The WHO Reproductive Health Library
A Training Manual
The WHO Reproductive Health Library

A Training Manual

World Health Organization
Regional Office for South-East Asia
New Delhi
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Preface

The World Health Organization is committed to the promotion and implementation of evidence-based practices in health care in all populations. Evidence-based health care may be defined as the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.

The WHO Reproductive Health Library (RHL), is a tool developed by the World Health Organization to help promote evidence-based reproductive health care. The library comprises reviews from The Cochrane Library, which are relevant to reproductive health with comments and recommendations on the applicability of the findings of these reviews in developing-country settings. It also includes implementation aids as well as other useful information related to reproductive health. The WHO RHL is updated annually.

The WHO Regional Office for South-East Asia organized a regional workshop on WHO RHL at Hat Yai, Songkhla, Thailand in August 2003. The workshop aimed to expand access to, and use of evidence-based reproductive health care by using the WHO RHL as a source of authoritative information on key reproductive health issues.

This training manual has been developed to assist in improving health care through principles and practices of evidence-based health care (EBHC) in reproductive health to health-care providers and policy-makers. The RHL training manual designed in a modular form may be used by an individual, or by groups of learners. In addition, the Facilitator’s Manual (available on a CD along with this manual) is designed to help facilitators to organize a training course on EBHC in reproductive health.

It is hoped that this manual will further strengthen the implementation of evidence-based practices in reproductive health throughout the South-East Asia Region.

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Regional Director
The first draft training manual was prepared by Dr Tippawan Liabsuetrakul from the Prince of Songkla University, Thailand. The draft manual was field-tested through a workshop with participation of invitees from six Member States. Dr Metin Gulmezoglu from the Department of Reproductive Health and Research, WHO/HQ and Dr Ricky Lu, representative from JHPIEGO (a non-profit international public health organization affiliated with John Hopkins University), participated in this workshop and provided invaluable inputs and support. Participants from countries provided suggestions to make the guidelines more user-friendly. Following the workshop, Dr Matthews Mathai from the Christian Medical College, Vellore, India, revised the draft training manual and used a similar document developed by the WHO Regional Office for Africa as reference to finalize this manual for the WHO Regional Office for South-East Asia.
Goal and objectives

The goal of this manual is to improve patient care by teaching principles and practices of evidence-based health care (EBHC) in reproductive health to health care providers and policy-makers. Evidence-based health care may be defined as the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.

The manual is designed in a modular form and may be used by individual learners, or by groups of learners attending a workshop on EBHC in reproductive health.

After using the manual, you should be able to:

• Formulate answerable clinical questions
• Search effectively for evidence using the WHO Reproductive Health Library
• Critically appraise clinical evidence for its validity and applicability
• Understand basic measures of efficacy such as Relative Risk and Numbers Needed to Treat

What are the basic requirements for using the manual?

To facilitate optimal learning, you should have:

• Working knowledge of English
• Basic computing skills
• A copy of the WHO-RHL to use with the manual.

You do not need detailed knowledge of statistics and computer software.

The WHO RHL can be used on any personal computer that has a Pentium processor with a minimum of 32 MB of RAM. RHL is currently produced only as a Microsoft Windows™ programme which can run from a Compact Disk drive. The programme can also be installed on the hard disk if about 650 MB of free space is available for installation. Instructions for installation of the programme are available with the RHL diskette.

How can you subscribe to RHL?

If you are using RHL for the first time, please remember to fill in and send your subscription form to:

The WHO Reproductive Health Library
Reproductive Health and Research
World Health Organization
1211 Geneva 27
Switzerland

Alternatively, you can send the same information to RHL@who.int.

Subscription to RHL is free to individuals from developing countries.
An Introduction to Evidence-based Reproductive Health Care

Objective
At the end of this chapter, you should be able to satisfactorily explain the term, “evidence-based reproductive health care” and what it implies.

What is Evidence-based Health Care?
The term “evidence-based health care” (EBHC) is a relatively new term. It may mean different things to different people. Essentially, this term may be defined as “the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients”.

To understand this, you could analyse the different terms used:
• “Conscientious” means carefully and with diligence
• “Explicit” means precisely and clearly
• “Judicious” means sensibly and with good judgement

You could rephrase this definition:

“Evidence-based health care is the use of current best evidence carefully, diligently, precisely, and with good judgement in making decisions about the care of individual patients.”

How do you practise EHBC?
In order to practise EHBC, you will need to integrate individual clinical expertise with the best available clinical evidence from systematic research.
• *Individual clinical expertise* means the skill and judgement which you as an individual health care worker have acquired through clinical experience and clinical practice.

• *Best available clinical evidence* means clinically relevant research from both basic medical sciences, and from patient-centred clinical research into the safety and efficacy of therapeutic interventions.

Why is it important to integrate these two components? Without clinical expertise, you will not be able to apply knowledge of best evidence to the care of the individual patient appropriately. Similarly, without knowledge of current best evidence, your clinical practices may soon become out of date and possibly harmful to your patients.

Thus, in order to practise EHBC, you will need to:

• Get the current best evidence

• Apply the current best evidence to individual settings.

There has been an explosion of information available these days. However, there are also newer opportunities to access this information. Evidence-based health care offers:

• The tools to apply the evidence to specific settings

• A systematic approach to the science of applying the evidence

• Explicit information regarding uncertainty within the information available

You will learn more about how to get the current best evidence as you go through this manual. However, it is important to remember that individual settings differ in terms of resources, background prevalence rates of illness, and community values, among others. Evidence may therefore apply differently to different settings.

Thus, while practising EHBC you should also consider other factors such as:

• Expertise of the caregiver

• The specific setting in which the patient is seen

• The values of the individual

• The values of the community in which that individual resides

• The costs involved

Experience, judgement and caring are indispensable for providing high quality EHBC.

**To summarize:**

EHBC is new in that it is more explicit and systematic in the collection and application of evidence. EHBC complements but does not replace experience, judgement and caring.
Objectives

At the end of this chapter, you should be able to:

• Formulate a clinical question in a way that facilitates the search for relevant information
• List the different sources of information with which to answer a clinical question and the relative merits of these sources
• Explain the different study designs used in clinical research

Step 1: Asking a clinical question

When you see a patient, it is likely that you will need new information about some aspect of his or her clinical problem. You may want some additional information on:

• Diagnosis – e.g., what tests are useful to confirm your clinical suspicion? – or
• Prognosis – e.g., what are the chances of complete recovery with this illness? – or
• Immediate management – e.g., which is the drug of choice for the management of this disease? – or
• Future risks – e.g., how can this condition be prevented in the next pregnancy?

Sometimes the information is readily available. Many times, however, the information has to be sought. There are more than 20,000 biomedical
For most health care providers, the efforts to track down the best evidence relevant to the question can be a daunting task given the limited time available for reading and keeping up-to-date in a busy clinical situation. This chapter will provide you with an overview of how you can ask a clinical question and get an answer from the “information overload”.

A well-built clinical question should include the following:

• The intervention – What is being done?
• The condition or health problem – What is being treated or prevented?
• The patient and setting – Who is being affected?

Take a few minutes to read the following example:

You are developing guidelines regarding ways to reduce mother-to-child transmission of HIV in your clinic. You specifically want to know if antiretroviral drugs reduce the viral load and, consequently, the transmission of HIV to the foetus around the time of birth.

How will you formulate the clinical question? Take a few minutes to think and formulate the three-part question:

• What is the condition or health problem?
• Who is being affected?
• What is being done?

Write down your answer:


Step 2: Searching for an answer

You have formulated the clinical question. How do you find the appropriate evidence that will give you the current best evidence in answer to your question?

You may have one or more of these options:

(a) Visit the local medical library

• Is your library well stocked with medical literature and up-to-date? If not, it may not be a good idea.
(b) **Consult an expert**

- This may be quicker but your results will depend on the expertise of the expert!

(c) **Look for the answer in text books**

- Text books take so long to write and publish that, on average, they are way out of date by the time they arrive at the sales point.

(d) **Look for answers in practice guidelines**

- Do you have practice guidelines? How up-to-date are those guidelines? If those guidelines were developed elsewhere, are they relevant to your situation?

(e) **Do a computer search**

- You will need a computer with reliable internet connection.
- If you have these, then you could use PubMed.
- PubMed, a service of the National Library of Medicine (USA), provides access to over 11 million MEDLINE citations back to the mid-1960s and additional life science journals. PubMed also includes links to many sites providing full text articles and related resources.
- MEDLINE is the National Library of Medicine’s database of 11 million indexed citations (articles) and abstracts covering nearly 4500 journals published in the United States and more than 70 other countries. You can access this through the following internet address: [http://www.nlm.nih.gov](http://www.nlm.nih.gov)
- There is a wealth of information available on the internet. However, you should be aware that much of this literature has not appeared in paper publications and may not therefore been subjected to a rigorous peer review process.

(f) **Look for the answer in randomized controlled trials**

- Evidence of the effect of an intervention is generated by the results of clinical trials. The clinical question that you have asked is the effect of an experimental intervention (giving antiretroviral drugs to the mother) compared to the effect of a controlled intervention (no treatment). You will learn more about randomized clinical trials later.

(g) **Look for the answer in systematic reviews**

- You will learn more about systematic reviews later in “Interpreting Information”.

Before you learn about randomized controlled trials and systematic reviews, you should learn a few epidemiological study designs:

**Study designs**

Study designs may be:

- **Observational** – where one or more groups of patients are “observed” by the researcher, and certain characteristics of the observed group or groups that are of relevance to the research question are recorded.
• **Experimental** – an intervention or “experiment” is performed (e.g. giving a drug) on one or more groups of patients, and the effects of the intervention are recorded by the researcher.

There are different types of observational studies

(a) **Case control studies**

(i) The study begins with the absence or presence of an outcome and the investigators then look backwards in time to try to detect possible causes or risk factors.

• *E.g., you could study a group of babies, some of whom are of low birthweight and others are normally grown, and compare the smoking habits of the parents in the two groups. The outcome here is low birthweight and the possible risk factor is parental smoking habits.*

(b) **Cross-sectional studies**

(i) The investigators analyze data collected on a group of subjects at one time rather than over a period of time. Cross-sectional studies are designed to determine “What is happening?” right now.

• *E.g., you could check haemoglobin levels at the first antenatal visit to study the prevalence of anaemia in early pregnancy.*

(c) **Cohort studies**

(i) A cohort is a group of people who have something in common and who remain part of a group over an extended period of time. Investigators record outcomes after observing the group over a period of time.

