

SUPPLEMENTARY MATERIAL FOR ONLINE PUBLICATION

for

“Toward Evaluation of Disseminated Effects of Medications for
Opioid Use Disorder within Provider-Based Clusters Using
Routinely-Collected Health Data”

April 12, 2022

Appendix: Supplemental Tables and Figures

Table A1: Cumulative incidence of overdose in Optum's de-identified Clinformatics® Data Mart Database, 2010-2015, United States

MOUD Coverage	All patients			
	Total Person	Overdose	Cum Inc (%)	(95%CI)
$\leq 33\%$	459	19	4.14	(2.3, 5.9)
$> 33\% - \leq 50\%$	605	25	4.13	(2.5, 5.7)
$> 50\%$	1,209	39	3.2	(2.2, 4.2)
All	2,273	83	3.7	(2.9, 4.5)

Table A2: Simulation results with equal cluster sizes for direct, disseminated, composite and overall effects with different distributions for the random intercepts in the cluster-level propensity score model for 1000 simulated data sets.^a

Estimand	Truth	Horvitz-Thompson				Hájek						
		IPW	%Bias	ESE	ASE	CP	Truth	IPW	%Bias	ESE	ASE	CP
Normal												
DE(0.33)	0.0127	0.0164	-0.2916	0.0122	0.0117	0.925	0.0127	0.0128	-0.0107	0.0119	0.0118	0.942
IE(0.33, 0.5)	0.0042	0.0057	-0.3703	0.0040	0.0038	0.927	0.0042	0.0040	0.0449	0.0036	0.0036	0.930
TE(0.33, 0.5)	0.0125	0.0159	-0.2657	0.0114	0.0108	0.926	0.0125	0.0126	-0.0019	0.0110	0.0107	0.941
OE(0.33, 0.5)	0.0042	0.0054	-0.2928	0.0035	0.0033	0.940	0.0042	0.0040	0.0290	0.0031	0.0030	0.931
DE(0.5)	0.0084	0.0101	-0.2136	0.0100	0.0095	0.928	0.0084	0.0086	-0.0252	0.0101	0.0099	0.941
IE(0.5, 0.67)	0.0040	0.0051	-0.2818	0.0036	0.0034	0.925	0.0040	0.0038	0.0469	0.0035	0.0033	0.941
TE(0.5, 0.67)	0.0082	0.0094	-0.1395	0.0097	0.0092	0.941	0.0082	0.0083	-0.0116	0.0097	0.0094	0.942
OE(0.5, 0.67)	0.0027	0.0029	-0.0909	0.0026	0.0025	0.944	0.0027	0.0025	0.0409	0.0025	0.0024	0.944
DE(0.67)	0.0042	0.0043	-0.0054	0.0094	0.0090	0.945	0.0042	0.0045	-0.0667	0.0097	0.0095	0.946
IE(0.33, 0.67)	0.0082	0.0108	-0.3270	0.0073	0.0070	0.925	0.0082	0.0078	0.0459	0.0069	0.0066	0.938
