Multiple conditional randomization tests for lagged and spillover treatment effects

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Abstract

We consider the problem of constructing multiple independent conditional randomization tests using a single dataset. Because the tests are independent, the randomization p-values can be interpreted individually and combined using standard methods for multiple testing. We give a simple, sequential construction of such tests, and then discuss its application to three problems: Rosenbaum’s evidence factors for observational studies, lagged treatment effect in stepped-wedge trials, and spillover effect in randomized trials with interference. We compare the proposed approach with some existing methods using simulated and real datasets. Finally, we establish a more general sufficient condition for independent conditional randomization tests.

1 Introduction

The growth of randomized experiments in social and biomedical sciences has created numerous opportunities for the application of randomization tests. These tests, dating

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back to Fisher [1935] and Pitman [1937], are based solely on the physical act of randomization, enabling them to yield p-values that are exact in finite samples without relying on any distributional assumptions. Variations of randomization tests have also found wide applications in non-randomized settings in which modelling the full data distribution is prohibitively difficult; see Zhang and Zhao [2023] for a recent review.

Many modern randomized experiments have a complex design, and it may be challenging to design simple randomization tests. This is a particularly difficult problem when the causal hypothesis is not strong enough to impute all possible potential outcomes. There is much methodological progress in the last decade on this problem by conditioning on a suitable statistic (usually a function of the treatment). Some notable examples of conditional randomization tests (CRTs) include those for meta-analysis [Zheng and Zelen, 2008], covariate adjustment [Hennessy et al., 2016], and unit interference [Athey et al., 2018, Basse et al., 2019, Puelz et al., 2022]. Here, conditioning can be viewed as a way to increase the precision of hypothesis testing. The theory for a single CRT is briefly reviewed in Section 2 below.

In practice, it is often of interest to conduct multiple CRTs to increase power or assess different causal hypotheses. This is the problem we will study in this paper. Before outlining our proposal, we will give three examples where multiple CRTs could be useful.

**Example 1** (Evidence factors). In a series of work, Rosenbaum [2010, 2017, 2021] developed a concept called “evidence factors” for observational studies, which are essentially pieces of evidence regarding different aspects of an abstract causal hypothesis. Roughly speaking, each evidence factor is characterized by a worst-case p-value in a sensitivity analysis for a different (partially) sharp null hypothesis. Rosenbaum’s key observation is that in certain settings, these evidence factors are “nearly independent” in the sense that the worst-case p-values stochastic dominate the multivariate uniform distribution over the unit hypercube.

**Example 2** (Lagged treatment effect). The stepped-wedge randomized controlled trial is a monotonic cross-over design in which all units begin in the control group and subsequently cross over to the treatment group at staggered time points [Hussey and Hughes, 2007]. This design is also known as “staggered adoption” in economics [Sun and Abraham, 2021, Athey and Imbens, 2022]. It has become a popular trial design in medical and policy research, especially in cases where it is impractical to administer the treatment to all units at the same time or where for ethical reasons the treatment should be given to everyone since it has shown effectiveness already. Because the treatment is administered at different times, the stepped-wedge design allows us to estimate time-lagged treatment effects. This is usually done using mixed-effects models [Hussey and Hughes, 2007, Hemming et al., 2018, Li et al., 2021], but the inference is not reliable when the models are misspecified [Thompson et al., 2017, Ji et al., 2017]. Randomization tests have been proposed as an alternative to test the global
null hypothesis that assumes no treatment effect whatsoever [Ji et al., 2017, Wang and De Gruttola, 2017, Thompson et al., 2018, Hughes et al., 2020]. However, to our knowledge, no randomization test for lagged treatment effects has been developed in this context.

**Example 3** (Testing the range of spillover effect). When experimental units are geographical regions or users connected through a social network, it is often of interest to know if the effect of a treatment can spill over to neighbouring units. For example, Jayachandran et al. [2017] conducted a randomized controlled trial to study if payments for ecosystem services can reduce deforestation in Uganda. After receiving these payments, forest owners were expected to engage in forest conservation within their respective villages. However, there was also a potential spillover effect, where these forest owners may deforest more in nearby untreated villages. CRTs for spillover effects have been studied recently by, among others, Aronow [2012], Athey et al. [2018], Basse et al. [2019], and Puelz et al. [2022]. However, a single CRT can only determine the presence of a spillover effect within a specified distance. Multiple CRTs can assess how far the treatment effect can spread so policymakers can determine, e.g., in the deforestation example, how to maximize forest conservation by allocating payments to selected villages.

A common challenge in these examples is that a naive application of existing CRTs for different causal hypotheses (e.g., different time lags or spillover distances) will give dependent p-values, which complicates the decision. In this paper, we will propose a general, sequential construction of conditional randomization tests that generate “nearly independent” p-values. These p-values can be viewed as independent pieces of evidence for different causal hypotheses (or as “evidence factors” in Rosenbaum’s terminology), and can be combined using standard multiple testing methods such as Fisher’s and Stouffer’s methods for testing the intersection of the causal hypotheses [Fisher, 1925, Stouffer et al., 1949], or Hommel’s method and more general closed testing procedures for controlling the family-wise error rate [Marcus et al., 1976]. We will illustrate this sequential testing approach by applying it to the problems in Examples 1 to 3 and use simulations to investigate the power of the proposed method. Some concluding remarks will be offered at the end of the article.

## 2 Review: A single conditional randomization test

Consider a randomized experiment on $N$ units. Let $Z \in \mathcal{Z}$ denote the treatment assignment that is randomized. For every unit $i \in [N] := \{1, \cdots, N\}$, we denote all its potential outcomes by $(Y_i(z) \mid z \in \mathcal{Z})$. Let $Y(z) = (Y_1(z), \ldots, Y_N(z))$. The collection of potential outcomes for all units and treatment assignments is referred to as the
**potential outcomes schedule**, which is denoted by \( W = (Y(z) : z \in Z) \in W \). After \( Z \) is randomized, we observe a single outcome \( Y_i \) for every unit \( i \). We assume that all the observed outcomes \( Y = (Y_1, \ldots, Y_N) \) are consistent, meaning that they match the potential outcomes for the realized assignment, i.e., \( Y = Y(Z) \).

Treatment effects such as lagged or spillover effects are often defined as contrasts between potential outcomes. By randomizing \( Z \), the experiment establishes independence between \( Z \) and \( W \) that eliminates all confounding factors between the treatment and the outcome. This heuristic is formalized by the assumption below.

**Assumption 1** (Randomized experiment). \( Z \perp W \) and the density function \( \pi(\cdot) \) of \( Z \) is known and positive everywhere in \( Z \).

In this paper, we are interested in testing causal hypotheses under which some unknown entries of \( W \) can be imputed from \( Y \). The simplest example is the global null: for all assignments \( z, z' \in Z \), the potential outcomes are identical, i.e., \( Y(z) = Y(z') \). This is also known as Fisher’s exact null. Under such a fully sharp hypothesis, all potential outcomes in \( W \) can be imputed using the observed outcome \( Y \). However, we are often interested in testing more granular hypotheses that can only impute part of \( W \). Such hypotheses are called "partially sharp" by Zhang and Zhao [2023]. Conditioning is a useful tool to exclude non-imputable potential outcomes. Specifically, a conditional randomization test is defined as follows.

**Definition 1.** A conditional randomization test (CRT) for the treatment \( Z \) is defined by a finite partition \( \mathcal{R} = \{S_m\}_{m=1}^M \) of \( Z \) and a test statistics \( T = t(Z,W) \) where \( t : Z \times W \to \mathbb{R} \) is a (measurable) function of \( Z \) and \( W \). With an abuse of notation, let \( S_z \) be the set in the partition \( \mathcal{R} \) that contains \( z \). The p-value of the CRT is then given by

\[
P = p(Z, W) = \mathbb{P}\{t(Z^*, W) \leq t(Z, W) \mid Z^* \in S_Z, Z, W\},
\]

where \( Z^* \) is an independent copy of \( Z \) conditional on \( W \), that is, \( Z^* \) has the same distribution as \( Z \) but is independent of \( Z \) given \( W \).

In (1), the CRT compares the test statistic evaluated at the observed treatment \( Z \) with all other potential treatment assignments \( Z^* \) that are in the same equivalence class as \( Z \). The equivalence class can be represented by a function \( v : Z \to [M] \) such that \( S_m \) is the preimage of \( \{m\} \), i.e.,

\[
S_m = v^{-1}(\{m\}) = \{z \in Z : v(z) = m\}, \text{ for all } m \in [M].
\]

With \( T^* = t(Z^*, W), V^* = v(Z^*) \) and \( V = v(Z) \), we can rewrite the p-value in (1) as

\[
P = \mathbb{P}(T^* \leq T \mid V^* = V, Z, W).
\]
Note that our p-value is a function of the potential outcomes schedule $W$ instead of the observed outcomes $Y$. This representation guarantees the CRT to be valid given $V$, as stated in the theorem below. With this in mind, the role of the null hypothesis is to impute the missing potential outcomes in $W$ and compute the p-value, which is not always possible when the causal hypothesis is partially sharp. In this case, the conditioning statistic $V$ needs to be carefully chosen. Examples of $V$ we will below include the (random) set of units that are treated at a given time point and the subvector $Z_I$ for some pre-selected subset $I$.

**Theorem 1.** Under Assumption 1, the p-value in (1) satisfies, for any $\alpha \in [0, 1]$, 
\[
P \{ P(Z, W) \leq \alpha \mid V, W \} := \sum_{m=1}^{M} 1_{\{Z \in S_m\}} P \{ P(Z, W) \leq \alpha \mid Z \in S_m, W \} \leq \alpha. \tag{4}
\]
In consequence, the CRT is valid in the sense that $P \{ P(Z, W) \leq \alpha \} \leq \alpha$ for all $\alpha \in [0, 1]$.

Theorem 1 is a well-known result in randomization inference, and a proof is included in Appendix D.1 for completeness. By randomizing the rejection, the inequality (4) can be replaced by equality; see Lehmann and Romano [2006, eq. 5.51]. For this reason, we refer to the CRT as “nearly exact” and the multiple CRTs introduced below as “nearly independent”.

## 3 Sequential conditional randomization tests

Next, we consider the problem of constructing $K$ CRTs for $K$ potentially different null hypotheses. Following (2) and (3), we define the CRTs using $K$ conditioning statistics:
\[
V^{(k)} = v^{(k)}(Z) \text{ for some function } v^{(k)} \text{ on } Z, \ k \in [K].
\]
The sequential CRTs are constructed by conditioning on more and more information as $k$ increases. Specifically, we compute the p-value in the $k$th CRT using the distribution of $V^{(k)}$ given $V^{[k-1]}$ and a test statistics $t^{(k)}(V^{[k]}, W)$:
\[
P^{(k)} = p^{(k)}(V^{[k]}, W) = P \{ t^{(k)}(V^{*^{[k]}}, W) \leq t^{(k)}(V^{[k]}, W) \mid V^{*^{[k-1]}}, Z, W \} = V^{[k-1]}, Z, W \}, \tag{5}
\]
where $V^{*^{(k)}} = v^{(k)}(Z^*)$ and $Z^*$ is an i.i.d. copy of $Z$.

The next result shows that this construction generates nearly independent p-values regardless of how the conditioning statistics $V^{(1)}, \ldots, V^{(K)}$ are chosen. Note that sometimes it is desirable to condition additionally on a global statistic $V^{(0)}$ in all the tests. Then the test statistics $t^{(1)}, \ldots, t^{(K)}$ may further depend on $V^{(0)} = v^{(0)}(Z)$ and equation (6) below holds given $V^{(0)}$. 

5
Theorem 2. Under Assumption 1 and the setup above, the p-values \( P^{(1)}, \ldots, P^{(K)} \) defined in (5) are valid and nearly independent in the sense that

\[
P\left( P^{(1)} \leq \alpha^{(1)}, \ldots, P^{(K)} \leq \alpha^{(K)} \mid W \right) \leq \prod_{k=1}^{K} \alpha^{(k)} \text{ for all } \alpha^{(1)}, \ldots, \alpha^{(K)} \in [0, 1]. \tag{6}
\]

Proof. Suppose \( K = 2 \). Let \( \psi^{(k)}(V^{[k]}, W) = 1_{\{P^{(k)} \leq \alpha^{(k)}\}} \) be the test function. By using the law of iterated expectations and Theorem 1,

\[
\begin{align*}
P \left\{ P^{(1)} \leq \alpha^{(1)}, P^{(2)} \leq \alpha^{(2)} \mid W \right\} &= \mathbb{E} \left[ \psi^{(1)}(V^{(1)}, W) \mathbb{E} \left\{ \psi^{(2)}(V^{[2]}, W) \mid V^{(1)} \right\} \mid W \right] \\
&\leq \alpha^{(2)} \mathbb{E} \left\{ \psi^{(1)}(V^{(1)}, W) \mid W \right\} \\
&\leq \alpha^{(1)} \alpha^{(2)}.
\end{align*}
\]

By using the above argument sequentially, this proof easily generalizes to \( K > 2 \). \( \square \)

In the next three sections, we will illustrate this sequential construction of CRTs using the three examples introduced in Section 1. Specifically, in Section 4 we will give a simple explanation of Rosenbaum’s evidence factors for observational studies, without using any special structure of permutation groups as suggested by Rosenbaum [2017]. In Sections 5 and 6, we will develop some new statistical methods to test lagged and spillover treatment effects. In Section 8, we will give a more general theorem that does not require a strictly sequential construction of CRTs.