• *E.g., you could study a group of women after menopause over several years to study the effects of menopause on women’s health.*
Among experimental studies, the different types of trials include:

(a) Non-randomized controlled trials

(i) A controlled trial compares an intervention group with a control group, the two arms of the trial. In a non-randomized trial, participants are not always allocated to the different arms of the trial in a random manner. This can lead to imbalances between the groups being compared and would have a negative influence on the results of the trial.

(b) Randomized controlled trial (RCT)

(i) This is the principal research design in the evaluation of medical interventions. The aim is to use a method of allocating the participants to the two arms of the trial that ensures that the participants will be similar in all respects other than the intervention being given, apart from the effect of chance. This is done by randomly assigning participants in a way that minimizes imbalances between the groups.

(ii) One of the factors that influence the value of a random controlled trial is the method of random allocation.

(c) Methods of randomization include

(i) Quasi-random allocation:

- A method of allocating participants that is not truly random, for example, allocation by date of birth, day of the week, medical record number, day of the year or the order in which participants are included in the study (e.g. allotting participants alternately to two arms of a trial).

(ii) True random allocation:

- A method of allocation that uses the play of chance to assign participants to comparison groups in a trial, e.g. by using a random numbers table or a computer-generated random sequence. Random allocation implies that each...
individual being entered into a trial has the same chance of receiving each of the possible interventions. It also implies that the probability that an individual will receive a particular intervention is independent of the probability that any other individual will receive the same intervention.

**Step 3: Finding the evidence**

It would be good if there is a recent article or report that summarizes all previous research in your area of interest. A review article summarizes a number of different studies and may draw conclusions about a particular intervention. Individual reports of studies may be misleading if we do not pay attention to certain details.

What are the basic requirements for a literature review?

You will need:

- A readable and understandable summary of all the evidence relevant to a particular problem;
- An unbiased summary of the evidence;
- A transparent summary showing clearly how the evidence was collected and summarized; and
- A summary which is kept up-to-date.

*A bias is any trend in the collection, analysis, interpretation, publication or review of data that can lead to conclusions that are systematically (as opposed to randomly) different from the true state of affairs. An unbiased summary of evidence avoids biases in all these steps of data review.*

*A transparent summary is one in which the methods which have been used to select the studies and summarize the data are obvious, apparent, and unambiguous.*

**Types of Literature Review**

There are two types of literature review – the traditional review and the systematic review.

The **Traditional Review** is the generic term for any attempt to synthesize (combine into a logical and consistent whole) the results and conclusions of two or more publications on a given topic. Such reviews are usually produced by a “content expert”.

What are the potential problems with a traditional review? The author of a traditional review may:

- Include only certain studies in the review, depending on the preferences (and friends) of the author. This preference is called **Selection bias**
- Choose only studies with statistically significant results. Studies with statistically significant results are a) more likely to be published and b) more likely to be published in
significant journals. Those studies with negative conclusions may not be published. This problem is called Publication bias.

- Choose studies to include in the review depending on the language in which they are written. Statistically significant results are more likely to be published in English but there may be equally important information published in languages which are unfamiliar to the reviewer, a preference referred to as Language bias.

- Look for the studies in databases using search terms that have only recently been included in the indexing of articles. This is called Indexing bias. Even the term “randomized controlled trials” has only recently been introduced into MEDLINE as an indexing term. Further, only 23% of medical journals are indexed on MEDLINE as you will see from this diagram representing the final number of RCTs that are indexed on MEDLINE.

Thus, you can see that in a traditional literature review, bias can clearly distort the results and is to be avoided at all costs.

The Systematic Review, in contrast to the traditional review, comprehensively locates, evaluates, and synthesizes all the available literature (primary research) on a given topic using a strict scientific design, which must itself be reported in the review.

A good systematic review reduces bias by:

- Addressing a clearly defined question;
- Explaining how studies for the review were located;
- Describes in detail the search strategy used for finding the studies;
Explaining what criteria were used to select studies, and on what basis studies were excluded from the review;
Explaining how data were collected from studies and how missing data were handled.

A systematic review is an important scientific research evidence in medicine because it:
- Collects large volume of information related to a question,
- Critically appraises individual research data with scientific techniques,
- Assures consistency (or inconsistency) of research results,
- Increases generalizability of the findings.

The evidence hierarchy

Systematic review
Randomized controlled trial
Cohort study
Case control study
Cross-sectional analytical study
Descriptive / narrative study

The best evidence for interventions comes from systematic reviews and RCTs. However, as we move down this hierarchy in evidence, we usually have less good information available.

Cochrane systematic reviews

A Cochrane systematic review is produced by the Cochrane Collaboration. The Cochrane Collaboration is an international organization that aims to help people make well-informed decisions about health care by preparing, maintaining and ensuring the accessibility of systematic reviews of the effects of health care interventions. The main work of the Collaboration is done by about 50 Collaborative Review Groups, within which Cochrane reviews are prepared and maintained. The members of these groups - researchers, health care professionals, people using the health services (consumers), and others - have come together because they share an interest in generating reliable, up-to-date evidence relevant to the prevention, treatment and rehabilitation of particular health problems or groups of problems. These reviews are available on payment of subscription fees.

The WHO Reproductive Health Library (RHL) includes Cochrane Reviews on reproductive health topics that are relevant to developing countries. Experts with experience in developing countries comment on these selected Cochrane Reviews with regard to the relevance and applicability of the findings in resource-poor settings. RHL also contains one-line summaries of the main findings of the Cochrane reviews, implementation aids and other useful information. RHL is available free of cost to subscribers in developing countries.
Finding answers to your clinical question

At the beginning of this chapter, you had formulated a three-part clinical question about use of antiretroviral drugs for reducing mother-to-child transmission of HIV.

Take a few minutes to read the Cochrane systematic review on “Antiretrovirals to reduce mother- to-child transmission of HIV”.

If the WHO RHL has not yet been installed on your computer, go to “An Introduction to The WHO Reproductive Health Library” for instructions on installation.

If the WHO RHL is already installed on your computer, open the library by clicking on the RHL icon. Then type in “Antiretrovirals” in the search box on the left and click “Go”. Next click on the following links serially

1. “Systematic Reviews and Commentaries”,
2. “Reproductive Tract Infections/STDs and HIV/AIDS”,
3. “Human Immunodeficiency virus”, and
4. ”Cochrane review: Antiretrovirals for reducing the risk of mother to child transmission of HIV infection”.

Then try to answer the following questions related to the systematic review:

Does this systematic review satisfy the criteria for a good systematic review?

**Specifically**, does it:

- Address a clearly defined question. If so, what was the question?
- List how studies were found?
- List the search strategy used for finding the studies?
- List what criteria were used to select studies?
- Explain on what basis studies were excluded from the review?
- Explain, and if so, list how data were collected from studies?

Later, as you learn to use the WHO Reproductive Health Library, you will find a detailed guide to the critical appraisal of systematic reviews in the RHL.
An Introduction to the WHO Reproductive Health Library

Objectives

At the end of this chapter, you should be able to:

- Work with the WHO Reproductive Health Library (RHL)
- Search for and access systematic reviews on the WHO RHL

Installing the WHO Reproductive Health Library (RHL)

The first step in learning to work with RHL is to have it installed on your computer. Information regarding the computer hardware and software that are required to run the programme are listed in “About this Manual”. In case the programme is already installed on your computer, you may skip this section and go on to the next.

To install the programme,

(a) Insert the RHL CD in the CD-ROM drive of your computer.
(b) Click the START button.
(c) Click the RUN command.
(d) Type X:\SETUP and click the OK button.
   - X refers to the drive letter of your CD-ROM drive. It is usually D, E or F. Insert the appropriate drive letter for your computer instead of X
(e) Follow instructions on the screen.

(f) You will be offered the option of installing the entire RHL on the hard disk of your computer, or of running it from the CD.

- If you choose to install the entire RHL on the hard disk, you will need about 650 MB of free space.
- If you choose to run it from the CD, you will need to insert the CD every time you use the RHL.

(g) The WHO RHL will be added to the list of programmes accessed from the START menu.

To run the programme:

- Click on the START button.
- Select PROGRAMMES and The WHO Reproductive Library to start the programme.
- Alternatively, you could double-click (click twice in quick succession) on the WHO RHL icon on the computer screen and this will start the programme.

You will see the opening screen as shown here:
The Opening Screen

The opening screen has three parts (each of which is highlighted in red in the following figures):

- **The menu bar** along the top of the screen

- **The content pane** on the left-hand side of the screen

- **The document pane** on the right-hand side of the screen

**The content pane:**

When you first open the library, the **content pane** displays the list of sections which make up the library. This display can be reloaded at any point by clicking **Clear**. You can **browse** the titles of the documents within any section.

The search window can be found at the top of the content pane. Use this to enter words or phrases when you are **searching** the library.

**The document pane:**

When you first open the Library, the **document pane** displays the name of the library, and a link to the files which describe the content of the library. When you are searching the library, you can **display** any item within the document pane by clicking the title of that document within the content pane.

You can clear both panes and return to the initial display at any time by clicking **Clear**.

The **opening screen** provides a series of links to descriptions of the library. You can reload this screen at any point by clicking **Clear**, and then selecting the appropriate links to the descriptions.
The menu bar:
The menu bar lies across the top of the screen. You will use the five buttons on the left-hand side to help you search the Library, and locate the documents you require.

The buttons on the right-hand side allow you to move around and manage documents, and leave the Library.

Here is a detailed description of the functions of the various buttons:

Buttons on the left hand side

Clear
Clicking the Clear button during a search will clear the display from the database and document panes, and reset them to their initial settings.

Records
The Records button enables you to display the results of your most recent search in the content pane. You can use this button to return to your search from the MeSH and History displays.

MeSH
The MeSH thesaurus is published by the National Library of Medicine in the USA. It provides a vocabulary of some 15,000 terms which can be used to describe very precisely the content of medical documents. You can find details on using them under MeSH searching.
From a MeSH display, you can click the **Records** button to display the results of your most recent search in the content pane.

1. Type: “antibiotic prophylaxis” in MeSH term
2. Click on definition
3. Window of definition appears on the screen

**History**

Clicking **History** opens a new display in the database pane, showing the results of searches to date. Each line of the search is numbered in blue text (the number being preceded by a # symbol), and shows the search term used (in black text), and the number of documents found (in red text).

You can continue a search within this display by entering new search terms in the **Search phrase** window.

