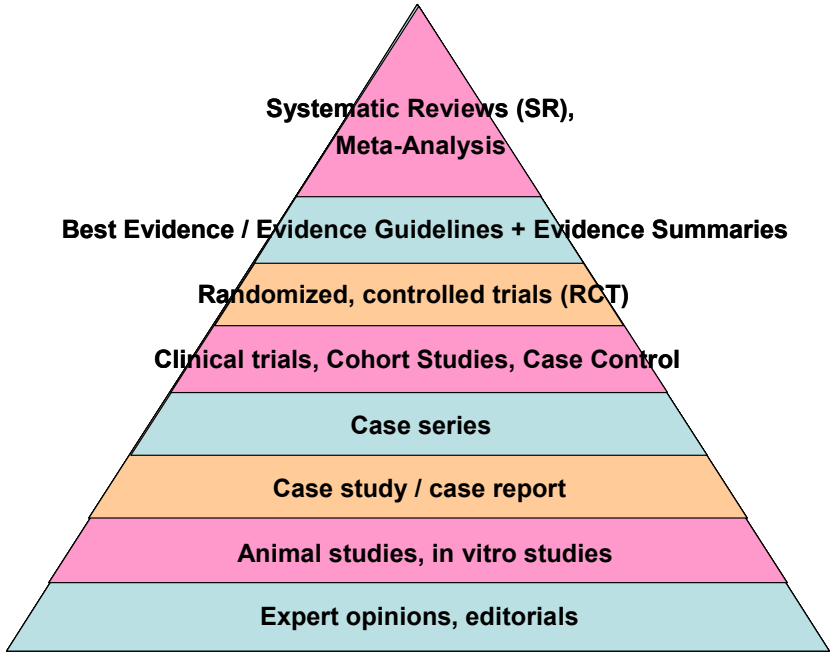
Overview of Study Designs in Clinical Research