4 Example 1: Evidence factors for observational studies

Rosenbaum [2010, 2017, 2021] developed a concept called “evidence factors” for observational studies, which are essentially pieces of evidence regarding different aspects of an abstract causal hypothesis. Roughly speaking, each evidence factor is characterized by a p-value upper bound for a different hypothesis and the factors together satisfy (6), as we detail below.

Consider the example in Rosenbaum [2017] that concerns the causal effect of smoking on periodontal disease. Each subject in this analysis is categorized as a “non-smoker”, “light smoker”, or “heavy smoker”. The main idea of Rosenbaum [2017] is to represent exposure as two indicators, one for smoking and one for heavy smoking. That is,
let the exposure be $Z = (Z^{(1)}, Z^{(2)})$, where $Z^{(1)}$ and $Z^{(2)}$ are $N$-dimensional binary variables, $Z^{(1)}_i = 1$ indicates subject $i$ is a smoker, and $Z^{(2)}_i = 1$ indicates subject $i$ is a heavy smoker. Rosenbaum then constructed a randomization test by comparing the outcomes of the smokers with the non-smokers, and another randomization test by comparing the outcomes of the heavy smokers with the light smokers.

Rosenbaum showed that the two tests are nearly independent by expressing the permutation group of $(Z_1, \ldots, Z_n)$ as a knit product of two smaller permutation groups, one for $(Z^{(1)}_1, \ldots, Z^{(1)}_N)$ and one for $(Z^{(2)}_1, \ldots, Z^{(2)}_N)$. A group $G$ is said to be the knit product of two subgroups $G_1$ and $G_2$, if every element $g \in G$ can be uniquely represented as $g = g_1g_2$ where $g_1 \in G_1$ and $g_2 \in G_2$. Intuitively, any permutation of the exposure status of the subjects can be obtained by first permuting the non-smokers with the smokers, then permuting the light smokers with the high smokers (within the set of smokers). Thus, the two permutation tests should be independent. Because smoking is not truly randomized in an observational study, Rosenbaum [2017] matched pairs of smokers and non-smokers in terms of age, gender, education, income, and ethnicity before running the randomization tests.

Rosenbaum’s observation is intuitive, but the argument is tailored to permutation tests. The mathematical proof in Rosenbaum [2017] is also quite involved. In view of our theory in Section 3, this can be simplified, as Rosenbaum’s two evidence factors are exactly the sequence of CRTs in Section 3 with $V^{(1)} = Z^{(1)}$ and $V^{(2)} = Z^{(2)}$. By Theorem 2, the p-value upper bounds are nearly independent. Suppose the first CRT assumes a collection $\Pi^{(1)}$ of randomization distributions of $Z^{(1)}$ and the second CRT assumes a collection $\Pi^{(2)}$ of randomization distributions of $Z^{(2)}$ given $Z^{(1)}$. Rosenbaum obtained closed-form expressions of the p-value upper bounds

$$P^{(k)} = \sup_{\pi^{(k)} \in \Pi^{(k)}} p^{(k)}(Z, W; \pi^{(k)}), \quad k = 1, 2,$$

where $p^{(k)}(Z, W; \pi^{(k)})$ is the p-value of the $k$th CRT under the distribution $\pi^{(k)}$. It directly follows from Theorem 2 that these p-values are valid and nearly independent for any distribution in $\pi = (\pi^{(1)}, \pi^{(2)}) \in \Pi^{(1)} \times \Pi^{(2)}$, where $\pi(z) = \pi^{(1)}(z^{(1)}) \cdot \pi^{(2)}(z^{(2)} \mid z^{(1)})$. That is,

$$\sup_{\pi \in \Pi^{(1)} \times \Pi^{(2)}} \mathbb{P}_\pi \left( P^{(1)} \leq \alpha^{(1)}, P^{(2)} \leq \alpha^{(2)} \right) \leq \alpha^{(1)} \alpha^{(2)}. \quad (7)$$

Thus, we can view $P^{(1)}$ and $P^{(2)}$ as independent pieces of evidence about two related causal hypotheses on the effect of smoking on periodontal disease. This argument does not rely on any specific algebraic structure of permutation groups (such as the knit product used by Rosenbaum) other than that they are constructed sequentially as described in Section 3.
5 Example 2: Testing lagged treatment effects in stepped-wedge trials

5.1 Sequential tests for lagged treatment effects

As introduced in Example 2, the stepped-wedge design randomizes cross-over times and thus presents an opportunity to investigate the time lag of treatment effect. In this section, we will describe a sequential construction of CRTs that will allow us to pool information from different time points. For simplicity, we assume that the randomization happens at the unit level, and note here that the method below is applicable to cluster-randomized trials by using aggregated cluster-level outcomes [Middleton and Aronow, 2015, Thompson et al., 2018].

We will consider a stepped-wedge trial on \( N \) units over an evenly spaced time grid \([T] = \{1, \cdots, T\}\). At time \( t \), a total of \( N_t \geq 0 \) units cross over from control to treatment, and for simplicity we assume \( \sum_{t=1}^{T} N_t = N \), so all units are treated when the trial is finished. The cross-overs can be represented by a binary \( N \times T \) matrix \( Z \), where \( Z_{it} = 1 \) indicates that unit \( i \) crosses over from control to treatment at time \( t \). Usually, the units stay in the treatment arm after crossing over, but this framework also covers the case of “one-shot treatment” by redefining treatment as whether the unit has received the one-shot treatment already. We consider the simple scenario of “complete randomization”, where \( Z \) is uniform assigned over \( Z = \{ z \in \{0, 1\}^{N \times T} : 1^T z = (N_1, \cdots, N_T) \} \) (\( 1 \) is a vector of ones). Thus, the treatment assignment mechanism is given by \( \pi(z) = 1/|Z| \) for \( z \in Z \) where \( |Z| = N!/(N_1! \cdots N_T!) \).

After the cross-overs at time \( t \), the experimenter immediately measures the outcomes of all units, denoted by \( Y_t \in \mathbb{R}^N \). The corresponding vector of potential outcomes under the assignment \( Z = z \) is denoted by \( Y_t(z) = (Y_{1t}(z), \ldots, Y_{nt}(z)) \). Let \( Y = (Y_1, \ldots, Y_T) \) be all the realized outcomes and \( \mathcal{Y}(z) \) be the collection of potential outcomes under treatment assignment \( z \in Z \). As before, we assume the observed outcomes are consistent, i.e., \( Y = \mathcal{Y}(Z) \). In this setting, several authors have developed unconditional randomization tests for the null hypothesis of no treatment effect whatsoever [Ji et al., 2017, Wang and De Gruttola, 2017, Hughes et al., 2020]:

\[
H : Y(z) = \mathcal{Y}(z^*), \quad \forall z, z^* \in Z, i \in [N], \text{ and } t \in [T].
\] (8)

Below, we will focus on less restrictive hypotheses about lagged treatment effects.

To make the problem more tractable, we assume no interference between units and no anticipation effect from treatment assignment in the future. See Athey and Imbens [2022] for some discussion on this assumption.

**Assumption 2** (No interference or anticipation). For all \( i \in [N] \) and \( t \in [T] \), \( Y_{it}(z) \) only depends on \( z \) through \( z_{i,[t]} \), i.e. the treatment history for unit \( i \) up to time \( t \).
Given this assumption, we can rewrite $Y_{it}(z)$ as $Y_{it}(z_{i,[t]})$. Given a fixed time lag $0 \leq l \leq T - 1$, we have a sequence of hypotheses about lag-$l$ treatment effect: for $t = 1, \ldots, T - l$,

$$H^{(t)}: Y_{i,t+l}(0_{t-1}, 1, 0_t) - Y_{i,t+l}(0_{t+l}) = \tau_l, \ \forall i \in [N].$$

(9)

In words, $H^{(t)}$ means that crossing over from control to treatment at time $t$ has a constant treatment effect $\tau_l$ on the outcome at time $t + l$.

Next, we will construct a sequence of CRTs for $H^{(1)}, \ldots, H^{(T-l)}$ and combine them to test the intersection hypothesis $\cap_t H^{(t)}$. This intersection hypothesis essentially asserts that the $l$-lagged treatment effect is always $\tau_l$, which is still much weaker claim than the fully sharp hypothesis $H$ in (8). Note that it is difficult to test the intersection $\cap_t H^{(t)}$ via a single CRT using outcomes across all time points. For every unit $i$, there exists some time steps $t$ such that both outcomes in $H^{(t)}$ are unobserved. Therefore, the CRT using all the potential outcomes in $\cap_t H^{(t)}$ is non-computable. This motivates us to test each $H^{(t)}$ individually using outcomes at fewer time steps.

We first show that the most straightforward CRTs for $H^{(1)}, \ldots, H^{(T-l)}$ are not independent. The hypothesis $H^{(t)}$ in (9) only concerns the potential outcomes of $Y_{i,t+l}$ when the cross-over occurs at time $t$ or after $t + l$. Thus, in order to test $H^{(t)}$, we can only compare units that crossed over at time $t$ with those crossed over after time $t + l$. We denote this random set of units as

$$v^{(t)}(Z) = \{i \in [N] : Z_{i,[t+l]} = (0_{t-1}, 1, 0_l) \text{ or } 0_{t+l}\}.$$  

(10)

Because the treatment assignment mechanism $\pi$ is uniform over $Z$, given the random set of units $v^{(t)}(Z)$, the treatment assignment $Z$ is still uniformly distributed over all permutations of the vectors $Z_{i,[t+l]}$ for $i \in v^{(t)}(Z)$. This shows that under Assumptions 1 and 2, the CRT given $v^{(t)}(Z)$ is a two-sample permutation test between the “treated” group that crosses over at time $t$ and the “control” group that crosses over after time $t + l$.

However, the above construction does not yield nearly independent CRTs for $l \geq 1$. We visualize this issue with $l = 1$ in Figure 1a. In this case, the CRT for $H^{(t)}$ is a permutation test that compares the time $t + 1$ outcome for crossing over at $t$ with those crossing over after $t + 1$. Specifically, the first CRT compares cross-overs at time 1 with cross-overs at time 2 and cross-overs at time 3, 4, …, the second CRT compares cross-overs at time 2 and cross-overs at time 4, 5, …, and so on. Thus, the conditioning statistics are not nested in the sense that $V^{(1)} = v^{(1)}(Z)$ can not be written as a function of $V^{(2)} = v^{(2)}(Z)$, and vice versa. In other words, suppose we let the second CRT condition on $v^{(1)}(Z)$ and $v^{(2)}(Z)$, as prescribed by Theorem 2. The second CRT will have a degenerated and powerless randomization distribution because the intersection $v^{(1)}(Z) \cap v^{(2)}(Z)$ exactly identifies the units that crossover at time 2.
To resolve this problem, we can gain some intuition by considering the $l = 0$ case, where the above construction does generate independent tests. Observe that the stepped-wedge trial can be viewed as a sequentially randomized experiment: the assignments $Z$ can be thought of as randomly starting the treatment for $N_t$ untreated units at every $t = 1, \ldots, T$. More precisely, let $Z_t$ denote the $t$-th column of $Z$, $Z_t = (z_1, \ldots, z_t) \in \{0, 1\}^{N \times t}$ and $N_t = \sum_{s=1}^{t} N_s$. We can decompose $\pi$ as

$$
\frac{N_1! \cdot N_T!}{N!} = \pi(z) = \pi_1(z_1) \pi_2(z_2 \mid z_1) \cdots \pi_T(z_T \mid z_{[t-1]}),
$$

where $\pi_t$ is a complete randomization that assigns $N_t$ out of $N - N_{[t-1]}$ units to treatment:

$$
\pi_t(z_t \mid z_{[t-1]}) = \frac{N_t!(N - N_{[t]}!}{(N - N_{[t-1]}!}, \forall z_t \in \{0, 1\}^N \text{ such that } (1_N - z_{[t-1]}1_{t-1})^T z_t = N_t,
$$

i.e. $Z_t$ is uniformly distributed over all assignments with $N_t$ crossovers. In the case of $l = 0$, the conditioning statistics $V^{(i)} = Z_t$ are nested: the first CRT compares cross-overs at time 1 with cross-overs at time 2, 3, \ldots, the second CRT compares cross-overs at time 2 with cross-overs at time 3, 4, \ldots, and so on. By Theorem 2, these CRTs are nearly independent.

