Logistic Regression for Clinical Risk Modeling of Heart Disease

Estimation, Variable Selection, and Statistical Inference

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Outline

1. Introduction
2. Data Visualization
3. Data Preprocessing
4. Model selection
5. Model comparison
6. Inference on selected model
7. Conclusion
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Problem Formulation

Objective:

- To model the relationship between patient-level clinical variables and the probability of heart disease.
- To identify statistically significant predictors and interactions.
- To construct a predictive model with strong generalization performance.

Setting:

- Observations: (Y_i, X_i) for $i = 1, \ldots, n$
- $Y_i \in \{0, 1\}$ indicates presence of heart disease
- $X_i \in \mathbb{R}^p$ includes clinical covariates

Goal:

$$\text{Estimate } \mathbb{P}(Y = 1 \mid X = x)$$

Logistic Regression Model

We model the conditional probability via a generalized linear model:

$$\mathbb{P}(Y = 1 \mid X) = \pi(X)$$

$$\log\left(\frac{\pi(X)}{1-\pi(X)}\right) = \eta(X) = X^\top \beta$$

Likelihood:

$$L(\beta) = \prod_{i=1}^{n} \pi(X_i)^{Y_i}(1-\pi(X_i))^{1-Y_i}$$

Estimation:

$$\hat{\beta} = \arg\max_{\beta} \ell(\beta)$$

where $\ell(\beta)$ is the log-likelihood.

Data Description and Study Design

Data Source:

- Clinical dataset collected from four hospitals
- Observational study with convenience sampling

Important Implication:

- Estimates are **associational**, not causal
- Potential selection bias must be acknowledged

Variables:

- Continuous: physiological measurements (e.g., cholesterol)
- Categorical: diagnostic indicators (e.g., chest pain type)

Variable	**Explanation**	**Min**	**Max**
Age	Age of the patient	29	77
Sex	(1 = male, 0 = female)	0	1
cp	Chest Pain Type	0	3
trestbps	Resting Blood Pressure	94	200
chol	Serum Cholesterol	126	564
fbs	Fasting Blood Sugar (= 1 if ≥ 120)	0	1
restecg	Resting Electrocardiographic Results	0	2

Table 1: Description of Variables (Part 1)

Variable	Explanation	Min	Max
thalach	Maximum Heart Rate Achieved	71	202
exang	Exercise-Induced Angina	0	1
oldpeak	ST Depression Induced by Exercise	0	6.2
slope	Slope of Peak Exercise ST Segment	0	2
ca	Number of Major Vessels	0	4
thal	Thalium Scintigraphy	0	3
target	Diagnosis of Heart Disease	0	1

Table 2: Description of Variables (Part 2)

