

Supplementary Material

Title: Leveraging contact network structure in the design of cluster randomized trials

Supplementary Table 1: Probability of rejecting null hypothesis of no effect of intervention comparing incidence in treatment cluster to control cluster

	$T_k + 1$	$T_k + 2$	$T_k + 3$	$T_k + 4$	$T_k + 5$	$T_k + 6$	$T_k + 7$	$T_k + 8$	$T_k + 9$	$T_k + 10$
Stepped Wedge designs										
Standard Stepped Wedge	61.8	82.7	90.4	93.5	94.4	95.4	96.1	96.4	96.6	97
Static Rank Fuzzy Order	47.1	59.8	64.5	67.9	69.5	70.5	71	71.2	71	72
Adaptive Rank Fuzzy Order	56.3	74.7	80.6	84.2	87.1	88.5	89.4	90.3	90.5	91
Static Rank Fuzzy Order Holdback-1	45.8	59.3	65.6	68.8	70.9	71.2	71.3	71.9	71.6	72

All dates are relative to week T_k , the cluster-specific date on which the intervention cluster in each pair received the intervention. Figures are power to reject a null hypothesis of no difference between the treatment and control cluster. Power is based on incidence in all weeks from the date of intervention, T_k , up to the week indicated. Probability is calculated across 19 paired comparisons except for Static Rank Order Holdback-1 with 18 paired comparisons. In all cases, the probability is calculated using a permutation test based on pairwise comparisons of incidence in 1000 simulations, with 2000 permutations per test.

Supplementary Table 2: Parameter values for primary simulations

Cluster characteristics †	
Number of clusters	20
Number of individuals per clusters	200
Mean (standard deviation) within-cluster degree	4.5 (0) & 5 (0)
Mean (standard deviation) between-cluster degree	1 (0.5) & 0.5 (0.5)
Infection characteristics	
Number of initial infections	4
Per-day risk of transmission from contact:	
Infectious at home (β_I)	7.5%
Hospitalized (β_H)	3.75%
Deceased, not buried (β_F)	10%
Mean duration in state (days):	
Incubation period (γ_E^{-1})	9
From symptom onset to hospitalization (γ_H^{-1})	5
From symptom onset to recovery (γ_I^{-1})	10
From symptom onset to death (γ_D^{-1})	10
From hospitalization to recovery (γ_{IH}^{-1})	5
From hospitalization to death (γ_{DH}^{-1})	5
From death to burial (γ_F^{-1})	2
Proportion of cases hospitalized (θ)	0.5
θ_I	0.33
Case-fatality rate:	
Without hospitalization (δ_I)	0.75
With hospitalization (δ_H)	0.65
Vaccination characteristics	
Time between vaccination rounds	7 days
Clusters vaccinated per round	1
Pause period for evaluation, Parallel trials	70 days
Proportion of cluster residents successfully vaccinated	80%
Probability of vaccination removing individual	95%

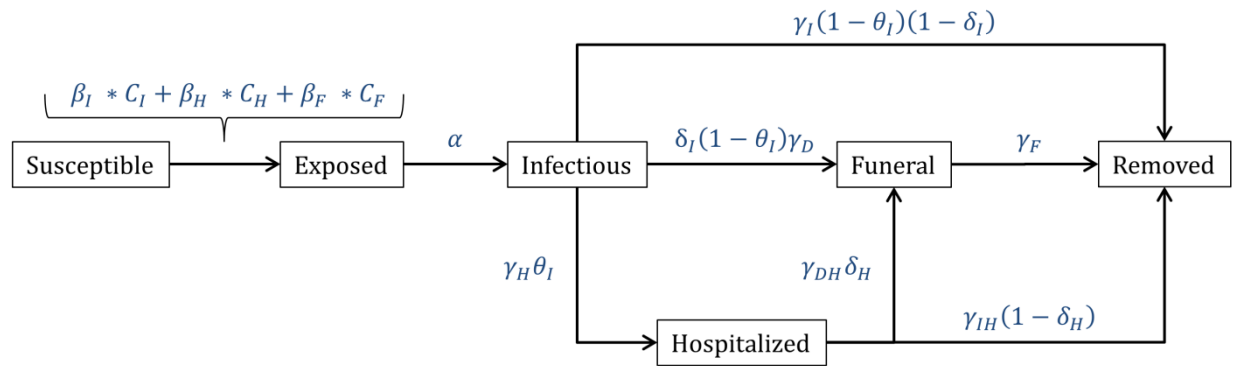
† The 20 study clusters were divided into two groups; both had the same mean number of contacts per person, but individuals in clusters in one group had (on average) twice as many between-cluster contacts as the other.

