

Guidelines for reading a Cohort Study

- I. Statement of Research Question
 - A. Prior Hypothesis?
 - B. Hypothesis Testing or Generating Study?
- II. Why was Cohort Methodology Chosen?
- III. Methods
 - A. Source of Cohort Population
 - i. Inclusion Criteria
 - ii. Exclusion Criteria
 - iii. Means of Recruitment
 - B. Follow-up Time
 - i. When were observations begun?
 - ii. When did follow-up time stop?
 - iii. How were censored observations handled?
 - C. Definition of Study Variables
 - i. Main Effect (dependent variable)
 - ii. Exposure (independent variable)
 - 1. estimation of exposure
 - 2. exposure opportunity
 - 3. duration/intensity: how were chronic exposures handled?
 - 4. Latency assumptions
 - iii. Confounding factors
 - D. Data Collection
 - i. Method (interview, questionnaire, record review, surrogate)
 - ii. Blinded?
 - iii. Independent validation?
 - iv. Repeated measurements?
- IV. Results/Analysis
 - A. Lost to follow-up: who & how many?
 - B. Analysis
 - i. Descriptive methods
 - ii. Measures of effect
 - iii. Dose response
 - C. Sources of confounding
 - i. Factors considered
 - ii. Means of assessing confounding/interaction
 - D. Sources of bias
 - i. Information bias
 - ii. Selection bias
 - 1. How complete was follow-up?
 - 2. Healthy worker/survival effect considered?

- V. Conclusions
 - A. Consistent with the data reported for the main effect of the study?
 - B. Results consistent with previous literature?
 - C. Interpretations of main effects fully explored?
 - i. Alternate hypotheses suggested?
 - ii. Study weakness and limitations noted?
- VI. Relevance
 - A. Findings new?
 - B. Findings original?
 - C. Findings hypothesis generating?
 - D. Implication for Public Health practice

References:

1. Breslow, NE, Day NE. *Statistical Methods in Cancer Research:II. The Design and Analysis of Cohort Studies*. International Agency for Research on Cancer, 1987, Lyon.
2. Dwyer JH, Feinleib M, Lippert P, Hoffmeister H. *Statistical Models for Longitudinal Studies of Health*. Monographs in Epidemiology and Biostatistics. Vol 16. Oxford University Press, 1992, New York.

Guidelines for reading a Case-Control Study

- I. Statement of Research Question
 - A. Prior Hypothesis?
 - B. Hypothesis Testing or Generating Study?
- II. Why was Case-Control Methodology Chosen?
- III. Methods
 - A. Sources of cases
 - 1. Case Definition/inclusion criteria
 - 2. Incident or prevalent cases?
 - 3. Exclusion criteria
 - 4. Means of Ascertainment
 - B. Sources of controls
 - 1. Exclusion criteria same as cases?
 - 2. Means of ascertainment
 - C. Matching procedure: if used
 - D. Definition of study variables
 - 1. Main effect (dependent variable)
 - 2. Exposure (independent variable)
 - 3. Confounding variables
 - E. Data Collection
 - 1. Method (interview, questionnaire, record review, surrogate)
 - 2. Blinded?
 - 3. Independent validation?
 - F. Estimation of exposure
 - 1. Exposure opportunity
 - 2. Duration/intensity
 - 3. Latency assumptions
- IV. Results/Analysis
 - A. Response/Nonresponse rates
 - B. Comparability of cases and controls
 - C. Analysis
 - 1. Descriptive Methods
 - 2. Measures of effects
 - 3. Dose response
 - D. Sources of confounding
 - 1. Factors considered
 - 2. Means of assessing confounding/interaction
 - E. Sources of bias
 - 1. Information bias
 - 2. Selection bias

- V. Conclusions
 - A. Consistent with the data reported for the main effect of the study?
 - B. Results consistent with the previous literature?
 - C. Interpretations of main effects of the study fully explored?
 - 1. Alternate hypotheses suggested?
 - 2. Study weaknesses and limitations noted?
- VI. Relevance
 - A. Findings new?
 - B. Findings original?
 - C. Finding hypothesis generating?
 - D. Implications for Public Health practice?

References:

1. Schlesselman JJ. Case Control Studies: Design, conduct and analysis. Oxford University Press, 1982, New York.
2. Breslow NE, Day NE. Statistical Methods in Cancer Research: I. The analysis of case-control studies. International Agency for Research on Cancer, 1980, Lyon.
3. Cornfield J. A method of estimating comparative rates from clinical data. Applications to cancer of the lung, breast, and cervix. *J Nat Can Inst* 1951; 11:1269-1275.
4. Dorn H. Some problems arising in prospective and retrospective studies of the etiology of disease. *NEJM* 1959; 261: 571-579.
5. Cole P. The evolving case-control study. *J Chronic Dis* 1979; 32: 15-27.
6. Greenland S, Thomas DC. On the need for the rare disease assumption in case-control studies. *Am J Epidemiol.* 1982; 116: 547-553.
7. Poole C. Exposure opportunity in case-control studies. *Am J Epidemiol* 1986; 122: 352-358.
8. Miettinen OS. Estimability and estimation in case referent studies. *Am J Epidemiol* 1976; 103: 226-234.

