

Survival and Prediction of Heart Disease Events

Cristina Iudica
Sofia Mongardi
Francesco Morettini
Davide Raffealli

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POLITECNICO
MILANO 1863



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What is Coronary Heart Disease?



Coronary Heart Disease

CHD develops when main arteries become clogged and start to harden and narrow. Untreated CHD may result in patients developing Heart Failure.

Coronary Angiography

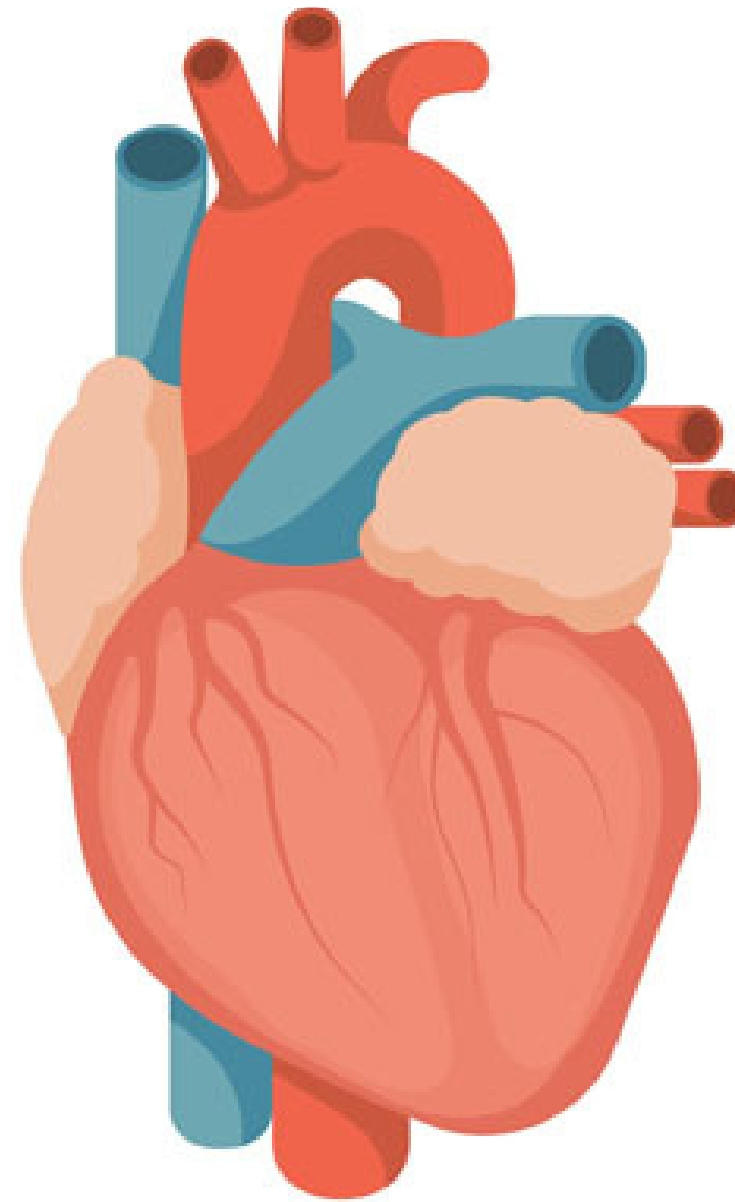
Angiography is an invasive medical procedure that uses contrast dye and x-ray in order to visualize the inside of blood vessels and detect blockages in the main arteries.

When to do Coronary Angiography

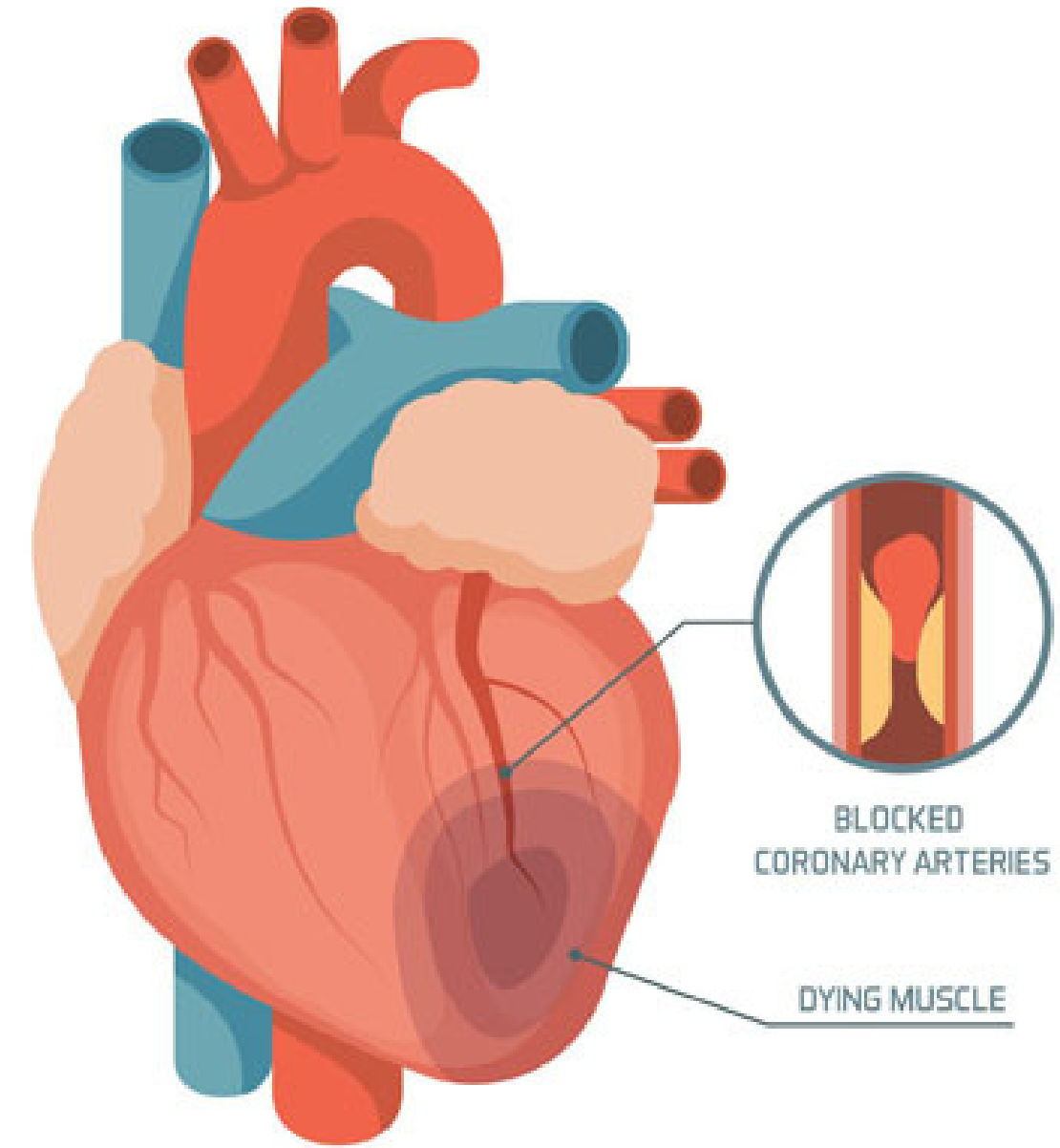
Your doctor may recommend it when you have increasing chest pain or other blood vessel problems.

