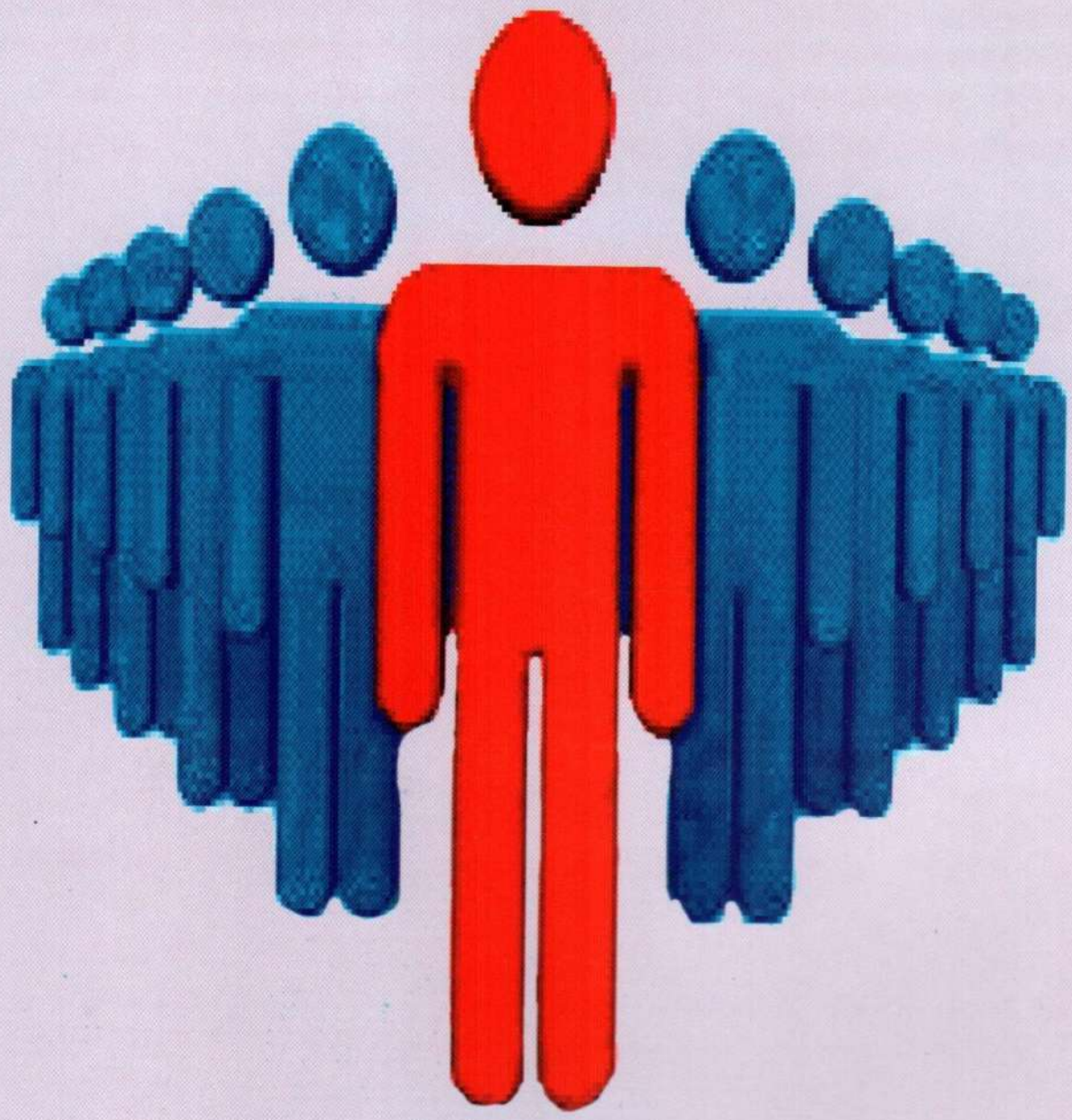
EVIDENCE BASED MEDICINE



Hospital Services Management. DGHS. Dhaka. Bangladesh
www.hsmdghs-bd.org

EVIDENCE BASED MEDICINE

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Message

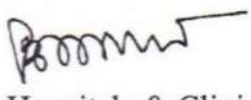
EBM is the integration of clinical expertise, patient values, and the best evidence into the decision making process for patients' care. Clinical expertise refers to the clinician's cumulated experience, knowledge and clinical skills. The patient brings to the encounter his or her own personal and unique concerns, expectations and values. The best evidence is usually found in clinically relevant research that has been conducted using sound methodology.

The evidence, by itself, does not make a decision for physicians, but it can help support the patient care process. The full integration of this component into clinical decisions enhances the opportunity for optimal clinical outcomes and quality of life. The practice of EBM is usually triggered by patients' encounters which generate questions about the effects of therapy, the utility of diagnostic tests, the prognosis of diseases, or the etiology of disorders.

In Practice, clinicians contextualize the best available research evidence by integrating it with their individual clinical experience and their patients' values and expectations. The incorporation of patients' values and clinical expertise in EBM party recognizes that many aspects of health care depend on individual factors. These include variations in individual physiology and pathology, quality-of-life and value-of-life judgments these factors are only partially subjected to scientific inquiry and sometimes cannot be assessed in controlled experimental settings. Application of available evidence is, therefore, dependent on patient circumstances and preferences, and remains subject to input from personal, political, philosophical, religious, ethical, economic, and aesthetic values.

The broad field of EBM includes rigorous and systematic analysis of published literature to synthesize high-quality evidence, such as systematic reviews. It could also be referring to a medical 'movement', where advocates work to popularize the method and usefulness of the practice of EBM in the public, patient communities, educational institutions, and continuing education of practicing professionals.

In this book, we have done our best to provide powerful and efficient ways to fulfill some of these information needs and describe a strategy for formulating answerable clinical questions as the first step.



Director-Hospitals & Clinics
& Line Director-HSM
Directorate General of Health Service
Mohakhali, Dhaka

Message

Along with rapid expansion of the National Health sector particularly that of the facilities of health service delivery and consequent commendable achievements made in last couple of years, the need of ensuring quality, state of the art clinical care is increasingly felt urgent. The urgency is well accommodated in different operational plans of the Health, Nutrition and Population Sector Development Program (HNPSDP) and in line of that Introducing Evidence Based Medicine (EBM) in clinical practice has been incorporated as an activity of the Hospital Service Management operational plan of HNPSDP.

EBM demands integration of best research evidence with individual clinical expertise and patient values through conscientious, explicit and judicious use of mathematical estimates of the risk of benefit and harm, derived from high-quality research on population samples, to inform clinical decision-making in the diagnosis, investigation or management of individual patients. Patient valuesrefer to individual patient's predicaments, rights, and preferences in making clinical decisions about their care. Proliferating from Archie Cochrane's insistence on need of evidence summarization of practices in clinical disciplines, Alvan Feinstein's focus on defining principles of quantitative clinical reasoning and David Sacketts's innovation in teaching critical appraisal, the concept and practice of EBM has been a dominant paradigm in academic medicine in developed world since 90s. However, in our context EBM is quiet a novel one and has just begun crystallization marked by establishment of organizational framework and initiation of operational frames and this manual is one step forward in the process.

Good medical practice uses both individual clinical expertise and best available external evidence, and neither alone is enough. Without clinical expertise, practice risks becoming tyrannised by evidence, for even excellent external evidence may be inapplicable to or inappropriate for an individual patient. Without current evidence, practice risks becoming rapidly out of date, to the detriment of patients. This is where paradigm of EBM stands establishing which in clinical practice throws several challenges, i.e. the need to develop skills in searching clinical evidences, the daunting task of critical appraisal and especially the complex job of knowledge translation into practice. Ensuring decisions are consistent with patients values is even more challenging. With the organizational framework, we have an encouraging start, appropriate strategies to address the challenges need to be operationalized to ensure practice of EBM in the country.

While I trust that this manual will meet the intended objectives I would like to express my sincere gratitude to all the contributors who made it possible.

Prof. Dr. A. F. M. Saiful Islam
President
EBM Core Committee
Directorate General of Health Services
Mohakhali, Dhaka-1212

Acknowledgement

Evidence-Based Medicine is the integration of best research evidence with clinical expertise and patient values.Best research evidence refers to clinically relevant research, often from the basic health and medical sciences, but especially from patient-centered clinical research. Clinical expertise means the ability to use clinical skills and past experience to rapidly identify each patient's unique health state and diagnosis, individual risks and benefits of potential interventions, and personal values and expectations .

Patient values refer to the unique preferences, concerns, and expectations that each patient brings to a clinical encounter and that must be integrated into clinical decisions if they are to serve the patient. Applying evidence to clinical practice is a requirement for best patient care. "Evidence-based medicine" takes many forms and is frequently viewed with some skepticism by practicing clinicians. However, fundamental to evidence-based practice is the concept that, although evidence can recommend particular diagnostic strategies, treatments or management plans, each plan must be individualized to reflect the specific characteristics of individual clinical circumstances.

Fundamental to understanding evidence-based practice and guideline development are systematic reviews. Systematic reviews use well-defined and reproducible literature search strategies to identify evidence that informs clinical problems; the data is then assessed for its methodological rigor and, when of sufficient quality and quantity, it may be confined mathematically using meta-analysis techniques, which provide more accurate estimates of effects as they incorporate larger numbers of patients than the source studies.

In the current sector programme, HPNSDP,Hospital Service Management is one of the important operational plan, is trying to develop the clinical skill & leadership of the clinicians on the basis of most modern clinical evidence practicing worldwide.

This Document is for clinicians at any stage of their service who want to learn how to practice andteach evidence-based medicine. Written for the busy practitioner, it is short, lean, and highly practical. Those who want, and have time for, more detailed discussions of the theoretical and methodological basesfor the tactics described here should consult one of the longer textbooks on clinical epidemiology.

This document differs from the others not only in its brevity. Its shift in focus reflects our growing ability to transform critical appraisals of evidence intodirect clinical action. This shift in focus also grows from the continuing clinical experiences development of several evidence-based information resources including different Journal Club, Evidence-Based Medicine, Evidence-Based Nursing, Evidence-Based Mental Health, and Best Evidence, to make iteasier for practitioners to get at the best current evidence.

In our experience, this is the hardest step that many people face in finding best current evidence to address clinical problems. Because EBM begins and ends with patients, will use a patient encounter to remind us how clinical questions arise and to show how they can be used to initiate evidence based learning. It will also introduce some teaching tactics that can help us coach others to develop their questioning skills.

Evidence-based guidelines use systematic reviews to inform specific clinical circumstances. Clinical questions are defined and systematic literature review is performed to identify evidence that addresses those clinical questions. The evidence is then summarized, graded and presented. Evidence-based guidelines can improve the quality of care of patients by supporting interventions of proven benefit, while discouraging interventions that are ineffective or potentially harmful. However, guidelines sometime can also be misleading and cause harm, particularly if recommendations are based on an incomplete or flawed dataset, if they are biased, or if the development process is incorrectly carried out. Rigorously developed evidence-based guidelines aim to minimize these potential harms.

We are really grateful to the core member of EBM who made their optimum sincere effort for this excellent document. We hope , in the current future, we will continue its up gradation for the best practices of the clinicians.

