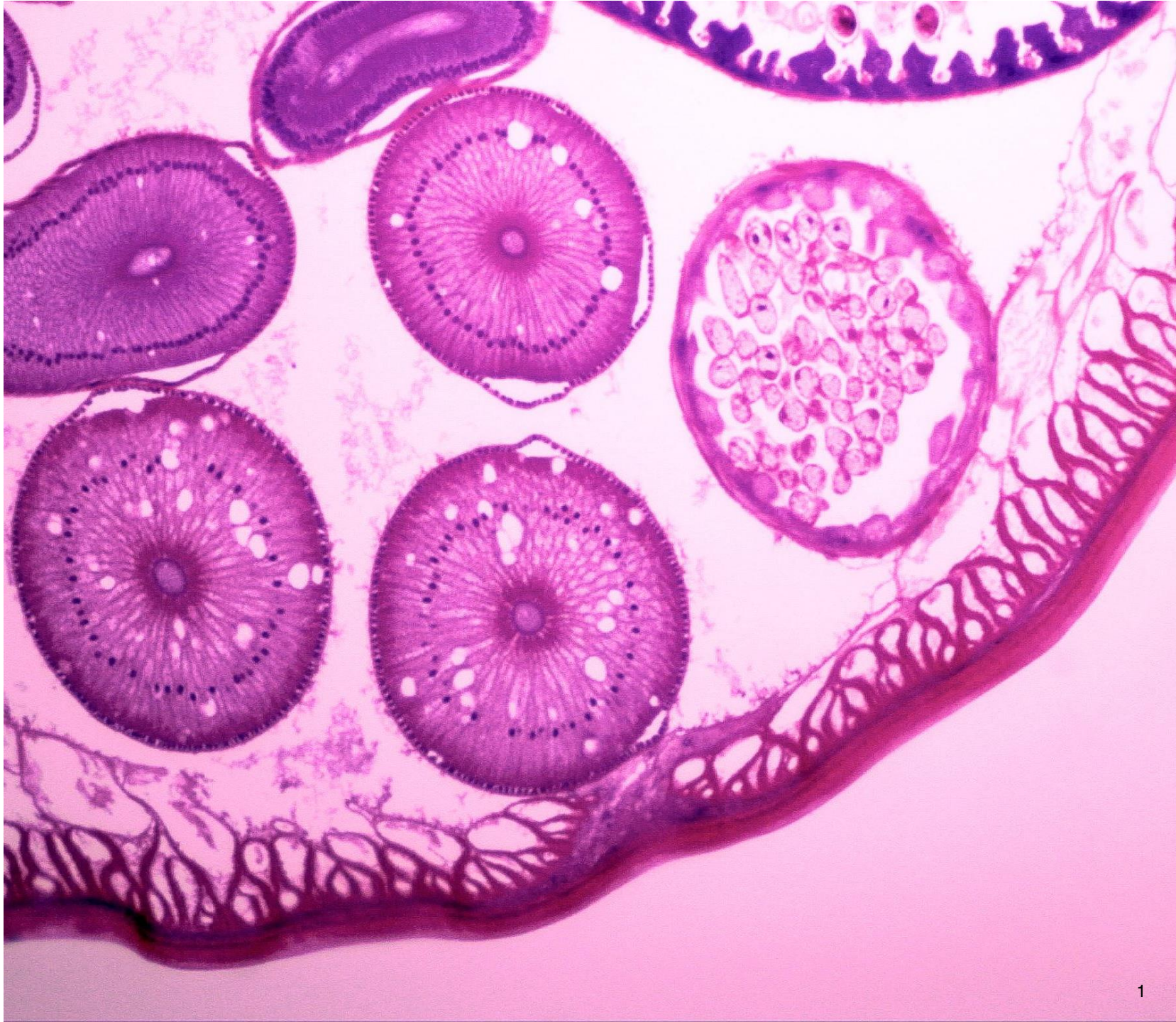
Early detection of Gastrointestinal cancers using Machine learning and blood biomarkers



INFO-I 501 – INTRO TO INFORMATICS

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Background & Significance:

Early Detection of GI Cancers: Challenges & Innovations

High Mortality

GI cancers (e g, gastric, colorectal) are leading causes of cancer deaths worldwide
Late-stage diagnosis due to vague symptoms & poor early detection tools

(Matsuoka & Yashiro, 2018; 2023)

Current Methods = Limitations

Endoscopy, imaging:
Invasive, costly, not scalable

Blood-Based Biomarkers = Game-Changer

Non-invasive, affordable, early-stage detection

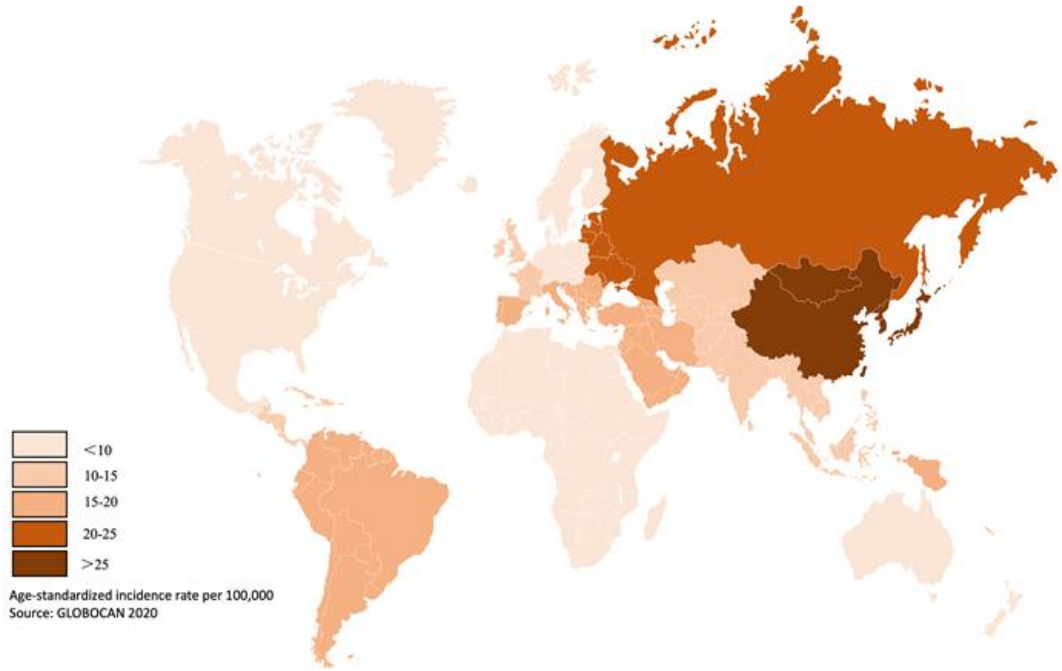
(Li et, 2021)

Machine Learning Power

Analyzes complex biomarker patterns
Enhances early, accurate cancer classification

(Sato et, 2023; Tabari et, 2022)

Global incidence rate of gastric cancer

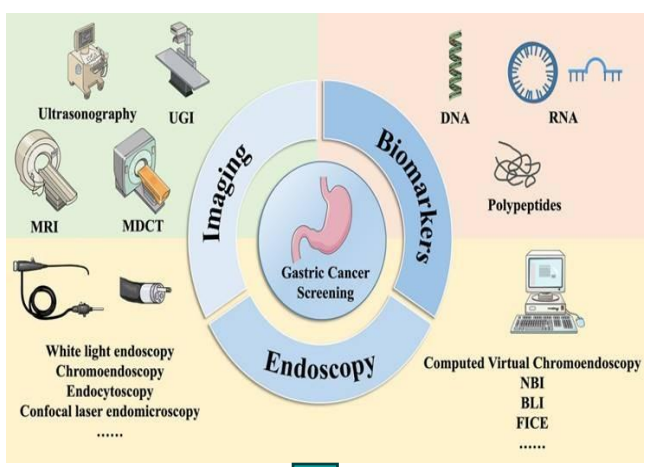


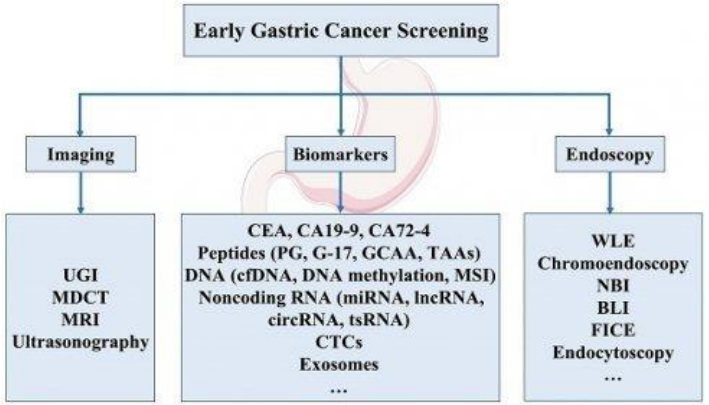
The incidence varies globally, especially high in East Asia and east Europe

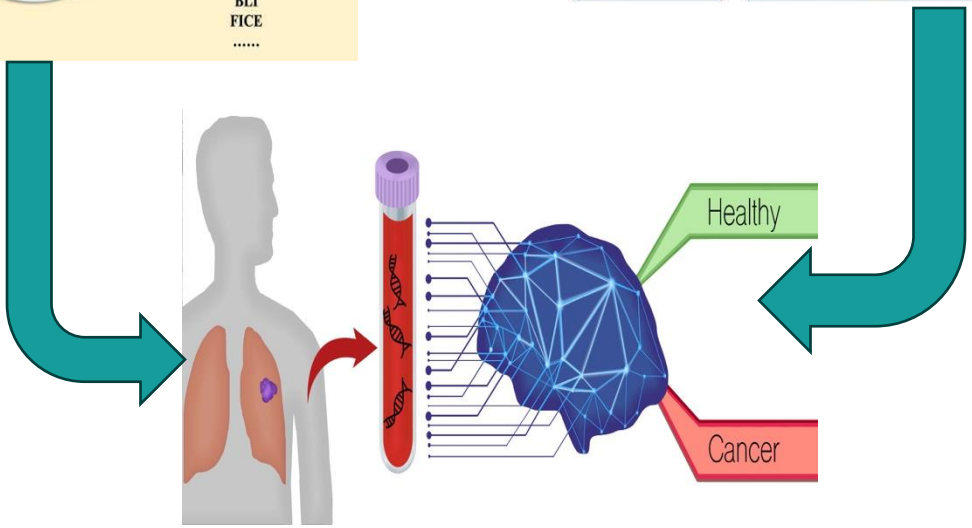
Introduction:

Gap in literature:

- Blood biomarkers are a non-invasive, scalable alternative.
- Their early detection potential is underused.
- ML is underapplied to multi-biomarker data.
- This project applies ML to CancerSeek for affordable, early GI cancer diagnosis.







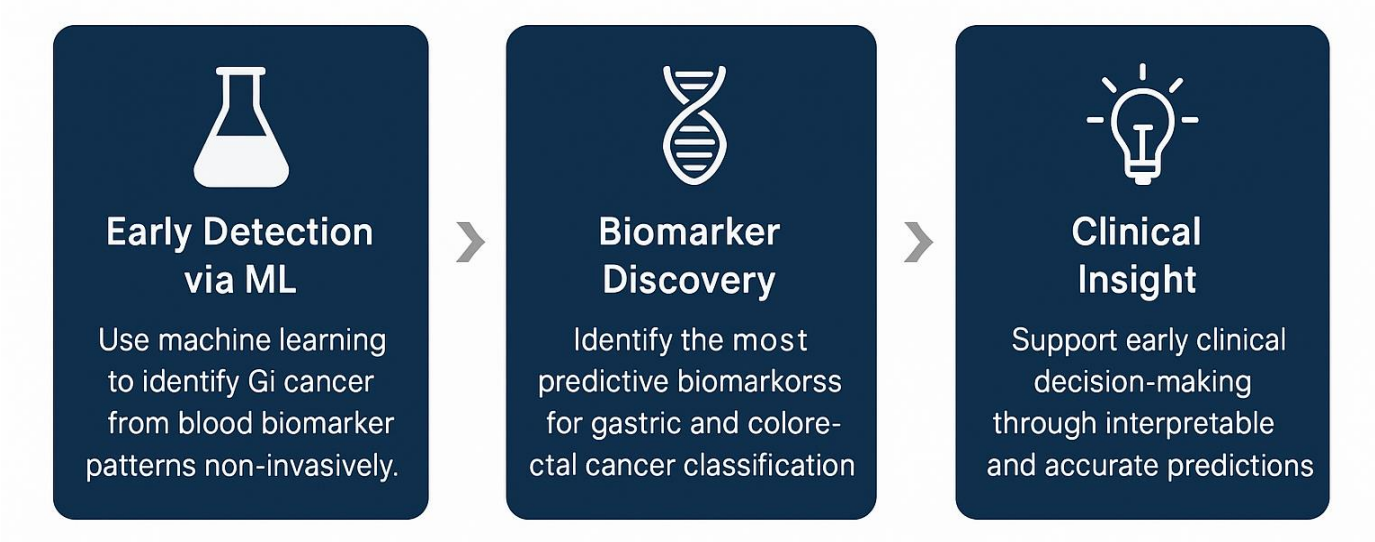
ML for non-invasive GI cancer detection

Project Overview

Aim:

To develop a machine learning model for the early detection of gastrointestinal (GI) cancers, specifically gastric and colon cancers, using blood biomarkers and classify GI cancer patients from normal individuals

Purpose:



