CAUSAL MACHINE LEARNING FOR TREATMENT OUTCOMES

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Why this article:

It provides a broad landscape about the currently used causal ML framework and workflow, and is easy to read for laypersons.

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Causal machine learning for predicting treatment outcomes

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Check for updates

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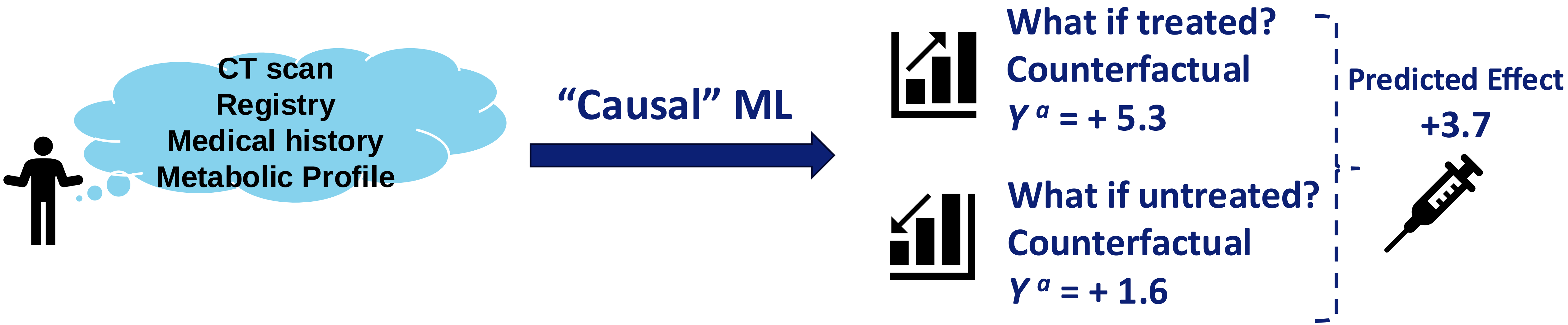
Causal machine learning (ML) offers flexible, data-driven methods for predicting treatment outcomes including efficacy and toxicity, thereby supporting the assessment and safety of drugs. A key benefit of causal ML is that it allows for estimating individualized treatment effects, so that clinical decision-making can be personalized to individual patient profiles. Causal ML can be used in combination with both clinical trial data and real-world data, such as clinical registries and electronic health records, but caution is needed to avoid biased or incorrect predictions. In this Perspective, we discuss the benefits of causal ML (relative to traditional statistical or ML approaches) and outline the key components and steps. Finally, we provide recommendations for the reliable use of causal ML and effective translation into the clinic.

1. INTRODUCTION

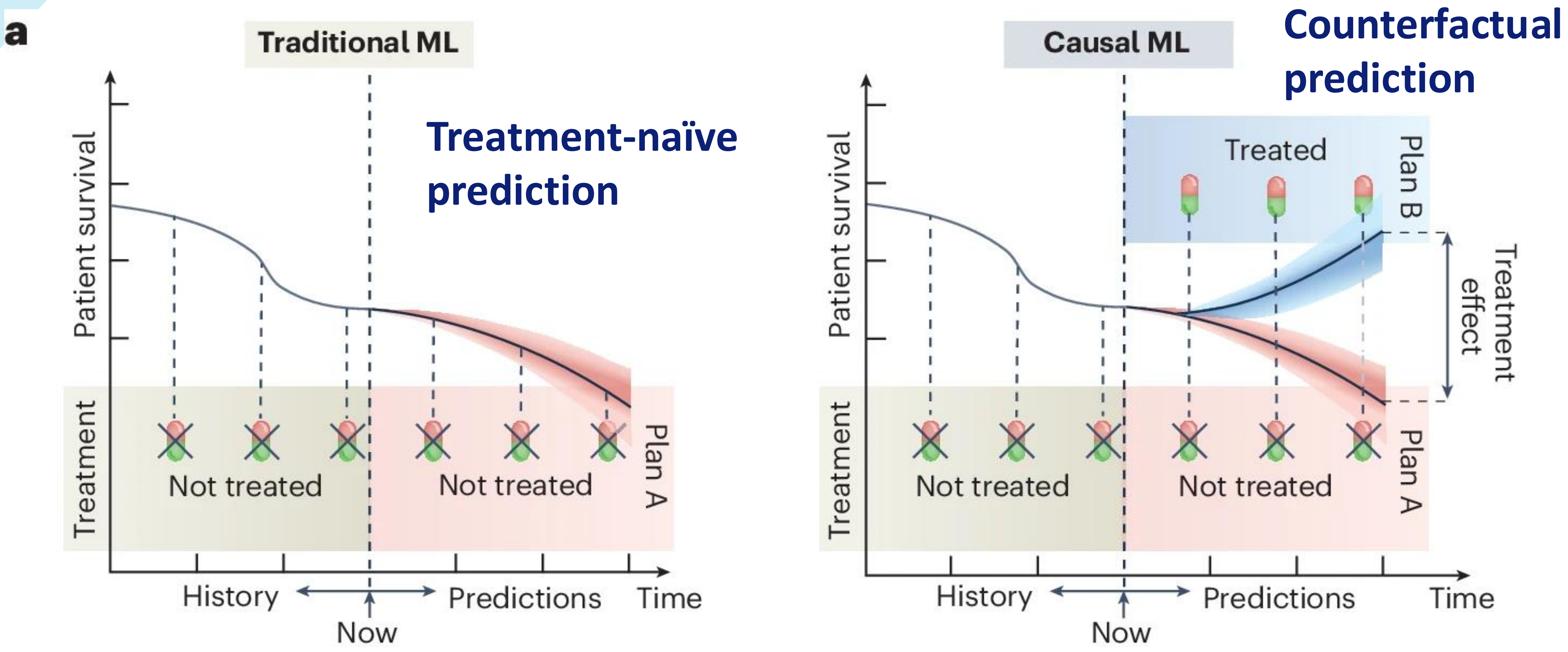
What is causal machine learning (ML) in medicine:

- A branch of ML that aims to estimate causal effects or counterfactual outcomes.



THREE TASKS...

Population --- Subgroup --- Individual



1. Prediction of Average Treatment Effect: Population level - ATE

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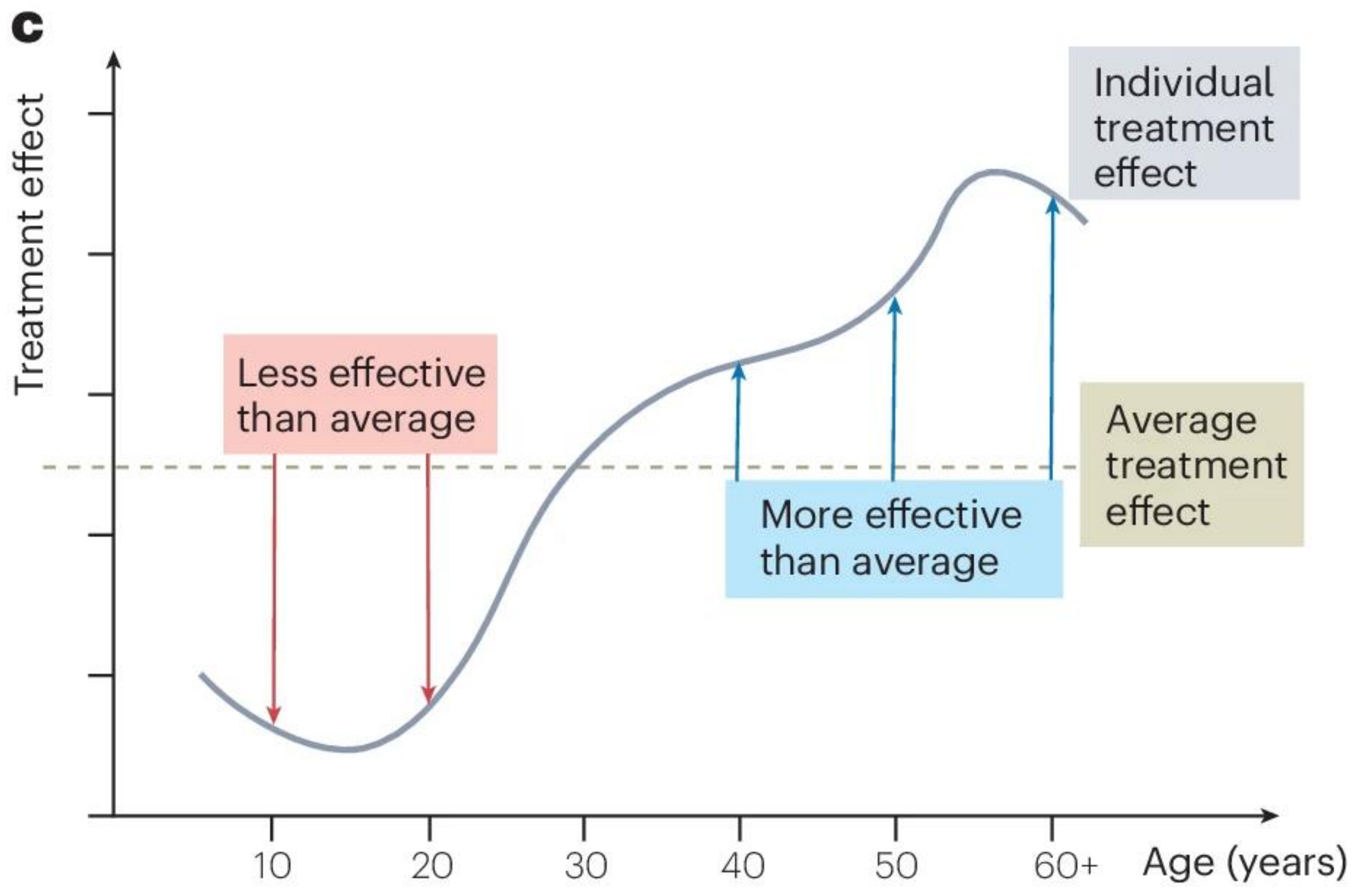


