12 (0.04, 0.20)
Andise 1975	984	376	0.21 (0.04)	0.21 (0.15, 0.27)	1.0	0.21 (0.15, 0.27)
Ashley 1977a	248	121	0.21 (0.08)	0.21 (0.08, 0.37)	0.8	0.21 (0.08, 0.37)
Blinkhorn 1983a	184	92	0.28 (0.09)	0.28 (0.09, 0.44)	0.7	0.28 (0.09, 0.44)
Brudevold 1986	906	223	0.21 (0.05)	0.21 (0.11, 0.31)	0.8	0.21 (0.11, 0.31)
Bube 1984	850	427	0.22 (0.03)	0.22 (0.19, 0.26)	1.0	0.22 (0.19, 0.26)
Cohen 1982	1200	708	0.13 (0.04)	0.13 (0.08, 0.21)	1.0	0.13 (0.08, 0.21)
Di Iagnello 1980	22	20	0.81 (0.03)	0.81 (0.76, 0.87)	1.0	0.81 (0.76, 0.87)
Dolles 1988	24	23	0.17 (0.32)	0.17 (-0.40, 0.80)	0.1	0.17 (-0.40, 0.80)
Fawcett 1988	422	422	0.21 (0.05)	0.21 (0.16, 0.27)	1.0	0.21 (0.16, 0.27)
Fujita 1979	880	440	0.18 (0.04)	0.18 (0.16, 0.20)	1.0	0.18 (0.16, 0.20)
Forsman 1974	614	148	0.18 (0.07)	0.18 (-0.03, 0.39)	0.7	0.18 (-0.03, 0.39)
Forsman 1974b	283	132	0.20 (0.08)	0.20 (-0.10, 0.50)	0.7	0.20 (-0.10, 0.50)
Glin 1988	164	82	0.28 (0.07)	0.28 (0.12, 0.44)	0.8	0.28 (0.12, 0.44)
Glass 1978	179	108	0.28 (0.07)	0.28 (0.12, 0.44)	0.8	0.28 (0.12, 0.44)
Glass 1983	167	208	0.28 (0.07)	0.28 (0.12, 0.44)	0.8	0.28 (0.12, 0.44)
Hannaford 1984	473	473	0.27 (0.05)	0.27 (0.19, 0.35)	1.0	0.27 (0.19, 0.35)
Hargreaves 1982	167	148	0.25 (0.07)	0.25 (0.11, 0.39)	0.8	0.25 (0.11, 0.39)
Hargreaves 1973a	148	138	0.26 (0.07)	0.26 (0.14, 0.42)	0.8	0.26 (0.14, 0.42)
Hargreaves 1973b	148	151	0.23 (0.08)	0.23 (0.11, 0.35)	0.8	0.23 (0.11, 0.35)
Hild 1988	22	21	0.88 (0.03)	0.88 (0.79, 0.98)	0.8	0.88 (0.79, 0.98)
Hild 1988b	18	17	0.71 (0.15)	0.71 (-0.08, 0.50)	0.3	0.71 (-0.08, 0.50)
Hild 1988c	14	18	-0.88 (0.20)	-0.88 (-1.74, 0.38)	0.1	-0.88 (-1.74, 0.38)
Hildje 1988	887	282	0.16 (0.05)	0.16 (0.08, 0.24)	0.8	0.16 (0.08, 0.24)
Hosomi 1988	229	280	0.17 (0.05)	0.17 (0.07, 0.27)	0.8	0.17 (0.07, 0.27)
Huang 1978	252	242	0.28 (0.05)	0.28 (0.14, 0.40)	0.8	0.28 (0.14, 0.40)
Jacobson 1982	488	420	0.12 (0.04)	0.12 (0.04, 0.20)	1.0	0.12 (0.04, 0.20)
Jones 1987	404	387	0.19 (0.07)	0.19 (0.04, 0.32)	0.8	0.19 (0.04, 0.32)
Jones 1987	489	379	0.21 (0.03)	0.21 (0.25, 0.37)	1.0	0.21 (0.25, 0.37)
King 1982	284	248	0.27 (0.08)	0.27 (0.28, 0.48)	0.8	0.27 (0.28, 0.48)

This will display a screen that allows you to manipulate how you want the data to be displayed.