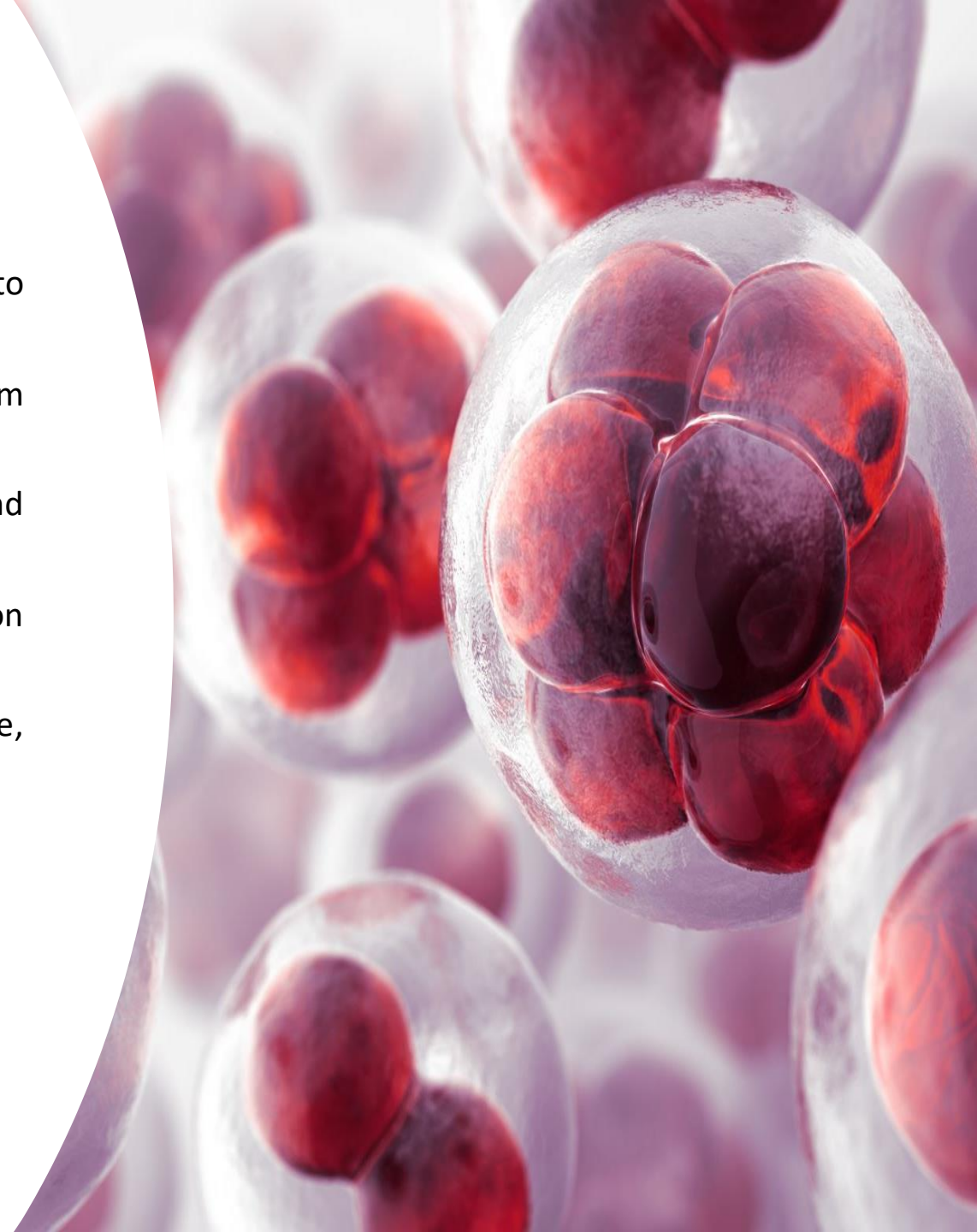
Project Overview

Objectives:

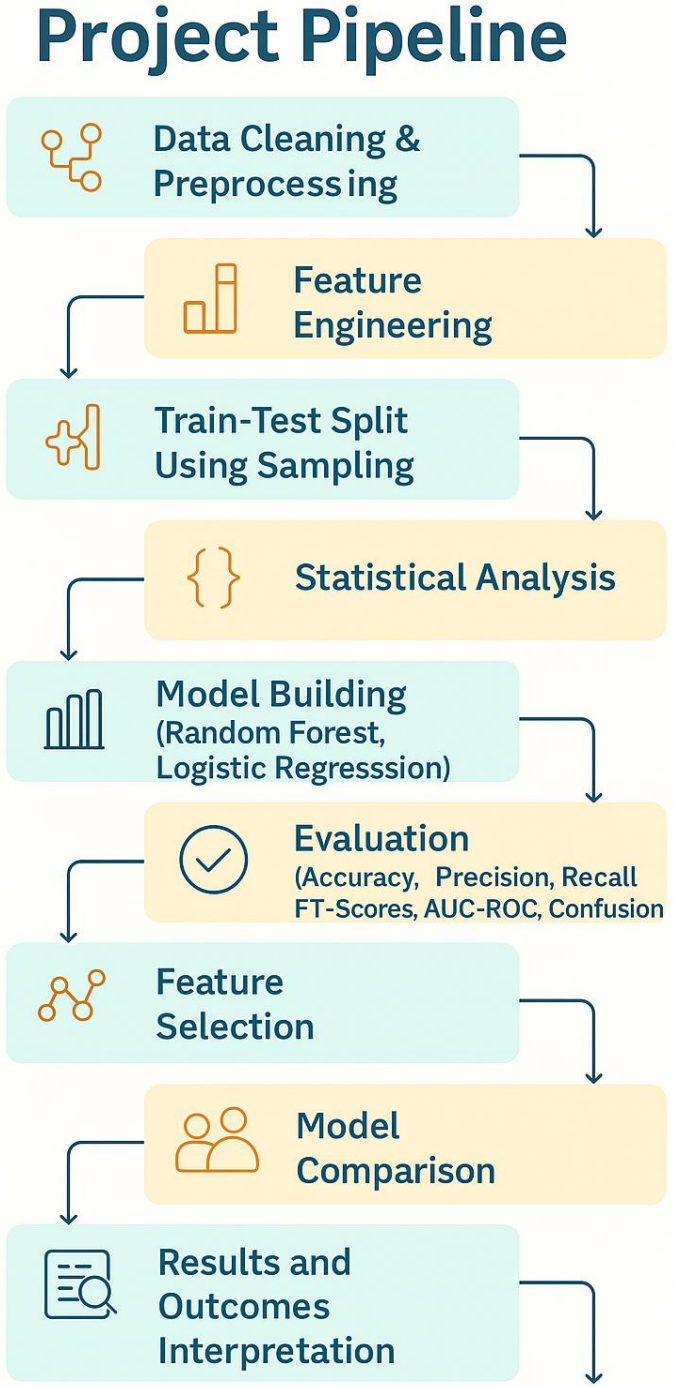
- Apply standard clinical thresholds to convert biomarker values into categorical flags indicating abnormality
- Identify statistically significant biomarkers differentiating cancer from normal using appropriate tests
- Address dataset imbalance through oversampling, undersampling, and bootstrapping methods
- Build and evaluate machine learning models to classify GI cancer based on biomarker profiles
- Analyze feature importance and explore demographic associations (age, sex, race) with cancer occurrence

Hypothesis:

- **Null Hypothesis (H0):** There is no statistically significant difference in biomarker values between GI cancer and normal patients.
- **Alternative Hypothesis (H1):** There is a statistically significant difference in biomarker values between GI cancer and normal patients.



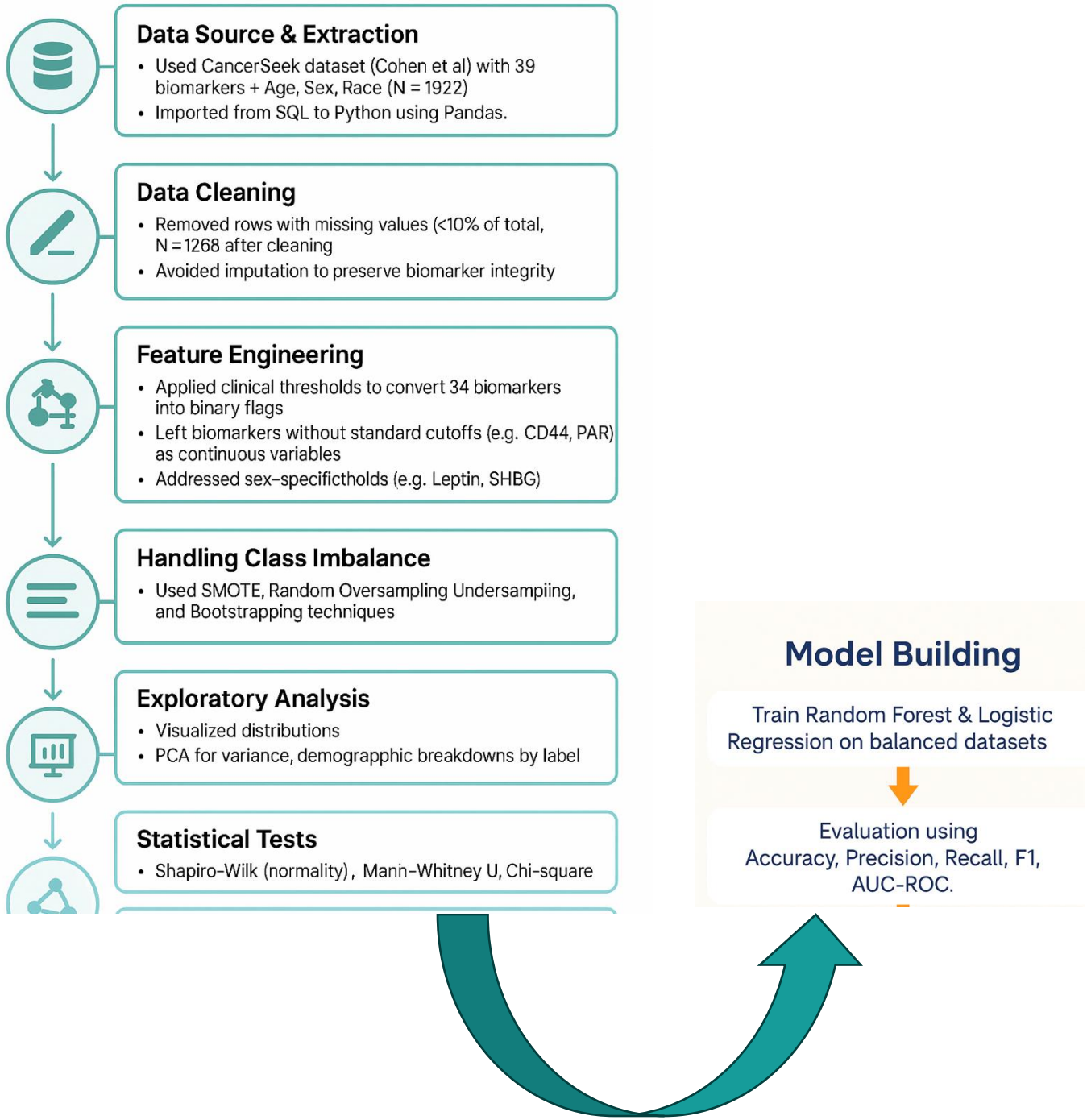
Step-by-Step Plan



Methodology

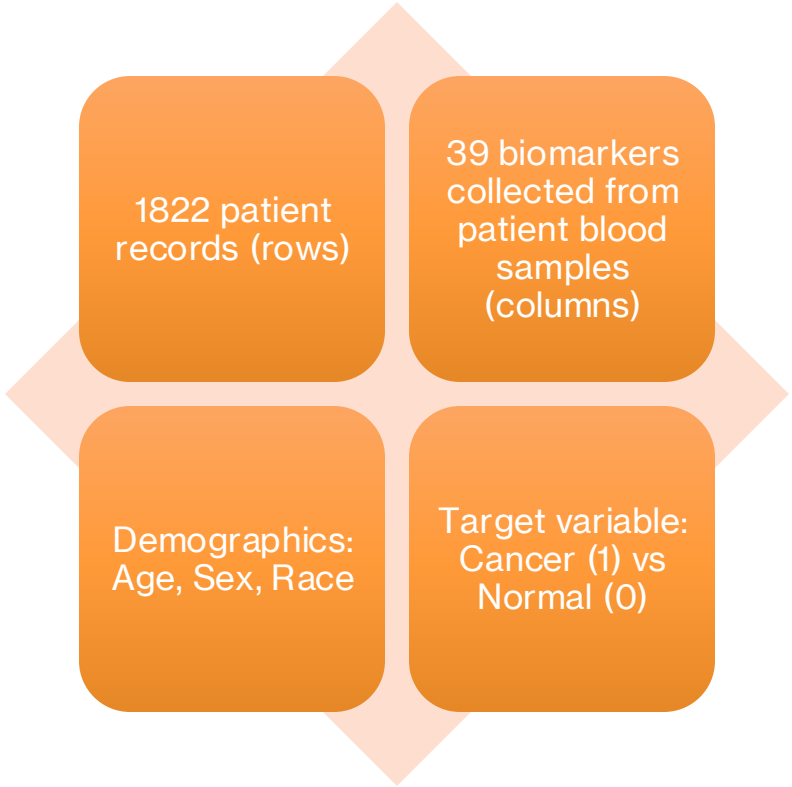
Study type:

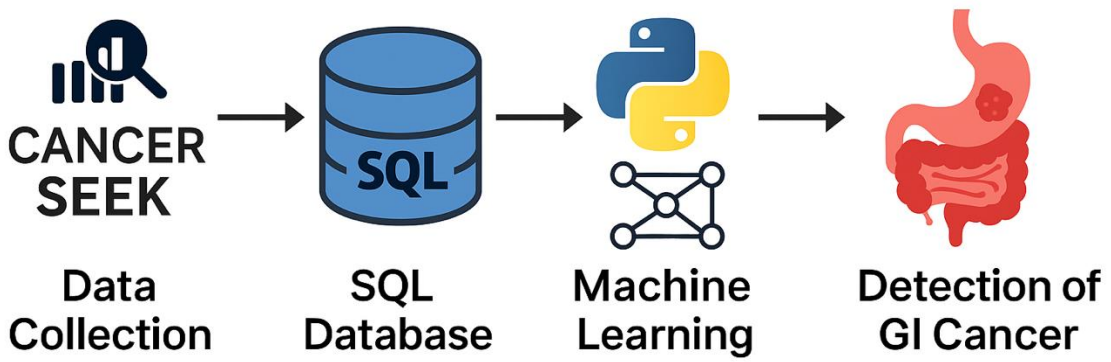
- Quantitative, retrospective ML study using blood biomarkers to detect GI cancers (gastric & colorectal).
- Combines statistical analysis and predictive modeling for binary classification (Normal vs Cancer).
- Dependent variable – Cancer status (Cancer vs Normal)
- Independent variable – 39 biomarkers