The above observation inspires the following construction of nearly independent CRTs for lag $l \geq 1$. Let us first consider $l = 1$. In this case, we divide the $T$ time steps into

Figure 1: Illustration of CRTs for lagged effect (lag $l = 1$) in a stepped-wedge trial.
two groups:
\[ C_{\text{odd}} = \{1, 3, \ldots\} \text{ and } C_{\text{even}} = \{2, 4, \ldots\}. \] (13)

Denote the set of units that cross over at odd time points as
\[ V^{(0)} = v^{(0)}(Z) = \left\{ i \in [N] : \sum_{t \in C_{\text{odd}}} Z_{i,t} = 1 \right\}. \]

Then we divide the treatment variables \( Z \) into two sets over time:
\[ V_{\text{odd}} = (V^{(1)}, V^{(3)}, \ldots) = (Z_1, Z_3, \ldots) \text{ and } V_{\text{even}} = (V^{(2)}, V^{(4)}, \ldots) = (Z_2, Z_4, \ldots). \]

We have \( V_{\text{odd}} \perp V_{\text{even}} \mid V^{(0)} \) given the following factorization of the randomization distribution:
\[
\pi(Z) = \pi(v^{(0)}) \pi_{\text{odd}}(v_{\text{odd}} \mid v^{(0)}) \pi_{\text{test}}(v_{\text{even}} \mid v^{(0)}) \\
= \frac{N_{\text{odd}}! N_{\text{even}}!}{N!} \times \prod_{t \in C_{\text{odd}}} \frac{N_t!}{N_{\text{odd}}!} \times \prod_{t \in C_{\text{even}}} \frac{N_t!}{N_{\text{even}}!}, \tag{14}
\]

where \( N_{\text{odd}} = \sum_{t \in C_{\text{odd}}} N_t \) and \( N_{\text{even}} = \sum_{t \in C_{\text{even}}} N_t \). Observe that the conditional distributions \( \pi_{\text{odd}}(v_{\text{odd}} \mid v^{(0)}) \) and \( \pi_{\text{test}}(v_{\text{even}} \mid v^{(0)}) \) can be further factorized in the same way as (11) and (12). This motivates us to construct two sequences of CRTs, one for the odd time steps and one for the even time steps. Specifically, in the odd sequence, CRT 1 compares cross-overs at time 1 with cross-overs at time 3, 5, \ldots; CRT 3 compares cross-overs at time 3 and cross-overs at time 5, 7, \ldots; and so on (see Figure 1b).

The above sequence of tests follows the sequential structure in Section 3, where the \( k \)th CRT conditions on \( (V^{(0)}, V^{(1)}, V^{(3)}, \ldots, V^{(k-2)}) \) for odd \( k \). The even sequence can be constructed similarly, and the \( k \)th CRT conditions on \( (V^{(0)}, V^{(2)}, V^{(4)}, \ldots, V^{(k-2)}) \) for even \( k \). By \( V_{\text{odd}} \perp V_{\text{even}} \mid V^{(0)} \) and Theorem 2, the p-values of all these CRTs are nearly independent given \( V^{(0)} \). For example, when \( T = 5 \), our theorem implies that
\[
\mathbb{P}(P^{(1)} \leq \alpha^{(1)}, P^{(2)} \leq \alpha^{(2)}, P^{(3)} \leq \alpha^{(3)}, P^{(4)} \leq \alpha^{(4)} \mid V^{(0)}) \\
= \mathbb{P}(P^{(1)} \leq \alpha^{(1)}, P^{(3)} \leq \alpha^{(3)} \mid V^{(0)}) \mathbb{P}(P^{(2)} \leq \alpha^{(2)}, P^{(4)} \leq \alpha^{(4)} \mid V^{(0)}) \\
\leq \alpha^{(1)} \alpha^{(3)} \alpha^{(2)} \alpha^{(4)}. \tag{By Theorem 2}
\]

These p-values can then be combined using Fisher’s or Stouffer’s method to test the intersection hypothesis \( \cap_l H^{(l)} \) about lag \( l = 1 \) effect. They use all the observed outcomes over time, so in this sense, this modified sequential construction uses all the information in the data.

The above construction can be easily generalized to \( l \geq 1 \). To test the lag \( l \) effect, we can emulate (13) to increase the gap and divide \([T]\) into disjoint subsets:
\[ C_1 = \{1, l + 2, 2l + 3, \ldots\}, C_2 = \{2, l + 3, 2l + 4, \ldots\}, \ldots, C_{l+1} = \{l + 1, 2l + 2, \ldots\}, \]
and let $V^{(0)}$ be the random sets \( \{ i \in [N] : \sum_{t \in C_1} Z_{i,t} = 1 \} \), \( \{ i \in [N] : \sum_{t \in C_2} Z_{i,t} = 1 \} \), . . . , which collects the crossover units in $C_1, C_2, \ldots$, respectively. Pseudocode for this algorithm with a general time lag $l$ is given in Appendix C, and we will call it multiple conditional randomization tests (MCRTs) in the examples below.

5.2 Real data examples

We next demonstrate our method using two real stepped-wedge randomized trials. Trial I was conducted to examine if a chronic care model was more effective than usual care in the Netherlands between 2010 and 2012 [Muntinga et al., 2012]. The study consists of 1,147 frail older adults in 35 primary care practices. The primary outcome in the dataset was quality of life measured by a mental health component score in a 12-item Short Form questionnaire (SF-12). Each adult’s outcome was measured at a baseline time point and every 6 months over the study. The trial randomly assigned some practices to start the chronic care model every 6 months. Each practice is an experimental unit, i.e., $N = 35$ and $T = 5$.

Trial II was a stepped-wedge trial performed over the pain clinics of 17 hospitals to estimate the effectiveness of an intervention in reducing chronic pain for patients [Twisk, 2021, Chapter 6.4]. The outcome was a pain score ranging from 1 (least pain) and 5 (most pain), and six measurements were taken over time: one at the baseline and five more equally spaced over a period of twenty weeks. After each measurement, intervention was started in a few randomly selected untreated hospitals. We considered each hospital as an experimental unit and estimated the lag $0$, $1$, $2$ and $3$ effects using hospital-level average outcomes ($N = 17$, $T = 6$).

In both trials, we implement all our CRTs as two-sample permutation tests using the difference-in-means statistic. We combine the p-values from MCRTs using Stouffer’s method based on z-scores; this will be denoted as MCRTs+Z. We compare it with mixed-effects models, with and without time-fixed effects. The 90%-confidence intervals (CIs) for the lagged treatment effects are reported in Figure 2. For Trial I in Figure 2(a), the mixed-effects model without time-fixed effects suggests an improvement in the quality of life with the new chronic care model. However, as noted by Twisk [2021, Section 6.3.1], this model overlooks the gradual increase in the quality of life over time. In contrast, both the mixed-effect model with time-fixed effects and our method MCRTs+Z show that the treatment effect is not statistically significant, and MCRTs+Z provides slightly wider confidence intervals. The difference between mixed-effect models with and without time fixed effects is even more pronounced in Trial II. In Figure 2(b), the confidence intervals generated by these models for the same time lag do not overlap. MCRTs+Z generated confidence intervals that lie in between, suggesting that the effectiveness of the intervention may increase over time. In conclusion, our method
Figure 2: Effect estimates from MCRTs+Z and mixed-effects models with and without time effect parameters: 90%-confidence intervals (CIs) of lagged effects on real data collected from four different stepped-wedge randomized trials.

(MCRTs) provides a robust and nonparametric alternative to existing mixed-effect models for inferring lagged treatment effects. In Section 7.2, we will investigate the coverage rates of the confidence intervals obtained by these methods using numerical simulations in cases where the mixed-effect models are misspecified.

6 Example 3: Range of spillover effect

6.1 Sequential CRTs for spillover effects

We now turn to the problem of testing spillover effects described in Example 3. To be more concrete, we consider the setting with N units in a spatial domain. Let \( z = (z_1, \ldots, z_N) \) denote the treatment assignment of all the units and \( Y_i(z) \) denote the potential outcome of unit \( i \) under treatment \( z \). The hypothesis of no interference can be written as

\[
H^{(1)}: Y_j(z) = Y_j(z') \text{ if } z_j = z'_j.
\]

Athey et al. [2018] proposes to test \( H^{(1)} \) on the potential outcomes of a (randomly) selected subset of “focal units” \( J \), while randomizing the treatment assignment of the other units. By conditioning on the assignment of \( J \), all the missing potential outcomes of \( J \) are imputable under \( H^{(1)} \). Other related methods can be found in Basse et al. [2019] and Puelz et al. [2022].

In applications with limited resources for treatment allocation, it is of interest to know not just whether interference exists but also the approximate range of the spillover
effect. We next propose a sequential construction of CRTs that test the spillover effect at increasing distances.

To formulate our hypotheses, suppose we are given a $N \times N$ symmetric matrix $D$ of pairwise distances between the units and a sequence of distance thresholds $0 = \epsilon^{(0)} < \epsilon^{(1)} < \epsilon^{(2)} < \cdots < \epsilon^{(K)}$. Let $B^{(-1)}$ be the $N \times N$ matrix of zeros, $B^{(0)}$ be the $N \times N$ identity matrix, and $B^{(k)}$ be the interference matrix with entries given by the indicator of $\{0 \leq D_{ij} \leq \epsilon^{(k)}\}$ for $i, j \in [N]$ and $k \in [K]$. With this definition, the diagonal of $B^{(k)}$ is one for $k = 0, 1, \ldots, K$.

We would like to test the following null hypothesis:

$$H^{(k)} : Y_j(z) = Y_j(z') \text{ if } B^{(k-1)}_{ij} z_i = B^{(k-1)}_{ij} z'_i \text{ for all } i \in [N],$$

which means that there is no spillover effect between any pair of units with distance larger than $\epsilon^{(k-1)}$ (using the convention $\epsilon^{(-1)} = -\infty$). Thus, $H^{(0)}$ corresponds to the hypothesis of no treatment effect whatsoever and $H^{(1)}$ is the hypothesis of no interference mentioned above. In the literature, authors also consider the hypothesis of no spillover effect on the control, which adds a condition $z_j = 0$ to the hypothesis $H^{(k)}$ in (15). This modification does not make a technical difference to the CRTs (including ours). A valid CRT requires the selection of focal units to be independent of the observed assignment $Z$. To test this new hypothesis, we can only remove the treated units from the test statistics, given that the treatment assignment of the focal units $j$ is fixed in the CRTs. To simplify the exposition, we will test the original $H^{(k)}$ in what follows.

To test different hypotheses $H^{(k)}$, we propose to randomize the treatment assignment of different subsets of units $\mathcal{I}^{(k)}$. Denote the subset

$$\mathcal{I}^{[k_1:k_2]} = \bigcup_{l=k_1}^{k_2} \mathcal{I}^{(l)} \text{ and } Z^{[k_1:k_2]} = Z_{\mathcal{I}^{[k_1:k_2]}}, \ 0 \leq k_1 \leq k_2 \leq K.$$

Our first method can be viewed as a sequential extension of the method in Athey et al. [2018]. Let $\mathcal{J}$ be a chosen set of “focal units”. Given $\mathcal{J}$, as $k$ increases, we iteratively define

$$\mathcal{I}^{(k)} = \left\{ i \in [N] \setminus \mathcal{I}^{[0:(k-1)]} : \sum_{j \in \mathcal{J}} B^{(k)}_{ij} \geq 1 \right\}, \ 0 \leq k \leq K. \quad (16)$$

In words, as $k$ increases, we let $\mathcal{I}^{(k)}$ collect all the units that fall in the $\epsilon^{(k)}$-balls centered at the focal units $\mathcal{J}$. But we have to remove $\mathcal{I}^{[0:(k-1)]}$ because $H^{(k)}$ is about the spillover effect at a distance larger than $\epsilon^{(k)}$. Figure 3 illustrates this unit selection procedure based on a static set of focal units. The construction in (16) implies that

$$\sum_{i \in \mathcal{I}^{[k:k]}_{[k]}} B^{(k-1)}_{ij} = 0 \text{ for all } j \in \mathcal{J}, 0 \leq k \leq K. \quad (17)$$
Consequently, the potential outcomes of the focal units are imputable under $H(k)$ given $z^{[0:(k-1)]}$:

$$Y_j(z) = Y_j \quad \text{for all } j \in J \text{ and } z \text{ such that } z^{[0:(k-1)]} = Z^{[0:(k-1)]}. \tag{18}$$

In principle, we can test $H(k)$ using any test statistic that only depends on the potential outcomes of $J$. A concrete example that will be used below is the difference-in-means statistic

$$t(k)(z, W) = \frac{\sum_{j \in J} A_j(z^{(k)}) Y_j(z)}{\sum_{j \in J} A_j(z^{(k)})} - \frac{\sum_{j \in J} \{1 - A_j(z^{(k)})\} Y_j(z)}{\sum_{j \in J} \{1 - A_j(z^{(k)})\}}, \tag{19}$$

where $A_j(z^{(k)})$ is an indicator for $\sum_{i \in I^{(k)}} z_i B^{(k)}_{ij} > 0$, i.e., it indicates whether unit $j \in J$ receives a spillover effect from $I^{(k)}$ if $H(k)$ is not true. When $k = 0$ so $B^{(0)}$ is the identity matrix, this reduces to $A_j(z) = z_j$ for all $j \in J^{(0)} = I^{(0)}$. Under $H(k)$, equation (18) shows that $T(k)(z, W)$ only depends on $z$ through $z^{[0:k]}$. Thus, by letting $V^{(k)} = Z^{(k)}$ for $k = 0, 1, \ldots, K$, we obtain a sequence of nearly independent p-values as defined in (5).

### 6.2 Adaptive selection of focal units

A limitation of the above construction is that the set $I^{(k)}$ is often quite small for large distances $\epsilon^{(k)}$; this will be exemplified using a real dataset in Section 6.3. Heuristically, it is difficult to select a single subset of focal units that lead to CRTs with decent power for all the spillover distances. If the subset $J$ is too dense (sparse) in the
spatial domain, the above tests have little power for spillover effect at longer (shorter) distances.