Guidelines for reading a Cross-Sectional Study

- I. Statement of research question
 - A. Prior hypothesis?
 - B. Hypothesis testing or generating?
- II. Why was cross-sectional methodology chosen?
- III. Methods
 - A. Source of population
 - 1. Inclusion and exclusion criteria
 - 2. Data sources for exposure and outcome measures
 - B. Definition of study variables
 - 1. Main Effect (dependent variable)
 - 2. Exposure (independent variable)
 - a. Estimation of exposure
 - b. Exposure opportunity
 - c. Duration/intensity; how were chronic exposures handled?
 - d. Latency assumptions
 - C. Confounding Factors
 - D. Data Collection
 - 1. Method (interview, questionnaire, record review, surrogate)
 - 2. Blinded?
 - 3. Independent validation?
 - 4. Repeated measurements?
- IV. Results/Analysis
 - A. Analysis
 - 1. Descriptive methods
 - 2. Measures of effect
 - 3. Dose response
 - B. Sources of confounding
 - 1. Factors considered
 - 2. Means of assessing confounding/interaction
 - C. Sources of bias
 - 1. Information bias
 - 2. Selection bias
- V. Conclusions
 - A. Consistent with the data reported for the main effect of the study?
 - B. Results consistent with the previous literature?
 - C. Interpretations of the main effects of study fully explored?
 - D. Study weaknesses/limitations noted?
- VI. Relevance
 - A. Findings new?
 - B. Findings original?
 - C. Findings hypothesis generating?
 - D. Implications for Public Health practice

Guidelines for reading a Randomized Controlled Clinical Trial

- I. Statement of research question or hypothesis
- II. Was randomized clinical trial methodology appropriate?
- III. Methods
 - A. Definition of study variables
 - 1. Independent variable (clinical intervention)
 - 2. Dependent variable (study outcome)
 - B. Sources of subjects
 - 1. Inclusion criteria
 - 2. Exclusion criteria
 - C. Informed consent prior to randomization
 - D. Means of random assignment
 - E. Sample size estimates reported?
 - F. Trial intervention
 - 1. Nature of clinical intervention
 - 2. Control conditions
 - a. Placebo/reference therapy
 - b. Site and conditions of treatment and follow-up
 - 3. Blinding of patients, investigators, and data analysts?
 - 4. Parallel or crossover design?
 - G. Follow-up
 - 1. Complete in both groups?
 - 2. How were drop-outs handled?
 - a. Intention to treat analysis?
 - b. Comparisons available between those completing the trial and those dropping out?
 - 3. Was compliance measured?
 - H. Were there interval looks at the data and was trial stopped before completion date?
 - 1. Were trial monitors independent?
 - 2. Were investigators blind to interval looks?
- IV. Results/Analysis
 - A. Was randomization successful?
 - B. Are within center and between center results comparable?
 - C. Possible sources of bias.
 - 1. Selection
 - a. Lost to follow-up
 - b. Variations in randomization procedure result in unequal distribution of prognostic factors (potential confounders)
 - c. Protocol variations

2. Measurement
 - a. Blinding incomplete
 - b. Specificity and sensitivity of measures of dependent variable (outcomes)
 - i. Hard vs. soft endpoints
 - ii. Detection or ascertainment bias
 - D. Analysis
 1. Descriptive measures used
 2. Outcomes
 - a. Person-time in trial accounted for
 - b. Main effects
 - c. Ad hoc, secondary analyses
 - d. Dose response reported?
- V. Conclusions
- A. Consistent with the data reported for the main effect of the study?
 - B. Results consistent with previous literature?
 - C. Interpretations of main effects of study fully explored?
 - D. Study weaknesses/limitations noted?
- VI. Relevance
- A. Findings new?
 - B. Findings original?
 - C. Findings hypothesis generating?
 - D. Implications for Public Health practice.