From the history display, you can click the **Records** button to display the results of your most recent search in the content pane.
There are three buttons immediately above the history display which allow you to manipulate the results of your search. These are **Clear**, **Save** and **Load**.

Clicking **Clear** will delete the entire search history.

You can save your search on your computer by clicking **Save**. This will open a new window in which you can choose a name and location for the search. Click **Save** to save the search.
Saved searches can be run by clicking **Load**, and selecting the name of the search. Click **Open** to run the search. Note that loading a search will overwrite any current search in the history display.

**Help**

You can open the full list of **Help files** by clicking the **Help** button on the menu bar.

The buttons on the right-hand side:

After viewing a number of documents, you can skip back to earlier ones by using the **Back** button. This enables you to move successively from the current document back to the first one viewed. You can move forwards again through these documents by using the **Forward** button.

**Forward**

After viewing earlier documents by paging **back** through them, you can move forwards again through the documents by clicking the **Forward** button.

**Outline**

Documents are divided into sections. By clicking **Outline**, you can view the list of section headings for any such document currently displayed. The outline will appear in the content pane.
In each library, the outline has a standard format. Headings in blue are used in the document currently being viewed. Headings not used in that document appear in grey. You can move directly to any section of a document by clicking the appropriate heading.

Feedback
The feedback facility enables you to send comments on documents found in the library. This feature can only be used if you have an internet connection, and is not available for all types of document. Clicking Feedback will open a new window permitting you to send your comments. If the document chosen does not have the feedback facility, a message will notify you of this.

Print
You can print any document which is currently displayed in the document pane by clicking the Print button. This will open the Internet Explorer “Print” window. You can select the options you require before clicking OK to print the document.

Find
The Find button lets you search for any word or phrase within a document. Clicking Find opens a new window in which you can type the text you wish to locate, and define the
options for the “find” function. Clicking Find Next within this window will then locate the chosen text in the document. The Find function will work on whichever document is currently displayed in the document pane.

About
The About button displays the Update Software disclaimer.

The opening screen provides a link to the full copyright statements for the library. You can reload this screen at any point by clicking Clear.

Exit
You can close the library and end your search session by clicking Exit.

Browsing titles of documents
When the list of sections is displayed in the content pane, you can browse the titles of documents by clicking the title of your chosen section. Clicking the section title again will close the list of documents.

Searching
You can search the library for documents on specific topics. The search window can be found at the top of the content pane. You can search in a number of ways. Follow the links below to learn more details of the different techniques.

- Simple search (for single words or phrases)
- Combining search terms (for combinations of words and phrases)
- Truncation (wildcards)
- Refining your search (for example, by date, by title, or by author name)
- Editing your search history (by modifying existing searches)
- Stop words (words for which you cannot search)
- MeSH searching

The results of a search will appear in the content pane. The search terms used, and the total number of documents found, are displayed in red text beneath the Search phrase window. The name of each section which contains records corresponding to the search will appear in blue text, followed by the number of records found. Section names displayed in grey text contain no documents corresponding to that search. To display the titles of records found by your search, click on the section name.

The results of each search carried out during a session are stored in the search history. This can be displayed in the database pane by clicking History.

You can clear the results of your search from the database pane by clicking Clear.
Simple searching

You can search for all documents containing a particular word or phrase by typing that term in the Search phrase window, and clicking Go.

The list of sections with the number of documents relative to the search will be displayed in the content pane. You can then browse the titles of documents by clicking the title of your chosen section.

Note that you do not need to place inverted commas around phrases.

Combining search terms

Words or phrases can be combined in a number of ways to modify the meaning of a search. Special words (known as “Boolean operators”) will relate the terms in specific ways. There are three of these “operators”:

(a) OR. If you use OR between search terms, you will retrieve documents containing at least one of those terms.
   - For example, the search “aspirin OR paracetamol” will locate documents containing the word “aspirin” or the word “paracetamol”.

(b) AND. If you use AND between terms, you will only retrieve documents that contain each of the terms specified.
   - For example, the search “corticosteroids AND preterm” will only retrieve documents containing the word “corticosteroids” and the word “preterm”.

(c) NOT. If you use NOT between terms, you will retrieve articles containing the first terms but not the second term.
   - For example, the search “corticosteroids NOT preterm” will only retrieve documents containing the word “corticosteroids” without the word “preterm”.

You can also use these operators to combine the results of previous searches from the History display. Use the search numbers (beginning with the # character), and combine them in the same way as outlined above. For example:

#1 OR #4
will retrieve any documents which occurred in either search #1 or search #4

#2 AND #4
will retrieve any documents which occur in both search #2 and search #4.

#3 NOT #4
will retrieve any documents found in search #3 with the exception of those also found in search #4
Displaying documents

Click the title of a document in the content pane to display the full document in the document pane. Selecting a different title within the content pane will display the new document in the document pane. You can move backwards and forwards through the documents selected during a session by clicking Back or Forward on the menu bar.

You can use the Page up and Page down keys to scroll up and down the document. The Clear key will move the display to the beginning of the document, and the End key will move it to the end.

Documents in certain databases are divided into sections. You can view the list of section headings for any such document displayed in the document pane by clicking Outline.

In each library, the outline has a standard format. Headings in blue are used in the document currently being viewed. Headings not used in that document appear in grey. You can move directly to any section of a document by clicking the appropriate heading. The outline is displayed in the database pane.

Print

To print a document, click on the Print button on the menu bar. You can clear the document pane and return to the initial display at any time by clicking Clear.
Objectives

At the end of this chapter you should:

- Have a basic knowledge of some common terms used in meta-analysis
- Be able to interpret information displayed in The WHO Reproductive Health Library

Introduction

In order to practise evidence-based reproductive health care, you will need to access certain skills which you most probably use every day. Understanding commonly used terms, definitions and calculations is a good place to start.

What is meta-analysis?

Individual clinical trials may mean little, especially when they are small or medium sized.

Small studies tend to be inconclusive - they may show no statistical difference between the treated and control groups. On the other hand they may be unable to exclude the possibility of there being a sizeable effect - because they have low power.

Aggregating studies in a systematic and unbiased way may allow a clearer picture to emerge. The question we are asking is whether, on average, a particular treatment confers significant benefits when used for specific patient groups. Meta-analysis allows this aggregate picture to emerge.
The terms “systematic review” and “meta-analysis” are often used as synonyms. They do not, however, mean the same thing.

A systematic review comprehensively locates, evaluates, and synthesizes all the available literature (primary research) on a given topic using a strict scientific design, which must itself be reported in the review. Meta-analysis is a statistical technique for combining the findings from independent studies that address the same question.

If, however, the individual studies in a systematic review are too diverse to combine statistically, a systematic review can be done without a meta-analysis.

The main requirement for a worthwhile meta-analysis is first and foremost a well-executed systematic review.

The Forest Plot

The most commonly used graphical presentation of the results of a meta-analysis is the forest plot. It is so named because it helps the reader to see the “forest” of evidence while still being able to focus on the “trees” of individual studies. The forest plot is also sometimes called a “blobbogram”.

In The WHO Reproductive Health Library practical sessions you will encounter forest plots in virtually every systematic review. The forest plot is a diagrammatic representation of the effectiveness of an intervention. Hence, interpreting the forest plot is a core skill in the practice of evidence-based reproductive health care.

| Review: Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection |
| Comparison: 01 Zidovudine vs placebos |
| Outcome: 01 HIV infection of the child |

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A forest plot usually displays the following:

- **Details of the systematic review**: name of review, comparison and outcome being studied
- **Odds ratio or relative risk**: statistical expressions of “estimate of effect” (estimate of the effect of the intervention) for each trial
- **Blobs or squares**: the midpoint is the visual expression of “estimate of effect” for each trial
- **Horizontal line through each blob or square**: Confidence Interval (CI) which represents the uncertainty of the estimate of the treatment effect for that study
- **Vertical line**: Line of no effect
- **Diamond**: Aggregate effect size for all the studies in the meta-analysis

Before you look at the forest plot and learn how to interpret it, you may need to learn or review some basic epidemiological concepts. Details of calculations and formula are included later in this manual.

**Review of epidemiological concepts**

**(a) Prevalence:**
- This refers to the number of existing cases of a particular disease or condition in a given population at a designated time
- E.g., the number of anaemic women seen in your antenatal clinic this month.

**(b) Incidence:**
- This gives the number of new cases of a particular disease or condition in a given population over a specific period of time
- E.g., the number of cases of neonatal eye infection seen in your nursery over 1 year.

**(c) Estimates of effect:**
- In studies of the effects of health care, the observed relationship between an intervention and an outcome are statistically expressed as an “estimate of effect” e.g. an odds ratio (OR) or a relative risk (RR).
- **Odds Ratio** (OR) is the ratio of the number of people in a group with an event to the number without an event. A more detailed explanation is included later in the manual. However, for interpreting forest plots, you need to know that if the OR = 1, the intervention has no effect.
- **Relative risk** (RR): The RR is the ratio of the cumulative incidence of disease in an exposed group (intervention group) to the cumulative incidence in the unexposed group (control group). For interpreting forest plots, you need to know that if the RR = 1, the intervention has no effect.
- **Confidence interval** (CI): The range within which the “true” value (e.g. size of the effect of the intervention) is expected to lie with a given degree of certainty (e.g. 95% or 99%).
• **Number needed to treat** (NNT): The NNT reflects the number of patients who need to be treated to prevent one bad outcome. It is an absolute value. NNT is often easier for clinicians to understand as it gives a clear answer as to the effect of the intervention in terms of patient numbers.

• **P-value**: The $P$-value measures the probability of an estimate of effect occurring if the null hypothesis was true, i.e. there is no effect. Convention measures the so-called statistical significance level at 0.05. If the $P$-value is less than 0.05, we say that the result is significant at the 5% level or that the probability of the result occurring by chance is less than 5%.

In the following pages, you can review a forest plot from a meta-analysis comparing giving zidovudine to placebo to the mother for prevention of HIV infection in the child.

As a preliminary exercise,

• Find the systematic review on *Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection* in The WHO Reproductive Health Library.

• Once you find the review, go to Outline view and then to Graphs and Tables

• Under *01. Zidovudine vs Placebo*, click on *01. HIV infection in the child* (Outcome Title) to display the forest plot shown below

**Forest Plot: Estimates of Effect**

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**Favours Zidovudine**

**Favours placebo**
### Forest Plot: Estimates of Effect

Estimate of effect is graphically displayed as the midpoint of a blob or square.

Estimate of effects of each study is expressed as an Odds Ratio (OR) or Relative Risk (RR).

