Detecting High-Risk of Alzheimer's Disease Using Statistics and Machine Learning

Data Science Project by Chuck Tucker

Alzheimer’s Disease

"Worldwide, 50 million people are living with Alzheimer's and other dementias."

Alzheimer’s disease is terminal unlike other dementias

Source: alz.org

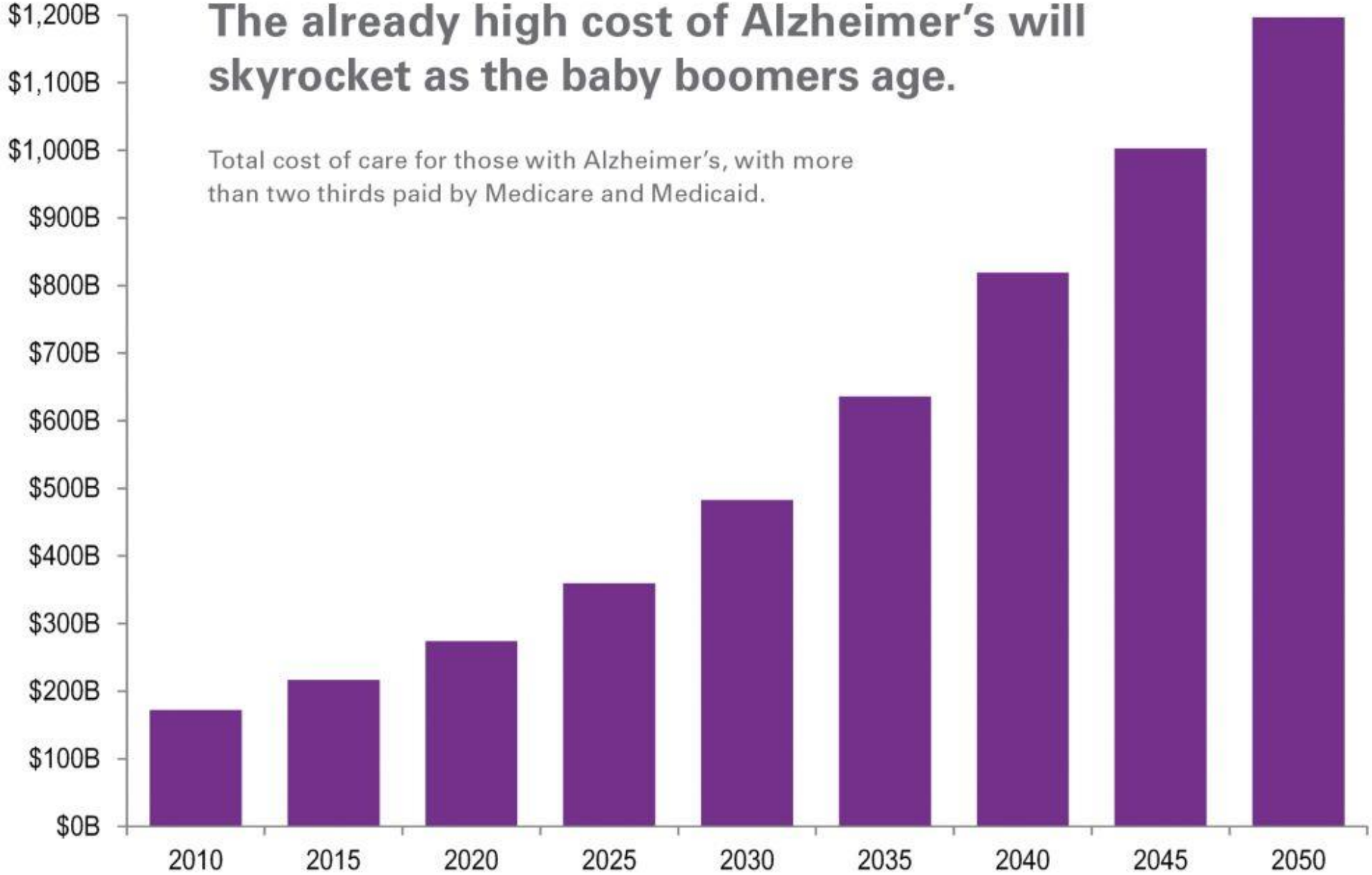
Cost of Care

- 15 million family members are providing 18.2 billion hours of unpaid care
- Economic value of this care is more than $230 billion

Source: alz.org

The already high cost of Alzheimer's will skyrocket as the baby boomers age.

Total cost of care for those with Alzheimer's, with more than two thirds paid by Medicare and Medicaid.



Source: Lewin Group Econometric Model of Alzheimer's and Dementia Costs (see: alz.org/trajectory).

Best Outcomes from Early Treatment

Early Treatment Options

- Changes in diet
- Taking supplements and/or antioxidants
- Avoid smoking and alcohol
- Social activities
- Exercising
- Brain stimulating activities

- Symptoms and disease progression are best mitigated with early treatment

- Early treatment options are inexpensive compared to medication costs

Source: alzheimers.net

Primary Goal for this Analysis

- Create tools that can detect or predict Alzheimer's disease to identify high-risk patients
- These patients can be referred for additional tests or begin early treatment

Target Audience

- Medical professionals diagnosing or treating Alzheimer's disease
- Patients or family members of patients suspecting early cognitive impairment

Data Source and Analysis Tools

- Data Source: Alzheimer's Disease Neuroimaging Initiative
  - Cognitive tests and brain scans
- Classical Statistical Methods
  - Threshold values that indicate high-risk
- Machine Learning Algorithms
  - Predict high-risk patients

Provide Patient Recommendations Based on:

Baseline Biomarkers	Change in Biomarkers	Screening Method
• Biomarker measurements at a patient's first exam • Predict Alzheimer's risk using only initial measurements	• Change in biomarkers over time for a patient • Change between first exam and most recent exam • Detect a progression to Alzheimer's disease	• Use only cognitive tests to create a recommendation system to refer patients for brain scans

Biomarkers = cognitive test results or scan results

Threshold Results

Baseline Biomarkers (first exam)

- Cognitive Test Thresholds:
- Very good detection rates
- Different thresholds for males and females

Biomarker	Threshold	Detection Rate
CDRSB Males	1.48	83 %
CDRSB Females	1.04	85 %
ADAS11 Males	10.46	81 %
ADAS11 Females	8.78	90 %
ADAS13 Males	16.74	86 %
ADAS13 Females	13.79	93 %
MMSE Males	27.37	80 %
MMSE Females	28.00	85 %
RAVLT Immed. Males	29.36	78 %
RAVLT Immed. Females	37.29	91 %

Calculations at 25% false positive rate

* Statistical tests showed males/females had different thresholds for all biomarkers

Recommended Usage

- Patients that exceed thresholds for one or more baseline cognitive tests
  - Refer patient for brain scans
  - Use the machine learning models (introduced later) to predict if patient is high-risk for Alzheimer's disease
  - Recommend patient begin early treatment as recommended by medical practitioner
  - Suggest continued monitoring of symptoms and regular exams

Baseline Biomarkers (first exam)

