Principal stratification (Frangakis and Rubin 2002) generalizes the binary Z/binary M studied in the previous lesson. This provides a general development of estimation within latent subpopulations (called principal strata) defined by post-treament potential outcomes.

One can estimate "principal stratum" effects

$$E(Y_i(1, M_i(1)) - Y_i(0, M_i(0)) \mid (M_i(0), M_i(1)) \in \mathcal{M})$$

 $E(Y_i(1, M_i(1)) - Y_i(0, M_i(0)) \mid (M_i(0), M_i(1)) \in \mathcal{M}, \mathbf{X}_{\flat}),$

where $\mathcal{M} \subset \Omega_M$.

These effects do not require the potential outcomes $Y_i(z, m)$ to be well defined.

Recall the case where the intermediate outcome M_i indexed whether or not a subject took up the assigned treatment or not. Under the exclusion restriction and the monotonicity condition, $M_i(1) \ge M_i(0)$, we saw the ITT,

$$E(Y_i(1, M_i(1)) - Y_i(0, M_i(0)) =$$

$$\sum_{m(1)=0}^{1} \sum_{m(0)=0}^{1} E(Y_i(1, M_i(1)) - Y_i(0, M_i(0)) \mid M_i(0) = m(0), M_i(1) = m(1)) \times$$

$$Pr(M_i(0) = m(0), M_i(1) = m(1))$$

reduced to the product of the CACE $E(Y_i(1, M_i(1)) - Y_i(0, M_i(0)) \mid M_i(0) = 0, M_i(1) = 1)$ and the complier probability $Pr(M_i(0) = 0, M_i(1) = 1)$.

More generally, M_i may have multiple categories or be continuous. Assignment to Z_i may depend on covariates \mathbf{X}_i and/or the investigator may be interested in treatment effects that vary with \mathbf{X}_i .

Consider the following question: Does coronary bypass surgery improve a subject's quality of life? We want to compare a subject's quality of life when he/she undergoes surgery with the quality of life when he/she foregoes bypass surgery.

A problem immediately arises. We can only ascertain the quality of life for subjects who survive. Let $Z_i = 1$ if subject i receives surgery, 0 otherwise, and let $M_i = 1$ if i survives, 0 otherwise. One solution is to simply define the quality of life as 0 for subjects who do not survive, but this seems arbitrary, hard to justify in general.

Another solution is to compare the survivors who received surgery with the survivors who did not. e.g. $E(Y \mid Z_i = 1, M_i = 1) - E(Y \mid Z_i = 0, M_i = 1)$.

But when assignment to Z_i is randomized, comparison $E(Y_i(1, M_i(1)) \mid M_i(1) = 1) - E(Y_i(0, M_i(0)) \mid M_i(0) = 1)$ is only descriptive. A causal comparison requires addition assumptions, e.g. assuming survival status M_i is conditionally independent of potential outcomes $Y_i(z, m)$.

However, if attention is confined to those who survive under either condition, we obtain estimand $E(Y_i(1, M_i(1)) - Y_i(0, M_i(0)) | M_i(0) = M_i(1) = 1)$. This is the so-called survivor causal effect. See Page, Feller, Grindall, Miratrix and Somers (2015).

The monotonicity assumption $M_i(1) \ge M_i(0)$ is often made to identify principal stratum effects. In many contexts this is reasonable, especially in randomized studies where the treatment is designed to operate through a mediating variable.

e.g. in a study of test outcomes, one might be willing to assume that a student studies more when encouraged to study than when not. n.b. the mediator here is continuous.

e.g. in a study of fitness, a subject assigned to an exercise program or a diet may be more likely to exercise more or diet more than had he/she not been assigned.

In some instances, it will also be reasonable to assume there is no effect on the outcome in strata with $M_i(0) = M_i(1)$.

More assumptions are required to identify causal effects within principal strata when M_i takes on more than two values.

e.g. if M_i takes 3 ordered values 0,1,2, there are 3 principal strata with $M_i(1) < M_i(0)$. Then, assuming monotonicity, 5 of the 9 principal stratum probabilities are identified, but without at least one additional restriction, the remaining probabilities are not. Further restrictions on the values of the principal strata effects may still be needed.

e.g. suppose we knew the principal strata probabilities. Then by the monotonicity condition, $Pr(M_i(0) = 0, M_i(1) = 0)) = Pr(M_i(1) = 0)$, so the principal stratum effect in this stratum is identified; similarly $Pr(M_i(0) = M_i(1) = 2) = Pr(M_i(0) = 2)$ so the principal stratum effect is identified in this stratum. However, it can be shown that the remaining principal stratum effects are not identified without imposing further restrictions on the effects.

When *M* takes more than 3 values, identification relies on even stronger assumptions. For continuous outcomes, one might use parametric mixture models with covariates. See see Jin and Rubin (2008) and Joffe, Small and Hsu (2007).