Table 4: Design effects calculations for hypothetical studies with different group distributions among centers.

4.a. Balanced designs ($n_1 = n_2$) with $N = 200$ subjects and $Q = 10$ centers of equal size (case of randomized trials with two treatment arms).

Group distribution	**Homogeneous**		**Slightly heterogeneous**		**S^* = 1**		**Heterogeneous**		**Strongly heterogeneous**		**Cluster design**	
Group sizes per center	m_{1j}	m_{2j}	m_{1j}	m_{2j}	m_{1j}	m_{2j}	m_{1j}	m_{2j}	m_{1j}	m_{2j}	m_{1j}	m_{2j}
Center 1	10	10	8	12	6	14	14	6	17	3	20	0
Center 2	10	10	11	9	12	8	8	12	6	14	0	20
Center 3	10	10	10	10	10	10	11	9	12	8	20	0
Center 4	10	10	11	9	11	9	6	14	4	16	0	20
Center 5	10	10	9	11	9	11	12	8	16	4	20	0
Center 6	10	10	11	9	13	7	5	15	3	17	0	20
Center 7	10	10	10	10	9	11	15	5	14	6	20	0
Center 8	10	10	10	10	10	10	7	13	2	18	0	20
Center 9	10	10	8	12	7	13	12	8	19	1	20	0
Center 10	10	10	12	8	13	7	10	10	7	13	0	20
S^*	0		0.32		1		2.08		7.20		20	
$\frac{n_1 n_2}{NQ} S^*$	0		1.6		5		10.4		36		100	
$Deff^{**}$ ($\rho = 0.01$)	0.990		0.993		1.000		1.011		1.062		1.190	
$Deff^{**}$ ($\rho = 0.1$)	0.900		0.932		1.000		1.108		1.620		2.900	

m_{ij} : size of group *i* in center *j*. * $S = \frac{N}{n_1 n_2} \sum_{j=1}^{Q} \left(m_{1j} - \frac{m_j n_1}{N} \right)^2$. ** Design effect.

4.b. Imbalanced designs ($n_1 = 140$, $n_2 = 60$) with $N = 200$ subjects and $Q = 10$ centers of equal size (case of observational studies with a binary risk factor).

Group distribution	**Homogeneous**		**Slightly heterogeneous**		**$S^* = 1$**		**Heterogeneous**		**Strongly heterogeneous**	
Group sizes per center	m_{1j}	m_{2j}	m_{1j}	m_{2j}	m_{1j}	m_{2j}	m_{1j}	m_{2j}	m_{1j}	m_{2j}
Center 1	14	6	15	5	14	6	18	2	20	0
Center 2	14	6	13	7	12	8	9	11	20	0
Center 3	14	6	14	6	16	4	13	7	8	12
Center 4	14	6	15	5	12	8	16	4	8	12
Center 5	14	6	16	4	17	3	12	8	20	0
Center 6	14	6	13	7	11	9	11	9	20	0
Center 7	14	6	12	8	16	4	16	4	20	0
Center 8	14	6	14	6	12	8	10	10	8	12
Center 9	14	6	15	5	14	6	17	3	8	12
Center 10	14	6	13	7	16	4	18	2	8	12
S^*	0		0.33		1		2.48		8.57	
$\frac{n_1 n_2}{NQ} S^*$	0		1.4		4.2		10.4		36	
$Deff^{**}$ ($\rho = 0.01$)	0.990		0.993		1.000		1.015		1.076	
$Deff^{**}$ ($\rho = 0.1$)	0.900		0.933		1.000		1.148		1.757	

m_{ij} : size of group i in center j. * $S = \frac{N}{n_1 n_2} \sum_{j=1}^{Q} \left(m_{1j} - \frac{m_j n_1}{N} \right)^2$. ** Design effect.