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臨床疫学をどう学ぶか

香川大学医療管理学
平尾智広
2004.11.27 乃木坂

臨床疫学をどう教えるか(学ぶか)

- EBMの過程そのものが臨床疫学
- いわゆる疫学をどう学ぶか
- 生物統計学をどう学ぶか

EBMの5ステップ

1. 患者の問題の定式化
2. 問題についての情報収集
3. 得た情報の批判的吟味 ←
4. 情報の患者への応用
5. 1-4のステップの評価

JAMA ガイドによる批判的吟味

- 結果は妥当か？
デザインの問題
- 結果は何か？
結果指標の問題
- 結果は自分の患者に役立つか？

その前に疫学のチェック

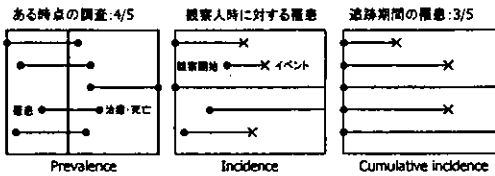
- 疫学研究の種類
- 疫学指標
- 疫学研究における誤差

疫学研究の種類

- 横断研究
- 縦断研究
 - 観察研究
 - ケースコントロール研究
 - コホート研究
 - 介入研究
 - コントロールなし前後比較
 - コントロールあり前後比較
 - コントロールあり無作為割付前後比較

疫学指標(1)

- 頻度の測定
 - Prevalence (有病)
 - Incidence (罹患)
 - Cumulative incidence (累積罹患)



疫学指標(2)

- 頻度の比較
 - 相対危険 (RR: relative risk) リスク比
 - 罹患率比 (IRR: incidence rate ratio)
 - 累積罹患率比 (CI: cumulative incidence rate ratio)
 - オッズ比 (OR)
 - 寄与危険 (attributable risk) リスク差
 - 罹患率差 (incidence rate difference)
 - 累積罹患率差 (cumulative incidence rate difference)
 - 寄与割合 (attributable proportion)
 - 人口寄与割合 (attributable population)

疫学研究における誤差

- 偶然
 - 検定、信頼区間
- バイアス
 - 研究終了後制御不能
- 交絡因子 (予後因子のことが多い)
 - 研究終了後でもある程度制御できる

JAMA ガイドによる批判的吟味

- 結果は妥当か？
 - デザインの問題
- 結果は何か？
 - 結果指標の問題
- 結果は自分の患者に役立つか？

デザインの問題 (治療編)

- 問題の定義
- 無作為性
- ITT分析
- ブラインド
- 観察期間
- 脱落数
- 割付られた群間の予後因子 (属性)

結果指標の問題 (治療編)

- 効果の大きさ
 - アウトカム (あり/なし)
 - リスク比
 - リスク差
 - 相対リスク減少率 (RRR)
 - 絶対リスク減少率 (ARR)
 - 治療必要数 (NNT)
- 効果の精度
 - 95%信頼区間 (CI)
 - P値

	治療群	対照群
あり	A	B
なし	C	D

治療群発生率 (EER) = $A/(A+C)$
 対照群発生率 (CER) = $B/(B+D)$
 相対リスク減少率 (RRR) = $(CER - EER)/CER$
 治療が対照に比してリスクを何%減らしたかを表わす。
 絶対リスク減少率 (ARR) = $CER - EER$
 治療が対照に比して減らした絶対リスクを表わす。
 治療必要数 (NNT) = $1/ARR$
 真のアウトカムを1人減らすのに必要な治療患者数

デザインの問題(診断編)

- 問題の定義
- 患者の選定
- ゴールドスタンダード(基準)
- ブラインド
- 診断非確定患者の追跡

結果指標の問題(診断編)

- 効果の大きさ
 - 感度
 - 特異度
 - 陽性的中率
 - 陰性的中率
 - 検査前確率
 - 尤度比(LR)

	疾患あり	疾患なし
陽性	A	B
陰性	C	D

- ①感度= $A/(A+C)$ SpPin
 ②特異度= $D/(B+D)$ SpNout
 陽性的中率= $A/(A+B)$
 陰性的中率= $D/(C+D)$
 ③陽性尤度比 $LR(+)=\text{感度}/(1-\text{特異度})$
 陰性尤度比 $LR(-)=(1-\text{感度})/\text{特異度}$
 ④ノモグラム
 検査前確率= $(A+C)/(A+B+C+D)$
 検査前オッズ=検査前確率/(1-検査前確率)
 検査後オッズ=検査前オッズ $\times LR(+)$
 検査後確率=検査後オッズ/(検査後オッズ+1)