What is Heart Failure?

Heart failure occurs when the heart is too weak or stiff and is not able to pump enough blood in order to maintain the normal blood flow necessary to meet the body's needs.



HEALTHY HEART



HEART FAILURE

Questions of interest

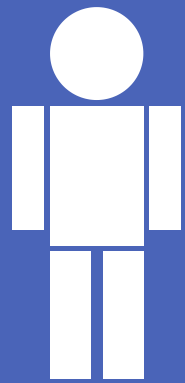
Are there variables that can help explain if a patient is at risk of developing coronary heart disease?

How different hospitals may affect the diagnosis of a coronary heart disease?

Once patients have been diagnosed with heart failure, which variables affect their survival? Can those variables successfully predict a death event?



Coronary Heart Disease Dataset



918 Patients
undergoing Coronary
Angiography



Coronary angiograms were
considered abnormal, i.e.
presence of CHD, if there was
greater than 50% luminal
narrowing of any major arteries



4 Hospitals

- Cleveland
- Hungary
- Long Beach
- Switzerland

Patient Information

- Age
- Sex
- Hospital

Clinical Data

- Resting Blood Pressure
- Max Heart Rate
- Peak (ST Segment)
- Fasting Blood Sugar
- Resting ECG
- Exercise Angina
- Chest Pain Type

Outcome of Interest
Presence of Coronary Heart Disease

Chest Pain



Typical Chest Pain

It consists of substernal chest pain or discomfort caused by exertion or stress and relieved by rest.

Atypical Chest Pain

It applies when not all of the symptoms for typical angina are present and therefore is also called probable angina.

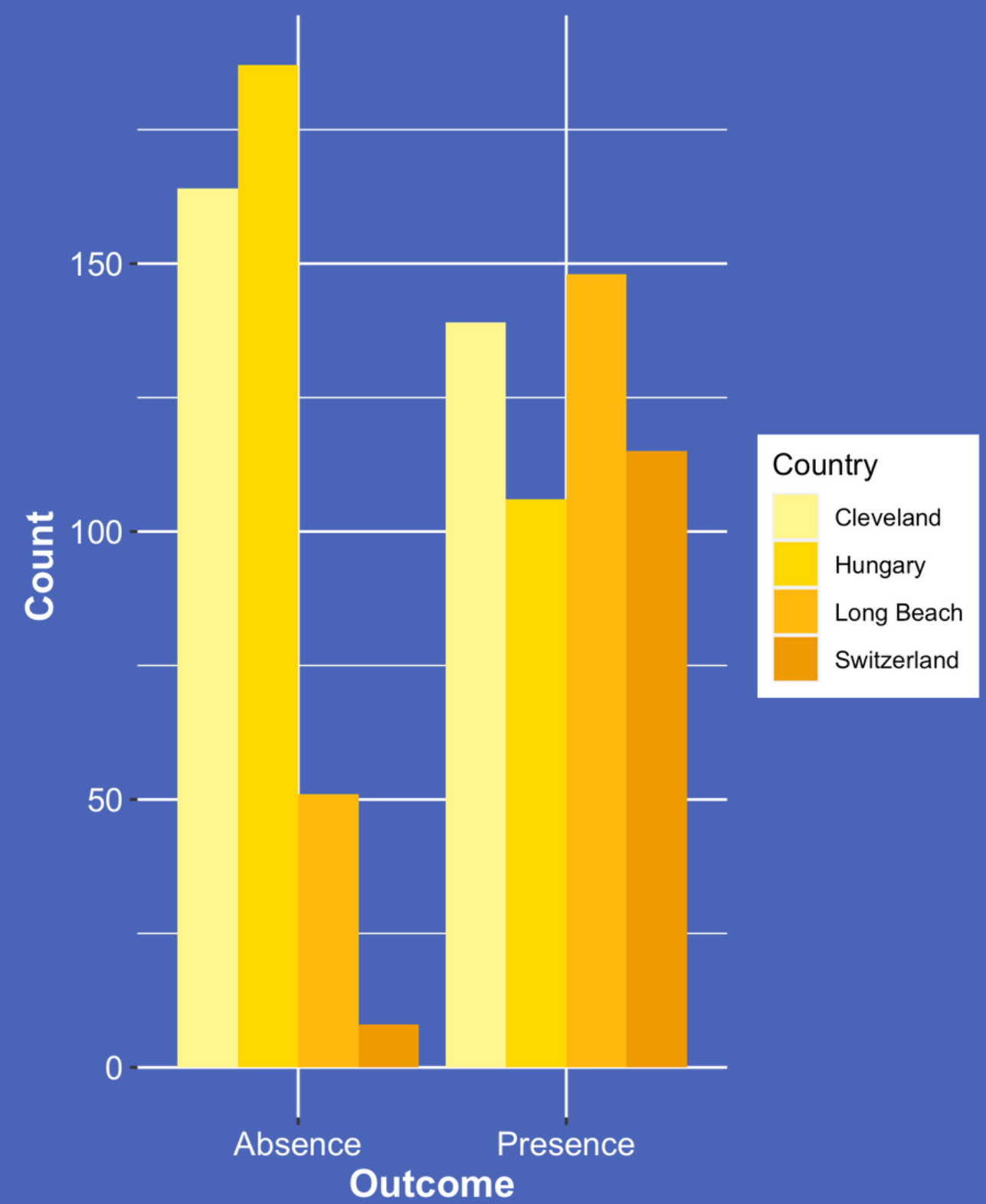
Non-anginal Chest Pain

It often feels like angina and is usually related to problems with the esophagus, lung conditions or chest bones.

