M3E2: Multi-gate Mixture-of-experts for Multi-treatment Effect Estimation

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Abstract

This work proposes the M3E2, a multi-task learning neural network model to estimate the effect of multiple treatments. In contrast to existing methods, M3E2 can handle multiple treatment effects applied simultaneously to the same unit, continuous and binary treatments, and many covariates. We compared M3E2 with three baselines in three synthetic benchmark datasets: two with multiple treatments and one with one treatment. Our analysis showed that our method has superior performance, making more assertive estimations of the multiple treatment effects.

1 Introduction

Consider the following setting extracted from Drögemöller et al. [5]: an exploratory study on hearing loss as an Adverse Drug Reaction (ADR) in children under cancer treatment with the drug Cisplatin. While Cisplatin is one of the most effective chemotherapeutic agents for children, reports have also demonstrated that 75-100% of infant patients have hearing loss. Note that patients often receive a drug cocktail, and while a single drug might not lead to ADR, the ADR is observed when we have a combination of these drugs. Drögemöller et al. [5] also point out that hearing loss is the result of a combination of factors, such as the patient’s age, genetic predisposition, dosage, and exposure to several drugs (more drugs, more heavy metals accumulation in the body, higher the chances of hearing loss). The study’s data are the patient’s clinical information (low-dimensional), genetic information (high-dimensional), the drugs given to the patient, and the observed ADR. Pharmacogenomics [5] is the name given to the field that explores the genomic predisposition to a particular response to medication (including both cure and adverse reactions).

In a Causal Inference notation, the covariates $X$ are the patients’ clinical information and genetic information; the outcome of interest is the hearing loss $Y$, and each drug taken by the patient would be a binary treatment ($T = [T_0, T_1, ..., T_K]$, where $K$ is the total number of drugs in the cocktail and $T_k \in \{0, 1\}, \forall k \in \{0, ..., K\}$). Note that treatment effect estimators designed for individual binary treatments could be adopted: For each drug $k \in \{0, ..., K\}$, we fit an estimator using all the other drugs as covariates. By conditioning the other drugs, one could close back-doors and estimate the treatment effect. However, such an approach assumes the estimator would perform covariate adjustment correctly - and here is where we argue that an estimator that considers the multiple treatments could be a better alternative.

These existing single binary treatments are considered single-task learning (STL) methods. Multi-task learning (MTL) methods [25][30], on the other hand, optimize a model to multiple tasks (or, in our context, treatments). The main argument in favor of MTL is that STL may fail to capture the synergy of multiple treatments, e.g., an additive effect or a genetic predisposition to a certain combination of treatments, but not to individual treatment. Currently, there are only a few methods capable of handling multiple treatments. Hi-CI [27] considers and models multiple treatments but assumes that only one is assigned to a unit at any given time. The Deconfounder Algorithm (DA) [32], a
probabilistic graphical model, works with multiple treatments but has received some recent criticism regarding its assumptions [4]. Seeing a clear need for a new treatment effect estimator, we propose Multi-gate Mixture-of-experts for Multi-treatment Effect Estimation (M3E2): an MTL-based neural network adapted to estimate the treatment effects of multiple treatments.

**Contributions:** The main contributions of this paper are as follows:

- We propose the Multi-gate Mixture-of-experts for Multi-treatment Effect Estimation (M3E2), a method to estimate multiple treatment effects with an MTL neural network architecture.
- We validate M3E2 in three synthetic datasets where the true causal effects are known. We also compare our method with three existing methods.
- We create a repository with an implementation of our methods, baselines, and datasets. We also share all the configuration files for reproducibility of our results, with hyperparameters and seeds adopted.

## 2 Related Work

This work combines estimation of treatment effects and multi-task learning (MTL).

**Estimating Treatment Effects:** BART [3,7], Causal Forests [31], CEVAE [14], and Dragonnet [28], have explored the estimation of a single treatment effect, using Bayesian Random Forests, Random Forests, VAEs, and neural networks (NN) respectively. Hernán and Robins [6] present an inverse propensity weighting-based method, also focused on single treatments. The Deconfounder Algorithm [32], Hi-CI [27], approaches based on the propensity score [11,13,17], and others [26,18] aim to estimate multiple treatment effects. However, many of these methods assume that only one treatment is applied to any given unit. Note that several works assume robustness to missing confounders [14,32,26,18,16]. Their robustness is often built on the assumption that extra information is known, such as a known number of hidden confounders or replacing unobserved confounders with proxies. There are, however, several concerns regarding some of these methods [4,33,22]. Our proposed method focuses on multiple treatment effect estimation through an outcome model in a multi-task learning neural network architecture and strong ignorability.