- Brain Scan Thresholds:
- Lower detection rates than cognitive tests
- Different thresholds for males and females

Biomarker	Threshold	Detection Rate
Hippocampus Males	6673.01	66 %
Hippocampus Females	6391.04	80 %
Ventricles Males	50797.64	45 %
Ventricles Females	37943.74	40 %
WholeBrain Males	1025582.00	48 %
WholeBrain Females	928774.86	56 %
Entorhinal Males	3474.42	67 %
Entorhinal Females	3152.40	76 %
MidTemp Males	19179.84	57 %
MidTemp Females	17617.11	70 %

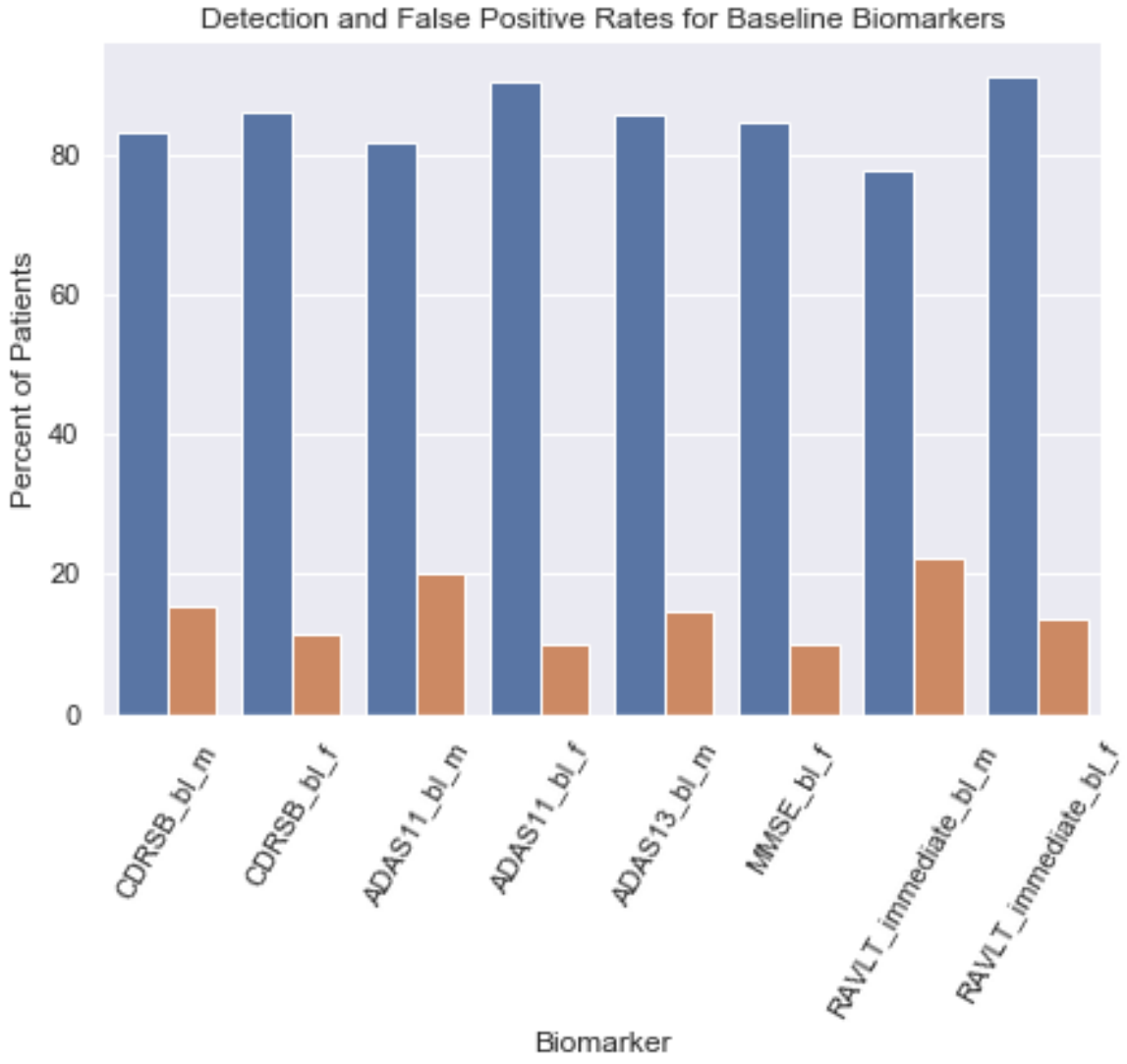
Calculations at 25% false positive rate

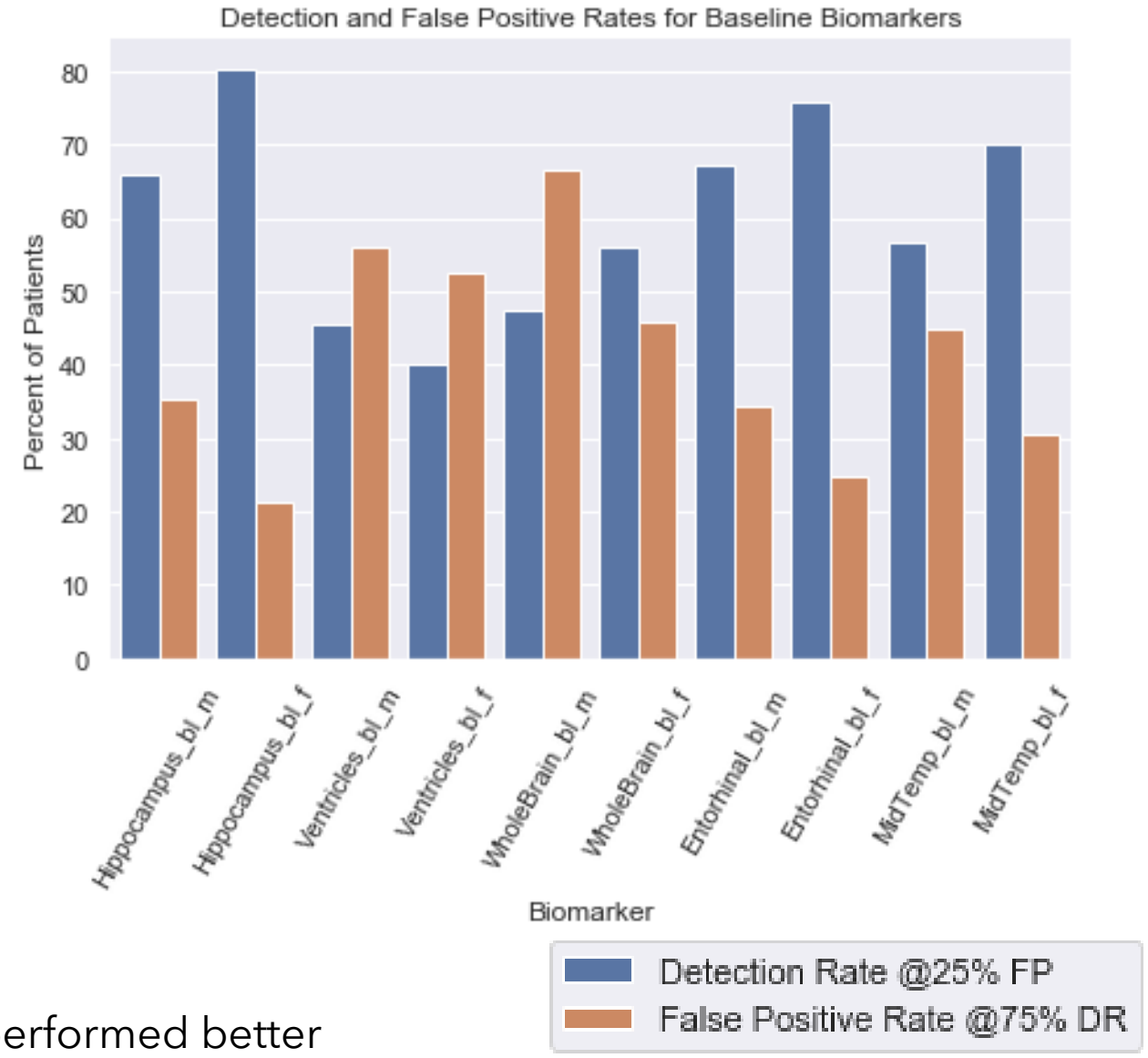
* Statistical tests showed males/females had different thresholds for all biomarkers

