Improved Neymanian analysis for $2^K$ factorial designs with binary outcomes

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Abstract

$2^K$ factorial designs are widely adopted by statisticians and the broader scientific community. In this short note, under the potential outcomes framework (Neyman, 1923; Rubin, 1974), we adopt the partial identification approach and derive the sharp lower bound of the sampling variance of the estimated factorial effects, which leads to an “improved” Neymanian variance estimator that mitigates the over-estimation issue suffered by the classic Neymanian variance estimator by Dasgupta et al. (2015).

Keywords: Partial identification; potential outcome; randomization; robust inference

1. INTRODUCTION

Originally introduced for agricultural research at the famous Rothamsted Experimental Station more than a century ago (Fisher 1926; Yates and Mather 1963), randomized controlled factorial designs (Fisher 1935) have been widely adopted by researchers in social, behavior and biomedical sciences to simultaneously assess the main and interactive effects of multiple treatment factors. In applied research, a frequently encountered scenario is where not only the treatments but also the outcomes of interests are binary. For example, Nair et al. (2008) explored how differentiating the

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format of a computer-aided encouragement program (e.g., single session vs. multiple occurrences, personalized vs. more general feedback and advice) affected the abstinence from smoking. Stampfer et al. (1985) investigated whether aspirin and β-carotene could help prevent cardiovascular mortality. For such studies, to guarantee trustworthy discovery and reporting of causal effects that are scientifically meaningful, it is imperative to adopt an interpretable and robust methodology for estimation and inference.

During recent years, the potential outcomes framework (Neyman, 1923; Rubin, 1974, 1990) has become increasingly popular, because it enjoys clear interpretability (causal effects are defined as comparisons between potential outcomes under different treatments), and can be flexibly combined with various inferential procedures (e.g., Fisherian, Neymanian and Bayesian; see Ding and Li (2018) for a comprehensive review). Realizing the salient features of the potential outcomes framework, Dasgupta et al. (2015) extended it to $2^K$ factorial designs, and claimed that the proposed Neymanian causal inference framework “results in better understanding of the estimands and allows greater flexibility in statistical inference of factorial effects, compared to the commonly used linear model based approach.” However, as acknowledged by the causal inference literature (e.g., Aronow et al., 2014; Ding, 2017; Imbens and Rubin, 2015, Section 6.5), a long-standing and fundamental challenge faced by the Neymanian framework is the over-estimation of the sampling variances of the estimated factorial effects, because we cannot jointly observe the potential outcomes under different treatments, and therefore directly identify the strengths of association between them. This missing data problem is sometimes referred to as the “fundamental problem of causal inference” (e.g., Holland, 1986; Imbens and Rubin, 2015, Section 1.3).

Among the numerous proposals that mitigate the variance over-estimation of the Neymanian causal inference framework, one solution that completely preserves the randomization-based “flavor” is the partial identification approach (c.f. Richardson et al., 2014), which is widely employed by both statisticians (e.g., Cheng and Small, 2006; Zhang and Rubin, 2003; Aronow et al., 2014; Ding and Dasgupta, 2016; Lu et al., 2018) and econometricians (e.g., Fan and Park, 2010). The key idea of partial identification, in the context of factorial designs, is that although we cannot directly identify the sampling variances of the estimated factorial effects, we can derive their sharp lower bounds which are identifiable from observed data, which leads to an “improved” Neymanian variance estimator that guarantees better performance, regardless of the underlying dependency
structure of the potential outcomes (however, the extent of performance improvement depends on the dependency structure). Along this line of research, Ding and Dasgupta (2016) solved the problem for treatment-control studies (i.e., $2^1$ factorial designs), and in a recent paper Lu (2017) proposed the said “improved” variance estimator for $2^2$ factorial designs. Nevertheless, we still need a unifying framework applicable to general $2^K$ factorial designs, which to the best of our knowledge is lacking from the existing literature. From a theoretical perspective, it seems non-trivial to generalize the main results in Lu (2017) to arbitrary $2^K$ factorial designs, because the complexity of the dependency structure of the potential outcomes grows exponentially as $K$ increases. From a practical perspective, although $2^2$ factorial designs seem common in applied research, high-order factorial designs were also frequently employed (Berkowitz and Daniels, 1964; Kim et al., 2008; Yuan et al., 2008) (e.g., to screen a large number of candidate treatment factors). In this paper, we fill this theoretical gap by deriving the desired “improved” Neymanian variance estimator, for arbitrary $2^K$ factorial designs.