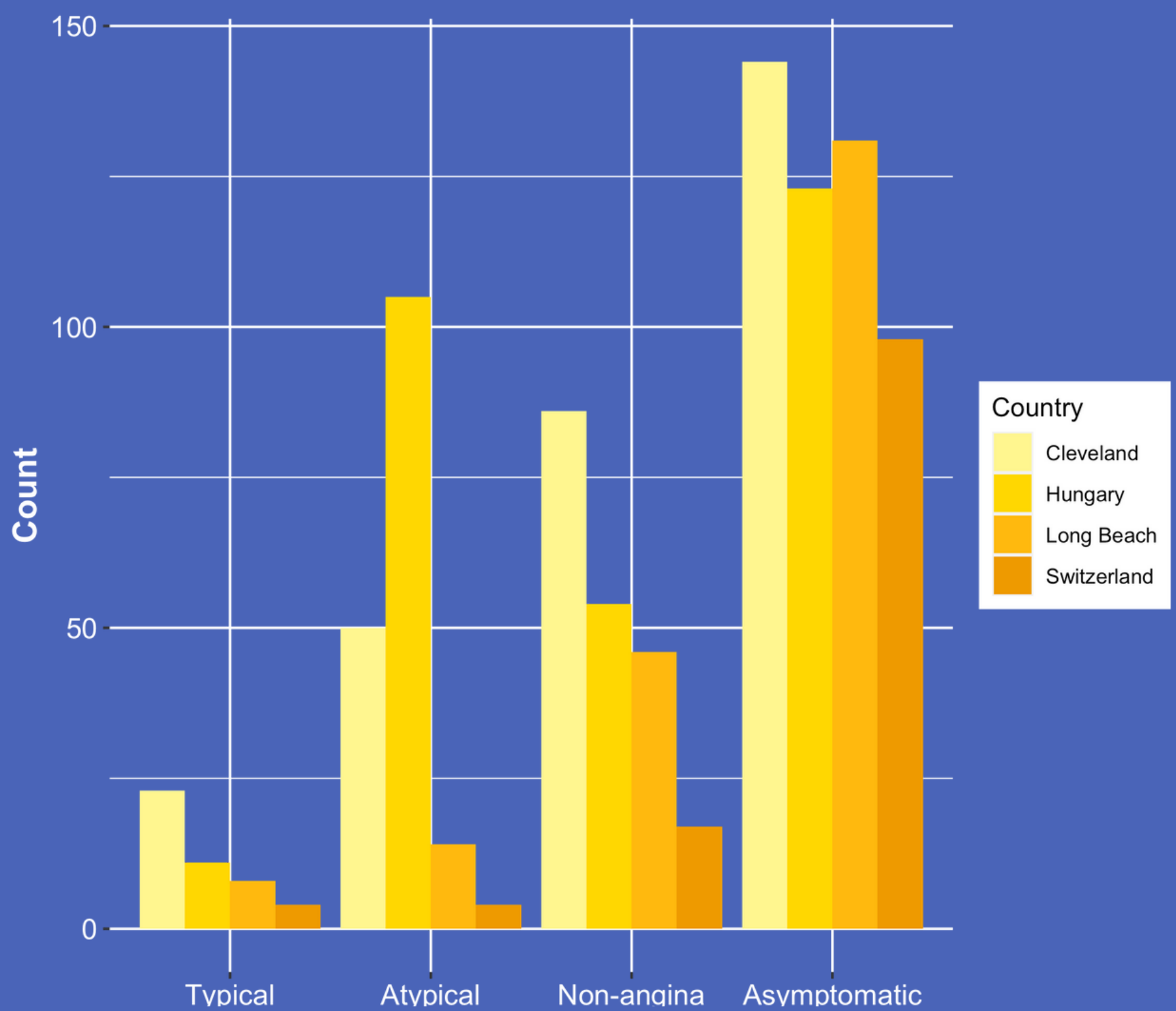
Asymptomatic

Patients do not feel any chest pain or discomfort. It is often related to silent myocardial infarction which is most likely to occur in middle-aged man.