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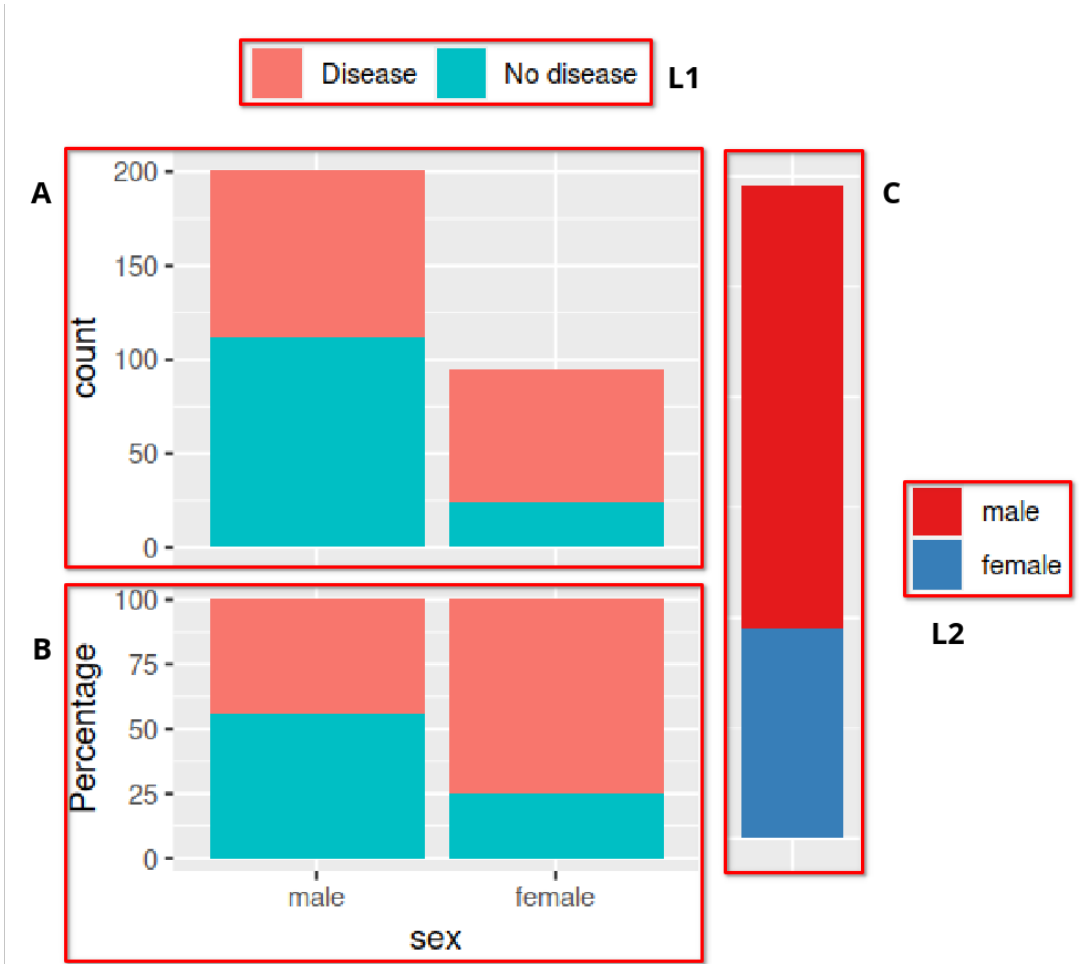
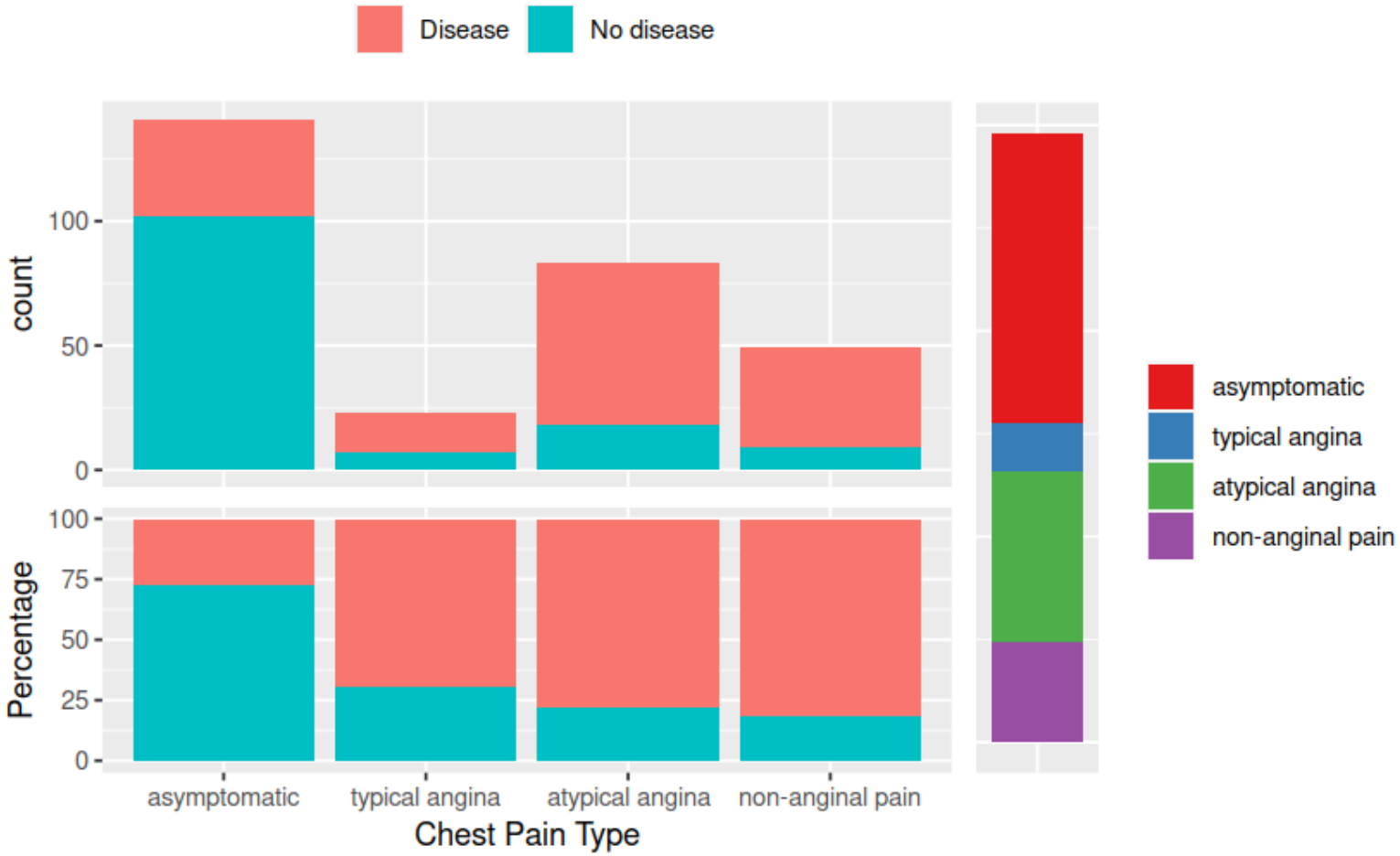
1. Categorical Variables