Dr. Md. Aminul Hasan
MBBS. MPH. PhD
Member Secretary of EBM Core Committee

Compiled by

Dr. A K M Saiedur Rahman
Asst. Director MBPC
DGHS, Mohakhali, Dhaka

National Core committee of EBM

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2. Dr. Md. Mumtazuddin Bhuiyan- Director Hospital & Clinics. DGHS- Member
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13. Dr. Md. Aminul Hasan, DPM, TQM, HSM, DGHS- Member Secretary

Preface

In clinical practice, we always try to provide the best treatment to our patients through the best available knowledge. The medical knowledge is so rapidly evolving that keeping up-to-date is a very difficult task. If we consider the treatment of a particular clinical problem then one physician may need to be adequately updated on that issue but for an individual there might have a gap in the clinical practice and the latest development on that particular issue. So the evidence based medicine (EBM) has emerged to meet that gap by contextualize the best available research evidence by integrating it with physician's clinical expertise and the patient's values and expectations. In 1996 David Sackett wrote that "evidence-based medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients."

Evidence-based medicine is the integration of best research evidence with clinical expertise and patient values in clinical practice. The best research evidencemeans clinically relevant research, often from the basic sciences of medicine, but especially from patient centered clinical research. New evidence from clinical research both invalidates previously accepted tests and treatments and replaces them with new ones that are more powerful, accurate and efficacious. The clinical expertisemeans the ability to use our clinical skills and past experience to rapidly identify each patient's unique health status and diagnosis, their individual risks and benefits of potential interventions. Patientvaluesmean the unique preferences, concerns and expectations each patient brings to a clinical encounter and which must be integrated into clinical decisions. When these three elements are integrated, clinicians and patients form a diagnostic and therapeutic alliance which optimizes clinical outcomes and quality of life. EBM is a process of life-long, problem-based learning. The process involves: converting the patients problems into focused questions, efficiently tracking down the best evidence with which to answer the question, critically appraising the evidence for validity and clinical usefulness, applying the results in clinical practice, and evaluating performance of the evidence in clinical application. The practice of EBM is a team work; all members of the team will have equal importance and the junior member of the team may have the latest information about the problem.

In our practice we do the evidence based medicine in piecemeal mostly depending on the text books and partly on the journals. In most of the situation we feel that there is gap between our knowledge and the patients' need.The text books are not dealing with all the specific questions and the information there is already out of date. So for the latest information we have to be dependent on the journals which are huge and also disorganized. If we consider the publications in the field of internal medicine where there

are 20 important clinical journals in which 6000 articles per year. So to keep up to date one need to read over 17 articles a day for every day of the year. This is next to impossible. So the there are groups of evidence based collaboration worldwide and they have the strategiesto create the systematic reviews and concise summaries of the primary articles of health care importance. The Cochrane Collaboration is pioneer among them. The creation of one-page summaries of the articles by ACP journal club and evidence based journal are also worth mentioning.Only the 2% of journal articles that are both valid and of immediate clinical use are summarized and published as the secondary publication.We can use these secondary evidence based article in our practice.

There are specific search strategies by which we can search the article of clinical relevance and by appraising that critically we can use the results in our daily practice or we can use those secondary articles which are appraised before publication. In the present document we try to present the ways by which we can formulate a question, search the literatures systematically and appraise those critically before applying them in our clinical practice.

Prof. Dr Md Mujibur Rahman
Coordinator, EBM Core Committee
Prof of Medicine, Shaheed Shurawardee Medical College, Dhaka

Content

1. Introduction

Evidence-based medicine (EBM) is the integration of best research evidence with clinical expertise and patient values.

By best research evidence we mean clinically relevant research, often from the basic sciences of medicine, but especially from patient centered clinical research into the accuracy and precision of diagnostic tests (including the clinical examination), the power of prognostic markers, and the efficacy and safety of therapeutic, rehabilitative, and preventive regimens. New evidence from clinical research both invalidates previously accepted diagnostic tests and treatments and replaces them with new ones that are more powerful, more accurate, more efficacious, and safer.

By clinical expertise we mean the ability to use our clinical skills and past experience to rapidly identify each patient's unique health state and diagnosis, their individual risks and benefits of potential interventions, and their personal values and expectations.

By patient values we mean the unique preferences, concerns and expectations each patient brings to a clinical encounter and which must be integrated into clinical decisions if they are to serve the patient. When these three elements are integrated, clinicians and patients form a diagnostic and therapeutic alliance which optimizes clinical outcomes and quality of life.

Rationale : These ideas have been around for a long time. Some authors identify with their expression in post-revolutionary Paris (when clinicians like Pierre Louis rejected the pronouncements of authorities* and sought the truth in systematic observation of patients), and a colleague has nominated a much earlier origin in ancient Chinese medicine†.

In the current era, they were consolidated and named EBM in 1992 by a group led by Gordon Guyatt at McMaster University in Canada[1]. Since then, the number of articles about evidence-based practice has grown exponentially (from 1 publication in 1992 to about a thousand in 1998) and international interest has led to the development of 6 evidence-based journals (published in up to 6 languages) that summarize the most relevant studies for clinical practice and have a combined world-wide circulation of over 175,000.

The subsequent rapid spread of EBM has arisen from 4 realizations and is made possible by 5 recent developments. The realizations, attested to by ever-increasing numbers of clinicians, are:

1. Our daily need for valid information about diagnosis, prognosis, therapy and prevention (up to 5 times per in-patient2 and twice for every 3 out-patients).
2. The inadequacy of traditional sources for this information because they are out-of-date frequently wrong (experts5), ineffective (didactic continuing medical education6) or too overwhelming in their volume and too variable in their validity for practical clinical use (medical journals).

3. the disparity between our diagnostic skills and clinical judgement, which increase with experience, and our up-to-date knowledge8 and clinical performance9 which decline.
4. our inability to afford more than a few seconds per patient for finding and assimilating this evidence or to set aside more than half an hour per week for general reading and study.

Until recently, these problems were insurmountable for full-time clinicians. However, 5 developments have permitted us to turn this state of affairs around:

1. The development of strategies for efficiently tracking down and appraising evidence (for its validity and relevance).
2. The creation of systematic reviews and concise summaries of the effects of health care (epitomized by the Cochrane Collaboration).
3. The creation of evidence-based journals of secondary publication (that publish the 2% of clinical articles that are both valid and of immediate clinical use).
4. The creation of information systems for bringing the foregoing to us in seconds.
5. The identification and application of effective strategies for life-long learning and for improving our clinical performance.

Challenges for practice EBM : First of all, do full-time clinicians really recognize working in these modes? It appears so. In a survey of UK GPs (in which responders were more likely to hold MRCP certification), the great majority reported practicing at least part of their time in the "searching" mode, using evidence- based summaries generated by others (72%) and evidence-based practice guidelines or protocols (84%)

On the other hand, far fewer claimed to understand (and be able to explain) the "appraising" tools of NNTs (35%) and confidence intervals (20%). Finally only 5% believed that "learning the skills of evidence-based medicine" (all five steps) was the most appropriate method for "moving from opinion-based medicine to evidence-based medicine.

Second, even if they recognize these modes, can they actually get at the evidence quickly enough to consider it on a busy clinical service? Again, it appears so, but examples are few. When a busy (180 admissions per month) in-patient medical service brought electronic summaries of evidence previously appraised either by team members ("CATs") or by the summary journals‡‡ to working rounds, it was documented that, on average, the former could be accessed in 10 seconds and the latter in 2510. Moreover, when assessed from the viewpoint of the most junior member of the team caring for the patient, this evidence changed 25% of their diagnostic and treatment suggestions and added to a further 23% of them. Third, even if they can get at it, can clinicians actually provide evidence-based care to their patients?

Again, it appears so from audits carried out on clinical services that attempt to operate in the searching and appraising modes. The first of these examined the evidence-base for the primary interventions applied to the primary diagnoses of consecutive patients on an in-patient medical service and documented that 82% of them were evidence-based (53% based on

randomized trials or systematic reviews of randomized trials and 29% based on convincing non-experimental evidence).16 Similar results have been obtained from audits of psychiatric17, surgical18, pediatric19 and general20 practice.

Outcome of Evidence Based Medicine : No such evidence is available from randomized trials because no investigative team or research granting agency has yet overcome the problems of sample-size, contamination, blinding, and long-term follow-up which such a trial requires. Moreover, there are ethical concerns with such a trial: is withholding access to evidence from the control clinicians ethical?

On the other hand, population-based "outcomes research" has repeatedly documented that those patients who do receive evidence-based therapies have better outcomes than those who don't. For positive examples, myocardial infarction survivors prescribed aspirin or betablockers have lower mortality rates than those who aren't prescribed these drugs21,22, and where clinicians use more warfarin and stroke unit referrals, stroke mortality declines by >20%.23 For a negative example, patients undergoing carotid surgery despite failing to meet evidence-based operative criteria, when compared with operated patients who meet those criteria, are more than 3 times as likely to suffer major stroke or death in the next month

Limitation : The examination of the concepts and practice of EBM by clinicians and academics has led to negative as well as positive reactions. The ensuing discussion and debate has reminded us of 3 limitations that are universal to science (whether basic or applied) and medicine (the shortage of coherent, consistent scientific evidence; difficulties in applying any evidence to the care of individual patients; barriers to any practice of high quality medicine). The debate has also identified 3 limitations that are unique to the practice of EBM.

First, the need to develop new skills in searching and critical appraisal can be daunting, although (as we pointed out above) evidence-based care can still be applied if only the former has been mastered and directed toward pre-appraised resources. Second, busy clinicians have limited time to master and apply these new skills, and the resources required for instant access to evidence are often woefully inadequate in clinical settings. Finally, evidence that EBM "works" has been late and slow to come.

On the other hand, the ensuing discussion and debate has clarified some "pseudo-limitations" that arise from misunderstandings of the definition of EBM. An examination of the definition and steps of EBM quickly dismisses the criticisms that it denigrates clinical expertise, is limited to clinical research, ignores patients' values and preferences, or promotes a cookbook approach to medicine. Moreover, it is not an effective cost-cutting tool, since providing evidence-based care directed toward maximizing patients' quality of life often increases the costs of their care and raises the ire of health economists27. In addition, the selfreported employment of the "searching" mode by a great majority of front line GPs dispels the contention that EBM is an ivory tower concept. Finally, we hope that the rest of this book will put to rest the concern that EBM leads to therapeutic nihilism in the absence of randomized trial evidence.

2. Concept of Evidence Based Medicine

What is evidence-based medicine?

"Evidence-based medicine is the integration of best research evidence with clinical expertise and patient values" - Dave Sackett

Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.

[Sackett DL, Rosenberg WMC, Gray JAM, Haynes RB, Richardson WS: Evidence based medicine: what it is and what it isn't. BMJ 1996;312:71-2]

By best available external clinical evidence we mean:

- Clinically relevant research
- Often from the basic sciences of medicine,
- Especially from patient centered clinical research
- Into the accuracy and precision of diagnostic tests
- The power of prognostic markers, and
- The efficacy and safety of therapeutic, rehabilitative, and preventive regimens

By individual clinical expertise we mean:

- The proficiency and judgment
- More effective and efficient diagnosis
- More thoughtful identification and use of individual patients' predicaments, rights, and preferences
- Collaborating patients' values in making clinical decisions about their care.

