Research Methodology and Medical Treatment Guidelines

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INTRODUCTION

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- Masters in Public Health
  - Focus in Epidemiology & Biostatistics
- Senior Research Methodologist
  - Colorado Division of Workers' Comp. (Medical Treatment Guidelines)

INTRODUCTION

Presentation Goals

- Why we create the MTGs
- The Colorado DOWC process
- Study quality / confidence based on study type and risk of bias

Why Evidence-Based Medical Treatment Guidelines?

WHY EVIDENCE-BASED MTGs?

Our goal is to make **decisions** that are **most likely** to achieve our **desired outcomes**.

WHY EVIDENCE-BASED MTGs?

Desired outcomes in Workers' Comp

- Healing →
  Functional improvement →
  Return to work
- Safety
- Resources / Cost-effectiveness

WHY EVIDENCE-BASED MTGs?

Medical **Decisions** in Workers' Comp

- Treatment options
  - When and for whom
  - How much, how long
  - When to try something different
- Diagnostic approaches

WHY EVIDENCE-BASED MTGs?

For these types of decisions, **medical research** is a valuable information source.

WHY EVIDENCE-BASED MTGs?

But there's a lot of research - of varying reliability – how do we navigate that?

WHY EVIDENCE-BASED MTGs?

How do we navigate that?

- It's often complicated
  - Specialized knowledge and experience
  - It's time consuming

OUR AIMS FOR THE MTGs

- Provide best evidence on available medical treatments
- Weigh appropriateness of treatment relative to functional outcomes
- Address emerging treatments and diagnostics
- Create actionable recommendations

Phases of the Colorado DOWC MTG Process

PHASES OF THE MTG PROCESS

- Expert interviews and scoping
- Finding and selecting studies
- Evaluating individual studies
- Combining evidence from multiple studies
- Writing recommendations and guidance
- Task Force process
- Advisory Panel and public input process

PHASES OF THE MTG PROCESS

- **Expert interviews and scoping**
  - What topics should we review?
    - Specify using PICO questions.
      - Population (including the medical condition)
      - Intervention (the treatment being studied)
      - Comparison (typically a traditional/proven treatment)
      - Outcome (function, pain, adverse events)
      - Timing (how long after treatment)

PHASES OF THE MTG PROCESS

- **Expert interviews and scoping**
  - Occ Med and PM&R Physicians
  - Physical and Occupational Therapists and Physiatrists
  - Psychiatrists and Psychologists
  - Claimant's and Respondent's Attorneys
  - Other Medical, Government, and Insurance Professionals

PHASES OF THE MTG PROCESS

- Expert interviews and scoping
- **Finding and selecting studies**
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PHASES OF THE MTG PROCESS

- **Finding and selecting studies**
  - Systematic search
    - PubMed and Cochrane Databases
    - Detailed search terms