We organize the remainder of the paper as follows. Section 2 reviews Dasgupta et al. (2015)’s Neymanian inference framework for $2^K$ factorial designs, with a primary focus on binary outcomes. Section 3 first highlights the variance over-estimation issue that the Neymanian causal inference framework suffers, and presents the “improved” Neymanian variance estimator that is guaranteed to be less biased than the standard Neymanian estimator. Section 4 concludes with a discussion.

2. NEYMANIAN INFERENCE FOR FACTORIAL DESIGNS

2.1. Factorial designs

We adapt some materials from Dasgupta et al. (2015) and Lu (2016a,b) to review the Neymanian causal inference framework for $2^K$ factorial designs. To maintain consistency, we inherit the set of notations from Lu (2017).

Consider $K(\geq 1)$ distinct treatment factors with two-levels -1 (placebo) and 1 (active treatment), resulting a total number of $J = 2^K$ treatment combinations, labelled as $z_1, \ldots, z_J$. Their definitions depend on the $J \times J$ model matrix $H = (h_0, \ldots, h_{J-1})$ (c.f. Wu and Hamada, 2009), constructed as follows:

1. Let $h_0 = 1_J$;
2. For $k=1,\ldots,K$, construct $h_k$ by letting its first $2^{K-k}$ entries be -1, the next $2^{K-k}$ entries be 1, and repeating $2^{k-1}$ times;

3. If $K \geq 2$, order all subsets of $\{1,\ldots,K\}$ with at least two elements, first by cardinality and then lexicography. For $k=1,\ldots,J-1-K$, let $\sigma_k$ be the $k$th subset and $h_{K+k} = \prod_{l \in \sigma_k} h_l$, where “$\prod$” stands for entry-wise product.

Given the resulting design matrix $H$, the $j$th row of the corresponding sub-matrix $(h_1,\ldots,h_K)$ is the $j$th treatment combination $z_j$, for $j=1,\ldots,J$. In the next section, we will use $(h_1,\ldots,h_J)$ to define the (main and interactive) factorial effects.

### 2.2. Potential outcomes and factorial effects

Consider $2^K$ factorial designs with $N (\geq 2^{K+1})$ experimental units. Under the Stable Unit Treatment Value Assumption (SUTVA, Rubin, 1980), for all $i=1,\ldots,N$, we let $Y_i(z_j) \in \{0,1\}$ be the potential outcome of unit $i$ under treatment $z_j$, and $Y_i = \{Y_i(z_1),\ldots,Y_i(z_J)\}'$. To simplify future notations, for all $\{j_1,\ldots,j_s\} \subset \{1,\ldots,J\}$, let

$$N_{j_1,\ldots,j_s} = \sum_{i=1}^N 1\{Y_i(z_{j_1})=1,\ldots,Y_i(z_{j_s})=1\} = \sum_{i=1}^N \prod_{r=1}^s Y_i(z_{j_r}).$$

Intuitively, $N_{j_1,\ldots,j_s}$ is the number of experimentation units with potential outcomes equal to one, under treatments $z_{j_1},\ldots,z_{j_s}$. We will use this set of notations frequently going forward.

For all $j=1,\ldots,J$, the average potential outcome for $z_j$ is $p_j = N_j/N$, and $p = (p_1,\ldots,p_J)'$.

For all $l = 1,\ldots,J-1$, Dasgupta et al. (2015) defined the $l$th individual- and population-level factorial effects as

$$\tau_{il} = 2^{-(K-1)}h_i'Y_i \quad (i=1,\ldots,N); \quad \bar{\tau}_l = 2^{-(K-1)}h_l'p. \quad (1)$$

We provide the following example to illustrate the concepts introduced above.