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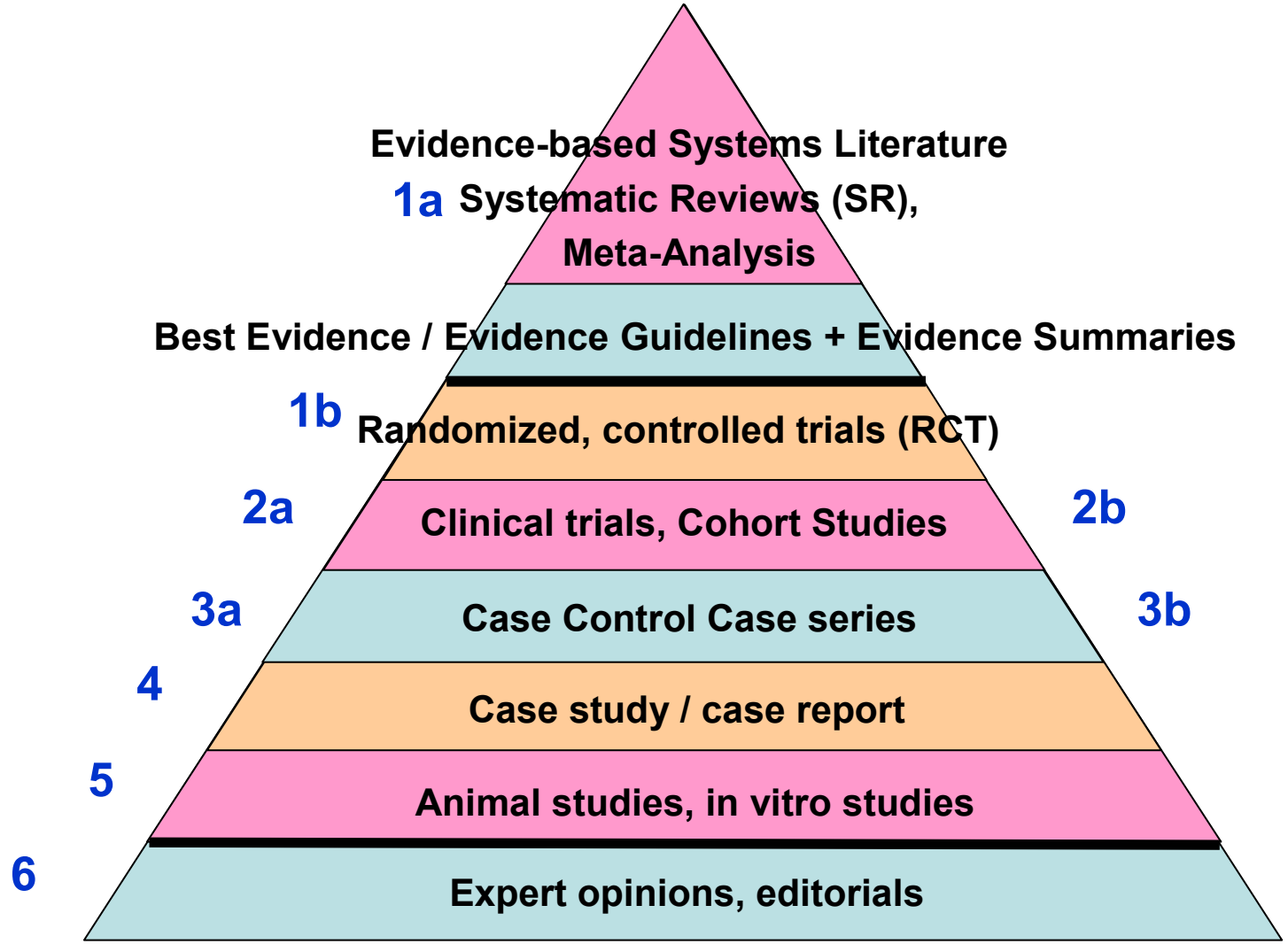
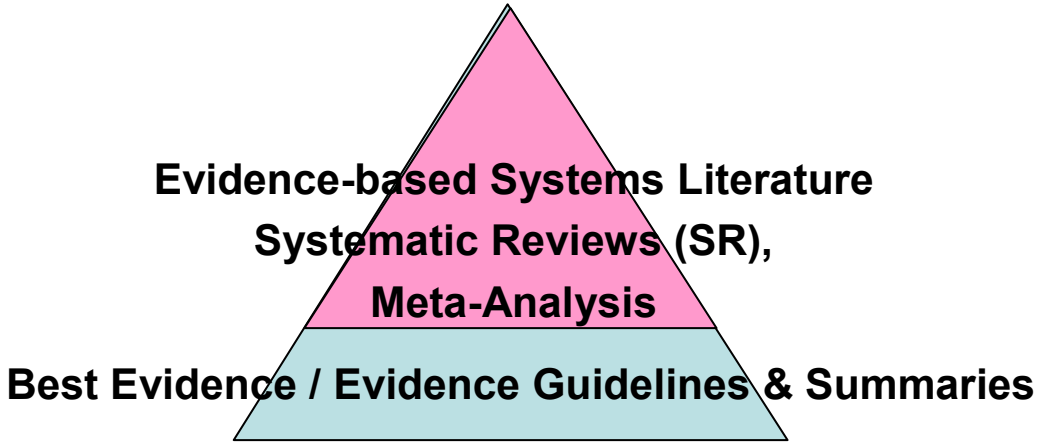
Hierarchy of Evidence: Strength of Study Design for Evidence Based Clinical Decision Making



Hierarchy of Evidence: strength of study design

- Systematic Reviews (SR), meta-analysis
- Best Evidence / Evidence Guidelines (AHRQ, CEBM, etc.), Evidence Summaries
- Randomized, controlled trials (RCT)
- Clinical trials, Cohort Studies, Case Control
- Case series
- Case study / case report
- Animal studies, in vitro studies