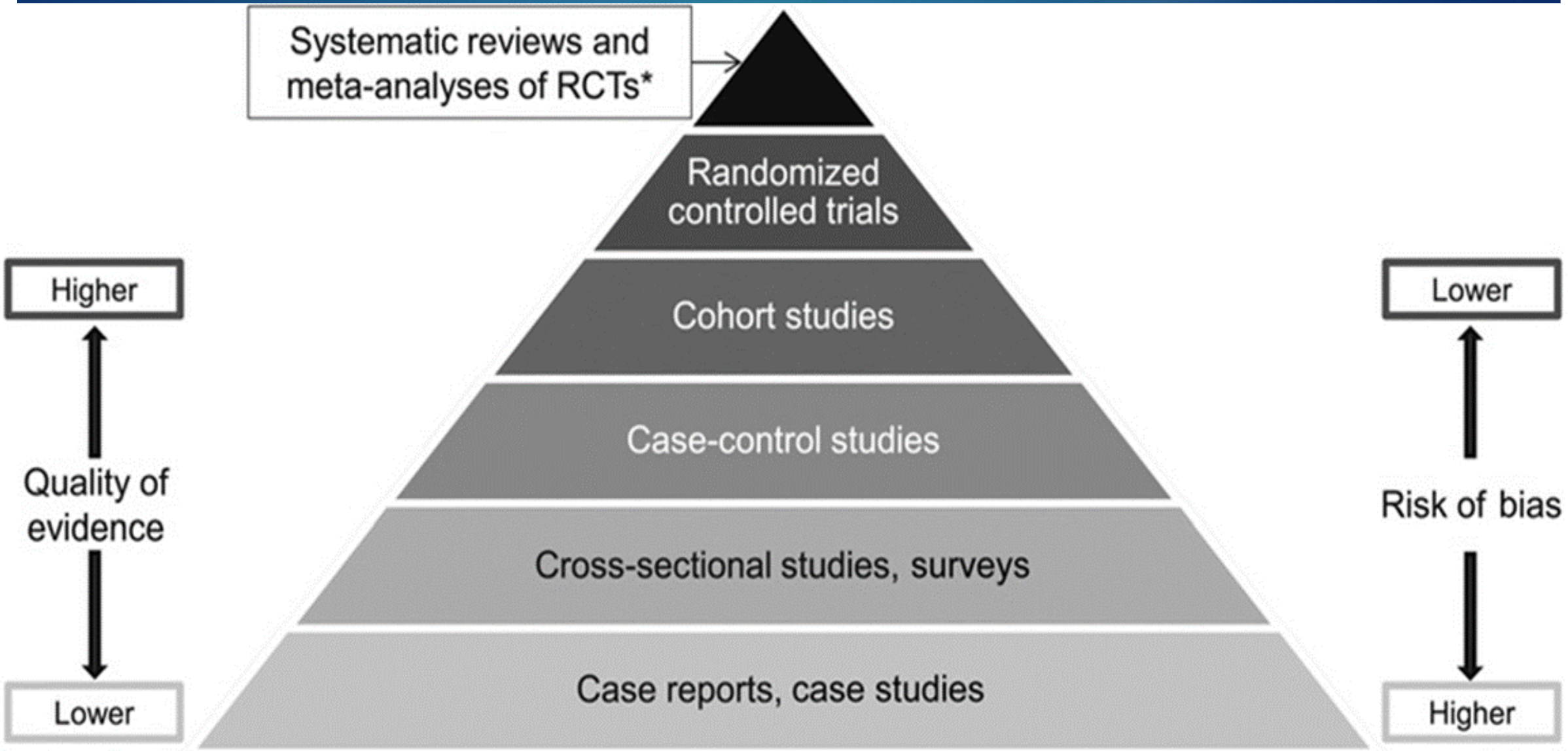
SEARCH TERMS

((cam[sb] OR Vertebroplasty[mh] OR "Cognitive Behavioral Therapy"[mh] OR "Combined Modality Therapy"[mh] OR Traction[mh] OR Laminectomy[mh] OR "Diskectomy, Percutaneous"[mh] OR "Diskectomy/methods"[MAJR] OR ("Injections"[mh] AND "Adrenal Cortex Hormones/pharmacology"[mh]) OR "Injections,Spinal"[mh] OR "directional preference" OR "centralization" OR "Spinal Fusion"[mh] OR "Low-Level Light Therapy"[mh] OR "Smoking Cessation" OR "Lumbar discography" OR myelography[mh] OR "Diathermy"[mh] OR "Nerve Block"[mh] OR "orthotic devices"[mh] OR Arthroplasty[mh] OR Phonophoresis[mh] OR "Decompression, Surgical"[mh] OR "interferential therapy" OR "interferential current therapy" OR "Electric Stimulation Therapy"[mh] OR "Vax-D" OR "McKenzie Assessment" OR "infrared therapy" OR "ergonomic" OR "Workers' Compensation"[mh] OR "Return to Work"[mh] OR "Occupational diseases"[mh] OR "Occupational Health"[mh] OR "diagnostic imaging" OR "Analgesics"[mh] OR "Spinal Stenosis" OR "Radiculopathy" OR "Patient Education as Topic"[mh] OR "Conservative Treatment"[mh]) OR "Physical Therapy Modalities"[mh] AND (back[mh] OR neck[mh] OR "Back Pain"[mh] OR "Neck Pain"[mh] OR Sacroiliac Joint[mh] OR "Spinal Fractures"[mh] OR "Back Injuries"[mh] OR "Neck Injuries"[mh] OR "Spinal Cord Injuries"[mh] OR "Thoracic Injuries"[mh] OR "Spinal Diseases"[mh] OR "Lumbar Vertebrae"[mh] OR Spine[mh] OR Lumbosacral Region[mh] OR "Spinal Nerve Roots"[mh] OR "Zygapophyseal Joint"[mh]) AND (systematic review[sb] OR meta-analysis[mh] OR RCT OR randomized controlled trial OR "Randomized Controlled Trial"[mh])) AND ("2017/08/01"[PDAT] : "3000"[PDAT]) AND human[mh] AND English[Language] NOT clinical protocols[mh] NOT "protocol" NOT "Animal Population Groups"[mh] NOT Neoplasms[mh] NOT cancer [sb] NOT child[mh] NOT Adolescent[mh] NOT "Cost-Benefit Analysis"[mh] NOT "healthy volunteers"[mh] NOT "Case-control studies"[mh]