TE(0.33, 0.67)	0.0124	0.0151	-0.2172	0.0111	0.0105	0.934	0.0124	0.0123	0.0074	0.0106	0.0102	0.933
OE(0.33, 0.67)	0.0068	0.0083	-0.2143	0.0058	0.0055	0.940	0.0068	0.0066	0.0336	0.0054	0.0052	0.944
Right Skewed												
DE(0.33)	0.0127	0.0153	-0.2090	0.0117	0.0116	0.941	0.0127	0.0124	0.0181	0.0114	0.0113	0.940
IE(0.33, 0.5)	0.0042	0.0055	-0.3159	0.0039	0.0037	0.934	0.0042	0.0042	-0.0079	0.0036	0.0034	0.938
TE(0.33, 0.5)	0.0125	0.0152	-0.2168	0.0107	0.0107	0.948	0.0125	0.0123	0.0172	0.0103	0.0104	0.947
OE(0.33, 0.5)	0.0042	0.0053	-0.2748	0.0033	0.0032	0.952	0.0042	0.0041	0.0134	0.0030	0.0030	0.935
DE(0.5)	0.0084	0.0098	-0.1675	0.0095	0.0094	0.946	0.0084	0.0081	0.0297	0.0095	0.0095	0.940
IE(0.5, 0.67)	0.0040	0.0053	-0.3314	0.0034	0.0033	0.919	0.0040	0.0039	0.0109	0.0033	0.0032	0.938
TE(0.5, 0.67)	0.0082	0.0091	-0.1122	0.0091	0.0091	0.947	0.0082	0.0080	0.0292	0.0091	0.0091	0.939
OE(0.5, 0.67)	0.0027	0.0030	-0.1314	0.0024	0.0025	0.954	0.0027	0.0026	0.0176	0.0023	0.0024	0.952
DE(0.67)	0.0042	0.0038	0.0946	0.0091	0.0089	0.937	0.0042	0.0040	0.0465	0.0093	0.0091	0.938
IE(0.33, 0.67)	0.0082	0.0108	-0.3234	0.0071	0.0068	0.933	0.0082	0.0081	0.0013	0.0067	0.0064	0.944
TE(0.33, 0.67)	0.0124	0.0146	-0.1807	0.0104	0.0104	0.950	0.0124	0.0122	0.0167	0.0099	0.0100	0.943
OE(0.33, 0.67)	0.0068	0.0083	-0.2191	0.0054	0.0055	0.955	0.0068	0.0067	0.0150	0.0050	0.0051	0.946
Left Skewed												
DE(0.33)	0.0127	0.0172	-0.3550	0.0122	0.0120	0.927	0.0127	0.0129	-0.0172	0.0119	0.0116	0.943
IE(0.33, 0.5)	0.0042	0.0066	-0.5916	0.0039	0.0039	0.937	0.0042	0.0045	-0.0714	0.0035	0.0036	0.956
TE(0.33, 0.5)	0.0125	0.0165	-0.3202	0.0110	0.0110	0.945	0.0125	0.0129	-0.0297	0.0106	0.0106	0.947
OE(0.33, 0.5)	0.0042	0.0059	-0.4218	0.0033	0.0034	0.942	0.0042	0.0045	-0.0753	0.0030	0.0031	0.951
DE(0.5)	0.0084	0.0099	-0.1849	0.0098	0.0096	0.941	0.0084	0.0084	-0.0089	0.0099	0.0097	0.935
