

Evidence-Based Medicine: Levels of Evidence and Guidelines



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Speaker: Dr. Jike Lu

Department: Orthopedic Surgery, BJU



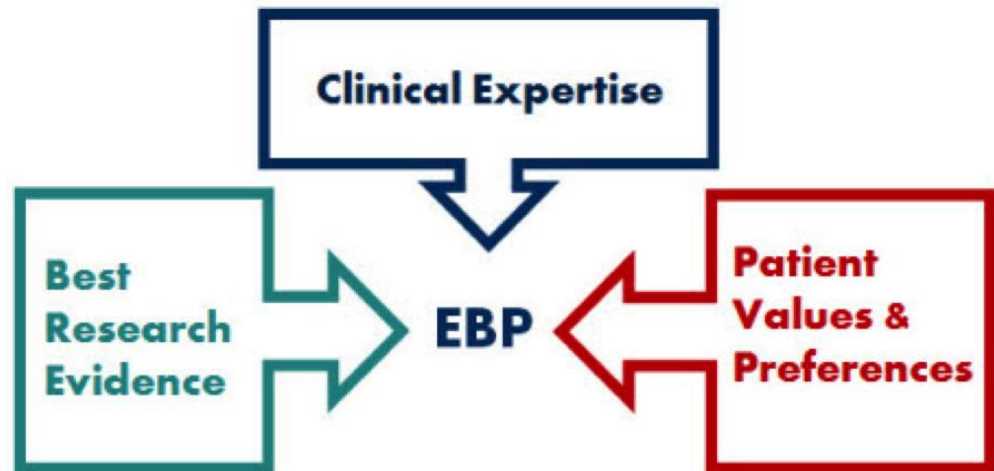
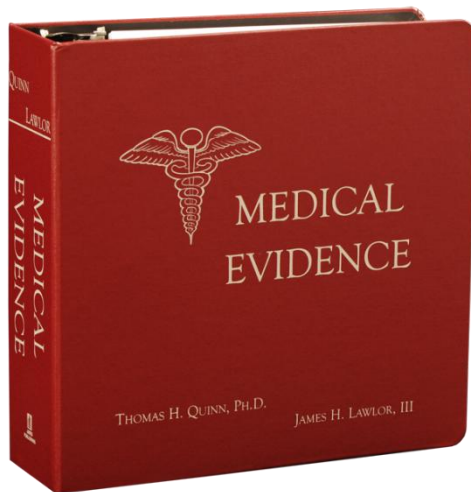
UFH is China's only healthcare network
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Evidence-based medicine

Defined as a conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.



Evidence-based medicine



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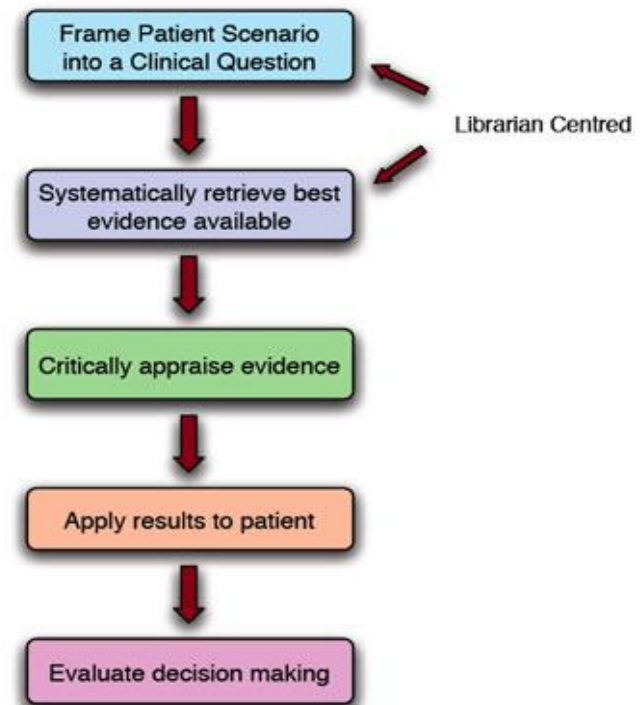
- Refers to an explicit process of using and evaluating information to make medical decisions.
- Requires its users to embrace uncertainty in medical decision making because information that is simultaneously true and complete cannot be attained.
- Recognizing medicine's inherent uncertainty, proponents of evidence-based medicine advocate.