- The following charts provide insight about relationships between our categorical variables and the target variable.
- In figures **A** and **B**, the count and percentage of each of the categories of our predictor is compared to the target class; in part **C** the number of observations in each category is compared to each other. **L1** and **L2** are legends for the plot.



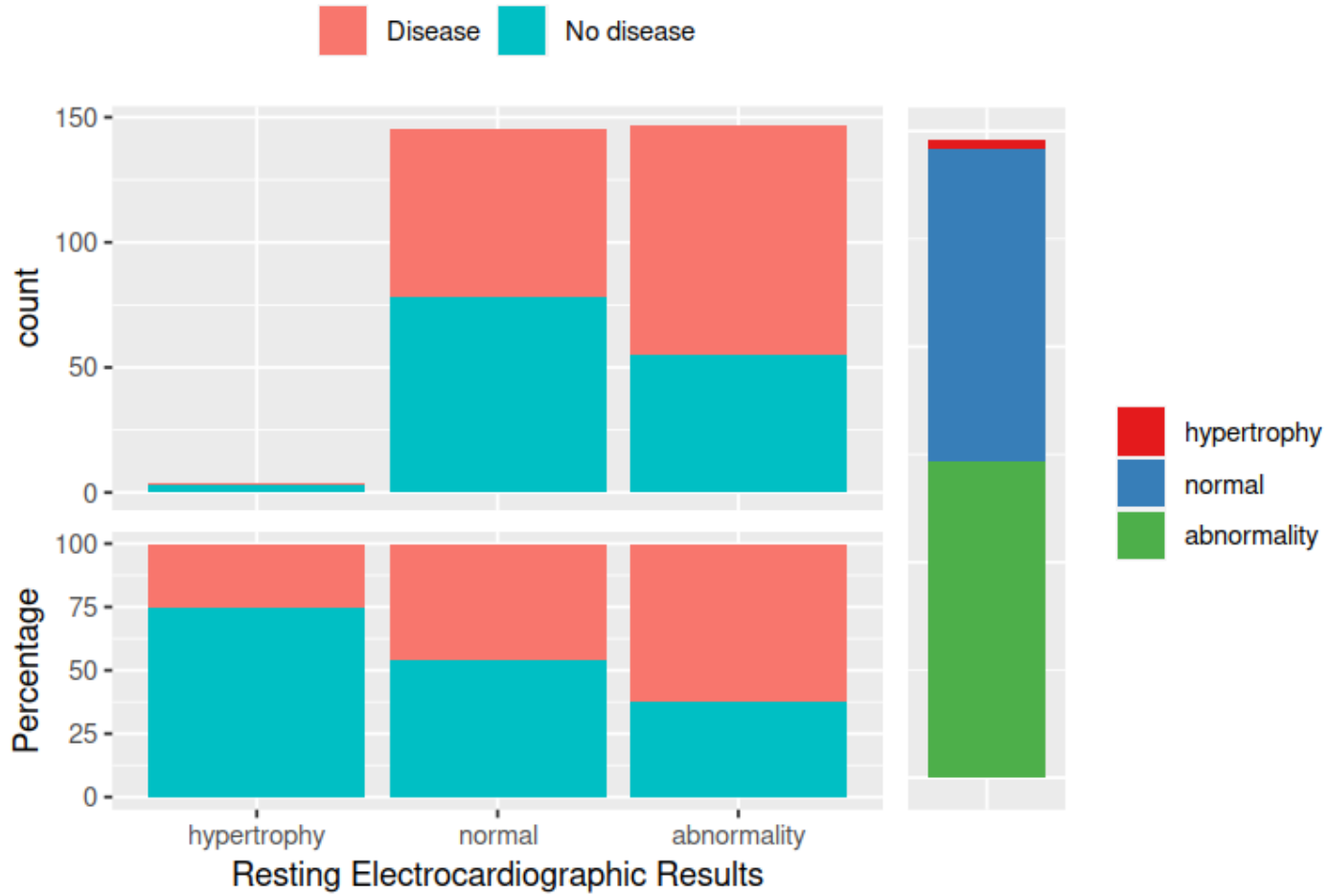

Disease
No disease
count
100
50
0
Percentage
100
75
50
25
0
asymptomatic
typical angina
atypical angina
non-anginal pain
Chest Pain Type
asymptomatic
typical angina
atypical angina
non-anginal pain

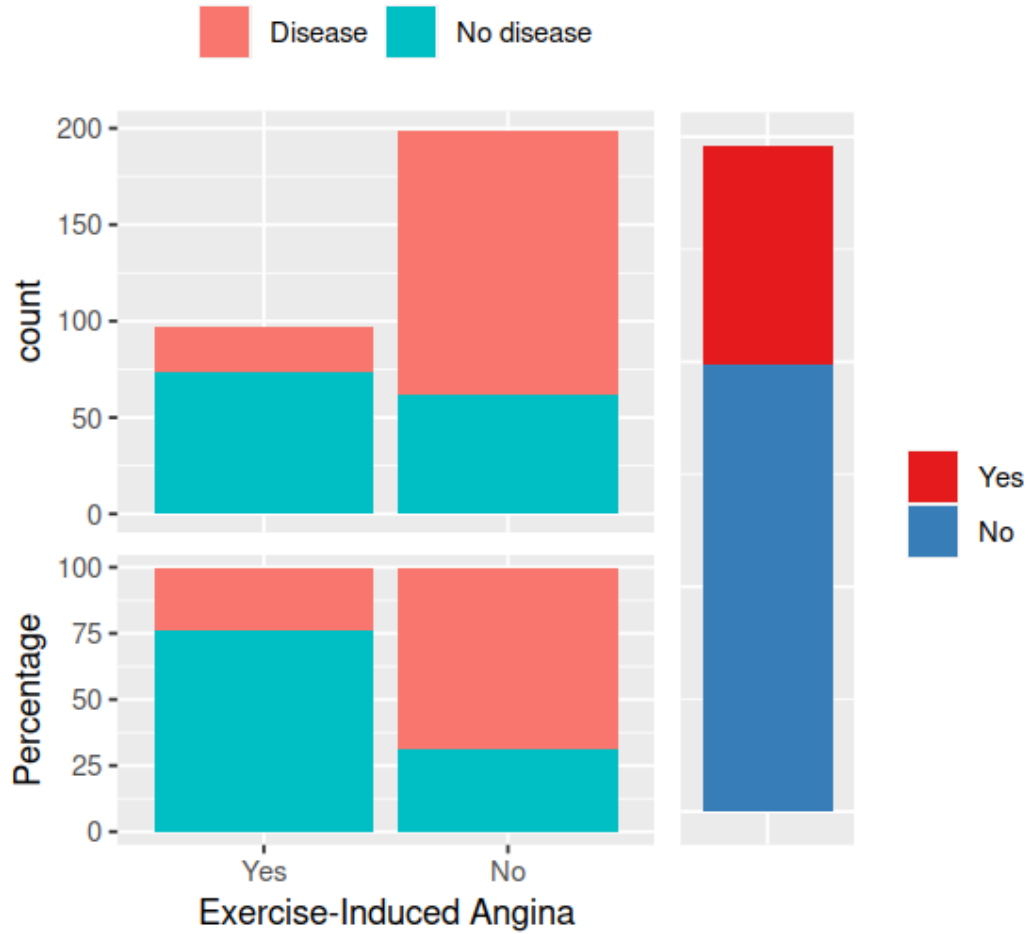
Observed Patterns:

- Strong separation in distribution of `cp`, `thal`, and `slope`
- Evidence of nonlinearity in `ca` and `oldpeak`
- Potential interactions:
  - Sex $\times$ physiological variables
  - Exercise-induced variables $\times$ cardiac stress indicators

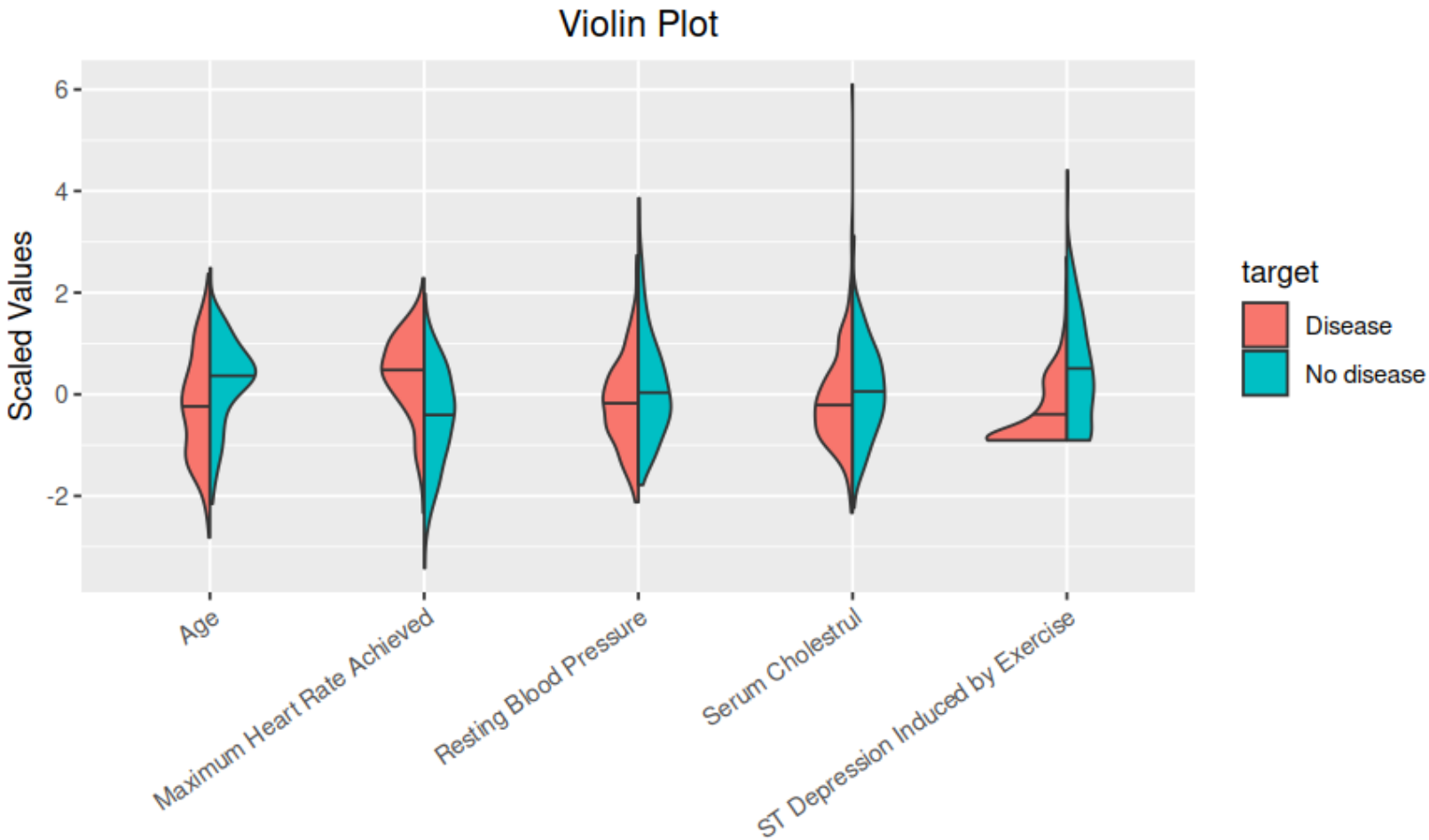
Implication:

- Motivates inclusion of interaction and nonlinear terms


Disease
No disease
150
100
50
0
count
100
75
50
25
0
Percentage
hypertrophy
normal
abnormality
Resting Electrocardiographic Results
hypertrophy
normal
abnormality


Disease
No disease
count
200
150
100
50
0
Percentage
100
75
50
25
0
Yes
No
Exercise-Induced Angina
Yes
No

2. Numerical Variables



3. Pairs Plot - Correlation Matrix for Quantitative Predictors

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Data Preprocessing and Quality Control

Data Cleaning Steps:

- Removal of duplicate observations ($n = 723$ removed)
- Removal of invalid categorical encodings
- Final sample size: $n = 296$

Standardization:

$$X_j^{\text{scaled}} = \frac{X_j - \mu_j}{\sigma_j}$$

- Ensures numerical stability of MLE
- Required for penalized methods (LASSO)

Remark: Standardization does not affect interpretability of signs, only scale.

Data Standardization

- We scaled all the 6 continuous variables (”age”, ”trestbps”, ”chol”, ”thalach”, ”oldpeak”, ”ca”) using the Z-score standardization technique.
- Standardized variables can contribute to better numerical stability in the computations involved in regression analysis.
- Standardization helps in reducing the impact of multicollinearity.
- When using regularization techniques like Ridge or Lasso regression, scaling becomes importantsince the penalty term is influenced by the scale of the variables.

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Logistic regression

- Logistic regression was used since the response variable ("target") was binary.
- The logit link function was used (the probit model performed slightly worse):

$$\eta = logit(p) = log(\frac{p}{1-p})$$

- We performed three main processes to build logistic regression models for our dataset:
  1. Variable selection with the full model
  2. Variable selection with the reduced model
  3. Variable selection via Lasso regression

Model Selection Framework

Challenge:

- Large model space with interactions and nonlinear terms

Strategies Used (bias-variance tradeoff)

- Stepwise selection (AIC-driven)
- Penalized likelihood (LASSO)
- Cross-validation for predictive risk

LASSO Regularization

Estimator:

$$\hat{\beta}^{\text{lasso}} = \arg\min_{\beta} \{-\ell(\beta) + \lambda \|\beta\|_1\}$$

Properties:

- Performs variable selection
- Shrinks coefficients toward zero
- Handles multicollinearity

Tuning:

- λ selected via cross-validation

(Process 1): Building from the full model

- We started with the full linear model which consists of all 13 predictors $\eta = \sum_{j=1}^{13} \beta_j X_j$

- We found that "ca" had a quadratic relationship with our response via the Wald test which we added to our full model. **(Model 1)**

- From scientific literature, we found that certain variables in our predictors were correlated and hence we added their corresponding interaction terms to the basic full model. **(Model 2)**
  - Females tend to have have lower blood pressure
  - Males tend to have higher levels of resting blood sugar

(Process 1): Other full models with two-way interactions

We explored other methods to decide which two-way interaction terms to include in our model:

- Backward stepwise selection on Full Model with all two-way interaction terms **(Model 3)**
- Forward stepwise selection with the maximum endpoint model as the Full model with all two-way interaction terms
  - Starting from the Model 2. This gave **(Model 4)**.
  - Starting from the intercept model. This gave **(Model 5)**.

(Process 2): Building from the reduced model

- From the basic full model, we used the Wald test to remove insignificant coefficients and added a quadratic term for the predictor "ca" (Wald test) **(Model 6)**.
- We added all possible two-way interactions to Model 6 to generate **Model 7**.
- To explore the effect of the intercept, we removed the intercept from Model 7 to generate **Model 8**.