IE(0.5, 0.67)	0.0040	0.0055	-0.3737	0.0034	0.0035	0.938	0.0040	0.0043	-0.0718	0.0033	0.0034	0.959
TE(0.5, 0.67)	0.0082	0.0093	-0.1268	0.0093	0.0092	0.937	0.0082	0.0084	-0.0207	0.0093	0.0093	0.941
OE(0.5, 0.67)	0.0027	0.0031	-0.1553	0.0024	0.0025	0.948	0.0027	0.0028	-0.0581	0.0023	0.0024	0.945
DE(0.67)	0.0042	0.0038	0.1061	0.0092	0.0090	0.934	0.0042	0.0041	0.0274	0.0095	0.0093	0.937
IE(0.33, 0.67)	0.0082	0.0121	-0.4850	0.0070	0.0072	0.933	0.0082	0.0087	-0.0716	0.0066	0.0068	0.960
TE(0.33, 0.67)	0.0124	0.0159	-0.2832	0.0106	0.0107	0.945	0.0124	0.0129	-0.0378	0.0101	0.0102	0.947
OE(0.33, 0.67)	0.0068	0.0090	-0.3183	0.0055	0.0056	0.942	0.0068	0.0073	-0.0686	0.0051	0.0052	0.957
Bimodal												
DE(0.33)	0.0127	0.0158	-0.2493	0.0121	0.0116	0.936	0.0127	0.0126	0.0032	0.0118	0.0114	0.946
IE(0.33, 0.5)	0.0042	0.0054	-0.2975	0.0037	0.0037	0.939	0.0042	0.0039	0.0540	0.0034	0.0034	0.940
TE(0.33, 0.5)	0.0125	0.0157	-0.2505	0.0111	0.0106	0.937	0.0125	0.0125	0.0050	0.0108	0.0104	0.936
OE(0.33, 0.5)	0.0042	0.0053	-0.2758	0.0033	0.0032	0.940	0.0042	0.0040	0.0381	0.0030	0.0030	0.924
DE(0.5)	0.0084	0.0103	-0.2271	0.0100	0.0095	0.938	0.0084	0.0085	-0.0194	0.0100	0.0096	0.934
IE(0.5, 0.67)	0.0040	0.0052	-0.2987	0.0033	0.0033	0.937	0.0040	0.0038	0.0533	0.0032	0.0032	0.945
TE(0.5, 0.67)	0.0082	0.0096	-0.1652	0.0097	0.0091	0.938	0.0082	0.0083	-0.0104	0.0097	0.0092	0.934
OE(0.5, 0.67)	0.0027	0.0030	-0.1313	0.0026	0.0025	0.932	0.0027	0.0026	0.0341	0.0025	0.0024	0.930
DE(0.67)	0.0042	0.0044	-0.0393	0.0095	0.0090	0.938	0.0042	0.0045	-0.0705	0.0097	0.0093	0.933
IE(0.33, 0.67)	0.0082	0.0106	-0.2981	0.0068	0.0067	0.940	0.0082	0.0077	0.0536	0.0064	0.0064	0.944
TE(0.33, 0.67)	0.0124	0.0150	-0.2097	0.0109	0.0103	0.934	0.0124	0.0123	0.0113	0.0104	0.0100	0.933
OE(0.33, 0.67)	0.0068	0.0083	-0.2197	0.0056	0.0054	0.938	0.0068	0.0066	0.0365	0.0052	0.0051	0.937