**Multi-task learning (MTL):** MTL neural network (NN) architectures aim to optimize a single model for two or more tasks simultaneously. Hard-parameter sharing NN, first proposed by Caruana [2], is one of the MTL pillars. Such architecture is composed of a set of layers shared among all tasks and a set of task-specific layers on the top. From the MTL perspective, the Dragonnet [28] has a hard-parameter sharing architecture. Building upon the hard-parameter sharing architectures, Ma et al. [15] proposed a Multi-gate Mixture-of-Experts (MMoE) architecture, where each expert can be seen as a hard-parameter sharing NN, and all the experts are combined through a gate function, which is also trainable. The core idea of such an approach is to improve the model’s generalization; plus, it allows experts to specialize in one of the tasks. To put into perspective, an MMoE is to hard-parameter sharing NN what a Random Forest Model is to a Decision Tree. Our proposed method M3E2 uses a MMoE [15] as a component. For more details on MTL architectures and optimization methods, Ruder [25] and Vandenhende et al. [30] present an overview of the most recent works.

Our work expands the MMoE architecture to satisfy causal inference assumptions and estimate multiple treatment effects simultaneously.

## 3 Multi-gate Mixture-of-experts for Multi-treatment Effect Estimation (M3E2)

This section describes our proposed method, the M3E2. Its multi-task learning architecture allows simultaneous prediction of the multiple propensity scores and the outcome.

It is always important to describe how one addresses confounders in observational studies. Some works assume no unobserved confounders [28], others try to reduce the bias through latent variables [14,32,27,16]: while others question if the latent variables are solving the problem at all [33,22]. While exploring alternatives to the strong ignorability assumption is an interesting research direction, the main focus of this work is the estimation of multiple treatments. Hence, in our work, we assume no unobserved confounders.
Figure 1 illustrates the proposed neural network architecture, with a MMoE [15], and a Latent Variable Model (LVM) as subcomponents. In the MTL context, each propensity score prediction $p_k, \forall k \in \{0, ..., K\}$ is a task, and the prediction of the outcome of interest $\hat{Y}$ is also a task. Therefore, if a given application has $K$ treatments, M3E2 would have $K + 1$ tasks. Note that, in the testing phase, the propensity score predictions are not used (See Appendix).

Figure 1: M3E2 training architecture. It receive as input the covariates $X = [X_{low}, X_{high}]$ and the treatment assignments $T = \{T_0, T_1, ..., T_K\}$. The outcome of interest is $Y$ and the treatment effects.

One of the strengths of M3E2 is its capacity to estimate the combined effect of a large number of treatments: the M3E2 network only grows linearly with the number of treatments, handling all potential combinations, something that other multi-treatment methods typically struggle to accomplish. Furthermore, the proposed architecture of M3E2 extends the MMoE architecture by incorporating causal inference assumptions through suitable regularizers and adding the outcome model to estimate the treatment effects.

3.1 Notation

We define low-dimensional covariates as $X_{low}$ and high-dimensional covariates as $X_{high}$. An example of the first is clinical variables and, from the latter, genomics information. The split of covariates into low-dimensional and high-dimensional will be explained in Section 3.3. We define the covariates concatenation as $X = [X_{low}, X_{high}]$. The continuous outcome is $Y$, and $K$ represents the number of treatments. $T = \{T_0 = t_0, T_1 = t_1, ..., T_K = t_K\}$, where $T$ could e.g. be the drug cocktail taken by a patient.

3.2 Assumptions

**Assumption 1**: The application contains a continuous outcome, binary or continuous treatments, and a set of covariates.

**Assumption 2 - Stable Unit Treatment Value Assumption (SUTVA) [24]**: the response of a particular unit depends only on the treatment(s) assigned, not the treatments of other units.

**Assumption 3 - Common Confounders and conditional independence [21]**: Treatments share confounders. Given the shared confounders, the treatments are independent.

$$T_i \perp T_j | X, \forall i, j \in \{0, ..., K\}, i \neq j$$
**Assumption 4: Strong ignorability** - There are no missing confounders.

Assumption 2 (SUTVA) is standard in Causal Inference. According to SUTVA, the samples are independent and do not interfere with each other. Assumptions 3 and 4 are related to the identifiability of the treatment effect. Assumption 3 assumes no links (dependencies) between the treatments given the covariates, and Assumption 4 assures all back-door paths can be blocked by conditioning on the observed covariates $X$ - guaranteeing the identifiability of the treatment effect [20]. Assumption 3 is also related to multi-task learning (MTL). The ideal use of MTL is when tasks (in our case, treatments) are somehow related. In that case, it is reasonable to assume they also share confounders.