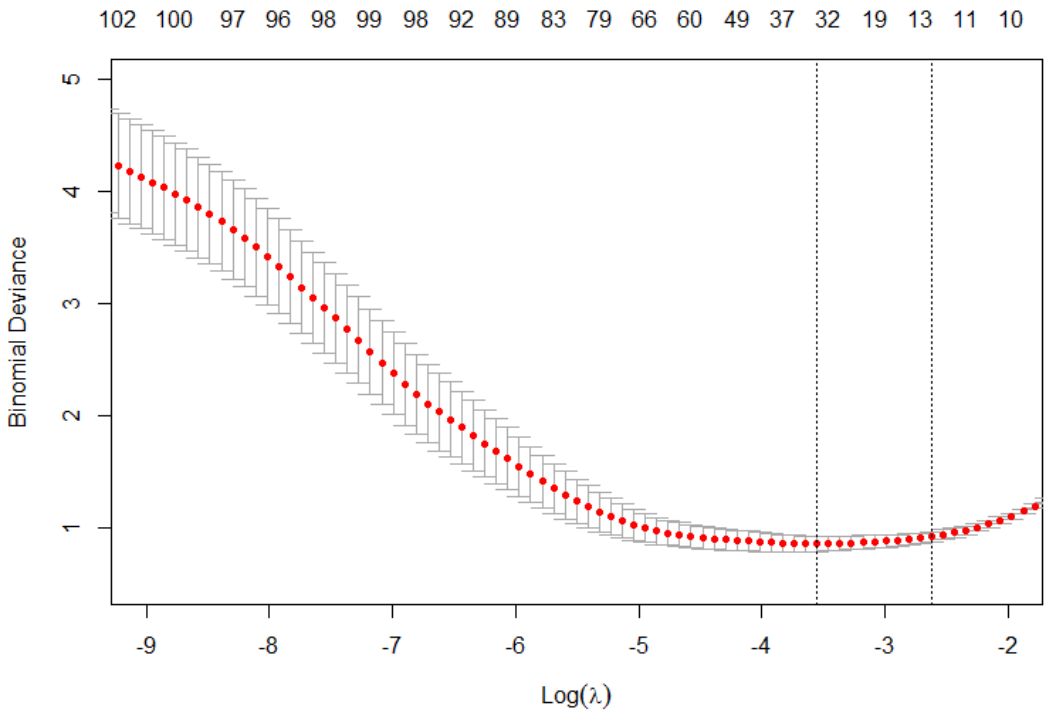
(Process 2): Other reduced models with two-way interactions

- We explored other methods to decide which two-way interaction terms to include in our model.
- Backward stepwise selection on the Reduced model with all possible two-way interaction terms **Model 9**
- Forward stepwise selection on with the maximum endpoint model as the reduced model with all possible two-way interaction terms
  - Starting from Model 6.
  - Starting from the intercept model
  - Both steps generated the **same** model which we named **Model 10**
- From scientific literature we found that "sex" and "trestbps" was correlated and hence we added their interaction term to Model 6 to generate **Model 11**.

(Process 3): Lasso regression

- In this section, we made use of lasso regression technique to perform variable selection on the data with all the 2-way interaction terms and ca^2. **(Model 12)**
- The Cross-Validation method offered $\lambda = 0.01977$ to be optimal, which resulted in 41 variables, and %58 of explained deviance
- The ridge penalty shrinks the coefficients of correlated predictors towards each other while the lasso tends to pick one of them and discard the others. This is why we have preferred LASSO over Ridge to conduct automatic variable selection.

(Process 3): Lasso regression



Over-Dispersion Check

- We checked for existence of over-dispersion, and we found that the dispersion parameter is less than 1.
- Hence the model is not suspect, and we did not use quasi-binomial models.