Data Overview

- Data collected from CancerSeek dataset (Cohen et al., Supplementary Material) from Zenodo, along with demographic variables such as sex, age, and race/ethnicity. Link for the dataset - https://www.science.org/doi/full/10.1126/science.aar3247





Data Cleaning & Preparation

1.Merged biomarker and clinical data into a single unified dataframe (merged_df)

merged_df

	Patient ID #_from_df1	Sample_ID	Primary tumor sample ID #	Age	Sex	Race	Tumor type_from_df1	AJCC Stage_from_df1	Histopathology	Plasma volume (mL)	Plasma DNA concentration (ng/mL)	CancerSEI Logist Regressi Score_from_d
0	CRC 455	CRC 455 PLS 1	Not available	60	Male	Caucasian	Colorectum	I	Adenocarcinoma	5	6.08	0.9
1	CRC 456	CRC 456 PLS 1	CRC 456 PT1	59	Female	Caucasian	Colorectum	I	Adenocarcinoma	4	46.01	0.9
2	CRC 457	CRC 457 PLS 1	CRC 457 PT1	69	Female	Caucasian	Colorectum	II	Adenocarcinoma	4.5	6.94	0.8
3	CRC 458	CRC 458 PLS 1	CRC 458 PT1	70	Female	Caucasian	Colorectum	II	Adenocarcinoma	7.5	7.15	0.6
4	CRC 459	CRC 459 PLS 1	CRC 459 PT1	43	Female	Caucasian	Colorectum	II	Adenocarcinoma	5	9.81	0.3
5	CRC 460	CRC 460 PLS 1	CRC 460 PT1	72	Male	Caucasian	Colorectum	II	Adenocarcinoma	5	16.33	0.9
6	CRC 461	CRC 461 PLS 1	CRC 461 PT1	70	Male	Caucasian	Colorectum	I	Adenocarcinoma	7.5	8.93	0.3

2. Removed unwanted characters such as asterisks (*), carets (^), white spaces, and commas from the dataset.

```
df = merged_df.applymap(lambda x: str(x).replace('*', '') if isinstance(x, str) else x)
df.head()
```

3.Dropped irrelevant columns that were not useful for analysis.

```
keywords = [
    'tumor type_from_df2', 'tumor type_from_df3',
    'patient id #_from_df1', 'patient id #_from_df2',
    'cancerseek logistic regression score_from_df1', 'cancerseek test result_from_df1',
    'cancerseek logistic regression score_from_df2', 'cancerseek test result_from_df2',
    'ajcc stage_from_df2', 'ajcc stage_from_df1', 'histopathology', 'primary tumor sample id #'
]

columns_to_drop = [col for col in merged_df.columns if any(key in col.lower() for key in keywords)]

print("Dropping columns:")
print(columns_to_drop)

df_cleaned = df.drop(columns=columns_to_drop)

df_cleaned.head()
```

```
Dropping columns:
['Patient ID #_from_df1', 'Primary tumor sample ID #', 'AJCC Stage_from_df1', 'Histopathology', 'CancerSEEK Logistic Regression Score_from_df1', 'Cancer
SEEK Test Result_from_df1', 'Patient ID #_from_df2', 'Tumor type_from_df2', 'AJCC Stage_from_df2', 'CancerSEEK Logistic Regression Score_from_df2', 'Can
cerSEEK Test Result_from_df2']
```

4. Filtered the dataset to keep only Gastric, Colorectal, and Normal samples

```
exclude_tumors = ['breast', 'esophagus', 'liver', 'lung', 'ovary', 'pancreas']

df_filtered = df_cleaned[~df_cleaned['Tumor type_from_df1'].str.lower().isin(exclude_tumors)]

print("Remaining tumor types:", df_filtered['Tumor type_from_df1'].unique())
print("Filtered dataset shape:", df_filtered.shape)
df_filtered
```

```
Remaining tumor types: ['Colorectum' 'Stomach' 'Normal']
Filtered dataset shape: (1255, 47)
```

	Sample_ID	Age	Sex	Race	Tumor type_from_df1	Plasma volume (mL)	Plasma DNA concentration (ng/mL)	AFP (pg/ml)	Angiopoietin-2 (pg/ml)	AXL (pg/ml)	CA-125 (U/ml)	CA 15-3 (U/ml)	CA19-9 (U/ml)	CD44 (ng/ml)
0	CRC 455 PLS 1	60	Male	Caucasian	Colorectum	5.00	6.08	1583.450	5598.500	3621.04	5.090	19.080	16.452	9.810
1	CRC 456 PLS 1	59	Female	Caucasian	Colorectum	4.00	46.01	715.308	20936.350	2772.96	7.270	10.040	40.910	27.570
2	CRC 457 PLS 1	69	Female	Caucasian	Colorectum	4.50	6.94	4365.530	2350.930	4120.77	4.854	16.960	16.452	14.590
3	CRC 458 PLS 1	70	Female	Caucasian	Colorectum	7.50	7.15	715.308	1604.340	2029.96	5.390	8.310	16.452	7.780

5. Removed unnecessary descriptive rows from the end of the dataset to retain only relevant data entries.

```
# Data cleaning 3. Delete unwanted rows
df_cleaned = df_filtered.iloc[:1268]
df_cleaned.tail()
```

6. Remove unwanted trailing spaces from column names and string entries.

```
merged_df.columns = merged_df.columns.str.strip()
for col in merged_df.select_dtypes(include='object').columns:
    merged_df[col] = merged_df[col].str.strip()
```

7. Converted numeric columns from integer to float for precise calculations during analysis.

```
Skipped 'Sex' – categorical
Skipped 'Race' – categorical
Cleaned and converted 'Plasma volume (mL)' to float.
Cleaned and converted 'Plasma DNA concentration (ng/mL)' to float.
Cleaned and converted 'AFP (pg/ml)' to float.
Cleaned and converted 'Angiopoietin-2 (pg/ml)' to float.
Cleaned and converted 'AXL (pg/ml)' to float.
Cleaned and converted 'CA-125 (U/ml)' to float.
Cleaned and converted 'CA 15-3 (U/ml)' to float.
Cleaned and converted 'CA19-9 (U/ml)' to float.
Cleaned and converted 'CD44 (ng/ml)' to float.
```

8. Converted cancer status into binary labels: "Label" - Cancer – 1, Normal – 0

```
df_cleaned['Label'] = df_cleaned['Tumor type_from_df1'].apply(lambda x: 0 if str(x).strip().lower() == 'normal' else 1)
df_cleaned.tail()
```

dase /ml)	NSE (ng/ml)	OPG (ng/ml)	OPN (pg/ml)	PAR (pg/ml)	Prolactin (pg/ml)	sEGFR (pg/ml)	sFas (pg/ml)	SHBG (nM)	sHER2/sEGFR2/sErbB2 (pg/ml)	sPECAM-1 (pg/ml)	TGFa (pg/ml)	Thrombospondin-2 (pg/ml)	TIMP-1 (pg/ml)	TIMP-2 (pg/ml)	Label
6.49	25.08	0.28	8913.64	11574.68	9851.43	4677.93	1072.020	32.15	6824.90	9314.25	15.258	4831.59	79549.74	42248.26	0
9.63	28.46	0.26	20352.33	4964.90	7244.91	5158.71	192.948	22.91	4776.64	3605.28	15.258	3678.90	59497.63	32619.49	0

9. Checked for missing values in the dataset after preprocessing.

```
import pandas as pd
df = pd.read_csv("draft_dataset4.csv")
missing_counts = df.isnull().sum()
missing_columns = missing_counts[missing_counts > 0]
if missing_columns.empty:
    print("No missing values in the dataset.")
else:
    print("Columns with missing values:")
    print(missing_columns.sort_values(ascending=False))
```

```
Columns with missing values:
AXL (pg/ml)                  6
CD44 (ng/ml)                 6
G-CSF (pg/ml)                6
Kallikrein-6 (pg/ml)         6
Mesothelin (ng/ml)           6
Midkine (pg/ml)              6
PAR (pg/ml)                  6
sEGFR (pg/ml)                6
sHER2/sEGFR2/sErbB2 (pg/ml)  6
sPECAM-1 (pg/ml)             6
Thrombospondin-2 (pg/ml)     6
sFas (pg/ml)                 1
```

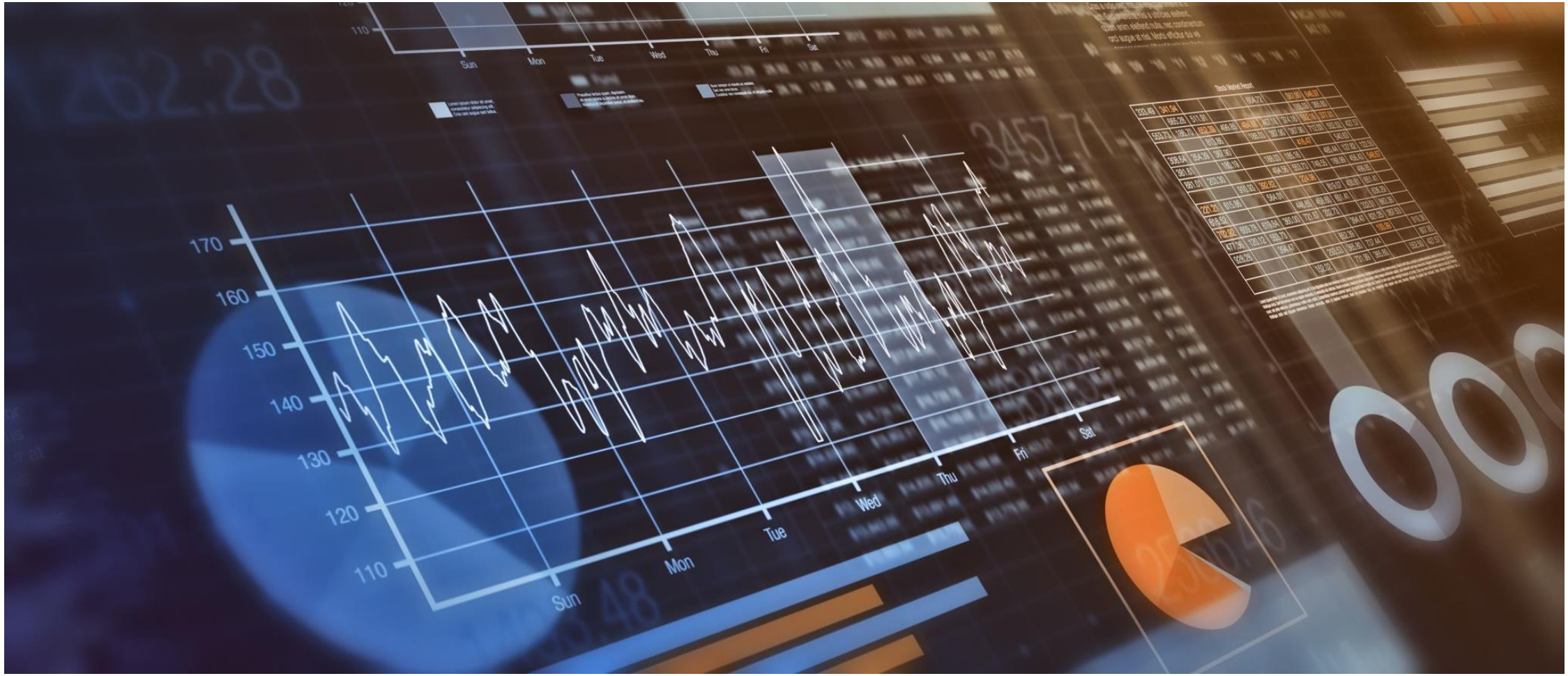
10. Dropped rows with missing values since they represented less than 10% of the data.

```
df_cleaned = df.dropna()

print("Remaining rows:", df_cleaned.shape[0])
```