**Theorem 1 - Sufficiency of Propensity Score [23, 28, 19]:** If the average treatment effect is identifiable from observational data by adjusting for $X$, i.e., $ATE = E[E[Y | X, T = 1] - E[Y | X, T = 0]]$, then adjusting for the propensity score also suffices: $ATE = E[E[Y | h(X), T = 1] - E[Y | h(X), T = 0]]$

In other words, it suffices to adjust only the information in $X$ that is relevant for predicting the treatment $T_k$, and this information is the output of $H_k(X_{L1})$. For multiple treatments, the generalization goes as follows [10, 9]:

$$ATE = E[E[Y | H(X_{L1})], T_1 = t_1, ..., T_K = t_K] - E[Y | H(X_{L1}), T_1 = 1 - t_1, ..., T_K = t_K]$$

The theorem is presented here as originally proposed, so for the proofs and demonstrations, please check the original publications Rosenbaum and Rubin [23] and Imbens [10]. Under these assumptions and theorem, the derivation of the identifiability comes from the Sufficiency of the Propensity Score and the following causal structure: $T \rightarrow Y, X \rightarrow T, X \rightarrow Y$.

### 3.3 Latent Variable Model (LVM)

M3E2 can handle different data types by dividing the input covariates $X$ into two groups, $X_{low}$ and $X_{high}$. While the Latent Variable Model (LVM) handles the covariates in $X_{high}$, the $X_{low}$ covariates are fed directly to the experts. The split of the covariates $X$ into $X_{low}$ and $X_{high}$ is defined by the user. Ideally, $X_{high}$ contains high-dimensional covariates, such as gene expression, single-cell data, or image data; and $X_{low}$ contains low-dimensional data, such as clinical variables. Note that, in applications with only one data type, both $X_{low} = \emptyset$ and $X_{high} = X$, and $X_{low} = X$ and $X_{high} = \emptyset$ are acceptable splits.

In applications where $X_{high} \neq \emptyset$, M3E2 uses a LVM to reduce the dimensionality of the covariates in $X_{high}$. Note that, while there are similarities with other works that adopt proxies to handle missing confounders, our LVM component is responsible only for reducing the dimensionality of $X_{high}$. As described in Section 3.2, our work assumes strong ignorability, a setting where there are no missing confounders. Under strong ignorability, however, we can still have confounding within the observed data. The LVM component, along with the experts, is responsible for extracting a meaningful representation of the input data. These features are used in the covariate adjustment $E[Y | X, T_1, ..., T_K]$, which should close the back-doors and make the treatment effect identifiable. In order to learn a meaningful representation of $X$ in applications with a mix of high-dimensional and low-dimensional covariates, it was important to find an approach that is capable of combining these different types of covariates. Without the LVM component, the experts could give a disproportional weight to $X_{high}$ covariates, as they would be the majority in $X$, and even ignore relevant information in $X_{low}$.

In our experiments, M3E2 adopts an autoencoder with two linear encoder layers and two linear decoder layers. Note, however, that one is free to choose a different architecture or factor model to extract a latent representation of $X_{high}$. Consider an application with $n$ samples, $c_2$ columns in $X_{high}$, $c_L$ as the latent variables size, and the input data $X_{high}$ as a matrix $n \times c_2$. The function $\omega_{enc}(X_{high})$ returns $L_{(n \times c_L)}$, a representation of $X_{high}$ in a lower dimension. Finally, $\omega_{dec}(X_{high})$ returns the reconstructed data $X_{high}$, back on $n \times c_2$ space. The autoencoder’s loss is the mean squared error between the input $X_{high}$ and the reconstructed input $X_{high}^r$.

### 3.4 MMoE Architecture

In multi-task learning, a hard-parameter sharing network combines shared layers and task-specific layers. In a multi-gate mixture-of-expert (MMoE) architecture [15], a hard-parameter sharing network
can be interpreted as a single expert model. Therefore, a model with several experts has several independent shared layers components. Ma et al. [15] shows that an MMoE architecture applied to multiple tasks generalizes better than other approaches. In our case, that translates to better propensity score estimates and outcome model.