Supplementary Table 3: Key epidemic and study outcomes for sensitivity analyses

	Standard Stepped Wedge		Static Rank Strict Order		Static Rank Fuzzy Order		Static Rank Holdback-1	
Time to end of epidemic (days)								
Baseline	226	[216 - 240]	229	[217 - 242]	227	[217 - 241]	226	[216 - 240]
Negative control	292	[272 - 315]	292	[270 - 314]	290	[271 - 314]	292	[270 - 316]
Poor vaccine	281	[255 - 314]	287	[259 - 323]	290	[262 - 325]	287	[260 - 325]
Perfect vaccine	210	[203 - 218]	207	[199 - 216]	208	[200 - 216]	208	[201 - 216]
Perfect vaccine incl. Exposed	221	[210 - 235]	219	[207 - 232]	219	[208 - 232]	219	[208 - 233]
Week 8 vaccine	233	[221 - 247]	238	[227 - 252]	237	[226 - 250]	238	[226 - 250]
Week 10 vaccine	240	[228 - 254]	245	[234 - 259]	244	[233 - 257]	244	[232 - 258]
Low between-cluster heterogeneity	229	[218 - 242]	229	[220 - 243]	230	[218 - 242]	228.5	[218 - 243]
High between-cluster heterogeneity	226	[215 - 240]	226	[214 - 238]	226	[214 - 239]	226	[216 - 240]
Lognormal within-cluster ties	227	[216 - 240]	228	[217 - 241]	228	[216 - 242]	228	[218 - 241]
14 days between interventions	273	[255 - 294]	292	[268 - 318]	290	[268 - 318]	288	[267 - 311]
21 days between interventions	284	[264 - 306]	299	[275 - 332]	299	[276 - 329]	296.5	[273 - 325]
Lower infectiousness	198	[173 - 217]	184	[156 - 204]	185	[156 - 205]	186	[155 - 205]
Outside population	260	[241 - 286]	277	[253 - 309]	278	[253 - 307]	274	[251 - 304]
Cumulative incidence (%)								
Baseline	35.8	[28.0 - 42.0]	29.7	[20.6 - 37.8]	29.6	[21.3 - 37.0]	31.2	[22.6 - 38.6]
Negative control	80.0	[78.9 - 80.9]	80.0	[78.9 - 80.9]	79.9	[78.7 - 80.9]	80.0	[78.8 - 81.0]
Poor vaccine	44.0	[36.4 - 49.4]	40.2	[31.6 - 47.6]	39.9	[31.3 - 47.0]	41.0	[31.7 - 48.3]
Perfect vaccine	31.3	[24.1 - 37.4]	24.5	[16.0 - 32.5]	25.6	[17.6 - 32.8]	25.2	[17.8 - 33.9]
Perfect vaccine incl. Exposed	30.2	[22.1 - 36.1]	24.5	[16.0 - 32.2]	24.6	[16.9 - 32.2]	24.9	[17.3 - 31.9]
Week 8 vaccine	43.8	[35.9 - 49.8]	40.4	[30.6 - 48.3]	40.7	[31.5 - 48.3]	40.9	[31.1 - 48.3]