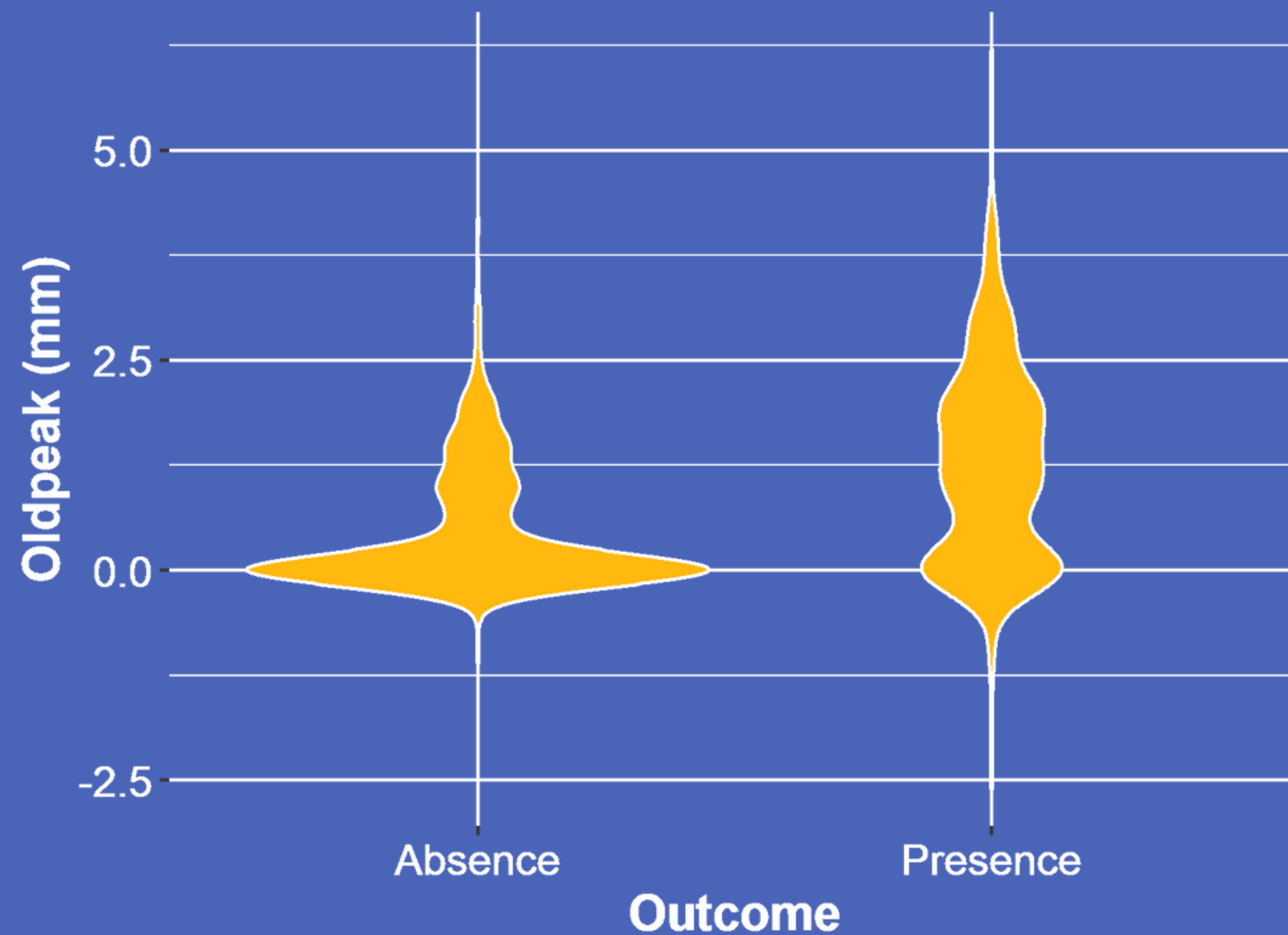
Presence of Heart Disease
by Country



Chest Pain Type by Country

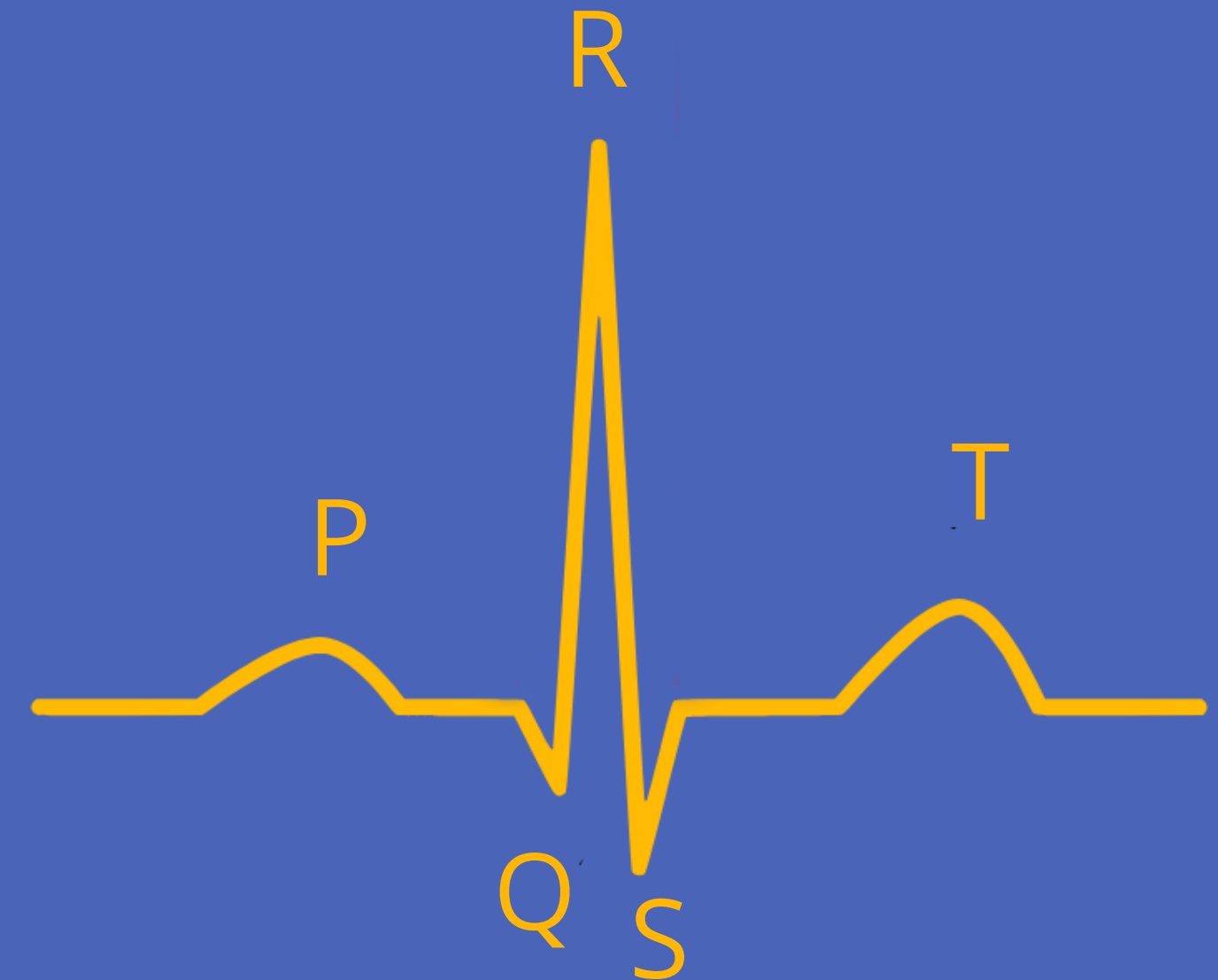


ST Segment



ST depression or elevation induced by exercise relative to rest.

ST segment as a categorical variable. Values between -1 and 1 are coded as Normal. Otherwise as Abnormal.



Generalized Mixed Effects Model

$$\text{logit}(p_{ij}) = \beta_0 + \beta_1 \text{MaxHeartRate}_{ij} + \beta_2 \text{OldPeak}_{ij} + \beta_3 \text{FastingBloodSugar}_{ij} + \beta_4 \text{ExerciseAngina}_{ij} + \beta_5 \text{Age}_{ij} + \beta_6 \text{Sex}_{ij} + \beta_7 \text{ChestPain}_{ij} + b_j \quad b_j \sim N(0, \sigma_b^2)$$

$$i = 1, 2, \dots, 918$$

$$j = 1, 2, 3, 4 \text{ Countries}$$

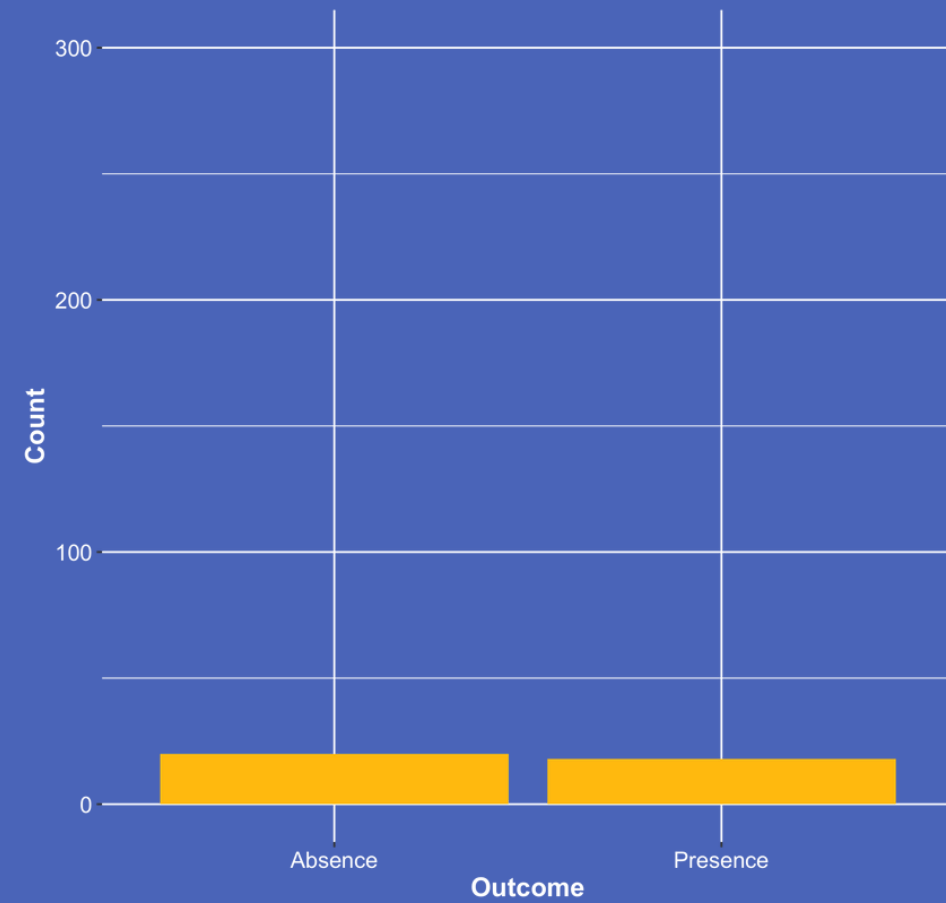
Variable	Estimate	CI Lower	CI Upper	Exponential
Intercept	-0.496	-2.751	1.758	-
Max Heart Rate	-0.011	-0.019	0.002	0.989
Peak (Abnormal)	1.084	0.682	1.486	2.956
Fasting Blood Sugar (High)	0.657	0.147	1.167	1.929
Exercise Angina (Yes)	0.990	0.587	1.393	2.691
Age	0.029	0.006	0.052	1.029
Sex (Male)	1.278	0.805	1.751	3.589
Chest Pain (Presence)	-1.713	-2.081	1.344	0.180

