Supplementary Online Content

Blanco N, Harris AD, Magder LS, et al. Sample size estimates for cluster-randomized trials in hospital infection control and antimicrobial stewardship. *JAMA Netw Open.* 2019;2(10):e1912644. doi:10.1001/jamanetworkopen.2019.12644

eTable 1. Sample Size Parameters and Estimations for Health Care–Associated Infection (HAI) Parallel Cluster Randomized Trials

eTable 2. Sample Size Parameters and Estimations for MRSA and VRE Acquisition Parallel Cluster Randomized Trials

eMethods. Equation to Estimate the Variance of Site-Specific Rates Given Data on Observed Rates at Multiple Sites

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Sample Size Parameters and Estimations for Health Care—Associated Infection (HAI) Parallel Cluster Randomized Trials

MRSA Bacteremia												
Anticipated incidence rate (intervention) (effect size)	(50%) 0.0000275	(30%) 0.000038 5	(10%) 0.000049 5	(50%) 0.000027 5	(30%) 0.000038 5	(10%) 0.000049 5	(50%) 0.000027 5	(30%) 0.000038 5	(10%) 0.000049 5	(50%) 0.0000275	(30%) 0.0000385	(10%) 0.0000495
Anticipated incidence rate (control)	0.000055	0.000055	0.000055	0.000055	0.000055	0.000055	0.000055	0.000055	0.000055	0.000055	0.000055	0.000055
Cluster size	219.4	219.4	219.4	219.4	219.4	219.4	219.4	219.4	219.4	219.4	219.4	219.4
CV	0.45	0.45	0.45	0.55	0.55	0.55	0.65	0.65	0.65	0.55	0.55	0.55
Power	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.9	0.9	0.9
TOTAL SAMPLE SIZE (hospitals)	20	60	626	24	73	768	29	89	938	31	98	1028
						CAUTI						
Anticipated incidence rate (intervention) (effect size)	(50%) 0.0004775	(30%) 0.000668 5	(10%) 0.000859 5	(50%) 0.000477 5	(30%) 0.000668 5	(10%) 0.000859 5	(50%) 0.000477 5	(30%) 0.000668 5	(10%) 0.000859 5	(50%) 0.0004775	(30%) 0.0006685	(10%) 0.0008595
Anticipated incidence rate (control)	0.000955	0.000955	0.000955	0.000955	0.000955	0.000955	0.000955	0.000955	0.000955	0.000955	0.000955	0.000955
Cluster size	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3
CV	0.60	0.60	0.60	0.70	0.70	0.70	0.80	0.80	0.80	0.70	0.70	0.70
Power	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.9	0.9	0.9
TOTAL SAMPLE SIZE (hospitals)	21	65	690	26	82	875	31	101	1088	34	109	1171
CLABSI												

Anticipated incidence rate	(50%) 0.0004075	(30%) 0.000570	(10%) 0.000733	(50%) 0.000407	(30%) 0.000570	(10%) 0.000733	(50%) 0.000407	(30%) 0.000570	(10%) 0.000733	(50%) 0.0004075	(30%) 0.0005705	(10%) 0.0007335
(intervention) (effect size)		5	5	5	5	5	5	5	5			
Anticipated incidence rate (control)	0.000815	0.000815	0.000815	0.000815	0.000815	0.000815	0.000815	0.000815	0.000815	0.000815	0.000815	0.000815
Cluster size	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0
CV	0.45	0.45	0.45	0.55	0.55	0.55	0.65	0.65	0.65	0.55	0.55	0.55
Power	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.9	0.9	0.9
TOTAL SAMPLE SIZE (hospitals)	16	47	489	20	60	631	24	75	801	26	80	844
C. difficile Infection												
Anticipated incidence rate (intervention) (effect size)	(50%) 0.0003080	(30%) 0.000431 2	(10%) 0.000554 4	(50%) 0.000308 0	(30%) 0.000431 2	(10%) 0.000554 4	(50%) 0.000308 0	(30%) 0.000431 2	(10%) 0.000554 4	(50%) 0.0003080	(30%) 0.0004312	(10%) 0.0005544
Anticipated incidence rate (control)	0.000616	0.000616	0.000616	0.000616	0.000616	0.000616	0.000616	0.000616	0.000616	0.000616	0.000616	0.000616
Cluster size	124.2	124.2	124.2	124.2	124.2	124.2	124.2	124.2	124.2	124.2	124.2	124.2
CV	0.34	0.34	0.34	0.44	0.44	0.44	0.54	0.54	0.54	0.44	0.44	0.44
Power	0.8	0.8	8.0	0.8	0.8	0.8	0.8	0.8	0.8	0.9	0.9	0.9
TOTAL SAMPLE SIZE (hospitals)	8	22	218	11	31	329	15	44	468	14	41	440

Anticipated incidence rate (intervention) (le) = The anticipated daily average incidence rate in the experimental group with the outcome.

Anticipated incidence rate (control) (Ic) = The anticipated daily average incidence rate in the control group with the outcome.