**Example 1.** For $K=3$, by the construction procedure described in Section 2.1, we obtain $h_0 = (1,1,1,1,1,1,1,1)'$, $h_1 = (-1,-1,-1,1,1,1,1,1)'$, $h_2 = (-1,-1,1,1,-1,-1,1,1)'$, and $h_3 = (-1,1,-1,1,1,1,1,1)'$. Moreover, $h_4 = h_1 \cdot h_2 = (1,1,-1,-1,1,1,1,1)'$, $h_5 = h_1 \cdot h_3,$
\[ h_6 = h_2 \cdot h_3, \text{ and } h_7 = h_1 \cdot h_2 \cdot h_3. \] Therefore, the design matrix

\[
H = \begin{pmatrix}
    h_0 & h_1 & h_2 & h_3 & h_4 & h_5 & h_6 & h_7 \\
    1 & -1 & -1 & 1 & 1 & 1 & 1 & -1 \\
    1 & -1 & 1 & 1 & -1 & -1 & 1 & 1 \\
    1 & -1 & 1 & -1 & -1 & 1 & 1 & 1 \\
    1 & -1 & 1 & -1 & -1 & 1 & 1 & 1 \\
    1 & 1 & -1 & -1 & -1 & 1 & 1 & 1 \\
    1 & 1 & -1 & -1 & -1 & 1 & 1 & 1 \\
    1 & 1 & 1 & 1 & 1 & 1 & 1 & 1
\end{pmatrix},
\]

and the treatment combinations are

\[ z_1 = (-1, -1, -1), \quad z_2 = (-1, -1, 1), \quad z_3 = (-1, 1, -1), \quad z_4 = (-1, 1, 1), \]

and

\[ z_5 = (1, -1, -1), \quad z_6 = (1, -1, 1), \quad z_7 = (1, 1, -1), \quad z_8 = (1, 1, 1), \]

respectively. For illustration we consider \( \bar{\tau}_{11} \), the main effect of the first treatment factor. By (1)

\[
\tau_{il} = \frac{1}{4} \sum_{j=1}^{4} Y_i(z_j) - \frac{1}{4} \sum_{j=5}^{8} Y_i(z_j),
\]

which is indeed difference between the average potential outcome where the first treatment factor is +1 and the one where the first treatment factor is -1.

### 2.3. Neymanian inference

We consider a completely randomized treatment assignment. Let \( n_1, \ldots, n_J \) be positive constants such that \( \sum n_j = N \). For all \( j = 1, \ldots, J \), randomly assign \( n_j \geq 2 \) units to \( z_j \). For all \( i = 1, \ldots, N \),
we let 
\[ W_i(z_j) = \begin{cases} 
1, & \text{if unit } i \text{ is assigned to } z_j, \\
0, & \text{otherwise} 
\end{cases} \quad (j = 1, \ldots, J). \]

The observed outcomes for unit \( i \) is therefore \( Y^{\text{obs}}_i = \sum_{j=1}^{J} W_i(z_j)Y_i(z_j) \). Let the average observed potential outcome for \( z_j \) be \( \hat{p}_j = n_j^{\text{obs}}/n_j \), where

\[ n_j^{\text{obs}} = \sum_{i=1}^{N} W_i(z_j)Y_i(z_j) = \sum_{i:W_i(z_j)=1} Y^{\text{obs}}_i \quad (j = 1, \ldots, J). \]

Denote \( \hat{p} = (\hat{p}_1, \ldots, \hat{p}_J)' \). An unbiased estimator of the factorial effect \( \bar{\tau}_l \) is

\[ \hat{\bar{\tau}}_l = 2^{-(K-1)}h'_l \hat{p} \quad (l = 1, \ldots, J - 1). \tag{2} \]

Dasgupta et al. (2015) derived the sampling variance of the estimator in (2) as

\[
\text{Var}(\hat{\bar{\tau}}_l) = \frac{1}{2^{2(K-1)}} \sum_{j=1}^{J} S^2_j/n_j - \frac{1}{N} S^2(\bar{\tau}_l),
\]

where

\[ S^2_j = (N-1)^{-1} \sum_{i=1}^{N} \left\{ Y_i(z_j) - \bar{Y}(z_j) \right\}^2 = \frac{N}{N-1} p_j (1 - p_j) \]

is the variance of potential outcomes for \( z_j \), and

\[ S^2(\bar{\tau}_l) = (N-1)^{-1} \sum_{i=1}^{N} (\tau_{il} - \bar{\tau}_l)^2 \]

is the variance of the \( l \)th individual-level factorial effects. To estimate the sampling variance \( \text{Var}(\hat{\bar{\tau}}_l) \), Dasgupta et al. (2015) substituted \( S^2_j \) with its unbiased estimate