Protective Factor

Risk Factors



Protective Factor



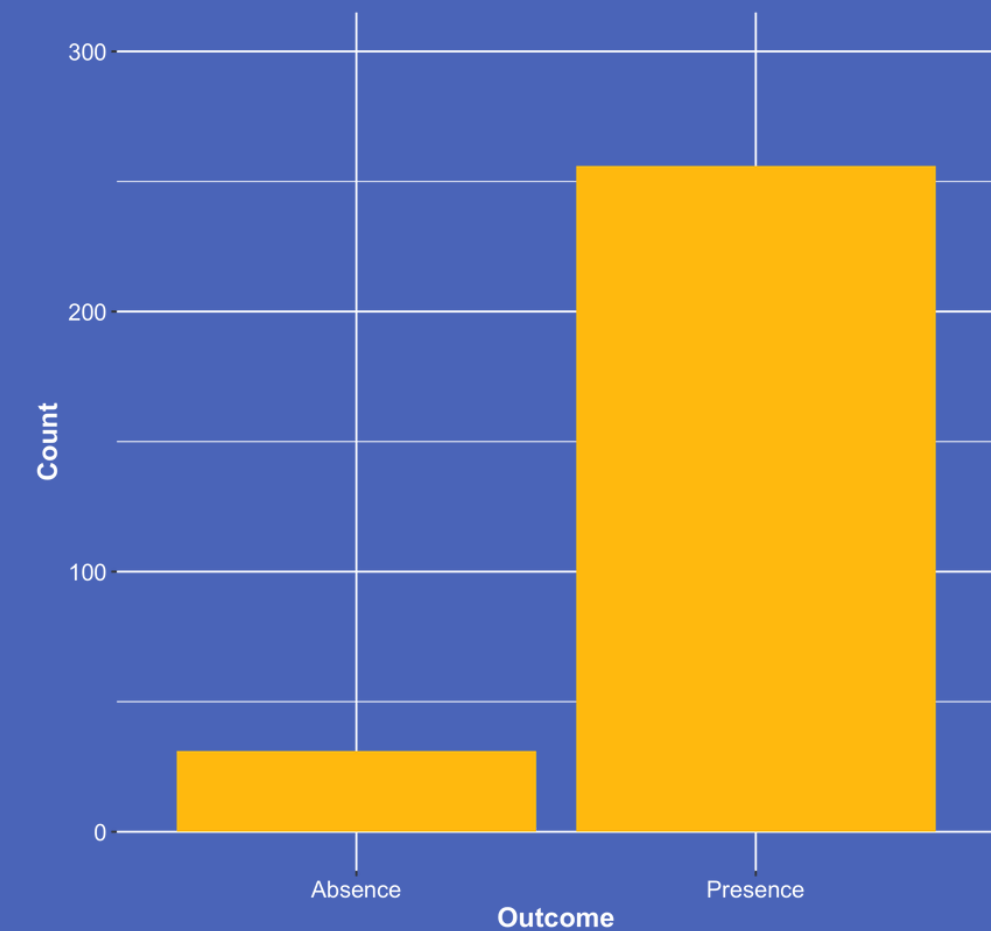
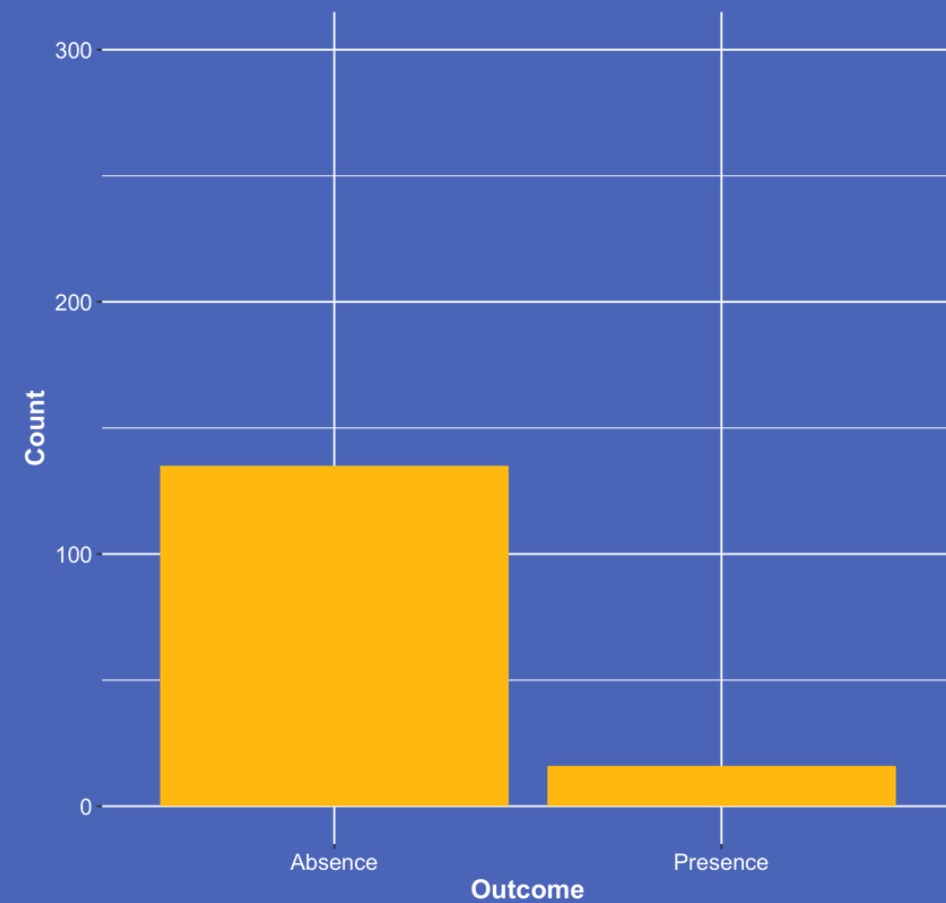
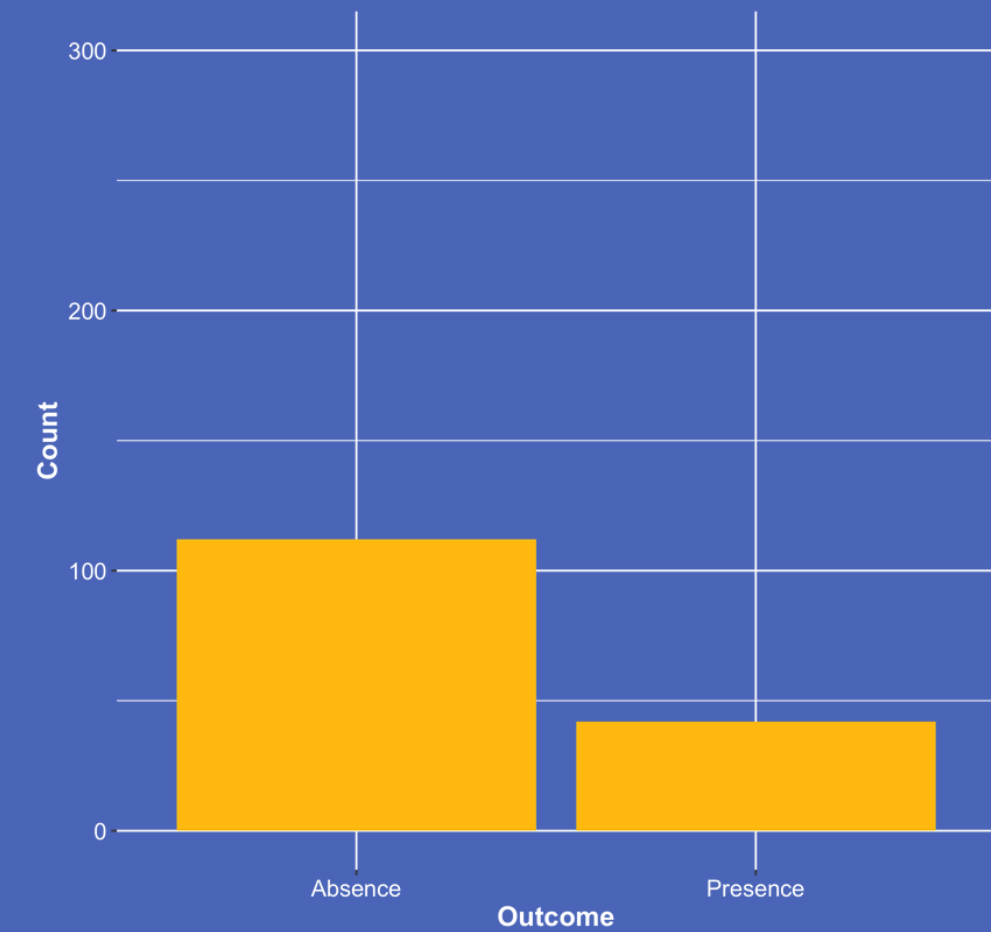
**No Exercise Angina and
Typical Angina Chest Pain**