The user defines the number of experts \( E \) and the \( f_e \) architecture. In the context of multiple treatment effect estimation, the tasks are the propensity score and the outcome \( Y \) prediction. The experts' input data is \( X_{L1} = \left[ \Omega_{\text{enc}}(X_{\text{high}}), X_{\text{low}} \right] \). The ideal number of experts depends on the tasks. Homogeneous tasks might not benefit from many experts and might overfit if the number of experts is too large; on the other hand, heterogeneous tasks tend to benefit from a larger number of experts. Here, we define applications whose tasks adopt the same loss as homogeneous tasks. An example would be an application with only classification tasks. On the other hand, heterogeneous tasks applications contain classification, regression, multi-label, and other potential tasks in the MTL model. The gates control the contribution of each expert to each task. There is a gate \( g_k \) per treatment defined as:

\[
g_k(X_{L1}) = \text{softmax}(W_k \times X_{L1}), \forall k \in \{1, \ldots, K\}
\]

where \( W_k \in \mathbb{R}^{E \times d} \) is a trainable matrix of weights, \( E \) is the number of experts defined by the user, and \( d \) the number of columns in \( X_{L1} \).

### 3.5 Task-specific Layers

The task-specific layers are responsible for predicting the propensity score \( p_k \) and the outcome of interest \( \hat{Y} \). Each treatment task-specific layer receives as input a weighted average of the experts, where the weights come from the gates associated with that given task. This relationship is formally defined as:

\[
H_k = h_k(\sum_{e=1}^{E} g_k(X_{L1}) f_e(X_{L1})), \forall k \in \{1, \ldots, K\}
\]

In the training phase (Figure 1), the treatment assignment is predicted with the propensity score \( p_k \), estimated as \( p_k = P(T_k = t|H_k) \) (for discrete treatments) or \( p_k = P(T_k \leq t|H) \) (for continuous treatments using the conditional density \( f_{T|X}(t, x) \) [8, 19]). To estimate the treatment assignment of \( T_k \) we only use \( H_k, \forall k \in \{1, \ldots, K\} \). For binary treatments, a softmax activation function will outputs, for each sample, the probability of \( P(T_k = 1|H_k) \) and \( P(T_k = 0|H_k) \). These predictions are used to calculate the loss of the neural network, as described in the Section 3.6. The propensity score losses are used to drive \( H_k \) to be sufficient (Theorem 1 - Section 3.2). Note that \( h_k \) can be a combination of one or more layers.

Finally, a layer with trainable weights \( \Phi \) is used to predict the final outcome. Consider the input data of this layer as \( X_{TH} = [T_1, \ldots, T_K, H] \), where \( T_1, \ldots, T_K \) are the observed treatment assignments, \( H = \sum_{k=1}^{K} H_k \), and \( c_{TH} \) is the number of columns. The trainable weights layer \( \Phi = [\tau_1, \ldots, \tau_k, \ldots, \tau_{c_{TH}}] \) estimates the final outcome as \( \hat{Y} = \Phi \times X_{TH} \). In our context of treatment effect estimation, \( \tau_k \) is the treatment effect of the treatment \( k \). In the testing set, if the true treatment assignment is unknown, it is also possible to adopt the propensity score predictions as a replacement of the observed treatment assignments. The \( \Phi \) works as an outcome model and each weight associated with a \( T_i, \forall i \in \{0, \ldots, K\} \) represents the average treatment effect of increasing the treatment \( i \) unit (or the counterfactual in binary treatments).

Note that our approach targets additive effects, which are fairly common in real-world applications. For instance, consider adversarial drug reactions in cancer therapy. Cancer therapy usually involves several treatments (drugs) simultaneously or through a certain period. Many of these drugs contain heavy metals, and their accumulation can result or contribute to observed adverse drug reactions. The inclusion of non-linear effects on the outcome model \( \Phi \) is left as future work, as it would require a different approach to estimate the treatment effects. Note, however, that the linearity limitation only applies to the last layer \( \Phi \) (to predict the main outcome).

### 3.6 Loss function

M3E2’s loss function is composed of:
1. Root mean square error loss $\ell_y(Y, \hat{Y}) = RMSE(Y, \hat{Y})$ for continuous outcomes and binary cross-entropy $\ell_y(Y, \hat{Y}) = BCE(Y, \hat{Y})$ for binary outcomes.

2. Similar to the outcome loss functions, we adopt $\ell_{g_k}(T, \hat{T}) = RMSE(T_k, \hat{T}_k)$ or/and $\ell_{g_k}(T, \hat{T}) = BCE(T_k, \hat{T}_k)$ as the propensity score losses, $\forall k \in \{0, ..., K\}$.

3. $\ell_A(X_2, \hat{X}_2) = RMSE(X_{high}, \hat{X}_{high}) = \sum^n \sum_j^f (x_{n,j} - \hat{x}_{n,j})^2$ is the the autoencoder loss function.