\[ s^2_j = (n_j - 1)^{-1} \sum_{i=1}^{N} W_i(z_j)\left( Y^{\text{obs}}_i - \bar{Y}^{\text{obs}}(z_j) \right)^2 = \frac{n_j}{n_j - 1} \hat{p}_j (1 - \hat{p}_j), \]

\[ \text{Var}(\hat{\bar{\tau}}_l) \]
and plugged in the lower bound of zero for $S^2(\bar{\tau})$. The resulted Neymanian estimator

$$\hat{\text{Var}}_{\text{Ney}}(\hat{\tau}_l) = 2^{-2(K-1)} \sum_{j=1}^{J} s_j^2 / n_j = 2^{-2(K-1)} \sum_{j=1}^{J} \hat{p}_j (1 - \hat{p}_j) / n_j - 1$$

(4)

is “conservative,” on average over-estimating the true sampling variance by

$$E\{\hat{\text{Var}}_{\text{Ney}}(\hat{\tau}_l)\} - \text{Var}(\hat{\tau}_l) = S^2(\bar{\tau}) / N.$$

The bias is generally positive, unless strict additivity (Dasgupta et al., 2015; Ding and Dasgupta, 2016; Ding, 2017) holds, i.e., $\tau_{il} = \tau_{i'lj}$ for all $i \neq i'$. In other words, all experimental units have identical treatment effects. Several researchers (e.g., LaVange et al., 2005; Rigdon and Hudgens, 2015) pointed out that this condition is too strong in practice, especially for binary outcomes. In cases where strict additivity does not hold, the estimator in (4) might be too conservative, as acknowledged by Aronow et al. (2014).

3. THE IMPROVED NEYMANIAN VARIANCE ESTIMATOR

The key to the partial identification approach is to derive a non-zero lower bound of $S^2(\bar{\tau})$. To achieve this goal, we rely on the following lemmas, which are “$2^K$ versions” of the corresponding “$2^2$ versions” in Lu (2017). However, it is worth mentioning that, the original proofs in Lu (2017) relied on the inclusion-exclusion principle and Boole’s inequality, and therefore are difficult to be generalized to arbitrary $2^K$ factorial designs. To partially circumvent this technical difficulty, we adopt a methodology that is simpler and more intuitive than the one used by Lu (2017).

**Lemma 1.** For all $l = 1, \ldots, J - 1$, let $\mathbf{h}_l = (h_{1l}, \ldots, h_{Jl})'$, and

$$S^2(\bar{\tau}_l) = \frac{1}{2^{2(K-1)} (N - 1)} \left( \sum_{j=1}^{J} N_j + \sum_{j \neq j'} h_{lj} h_{lj'} N_{jj'} \right) - \frac{N}{N - 1} \bar{\tau}_l^2.$$
Proof. The proof largely follows Lu (2017). First, by (1)

\[
\sum_{i=1}^{N} \tau_{it}^2 = 2^{-2(K-1)} \sum_{i=1}^{N} (h_{it}^2 Y_i)^2
\]

\[
= 2^{-2(K-1)} \sum_{i=1}^{N} \left\{ \sum_{j=1}^{J} h_{ij} Y_i(z_j) \right\}^2
\]

\[
= 2^{-2(K-1)} \sum_{i=1}^{N} \left\{ \sum_{j=1}^{J} h_{ij}^2 Y_i^2(z_j) + \sum_{j \neq j'} h_{ij} h_{ij'} Y_i(z_j) Y_i(z_{j'}) \right\}
\]

\[
= 2^{-2(K-1)} \left( \sum_{j=1}^{J} N_j + \sum_{j \neq j'} h_{ij} h_{ij'} N_{jj'} \right).
\]

Therefore

\[
S^2(\bar{\tau}_l) = (N - 1)^{-1} \left( \sum_{i=1}^{N} \tau_{it}^2 - N \bar{\tau}_l^2 \right)
\]

\[
= \frac{1}{2^{2(K-1)}(N-1)} \left( \sum_{j=1}^{J} N_j + \sum_{j \neq j'} h_{ij} h_{ij'} N_{jj'} \right) - \frac{N}{N - 1} \bar{\tau}_l^2,
\]

which completes the proof.