PHASES OF THE MTG PROCESS

- **Finding and selecting studies**
  - Inclusion / exclusion criteria
    - RCT or SR/MA of RCTs
    - Published in a peer-reviewed journal in English
    - Fits our scope (PICOTs)
    - Sufficient size (20 subjects per group)

STUDY TYPE


Systematic reviews and meta-analyses of RCTs*
Randomized controlled trials
Cohort studies
Case-control studies
Cross-sectional studies, surveys
Case reports, case studies
Higher
Quality of evidence
Lower
Lower
Risk of bias
Higher

PHASES OF THE MTG PROCESS

- Expert interviews and scoping
- Finding and selecting studies
- **Evaluating individual studies**
- Combining evidence from multiple studies
- Writing recommendations and guidance
- Task Force process
- Advisory Panel and public input process

PHASES OF THE MTG PROCESS

- **Evaluating individual studies**
  - Which results are we interested in?
    - Direct comparison of the amount of change
  - How confident are we that those results represent the true effect of the treatment?
    - Risk of bias – many factors can potentially bias the results
      - We currently use Cochrane's updated risk-of-bias tool (RoB 2)
    - Also called "internal validity"

PHASES OF THE MTG PROCESS

- Expert interviews and scoping
- Finding and selecting studies
- Evaluating individual studies
- **Combining evidence from multiple studies**
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PHASES OF THE MTG PROCESS

- **Combining evidence from multiple studies**
  - Systematic review – the "qualitative" questions:
    - Which studies can be combined based on their scope (PICOs)?
      - For example: Different age ranges; Different methods of delivering the treatment; Different outcome measures
    - Do the study results agree?
      - If not, look for explanations of the inconsistency.

PHASES OF THE MTG PROCESS

- **Combining evidence from multiple studies**
  - Meta-analysis – the "quantitative" analysis:
    - Results in a "pooled estimate" of the effect
    - Is there evidence of publication bias (unpublished studies)?
    - Do any low-quality studies bias the pooled estimate?
    - How certain is the pooled estimate (confidence interval)?

PHASES OF THE MTG PROCESS

- Expert interviews and scoping
- Finding and selecting studies
- Evaluating individual studies
- Combining evidence from multiple studies
- **Writing recommendations and guidance**
- **Task Force process**
- Advisory Panel and public input process

PHASES OF THE MTG PROCESS

- **Writing recommendations and guidance**
- **Task Force process**
  - Consider multiple factors that go into recommendations:
    - Study results
    - Risks/harms
    - Other factors like availability and cost
    - Expert perspectives

PHASES OF THE MTG PROCESS

- **Writing recommendations and guidance**
- **Task Force process**
  - Consider details that inform the guidance around recs:
    - Study population and condition – informs the indications
    - Details of the study treatment – informs dose and duration
    - Other factors like co-interventions in the studies