Evidence-based medicine

Evidence Based Medicine (EBM) and describes 5 step process of making medical decisions based on the available, and often limited, evidence

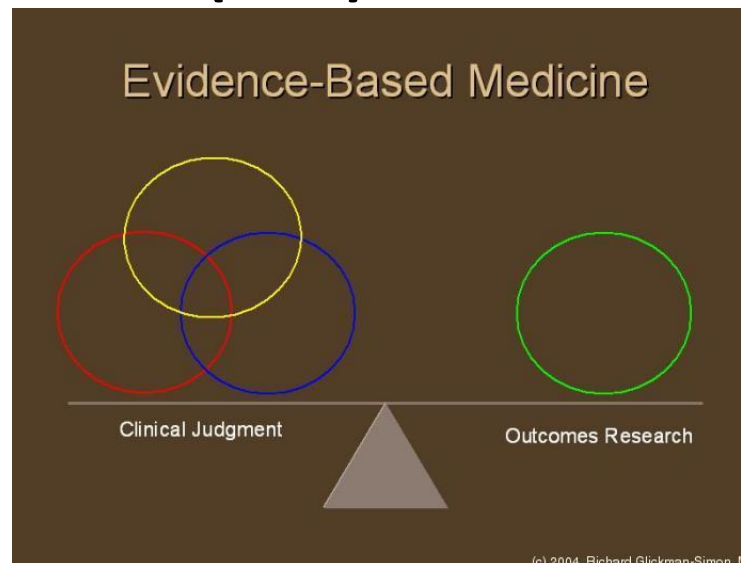
- 1) Formulate answerable questions.
- 2) Gather the evidence.
- 3) Appraise the evidence.
- 4) Implement the evidence.
- 5) Evaluate the process.

