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Clinically Meaningful Treatment Effect Subgroups Exist following Anterior Cruciate Ligament Reconstruction

Optimizing Patient Selection through a Machine Learning Approach

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I (and/or my co-authors) have something to disclose.

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THE QUESTION

- Surgical indications for anterior cruciate ligament reconstruction (ACLR) are
  - Return to cutting and pivoting activities
  - Risks of contralateral injury
  - Meniscal injury
  - Post-traumatic osteoarthritis (PTOA)
- Differential treatment effect of ACLR compared to nonoperative management on a patient-specific level is useful information

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THE GOAL

- Utilize unsupervised machine learning clustering to identify clinically meaningful patient outcomes subgroups after ACL injury
- Estimate subgroup-specific treatment effect of ACLR
- Identify patient-specific risk factors for poor outcomes

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THE APPROACH

- Combine
  - Unsupervised clustering
  - Nonparametric inference
- Can not only identify unique patient subgroups from aggregated data, but also assess the subgroup-specific treatment effect of particular interventions with comparatively less bias

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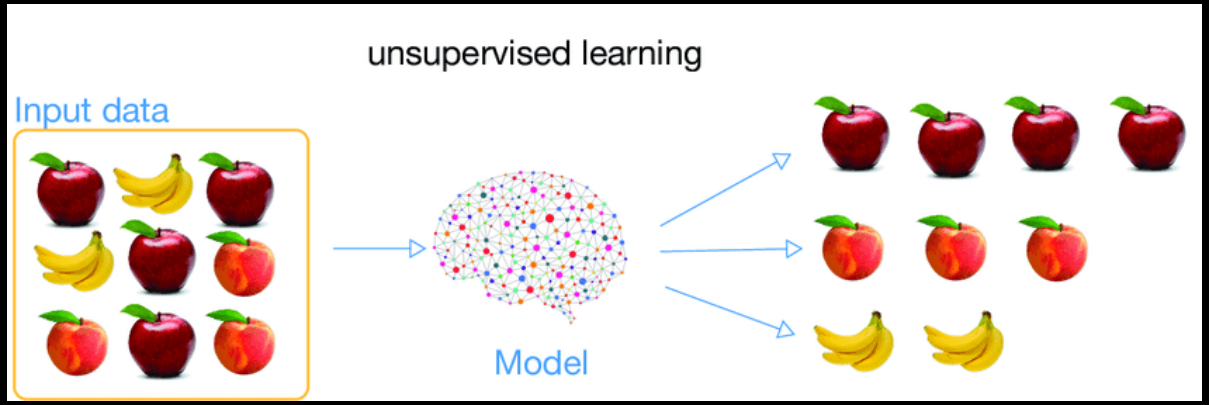
UNSUPERVISED LEARNING



- Identify hidden patterns
- Takes all features and group data points based on similarity to each other

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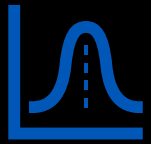
TARGETED INFERENCE



Statistics

- For inference
- Usually parametric model
- Coefficients with standard errors

Machine learning

- For prediction
- Data-adaptive and nonparametric
- Performance metrics such as AUC

- A semiparametric method for causal inference
- Produces coefficients with machine learning models
- Makes no assumptions on the underlying distribution of data

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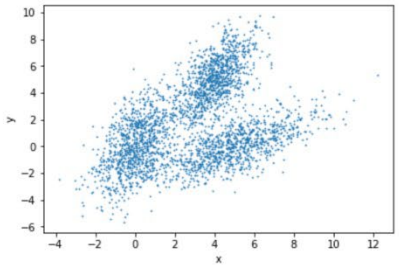
METHODS: DATA AND WORKFLOW

- A longitudinal geographic database registry queried for all patients with ACL injuries from 1990 to 2016
  - Demographics, injury characteristics, radiographical findings and clinical course were collected

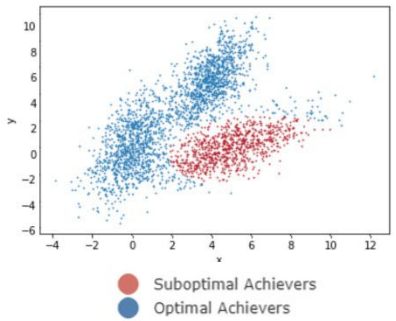
Before



Patients with all features (age, sex, BMI, tear size, etc)

