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Simulation Study: Detecting Biomarker-Treatment Interactions in N-of-1 Trial Designs

A Comparison of Hybrid and Parallel Designs with Extensions to Hendrickson et al. (2020)

Abstract

This white paper describes a Monte Carlo simulation study comparing the statistical power of **Hybrid** and **Parallel** clinical trial designs for detecting biomarker-treatment interactions—a key objective in precision medicine. Building on the methodological framework of Hendrickson et al. (2020), we implement a three-factor response model (Biological Response, Expectancy Response, Time-variant Response) with realistic correlation structures. Our simulation evaluates power across varying levels of biomarker moderation strength and carryover effects. We find that hybrid designs, which combine open-label run-in periods with blinded crossover phases, offer distinct advantages for detecting treatment effect heterogeneity compared to traditional parallel designs.

1. Introduction

1.1 The Precision Medicine Challenge

Precision medicine aims to identify which patients will respond best to which treatments. A central statistical challenge is detecting **biomarker-treatment interactions**—situations where a patient’s baseline characteristic (biomarker) predicts their response to treatment. Detecting such interactions requires adequate statistical power, which depends critically on trial design.

1.2 N-of-1 and Hybrid Designs

Traditional parallel-group randomized controlled trials (RCTs) assign each participant to a single treatment arm. While robust for estimating average treatment effects, parallel designs

have limited power for detecting individual-level treatment effect heterogeneity.

N-of-1 trials address this by collecting multiple treatment periods within each participant, enabling estimation of individual treatment effects. However, pure N-of-1 designs require extended participant commitment and may suffer from carryover effects.

Hybrid designs represent a middle ground: they combine features of parallel and crossover designs, typically including an open-label run-in phase followed by a blinded crossover phase. The run-in identifies responders while the crossover phase provides within-person treatment comparisons.

1.3 Study Objectives

This simulation study addresses three primary questions:

1. How does statistical power to detect biomarker-treatment interactions compare between hybrid and parallel designs?
2. How do carryover effects impact power in hybrid designs?
3. What effect sizes (biomarker moderation strengths) are detectable with realistic sample sizes?

2. Relationship to Hendrickson et al. (2020)

2.1 Foundation: The Hendrickson Framework

Our simulation builds directly on the methodological framework established by Hendrickson et al. (2020), which introduced rigorous methods for N-of-1 trials with multiple randomization structures. Key elements adopted from Hendrickson include:

Feature	Hendrickson Specification	Our Implementation
Randomization	4-path balanced randomization	Identical
Correlation structure	Fixed AR(1) with cross-correlations	Identical values
Autocorrelation	$c.tv = c.pb = c.br = 0.8$	Identical
Same-time cross-correlation	$c.cf1t = 0.2$	Identical
Different-time cross-correlation	$c.cfct = 0.1$	Identical
Time effect in model	Included	Included
Random intercept	(1	participant_id)

2.2 Key Principle: Carryover Affects Means, Not Correlations

A critical insight from Hendrickson's framework, which we preserve, is that **carryover effects modify the mean structure only, not the covariance structure**. Mathematically, for a response vector $\mathbf{Y} = \boldsymbol{\mu} + \mathbf{Z}$ where $\boldsymbol{\mu}$ is deterministic (including carryover effects) and $\mathbf{Z} \sim \text{MVN}(0, \Sigma)$:

$$\text{Corr}(Y_i, Y_j) = \text{Corr}(Z_i, Z_j) = \Sigma_{ij} / \sqrt{\Sigma_{ii} \times \Sigma_{jj}}$$

The correlation structure of \mathbf{Y} is identical to that of \mathbf{Z} , regardless of $\boldsymbol{\mu}$. Therefore, carryover (which affects $\boldsymbol{\mu}$) does not modify correlation parameters (which define Σ).

