

Systematic Reviews



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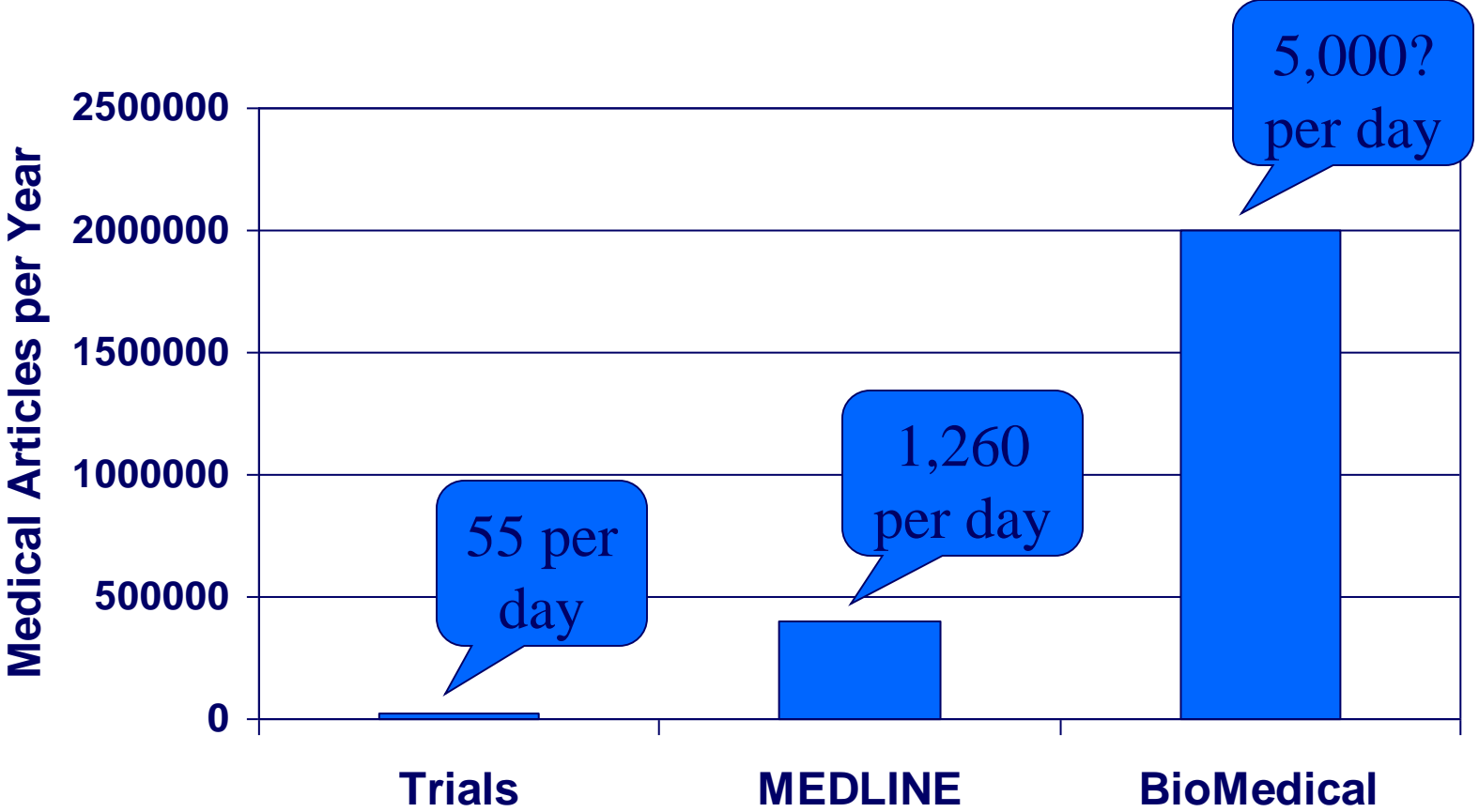
Information Overload



- 20,000 biomedical periodicals (6M articles)
- 17,000 biomedical books annually
- 30,000 recognized diseases
- 15,000 therapeutic agents (250/yr)