Fortunately, the construction in Section 6.1 can be easily modified to allow adaptive selection of focal units. The key idea is to partition \([N]\) into subsets \(\mathcal{I}^{(0)}, \ldots, \mathcal{I}^{(K)}\) first and then use the largest possible set \(\mathcal{J}^{(k)}\) of focal units for every distance threshold \(\epsilon^{(k)}\). In the following, we first treat \(\mathcal{I}^{(0)}, \ldots, \mathcal{I}^{(K)}\) as given and discuss our choice of \(\mathcal{J}^{(k)}\).

The CRT for \(H^{(k)}\) uses the potential outcomes of the following set of “focal units”:

\[
\mathcal{J}^{(k)} = \left\{ j \in [N] : \sum_{i \in \mathcal{I}^{(k)}} B_{ij}^{(k)} \geq 1 \text{ and } \sum_{i \in \mathcal{I}^{[k-1]}} B_{ij}^{(k-1)} = 0 \right\}. \tag{20}
\]

The first condition in (20) ensures that for every focal unit \(j \in \mathcal{J}^{(k)}\), there exists at least one unit \(i \in \mathcal{I}^{(k)}\) with distance \(D_{ij} \in (\epsilon^{(k-1)}, \epsilon^{(k)})\). In other words, the focal units are “on the edge” of experiencing a spillover effect from \(\mathcal{I}^{(k)}\) when we randomize \(Z^{[k:K]}\) and \(H^{(k)}\) is not true.

Like (17), the second condition in (20) implies that the distances between the focal units and \(\mathcal{I}^{[k:K]}\) are larger than \(\epsilon^{(k-1)}\). The definition in (20) implies that \(\mathcal{J}^{(0)} = \mathcal{I}^{(0)}\) and \(\mathcal{J}^{(k)} \subseteq \mathcal{I}^{[0:(k-1)]}\) for \(k \geq 1\). Equation (18) holds with \(\mathcal{J}\) replaced by \(\mathcal{J}^{(k)}\). Then we can use the same test statistic in (19) but with \(\mathcal{J}\) replaced by \(\mathcal{J}^{(k)}\). Then we have a sequence of nearly independent p-values in (5) by choosing \(V^{(k)} = Z^{(k)}\) for \(k = 0, 1, \ldots, K\) as above.

Next, we describe a procedure for selecting the subsets \(\mathcal{I}^{(k)}\), with the aim of generating large \(\mathcal{I}^{(k)}\) and \(\mathcal{J}^{(k)}\) to increase the statistical power. We say \(\mathcal{U}\) is an \(\epsilon\)-cover of a set of units \(\mathcal{M} \subseteq [N]\), if the \(\epsilon\)-balls of the units in \(\mathcal{U}\) cover all units in \(\mathcal{M}\). Finding the minimum cover is an NP-hard problem, but an approximate solution can be obtained by solving its linear program relaxation. Let \(\mathcal{I}^{[1:0]} = \emptyset\). As \(k\) increases from 1 to \(K\), our algorithm iteratively finds the minimum \(\epsilon^{(k)}\)-cover \(\mathcal{U}^{(k)}\) of the units \([N] \setminus \mathcal{I}^{[1:(k-1)]}\) and selects its subset

\[
\mathcal{I}^{(k)} = \left\{ i \in \mathcal{U}^{(k)} : \sum_{j \neq i} B_{ij}^{(k)} \geq 1 \right\}, \tag{21}
\]

which are essentially the units whose \(\epsilon^{(k)}\)-balls contain not only themselves. Finally, we let \(\mathcal{I}^{(0)} = [N] \setminus \mathcal{I}^{[1:K]}\). Our algorithm ensures that \(\mathcal{I}^{(0)}, \mathcal{I}^{(1)}, \ldots, \mathcal{I}^{(K)}\) are disjoint and form a partition of \([N]\), which is required in our construction of sequential CRTs.

Through the definition in (21), all the units in \(\mathcal{I}^{[1:k-1]}\) have at least one neighbours left in \([N] \setminus \mathcal{I}^{[1:(k-1)]}\). Heuristically, solving the covering problem with and without \(\mathcal{I}^{[1:k-1]}\) will lead to a similar cover \(\mathcal{U}^{(k)}\), given that the \(\epsilon^{(k)}\)-balls get larger as \(k\) increases. In other words, every \(\mathcal{U}^{(k)}\) remains as an approximate cover of all the units in \([N]\).
Consequentially, there are always focal units $\mathcal{J}(k)$ to use in the neighbourhoods of $\mathcal{I}(k) \subseteq \mathcal{U}(k)$. Below, we compare this adaptive approach of selecting focal units with the static approach in Section 6.1 on a real-world dataset.

### 6.3 A real data example

We illustrate our method with a real data example [Jayachandran et al., 2017]. The dataset comprises 121 villages located in Hoima district and northern Kibaale district in Uganda, with 60 of these villages randomly assigned to receive annual payments for forest preservation from 2011 to 2013. The cash payments should reduce deforestation in the treated units, but one concern is that they may increase deforestation in nearby, untreated villages. Following Wang et al. [2020], we use change in the land area covered by trees as the outcome, which is measured from satellite images [Hansen et al., 2013]. We set $\epsilon(k) = 3k$ and $K = 4$. The minimum set covering problem is solved approximately using setcover in the R-package adagio [Borchers, 2016].

To test the spillover effects within a distance of 12, the static approach fixes the focal units in all the CRTs to the minimum 9-cover $\mathcal{U}$ of the units in $[N]$, which are those green points in each upper panel of Figure 4. We then select $\mathcal{I}^{(1)}$ to be the 3-neighbours of $\mathcal{U}$, which are the red dots in panel (a). Recall that $H^{(k)}$ is about no
Table 1: P-values for testing spillover effects at different distances in the forest example.

| Method       | Distance | 3  | 6  | 9  | 12 |
|--------------|----------|----|----|----|----|
| Static       |          | 0.564 | 0.056 | 0.404 | 1.000 |
| MCRTs        |          | 0.013 | 0.120 | 0.503 | 0.713 |
| MCRTs+F      |          | 0.058 | 0.392 | 0.726 | 0.713 |

spillover effect at a distance larger than $3(k - 1)$. In its CRT, we take $I^{(k)}$ as the $3k$-neighbours of $U$ but with $I^{[k-1]}$ removed. As shown in panels (a) and (d), this method leads to a small $I^{(1)}$ and empty $I^{(4)}$, respectively. In comparison, the lower panels of Figure 4 show that our adaptive method generates large enough $I^{(k)}$ and $J^{(k)}$ while keeping the CRTs nearly independent. The distances between red and green units increase in the panels from left to right, indicating that we are testing the spillover effect at greater distances.

Table 1 shows the p-values produced by the static method, our method MCRTs and its variant MCRTs+F. MCRTs+F tests $H^{(k)}$ by combining the p-values $P^{(k)}, \ldots, P^{(4)}$ from MCRTs using Fisher’s method. This strategy assumes that the spillover effect is decreasing as the spillover distance increases. MCRTs and MCRTs+F agree that the payments can encourage more forest conservation within a distance of 3, and there is no displacement of deforestation. The combined p-values in MCRTs+F are larger than the ones in MCRTs. This is because the statistical power for testing spillover effects is complicated. It depends not only on the spillover distance but also on other factors, such as units’ location and the design. Nevertheless, the simulations in Section 7.3 show that combining p-values can be useful when the CRT is not well powered at some distance.

7 Numerical experiments

7.1 Stepped-wedge design: size and power

We examine the performance of the MCRTs method in Section 5 by comparing it with Bonferroni’s Method and checking its validity in the presence of unit-by-time interactions. We use the notations MCRTs+F and MCRTs+Z to represent the combination of MCRTs with Fisher’s combination method [Fisher, 1925] and Stouffer’s method using the Z-scores, respectively; more details can be found in Appendix A. In all the CRTs, we use the difference-in-means statistic and 1000 permutations.

As shown in Figure 1, the non-nested CRTs have larger control groups compared to our nested CRTs created in MCRTs. However, the non-nested CRTs are not independent,
and there are limited ways to combine them. The most commonly used method in this case is Bonferroni’s method, which rejects the intersection of $K$ hypotheses if the smallest p-value is less than $\alpha/K$. A remaining question is whether the reduced sample size in MCRTs can indeed be compensated by combining p-values. To answer this question empirically, we conducted a simulation with variations in the sample size $N$, trial length $T$, time lag $l$, and effect sizes $\tau_l$, respectively.

We fix $N_1 = \ldots = N_T = N/T$ and $N_T = N - \sum_{t=1}^{T-1} N_t$ in the stepped-wedge design. Let $A_i$ denote the treatment starting time of unit $i$, i.e., the index of the non-zero entry of $Z_i$. The outcomes were generated by a linear mixed-effects model,

$$Y_{it} = \mu_i + 0.5(X_i + t) + \sum_{t=0}^{T-1} 1_{\{A_i-t=l\}} \tau_l + \epsilon_{it}, \quad i = 1, \ldots, N, \quad t = 0, \ldots, T,$$

where $\mu_i \sim \mathcal{N}(0, 0.25)$, $X_i \sim \mathcal{N}(0, 0.25)$ and $\epsilon_{it} \sim \mathcal{N}(0, 0.1)$. This assumes that the baseline outcome $Y_{i0}$ is measured, which is not uncommon in real clinical trials. Basic parameters were varied in the following ranges: (i) number of units $N \in \{100, 200, 300, 400, 500\}$; (ii) number of time steps $T \in \{4, 6, 8, 10, 12\}$; (iii) time lag $l \in \{0, 1, 2, 3, 4\}$; effect size $\tau_l \in \{0.01, 0.02, 0.03, 0.04, 0.05\}$. The performance of the methods was examined when one of $N, T,$ and $l$ is changed while the other two are
fixed at the medians of their ranges, respectively. For example, we increased \(N\) from 100 to 500 while keeping \(T = 8\) and \(l = 2\). In these simulations, \(\tau_l\) was set to 0 and 0.03 to investigate the level and power of the methods, respectively. One more simulation was created to study the power as the effect size \(\tau_l\) varies, in which we keep the first three parameters at their medians \((N = 300, T = 8, l = 2)\) and increase \(\tau_l\) from 0.01 to 0.05.

The upper panels of Figure 5 show that all the methods control the type I errors at any number of units, time steps and time lags. The lower panel shows that our methods are more powerful than Bonferroni’s method in all the simulations. MCRTs+Z is slightly more powerful than MCRTs+F in all experiments. This shows that the weighted z-score is more effective than Fisher’s combination method for MCRTs. Panels (d) and (g) show that our methods outperform Bonferroni’s method by a wider margin as the sample size or the effect size increases. Panel (e) establishes the same observation for trial length, which can be explained by the fixed sample size (so fewer units start treatment at each step as trial length increases). This is not an ideal scenario for applying Bonferroni’s method, as the individual tests have diminishing power. Finally, panel (f) shows that all the methods have smaller power as the lag size increases, and our methods are particularly powerful when the time lag is small. This is because there are fewer permutation tests available for larger time lags. Moreover, by only including the units that are treated after a large time lag, the control groups in the permutation tests are small. Overall, the reduced sample size in MCRTs may not be as damaging as it might first appear because every outcome relevant to lag \(l\) effect is still used in at least one test in MCRTs.

### 7.2 Stepped-wedge design: misspecified mixed-effects models

We next investigate the finite-sample properties of confidence intervals obtained by inverting conditional randomization tests (see Appendix B for more details). We compare its efficiency and robustness with mixed-effects models for estimating lagged treatment effects.

The treatment generating process was kept the same as above. Simulation parameters are set as \(N = 200\), \(T = 8\) and lagged effects \((\tau_0, \ldots, \tau_7) = (0.1, 0.3, 0.6, 0.4, 0.2, 0, 0, 0)\). The treatment effect is gradually realized and then decays to 0 over time. For every \(i \in [N]\) and \(t = 0, 1, \ldots, T\), we generate the outcome \(Y_{it}\) using a mixed-effects model,

\[
Y_{it} = \mu_i + 0.5(1 - 0.1 \cdot 1_{\{m \neq 0\}})(X_i + t) + 0.1 f_m(X_i + t) + \sum_{l=0}^{7} 1_{\{A_i - t = l\}} \tau_l + \epsilon_{it},
\]

where \(\mu_i \sim \mathcal{N}(0, 0.25)\), \(X_i \sim \mathcal{N}(0, 0.25)\), \(\epsilon_{it} \sim \mathcal{N}(0, 0.1)\) and the unit-by-time interaction \(f_m(X_i + t) = 0\) if \(m = 0\) (no interaction), \((X_i + t)^2\) if \(m = 1\) (quadratic interaction),
Figure 6: Performance of MCRTs+F, MCRTs+Z and the mixed-effects model: coverage rates and lengths of confidence intervals (CIs) under the outcome generating processes with no interaction effect and with three different types of covariate-and-time interactions.

\[ Y_{it} = \beta_{0i} + \beta_1 x_i + \beta_2 t + \sum_{l=0}^{7} \xi_l I_{\{A_i = t = l\}} + \epsilon_{it}, \quad (22) \]

where \( \beta_{0i} \) is a random unit effect, \( \beta_1, \beta_2 \) are fixed effects and \( \xi_0, \ldots, \xi_7 \) are lagged effects, and were fitted using the R-package lme4 [Bates et al., 2015]. Recently, Kenny et al. [2022] proposed mixed-effects models that can leverage the shapes of time-varying treatment effects. Their models are given by specifying some parametric effect curves with the help of basis functions (e.g. cubic spline). Besides the unit-by-time interaction, the model (22) is already correctly specified for modelling the treatment effects and other parts of the outcome generating process above. Excluding some of the lagged effect parameters \( \xi_5, \ldots, \xi_7 \) from the model may change the effect estimates but not the validity of its CIs.