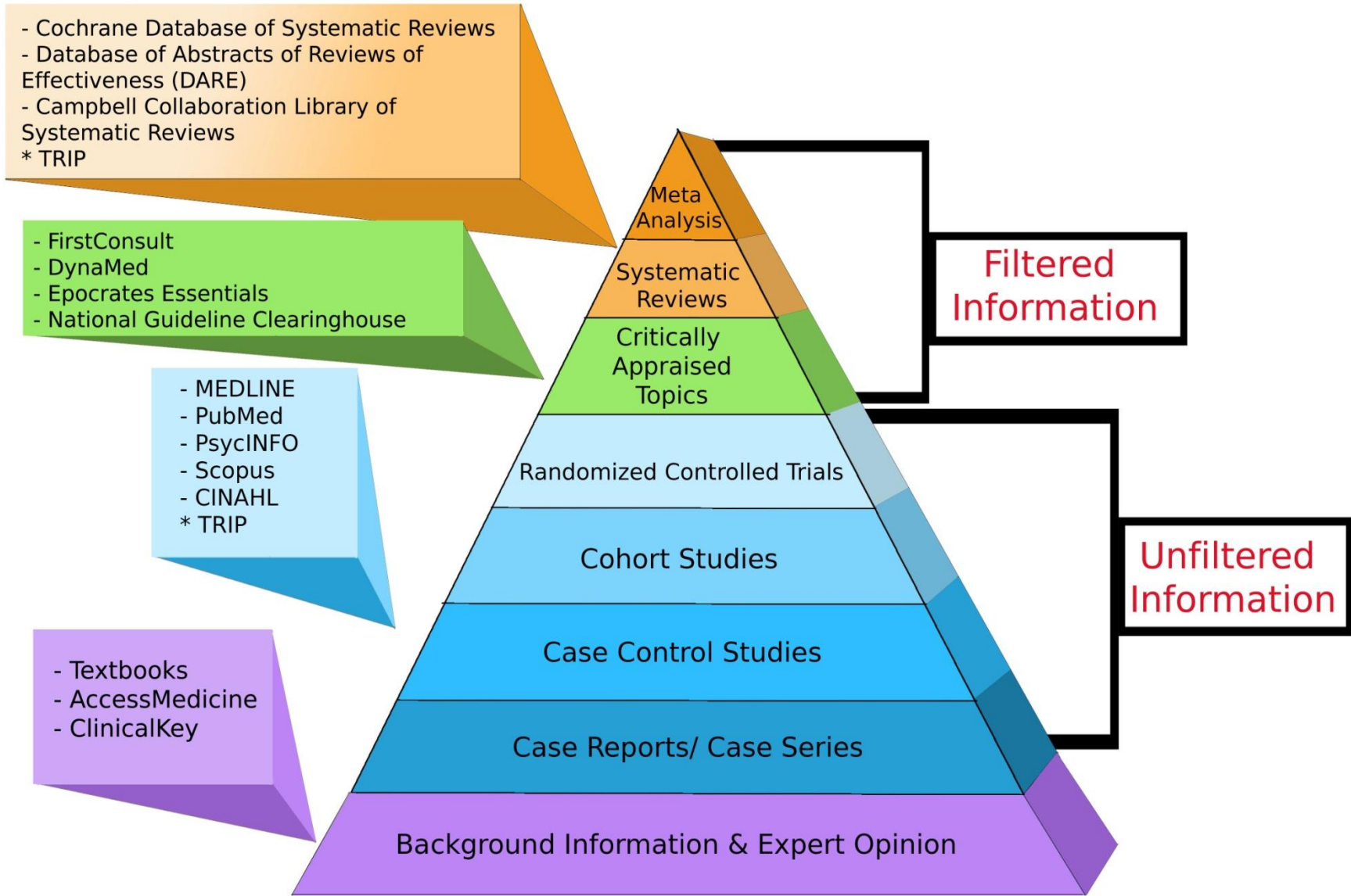
The Five Steps of EBM



Evidence-based medicine (EBM)

- **Meta-Analysis (MA)**
- **Systematic Review (SRV)**
- **Randomized Controlled Trial (RCT)**
- **Case Report (CR)**
- **Practice Guideline (PGL)**





*TRIP searches filtered AND unfiltered information simultaneously.

PROSPECTIVE STUDIES

- Designed to assess outcomes occurring forward in time
- Exposure has occurred or risk factor has developed; patients are monitored forward in time to determine the occurrence of an outcome of interest.

RETROSPECTIVE STUDIES

- Designed to assess outcomes that have already occurred or data that has been collected in the past

LONGITUDINAL STUDIES

- Designed to assess outcomes at multiple points (i.e., repeated measures) over time

CASE REPORTS

- Descriptions of unique injuries, disease occurrences, or outcomes in a single patient
- No attempts at advanced data analysis are made.
- Cause-effect relationships are not discussed, and generalizations are not made.

CASE SERIES

- Outcomes are measured in patients with a particular disease or injury.
- These studies are typically retrospective and involve a thorough review of medical records.

CASE CONTROL STUDIES

- Outcomes measured in patients with a particular disease or injury are compared with outcomes in a control group
- Odds ratios (not relative risks) are appropriate measures of association from data collected in these study designs

COHORT STUDY

- Groups of patients with a similar characteristic or similar exposure or risk factors are studied forward in time (prospective) or from existing data (retrospective).
- Cohort studies are appropriate for estimating incidence of disease or injury and the relative risks.

Different Levels of Evidence

Level 1

- **Randomized controlled trial (RCT)**
- a study in which patients are randomly assigned to the treatment or control group and are followed prospectively
- **Meta-analysis of randomized trials with homogeneous results**

Level 2

- **Prospective comparative study (therapeutic)**
- a study in which patient groups are separated non-randomly by exposure or treatment, with exposure occurring after the initiation of the study
- **Meta-analysis of Level 2 studies or Level 1 studies with inconsistent results**

Level 3

- **Retrospective cohort study**
- a study in which patient groups are separated non-randomly by exposure or treatment, with exposure occurring before the initiation of the study
- **Case-control study**
- a study in which patient groups are separated by the current presence or absence of disease and examined for the prior exposure of interest
- **Meta-analysis of Level 3 studies**

Level 4

- **Case series**
- a report of multiple patients with the same treatment, but no control group or comparison group

Level 5

- **Case report** (a report of a single case)
- **Expert opinion**
- **Personal observation**

The Principles of Evidence-based Medicine Meta-analysis

- Gaining acceptance
- Requires a careful, systematic review of the literature to appropriately value the merit of studies.
- Systematic review assists the orthopaedic surgeon in interpreting study results and in understanding the relative validity of these results in the hierarchy of evidence.
- Sufficiently valid evidence-based information ultimately will help in making decisions regarding patient care.