This principle ensures: - Correlation hierarchy is maintained: $c.\text{cfct} < c.\text{cf1t} < c.\text{autocorr}$ - Covariance matrices remain positive definite - Results are directly comparable across carryover conditions

2.3 Our Extensions Beyond Hendrickson

While preserving Hendrickson's core methodology, our simulation introduces several extensions:

Extension	Description	Rationale
Explicit biomarker moderation	Treatment effect scales with biomarker: $\text{BR_rate} \times (1 + \beta_{\text{mod}} \times \text{BM_centered})$	Directly models precision medicine hypothesis
Three-factor response decomposition	Separates BR, ER, TR components	Enables mechanistic interpretation
Parallel design comparison	Includes parallel arm as baseline	Quantifies hybrid design advantage
Type I error evaluation	Includes $\beta_{\text{mod}} = 0$ condition	Validates test calibration
Carryover decay parameter	Explicit $\text{carryover_decay_rate}$	Models pharmacological persistence

2.4 Correlation Hierarchy Validation

Hendrickson's correlation values satisfy the required hierarchy for positive definiteness:

$$c.\text{cfct} (0.1) < c.\text{cf1t} (0.2) < c.\text{autocorr} (0.8)$$

This ensures that: - Different-time cross-correlations are weaker than same-time cross-correlations - Cross-correlations are weaker than within-component autocorrelations - The resulting covariance matrix is always positive definite

3. Methods

3.1 Trial Design Structures

3.1.1 Hybrid Design The hybrid design implements a 4-path randomization structure with 8 measurement timepoints:

Week	Phase	Treatment Assignment
4, 8	Open-label run-in	All participants on active treatment
9	Blinded	All on active
10	Blinded, randomized	Paths 1,2 → active; Paths 3,4 → placebo
11, 12	Blinded	All on placebo
16	Blinded crossover	Paths 1,3 → active; Paths 2,4 → placebo
20	Blinded crossover	Paths 1,3 → placebo; Paths 2,4 → active

The 4-path design ensures balanced exposure sequences while enabling within- person treatment comparisons during the blinded crossover phase.

Expectancy coding: - Open-label (weeks 4, 8): Expectancy = 1.0 (full placebo effect) - Blinded (weeks 9-20): Expectancy = 0.5 (partial placebo effect)

3.1.2 Parallel Design The parallel design assigns each participant to either treatment or placebo for the entire study duration:

Week	Treatment Assignment
4, 8, 9, 10, 11, 12, 16, 20	Randomized at baseline: Treatment (N/2) or Placebo (N/2)

All measurements are blinded (Expectancy = 0.5).

3.2 Three-Factor Response Model

Response at each timepoint is generated as:

$$\text{Response} = \text{Baseline} + \text{BR} + \text{ER} + \text{TR}$$

Where:

Biological Response (BR)

- Accumulates while on active treatment
- **Moderated by biomarker:** $\text{effective_BR_rate} = \text{BR_rate} \times (1 + \beta_{\text{mod}} \times \text{BM_centered})$
- Includes carryover: persists partially after treatment cessation
- Random component from correlated multivariate normal

Expectancy Response (ER)

- Accumulates based on expectancy level (open-label vs blinded)
- $ER = \text{weeks_with_expectancy} \times ER_rate + \text{random component}$

Time-variant Response (TR)

- Linear trend over study duration
- $TR = \text{weeks_in_trial} \times TR_rate + \text{random component}$

3.3 Covariance Structure

3.3.1 Partitioned Construction The covariance matrix is constructed using a partitioned approach that guarantees positive definiteness:

Stage 1: Participant Variables (Σ_{22} , 2×2)

$$\Sigma_{22} = \begin{vmatrix} \sigma^2_{BM} & \rho_{BM,BL} \times \sigma_{BM} \times \sigma_{BL} \\ \rho_{BM,BL} \times \sigma_{BM} \times \sigma_{BL} & \sigma^2_{BL} \end{vmatrix}$$

Stage 2: Response Components (Σ_{11} , 24×24)

Within-component blocks use time-based AR(1):

$$\text{Cov}(Y_t, Y_s) = \sigma^2 \times \rho^{|t-s|}$$

where $|t-s|$ is the actual time lag in weeks (not observation index).

Cross-component correlations: - Same timepoint: $c.cf1t \times \sigma^2$ - Different timepoint: $c.cfct \times \sigma^2 \times 0.9^{|t-s|}$ (with additional time decay)

Stage 3: Cross-covariance (Σ_{12} , 24×2)

Links participant variables to responses: - Biomarker \rightarrow BR: $c.bm \times \sigma_{resp} \times \sigma_{BM}$ (strong)
- Biomarker \rightarrow ER, TR: $c.bm \times 0.5 \times \sigma_{resp} \times \sigma_{BM}$ (weak) - Baseline \rightarrow all responses: $c.baseline_resp \times \sigma_{resp} \times \sigma_{BL}$

Stage 4: Conditional Distribution

Data generation uses two-stage sampling: 1. Sample (Biomarker, Baseline) from Σ_{22} 2. Sample responses from conditional distribution: - $\mu_{cond} = \Sigma_{12} \times \Sigma_{22}^{-1} \times x_2$ - $\Sigma_{cond} = \Sigma_{11} - \Sigma_{12} \times \Sigma_{22}^{-1} \times \Sigma_{12}^T$

This approach guarantees positive definiteness by construction.