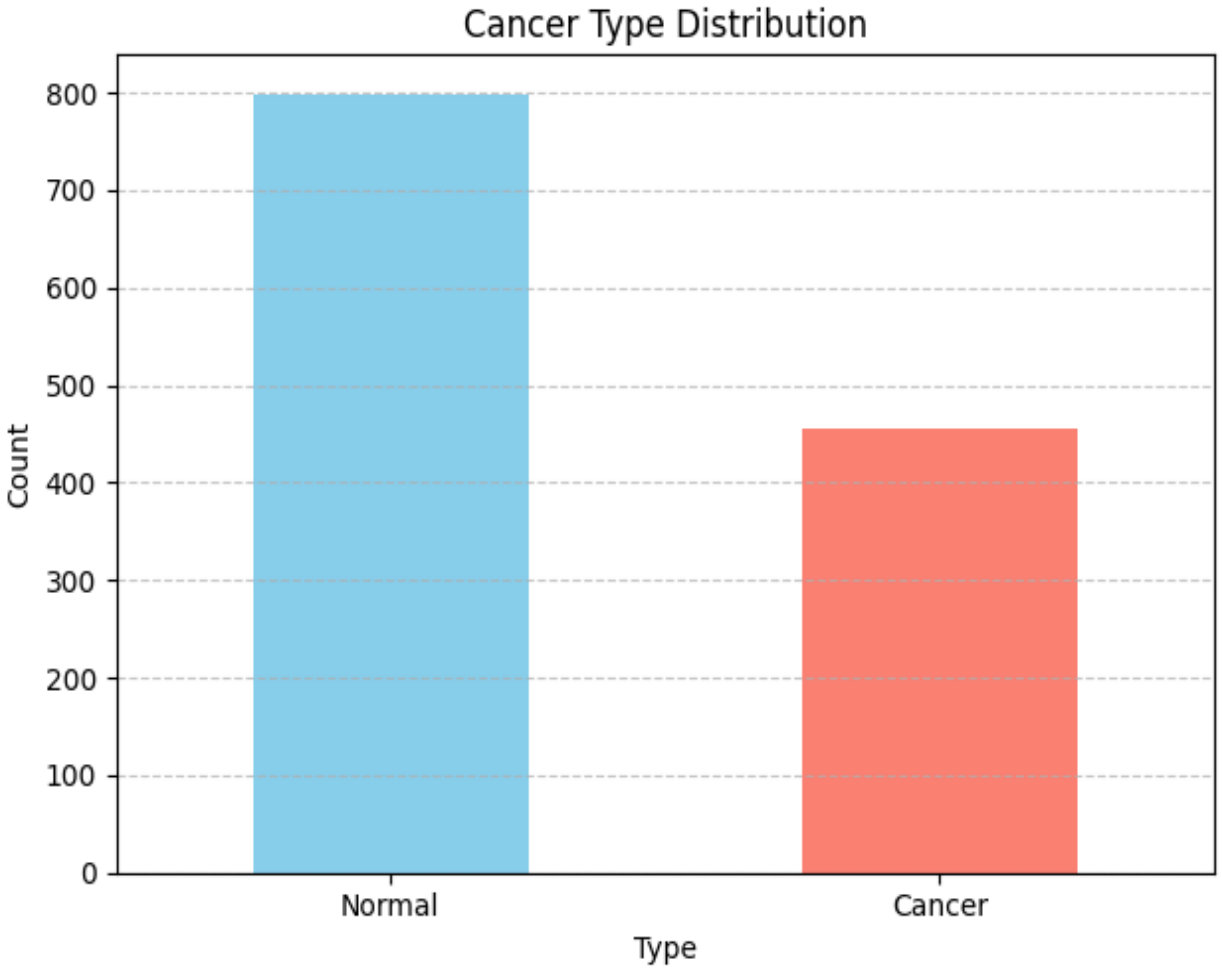
```
Remaining rows: 1255
```

Data visualization and analysis



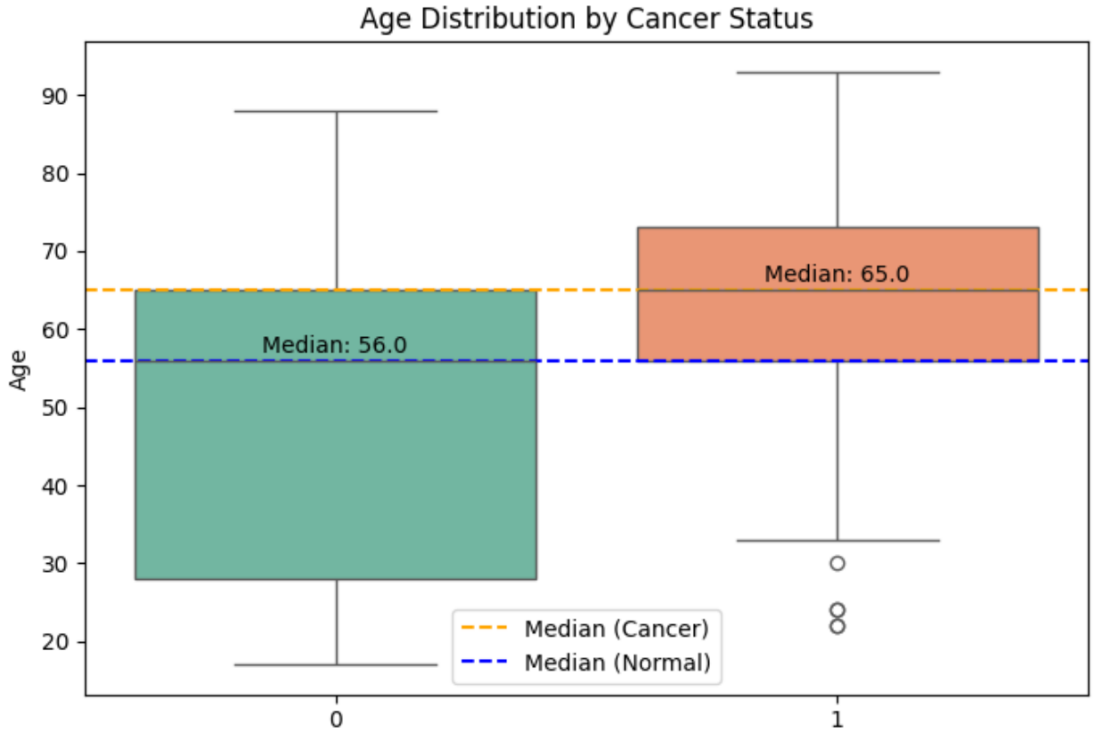
Class distribution – Normal vs Cancer

The graph shows a clear class imbalance with 812 Normal samples and 453 Cancer samples in the dataset. N=1255



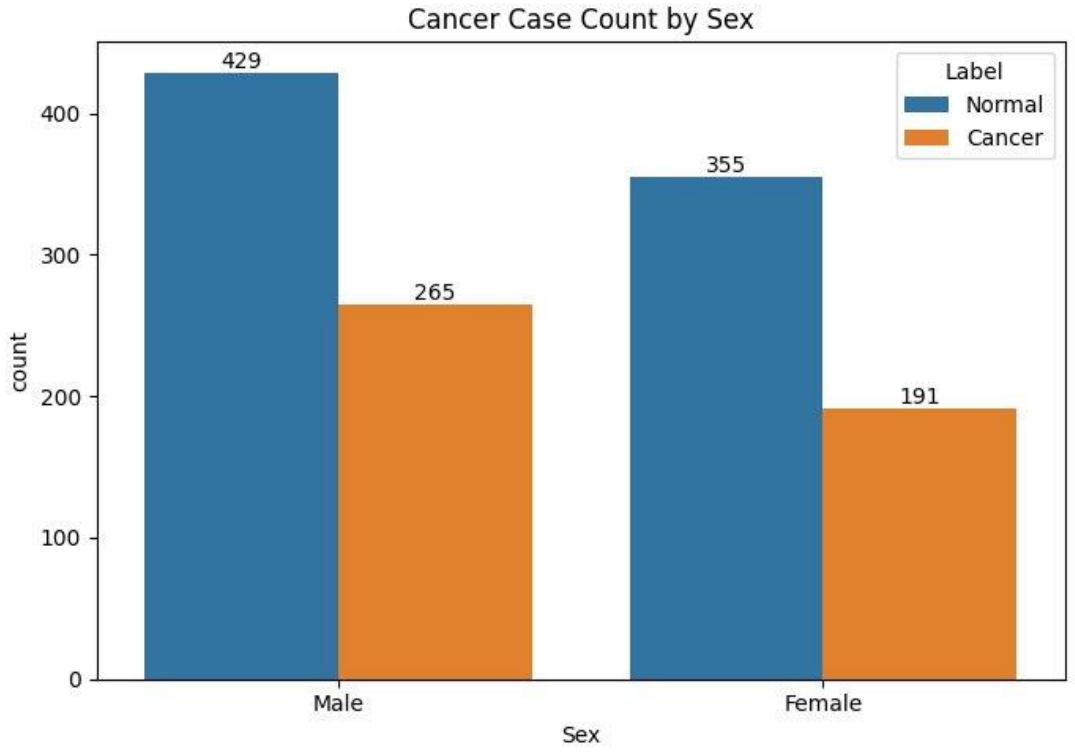
Age distribution:

- Interpretation:
- Median age for cancer patients from the results is 65. However, patients aged 20, tested positive for GI cancer, indicating a sociodemographic shift



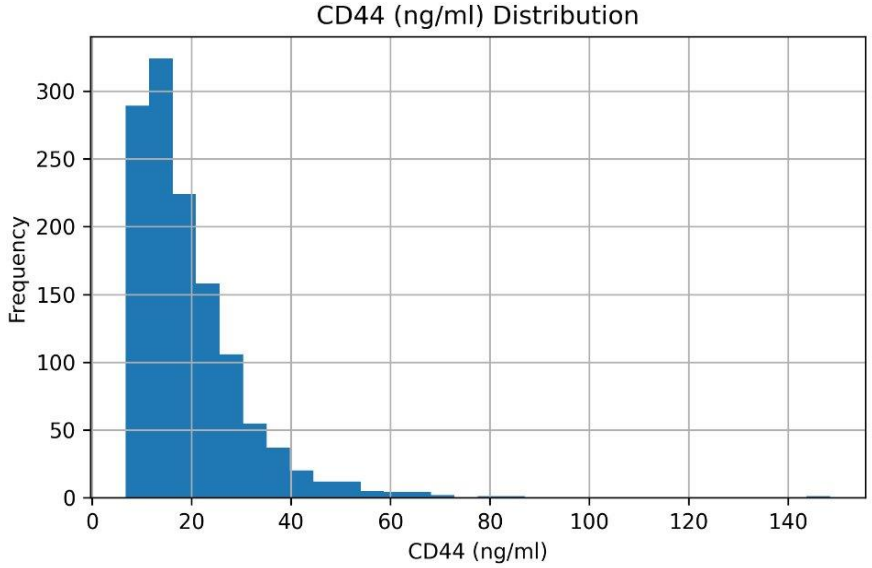
Sex: Cancer rate by gender

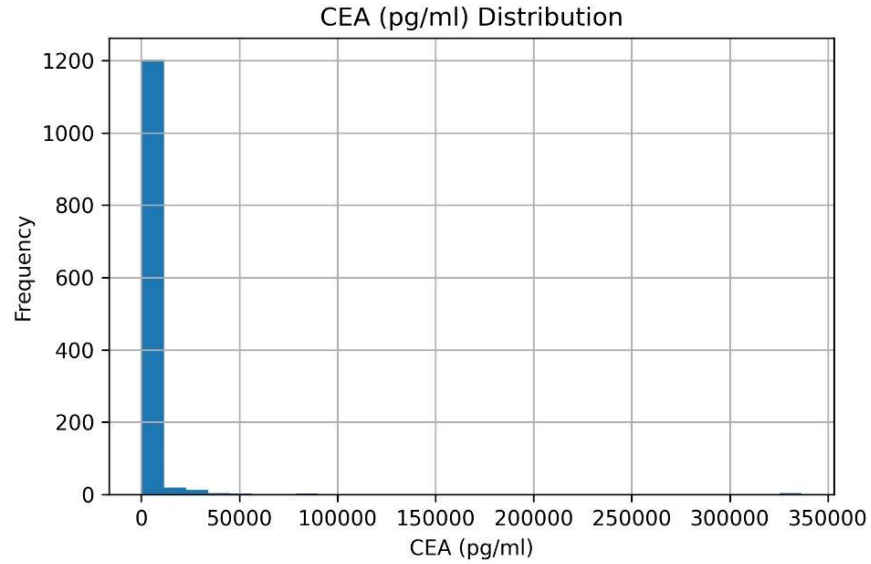
- Interpretation: The results indicate that most of the cancer patients in the data set were males n=265



Biomarkers distribution

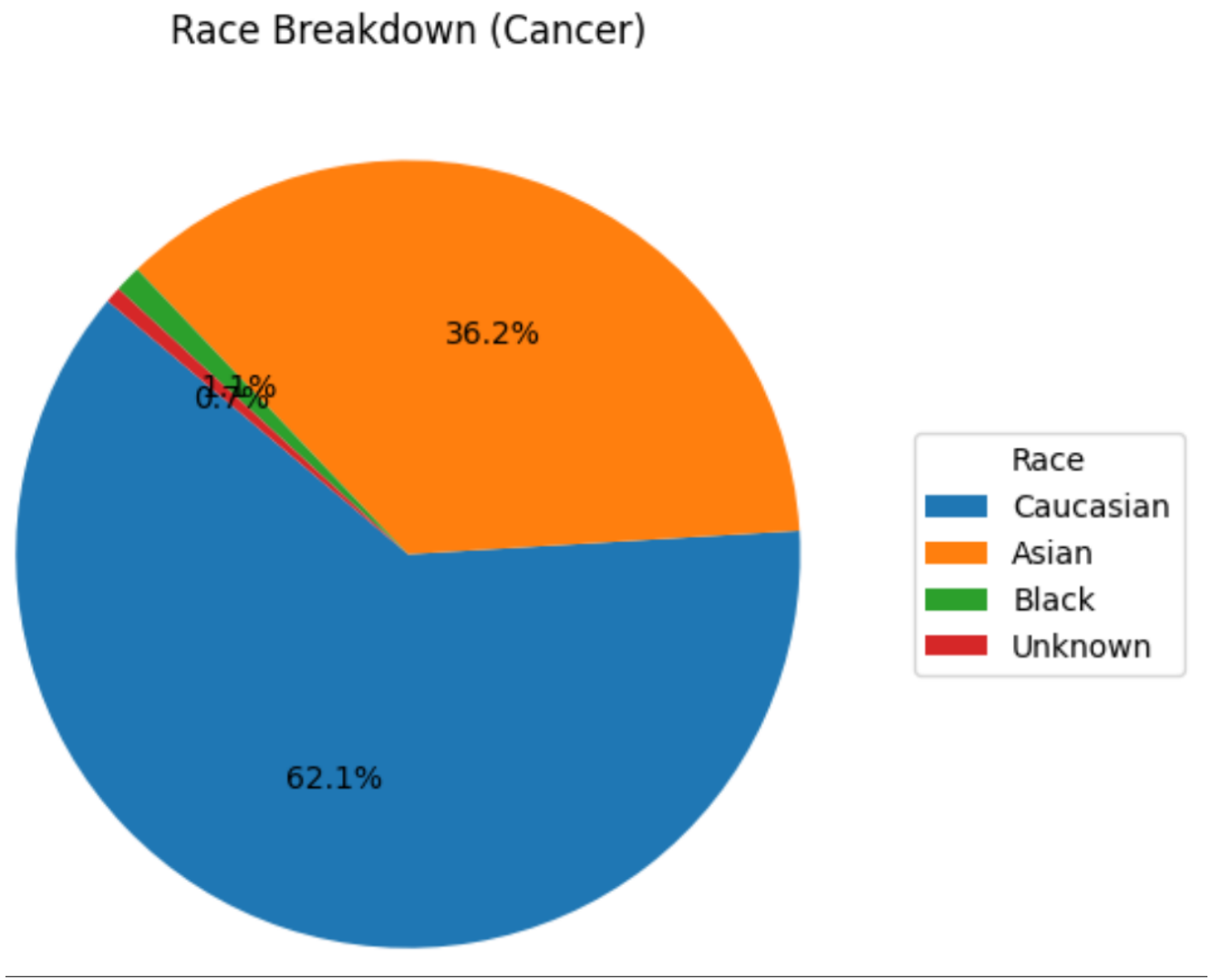
The distributions of biomarkers are skewed, with most samples showing lower expression levels and a few showing very high values.