References:

1. Peto R, Pike MC, Armitage P, Breslow NE, Cox DR, Howard SV, Mantel N, McPherson K, Peto J, Smith PG. Design and analysis of randomized clinical trials requiring prolonged observation of each patient: I. Introduction and design. *Br J Cancer* 1976; 34: 585-612.
2. Peto R, Pike MC, Armitage P, Breslow NE, Cox DR, Howard SV, Mantel N, McPherson K, Peto J, Smith PG. Design and analysis of randomized clinical trials requiring prolonged observation of each patient: II. Analysis and examples. *Br J Cancer* 1976; 34: 585-612.
3. Meinert CL. *Clinical trials: Design, conduct, and analysis*. 1986. Oxford University Press, London.
4. Dupont WD. Randomized vs. historical clinical trials: are the benefits worth the costs? *Am J Epidemiol* 1985; 122: 940-946.
5. Sackett DL, Gent M. Controversy in counting and attributing events in clinical trials. *NEJM* 1979; 301: 1410-1412.

Guidelines for reading a Meta-Analysis

- I. Statement of research question or hypothesis
 - A. Did meta-analysis pool data from clinical trials or observational studies?
 - B. Do authors define a specific question involving 5 specific components: population, exposures, outcomes, comparison groups, and study types?
- II. Qualitative Methods
 - A. Literature Search
 1. Is procedure for literature search described?
 2. Do authors account for 'gray' literature (not found in PubMed)?
 3. Is there a documented method for the study identification and selection strategy?
 4. Are inclusion and exclusion criteria for studies adequately described?
 5. Is there a flow diagram enumerating study selection process from initial search to final inclusion?
 - B. Publication Bias
 1. Is issue of publication bias addressed (i.e. that studies with 'positive' or 'significant' results are more likely to be published in journals)
 2. Is there a presentation of a funnel plot showing potential bias?
 - C. Evidence Table
 1. Are key components of identified research presented in a table?
 2. Should include reference, year published, study sample size, setting, and population characteristics.
 3. Exposure and outcome measurements should be described.
 4. Is there a risk estimate (with confidence interval) for the main finding?
 5. Are important adjustment variables or confounders listed?
 - D. Quality Indicators
 1. Do the authors assign scores to studies based on pre-specified criteria?
 2. Does the quality index include indicators of representativeness, validity, reliability, assessment of control of bias and confounding, durations of follow-up, and use of statistical tests and interpretations?
 3. Are the included studies stratified by quality scores?
 4. Are limitations of this method discussed: lack of gold standard, application of subjective scoring, use as weighting index?
 - E. Heterogeneity evaluation
 1. Is it plausible to combine studies that have been selected?
 2. Do the authors discuss study heterogeneity?
 3. Is there a statistical test of heterogeneity (such as a chi-square)?
 4. Are explanations of heterogeneity given, such as chance, exposure and outcome measures, design differences, adjustment factors, and bias?
 - F. Qualitative Synthesis
 1. Do the authors describe the motivation for the meta-analysis?
 2. Is the search strategy and results of it discussed adequately?

3. Are there transparent eligibility criteria for study selection?
 4. Are there presentations of data abstraction and evidence tables?
- III. Quantitative Analysis and Results
- A. Are the risk estimates pooled using similar measures?
 - B. Is there homogeneity among estimates in order to pool results?
 - C. What graphical techniques have been used to represent data?
 1. Forest plots
 2. L'Abbé plots (scatterplots)
 3. Funnel plots
 - D. Do the authors perform sensitivity analyses?
 1. How do the investigators weight their studies?
 2. Do pooled estimate vary using different sensitivity indicators?
 3. Have the authors repeated quantitative analyses with different selections of studies? Different statistical procedures?
 - E. Model Choice
 1. Do the authors use fixed effects models that assume that each study has the same common effect?
 2. Are random effects models employed that assume individual variability among pooled studies?
- IV. Reporting Results
- A. Do the authors present the design and motivating questions?
 - B. Is the protocol for publication search and selection easily duplicated?
 - C. Are results consistent with previous literature? With body of evidence?
 - D. Interpretations of main effects of study fully explored?
 - E. Study weaknesses/limitations noted?
- V. Conclusions and Relevance
- A. Are the findings original and important?
 - B. Do the findings generate further hypotheses?
 - C. Are the implications for public health practice discussed?

References:

1. Petitti DB. *Meta-Analysis, Decision Analysis, and Cost-Effectiveness Analysis: Methods for Quantitative Synthesis in Medicine*, 2nd Edition. New York: Oxford University Press; 2000.
2. Mulrow C and Cook D, editors. *Systematic Reviews: Synthesis of Best Evidence for Health Care Decisions*. Philadelphia, PA: American College of Physicians; 1998.
3. Egger M, Smith GD, Altman DG, editors. *Systematic Reviews in Health Care: Meta-Analysis in Context*, 2nd Edition. London: BMJ Publishing Group; 2001.
4. Goodman SN, Powe N, and Guallar E. *Notes for Course 340.606: Meta-Analysis*. Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology; 2002.