Hierarchy of Evidence for Clinical Decision Making



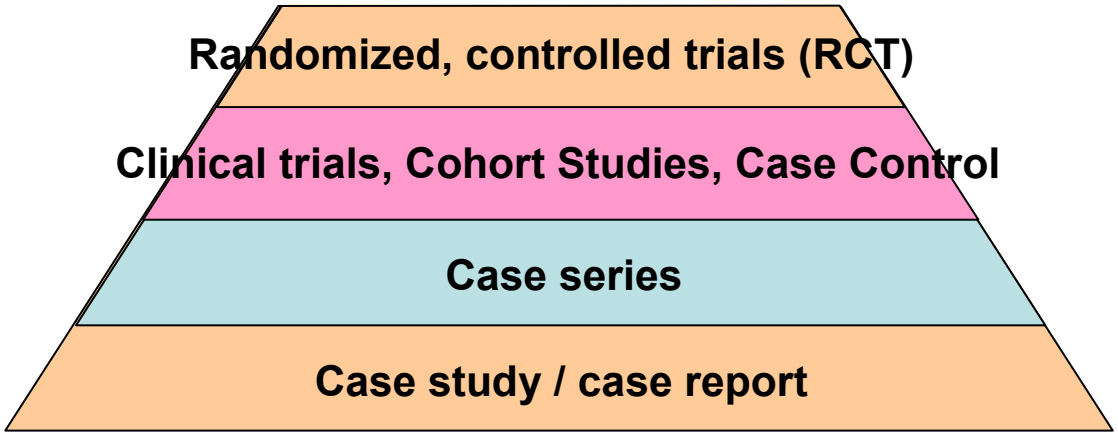
- Summarized & synthesized by experts
  - "systems research"
- Usually extremely reliable & high quality (authoritative)
- Useful for quick reads and sound decisions
- "Remove the practitioner from the primary literature."
- "Remove the patient from the picture."
- Limited in number, scope and "perspective"
- Often a lag between study results, analysis, publication, summary

Hierarchy of Evidence for Clinical Decision Making

- Expert opinions, editorials, perspective, ideas are based on professional experience – a key aspect of EBP!
- Animal studies often ARE the basic research studies!
- "Provide a substantial foundation"
- "Difficult to generalize to the patient sitting in front of the practitioner."
- Not low quality

Hierarchy of Evidence for Clinical Decision Making

Key study designs for clinical research studies:



Overview of Primary Research Study Designs

EXPERIMENTAL

- Investigator assigns, chooses, tests intervention, treatment or exposure
- Control / comparison
- Random allocation of study subjects

- Randomized Controlled Trials
- Clinical Trials
- Community Trials
- Laboratory Trials

OBSERVATIONAL

- Investigators study people and exposures "in nature"

Comparison / control group?

YES — NO

ANALYTIC

- Case-Control
- Cohort

DESCRIPTIVE

- Correlational
- Case Series
- Case Reports
- Cross-Sectional
- Migrant studies

Primary Clinical Research Study Designs

Randomized, controlled trials (RCT)

- Considered the "Gold Standard"
- Participants are **randomly allocated** into

intervention (treatment) and control (placebo) groups

  - Randomization (if done) method is key
  - "other clinical trial" or "clinical trial" may have limited or no randomization
  - Random allocation vs.
    random selection (for surveys)

Primary Clinical Research Study Designs

Randomized, controlled trials (RCT)

- Allows rigorous evaluation of a single variable
- Prospective: data is collected after the study is designed and in progress
- Seeks to falsify (not confirm) its own hypothesis
- Seeks to eradicate bias through comparison and blinding
- Allows for "meta-analysis" (combining numerical results) at a later date
- Strongest study design for **therapy** questions

Primary Clinical Research Study Designs

Randomized, controlled trials (RCT)

- Expensive and time consuming
- True randomization is difficult to achieve
  - Incomplete randomization
  - Bias in selection and randomization
- Often impractical
- Could be unethical
- Other study designs may be more appropriate

Primary Clinical Research Study Designs

Cohort Studies

- Observational
- Measurement of the same characteristic / outcome / issue / disease
  - Patients suffering from low back pain
  - Death from heart attack
- Two groups of patients differ in one characteristic
  - For example, smokers or non-smokers
  - Surgery vs. other intervention
- Most often not randomized to intervention (selected)
- Eligibility and outcome assessments can be standardized