Are systematically developed statements that aim to help physicians and patients reach the best health care decisions. Appropriately developed guidelines incorporate validity, reliability, reproducibility, clinical applicability and flexibility, clarity, development through a multidisciplinary process, scheduled reviews, and documentation. Thus, evidence-based clinical practice guidelines represent statements developed to improve the quality of care, patient access, treatment outcomes, appropriateness of care, efficiency and effectiveness and achieve cost containment by improving the cost benefit ratio.

AAOS Evidence-Based Practice Committee Recommendations in Clinical Practice Guidelines



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- **Strong**-Level I evidence from more than 1 study with consistent findings for recommending for/against the intervention/diagnostic
- **Moderate**-Level II or III evidence from more than 1 study with consistent findings for recommending for/against the intervention/diagnostic Level I evidence from a single study for recommending for/against the intervention/diagnostic
- **Weak**-Level IV or V evidence from more than 1 study with consistent findings for recommending for/against the intervention/diagnostic Level II or III evidence from a single study for recommending for/against the intervention/ diagnostic
- **Inconclusive**-Insufficient/conflicting evidence not allowing a recommendation for/against intervention
- **Opinion**-There is no supporting evidence. The work group is making a recommendation based on their clinical opinion.

Although clinical practice guidelines have generally been welcomed by the evidence-based medicine community, this reception has not been universal. Some argue, for example, that clinical practice guidelines erode physician autonomy and run the risk of transforming clinical practice into “cookbook medicine.” Others complain that existing guidelines are too comprehensive or too narrowly focused, and quickly become outdated. Still others voice fears that guidelines will be used to critique the treatment decisions of physicians in legal and pay-for-performance settings.

- Shaneyfelt TM, Centor RM: Reassessment of clinical practice guidelines: Go gently into that good night. *JAMA* 2009;301(8):868-869.
- The authors describe the shortcomings of clinical practice guidelines as they currently exist and argue that they should undergo major changes or be abandoned.

Levels of Evidence for Primary Research Question

Types of Studies

	Therapeutic Studies— Investigating the Results of Treatment	Prognostic Studies— Investigating the Outcome of Disease	Diagnostic Studies— Investigating a Diagnostic Test	Economic and Decision Analyses—Developing an Economic or Decision Model
Level I	<ol style="list-style-type: none"> 1. Randomized controlled trial <ol style="list-style-type: none"> a. Significant difference b. No significant difference but narrow confidence intervals 2. Systematic review² of Level-I randomized controlled trials (studies were homogeneous) 	<ol style="list-style-type: none"> 1. Prospective study¹ 2. Systematic review² of Level-I studies 	<ol style="list-style-type: none"> 1. Testing of previously developed diagnostic criteria in series of consecutive patients (with universally applied reference “gold” standard) 2. Systematic review² of Level-I studies 	<ol style="list-style-type: none"> 1. Clinically sensible costs and alternatives; values obtained from many studies; multiway sensitivity analyses 2. Systematic review² of Level-I studies
Level II	<ol style="list-style-type: none"> 1. Prospective cohort study³ 2. Poor-quality randomized controlled trial (e.g., <80% follow-up) 3. Systematic review² <ol style="list-style-type: none"> a. Level-II studies b. nonhomogeneous Level-I studies 	<ol style="list-style-type: none"> 1. Retrospective study⁴ 2. Study of untreated controls from a previous randomized controlled trial 3. Systematic review² of Level-II studies 	<ol style="list-style-type: none"> 1. Development of diagnostic criteria on basis of consecutive patients (with universally applied reference “gold” standard) 2. Systematic review² of Level-II studies 	<ol style="list-style-type: none"> 1. Clinically sensible costs and alternatives; values obtained from limited studies; multiway sensitivity analyses 2. Systematic review² of Level-II studies
Level III	<ol style="list-style-type: none"> 1. Case-control study⁵ 2. Retrospective cohort study⁴ 3. Systematic review² of Level-III studies 		<ol style="list-style-type: none"> 1. Study of nonconsecutive patients (no consistently applied reference “gold” standard) 2. Systematic review² of Level-III studies 	<ol style="list-style-type: none"> 1. Limited alternatives and costs; poor estimates 2. Systematic review² of Level-III studies
Level IV	Case series (no, or historical, control group)	Case series	<ol style="list-style-type: none"> 1. Case-control study 2. Poor reference standard 	No sensitivity analyses
Level V	Expert opinion	Expert opinion	Expert opinion	Expert opinion