尤度比

- $>10, <0.1$
 - 検査前後の確率に大きな変化をもたらす
- 5-10, 0.1-0.2
 - 中等度の変化をもたらす
- 2-5, 0.2-0.5
 - 小さな変化をもたらす
- 1-2, 0.5-1
 - わずかな変化をもたらす

統計モデル

- 単変量
- 多変量
 - 重回帰
 - 共分散
 - 多重ロジスティック
 - 比例ハザード

線形モデル
 $Y=A+B_1X_1+B_2X_2+\dots+E$ (誤差)
 Y: 目的変数 X_1, X_2, \dots : 説明変数 E: 誤差
 B: 係数
 多変量解析のこころ
 例えばX1について見てみると、他の説明変数(X2等)が、一定不変とした場合、X1が1変化するるとYはB1変化すると言う意味。
 ロジスティック回帰では、Bがそのままオッズ比となる。

指導医の悩み

- いわゆる疫学をどう学ぶか
- 生物統計学をどう学ぶか
- へたをすると研修医の方が詳しいかも
- じっくり学びたいが時間が無い
- 何回読んでもすぐ忘れる

教えると言うよりはいっしょに学ぶ

- 教科書から
- ケースから
- 詳読会
- ...
- 日々じっくりと実践

EBM理解のための

生物統計学

のヒント

鎌江伊三夫
神戸大学大学院医学系研究科
応用統計医学

EBM教育者講習会
2004年11月

アウトライン
プロローグ

- EBMの基本研究デザイン
 - 1) コホート研究
 - 2) ケース・コントロール研究
 - 3) ランダム化比較臨床試験 (RCT)
- 生物統計学のキーワード
 - 1) ランダムサンプリング / 中心極限定理
 - 2) 標準偏差 (SD) と標準誤差 (SE)
 - 3) P値とは?
 - 4) 95%信頼区間 (95CI) とは?
 - 5) 標本サイズ
 - 6) 解析のエラー “ α と β ”
 - 7) ITT
 - 8) コクランのシンボル - メタアナリシス -
- EBMの新キーワード
 - 1) NNT
 - 2) NNTの切り替え効果
 - 3) NNTと2項分布
 - 4) NNTの問題点
- EBMでよく聞かれる誤り
おわりに

プロローグ

- ケース・コントロール研究では、オッズがよい指標となる。
- RCTのエビデンスを個別の患者に主観的に適用することがEBMである。
- 有意差の出ない研究は失敗。
- NNTは、ARRの逆数で定義される定数である。
- NNT=31は、31人に新薬を使って1人が有効、30人が無効となることである。
- EBMはガイドライン作り、あるいはCook book Medicineである。
- 日本流EBMを目指すべきである。

1. EBMの基本研究デザイン

1) コホート研究

コホート

疾病

健康

追跡研究(コホート)

		疾患	
		あり	なし
要因	あり	A	B
	なし	C	D

要因ありの時の罹患リスク = $\frac{A}{A+B}$

要因なしの時の罹患リスク = $\frac{C}{C+D}$

→ リスク比 (Risk Ratio, RR) = $\frac{A}{C} \div \frac{B}{D}$

または Relative Risk

- 要因から疾患をさぐる (前向き: プロスペクティブ)
- 手間/コストがかかる
- バイアスは取り除きやすい
 - 層化 (Stratification): マンテル・ヘンツェル検定
 - マッチング
- ☆ 罹患リスクがわかる

2) ケース・コントロール研究

要因

あり

なし

疾病

健康

症例対照研究(ケース・コントロール)

疾患

- ・疾患ありの時の要因 $P_1 = \dots$
- ・疾患なしの時の要因 $P_2 = \dots$

→オッズ比 (Odds Ratio, OR) = $\frac{P_1}{P_2}$

- 疾患から要因をさぐる (後向き; レトロスペクティブ)
- 比較的容易に行える (手間/コスト)
- バイアスの影響を受けやすい
- ☆ 罹患リスクがわからない

3) ランダム化比較臨床試験(RCT)

RCT: Randomized Controlled Clinical Trial

- 基本的には、コホートと同じ前向き研究
- ランダム化により科学性が期待
- EBMでは、罹患リスク P_1 は、EER または ART
罹患リスク P_2 は、CER または ARC
- マスキング (2重/3重)
- キー割り付け (封筒法、センター管理方式) 固定/動的

