**eAPPENDICES**

**Generalized Difference-in-Differences**

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eAPPENDIX 1. Identification of the treatment effect.

eAPPENDIX 2. Example computer code.

eAPPENDIX 3. Additional simulations.

eAPPENDIX 1. Identification of the treatment effect.

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Graphical user interface, text, application

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eAPPENDIX 2. Example computer code.

*SAS code for a generalized DID estimator.*

We assume an exposure variable of primary interest (A), covariate (Z1), and outcome variables (Y0 and Y1) measured at times 0 and 1, respectively. In the example, the original dataset is named *ONE*.

\* Calculate difference between post- and pre-treatment outcomes;

**data** TWO;

set ONE;

DIFFY=Y1-Y0;

\*Fit proposed generalized DID;

**proc** **model** data=TWO;

exogenous Z1;

endogenous A DIFFY;

DIFFY = p0 + p1 \*A;

A = intercep + p2\*Z1;

fit DIFFY A / n2sls FSRSQ;

instruments Z1; **run**;

*R code for a generalized DID estimator*

We assume an exposure variable of primary interest (a), covariate (z1), and outcome variables (y\_pre and y\_post) measured at times 0 and 1, respectively.

library(ivreg)

library(lmtest)

library(sandwich)

gdid<-function(y\_pre,y\_post,a,z1,robust.se=FALSE){

y\_diff<-y\_post-y\_pre

fit\_gdid<-ivreg(y\_diff~a|z1)

if(robust.se==TRUE){

se<-coeftest(fit\_gdid, vcov = vcovHC, type = "HC3")[2,2]

}else{

se<-summary(fit\_gdid)$coefficients[2,2]

}

return(list(est=summary(fit\_gdid)$coefficients[2,1],

se=se,

f.statistic=summary(fit\_gdid)$diagnostic[1,3]))

}

eAPPENDIX 3. Additional simulations.

Additional simulations were conducted. In each scenario, we considered respectively the case when *Z*1 is strongly *(*=2)*, moderately (*=1)*, and* weakly *(*=0.4)associated with *A.*

In simulation A1, *U*1 affected *Z*1, but otherwise the simulation conformed to the ‘parallel trends’ assumption in simulation scenario 1. We generated an unmeasured covariate, denoted *U*1, as a random binary variable. *U*1 affected the measured covariate, denoted *Z*1, which was a random variable with probability 0.4+0.2 *U*1. We assigned *A* as a random binary variable that took a value of 1 with probability 1/(1+exp(-(-0.1 -0.5×*U*1 +×*Z*1))). The pre-treatment outcome variable, *Y*(*t*=0), took a value of (1 +1×*U*1 +1×*Z*1 + *ε*), where *ε* ~*N*(0,1); and, the post-treatment outcome variable, *Y*(*t*=1), took a value of (1 +1×*U*1 +1×*Z*1 +1×*A*+ *ε*).

In simulation A2, *U*1 affected *Z*1, but otherwise conformed to the second scenario, which violated the ‘parallel trends’ assumption. We generated an unmeasured covariate, denoted *U*1, as a random binary variable. *U*1 affected the measured covariate, denoted *Z*1, which was a random variable with probability 0.4+0.2 *U*1. We generated an additional covariate, denoted *U*2, that was a continuous variable assigned by sampling from a normal (0,1) distribution. We assigned *A* as a random binary variable that took a value of 1 with probability 1/(1+exp(-(-0.1 -0.5×*U*1 -0.5×*U*2 +×*Z*1))). The pre-treatment outcome, *Y*(*t*=0), took a value of (1 +1×*U*1 +1×*U*2 +1×*Z*1 + *ε*); and, the post-treatment outcome, *Y*(*t*=1), took a value of (1 +1×*U*1 +1×*Z*1 +1×*A*+ *ε*).

In simulation A3, *U*2 affected *Z*1, but otherwise conformed to the second scenario, which violated the ‘parallel trends’ assumption. We generated an unmeasured covariate, denoted *U*1, as a random binary variable. We generated an additional covariate, denoted *U*2, that was a continuous variable assigned by sampling from a normal (0,1) distribution. *U*2 affected the measured covariate, denoted *Z*1, which was a random variable with probability 1/(1+exp(-(-0.5+0.5 *U*2). We assigned *A* as a random binary variable that took a value of 1 with probability 1/(1+exp(-(-0.1 -0.5×*U*1 -0.5×*U*2 +×*Z*1))). The pre-treatment outcome, *Y*(*t*=0), took a value of (1 +1×*U*1 +1×*U*2 +1×*Z*1 + *ε*); and, the post-treatment outcome, *Y*(*t*=1), took a value of (1 +1×*U*1 +1×*Z*1 +1×*A*+ *ε*).

eTable. Monte Carlo mean, standard deviation (SD), and root MSE (RMSE), average standard error (SE), and coverage probability (CP) of 95% asymptotic confidence interval for 1000 cohorts with 5,000 observations each. Results of simulations of association between exposure, *A*, measured covariate, *Z*, unmeasured covariate, *U*, and outcome, *Y*.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Scenario | Mean | SD | RMSE | SE | CP |
| **Scenario A1**  *Strong bespoke IV (Mean F-statistic 1050.5)* |  |  |  |  |  |
| GDID method  Standard DID method | 1.00  1.00 | 0.10  0.04 | 0.10  0.04 | 0.10  0.04 | 95.1  96.1 |
|  |  |  |  |  |  |
| *Moderate bespoke IV (Mean F-statistic 248.7)* |  |  |  |  |  |
| GDID method | 1.00 | 0.18 | 0.18 | 0.19 | 95.3 |
| Standard DID method  *Weak bespoke IV (Mean F-statistic 27.8)*  GDID method  Standard DID method | 1.00  1.00  1.00 | 0.04  0.58  0.04 | 0.04  0.58  0.04 | 0.04  0.59  0.04 | 95.3  97.1  95.7 |
| **Scenario A2**  *Strong bespoke IV (Mean F-statistic 956.0)* |  |  |  |  |  |
| GDID method  Standard DID method | 1.00  1.39 | 0.13  0.05 | 0.13  0.40 | 0.13  0.05 | 95.6  0.0 |
|  |  |  |  |  |  |
| *Moderate bespoke IV (Mean F-statistic 223.4)* |  |  |  |  |  |
| GDID method | 1.00 | 0.24 | 0.24 | 0.24 | 96.1 |
| Standard DID method  *Weak bespoke IV (Mean F-statistic 25.2)*  GDID method  Standard DID method | 1.45  0.97  1.47 | 0.05  0.77  0.05 | 0.45  0.77  0.47 | 0.05  0.77  0.05 | 0.0  97.1  0.0 |
|  |  |  |  |  |  |
| **Scenario A3**  *Strong bespoke IV (Mean F-statistic 744.9)*  GDID method  Standard DID method | -0.30  1.22 | 0.15  0.05 | 1.30  0.22 | 0.15  0.05 | 0.0  0.7 |
| *Moderate bespoke IV (Mean F-statistic 151.1)* |  |  |  |  |  |
| GDID method | -1.71 | 0.38 | 2.74 | 0.39 | 0.0 |
| Standard DID method  *Weak bespoke IV (Mean F-statistic 7.8)*  GDID method  Standard DID method | 1.35  -15.68  1.42 | 0.05  55.78  0.05 | 0.35  58.20  0.42 | 0.05  99.61  0.05 | 0.0  28.8  0.0 |