



TEN COMMANDMENTS FOR DEALING WITH CONFOUNDING



- I. Always worry about confounding in your research, especially at the design/protocol stage. Try to use design elements (e.g. randomization) that will help reduce potential confounding.
- II. Prior to the study, review the literature and consider the underlying causal mechanisms (e.g. draw causal diagrams such as directed acyclic graphs [DAGs]). Then make sure you collect data on all potential confounders; otherwise you will not be able to adjust for them in your analyses.
- III. Know your field or collaborate with an expert who does! Subject-matter knowledge is important to recognize (e.g. draw causal diagrams) and adjust for confounding.
- IV. Use *a priori* and data-based methods to check if the potential confounders are indeed confounders that should be adjusted for.
 - V. Use stratified analyses and multivariable methods to handle confounding at the analysis stage. Choose the multivariate model that best suits the type of data (e.g. dichotomous vs. continuous) you collected and the design you employed (e.g. case-control vs. cohort).
- VI. Do not adjust for covariates that may be intermediate causes (on the causal pathway between the exposure and disease). Do not adjust for covariates that may not be genuine confounders. And beware of time-varying covariates that will need special approaches.
- VII. Use matching with great caution. Use analytic methods that are appropriate for the design used; for example, if matching was done, use methods that take matching into account (e.g. conditional logistic regression, matched pairs analyses).
- VIII. Always consider effect measure modification, but perform and interpret subgroup analyses with caution. The subgroup analysis should be one of a small number of hypotheses tested, and the hypothesis should precede rather than follow the analysis (i.e. subgroups must be pre-specified).
- IX. Always remember that adjustment for confounding can be inadequate due to residual confounding because of unmeasured confounders, misclassification of confounders, and inadequate adjustment procedures (e.g. model misspecification, categorization of continuous covariates).
- X. If conventional methods prove to be inadequate, consider using newer approaches such as propensity scores, matched sampling, instrumental variables and marginal structural models. However, make sure you work with statisticians who understand these new methods (not many do).

When all else fails, pray! If prayer fails, consider changing professions!!