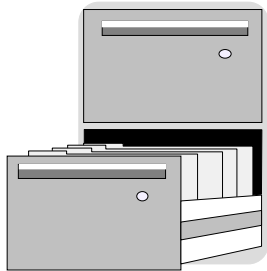
- MEDLINE
 - 4,000 journals surveyed
 - 11,000,000 citations
 - 1.27 million articles related to oncology
 - 35,000 articles related to ear, nose, or throat surgery

Review the World Literature Fortnightly*



SYSTEMATIC Review: Steps

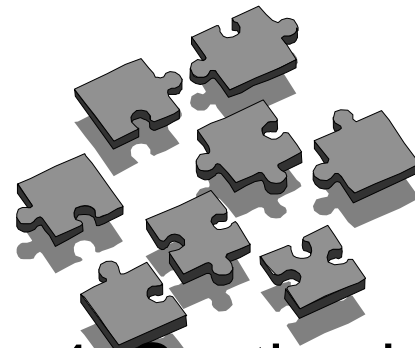
1. Formulate question(s)



2. Find
All studies



3. Assess



4. Synthesise

5. Applicability analysis

EBM and Systematic Review



- EBM
 - Steps
 - Answerable Question
 - Search
 - Appraise
 - Apply
 - Time: 30 seconds
- Systematic Review
 - Steps
 - Answerable Question
 - Search +++++
 - Appraise x 2
 - Synthesize
 - Apply
 - Time: 6 months

Origin of Clinical Questions



Diagnosis: how to select and interpret diagnostic tests

Prognosis: how to anticipate the patient's likely course

Therapy: how to select treatments that do more good than harm

Prevention: how to screen and reduce the risk for disease

Step 1- Framing the Question (Q)



- Clear, unambiguous, *structured* question
- Questions formulated re:
 - **P**opulations of interest
 - **I**nterventions
 - **C**ontrol
 - **O**utcomes

Unstructured Question



- Is self-management effective?
 - For what?
 - For whom?
 - Compared to what?
 - What is meant by “effective”?

Structured Question



population

Do adults (aged > 18) using oral

outcome

anticoagulation therapy have fewer

intervention

episodes of thrombotic events if they are

self-managed than those that are *control*

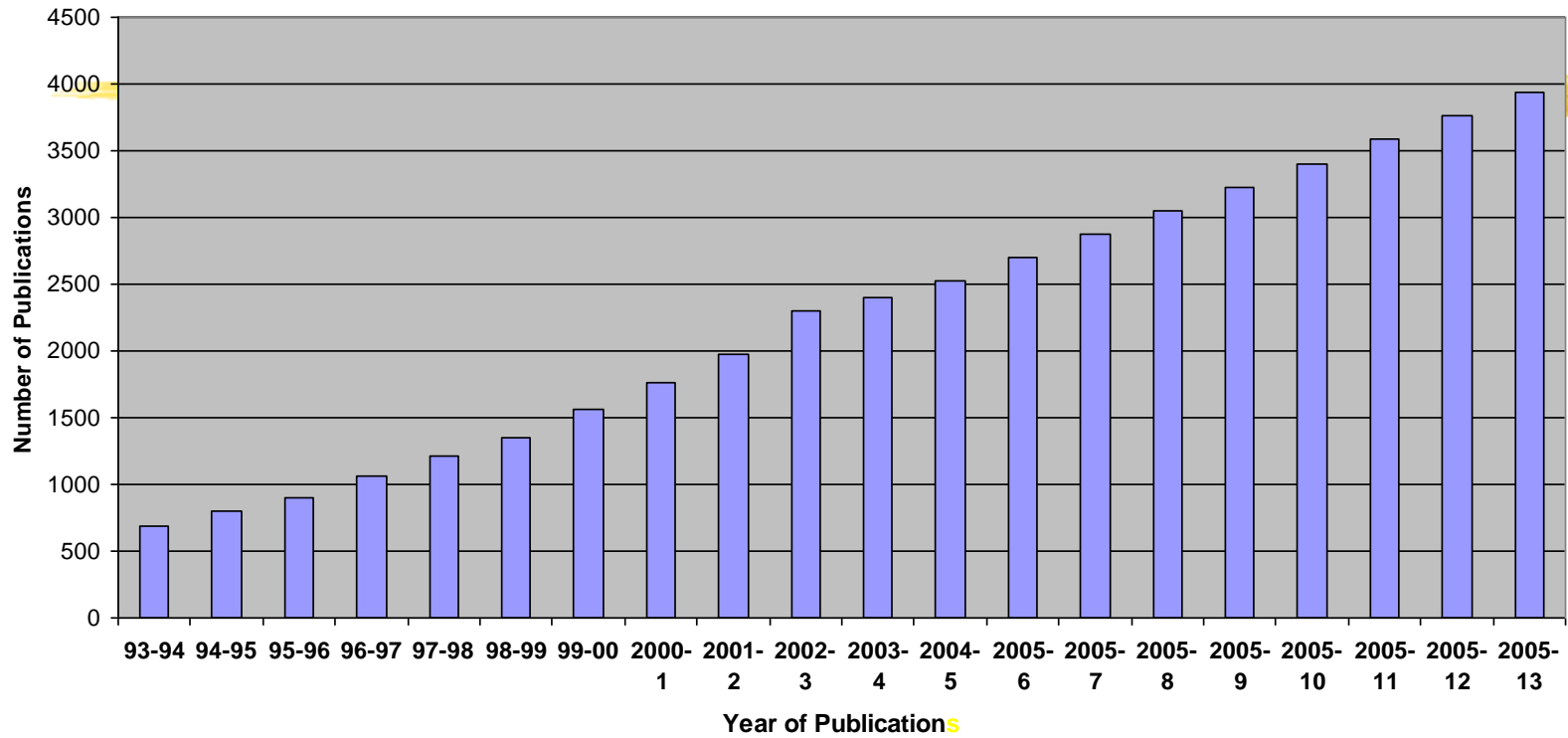
managed by doctor/health practitioner?