To add 'Clinical Expertise and Patient's Biology & Values:

- First and foremost: Is my patient so different from those in the trial?
- What is my patient's RISK?
  - of the event the treatment strives to prevent?
  - of the side-effect of treatment?
- What is my pt's RESPONSIVENESS?
- What is the treatment's FEASIBILITY in my practice/setting?
- What is my patient's VALUES?

Principles of EBM:

Five linked ideas-

- Health care and clinical decisions should be based on the best available evidence.
- The health care/clinical problem-rather than habits or protocols determines the evidence to be sought
- Identifying the best evidence requires mastering search skills and means using epidemiological and bio-statistical ways of thinking
- Conclusions derived from critically appraising the evidence are useful only if put into action in managing patients/making health care decisions
- Performance should be constantly evaluated

Skills, knowledge and attitudes for EBM-

- Questioning attitude to existing knowledge and accepted practices, which should be based on the be available evidence
- Ability to link the question/problem to the appropriate type of evidence
- Ability to seek out the evidence
- Ability to critically appraise that evidence
- Store relevant information
- Audit

Questions that Spark a Spirit of Inquiry-

- Which of my practices are currently evidence based?
- Which don't have any evidence in support?
- When is the best time to question my current clinical practices?
- Where can I find the best evidence to answer my clinical questions?
- Why am I doing what I do with my patients?
- How can I become more skilled in EBM and mentor others to implement evidence-based care?

Summary-

- Good doctor use both individual clinical expertise and the best available external evidence, and neither alone is enough.
- Without clinical expertise, practice risks becomes tyrannised by evidence, for even excellent external evidence may be inappropriate for an individual patient.
- Without current best evidence, practice risks becoming rapidly out of date, to the detriment of patients.

How did it evolve?

- Traces of evidence-based medicine's origin can be found in ancient Greece (Woolf SH, George JN (August 2000). "Evidence-based medicine. Interpreting studies and setting policy". Hematol. Oncol. Clin. North Am. 14 (4): 761–84).
- Although testing medical interventions for efficacy has existed since the time of Avicenna's The Canon of Medicine in the 11th century (Daly WJ, Brater DC (2000). "Medieval contributions to the search for truth in clinical medicine". Perspect. Biol. Med. 43 (4): 530–40. PMID 11058989. "p. 536)
- It was only in the 20th century that this effort evolved to impact almost all fields of health care and policy. Professor Archie Cochrane, a Scottish epidemiologist, through his book Effectiveness and Efficiency: Random Reflections on Health Services (1972) and subsequent advocacy, caused increasing acceptance of the concepts behind evidence-based practice. Cochrane's ideal was for each specialty to produce a series of meta-analyses of all the trials in the discipline, and to regularly update these meta-analyses.
- Centres of evidence-based medical research 'Cochrane Centres' and an international organization, the 'Cochrane Collaboration' is named to honour Prof. Cochrane's effort.
- The explicit methodologies used to determine "best evidence" was largely established by the McMaster University research group led by David Sackett and Gordon Guyatt.
- Guyatt later coined the term "evidence-based" in 1990.[32] The term "evidence-based medicine" first appeared in the medical literature in 1992 in a paper by Guyatt et al [Evidence-Based Medicine Working Group (November 1992). "Evidence-based medicine. A new approach to teaching the practice of medicine". JAMA 268 (17): 2420–5)].
- Mile stones of EBM-
  - At McMaster University David Sackett founded the world's first department of clinical epidemiology.
  - In 1988 the Oxford Database of Perinatal Trials was launched. This developed into the Cochrane Collaboration and its Cochrane Library
  - In 1991 the ACP journal club was launched by the American College of Physicians.
  - In 1995 the journal Evidence based medicine for primary care and internal medicine was launched.

Why is EBM important?

- Practitioners limited time and little understanding of research methods
- Awareness of the gaps between scientific evidence and health care practice
- Awareness of the consequences of the adoption of ineffective, or even harmful procedures in practice
- Science and technology innovations-new tools/resources, text books are often out-dated
- Patients do benefit-

- E-B practise vs. Outcome in stroke (US):
  - When cared for by E-B neurologists, patients were 44% more likely to receive warfarin, and much more likely to be placed in a stroke care unit,
  - And were 22% less likely to die in the next 90 days. (Mitchell et al: stroke 1996;27:1937-43)

What are the barriers?

- Patient-values & preferences
- Geography
- Economics
- Administration/Organisation
- Tradition
- "Expert" opinion

Three solutions:

Clinical performance can keep up to date by:

1 Learning how to practice evidence-based medicine ourselves.

2 Seeking and applying evidence-based medical summaries generated by others.

3 Applying evidence-based strategies for changing our clinical behaviour.

Conclusion:

- **EBM integrates evidence, expertise, and the unique biology and values of individual patients.**
- **Local EB Provision ought to integrate evidence, expertise, and the unique biology and values of the local scene.**

3. Concept of Evidence Based Practice

Objectives:

General : To understand the practical application of the concepts of evidence based medicine

Specific: After the session participants should know:

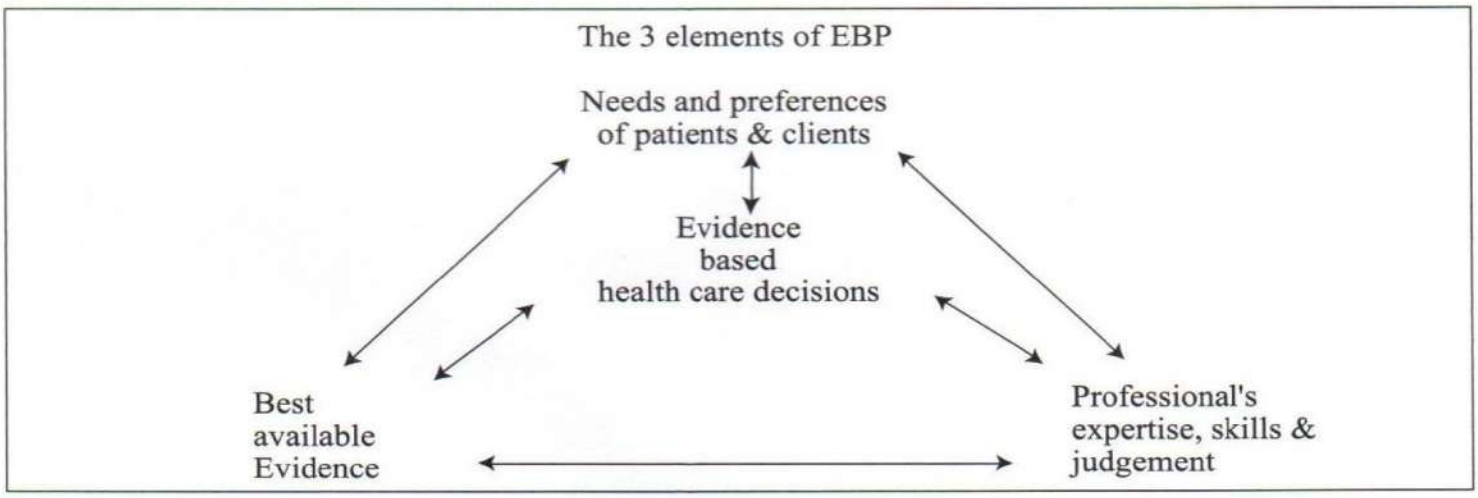
- Principals of EBP
- Five steps of EBP
- Basics of step 1: 'formulation of an answerable question'
- Structure and organization of researchable questions – PICO

Principals of Evidence Based Practice

The practice of evidence-based medicine is an ongoing process involving clinicians and patients: staying abreast of science, filtering science through the patient's preferences, and shared decision-making with patients are its keys.

3 critical integrated processes involved in the practice of evidence-based medicine:

1. Evidence-based practice involves *ongoing systematic review of the "science"* supporting the diagnosis and treatment planning for a condition by clinicians and patients. Often, the science is incorporated into guidelines, or a "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.
2. Evidence-based practice involves *the integration of the science with the clinician's training and practice experience.*
3. Evidence-based practice involves the active participation of patients in making decisions about their care. Though foreboding in concept, the premise is simple: evidence-based decision-making requires that *consumers comprehend their diagnosis and engage in a reasoned assessment of available treatment options* and the benefits and risks associated with each.



Five steps of Evidence Based Practice

1. Formulate an answerable question
2. Track down the best evidence
3. Critically appraise the evidence for:
    - Validity
    - Impact (size of the benefit)
    - Applicability
4. Integrate with clinical expertise and patient values
5. Evaluate our effectiveness and efficiency
    - keep a record; improve the process

Step 1: Ask clinical questions in PICO format.

Inquiries in this format take into account:

- Patient population of interest (P)
- Intervention or area of interest (I)
- Comparison intervention or group (C)
- Outcome (O), and
- [Time (T)]

The PICO format provides an efficient framework for searching electronic databases, one designed to retrieve only those articles relevant to the clinical question.

Step 2: Search for the best evidence.

Using the PICO format helps to identify key words or phrases that, when entered into search successively and then combined, expedite the location of relevant articles in massive research databases such as MEDLINE.

Step 3: Critically appraise the evidence.

Once articles are selected for review, they must be rapidly appraised to determine which are-

- most relevant,
- valid,
- reliable, and
- applicable to the clinical question.

Step 4: Integrate the evidence with clinical expertise and patient preferences and values.

- Research evidence alone is not sufficient to justify a change in practice.
- Evidences must be integrated with
    - Clinical expertise, based on patient assessments, data from laboratory and outcomes management programs, and

- Patients' preferences and values
- These are important components of EBP.

Step 5: Evaluate the outcomes of the practice decisions or changes based on evidence.

- After implementing EBP, it's important to monitor and evaluate any changes in outcomes so that positive effects can be supported and negative ones remedied.
- Just because an intervention was effective in a rigorously controlled trial doesn't mean it will work exactly the same way in the clinical setting.

Questions

- Recognize: your questions
- Select: which questions to pursue
- Guide: how to ask and answer
- Assess: how well & what to improve

Importance:

- The importance of a well framed question cannot be overstated
- The type of question directs the search for evidence, and
- The components of the question become the search terms for the resources

Types of Question

- "Background" questions ask for general knowledge about a condition or thing
- "Foreground" questions ask for specific knowledge for clinical decisions or actions.

Background Question

- Have two essential components:
- A question root (who, what, etc.) with a verb
- A disorder, test, treatment, or other healthcare
- Example: What causes migraines? Or

  How often should women>40 have a mammogram?
- The background question is usually asked because of the need for basic information. It is not normally asked because of a need to make a clinical decision about a specific patient.

Foreground Questions:

- Ask for specific knowledge about managing patients with a disease
- Have 3 or 4 essential components
  - Patient and/or problem
  - Intervention
  - Comparative intervention (optional, include if relevant)
  - Clinical outcome

Case scenario: A 42 year old woman comes to her primary care practitioner's office for follow up of her type II diabetes. She is currently on glyburide 10 mg twice daily. However, her morning and evening blood sugars still fall above 200 mg/dl. You are the medical student who sees this patient with your attending. When you leave the patient's room, your attending asks whether you think she should add metformin to her regimen. You haven't taken the endocrine sequence yet, so your knowledge of this medication is sketchy.