^a IPW = Mean of inverse probability weighted estimates; ESE = empirical standard error; ASE = average estimated standard error; CP = empirical coverage probability).

Table A3: Simulation results with unequal cluster sizes for direct, disseminated, composite and overall effects with different distributions for the random intercepts in the cluster-level propensity score model for 1000 simulated data sets.^a

Estimand	Truth	Horvitz-Thompson				Hájek						
		IPW	%Bias	ESE	ASE	CP	Truth	IPW	%Bias	ESE	ASE	CP
Normal												
DE(0.33)	0.0132	0.0165	-0.2500	0.0123	0.0122	0.939	0.0132	0.0116	0.1212	0.0124	0.0134	0.945
IE(0.33, 0.5)	0.0039	0.0051	-0.3333	0.0036	0.0036	0.948	0.0039	0.0042	-0.0769	0.0045	0.0053	0.959
TE(0.33, 0.5)	0.0132	0.0163	-0.2424	0.0115	0.0114	0.943	0.0132	0.0116	0.1212	0.0111	0.0120	0.930
OE(0.33, 0.5)	0.0042	0.0053	-0.2619	0.0033	0.0032	0.935	0.0042	0.0040	0.0238	0.0038	0.0044	0.932
DE(0.5)	0.0093	0.0112	-0.2043	0.0105	0.0103	0.938	0.0093	0.0074	0.2043	0.0099	0.0102	0.930
IE(0.5, 0.67)	0.0037	0.0046	-0.2162	0.0034	0.0033	0.929	0.0037	0.0039	-0.0270	0.0043	0.0043	0.934
TE(0.5, 0.67)	0.0092	0.0107	-0.1522	0.0101	0.0100	0.937	0.0092	0.0075	0.1848	0.0095	0.0097	0.929
OE(0.5, 0.67)	0.0028	0.0031	-0.1071	0.0026	0.0025	0.948	0.0028	0.0026	0.0357	0.0031	0.0030	0.927
DE(0.67)	0.0055	0.0061	-0.1091	0.0099	0.0098	0.940	0.0055	0.0037	0.3455	0.0093	0.0095	0.930
IE(0.33, 0.67)	0.0076	0.0097	-0.2763	0.0068	0.0067	0.931	0.0076	0.0081	-0.0658	0.0079	0.0088	0.947
TE(0.33, 0.67)	0.0131	0.0158	-0.2061	0.0112	0.0111	0.940	0.0131	0.0117	0.1069	0.0106	0.0115	0.928
OE(0.33, 0.67)	0.0069	0.0083	-0.2029	0.0056	0.0055	0.947	0.0069	0.0067	0.0290	0.0061	0.0067	0.922
Right Skewed												
DE(0.33)	0.0132	0.0589	-3.4545	0.0178	0.0172	0.271	0.0132	0.0347	-1.6212	0.0155	0.0160	0.585
IE(0.33, 0.5)	0.0039	0.0033	0.1282	0.0044	0.0045	0.943	0.0039	0.0038	0.0256	0.0036	0.0040	0.955
TE(0.33, 0.5)	0.0132	0.0592	-3.4848	0.0159	0.0155	0.178	0.0132	0.0327	-1.4773	0.0133	0.0140	0.602
OE(0.33, 0.5)	0.0042	0.0118	-1.8333	0.0041	0.0041	0.536	0.0042	0.0064	-0.5476	0.0033	0.0035	0.916
DE(0.5)	0.0093	0.0559	-5.0108	0.0142	0.0137	0.132	0.0093	0.0289	-2.1075	0.0121	0.0124	0.527
IE(0.5, 0.67)	0.0037	0.0033	0.1081	0.0044	0.0045	0.945	0.0037	0.0046	-0.2432	0.0034	0.0034	0.953
TE(0.5, 0.67)	0.0092	0.0556	-5.0326	0.0126	0.0123	0.049	0.0092	0.0266	-1.8913	0.0101	0.0108	0.564
OE(0.5, 0.67)	0.0028	0.0104	-2.7143	0.0031	0.0031	0.267	0.0028	0.0051	-0.8214	0.0027	0.0028	0.886
DE(0.67)	0.0055	0.0522	-8.4909	0.0121	0.0117	0.037	0.0055	0.0220	-3.0000	0.0097	0.0103	0.558