Recommended Usage

- Patients that exceed thresholds for one or more baseline brain scans
  - Use the machine learning models (introduced later) to predict if patient is high-risk for Alzheimer's disease
  - Recommend patient begin early treatment as recommended by medical practitioner
  - Suggest continued monitoring of symptoms and regular exams

Baseline Thresholds Performance Summary





* Cognitive tests performed better

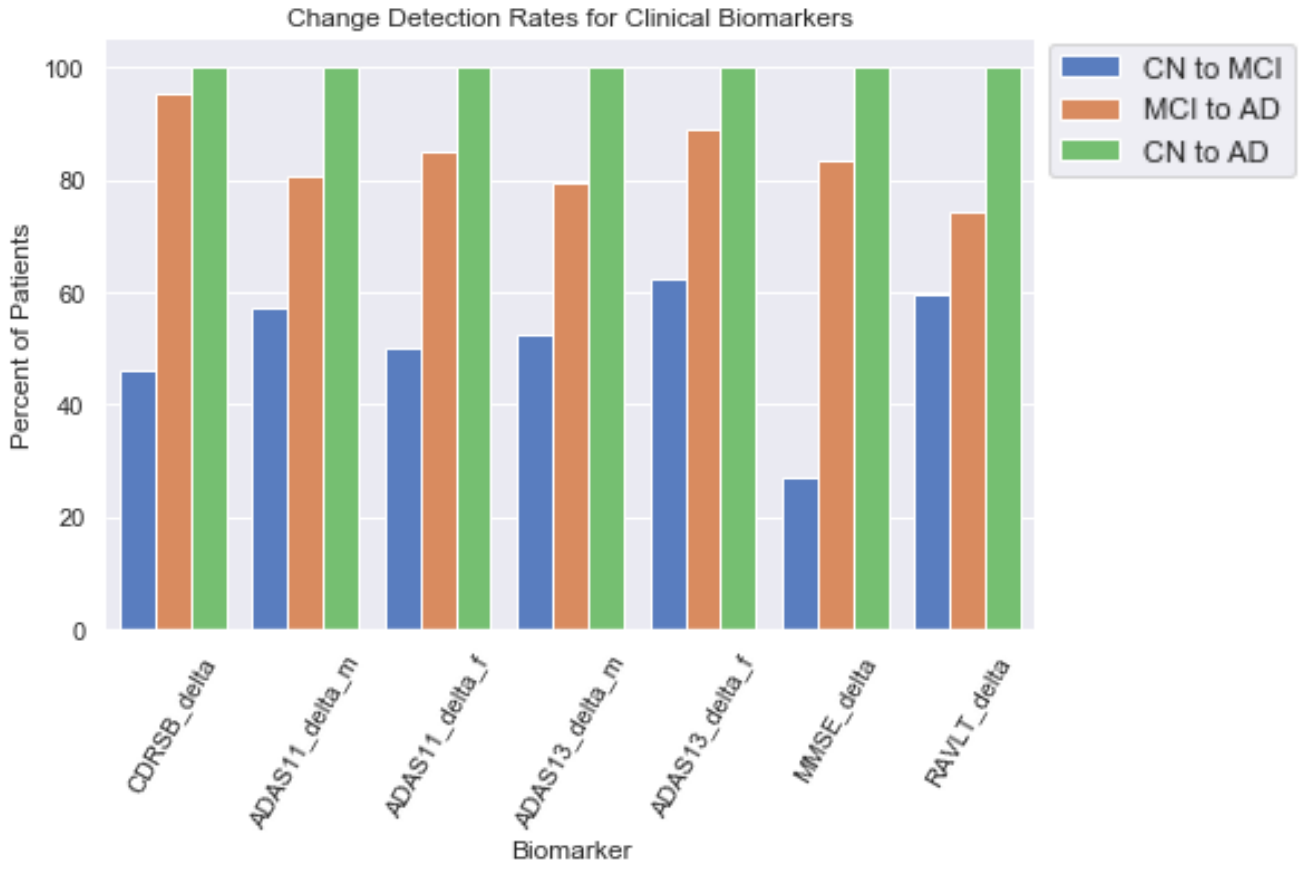
Change in Biomarkers

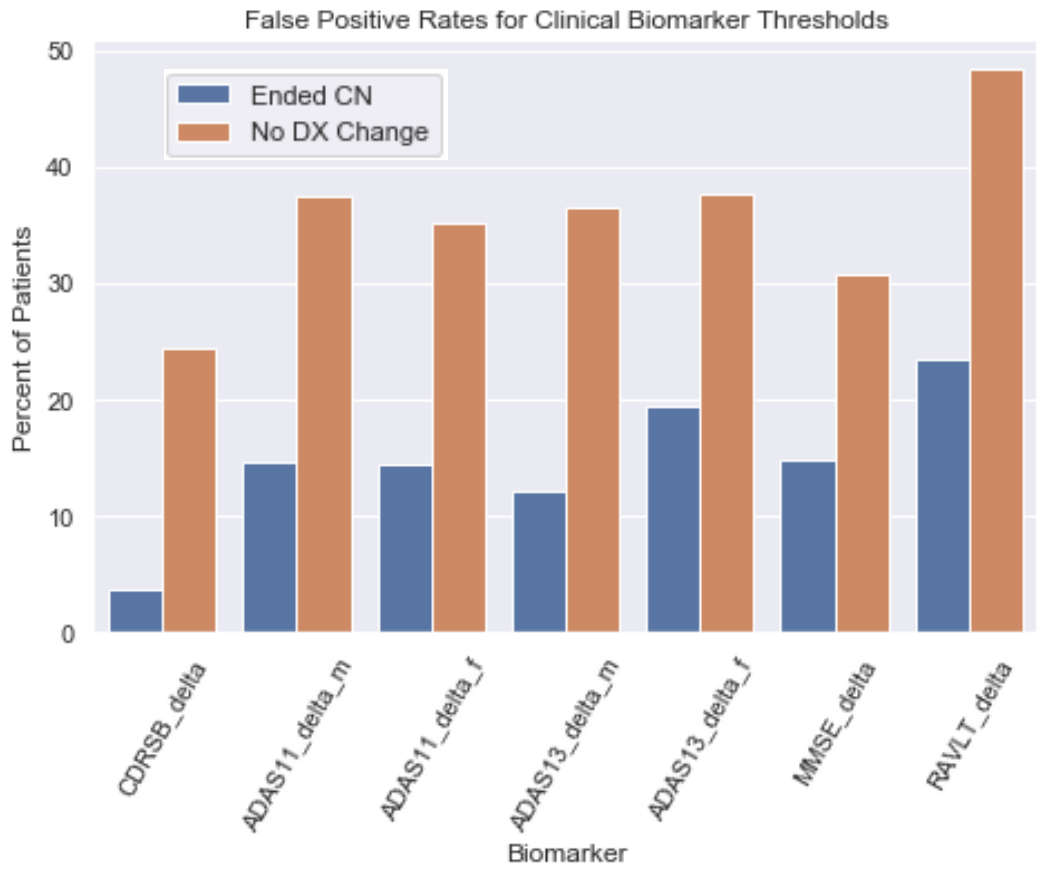
Cognitive Test Thresholds: high detection rates & low false positive rates

Biomarker	Threshold	CN to AD Detect Rate	MCI to AD Detect Rate	False Positive Rate
CDRSB	+ 2.07	100 %	95 %	4 %
ADAS11 Males*	+ 1.69	100 %	81 %	15 %
ADAS11 Females*	+ 2.41	100 %	85 %	14 %
ADAS13 Males*	+ 2.13	100 %	80 %	12 %
ADAS13 Females*	+ 0.60	100 %	89 %	19 %
MMSE	- 176.0	100 %	84 %	15 %
RAVLT Immediate	- 281.7	100 %	74 %	23 %

* Statistical ADAS tests showed males/females had different thresholds
+ indicates in increase, – indicates a decrease

Change in Cognitive Tests
Performance of Thresholds





* Good detection rates and acceptable false positive rates for recommended purpose

Recommended Usage

- Patients that exceed thresholds for changes in one or more cognitive tests
  - Refer for brain scans
  - Use the machine learning models (introduced later) to predict if patient is high-risk for Alzheimer's disease
  - Recommend patient begin early treatment as recommended by medical practitioner
  - Suggest continued monitoring of symptoms and regular exams

