Cross-validation Approaches for Multi-study Predictions

Boyu Ren\textsuperscript{1,2}, Prasad Patil\textsuperscript{3}, Francesca Dominici\textsuperscript{4}, Giovanni Parmigiani\textsuperscript{4,5}, and Lorenzo Trippa\textsuperscript{4,5}

\textsuperscript{1}Laboratory for Psychiatric Biostatistics, McLean Hospital
\textsuperscript{2}Department of Psychiatry, Harvard Medical School
\textsuperscript{3}Department of Biostatistics, Boston University School of Public Health
\textsuperscript{4}Department of Biostatistics, Harvard T.H. Chan School of Public Health
\textsuperscript{5}Department of Data Sciences, Dana-Farber Cancer Institute

Abstract

We consider prediction in multiple studies with potential differences in the relationships between predictors and outcomes. Our objective is to integrate data from multiple studies to develop prediction models for unseen studies. We propose and investigate two cross-validation approaches applicable to \textit{multi-study stacking}, an ensemble method that linearly combines study-specific ensemble members to produce generalizable predictions. Among our cross-validation approaches are some that avoid reuse of the same data in both the training and stacking steps, as done in earlier multi-study stacking. We prove that under mild regularity conditions the proposed cross-validation approaches produce stacked prediction functions with oracle properties. We also identify analytically in which scenarios the proposed cross-validation approaches increase prediction accuracy compared to stacking with data reuse. We perform a simulation study to illustrate these results. Finally, we apply our method to predicting mortality from long-term exposure to air pollutants, using collections of datasets.
1 Introduction

It is increasingly common for researchers to have access to multiple studies and datasets to address the same or closely related prediction questions (Kannan et al., 2016; Manzoni et al., 2018). Although datasets from $K > 1$ studies may contain the same outcome variable $Y$ (e.g., patient survival) and predictors $X$ (e.g., pre-treatment prognostic profiles in clinical studies), the joint distributions $P_1, \ldots, P_K$ of $(X, Y)$ across these $K$ studies are typically different, owing to distinct study populations, study designs and study-specific technological artifacts (Patil et al., 2015; Sinha et al., 2017). In this article, we consider building prediction functions (PFs) for future unseen studies using multiple datasets, while accounting for potential differences in the study-specific distributions $P_1, \ldots, P_K$. We consider $P_k$’s to be random objects and the heterogeneity across them to be described by a hyper-distribution of distributions.

We use the term generalist, as in Bernau et al. (2014), to indicate that we wish to make prediction in studies $K + 1, K + 2, \ldots$ that are not included in the training data collection. Strategies to develop a generalist PF depend on relations and similarities between studies. If studies can be considered exchangeable, i.e. $P_k$ can be assumed to be invariant to permutations of the study indices $1, \ldots, K$, then a model that consistently predicts accurately across all $K$ training studies is a good candidate for generalist predictions in unseen studies $k > K$. Generalist PFs have been studied from meta-analytic perspectives (Tseng et al., 2012; Pasolli et al., 2016) and using hierarchical models (Ventz et al., 2020; Rashid et al., 2020), often assuming study exchangeability. If the exchangeability assumption is inadequate, joint models for multiple studies can incorporate information on relevant relations between studies (Moreno-Torres et al., 2012). For example, when $K$ datasets are representative of different time points, one can incorporate potential cycles or long-term trends.

The goal of generalist prediction is akin to that of domain generalization (DG) (Wang et al., 2021) in machine learning, if each study can be thought of as a domain, that is, a factor known to substantially affect the data generating distribution $P_k$. One of the goals of DG is to leverage the information of all $K$ observed domains to construct a PF that can generalize to an unseen target domain. Some algorithms in DG use representation learning to identify transformations of $X$ to serve as the predicting features for better generalizability. One strategy, domain invariant representation learning, finds such transformations of $X$ whose distributions are invariant across domains (Shao et al., 2019; Deng et al., 2020). Another, feature disentanglement, relaxes the assumption that invariant representations exist and instead learns transformations of $X$ that
later are identified as domain-shared and domain-specific features. This strategy uses only the
domain-shared features for predictions while minimizing the information loss of ignoring the
domain-specific features (Ilse et al., 2020; Wang et al., 2021).

Recently, ensemble methods have been proposed for DG (Nozza et al., 2016; Ding and Fu,
2017; Zhou et al., 2020), as well as multi-study learning (Patil and Parmigiani, 2018; Ramchan-
dran et al., 2020). An important building block for these methods is stacking (Wolpert, 1992;
Breiman, 1996). In a single study setting, stacking combines an ensemble of PFs, each trained
in a subset of the available data, into a single PF. The weights assigned to each model are often
selected by maximizing a utility function representative of the accuracy of the combined PF.
Stacking is computationally efficient and finds the optimal PF within the convex hull of the
ensemble (Juditsky et al., 2008; Yao et al., 2018). When PFs are derived from flexible machine
learning algorithms, their convex hull contains a large class of models, and hence stacking is
more likely to recover the true data generating mechanism (Yao et al., 2018).

Patil and Parmigiani (2018) extended stacking to the multi-study setting via two-stage al-
gorithms that, in the first stage, train learners on individual studies to generate a collection of
single-study prediction functions (SPFs) with arbitrary machine learning methods. Then, at
the second stage, they select ensemble weights using stacking on a merged dataset including
all labels and all predictions. This rewards SPFs that do well outside their training studies.
This approach does not require exchangeability, and the derivation of the ensemble weights can
be tailored to settings where exchangeability is implausible. Loewinger et al. (2021) further
extended this method to studies generated by resampling of the K training datasets. In this
article we formulate the second stage of the multi-study stacking approach as a formal opti-
mization wherein stacking weights approximately maximize an expected utility function. The
expectation is estimated using the entire collection of K training studies. Our contribution is
two-fold.

First, we introduce cross-validation (CV) procedures specific for the multi-study settings,
with the aim to mitigate the potential over-fitting associated with data reuse (DR) in two-stage
stacking. This issue arises from the partial overlap of the data points used to train each SPF
and to estimate stacking weights. Depending on how a multi-study dataset is partitioned into
different folds for training SPFs and estimating weights, we propose two CV procedures: within-
study CV (CV_{ws}) and cross-study CV (CV_{cs}). CV_{ws} uses a subset of the data in each study to
form a fold while CV_{cs} treats each study as a fold. This approach shares similarities with the
multi-source CV strategy discussed in Geras and Sutton (2013), but with a key difference: at each
iteration, CV_{cs} evaluate the out-of-study prediction accuracy of a weighted combination of SPF s, instead of a re-trained PF based on the aggregated training studies, to explicitly accommodates the utility function defined for multi-study stacking. We characterize the behavior of CV_{ws} and CV_{cs} when applied for generalist predictions, with particular focus on the bias and variance of the estimated expected utilities (Bengio and Grandvalet, 2003).

Second, we derive asymptotic results and provide empirical comparisons between the multi-study stacking PFs trained with DR and CV procedures. We evaluate these procedures using mean squared error (MSE) of prediction. Ours is the first theoretical investigation of the two-stage stacking with CV in multi-study settings. Our results supplement generalization error bounds for DG (Blanchard et al., 2021) and show that, when the number of studies $K$ and the sample sizes $n_k$ become large, both DR and CV stacking achieve a generalization error similar to an asymptotic oracle benchmark. The asymptotic oracle is defined as the linear combination of the SPF s’ limits $\lim_{n_k \to \infty} \hat{Y}_k$ for $k = 1, \ldots, K$ that minimizes the MSE in future studies, that is for $k > K$. Our results bound the MSE difference between the oracle ensemble and two stacking procedures, with and without DR. Related bounds have been studied in the single-study setting (van der Laan et al., 2006) and in the functional aggregation literature (Juditsky and Nemirovski, 2000; Juditsky et al., 2008; Li et al., 2022).

We apply our DR and CV stacking procedures to predicting pollution-related mortality. We use information on Medicare beneficiaries and measurements of air pollutants at the ZIP code level. We are interested in predicting the number of deaths per 10,000 person-years. In separate analyses, we partitioned the database into studies defined by state and by county. We compare the relative performance of DR and CV stacking.

2 Generalist predictions

2.1 Notation

We use data from $K$ studies $k = 1, \ldots, K$, with sample sizes $n_k$. For individual $i$ in study $k$ we have a vector of $p$-dimensional characteristics $x_{i,k} \in X \subseteq \mathbb{R}^p$ and the individual outcome $y_{i,k} \in \mathbb{R}$. Let $S_k = \{(x_{i,k}, y_{i,k}), i = 1, \ldots, n_k\}$ denote all data from study $k$ and $S = \{S_k, k = 1, \ldots, K\}$ the collection of all $K$ datasets. Extending earlier multi-study architectures, we define a list $\mathcal{D}$ of training sets, which includes $T$ disjoint members $D_1, \ldots, D_T$. Each $D_t$ is a set of $(i, k)$ indices, where $i \in \{1, 2, \ldots, n_k\}$ is the sample index within a study $k$. The set $D_t$ can include indices with different $k$ values (see for example $D_2$ and $D_3$ in Figure 1). We call a collection $\mathcal{D}$
partitioned by study if $T = K$ and $D_t = \bar{D}_t = \{(1, t), \ldots, (n_t, t)\}$ for $t = 1, \ldots, K$.

$$
\begin{array}{c|cccc}
  k & 1 & 2 & \cdots & K \\
  \hline
  1 & (1,1) & (2,1) & \cdots & (n,1) \\
  2 & (1,2) & (2,2) & \cdots & (n,2) \\
  \vdots & \vdots & \vdots & \ddots & \vdots \\
  K & (1,K) & (2,K) & \cdots & (n,K) \\
\end{array}
$$

**Figure 1**: Illustration of the relation between studies and training sets for $D = \{D_1, D_2, D_3\}$ when all studies are of equal size $(n_k = n, k = 1, \ldots, K)$.

We consider $L$ different learners. A learner is a method for generating a PF, such as linear regression, random forests or a neural network. Note that we do not require a learner to have the ability to assess the evidential uncertainty associated with its output PF. Training the learner $\ell$ on $D_t$ generates an SPF denoted as $\hat{Y}_t^\ell : \mathcal{X} \rightarrow \mathbb{R}$. The set of SPFs is $\hat{Y} = \{\hat{Y}_t^\ell(\cdot); \ell = 1, \ldots, L, t = 1, \ldots, T\}$. Let $W$ be a subset of $\mathbb{R}^{TL}$, where $\mathbb{R}^{TL}$ is the $TL$-dimensional Euclidean space. We combine the SPFs in $\hat{Y}$ into $\hat{Y}_w : \mathcal{X} \rightarrow \mathbb{R}$,

$$
\hat{Y}_w(\cdot) = \sum_{\ell=1}^{L} \sum_{t=1}^{T} w_{\ell,t} \hat{Y}_t^\ell(\cdot),
$$

where $w = (w_{\ell,t}; \ell \leq L, t \leq T) \in W$ are weights trained using multi-study stacking. In the remainder of this manuscript, if not otherwise specified, we suppress the range of the summations and assume that the range for $i$ is $1$ to $n_k$, $1$ to $K$ for $k$, $1$ to $T$ for $t$, and $1$ to $L$ for $\ell$.

### 2.2 Utility function for generalist prediction

We want to use $\hat{Y}_w$ for prediction in a target population with unknown joint distribution $\pi$ on $(X, Y)$. The objective is to maximize the expected utility $U$ of $\hat{Y}_w$ in the target population:

$$
U(w; \pi) = \int_{(x,y)} u(\hat{Y}_w(x), y) \, d\pi(x, y),
$$

where $u(y, y')$ is a utility function, such as the negative squared difference $u(y, y') = -(y - y')^2$.

Generalist predictions are designed to target all future studies $K + 1, K + 2, \ldots$. The corresponding utility function is defined through a limit:

$$
U_g(w) = \lim_{I \to \infty} \frac{1}{I} \sum_{i=1}^{I} U(w; P_{K+i}).
$$
We will only consider scenarios where the above limit is well defined. In particular, if $P_1, P_2, \ldots$ are exchangeable, there exists a fixed distribution $Q$ of random distributions such that $P_k \overset{iid}{\sim} Q$ for $k = 1, 2, \ldots$. In this case, $U_g(w)$ can be rewritten, for a generic $P \sim Q$, as

$$U_g(w) = \int \left[ \int_{(x,y)} u(\hat{Y}_w(x), y) dP(x,y) \right] dQ.$$  

Changing the order of integration, and defining $P_0(\cdot) = \int P(\cdot) dQ$,

$$U_g(w) = U(w; P_0) = \int_{(x,y)} u(\hat{Y}_w(x), y) dP_0(x,y).$$

Note that when exchangeability across $P_k$ holds, $P_0$ can be estimated with the empirical distribution $\hat{P}_0(x,y) = K^{-1} \sum_{k,i} \mathbb{I}(x = x_{i,k}, y = y_{i,k})/n_k$. Hence, a direct estimator of $U_g(w)$ is

$$\hat{U}^{DR}(w) = \sum_k \frac{1}{K} \cdot \frac{1}{n_k} \sum_i u(\hat{Y}_w(x_{i,k}), y_{i,k}),$$

where DR indicates that the estimate of $U$ involves DR. See Section 3 for a discussion of DR.

If the sequence $P_1, P_2, \ldots$ is not exchangeable, for example when the sequence satisfies a Markov relation $[P_k|P_1, \ldots, P_{k-1}] \overset{d}{=} [P_k|P_{k-1}]$ as in Shumway and Stoffer (2017), we can replace $1/K$ by weights $\nu_k$ varying with $k$ (e.g., $\nu_k$ is larger when $k$ gets closer to $K$). Throughout this article we will not specify $Q$, but we will assume exchangeability of $P_1, P_2, \ldots$.

## 3 Multi-study Stacking Approaches

In this section, we introduce three approaches to train generalist PFs in the multi-study setting.

We begin by defining the oracle weights as

$$w_g = \arg \max_{w \in W} U_g(w).$$

In what follows, if not otherwise specified, $u(y, y') = -(y-y')^2$. For the oracle case the generalist prediction error of the PF $\hat{Y}$ is

$$\text{MSE}_0(\hat{Y}) = \int_{(x,y)} \left( y - \hat{Y}(x) \right)^2 dP_0. \quad (1)$$

We consider three multi-study stacking approaches: the original multi-study stacking (Patil and Parmigiani, 2018), which involves data reuse (DR stacking, for short) and two novel CV
stacking approaches: *within-study cross-validated stacking* (CV_{ws}) and *cross-study cross-validated stacking* (CV_{cs}). These three approaches select \( w \) by maximizing different estimates of the expected utility \( U_g(w) \). We discuss the estimators of \( U_g(w) \) underlying these approaches. We study the accuracy of an estimator \( \hat{U}(w) \) by examining its deviation from the truth \( \hat{U}(w) - U_g(w) \) and we focus mainly on the mean \( E_S(\hat{U}(w) - U_g(w)) \) and variance \( \text{var}_S(\hat{U}(w) - U_g(w)) \) over different realizations of \( S \), the data from the entire collection of \( K \) studies. We refer to \( E_S(\hat{U}(w) - U_g(w)) \) as the bias of \( \hat{U}(w) \).