Week 10 vaccine	50.9	[43.1 - 57.0]	49.1	[40.1 - 56.6]	50.3	[41.1 - 57.7]	50.3	[41.0 - 58.0]
Low between-cluster heterogeneity	35.2	[27.6 - 40.2]	31.4	[22.8 - 38.6]	31.5	[23.3 - 38.6]	31.6	[23.7 - 38.3]
High between-cluster heterogeneity	36.3	[28.0 - 43.6]	28.9	[19.3 - 38.0]	29.1	[19.0 - 37.6]	30.5	[21.2 - 39.2]
Lognormal within-cluster ties	34.7	[26.8 - 41.0]	29.4	[20.2 - 36.9]	29.2	[20.5 - 37.1]	30.2	[21.3 - 38.2]
14 days between interventions	56.1	[51.4 - 59.8]	54.4	[48.9 - 59.2]	55.2	[49.4 - 59.3]	55.4	[50.0 - 59.7]
21 days between interventions	63.5	[60.4 - 66.3]	63.2	[59.2 - 66.5]	63.4	[59.1 - 66.2]	63.4	[59.8 - 66.3]
Lower infectiousness	3.4	[1.8 - 5.5]	3.1	[1.7 - 4.6]	2.9	[1.6 - 4.8]	3.1	[1.7 - 4.8]
Outside population	18.5	[15.9 - 20.9]	16.6	[13.6 - 19.6]	16.8	[13.3 - 19.8]	16.8	[13.9 - 19.8]
Power after one week								
Baseline	61.8	[58.8 - 64.8]			45.8	[42.7 - 48.9]	56.3	[53.2 - 59.4]
Negative control	4.5	[3.2 - 5.8]			4.7	[3.4 - 6.0]	3.7	[2.5 - 4.9]
Poor vaccine	29.9	[27.1 - 32.7]			24.5	[21.8 - 27.2]	28.6	[25.8 - 31.4]
Perfect vaccine	81.2	[78.8 - 83.6]			62.4	[59.4 - 65.4]	69.8	[67.0 - 72.6]
Perfect vaccine incl. Exposed	91.1	[89.3 - 92.9]			70.9	[68.1 - 73.7]	87.4	[85.3 - 89.5]
Week 8 vaccine	60.9	[57.9 - 63.9]			58.1	[55.0 - 61.2]	66.4	[63.5 - 69.3]
Week 10 vaccine	63.9	[60.9 - 66.9]			59.8	[56.8 - 62.8]	70.0	[67.2 - 72.8]
Low between-cluster heterogeneity	62.9	[59.9 - 65.9]			48.7	[45.6 - 51.8]	59.4	[56.4 - 62.4]
High between-cluster heterogeneity	60.9	[57.9 - 63.9]			48.0	[44.9 - 51.1]	56.0	[52.9 - 59.1]
Lognormal within-cluster ties	60.2	[57.2 - 63.2]			47.2	[44.1 - 50.3]	56.3	[53.2 - 59.4]
14 days between interventions	4.2	[3.0 - 5.4]			5.2	[3.8 - 6.6]	5.6	[4.2 - 7.0]
21 days between interventions	4.2	[3.0 - 5.4]			4.7	[3.4 - 6.0]	4.7	[3.4 - 6.0]
Lower infectiousness	10.4	[8.5 - 12.3]			6.7	[5.2 - 8.2]	7.0	[5.4 - 8.6]
Outside population	72.0	[69.2 - 74.8]			67.1	[64.2 - 70.0]	75.6	[72.9 - 78.3]

