## S3 Appendix General flowchart for all designs.

All of the designs can be illustrated in a single flowchart (Fig A). In the two-arm single-stage designs K = 1 and J = 1. In the multi-arm designs in our simulations K = 5 and J = 4. For the frequentist designs the efficacy and futility measures are always equal to the standardized test statistic, i.e.  $e_{kj} = f_{kj} = Z_{kj}$  and the efficacy and futility thresholds are the upper and lower stopping boundaries with  $a_K = b_K$  in order to force a decision at the final analysis.

For the Bayesian designs the efficacy measure is the probability  $e_{kj} = P(p_j < p_0 | \text{Data}_k)$  given the data Data<sub>k</sub> at the k-th analysis. The futility measure is  $f_{kj} = P(p_j < p_0 + 0.1 | \text{Data}_k)$ . The efficacy and futility thresholds are  $a_k = 0.1$  and  $b_k = 0.99$  (k = 1, ..., K).

For the designs with complete randomization the allocation probabilities are  $q_j = 1/(\tilde{K}+1)$  for all j = 1, ..., J, where  $\tilde{K}$  is the number of remaining treatment arms at stage k. For the responseadaptive randomization designs the allocation probabilities are initially  $q_j = 1/(K+1)$  and are then updated at the interim analysis according to Eq (2).

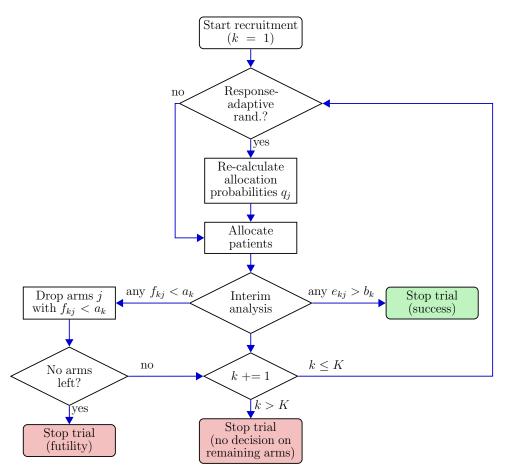


Figure A: General flowchart for all designs. At each of the at most K (interim) analyses the design-specific efficacy measures  $e_{kj}$  and futility measures  $f_{kj}$  (k = 1, ..., K; j = 1, ..., J) for all remaining treatment arms are compared to efficacy thresholds  $b_k$  and futility thresholds  $a_k$ . Patients are allocated according to allocation probabilities  $q_{kj}$ .