In two examples we illustrate that DR stacking and CV_{ws} tend to over-estimate the utility function \( U_g \) (\( E_S(\hat{U}(w) - U_g(w)) > 0 \)) and have smaller variance compared to CV_{cs}, which in turn tends to under-estimate \( U_g \).

### 3.1 DR stacking

A direct approach to selecting \( w \) for generalist predictions is to maximize the estimate \( \hat{U}^{DR}(w) \) of \( U_g(w) \). Let \( \hat{w}^{DR} = \arg \max_{w \in W} \hat{U}^{DR}(w) \) and \( \hat{Y}^{DR} = \sum_{t,\ell} \hat{w}^{DR}_{t,\ell} \hat{Y}_t^\ell \). Training the SPFs \( \hat{Y}_t^\ell \) uses data in \( D_t \), which in this case is later re-used to compute \( \hat{U}^{DR}(w) \). This could lead to a non-zero bias \( E_S(\hat{U}^{DR}(w) - U_g(w)) \) that may also depend on \( w \). To see this, note that the difference between \( U_g(w) \) and \( \hat{U}^{DR}(w) \) can be expressed as

\[
\hat{U}^{DR}(w) - U_g(w) = -w^\top (\hat{\Sigma}^{DR} - \Sigma) w + 2w^\top (\hat{b}^{DR} - b) + C,
\]

where \( E_S(C) = 0 \). Here \( \hat{\Sigma}^{DR} \) and \( \Sigma \) are \( TL \times TL \) matrices and their components corresponding to \( w_{t,\ell} \times w_{t',\ell'} \) are

\[
\hat{\Sigma}^{DR}_{t,\ell; t',\ell'} = \frac{1}{Kn_k} \sum_i \hat{Y}_t^\ell(x_{i,k}) \hat{Y}_t^{\ell'}(x_{i,k}), \text{ and } \Sigma_{t,\ell; t',\ell'} = \langle \hat{Y}_t^\ell, \hat{Y}_t^{\ell'} \rangle,
\]

where \( \langle \hat{Y}_t^\ell, \hat{Y}_t^{\ell'} \rangle = E_{x \sim P_0} (\hat{Y}_t^\ell(x) \hat{Y}_t^{\ell'}(x)|S) \). Also, \( \hat{b}^{DR} \) and \( b \) are \( TL \)-dimensional vectors:

\[
\hat{b}^{DR}_{k,\ell} = \frac{1}{Kn_k} \hat{Y}_t^\ell(x_{i,k}) y_{i,k}, \text{ and } b_{t,\ell} = \langle \hat{Y}_t^\ell, Y_0 \rangle,
\]

where \( \langle \hat{Y}_t^\ell, Y_0 \rangle = E_{(x,y) \sim P_0} (y \hat{Y}_t^\ell(x)|S) \).

Consider \( D \) partitioned by study. If \( k \notin \{t, t'\} \), then

\[
E_S(\hat{Y}_t^\ell(x_{i,k}) \hat{Y}_t^{\ell'}(x_{i,k})|S_t, S_{t'}) = \langle \hat{Y}_t^\ell, \hat{Y}_t^{\ell'} \rangle, \text{ and } E_S(\hat{Y}_t^\ell(x_{i,k}) y_{i,k}|S_t) = \langle \hat{Y}_t^\ell, Y_0 \rangle.
\]
If \( k \in \{t, t'\} \), the first equality does not hold since conditioning on \( S_t \) and \( S_{t'} \), \( \hat{Y}^{t'}_t(x_{i,k})\hat{Y}^{t'}_{t'}(x_{i,k}) \) is a constant in the expectation, and this constant depends on \( x_{i,k} \). Hence, it cannot be equal to \( \langle \hat{Y}^t_t, \hat{Y}^{t'}_{t'} \rangle \), which is independent of \( x_{i,k} \). Similarly, if \( k = t \), the second equality does not hold. Specifically,

\[
\mathbb{E}_S \left( \Sigma_{t,t',t',t'}^{\text{DR}} - \Sigma_{t,t',t',t'} \big| S_t, S_{t'} \right) = \sum_{k \in \{t,t'\}} \sum_i \frac{\left( \hat{Y}^t_t(x_{i,k})\hat{Y}^{t'}_{t'}(x_{i,k}) - \langle \hat{Y}^t_t, \hat{Y}^{t'}_{t'} \rangle \right)}{K_n_k},
\]

and

\[
\mathbb{E}_S \left( \hat{b}^{\text{DR}}_{t,t} - b_{t,t} \big| S_t \right) = \sum_i \frac{1}{K_n_t} \left( \hat{Y}^t_t(x_{i,t})y_{i,t} - \langle \hat{Y}^t_t, Y_0 \rangle \right).
\]

Integrating out \( S_t \) and \( S_{t'} \) in the first equation, we have

\[
\mathbb{E}_S \left( \Sigma_{t,t',t',t'}^{\text{DR}} - \Sigma_{t,t',t',t'} \big| S_t, S_{t'} \right) = \sum_{k \in \{t,t'\}} \sum_i \frac{\left( \mathbb{E}(\hat{Y}^t_t(x_{i,k})\hat{Y}^{t'}_{t'}(x_{i,k})) - \mathbb{E}\langle \hat{Y}^t_t, \hat{Y}^{t'}_{t'} \rangle \right)}{K_n_k}.
\]

At least one of \( \hat{Y}^t_t \) and \( \hat{Y}^{t'}_{t'} \) has been trained with data including \( x_{i,k} \). Hence there is no guarantee that the expectation above is zero as it involves a difference between “in-sample” estimate \( \hat{Y}^t_t(x_{i,k})\hat{Y}^{t'}_{t'}(x_{i,k}) \) of an “out-of-sample” target \( \langle \hat{Y}^t_t, \hat{Y}^{t'}_{t'} \rangle \). The same result applies to \( \hat{b}^{\text{DR}} \), which implies that \( \hat{U}^{\text{DR}} \) is potentially biased.

**Example 1** (No predictors, DR). This example illustrates key points using two studies and no predictors. Here the oracle solution favors the SPF with higher generalist prediction accuracy, while DR stacking does not. Also, DR over-estimates \( U_g \), and its bias grows with inter-study heterogeneity. We will revisit this example to discuss various stacking procedures throughout the manuscript. See Appendix for detailed derivations.

Consider a \( D \) partitioned by study with \( K = 2 \). Assume we observe outcomes \( y_{i,k} \sim N(\mu_k, 1) \) for \( k = 1, 2 \) and \( n_1 = n_2 = n \). Across studies, \( \mu_k \sim N(0, \sigma^2) \). Consider the two SPFs \( \hat{Y}_1(\cdot) = \hat{y}_1 \) and \( \hat{Y}_2(\cdot) = \hat{y}_2 \), where \( \hat{y}_k = n_k^{-1} \sum_i y_{i,k} \). Set \( W = \Delta_1 \), the 1-simplex.

**Oracle weights** \( w_g \). The oracle weight for the SPF \( \hat{Y}_1, w_{g;1} \), is

\[
w_{g;1} = \begin{cases} 
\frac{|\hat{y}_2|}{|\hat{y}_1| + |\hat{y}_2|} & \hat{y}_1 \cdot \hat{y}_2 < 0, \\
1 & \hat{y}_1 \cdot \hat{y}_2 \geq 0, |\hat{y}_1| \leq |\hat{y}_2|, \\
0 & \hat{y}_1 \cdot \hat{y}_2 \geq 0, |\hat{y}_1| > |\hat{y}_2|.
\end{cases}
\]

Thus, the oracle favors \( \hat{Y}_1 \), i.e. \( w_{g;1} > w_{g;2} \), whenever \( \text{MSE}_0(\hat{Y}_1) < \text{MSE}_0(\hat{Y}_2) \).

**DR stacking weights**. The DR stacking weights turn out to be \( \hat{w}^{\text{DR}} = (1/2, 1/2) \). In other words,
DR stacking does not place more weight on the PF with smaller MSE. Also, the mean and variance of $\hat{U}_{DR}(w) - U_g(w)$ are

$$
\mathbb{E}_S(\hat{U}_{DR}(w) - U_g(w)) = \sigma^2 + 1/n, \\
\text{var}_S(\hat{U}_{DR}(w) - U_g(w)) = (\sigma^2 + 1/n)^2 \left(1 + 2(w_1^2 + w_2^2)\right).
$$

Thus $\hat{U}_{DR}(w)$ over-estimates $U_g(w)$. Bias and variance remain positive when $n \to \infty$ and are increasing functions of $\sigma^2$, which quantifies the inter-study heterogeneity.

### 3.2 CV stacking

In single-study stacking, CV is implemented by using part of the data for the training of the PFs $\hat{Y}$ and the rest for the selection of $w$ (see for example Breiman (1996)). We introduce two approaches to generalize CV to the multi-study setting. **Within-study CV** ($CV_{ws}$), in Section 3.2.1, partitions each study in folds. For each learner, one fold is set aside for selecting the multi-study stacking weight, while the others are used for training SPFs. **Cross-set CV** ($CV_{cs}$), in Section 3.2.2, treats studies as folds. At iteration $k = 1, \ldots, K$, we build the library of SPFs using all $D_t$ that do not contain samples from study $k$. We then combine this restricted library of SPFs to predict for study $k$. The optimal $w$ maximizes a utility estimate based on the predictions generated across all $K$ iterations.

#### 3.2.1 Within-study CV

This approach includes $M$ iterations and the four steps below. For simplicity, we assume that $|\tilde{D}_k|$ is divisible by $M$ for $k = 1, \ldots, K$, where $|D|$ is the cardinality of $D$.

1. Randomly partition each index set $\tilde{D}_k$ into $M$ equal-size subsets $\tilde{D}_{k,1}, \ldots, \tilde{D}_{k,M}$.
2. For every $m = 1, \ldots, M$, we train SPFs $\hat{Y}_{t,m}$ using data in $D_t$ that is not included in the $m$-th fold, that is, $\{(x_{i,k}, y_{i,k}); (i, k) \in D_t \cap (\bigcup_{k,m \neq m} D_{k,m'})\}$, for $\ell = 1, \ldots, L$ and $t = 1, \ldots, T$.
3. For each sample $(i, k)$, denote by $m(i, k)$ the single index $m$ such that $(i, k) \in \tilde{D}_{k,m}$. The estimated utility function for the generalist predictions is

$$
\hat{U}^{WS}(w) = \sum_k \frac{1}{Kn_k} \sum_i u \left( \sum_{\ell,t} w_{\ell,t} \hat{Y}_{\ell,t,m(i,k)}(x_{i,k}), y_{i,k} \right),
$$
and the optimal weights solve

\[ w^{WS} = \arg \max_{w \in W} \hat{U}^{WS}(w). \]

4. The CV$_{ws}$ stacked PF is \( \hat{Y}^{WS} = \sum_{\ell,t} \hat{w}_{\ell,t}^{WS} \hat{Y}_\ell^{t}. \)

We could also repeat steps 1-3 for multiple random partitions of the data collection \( S \) into \( M \) folds. Each repetition results in an estimate \( \hat{U}^{WS}(w) \). Although each repetition generates a similar but not identical set of SPFs, it may still be useful to consider consensus weights \( \hat{U}^{WS} \) obtained, for example, by optimizing the average over all the estimated utilities.

Although CV$_{ws}$ seemingly avoids DR through holding out part of \( S \) for the selection of \( w \), this strategy turns out to be insufficient in many cases and leads to a utility estimator \( \hat{U}^{WS} \) that is almost identical to \( \hat{U}^{DR} \). We illustrate this phenomenon in the setting of Example 1 and in a regression setting (see Appendix for derivations).

**Example 1** (No predictors, CV$_{ws}$). When applying CV$_{ws}$ in this example, we have

\[ |\hat{U}^{WS}(w) - \hat{U}^{DR}(w)| = o_p(|\hat{U}^{DR}(w) - \lim_{n \to \infty} \hat{U}^{DR}(w)|). \]

Specifically, we can show that \( |\hat{U}^{WS}(w) - \hat{U}^{DR}(w)| = O_p(1/n) \). In contrast, \( \sqrt{n}((\hat{\bar{y}}_1, \hat{\bar{y}}_2)^T - \mu) \to^d N(0, I_2) \) as \( n \to \infty \), where \( I_2 \) is the identify matrix, and therefore \( \hat{U}^{DR}(w) - \lim_{n \to \infty} \hat{U}^{DR}(w) = O_p(1/\sqrt{n}) \). This result suggests with moderate sample size \( n \), the difference between the two utility estimators is of smaller magnitude than the variability of the DR stacking estimator itself, and the two estimators can be regarded as identical in practice.

**Example 2** (Regression, CV$_{ws}$ vs. DR). Consider a scenario with \( K \) studies, and

\[
y_{i,k} = \beta_k^T x_{i,k} + \epsilon_{i,k}, \quad \beta_k \sim N(\beta_0, \sigma^2 \beta I_p), \quad \epsilon_{i,k} \sim N(0, \sigma^2), \tag{2}
\]

where \( \beta_k \in \mathbb{R}^p \) are study-specific regression coefficients and \( \epsilon_{i,k} \) is a noise term. We also assume that the \( p \)-dimensional vector \( x_{i,k} \) follows a \( N(0, I_p) \) distribution. We prove that again, \( |\hat{U}^{WS}(w) - \hat{U}^{DR}(w)| = o_p(|\hat{U}^{DR}(w) - \lim_{n \to \infty} \hat{U}^{DR}(w)|) \) as \( n \to \infty \) in Proposition 1.

**Proposition 1.** Assume \( D \) is partitioned by study and \( n_k = n \) for \( k \in \{1, 2, \ldots, K\} \). Fix \( \beta_1, \ldots, \beta_K \) in model (2). Let \( L = 1 \) and SPFs \( \hat{Y}_k^{t} \) be OLS regression functions. For any \( w \in W \),
where $W$ is a bounded set in $\mathbb{R}^K$, the following results hold:

$$\sup_{w \in W} \left| \hat{U}^{DR}(w) - \hat{U}^{WS}(w) \right| = O_p(1/n),$$

$$\sqrt{n} \left( \hat{U}^{DR}(w) - \lim_{n \to \infty} \hat{U}^{DR}(w) \right) \xrightarrow{d} Z.$$

Here $Z$ a non-degenerate normally distributed random variable.

In Figure 2(a), we plot $\hat{U}^{DR}(w) - \hat{U}^{WS}(w)$ and $\hat{U}^{DR}(w) - \lim_{n \to \infty} \hat{U}^{DR}(w)$ at $w = 1_K/K$ as a function of $n$. We find that $\log \left| \hat{U}^{DR}(w) - \hat{U}^{WS}(w) \right|$ can be approximated by $(- \log n + c_0)$ while $\log \left| \hat{U}^{DR}(w) - \lim_{n \to \infty} \hat{U}^{DR}(w) \right|$ can be approximated by $(-0.5 \log n + c_1)$, where $c_0$ and $c_1$ are constants. The results are concordant with the rates of convergence in Proposition 1.

### 3.2.2 Cross-set CV

In this section, we introduce $CV_{cs}$ by focusing on the special case of leave-one-study-out $CV_{cs}$ and when $D$ is partitioned by study. The estimator of $U_g(w)$ is constructed as follows.

1. Generate the library of SPFs $\hat{Y}$ using every set in $D$ (i.e. every study in this case). This library remains identical across the $K$ iterations.

