DESIGN OF OBSERVATIONAL LONGITUDINAL STUDIES WITH A TIME-VARYING EXPOSURE

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Existing study design formulas for longitudinal studies assume that the exposure is time-invariant or that it varies in a manner that is controlled by design. However, in observational studies, the investigator does not control how exposure varies within subjects over time. Typically, a large number of exposure patterns are observed, with large differences in the number of exposed periods per participant and changes in the cross-sectional prevalence of exposure over time. We developed formulas for study design calculations that address these issues for studies with a continuous outcome and a binary, time-varying exposure. We covered studies where the interest is the effect of a time-varying exposure on either the mean levels of the response or on the rate of change of the response over time. It is shown that, in some cases, the mean prevalence and the intraclass correlation of exposure are the only two additional parameters that need to be provided to obtain exact solutions for the required sample size. Even when these two parameters, for which an investigator can reasonably provide plausible values, do not suffice to produce exact solutions, they provide good approximations. The effects of having a time-varying exposure on efficiency are also studied. In particular, it is shown that, when the interest is in comparing the mean response levels according to exposure, studies with a time-varying exposure may have substantial gains in efficiency. On the other hand, for studies comparing rates of change, there are circumstances where having a time-varying exposure can produce substantial losses in efficiency. Therefore, the use of the existing study design formulas for time-invariant exposure is discouraged if the exposure is believed to change over time within participants. We developed user-friendly software that implements our formulas and covers a wide range of common scenarios. This software is publicly available at
http://www.hsph.harvard.edu/faculty/spiegelman/optitxs.html