**No Exercise Angina and
Non-angina Chest Pain**

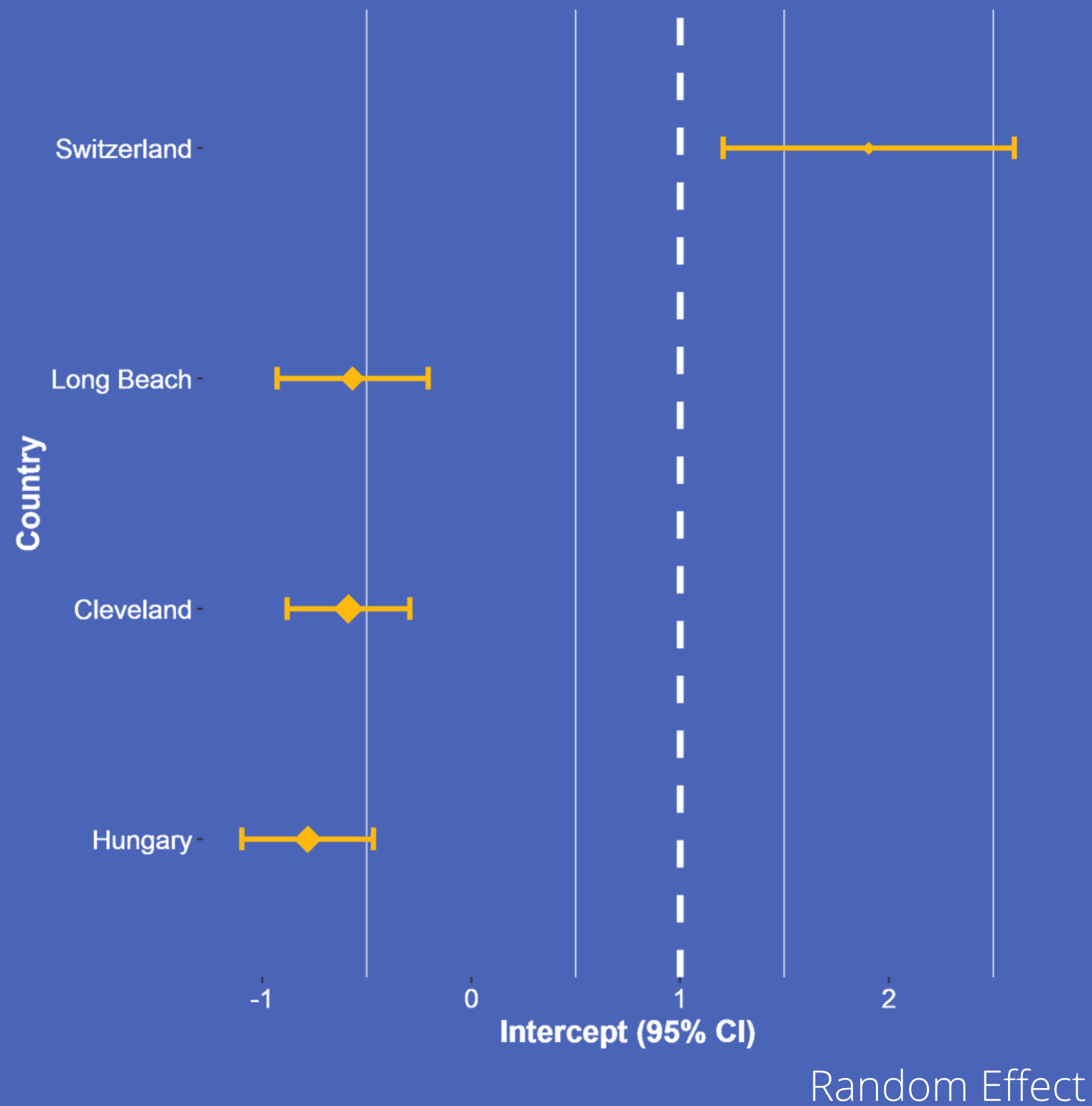
**Chest Pain
Protective?**

**No Exercise Angina and
Atypical Chest Pain**

**Exercise Angina and No
Chest Pain**



Variability between Countries



VPC = 28.5%



As shown in the plot, there is a huge variability between the countries.

Data from Switzerland suggests there may be a difference in protocols as to when the coronary angiography should be carried out.

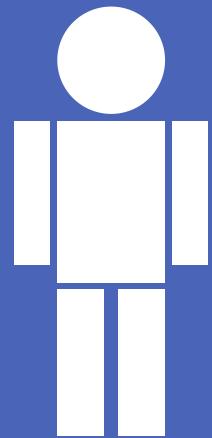
It has been shown how some features (exercise angina, ST segment) explain the risk of having coronary heart disease.

But in many cases, patients are not diagnosed with coronary heart disease until they have a heart failure due to the possible lack of classic symptoms.

Heart failure represents one of the most common complications of heart disease. Narrowed arteries may limit your heart's supply of oxygen-rich blood, resulting in weakened heart muscle.