	Randomized Controlled Trial (RCT)	Cohort Design
Populations studied	Highly characterized, selected populations recruited on the basis of detailed criteria Treated at selected sites	Diverse populations observed in a broad range of settings (natural environment)
Allocation to intervention	Based on chance Not controlled or influenced by investigators or patient choice	Not randomized Allocated based on decisions made by providers or patients
Outcomes	Primary outcomes determined before patients enrolled in study; focused on predicted benefits and risks	Can be defined after the intervention (exposure) Can include rare or unexpected events
Follow-up	Prospective studies; often short follow-up due to costs and pressure to produce timely evidence	May rely on history / existing experience (retrospective studies) Can provide opportunity for long follow-up
Analysis	Analysis is straightforward	Sophisticated multivariate techniques may be required to deal with confounding
Validity	Internal validity enhanced by minimizing selection bias and confounding	Vulnerable to selection bias - groups may differ in some factor related to outcome

Primary Clinical Research Study Designs

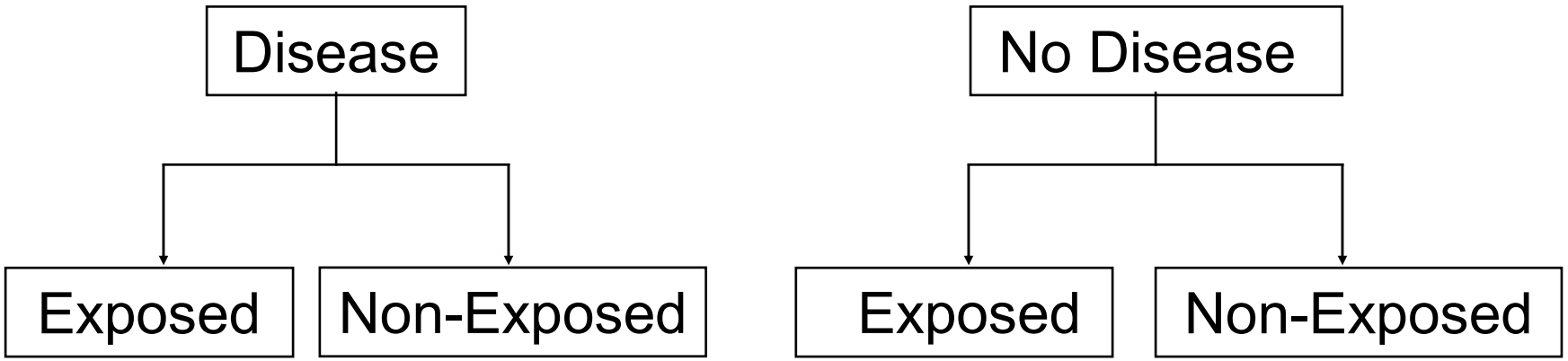
Case Control

- Observational
- Possible associations between
  - Disease/ disorder / health issue
  - and one or more hypothesized risk factors
- Focus on the etiology of a disease or disorder
- Strongest study for questions of cause (etiology)

Primary Clinical Research Study Designs

Case Control

- Observational
- Possible associations between a disease and one or more hypothesized risk factors
- Focus on the etiology of a disease or health issue