2. Heterogeneity of Treatment Effect (HTE) Prediction: Group level - CATE

b

Traditional ML

	Patient	Covariates	Treatment	Patient outcome
Data	1	Age, sex, etc.	0	–1.0
	2		1	2.3
	3		1	0.3

	Patient	Covariates	Treatment	Patient outcome
Task	1	Age, sex, etc.	1	?
	2		0	?

Causal ML

	Patient	Covariates	Treatment	Patient outcome	
				If not treated	If treated
Data	1	Age, sex, etc.	0	–1.0	
	2		1		2.3
	3		1		0.3

	Patient	Covariates	Potential outcomes		Treatment effect
			If not treated	If treated	If treated → If not treated
Task	1	Age, sex, etc.	?	?	?
	2		?	?	?

☐ Missing observations ? Prediction targets

3. Individual effect prediction: individual level - ITE

2. WHEN TO USE?

Predictimand (estimand for prediction) for causal ML prediction:

- **EVERYTHING** related to effect: everything concerning counterfactual outcomes but not only observed outcomes.

When to prefer causal ML over traditional methods?

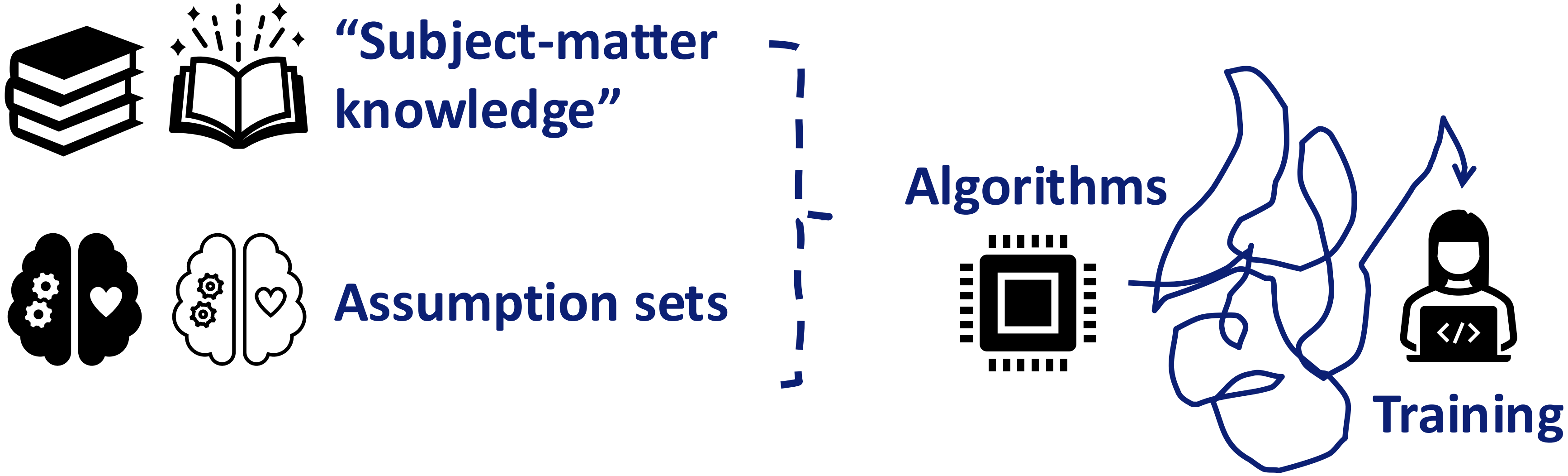
(This is the authors' argument not mine)

- Dealing with ***high-dimensional data***: imaging; omics; health records; unstructured text; etc.
- High risk for model misspecification when using traditional statistical methods.