#### Review: Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection

**Comparison:** 01 Zidovudine vs placebo

**Outcome:** 01 HIV infection of the child

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Favours Zidovudine

Favours placebo

- Overall effect size: This denotes the overall statistical result of the meta-analysis (the Combined OR and the diamond)

- Favours Zidovudine

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Forest Plot: Estimates of Effect

Line of no effect:
At this point there is no difference between the intervention group and the control group.

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**Weight of study:** Area of each blob or square represents the weight given to each trial during the analysis. This is also expressed as a percentage.

One of the things that determine the **weight** given to a trial during a meta-analysis is the size of the trial. Large trials tend to give more precise answers and hence carry more weight.

**Favours Zidovudine**       **Favours placebo**
The WHO Reproductive Health Library
A Training Manual

Forest Plot: Confidence interval

Confidence interval (CI) shows range within which true size of effect of intervention is likely to lie.

CI that crosses the line of no effect indicates: intervention not statistically significantly different from control.

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A 95% confidence interval (CI) means that if the trial was to be repeated 100 times under identical conditions, the estimate of effect would lie within this range 95 out of 100 times.

A wide CI indicates a less precise estimate of effect.

Overall effect size is also known as the “overall estimate of effect”. The CI of the overall effect size is indicated by the width of the “diamond”. 

Favours Zidovudine       Favours placebo

0.1 0.2 1 5 10
Favours treatment Favours control
You should now attempt to interpret these forest plots:

1. Which statistical estimate of effect is being reported?

2. What comparison is being made?

3. What is the outcome under investigation?

4. On which side of the line of no effect does the overall estimate of effect lie?

5. Does the confidence interval touch or cross the line of no effect? (If the confidence interval does touch or cross the line of no effect, this indicates that the result is NOT significant.)

6. What conclusions can be drawn from the forest plot?

Here are some additional epidemiological concepts for the really keen! You may skip the following until the end of the chapter if you are not interested in the statistical basis of these concepts.

**How to calculate relative risk and odds ratio**

The Two-way table (two by two or fourfold table)
Data from epidemiological studies can often be displayed in “two-way” tables. These tables are a convenient way of organizing study data so that results such as the appropriate measures of effect can be calculated.

If subjects in a trial are followed up from the time of exposure to an intervention to see what the effect of the intervention is on a disease (or event), the data can be summarized as follows in what is known as a “two-way” table. The letters a, b, c and d denote the number of subjects who end up in each category:

<table>
<thead>
<tr>
<th></th>
<th>Event</th>
<th>No Event</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention</strong></td>
<td>a</td>
<td>b</td>
<td>a+b</td>
</tr>
<tr>
<td><strong>Control</strong></td>
<td>c</td>
<td>d</td>
<td>c+d</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>a+c</td>
<td>b+d</td>
<td></td>
</tr>
</tbody>
</table>

This table can be used to compute two of the commonly used measures of effect, namely, the relative risk and the odds ratio.

**Odds ratio**

Odds ratio is:

- the ratio of the odds of an event in the experimental (intervention) group to the odds of an event in the control group, or
- the ratio of the number of people in a group with an event to the number without an event, or
- the ratio of the number of times we believe the event is likely to occur to the number of times we believe it is likely not to occur.

To calculate the odds ratio (OR), we can use the following:

- Odds of an event in the intervention group: \( \frac{a}{c} \)
- Odds of an event in the control group: \( \frac{b}{d} \)
- The OR is therefore: \( \frac{a/c}{b/d} = \frac{a \times d}{b \times c} \)

For undesirable outcomes an OR that is less than one indicates that the intervention was effective in reducing the risk of that outcome. Similarly, when an OR is more than one, then the outcome occurs more often in the intervention group i.e. the intervention results in worse outcomes. When the event rate is small, odds ratios are very similar to relative risks.

**Relative risk (RR)**

The Relative Risk is the ratio of the risk of the event in the intervention group to the risk of the event in the placebo group.
To calculate the RR

- The risk of the event in the intervention group is \( \frac{a}{a + b} \)
- The risk of the event in the control group is \( \frac{c}{c + d} \)
- The relative risk (RR) is \( \frac{\frac{a}{a + b}}{\frac{c}{c + d}} \)

RR is usually expressed as a decimal proportion, sometimes as a percentage.

If the RR = 2, the risk of the event occurring in the intervention group is twice that of the risk of the event occurring in the control group. If the RR = 0.5, the risk of the event occurring in the intervention group is half that of the risk of the event occurring in the control group.

Remember that a RR = 1 or RR = 100% means “No effect of intervention”.

**Number needed to treat**

The number needed to treat (NNT) is becoming a popular way for expressing the effectiveness of interventions. The NNT reflects the number of patients who need to be treated to prevent one bad outcome.

Suppose a new treatment leads to 50% of patients surviving five years after the start of treatment rather than 30% on the traditional treatment. If patients who might have been managed traditionally are instead given the new treatment, an additional 20% of them will be expected to benefit. For at least one patient to benefit from the new treatment, five would have to receive it. This is referred to as the number needed to treat (NNT).

The NNT is also the inverse of the risk difference (RD). The risk difference is the absolute difference in the event rate between two comparison groups. A risk difference of zero indicates no difference between comparison groups. A RD that is less than zero indicates that the intervention was effective in reducing the risk of that outcome.

\[
\text{Risk difference} = \text{Incidence in exposed} - \text{Incidence in unexposed}
\]

\[
\text{NNT} = \frac{1}{\text{Risk difference}}
\]

The appendix includes a list of terms often used in statistics and epidemiology. You could refer to this list if you need further information on any other terms used in The WHO Reproductive Health Library.
Objective
At the end of this session, you should be able to:

- Ask relevant questions related to a clinical situation
- Obtain the relevant information from the WHO RHL
- Interpret the information in the context of the clinical situation

Introduction
During this session, you will be given certain clinical situations. In each case, take a few minutes to read the scenario. Then frame a relevant question if required, search the WHO Reproductive Library for information to answer the question, and finally interpret the information obtained in the clinical context. You should be aware that the required information may be available in one or more document in the Library. You will therefore have to do a thorough search of the Library.

Clinical Situation 1
A 21-year-old woman visits your clinic for antenatal care. She has been married for a year to a truck driver. This is her first pregnancy. The gestational age is 18 weeks. During routine tests, she was found to be HIV positive. You explain to her the problem and its effects on the baby. She is keen to have this baby and wants to know if you can give her medicines to prevent the baby from getting infected.
1. What is the question that you will want to ask in this clinical situation?

2. List some drugs used to reduce the risk of HIV transmission to babies.

3. In the trials reviewed, did these drugs reduce the risk of HIV transmission to babies? If yes, how much was the reduction achieved?

4. Among the groups that received these drugs, were there some subgroups of babies who had significantly lower risks of HIV infection than the remainder? If yes, what were the characteristics of these subgroups?

5. Do these drugs have any effect on the risk of infant or maternal mortality?

6. Among the various regimens of Zidovudine that have been tried, which is the most effective?
7. Finally, what would you advise your patient about drugs to prevent HIV transmission to the baby?

Clinical situation 2

A 28-year-old woman attends your clinic for antenatal care. This is her second pregnancy. She has no significant medical problems. You have confirmed that she is about 12 weeks pregnant. You ask her to come regularly for antenatal care once a month for the next four months, once in 2 weeks after that until her pregnancy reaches 36 weeks, and every week thereafter until delivery. You advise her on the importance of regular antenatal visits as suggested. However, she tells you that she cannot come very often as she has a small child, has no help at home, and has a long way to travel to your clinic. She asks you, “Can I come less often than what you have advised? Will I have major problems if I can come only less often?”

1. Use the WHO RHL to locate the evidence about antenatal care.

2. How often should women with low risk pregnancy visit the antenatal clinic?

3. Are there any significant differences in pregnancy outcomes between women who received fewer but focused antenatal care and those who had more frequent antenatal clinic visits?
4. Your patient tells you that a trained midwife conducts a clinic near her house. She wants to know if she can go there for her antenatal care. What will you, as a specialist obstetrician advise her based on the evidence from WHO RHL?

5. After having read the evidence, how will you implement evidence-based antenatal care?

Clinical Scenario 3

A 32-year-old woman has been admitted to the labour ward. This is her first pregnancy. The gestational age is 32 weeks. She complains of low abdominal pain and you suspect that she may be in preterm labour. She is worried that if the baby is born now, it will suffer from many problems related to prematurity. You have heard that giving corticosteroids to the mother with preterm labour may benefit the baby.

1. Find the evidence in the WHO RHL regarding corticosteroids in preterm labour.

2. List some of the major complications related to prematurity.
3. Do corticosteroids have any beneficial effect on these complications? If yes, what is the magnitude of the benefit?

4. Will corticosteroids increase the risk of infection in the mother or baby?

5. Should this woman receive corticosteroids? Give reasons for your answer.

**Clinical Scenario 4**

You have just seen a primigravida at 38 weeks with a breech presentation. You estimate that the foetus is appropriately grown. The mother has no other complications. She wants to know what the risks of having a breech delivery are and wants your advice on further care.

1. What are the risks of having a breech delivery?

2. List the possible options for her management?
3. Is there any procedure that can be carried out in the clinic which will reduce the chances of a breech delivery? If yes, describe the procedure. What are its benefits and risks? Are there any other procedures that can aid you in reducing the chances of breech delivery?

4. Is caesarean delivery an option? If yes, what is the evidence in support of this option? Are there any disadvantages of caesarean section for breech presentation?

Clinical Scenario 5

You have been posted to a new health facility which has a delivery room. However, there is no facility for assisted vaginal delivery. You would like to purchase an instrument for facilitating instrumental vaginal delivery. Which instrument would you prefer to buy – a vacuum extractor or a forceps?

1. What are the complications that may result from instrumental vaginal delivery?

2. Which is associated with more complications – vacuum extraction or forceps delivery? Give reasons for your answer.

Clinical Scenario 6

The mother of your patient, an 18-year-old primigravida in labour has asked you if she could be allowed to stay with her daughter in the labour ward. The nursing staff does not
want to allow the mother into the labour ward as she is worried that the older lady’s presence would cause more problems in labour and increase the risk of newborn infection. You feel sympathetic to the mother and would like to help her.

1. Search the WHO RHL for the evidence that you can use to support your decision.

2. What are the advantages that have been found with use of social support in labour? What is the magnitude of benefits of each of these advantages?