Effect size= % difference between the anticipated daily average incidence rate in the experimental group with the outcome and the anticipated daily average incidence rate in the control group with the outcome

Cluster size (m)= The anticipated average (or actual) cluster size

CV = The coefficient of variation of cluster-specific incidence rates, assumed constant over both the treatment and control groups. The bolded CV was estimated from Hospital Compare data.

Power = The desired level of power, recall power = 1 - type II error

Other parameters included (and held constant) but not shown in table:

Planned follow-up time (t) for the study (days)= 365

Allocation Ratio (AR) of patients in intervention group to control group=1 Alpha or the desired type I error rate= 0.05

eTable 2. Sample Size Parameters and Estimations for MRSA and VRE Acquisition Parallel Cluster Randomized Trials

					MARCA	cquisition						
					IVINSA	icquisition						
Anticipated incidence rate (intervention) (effect size)	(50%) 0.004160	(30%) 0.005824	(10%) 0.007488									
Anticipated incidence rate (control)	0.008320	0.008320	0.008320	0.008320	0.008320	0.008320	0.008320	0.008320	0.008320	0.008320	0.008320	0.008320
Cluster size	7.1	7.1	7.1	7.1	7.1	7.1	7.1	7.1	7.1	7.1	7.1	7.1
CV	0.48	0.48	0.48	0.58	0.58	0.58	0.68	0.68	0.68	0.58	0.58	0.58
Power	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.9	0.9	0.9
TOTAL SAMPLE SIZE (hospitals)	13	37	389	17	50	540	22	67	719	22	67	722
					VRE A	equisition						
Anticipated incidence rate (intervention) (effect size)	(50%) 0.007130	(30%) 0.00998	(10%) 0.012834									
Anticipated incidence rate (control)	0.014260	0.014260	0.014260	0.014260	0.014260	0.014260	0.014260	0.014260	0.014260	0.014260	0.014260	0.014260
Cluster size	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9
CV	0.42	0.42	0.42	0.52	0.52	0.52	0.62	0.62	0.62	0.52	0.52	0.52
Power	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.9	0.9	0.9
TOTAL SAMPLE SIZE (hospitals)	10	28	292	13	40	426	18	54	588	17	53	570

Anticipated incidence rate (intervention) (le) = The anticipated daily average incidence rate in the experimental group with the outcome.

Anticipated incidence rate (control) (Ic) = The anticipated daily average incidence rate in the control group with the outcome.

Effect size= % difference between the anticipated daily average incidence rate in the experimental group with the outcome and the anticipated daily average incidence rate in the control group with the outcome

Cluster size (m)= The anticipated average (or actual) cluster size

CV = The coefficient of variation of cluster-specific incidence rates, assumed constant over both the treatment and control groups. The bolded CV was estimated from Hospital Compare data.

Power = The desired level of power, recall power = 1 - type II error

Other parameters included (and held constant) but not shown in table:

Planned follow-up time (t) for the study (days)= 120 Allocation Ratio (AR) of patients in intervention group to control group=1 Alpha or the desired type I error rate= 0.05= **eMethods.** Equation to Estimate the Variance of Site-Specific Rates Given Data on Observed Rates at Multiple Sites

Let Yi and Ti stand for the number of acquired infections, and the total patient-time observed in cluster "i".

Assume:

Yi $|\lambda_i|^{\infty}$ Poisson(λ_i , Ti) where λ_i is the site-specific rate of acquired infections.

Let σ^2_{λ} stand for the variance of the site-specific rates. This is the parameter of interest.

Define $\hat{\lambda}_i = \text{Yi/Ti}$

Now

$$\begin{aligned} \mathsf{Var}(\hat{\lambda}_i) &= \; \mathsf{E}(\mathsf{Var}(\hat{\lambda}_i \,|\, \lambda \mathsf{i})) &+ \; \mathsf{Var}(\mathsf{E}(\hat{\lambda}_i \,|\, \lambda \mathsf{i})) \\ &= \; \mathsf{E}(\lambda \mathsf{i}/\mathsf{Ti}) &+ \; \mathsf{Var}(\lambda \mathsf{i}) \\ &= \; \lambda/\mathsf{Ti} &+ \; \sigma^2_\lambda \end{aligned}$$

Now suppose we observe a set of independent Yi, i=1 to n, and we want to estimate σ^2_{λ} and λ

However, let AVEvar=Average ($Var(\hat{\lambda}_i)$) which equals:

AVEvar =
$$\frac{1}{n}\sum \left((\lambda/T_i) + \sigma_{\lambda}^2\right) = \frac{1}{n}\lambda\sum (1/T_i) + \sigma_{\lambda}^2$$

Which implies that

$$\sigma^2_{\lambda} = \text{AVEvar} - \frac{1}{n} \lambda \sum_{i=1}^{n} \frac{1}{T_i}$$
 (1)

Note, we can get a natural estimate of the AVEvar using

$$\sum_{i=1}^{n} (\widehat{\lambda}_{i} - \lambda)^{2}$$

where λ is estimated as the mean or a weighted mean of the $\hat{\lambda}_i$.

Plugging that estimate for AVEvar into equation (1) gives us an estimate of σ^2_{λ} .