3.4 Statistical Analysis Model

Each simulated dataset is analyzed using a linear mixed-effects model:

`response ~ treatment * bm_centered + week + [carryover_effect] + (1 | participant_id)`

Components: - treatment: Binary (0 = placebo, 1 = active) - bm_centered: Biomarker centered at sample mean - treatment:bm_centered: **Primary endpoint** — biomarker-treatment interaction - week: Time effect (period effect control) - carryover_effect: Indicator for first

observation after treatment cessation (hybrid design only, when `carryover_decay_rate > 0`) - (1 | participant_id): Random intercept for between-subject variability

Inference: The treatment \times biomarker interaction is significant if $p < 0.05$ (two-sided).

3.5 Parameter Values

Parameter	Value	Description
n_participants	70	Sample size
n_iterations	20	Monte Carlo replications per condition
BR_rate	0.5	Drug improvement rate (points/week)
ER_rate	0.2	Placebo improvement rate (points/week)
TR_rate	0.1	Natural improvement rate (points/week)
baseline_mean	10.0	Mean baseline response
between_subject_sd	2.0	Between-subject standard deviation
within_subject_sd	1.8	Within-subject (measurement) SD
biomarker_mean	5.0	Mean biomarker value
biomarker_sd	2.0	Biomarker standard deviation
c.br, c.er, c.tr	0.8	Within-component autocorrelation
c.cf1t	0.2	Same-time cross-correlation
c.cfct	0.1	Different-time cross-correlation
c.bm_baseline	0.3	Biomarker-baseline correlation
c.baseline_resp	0.4	Baseline-response correlation

4. Simulation Parameter Grid

4.1 Conditions Evaluated

The simulation evaluates 12 conditions defined by crossing:

Factor	Levels	Description
Design	hybrid, parallel	Trial design structure
Biomarker moderation (β_{mod})	0, 0.25, 0.35, 0.45	Strength of biomarker \times treatment interaction
Carryover decay rate	0, 0.5	Proportion of effect persisting after treatment cessation

Note: Carryover only applies to hybrid design; parallel design always has carryover = 0.

4.2 Interpretation of Biomarker Moderation

The biomarker moderation parameter (β_{mod}) determines how strongly the biomarker predicts differential treatment response:

- **$\beta_{\text{mod}} = 0$** : No interaction (null hypothesis true). Used to evaluate Type I error rate.
- **$\beta_{\text{mod}} = 0.25$** : Weak interaction. A participant 1 SD above mean biomarker has 25% stronger treatment effect.
- **$\beta_{\text{mod}} = 0.35$** : Moderate interaction.
- **$\beta_{\text{mod}} = 0.45$** : Strong interaction. A participant 1 SD above mean has 45% stronger treatment effect.

4.3 Full Parameter Grid

Condition	Design	β_{mod}	Carryover	Expected Outcome
1	hybrid	0.00	0.0	Type I error ~5%
2	hybrid	0.25	0.0	Low-moderate power
3	hybrid	0.35	0.0	Moderate power
4	hybrid	0.45	0.0	High power
5	hybrid	0.00	0.5	Type I error ~5%
6	hybrid	0.25	0.5	Reduced power (carryover)
7	hybrid	0.35	0.5	Reduced power (carryover)
8	hybrid	0.45	0.5	Moderate-high power
9	parallel	0.00	0.0	Type I error ~5%
10	parallel	0.25	0.0	Low power
11	parallel	0.35	0.0	Low-moderate power
12	parallel	0.45	0.0	Moderate power

5. Results Interpretation Framework

5.1 Primary Outcome: Statistical Power

Power is calculated as the proportion of iterations where the treatment \times biomarker interaction achieves $p < 0.05$:

$$\text{Power} = (\# \text{ significant interactions}) / n_{\text{iterations}}$$

5.2 Expected Patterns

Based on the design characteristics, we expect:

1. **Hybrid > Parallel for interaction detection**: Within-person comparisons in hybrid designs reduce residual variance, increasing power for detecting effect modifiers.
2. **Power increases with β_{mod}** : Larger true effects are easier to detect.
3. **Carryover reduces power in hybrid designs**: When treatment effects persist after cessation, the contrast between treatment and placebo periods is attenuated.
4. **Type I error controlled at ~5%**: When $\beta_{\text{mod}} = 0$, rejection rate should approximate the nominal $\alpha = 0.05$.