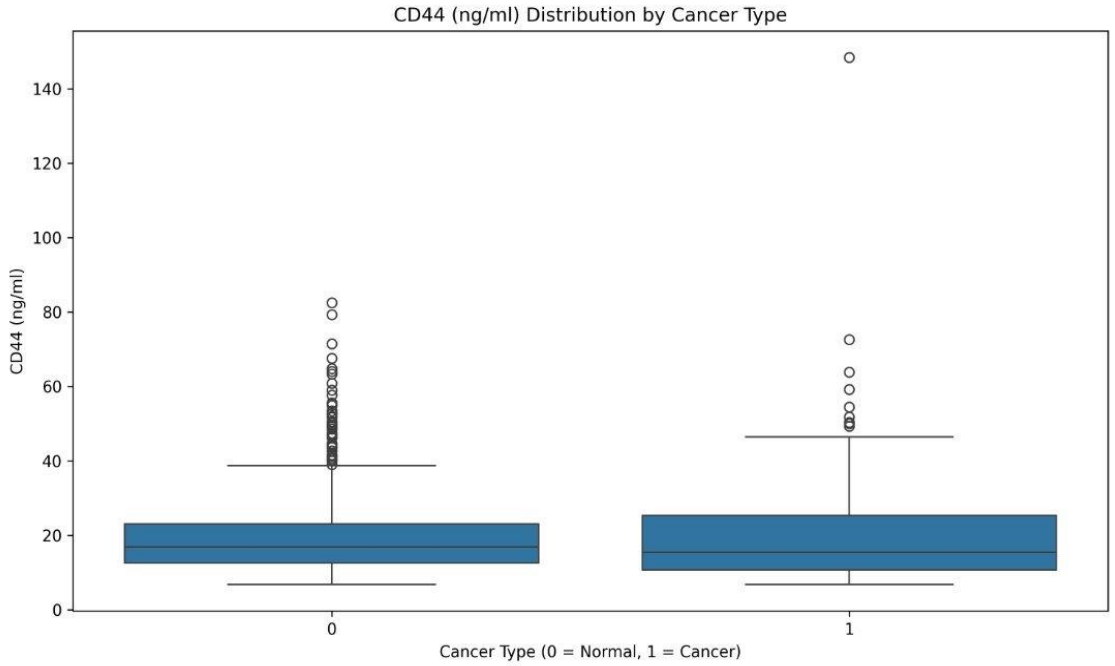
Race: Pie chart for class split

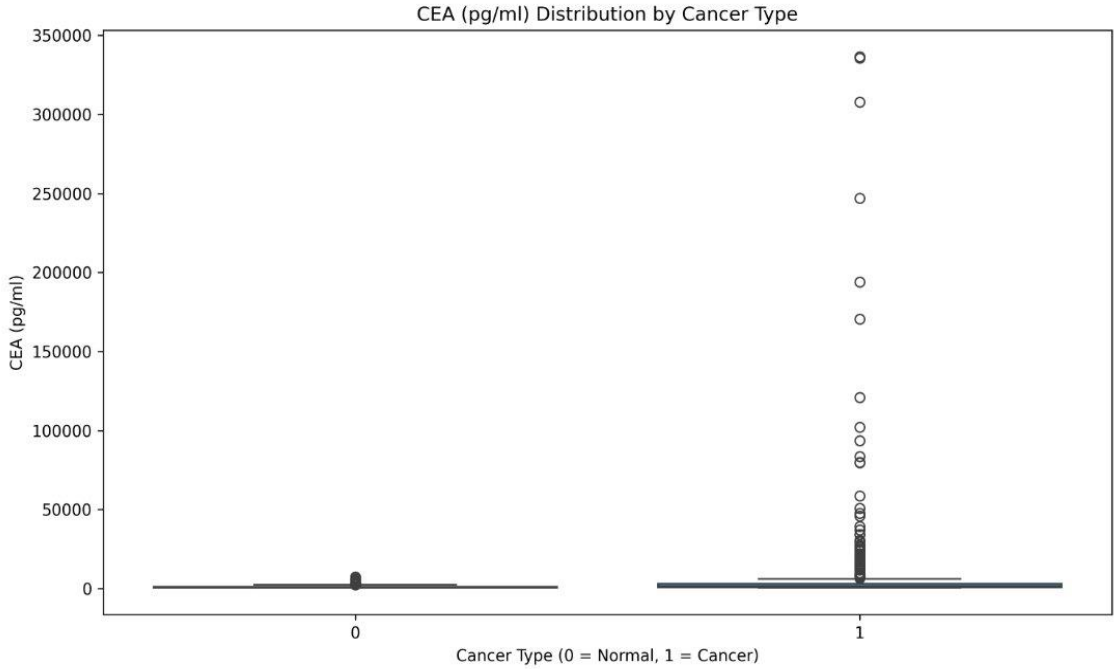
Interpretation: the Caucasians formed a majority of the GI cancer patients (62.1%) followed by Asians 36.2 %



Box plots of biomarkers to visualize outliers

Box plot of biomarkers exhibit a high number of outliers, especially in cancer cases, reflecting biological variability and heterogeneity among patients.





Outliers' summary:

- Several biomarkers, including CEA, AFP, and Thrombospondin-2, exhibited extreme outliers in both normal and GI cancer groups, which can distort statistical analyses and model performance.
- To address this, we applied standard clinical thresholds to convert continuous biomarker values into categorical flags indicating abnormality.

Biomarker	Label	Num Outliers	Outlier Min	Outlier Max
CEA (pg/ml)	Normal	39	2575.2	7377.64
CEA (pg/ml)	GI Cancer	69	6637.5	336427.99
AFP (pg/ml)	Normal	85	2811.58	171255.75
AFP (pg/ml)	GI Cancer	66	3066.13	592312.72
CA-125 (U/ml)	Normal	167	5.24	33.07
CA-125 (U/ml)	GI Cancer	70	9.88	111.49
CD44 (ng/ml)	Normal	45	38.62	82.53
CD44 (ng/ml)	GI Cancer	9	49.31	148.44
GDF15 (ng/ml)	Normal	56	1.08	8.56
GDF15 (ng/ml)	GI Cancer	39	2.27	24.29
IL-6 (pg/ml)	Normal	156	6.9	356.64
IL-6 (pg/ml)	GI Cancer	61	92.08	2818.46
CA 15-3 (U/ml)	Normal	32	36.17	102.98
CA 15-3 (U/ml)	GI Cancer	21	29.75	336.25
CYFRA 21-1 (pg/ml)	Normal	108	1816.46	13499.0
CYFRA 21-1 (pg/ml)	GI Cancer	66	4541.87	722034.0
Thrombospondin-2 (pg/ml)	Normal	76	10756.08	131014.81
Thrombospondin-2 (pg/ml)	GI Cancer	52	12973.51	157461.07

Normality test summary

None of the key biomarkers in this dataset follow a normal distribution, as indicated by the Shapiro-Wilk test.

As a result, the next step involves applying clinical thresholds to convert continuous biomarker values into categorical flags indicating abnormality.

```
from scipy.stats import shapiro
import pandas as pd

normality_results = []

for col in key_biomarkers:
    stat, p_value = shapiro(df_cleaned[col].dropna())
    normality_results.append({
        'Biomarker': col,
        'Shapiro-Wilk p-value': round(p_value, 5),
        'Normality': 'Not Normal' if p_value < 0.05 else 'Normal'
    })

normality_df = pd.DataFrame(normality_results)
print(normality_df)
normality_df.to_csv("Normality_test_results.csv", index=False)
```

	Biomarker	Shapiro-Wilk p-value	Normality
0	CEA (pg/ml)	0.0	Not Normal
1	AFP (pg/ml)	0.0	Not Normal
2	CA-125 (U/ml)	0.0	Not Normal
3	CD44 (ng/ml)	0.0	Not Normal
4	GDF15 (ng/ml)	0.0	Not Normal
5	IL-6 (pg/ml)	0.0	Not Normal
6	CA 15-3 (U/ml)	0.0	Not Normal
7	CYFRA 21-1 (pg/ml)	0.0	Not Normal
8	Thrombospondin-2 (pg/ml)	0.0	Not Normal

Feature engineering and Threshold Flagging

Clinical thresholds gathered from literature for 34 biomarkers and applied known thresholds to flag values (0 – Normal (low), 1 – Abnormal (elevated))

Handled sex-specific biomarkers by applying variable thresholds : Leptin, Prolactin and SHBG

Few biomarkers with no universal thresholds were kept as numerical : CD44, PAR, TIMP-2, sEGFR and sPECAM-1

```python
import pandas as pd

df_cleaned = pd.read_csv("Dropped_rows_dataset.csv")
clinical_thresholds = {
    'AFP (pg/ml)': 20000,
    'Angiopoietin-2 (pg/ml)': 4141,
    'AXL (pg/ml)': 1243,
    'CA-125 (U/ml)': 35,
    'CA 15-3 (U/ml)': 30,
    'CA19-9 (U/ml)': 37,
    'CYFRA 21-1 (pg/ml)': 3500,
    'CEA (pg/ml)': 5000,
    'DKK1 (ng/ml)': 2.03 * 1000,  # ng/ml to pg/ml
    'Endoglin (pg/ml)': 2000,
    'FGF2 (pg/ml)': 10,
    'Follistatin (pg/ml)': 4700,
    'Galectin-3 (ng/ml)': 22.1 * 1000,
    'G-CSF (pg/ml)': 15,
    'GDF15 (ng/ml)': 1200 * 1000,
    'HE4 (pg/ml)': 3500,
    'HGF (pg/ml)': 1000,
    'IL-6 (pg/ml)': 5,
    'IL-8 (pg/ml)': 57.7,
    'Kallikrein-6 (pg/ml)': 1000,
    'Mesothelin (ng/ml)': 2 * 1000,
    'Midkine (pg/ml)': 400,
    'Myeloperoxidase (ng/ml)': 220 * 1000,
    'NSE (ng/ml)': 16.3 * 1000,
    'OPG (ng/ml)': 0.2 * 1000,
    'OPN (pg/ml)': 200000,
    'sFas (pg/ml)': 150,
    'sHER2/sEGFR2/sErbB2 (pg/ml)': 15000,
    'TGFa (pg/ml)': 100,
    'Thrombospondin-2 (pg/ml)': 45000,
    'TIMP-1 (pg/ml)': 126000,
}
```

```python
#Sex-specific thresholds
sex_specific_thresholds = {
    'Leptin (pg/ml)': {'Male': 15200, 'Female': 12500},
    'Prolactin (pg/ml)': {'Male': 18000, 'Female': 25000},
    'SHBG (nM)': {'Male': 54, 'Female': 145},
}

#Convert biomarker columns to numeric
for col in df_cleaned.columns:
    df[col] = pd.to_numeric(df_cleaned[col], errors='coerce')

#clinical threshold flags
for biomarker, threshold in clinical_thresholds.items():
    if biomarker in df_cleaned.columns:
        df_cleaned[f"{biomarker}_flag"] = (df_cleaned[biomarker] > threshold).astype(int)

#sex-specific thresholds
for biomarker, thresholds in sex_specific_thresholds.items():
    if biomarker in df_cleaned.columns and 'Sex' in df_cleaned.columns:
        df_cleaned[f"{biomarker}_flag"] = df_cleaned.apply(
            lambda row: int(row[biomarker] > thresholds.get(row['Sex'], float('inf'))), axis=1
        )

#Remove any mistakenly flagged non-biomarker
non_biomarker_flags = ['Sex_flag', 'Sample_ID_flag']
df_cleaned.drop(columns=[col for col in non_biomarker_flags if col in df_cleaned.columns], inplace=True)

df_cleaned.to_csv("threshold_flagged_dataset_final.csv", index=False)
df_cleaned.head()
```

Threshold flagging:

Label	AFP (pg/ml	Angiopoiet	AXL (pg/ml	CA-125 (U/	CA 15-3 (U	CA19-9 (U/	CYFRA 21-	CEA (pg/m	DKK1 (ng/r	Endoglin (p	FGF2 (pg/r	Follistatin (	Galectin-3	G-CSF (pg/	GDF15 (ng	HE4 (pg/m	HGF (pg/m	IL-6 (pg/ml	IL-8 (pg/ml	Kallikrein-(	Mesothelir	Midkine (p	M
1	0	1	1	0	0	0	0	0	0	1	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	1	1	0	0	1	0	1	0	1	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	1	0	0	0	0	0	0	1	1	0	0	1	0	1	0	1	0	1	0	1	
1	0	0	1	0	0	0	0	0	0	0	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	1	0	0	0	0	0	0	1	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	1	0	0	1	0	0	0	1	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	1	0	0	0	0	0	0	0	1	0	0	1	0	1	0	1	1	1	0	0	
1	0	0	1	0	0	0	0	0	0	0	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	1	0	0	0	0	0	0	1	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	1	0	0	1	0	0	0	0	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	1	0	0	0	0	0	0	1	1	0	0	1	0	1	0	1	0	1	0	1	
1	0	0	1	0	0	0	0	1	0	1	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	1	0	0	0	0	1	0	0	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	0	0	0	0	0	0	0	1	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	1	0	1	1	1	0	0	
1	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	1	0	0	1	0	1	0	0	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	1	0	0	0	0	0	0	0	1	0	0	1	0	1	0	1	0	1	0	0	
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1	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	1	0	1	0	1	0	0	
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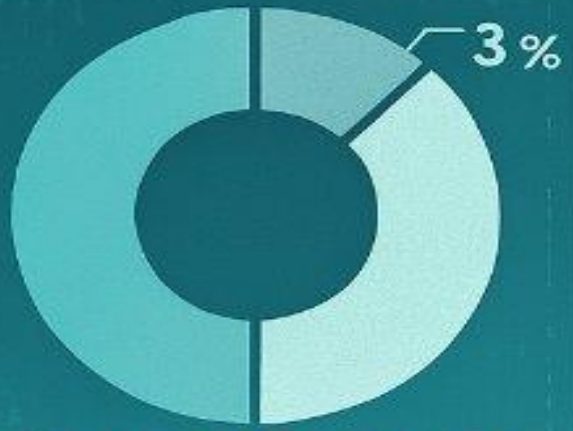
1	0	0	1	0	0	0	0	0	0	1	1	0	0	1	0	1	0	1	0	1	0	0	
1	0	0	1	0	0	0	0	0	0	0	1	0	0	1	0	1	0	1	0	1	0	0	

STATISTICAL TESTING

COTAGENCY TABLE



CHI-SQUARE P-VALUE

CHI-SQUARE CONTIGENCY TABLE

Statistical Analysis

- **Categorical data:** Flagged biomarkers
- **Method:** Chi-Square Test was applied to categorical biomarker variables
- **Result:** A majority of biomarker flags show statistically significant differences ($p < 0.05$) between cancer and normal groups. This highlights their potential utility in classification and feature selection for predictive modeling. Non-significant ones retained for biological relevance.