2. At iterations $k = 1, \ldots, K$, evaluate the utility of $w$ using $D_k$ as validation set, excluding SPFs trained on $D_k$: 
   $$\hat{U}_{CS}^k(w) = \frac{1}{n_k} \sum_i u \left( \sum_{\ell,k'} I(k' \neq k) w_{\ell,k'} \hat{Y}_{k'}(x_{i,k'}, y_{i,k}) \right).$$

3. Obtain the utility estimator $\hat{U}^{CS}(w)$ by combining all $\hat{U}_{CS}^k$ across the $K$ iterations:
   $$\hat{U}^{CS}(w) = \frac{1}{K} \sum_k \hat{U}_{CS}^k \left( \frac{w}{1 - 1/K} \right).$$

4. Select $w$ as $\hat{w}^{CS} = \arg \max_{w \in W} \hat{U}^{CS}(w)$. The $CV_{cs}$ stacked PF is $\hat{Y}^{CS} = \sum_{\ell,k} \hat{w}^{CS}_{\ell,k} \hat{Y}_\ell^k$.

**Interpretation of $CV_{cs}$.** Expression (4) and $\hat{Y}^{CS}$ are simple to interpret when each study is regarded as a “fold”. Our goal is to obtain an accurate estimate of the generalist utility for stacking weights. Similar to single-study CV, $CV_{cs}$ will sequentially hold out each study (fold) and use it to test the stacked PF’s generalist prediction performance. When study $k$ is held out, SPFs $\hat{Y}_\ell^k$, $\ell = 1, \ldots, L$ from study $k$ are removed from the stacking stage to avoid data reuse.
The stacked PF using this reduced list of SPF can approximate \( \hat{Y}_w \) by rescaling \( w \). If we assume that the total contribution of all SPF of a study \( k \) to the final prediction is roughly identical across \( k = 1, \ldots, K \), which is not too unreasonable given that \( P_1, P_2, \ldots \) are exchangeable, then \( \hat{Y}_w \approx \sum_{k' \neq k, \ell} w_{k', \ell} / (1 - 1/K) \hat{Y}_{k'}^{\ell} \). The estimated generalist utility for the original library of SPF with study \( k \) as the hold-out is thus \( \hat{U}_k^{CS}(w/(1 - 1/K)) \). The overall estimated generalist utility, after iterating over all studies, is the average of \( \hat{U}_k^{CS}(w/(1 - 1/K)) \), as defined in (4).

See the following paragraph for a more concrete discussion.

**Rationale of CV\textsubscript{cs}.** We motivate CV\textsubscript{cs} as an approximated unbiased estimator of \( U_g \). Define \( w_{-k} \) to be equal to \( w \) except for components \( w_{\ell,k} \), \( \ell = 1, \ldots, L \), which are set to zero. With exchangeable \( P_k \) distributions, \( \hat{U}_k^{CS}(w) \) is an unbiased estimator of \( U_g(w_{-k}) \), that is:

\[
E[\hat{U}_k^{CS}(w) | S_{-k}] = U_g(w_{-k}),
\]

where \( S_{-k} = \{S_{k'}; k' \neq k\} \). It follows that

\[
\sum_k E[\hat{U}_k^{CS}(w) | S_{-k}] / K = \sum_{k=1}^K U_g(w_{-k}) / K.
\]

Consider the Taylor expansion of \( \sum_k U_g(w_{-k}) / K \) around \( 1_K / K \):

\[
\sum_k U_g(w_{-k}) / K \approx U_g(1_K / K) + \frac{\partial U_g}{\partial w^T}(1_K / K) \left( \sum_k w_{-k} / K - 1_K / K \right).
\]

By construction, \( \sum_k w_{-k} / K = (1 - K^{-1})w \). It follows that

\[
\sum_k E[\hat{U}_k^{CS}(w) | S_{-k}] / K \approx U_g(1_K / K) + \frac{\partial U_g}{\partial w^T}(1_K / K) \left( (1 - K^{-1})w - 1_K / K \right)
\]

\[
\approx U_g((1 - K^{-1})w).
\]

The last approximation holds because the first approximation is the Taylor expansion of \( U_g((1 - K^{-1})w) \) at \( w = 1_K / K \) up to the first order. Note that \( \hat{U}^{CS}(w) = \sum_k \hat{U}_k^{CS}(w/(1 - K^{-1})) / K \), therefore

\[
E(\hat{U}^{CS}(w) | S) = K^{-1} \sum_k E[\hat{U}_k^{CS}\left(\frac{w}{1 - K^{-1}}\right) | S_{-k}] \approx U_g(w),
\]

for \( w \) close to \( 1_K / K \).
We next illustrate that the finite-sample behavior of $\text{CV}_{cs}$ stacking is distinct from that of DR stacking and $\text{CV}_{ws}$ in Examples 1 and 2. We also introduce Example 3 to illustrate the important differences between $\text{CV}_{cs}$ and $\text{CV}_{ws}$ in generalist predictions.

**Example 1** (No predictors, $\text{CV}_{cs}$). We consider $\hat{U}_{CS}(w)$ for generalist predictions. See Appendix for detailed derivations of results below. In this example $\mathcal{D}$ is partitioned by study, and

$$\hat{U}_{CS}(w) = -\left(2w_1^2\bar{y}_1^2 + 2w_2^2\bar{y}_2^2 - 2\bar{y}_1\bar{y}_2 + \frac{\bar{y}_1^2 + \bar{y}_2^2}{2}\right),$$

It follows that

$$\mathbb{E}\left(\hat{U}_{CS}(w) - U_g(w)\right) = -(\sigma^2 + 1/n)(w_1^2 + w_2^2),$$

$$\text{var}\left(\hat{U}_{CS}(w) - U_g(w)\right) = 2(\sigma^2 + 1/n)^2 (w_1^2 + w_2^2)^2.$$

Therefore, $\hat{U}_{CS}(w)$ underestimates $U_g(w)$. Also, for every $w \in \Delta_1$, $\hat{U}_{CS}$ has a smaller bias and variance compared to $\hat{U}_{DR}$:

$$|\mathbb{E}\left(\hat{U}_{CS}(w) - U_g(w)\right)| < |\mathbb{E}\left(\hat{U}_{DR}(w) - U_g(w)\right)|,$$

$$\text{var}\left(\hat{U}_{CS}(w) - U_g(w)\right) < \text{var}\left(\hat{U}_{DR}(w) - U_g(w)\right).$$

The maximizer of $\hat{U}_{CS}(w)$ is $\hat{w}^{CS} = (\bar{y}_2^2/\bar{y}_1^2 + \bar{y}_2^2), \bar{y}_1^2/\bar{y}_1^2 + \bar{y}_2^2))$. Like the oracle weights $w_g$, $w^{CS}$ favors the SPF with lower MSE$_0$ (see equation 1). More importantly, $\text{CV}_{cs}$ has smaller generalist prediction error MSE$_0$ than DR stacking:

$$\text{MSE}_0\left(\hat{Y}_{CS}\right) - \text{MSE}_0\left(\hat{Y}_{DR}\right) = \frac{-(\bar{y}_1^2 - \bar{y}_2^2)^2(\bar{y}_1 + \bar{y}_2)^2}{4(\bar{y}_1^2 + \bar{y}_2^2)^2} \leq 0.$$

The equality holds if and only if $\bar{y}_1 = \bar{y}_2$.

**Example 2** (Regression, $\text{CV}_{cs}$). We revisit the regression setting to compare $\text{CV}_{cs}$, DR stacking and $\text{CV}_{ws}$. As $n \to \infty$, $\text{CV}_{cs}$ behaves differently compared to $\text{CV}_{ws}$. Under mild assumptions (cf. Prop. 1), $\hat{U}_{WS}(w) - \hat{U}_{DR}(w) \overset{P}{\to} 0$ as $n \to \infty$ when $K$ is fixed. This is not the case for $\text{CV}_{cs}$.

As $n \to \infty$, we have

$$\hat{U}_{CS}(w) \overset{P}{\to} \sum_{k,k'} \frac{K(K - 2 + \delta_{k,k'})}{(K - 1)^2} w_k\beta_k^\top \beta_{k'} w_{k'} - 2 \sum_k w_k\beta_k^\top \beta_{-k} + \frac{\sum_k \beta_k^\top \beta_{k}}{K} + \sigma^2,$$

where $\delta_{k,k'} = \mathbb{I}(k = k')$ and $\beta_{-k} = \sum_{k' \neq k} \beta_{k'}/(K - 1)$. This limit is different from the limit of
Both DR stacking and CV\textsubscript{ws} overestimate \( U_g \). We compute by Monte Carlo simulations the bias and variance for DR stacking, CV\textsubscript{ws} and CV\textsubscript{cs} (Fig. 2(b-c)). We assume that \( \sigma = \sigma_\beta = 1 \), \( K = 20 \), \( p = 10 \) and \( n_k = 100 \). The only learner \((L = 1)\) is OLS. The means and variances are derived based on 50 replicates. The data generating model is defined by expression (2), and we generate a new set of \( \beta_1, \ldots, \beta_K \) in each simulation replicate. The bias and variance for DR and CV\textsubscript{ws} are nearly identical (cf. Prop. 1). In 2(c), the curves for DR and CV\textsubscript{ws} even overlap with each other. On the other hand, CV\textsubscript{cs} has smaller bias but larger variance compared to DR stacking and CV\textsubscript{ws}, indicating a bias-variance trade-off of the CV\textsubscript{cs} strategy.

**Example 3.** We consider the data generating model in (2), with a different distribution of \( \beta_k \)'s such that \( \beta_k \overset{iid}{\sim} 0.5\delta_{\beta_0} + 0.5N(\beta_0, \sigma_\beta^2I_p) \), where \( \delta_{\beta_0} \) is the point-mass distribution at \( \beta_0 \). The oracle PF is \( Y_g(x) = \beta_0^\top x \). Assume \( K = 3 \), \( n_k = 10,000 \), \( k = 1, 2, 3 \), and \( \sigma^2 = 10 \). In a single simulation of the multi-study collection \( S \), we set \( \beta_1 = \beta_2 = \beta_0 \) and \( \beta_3 \neq \beta_0 \). We train three SPFs: \( \hat{Y}_k(x) = \hat{\beta}_k^\top x, k = 1, 2, 3 \), where \( \hat{\beta}_k \) is the OLS estimate of \( \beta_k \) using \( \bar{D}_k \). We consider CV\textsubscript{cs} and CV\textsubscript{ws} for generalist predictions.

In Figure 2(d-e), we plot \( \hat{U}_{\text{WS}}(w) \) and \( \hat{U}_{\text{CS}}(w) \) as a function of \((w_1, w_2)\) when \( w \in \Delta_2 \). The contour lines are straight for \( \hat{U}_{\text{WS}} \) and curved for \( \hat{U}_{\text{CS}} \). This illustrates that the geometries of the estimated utilities from CV\textsubscript{ws} and CV\textsubscript{cs} are generally different. We compare CV\textsubscript{ws} and CV\textsubscript{cs} in generalist predictions. Specifically, we simulate a dataset with size \( n = 10,000 \), \( \{(x_i, y_i); i = 1, \ldots, n\} \) from \( P_0 \). We calculate the predicted values for all samples using different PFs. Denote the vectors of predicted values using the three SPFs by \( \hat{Y}_k(X) = (\hat{Y}_k(x_i), i = 1, \ldots, n), k = 1, 2, 3 \), predicted values of CV\textsubscript{ws} by \( \hat{Y}_{\text{WS}}(X) = (\hat{Y}_{\text{WS}}(x_i), i = 1, \ldots, n), \) CV\textsubscript{cs} by \( \hat{Y}_{\text{CS}}(X) = (\hat{Y}_{\text{CS}}(x_i), i = 1, \ldots, n) \) and oracle by \( Y_g(X) = (Y_g(x_i), i = 1, \ldots, n) \). We then project vectors \( \hat{Y}_k(X), k = 1, 2, 3 \), \( \hat{Y}_{\text{WS}}(X), \hat{Y}_{\text{CS}}(X) \) and \( Y_g(X) \) into \( \mathbb{R}^2 \) using principal component analysis (PCA), see Figure 2(f). We note that \( \hat{Y}_{\text{WS}} \) in this example deviates substantially from the oracle \( Y_g \). On the other hand, \( \hat{Y}_{\text{CS}} \) is close to \( Y_g \).

**CV\textsubscript{cs} with arbitrary \( D_t \)'s.** CV\textsubscript{cs} can also be applied when \( D \) is not partitioned by study. In this case, we extend the definition of \( \hat{U}_k^{\text{CS}}(w) \) to

\[
\hat{U}_k^{\text{CS}}(w) = \frac{1}{n_k} \sum_i u \left( \sum_{\ell, t} \mathbb{1}(k \neq s_t) w_{\ell, t} \hat{y}_\ell(x_i, k), y_{i, k} \right),
\]

where \( \mathbb{1}(k \neq s_t) \) is an indicator function that equals 1 if \( k \neq s_t \) and 0 otherwise.
Figure 2: (a) Comparisons of DR and $CV_{ws}$ in Example 1. We illustrate $|\hat{U}^{DR}(w) - \hat{U}^{WS}(w)|$ (black) and $|\hat{U}^{DR}(w) - \lim_{n \to \infty} \hat{U}^{DR}(w)|$ (red) at $w = 1_K/K$ as a function of $n$. The dashed lines indicate the upper and lower fifth percentile of the differences simulation replicates. The solid lines illustrate the linear approximation of log-transformed average difference (black and red dots). The slopes approximate the rate of convergence of the differences when $n \to \infty$. (b-c) Comparisons of bias and standard deviation of the utility estimates from DR, $CV_{ws}$, $CV_{cs}$ stacking in Example 2. Note that in (c) the curves for DR and $CV_{ws}$ stacking overlap with each other. (d-f) Comparisons of $CV_{ws}$ and $CV_{cs}$ in generalist predictions (Example 3). We visualize the contour plots of $\hat{U}^{WS}(w)$ (d) and $\hat{U}^{CS}(w)$ (e). We use a dashed line and a dot to illustrate the maximizers of $\hat{U}^{WS}(w)$ and $\hat{U}^{CS}(w)$ respectively. (f) PCA of different PFs. We include three SPF $\hat{Y}_k$, two stacked PFs $\hat{Y}^{WS}$ and $\hat{Y}^{CS}$, and the oracle PF $Y_g$. 
where $s_t = \{k: (i, k) \in D_t \text{ for some } i = 1, \ldots, n_k\}$ is the set of study indices that are present in $D_t$. Similar to the partitioned by study setting, with exchangeable distributions $(P_1, P_2, \ldots)$, we have $\mathbb{E}\left[\hat{U}_{k}^{CS}(w) \mid s_{-k}\right] = U_g(w_{-k})$, where $w_{-k}$ is now equal to $w$ except for all elements $w_{\ell,t}$ with $s_t$ containing $k$, which are set to zero. $\hat{U}_{k}^{CS}(w)$ are combined into $\hat{U}^{CS}(w)$. Using the same Taylor expansion argument as in the previous derivations,

$$\sum_k \mathbb{E}\left[\hat{U}_{k}^{CS}(w) \mid S_{-k}\right] / K \approx U_g(\Gamma w),$$

where $\Gamma$ is a $KT \times KT$ diagonal matrix with the term corresponding to $w_{\ell,t}$ equal to $1 - \#\{k \in s_t\}/K$.