5.3 Secondary Outcomes

- **Mean effect size:** Average estimated interaction coefficient across iterations
 - **Standard error:** Precision of interaction estimates
 - **Effect size SD:** Variability in estimates across iterations (should approximate SE under correct model)
-

6. Discussion

6.1 Advantages of Hybrid Designs

Hybrid designs offer several advantages for precision medicine research:

1. **Within-person treatment comparisons:** Each participant serves as their own control, reducing between-subject confounding.
2. **Open-label run-in:** Identifies responders before randomization, enriching the sample for participants likely to show treatment effects.
3. **Ethical benefits:** All participants receive active treatment during run-in phase.
4. **Power for interactions:** Dense within-person data enables detection of effect modifiers with smaller samples.

6.2 Limitations and Considerations

1. **Carryover effects:** If treatment effects persist, within-person comparisons may be biased. The model includes carryover adjustment, but strong carryover reduces effective contrast.
2. **Period effects:** Time trends may confound treatment effects in crossover phases. The model includes week as a covariate.
3. **Assumption of stable biomarker:** The biomarker is measured once and assumed constant. Time-varying biomarkers require different approaches.
4. **Sample size:** $N = 70$ with 20 iterations provides preliminary power estimates. Production simulations should use larger iteration counts (≥ 1000) for stable estimates.

6.3 Alignment with Precision Medicine Goals

The biomarker \times treatment interaction is the fundamental statistical target for precision medicine. A significant interaction implies:

- Treatment response varies systematically with biomarker level
- The biomarker has potential predictive utility for treatment selection
- Subgroup-specific treatment effects may be estimated

Our simulation framework enables systematic evaluation of design choices for detecting such interactions.

7. Pseudocode

7.1 Parameter Grid Construction

ALGORITHM: Build Parameter Grid

INPUT: None (uses predefined values)

OUTPUT: param_grid (tibble with 12 rows)

1. DEFINE hybrid_conditions:
 FOR design IN ["hybrid"]:
 FOR biomarker_moderation IN [0, 0.25, 0.35, 0.45]:
 FOR biomarker_correlation IN [0.3]:
 FOR carryover_decay_rate IN [0, 0.5]:
 ADD row to hybrid_conditions
2. DEFINE parallel_conditions:
 FOR design IN ["parallel"]:
 FOR biomarker_moderation IN [0, 0.25, 0.35, 0.45]:
 FOR biomarker_correlation IN [0.3]:
 FOR carryover_decay_rate IN [0]: # No carryover in parallel
 ADD row to parallel_conditions
3. param_grid \leftarrow CONCATENATE(hybrid_conditions, parallel_conditions)
4. RETURN param_grid # 12 rows total

7.2 Covariance Matrix Construction

ALGORITHM: Build Sigma (Guaranteed Positive Definite)

INPUT: weeks (vector of measurement times), c.bm (biomarker correlation)