4. $\frac{1}{2n} \sum w w^2$ as the $L_2$ regularization.

The modification of both $\ell_{g_k}$ and $\ell_y$ to other loss functions is quite straightforward.

As a reminder, while our architecture minimizes the propensity score and the outcome losses, our main target is to obtain estimates of the treatment effects. The treatment effects are a co-product of this model, i.e., the weights associated with the treatments in the trainable layer $\Phi$ (See Section 3.5). The model also learns weights in $\Phi$ associated with the $H$; however, these are not considered treatment effects. The total loss is shown in Equation 1.

$$L = \alpha \ell_y + \beta \sum_k \ell_{p_k} + \gamma \ell_A + \frac{\lambda}{2n} \sum w w^2$$ (1)

The $\alpha$, $\beta$ and $\gamma$ from Equation 1 are weights. There are two possible ways to define these weights: adopting them as a hyper-parameter or through the adoption of an MTL task balancing approach. For example, Liu et al. [12] dynamically sets these weights based on the losses values to minimize negative transfer between tasks. For more heterogeneous treatments, such as a mix between continuous and discrete treatments, adopting a weight per propensity score can also help with task-balancing.

4 Experiments

In causal inference, the lack of ground truth for real-world applications poses a challenge to its evaluation. Therefore, we adopt three synthetic datasets[1] that have known treatment effects:

- GWAS [32, 1]: this semi-simulated dataset explores sparse settings, with a large number of confounders, 3-10 binary treatments, and continuous outcome.
- Copula [33]: this synthetic dataset contains four treatments, fewer confounders, and a binary outcome. We adopt the same treatment effects described in [33].
- IHDP [7, 14, 28]: this is a traditional benchmark for single binary treatments. It has 24 covariates and a continuous outcome. We adopt this dataset to compare with some of our single-treatment estimation baselines that have been evaluated on the IHDP dataset.

For more details about the synthetic benchmark datasets, check Appendix B.

We adopted the mean absolute error (MAE) as an evaluation metric to compare M3E2 and the baselines. We define $\tau_k$ as the true treatment effect of $T_k$, and $\hat{\tau}_k$ as its estimated value. As we have multiple treatment effects, we report their average error $\frac{\sum_{k=0}^K |\tau_k - \hat{\tau}_k|}{K}$, where $K$ is the total number of treatments. We repeat each combination of (data $\times$ model $\times$ setting) $B$ times, and in our plots, we show the MAE calculated over all these runs:

$$MAE = \sum_{b=0}^B \left( \frac{\sum_{k=0}^K |\tau_k - \hat{\tau}_k|}{K} \right) \frac{1}{B}$$ (2)

The goal is to minimize the difference between estimated and true treatment effects; therefore, low MAE values are desirable.

We adopt an experimental setting similar to the multi-task learning settings [15], where the proposed multi-task learning method is compared with other multi-task learning methods and single-task

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1 The code to generate the datasets is available at [github.com/HIDDEN_FOR_ANONYMIZATION](https://github.com/HIDDEN_FOR_ANONYMIZATION)
learning models, specialized and designed to optimize a single task. Among our baselines, the DA$[32]$ is the only method that can estimate the effect of multiple treatments with one model. The CEVAE$[14]$ and Dragonnet$[28]$, on the other hand, are single-treatment methods. In this case, we ran one independent model for each treatment. We utilized the author’s implementation of the baselines when available. We also performed experiments with BART. However, since CEVAE and Dragonnet achieved better performance results in the recent publications$[14,28]$, and since BART performed poorly on the GWAS and Copula datasets, we decided not to discuss BART in the experimental section.

For single treatment baseline methods, the multiple treatment effects were estimated as follows: to estimate $\tau_1$, the baseline methods receive as input $T_1$ as the treatment assignment, and the columns $T_0, T_2, ..., T_K$ are added to $X_{low}$. We follow this setup for all $K$ treatments.

We generate four datasets using different seeds for each configuration explored in the GWAS and Copula datasets. For the IHDP, we adopted the ten replications previously generated by Louizos et al.$[14]$. We set $B = 20$ (number of repetitions of each $(data \times model \times setting)$). To run the experiments, we use GPUs on Colab Pro. Check Appendix C for more details on the experimental settings.