Next we assume that $1 - \#\{k \in s_t\}/K > 0$, that is, $D_t$ does not contain samples from all studies $k = 1, \ldots, K$. Then the estimator of utility is

$$\hat{U}^{CS}(w) = \sum_k \frac{1}{K n_k} \sum_{i=1}^{n_k} \left( \sum_{\ell,t} \frac{\mathbb{I}(k \notin s_t)}{1 - \#\{k \in s_t\}/K} w_{\ell,t} \hat{Y}_t(x_{i,k}, y_{i,k}) \right),$$

which again has the approximate unbiasedness property as in the case where $D$ is partitioned by study.

4 Properties of stacking PFs for generalist predictions

In consideration of the similarity of $\hat{Y}_w^{DR}$ and $\hat{Y}_w^{WS}$, we focus on the comparison between $\text{CV}_{cs}$ and DR stacking. We will assume that the data is generated from a hierarchical model, and that $D$ is partitioned by study. We will only consider the scenario where studies differ in the conditional distribution $P(Y|X)$ while $P(X)$ remains the same across all studies.

We show that, with $\hat{w}^{DR}$ and $\hat{w}^{CS}$, the expected prediction error of the generalist PFs in future study $k > K$ is close to the prediction error of an asymptotic oracle PF when $n_k$ and $K$ are large. The discrepancy between the prediction errors can be bounded by a monotone function of $K$ and $\min_k n_k$.

We consider arbitrary regression functions $\mathbb{E}(y_{i,k}|x_{i,k})$ with additive error:

$$y_{i,k} = f_k(x_{i,k}) + \epsilon_{i,k}, \quad f_k \sim F_f, \quad x_{i,k} \sim F_X, \quad (5)$$

for $i = 1, \ldots, n_k$ and $k = 1, 2, \ldots$. Here $f_k: \mathbb{R}^p \rightarrow \mathbb{R}, k \geq 1$, are random functions. The mean of $F_f$ is indicated as $f_0$. The noise terms $\epsilon_{i,k}$ are independent with mean zero and variance $\sigma^2$. 

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Our bound is stated in Proposition 2 below, which requires the following assumptions:

A1. There exists an \( M_1 < \infty \) such that a.e. (i.e., with probability 1) for any \( k > 0 \) and \( \ell \leq L \),

\[
\sup_{x \in \mathcal{X}} |f_k(x)| \leq M_1, \quad \sup_{x \in \mathcal{X}} |\hat{Y}_k^\ell(x)| \leq M_1, \quad \text{and, } |y_{i,k}| \leq M_1.
\]

We require the first inequality to have probability 1 with respect to \( F_f \). We require the second and third inequalities to have probability 1 with respect to the distribution of \( S \).

These assumptions are not restrictive. For example, if \( \mathcal{X} \) is a compact set and the outcomes \( Y \) are bounded, then the SPFs trained with a penalized linear regression model, e.g. a LASSO regression, or with tree-based regression models satisfy the assumption.

A2. There exist constants \( M_2 < \infty \), \( p_\ell > 0 \) and random functions \( Y_\ell^\ell \) for \( k = 1, \ldots, K \), \( \ell = 1, \ldots, L \), such that \( \sup_{x \in \mathcal{X}} |Y_k^\ell(x)| \leq M_1 \) a.e., and for sufficiently large \( n_k \), \( k = 1, \ldots, K \),

\[
\mathbb{E} \left[ \int_x n_k^{2p_\ell} \left( \hat{Y}_k^\ell(x) - Y_k^\ell(x) \right)^2 dF_X(x) \right] \leq M_2.
\]

Here the expectation is with respect to the distribution of \( S \) and \( Y_k^\ell = \lim_{n_k \to \infty} \hat{Y}_k^\ell \). For example, if \( \|E((X_k^\ell X_k)^{-1})\|_F = O(1/n_k) \), where \( \| \cdot \|_F \) is the Frobenius norm, and \( \hat{Y}_k^\ell \) is an OLS regression function, then \( Y_k^\ell(x) = (\lim \hat{\beta}_k)^\top x \) and \( p_\ell < 1/2 \) satisfy the above inequality.

The asymptotic oracle PF is based on the limiting oracle generalist stacking weights \( w_g^0 \), which combine the limiting SPFs \( Y_k^\ell \), \( k = 1, \ldots, K \), \( \ell = 1, \ldots, L \):

\[
w_g^0 = \arg \max_{w \in W} \int_{x,y} u(Y_w(x), y) dP_0(x, y),
\]

where \( Y_w = \sum_{\ell,t} w_{\ell,t} Y_\ell^t \) and \( P_0 \) (defined in Section 2.2) is the average joint distribution of \((X, Y)\) across studies \( k \geq 1 \). The generalist prediction error of \( Y_w \) is

\[
\psi(w) = \int_{x,y} (y - Y_w(x))^2 dP_0(x, y) = w^\top \Sigma w - 2b^\top w + \int_y y^2 dP_0(y).
\]

In Proposition 2 we compare \( \hat{Y}_w^{DR} \) and \( \hat{Y}_w^{CS} \) to the asymptotic oracle PF, using the metrics \( \mathbb{E}[\psi(\hat{w}^{DR}) - \psi(w_g^0)] \) and \( \mathbb{E}[\psi(\hat{w}^{CS}) - \psi(w_g^0)] \). We show that both CV_{ws} and CV_{cs} have the oracle property in the sense that their generalist prediction error converge to that of the asymptotic oracle PF as the size of the studies \( \min_k n_k \) and the number of studies \( K \) both go to infinity.
Proposition 2. Let $K \geq 2$ and $w \in \Delta_{KL-1}$. Consider $K$ training datasets and all future studies $k = K + 1, \ldots$ from model (5). If (A1) and (A2) hold, then

$$
E(\psi(\hat{w}^{DR}) - \psi(w_0^0)) \leq C_0 \sqrt{\log(KL)}K^{-1/2} + C_1(\min_k n_k)^{-\min_p p_c},
$$

$$
E(\psi(\hat{w}^{CS}) - \psi(w_0^0)) \leq C'_0 \sqrt{\log(KL)}K^{-1/2} + C'_1(\min_k n_k)^{-\min_p p_c},
$$

where the expectations are taken over the joint distribution of the data $S$. $C_0$, $C'_0$, $C_1$ and $C'_1$ are constants, independent of $K$ and $n_k$.

We then compare the performance of DR and CV$_{cs}$ stacking. Consider first the setting in Example 2 (see Appendix for derivations).

Example 2 (DR and CV$_{cs}$). We set $n_k = n$ for $k = 1, \ldots, K$. Consider first the bias (see Appendix for details):

$$
E(\hat{U}^{DR}(w) - U_g(w)) = \frac{p(p+1)\sigma^2}{Kn(n-p-1)}\|w\|_2^2 + \frac{2(p\sigma^2 + p\sigma^2/n)}{K}w^T1_K
$$

$$
E(\hat{U}^{CS}(w), U_g(w)) = \frac{\|\beta_0\|_2^2 \sum_{k \neq k'} w_k w_{k'}}{(K-1)^2} - \frac{\|\beta_0\|_2^2 + p(\sigma^2 + \sigma^2/n)}{K-1}\|w\|_2^2.
$$

$E(\hat{U}^{DR}(w) - U_g(w)) \geq 0$ and $E(\hat{U}^{CS}(w) - U_g(w)) \leq 0$ for any $w \in \Delta_{K-1}$. As $\|\beta_0\|_2/\sigma \beta \rightarrow 0$, the absolute bias of DR stacking becomes uniformly larger than CV$_{cs}$. On contrary, as $\|\beta_0\|_2/\sigma \beta \rightarrow \infty$, the absolute bias of DR stacking becomes uniformly smaller than CV$_{cs}$.

Although smaller absolute bias does not necessarily imply better generalist prediction accuracy, the relative prediction error of DR stacking to CV$_{cs}$, measured by $E(\psi(\hat{w}^{DR}) - \psi(\hat{w}^{CS}))$, follows a similar trend as $\sigma \beta$ changes. In Figure 3, we use simulated data to illustrate $E[\psi(\hat{w}^{DR}) - \psi(\hat{w}^{CS})]$ as a function of $\sigma \beta$. We generate data from the model in (2) and set $p = 10$, $\beta_0 = 1_p$ and $n = 200$. We examine two scenarios $K = 2$ and $K = 9$. $E(\psi(w))$ is calculated with 1,000 replicates. As shown in the figures, when $\sigma \beta$ is small, CV$_{cs}$ has lower generalist prediction accuracy than DR stacking ($E(\psi(\hat{w}^{DR}) - \psi(\hat{w}^{CS})) < 0$). When $\sigma \beta$ is large, CV$_{cs}$ outperforms DR stacking.

In Proposition 3, we derive the relationship between $\sigma \beta$ and $E(\psi(\hat{w}^{DR}) - \psi(\hat{w}^{CS}))$ when $n_k = n \rightarrow \infty$, $k = 1, \ldots, K$, and $K \leq p/2$ is fixed.

Proposition 3. Consider the model in Example 2 with an OLS learner ($L = 1$). Assume $p > 4$, $K \leq p/2$ and $W = \mathbb{R}^K$. If $\beta_0 = 0$, then $\lim_{n \rightarrow \infty} E(\psi(\hat{w}^{DR}) - \psi(\hat{w}^{CS})) > 0$ for every $\sigma \beta > 0$. If
\( \beta_0 \neq 0, \)

\[
\lim_{\sigma_\beta \to \infty} \lim_{n \to \infty} E(\psi(\hat{w}^{DR}) - \psi(\hat{w}^{CS})) \rightarrow \infty,
\]

and \( \lim_{n \to \infty} E(\psi(\hat{w}^{DR}) - \psi(\hat{w}^{CS})) \uparrow 0 \) as \( \sigma_\beta \downarrow 0. \)

In Example 2 with large sample sizes and relatively small number of studies, if the level of heterogeneity across studies \( \sigma_\beta \) is sufficiently large, CV\(_{CS}\) outperforms DR stacking. On the other hand, if \( \sigma_\beta \) is close to zero, DR stacking tends to work better. Of note, if \( \sigma_\beta \) is exceedingly high, neither approaches could work as cross-study predictions of a SPF would be problematic.

![Figure 3: Comparison of DR stacking and CV\(_{CS}\) when \( K = 2 \) (left) and \( K = 9 \) (right). The plots illustrate the differences \( E(\psi(\hat{w}^{DR}) - \psi(\hat{w}^{CS})) \) (CV\(_{CS}\)) and \( E(\psi(\hat{w}^{DR}) - \psi(\hat{w}_g^0)) \) (oracle). We set \( p = 10, \beta_0 = 1_K, n = 200, \) and vary \( \sigma_\beta. \) The expected values are calculated with 1,000 replicates.](image)

5 Simulation studies

We investigate empirically whether the error bounds in Proposition 2 are tight, and how the difference \( E(\psi(\hat{w}^{DR})) - E(\psi(\hat{w}^{CS})) \) changes as \( K \) and the inter-study heterogeneity \( \sigma_\beta \) vary.

We illustrate the behavior of \( E(\psi(\hat{w}^{DR}) - \psi(w_0^0)) \) from Proposition 2 with a numeric example and compare the actual difference to the analytic upper bound as \( n_k \) and \( K \) change. We use the simulation setting in Example 2 with each component of \( \beta_k \) uniformly distributed in \([0, 1]\). Each component of \( x_{i,k} \) is uniform in \([-1, 1]\) and \( \epsilon_{i,k} \) is uniform in \([-1, 1]\). We set \( n_k = n \) for all \( k \) and approximate \( E(\psi(\hat{w}^{DR}) - \psi(w_0^0)) \) with Monte Carlo simulations, for \( n = 100, 200, 400 \) as \( K \) increases from 20 to 50 (Fig. 4(a)) and for \( K = 5, 15, 20 \) as \( n \) increases from 20 to 100 (Fig. 4(b)). We use the constraint \( w \in \Delta_{K-1} \). We simulate 1000 replicates. The difference \( E(\psi(\hat{w}^{DR}) - \psi(w_g^0)) \) is approximately a linear function of \( \sqrt{\log K/K} \) (Fig. 4(a)) and \( n^{-1/2} \) (Fig. 4(b)). The results for \( E(\psi(\hat{w}^{CS}) - \psi(w_g^0)) \) are similar (see Figure E.1).

We then perform a simulation analysis focused on the main results in Proposition 3. This analysis identifies regions where \( E(\psi(\hat{w}^{DR}) - \psi(\hat{w}^{CS})) > 0 \). We use the data generating model in
Figure 4: (a-b) $E(\psi(\hat{w}^{DR}) - \psi(w_0^{0}))$ as a function of $K$ and $n$. Dots represent results from the Monte Carlo simulation. Lines illustrate the fitted functions $c_0 + c_1 \log(K)/K$ (a) and $c_0 + c_1/\sqrt{n}$ (b) to the Monte Carlo results. (c) Comparison of generalist prediction accuracy of DR stacking and $CV_{cs}$ as measured by $E(\psi(\hat{w}^{DR}) - \psi(\hat{w}^{CS}))$.

Example 2. We fix $\beta_0 = 1_{10}$, vary $\sigma_\beta$ between 0 and 4, and the number of studies $K$ between 3 and 50. We then approximate $E(\psi(\hat{w}^{DR}) - \psi(\hat{w}^{CS}))$ with Monte Carlo simulations (Fig. 4(c)). In this figure the regions of $K$ and $\sigma_\beta$ in which $E(\psi(\hat{w}^{DR}) - \psi(\hat{w}^{CS})) < 0$ are in blue. We can see that when $\sigma_\beta$ is large, it is preferable to use $CV_{cs}$ for generalist predictions, while at smaller values of $\sigma_\beta$ the choice depends on the number of studies, and there remains a region where data reuse is preferable.

6 Application

As an illustration of the methods proposed in this article, we develop generalist PFs in an environmental health application. Our data consists of annual mortality rates for years 2000 to 2016 in 41,337 unique zip codes across the U.S. The annual average exposure to PM$_{2.5}$ is available for each zip code (Di et al., 2019). In addition to the measurement of PM$_{2.5}$ and the annual mortality rate, we consider several zip code-level demographic variables, which include the percentage of ever smokers, percentage of the population who are black, median household income, median value of housing, percentage of the population below the poverty level, percentage of the population with education below high school, percentage of owner-occupied housing units, and population density.

Our goal is the generalist prediction of zip code-level annual mortality rates from 2000 to 2016 based on yearly exposure to PM$_{2.5}$ and zip-code-level demographic predictors in unseen studies. We also include year as a predictor to capture temporal trends of mortality rate. The zip codes are the sampling units, while studies are either States in one analysis or Counties in another. For generalist predictions at the state level, we randomly select 10 states to train an ensemble of state-specific PFs with random forest, and use DR stacking and $CV_{cs}$ to combine
Figure 5: Comparison of DR stacking and CVcs in generalist predictions of mortality. Boxplots show the distributions of the differences in accuracy of the two stacking methods across 20 replicates, evaluated as average RMSE across all validation regions and years. In each replicate, we randomly select 10 regions to train, and evaluate the stacked PF on the remaining regions (39 test states in the U.S. and 47 test counties in California).

them and predict mortality in the remaining unseen 40 states. Here $k = 1, \ldots, 10$. Each state contains on average 980 unique zip codes and 13,936 zip-code-by-year records. The metric we use to evaluate the accuracy of the stacked PF is the average RMSE across all years in the set-aside testing states or counties. We repeat this procedure 20 times. The county-level analysis is performed by restricting the analysis to the state of California and considering counties within it to be studied. For this county-level dataset, we combine 10 county-specific PFs and validate the stacked PFs using the remaining 47 counties. Each county contains on average 23 unique zip codes and 657 zip code by-year records. The results are shown in Figure 5.