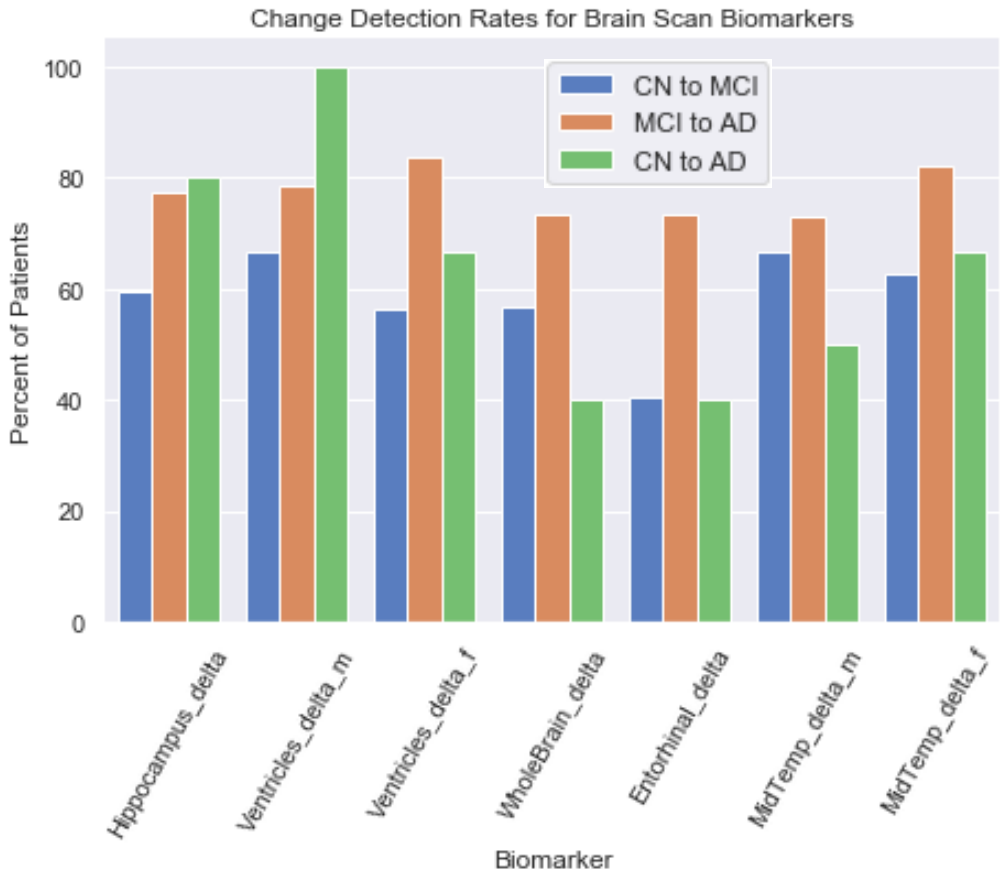
Change in Biomarkers

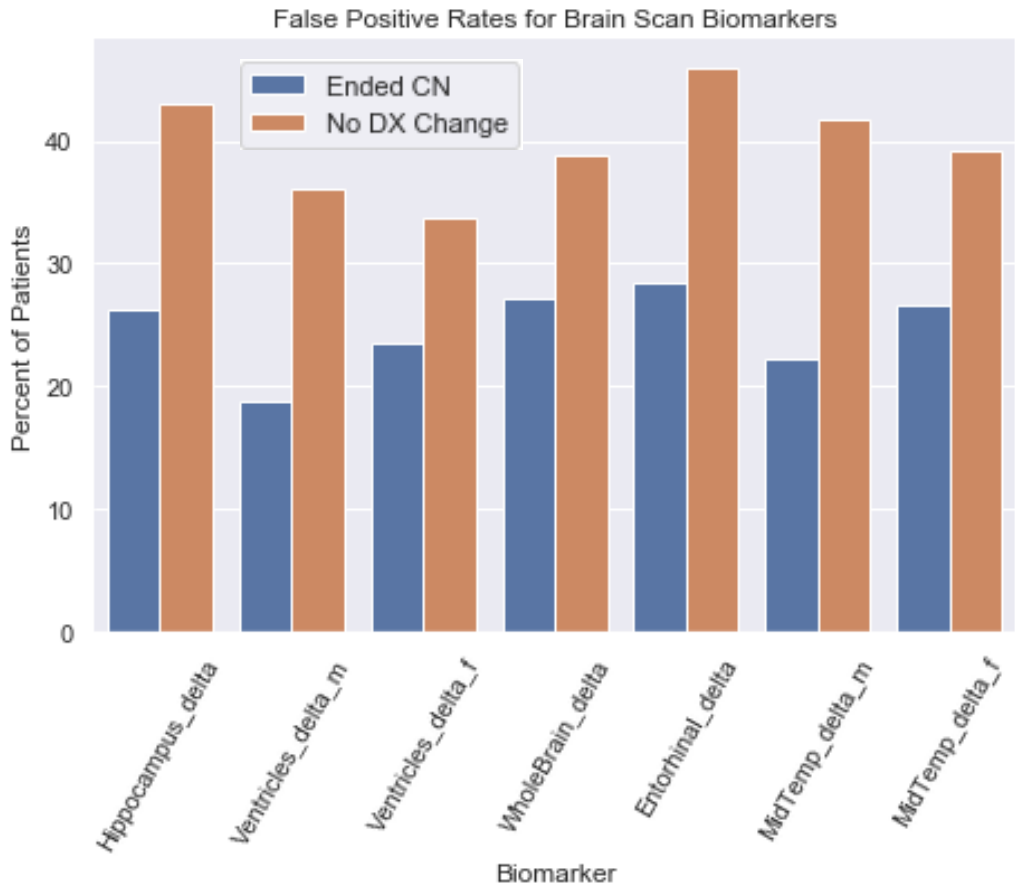
Brain Scan Thresholds: less accurate than cognitive thresholds

Biomarker	Threshold	CN to AD Detect Rate	MCI to AD Detect Rate	False Positive Rate
Hippocampus	- 1.0	80 %	77 %	26 %
Ventricles Males*	- 772.8	100 %	79 %	19 %
Ventricles Females*	- 684.1	66 %	84 %	24 %
WholeBrain	- 1.9	40 %	73 %	27 %
Entorhinal	+ 4684.0	40 %	73 %	29 %
MidTemp Males*	+ 5764.3	50 %	73 %	22 %
MidTemp Females*	- 21220.4	67 %	82 %	27 %

* Statistical tests for Ventricles and MidTemp showed males/females had different thresholds
+ indicates an increase, – indicates a decrease

Change in Brain Scans
Performance of Thresholds