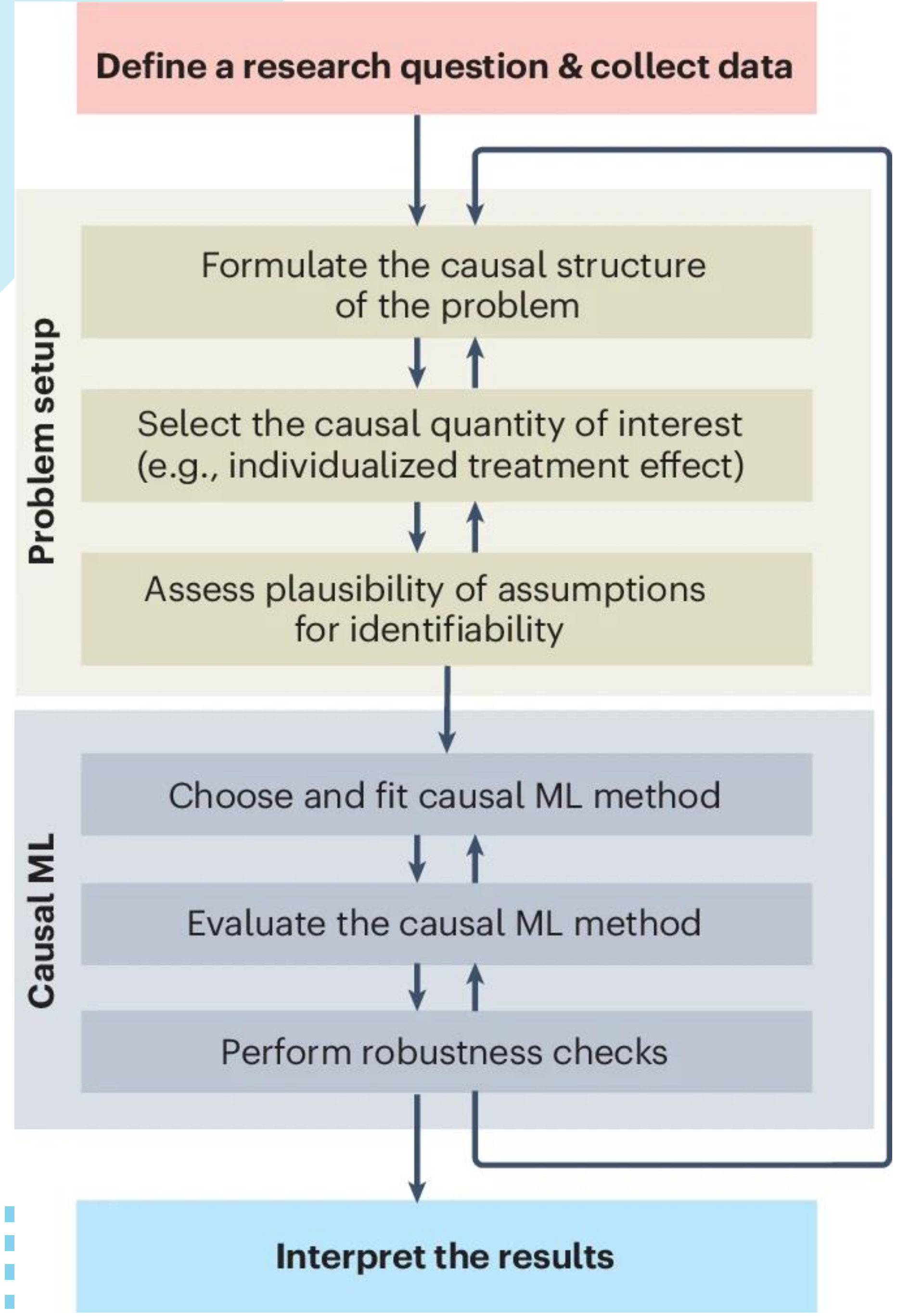
3. FUNDAMENTAL PROBLEMS

Causal ML is often Strongly-Supervised:

- One has to embed causal framework knowledge and assumptions into a ML process.



4. WORKFLOW



Still the researchers' responsibility for assumptions and subject-matter knowledge!