As the unit-by-time interactions are unknown and fully specifying them would render
the model unidentifiable, they are typically not considered in mixed-effect models. If
the stepped-wedge trial is randomized at the cluster levels, one can introduce cluster-
by-time interaction effects in a mixed-effects model; see Ji et al. [2017, Equation 3.1]
for an example. However, the cluster-by-time interactions are not exactly the same as
the interaction between time and some covariates of the units. It depends on if the
interaction varies within each cluster and the clusters are defined by the covariates
which interact with time.

The upper panels in Figure 6 show that the CIs of the mixed-effects model only achieve
the target coverage rate of 90% for all the lagged effects when there is no unit-by-time
interaction (panel a). In contrast, the CIs of our methods fulfil the target coverage
rate of 90% in all scenarios. The lower panels show that the valid CIs given by our
methods have reasonable lengths between 0.05 and 0.10 for covering the true lagged
effects \((\tau_0, \ldots, \tau_4) = (0.1, 0.3, 0.6, 0.4, 0.2)\). Finally, panel (e) shows that when the
mixed-effects model is indeed specified correctly, it gives valid CIs that are narrower
than our nonparametric tests.

7.3 Simulation II: general interference

We next assess the validity and power of the static method and the MCRTs(+F)
method from Section 6. Our simulation has three parameters: sample size \(N \in \{100, 150, 200, 250, 300\}\), proportion of treated units \(P_N \in \{0.1, 0.2, 0.3, 0.4, 0.5\}\) and
signal strength \(\beta \in \{0, 0.5, 1.0, 1.5, 2.0\}\). For \(i \in [N]\), unit \(i\)'s location \(X_i = (X_{i1}, X_{i2})\)
is drawn independently from a mixture of bivariate normal distributions,

\[
X_{i1} \sim 0.5\mathcal{N}(50, 100) + 0.3\mathcal{N}(30, 56.25) + 0.2\mathcal{N}(40, 56.25),
\]
\[
X_{i2} \sim 0.5\mathcal{N}(50, 100) + 0.3\mathcal{N}(60, 56.25) + 0.2\mathcal{N}(20, 56.25).
\]

Let \(D_{ij}\) denote the Euclidean distance between units \(i\) and \(j\). The outcome of each
unit \(i\) is given by

\[
Y_i = 4Z_i + \sum_{j \in [N] \setminus \{i\}} \sum_{k \in [5]} 1_{\{D_{ij} \in (k-1,k]\}} Z_j \beta \tau_k + E_i,
\]

where \(E_i \sim \mathcal{N}(0, 1)\) and \((\tau_1, \tau_2, \tau_3, \tau_4, \tau_5) = (2.0, 1.6, 1.2, 0.8, 0.4)\) is a decreasing
spillover effect vector. As we vary one of the parameters \(N, P_N\) and \(\beta\), we fix the
other two at the median of their respective ranges. In all the CRTs, we use the
difference-in-means statistic and fix the number of permutations at 1000.

The results of all the methods are reported in Figure 7. In the static method, we let
the focal units be the minimum 3-cover of all the units. The top panels show that
the static method is powerful in testing the hypothesis of no spillover effect between
Figure 7: Performance of the static method and the MCRTs(+F) method in testing the hypotheses $H^{(k)}$ for $k \in [5]$. The upper panels use the p-values from the static method. The middle panels use the p-values from MCRTs. The lower panels combine the p-values from MCRTs using Fisher’s method, denoted by MCRTs+F. The results are averaged over 1000 independent runs.

units with distance more than 3, but has no power for longer distances because no units can be found for the randomization test (similar to Figure 4(d) in the real data example). The middle panels show that the power of our adaptive MCRTs is not a simple decreasing function of the distance $k$. The bottom panels show that this can be addressed by combining the tests at different distances (for example, we use Fisher’s method that combines $P^{(k)}, \ldots, P^{(5)}$ to test $H^{(k)}$) because the hypotheses are nested and the p-values are nearly independent. Panels (c,g,f) verify that the CRTs control the type I error rate at the significance level $\alpha = 0.1$. 

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8  Multiple conditional randomization tests

We next generalize the theory of sequential CRTs in Section 3. For any subset of the CRTs $J \subseteq [K]$, we define the union, refinement and coarsening of their conditioning sets as

$$
R^J = \bigcup_{k \in J} R^{(k)}, \quad R^J = \left\{ \bigcap_{j \in J} S_z^{(j)} : z \in Z \right\}, \quad \text{and} \quad \overline{R}^J = \left\{ \bigcup_{j \in J} S_z^{(j)} : z \in Z \right\}.
$$

Let $G^J$ be the $\sigma$-algebra generated by the sets in $R^J$, so $G^J = \sigma(R^J)$. Similarly, the refinement and coarsening $\sigma$-algebras are defined as $G^{J} = \sigma(R^{J})$ and $\overline{G}^{J} = \sigma(\overline{R}^{J})$.

**Theorem 3.** Suppose the following two conditions are satisfied for all $j, k \in [K]$, $j \neq k$.

$$
R^{\{j,k\}} \subseteq R^{\{j,k\}},
$$

$$
(t^{(j)}(Z, W))_{j \in J} \text{ are independent given } G^J, W \text{ for all } J \subseteq [K],
$$

where conditioning on $G^J$ means conditioning on $Z \in S$ for any set $S \in R^J$. Under Assumption 1, for any $\alpha^{(1)}, \ldots, \alpha^{(K)} \in [0, 1]$,

$$
\mathbb{P} \left\{ P^{(1)}(Z, W) \leq \alpha^{(1)}, \ldots, P^{(K)}(Z, W) \leq \alpha^{(K)} | G^J, W \right\} \leq \prod_{k=1}^{K} \alpha^{(k)}.
$$

In consequence, (6) holds for any $\alpha^{(1)}, \ldots, \alpha^{(K)} \in [0, 1]$.

The proof of Theorem 3 is not straightforward and can be found in Appendix D. Comparing to Theorem 2, it is allowed that $S_z^{(1)} \subseteq S_z^{(2)}$ for some $z$ but $S_z^{(1)} \supseteq S_z^{(2)}$ for another $z^* \neq z$. When $K = 2$, condition (24) is equivalent to

$$
t^{(1)}(Z, W) \perp \perp t^{(2)}(Z, W) \mid Z \in S_z^{(1)} \cap S_z^{(2)}, W, \quad \forall z \in Z,
$$

Equation (26) is satisfied by our sequential CRTs in Section 3, where $t^{(j)}(Z, W)$ is a function of $V^{[j]}$ and $W$ and the condition $Z \in S_z^{(k)}$ fixes all the randomness in $V^{(j)}$ for $j < k$.

9  Discussion

In this article, we demonstrated how to generate nearly independent and powerful $p$-values through a sequential construction of multiple conditional randomization tests. Our idea led to new methods for testing lagged treatment effects in stepped-wedge...
randomized trials and spillover effects in spatial experiments. Our methods are model-free and thus robust against model misspecification, as confirmed by our numerical experiments.

Our theory assumes a randomized experiment. In observational studies, matching by observed confounders is often used to mimic a randomized experiment using observational study [Rosenbaum, 2002]. This heuristic has been more formally investigated recently [Pimentel, 2022, Guo and Rothenhäusler, 2023]. It would be interesting to study if the theory presented here can be extended to randomization inference for observational studies.

In another line of research, it has been shown that a two-sample permutation test or randomization test with a carefully constructed test statistic is asymptotically valid for testing equality of a summary parameter between the samples [Chung and Romano, 2013, Bertanha and Chung, 2023], average treatment effects [Cohen and Fogarty, 2022, Fogarty, 2021, Zhao and Ding, 2021], “bounded” null hypotheses [Caughey et al., 2023], or quantiles of individual treatment effects [Caughey et al., 2023]. It may be possible to combine these techniques and the sequential construction in this article to composite null hypotheses and obtain nearly independent p-values.

It would also be interesting to consider more complex design spaces and their topological structures in future works. For example, Auerbach [2022] recently introduced a randomization test for the hypothesis that two networks are drawn from the same random graph model. As another example, unlike in the stepped-wedge design, a unit can switch to any treatment arm at any time in general cross-over designs or panel experiments [Bojinov et al., 2021, Shahn et al., 2023]. The theory outlined in this article in principle applies to any experimental design, but some non-trivial adaptions are needed for each specific setting as shown in the examples above.

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Appendices

A Method of combining p-values

A remaining question is how to combine the permutation tests obtained from Algorithm 1 (MCRTs) efficiently for testing spillover effects in Section 5. Heard and Rubin-Delanchy [2018] compared several p-value combination methods in the literature. By recasting them as likelihood ratio tests, they demonstrated that the power of a combiner crucially depends on the distribution of the p-values under the alternative hypotheses. In large samples, the behaviour of permutation tests is well-studied in the literature. Lehmann and Romano [2006, Theorem 15.2.3] showed that if the test statistics in a permutation test converges in distribution, the permutation distribution will converge to the same limiting distribution in probability. These results form the basis of our investigation of combining CRTs.

Suppose that \( K \) permutation p-values \( P^{(1)}, \ldots, P^{(K)} \) are obtained from Algorithm 1. Suppose the \( k \)th test statistic, when scaled by \( \sqrt{N} \), is asymptotically normal so that it converges in distribution to \( T^{(k)}_\infty \sim \mathcal{N}(\tau, V^{(k)}_\infty) \) under the null hypothesis \( (\tau = 0) \) and some local alternative hypothesis \( (\tau = h/\sqrt{N}) \) indexed by \( h \). The limiting distributions have the same mean but different variances. Suppose that we define the p-value likelihood ratio as the product of the alternative p-value distributions for all \( k \) divided by the product of the null p-value distributions for all \( k \). Since the permutation p-values are standard uniform, it is easy to verify that the logarithm of this p-value likelihood ratio is proportion to a weighted sum of Z-scores,

\[
\Phi^{-1}(P^{(k)}) \sim N(0, 1)
\]

This motivates a weighted Stouffer’s method [Stouffer et al., 1949] for combining the p-values. The weights are non-negative and sum to one, thus \( T^{(k)}_\infty \sim N(0, 1) \) if the p-values are independent. Then we can reject \( \bigcap_{k \in [K]} H_0^{(k)} \) if \( \Phi(T^{(k)}_\infty) \leq \alpha \). This test is shown to be uniformly most powerful for all \( h \) in the normal location problem [Heard and Rubin-Delanchy, 2018].

To formalize the discussion above, we consider the difference-in-means statistics as an example. Following the notation in Algorithm 1 (see lines 6 and 11), the treated group \( I_1^{(k)} \) for the \( k \)th CRT crosses over at time \( k \) and the control group \( I_0^{(k)} \) crosses over time \( t \in T^{(k)} \setminus \{k\} \), where \( T^{(k)} \setminus \{k\} \) is a subset of \( C_j \) that collects some time points after \( k + l \).

Let \( N_1^{(k)} = |I_1^{(k)}|, N_0^{(k)} = |I_0^{(k)}| \) and \( N^{(k)} = N_0^{(k)} + N_1^{(k)} \) Let \( A_i^{(k)} = 1 \) or \( 0 \) denote unit \( i \in I_0^{(k)} \cup I_1^{(k)} \) starting the treatment at time \( k \) or after \( k + l \), i.e., \( Z_{i,k+l} = (0_{k-1}, 1, 0_l) \) or \( 0_{k+l} \). To simplify the exposition in the results below, we use the
Abbreviations

\[ Y_i^{(k)} = Y_{i,k+1}, \quad Y_i^{(k)}(1) = Y_{i,k+1}(0_{k-1}, 1, 0_i) \quad \text{and} \quad Y_i^{(k)}(0) = Y_{i,k+1}(0_{k+1}) \]

We further assume that the \( N \) units are i.i.d draws from a super-population model, and every unit’s potential outcome \( Y_i^{(k)}(a) \) is a random copy of some generic \( Y^{(k)}(a) \) for \( a \in \{0,1\} \) and \( k \in K \).

**Proposition 1.** Suppose that the \( K \) permutation tests in Algorithm 1 use the difference-in-means statistics. We assume that for every \( k \in [K] \) and \( a \in \{0,1\} \),

(i) \( Y^{(k)}(a) \) has a finite and nonzero variance;

(ii) \( N_1^{(k)}/N \) and \( N_0^{(k)}/N \) are fixed as \( N \to \infty \);

The weighted Z-score combiner \( T_\infty \) is then given with weights \( w_\infty^{(k)} = \frac{\Lambda^{(k)}}{\sum_{j=1}^{K} \Lambda^{(j)}} \), where

\[
\Lambda^{(k)} = \left( \frac{N}{N_0^{(k)}} \text{Var}[Y^{(k)}(1)] + \frac{N}{N_1^{(k)}} \text{Var}[Y^{(k)}(0)] \right)^{-1} \tag{27}
\]

is the inverse of the asymptotic variance \( V^{(k)}_\infty \) of the statistics in the \( k \)-th test.