4.1 Overall Performance

Figure 2 shows, for each dataset, the average MAE across all settings. Our proposed method, M3E2, clearly outperforms all baselines on the multi-treatment datasets GWAS and COPULA. On IHDP, a single-treatment dataset, M3E2 was outperformed by Dragonnet, yet, it was better than the other two baselines. Note that our results for Dragonnet on IHDP match the results previously reported by Shi et al.$[28]$, and the estimators’ larger variance on the IHDP dataset can be explained by the scale of the true treatment effect. Our main take from Figure 2 is that our method outperforms all the baselines on its ideal use-case: applications with multiple treatment effects. In single-treatment applications, while achieving reasonable results, simpler architectures that target single-treatment estimation like the Dragonnet tend to achieve better performance.

Figure 3 shows a deeper analysis of the Copula dataset. Figure 3.a shows that M3E2 has the lowest MAE values compared to the other baselines. Figure 3.b shows the total run time of each method in seconds. As a reminder, both DA and M3E2 fit one model for all treatments; Dragonnet and CEVAE, on the other hand, fit one model for each treatment. DA, a probabilistic model, has the fastest running time; M3E2 has the lowest running time among the NN methods. A comparison between the true $\tau$ (line in red) and the estimated treatment effects (dots) is shown in Figures 3.c-f. Note that for $\tau_0$ and $\tau_2$, M3E2 is the only method whose estimates are centered around the true value. For $\tau_1$ and $\tau_3$, M3E2 overestimates the treatment effects, yet, it still produces reasonably good estimates. Overall, M3E2 has a good performance. However, we noticed two limitations: First, M3E2 has a larger variance than the other methods; second, for some runs, it estimated values very far from the true treatment effect $\tau_0$. Considering our baselines, while they have a smaller variance, we noticed...
that DA and Dragonnet often estimated the treatment effect as 0, indicating that these methods might fail to estimate the treatment effect in this dataset correctly, despite achieving reasonable predictive performance. CEVAE was the second-best method; still, its results were never centered around the true values (red lines) and often underestimated the magnitude of the treatment effect.

4.2 Impact of Dataset Hyperparameters

We also explored the impact of the dataset parameters in estimating the multiple treatment effects. We focused on three parameters: the sample size, number of treatments, and covariates. Figure 4 shows, in detail, the average MAE and the 95% confidence interval (colored area) for the several settings. Figure 4a and 4d show the impact of the sample size on the GWAS and Copula dataset, respectively. Our proposed method, M3E2, is the method that benefits the most from increasing the sample size. We noticed that all methods are robust to the increase in the number of covariates (Figures 4b and 4e), with M3E2 having a small increase on MAE on the Copula dataset with 125 covariates. The most surprising result of all is shown in Figure 4c. The MAE increases in all baselines with the increase in the number of treatments. Nevertheless, M3E2 achieves better results with nine treatments than with six treatments. Such a result shows that, while the methods are similar regarding the dataset impact on MAE and are quite robust to variations in the number of covariates, M3E2 significantly outperforms all other methods when a larger number of treatment effects are considered.
5 Discussion and Conclusion

In this paper, we have investigated the problem of estimating the combined effect of multiple treatments from observational data. We propose M3E2, a neural network adopting a multi-task learning architecture. Various architecture components can be replaced by alternative implementations, e.g., by different experts, latent variable models, or propensity score predictors. We experimentally compared M3E2 against three baselines on three synthetic benchmark datasets. The online repository [github.com/HIDDEN_FOR_ANONYMIZATION](http://github.com/HIDDEN_FOR_ANONYMIZATION) contains the code to replicate all the experiments, and we put extra effort into making the M3E2 implementation agnostic to the application; therefore, its deployment in other applications should be straightforward. M3E2 demonstrated promising experimental results and strong evidence that the multi-task learning contributed to better estimating the treatment effects. Nevertheless, there remain several directions for future research. As discussed in Section 3.2, our method assumes strong ignorability, which is quite limiting in real-life applications. M3E2 also inherits the limitations of other multi-task learning models, in particular, the susceptibility to imbalanced tasks and overfitting.

A potential negative societal impact of estimating treatment effects from observational data is the lack of a standard approach to evaluate such results in real-world applications. Most publications evaluate their methods using the method’s predictive power or expert knowledge. However, both are susceptible to mistakes because they are indirect and non-objective measures of the treatment effect, which opens room for potential misuse. Furthermore, the success of observational causal inference methods might lead researchers to rely on such methods even in settings where they are not needed. Randomized controlled trials are still the gold standard for treatment effect estimation and, if available, should always be the first choice.