PHASES OF THE MTG PROCESS

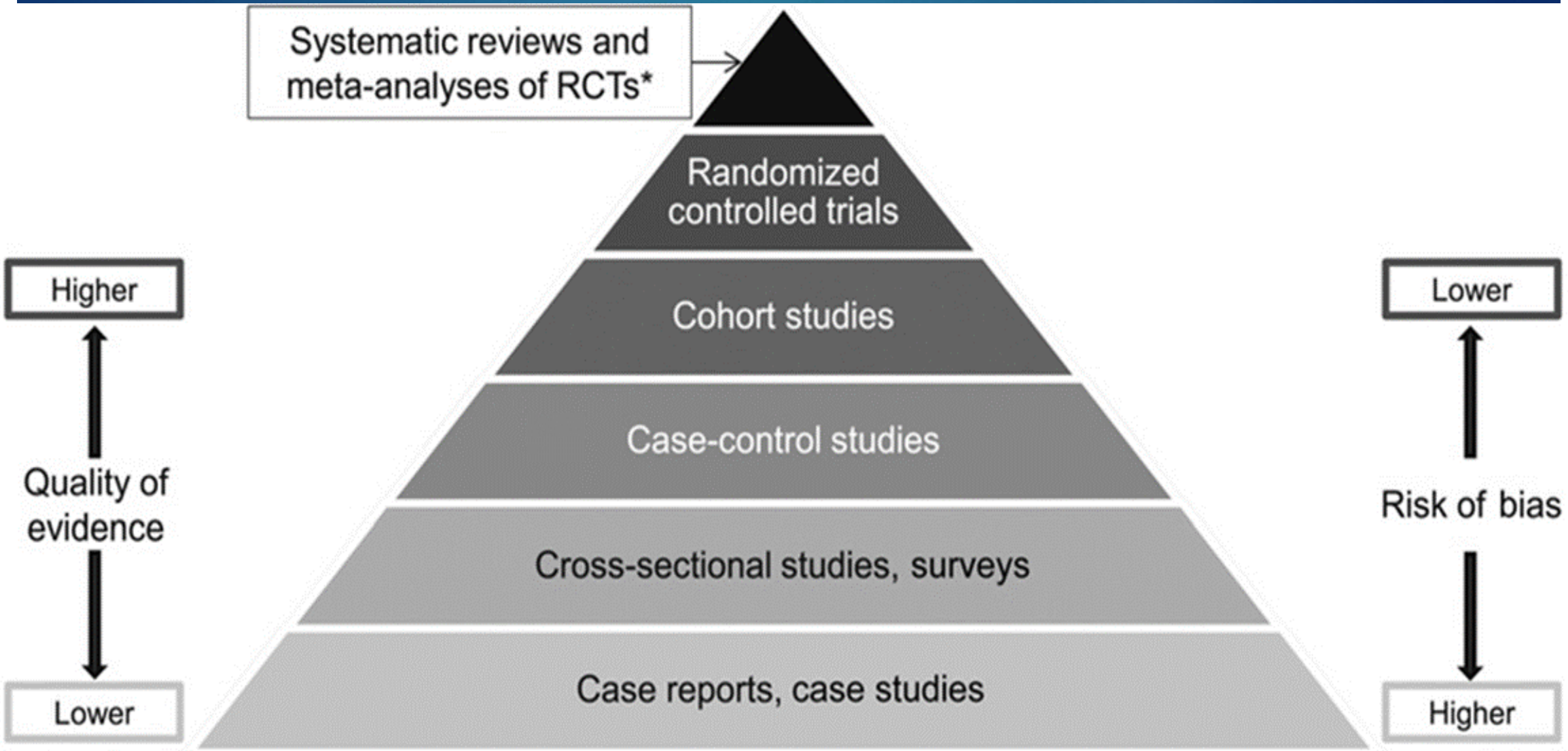
- Expert interviews and scoping
- Finding and selecting studies
- Evaluating individual studies
- Combining evidence from multiple studies
- Writing recommendations and guidance
- Task Force process
- **Advisory Panel and public input process**

PHASES OF THE MTG PROCESS

- **Advisory Panel and public input process**
  - 35 member Advisory panel for the spine guidelines
  - Public comment period of at least 1 month
    - Actively solicit input by emailing all prior stakeholders

Study design

STUDY TYPE


Systematic reviews and meta-analyses of RCTs*
Randomized controlled trials
Cohort studies
Case-control studies
Cross-sectional studies, surveys
Case reports, case studies
Higher
Quality of evidence
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Lower
Risk of bias
Higher

CASE REPORTS AND CASE SERIES

- One or more people with a particular condition are given a treatment and improve
- Strengths:
  - Hypothesis generating about possibly effective treatments
  - Provides information about possible dose, duration, etc.