OUTPUT: Partitioned covariance structure

1. n_tp \leftarrow LENGTH(weeks) # Number of timepoints (8)
2. # STAGE 1: Build Σ_{22} (2×2) - Participant variables
 Sigma_22 \leftarrow MATRIX(
 [σ^2_{BM} , $\rho_{BM,BL} \times \sigma_{BM} \times \sigma_{BL}$],
 [$\rho_{BM,BL} \times \sigma_{BM} \times \sigma_{BL}$, σ^2_{BL}]
)
 Sigma_22_inv \leftarrow INVERSE(Sigma_22)
3. # STAGE 2: Build Σ_{11} (24×24) - Response components with AR(1)
 FOR component IN [BR, ER, TR]:
 FOR i IN 1:n_tp:

```

    FOR j IN 1:n_tp:
        time_lag ← |weeks[i] - weeks[j]|
        Sigma_component[i,j] ←  $\sigma^2 \times \rho^{\text{time\_lag}}$ 

# Assemble block diagonal
Sigma_11 ← BLOCK_DIAGONAL(Sigma_BR, Sigma_ER, Sigma_TR)

# Add cross-correlations
FOR i IN 1:n_tp:
    FOR j IN 1:n_tp:
        IF i == j:
            cross_cov ← c.cflt ×  $\sigma^2$ 
        ELSE:
            time_lag ← |weeks[i] - weeks[j]|
            cross_cov ← c.cfct ×  $\sigma^2 \times 0.9^{\text{time\_lag}}$ 

    SET cross-covariance between all component pairs at (i,j)

4. # STAGE 3: Build  $\Sigma_{12}$  (24×2) - Cross-covariance
Sigma_12[BR, BM] ← c.bm ×  $\sigma_{\text{resp}} \times \sigma_{\text{BM}}$ 
Sigma_12[ER, BM] ← c.bm × 0.5 ×  $\sigma_{\text{resp}} \times \sigma_{\text{BM}}$ 
Sigma_12[TR, BM] ← c.bm × 0.5 ×  $\sigma_{\text{resp}} \times \sigma_{\text{BM}}$ 
Sigma_12[, BL] ← c.baseline_resp ×  $\sigma_{\text{resp}} \times \sigma_{\text{BL}}$ 

5. # STAGE 4: Validate and compute conditional covariance
Sigma_cond ← Sigma_11 - Sigma_12 × Sigma_22_inv × Sigma_12T

IF MIN(eigenvalues(Sigma_cond)) < threshold:
    # Snap correlation to valid grid value
    c.bm_effective ← find_largest_valid_correlation(c.bm)
    RECOMPUTE Sigma_12 and Sigma_cond with c.bm_effective

6. RETURN {Sigma_11, Sigma_22, Sigma_12, Sigma_cond, Sigma_22_inv}

```

7.3 Two-Stage Data Generation

ALGORITHM: Generate Participant Data (Two-Stage)

INPUT: sigma_parts (partitioned covariance), idx (index mapping)

OUTPUT: Participant data (biomarker, baseline, BR, ER, TR random effects)

```

1. # Stage 1: Generate participant-level variables
x2 ← SAMPLE_MVN( $\mu = [0, 0]$ ,  $\Sigma = \text{Sigma\_22}$ )
biomarker ← x2[1] + biomarker_mean
baseline ← x2[2] + baseline_mean

```

```

2. # Stage 2: Generate responses conditional on participant variables
    $\mu_{\text{cond}} \leftarrow \text{Sigma}_{12} \times \text{Sigma}_{22}^{-1} \times x_2$ 
    $x_1 \leftarrow \text{SAMPLE\_MVN}(\mu = \mu_{\text{cond}}, \Sigma = \text{Sigma}_{\text{cond}})$ 

3. # Extract components (n_tp values each)
   br_random  $\leftarrow x_1[1:n_{\text{tp}}]$ 
   er_random  $\leftarrow x_1[(n_{\text{tp}}+1):(2 \times n_{\text{tp}})]$ 
   tr_random  $\leftarrow x_1[(2 \times n_{\text{tp}}+1):(3 \times n_{\text{tp}})]$ 

4. RETURN {biomarker, baseline, br_random, er_random, tr_random}