All strengths and limitations considered, we believe that M3E2 has a very good use case with manageable limitations. In future research, we want to explore applications with very heterogeneous treatments, such as temporal versus non-temporal treatments and non-linear effects. We also want to apply our proposed method to a real-world dataset that explores adverse drug reactions in therapies for treating cancer in infants.
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6 Extra Details on the Architecture

Figure 5.a shows the testing architecture. The main difference is that we do not need to use the predicted propensity score for the testing phase. Instead, we use the observed assigned treatments. For comparison, Figure 5.b shows the original MMoE architecture, as proposed by Ma et al. [15]. While the backbone is very similar, our M3E2 architecture has an extra layer with the autoencoder, and the top layers are also different. M3E2 top layer modifies the architecture for the outcome model, which estimates the treatment effect.

7 Datasets

Here we will present a broader description of the datasets adopted to validate our proposed architecture, M3E2. The main goal of our project is to estimate multiple treatment effects by adopting an multi-task learning approach. Furthermore, a given sample can be assigned one or more treatments. First, Table 1 shows all architectures considered.
Figure 5: (a) M3E2 architecture testing architecture. Shows the testing architecture, where the propensity score prediction is not required. (b) The Original MMoE architecture (Figure from [15]).

Table 1: Datasets settings explored. Example: Setting a indicates a study on the sample size effect on the GWAS dataset. We compared the models’ MAE with $2000 \times 4000 \times 6000$ samples, with 5 treatments and 995 covariates.

| Setting | Data | Sample Size | Number of Treatments | Number of Covariates |
|---------|------|-------------|----------------------|----------------------|
| a       | GWAS| 2000, 4000, 6000 | 5                    | 995                  |
| b       | GWAS| 6000        | 5                    | 100, 500, 1000        |
| c       | GWAS| 6000        | 3, 6, 9              | 500                  |
| d       | Copula| 2500, 5000, 10000 | 4                    | 10                   |
| e       | Copula| 10000       | 4                    | 5, 25, 125           |
| f       | IHDP | 747         | 1                    | 24                   |

7.1 GWAS

We follow the same simulation process available in the literature [29, 32, 1]. The covariates and treatments are single-nucleotide polymorphisms (SNPs), and the target, also referred as the outcome of interest, is a clinical trait. The outcome is continuous, and treatments, binary. We set a small number of SNPs to be causal, meaning they affect the outcome of interest. These causal SNPs are the treatments we want to estimate the treatment effect for. The dataset generation uses as a base the 1000 Genome Project (TGP), used to calculate the matrix of allele frequency $F_{J,V}$, where $J$ is the number of samples and $V$ the number of SNPs. See below the steps to generate the covariates of the simulated dataset:

1. We remove highly correlated SNPs with linkage disequilibrium.
2. $S_{L \times V} = PCA(TGP)$: First, we extract $L$ principal components from a PCA fitted to the TGP data base. For this project, $L = 3$
3. We append a new column to $S$ such that $S_{3,V} = 1$ to be the intercept.
4. We created a new matrix, $\Gamma_{J,L}$, to represent the simulated samples:
   \[ \Gamma_{j,d} \sim 0.9 \times Uniform(0, 0.5) \forall j \in \{1, ..., J\}, d \in \{0, 1, 2\}. \]  
   and $\Gamma_{j,3} = 0.05$
5. The matrix of allele frequency is obtained from $F_{J,V} = \Gamma_{J,L} \times S_{L,V}$.
6. This matrix is then used to simulate the covariates:
   \[ X_{J,V} \sim Binomial(1, F_{J,V}) \]
After simulating the covariates, we simulate the outcome of interest.

1. We define an array $\tau_v, \forall v \in \{0, ..., V\}$. We set $\tau_v \neq 0$ for the SNPs used as a treatment, and $\tau_v = 0$ otherwise.

2. Defining the set treatments as K, if $v \in K$, the treatment effect is simulated as $\tau_v \sim \text{Normal}(0, 0.5)$.

3. To add confounding effect, we group individuals using $\text{kmeans}(X)$ and three clusters $c$. These clusters are used as per-group intercept $\gamma_c$, and to define the error variance $\epsilon \sim \text{Normal}(0, \sigma_c)$, where $\sigma_1, \sigma_2, \sigma_3 \sim \text{InvGamma}(3, 1)$.