3. Are there any disadvantages? If yes, what is the magnitude of these disadvantages?

4. Does the presence of a person providing supportive care in labour increase the risk of infection in the mother or baby?
Appendix

Glossary of Terms

When you use The WHO Reproductive Health Library, you may come across some terms that you may not understand. The following alphabetical list of terms with their meanings should help you to understand these terms.

Allocation concealment
See concealment of allocation.

Attrition bias
Systematic differences between comparison groups in withdrawals or exclusions of participants from the results of a study. For example, patients may drop out of a study because of side-effects of the intervention. Excluding these patients from the analysis could result in an overestimate of the effectiveness of the intervention.

Bias
Systematic error or deviation in results or inferences. In studies of the effects of health care, bias can arise from systematic differences in the groups that are compared (selection bias), the care that is provided, or exposure to other factors apart from the intervention of interest (performance bias), withdrawals or exclusions of people entered into the study (attrition bias) or how outcomes are assessed (detection bias). Bias does not necessarily carry an imputation of prejudice, such as the investigators’ desire for particular results. This differs from conventional use of the word in which bias refers to a partisan point of view. Many varieties of biases have been described. See also methodological quality, validity.
Blinding (synonym: masking)
Keeping group assignment (e.g. to treatment or control) secret from the study participants or investigators. Blinding is used to protect against the possibility that knowledge of assignment may affect patient response to treatment, provider behaviours (performance bias) or outcome assessment (detection bias). Blinding is not always practical (e.g. when comparing surgery to drug treatment). The importance of blinding depends on how objective the outcome measure is; blinding is more important for less objective outcome measures such as pain or quality of life. See also single blind, double blind and triple blind.

Case study (synonyms: anecdote, case history, single case report)
An uncontrolled observational study involving an intervention and outcome for a single person.

Case-control study (synonyms: case referent study, retrospective study)
A study that starts with the identification of people with the disease or outcome of interest (cases) and a suitable control group without the disease or outcome. The relationship of an attribute (intervention, exposure or risk factor) to the outcome of interest is examined by comparing the frequency or level of the attribute in the cases and controls. For example, to determine whether thalidomide caused birth defects, a group of children with birth defects (cases) could be compared to a group of children without birth defects (controls). The groups would then be compared with respect to the proportion exposed to thalidomide through their mothers taking the tablets. Case-control studies are sometimes described as being retrospective studies as they are always performed looking back in time.

CD-ROM (Compact Disc – Read Only Memory)
A computer storage medium. A CD-ROM can contain a database of information (e.g. MEDLINE, or the Cochrane Controlled Trials Register) that may be searched either on a personal computer or a computer linked to a network.

CDSR
See Cochrane Database of Systematic Reviews.

CL
See Cochrane Library

Clinical trial (synonyms: therapeutic trial, intervention study)
A trial that tests out a drug or other intervention to assess its effectiveness and safety. This general term encompasses randomized-controlled trials and controlled clinical trials.

Cochrane Collaboration
An international organization that aims to help people make well-informed decisions about health by preparing, maintaining and ensuring the accessibility of systematic reviews of the
benefits and risks of health care interventions. More information on the Cochrane Collaboration is available from the Cochrane Library.

**Cochrane Controlled Trials Register (CCTR)**
A database of references to controlled trials in health care. Cochrane groups and other organizations have been invited to contribute their specialized registers, and these registers, together with references to clinical trials identified on MEDLINE, form the CENTRAL register of studies. Records from CENTRAL, following quality control to try to ensure that only reports of definite randomized controlled trials or controlled clinical trials are included, make up The Cochrane Controlled Trials Register (CCTR).

**Cochrane Database of Systematic Reviews (CDSR)**
The major product of the Cochrane Collaboration. It brings together all the currently available Cochrane Reviews and is updated quarterly. It also contains information about the Collaboration. See Cochrane Library.

**Cochrane Library (CL)**
A collection of databases, published on disk and CD-ROM and updated quarterly, containing the Cochrane Database of Systematic Reviews, the Cochrane Controlled Trials Register, the Database of Abstracts of Reviews of Effectiveness, the Cochrane Review Methodology Database, and information about the Cochrane Collaboration.

**Cohort study (synonyms: follow-up, incidence, longitudinal, prospective study)**
An observational study in which a defined group of people (the cohort) is followed over time and outcomes are compared in subsets of the cohort who were exposed or not exposed, or exposed at different levels, to an intervention or other factor of interest. Cohorts can be assembled in the present and followed into the future (a “concurrent cohort study”), or identified from past records and followed forward from that time up to the present (a “historical cohort study”). Because random allocation is not used, matching or statistical adjustment must be used to ensure that the comparison groups are as similar as possible.

**Concealment of allocation**
The process used to prevent foreknowledge of group assignment in a randomized-controlled trial, which should be seen as distinct from blinding. The allocation process should be impervious to any influence by the individual making the allocation by having the randomization process administered by someone who is not responsible for recruiting participants; for example, a hospital pharmacy, or a central office. Using methods of assignment such as date of birth and case record numbers (see quasi-random allocation) are open to manipulation. Adequate methods of allocation concealment include: centralized randomization schemes; randomization schemes controlled by a pharmacy; numbered or coded containers in which capsules from identical-looking, numbered bottles are administered sequentially; on-site computer systems, where allocations are in a locked, unreadable file; and sequentially numbered opaque, sealed envelopes.
Confidence interval (CI)
The range within which the “true” values (e.g. size of effect of an intervention) are expected to lie with a given degree of certainty (e.g. 95% or 99%). Note: Confidence intervals represent the probability of random errors, but not systematic errors (bias).

Confounding
A situation in which a measure of the effect of an intervention or exposure is distorted because of the association of exposure with other factor(s) that influence the outcome under study.

Consumer (health care consumer)
Someone, who uses, is affected by, or who is entitled or compelled to use a health-related service.

Control
1. In clinical trials comparing two or more interventions, a control is a person in the comparison group that receives a placebo, no intervention, usual care or another form of care.
2. In case-control studies a control is a person in the comparison group without the disease or outcome of interest.
3. In statistics control means to adjust for or take into account extraneous influences or observations.
4. Control can also mean programmes aimed at reducing or eliminating the disease when applied to communicable (infectious) diseases.

Controlled clinical trial (CCT)
Refers to a study that compares one or more intervention groups to one or more comparison (control) groups. Whilst not all controlled studies are randomized, all randomized trials are controlled.

Critical appraisal
The process of assessing and interpreting evidence by systematically considering its validity, results and relevance.

Cross-sectional study (synonym: prevalence study)
A study that examines the relationship between diseases (or other health-related characteristics) and other variables of interest as they exist in a defined population at one particular time. The temporal sequence of cause and effect cannot necessarily be determined in a cross-sectional study.

Cross-over trial
A type of clinical trial comparing two or more interventions in which the participants, upon completion of the course of one treatment are switched to another. For example, for a
comparison of treatments A and B, half the participants are randomly allocated to receive them in the order A, B and half to receive them in the order B, A. A problem with this design is that the effects of the first treatment may carry over into the period when the second is given.

**Database**
A collection of organized information usually held on a computer. In some ways a database is similar to a filing system, but with important advantages: the information can be revised and kept up to date easily, and the computer can retrieve information from it very quickly. Electronic databases such as MEDLINE, EMBASE and the CDSR can be distributed on disk, CD-ROM or via the Internet.

**Database of Abstracts of Reviews of Effectiveness (DARE)**
A collection of structured abstracts and bibliographic references of systematic reviews of the effects of healthcare. See the Cochrane Library.

**Detection bias (synonym: ascertainment bias)**
Systematic differences between comparison groups in how outcomes are ascertained, diagnosed or verified.

**Dichotomous data (synonym: binary data)**
Observations with two possible categories such as dead/alive, smoker/non-smoker, present/not present.

**Double blind (synonym: double masked)**
Neither the participants in a trial nor the investigators (outcome assessors) are aware of which intervention participants are given. The purpose of blinding the participants (recipients and providers of care) is to prevent performance bias. The purpose of blinding the investigators (outcome assessors, who might also be the care providers) is to protect against detection bias. See also blinding, single blind, triple blind, concealment of allocation.

**Effect size**
1. A generic term for the estimate of effect for a study.
2. A dimensionless measure of effect that is typically used for continuous data when different scales (e.g. for measuring pain) are used to measure an outcome and is usually defined as the difference in means between the intervention and control groups divided by the standard deviation of the control or both groups. See standardized mean difference.

**Effectiveness**
The extent to which a specific intervention, when used under ordinary circumstances, does what it is intended to do. Clinical trials that assess effectiveness are sometimes called management trials. See also intention-to-treat.
Efficacy
The extent to which an intervention produces a beneficial result under ideal conditions. Clinical trials that assess efficacy are sometimes called explanatory trials and are restricted to participants who fully co-operate.

EMBASE (Excerpta Medica database)
A European-based electronic database of pharmacological and biomedical literature covering 3500 journals from 110 countries. Years of coverage: 1974 to the present.

Epidemiology
The study of the distribution and determinants of health-related states or events in specified populations.

Estimate of effect (synonym: treatment effect)
In studies of the effects of health care, the observed relationship between an intervention and an outcome expressed as, for example, a number needed to treat, odds ratio, risk difference, relative risk, standardized mean difference, or weighted mean difference.

Event rate
The proportion of participants in a group in whom an event is observed. Thus, if out of 100 patients the event (e.g. a stroke) is observed in 32, the event rate is 0.32.

Evidence-based health care
The conscientious use of current best evidence in making decisions about the care of individual patients or the delivery of health services.

External peer reviewer
A person with relevant content, methodological or user expertise who critically examines reviews in her/his area of expertise.

External validity (synonyms: external validity, generalizability, relevance, transferability)
The degree to which the results of an observation hold true in other settings. See also validity.

Fixed effect model
A statistical model that stipulates that the units under analysis (e.g. people in a trial or study in a meta-analysis) are the ones of interest, and thus constitute the entire population of units. Only within-study variation is taken to influence the uncertainty of results (as reflected in the confidence interval) of a meta-analysis using a fixed effect model. Variation between the estimates of effect from each study (heterogeneity) does not affect the confidence interval in a fixed effect model. See random effects model.
Generalizability (synonyms: applicability, external validity, relevance, and transferability)

Generalizability is the degree to which the results of a study or systematic review can be extrapolated to other circumstances, in particular to routine health care situations.

