

MrOS case-cohort data

Many MrOS studies have utilized a case-cohort design. In these studies, the measure of interest is only obtained in a subset of MrOS participants, some of which (the “subcohort”) were sampled to represent the MrOS cohort and others of which were selected based on their case status. The data from the subcohorts are available on the MrOS data CDs. The data from the additional case groups are released directly to investigators and analysts conducting case-cohort analyses. This document provides an overview of case-cohort designs and the relevant analytical considerations.

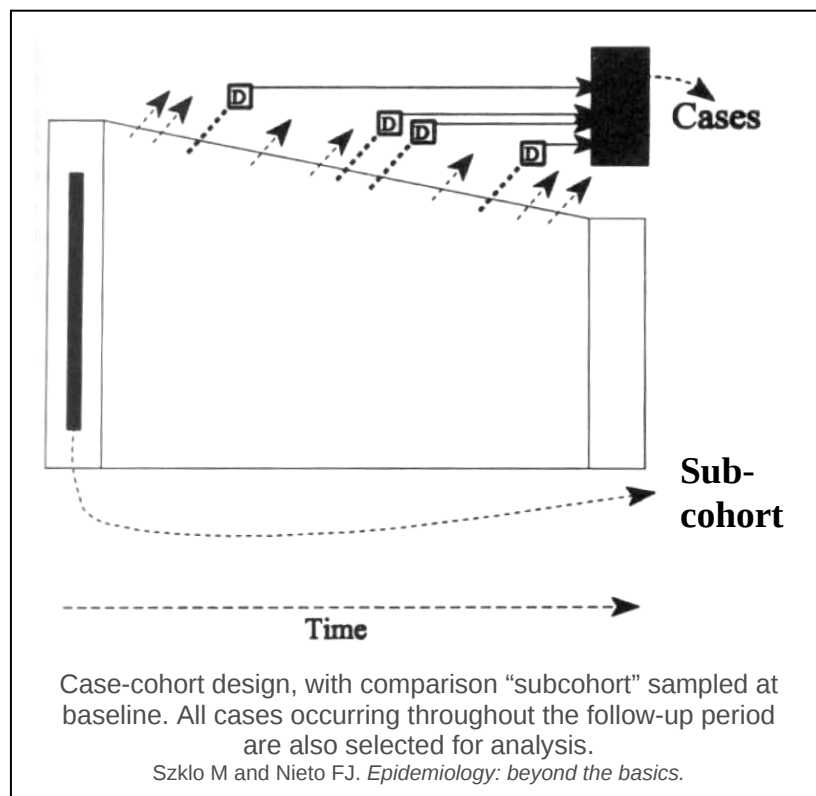
Case-cohort definition and special analytical considerations

The case-cohort study design is used to examine time-to-event outcomes when limited resources prohibit assessment of certain exposure information on all members of a large cohort. In the case-cohort design, members of the cohort who are eligible for follow-up are sampled at baseline in order to represent the person-time experience of the entire cohort. This group is referred to as the subcohort. All cases that subsequently occur during a specified follow-up period—regardless of whether they were included in the subcohort sample—are included in the design as well.

Typically, the subcohort comprises a simple random sample. However, stratified sampling designs can also be employed to ensure that exposure categories with low frequency are adequately represented in the analysis. In MrOS, a random sample of all cohort members was augmented with all additional minority members, forming two strata (random sample and minority sample).

Case-cohort designs can be analyzed using Cox proportional hazards models. However,

special consideration must be made for the additional case group that is added at the moment of their “event” (e.g., fracture or death). Person-time is therefore weighted in the Cox model partial likelihood, which is known as a ‘pseudo-likelihood’ for the case-cohort design (1). Methods of weighting vary in their treatment of cases that occur outside the randomly selected subcohort, as well as by whether the probability of selection into the subcohort is incorporated into weights. Weighting methods are described in detail in references (1, 2). Robust variance estimates for Cox proportional hazards models using these weights can be calculated using the ROBVAR macro referenced in (1) or the



COVSANDWICH option in PROC PHREG. Note that the COVSANDWICH option requires installation of SAS 9.1.3 Service Pack 4. (Previous versions give erroneous robust variance results.) Analysts at the Administrative Center can provide sample code and are available to assist with the analytic approach and selection of weights.

References

1. Barlow WE, Ichikawa L, Rosner D, et al. Analysis of case-cohort designs. *J Clin Epidemiol* 1999;52:1165-72.
2. Borgan O, Langholz B, Samuelsen SO, et al. Exposure stratified case-cohort designs. *Lifetime Data Anal* 2000;6:39-58.