IE(0.33, 0.67)	0.0076	0.0067	0.1184	0.0088	0.0089	0.943	0.0076	0.0084	-0.1053	0.0069	0.0074	0.956
TE(0.33, 0.67)	0.0131	0.0589	-3.4962	0.0145	0.0143	0.097	0.0131	0.0304	-1.3206	0.0116	0.0126	0.666
OE(0.33, 0.67)	0.0069	0.0222	-2.2174	0.0070	0.0069	0.399	0.0069	0.0115	-0.6667	0.0057	0.0060	0.904
Left Skewed												
DE(0.33)	0.0132	0.0626	-3.7348	0.0240	0.0221	0.304	0.0132	0.0267	-1.0227	0.0198	0.0178	0.689
IE(0.33, 0.5)	0.0039	0.0058	-0.4872	0.0057	0.0056	0.928	0.0039	0.0025	0.3333	0.0039	0.0039	0.931
TE(0.33, 0.5)	0.0132	0.0623	-3.7197	0.0211	0.0199	0.265	0.0132	0.0244	-0.8561	0.0162	0.0153	0.808
OE(0.33, 0.5)	0.0042	0.0134	-2.1905	0.0051	0.0050	0.574	0.0042	0.0048	-0.1429	0.0035	0.0036	0.947
DE(0.5)	0.0093	0.0565	-5.0753	0.0193	0.0177	0.236	0.0093	0.0219	-1.3548	0.0156	0.0143	0.694
IE(0.5, 0.67)	0.0037	0.0055	-0.4595	0.0057	0.0056	0.930	0.0037	0.0037	0.0270	0.0038	0.0038	0.938
TE(0.5, 0.67)	0.0092	0.0556	-5.0326	0.0168	0.0159	0.174	0.0092	0.0197	-1.1304	0.0124	0.0121	0.829
OE(0.5, 0.67)	0.0028	0.0108	-2.8571	0.0038	0.0037	0.425	0.0028	0.0039	-0.4286	0.0029	0.0030	0.947
DE(0.67)	0.0055	0.0501	-8.1091	0.0166	0.0154	0.179	0.0055	0.0160	-1.9091	0.0125	0.0119	0.811
IE(0.33, 0.67)	0.0076	0.0112	-0.4737	0.0114	0.0111	0.930	0.0076	0.0062	0.1842	0.0077	0.0076	0.938
TE(0.33, 0.67)	0.0131	0.0613	-3.6794	0.0188	0.0182	0.213	0.0131	0.0222	-0.6947	0.0132	0.0132	0.898
OE(0.33, 0.67)	0.0069	0.0242	-2.4928	0.0086	0.0085	0.475	0.0069	0.0087	-0.2609	0.0060	0.0062	0.953
Bimodal												
DE(0.33)	0.0132	0.0161	-0.2121	0.0126	0.0122	0.941	0.0132	0.0114	0.1439	0.0109	0.0108	0.944
IE(0.33, 0.5)	0.0039	0.0049	-0.2821	0.0036	0.0035	0.928	0.0039	0.0036	0.0513	0.0040	0.0037	0.944
TE(0.33, 0.5)	0.0132	0.0163	-0.2424	0.0116	0.0113	0.944	0.0132	0.0113	0.1364	0.0098	0.0098	0.943
OE(0.33, 0.5)	0.0042	0.0053	-0.2857	0.0033	0.0032	0.947	0.0042	0.0037	0.1190	0.0032	0.0031	0.925
DE(0.5)	0.0093	0.0114	-0.2258	0.0104	0.0103	0.946	0.0093	0.0077	0.1720	0.0094	0.0093	0.939
IE(0.5, 0.67)	0.0037	0.0049	-0.3243	0.0035	0.0033	0.924	0.0037	0.0035	0.0541	0.0043	0.0039	0.940
TE(0.5, 0.67)	0.0092	0.0110	-0.1957	0.0100	0.0100	0.944	0.0092	0.0077	0.1630	0.0092	0.0090	0.935
OE(0.5, 0.67)	0.0028	0.0033	-0.1786	0.0025	0.0025	0.947	0.0028	0.0025	0.0714	0.0031	0.0029	0.932
DE(0.67)	0.0055	0.0061	-0.1091	0.0099	0.0098	0.952	0.0055	0.0042	0.2364	0.0098	0.0094	0.936
IE(0.33, 0.67)	0.0076	0.0099	-0.3026	0.0068	0.0066	0.933	0.0076	0.0071	0.0658	0.0073	0.0069	0.946
TE(0.33, 0.67)	0.0131	0.0160	-0.2137	0.0112	0.0110	0.947	0.0131	0.0113	0.1374	0.0097	0.0095	0.937
OE(0.33, 0.67)	0.0069	0.0086	-0.2464	0.0055	0.0054	0.952	0.0069	0.0062	0.1014	0.0056	0.0053	0.924