Biomarker	p_value	Significant
IL-6 (pg/ml)_flag	0.0	Yes
Leptin (pg/ml)_flag	0.0	Yes
TIMP-1 (pg/ml)_flag	0.0	Yes
OPN (pg/ml)_flag	0.0	Yes
CA19-9 (U/ml)_flag	0.0	Yes
CYFRA 21-1 (pg/ml)_flag	0.0	Yes
CEA (pg/ml)_flag	0.0	Yes
Midkine (pg/ml)_flag	0.0	Yes
IL-8 (pg/ml)_flag	0.0	Yes
HGF (pg/ml)_flag	0.0	Yes
Prolactin (pg/ml)_flag	0.0	Yes
ngiopoietin-2 (pg/ml)_flag	1e-05	Yes
SHBG (nM)_flag	2e-05	Yes
CA-125 (U/ml)_flag	2e-05	Yes
AFP (pg/ml)_flag	0.00886	Yes
Kallikrein-6 (pg/ml)_flag	0.02145	Yes
CA 15-3 (U/ml)_flag	0.05517	No
TGFa (pg/ml)_flag	0.09993	No
AXL (pg/ml)_flag	0.14044	No
Endoglin (pg/ml)_flag	0.8987	No
GFR2/sErbB2 (pg/ml)_flag	1.0	No
bospondin-2 (pg/ml)_flag	1.0	No
Follistatin (pg/ml)_flag	1.0	No

Statistical Analysis – Continuous Biomarkers

- **Method:** Mann-Whitney U Test
- **Biomarkers Tested:** CD44, PAR, sEGFR, TIMP-2, sPECAM-1

Most numerical features showed statistically significant differences between cancer and normal groups, indicating strong discriminatory potential.

	Biomarker	Mann-Whitney U	p-value	Significant
2	sEGFR (pg/ml)	248907.0	0.00000	Yes
1	PAR (pg/ml)	159440.5	0.00149	Yes
4	TIMP-2 (pg/ml)	197661.0	0.00187	Yes
0	CD44 (ng/ml)	191261.5	0.03966	Yes
3	sPECAM-1 (pg/ml)	187833.5	0.13531	No

Machine learning

Train/Test Splitting:

Stratified 80-20 train/test split and applied four sampling techniques

```python
import pandas as pd
from sklearn.model_selection import train_test_split
from sklearn.preprocessing import StandardScaler

df = pd.read_csv("threshold_flagged_dataset_final.csv")

y = df["Label"]

flagged_features = [col for col in df.columns if col.endswith('_flag')]
continuous_features = [
    "CD44 (ng/ml)", "PAR (pg/ml)", "sEGFR (pg/ml)",
    "sPECAM-1 (pg/ml)", "TIMP-2 (pg/ml)"
]

X_categorical = df[flagged_features]
X_continuous = df[continuous_features]
X_full = pd.concat([X_categorical, X_continuous], axis=1)

#Splitting before scaling to avoid data leakage
X_train, X_test, y_train, y_test = train_test_split(
    X_full, y, test_size=0.2, stratify=y, random_state=42
)

scaler = StandardScaler()
X_train_cont = scaler.fit_transform(X_train[continuous_features])
X_test_cont = scaler.transform(X_test[continuous_features])

X_train_scaled = X_train.copy()
X_test_scaled = X_test.copy()
X_train_scaled[continuous_features] = X_train_cont
X_test_scaled[continuous_features] = X_test_cont

X_train_scaled.to_csv("X_train_prepared.csv", index=False)
X_test_scaled.to_csv("X_test_prepared.csv", index=False)
y_train.to_csv("y_train.csv", index=False)
y_test.to_csv("y_test.csv", index=False)
```

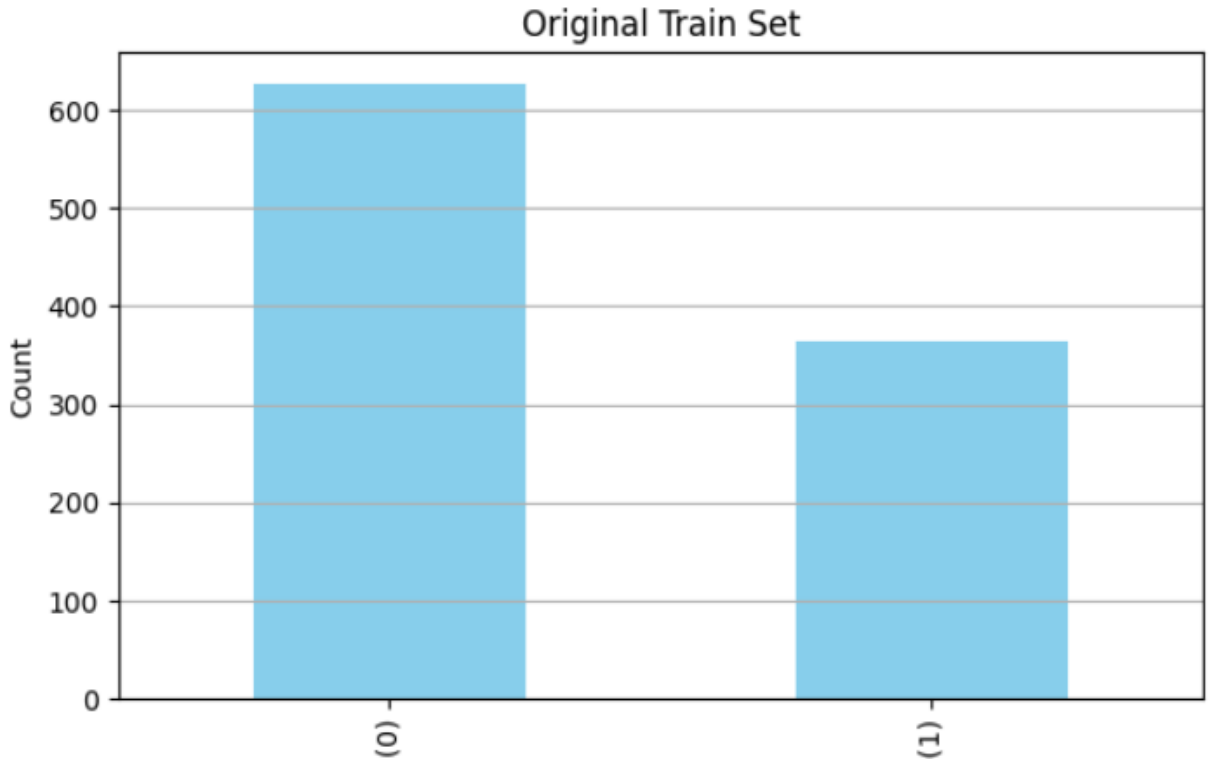
```python
from imblearn.over_sampling import SMOTE, RandomOverSampler
from imblearn.under_sampling import RandomUnderSampler
from sklearn.utils import resample
from collections import Counter
import pandas as pd

# 1. SMOTE
smote = SMOTE(random_state=42)
X_train_smote, y_train_smote = smote.fit_resample(X_train_scaled, y_train)

# 2. Random Oversampling
ros = RandomOverSampler(random_state=42)
X_train_ros, y_train_ros = ros.fit_resample(X_train_scaled, y_train)

# 3. Random Undersampling
rus = RandomUnderSampler(random_state=42)
X_train_rus, y_train_rus = rus.fit_resample(X_train_scaled, y_train)

# 4. Bootstrapping the minority class
df_train = X_train_scaled.copy()
df_train['Label'] = y_train.values

df_majority = df_train[df_train.Label == 0]
df_minority = df_train[df_train.Label == 1]

df_minority_boot = resample(
    df_minority,
    replace=True,
    n_samples=len(df_majority),
    random_state=42
)

df_bootstrap = pd.concat([df_majority, df_minority_boot])
X_train_bootstrap = df_bootstrap.drop(columns=['Label'])
y_train_bootstrap = df_bootstrap['Label']
```

```python
# Summary of class balance
print("Original:", Counter(y_train))
print("SMOTE:", Counter(y_train_smote))
print("Random Oversampling:", Counter(y_train_ros))
print("Random Undersampling:", Counter(y_train_rus))
print("Bootstrapped:", Counter(y_train_bootstrap))
```

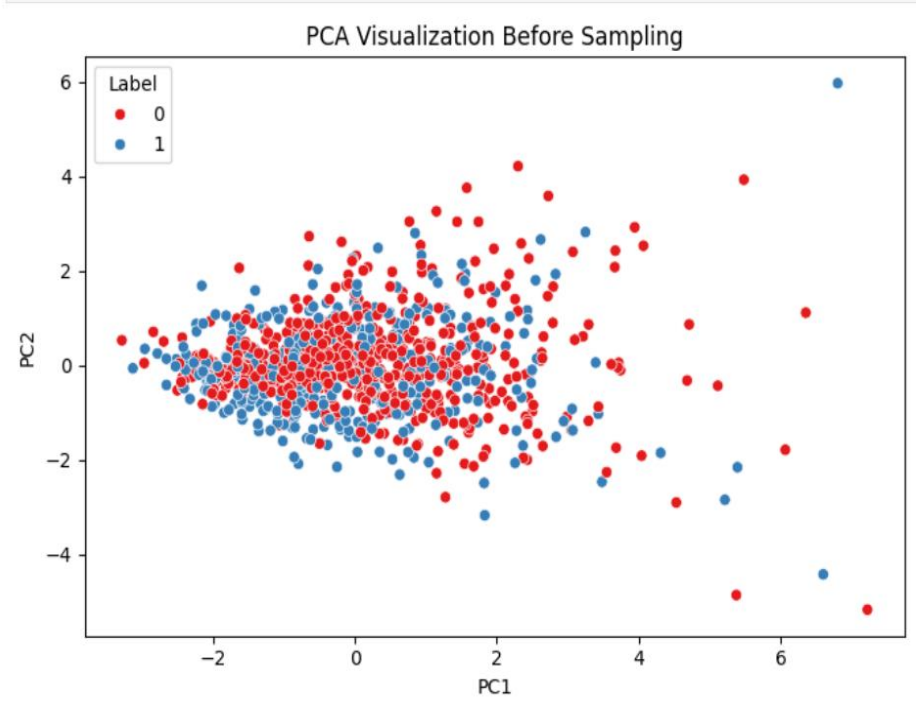
```
Original: Counter({0: 627, 1: 365})
SMOTE: Counter({0: 627, 1: 627})
Random Oversampling: Counter({0: 627, 1: 627})
Random Undersampling: Counter({0: 365, 1: 365})
Bootstrapped: Counter({0: 627, 1: 627})
```

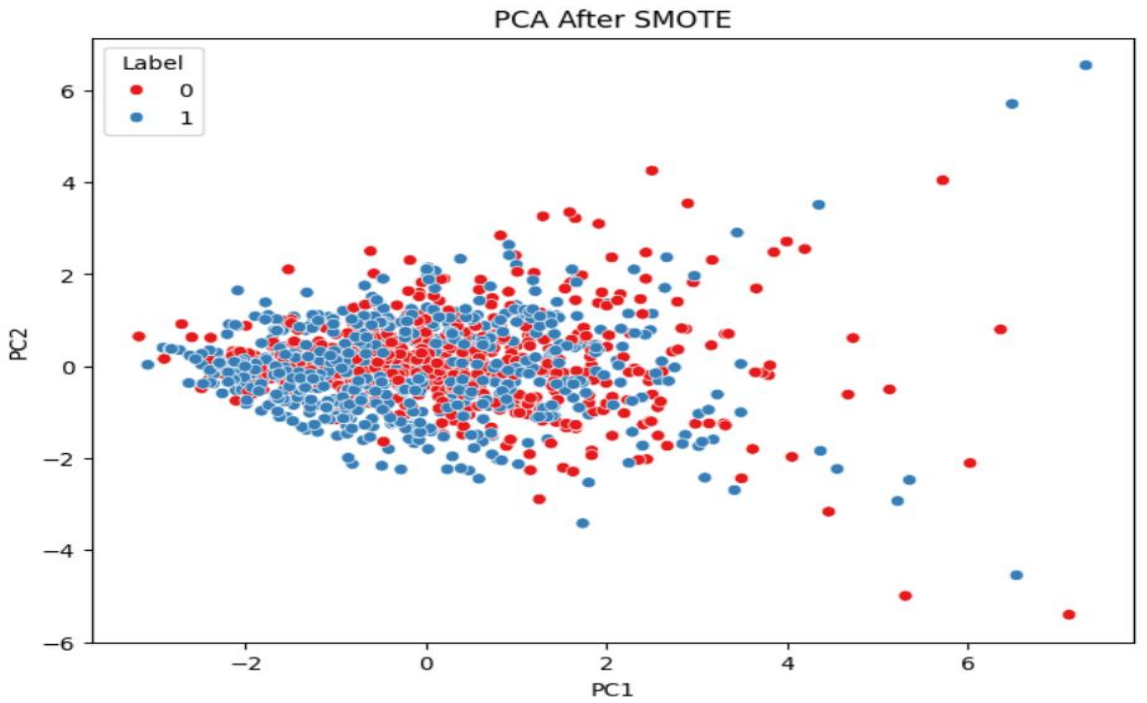
Class Imbalance & Sampling

- Initial imbalance: 455 cancer vs. 800 non-cancer (Normal) cases (35-65%)
- Applied techniques:
  - SMOTE to generate synthetic cancer samples
  - Random Oversampling /Undersampling for balance
  - Bootstrapping to improve training diversity