Primary Clinical Research Study Designs

Case Control

- **compare** the prevalence or level of the possible risk factor between

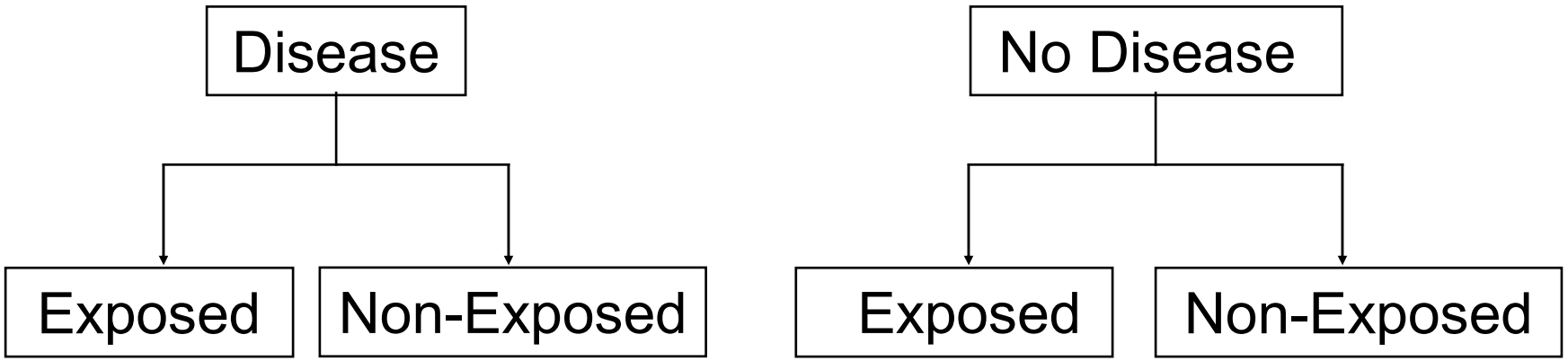
Case

∗ representative group of disease subjects (cases)

Control

∗ representative group of disease-free subjects (controls)

- derived from the same population



Primary Clinical Research Study Designs

Case control

- Patients with a particular health concern / characteristic / disease /disorder
- Matched with "controls:"
  - Identical patients *without* that issue
  - Identical patients with a different disease
  - General population
- Data is collected by searching through patient histories or through patient recall surveys
- Used to study rare conditions (strong study design)

Primary Clinical Research Study Designs

Cross-sectional surveys

- Representative sample of subjects or patients
- Interview, survey, study
- Data is collected at a single time point
- Data collection may depend on history or recall
- Establishes association, not causality
- Often used to develop further clinical research

Primary Clinical Research Study Designs

Case Study

- Detailed description a single case
- 10-30 patients = case series
- Rare events, early trends, unusual manifestations, responses
- Elucidate disease mechanisms and treatment
- Detailed, well-defined patient description
- Highly detailed and methodologically sophisticated

Primary Clinical Research Study Designs

Case Study

- Rich source of ideas, hypotheses about disease, conditions, risk, prognosis and treatment.
- Not typically useful or strong enough to test a hypothesis
- Initiate issues and trigger more decisive studies
- No statistical analysis: no determination of “chance”
- Often retrospective (looking back)

Primary Clinical Research Study Designs

Case Series

- 10 to 30 patients
- Detailed description
- Well described treatment or intervention
- All subjects receive same treatment
  - No comparison group
  - If inclusion and exclusion data were used, explicit definitions and descriptions should be provided
- Larger number of cases (than a case study) allows statistical analysis (p values, means, standard deviations)
  - Allows determination of chance

Primary Clinical Research Study Designs

Case Series

- Often retrospective (look back in time)
  - restricts value as prognosis study or determining cause and effect relationships
- Prospective (looking forward) case series studies are often designed as prospective cohort studies
  - including a control group (a benefit, strength).

Suggested Practice:

Objective:

- To search the professional biomedical literature databases for professional journal articles (papers) describing primary research studies which support clinical decisions regarding a specific patient scenario.
- Identify study design by abstract, methods

- Selected journal article characteristics:
  - Primary research study
    - Human subjects or patients who are analyzed
    - NOT reviews, analyses, guidelines, economic analyses based on primary studies etc.
    - NOT about other studies (compiled evidence reviews, systematic reviews, meta-analyses, narrative reviews, etc.)
  - Published within 3 years or less)
  - Written by the researchers who conducted the study
  - From a peer reviewed journal to ensure high quality