Gold standard

The method, procedure or measurement that is widely accepted as being the best available against which new interventions should be compared. It is particularly important in studies of the accuracy of diagnostic tests. For example, handsearching is sometimes used as the gold standard for identifying trials against which electronic searches of databases, such as MEDLINE are compared.

Heterogeneity

In systematic reviews heterogeneity refers to variability or differences between studies in the estimates of effects. A distinction is sometimes made between “statistical heterogeneity” (differences in the reported effects), “methodological heterogeneity” (differences in study design) and “clinical heterogeneity” (differences between studies in key characteristics of the participants, interventions or outcome measures). Statistical tests of heterogeneity are used to assess whether the observed variability in study results (effect sizes) is greater than that expected to occur by chance. However, these tests have low statistical power. See also homogeneity.

Incidence

The number of new cases of a disease, or event, in a population during a specific period of time.

Individual patient data

In systematic reviews this term refers to the availability of raw data for each study participant in each included trial, as opposed to aggregate data (summary data for the comparison groups in each study). Reviews using individual patient data require collaboration of the investigators who conducted the original trials, who must provide the necessary data.

Intention-to-treat

An intention-to-treat analysis is one in which all the participants in a trial are analysed according to the intervention to which they were allocated, whether they received it or not. Intention-to-treat analyses are favoured in assessments of effectiveness as they mirror the noncompliance and treatment changes that are likely to occur when the intervention is used in practice, and because of the risk of attrition bias when participants are excluded from the analysis.

Mean (synonyms: arithmetic mean, average)

The average value calculated by adding all the observations and dividing by the number of observations.
MEDLINE (MEDlars onLINE)
An electronic database produced by the United States National Library of Medicine. It indexes millions of articles in selected (about 3700) journals. It is available through most medical libraries, and can be accessed on CD-ROM, the Internet and by other means. Years of coverage: 1966 to the present.

MeSH headings (Medical Subject Headings)
Terms used by the United States National Library of Medicine to index articles in Index Medicus and MEDLINE. Designed to reduce problems that arise from, for example, differences in British and American spelling. The MeSH system has a tree structure in which broad subject terms branch into a series of progressively narrower subject terms.

Meta-analysis
The use of statistical techniques in a systematic review to integrate the results of the included studies. Also used to refer to systematic reviews that use meta-analysis.

Meta-regression
Multivariate meta-analytic techniques, such as logistic regression, used to explore the relationship between study characteristics (e.g. allocation concealment, baseline risk, timing of the intervention) and study results (the magnitude of effect observed in each study) in a systematic review.

Methodological quality (synonyms: validity, internal validity)
The extent to which the design and conduct of a trial are likely to have prevented systematic errors (bias). Variation in quality can explain variation in the results of trials included in a systematic review. More rigorously designed (better “quality”) trials are more likely to yield results that are closer to the “truth”. See also external validity, validity.

Negative study
A term used to refer to a study that does not have “statistically significant” (positive) results indicating a beneficial effect of the intervention being studied. The term can generate confusion because it refers to both statistical significance and the direction of effect. Studies often have multiple outcomes, the criteria for classifying studies as “negative” are not always clear and, in the case of studies of risk or undesirable effects, “negative” studies are ones that do not show a harmful effect. See also positive study.

Null hypothesis
The statistical hypothesis that one variable (e.g. whether or not a study participant was allocated to receive an intervention) has no association with another variable or set of variables (e.g. whether or not a study participant died), or that two or more population distributions do not differ from one another. In simplest terms, the null hypothesis states that the results observed in a study are no different from what might have occurred as a result of the play of chance.
Number needed to treat (NNT)
The number of patients who need to be treated to prevent one bad outcome. It is the inverse of the risk difference.

Observational study (synonym: non-experimental study)
A study in which nature is allowed to take its course. Changes or differences in one characteristic (e.g. whether or not people received the intervention of interest) are studied in relation to changes or differences in other(s) (e.g. whether or not they died), without the intervention of the investigator. There is a greater risk of selection bias than in experimental studies (randomized controlled trials).

Odds ratio (OR)
The ratio of the odds of an event in the experimental (intervention) group to the odds of an event in the control group. Odds are the ratio of the number of people in a group with an event to the number without an event. Thus, if a group of 100 people had an event rate of 0.20, 20 people had the event and 80 did not, and the odds would be 20/80 or 0.25. An odds ratio of one indicates no difference between comparison groups. For undesirable outcomes an OR that is less than one indicates that the intervention was effective in reducing the risk of that outcome. When the event rate is small, odds ratios are very similar to relative risks.

Peer review
A refereeing process used to check the quality and importance of reports of research. An article submitted for publication in a peer reviewed journal is reviewed by other experts in the area. It aims to provide a wider check on the quality and interpretation of a report and to improve its quality. See also external peer reviewer.

Performance bias
Systematic differences in care provided apart from the intervention being evaluated. For example, if patients know they are in the control group they may be more likely to use other forms of care, patients who know they are in the experimental (intervention) group may experience placebo effects, and care providers may treat patients differently according to what group they are in. Blinding of study participants (both the recipients and providers of care) is used to protect against performance bias.

Placebo
An inactive substance or procedure administered to a patient, usually to compare its effects with those of a real drug or other intervention, but sometimes for the psychological benefit to the patient through a belief that s/he is receiving treatment. Placebos are used in clinical trials to blind people to their treatment allocation. Placebos should be indistinguishable from the active intervention to ensure adequate blinding.

Placebo effect
A favourable response to an intervention, regardless of whether it is the real thing or a placebo, attributable to the expectation of an effect, i.e. the power of suggestion. The effects
of many health care interventions are attributable to a combination of both placebo and “active” (non-placebo) effects.

**Positive study**
A term used to refer to a study with results indicating a beneficial effect of the intervention being studied. The term can generate confusion because it can refer to both statistical significance and the direction of effect. Studies often have multiple outcomes, the criteria for classifying studies as negative or positive are not always clear and, in the case of studies of risk or undesirable effects, “positive” studies are ones that show a harmful effect. See also negative study.

**Precision**
1. A measure of the likelihood of random errors in the results of a study, meta-analysis or measurement. Confidence intervals around the estimate of effect from each study are a measure of precision, and the weight given to the results of each study in a meta-analysis (typically the inverse of the variance of the estimate of effect) is a measure of precision (i.e. the degree to which a study influences the overall estimate of effect in a meta-analysis is determined by the precision of its estimate of effect).
2. The proportion of relevant citations located using a specific search strategy, i.e. the number of relevant studies (meeting the inclusion criteria for a trials register or a review) divided by the total number of citations retrieved.

**Prevalence**
The number of existing cases of a particular disease or condition in a given population at a designated time.

**Probability distribution**
The function that gives the probabilities that a variable equals each of a sequence of possible values. Examples include the binomial, chi square, normal and Poisson distributions.

**Prospective study**
In evaluations of the effects of health care interventions, a study in which people are divided into groups that are exposed or not exposed to the intervention(s) of interest before the outcomes have occurred. Randomized controlled trials are always prospective studies and case control studies never are. Concurrent cohort studies are prospective studies, whereas historical cohort studies are not (see cohort study), although in epidemiology a prospective study is sometimes used as a synonym for cohort study. See also retrospective study.

**Publication bias**
A bias in the published literature where the publication of research depends on the nature and direction of the study results. Studies in which an intervention is not found to be effective are sometimes not published. Because of this, systematic reviews that fail to include unpublished studies may overestimate the true effect of an intervention.
**P-value**
The probability (ranging from zero to one) that the observed results in a study, or results more extreme, could have occurred by chance. In a meta-analysis the P-value for the overall effect assesses the overall statistical significance of the difference between the treatment and control groups, whilst the P-value for the heterogeneity statistic assesses the statistical significance of differences between the effects observed in each study.

**Quasi-random allocation**
A method of allocating participants to different forms of care that is not truly random; for example, allocation by date of birth, day of the week, medical record number, month of the year, or the order in which participants are included in the study (e.g. alternation).

**Quasi-randomised trial**
A trial using a quasi-random method of allocating participants to different forms of care. There is a greater risk of selection bias in quasi-random trials where allocation is not adequately concealed compared with randomized controlled trials with adequate concealment of allocation.

**Random allocation**
A method that uses the play of chance to assign participants to comparison groups in a trial, e.g. by using a random numbers table or a computer-generated random sequence. Random allocation implies that each individual or unit being entered into a trial has the same chance of receiving each of the possible interventions. It also implies that the probability that an individual will receive a particular intervention is independent of the probability that any other individual will receive the same intervention. See also concealment of allocation, quasi-random allocation, randomization.

**Random effects model**
A statistical model sometimes used in meta-analysis in which both within-study sampling error (variance) and between-studies variation are included in the assessment of the uncertainty (confidence interval) of the results of a meta-analysis. See fixed effect model. If there is significant heterogeneity among the results of the included studies, random effects models will give wider confidence intervals than fixed effect models.

**Random selection (synonym: random sampling)**
A method of obtaining a representative, unbiased group of people from a larger population. Random selection which is not related to how participants are allocated to comparison groups is frequently used in cross-sectional and cohort studies, which are not randomised controlled trials, and it is frequently not used in randomised controlled trials. In older trial reports, however, the term is occasionally used instead of random allocation or randomisation.

**Randomization**
Method used to generate a random allocation sequence, such as using tables of random numbers or computer-generated random sequences. The method of randomization should be distinguished from concealment of allocation because of the risk of selection bias despite
the use of randomization, if there is not adequate allocation concealment. For instance, a list of random numbers may be used to randomize participants, but if the list is open to the individuals responsible for recruiting and allocating participants, those individuals can influence the allocation process, either knowingly or unknowingly.

**Randomized controlled trial (RCT) (Synonym: randomized clinical trial)**
An experiment in which investigators randomly allocate eligible people into (e.g. treatment and control) groups to receive or not to receive one or more interventions that are being compared. The results are assessed by comparing outcomes in the treatment and control groups. NOTE: when using randomized controlled trial as a search term (publication type) in MEDLINE, the US spelling (randomized) must be used.

**Relative risk (RR) (synonym: risk ratio)**
The ratio of risk in the intervention group to the risk in the control group. The risk (proportion, probability or rate) is the ratio of people with an event in a group to the total in the group. A relative risk of one indicates no difference between comparison groups. For undesirable outcomes a RR that is less than one indicates that the intervention was effective in reducing the risk of that outcome.

**Reliability**
Refers to the degree to which results obtained by a measurement procedure can be replicated. Lack of reliability can arise from divergences between observers or measurement instruments, or instability in the attribute being measured.