Notes. All outcome figures are medians and interquartile ranges of result from 1000 simulation realizations. Time to end of epidemic measured in days since first infections; cumulative incidence measured as percentage of all individuals ever infected.

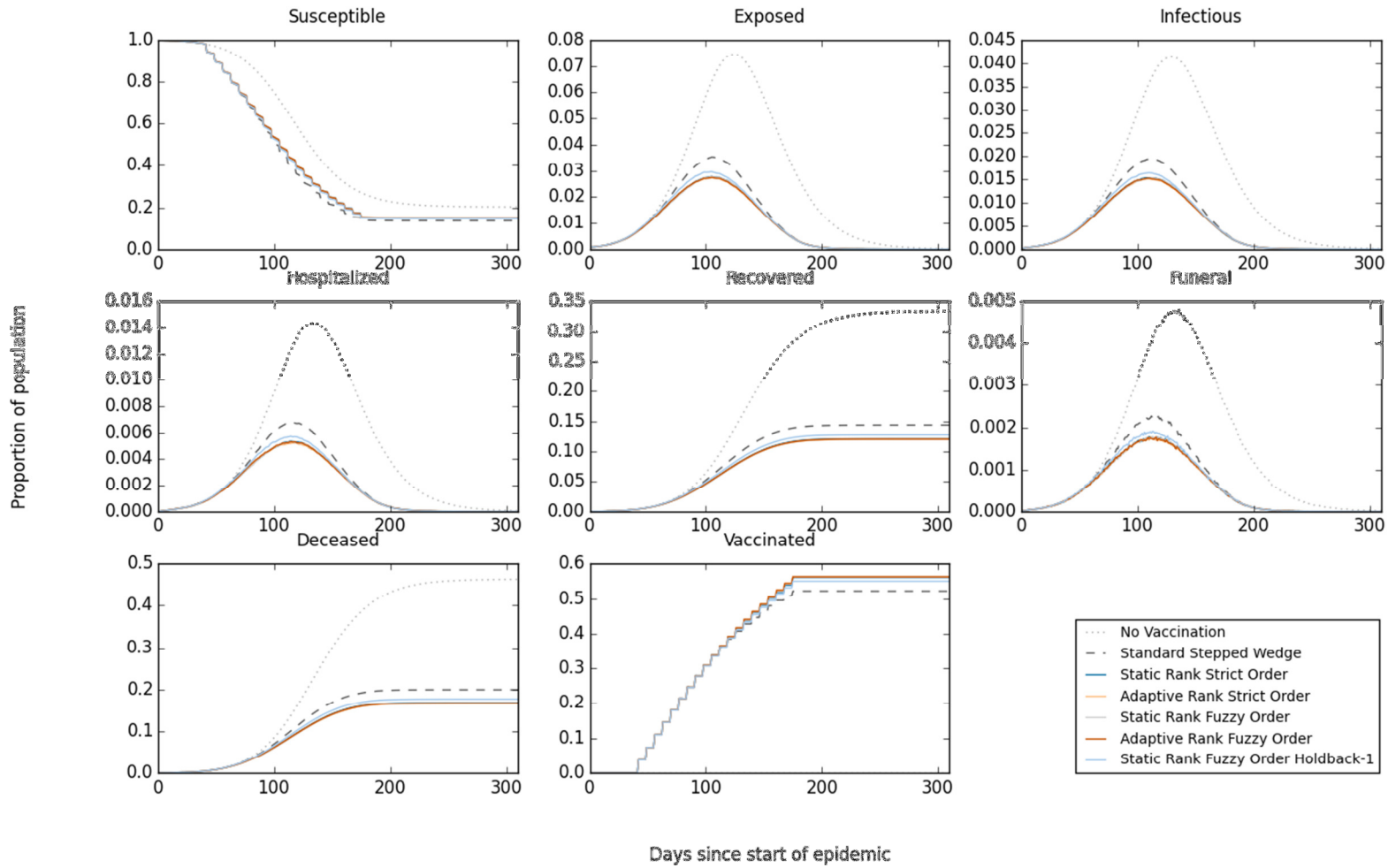
Supplementary Figure 1: Schematic of state transition model