The State and County level analyses provide a useful contrast, as they reflect different degrees of heterogeneity in the underlying data distributions. For summary quantification, we estimate between-study heterogeneity by the variance of the predicted values from the 10 PFs on a single sample, with all predictors fixed at the national means. Across the 20 replicates, the mean of this heterogeneity metric is 0.017 for the state-specific PFs and 0.0029 for the county-specific PFs. In the state-level analysis, we thus combine study-specific PFs that reflect higher heterogeneity, and the performance of CVcs is slightly but consistently better compared to DR stacking (19 out of 20 replicates). In contrast, when we consider California and combine county-level models, with less heterogeneity, DR stacking has a smaller mean RMSE than CVcs (18 out of 20 replicates). This result is aligned with Proposition 3, which indicates for a fixed $K$, CVcs can outperform DR when the inter-study heterogeneity is large.
We studied a multi-study ensemble learning framework based on stacking for generalist predictions. We compared CV and DR approaches for the selection of stacking weights of SPFs in the ensemble. We discussed oracle properties of the generalist PFs and provided a condition under which CV\textsubscript{cs} can outperform DR stacking. We illustrated these developments with simulations and applied our approach to predict mortality based on multi-state and multi-county datasets.

We illustrated in examples that DR stacking is nearly identical to CV\textsubscript{ws} for generalist predictions, while CV\textsubscript{cs} is substantially different from both. We examined the differences \( E(\psi(\hat{w}^{\text{DR}}) - \psi(w^0)) \) and \( E(\psi(\hat{w}^{\text{CS}}) - \psi(w^0)) \) with Monte Carlo simulations and observed in simulations that they can be approximated by the bounds in Proposition 2. We also confirmed with numerical experiments and analytic results that CV\textsubscript{cs} outperforms DR stacking (\( E(\psi(\hat{w}^{\text{DR}}) - \psi(\hat{w}^{\text{CS}})) > 0 \)) when the heterogeneity of \( E(Y|X) \) across studies is high.

There are a couple of topics we would like to pursue further in future research. The procedure that we developed are applicable to any \( D \), beyond the partitioned-by-study case where \( D = \{\bar{D}_k; k = 1, \ldots, K\} \), as indicated by Figure 1. We would like to investigate the performance of our procedure for generic \( D \). We expect that a scenario where non-study-specific \( D \) is beneficial is when the multi-study dataset exhibits cluster structure with subsets of studies that share identical conditional distribution \( P(Y|X) \). In this case, merging studies from the same cluster to form a training set \( D \) increases the prediction accuracy of SPFs and in turn improves the performance of the resulting PFs. The other topic will target at non-exchangeable studies. As we discussed in Section 3, study weights \( \nu \) enable us to work with non-exchangeable studies, by specifying a set of \( \nu_k \) that reflects the relationship between the individual studies, which might be informed by some external variables, such as time and geographic locations.

\section{A \ Proof of Proposition 1}

Let \( M \) be such that \( n \) is divisible by \( M \). To prove \( \sqrt{n}(\hat{U}^{\text{DR}}(w) - \lim_{n \to \infty} \hat{U}^{\text{DR}}(w)) \) converges in distribution to \( Z \), we note that \( \hat{U}^{\text{DR}} \) is a continuous function of \( \hat{\beta}_k, k = 1, \ldots, K \). The result follows from central limit theorem and delta method.

We now prove the other equality. Partition each study evenly into \( M \) components and denote the \( m \)-th component of \( X_k \) as \( X_{k,m} \) and the responses as \( Y_{k,m} \). Let \( X_{k,-m} \) and \( Y_{k,-m} \) denote the complements of \( X_{k,m} \) and \( Y_{k,m} \) respectively. The estimated regression coefficients are \( \hat{\beta}_{k,m} = (X_{k,-m}^T X_{k,-m})^{-1} X_{k,-m}^T Y_{k,-m} \). Define \( \delta \hat{\beta}_{k,m} = \hat{\beta}_{k,m} - \hat{\beta}_k \), where \( \hat{\beta}_k = (X_k^T X_k)^{-1} X_k^T Y_k \) is
the OLS estimate using all data in study $k$.

**Lemma A.1.** Under the assumption of Proposition 1, $\| \sum_m \delta \hat{\beta}_{k,m} \|_2 = O_p(1)$.

**Proof.** First note the following relationship between $\hat{\beta}_{k,m}$ and $\hat{\beta}_k$ (Zhang, 1993):

$$\hat{\beta}_{k,m} = \hat{\beta}_k + (X_k^TX_k)^{-1}X_k^T(I_{n/M} - P_{k,m})^{-1}(X_{k,m}\hat{\beta}_k - Y_{k,m}), \quad (6)$$

where $P_{k,m} = X_{k,m}(X_k^TX_k)^{-1}X_k^T$ and $I_{n/M}$ is the identity matrix of size $n/M$. With central limit theorem, we have

$$\left\| \frac{X_k^TX_k}{n} - I_p \right\|_F = O_p\left(\frac{1}{\sqrt{n}}\right), \quad \left\| \frac{X_k^TX_{k,m}}{n} - \frac{1}{M} I_p \right\|_F = O_p\left(\frac{1}{\sqrt{n}}\right), \quad \|\delta \hat{\beta}_{k,m}\|_2 = O_p\left(\frac{1}{\sqrt{n}}\right), \quad (7)$$

where $\| \cdot \|_F$ is the Frobenius norm. From (6), it follows

$$\sum_m \delta \hat{\beta}_{k,m} = \frac{(X_k^TX_k)^{-1}}{M} \sum_m X_k^T(I_{n/M} - P_{k,m})^{-1}(X_{k,m}\hat{\beta}_k - Y_{k,m})$$

$$= \frac{(X_k^TX_k)^{-1}}{M} \sum_m X_k^T(I_{n/M} + \sum_l P_{k,m,l})(X_{k,m}\hat{\beta}_k - Y_{k,m})$$

$$= \frac{(X_k^TX_k)^{-1}}{M} \sum_m \sum_l X_{k,m}^T P_{k,m,l}(X_{k,m}\hat{\beta}_k - Y_{k,m}),$$

where the second equation holds since the spectral norm (maximum eigenvalue) of $P_{k,m}$ is smaller than 1 when $n$ is large. Indeed, the spectral norm converges to $1/M$ as $n \to \infty$. The last equation holds since $(\sum_m X_{k,m}^TX_{k,m})\hat{\beta}_k = X_k^TY_k = \sum_m X_{k,m}^TY_{k,m}$.

We prove that $\| \sum_m X_{k,m}^TP_{k,m,l}(X_{k,m}\hat{\beta}_k - Y_{k,m}) \|_2 = O_p(1)$ for $l = 1, 2, \ldots$, which will prove the lemma immediately. Indeed, since $Y_k = X_k\beta_k + \epsilon_k$, where $\epsilon_k = (\epsilon_{i,k}; i = 1, \ldots, n)$, we have

$$\sum_m X_{k,m}^TP_{k,m,l}(X_{k,m}\hat{\beta}_k - Y_{k,m})$$

$$= \sum_m X_{k,m}^TP_{k,m,l}(X_{k,m}\hat{\beta}_k - Y_{k,m})$$

$$= \sum_m X_{k,m}^TP_{k,m,l}X_{k,m}(X_k^TX_k)^{-1}X_k^T\epsilon_k - \sum_m X_{k,m}^TP_{k,m,l} \epsilon_{k,m},$$

where $\epsilon_{k,m}$ is the $m$-th component of $\epsilon_k$. Using the assumption in Proposition 1, we know $\|X_{k,m}^T\epsilon_{k,m}\|_2 = O_p(\sqrt{n})$ since $X_{k,m}^T\epsilon_{k,m}$ is mean zero and its variance-covariance matrix is
\(n\sigma^2/MI_p\). From (7), we also have

\[\|X_{k,m}^TX_{k,m}(X_k^TX_k)^{-1} - I_p/M\|_F = O_p(1/\sqrt{n})\]

\[\|\sum_m X_{k,m}^TP_{k,m}X_{k,m} - X_k^TX_k/M\|_F = O_p(\sqrt{n}),\]

\[\|\sum_m X_{k,m}^TP_{k,m}^{\epsilon_k} - X_k^T\epsilon_k/M\|_2 = O_p(1).\]

It then follows that

\[\left\|\left(\sum_m X_{k,m}^TP_{k,m}X_{k,m}\right)(X_k^TX_k)^{-1}X_k^T\epsilon_k - \sum_m X_{k,m}^TP_{k,m}^{\epsilon_k}\right\|_2 = O_p(1).\]

The proof is completed by noting that \(\|X_k^TX_k\|_F = O_p(1/n)\).

We know

\[\hat{\Sigma}_{i,i'}^{\text{DR}} = (Kn)^{-1}\sum_k X_k^TX_k\hat{\beta}_{k,i'} \quad \hat{b}_{i}^{\text{DR}} = (Kn)^{-1}\sum_k X_k^TY_k,\]

\[\hat{\Sigma}_{i,i'}^{\text{WS}} = (Kn)^{-1}\sum_k \sum_{m=1}^M X_{k,m}^TX_{k,m}\beta_{k,m}' \quad \hat{b}_{i}^{\text{WS}} = (Kn)^{-1}\sum_k \sum_{m=1}^M \beta_{k,m}' X_{k,m} Y_{k,m}.\]

It follows that

\[n^{-1}\sum_m \beta_{k,m}' X_{k,m}^TX_{k,m}\beta_{k,m}' = \hat{\beta}_i(n^{-1}X_k^TX_k)\beta_{k,m}' + 2\sum_m \delta\beta_{k,m}' (n^{-1}X_k^TX_k)\hat{\beta}_{k,m}' + n^{-1}\sum_m \delta\hat{\beta}_{k,m}' (n^{-1}X_k^TX_k)\beta_{k,m}'\]

(7) indicates that \(\|\sum_m \delta\beta_{k,m}' (n^{-1}X_k^TX_k)\delta\hat{\beta}_{k,m}'\|_2 = O_p(1/n)\). And by invoking Lemma A.1, \(\|\sum_m \delta\beta_{k,m}' (n^{-1}X_k^TX_k)\beta_{k,m}'\|_2 = O_p(1/n)\). Therefore, \(|\hat{\Sigma}_{i,i'}^{\text{DR}} - \hat{\Sigma}_{i,i'}^{\text{WS}}| = O_p(1/n)\) for \(i, i' = 1, \ldots, K\). Similarly, we can prove \(|\hat{b}_{i}^{\text{DR}} - \hat{b}_{i}^{\text{WS}}| = O_p(1/n)\) for \(i = 1, \ldots, K\).

**B Proof of Proposition 2**

Define \(\hat{\psi}(w)\) as

\[\hat{\psi}^{\text{DR}}(w) = \hat{\psi}^{\text{DR}}(w) - \frac{\sum_k n_k^{-1}Y_k^TY_k}{K} + \int_y y^2 dP_0(y).\]

Similarly, let \(\hat{\psi}^{\text{CS}}(w) = \hat{\psi}^{\text{CS}}(w) - K^{-1}\sum_k n_k^{-1}Y_k^TY_k + \int_y y^2 dP_0(y).\)

We first prove the following lemma on upper bounds of two differences \(|\psi(\hat{w}^{\text{DR}}) - \psi(w_0)|\)
and $|\psi(\hat{w}^{CS}) - \psi(w^0_g)|$.

**Lemma B.1.** $|\psi(\hat{w}^{DR}) - \psi(w^0_g)|$ and $\psi(\hat{w}^{CS}) - \psi(w^0_g)$ can be bounded as follows.

\[
|\psi(\hat{w}^{DR}) - \psi(w^0_g)| \leq 2 \sup_{w \in W} |\psi(w) - \hat{\psi}^{DR}(w)|, \\
|\psi(\hat{w}^{CS}) - \psi(w^0_g)| \leq 2 \sup_{w \in W} |\psi(w) - \hat{\psi}^{CS}(w)|.
\]

**Proof.** We prove the inequality for $\hat{w}^{DR}$ and similar steps can be followed to verify the other inequality. Note that

\[
\psi(\hat{w}^{DR}) - \psi(w^0_g) = \psi(\hat{w}^{DR}) - \hat{\psi}^{DR}(\hat{w}^{DR}) + \hat{\psi}^{DR}(\hat{w}^{DR}) - \hat{\psi}^{DR}(w^0_g) + \hat{\psi}^{DR}(w^0_g) - \psi(w^0_g).
\]

By definition $\psi(\hat{w}^{DR}) - \psi(w^0_g) \geq 0$ and $\hat{\psi}^{DR}(\hat{w}^{DR}) - \hat{\psi}^{DR}(w^0_g) \leq 0$, therefore

\[
|\psi(\hat{w}^{DR}) - \psi(w^0_g)| \leq |\psi(\hat{w}^{DR}) - \hat{\psi}^{DR}(\hat{w}^{DR})| + |\hat{\psi}^{DR}(w^0_g) - \psi(w^0_g)| \leq 2 \sup_{w \in W} |\psi(w) - \hat{\psi}^{DR}(w)|.
\]

When $W = \Delta_{K-1}$, we have $\sup_{w \in W} |\psi(w) - \hat{\psi}^{DR}(w)| \leq \|\text{vec}(\Sigma - \hat{\Sigma}^{DR})\|_\infty + \|b - \hat{b}^{DR}\|_\infty$, where $\|\cdot\|_\infty$ is the $L^\infty$-norm of a vector and vec($\cdot$) is the vectorization of a matrix. With Lemma B.1, it follows

\[
\mathbb{E}[\psi(\hat{w}^{DR}) - \psi(w^0_g)] \leq 2\mathbb{E}\|\text{vec}(\Sigma - \hat{\Sigma}^{DR})\|_\infty + 2\mathbb{E}\|b - \hat{b}^{DR}\|_\infty. \quad (8)
\]

Similar results hold for $\mathbb{E}[\psi(\hat{w}^{CS}) - \psi(w^0_g)]$. The following lemma provides an upper bound for $\mathbb{E}\|\text{vec}(\Sigma - \hat{\Sigma}^{DR})\|$ and $\mathbb{E}\|\text{vec}(\Sigma - \hat{\Sigma}^{CS})\|$. 