4. Following a high signal-to-noise ration, the SNP’s and the per-group intercept are responsible for 40% ($v_{\text{gene}} = v_{\text{group}} = 0$) of the variance each, and the error is responsible for 20% ($v_{\text{noise}} = 0$) of the variance. To re-scale the noise and intercept:

   $$\gamma_j \leftarrow \left[ \frac{sd(\sum_v \tau_v X_{v,j})}{\sqrt{v_{\text{gene}}}} \right] \left[ \frac{\sqrt{v_{\text{group}}}}{sd(\gamma_j)} \right] \gamma_j$$ (5)

   $$\epsilon_j \leftarrow \left[ \frac{sd(\sum_v \tau_v X_{v,j})}{\sqrt{v_{\text{gene}}}} \right] \left[ \frac{\sqrt{v_{\text{noise}}}}{sd(\epsilon_j)} \right] \epsilon_j$$ (6)

5. Finally, the outcomes are generated as:

   $$Y = \sum_v \tau_v X_{v,j} + \gamma_c + \epsilon_j$$

### 7.2 Copula

Copula dataset was proposed by Zheng et al. [33]. We adopted the setting where the outcome is a non-linear function of the treatments. The target adopted can be either continuous or binary, and in our experiments, we used the continuous $Y$. See below how to simulate this dataset:

1. Generate $u_{n,s} \sim \text{Normal}(0, 1)$, where $n$ is the sample size and $s$ the number of covariates not associated with the outcome.

2. If $s > 1$, define the confounding effect $c$ as the first component of $\text{PCA}(u)$; else, $c = u$.

3. To help us to simulate the treatment effect, we define $B = []$ and $T = [c, ..., c]_{n \times k}$, meaning $c$ is repeated $k$ times, where $k$ is the number of treatments. Then, $T = \text{Normal}(0, \sigma_t) + T$.

4. To help explain the outcome construction, we define the outcome as the sum of three quantities: $y = y_1 + y_2 + y_3$.
   - (a) $y_1 \sim \text{Normal}(0, \sigma_y)_{n \times 1}$, represents random noise.
   - (b) $y_2 = [c \ast \gamma]_{n \times 1}$, where $\gamma$ represents the proportion of confounding effect in $y$, and $\gamma = 0$ means no confounding effect.
   - (c) $y_3 = 3T_1 - T^2 + T_3 I_{T_3 > 0} + 0.7 \ast T_3 I_{T_3 \leq 0} - 0.06T_4 - 4T_5^2$, which is the contribution of the treatment effects in $y$.

The implementation followed closely the code made available by Zheng et al. [33] in https://github.com/JiajingZ/CopulaSensitivity. One of the main changes was we changed the implementation from R to Python, as you can see in our repository HIDDEN_FOR_DOUBLE_BLIND_SUBMISSION.

### 7.3 IHDP

We adopted the repetitions available in the literature. In particular, we used the datasets available at https://github.com/AMLab-Amsterdam/
8 Code usage and Hyperparameters

The code is available in the repository [github.com/HIDDEN_FOR_ANONYMIZATION](https://github.com/HIDDEN_FOR_ANONYMIZATION). We used Colab Pro with GPUs. The file `model_m3e2.py` contains our method implementation, and the folder `resources` contains the baselines. To train the models, we use the file `train_models.py`, which takes three parameters: the config files in `yaml` format, number of dataset replications, and number of model replications. The folder `config` contains all the config files adopted by our experiments, which contains datasets generation parameters, such as dataset name, sample size, covariates size, and the number of treatments. The config file also contains model parameters, such as batch size, number of epochs, optimization parameters, size of hidden layers, type of target and treatment, baselines available to run, and losses weights. Check the file `config_instructions.md` for a complete description of the parameters. The number of dataset and model replications are also used as seeds. For example, if the number of dataset replications is 4, we adopt the seeds 1, 2, 3, and 4 to generate each of the datasets. For our proposed method M3E2, the user needs to define the following hyperparameters:

- (Required) Number of experts (`num_exp`): the ideal number depends on the complexity of the treatments and outcome. The current implementation requires the user to test different sizes manually. Most applications active the best results with 4 to 12 experts.
- `expert`: Define the architecture of the experts. The user can pass a `torch.nn.Module` as an expert. The default option has one linear layer with 4 units. The number of units of the default option can also be changed with the parameter `units_exp`.
- $X_{low}$ and $X_{high}$: Default option is $X_{high} = X$ and $X_{low} = \emptyset$. The default factor model is an autoencoder with two layers of size $hidden_1$ (default 64) and $hidden_2$ (default 8).
- `type_treatment` and `type_target`: the implemented options are `binary` and `continuous`. These values define the type of loss function. We assume all treatments have the same type (all binary or all continuous); therefore, only one value needs to be defined.
- `loss_target`, `loss_da`, `loss_treat`, `loss_reg`: losses weights for the target/outcome, autoencoder, treatments, and regularization, respectively. Default value is 1.

As previously mentioned, the user also needs to define optimization parameters as any other neural network (learning rate, batch size, number of epochs, etc.).