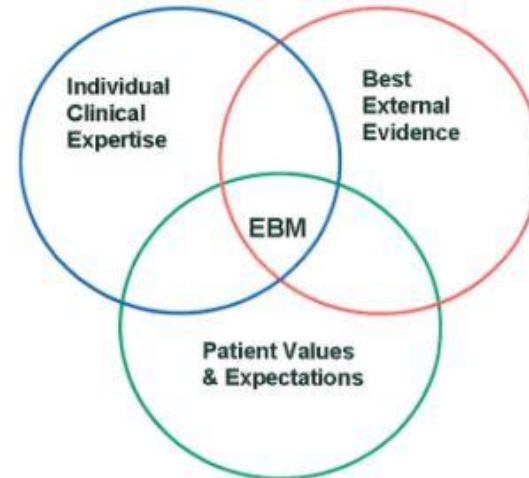
1. All patients were enrolled at the same point in their disease course (inception cohort) with ≥80% follow-up of enrolled patients.
2. A study of results from two or more previous studies.
3. Patients were compared with a control group of patients treated at the same time and institution.
4. The study was initiated after treatment was performed.
5. Patients with a particular outcome (“cases” with, for example, a failed total arthroplasty) were compared with those who did not have the outcome (“controls” with, for example, a total hip arthroplasty that did not fail).

Therapeutic Studies



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Therapeutic studies investigate the effect of treatment on the outcome of disease and represent the most common type of study in the literature.



Level I therapeutic studies are high-quality randomized controlled trials (RCTs), which are generally considered to represent the best possible evidence available.

To be considered a high-quality study, an RCT must satisfy several criteria. It must be appropriately powered, either by detecting a significant difference (in the case of a “positive” trial) or documenting sufficient power (in the case of a “negative” trial). High-quality RCTs must use an appropriate randomization technique, in which allocation of the next study participant cannot be determined by members of the research team before the patient receives his or her treatment allocation. Rates of follow-up must be high – generally above 80%. Whenever possible, patients, caregivers, and researchers should be blinded to the treatment assignment. This is by no means an exhaustive list, and there are several other characteristics that must be fulfilled for a trial to be considered of high quality. However, one can reliably assume that studies not fulfilling the above criteria will generally not be considered level I evidence.

Level II therapeutic studies include lesser-quality RCTs (as previously discussed), as well as prospective comparative studies.

Comparative studies (also known as cohort studies) involve the comparison of one group of patients treated in a particular way with another group of patients treated in another way. For example, a study comparing the outcomes of patients with inter-trochanteric hip fractures treated with a sliding hip screw or a cephalomedullary device would be considered a comparative (or cohort) study. Although the distinction between prospective and retrospective can sometimes be confusing, it has been considered prospective investigations to be those in which the study was initiated (the research question was posed) before the first patient was enrolled or treated.

Level III therapeutic studies include retrospective comparative studies, as well as case-control studies.

Case-control studies, which are retrospective, involve the comparison of one group of patients who have a particular outcome with another group of patients who do not have the outcome of interest. These “case” and “control” groups are compared to each other on the basis of characteristics plausibly associated with the outcome of interest. For example, a comparison of children who developed slipped capital femoral epiphysis to a similar group of children who did not develop this condition would be considered to be a case-control study. Such a comparison could be made on the basis of risk factors, such as obesity or sex.

Expert opinion, without the support of clinical data, is considered to be **level V evidence**. This is true for all study types, including therapeutic studies.

The terms “systematic review” and “meta-analysis” are often assumed to be interchangeable, but their definitions do differ slightly. Whereas a systematic review is a comprehensive literature search to identify studies appropriate for answering a particular clinical question, a meta-analysis is a statistical method of combining the data provided by these studies. Combining multiple studies into a single meta-analysis may address problems of small sample size and insufficient power, but it will not alter the level of evidence because meta-analyses are assigned levels of evidence based on the quality of the studies used in the meta-analysis.

