Web-based Supplementary Material for Manuscript

**Blinded sample size recalculation in clinical trials with binary
composite endpoints**

Anja Sander, Geraldine Rauch and Meinhard Kieser

1. Description of considered scenarios

Table 1: Considered scenario 1: $\Delta_{CE}=0.06$, $p_{MC}=0.0125$, $\Delta_{MC}=0.003$, $\alpha_{MC}=0.0125$.

p_{CE}^C	p_{CE}^I	p_{CE}	$Corr_{H_0}(T_{CE}, T_{MC})$	$Corr_{H_1}(T_{CE}, T_{MC})$	α_{CE}	n_0	$\mathbb{E}(Corr^{blind})$
0.09	0.03	0.06	0.379	0.447	0.01368	291	0.445
0.10	0.04	0.07	0.357	0.411	0.01358	337	0.410
0.11	0.05	0.08	0.339	0.382	0.01349	381	0.382
0.12	0.06	0.09	0.323	0.358	0.01342	424	0.358
0.13	0.07	0.10	0.308	0.338	0.01336	466	0.338
0.14	0.08	0.11	0.295	0.320	0.01331	507	0.320
0.15	0.09	0.12	0.284	0.305	0.01327	547	0.305
0.16	0.10	0.13	0.273	0.291	0.01323	586	0.291
0.17	0.11	0.14	0.263	0.279	0.01320	624	0.279
0.18	0.12	0.15	0.254	0.268	0.01317	660	0.268
0.19	0.13	0.16	0.246	0.258	0.01314	696	0.258
0.20	0.14	0.17	0.238	0.248	0.01312	731	0.249
0.21	0.15	0.18	0.231	0.240	0.01310	764	0.240
0.22	0.16	0.19	0.224	0.232	0.01308	797	0.232
0.23	0.17	0.20	0.218	0.225	0.01306	828	0.225
0.24	0.18	0.21	0.212	0.218	0.01304	858	0.218
0.25	0.19	0.22	0.206	0.211	0.01303	888	0.212

Table 2: Considered scenario 2: $\Delta_{CE}=0.1$, $p_{MC}=0.075$, $\Delta_{MC}=0.05$, $\alpha_{MC}=0.0125$.

p_{CE}^C	p_{CE}^I	p_{CE}	$Corr_{H_0}(T_{CE}, T_{MC})$	$Corr_{H_1}(T_{CE}, T_{MC})$	α_{CE}	n_0	$\mathbb{E}(Corr^{blind})$
0.15	0.05	0.10	0.793	0.854	0.01843	155	0.854
0.20	0.10	0.15	0.667	0.674	0.01619	219	0.678
0.25	0.15	0.20	0.577	0.565	0.01513	262	0.569
0.30	0.20	0.25	0.509	0.488	0.01452	290	0.493
0.35	0.25	0.30	0.454	0.429	0.01412	308	0.435
0.40	0.30	0.35	0.408	0.382	0.01384	319	0.388
0.45	0.35	0.40	0.369	0.342	0.01363	325	0.349
0.50	0.40	0.45	0.333	0.308	0.01347	327	0.315
0.55	0.45	0.50	0.302	0.278	0.01334	326	0.285

Table 3: Considered scenario 3: $\Delta_{CE}=0.18$, $p_{MC}=0.08$, $\Delta_{MC}=0.06$, $\alpha_{MC}=0.0125$.

p_{CE}^C	p_{CE}^I	p_{CE}	$Corr_{H_0}(T_{CE}, T_{MC})$	$Corr_{H_1}(T_{CE}, T_{MC})$	α_{CE}	n_0	$\mathbb{E}(Corr^{blind})$
0.24	0.06	0.15	0.626	0.701	0.01566	71	0.702
0.29	0.11	0.20	0.550	0.583	0.01487	89	0.590
0.34	0.16	0.25	0.490	0.502	0.01437	103	0.511
0.39	0.21	0.30	0.440	0.440	0.01403	114	0.450
0.44	0.26	0.35	0.397	0.390	0.01378	122	0.402
0.49	0.31	0.40	0.359	0.349	0.01358	127	0.361
0.54	0.36	0.45	0.324	0.313	0.01343	129	0.326
0.59	0.41	0.50	0.293	0.281	0.01331	130	0.295

2. Results for the unrestricted recalculation approach

Figure 1: The calculated actual type I error rate (left panel) and power (right panel) for the fixed sample size design (black line) and simulated results for the internal pilot study design (grey lines). Results are shown for investigated scenarios 1 (top), 2 (middle), and 3 (bottom), applying three different sample sizes of internal pilot study using the unrestricted recalculation approach (as described in Section 5.1). Underlying parameters are as follows: $\Delta_{CE} = 0.06$, $p_{MC} = 0.0125$, and $\Delta_{MC} = 0.003$ (scenario 1); $\Delta_{CE} = 0.1$, $p_{MC} = 0.075$, and $\Delta_{MC} = 0.05$ (scenario 2); $\Delta_{CE} = 0.18$, $p_{MC} = 0.08$, and $\Delta_{MC} = 0.06$ (scenario 3); with the initial assumption for p_{CE}^C of 0.15, 0.35, and 0.34, respectively. The vertical reference line indicates the setting matching the initial assumptions. Below the plots, true required sample sizes per group n_0 are given in grey color.

Figure 2: Simulated empirical distribution of the final sample size. The boxes show the median value and interquartile range of the final sample size ($n_1 + n_2$) and the whiskers indicate minimum and maximum. Results are shown for investigated scenarios 1 (top), 2 (middle), and 3 (bottom), applying three different sample sizes of internal pilot study using the unrestricted recalculation approach (as described in Section 5.1). Underlying parameters are as follows: $\Delta_{CE} = 0.06$, $p_{MC} = 0.0125$, and $\Delta_{MC} = 0.003$ (scenario 1); $\Delta_{CE} = 0.1$, $p_{MC} = 0.075$, and $\Delta_{MC} = 0.05$ (scenario 2); $\Delta_{CE} = 0.18$, $p_{MC} = 0.08$, and $\Delta_{MC} = 0.06$ (scenario 3); with the initial assumption for p_{CE}^C of 0.15, 0.35, and 0.34, respectively. Below the plots, true required sample sizes per group n_0 are given in grey color.