The weights in eq. (27) are obtained by inverting the asymptotic variance of the difference-in-means statistics; see Imbens and Rubin [2015, Section 6.4] and Li and Ding [2017]. We can estimate \( \text{Var}[Y^{(k)}(a)] \) in \( \Lambda^{(k)} \) consistently using the sample variance of \( Y_i^{(k)}, \forall i \in I_a^{(k)} \). We denote the estimator of \( \Lambda^{(k)} \) by \( \hat{\Lambda}^{(k)} \). The empirical version of \( T_\infty \) is given by

\[
\hat{T} = \sum_{k=1}^{K} \hat{w}^{(k)} \Phi^{-1}(P^{(k)}) \quad \text{where} \quad \hat{w}^{(k)} = \sqrt{\frac{\hat{\Lambda}^{(k)}}{\sum_{j=1}^{K} \hat{\Lambda}^{(j)}}} \tag{28}
\]

**Proposition 2.** Suppose that the p-values \( P^{(1)}, \ldots, P^{(K)} \) from Algorithm 1 are valid, the combined p-value \( \hat{P}(Z, W) = \Phi(\hat{T}) \) is also valid such that under the null hypotheses,

\[
P\{\hat{P}(Z, W) \leq \alpha\} \leq \alpha.
\]

In general, improving the statistical power in combining multiple CRTs is an independent task after choosing an efficient test statistics. Different test statistics may have different asymptotic distributions and the optimal p-value combiners (if exist) may be different. Nonetheless, a key insight from the discussion above is that we should weight the CRTs appropriately, often according to their sample size.
B Confidence intervals from randomization tests

Here we describe how to invert (a combination of) permutation tests and the complexity involves; see also Ernst [2004, Section 3.4] for an introduction. Consider a completely randomized experiment with treated outcomes \((Y_1, \ldots, Y_m)\) and control outcomes \((Y_{m+1}, \ldots, Y_{m+n})\).

Consider the constant effect null hypothesis

\[ H_0 : Y_i(1) = Y_i(0) + \Delta, \forall i \in [m + n]. \]

We can implement a permutation test for \(H_0\) by testing the zero-effect hypothesis on the shifted outcomes \(Y_\Delta = (Y_1 - \Delta, \ldots, Y_m - \Delta, Y_{m+1}, \ldots, Y_{m+n})\). To construct a confidence interval for the true constant treatment effect \(\tau\), we can consider all values of \(\Delta\) for which we do not reject \(H_0\). We define the left and right tails of the randomization distribution of \(t(Z^*, Y_\Delta)\) by

\[
P_1(\Delta) = \mathbb{P}^*\{t(Z^*, Y_\Delta) \leq t(Z, Y_\Delta)\} \quad \text{and} \quad P_2(\Delta) = \mathbb{P}^*\{t(Z^*, Y_\Delta) \geq t(Z, Y_\Delta)\},
\]

where \(Z = [1_m/m, -1_n/n]\) is observed assignment, \(Z^*\) is a permutation of \(Z\), \(T\) is the test statistics, e.g., difference-in-means, \(t(Z, Y_\Delta) = Z^\top Y_\Delta\). The complexity of computing \(P_1(\Delta)\) and \(P_2(\Delta)\) with \(b\) different permutations is \(O(mb+nb)\). The two-sided \((1-\alpha)\)-confidence interval for \(\Delta\) is given by \([\Delta_L, \Delta_U]\) := \([\min_{P_1(\Delta) > \alpha/2} \Delta, \max_{P_1(\Delta) > \alpha/2} \Delta]\).

We use a grid search to approximately find the minimum and maximum \(\Delta\) in \([\Delta_L, \Delta_U]\). Since \(P_1(\Delta)\) and \(P_2(\Delta)\) are monotone functions of \(\Delta\), we can also consider obtaining the optimal \(\Delta\)’s via a root-finding numerical method [see e.g. Garthwaite, 1996].

Inverting a combination of permutation tests can be done similarly. For example, by searching the same \(\Delta\)’s for every permutation test, the lower confidence bound \(\Delta_L\) is given by the minimum \(\Delta\) under which the p-value of the combined test (e.g. \(\hat{P}\) in Proposition 2) is larger than \(\alpha/2\). The complexity of inverting a combined test scales linearly in terms of the number of tests. The total complexity is manageable as long as the numbers of units and permutations are not very large at the same time.

If we have covariates information in the dataset, we can consider fitting a linear regression model (with basis functions for nonlinearity). We can compute the matrix inversion in the least-squares solution once, then update the solution by shifting the outcome vector with different \(\Delta\)’s. Inverting the test returns an interval with coverage probability approximately equal to \(1 - \alpha\). When the probability is slightly below \(1 - \alpha\), we can decrease \(\alpha\) by a small value (e.g. 0.0025) gradually and reconstruct the interval based on the previously searched \(\Delta\)’s. We stop if we obtain an interval with coverage probability above \(1 - \alpha\).
### C Pseudocode for multiple conditional randomization tests (MCRTs)

See Algorithm 1.

**Algorithm 1** Multiple conditional randomization tests (MCRTs) for testing lag-\(l\) treatment effect in stepped-wedge randomized controlled trials

1: **Input:** Number of units \(N\), Number of time steps \(T\), Time lag \(l\), Outcomes \(Y = (Y_{it} : i \in [N], t \in [T])\), Assignments \(Z = (Z_{it} : i \in [N], t \in [T])\), Statistics \(T\).
2: **Initialization:** \(J \leftarrow \min(l + 1, T - l - 1)\) and \(I_t \in \{i \in [N] : Z_{it} = 1\}, \forall t \in [T]\)
3: for \(j \in [J]\) do
   4: \( t \leftarrow j, C_j \leftarrow \{t\} \)
   5: while \(t + l + 1 \leq T\) do
   6: \( t \leftarrow t + l + 1, C_j \leftarrow C_j \cup \{t\} \)
   7: end while
4: for \(j \in [J]\) do
5: for \(k \in C_j\) do
   6: \( T^{(k)} \leftarrow \{t \in C_j : t \geq k\} \)
   7: \( I^{(k)} \leftarrow I_k, Y_{\text{treated}}^{(k)} \leftarrow \{Y_{i,k+l} : i \in I^{(k)}_k\} \)
   8: \( I^{(0)}_k \leftarrow (\bigcup_{t \in T^{(k)}} I_t) \setminus I_k, Y_{\text{control}}^{(k)} \leftarrow \{Y_{i,k+l} : i \in I^{(0)}_k\} \)
   9: \( P^{(k)}(Z, Y) \leftarrow \text{Permutation Test}(Y_{\text{treated}}^{(k)}, Y_{\text{control}}^{(k)}; T) \)
5: end for
4: end for
3: end for
2: Output: P-values \(\{P^{(k)} := P^{(k)}(Z, Y)\}\)

### D Technical Proofs

#### D.1 Proof of Theorem 1

**Proof.** We first write the p-value in eq. (1) as a probability integral transform. For any fixed \(z \in Z\), let \(F_z(\cdot; W)\) denote the distribution function of \(T(Z, W)\) given \(W\) and \(Z \in S_z\). Given \(Z \in S_z\) (so \(S_Z = S_z\) by Definition 1), the p-value can be written as \(P(Z, W) = F_z(T_z(Z, W); W)\). For any random variable \(T\) and its distribution function \(F(t) = \mathbb{P}(T \leq t)\) we have \(\mathbb{P}(F(T) \leq \alpha) \leq \alpha\) for all \(0 \leq \alpha \leq 1\); see Lemma 1
By the law of total probability,

\[
\mathbb{P}\{P(Z, W) \leq \alpha \mid V, W\} = \sum_{m=1}^{M} \mathbb{P}\{P(Z, W) \leq \alpha \mid Z \in S_m, W\} \mathbbm{1}_{\{V=m\}} \leq \sum_{m=1}^{M} \alpha \mathbbm{1}_{\{Z \in S_m\}} = \alpha.
\]

Marginalizing over the potential outcomes schedule \(W\), we attain the last claim in the theorem.

**Lemma 1.** Let \(T\) be a random variable and \(F(t) = \mathbb{P}(T \leq t)\) be its distribution function. Then \(F(T)\) has a distribution that stochastically dominates the uniform distribution on \([0, 1]\).

**Proof.** Let \(F^{-1}(\alpha) = \sup\{t \in \mathbb{R} \mid F(t) \leq \alpha\}\). We claim that \(\mathbb{P}\{F(T) \leq \alpha\} = \mathbb{P}\{T < F^{-1}(\alpha)\}\); this can be verified by considering whether \(T\) has a positive mass at \(F^{-1}(\alpha)\) (equivalently, by considering whether \(F(t)\) jumps at \(t = F^{-1}(\alpha)\)). Then, we have

\[
\mathbb{P}\{F(T) \leq \alpha\} = \mathbb{P}\{T < F^{-1}(\alpha)\} = \lim_{t \uparrow F^{-1}(\alpha)} F(t) \leq \alpha,
\]

using the fact that \(F(t)\) is non-decreasing and right-continuous.

**D.2 Proof outline of Theorem 3**

We now outline a proof of Theorem 3. We start with the following observation. (All proofs of the technical results can be found in the following sections.)

**Lemma 2.** Suppose eq. (23) is satisfied. Then for any \(J \subseteq [K]\) and \(S, S' \in \mathcal{R}^J\), the sets \(S\) and \(S'\) are either disjoint or nested, that is,

\[
S \cap S' \in \{\emptyset, S, S'\}.
\]

Furthermore, we have \(\mathcal{R}^{|K|} \subseteq \mathcal{R}^{|K|}\) and \(\overline{\mathcal{R}}^{|K|} \subseteq \mathcal{R}^{|K|}\).

The sets in \(\mathcal{R}^{|K|}\) can be partially ordered by set inclusion. This induces a graphical structure on \(\mathcal{R}^{|K|}\):

**Definition 2.** The Hasse diagram for \(\mathcal{R}^{|K|} = \{S^k_z : z \in Z, k \in [K]\}\) is a graph where each node in the graph is a set in \(\mathcal{R}^{|K|}\) and a directed edge \(S \to S'\) exists between two distinct nodes \(S, S' \in \mathcal{R}^{|K|}\) if \(S \supset S'\) and there is no \(S'' \in \mathcal{R}^{|K|}\) such that \(S \supset S'' \supset S'\).
It is straightforward to show that all edges in the Hasse diagram for $R[K]$ are directed and this graph has no cycles. Thus, the Hasse diagram is a directed acyclic graph.

For any node $S \in R[K]$ in this graph, we can further define its parent set as

$$\text{pa}(S) = \{S' \in R[K] : S' \rightarrow S\},$$

child set as $\text{ch}(S) = \{S' \in R[K] : S \rightarrow S'\}$, ancestor set as $\text{an}(S) = \{S' \in R[K] : S' \supset S\}$, and descendant set as $\text{de}(S) = \{S' \in R[K] : S \supset S'\}$. We note that one conditioning set $S \in R[K]$ can be used in multiple CRTs. To fully characterize this structure, we introduce an additional notation.

**Definition 3.** For any $S \in R[K]$, let $K(S) = \{k \in [K] : S \in R^{(k)}\}$ be the collection of indices such that $S$ is a conditioning set in the corresponding test. Furthermore, for any collection of conditioning sets $R \subseteq R[K]$, denote $K(R) = \bigcup_{S \in R} K(S)$.

**Lemma 3.** Suppose eq. (23) is satisfied. Then for any $S \in R[K]$, we have

(i) If $\text{ch}(S) \neq \emptyset$, then $\text{ch}(S)$ is a partition of $S$;

(ii) $\{K(\text{an}(S)), K(S), K(\text{de}(S))\}$ forms a partition of $[K]$.

(iii) For any $S' \in \text{ch}(S)$, $K(\text{an}(S')) = K(\text{an}(S) \cup \{S\})$ and $K(\{S'\} \cup \text{de}(S')) = K(\text{de}(S))$.

Using Lemma 3, we can prove the following key lemma that establishes the conditional independence between the p-values.

**Lemma 4.** Suppose eq. (23) and eq. (24) are satisfied. Then for any $S \in R[K]$ and $j \in K(S)$,

$$P^{(j)}(Z, W) \perp \perp (P^{(k)}(Z, W))_{k \in K(\text{an}(S) \cup \{S\}) \setminus \{j\}} \mid Z \in S, W.$$

Finally, we state a general result based on the above Hasse diagram, from which Theorem 3 almost immediately follows.