* Lower detection rates and higher false positive rates than cognitive tests

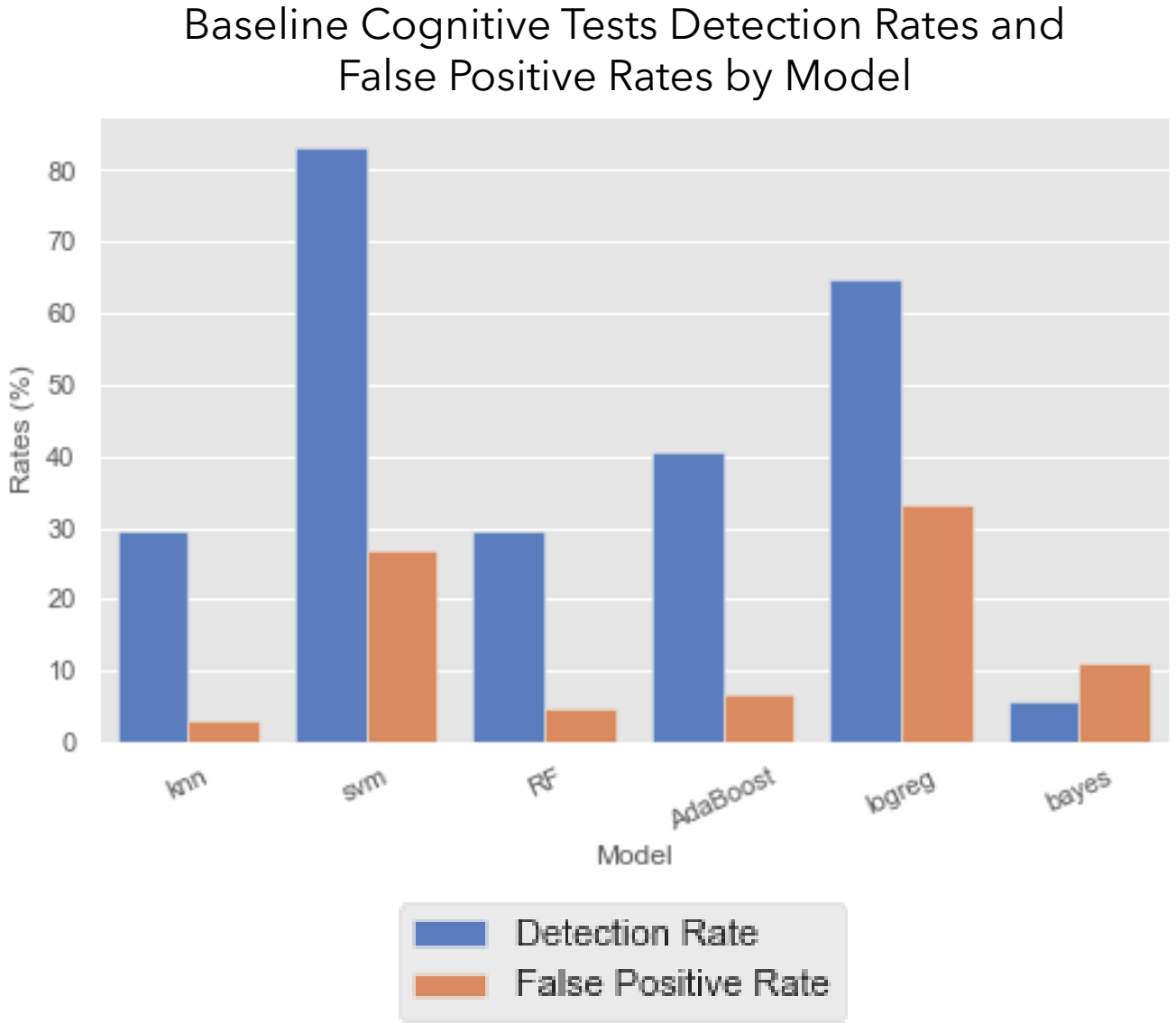
Recommended Usage

- Patients that exceed thresholds for changes in one or more brain scans
  - Use the machine learning models (introduced later) to predict if patient is high-risk for Alzheimer's disease
  - Recommend patient begin early treatment as recommended by medical practitioner
  - Suggest continued monitoring of symptoms and regular exams

Machine Learning and Predictive Modeling Results

Machine Learning Models: Baseline Cognitive Tests

- Support Vector Machines
  - 83% detection and 27% false positive
- Other models inaccurate with no brain scan data