Lemma 2. For all $l = 1, \ldots, J - 1$,

\[
\sum_{j=1}^{J} N_j + \sum_{j \neq j'} h_{ij} h_{ij'} N_{jj'} \geq \left| \sum_{j=1}^{J} h_{ij} N_l \right|,
\]

and the equality in (5) holds if and only if

\[
\tau_{il} \left\{ \tau_{il} + 2^{-(K-1)} \right\} = 0 \quad (\forall i = 1, \ldots, N)
\]

or

\[
\tau_{il} \left\{ \tau_{il} - 2^{-(K-1)} \right\} = 0 \quad (\forall i = 1, \ldots, N).
\]
Proof. To prove (5), we break it down into two parts:

\[ \sum_{j=1}^{J} N_j + \sum_{j \neq j'} h_{lj} h_{lj'} N_{jj'} \geq \sum_{j=1}^{J} h_{lj} N_l \]  

(8)

and

\[ \sum_{j=1}^{J} N_j + \sum_{j \neq j'} h_{lj} h_{lj'} N_{jj'} \geq -\sum_{j=1}^{J} h_{lj} N_l. \]  

(9)

Note that

1. The inequality in (5) holds if and only if both the inequalities in (8) and (9) hold;
2. The equality in (5) holds if and only if either the equalities in both (8) and (9) hold.

We first prove (8), and derive the sufficient and necessary condition for the equality to hold. To simplify notations, denote

\[ J_{l}^{-} = \{ j : h_{lj} = -1 \}, \quad J_{l}^{+} = \{ j : h_{lj} = 1 \}. \]

Simple algebra suggests that (8) is equivalent to

\[ 2 \sum_{j \in J_{l}^{-}} N_j + \sum_{j, j' \in J_{l}^{-} : j \neq j'} N_{jj'} + \sum_{j, j' \in J_{l}^{+} : j \neq j'} N_{jj'} \geq 2 \sum_{j \in J_{l}^{-}, j' \in J_{l}^{+}} N_{jj'}. \]  

(10)

To prove (10), for all \( i = 1, \ldots, N \), we let \( \lambda_{il} = \sum_{j \in J_{l}^{-}} Y_i(z_j) \) and \( \lambda_{il} = \sum_{j' \in J_{l}^{+}} Y_i(z_{j'}) \), which are two integer constants. Therefore, for \( i = 1, \ldots, N \), it is obvious that \( (\lambda_{il} - \lambda_{il}) + (\lambda_{il} - \lambda_{il})^2 \geq 0 \), or equivalently

\[ 2\lambda_{il} - \lambda_{il} - (\lambda_{il} - 1) + \lambda_{il} - (\lambda_{il} - 1) \geq 2\lambda_{il} - \lambda_{il}. \]  

(11)

Note that (11) immediately implies (8), because

\[ \sum_{j \in J_{l}^{-}} N_j = \sum_{i=1}^{N} \lambda_{il}, \quad \sum_{j, j' \in J_{l}^{+} : j \neq j'} N_{jj'} = \sum_{i=1}^{N} \lambda_{il} - \lambda_{il}, \]

and

\[ \sum_{j, j' \in J_{l}^{+} : j \neq j'} N_{jj'} = \sum_{i=1}^{N} \lambda_{ils} (\lambda_{ils} - 1) \quad (s = -, +). \]
Moreover, the equality in (8) holds if and only if the equality in (11) holds for all \( i = 1, \ldots, N \), which is equivalent to (6), because by definition \( \lambda_{il} - \lambda_{ip} = 2^{K-1}r_{il} \).

Similarly, we can prove (9), and its equality holds if and only if (7) holds.

With the help of Lemmas 1 and 2 along with the definition of factorial effect in (1), we can derive the main theoretical result of the paper.

**Theorem 1.** The sharp lower bound for \( S^2(\bar{\tau}_l) \) is

\[
S^2(\bar{\tau}_l) \geq \frac{N}{N-1} \max \{ 2^{-(K-1)}|\bar{\tau}_l| - \bar{\tau}_l^2, 0 \}.
\]  

The equality in (12) holds if and only if (6) or (7) holds.