CASE REPORTS AND CASE SERIES

- Limitations:
  - Only positive results usually get reported
  - The authors often have a vested interest in the treatment
  - Many factors other than the treatment could be the reason for improvement
    - No control comparison

CROSS-SECTIONAL STUDIES

- All information is gathered at one point in time
- Surveys are typical, though some include other data collection
- Used more to investigate risk factors than treatments
- Diagnostic studies are similar:
  - Results of the diagnostic tool being studied are compared with results of a gold-standard diagnosis

CASE-CONTROL STUDIES

- Used most often to look for links between risk factors and diseases
- Cases are individuals who developed the disease
- Controls are selected from a similar population, often matched for key demographics
- The history of possible risk factors are compared
- Not relevant for evaluating treatments

COHORT STUDIES

- Two groups with a key difference at the starting point are followed over time to detect possible outcomes
  - For example: people who got a certain treatment vs. others who didn't get that treatment are followed for improvement
  - More commonly used to link risk factors and disease

COHORT STUDIES

- Strengths:
  - Less expensive and less red tape than a trial
  - Can be used when randomization isn't feasible
- Limitations:
  - Much greater risk of bias, especially related to the selection of who is in each group

COMPARATIVE TRIAL (INCLUDING RCTs)

- Divide patients with a condition into two groups: treatment A vs treatment B
- Randomized – each individual has an equal chance of being in each group. This eliminates possible selection bias.
- Controlled – treatment B is a "control." Thus, if group A improves more than group B, it's reasonable to conclude it's from treatment A.

COMPARATIVE TRIALS (INCLUDING RCTs)

- Strengths of RCTs:
  - If well designed and executed, eliminates many possible sources of bias.
  - Is therefore the strongest study type to demonstrate causation.

COMPARATIVE TRIALS (INCLUDING RCTs)

- Limitations of RCTs:
  - Expensive.
  - Recruitment can be difficult.
    - Can be "underpowered" due to small numbers.
  - Many requirements to ensure ethical study practices.
  - Must balance getting similar groups with representing the general population.

SYSTEMATIC REVIEWS AND META-ANALYSES

- Systematic review
  - Formal, rigorous methods to identify all relevant research (such as our MTG process)
- Non-systematic review examples
  - The latest studies receiving press coverage
  - A selection of research provided by a drug representative or device manufacturer

SYSTEMATIC REVIEWS AND META-ANALYSES

- Meta-analysis
  - Statistical combination of study results to generate a "pooled" estimate of effect
- Our confidence in the findings of systematic reviews and meta-analyses **depend on the quality of the included studies**

(Minimizing) Risk of Bias

RANDOM SEQUENCE GENERATION

- Determines a random order for assigning people into the intervention and control groups
- Occurs at the start of the trial before allocation
- Helps to eliminate confounders
  - Confounder = a difference in some characteristic between the groups that affects outcomes
- Avoids **selection bias**

ALLOCATION CONCEALMENT

- When a person is recruited to the study, no one can predict which group they will be allocated to
- Ensures the strict implementation of the random sequence
  - Prevents changing the order
  - Prevents selecting who to recruit based on knowledge of which group they would be in
- Avoids **selection bias**

BLINDING OF PARTICIPANTS & PROVIDERS

- Patients don't know which group they are in for the duration of the study – and neither do their providers
- Ensures there are not differences in additional treatments or patient behaviors resulting from knowledge of group assignment
- Avoids **performance bias**
- In some cases, blinding might not be possible

BLINDING OF OUTCOME ASSESSMENT

- Individuals measuring the outcomes don't know which group each patient is in
- Prevents psychological biasing of outcome measurement, especially any that are subjective
- The patient may also be an outcome assessor
- Avoids **detection bias**

SUFFICIENT FOLLOW-UP

- There isn't a firm rule, but 95% is generally good
- Can be hard to control lost patients & data
  - Patient withdrawal or loss to follow up
  - Missing data, such as incomplete assessments
- Could "missingness" be related to outcomes for those patients?
- Avoids **attrition bias**

FULL REPORTING AND APPROPRIATE ANALYSIS

- Outcome measures are appropriate
- All outcome measures are reported
  - No selective reporting
- Analysis should be based on group assignment (intention-to-treat
  - If multiple analyses were done, all are reported
- Avoids **reporting bias**

PRE-REGISTERED STUDY PROTOCOL

- This is becoming standard practice
- A protocol should be registered prior to enrollment
- There should be no major changes in study design from the early protocol to the final study report
- Provides assurance against multiple types of potential bias

Any questions?

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(or via Dr. Cook-Shimanek)