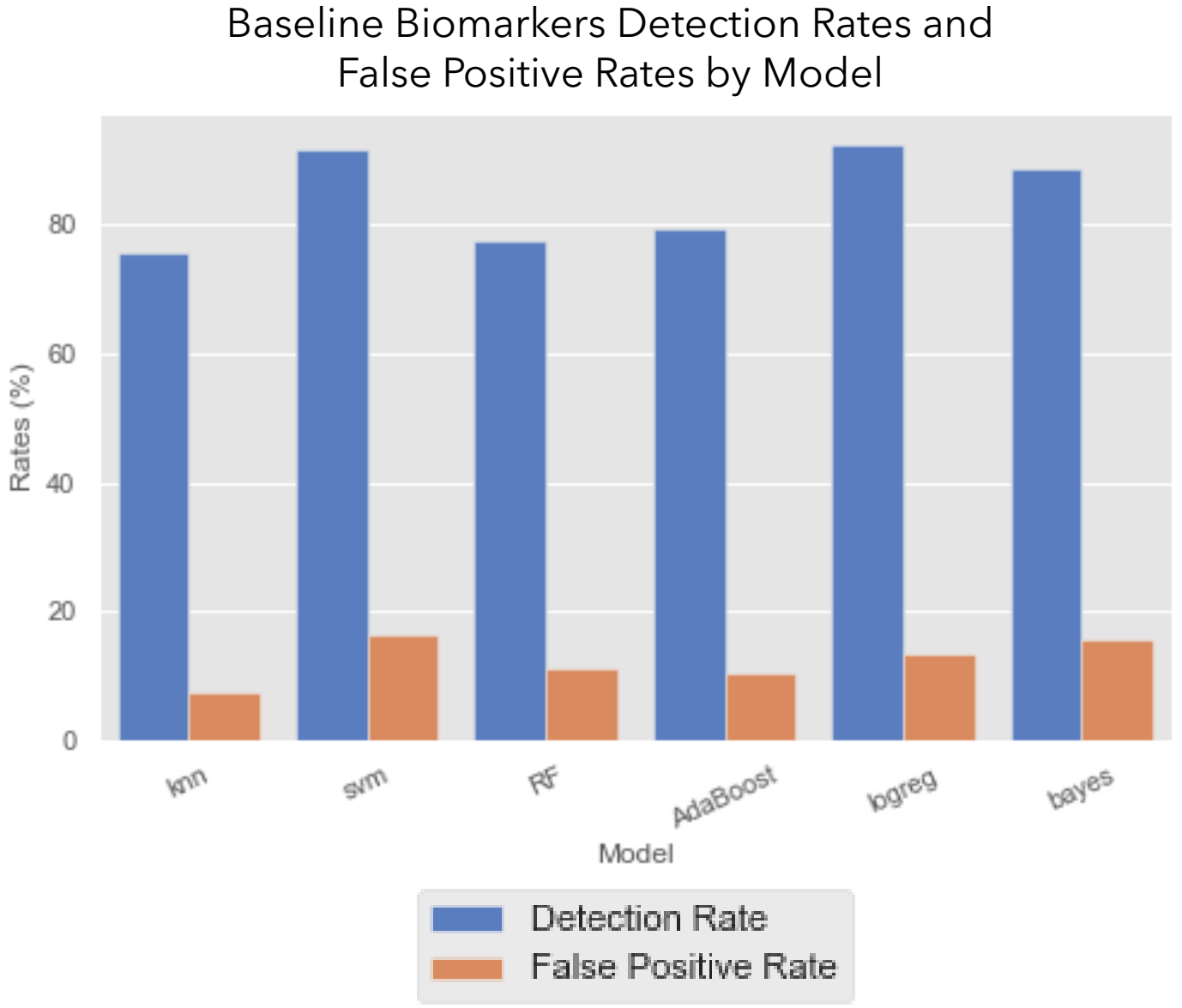
Recommended Usage

- Patients that are predicted as high-risk using baseline cognitive test SVM model
  - Refer patient for brain scans
  - Recommend patient begin early treatment as recommended by medical practitioner
  - Suggest continued monitoring of symptoms and regular exams

Machine Learning Models: Baseline Biomarkers

(Cognitive tests and brain scans)

- High Value Models
- Over 85% detection rates and less than 20% false positive rates
  - Support Vector Machines
  - Logistic Regression
  - Naïve Bayes
- Every model over 75% detection
- Every model under 20% false positive