2. 生物統計学のキーワード

1) ランダムサンプリング

母集団: 平均 μ_0 , 分散 σ^2

標本サイズ n : 平均 \bar{X} , 分散 s^2 , $N\left(\mu_0, \frac{\sigma^2}{n}\right)$

中心極限定理

- 1) 母集団: $N(\mu, \sigma^2) \rightarrow$ 標本分布: $N(\mu, \sigma^2/n)$
- 2) サンプルサイズ大 (通常、 $n \geq 30$) のとき \rightarrow 標本分布は正規

2) 標準偏差 (SD) と標準誤差 (SE)

標準偏差 (SD)

$$SD = \sqrt{\frac{\sum (x_i - \bar{x})^2}{n-1}}$$

n はサンプル数
 $n-1$ は自由度

標準誤差 (SE) 無限母集団の場合

$$SE = \frac{\sigma}{\sqrt{n}}$$

σ は母集団の標準偏差
 n はサンプル数

3) P値とは?

$P = \text{Prob}(X \geq x_0)$

$z = \frac{x - \mu}{\sigma}$

> 2群の比較 $H_0: \mu_0 = \mu_1$

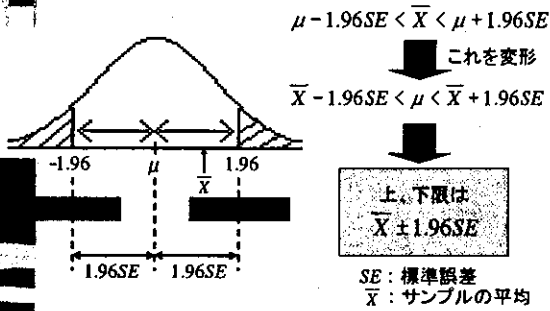
$H_0: \mu_0 = \mu_1$ 対照群の分布

$H_1: \mu_0 < \mu_1$ 実験群の分布

対照群の平均 μ_0 , 実験群の平均 μ_1

$P = \text{Prob}(X \geq x_0) < 0.05$ ならば
 $H_1: \mu_0 < \mu_1$ が成立することにする
 \rightarrow (偶然のゆらぎかもしれない; α エラー)

4) 95%信頼区間(95CI)とは？



95CIの解釈

同じ母集団において、同じ症例数・デザインでの研究を無限回くりかえした場合に得られる無限個の95CIの95%が、 μ を含む。

▶ 注意

「 μ が信頼区間内に入る可能性が95%である」という表現は不十分

P値か95CIか

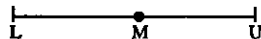
P値が5%より小 (有意差あり)

↔ RRの95%CIが1を含まない (OR)

↔ ARRの95%CIが0(ゼロ)を含まない

▶ 95%CIの利点

- 幅を持たせた推定ができる



- 検定(又はP値)が不要

信頼区間(95%CI)

母集団の平均値が95%の確率で存在する推定値の範囲

例) サンプル平均の95%CI = $(\bar{X} - 1.96 \frac{\sigma}{\sqrt{n}}, \bar{X} + 1.96 \frac{\sigma}{\sqrt{n}})$

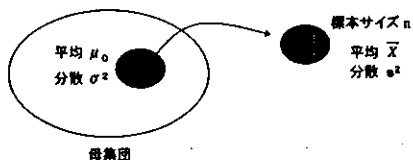
★ RRの95%CI $\Rightarrow RR \cdot e^{\pm 1.96 \cdot \ln RR}$

ただし、 $\ln = \frac{a_1 + a_2 + \dots + a_n}{N}$, $\ln = \frac{b_1 + b_2 + \dots + b_n}{N}$

★ ORの95%CI $\Rightarrow OR \cdot e^{\pm 1.96 \cdot \ln OR}$

ただし、 $\ln = \frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}$

5) 標本サイズ



標本サイズnは、 $\alpha(Z_\alpha)$ 、 $\beta(Z_\beta)$ 、平均の差 Δ 及び標準偏差 σ のバランスで決まる。

$$n = \left[\frac{(Z_\alpha + Z_\beta) \sigma}{\Delta} \right]^2$$

ただし $\Delta = \mu_1 - \mu_0$

6) 解析のエラー “ α と β ”

■ 検定の結果が真実と異なることがある。これをエラーと呼ぶ。

- 真実は有意差がないのに、検定では「差あり」と判断されてしまう

$\Rightarrow \alpha$ エラー (第1種の誤り)

- 真実は有意差があるのに、検定では「差なし」と判断されてしまう

$\Rightarrow \beta$ エラー (第2種の誤り)

エラーと検出力

	真実	
	差あり O.K.	差なし αエラー
結論	差あり 検出力(1-β) βエラー (第2種の過誤)	差なし αエラー (第1種の過誤) O.K.