**Lemma B.2.** If assumption A1 and A2 hold, we have the following bounds for $\mathbb{E}\|\text{vec}(\Sigma - \hat{\Sigma}^{DR})\|_\infty$ and $\mathbb{E}\|\text{vec}(\Sigma - \hat{\Sigma}^{CS})\|_\infty$.

\[
\mathbb{E}\|\text{vec}(\Sigma - \hat{\Sigma}^{DR})\|_\infty \leq 4\sqrt{2e}M_2^2\sqrt{\log(KL)/K} + 2M_1M_2\min_k n_k^{-\min \ell_p}, \\
\mathbb{E}\|\text{vec}(\Sigma - \hat{\Sigma}^{CS})\|_\infty \leq (4\sqrt{2e} + 8)M_1^2\sqrt{\log(KL)/K} + 2M_1M_2\min_k n_k^{-\min \ell_p}.
\]
Proof. First note that
\[
\hat{\Sigma}_{k,l,k',l'}^{\text{DR}} - \Sigma_{k,l,k',l'} = K^{-1} \sum_{s=1}^{K} n_s^{-1} \sum_{i=1}^{n_s} \left( \hat{Y}_k^e(x_{i,s}) \hat{Y}_{k'}^e(x_{i,s}) - \int_x Y_k^e(x) Y_{k'}^e(x) dF_X(x) \right).
\]
Denote \( \int_x Y_k^e(x) Y_{k'}^e(x) dF_X(x) \) as \( (Y_k^e, Y_{k'}^e) \), we have
\[
\| \hat{\Sigma}^{\text{DR}} - \Sigma \|_\infty \leq K^{-1} \sum_{s=1}^{K} n_s^{-1} \sum_{i=1}^{n_s} \left\| \left( \hat{Y}_k^e(x_{i,s}) \left( \hat{Y}_{k'}^e(x_{i,s}) - Y_{k'}^e(x_{i,s}) \right) \right) ; k, k' \leq K, l, l' \leq L \right\|_\infty
\]
\[+ K^{-1} \sum_{s=1}^{K} n_s^{-1} \sum_{i=1}^{n_s} \left\| \left( Y_{k'}^e(x_{i,s}) \left( \hat{Y}_k^e(x_{i,s}) - Y_k^e(x_{i,s}) \right) \right) ; k, k' \leq K, l, l' \leq L \right\|_\infty \tag{9}
\]
By assumption A1, we have
\[
\left| \hat{Y}_k^e(x_{i,s}) \left( \hat{Y}_{k'}^e(x_{i,s}) - Y_{k'}^e(x_{i,s}) \right) \right| \leq M_1 |\hat{Y}_{k'}^e(x_{i,s}) - Y_{k'}^e(x_{i,s})|.
\]
Combined with assumption A2, we have
\[
E \left\| \left( \hat{Y}_k^e(x_{i,s}) \left( \hat{Y}_{k'}^e(x_{i,s}) - Y_{k'}^e(x_{i,s}) \right) \right) ; k, k' \leq K, l, l' \leq L \right\|_\infty \leq M_1 M_2 (\min_k n_k)^{-\min_{l'} p_{l'}}.
\]
The same upper bound holds for the second term on the right-hand side of (9).
Define vector \( \alpha_{i,s} = \left( Y_k^e(x_{i,s}) Y_{k'}^e(x_{i,s}) - \langle Y_k^e, Y_{k'}^e \rangle ; k, k' \leq K, l, l' \leq L \right) \). Based on Lemma 2.1 in Juditsky and Nemirovski (2000), we have
\[
V \left( \sum_{i=1}^{n_s} \sum_{i=s}^{n_s} \alpha_{i,s} \right) \leq V \left( \sum_{i=1}^{n_s} \sum_{i=s}^{n_s} \alpha_{i,s} \right) + (n_K - \sum_{i=1}^{n_K} \alpha_{i,K})^T \nabla V \left( \sum_{i=1}^{n_s} \sum_{i=s}^{n_s} \alpha_{i,s} \right)
\]
\[+ c^*(M) n_K^{-1} \sum_{i=1}^{n_K} \alpha_{i,K}^2, \]
where \( M = K^2 L^2, c^*(M) = 4 e \log M, V(z) = 1/2 z^2 \rightarrow \mathbb{R}^M \rightarrow \mathbb{R} \) and \( q = 2 \log M \). It follows that
\[
E \left[ V \left( \sum_{i=1}^{n_s} \sum_{i=s}^{n_s} \alpha_{i,s} \right) \right] \leq E \left[ V \left( \sum_{i=1}^{n_s} \sum_{i=s}^{n_s} \alpha_{i,s} \right) \right] + c^*(M) E \| n_K^{-1} \sum_{i=1}^{n_K} \alpha_{i,K}^2 \|	ag{10}
\]
since \( \alpha_{i,s} \) and \( \alpha_{i,s'} \) are independent conditioned on \( f_1, \ldots, f_K \) when \( s \neq s' \) and \( E(\alpha_{i,k}) = 0 \). The
inequality in (10) implies a recursive relationship and repeatedly applying for $K$ times we get

$$E \left[ V \left( \sum_{s=1}^{K} n_s^{-1} \sum_{i=1}^{n_s} \alpha_{i,s} \right) \right] \leq c^*(M) \sum_{s=1}^{K} n_s^{-2} \mathbb{E} \left\| \sum_i \alpha_{i,s} \right\|_\infty^2.$$

By assumptions A1 and A2 again, we have $|Y_k^\ell(x_{i,s})Y_{k'}^\ell(x_{i,s}) - \langle Y_k^\ell, Y_{k'}^\ell \rangle| \leq 2M_1^2$, a.e. Therefore,

$$E \left[ V \left( \sum_{s=1}^{K} n_s^{-1} \sum_{i=1}^{n_s} \alpha_{i,s} \right) \right] \leq c^*(M)4KM_1^4 = 32e \log(KL)KM_1^4.$$

Since $V(z) \geq 1/2 \|z\|_\infty^2$, it follows

$$K^{-1}E\| \sum_s n_s^{-1} \sum_i \alpha_{i,s} \|_\infty \leq K^{-1} \sqrt{32e \log(KL)KM_1^4} = 4\sqrt{2eM_1^2} \sqrt{\log(KL)/K}.$$

The above steps also apply to prove of the bound of $E\| \hat{\Sigma}_{CS} - \Sigma \|_\infty$ by noting that

$$|\hat{\Sigma}_{k,\ell,k',\ell'} - \Sigma_{k,\ell,k',\ell'}| \leq \sum_s \sum_i n_s^{-1} \left( \hat{Y}_k^\ell(x_{i,s})\hat{Y}_{k'}^\ell(x_{i,s}) - \langle Y_k^\ell, Y_{k'}^\ell \rangle \right) + \frac{4M_1^2}{K-1}$$

$$\leq \sum_s \sum_i n_s^{-1} \left( \hat{Y}_k^\ell(x_{i,s})\hat{Y}_{k'}^\ell(x_{i,s}) - \langle Y_k^\ell, Y_{k'}^\ell \rangle \right) + 8M_1^2 \sqrt{\log(KL)/K}.$$

**Lemma B.3.** If assumption A1 and A2 hold, then

$$E\|b - \hat{b}^{DR}\|_\infty \leq M_1M_2(M \min_k n_k)^{-\min_{\ell} p_\ell} + (8\sqrt{2e} + 2)M_1^2 \sqrt{\log(KL)/K},$$

$$E\|b - \hat{b}^{CS}\|_\infty \leq 2M_1M_2(M \min_k n_k)^{-\min_{\ell} p_\ell} + (16\sqrt{2e} + 6)M_1^2 \sqrt{\log(KL)/K}.$$

**Proof.** Note that

$$\| \hat{b}^{DR} - b \|_\infty \leq K^{-1} \sum_s n_s^{-1} \sum_i \left( \hat{Y}_k^\ell(x_{i,s})y_{i,s} - Y_k^\ell(x_{i,s})y_{i,s}; k \leq K, \ell \leq L \right) \|_\infty +$$

$$K^{-1} \sum_s n_s^{-1} \sum_i \left( Y_k^\ell(x_{i,s})(y_{i,s} - f_s(x_{i,s})); k \leq K, \ell \leq L \right) \|_\infty +$$

$$K^{-1} \sum_s n_s^{-1} \sum_i \left( Y_k^\ell(x_{i,s})f_s(x_{i,s}) - \langle Y_k^\ell, f_0 \rangle; k \leq K, \ell \leq L \right) \|_\infty.$$
With assumption A1 and A2, we have
\[
\mathbb{E} \left( K^{-1} \sum_s n_s^{-1} \sum_i \left\| (\hat{Y}_k^e(x_{i,s}) - Y_k^e(x_{i,s})) y_{i,s}; k \leq K, \ell \leq L \right\|_\infty \right) \leq M_1 M_2 (\min_k n_k)^{-\min \nu_k}.
\]

Since \( \epsilon_{i,s} = y_{i,s} - f_s(x_{i,s}) \) is independent of \( Y_k^e \) and \( \mathbb{E} \epsilon_{i,s} = 0 \), applying a similar recursive relationship as in (10), we have
\[
\mathbb{E} \left( V \left( \sum_s n_s^{-1} \sum_i \left( Y_k^e(x_{i,s})(y_{i,s} - f_s(x_{i,s})); k \leq K, \ell \leq L \right) \right) \right) \leq c^*(M) \sum_{s=1}^K n_s^{-2} \mathbb{E} \left( \sum_i (Y_k^e(x_{i,s}) \epsilon_{i,s}; k \leq K, \ell \leq L) \right)^2 \leq 4K c^*(M) M_1^4.
\]

The last inequality holds due to Assumption A1. Therefore
\[
K^{-1} \mathbb{E} \left( \left\| \sum_s n_s^{-1} \sum_i \left( Y_k^e(x_{i,s})(y_{i,s} - f_s(x_{i,s})); k \leq K, \ell \leq L \right) \right\|_\infty \right) \leq 4 \sqrt{2e} M_1^2 \sqrt{\log(KL)/K}.
\]

Denote \( \tilde{\alpha}_{i,s} = ((Y_k^e(x_{i,s}) f_s(x_{i,s}) - \langle Y_k^e, f_0 \rangle) 1(s \neq k); k \leq K, \ell \leq L) \). It follows that
\[
\left\| \sum_s n_s^{-1} \sum_i \left( Y_k^e(x_{i,s}) f_s(x_{i,s}) - \langle Y_k^e, f_0 \rangle; k \leq K, \ell \leq L \right) \right\|_\infty \leq \left\| \sum_s n_s^{-1} \sum_i \tilde{\alpha}_{i,s} \right\|_\infty + \left\| \left( n_k^{-1} \sum_i (Y_k^e(x_{i,k}) f_k(x_{i,k}) - \langle Y_k^e, f_0 \rangle); k \leq K, \ell \leq L \right) \right\|_\infty \leq \left\| \sum_s n_s^{-1} \sum_i \tilde{\alpha}_{i,s} \right\|_\infty + 2M_1^2.
\]

Note that by definition, \( \mathbb{E}(\tilde{\alpha}_{i,s}) = 0 \) and \( \tilde{\alpha}_{i,s} \) is independent to \( \tilde{\alpha}_{i,1}, \ldots, \tilde{\alpha}_{i,s-1} \) conditioning on \( f_1, \ldots, f_{s-1} \). Applying (10), we have \( \left\| \sum_s n_s^{-1} \sum_i \tilde{\alpha}_{i,s} \right\|_\infty \leq 2 \sqrt{K c^*(M)} M_1^2 \) and
\[
\left\| \sum_s n_s^{-1} \sum_i \left( Y_k^e(x_{i,s}) f_s(x_{i,s}) - \langle Y_k^e, f_0 \rangle; k \leq K, \ell \leq L \right) \right\|_\infty \leq 4 \sqrt{2e} M_1^2 \sqrt{\log(KL)/K} + 2M_1^2 \leq (4 \sqrt{2e} + 2) M_1^2 \sqrt{\log(KL)/K}.
\]

Therefore, we have
\[
\mathbb{E} \| \hat{b}^{DR} - b \|_\infty \leq M_1 M_2 (\min_k n_k)^{-\min \nu_k} + (8 \sqrt{2e} + 2) M_1^2 \sqrt{\log(KL)/K}.
\]
The proof is completed by noting that
\[
\|\hat{b}^{CS} - b\|_\infty = \left\| \frac{K}{K-1}(\hat{b}^{DR} - b) + \frac{1}{K-1} \left( n_k^{-1} \sum_{i=1}^{n_k} \hat{Y}_k (x_i, y_i, k; k \leq K) \right) \right\|_\infty 
\leq \frac{K}{K-1} \|\hat{b}^{DR} - b\|_\infty + \frac{M_1^2}{K-1} \leq 2\|\hat{b}^{DR} - b\|_\infty + 2M_1^2 \sqrt{\log(KL)/K}.
\]

Combining the results in Lemma B.2 and Lemma B.3, we have
\[
2E\|\text{vec}(\Sigma - \Sigma^{DR})\|_\infty + 2E\|b - \hat{b}^{DR}\|_\infty \leq 6M_1M_2(\min_k n_k)^{-\min p_t} + (24\sqrt{2e} + 4)M_1^2 \sqrt{\log(KL)/K},
\]
\[
2E\|\text{vec}(\Sigma - \Sigma^{CS})\|_\infty + 2E\|b - \hat{b}^{CS}\|_\infty \leq 8M_1M_2(\min_k n_k)^{-\min p_t} + (40\sqrt{2e} + 28)M_1^2 \sqrt{\log(KL)/K}.
\]

The proof is completed by applying Lemma B.1 on the above two inequalities.

## C Proof of Proposition 3

When \( n \to \infty \), we have \( \hat{Y}_k (x) \to \beta_k^tx = Y_k(x) \). Therefore \( \lim_{n \to \infty} \psi(w) = (\beta w)^T (\beta w) - 2(\beta w)^T \beta_0 + (\|\beta_0\|^2_2 + p\sigma_\beta^2 + 1) \), where \( \beta = (\beta_1, \ldots, \beta_K) \), and

\[
\hat{U}^{DR}(w) \to (\beta w)^T (\beta w) - 2(\beta w)^T \bar{\beta} + (\|\beta_0\|^2_2 + p\sigma_\beta^2 + 1),
\]
\[
\hat{U}^{CS}(w) \to \frac{K^2 - 2K}{(K-1)^2} (\beta w)^T (\beta w) + \frac{K}{(K-1)^2} w^TDw - \frac{2(\beta w)^T \beta 1_K - 2w^TD1_K}{K-1} + (\|\beta_0\|^2_2 + p\sigma_\beta^2 + 1),
\]

where \( \bar{\beta} = K^{-1} \sum_k \beta_k \) and \( D = \text{diag}\{\|\beta_k\|^2_2, k \leq K\} \). If follows that \( \hat{w}^{DR} = 1_K/K \) and

\[
\hat{w}^{CS} = \frac{K-1}{K} ((K-2)\beta^T \beta + D)^{-1} (\beta^T \beta - D) 1_K.
\]

Since \( K > 2 \), with Woodbury matrix identity

\[
((K-2)\beta^T \beta + D)^{-1} = D^{-1} - D^{-1} \beta^T \left( \frac{I_p}{K-2} + \beta D^{-1} \beta^T \right)^{-1} \beta D^{-1},
\]

hence

\[
\hat{w}^{CS} = \frac{K-1}{K} \left( I_K - D^{-1} \beta^T \left( \frac{I_p}{K-2} + \beta D^{-1} \beta^T \right)^{-1} \beta \right) (D^{-1} \beta^T \beta - I_K) 1_K,
\]

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and
\[
\beta \hat{w}^{\text{CS}} = \frac{K-1}{K-2} \left( I_p - \frac{K-1}{K-2} \left( \beta D^{-1} \beta^T + \frac{I_p}{K-2} \right)^{-1} \right) \bar{\beta}.
\]

We have
\[
\lim_{n \to \infty} (\psi(\hat{w}^{\text{DR}}) - \psi(\hat{w}^{\text{CS}})) = \| \beta \hat{w}^{\text{DR}} - \beta_0 \|^2 - \| \beta \hat{w}^{\text{CS}} - \beta_0 \|^2.
\]

If \( \beta_0 = 0 \), we only need to study the case where \( \sigma_\beta = 1 \) since \( \mathbb{E}(\psi(\hat{w}^{\text{DR}}) - \psi(\hat{w}^{\text{CS}})) = \sigma_\beta^2 \mathbb{E}(\psi(\hat{w}_1^{\text{DR}}) - \psi(\hat{w}_1^{\text{CS}})) \), where \( \hat{w}_1^{\text{DR}} \) and \( \hat{w}_1^{\text{CS}} \) are the stacking weights derived when \( \sigma_\beta = 1 \).