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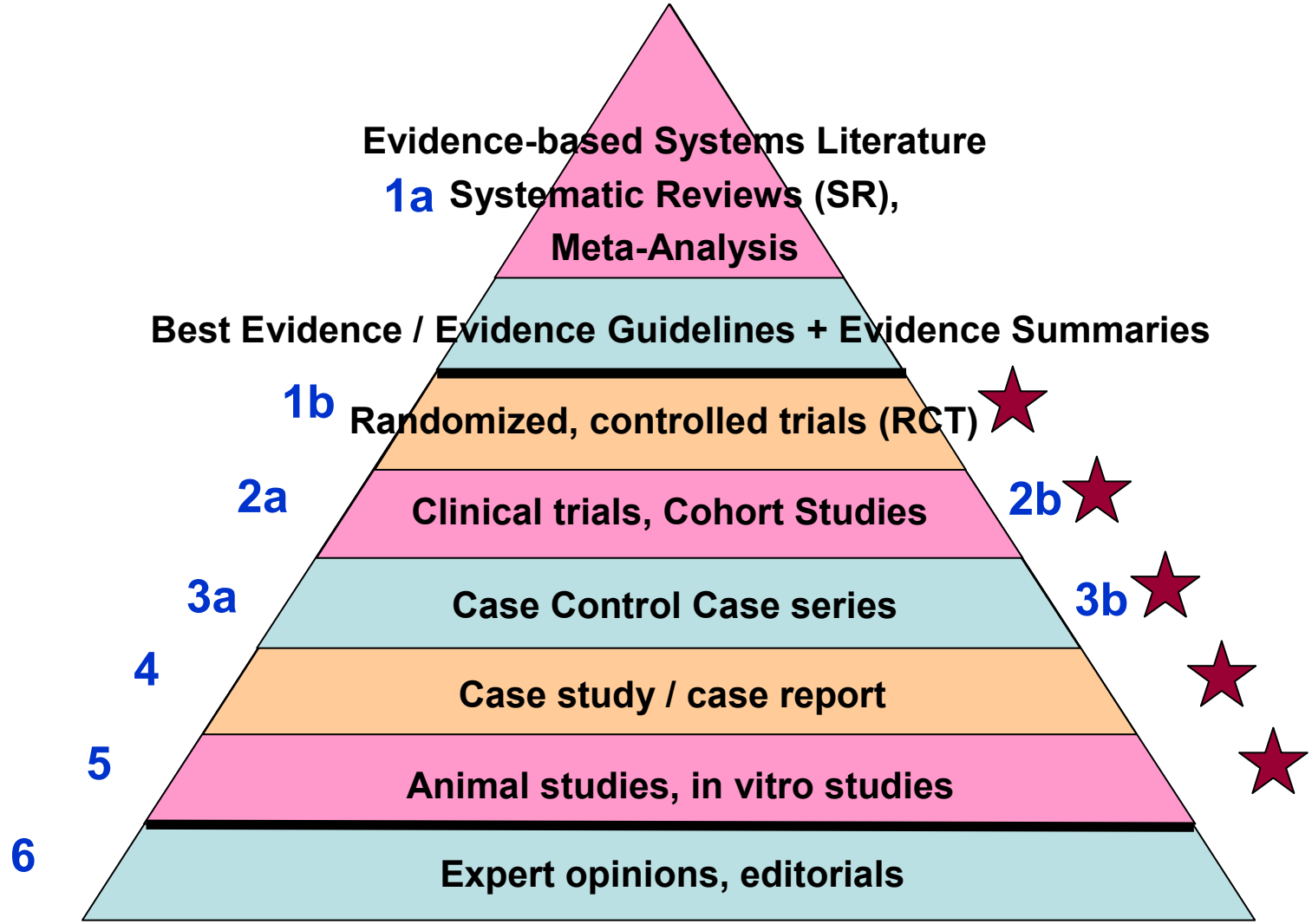

Reading Resources:

- Haneline M, Cooperstein R. Appraisal of Journal Articles: Asking the Right Questions. JACA 2006 May/June:20-24.
- Greenhalgh T. Assessing the methodological quality of published papers. BMJ 1997 2 Aug;315:305-8.