Using Secondary Data in Statistical Analysis

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Meta-analysis Definition

Glass 1976, “the statistical analysis of a large collection of results from individual literature for the purpose of integrating their respective findings.”

Two basic purposes:

Determine if similar treatment effects exist for a therapy in independent studies to estimate a net effect for this therapy

Alternatively, if treatment effects differ substantially for a therapy among independent studies, to examine factors that may explain these differing effects

Education Research 1976

Techniques of Meta-Analysis

Step One: Formulating the Question

Validity and importance are contingent on this step

Poorly conceived research hypothesis will usually lead to an analysis of dubious value

Techniques of Meta-Analysis

Step Two: Defining Eligibility Criteria

Protocols for study inclusion should be prospective, systematic, and explicit

Ideally, randomized trials similar in diagnosis, outcome, patient characteristics, and treatment groups

Techniques of Meta-Analysis

Step Two: Defining Eligibility Criteria Cont'd

Including all available studies, regardless of size, design, or quality results in an analysis that is broadly representative but may compromise accuracy

Alternatively, exclusion of poorly done studies may increase the statistical validity but limit the ability to generalize findings

Techniques of Meta-Analysis

Step Three: Identifying Studies and Data Abstraction

Usually begins with a search of online databases such as MEDLINE, Current Contents, Best Evidence, Cochrane, and HealthSTAR

Title and abstract perused to exclude studies

Techniques of Meta-Analysis

Step Three: Identifying Studies and Data Abstraction Cont'd

Full texts of the remaining articles retrieved and thoroughly studied

Reference lists of these articles are reviewed

Once a study selected for inclusion, data should be extracted by more than one reviewer onto structured forms

Techniques of Meta-Analysis

Step Four: Analysis

A common measure of treatment effect must be determined

Fixed versus random effect model used to combine data

Techniques of Meta-Analysis

Step Four: Analysis Cont'd

Cochran's Q statistic and I2 calculated

Consider metaregression when $I2 > 30\%$ and $P < 0.10$

Publication bias examined

Funnel Plot

Techniques of Meta-Analysis

Step Five: Reporting and Interpreting Results

To improve overall quality of reporting for meta-analysis, a checklist and a flow chart should be constructed

Quality of Reporting of Meta-analyses (QUOROM) conference provides guidelines for reporting searches, study selection, validity assessment, data abstraction, study characteristics and data synthesis

Meta-analysis of Clinical Trials in Sepsis

The Host Inflammatory Response Hypothesis: What went wrong?

Human Clinical Trials of Anti-Inflammatory Therapies in Sepsis Ranked by Size

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Summary

Anti-Inflammatory Agents in Sepsis

Meta-analysis:

treatment effects are small (3%), but statistically significant

Meta-regression analysis:

Efficacy dependent on risk of death

Beneficial at high risks of death,

ineffective or harmful when risk was moderate or low

Paradox of
Corticosteroids in Sepsis

Less may have benefits, but only in sickest patients

Corticosteroids in Sepsis

Investigated since the 1960s

By early 1990s, shown to be ineffective or possibly harmful

Renewed interest and new trials over the last decade

How is Corticus Different from the 11 Other Trials of Low-Dose Steroids?

Funnel Plot of Sepsis Trials of Low Dose Steroids

Corticosteroid Effect on Shock

Summary

Corticosteroid effects during sepsis depend on dose and severity of illness

Low dose steroids decrease vasopressor requirements and enhance shock reversal

Limitations

At present, the beneficial effects of low doses of corticosteroids are based on small trials (median 40 patients, IQR 41-44) confounded by publication bias

The largest trial of low dose cortico-steroids (CORTICUS, n = 499) studied a relatively low risk population

Benefit from low dose corticosteroids has not been confirmed in a large multicenter trial of high risk patients

Until new data are available, the decision to administer low dose steroids for septic shock should be individualized:

Severity of illness

Assessment of risk

Intensive Insulin Therapy
in Patients with Sepsis

How much risk and how much benefit?

Endorsement of Glycemic Control as
Standard of Care for the Critically Ill

JCAHO

Core quality of care - all Medicare hospitals

American College of Endocrinology

Volunteer Hospital Association

Care bundle

Institute for Healthcare Improvement

Sepsis bundle

Post cardiac surgery

Surviving Sepsis Campaign

Sepsis bundle

Selected Baseline Characteristics

Mortality Associated with Conventional versus Intensive Insulin

Limitations

Single center, unblinded study

Relatively high mortality among cardiac surgery patients in control group (5.1%)

Immediate post-operative i.v. glucose (200-300 g per day: ~ 2 - 3 L D10 or D20) and early feeding (enteral or parenteral)

Not routine care for cardiothoracic surgery patients

NICE-Sugar Trial
Baseline Characteristics

NICE-Sugar Trial
Outcomes

Meta-analyses of Sepsis Trials with at Least One Significant Benefical Trial

Summary

The randomized control trial minimizes bias but does not eliminate the need for reproducibility which is the sine qua non (i.e. the indispensable and essential condition) of scientific evidence