**Lemma 5.** Given conditions eq. (23) and eq. (24), we have, for any $S \in R[K]$,

$$\mathbb{P}\left\{ P^{(1)}(Z, W) \leq \alpha^{(1)}, \ldots, P^{(K)}(Z, W) \leq \alpha^{(K)} \mid Z \in S, W \right\} \leq \mathbb{P}\left\{ P^{(k)}(Z, W) \leq \alpha^{(k)} \text{ for } k \in K(\text{an}(S)) \mid Z \in S, W \right\} \prod_{j \in K(\{S\} \cup \text{de}(S))} \alpha_j.$$

(29)
D.3 Proof of Lemma 2

Proof. Consider $S \in \mathcal{R}^{(j)}$ and $S' \in \mathcal{R}^{(k)}$ for some $j, k \in [K]$ and $S \cap S' \neq \emptyset$. By the definition of refinement and eq. (23),

$$S \cap S' \in \mathcal{R}^{(j,k)} \subseteq \mathcal{R}^{(j)} \cup \mathcal{R}^{(k)},$$

so there exists integers $m$ such that $S \cap S' = S_m^{(j)}$ or $S_m^{(k)}$. Because $\mathcal{R}^{(j)}$ and $\mathcal{R}^{(k)}$ are partitions, this means that $S = S_m^{(j)}$ or $S' = S_m^{(k)}$. In either case, $S \cap S' = S$ or $S'$.

Now consider any $z \in Z$ and $j, k \in [K]$. Because $S_z^{(j)}, S_z^{(k)} \in \mathcal{R}^{[K]}$ and $S_z^{(j)} \cap S_z^{(k)} \neq \emptyset$ (because they contain at least $z$), either $S_z^{(j)} \supseteq S_z^{(k)}$ or $S_z^{(k)} \supseteq S_z^{(j)}$ must be true. We can order the conditioning events $S_z^{(k)}, k \in [K]$ according to the relation $\supseteq$. Without loss of generality, we assume that, at $z$,

$$S_z^{(1)} \supseteq S_z^{(2)} \supseteq \ldots \supseteq S_z^{(K-1)} \supseteq S_z^{(K)}.$$

Then $\bigcap_{k=1}^{K} S_z^{(k)} = S_z^{(K)}$ and $\bigcup_{k=1}^{K} S_z^{(k)} = S_z^{(1)}$. Thus the intersection and the union of $\{S_z^{(k)} \}_{k=1}^{K}$ are contained in $\mathcal{R}^{[K]}$ which collects all $S_z^{(k)}$ by the definition. As this is true for all $z \in Z$, we have $\mathcal{R}^{[K]} \subseteq \mathcal{R}^{[K]}$ and $\overline{\mathcal{R}}^{[K]} \subseteq \mathcal{R}^{[K]}$. \qed

D.4 Proof of Lemma 3

Proof. (i) Suppose $S', S''$ are two distinct nodes in $\text{ch}(S)$. By Lemma 2, they are either disjoint or nested. If they are nested, without loss of generality, suppose $S'' \supseteq S'$. However, this contradicts with the definition of the edge $S \rightarrow S'$, as by Definition 2 there should be no $S''$ satisfying $S \supseteq S'' \supseteq S'$. This shows that any two nodes in $\text{ch}(S)$ are disjoint.

Next we show that the union of the sets in $\text{ch}(S)$ is $S$. Suppose there exists $z \in S$ such that $z \notin S'$ for all $S' \in \text{ch}(S)$. In consequence, $z \notin S'$ for all $S' \in \text{de}(S)$. Similar to the proof of Lemma 2, we can order $S_z^{(k)}, k \in [K]$ according to set inclusion. Without loss of generality, suppose

$$S_z^{(1)} \supseteq S_z^{(2)} \supseteq \ldots \supseteq S_z^{(K-1)} \supseteq S_z^{(K)}.$$

This shows that $S = S_z^{(K)}$, so $\text{ch}(S) = \text{de}(S) = \emptyset$. This contradicts the assumption.

(ii) Consider any $S \in \mathcal{R}^{[K]}$, $S' \in \text{an}(S)$ and $S'' \in \text{de}(S)$. By definition, $S' \supseteq S \supseteq S''$. Because the sets in any partition $\mathcal{R}^{(k)}$ are disjoint, this shows that no pairs of $S, S', S''$ can belong to the same partition $\mathcal{R}^{(k)}$. Thus, $\mathcal{K}(S'), \mathcal{K}(S), \mathcal{K}(S'')$ are disjoint. Because this is true for any $S' \in \text{an}(S)$ and $S'' \in \text{de}(S)$, this shows $\mathcal{K}(\text{an}(S)), \mathcal{K}(S)$, and $\mathcal{K}(\text{de}(S))$ are disjoint.
By the proof of (i), for any \( z \in S \), \( S \) is in a nested sequence consisting of \( S_z^{(1)}, \ldots, S_z^{(K)} \). Hence,
\[
\mathcal{K}(\text{an}(S)) \cup \mathcal{K}(S) \cup \mathcal{K}(\text{de}(S)) = \mathcal{K}(\text{an}(S) \cup \{S\} \cup \text{de}(S)) = [K].
\]

(iii) The first result follows from the fact that \( \text{an}(S') = \text{an}(S) \cup \{S\} \). The second result is true because both \( \mathcal{K}(\{S'\} \cup \text{de}(S')) \) and \( \mathcal{K}(\text{de}(S)) \) are equal to \([K] \setminus \mathcal{K}(\text{an}(S) \cup \{S\})\). \( \square \)

D.5 Proof of Lemma 4

Proof. First, we claim that for any \( j, k \in [K] \) and \( z \in Z \), given that \( Z \in S_z^{(j)} \cap S_z^{(k)} \), \( P^{(k)}(Z, W) \) only depends on \( Z \) through \( T^{(k)}(Z, W) \). This is true because of the definition of the p-value eq. (1) and the invariance of the conditioning sets, i.e., \( S_Z^{(k)} = S_z^{(k)} \). Now fix \( S \in \mathcal{R}^{[K]} \) (which means \( S = S_z \) for some \( z \)) and consider any \( j \in \mathcal{K}(S) \). Let \( J = \mathcal{K}(\text{an}(S) \cup \{S\}) \). By Lemma 2, \( S_z^{(j)} \cap S_z^{(k)} = S_z^{(j)} = S \) for any \( k \in J \). Thus, the conditional independence eq. (24) implies that
\[
t^{(j)}(Z, W) \perp \perp t^{(k)}(Z, W)_{k \in J \setminus \{j\}} \mid Z \in S, W.
\]
Using the claim in the previous paragraph, this verifies the conclusion in Lemma 4. \( \square \)

D.6 Proof of Lemma 5

Proof. Let \( \psi^{(k)} = \psi^{(k)}(Z, W) = 1_{\{P^{(k)}(Z, W) \leq \alpha^{(k)}\}} \) for \( k \in [K] \) and rewrite the L.H.S of eq. (29):
\[
\mathbb{P}\{P^{(1)}(Z, W) \leq \alpha^{(1)} , \ldots , P^{(K)}(Z, W) \leq \alpha^{(K)} \mid Z \in S, W\} = \mathbb{E}\left\{ \prod_{k=1}^{K} \psi^{(k)} \mid Z \in S, W\right\}.
\]
We prove Lemma 5 by induction. First, consider any leaf node in the Hasse diagram, that is, any \( S \in \mathcal{R}^{[K]} \) such that \( \text{ch}(S) = \emptyset \). By Lemma 3, \( \mathcal{K}(S) \cup \mathcal{K}(\text{an}(S)) = [K] \). By Lemma 4,
\[
\psi^{(j)} \perp \perp \left( \psi^{(k)}\right)_{k \in \mathcal{K}(S) \setminus \{j\}} , \forall j \in \mathcal{K}(S).
\]
Using the validity of each CRT (Theorem 1),
\[
\mathbb{E}\left\{ \prod_{k=1}^{K} \psi^{(k)} \mid Z \in S, W\right\} = \mathbb{E}\left\{ \prod_{k \in \mathcal{K}(\text{an}(S))} \psi^{(k)} \mid Z \in S, W\right\} \prod_{j \in \mathcal{K}(S)} \mathbb{E}\{\psi^{(j)} \mid Z \in S, W\}.
\]
This is exactly eq. (29) for a leaf node. Now consider a non-leaf node $S \in \mathcal{R}^{|K|}$ (so $\text{ch}(S) \neq \emptyset$) and suppose eq. (29) holds for any descendant of $S$. We have

\[
\mathbb{E}\left\{ \prod_{k \in \mathcal{K}(\text{an}(S))} \psi^{(k)} \mid Z \in S, W \right\} \prod_{j \in \mathcal{K}(\text{de}(S))} \alpha^{(j)}.
\]

(By Theorem 1)

By induction, this shows that eq. (29) holds for all $S \in \mathcal{R}^{|K|}$.

\[\square\]

**D.7 Proof of Theorem 3**

*Proof. Lemma 2 shows that $\mathcal{R}^{|K|} \subseteq \mathcal{R}^{|K|}$, thus eq. (29) holds for every $S \in \overline{\mathcal{R}}^{|K|} \subseteq \mathcal{R}^{|K|}$. Moreover, any $S \in \overline{\mathcal{R}}^{|K|}$ has no superset in $\mathcal{R}^{|K|}$ and thus has no ancestors in the Hasse diagram. This means that the right-hand side of eq. (29) is simply $\prod_{k=1}^{K} \alpha^{(k)}$. Because $\overline{\mathcal{G}}^{|K|}$ is the $\sigma$-algebra generated by the sets in $\overline{\mathcal{R}}^{|K|}$, equation eq. (25) holds. Finally, equation eq. (6) holds trivially by taking the expectation of eq. (25) over $\overline{\mathcal{G}}^{|K|}$.*

\[\square\]
D.8 Proof of Proposition 1 in Appendix A

We denote the units used in the $k$-th test by $I^{(k)} = I_0^{(k)} \cup I_1^{(k)}$. We denote the treatment variables and outcomes used in the $k$-th test by $A^{(k)} = (A_i : i \in I^{(k)})$ and $Y^{(k)} = (Y_i^{(k)} : i \in I^{(k)})$, respectively. We define the difference-in-means statistics in the $k$-th test as

$$t(A^{(k)}, Y^{(k)}) = \sqrt{N}(\bar{Y}^{(k)}_1 - \bar{Y}^{(k)}_0), \quad (30)$$

where the average outcomes are given by

$$\bar{Y}^{(k)}_1 = (N_1^{(k)})^{-1} \sum_{i \in I^{(k)}} A_i^{(k)} Y_{ik} \quad \text{and} \quad \bar{Y}^{(k)}_0 = (N_0^{(k)})^{-1} \sum_{i \in I^{(k)}} (1 - A_i^{(k)}) Y_{ik}.$$ 

Let $W^{(k)} = (Y_i^{(k)}(0), Y_i^{(k)}(1) : i \in I^{(k)})$. The randomization distribution in the $k$-th test is

$$\hat{G}(b^{(k)}) = \mathbb{P}^* \left\{ t(A_i^{(k)}, Y^{(k)}(A_i^{(k)})) \leq b^{(k)} \mid W^{(k)} \right\},$$

where $A_i^{(k)}$ is a permutation of $A^{(k)}$, i.e., $A_i^{(k)}$ is drawn from the same uniform assignment distribution as $A^{(k)}$. Under assumption (i), using the bivariate Central Limit Theorem,

$$\left( t(A^{(k)}, Y^{(k)}), t(A_i^{(k)}, Y^{(k)}(A_i^{(k)})) \right) \overset{d}{\to} (T^{(k)}_{\infty}, T^{(k)}_{\infty,*}),$$

where $T^{(k)}_{\infty}$ and $T^{(k)}_{\infty,*}$ are independent, each with a common c.d.f $G^{(k)}(\cdot)$. By Lehmann and Romano [2006, Theorem 15.2.3], $\hat{G}(b^{(k)}) \overset{L}{\to} G^{(k)}(b^{(k)})$ for every $b^{(k)}$ which is a continuity point of $G^{(k)}(\cdot)$.