Heart Failure Dataset



299 Patients suffering from Heart Failure



Faisalabad Institute of Cardiology
Allied Hospital in Faisalabad
(Pakistan)

Patient Information

- Age
- Sex
- Smoking
- Diabetes

Clinical Data

- Anemia
- Creatinine Phosphokinase
- Ejection Fraction
- Blood Pressure
- Platelets
- Serum Creatinine
- Serum Sodium

Outcome of Interest

- Death Event
- Time-to-event

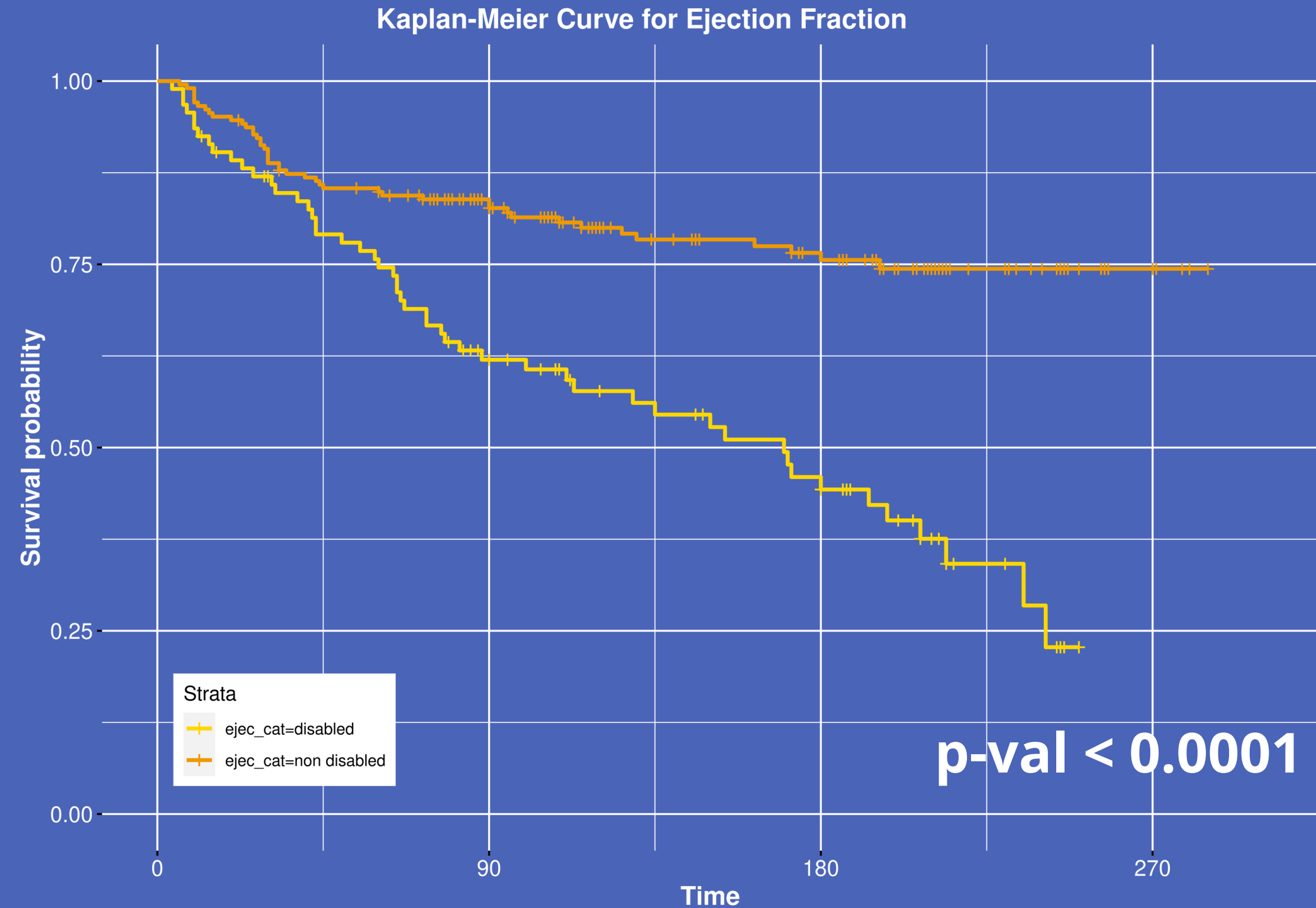
Ejection Fraction

Percentage of how much blood is pumped out of the left ventricle with each contraction. As the heart muscle becomes more stiff and thick, less blood can enter the ventricle.

Reduction of EF is strictly connected to HF

- Normal LVEF >50%
- Reduced LVEF 30%-50%
- Low LVEF <30%

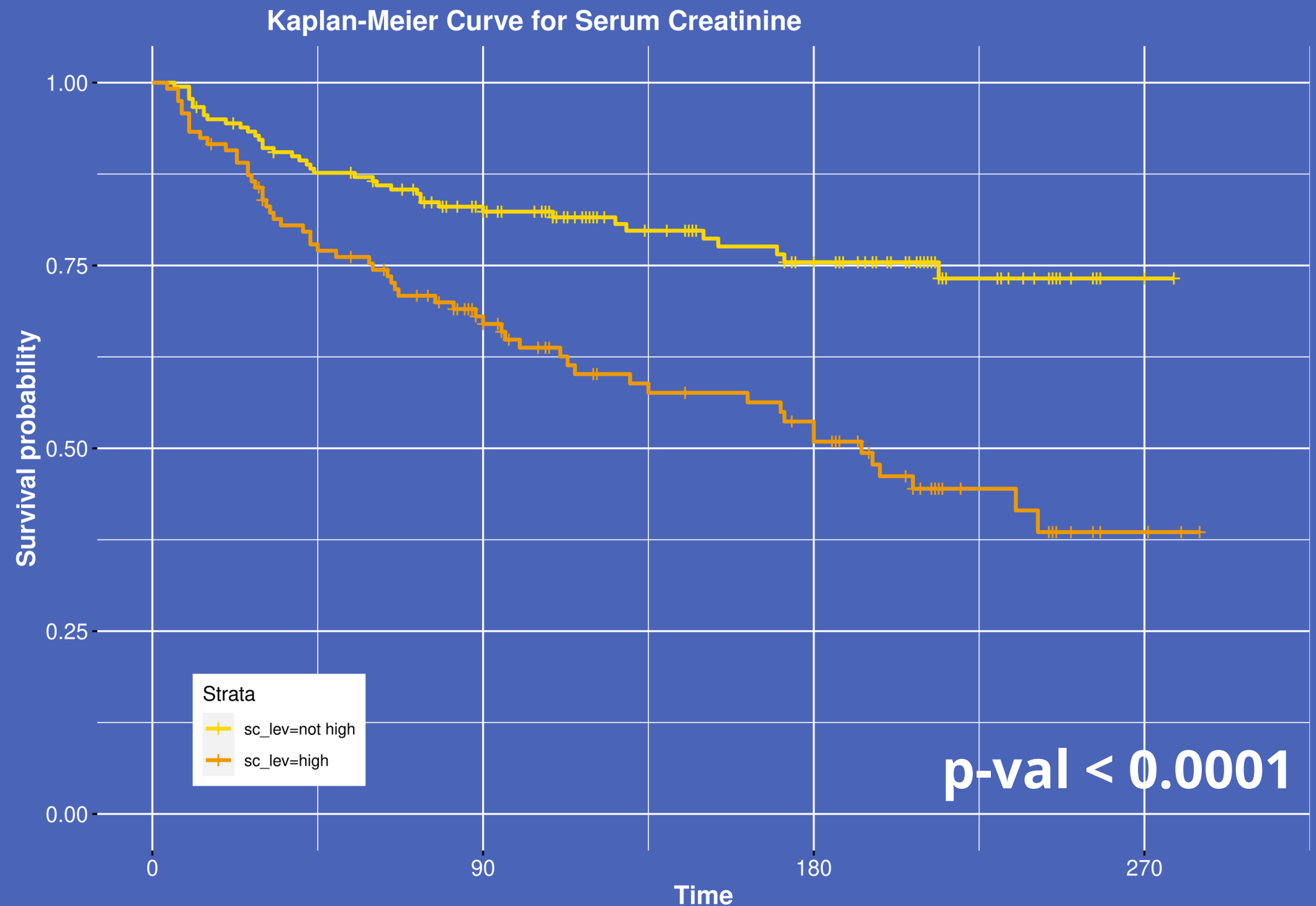
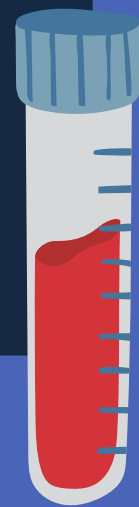
**LVEF < 30% is a
threshold for
disability benefits**



Serum Creatinine Levels

Levels of creatinine in the blood. It is a measure of how well your kidneys are working. Patients with severe heart failure are usually prescribed ACE inhibitor as medication that can increase SC concentration.