But causal ML aims to provide an alternative for traditional statistical methods (like g-methods) here.

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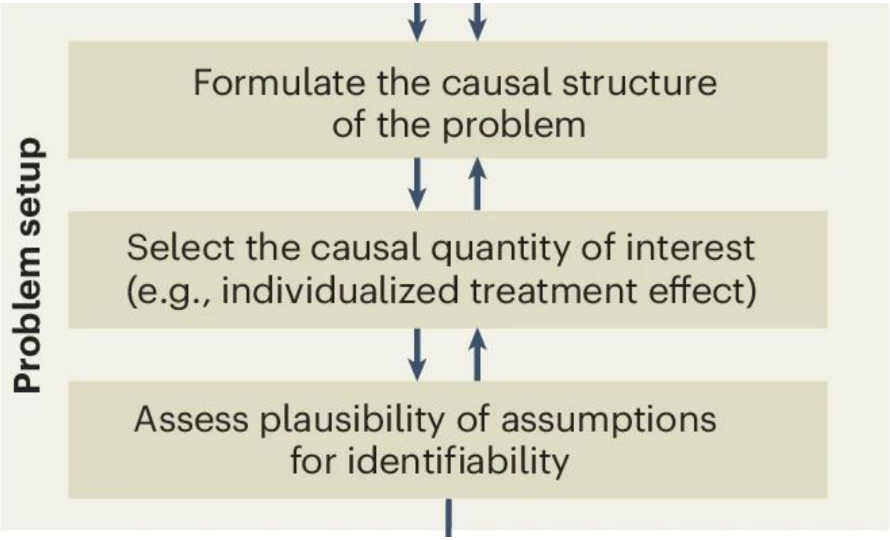
4. WORKFLOW



Causal structure:

- Treatment, outcome, covariates, time frame, confounding structure, selection, effect modification, …

Causal Estimand:

- ATE, CATE, ITE, counterfactual outcome, …

Assumptions:

- Dealing with identifiability conditions.

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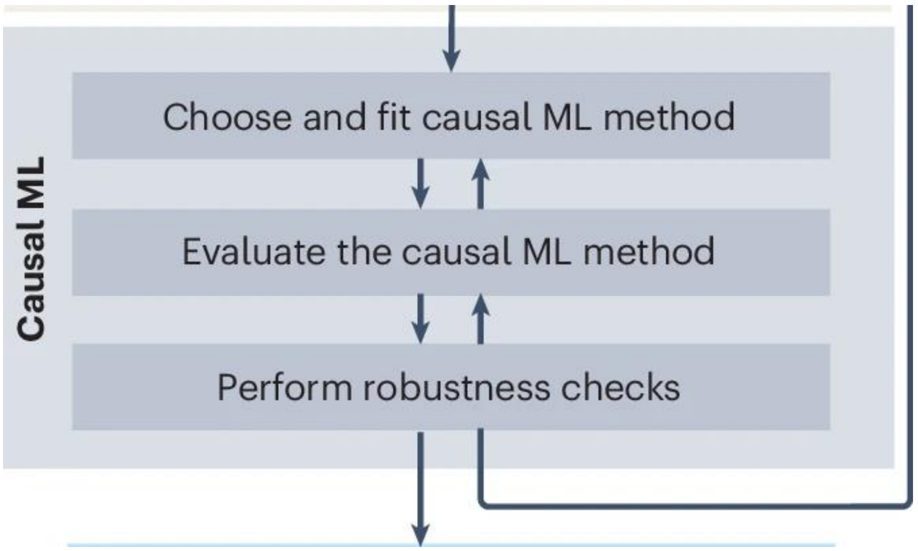
4. WORKFLOW



ML Algorithm:

- Model-agnostic methods and adapted model-based methods

Performance/benchmarking:

- Using RCT data: heterogeneity prediction; using factual prediction or a secondary model for benchmarking.

Robustness check:

- Add noise; replace treatment; change data generation mechanisms.

5. PRACTICE AND CHALLENGES

Practical use:

1. Average treatment effect:

- help to define inclusion criteria for clinical trials or to identify predictive biomarkers

2. Conditional average treatment effect:

- flexible, data-driven methods to analyze treatment effect heterogeneity in real-world data

3. Conditional/individual treatment effect:

- Clinical treatment decision-making

5. PRACTICE AND CHALLENGES

Challenges

1. Requires strong predictors and large sample size

2. Uncertainty should be estimated

3. No standard software implementation

4. Simulation is different from real-world data

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QUESTIONS?