Note in this case \( \lim_{n \to \infty} (\psi(\hat{w}^{\text{DR}}) - \psi(\hat{w}^{\text{CS}})) = \| \beta \hat{w}^{\text{DR}} \|^2 - \| \beta \hat{w}^{\text{CS}} \|^2 \). Denote \( \tilde{\beta} = \beta_k / \| \beta_k \|_2 \) and \( \bar{\beta} = (\tilde{\beta}_1, \ldots, \tilde{\beta}_K) \). Denote all non-zero \( K \) eigenvalues and the corresponding eigenvectors of \( \beta D^{-1} \beta \) as \( \lambda_1, \ldots, \lambda_K \) and \( v_1, \ldots, v_K \). It follows that
\[
\frac{K-1}{K-2} \left( I_p - \frac{K-1}{K-2} \left( \beta D^{-1} \beta^T + \frac{I_p}{K-2} \right)^{-1} \right) = \sum_{k=1}^K \frac{(\lambda_k-1)(K-1)}{\lambda_k(K-2)+1} v_k v_k^T,
\]
and
\[
\beta \hat{w}^{\text{CS}} = \sum_{k=1}^K \frac{(\lambda_k-1)(K-1)}{\lambda_k(K-2)+1} v_k \omega_k,
\]
where \( \omega_k = v_k^T \bar{\beta} \). It follows that
\[
\lim_{n \to \infty} (\psi(\hat{w}^{\text{CS}}) - \psi(\hat{w}^{\text{DR}})) = \sum_{k=1}^K \left( \left( \frac{(\lambda_k-1)(K-1)}{\lambda_k(K-2)+1} \right)^2 - 1 \right) \omega_k^2.
\]

We note that \( \tilde{\beta}_k \) follows a uniform distribution on a unit sphere. Based on the properties of spherical uniform distribution (Watson, 1983), we can show that when \( K \leq p/2 \),
\[
\sum_{k=1}^K \mathbb{E} \left[ \left( \frac{(\lambda_k-1)(K-1)}{\lambda_k(K-2)+1} \right)^2 - 1 \right] \omega_k^2 < 0.
\]

Therefore when \( \beta_0 = 0 \), \( \lim_{n \to \infty} \mathbb{E}(\psi(\hat{w}^{\text{DR}}) - \psi(\hat{w}^{\text{CS}})) > 0 \) for any \( K > 2 \).

If \( \beta_0 \neq 0 \), denote \( \tilde{\beta}_0 = \beta_0 / \| \beta_0 \|_2 \). When \( \sigma_\beta = 0 \),
\[
(\beta D^{-1} \beta^T + I_p/(K-2))^{-1} = (K-2)I_p - \frac{K(K-2)}{(K-1)^2} \tilde{\beta}_0 \tilde{\beta}_0^T,
\]
and \( \beta \hat{w}^{\text{CS}} = \beta_0 = \beta \hat{w}^{\text{DR}} \). Therefore \( \lim_{n \to \infty} \mathbb{E}(\psi(\hat{w}^{\text{DR}}) - \psi(\hat{w}^{\text{CS}})) = 0 \). When \( \sigma_\beta = o(\| \beta_0 \|_2) \), we have \( \beta_k = \beta_0 + \eta_k \), where \( \eta_k \sim N(0, \sigma_\beta^2 I_p) \) and \( \| \eta_k \|^2 = o_p(\| \beta_0 \|_2^2) \). \( \beta \hat{w}^{\text{DR}} = \beta_0 + \bar{\eta} \), where \( \bar{\eta} = \sum_k \eta_k / K \). It follows that \( \| \beta_k \|^2 \sim \| \beta_0 \|^2 (1 - \beta_0^T \eta_k / \| \beta_0 \|^2) / 2 \). Thus \( \bar{\beta}_k = \beta_k / \| \beta_k \|_2 \approx \)
\[ \beta_0 + \| \beta_0 \|^2 (I_p - \beta_0 \beta_0^\top) \eta_k, \text{ and } \beta D^{-1} \beta \approx K(\beta_0 + \eta) (\beta_0 + \eta)^\top, \text{ where } \eta = \| \beta_0 \|^2 (I_p - \beta_0 \beta_0^\top) \eta. \]

By noting that \( \beta_0^\top \eta = 0, \)

\[ (\beta D^{-1} \beta + I_p/(K - 2))^{-1} \approx (K - 2)I_p - \frac{K(K - 2)^2}{(K - 1)^2} \left( \beta_0 \beta_0^\top + \beta_0 \eta \eta^\top + \eta \beta_0^\top \right). \]

Therefore, \( \beta w^{CS} \approx K(\beta_0 \beta_0^\top + \beta_0 \eta \eta^\top + \eta \beta_0^\top) \beta - (K - 1) \beta = \beta_0 + \eta + \beta_0 \eta \eta^\top + \eta \beta_0^\top \eta, \text{ and } \)

\[
\lim_{n \to \infty} \mathbb{E}(\psi(\hat{w}^{\text{DR}}) - \psi(\hat{w}^{\text{CS}})) \approx \mathbb{E}(\eta^\top \eta - (\eta + \beta_0 \eta \eta^\top \eta + \eta \beta_0^\top \eta)) \approx -4 \mathbb{E}(\eta^\top \eta)(\beta_0^\top \eta) - \mathbb{E}((\eta^\top \eta)^2) - 3 \mathbb{E}(\eta^\top \eta)(\eta^\top \beta_0)(\eta^\top \beta_0) \approx -4 \mathbb{E}(\eta^\top \eta)^2.
\]

Since \( \eta \sim N(0, \sigma_\beta^2/K I_p), \)

\[ | \lim_{n \to \infty} \mathbb{E}(\psi(\hat{w}^{\text{DR}}) - \psi(\hat{w}^{\text{CS}}))| = O(\sigma_\beta^4). \]

Therefore as \( \sigma_\beta \downarrow 0, \)

\[ \mathbb{E}(\psi(\hat{w}^{\text{DR}}) - \psi(\hat{w}^{\text{CS}})) \uparrow 0. \]

When \( \sigma_\beta \to \infty, \) we note that \( \beta_k' = \beta_k/\sigma_\beta \) converges in distribution to \( N(0, I_p). \) Denote \( \beta' = (\beta'_1, \ldots, \beta'_K). \) Based on the results when \( \beta_0 = 0, \) we know that \( \lim_{n \to \infty} \mathbb{E}(\| \beta' \hat{w}^{\text{DR}} \|^2_2 - \| \beta' \hat{w}^{\text{CS}} \|^2_2) \) converges to a positive constant as \( \sigma_\beta \to \infty. \) By noting that \( \lim_{n \to \infty} (\psi(\hat{w}^{\text{DR}}) - \psi(\hat{w}^{\text{CS}})) = \sigma_\beta^2(\| \beta' \hat{w}^{\text{DR}} \|^2_2 - \| \beta' \hat{w}^{\text{CS}} \|^2_2), \) we have \( \lim_{n \to \infty} [\lim_{\sigma_\beta \to \infty} \mathbb{E}(\psi(\hat{w}^{\text{DR}}) - \psi(\hat{w}^{\text{CS}}))] = \infty. \)

### D Derivations in Example 1 and 2

**Example 1, Oracle.** We begin with the oracle case. Since \( w \in \Delta_1, \) the expected generalist utility is \( U_g(w) = -(w_1 \bar{y}_1 + w_2 \bar{y}_2)^2 - 2 = -(w_1 (\bar{y}_1 - \bar{y}_2) + \bar{y}_2)^2 - 2, \) \( w_1 \in [0, 1]. \) If \( \bar{y}_1 = \bar{y}_2, \) any \( w \in \Delta_1 \) maximizes \( U_g(w). \) If \( \bar{y}_1 \neq \bar{y}_2 \) and \( \bar{y}_2/(\bar{y}_1 - \bar{y}_2) \in [0, 1], \) \( U_g(w) \) is maximized at \( w_g = (\bar{y}_2/(\bar{y}_2 - \bar{y}_1), \bar{y}_1/(\bar{y}_1 - \bar{y}_2)). \) Note \( \bar{y}_2/(\bar{y}_2 - \bar{y}_1) \in [0, 1] \) if and only if \( \bar{y}_1 \cdot \bar{y}_2 \leq 0, \) in which case \( \bar{y}_2/(\bar{y}_2 - \bar{y}_1) = |\bar{y}_2|/(|\bar{y}_1| + |\bar{y}_2|). \) If \( \bar{y}_2/(\bar{y}_2 - \bar{y}_1) < 0, \) that is, \( \bar{y}_1 \cdot \bar{y}_2 > 0 \) and \( |\bar{y}_1| > |\bar{y}_2|, \)

\( w_g = (0, 1). \) If \( \bar{y}_1 \cdot \bar{y}_2 > 0 \) and \( |\bar{y}_1| < |\bar{y}_2|, \) \( \bar{y}_2/(\bar{y}_2 - \bar{y}_1) > 1 \) and \( w_g = (1, 0). \)

**Example 1, DR.** Moving to DR stacking, the estimated generalist utility is

\[
\hat{U}^{\text{DR}}(w) = -(w_1 \bar{y}_1 + w_2 \bar{y}_2)^2 + (\bar{y}_1 + \bar{y}_2)(w_1 \bar{y}_1 + w_2 \bar{y}_2) - \bar{y}_1^2/2 - \bar{y}_2^2/2,
\]

and it follows that \( \hat{w}^{\text{DR}} = (1/2, 1/2) \) and \( \mathbb{E}(\hat{U}^{\text{DR}}(w) - U_g(w)) = \mathbb{E}((\bar{y}_1 + \bar{y}_2)(w_1 \bar{y}_1 + w_2 \bar{y}_2)). \) We
note that \( \bar{y}_1 \) and \( \bar{y}_2 \) are independent \( N(0, \sigma^2 + 1/n) \). Therefore,

\[
\begin{align*}
\mathbb{E} \left( \hat{U}^{\text{DR}}(w) - U_g(w) \right) &= w_1 \mathbb{E}(\bar{y}_1^2) + w_2 \mathbb{E}(\bar{y}_2^2) = \sigma^2 + 1/n, \\
\mathbb{E} \left( (\hat{U}^{\text{DR}}(w) - U_g(w))^2 \right) &= w_1^2 \mathbb{E}(\bar{y}_1^4) + w_2^2 \mathbb{E}(\bar{y}_2^4) + \left(1 + 2w_1w_2\right)\mathbb{E}(\bar{y}_1^2 \bar{y}_2^2) \\
&= (3w_1^2 + 3w_2^2 + 2w_1w_2 + 1)(\sigma^2 + 1/n)^2.
\end{align*}
\]

Since \( w \in \Delta_1 \), we have \( \text{var}(\hat{U}^{\text{DR}}(w) - U_g(w)) = (2w_1^2 + 2w_2^2 + 1)(\sigma^2 + 1/n)^2 \).

**Example 1, CV\textsubscript{ws}.** To show that \( |\hat{U}^{\text{WS}}(w) - \hat{U}^{\text{DR}}(w)| = O_p(1/n) \), we fix \( \mu = (\mu_1, \mu_2)^T \) and it follows

\[
\begin{align*}
\hat{\Sigma}^{\text{WS}} &= \hat{\Sigma}^{\text{DR}} + \frac{1}{(M-1)^2} \left[ \begin{array}{cc}
\frac{1}{M} \sum_m \bar{y}_{1,m}^2 - \bar{y}_1^2, & \frac{1}{M} \sum_m \bar{y}_{1,m} \bar{y}_{2,m} - \bar{y}_1 \bar{y}_2 \\
\frac{1}{M} \sum_m \bar{y}_{2,m}^2 - \bar{y}_2 \end{array} \right], \\
\hat{\mu}^{\text{WS}} &= \hat{\mu}^{\text{DR}} - \frac{1}{2(M-1)} \left[ \begin{array}{c}
\frac{1}{M} \sum_m \bar{y}_{1,m}^2 - \bar{y}_1^2 + \frac{1}{M} \sum_m \bar{y}_{1,m} \bar{y}_{2,m} - \bar{y}_1 \bar{y}_2 \\
\frac{1}{M} \sum_m \bar{y}_{2,m}^2 - \bar{y}_2 \end{array} \right],
\end{align*}
\]

where \( \bar{y}_{k,m} \) is the average of \( y_{i,k} \)'s in the \( m \)-th fold. Note that \( n(\sum_m \bar{y}_{k,m}^2/M - \bar{y}_k^2) \sim \chi^2_{M-1} \), \( \mathbb{E}(\sum_m \bar{y}_{1,m} \bar{y}_{2,m}/M - \bar{y}_1 \bar{y}_2) = 0 \) and \( \text{var}(\sum_m \bar{y}_{1,m} \bar{y}_{2,m}/M - \bar{y}_1 \bar{y}_2) = M^2/((M-1)n^2) \). It follows that \( \sum_m \bar{y}_{k,m}^2/M - \bar{y}_k^2 = O_p(1/n) \) and \( \sum_m \bar{y}_{1,m} \bar{y}_{2,m}/M - \bar{y}_1 \bar{y}_2 = O_p(1/n) \).