Sampling balance visualization - PCA scatter plot:

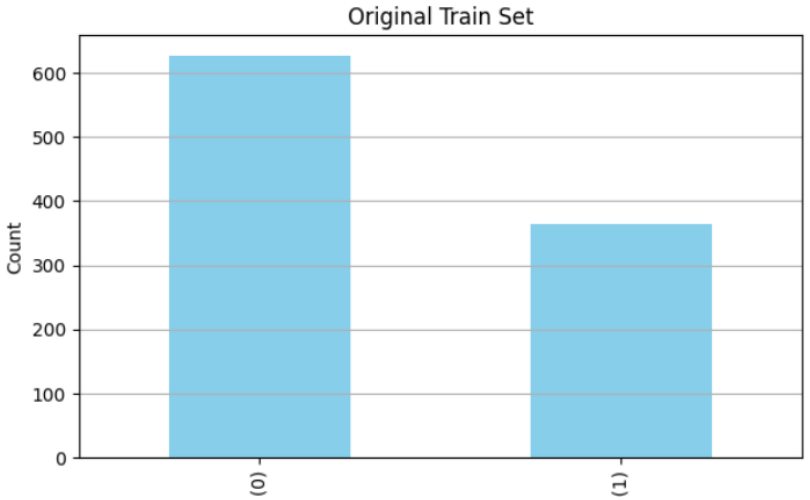


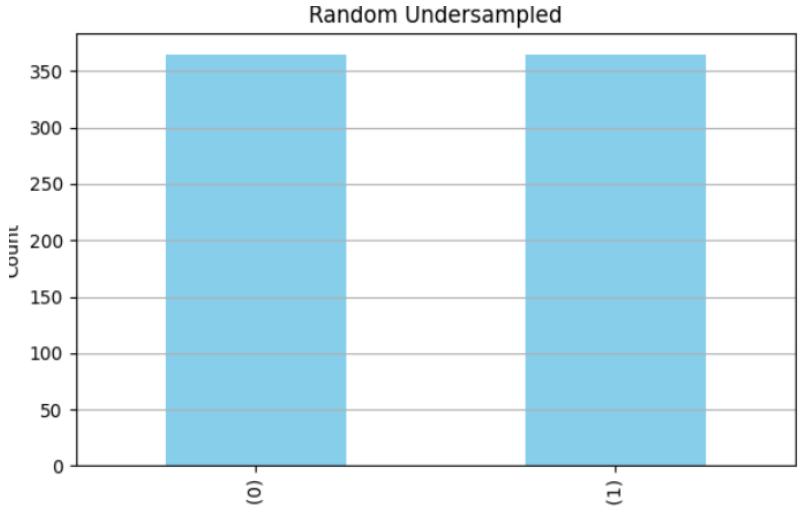


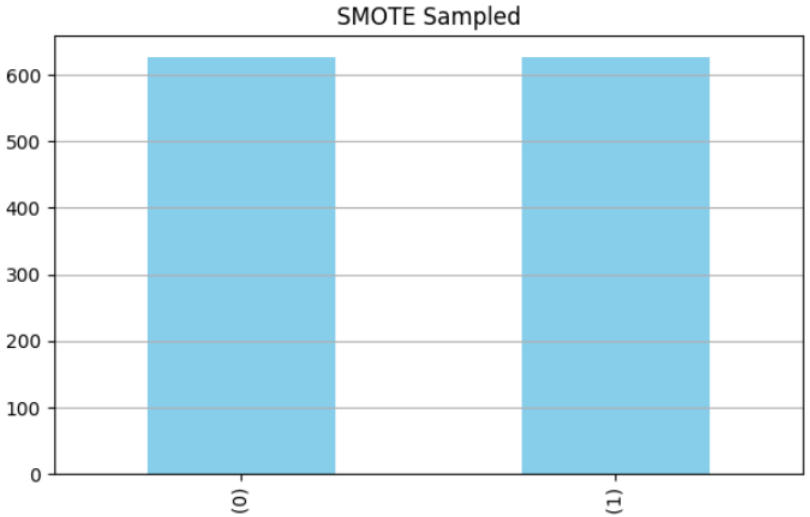
Before SMOTE: Data is imbalanced; the model favors the majority class (red)

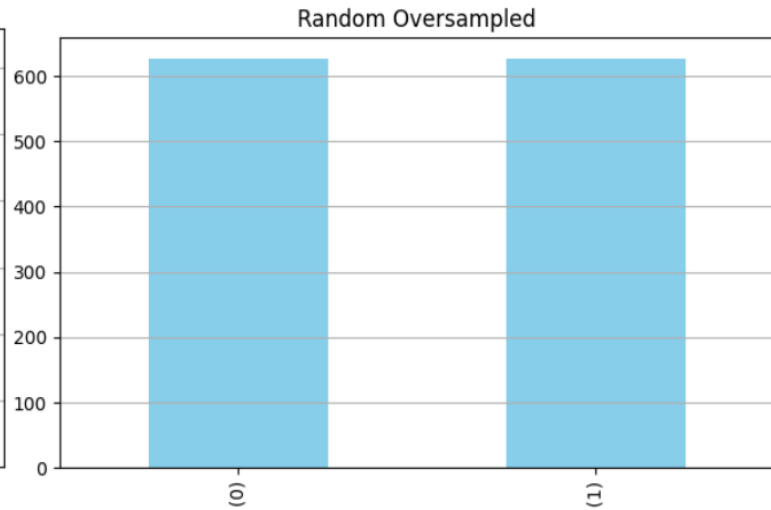
After SMOTE: Classes are balanced; model learns both classes more effectively, improving fairness and recall (balance between red and blue).

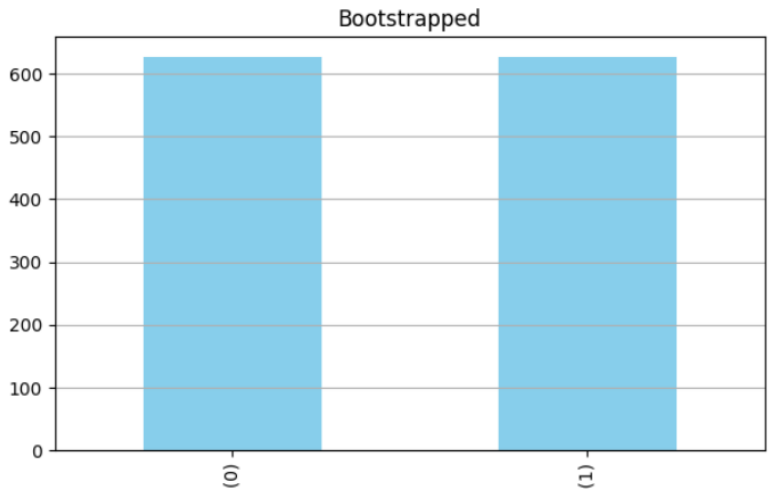
Sampling balance visualization – Data distribution





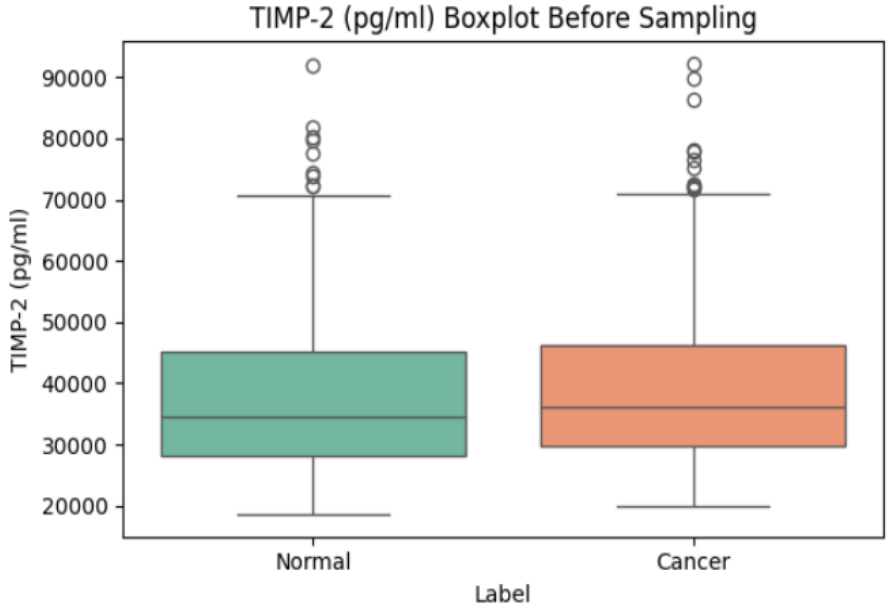


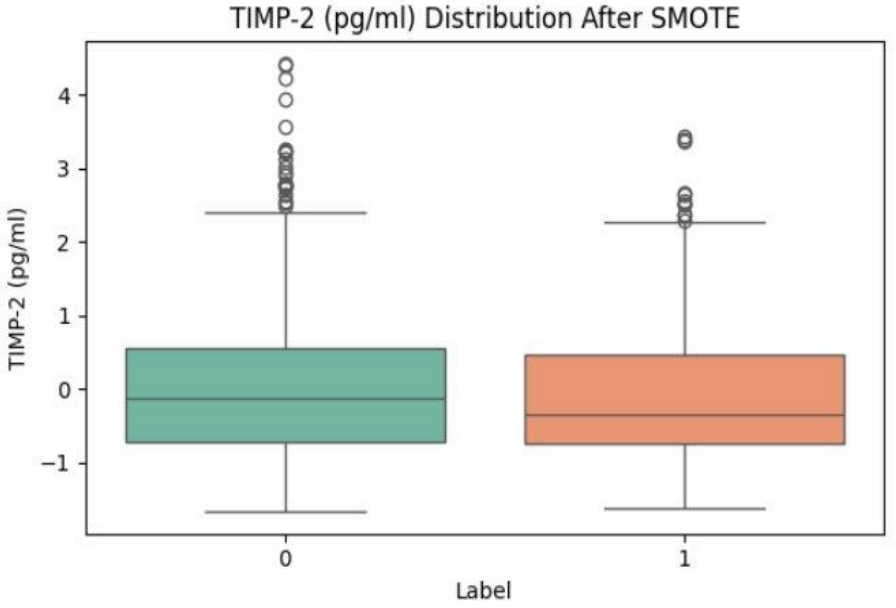




Sampling balance visualization – Box plots:

- Before sampling, the distribution of TIMP-2 values was imbalanced between the normal and cancer groups, with visible differences in spread and medians.
- After applying SMOTE (Synthetic Minority Over-sampling Technique), the sample size was balanced, leading to more symmetrical box plots for both classes.
- The SMOTE-adjusted distribution helps ensure that the model is trained on balanced data, improving fairness and reducing bias during classification.





Model building - Overview

Why? Classification problem

Models Used:

Random Forest and logistic regression

Supported by : (Du et al., 2024)

Random Forest (RF):
An ensemble learning method that combines multiple decision trees to improve prediction accuracy and control overfitting.

Logistic Regression (LR):
A linear model used for binary classification, useful for interpretability and identifying relationships between biomarkers and cancer outcome.

Why These Models?
Both models perform well on imbalanced biomedical data and allow for feature importance interpretation.

Random forest

- Suitable for binary classification, such as predicting GI cancer presence.

```
from sklearn.ensemble import RandomForestClassifier
from sklearn.metrics import classification_report

rf_model = RandomForestClassifier(n_estimators=100, random_state=42)

#SMOTE
rf_model.fit(X_train_smote, y_train_smote)
y_pred_smote = rf_model.predict(X_test_scaled)
print("SMOTE")
print(classification_report(y_test, y_pred_smote))

#Random Oversampling
rf_model.fit(X_train_ros, y_train_ros)
y_pred_ros = rf_model.predict(X_test_scaled)
print("Random Oversampling")
print(classification_report(y_test, y_pred_ros))

#Random Undersampling
rf_model.fit(X_train_rus, y_train_rus)
y_pred_rus = rf_model.predict(X_test_scaled)
print("Random Undersampling")
print(classification_report(y_test, y_pred_rus))

#Bootstrapping
rf_model.fit(X_train_bootstrap, y_train_bootstrap)
y_pred_boot = rf_model.predict(X_test_scaled)
print("Bootstrapping")
print(classification_report(y_test, y_pred_boot))
```

Random Forest overview and results:

- SMOTE AUC (0.92): 92% chance of correctly ranking positive cases higher.
- Undersampling AUC (0.94): 94% chance, slightly better performance.
- Oversampling AUC (0.93) and Bootstrapping AUC (0.93): Strong but slightly lower than undersampling.