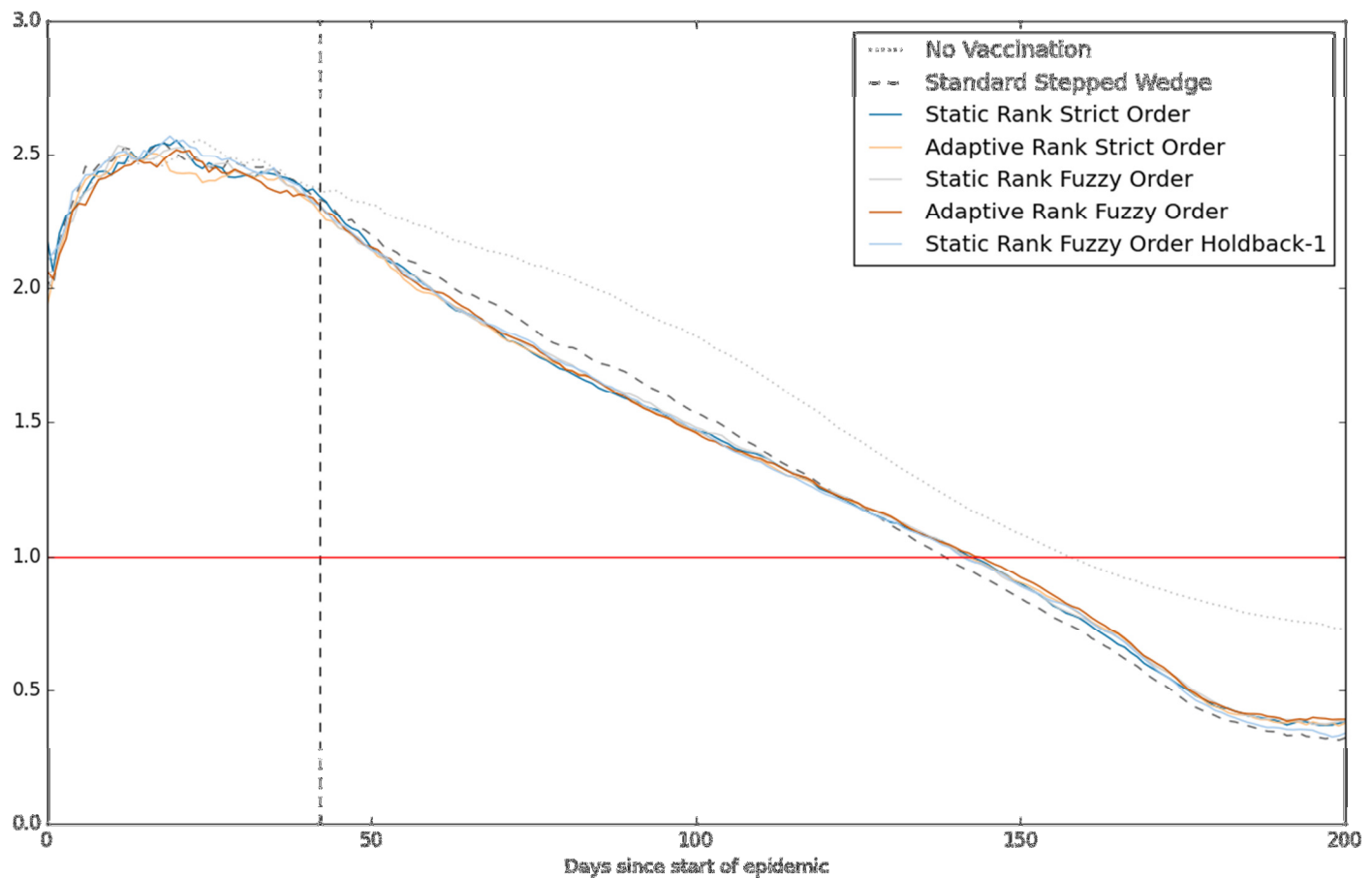
β_I, β_H and β_F are the transmission risk to a susceptible individual if one of their contacts is, respectively, infectious at home (C_I), hospitalized (C_H) or deceased but not yet buried (C_F). The inverse of each γ term reflects the mean duration in a state: incubation period (γ_E); time from symptom onset to hospitalization (γ_H); time from symptom onset to recovery without hospitalization (γ_I); time from symptom onset to death without hospitalization (γ_D); time from hospitalization to recovery (γ_{IH}); time from hospitalization to death (γ_{DH}); and time to burial from death (γ_F).

θ_I is computed to fix the proportion of individuals hospitalized, allowing for competing risks of death or recovery, δ_I and δ_H are computed to fix the overall case-fatality ratio. Details, including equations for θ_I, δ_I and δ_H , can be found in Tables 2 and 3 of [23].

Supplementary Figure 2: Mean state values for each day since the start of the epidemic across 1000 simulations



Supplementary Figure 3: Mean daily effective reproductive rate for each vaccination study design across 1000 simulations



Vertical dashed line represents date of first cluster vaccination; horizontal solid line represents $R_e=1$.

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