**Example 1, CV\textsubscript{cs}.** Note that

\[
\begin{align*}
\mathbb{E} \left( \hat{U}^{\text{CS}}(w) - U_g(w) \right) &= -w_1^2 \mathbb{E}(\bar{y}_1^2) - w_2^2 \mathbb{E}(\bar{y}_2^2) = -(w_1^2 + w_2^2)(\sigma^2 + 1/n), \\
\mathbb{E} \left( (\hat{U}^{\text{CS}}(w) - U_g(w))^2 \right) &= w_1^4 \mathbb{E}(\bar{y}_1^4) + w_2^4 \mathbb{E}(\bar{y}_2^4) + 6w_1^2 w_2^2 \mathbb{E}(\bar{y}_1^2 \bar{y}_2^2) = 3(\sigma^2 + 1/n)^2 (w_1^2 + w_2^2)^2.
\end{align*}
\]

It follows that \( \text{var}(\hat{U}^{\text{CS}}(w; 1/2, 1/2) - U_g(w)) = 2(\sigma^2 + 1/n)(w_1^2 + w_2^2)^2 \). The MSE\textsubscript{0} for DR stacking and CV\textsubscript{cs} are

\[
\text{MSE}_0(\hat{w}^{\text{DR}}) = \frac{(\bar{y}_1 + \bar{y}_2)^2}{4} + 2, \quad \text{MSE}_0(\hat{w}^{\text{CS}}) = \frac{(\bar{y}_1 + \bar{y}_2)^2 \bar{y}_1^2 \bar{y}_2^2}{(\bar{y}_1^2 + \bar{y}_2^2)^2} + 2,
\]

and

\[
\text{MSE}_0(\hat{w}^{\text{CS}}) - \text{MSE}_0(\hat{w}^{\text{DR}}) = \frac{(\bar{y}_1 + \bar{y}_2)^2 (4\bar{y}_1^2 \bar{y}_2^2 - (\bar{y}_1^2 + \bar{y}_2^2)^2)}{4(\bar{y}_1^2 + \bar{y}_2^2)^2} = -\frac{(\bar{y}_1 + \bar{y}_2)^2 (\bar{y}_1^2 - \bar{y}_2^2)^2}{4(\bar{y}_1^2 + \bar{y}_2^2)^2}.
\]
Example 2, CVcs. Let $X_k = (x_{1,k}, \ldots, x_{n,k})^T$, $Y_k = (y_{1,k}, \ldots, y_{n,k})^T$, and $\hat{Y}_k^T(X_k) = (\hat{Y}_{k,k}(x_{i,k}); i \leq n_k)^T$. We have

$$\hat{U}^{\text{DR}}(w) = w^T\hat{\Sigma}^{\text{DR}} w - 2(\hat{b}^{\text{DR}})^T w + K^{-1} \sum_k n_k^{-1} \sum_i y_{i,k}^2,$$

$$\hat{U}^{\text{CS}}(w) = w^T\hat{\Sigma}^{\text{CS}} w - 2(\hat{b}^{\text{CS}})^T w + K^{-1} \sum_k n_k^{-1} \sum_i y_{i,k}^2.$$

Recall that

$$\hat{\Sigma}^{\text{DR}}_{k,k',\ell,\ell'} = \sum_{i=1}^K \frac{(\hat{Y}_k(X_i))^T \hat{Y}_{k'}(X_i)}{n_i K}, \quad \hat{b}^{\text{DR}}_{k;\ell} = \sum_{i=1}^K \frac{(\hat{Y}_k(X_i))^T Y_i}{n_i K},$$

$$\hat{\Sigma}^{\text{CS}}_{k,k',\ell,\ell'} = \sum_{i \neq k, i \neq k'} \frac{K (\hat{Y}_k(X_i))^T \hat{Y}_{k'}(X_i)}{n_i (K-1)^2}, \quad \hat{b}^{\text{CS}}_{k;\ell} = \sum_{i \neq k} \frac{(\hat{Y}_k(X_i))^T Y_i}{n_i (K-1)}.$$

Here $\hat{\Sigma}^{\text{DR}}$ and $\hat{\Sigma}^{\text{CS}}$ are $KL \times KL$ matrices, and $w$, $\hat{b}^{\text{DR}}$ and $\hat{b}^{\text{CS}}$ are $KL$-dimensional vectors. $\hat{\Sigma}_{k,k',\ell,\ell'}$ is the element corresponding to $w_{k,\ell}$ and $w_{k',\ell'}$ while $\hat{b}_{k;\ell}$ corresponds to $w_{k,\ell}$. Since each row of $X_k$ follows $N(0, I_p)$, $X_k^T X_k$ follows a Wishart distribution with $\mathbb{E}(X_k^T X_k) = n I_p$ and $(X_k^T X_k)^{-1}$ follows an inverse-Wishart distribution with $\mathbb{E}((X_k^T X_k)^{-1}) = I_p/(n - p - 1)$. Therefore,

$$\mathbb{E}(\beta_k^T X_k^T X_k^T \beta_{k'}) = \mathbb{E}(\beta_k^T X_k^T X_k X_{k'} + \mathbb{E}(\epsilon_k X_k (X_k^T X_k)^{-1} X_k^T X_{k'})^T X_k^T \epsilon_{k'})$$

$$= \begin{cases} 
2n\|\beta_k\|_2^2 + np\sigma_\beta^2 + p\sigma^2, & k = k' = s, \\
2n\|\beta_k\|_2^2 + np\sigma_\beta^2 + p\sigma^2/n-p-1, & k = k' \neq s, \\
n\|\beta_k\|_2^2, & k \neq k'.
\end{cases}$$

$$\mathbb{E}(\hat{\beta}_k^T X_k^T Y_s) = \mathbb{E}(\hat{\beta}_k^T X_k^T X_k \beta_{s}) + \mathbb{E}(\epsilon_k X_k (X_k^T X_k)^{-1} X_k^T \epsilon_{s}) = n\|\beta_0\|_2^2 + I(k = s)(np\sigma_\beta^2 + p\sigma^2).$$

In addition, $\mathbb{E}(\Sigma_{g,k,k'}) = \|\beta_0\|_2^2 + I(k = k')(np\sigma_\beta^2 + p\sigma^2/(n - p - 1))$ and $\mathbb{E}(b_k) = \|\beta_0\|_2^2$. It follows that $\mathbb{E}(\Sigma^{\text{DR}}_{k,k'} - \Sigma_{g,k,k'}) = -I(k = k') p(1 + p)/K(n - p - 1)$ and $\mathbb{E}(\Sigma^{\text{CS}}_{k,k'} - \Sigma_{k,k'}) = (\|\beta_0\|_2^2 + p\sigma_\beta^2 + Kp\sigma^2/(n - p - 1))/(K - 1)$ if $k = k'$ and $\mathbb{E}(\Sigma^{\text{CS}}_{k,k'} - \Sigma_{k,k'}) = \|\beta_0\|_2^2/(K - 1)^2$ otherwise. $\mathbb{E}(\hat{b}^{\text{DR}}_k - b_k) = p(\sigma_\beta^2 + \sigma^2/n)/K$ and $\mathbb{E}(\hat{b}^{\text{CS}}_k - b_k) = 0$. As a result,

$$\mathbb{E} \left( \hat{U}^{\text{DR}}(w) - U_g(w) \right) = \frac{p(p+1)\sigma^2}{Kn(n-p-1)} \|w\|_2^2 + \frac{2(p\sigma_\beta^2 + p\sigma^2/n)}{K} w^T 1_K,$$

$$\mathbb{E} \left( \hat{U}^{\text{CS}}(w) - U_g(w) \right) = \frac{\|\beta_0\|_2^2}{(K - 1)^2} \sum_{k \neq k'} w_k w_{k'} - \frac{\|\beta_0\|_2^2 + p\sigma_\beta^2 + p\sigma^2/(n - p - 1)}{K - 1} \|w\|_2^2.$$
\( \mathbb{E}(\hat{U}^{\text{DR}}(w) - U_g(w)) \geq 0 \) for any \( w \in \Delta_{K-1} \) and \( \min(\mathbb{E}(\hat{U}^{\text{DR}}(w) - U_g(w))) = p\sigma^2(2 + (p + 1)/K/(n - p - 1))/(K_n) + 2p\sigma^2_\beta/K \). \( \mathbb{E}(\hat{U}^{\text{CS}}(w) - U_g(w)) \leq 0 \) for any \( w \in \Delta_{K-1} \) and \( \max(\mathbb{E}(\hat{U}^{\text{CS}}(w) - U_g(w))) = (\|\beta_0\|^2 + p\sigma^2_\beta + p\sigma^2/(n - p - 1))/(K - 1) \). When \( \|\beta_0\|_2 = o(\sigma_\beta) \) and \( 2p \leq n \), \( |\mathbb{E}(\hat{U}^{\text{DR}}(w) - U_g(w))| \geq |\mathbb{E}(\hat{U}^{\text{CS}}(w) - U_g(w))| \) for any \( w \in \Delta_{K-1} \). When \( \sigma_\beta = o(\|\beta_0\|_2) \) and \( \sigma = O(\sigma_\beta) \), \( |\mathbb{E}(\hat{U}^{\text{DR}}(w) - U_g(w))| \leq |\mathbb{E}(\hat{U}^{\text{CS}}(w) - U_g(w))| \).

**E Figure for \( \mathbb{E}(\psi(\hat{w}^{\text{CS}}) - \psi(w^0_g)) \)**

Figure E.1: \( \mathbb{E}(\psi(\hat{w}^{\text{CS}}) - \psi(w^0_g)) \) as a function of \( K \) and \( n \). Dots represent results from the Monte Carlo simulation. Lines illustrate the fitted functions \( c_0 + c_1 \log(K)/K \) (Left) and \( c_0 + c_1/\sqrt{n} \) (Right) to the Monte Carlo results. Simulation settings are described in Section 5.

**Acknowledgements**

Research was supported by the U.S.A.’s National Science Foundation grant NSF-DMS1810829, the U.S.A.’s National Institutes of Health grant NCI-5P30CA006516-54, NIA-R01AG066670, NIDA-R33DA042847, NIMH-R01MH120400 and NIH-UL1TR002541 and Gunderson Legacy Fund 041662.

**References**

Bengio, Y. and Y. Grandvalet (2003). No unbiased estimator of the variance of k-fold cross-validation. *Advances in Neural Information Processing Systems 16.*

Bernau, C., M. Riester, A.-L. Boulesteix, G. Parmigiani, C. Huttenhower, L. Waldron, et al. (2014). Cross-study validation for the assessment of prediction algorithms. *Bioinformatics 30*(12), i105–i112.
Blanchard, G., A. A. Deshmukh, U. Dogan, G. Lee, and C. Scott (2021). Domain generalization by marginal transfer learning. *Journal of Machine Learning Research* 22, 1–55.

Breiman, L. (1996). Stacked regressions. *Machine learning* 24(1), 49–64.

Deng, Z., F. Ding, C. Dwork, R. Hong, G. Parmigiani, P. Patil, et al. (2020). Representation via representations: Domain generalization via adversarially learned invariant representations. *arXiv preprint arXiv:2006.11478*.

Di, Q., H. Amini, L. Shi, I. Kloog, R. Silvern, J. Kelly, et al. (2019). An ensemble-based model of pm2.5 concentration across the contiguous united states with high spatiotemporal resolution. *Environment international* 130, 104909.

Ding, Z. and Y. Fu (2017). Deep domain generalization with structured low-rank constraint. *IEEE Transactions on Image Processing* 27(1), 304–313.

Geras, K. and C. Sutton (2013). Multiple-source cross-validation. In *International Conference on Machine Learning*, pp. 1292–1300. PMLR.

Ilse, M., J. M. Tomczak, C. Louizos, and M. Welling (2020). Diva: Domain invariant variational autoencoders. In *Medical Imaging with Deep Learning*, pp. 322–348. PMLR.

Juditsky, A. and A. Nemirovski (2000). Functional aggregation for nonparametric regression. *Annals of Statistics*, 681–712.

Juditsky, A., P. Rigollet, A. B. Tsybakov, et al. (2008). Learning by mirror averaging. *The Annals of Statistics* 36(5), 2183–2206.

Kannan, L., M. Ramos, A. Re, N. El-Hachem, Z. Safikhani, D. M. Gendoo, et al. (2016). Public data and open source tools for multi-assay genomic investigation of disease. *Briefings in bioinformatics* 17(4), 603–615.

Li, S., T. T. Cai, and H. Li (2022). Transfer learning for high-dimensional linear regression: Prediction, estimation and minimax optimality. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)* 84(1), 149–173.

Loewinger, G., P. Patil, K. T. Kishida, and G. Parmigiani (2021). Multi-study learning for real-time neurochemical sensing in humans using the “study strap ensemble”. *Annals of Applied Statistics*, in press.
Manzoni, C., D. A. Kia, J. Vandrovcova, J. Hardy, N. W. Wood, P. A. Lewis, et al. (2018). Genome, transcriptome and proteome: the rise of omics data and their integration in biomedical sciences. *Briefings in bioinformatics* 19(2), 286–302.

Moreno-Torres, J. G., T. Raeder, R. Alaiz-Rodríguez, N. V. Chawla, and F. Herrera (2012). A unifying view on dataset shift in classification. *Pattern recognition* 45(1), 521–530.

Nozza, D., E. Fersini, and E. Messina (2016). Deep learning and ensemble methods for domain adaptation. In *2016 IEEE 28th International Conference on Tools with Artificial Intelligence (ICTAI)*, pp. 184–189. IEEE.

Pasolli, E., D. T. Truong, F. Malik, L. Waldron, and N. Segata (2016). Machine learning meta-analysis of large metagenomic datasets: tools and biological insights. *PLoS computational biology* 12(7), e1004977.

Patil, P., P.-O. Bachant-Winner, B. Haibe-Kains, and J. T. Leek (2015). Test set bias affects reproducibility of gene signatures. *Bioinformatics* 31(14), 2318–2323.

Patil, P. and G. Parmigiani (2018). Training replicable predictors in multiple studies. *Proceedings of the National Academy of Sciences* 115(11), 2578–2583.

Ramchandran, M., P. Patil, and G. Parmigiani (2020). Tree-weighting for multi-study ensemble learners. *Pacific Symposium on Biocomputing* (25), 451–462.

Rashid, N. U., Q. Li, J. J. Yeh, and J. G. Ibrahim (2020). Modeling between-study heterogeneity for improved replicability in gene signature selection and clinical prediction. *Journal of the American Statistical Association* 115(531), 1125–1138.

Shao, R., X. Lan, J. Li, and P. C. Yuen (2019). Multi-adversarial discriminative deep domain generalization for face presentation attack detection. In *Proceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition*, pp. 10023–10031.

Shumway, R. H. and D. S. Stoffer (2017). *Time series analysis and its applications: with R examples*. Springer.

Sinha, R., G. Abu-Ali, E. Vogtmann, A. A. Fodor, B. Ren, A. Amir, et al. (2017). Assessment of variation in microbial community amplicon sequencing by the microbiome quality control (mbqc) project consortium. *Nature biotechnology* 35(11), 1077.
Tseng, G. C., D. Ghosh, and E. Feingold (2012). Comprehensive literature review and statistical considerations for microarray meta-analysis. *Nucleic acids research* 40(9), 3785–3799.

van der Laan, M. J., S. Dudoit, and A. W. van der Vaart (2006). The cross-validated adaptive epsilon-net estimator. *Statistics & Decisions* 24(3), 373–395.

Ventz, S., R. Mazumder, and L. Trippa (2020). Integration of survival data from multiple studies. *arXiv preprint arXiv:2007.08594*.

Wang, J., C. Lan, C. Liu, Y. Ouyang, W. Zeng, and T. Qin (2021). Generalizing to unseen domains: A survey on domain generalization. *arXiv preprint arXiv:2103.03097*.

Wang, Y., H. Li, L.-P. Chau, and A. C. Kot (2021). Variational disentanglement for domain generalization. *arXiv preprint arXiv:2109.05826*.

Watson, G. S. (1983). *Statistics on spheres*. The University of Arkansas lecture notes in the mathematical sciences; v. 6. New York: Wiley.

Wolpert, D. H. (1992). Stacked generalization. *Neural networks* 5(2), 241–259.

Yao, Y., A. Vehtari, D. Simpson, and A. Gelman (2018). Using stacking to average bayesian predictive distributions (with discussion). *Bayesian Analysis* 13(3), 917–1007.

Zhang, P. (1993). Model selection via multifold cross validation. *The annals of statistics*, 299–313.

Zhou, K., Y. Yang, Y. Qiao, and T. Xiang (2020). Domain adaptive ensemble learning. *arXiv preprint arXiv:2003.07325*.