**Retrospective study**
A study in which the outcomes have occurred to the participants before the study commenced. Case control studies are always retrospective, cohort studies sometimes are, randomized controlled trials never are. See prospective study.

**Review**
1. A systematic review.
2. A review article in the medical literature, which summarizes a number of different studies and may draw conclusions about a particular intervention. Review articles are often not systematic. Review articles are also sometimes called overviews.
3. To referee a paper. See referee, referee process, external peer reviewer.

**Risk difference (RD) (synonym: absolute risk reduction)**
The absolute difference in the event rate between two comparison groups. A risk difference of zero indicates no difference between comparison groups. For undesirable outcomes a RD that is less than zero indicates that the intervention was effective in reducing the risk of that outcome.

**Risk factor**
Aspects of a person’s condition, lifestyle or environment that increase the probability of occurrence of a disease. For example, cigarette smoking is a risk factor for lung cancer.
**Selection bias**

1. In assessments of the validity of studies of health care interventions, selection bias refers to systematic differences between comparison groups in prognosis or responsiveness to treatment. Random allocation with adequate concealment of allocation protects against selection bias. Other means of selecting who receives the intervention of interest, particularly leaving it up to the providers and recipients of care, are more prone to bias because decisions about care can be related to prognosis and responsiveness to treatment.

2. Selection bias is sometimes used to describe a systematic error in reviews due to how studies are selected for inclusion. Publication bias is an example of this type of selection bias.

3. Selection bias, confusingly, is also sometimes used to describe a systematic difference in characteristics between those who are selected for study and those who are not. This affects the generalizability (external validity) of a study but not its (internal) validity.

**Sensitivity analysis**

An analysis used to determine how sensitive the results of a study or systematic review are to changes in how it was done. Sensitivity analyses are used to assess how robust the results are to uncertain decisions or assumptions about the data and the methods that were used.

**Single blind (synonym: single masked)**

The investigator is aware of the treatment/intervention the participant is getting, but the participant is unaware. See also blinding, double blind, triple blind.

**Standardized mean difference**

The difference between two means divided by an estimate of the within-group standard deviation. When an outcome (such as pain) is measured in a variety of ways across studies (using different scales) it may not be possible directly to compare or combine study results in a systematic review. By expressing the effects as a standardized value the results can be combined since they have no units. Standardized mean differences are sometimes referred to as a “d” index.

**Statistical power**

The probability that the null hypothesis will be rejected if it is indeed false. In studies of the effectiveness of health care interventions, power is a measure of the certainty of avoiding a false negative conclusion that an intervention is not effective when in truth it is effective. The power of a study is determined by how large it is (the number of participants), the number of events (e.g. strokes) or the degree of variation in a continuous outcome (such as weight), how small an effect one believes is important (i.e. the smallest difference in outcomes between the intervention and the control groups that is considered to be important), and how certain one wants to be of avoiding a false positive conclusion (i.e. the cut-off that is used for statistical significance).
**Statistical significance**
An estimate of the probability of an association (effect) as large or larger than what is observed in a study occurring by chance, usually expressed as a $P$-value. For example, a $P$-value of 0.049 for a risk difference of 10% means that there is less than a one in 20 (0.05) chance of an association that is as large or larger having occurred by chance and it could be said that the results are “statistically significant” at $P = 0.05$). The cut-off for statistical significance is usually taken at 0.05, but sometimes at 0.01 or 0.10. These cut-offs are arbitrary and have no specific importance. Although it is often done, it is inappropriate to interpret the results of a study differently according to whether the $P$-value is, say, 0.055 or 0.045 (which are quite similar values, not diametrically opposed ones).

**Systematic review (synonym: systematic overview)**
A review of a clearly formulated question that uses systematic and explicit methods to identify, select and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarize the results of the included studies.

**Trials register**
In the Cochrane Collaboration, this is a database of bibliographic references to randomized controlled trials and controlled clinical trials relevant to a Collaborative Review Group or Field, that is maintained at the editorial base. Software such as ProCite or Reference Manager is used to manage the database. Once a relevant report of a trial is identified, it is photocopied, coded and entered onto the register. Wherever possible, relevant trial reports are downloaded directly into the register from an electronic database such as MEDLINE. Information about unpublished and ongoing trials is also included in trials registers.

**Triple blind (synonym: triple masked)**
An expression that is sometimes used to indicate that in addition to the participants and the investigators (outcome assessors) being unaware of which is the experimental group and which is the control group, the person doing the analysis is also unaware of the study group allocation.

**Validity (synonym: internal validity)**
Validity is the degree to which a result (of a measurement or study) is likely to be true and free of bias (systematic errors). Validity has several other meanings, usually accompanied by a qualifying word or phrase; for example, in the context of measurement, expressions such as “construct validity”, “content validity” and “criterion validity” are used. The expression “internal validity” is sometimes used to distinguish validity (the extent to which the observed effects are true for the people in a study) from external validity or generalizability (the extent to which the effects observed in a study truly reflect what can be expected in a target population beyond the people included in the study).

**Variable**
Any quantity that varies. A factor that can have different values.
You are developing guidelines regarding ways to reduce mother-to-child transmission of HIV in your clinic. You specifically want to know if antiretroviral drugs reduce the viral load and consequently the transmission of HIV to the foetus around the time of birth.

How will you formulate the clinical question? Take a few minutes to think and formulate the three-part question:

- What is the condition or health problem?
- Who is being affected?
- What is being done?

Write down your answer:

- Mother-to-child transmission of HIV
- The mother and her baby
- Interventions (antiretroviral drugs) to reduce transmission of HIV to the baby
- Can antiretroviral drugs reduce transmission of HIV infection from the mother to her baby?

Finding answers to your clinical question

"Antiretrovirals to reduce mother-to-child transmission of HIV"
Does this systematic review satisfy the criteria for a good systematic review?

Specifically, does it:

- Address a clearly defined question. If so, what was the question?
  Yes. "Are antiretroviral drugs effective in reducing the mother to child transmission of HIV infection?"

- List how studies were found?
  The authors searched the Cochrane Pregnancy and Childbirth Group trials register and the Cochrane Controlled Trials Register. They also searched conference abstracts from the International AIDS Conferences and Conference on Retroviruses and Opportunistic Infections.

- List the search strategy used for finding the studies?
  The reviewers used the search strategy used by the Cochrane HIV/AIDS group and that developed for the Pregnancy and Childbirth Group as a whole. Relevant trials were identified in the Group’s Specialized Register of Controlled Trials. In addition the Cochrane Controlled Trials Register was searched with each new edition of the Cochrane Library. Conference abstracts from the International AIDS Conferences and Conference on Retroviruses and Opportunistic Infections were also searched.

- List what criteria were used to select studies?
  The authors selected only randomized trials comparing any antiretroviral therapy aimed at decreasing the risk of mother-to-child transmission of HIV infection with placebo or no treatment, or any two or more antiretroviral therapies or regimens aimed at decreasing the risk of mother-to-child transmission of HIV infection.

- Explain on what basis studies were excluded from the review?
  The reviewers would have excluded studies which did not fulfil the entry criteria.

- Explain, and if so, list how data were collected from studies?
  The reviewers had defined the outcome measures for the mother and the child. Then all included trials were selected for eligibility according to the criteria specified. The information related to the pre-stated outcomes for the review was abstracted from the trial reports. Any additional information was requested from the authors. The reviewers also assessed all trials for Allocation Concealment using standard Cochrane criteria. In addition, the reviewers assessed the degree of blinding of the trial interventions and documented loss to follow up. The reviewers also contacted the authors of the trials when more information was required.
Interpreting information

1. Which statistical estimate of effect is being reported?
   The statistical estimates of effect being reported are the Odds Ratio, Overall Effect Size and 95% Confidence intervals.

2. What comparison is being made?
   The studies compare zidovudine with placebo in reducing mother-to-child transmission of HIV.

3. What is the outcome under investigation?
   HIV infection in the child.

4. On which side of the line of no effect does the overall estimate of effect lie?
   On the left of the line of no effect – shows that the drug is beneficial.

5. Does the confidence interval touch or cross the line of no effect? (If the confidence interval does touch or cross the line of no effect, this indicates that the result is NOT significant.)
   No.

6. What conclusions can be drawn from the forest plot?
   Most studies show a significant protective effect of zidovudine. The overall estimate is 0.44 and the 95% confidence interval is 0.33 - 0.51. This means that zidovudine reduces the risk of mother-to-child transmission of HIV infection by 56%. If these trials were repeated 100 times, the magnitude of reduction may vary from 49% to 67%.

Practising with the WHO RHL

Clinical Situation 1

A 21 year old woman visits your clinic for antenatal care. She has been married for a year to a truck driver. This is her first pregnancy. The gestational age is 18 weeks. During routine tests, she was found to be HIV positive. You explain to her the problem and its effects on the baby. She is keen to have this baby and wants to know if you can give her medicines to prevent the baby from getting infected.

1. What is the question that you will want to ask in this clinical situation?
   Can medicines reduce the risk of transmitting HIV infection from the mother to the baby?
2. List some drugs used to reduce the risk of HIV transmission to babies.

Drugs used to reduce the risk of HIV transmission to babies include:

A. Nucleoside analogue reverse transcriptase inhibitors like zidovudine (ZDV, also known as AZT), lamivudine (3TC), didanosine (ddI), stavudine (d4T) and abacavir (ABC).

B. Non-nucleoside analogue reverse transcriptase inhibitors like nevirapine (NVP), delavirdine and efavirenz.

C. Protease inhibitors like indinavir, ritonavir, nelfinavir and saquinavir.

(See Background in the Cochrane review)

3. In the trials reviewed, did these drugs reduce the risk of HIV transmission to babies? If yes, how much reduction was achieved?

Zidovudine reduced mother-to-child HIV transmission by 56% (See comparison of Zidovudine versus placebo)

4. Among the groups that received these drugs, were there some subgroups of babies who had significantly lower risks of HIV infection than the remainder? If yes, what were the characteristics of these subgroups?

Babies born to mothers who had only a short course of zidovudine before delivery and had themselves received only a short course of zidovudine after birth were 2.46 times more likely to get HIV infection compared to those babies whose mothers had received a long course of zidovudine and who themselves had received a long course of zidovudine after birth. The long-long course of zidovudine was more protective than the short-short course. Also, in a group of breast-feeding women, nevirapine given just before delivery and within 72 hours of birth (when compared with intrapartum and neonatal zidovudine) was associated with a greater (50%) reduction in mother-to-child transmission of HIV.