Background questions: What class of medication does metformin fall in?

What is the initial dosage of metformin?

What are the adverse effects of metformin?

Foreground questions: Does the addition of metformin to a sulfonylurea in patients with type II diabetes mellitus improve glycemic control?

Does metformin + glyburide make type II diabetics more prone to hypoglycemic side effects than glyburide alone?

Structure of researchable questions – PICO

- Population/Patients
- Intervention
- Comparison
- Outcome

Population can be-

- General or specific (eg. Male children < 1 yr)
- Patient situation
- Problem of interest

An intervention can be-

- An exposure
- A diagnostic test
- A prognostic factor
- A treatment
- A patient perception, etc.

A comparison can be-

- An alternative intervention
- No intervention
- An exposure

An outcome can be-

- What are the findings/ results of the research?

Asking the question

- Write your question out as a full sentence

Examples-

- In the general population, is duct tape as effective as cryotherapy for the treatment of cuteneous warts?
- Can Vitamin D supplements help prevent falls in the elderly?

	Patient or Problem	**Intervention** (a cause, prognostic factor, treatment, etc.)	**Comparison Intervention** (if necessary)	**Outcomes**
Tips for Building	Starting with your patient, ask "How would I describe a group similar to mine?" Eg. General population	Ask "Which main intervention is consideried?" Be specific Eg. Duct tape	Ask "What is the main alternative to compare with the intervention?" Again, be specific. Eg. Cryotherapy	Ask "What can I hope to accomplish?" or "What could this exposure really affect?" Again, be specific Eg. Rx of cuteneous warts

- P= In the general population
- I= Is duct tape as effective as
- C= cryotherapy
- O= for the treatment of cuteneous warts
- P= In the elderly
- I= doViamin D supplements
- C= (implied- compared to no intervention/ placebo)
- O= help prevent falls

Question type	Definition	Template
Intervention or therapy	To determine which treatment leads to the best outcome	In _____ (P), how does _____ (I) compared with _____ (C) affect _____ (O) within _____ (T)?
Etiology	To determine the greatest risk factors or causes of a condition	Are _____ (P) who have _____ (I), compared with those without _____ (C), at _____ risk for _____ (O) over _____ (T)?
Diagnosis or diagnostic test	To determine which test is more accurate and precise in diagnosing a condition	In _____ (P), are/is _____ (I) compared with _____ (C) more accurate in diagnosing _____ (O)?
Prognosis or prediction	To determine the clinical course over time and likely complications of a condition	In _____ (P), how does _____ (I) compared with _____ (C), influence _____ (O) over _____ (T)?
Meaning	To understand the meaning of an experience for a particular individual, group, or community	How do _____ (P) with _____ (I) perceive _____ (O) during _____ (T)?

Table 1: PICO Templates for common questions

Sites for framing your questions:

- Centre for Evidence Based medicine (Oxford University)
- Formulating a clinical question tutorial (Boston University Medical Center)
- Formulating evidence based question (University of Toronto)

4. Finding the Best Evidence

Objectives :

General: To give an overview of the evidences to be sought on the basis of the question

Specific: The clinician must know:

- Type of information sought
- Species of literature to be searched
- The range of sources available

After a well built clinical question, the next step is performing a literature search

The clinician must decide the type of evidence the PICO question is related to and the species of literature to be searched.

Type of Evidence on the basis of question

- Phenomena: Observation / qualitative studies
- Aetiology: Cohort studies (or Case-control studies)
- Diagnosis and screening: Cross-sectional analytical
- Prognosis: Cohort studies
- Intervention: Randomised Controlled Trials

To answer a broad clinical question

- Traditional review articles from peer-reviewed journals
- Well referenced chapters from current text books
- Practice guidelines

To answer a specific question

- Systematic reviews
- Meta-analysis
- Original research (RCTs) in peer-reviewed journals

Types of Evidence:

- **Primary studies: reports research first hand**
  - Case studies
  - Experiments
  - Surveys
  - Clinical Trials
- **Secondary studies: attempts to summarise and draw conclusions from primary studies**

- Non-systematic reviews
- Systematic reviews
- Meta-analyses
- Guidelines
- Decision analyses
- Economic analyses

Types of Primary Evidence: Clinical trials:

1. **Observational Studies**

   A. Descriptive studies- case series, cross-sectional surveys

   B. Analytical studies- case control, cohort

2. **Intervention Studies**

   A. Randomized control trials

   B. Quasi-randomized trials

Types	Design	Questions answered	Advantage/disadvantage
RCT	Randomly allocated participants	Is this drug better than placebo?	Rigorous evaluation of a single variable. Prospective design, BUT Expensive and time consuming Controversial funding
Cohort	Two or more groups with different exposures are followed up for outcome	Does high blood pressure get better over time?	Examines multiple effects of single exposure. Particularly valuable when exposure is rare. BUT, Blinding is difficult; randomisation not present; large sample sizes or long follow-up necessary.
Case control	patients with a particular disease or condition are identified and "matched" with controls	Does whooping cough vaccine cause brain damage?	Quick and cheap; only feasible method for very rare disorders or those with long lag between exposure and outcome; Fewer subjects needed than cross-sectional studies. But, confounders; selection of control groups is difficult; potential bias: recall, selection.
Cross-Sectional study	Examines the relationship between diseases and variables in a defined population at one particular time	What is the prevalence of a disease or risk factor?	Cheap and simple; ethically safe. But, establishes association at most, not causality; recall bias susceptibility; confounders may be unequally distributed

Secondary studies:

- [Non-systematic] reviews, which summarise primary studies;
- Systematic reviews, which do this according to a rigorous and predefined methodology; and
- Meta-analyses, which integrate the numerical data from more than one study.
- Guidelines, which draw conclusions from primary studies about how clinicians should be behaving.

Advantage/disadvantages:

Type	Advantages	Disadvantages
Primary Study	Very specific information	Not comprehensive
Systematic Review	Summarises all research about an intervention.	Usually only one of several possible interventions is considered. May not explore benfits vs harms.
Evidence-based Guideline	Summarises all relevant research about all possible interventions for a clinical problem. Explores benefits and harms.	May become out-of-date quickly. Expert opinion often fills gaps in evidence.

The hierarchy of evidence:

- Guide lines
- Systematic reviews and meta-analyses
- Randomised controlled trials with definitive results (confidence intervals that do not overlap the threshold clinically significant effect)
- Randomised controlled trials with non-definitive results (a point estimate that suggests a clinically significant effect but with confidence intervals overlapping the threshold for this effect)
- Cohort studies
- Case-control studies
- Cross sectional surveys
- Case reports.

5. Where and how to search Evidence

Objective :

Genereal: To understand the resources of medical evidence and learn how to extract evidence from them

Specific: To learn how to-

1. Chose resources
2. Translating the PICO to appropriate search terms
3. How to search the internet?

Searching for evidence using the Internet is an ideal way to efficiently retrieve high quality medical information.

Steps:

1. **Formulate the PICO and arrange the key words**
2. **Select resources according to question type**
3. **Search every key word, combine the search results, search for the best single article**
4. **Print the abstract and write down your search strategy**

p **Formulate the PICO and arrange the key words:**

Scenario - You are interested in checking the hearing of elderly patients, and have heard that the 'whispered voice test' is good.

Question

- Population – in elderly patients does
- Indicator – a 'poor' whispered voice test
- Comparator – a 'normal' whispered voice test
- Outcome – predict abnormal audiogram

Arrange the key words:

- Underline the key terms
- Number the order of importance from 1-4
- Think of alternate spellings, synonyms, & truncations

Eg.

1. Indicator – a 'poor' whispered voice test
2. Outcome – predict poor hearing (audiogram)
3. Population – in elderly patients does
4. Comparator – a 'normal' whispered voice test

p **Select resources according to question type**

For broad questions-

1. Text books: The Merck Manual
   Scientefic American medicine
   Up to Date
   MD Consult
2. Traditional review articles: OVID
3. Practice guidelines: "National Guidelines Clearinghouse"

For specific questions

- MEDLINE- Pubmed
- Meta search- Smart search, etc.

p **Stepwise searching in PUBMED**

Basics:

1. Know the short cuts of your internet browser and operating system

   Eg. 1. In Microsoft explorer clicking links with right button opens documents in a new window, retrieving the original one.

   2. 'Find" is an important function under 'edit' menu to locate specific terms in large articles

2. Start Explorer and enter- www.pubmed.gov
3. Put on CAPS lock- So that AND and OR are in CAPITALS

   Boo-le-ans*

   - AND = both terms
   - OR = either term
   - NOT = not this term

4. Search with #1 PICO item
   - Whisper*
   - Then go to "Clinical Queries": diagnosis
   - Whisper* (again)
   - Add #2 PICO item

   whisper AND (hear* OR audiogram)

p **PUBMED search guideline: WWW.LIBRARY.UBC.CA**

Start:

1. To perform a search, enter search terms in the PubMed Search Box and select Search. For example, to find information on the relation between heart attack and diet; enter heart attack diet in the Search Box and select Search (Fig. 1).
2. Multiple terms are automatically combined with AND
3. In a PubMed search the search terms are automatically mapped to MeSH (Medical Subject Headings). MeSH are standardized subject headings used to describe the contents of an article.

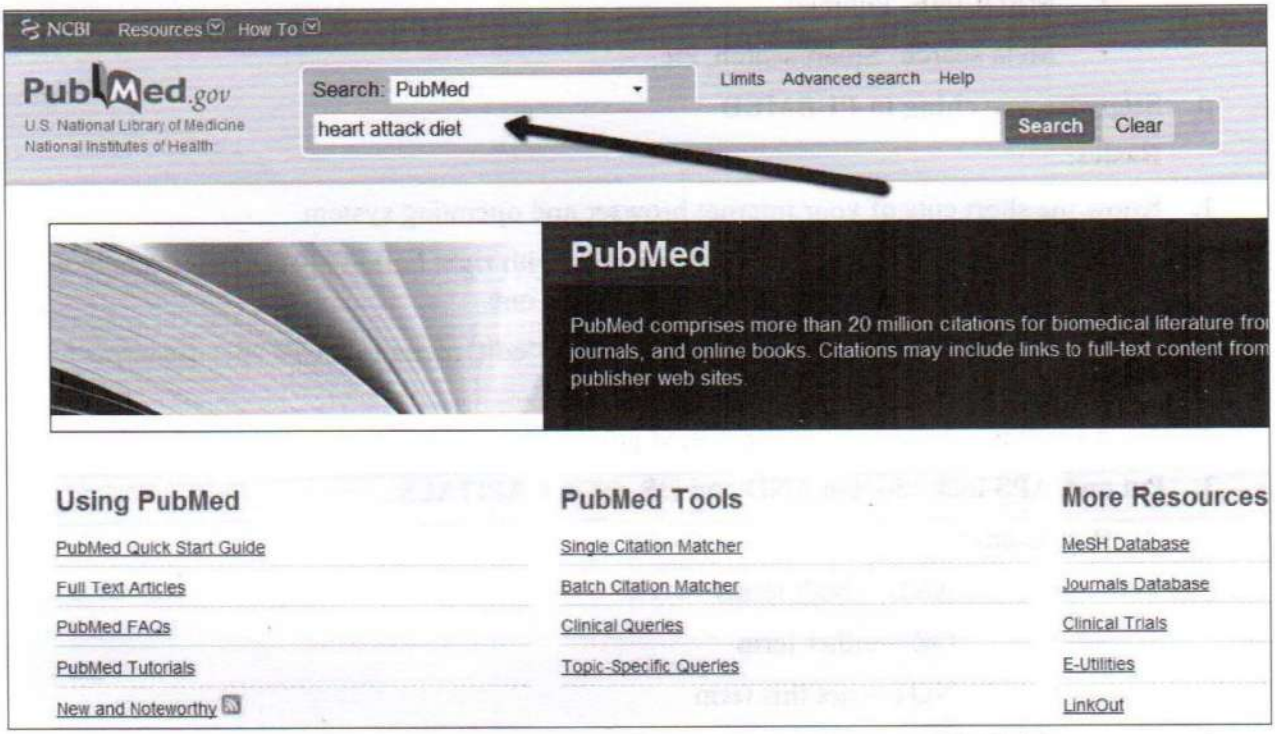


Figure 1: PubMed home page

Note: If you search for an exact phrase e.g. "heart attack" using quotation marks, or use truncation (*) to search for variations in spelling, the mapping to MESH terms will be switched off.

