There are no translations available.

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Models for Survival in Matched Pairs

Co-twin control designs are useful in identification of causal effects and have been applied to a vast number of different research questions within the fields of epidemiology and psychology. The logic of the co-twin control design assumes that twins who have been brought up together are matched on early environmental factors. Moreover, twins have partly or fully identical genetic setups at birth, depending on their zygosity. This implies that a number of factors - that are usually diffcult to measure - are held constant in within-pair comparisons. Hence confounding from these factors is controlled for per design thus providing less biased estimates of effect. Aside from confounder control, the differences in genetic relatedness between monozygotic (MZ) (genetically identical) and dizygotic (DZ) twins (share on average half of segregating genes) can be used for the purpose of making inferences about the source of confounding, i.e. genetic or environmental confounding, respectively. Assuming an association in the unpaired analysis, genetic confounding would be indicated if the within-pair analysis showed a partial attenuation of the association in DZ twins and a full attenuation in the MZ twins. Similarly, a full attenuation in both DZ and MZ twins would be compatible with shared environmental confounding. Finally to support a causal effect of exposure the association would have to persist in both DZ and MZ twins.

An application of the co-twin control design will be presented using a Danish twin study of the effect of education on breast cancer incidence (Madsen et al, 2011). Furthermore, I will discuss which survival models are appropriate to use in this context. One possibility is to use a shared frailty model. However, inference in the frailty model requires independence between the frailty variable and the explanatory variables (education in the above example). We study how violations of this assumption affects inference for the regression coeffcients, and conclude that substantial bias may occur.

Instead, we propose making inference by means of a stratified Cox model (Holt and Prentice, 1974) and we demonstrate that this model gives unbiased estimates regardless of a possible dependence between the frailty variable and the explanatory variable.

References: Madsen, M, Andersen PK, Gerster, M, Andersen, A-MN (2011). Education and incidence of breast cancer: Does the association replicate within twin pairs?, Br. J. Cancer, 104, 520-523. Holt, JD, Prentice, RL (1974). Survival analysis in twin studies and matched pairs experiments. Biometrika, 61, 17-30.