(See details under Results, Graphs and Tables)

5. Do these drugs have any effect on the risk of infant or maternal mortality?

When compared to placebo, giving zidovudine to reduce mother-to-child HIV transmission was associated with a 43% reduction in infant mortality and a 70% reduction in maternal mortality.

6. Among the various regimens of zidovudine that have been tried, which is the most effective?

The long-long course i.e. giving zidovudine to the mother from 28 weeks and to the baby for 6 weeks was better than the short-short course (giving zidovudine after 36 weeks to the mother and to the baby for 3 days). However, the results of the long-long course were comparable with those from the long-short course and the short-long course. (See Results, Graphs and Tables.)
7. Finally, what would you advise your patient about drugs to prevent HIV transmission to the baby?

I would advise on the use of antiretroviral drugs (zidovudine) starting from 28 weeks of pregnancy and giving the drug to the baby for 6 weeks after birth.

Clinical situation 2

A 28-year-old woman attends your clinic for antenatal care. This is her second pregnancy. She has no significant medical problems. You have confirmed that she is about 12 weeks pregnant. You ask her to come regularly for antenatal care once a month for the next four months, once in 2 weeks after that until her pregnancy reaches 36 weeks, and every week thereafter until delivery. You advise her on the importance of regular antenatal visits as suggested. However, she tells you that she cannot come very often as she has a small child, has no help at home, and has a long way to travel to your clinic. She asks you, "Can I come less often than what you have advised? Will I have major problems if I can come only less often?"

1. Use the WHO RHL to locate the evidence about antenatal care.
   Enter "antenatal care" in Search. You should get several links to antenatal care. Use the relevant link to get to the Cochrane review titled, "Patterns of routine antenatal care for low-risk pregnancy".

2. How often should women with low risk pregnancy visit the antenatal clinic?
   Fewer goal-oriented and focused visits for antenatal care appear to be as good as the conventional recommendation for several antenatal visits. (See Results)

3. Are there any significant differences in pregnancy outcomes between women who received fewer but focused antenatal care and those who had more frequent antenatal clinic visits?
   There were no significant differences in pregnancy outcomes (e.g., preeclampsia, anaemia, urinary infection, low birth weight) between women who received focused antenatal care and those who had more frequent antenatal clinic visits. (See Results.)

4. Your patient tells you that a trained midwife conducts a clinic near her house. She wants to know if she can go there for her antenatal care. What will you, as a specialist obstetrician advise her based on the evidence from WHO RHL?
   Midwife and general practitioner-led antenatal care appears to be equally effective as that provided by specialist obstetricians. Less women in the midwife-GP led care group developed pregnancy induced hypertension and pre-eclampsia. (See Results, Graphs and Tables.)

5. After having read the evidence, how will you implement evidence-based antenatal care?
   I would go through the Implementation aid, "WHO Antenatal Care Randomized Trial: Manual for the implementation of the New Model", which gives the required information.
Clinical Scenario 3

A 32-year-old woman has been admitted to the labour ward. This is her first pregnancy. The gestational age is 32 weeks. She complains of low abdominal pain and you suspect that she may be in preterm labour. She is worried that if the baby is born now, it will suffer from many problems related to prematurity. You have heard that giving corticosteroids to the mother with preterm labour may benefit the baby.

1. Find the evidence in the WHO RHL regarding corticosteroids in preterm labour.
   Type "corticosteroids" in Search and follow the links under Beneficial Forms of Care to the Cochrane review titled "Prophylactic corticosteroids for preterm birth".

2. List some of the major complications related to prematurity.
   Respiratory distress is a major complication of prematurity. Other complications of prematurity include intraventricular haemorrhage, necrotising enterocolitis and chronic lung disease (See Background and Objectives).

3. Do corticosteroids have any beneficial effect on these complications? If yes, what is the magnitude of the benefit?
   There is a 47% reduction in respiratory distress following antenatal corticosteroids administration. Other benefits include 40% reduction in neonatal deaths, 52% reduction in intraventricular haemorrhage diagnosed by ultrasound and over 8 days less specialized neonatal care. (See Results, Graphs and Tables.)

4. Will corticosteroids increase the risk of infection in the mother or baby?
   There is no increase in neonatal infection after antenatal steroids but there is a non-statistically significant trend towards increased maternal infection in those given antenatal steroids. (See Graphs and Tables.)

5. Should this woman receive corticosteroids? Give reasons for your answer.
   Yes, she should receive corticosteroids because of the potential risk of premature delivery. If she is delivered after a dose of corticosteroids, there will be less risk of respiratory distress, intraventricular haemorrhage, neonatal mortality, less need for surfactant therapy and shorter duration of neonatal intensive care.

Clinical Scenario 4

You have just seen a primigravida at 38 weeks with a breech presentation. You estimate that the foetus is appropriately grown. The mother has no other complications. She wants to know what the risks of having a breech delivery are and wants your advice on further care.

1. What are the risks of having a breech delivery?
   Vaginal delivery requires the assistance of a skilled obstetrician, and even then the risks of birth asphyxia and birth injury are more than the risks during delivery of a
baby presenting by vertex. (See Introduction in Cochrane review on "External cephalic version for breech presentation at term" and RHL Commentary on "External Cephalic version").

2. List the possible options for her management.
Vaginal delivery of the breech is associated with increased newborn mortality and morbidity. Caesarean section is the other option recommended for breech delivery but delivery by caesarean section does not exclude the risk of morbidity. (See Cochrane Review on "Planned caesarean section for term breech delivery"). External cephalic version is an option which can be attempted before delivery to change the presentation from breech to a vertex presentation.

3. Is there any procedure that can be carried out in the clinic which will reduce the chances of a breech delivery? If yes, describe the procedure. What are its benefits and risks? Are there any other procedures that can aid you in reducing the chances of breech delivery?
An external cephalic version (ECV) can be carried out in the clinic. (RHL has a video presentation which describes the procedure. Click on the video on external cephalic version under Implementation Aids). ECV reduces the occurrence of non-vertex presentations at term by 58% and caesarean sections by 48%. There were no significant risks for the foetus and mother.
Use of tocolysis during external version increases the success rate of version but foetal acoustic stimulation is not of proven benefit (See Cochrane review on "Interventions to help external cephalic version for breech presentation at term"). Attempts to change breech presentation to vertex presentation by postural management have not been successful. (See Cochrane Review on "Cephalic version by postural management for breech presentation").

4. Is caesarean delivery an option? If yes, what is the evidence in support of this option? Are there any disadvantages of caesarean section for breech presentation?
Caesarean delivery is an option. The Cochrane review on "Planned caesarean section for term breech delivery" shows that planned caesarean section reduces perinatal and neonatal death and severe neonatal morbidity by 67%. When congenital anomalies were excluded, there was a 71% reduction in neonatal mortality with planned caesarean section. The short term maternal morbidity is 1.29 times higher following caesarean delivery and abdominal pain is 1.89 times more common in women undergoing caesarean delivery. Urinary incontinence and perineal pain were 38% and 68% less common respectively in women undergoing caesarean delivery. However, the beneficial effects of caesarean section appear to be more in countries with low perinatal mortality than in those with high perinatal mortality. The number of additional caesarean sections necessary to avoid having one dead or compromised infant was around seven in countries with a low perinatal mortality rate and 39 in countries with a high perinatal mortality rate. Performing planned caesarean section...
for all term foetuses in the breech presentation would require large additional investments in most developing countries. Furthermore, in these countries where there are poor facilities for regional anaesthesia, blood transfusion and aseptic conditions, etc., a policy of caesarean section for all breech presentations would increase the risk to women as well as put them at greater risk in their future pregnancies due to the presence of the scar in the uterus. Thus, in some settings the risk of caesarean section may outweigh the risk of vaginal birth. (See also the RHL Commentary on "Planned caesarean section for term breech delivery").

Clinical Scenario 5

You have been posted to a new health facility which has a delivery room. However there is no facility for assisted vaginal delivery. You would like to purchase an instrument for facilitating instrumental vaginal delivery. Which instrument would you prefer to buy - a vacuum extractor or a forceps?

1. What are the complications that may result from instrumental vaginal delivery?
   (This information may be obtained from the Cochrane review titled, "Vacuum extraction versus forceps for assisted vaginal delivery").
   The complications that may occur from instrumental vaginal delivery include maternal injury - perineal and vaginal trauma and resultant pain, and neonatal injury - cephalhaematoma, intracranial haemorrhage, retinal haemorrhage, skull fractures, nerve injuries.

2. Which is associated with more complications - vacuum extraction or forceps delivery?
   Give reasons for your answer.
   Forceps delivery was associated with more maternal injury than vacuum extraction. More women who had forceps delivery complained of severe perineal pain 24 hours after delivery. However, neonatal morbidity was more in babies born after vacuum extraction. Cephalhaematoma and retinal haemorrhages were common in these babies. Women who were delivered by vacuum extraction were more worried about their babies than women who were delivered by forceps. The reviewers concluded that, "Use of the vacuum extractor reduces severe maternal injuries. The reduction in cephalhaematomas and retinal haemorrhages may be regarded as compensating foetal 'benefits' to support the choice of forceps. Maternal and neonatal injury may be increased when a difficult failure of vacuum extraction is followed by an attempt to deliver with forceps."

Clinical Scenario 6

The mother of your patient, an 18-year-old primigravida in labour has asked you if she could be allowed to stay with her daughter in the labour ward. The nursing staff does not want to allow the mother into the labour ward as she is worried that the older lady's
presence would cause more problems in labour and increase the risk of newborn infection. You feel sympathetic to the mother and would like to help her.

1. Search the WHO RHL for the evidence that you can use to support your decision.
   You can access the relevant Cochrane review, "Continuous support for women during childbirth" by using "female relative" in Search. You can also click on the Labour Companionship video under Implementation Aids for a video demonstration of the benefits of social support in labour.

2. What are the advantages that have been found with use of social support in labour? What is the magnitude of benefits of each of these advantages?
   Women who had continuous support in labour required 13% less analgesia, had shorter labours (mean 28 min), 13% less operative vaginal deliveries and 10% less caesarean deliveries. Less women (45%) reported difficulty in coping with labour.

3. Are there any disadvantages? If yes, what is the magnitude of these disadvantages?
   Social support was not associated with disadvantage in any of the outcomes reviewed.

4. Does the presence of a person providing supportive care in labour increase the risk of infection in the mother or baby?
   There is no evidence of increased risk of infection in the mother or the baby from the Cochrane review.