**Proof.** By Lemmas 1 and 2

\[
S^2(\bar{\tau}_l) \geq \frac{1}{2^{2(K-1)}(N-1)} \sum_{j=1}^{J} h_{lj}N_j \bigg| j \bigg| - \frac{N}{N-1} \bar{\tau}_l^2.
\]

Moreover, by (1),

\[
N2^{K-1}|\bar{\tau}_l| = N \sum_{j=1}^{J} h_{lj}p_j = \sum_{j=1}^{J} h_{lj}N_j,
\]

which completes the proof.

The lower bound in (12) is “sharp,” in the sense that it is the minimum of all possible values of \( S^2(\bar{\tau}_l) \) compatible with the marginal distributions of the potential outcomes (i.e., \( N_j \) for \( j = 1, \ldots, J \)). To facilitate a better understanding of Theorem 1 we consider two special cases. First, when \( K = 1 \), we have the classic treatment-control studies. In this case, Theorem 1 reduces to the main result of Ding and Dasgupta (2016). Moreover, the condition in (6) reduces to

\[
Y_i(1) = Y_i(-1) \text{ or } Y_i(-1) - 1 \quad (\forall i = 1, \ldots, N),
\]

or equivalently

\[
Y_i(1) \leq Y_i(-1) \quad (i = 1, \ldots, N),
\]
because \( Y_i(1) \) and \( Y_i(0) \) are both binary. Similarly, (6) is equivalent to

\[
Y_i(1) \geq Y_i(-1) \quad (i = 1, \ldots, N).
\]

The above two conditions are termed *monotonicity* by Ding and Dasgupta (2016). Second, when \( K = 2 \), Theorem 1 reduces to the main result of Lu (2017).

Theorem 1 leads to the “improved” Neymanian variance estimator

\[
\tilde{\text{Var}}_{\text{IN}}(\hat{\tau}_l) = \tilde{\text{Var}}_{\text{Ney}}(\hat{\tau}_l) - \frac{1}{N-1} \max\{2^{-(K-1)}|\hat{\tau}_l| - \hat{\tau}_l^2, 0\}. \tag{13}
\]

This bias-correction term on the right hand side of (13) is always non-negative, implying a guaranteed improvement of variance estimation, for any observed data-set.

To compare the performances of the “improved” and original Neymanian variance estimators, we extend Lu (2017) and provide the following example.

**Example 2.** Consider a \( 2^3 \) factorial design with 400 experimental units. We independently sample 5000 times, in each of which let \( n_{j}^{\text{obs}} \sim \lfloor \text{Unif}(0, 100) \rfloor \), for \( j = 1, \ldots, 8 \). Figure 2 contains the ratios of the “improved” and original Neymanian variance estimates of \( \hat{\tau}_1 \), defined in (13) and (4) respectively. Figure 2 suggests that the “improved” variance estimate is always smaller, and 11% of the times the improvement is more than 10%.

### 4. CONCLUDING REMARKS

Under the potential outcomes framework, we have proposed an “improved” Neymanian variance estimator for \( 2^K \) factorial designs with binary outcomes. Comparing to the classic variance estimator by Dasgupta et al. (2015), the newly proposed estimator guarantees bias-correction, regardless of the underlying dependency structure of the potential outcomes. The core idea behind the new estimator is the sharp lower bound of the sampling variance of the estimated factorial effects.

We point out three directions of future research. First, although we focus on binary outcomes, it would be interesting to generalize the current work to general outcomes (e.g., continuous, time to event). The proof of Lemma 1 suggest that the key is to sharply bound \( \sum_{j \neq j'} h_{ij} h_{ij'} Y_i(z_j) Y_i(z_{j'}) \) For \( K = 1 \), Aronow et al. (2014) solved this problem by using the arrangement inequality (Hardy
Figure 1: The ratios of the “improved” and original Naymanian variance estimates for a balanced $2^3$ factorial design with 400 experimental units, illustrated by 5000 repeated sampling of $(n_1^{obs}, \ldots, n_8^{obs})$ from the Uniform distribution.
et al. [1988]. However, generalizing their results to factorial designs seems non-trivial, because there is no “multivariate” rearrangement inequality readily available, to the best of our knowledge. Second, in a recent paper Mukerjee et al. (2018) extended the potential outcomes framework to more complex experimental designs beyond $2^k$ factorial (e.g., Latin square and split-plot), and it is possible to study partial identification for those scenarios.

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