RND-1: ???????? ?? ????????????? ???????? ? A/A-???????? ??????? ? ? ?????? A/B, ????? ? ?????????

??????: Draft
???????: A/B ????????????, pre-check (A/A), ????????????/???????

1. ???????? ? ??????????

? ????????????????? ????????? ???? ??? ?????? ?? ?????? ????? ????????:

1) **???????? ?????? A/B** ?? ????? ??? ?????????? ??????? ???????? (endpoints), ?? ??????? ??????????? ??????? ? ?????????.

2) **????????????????????? ???????? ?????????** (????? ?????????? A/A), ??? ??????????? ?????????????? ????? ?? ?????? ???????? (??????? ???? ??????? ? ?????????????? ????????). ?????? ??? ??????????? ??? ????????? ?????? (t-test/KS/?) ? ??????? ?? p-value. ??? ?????? ?????????? ??????????? ????????????? ????????? (?????????????).

????????: ??? ????? ????? ???????? ??????????? ???? ?? ?????? ????????? ??????? ?????? ?????? ???? ??? ?????????? ????????????. ??? ??????????? ?????? ???????? ? ??????? ?????? ???????? ?????????????? ??????.

2. ???????

? Q1. ????? ?? ???????? ?? ????????????? ???????? ??? ?????????? ?????? A/B ?? ?????????? ??????? ?????????
? Q2. ????? ?? ???????? ?? ????????????? ???????? ??? ???????? ??????? ?? ??????, ???? ???????????? p-value-??????? ?? ?????? ???????????
? Q3. ??? ????????? ????????????? accept/reject ? ?????????????? ? ?? ?????????? ??????? ? p-hacking ?? ????????
? Q4. ??? ??? ??????? ? ????????? ? ??????????? ???????????????

3. ??????

3.1 ????? A/B ?? ?????????? ????????: ???????? ?????? ?????

???? ??????? ?????? ???????? ??? ?????, ???? ??????? ???? ?? ???? ?? m ??????, ?? ??? ???????? ?????????????? ?????? ?????????? ?????????????????? ?????? ?? ?????? ????????????. ? ????? ??????? ????????? ??????? ??????? ????????? ???????? ??????:

? FWER: Bonferroni / Holm (????? ???? ??????? ?????? ??????),
? FDR: Benjamini?Hochberg (????? ?????? ????? ? ?????? ?????? exploratory),
? ???? ???????? endpoints (primary ? secondary).

???? ??????? ????????????? primary-???????, ?? ??????? ?????????? ???????, ? ????????? ??????? ?? ????????????? ??? ??????/?? ??????, ?? ??????? ???????? ??? ????????? ????? ???? ?? ????? (??? ?????????? pre-registration ???????).

3.2 ???????? ??????? ?? ??????: P-VALUES ?? ???????? ??????? ????????? ????????????

Baseline-p-values ??????? ?? N ? ?? ???????? ???????? ??????????. ??? ??????? ????? ????????
?????? ???????????? ???????? ???? ??? ????????? ???????. ??????? ??????? ?????? ????????
????????? ?? ??????????????? ? baseline-?????? (????????, Bonferroni) ? ???? ??????????
??????????? ????????? ?????, ? ?? ????????? ????????????? ??????????.

???????????? ??????: ?????? ??? ??????????? (effect size), ? accept/reject ??????? ?????
???? ????????????? ???????? ??????????.

3.3 ??????????????: ?????????? ??????? ???????? ???????

?????????????? (rejection sampling of assignments) ?????? ???? ?????? ??????? ????????????:

1) ?? ????????? ????????? ????????? ?????? ???????? ? ?? ?????????? (tiers/weights).
2) ???????? ??????? ?????????? (????????, max|SMD| ?? ???????? ??????????; ???????????
???????????? ?????????).
3) ???????? ????? ? **????????????**, ??????????????? ????? ??????? ???? ???????? ?????????
(acceptance rate p_a, ???????? 1?10%).
4) ???????????? ??????: max_iter / time-limit.
5) Fail-safe: ???? max_iter ???????? ? ???????? ?????????? ?????? ?? low-priority ??????????
??? ????????? ? ???????????? ?? 1?2 ???????? ??????????.
6) ????????: seed, ????? ???????, ???????? ????????.

4. ???????????? ??? ?????????? ? ??????????

1) **????? A/B:** ???????? ????? Holm / Bonferroni / BH-FDR, ????????? ???????? endpoints
(primary -> secondary).
2) **Pre-check (A/A):** ???????? ???? ?? ????????? p-values ??:
? ????? ?? SMD/????????? ????? (???????????),
? ???????????? ???????? ???????? (???????? max|SMD| ?? top-covariates).
3) **??????????????:** ????????????? API: criterion, threshold/acceptance_rate, max_iter,
tiers/weights, seed, ???????????? ???????????.

5. ???? ????????????? ?? ????????? (??? NOTEBOOK.IPYNB)

? ???? ??????????? ???? ?? ?????? ??????? ????? ??? ????? ????? ???????? K ??? ???????
???????.
? ????????? ??????? ?????? ??????: ??? ????????? vs Bonferroni vs Holm vs BH.
? ????????? ????? ???????? ????????????? ? ???????? ???????:
? p-value-???? (??? baseline),
? max|SMD|-???? (??? ???????????? ???????).

6. ??????????

? FDA. *Multiple Endpoints in Clinical Trials: Guidance for Industry* (Oct 2022).

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/multiple-endpoints-clinical-trials

? de Boer et al. (2015). *Testing for baseline differences in randomized controlled trials: an unhealthy research behavior that is hard to eradicate.*

   https://pmc.ncbi.nlm.nih.gov/articles/PMC4310023/

? Senn S. (1994). *Testing for baseline balance in clinical trials.* Stat Med. DOI: 10.1002/sim.4780131703.

   https://pubmed.ncbi.nlm.nih.gov/7997705/

? Benjamini Y., Hochberg Y. (1995). *Controlling the False Discovery Rate...* DOI: 10.1111/j.2517-6161.1995.tb02031.x

   https://doi.org/10.1111/j.2517-6161.1995.tb02031.x