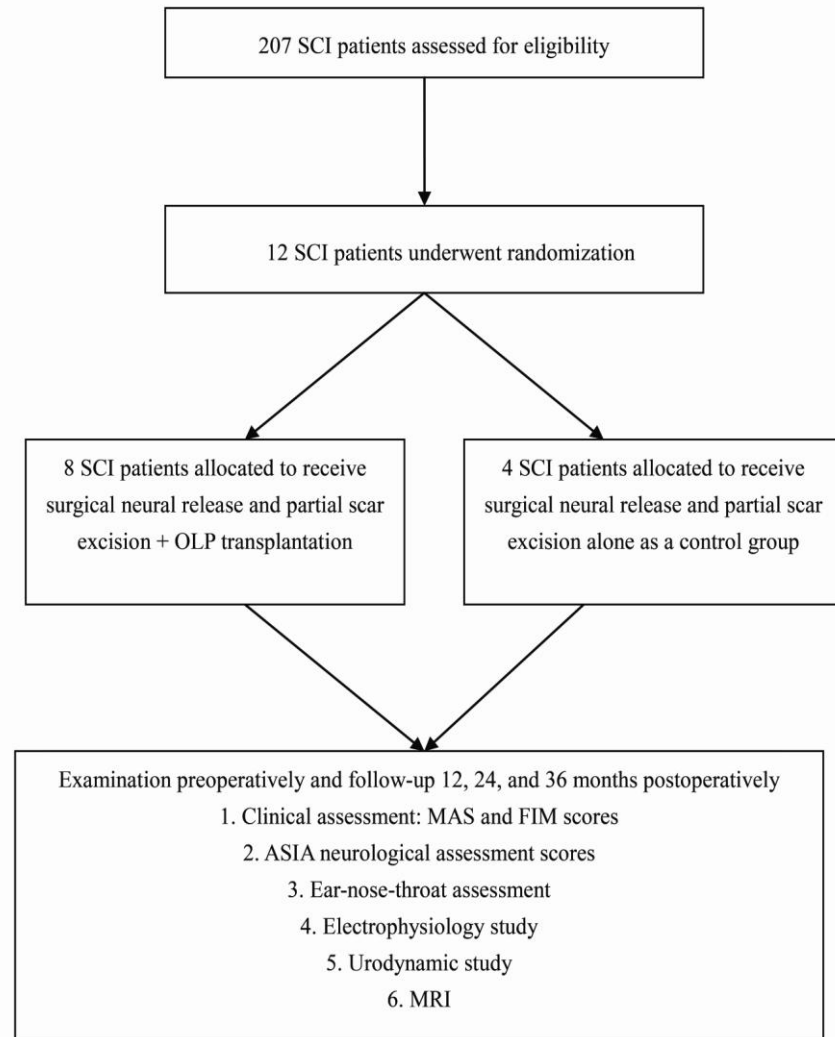
Nontherapeutic Studies



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- Prognostic studies, which represent the second most common type of study in the orthopaedic literature, investigate the effect of a patient characteristic on the outcome of disease.
- Differentiating between therapeutic and prognostic studies can be difficult because both examine the effects of factors with the potential to influence the outcome of disease.

Autologous olfactory lamina propria transplantation for chronic spinal cord injury - prospective double blinded clinical trial: 3-year follow-up outcomes



- Levels of evidence and clinical practice guidelines are tools of the evidence-based medicine movement that can help physicians provide better care for their patients. They do not represent “cookbook” instructions to be followed blindly, but rather instruments to be carefully evaluated and integrated with clinical expertise.
- There is reason to be optimistic regarding evidence-based practice. Levels of evidence are steadily increasing in the literature, and randomized trials are becoming more common. A lot carefully researched clinical practice guidelines have recently been approved, and others are under development. These advances have the potential to not only enhance evidence based medicine but also improve patient care.



Thank You

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Address: #2 Jiangtai Lu, Chaoyang District,
Beijing 100015 P.R.C.
Tel: 4008 919191 Fax: +86 (10) 5927 7200
24 Hour Emergency Hotline: (010) 5927 7120
www.ufh.com.cn



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