TESTING EQUALITY OF MEANS IN PARTIALLY MATCHED DATA

**Introduction**

It is common in biostatistics to test the equality of two means. In study designs with two independent, normally distributed samples, the two-sample *t*-test is appropriate. In study designs with two *paired* samples, at least two approaches are available. First, the one-sample *t*-test can be used on the unit-level differences between the first measurement and the second measurement. Second, although less routine, the two-sample *t*-test modified for correlated data can be used, assuming the correlation coefficient is known or estimated (Zimmerman 2012). This second approach can yield improved power compared to the first, as the test statistic has 2*n* – 2 degrees of freedom rather than *n* – 1.

Some study designs may include a hybrid of independent samples and repeated measures. For example, a subset of participants in a drug trial may be lost to follow-up, precluding the calculation of difference scores, but the remainder of participants may have pre- and post-intervention measurements available. Such designs have been called partially paired (Guo and Yuan 2017), or partially correlated (Samawi and Vogel 2014).

Recently, methods have been proposed to evaluate the equality of means in study designs with partially paired data (Lin and Stivers 1974, Samawi and Vogel 2014, Guo and Yuan 2017). Such methods involve tests based on modified maximum likelihood, multiple imputation, or pooling statistics across the paired and unpaired subsets of data.

A separate type of disconnected data called *unmatched data* arise in paired or repeated measures study designs when unit-level identifiers have been lost or withheld, sometimes in the interest of anonymity. For example, an online survey is administered anonymously to an employee pool, with each employee submitting a response before and after an intervention. The feature of this dataset that would qualify it as unmatched is the absence of any identifier that could link one employee’s response from pre-intervention to the same employee’s response post-intervention. For convenience, we refer to such study designs as *paired but unmatched.* Study designs with paired but unmatched observations have received relatively less attention.

Data from paired but unmatched studies present a challenge for testing the equality of means. The one-sample *t*-test cannot be used, due to the inability to match samples and calculate difference scores. Using the two-sample ­*t*-test is equivalent to assuming samples are uncorrelated, which is often an unrealistic assumption of repeated measures data in biostatistics. An alternative approach involves calculating the minimum possible correlation coefficient given the observed data; this value can be used as the estimated correlation in the two-sample *t*-test modified for correlated data. However, this approach yields a maximally conservative test statistic and thus is poorly powered.

In cases where even a small number of observations can be matched, an opportunity exists to construct a test for mean differences that uses the matched pairs to inform an estimate of the correlation between all pairs. We refer to the study design in which observations are paired but only some observations are matched as *paired but partially matched,* or more concisely, *partially matched*. In this work, we show that several methods can powerfully test for the equality of means in partially matched data, while controlling Type I error rates at a nominal level.

**Methods**

Part A: Simulation study

Part B: Real world application