Search Details:

1. To see how PubMed interpreted a search, scroll down to the Search Details box on the right of the results screen. Click See more and Search Details are displayed as shown in Fig. 2.
2. In this example heart attack was mapped to the MeSH term myocardial infarction and terms were searched as both keywords and as MESH terms
3. The search can be edited here and re-run by selecting Search.

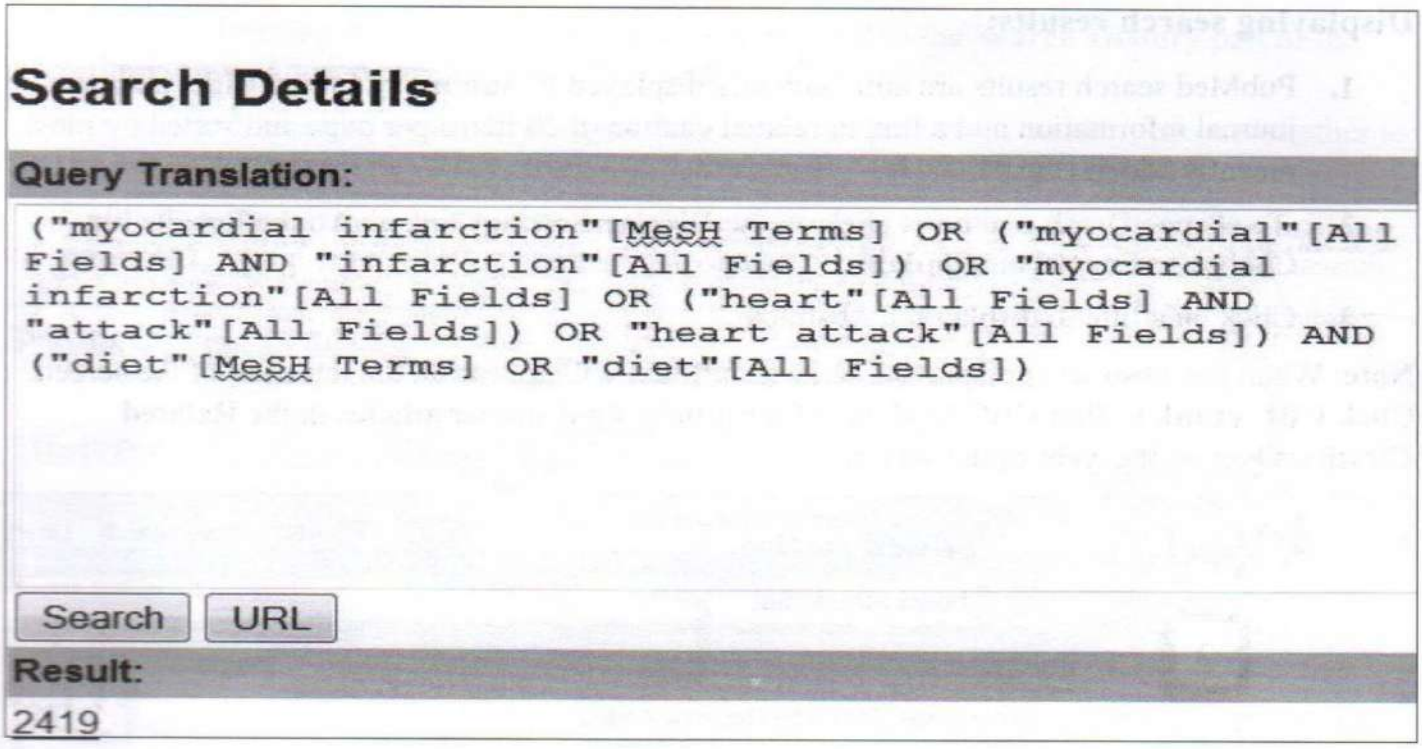


Figure 2: Search Details

Limiting a search:

1. Click **Limits** above the PubMed Search box
2. Select limits by checking the boxes beside limit options such as type of article, language, age etc. (Fig.3), then **Search.**

Note: A yellow triangle will be displayed at the top of the results screen when limits have been set. **Change** or **Remove** limits here too. A green check box is displayed when limits have been removed.

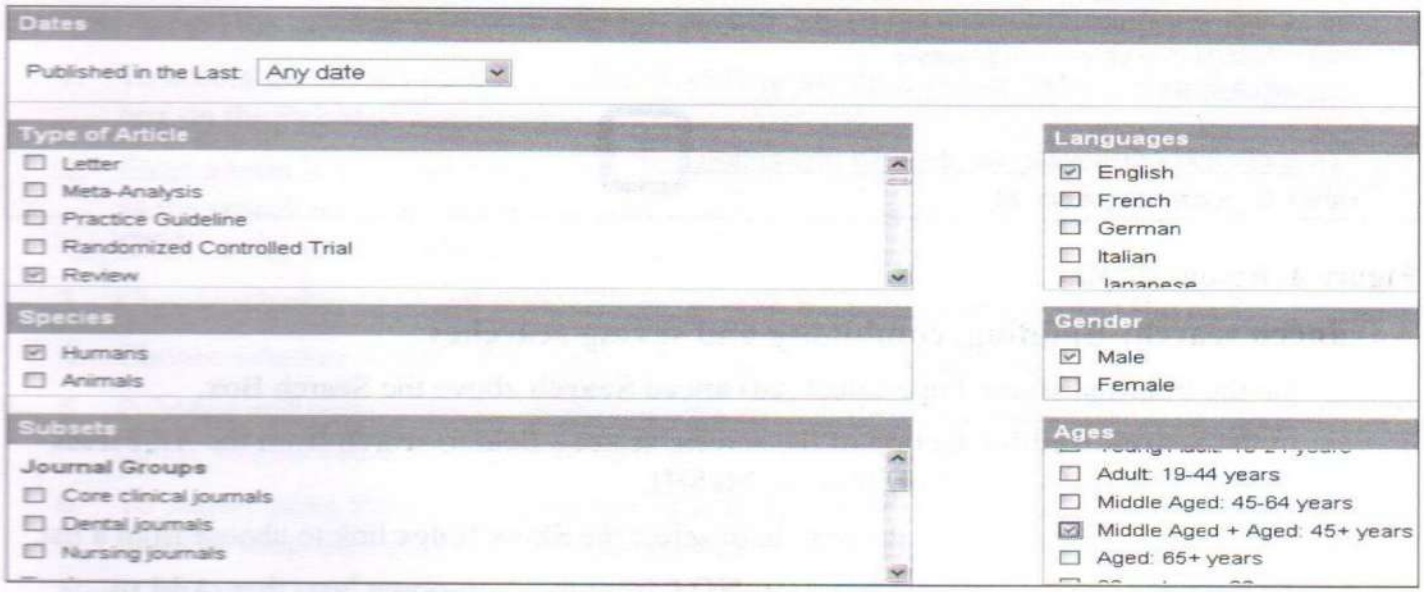


Figure 3: Applying Search Limits

Displaying search results:

1. PubMed search results are automatically displayed in **Summary** format (title, author, journal information and a link to related citations), 20 items per page and sorted by most recently added (Fig.4).
2. To change Display settings click on the **Display Settings** link above the Results list. Choose settings, then **Apply**.
3. Click on a title to display the Abstract.

Note: When the Abstract is displayed, links to full-text will appear on the top right of the screen. Click **UBC eLink** to find UBC holdings of the article. Find similar articles in the **Related Citations** box on the right of the screen.