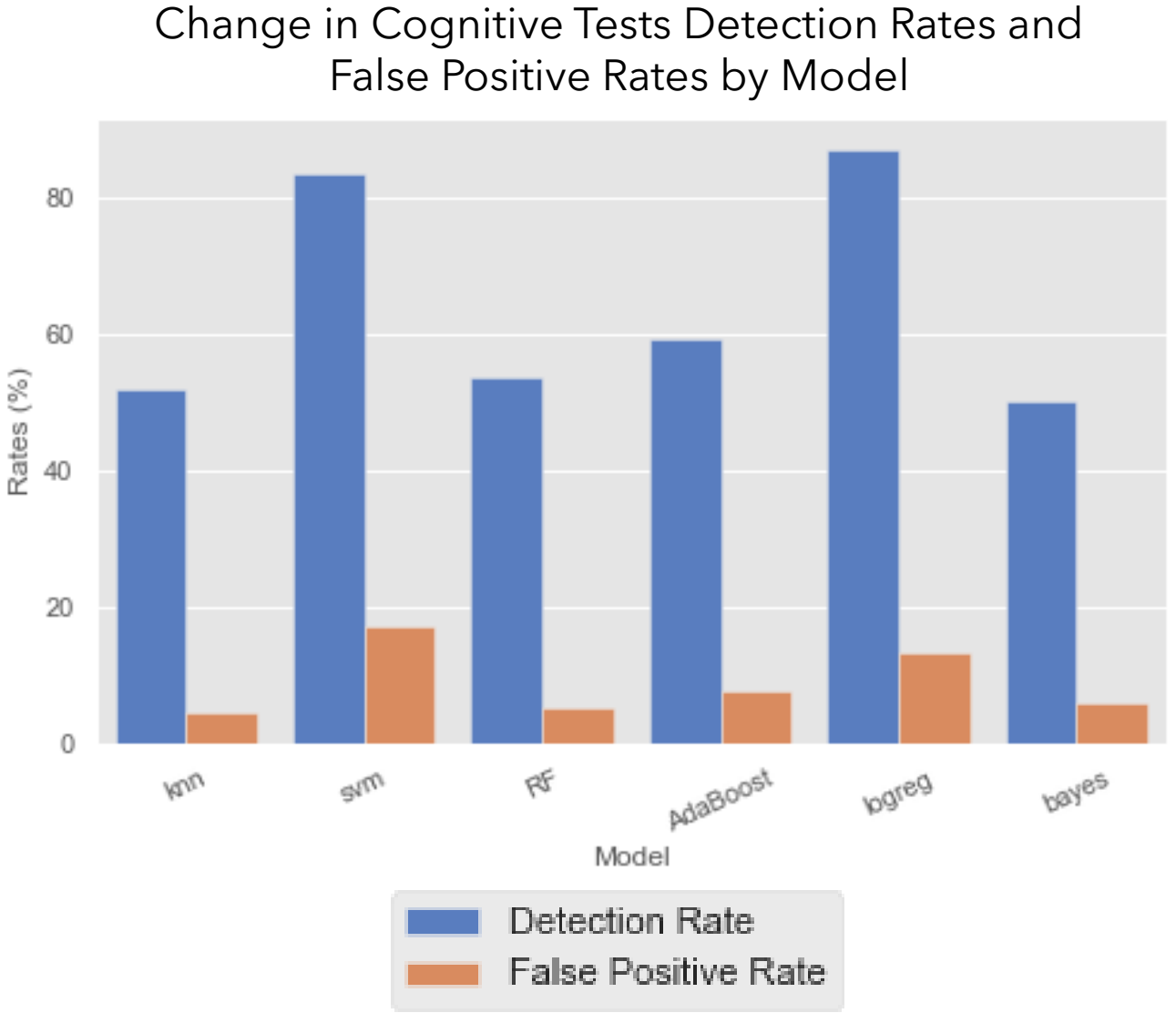


Recommended Usage

- Patients that are predicted as high-risk by the baseline biomarker models
  - Recommend patient begin early treatment as recommended by medical practitioner
  - Suggest continued monitoring of symptoms and regular exams

Machine Learning Models: Change in Cognitive Tests

- High Value Models
- Detection Rates over 80% and false positive rates 15-17%
  - Support Vector Machines
  - Logistic Regression
- Other models not as accurate



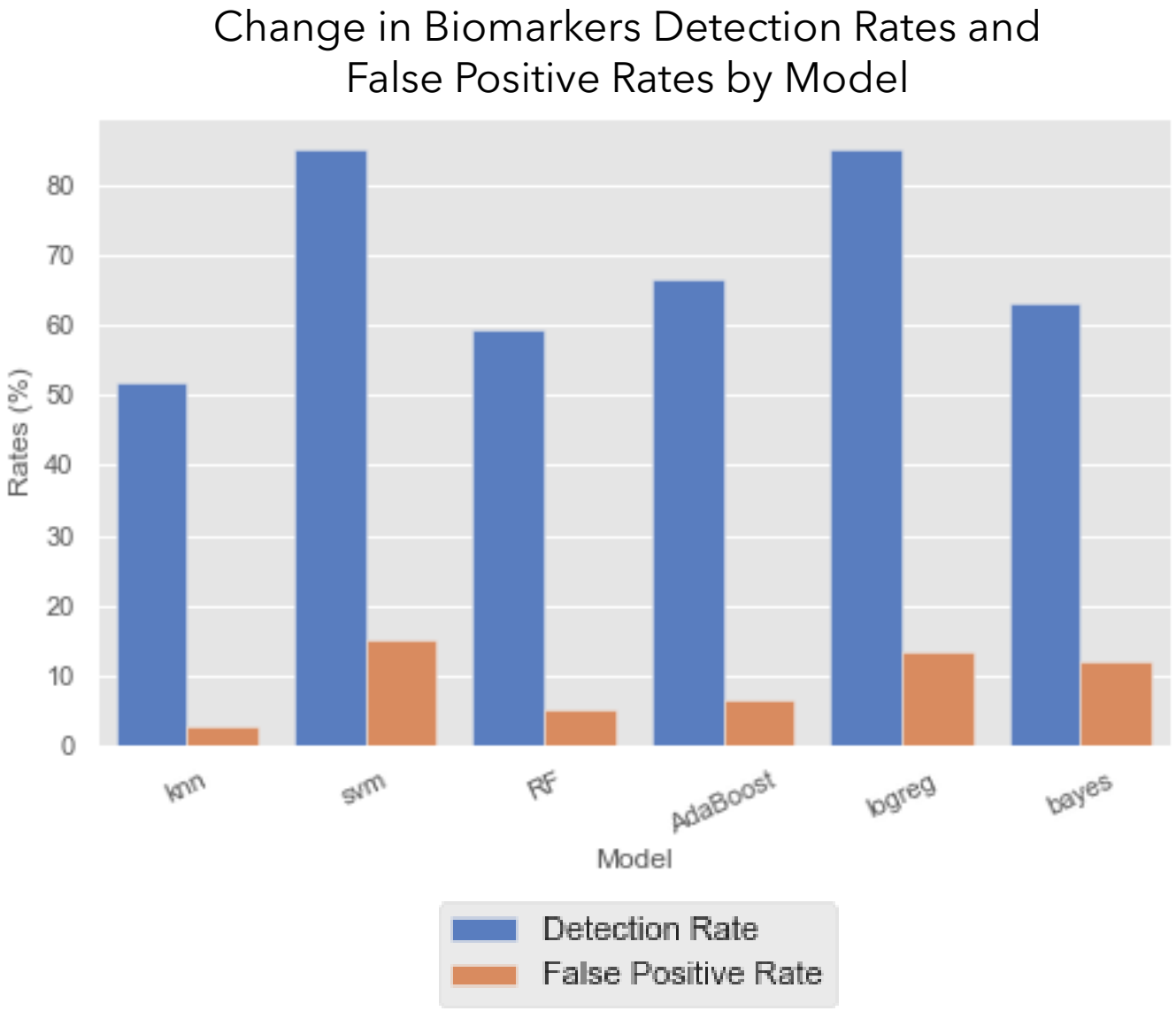
Recommended Usage

- Patients that are predicted as high-risk using change in cognitive test models
  - Refer patient for brain scans
  - Recommend patient begin early treatment as recommended by medical practitioner
  - Suggest continued monitoring of symptoms and regular exams

Machine Learning Models: Change in Biomarkers

(Cognitive tests and brain scans)

- High Value Models
- About 85% detection rates and less than 15% false positive rates
  - Support Vector Machines
  - Logistic Regression
- Other models not as accurate



Recommended Usage

- Patients predicted as being high-risk by the change in biomarkers models
  - Recommend patient begin all early treatment options as recommended by the patient's medical practitioner
  - Suggest continued monitoring of symptoms and regular exams

Model Tuning

- Hyperparameters were chosen using 5-fold cross validation
- Feature selection tools
  - Built-in attributes of models
  - Feature selector module
  - Principal component analysis
  - Ultimately made little improvement over the basic model
- Ensemble model comprised of the best performing models

Ensemble Models

- Individual models showed high detection rates and low false positive rates
- The best models were combined into ensemble models
  - These were generally 85% or higher detection and 20% or lower false positives
  - Majority voting by individual models decides the prediction for each patient
- Ensemble models should be better at generalizing to new patient data

Ensemble Models

Baseline Biomarkers

- Support Vector Machines (SVM)
- Logistic Regression (LR)
- SVM with 9 principal components
- LR with 9 principal components
- LR omitting 2 features