あわてもののα(危険率)
ぼんやりのβ

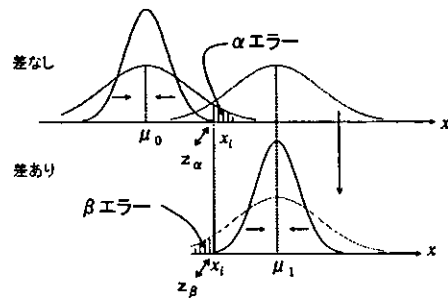
真実差があるとき、「差あり」の結論を得る確率を

検出力(パワー)と呼ぶ。

$$\text{検出力} = 1 - \beta$$

確率分布とエラー部分

標本サイズ n 平均差 Δ } の関係
αエラー → z_α βエラー → z_β



7) ITT

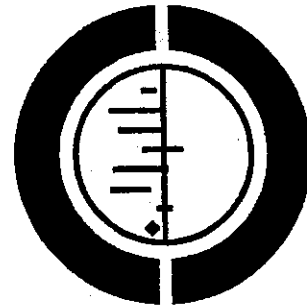
RCTにおいて脱落例を除外する完了者解析(CLT解析)では、ランダム化のバランス(compatibility)が崩れるため、その対策として、最初に割り付けたデザインで解析することを

Intention to treat (ITT)解析

と呼ぶ。

- ランダム化は？ マスキングは？ 検出力は？ サンプルサイズは？
- 一般化は？ 生物学的/生理学的妥当性は？

8) コ克蘭のシンボル — メタアナリシス



メタアナリシス

- 定義 多数のRCTの結果を統合する分析法
- 例 ある高血圧治療薬の既知の3つのRR 1.0, 1.8, 3.2を統合すれば1.6となった
- 意義 臨床では一つの指標がわかりやすい

メタアナリシスの手法

- 固定効果モデル
研究間の変動は、ランダムサンプリングに起因
- ランダム効果モデル
研究間の変動は、真の効果が異なることに起因
- ベイズモデル

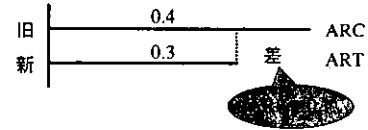
3. EBMの新キーワード

1) NNT(治療必要数)

- 定義 NNT = 1 ÷ 有効率の差
- 例 高血圧治療の有効率がA薬、B薬、各々50%、40%のとき、
NNT = 1 ÷ (0.5 - 0.4) = 10
- 注意 B薬からA薬への切り替え効果は10人に1人の割合で生じる

2) NNTの切り替え効果

➤ NNTは切り替え効果の目安



1) 旧→新: $NNT = \frac{1}{0.1} = 10$

2) 新→旧: $NNH = \frac{1}{ARI} = \frac{1}{0.1} = 10$

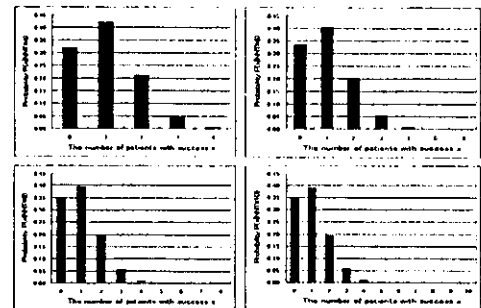
ARI : 絶対リスク増加

◇ 切り替えの方向に要注意

3) NNTの問題点

- ベースラインの無視
- 時間依存性
- 非直線性(非線形)
- 適正なカットオフ値
- 無効確率の存在

4) NNTと2項分布



The probability profile of binomial events in a new therapy regarding the NNT of 4, 6, 8 and 10.

4. EBMでよく聞かれる誤り

- ケース・コントロール研究では、オッズがよい指標となる。
- RCTのエビデンスを個別の患者に主観的に適用することがEBMである。
- 有意差の出ない研究は失敗。
- NNTは、ARRの逆数で定義される定数である。
- NNT=31は、31人に新薬を使って1人が有効、30人が無効となることである。
- EBMはガイドライン作り、あるいはCook book Medicineである。
- 日本流EBMを目指すべきである。

おわりに

科学的な医療の実現