What makes a Review “Systematic”?

- Based on a clearly formulated question
- Identifies relevant studies
- Appraises quality of studies
- Summarizes evidence by use of explicit methodology
- Comments based on evidence gathered

The popularity of meta analyses

publications



Systematics Reviews



- Finding
 - Electronic search
 - Supplementary search
- Appraising
 - Quality Assessment
 - Selection & extraction
- Synthesis
 - Summary Table
 - Plots: summary & diagnostic
 - Summary estimators

FINDING all Studies



- Is there an existing systematic review?
- Electronic Search
 - Initial Search
 - MEDLINE
 - Other databases: EMBASE, CINAHL, CCTR, ...
 - Further search
 - Check references of relevant papers & reviews and
 - Find terms (words or MeSH terms) you didn't use
 - Search again! (*snowballing*)
- Supplementary search
 - Hand search
 - Write to researchers

Problems with searching



- *Finding **overpublished** work*
 - Duplicate publications common
- *Finding **unpublished** work*
 - Negative trials unpublished?

Publication Bias: the problem



- Negative studies less likely to be published than 'Positive'
- How does this happen?
- Follow-up of 737 studies at Johns Hopkins
(Dickersin, JAMA, 1992)
 - Positive SUBMITTED more than negative (2.5 times)

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Assessment of Quality and Selection of Studies



- Quality varies, therefore
Standardized Assessment (?blind*)
Group/Rank by quality
- Select a threshold, e.g. all prospective studies with blind reading of reference and index tests.

* assessment of quality blind to study outcome

Assessing a Study of a Test

(Jaeschke et al, JAMA, 1994, 271: 389-91)