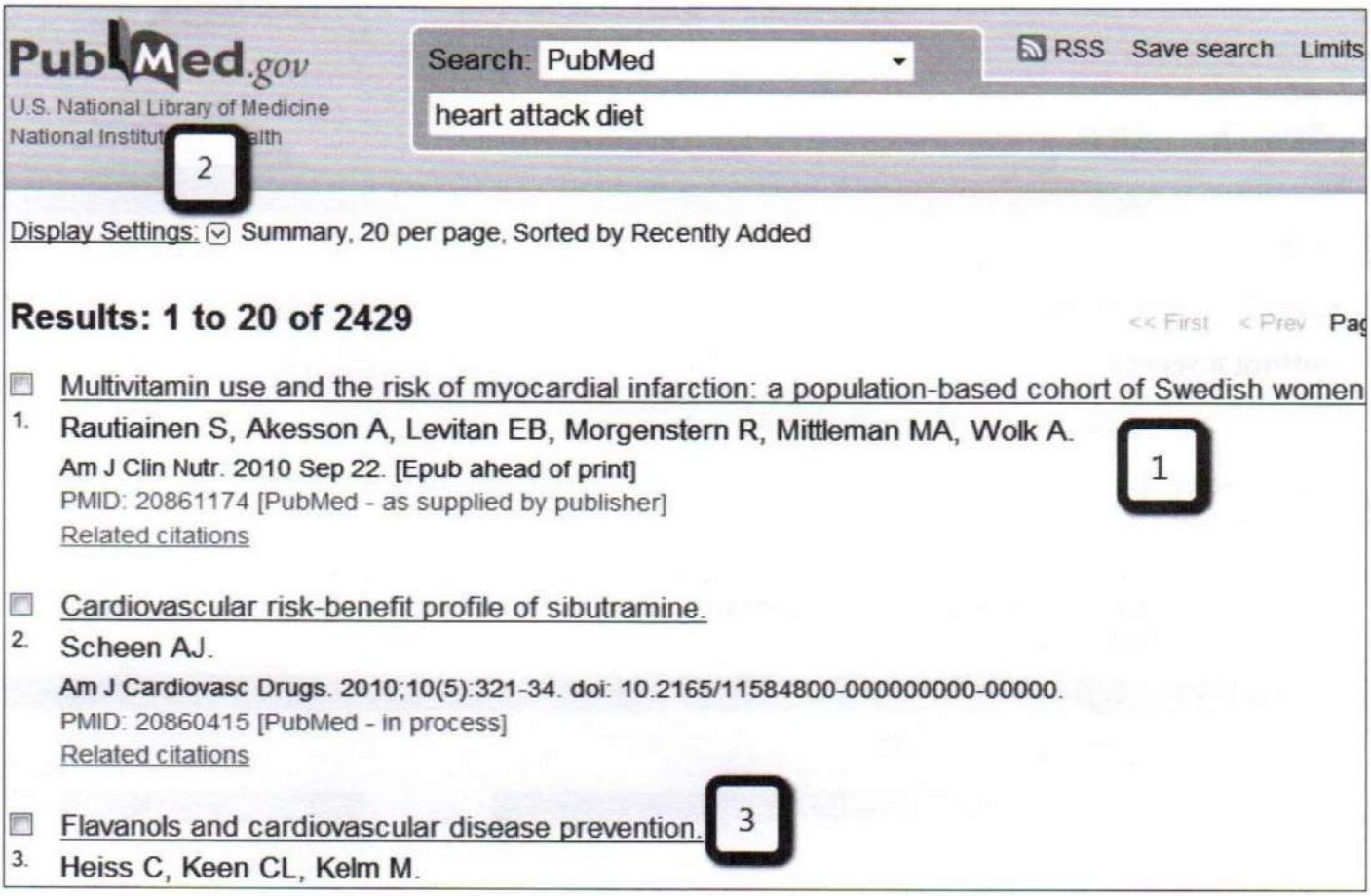


Figure 4: Results display

Advanced search: Building, combining and saving searches

1. On the PubMed Home Page select **Advanced Search** above the Search Box.
2. In the **Search Builder** section of the screen, select a field to search from the **All Fields** drop-down box (e.g. Author, Journal, MeSH).
3. Enter a search term and run the search, or select the **Show Index** link to choose from a list.
4. To build the search, Select **AND**, **OR**, **NOT** from the drop-down box, then **Add to Search Box.**

5. Select **Preview** to see the number of results returned in the **Search History** part of the screen, or Click **Search** to view the results.
6. To combine searches use **Search History**. Click on the search number, choose whether to combine terms with AND, OR, NOT, for example **#4 AND #5,** then **Search**.

Note: To Save a search, click on the search number, choose **Save in My NCBI**. You will be prompted to give your search a name and to choose whether to receive updates of the search.

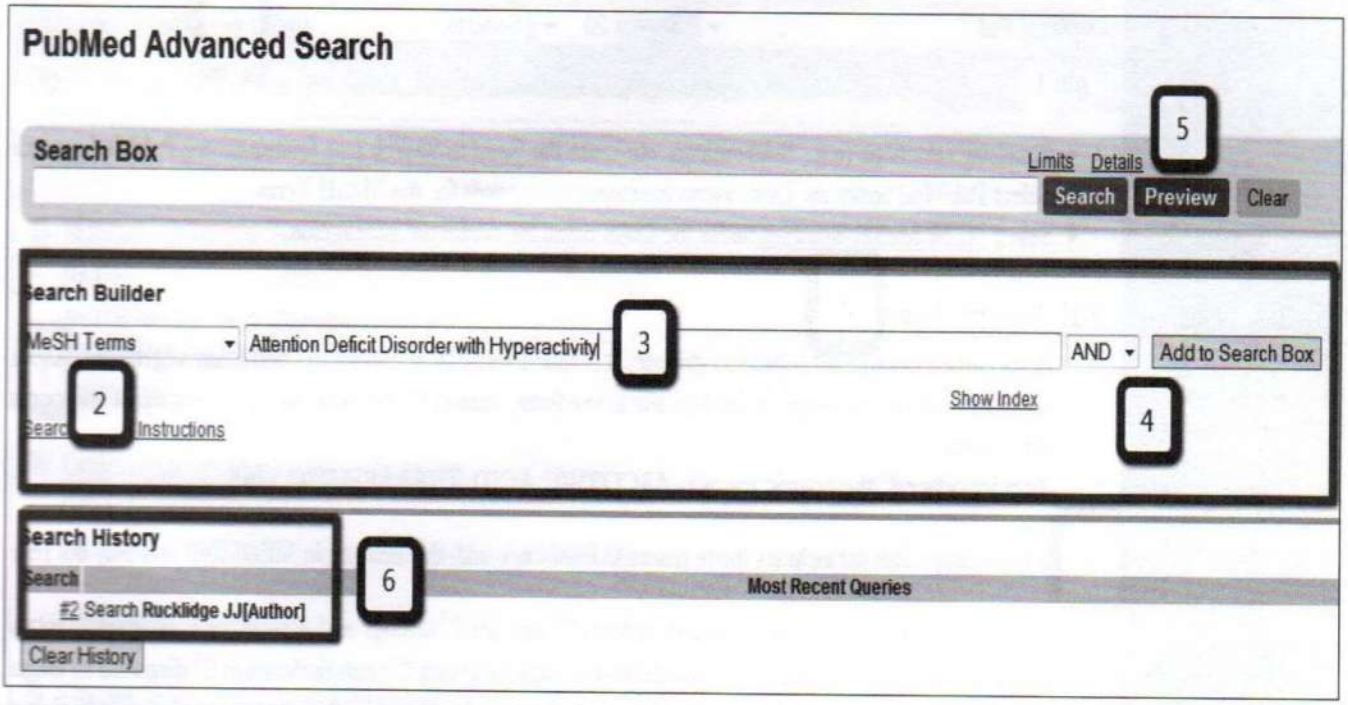


Figure 5: Buliding, combining, saving searches

Advanced search: Using MeSH terms

Records in PubMed are tagged with Medical Subject Headings (MeSH). Using the MeSH database to find the best MeSH terms will increase the relevance of your search results.

1. To access the MeSH database, select **MeSH** in the drop-down menu above the Search box on the PubMed home page.
2. Enter a term in the search box, then **Search.**As shown in Fig. 6, **Vitamin C** was entered as the search term and **Ascorbic acid** was displayed as the corresponding MeSH term. Click on the term to display the full record.
3. Choose whether to attach subheadings, to search a particular aspect of the topic.
4. Choose whether to restrict the search to major Subject Headings.
5. PubMed will automatically explode a term to include all narrower terms, so check the box if you do not want this to occur.
6. To search using the MeSH term, first check the box beside **Ascorbic Acid.** From the **Send to** drop-down box choose **Search box with AND,** then **Search PubMed.**

Note: The MeSH database also provides a definition of the term, shows where the term is in the MeSH tree structure, and gives examples of keywords to use to expand the search.

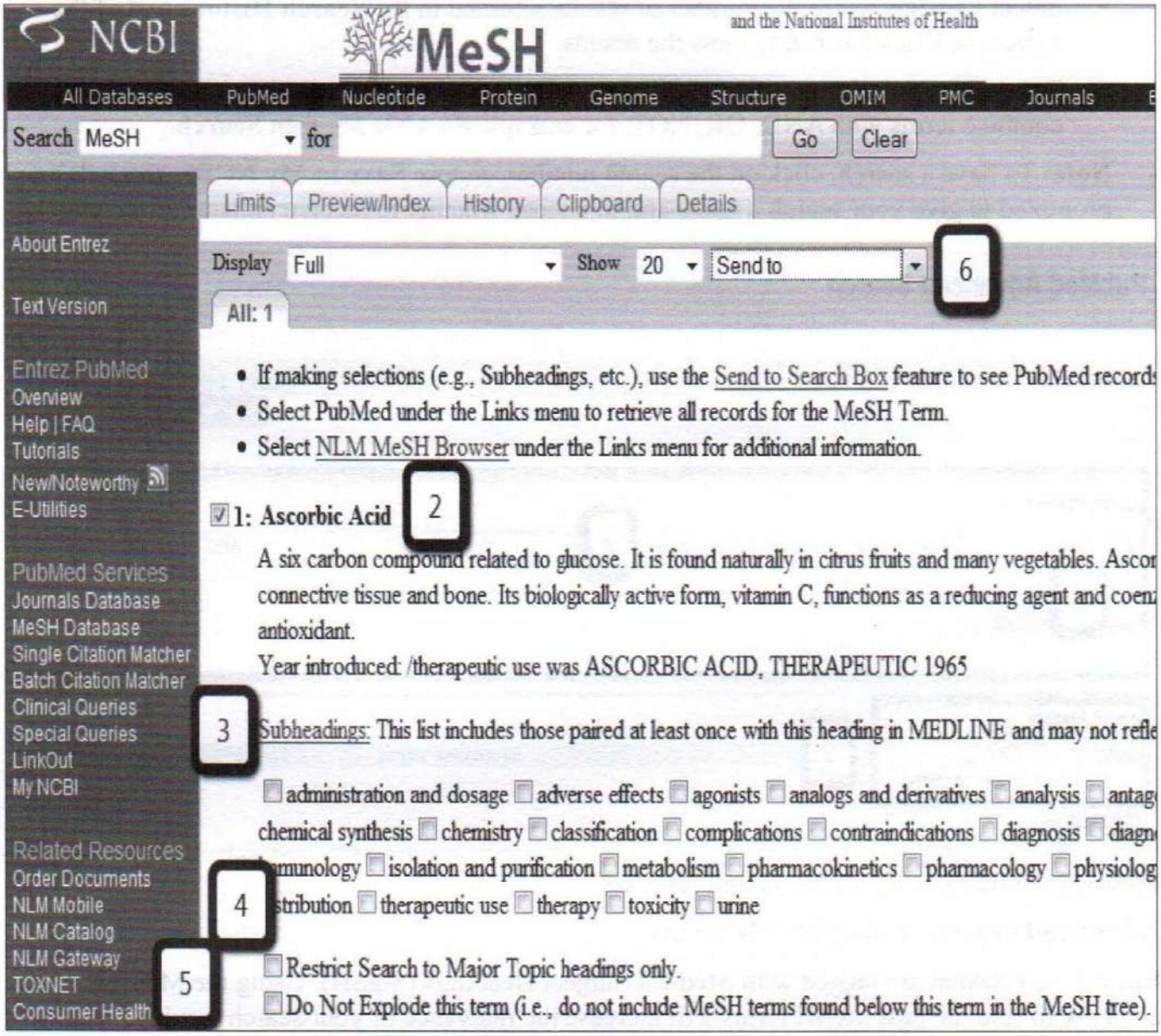


Figure 6: Searching using MeSH

Saving results:

A. Temporary storage: Save to clip boards

1. On the PubMed results page mark the PubMed search results that you want to save to the Clipboard.
2. From the **Send to** drop-down menu at the top right of the PubMed Results page, select **Clipboard** as the destination, then **Add to Clipboard**.
3. A green checkmark box at the top of the screen shows that items have been added to the Clipboard.
4. To see details of items that have been saved to the Clipboard, click on the link by the Clipboard icon at the top right of the screen.

Note: Items saved to the Clipboard are lost after 8 hr. of inactivity.