Change in Biomarkers

- Support Vector Machines
- Logistic Regression
- LR omitting 2 features

* Only three models with high enough detection rates

Ensemble Model Performance

Baseline Biomarkers

- 92% detection rate
- 15% false positive rate

Change in Biomarkers

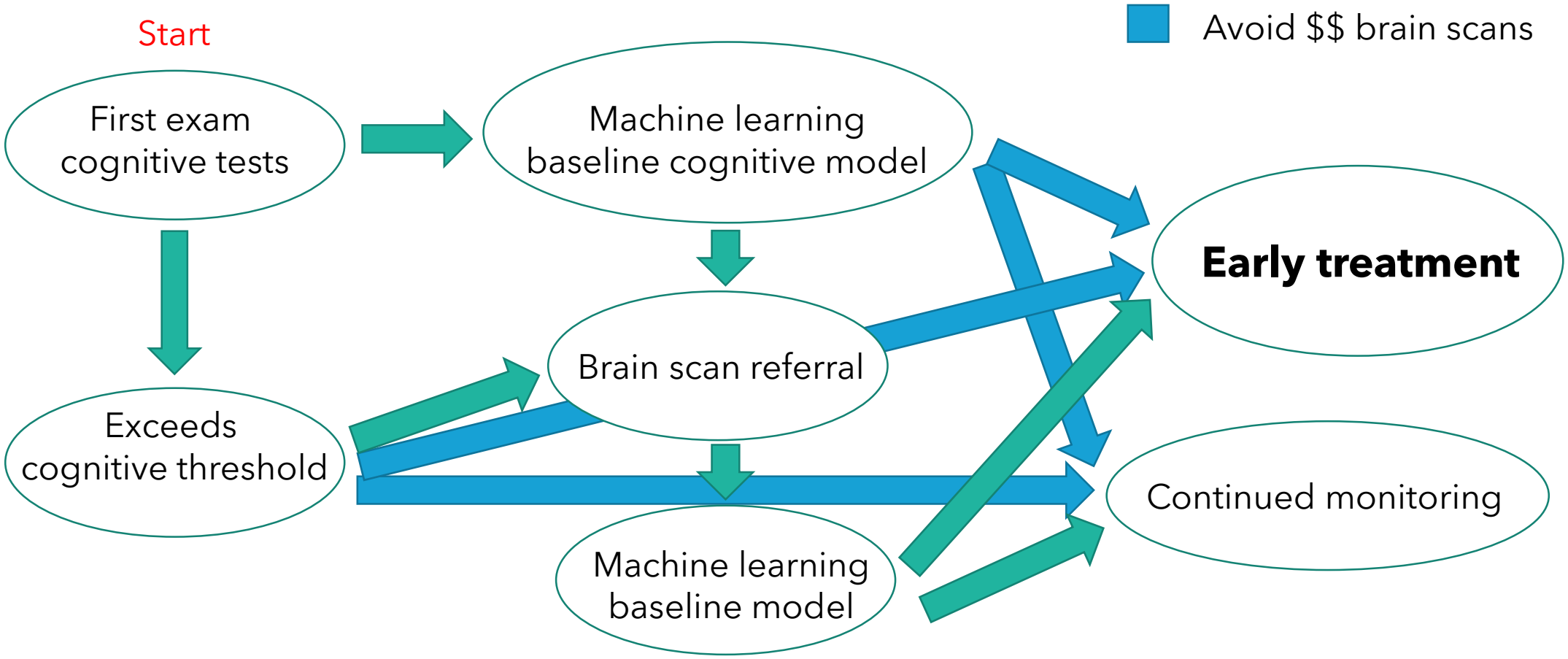
- 85% detection rate
- 14% false positive rate

These are the recommended models to use when there is data for cognitive tests and brain scans

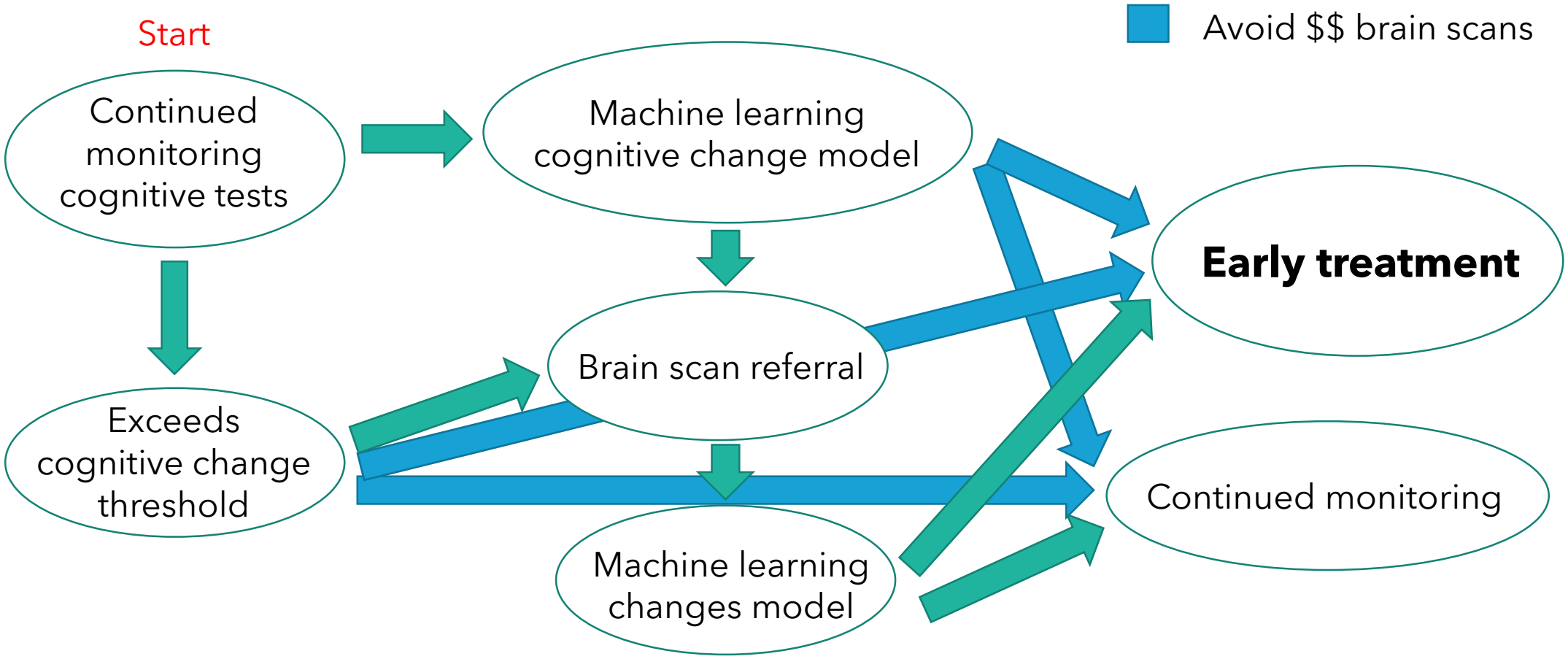
Practical Applications

- High detection rates make the model useful
- Low false positive rates mean not unduly alarming patients
- Early detection -> early treatment -> better outcomes

Baseline First Exam Decision Chart



Continued Monitoring Decision Chart



Final Thought:
Better Early than Late

"Although the adage, 'better late than never' certainly applies, waiting for a full blown diagnosis of Alzheimer's disease before making healthy diet and lifestyle changes, is not a very effective prevention plan."

Quote: alzheimers.net