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Model comparison metrics

The following metrics were investigated for model comparison:

- Residual deviance
- Akaike information criterion (AIC)
- McFadden's Pseudo-R^2
- Likelihood ratio test (comparison to the minimal model)
- Mean-squared prediction error (MSE)
  - Computed via cross-validation with 10 folds for 10 iterations

Candidate Models

Metrics for Model Comparison

Model	Deviance	AIC	q	R2	lrt_pval	MSE
Model 1	178.21	218.21	19	0.56	3.09e-38	0.12
Model 2	174.19	224.19	24	0.57	2.18e-36	0.12
Model 3	0.00	118.00	58	1.00	3.79e-54	0.22
Model 4	0.00	106.00	52	1.00	8.61e-57	0.18
Model 5	145.44	199.44	26	0.64	4.86e-41	0.12
Model 6	193.34	217.34	11	0.53	5.52e-40	0.11
Model 7	141.91	265.91	62	0.65	3.63e-27	0.18
Model 8	141.91	265.91	61	0.65	8.03e-28	0.18
Model 9	193.34	217.34	11	0.53	5.52e-40	0.11
Model 10	186.49	214.49	13	0.54	4.22e-40	0.11
Model 11	191.77	217.77	12	0.53	1.19e-39	0.11
Model 12	236.62	0.00	41	0.42	6.15e-18	0.66

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Final model: reason for selection

- The final model we selected is **Model 5** (forward stepwise algorithm from intercept model)
- The model contains the following **coefficients** (10): thal, ca, cp, slope, sex, ca^2, oldpeak, trestbps, thalach, chol
- The model contains the following **two-way interactions** (7): thal:ca, slope:trestbps, thal;oldpeak, slope:oldpeak, slope:sex, sex:oldpeak, trestbps:chol

Final model: confidence intervals

Confidence intervals - Part 1

	2.5 %	97.5 %
(Intercept)	-8.2715	-2.3654
factor(thal)normal	-20.1729	215.7082
factor(thal)reversable defect	0.9988	3.1807
ca	1.7209	3.6448
factor(cp)atypical angina	-3.8968	-1.4104
factor(cp)non-anginal pain	-2.6526	-0.0844
factor(cp)typical angina	-5.0925	-1.5796
factor(slope)flat	2.7296	8.6153
factor(slope)upsloping	3.3983	18.2094
factor(sex)male	3.0715	9.0023
I(ca^2)	-1.4479	-0.4077
oldpeak	-6.1414	-1.1812
trestbps	-0.1417	1.1154
thalach	-1.3023	-0.1542
chol	-0.0137	1.0360

Final model: confidence intervals

Confidence intervals - Part 2

	2.5 %	97.5 %
factor(thal)normal:ca	-22.0445	309.4746
factor(thal)reversable defect:ca	-2.1022	-0.1259
factor(slope)flat:trestbps	-0.3480	1.5094
factor(slope)upsloping:trestbps	-6.8918	-1.2133
factor(thal)normal:oldpeak	-2.1616	16.4485
factor(thal)reversable defect:oldpeak	0.5519	3.4193
factor(slope)flat:oldpeak	1.0176	4.5627
factor(slope)upsloping:oldpeak	0.2300	7.1003
factor(slope)flat:factor(sex)male	-7.0118	-1.1682
factor(slope)upsloping:factor(sex)male	-21.2604	-4.5967
factor(sex)male:oldpeak	0.4662	4.3731
trestbps:chol	-0.0837	0.9121

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Conclusion

- In order to double-check the relations found between the variables from the data visualization, we made use of the interaction models to further verify those interactions in model selection techniques (backward, forward, lasso, etc.)
- Based on our analysis of the heart disease dataset, conducted the process of data exploration, preprocessing, and model building. We considered various logistic regression models, including those with interaction terms and exponents to consider the relations of the predictors as well. The models were evaluated using different metrics such as deviance, AIC, pseudo-R^2, likelihood ratio test, and mean-squared prediction error.
- After comparison of these models, we selected the final model based on its performance metrics and the number of variables it had, but one can use other models based on different interests.
- In conclusion, the logistic regression model provides insights into the relationships between various patient attributes and the likelihood of heart disease. The selected model can serve as a tool for understanding and predicting heart disease based on a given new patient. Further research and validation may enhance the robustness of our findings.

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[1] Dataset: Heart Disease Dataset (Public Health Dataset)
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[4] Annette J. Dobson, Adrian G. Barnett (2018), An Introduction to Generalized Linear Models, Fourth Edition: Spring New York. Wickham and Grollemu; CRC Press

Thank You for your attention!

Questions...