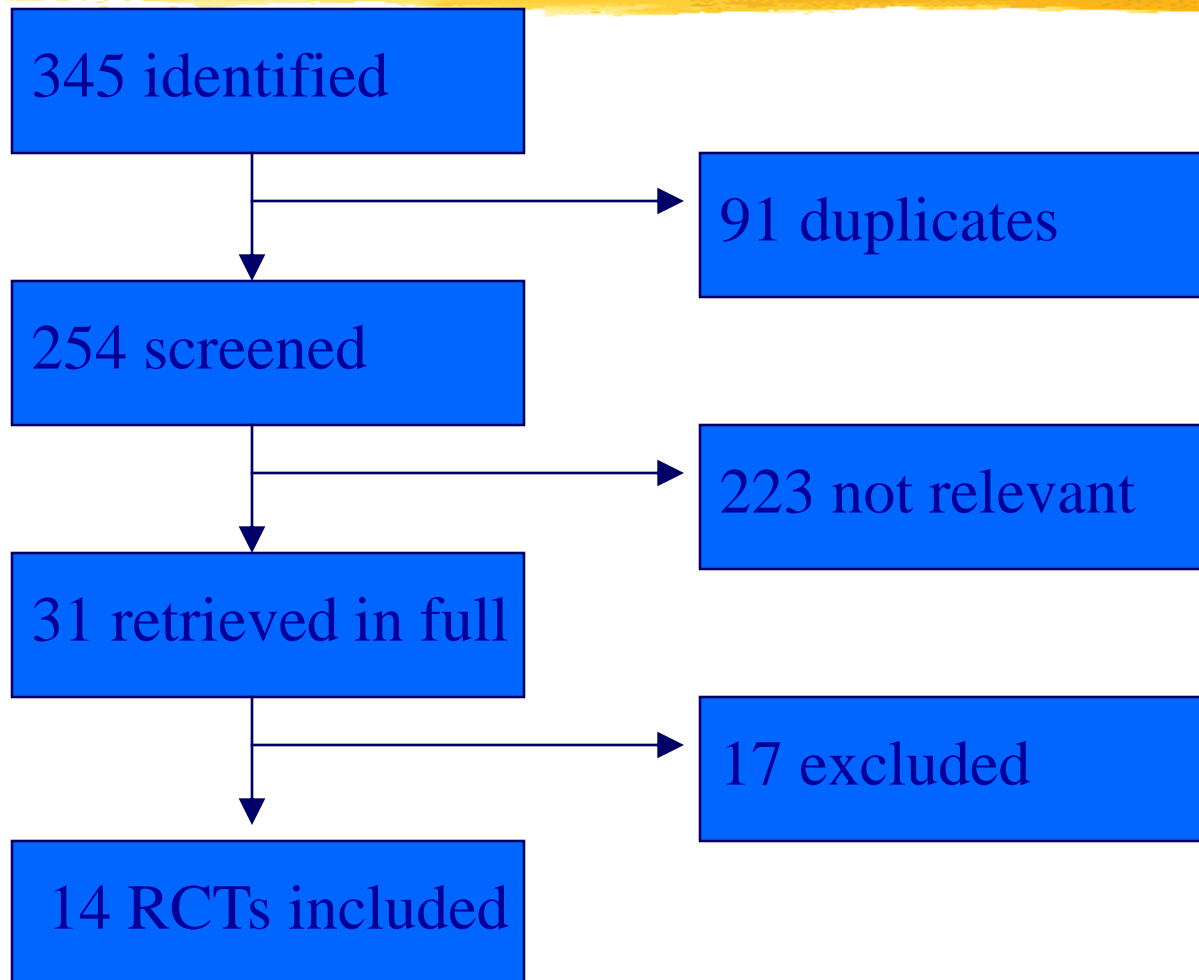
- Was an appropriate spectrum of patients included?
 - (Spectrum Bias)
- All patients subjected to a Gold Standard?
 - (Verification Bias)
- Was there an independent, "blind" comparison with a Gold Standard?
 - Observer Bias; Differential Reference Bias
- Methods described so you could repeat test?

Identifying relevant publications



- Relevance to focused question
 - Population of interest
 - Intervention of interest
 - Comparator of interest
 - Outcome of interest

Flowchart



Assessing Study Quality

Quality categories	High	Moderate	Low
Design	Prospective	Prospective	Prospective or retrospective
Ascertain outcome	Long follow-up and blind assessment	Long follow-up or blind assessment	Short follow-up and unblinded assessment
Control for confounders	Randomized	Adjustment for some factors	No adjustment

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Are the studies consistent?



- Are variations in results between studies consistent with chance?
(Test of homogeneity: has low power)
- If NO, then WHY?
 - Variation in study methods (biases)
 - Variation in intervention
 - Variation in outcome measure (e.g. timing)
 - Variation in population

**“... doing a meta-analysis is
easy, doing one well is hard.”**

A thick, horizontal yellow brushstroke with a textured, painterly appearance, spanning across the width of the slide below the quote.

Ingram Olkin