Under assumptions (i), (ii) and the zero-effect null hypothesis $H_0^{(k)}$, using the result in Lehmann and Romano [2006, Theorem 15.2.5], we have

$$T^{(k)}_{\infty} \sim g^{(k)}_0 = \mathcal{N}(0, V^{(k)}_{\infty}), \quad (31)$$

where the variance $V^{(k)}_{\infty}$ takes the form

$$V^{(k)}_{\infty} = 1/\Lambda^{(k)} = \frac{N}{N_0^{(k)}} \text{Var} \left[ Y^{(k)}(1) \right] + \frac{N}{N_1^{(k)}} \text{Var} \left[ Y^{(k)}(0) \right]. \quad (32)$$

This expression of the asymptotic variance can be found in Imbens and Rubin [2015, Section 6.4]. For completeness, an alternative derivation is provided in Appendix D.9. Under assumptions (i), (ii) and the constant effect alternative hypothesis $H_1^{(k)}$ (with $\tau = h/\sqrt{N}$),

$$T^{(k)}_{\infty} \sim g^{(k)}_1 = \mathcal{N}(h, V^{(k)}_{\infty}). \quad (33)$$
The c.d.f of $T_{\infty}^{(k)}$ under $H_{0}^{(k)}$ and $H_{1}^{(k)}$ are given by

$$G_{0}^{(k)}(b^{(k)}) = \Phi\left(\frac{b^{(k)}}{\sqrt{V^{(k)}}}\right) \quad \text{and} \quad G_{1}^{(k)}(b^{(k)}) = \Phi\left(\frac{b^{(k)} - h}{\sqrt{V^{(k)}}}\right).$$

Let $\tilde{b}^{(k)} = [G_{0}^{(k)}]^{-1}(p^{(k)})$. The p-value density function under $H_{1}^{(k)}$ can be rewritten as

$$f_{1}^{(k)}(p^{(k)}) = g_{1}^{(k)}(\tilde{b}^{(k)}) \left| \frac{d\tilde{b}^{(k)}}{dp^{(k)}} \right| = g_{1}^{(k)}(\tilde{b}^{(k)}) \left| \left[ G_{0}^{(k)} \right]'(\tilde{b}^{(k)}) \right|^{-1} = g_{1}^{(k)}(\tilde{b}^{(k)})/g_{0}^{(k)}(\tilde{b}^{(k)}).$$

Since the p-values from the permutation tests follow a standard uniform distribution under the null, the log-likelihood ratio of the p-values $P^{(1)} \ldots P^{(K)}$ is given by

$$\sum_{k=1}^{K} \log \left[ f_{1}^{(k)}(p^{(k)}) \right] = \sum_{k=1}^{K} \log \left[ \frac{g_{1}^{(k)}(\tilde{b}^{(k)})}{g_{0}^{(k)}(\tilde{b}^{(k)})} \right] \propto \sum_{k=1}^{K} \sqrt{\Lambda^{(k)}(\tilde{p}^{(k)})}.$$ 

Using the p-value weights $\Lambda^{(k), k \in [K]}$, from the log-likelihood ratio, we obtain

$$T_{\infty} = \sum_{k=1}^{K} w_{\infty}^{(k)} \Phi^{-1}(P^{(k)}) \quad \text{where} \quad w_{\infty}^{(k)} = \sqrt{\frac{\Lambda^{(k)}}{\sum_{j=1}^{K} \Lambda^{(j)}}}. \quad (34)$$

D.9 Proof of eq. (32) in Appendix D.8

Lehmann and Romano [2006, Theorem 15.2.3] uses the fact that under assumptions (i) and (ii), $V_{\infty}^{(k)} = \text{Var}[T(A^{(k)}, Y^{(k)})]$, but leaves the calculation of $\text{Var}[T(A^{(k)}, Y^{(k)})]$ (their Equation 15.15) as an exercise for readers. Here we provide the calculation to complete our proof for eq. (32). To simplify the exposition, we let $m = N_{1}^{(k)}$, $n = N_{0}^{(k)}$. Suppose that $T^{(k)} = [m + n]$, $\mathcal{T}^{(k)} = [m]$, $\mathcal{T}_{0}^{(k)} = \{m + 1, \ldots, m + n\}$ and

$$Y^{(k)} = \begin{cases} Y^{(k)}_{1}, \ldots, Y^{(k)}_{m}, & \text{treated outcomes} \\ Y^{(k)}_{m+1}, \ldots, Y^{(k)}_{m+n}, & \text{control outcomes} \end{cases}.$$ 

Let $\Pi = [\Pi(1), \ldots, \Pi(m+n)]$ be an independent random permutation of $1, \ldots, m+n$. We rewrite the difference-in-means statistics eq. (30) as

$$T := t(A^{(k)}, Y^{(k)}) = \sqrt{\frac{N}{m}} \sum_{i=1}^{m+n} E_{i} Y_{i}^{(k)}, \quad \text{where} \quad E_{i} = \begin{cases} 1 & \text{if } \Pi(i) \leq m \\ -m/n & \text{otherwise} \end{cases}, \forall i \in [m+n].$$

Let $D$ be the number of $i \leq m$ such that $\Pi(i) \leq m$. The value of $T$ is determined by $m - D$, the number of units swapped between the treated group ($i = 1, \ldots m$) and control group ($i = m + 1, \ldots, m+n$). Since all the treated (control) units have the
same outcome variance, it does not matter which units are swapped in computing the variance of $T$. We first consider the case that $m \leq n$. Using the expectation of the hypergeometric distribution,

$$E[D] = \sum_{d=0}^{m} \binom{m}{d} \binom{n-d}{m+n} d = \frac{m^2}{m+n}.$$

Let $\sigma^2_1 = \text{Var}[Y^{(k)}(1)]$ and $\sigma^2_0 = \text{Var}[Y^{(k)}(0)]$. The variance of $T$ is given by

$$\text{Var}(T) = \frac{N}{m^2} \sum_{d=0}^{m} \left( \frac{m}{d} \right) \left( \frac{n-m}{n} \right) \left[ d\sigma^2_1 + (m-d)\sigma^2_0 + (m-d)\frac{m^2}{n^2}\sigma^2_1 + (n-m+d)\frac{m^2}{n^2}\sigma^2_0 \right]$$

$$= \frac{N}{m^2} \left[ m^2 \sigma^2_1 + \frac{m n}{m+n} \sigma^2_0 + \frac{m n}{m+n} \frac{m^2}{n^2} \sigma^2_1 + \frac{m^2}{m+n} \sigma^2_0 \right]$$

$$= \frac{N}{m^2} \left[ \frac{m^2}{n} \sigma^2_1 + m \sigma^2_0 \right]$$

$$= \frac{N}{m} \sigma^2_1 + \frac{N}{m} \sigma^2_0.$$

If $m > n$, we let $D$ denote the number of $i \in \{m+1, \ldots, m+n\}$ such that $\Pi(i) \in \{m+1, \ldots, m+n\}$. Then, $E[D] = \frac{n^2}{m+n}$, and

$$\text{Var}(T) = \frac{N}{m^2} \sum_{d=0}^{n} \left( \frac{m}{d} \right) \left( \frac{n-m}{n} \right) \left[ d\frac{m^2}{n^2}\sigma^2_0 + (n-d)\frac{m^2}{n^2}\sigma^2_1 + (n-d)\sigma^2_0 + (m-n+d)\sigma^2_1 \right]$$

$$= \frac{N}{m^2} \left[ m^2 \sigma^2_0 + \frac{m n}{m+n} \frac{m^2}{n^2} \sigma^2_1 + \frac{m n}{m+n} \sigma^2_0 + \frac{m^2}{m+n} \sigma^2_1 \right]$$

$$= \frac{N}{m^2} \left[ \frac{m^2}{n} \sigma^2_1 + m \sigma^2_0 \right]$$

$$= \frac{N}{m} \sigma^2_1 + \frac{N}{m} \sigma^2_0.$$

The variance is the same for $m \leq n$ and $m > n$. This proves our claim and Equation 15.15 in Lehmann and Romano [2006]: $\text{Var}(m^{-1/2} \sum_{i=1}^{m+n} E_i Y_i^{(k)}) = \text{Var}(\sqrt{\frac{1}{N}} T) = \frac{m}{n} \sigma^2_1 + \sigma^2_0$.

**D.10 Proof of Proposition 2 in Appendix A**

In Algorithm 1, the time steps in $C_j$ define a sequence of nested permutation tests. For example, $C_1 = \{1, 3, 5, 7\}$ defines CRTs 1,3,5 and $C_2 = \{2, 4, 6, 8\}$ defines CRTs 2,4,6 in Figure 1. Suppose that we only have one subset $C = \{c_1, \ldots, c_K\}$ consists of $K$ time points.
We next prove that the tests defined on $\mathcal{C}$ are valid to combine. It is suffices to show that the test statistics $\hat{T} = \sum_{k=1}^{K} \hat{\omega}^{(k)} \Phi^{-1}(P^{(k)})$ stochastically dominates the random variable

$$
\hat{T} := \sum_{k=1}^{K} \hat{\omega}^{(k)} \Phi^{-1}(U^{(k)}) \sim \mathcal{N} \left( 0, \sum_{k=1}^{K} \left[ \hat{\omega}^{(k)} \right]^{2} \right) = \mathcal{N}(0, 1).
$$

where each $U^{(k)}$ is a standard uniform. The second equality is achieved by the definition of $\hat{\omega}^{(k)}$, $k \in [K]$.

By conditioning on the potential outcomes $(W^{(k)}, k \in [K])$, the weights $\hat{\omega}^{(k)}$, $k \in [K]$, are fixed. The derivation follows the same steps as Theorem 2 (the conditioning on $W$’s is suppressed). By construction, $c_{1} < \ldots < c_{K}$ and the conditioning sets $S^{(1)} \supseteq \cdots \supseteq S^{(K)}$ for all $z \in \mathcal{Z}$. Then, the corresponding $\sigma$-algebras generated by the conditioning sets satisfy that $G^{(1)} \subseteq \cdots \subseteq G^{(K)}$. Conditioning on $G^{(k)}$, the term $\sum_{k=1}^{K} \hat{\omega}^{(k)} \Phi^{-1}(P^{(k)})$ is fixed. By the law of iterated expectation,

\[
\mathbb{E} \left[ 1 \left\{ \hat{T} \leq b \right\} \right] = \mathbb{E} \left[ 1 \left\{ \hat{\omega}^{(K)} \Phi^{-1}(P^{(K)}) \leq b - \sum_{k=1}^{K-1} \hat{\omega}^{(k)} \Phi^{-1}(P^{(k)}) \right\} \right] \\
= \mathbb{E} \left( \mathbb{E} \left[ 1 \left\{ \hat{\omega}^{(K)} \Phi^{-1}(P^{(K)}) \leq b - \sum_{k=1}^{K-1} \hat{\omega}^{(k)} \Phi^{-1}(P^{(k)}) \right\} \mid G^{(K)} \right] \right) \\
\leq \mathbb{E}_{U^{(K)}} \left( \mathbb{E} \left[ 1 \left\{ \hat{\omega}^{(K)} \Phi^{-1}(U^{(K)}) \leq b - \sum_{k=1}^{K-1} \hat{\omega}^{(k)} \Phi^{-1}(P^{(k)}) \right\} \mid U^{(K)} \right] \right) \\
= \mathbb{E}_{U^{(K)}} \left( \mathbb{E} \left[ 1 \left\{ \hat{\omega}^{(K-1)} \Phi^{-1}(P^{(K-1)}) \leq b - \sum_{k=1}^{K-2} \hat{\omega}^{(k)} \Phi^{-1}(P^{(k)}) - \hat{\omega}^{(K)} \Phi^{-1}(U^{(K)}) \right\} \mid G^{(K-1)}, U^{(K)} \right] \right) \\
\leq \mathbb{E}_{U^{(K-1)}, U^{(K)}} \left( \mathbb{E} \left[ 1 \left\{ \hat{\omega}^{(K-1)} \Phi^{-1}(U^{(K-1)}) \leq b - \sum_{k=1}^{K-2} \hat{\omega}^{(k)} \Phi^{-1}(P^{(k)}) - \hat{\omega}^{(K)} \Phi^{-1}(U^{(K)}) \right\} \mid U^{(K-1)}, U^{(K)} \right] \right) \\
\vdots \\
\leq \mathbb{E}_{U^{(1)}, \ldots, U^{(K)}} \left( \mathbb{E} \left[ 1 \left\{ \sum_{k=1}^{K} \hat{\omega}^{(k)} \Phi^{-1}(U^{(k)}) \leq b \right\} \mid U^{(1)}, \ldots, U^{(K)} \right] \right) \\
= \mathbb{E} \left[ 1 \left\{ \hat{T} \leq b \right\} \right].
\]

The inequalities are attained by the validity of the p-values $P^{(1)}, \ldots, P^{(K)}$, i.e., each $P^{(k)}$ stochastically dominates the standard uniform variable $U^{(k)}$. Since $\hat{T}$ stochastically
dominates the standard normal random variable $\tilde{T}$,

$$\mathbb{P}\{\hat{P} \leq \alpha\} = \mathbb{P}\{\Phi(\hat{T}) \leq \alpha\} \leq \mathbb{P}\{\Phi(\tilde{T}) \leq \alpha\} = \alpha$$

The last equality is achieved by the fact that $\Phi(\tilde{T})$ is a standard uniform random variable. Suppose that Algorithm 1 creates multiple subsets $\mathcal{C}_j, j \in [J]$. Applying the same proof to the tests defined on each $\mathcal{C}_j$,

$$\mathbb{E}\left[1\{\hat{T}_j \leq b\}\right] \leq \mathbb{E}\left[1\{\tilde{T}_j \leq b\}\right].$$

where $\hat{T}_j = \sum_{c \in \mathcal{C}_j} \hat{w}^{(c)} \Phi(P^{(c)})$ and $\tilde{T}_j = \sum_{c \in \mathcal{C}_j} \hat{w}^{(c)} \Phi(U^{(c)}) \sim \mathcal{N}(0, \sum_{c \in \mathcal{C}_j}[\hat{w}^{(c)}]^2)$. By splitting the time steps, we make sure that the p-values from the tests based on different $\mathcal{C}_j$ can be combined. The test statistics $\hat{T} = \sum_{j \in \mathcal{J}} \hat{T}_j$ stochastically dominates the random variable

$$\tilde{T} = \sum_{j \in \mathcal{J}} \tilde{T}_j \sim \mathcal{N}\left(0, \sum_{j \in \mathcal{J}} \sum_{c \in \mathcal{C}_j} [\hat{w}^{(c)}]^2\right) = \mathcal{N}(0, 1),$$

which implies that eq. (35) still holds for the combined p-value $\hat{P} = \Phi(\tilde{T})$. 

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