Normal levels for women are **0.5 mg/dL to 1.0 mg/dL**
Normal levels for men are **0.7 mg/dL to 1.2 mg/dL**.



Cox Model

Variable	Hazard Ratio	CI Lower	CI Upper	P-val <i>Cox.zph()</i>
Age	1.047	1.028	1.066	0.552
Blood Pressure (High)	1.702	1.124	2.575	0.767
Ejection Fraction (Low)	3.041	2.001	4.623	0.002
Serum Creatinine (High)	1.813	1.189	2.765	0.145

PH assumption is not satisfied by Ejection Fraction

Two Baseline Hazards for the different levels of Ejection Fraction

Stratified Cox Model

Risk Factors



Variable	Hazard Ratio	CI Lower	CI Upper	P-val <i>Cox.zph()</i>
Age	1.049	1.030	1.069	0.89
Blood Pressure (High)	1.721	1.136	2.607	0.77
Serum Creatinine (High)	1.814	1.190	2.764	0.39

Prediction - Logistic Regression

Can the variables in the Cox Model be used to determine whether patients diagnosed with heart failure will survive?

$$\text{logit}(p_i) = \beta_0 + \beta_1 \text{Age}_i + \beta_2 \text{BloodPressure}_i + \beta_3 \text{EjectionFraction}_i + \beta_4 \text{SerumCreatinine}_i$$

Variable	Estimate	Odds Ratio	P-value
Intercept	-5.255	-	7.12×10^{-10}
Age	0.054	1.055	1.85×10^{-5}
Blood Pressure (High)	0.383	1.467	0.192
Ejection Fraction (Low)	1.642	5.165	4.84×10^{-8}
Serum Creatinine (High)	0.985	2.678	5.4×10^{-4}



Risk Factors



Model Accuracy

Empirical Threshold = 0.321



Predicted Dead

Observed Dead

Observed Alive

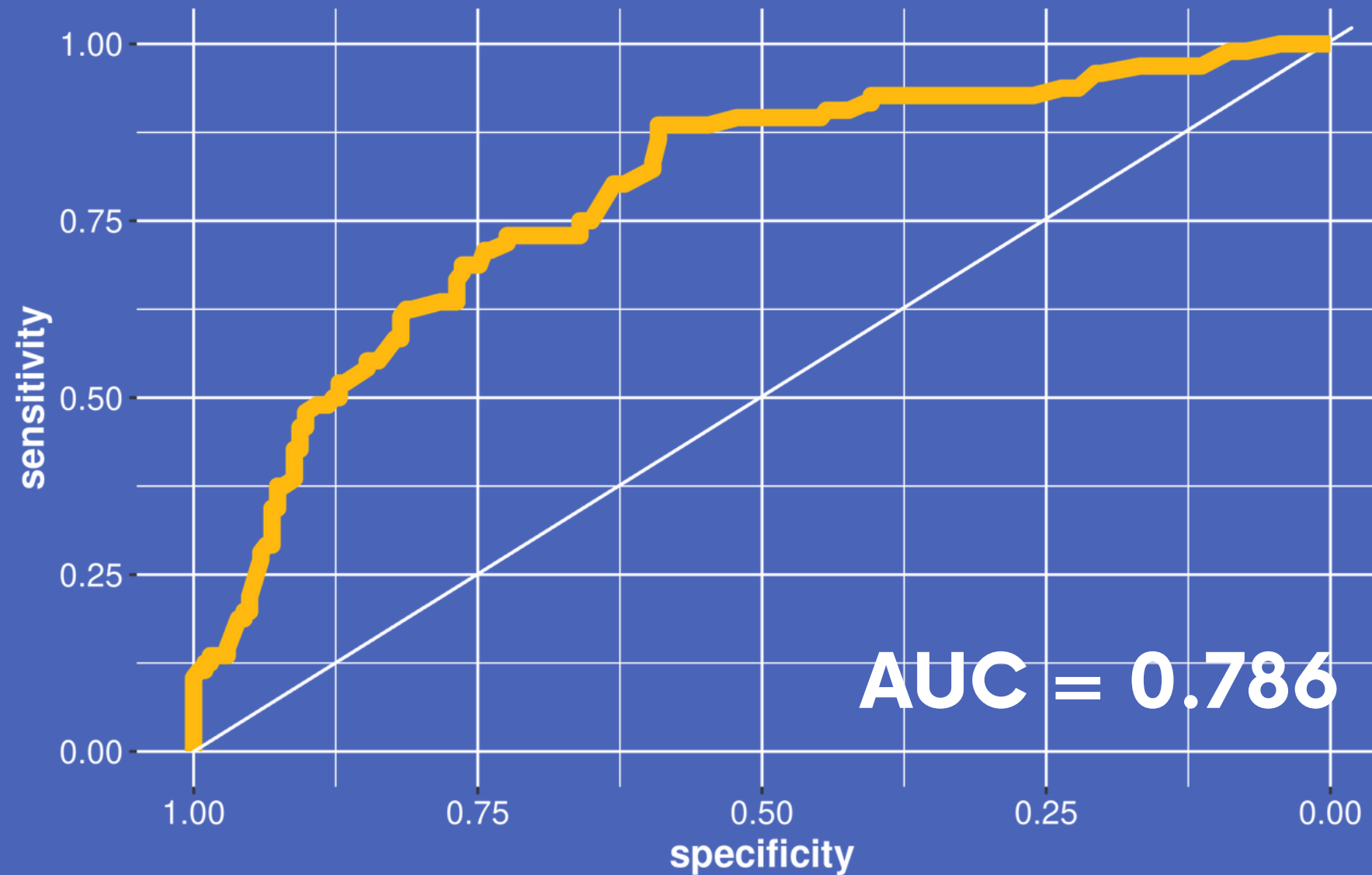
68

53

Predicted Alive

28

150



Sensitivity = 0.708

Specificity = 0.739

Accuracy = 0.729



Conclusions

- From our analysis, ST segment, Exercise Angina and Fasting Blood Sugar are the main risk factors for developing Coronary Heart Disease.
- The presence of any kind of Chest Pain appears to be a protective factor, suggesting CHD may go unnoticed unless proper tests are carried out.
- There is variability in the outcome between hospitals indicating there may exist a difference in protocols.

- Once patients have been diagnosed with Heart Failure, Serum creatinine levels, Age and High Blood Pressure are the main risk factors that will shorten their survival.
- We have different survival curves for patients with disability benefits, low ejection fraction, and no benefits.



**Thanks for your
Attention!**