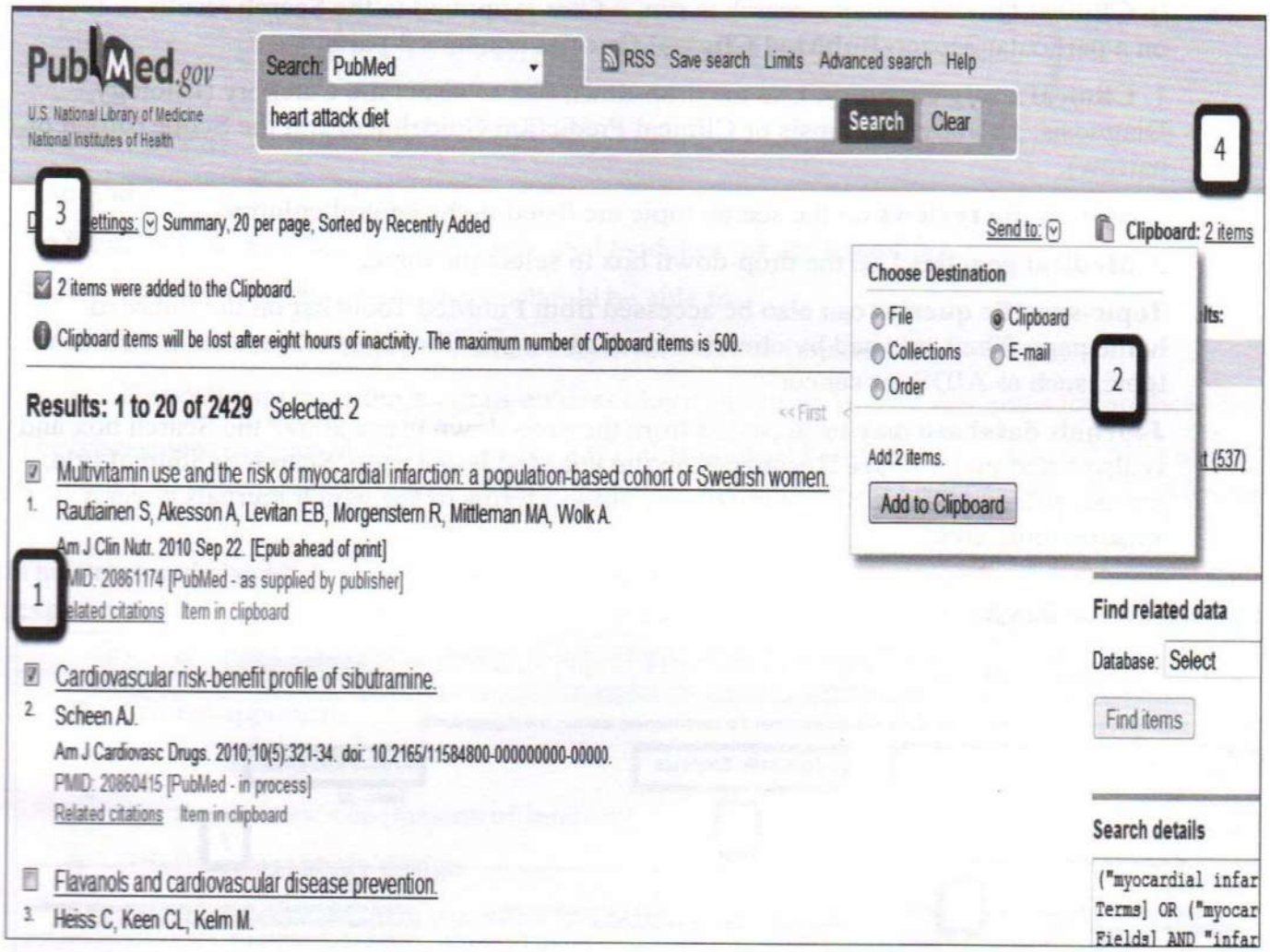


Figure 7: Saving to clipboard

B. Permanent storage:

1. To save Clipboard items permanently, use the **Send to** drop-down menu and select **E-mail, File** (save to your computer) or **Collections** (to add items to an NCBI collection). OR
2. Select **Save Search** above the Search box on the PubMed Home Page to save to your My NCBI account.

PubMed tools:

Other useful features of PubMed can be accessed from the **PubMed Tools** list on the PubMed home page

- Use Single Citation Matcher to locate PubMed citations even though you have limited information on title, author etc.
- Batch Citation Matcher for multiple citations
- Clinical queries and Topic-specific queries help clinicians and researchers improve the specificity of their searches.

- In **Clinical Queries** when a search is run, a filter is applied to the Search results to focus on a particular aspect. **PubMed Clinical Queries** contains 3 parts.

  1. **Clinical study category.** Use the drop-down box to select the Category (Etiology, Diagnosis, Therapy, Prognosis or Clinical Prediction Guidelines) and the Scope (broad or narrow).

  2. **Systematic reviews** on the search topic are listed in the central column.

  3. **Medical genetics** Use the drop-down box to select the topic.

- **Topic-specific queries** can also be accessed from PubMed Tools list on the PubMed home page. They are used by clinicians to locate a pre-filtered set of results on a clinical topic, such as AIDS, or cancer.

- **Journals database** may be accessed from the drop-down menu above the Search box and is also listed under **More Resources** on the PubMed home page. Search by journal title, journal abbreviation, ISSN, or browse by subject terms to see which journals cover a specific topic area.

PubMed Clinical Queries

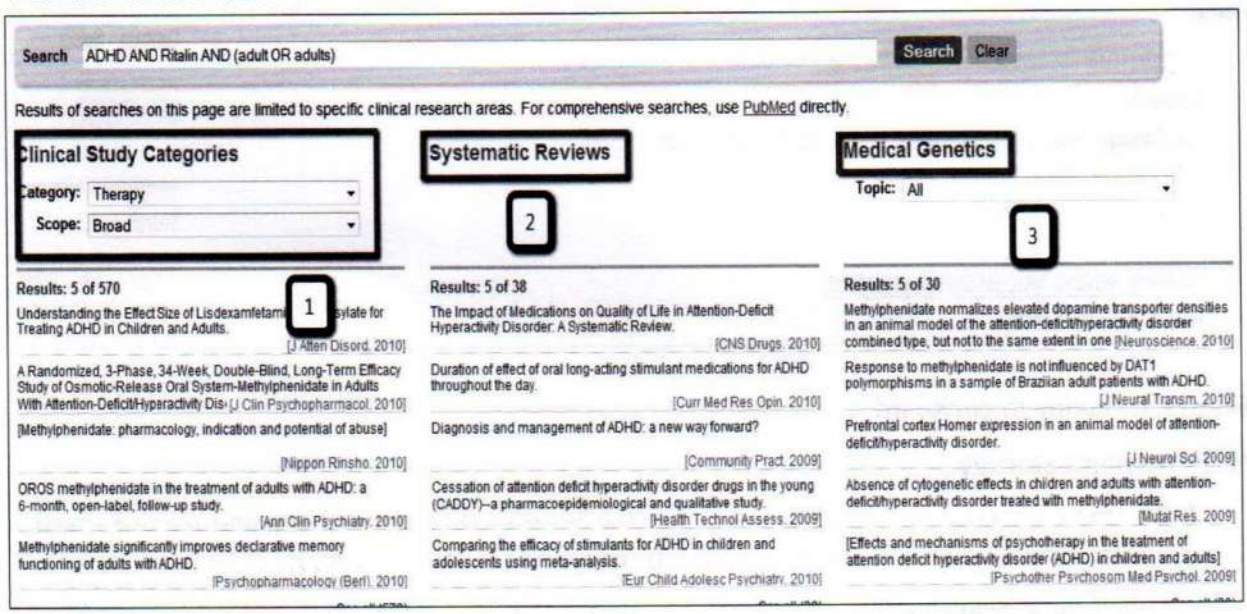


Figure 9: PubMed Clinical Queries

Retrieving search results:

After the search is performed, the next step is to review abstracts of relevant articles and decide whether full text retrieval is necessary. HINARY provides a good source of full text articles.

6. Critical Appraisal of Evidences

OBJECTIVES:

General:

To know how to read and assess the searched evidence for applicability

Specific: After the lecture participants should be able to-

- Read a scientific paper systematically with focus to important information.
- Critically appraise the sections epidemiologically to make own decisions for applicability

The assessment of methodological quality (critical appraisal) has been covered in detail in many textbooks on evidence based medicineand in Sackett and colleagues' Users' Guides to the Medical Literature in *JAMA*.

The structured checklists produced by these authors will be largely self explanatory for an experienced journal reader but for someone new the following preliminary steps should be tried:

- General scheme to read a paper: Structure and contents
- Critical appraisal:
  - Scan **abstract**
  - Are the authors' conclusions of interest?
  - Briefly assess study design
  - Briefly assess statistical precision of results
  - Formulate a brief summary
    - Critically appraise **methods & results** sections for validity
    - Critically appraise **results** section (especially the tables and figures) for relevance
    - Draw your own conclusions about clinical applicability

General scheme to read a paper:

Citation:

The citation includes

- the title of the study,
- all of the authors (last name, first name or initials)
- the information about the journal

  –full name, volume, issue and year of publication.

Introduction and background information:

- The purpose of the study: stated either as a statement or question.
- The literature review: provides a brief synthesis of previous research and background information that lead to the performance of the study.
- Any hypotheses (i.e. expectations) of the study's outcomes: "It is hypothesized that…", "We expect that…", or "It is anticipated that…"

Methodology:

- The study design
- The sampling technique:
  - The number of participants/subjects (the "N")
  - Evidence of random sampling and/or random selection
  - The characteristics of the participants (subjects)
  - The length of time the subjects were part of the study, any drop out
- The intervention or treatments
- The measurements or outcomes
- The study is approved by an appropriate Research Ethics Committee (or Board)

Results & analyses:

- The outcomes (variables) reported are important and of interest to the researchers.
- Statistical information is provided for all results for validity.
- The clinical importance of the findings is reported

Conclusions & discussion:

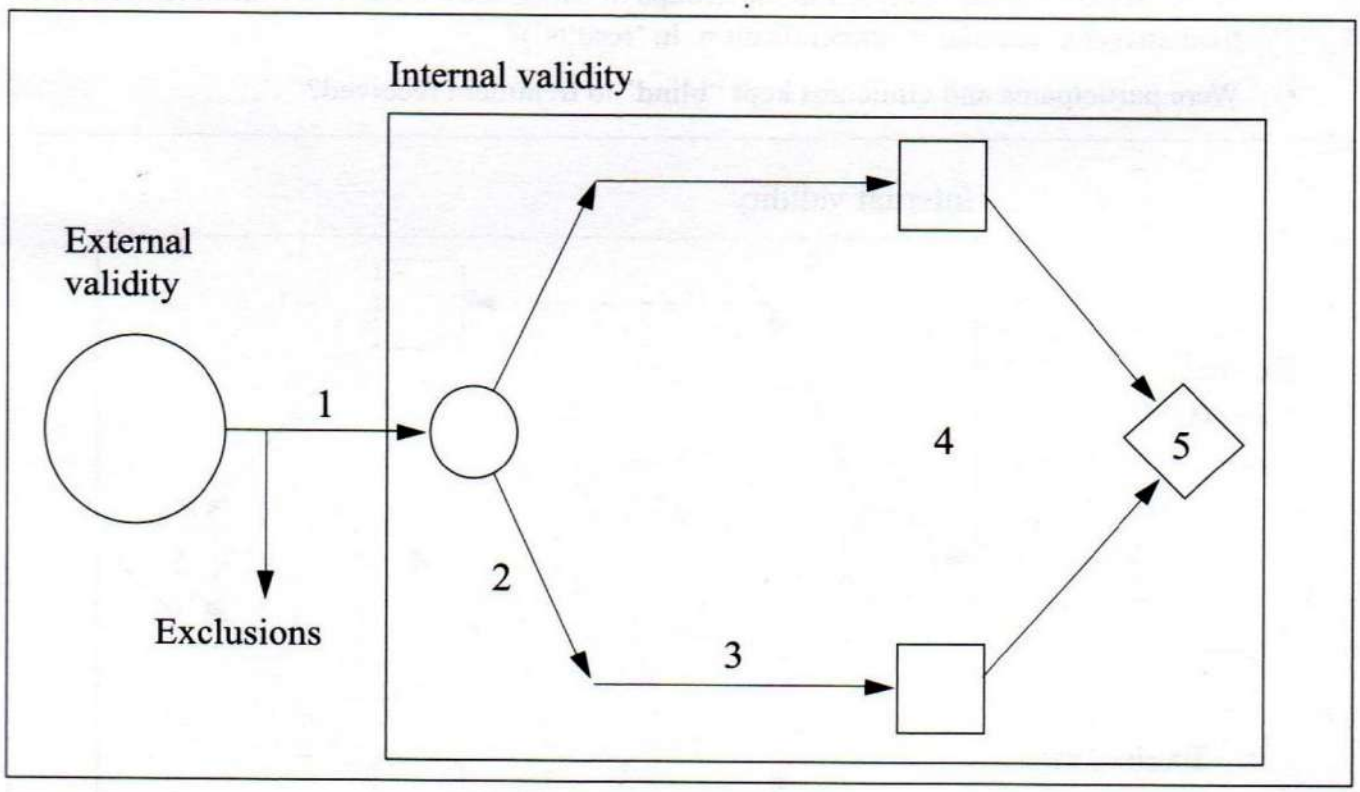
- The conclusions made by the authors are directly related to the findings from the study.
- Author's view regarding the relevance, importance and strength as well as limitations of the study is discussed.
- The funding source for the study is identified.•

Critical Appraisal

p **Scanning Abstracts: Points to look at**

- Type of study
- Size
- Study Population
- Intervention
- Comparator
- Duration
- Outcome(s)
- Main findings (with relevant statistics)
- Conclusion(s)

p **Critically appraise methods & results sections for validity**



Flow Diagram for a RCT / cohort study

1 Selection and sampling
2 Allocation (with or without Randomisation)
3 Follow-up
4 Outcomes
5 Analysis

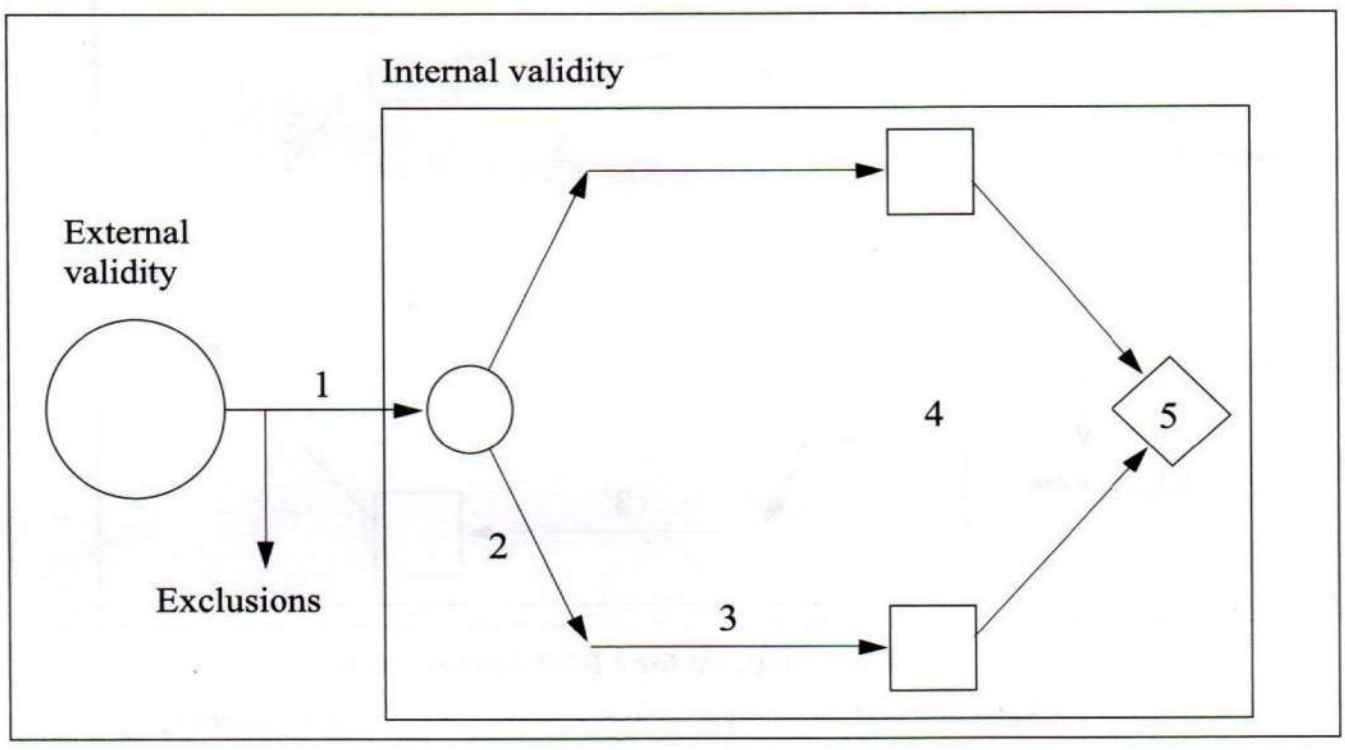
External validity appraisal:

- Where were the participants recruited from (primary care / referral centre)?

- Do the inclusion and exclusion criteria make sense?
- What proportion of the screened population was recruited?
- To whom do the results of this trial apply?
- Can the results be reasonably applied to a definable group of patients in a particular clinical setting in routine practice?
- Can the results be generalized beyond the trial setting?

Internal validity appraisal:

- Was assignment of patients to treatments randomised? (look in 'Methods')
- Were groups similar at start of trial? (Table of baseline characteristics in 'Results')
- Were groups treated similarly, apart from the experimental treatment? (Methods/Results)
- Were all participants accounted for in the conclusions? (Loss to follow up- 5% is OK; >20% - validity doubtful AND must not exceed outcome event rate. In 'results')
- Were all participants analysed in the groups to which they were randomised (Intention to treat analysis- maintains randomisation. In 'results')?
- Were participants and clinicians kept "blind" to treatment received?



• **Fig: Bias in RCTs:** 2 Allocation Bias (Failure of Randomisation)
3 Follow-up – Performance Bias and Attrition Bias
4 Outcomes – Detection Bias (Failure of Blinding)

Internal Validity - Sources of Bias in a RCT

- **Allocation (Selection) Bias** – Failure of randomisation
  - Systematic differences in comparison groups
- **Performance Bias**
  - Systematic differences in interventions received by the two groups due to contamination/compliance/co-intervention
- **Attrition Bias**
  - Systematic differences in withdrawals from the trial
  - eg. loss to follow up rate
- **Detection (Measurement) Bias** – Failure of blinding.
  - Systematic differences in outcome assessment
  - Best: Double blind

Fundamentals of Epidemiology and Biostatistics to appraise evidence:

Epidemiology is the basic science that provides a foundation for understanding the distribution of disease in the population and statistics provide essential techniques for these understandings.

The following discussion provides only an introduction to the fundamental principles that guide quantitative approaches to the study of disease etiology, treatment, and prognosis.

Descriptive studies that assess patterns of exposures or disease within a population often make use of *rates* and *risks*.

Rates are technically defined as a change per unit time, and for epidemiologic studies these are usually expressed as disease events per year, for a given population. For example, the *incidence rate, etc.*

Risk is defined as the probability of an event occurring over a specific interval of time. Risks are particularly useful statistics in clinical medicine, especially when communicating information about the probability that a patient will develop a particular outcome in a given interval.

Eg. If a woman is informed that her calculated risk for developing breast cancer in her life time is 16%, this is far more meaningful to her than describing the age-specific incidence rates for women with her particular risk profile.

However, it should be clear that *rates* and *risks* are different ways of communicating the same information.

Analytic studies that are intended to test specific hypotheses require *measures of association* to quantify relationships between the groups that are being compared.

The choice of an appropriate measure of association depends on the study design, but in simple terms, measures of association usually rely on comparisons of rates or risks.

Most measures of association are expressed as ratios and the literature is dominated by examples of rate ratios, risk ratios or odds ratio, which are sometimes referred to as a relative risk. 'Relative risk' is often used as a general term describing strength of an association between an exposure and disease.

Occurrence of disease= No. of outcomes ÷ No. of participants

Relative difference or Relative Risk = EGO ÷ CGO (EGO- exposure group occurance;

CGO- control group occurance)

Absolute Difference or Risk Difference(RD) = EGO - CGO

Number Needed To Treat (NNT) = 1 ÷ RD

Inferential statistics provide methods for drawing conclusions about a population based on a limited number of observations from a sample of the population, and serve as the foundation for clinical trials and observational epidemiology.

Thus inferential statistics also provide the tools for understanding whether an observed association is likely to be explained by chance, also known as sampling variation.

Followings are some commonly used statistical measures:

There are several ways to describe the range of plausible values around a statistical measure and gain a sense of their statistical stability.

Range is calculated as the highest value minus the lowest value and one can get a sense about the variation around a measure simply by examining it.

Variance describes the sampling variation and is accomplished by examining the deviation of each observation from the mean.

$V(x) = \sum_{i=1-j} (x - \bar{x})^2 / (n-1)$, where x is the value of an observation, is the mean, and n is the sample size

Standard deviation is square root of the variance in order to get the units back to their original form. $SD = \sqrt{V(x)}$

As a general rule of thumb for variables that are normally distributed, it is useful to know that:

Mean +/- 1 SD includes approximately 2/3 of all observations, and

Mean +/- 2 SD includes ~95% of all observations, and

Mean +/- 3SD includes essentially all observations.

Statistical testing: p-values and confidence intervals

Statistical testing also takes advantage of measures of variance, with critical ratio tests using variance informing estimates of probability.

These probability estimates are usually expressed in the medical literature as a ***p-value***, where p represents the probability that the observed result arose on the basis of sampling variation. A p-value of <0.05, states that the result had a probability of <5% that it arose by chance.

Estimates of variance can also be used to calculate confidence intervals for measures of association. 95% confidence intervals mean that there is only a 5% chance that the true value of the measure of association is not contained within the 95% confidence intervals.

- **Critically appraise results section (especially the tables and figures) for relevance**

- Were all the outcomes studied important?
- Were all the important outcomes studied?
- Was sub-group analysis pre-planned?
- Could the treatment effect have arisen by chance?
- How large was the treatment effect?

p **Draw your own conclusion- Appraising applicability:**

- Is my patient similar to the study population?
- Is the treatment feasible in my clinical setting?
- Will potential benefits of treatment outweigh potential harms of treatment for my patient?

The End