^a IPW = Mean of inverse probability weighted estimates; ESE = empirical standard error; ASE = average estimated standard error; CP = empirical coverage probability).

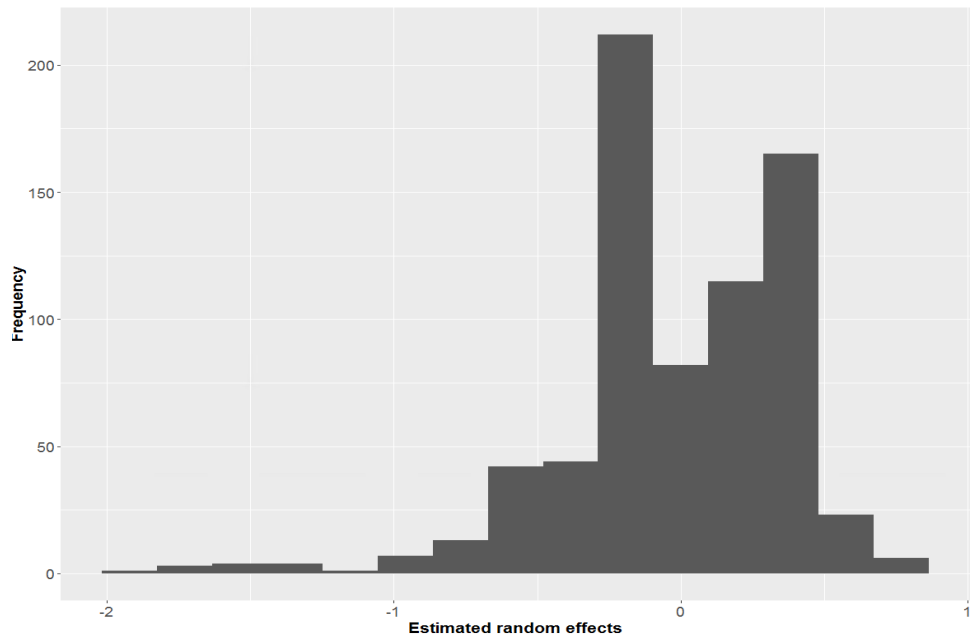


Figure 1: Distribution of the estimated random effects from the cluster-level propensity score model used in the analysis of disseminated effects in Optum’s de-identified Clinformatics® Data Mart Database, 2010-2017, United States.

Table A4: International Classification of Diseases (ICD)-9/10-CM codes for opioid use disorder, opioid overdose and other comorbidities used in the analysis of disseminated effects in Optum’s de-identified Clinformatics® Data Mart Database, 2010-2015, United States

Condition	ICD Version	Code	Description
Opioid use disorder ¹	9	304.00-304.03	Opioid type dependence (unspecified; continuous; episodic)
		304.70-304.73	Combinations of opioid type drug with any other drug dependence (unspecified; continuous; episodic)
		305.50-305.53	Opioid abuse (unspecified; continuous; episodic)
Opioid overdose ^{2,3}	9	965.0x	Poisoning by opiates and related narcotics
		E850.0 - E850.2	Accidental poisoning by heroin, methadone, or other opiates
	10	T40.0	Poisoning by, adverse effect of and underdosing of opium
		T40.1	Poisoning by and adverse effect of heroin
		T40.2	Poisoning by, adverse effect of and underdosing of other opioids
		T40.3	Poisoning by, adverse effect of and underdosing of methadone
T40.6 ⁴	Poisoning by, adverse effect of and underdosing of other and unspecified narcotics		
Depression ⁵	9	296.2	Major depressive disorder single episode
		296.3	Major depressive disorder recurrent episode
		296.5	Bipolar i disorder, most recent episode (or current) depressed
		300.4	Dysthymic disorder
		309	Adjustment reaction
		311	Depressive disorder, not elsewhere classified

¹ Olfson, M., Wall, M., Wang, S., Crystal, S., and Blanco, C. (2018). Service use preceding opioid-related fatality. *American Journal of Psychiatry*, 175(6), 538-544..

² Frazier, W., Cochran, G., Lo-Ciganic, W. H., Gellad, W. F., Gordon, A. J., Chang, C. C. H., and Donohue, J. M. (2017). Medication-assisted treatment and opioid use before and after overdose in Pennsylvania Medicaid. *JAMA*, 318(8), 750-752.

³ Daly, E. R., Dufault, K., Swenson, D. J., Lakevicius, P., Metcalf, E., and Chan, B. P. (2017). Use of emergency department data to monitor and respond to an increase in opioid overdoses in New Hampshire, 2011-2015. *Public Health Reports*, 132(suppl), 73S-79S.

⁴ Excluding T406.06 and T40.696.

⁵ Tonelli, M., Wiebe, N., Fortin, M., Guthrie, B., Hemmelgarn, B. R., James, M. T., ... and Sargious, P. (2016). Methods for identifying 30 chronic conditions: application to administrative data. *BMC Medical Informatics and Decision Making*, 15(1), 1-11.