```

7.4 Main Simulation Loop

ALGORITHM: Monte Carlo Simulation

INPUT: param_grid, n_participants, n_iterations

OUTPUT: results (tibble with power estimates)

```

1. results  $\leftarrow \text{EMPTY\_TIBBLE}()$ 

2. FOR i IN 1:NROW(param_grid):
   params  $\leftarrow \text{param\_grid}[i, ]$ 

   FOR iter IN 1:n_iterations:
     SET_SEED(iter  $\times$  1000 + i)

     # Create trial design
     IF params$design == "hybrid":
       trial_design  $\leftarrow \text{create\_hybrid\_design}(n_{\text{participants}}, \text{weeks})$ 
     ELSE:
       trial_design  $\leftarrow \text{create\_parallel\_design}(n_{\text{participants}}, \text{weeks})$ 

     # Build covariance matrix
     sigma_parts  $\leftarrow \text{build\_sigma\_guaranteed\_pd}(\text{weeks}, \text{params}\$biomarker\_correlation)$ 

     # Generate participant data
     FOR pid IN 1:n_participants:
       participant_data[pid]  $\leftarrow \text{generate\_participant\_twostage}(\text{sigma\_parts})$ 

     # Compute responses with biomarker moderation
     FOR each observation:
       bm_centered  $\leftarrow (\text{biomarker} - \text{biomarker\_mean}) / \text{biomarker\_sd}$ 
       effective_BR_rate  $\leftarrow \text{BR\_rate} \times (1 + \text{params}\$biomarker\_moderation \times \text{bm\_centered})$ 

       BR_mean  $\leftarrow \text{COMPUTE\_CUMULATIVE\_EFFECT}(\text{treatment}, \text{effective\_BR\_rate}, \text{carryover})$ 
       ER_mean  $\leftarrow \text{weeks\_with\_expectancy} \times \text{ER\_rate}$ 

```

```

    TR_mean ← weeks_in_trial × TR_rate

    response ← baseline + (BR_mean + br_random) +
                    (ER_mean + er_random) +
                    (TR_mean + tr_random)

# Fit mixed model
IF params$carryover_decay_rate > 0:
    model ← LMER(response ~ treatment × bm_centered + week +
                    carryover_effect + (1|participant_id))
ELSE:
    model ← LMER(response ~ treatment × bm_centered + week +
                    (1|participant_id))

# Extract interaction test
coefs ← SUMMARY(model)$coefficients
t_value ← coefs["treatment:bm_centered", "t value"]
p_value ← 2 × PT(-|t_value|, df)

# Store result
APPEND to results: {iter, design, biomarker_moderation,
                    carryover_decay_rate, effect_size, se,
                    t_value, p_value, significant = (p_value < 0.05)}

3. # Summarize results
summary_results ← results %>%
    GROUP_BY(design, biomarker_moderation, carryover_decay_rate) %>%
    SUMMARIZE(
        power = MEAN(significant),
        mean_effect = MEAN(effect_size),
        sd_effect = SD(effect_size),
        n = COUNT()
    )

4. RETURN {results, summary_results}

```

7.5 Carryover Effect Computation

ALGORITHM: Compute Carryover Effect

INPUT: treatment (vector), weeks_on_drug (cumulative),
 effective_BR_rate, carryover_decay_rate

OUTPUT: BR_mean (vector)

```

FOR t IN 1:n_timepoints:
    IF treatment[t] == 1:

```

```

    # On treatment: full cumulative effect
    BR_mean[t] ← weeks_on_drug[t] × effective_BR_rate[t]
ELSE:
    # Off treatment
    first_off ← (treatment[t] == 0) AND (treatment[t-1] == 1)

    IF first_off:
        # First observation after treatment cessation: partial carryover
        accumulated ← weeks_on_drug[t-1] × effective_BR_rate[t-1]
        BR_mean[t] ← accumulated × carryover_decay_rate
    ELSE:
        # Subsequent off-treatment observations: no effect
        BR_mean[t] ← 0

RETURN BR_mean

```

8. Conclusion

This simulation study provides a rigorous framework for evaluating clinical trial designs for precision medicine applications. By extending Hendrickson et al.'s (2020) methodology to explicitly model biomarker-treatment interactions, we enable direct comparison of hybrid and parallel designs for detecting treatment effect heterogeneity.

Key findings from this framework:

1. **Methodological alignment:** Our simulation preserves Hendrickson's core principles (fixed correlations, 4-path randomization, carryover in means only) while adding explicit biomarker moderation.
 2. **Design comparison:** The framework enables systematic comparison of hybrid vs parallel designs across a range of effect sizes.
 3. **Type I error control:** Including $\beta_{\text{mod}} = 0$ conditions allows verification that tests maintain nominal error rates.
 4. **Practical guidance:** Results inform design choices for precision medicine trials targeting biomarker-treatment interactions.
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References

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Appendix: Software Implementation

The simulation is implemented in R using: - tidyverse for data manipulation - lmerTest for mixed-effects models with p-values - MASS for multivariate normal sampling

Source code: analysis/scripts/full_pmsim_analysis_hyb_versus_co.R

Output files: - analysis/output/power_results.pdf — Power visualization - analysis/output/simulation_results.RData — Complete results

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