Random Forest Clustering

After



Targeted Inference

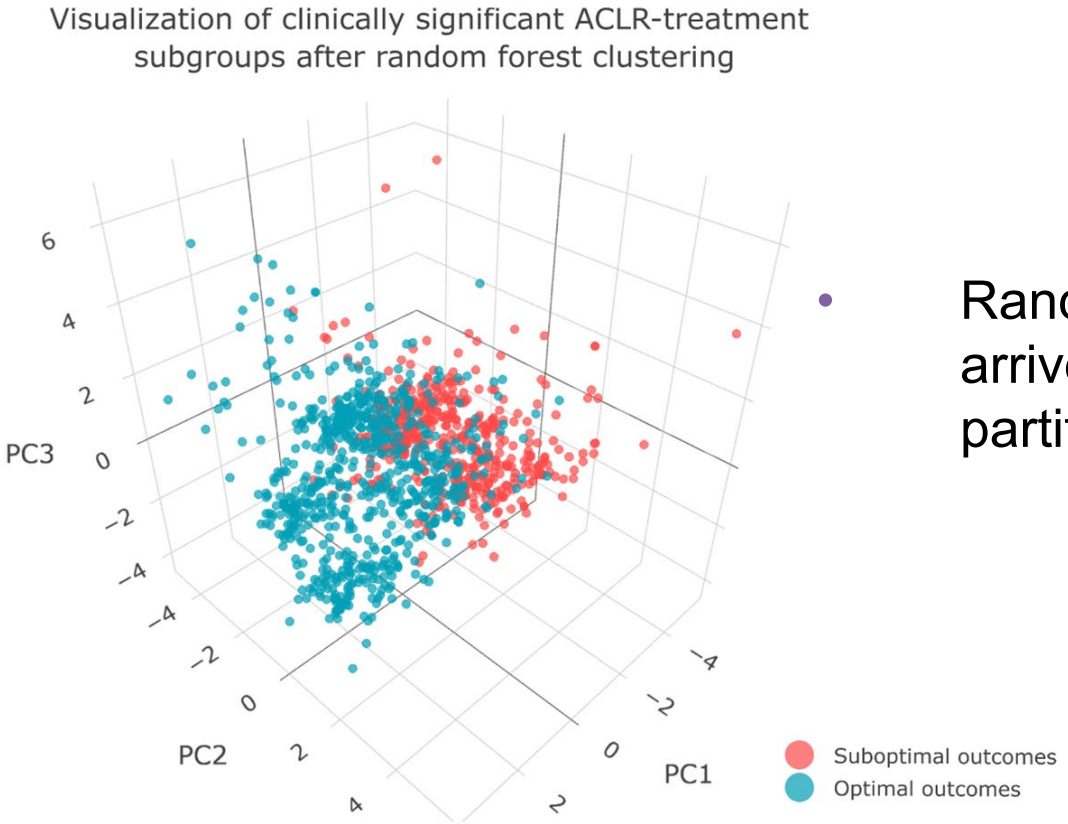
Odd ratios for suboptimal achievement for risk factor X, Y, Z

Primary outcomes:

Meniscus injury
Contralateral ACL injury
Development of PTOA
Progression to TKA

RESULTS

A



- Random forest algorithm arrived at an optimal partition of 2 subgroups

RESULTS

Table 1: Treatment effect of ACL reconstruction on subgroup outcomes via TMLE

	Suboptimal subgroup		Optimal subgroup	
Outcomes	Treatment effect	OR	Treatment effect	OR
Meniscus injury	-0.014 (-0.037--0.009)	0.87 (0.69-1.1)	**-0.53 (-0.55- -0.51)**	**0.08 (0.07-0.09)**
Contralateral ACL injury	-0.028 (-0.058-0.003)	0.61 (0.35-1.06)	**-0.07 (-0.10--0.049)**	**0.16 (0.06-0.41)**
Development of PTOA	**-0.14 (-0.17--0.099)**	**0.58 (0.49-0.67)**	**-0.079 (-0.1- -0.055)**	**0.59 (0.49-0.72)**
Progression to TKA	**-0.04 (-0.071 - -0.02)**	**0.69 (0.56-0.95)**	**-0.06 (-0.069- -0.050)**	**0.049 (0.01-0.16)**

Bold indicates statistically significant values (P <0.01)

ATE: average treatment effect prior to percentage conversion, negative values indicate protective effect against outcome

OR: odd ratio between treated and controls

RESULTS

- Predictors of suboptimal outcomes
  - **Older age at injury** (odd ratio [OR]: 0.89, 95% CI: 0.87-0.92), **greater BMI** (OR: 0.77, 95% CI: 0.72-0.82), **previous arthroscopic knee surgery** (OR: 0.04, 95% CI: 0.02-0.09), **concomitant medial meniscus injury** (OR: 0.05, 95% CI: 0.02-0.01, all P<0.01)
- Positive predictors for optimal outcomes included **sports participation**. (OR: 4.50, 95% CI: 1.96-10.35).

CONCLUSION

- Clinically meaningful subgroups exist following ACL injuries.
- ACLR exerted a protective effect on the development of PTOA and TKA in both subgroups but was not as effective in preventing secondary meniscus injuries or contralateral ACL injuries in patients who were older, heavier, or had concomitant medial meniscus injuries.

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