SMOTE

	precision	recall	f1-score	support
0	0.90	0.85	0.87	157
1	0.76	0.84	0.80	91
accuracy			0.84	248
macro avg	0.83	0.84	0.83	248
weighted avg	0.85	0.84	0.84	248

Random Oversampling

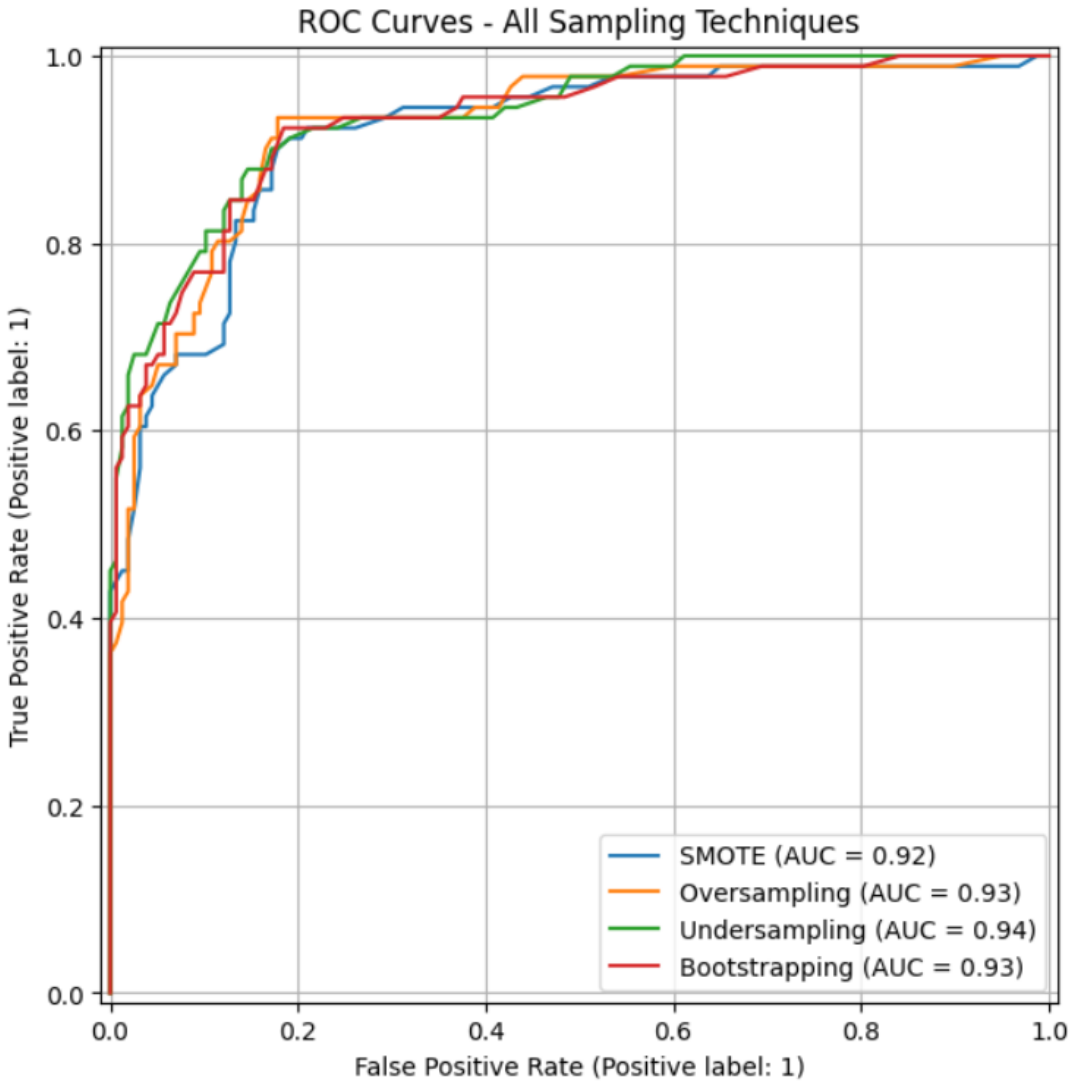
	precision	recall	f1-score	support
0	0.88	0.87	0.88	157
1	0.78	0.80	0.79	91
accuracy			0.85	248
macro avg	0.83	0.84	0.84	248
weighted avg	0.85	0.85	0.85	248

Random Undersampling

	precision	recall	f1-score	support
0	0.92	0.86	0.89	157
1	0.78	0.87	0.82	91
accuracy			0.86	248
macro avg	0.85	0.86	0.86	248
weighted avg	0.87	0.86	0.86	248

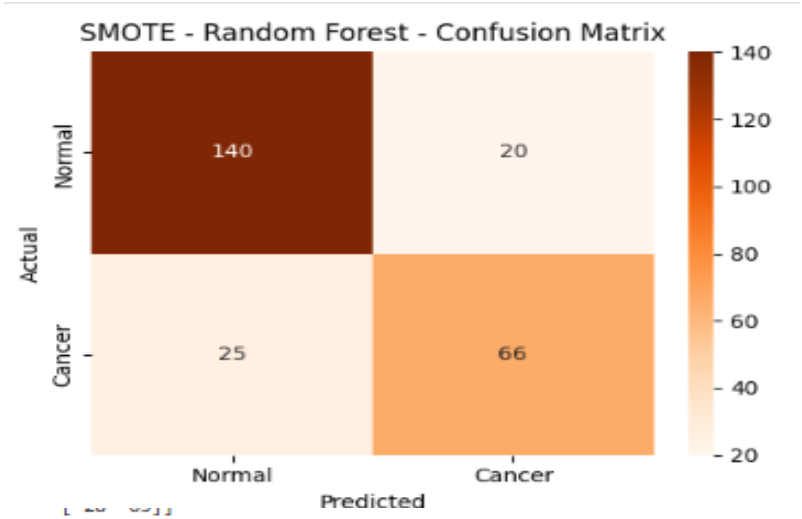
Bootstrapping

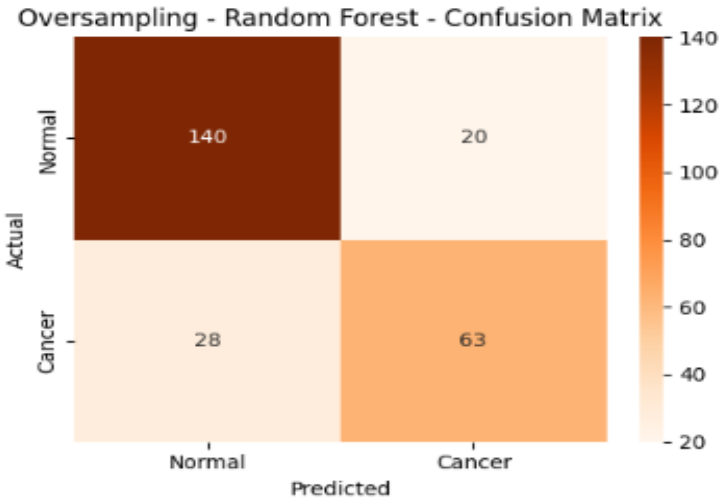
	precision	recall	f1-score	support
0	0.86	0.92	0.89	157
1	0.85	0.75	0.80	91
accuracy			0.86	248
macro avg	0.86	0.84	0.84	248
weighted avg	0.86	0.86	0.86	248

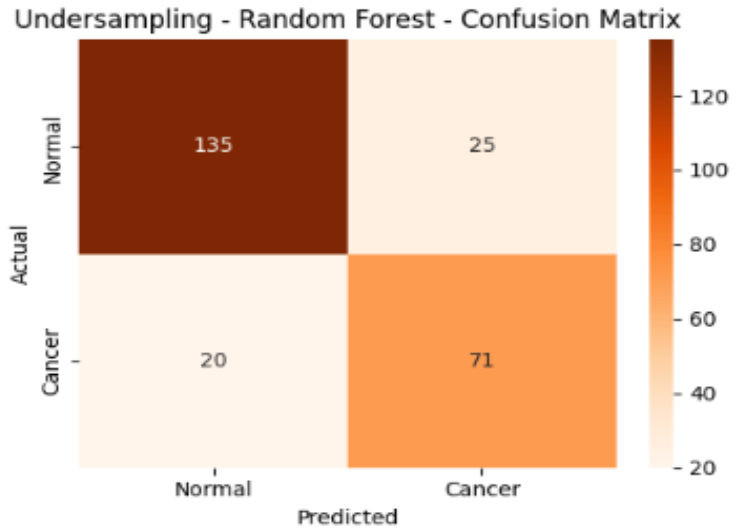


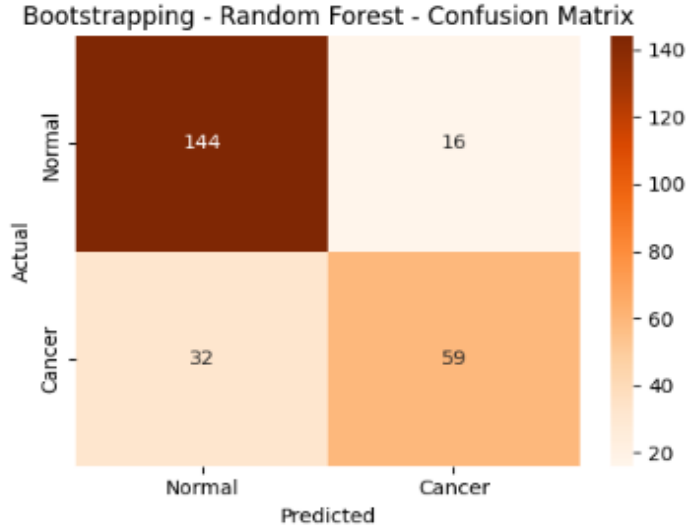
Random Forest overview and results:

- SMOTE and Undersampling gave the best cancer detection.
- Bootstrapping had the lowest sensitivity for cancer cases.
- SMOTE offered a balanced trade-off between precision and recall.









Logistic regression

- Ideal for binary classification tasks like predicting GI cancer.
- Offers clear interpretability of how biomarkers affect cancer risk.

```
from sklearn.linear_model import LogisticRegression
from sklearn.metrics import classification_report

lr_model = LogisticRegression(max_iter=1000, random_state=42)

#SMOTE
lr_model.fit(X_train_smote, y_train_smote)
y_pred_smote_lr = lr_model.predict(X_test_scaled)
print("SMOTE - Logistic Regression")
print(classification_report(y_test, y_pred_smote_lr))

#Random Oversampling
lr_model.fit(X_train_ros, y_train_ros)
y_pred_ros_lr = lr_model.predict(X_test_scaled)
print("Oversampling - Logistic Regression")
print(classification_report(y_test, y_pred_ros_lr))

#Random Undersampling
lr_model.fit(X_train_rus, y_train_rus)
y_pred_rus_lr = lr_model.predict(X_test_scaled)
print("Undersampling - Logistic Regression")
print(classification_report(y_test, y_pred_rus_lr))

#Bootstrapping
lr_model.fit(X_train_bootstrap, y_train_bootstrap)
y_pred_boot_lr = lr_model.predict(X_test_scaled)
print("Bootstrapping - Logistic Regression")
print(classification_report(y_test, y_pred_boot_lr))
```

Logistic Regression overview and results:

- **SMOTE AUC (0.89)**: 89% chance of correctly ranking positive cases higher.
- **Oversampling AUC (0.91)**: 91% chance, good model performance.
- **Undersampling AUC (0.91)** and **Bootstrapping AUC (0.91)**: All show similar, strong results.

SMOTE - Logistic Regression

	precision	recall	f1-score	support
0	0.87	0.84	0.86	157
1	0.74	0.79	0.77	91
accuracy			0.82	248
macro avg	0.81	0.82	0.81	248
weighted avg	0.83	0.82	0.82	248

Oversampling - Logistic Regression

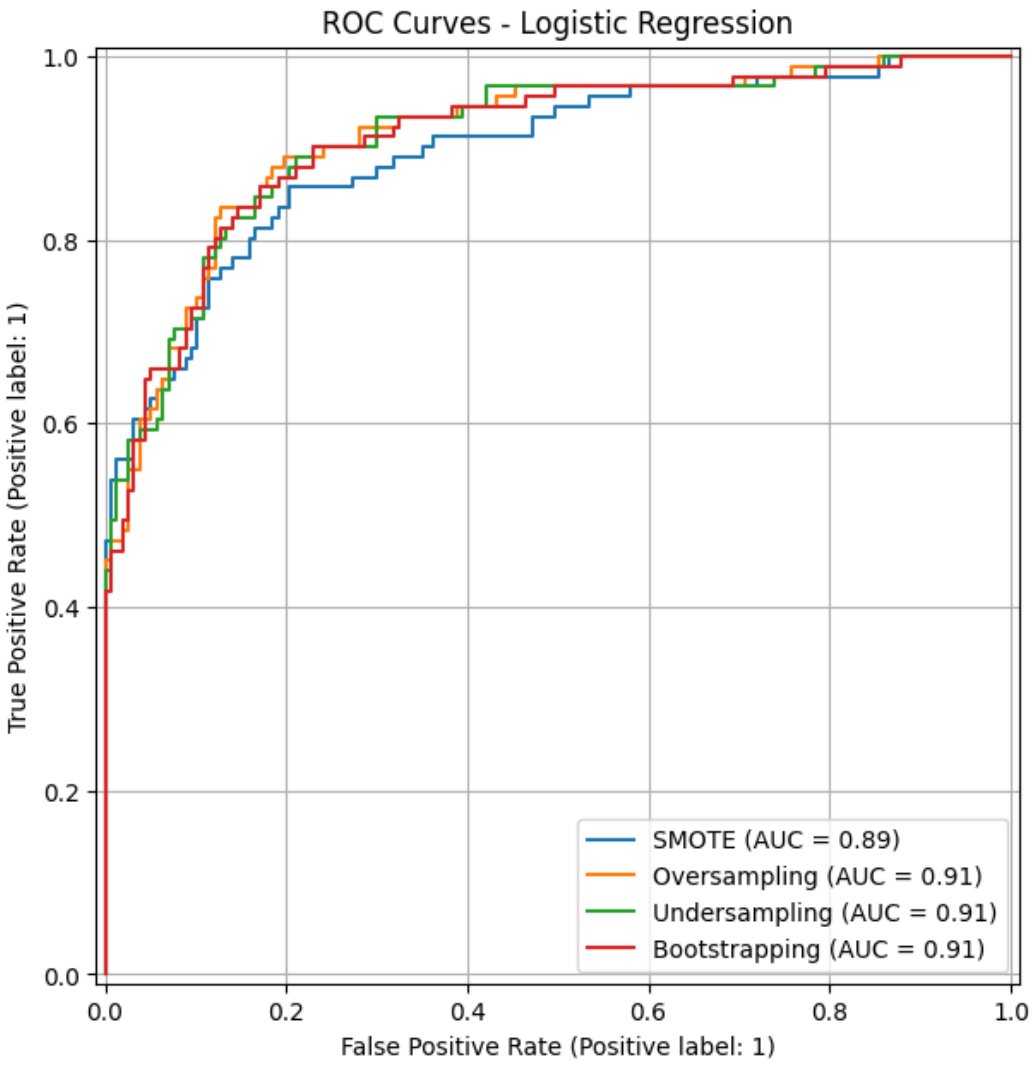
	precision	recall	f1-score	support
0	0.88	0.88	0.88	157
1	0.79	0.80	0.80	91
accuracy			0.85	248
macro avg	0.84	0.84	0.84	248
weighted avg	0.85	0.85	0.85	248

Undersampling - Logistic Regression

	precision	recall	f1-score	support
0	0.89	0.85	0.87	157
1	0.77	0.82	0.79	91
accuracy			0.84	248
macro avg	0.83	0.84	0.83	248
weighted avg	0.85	0.84	0.84	248

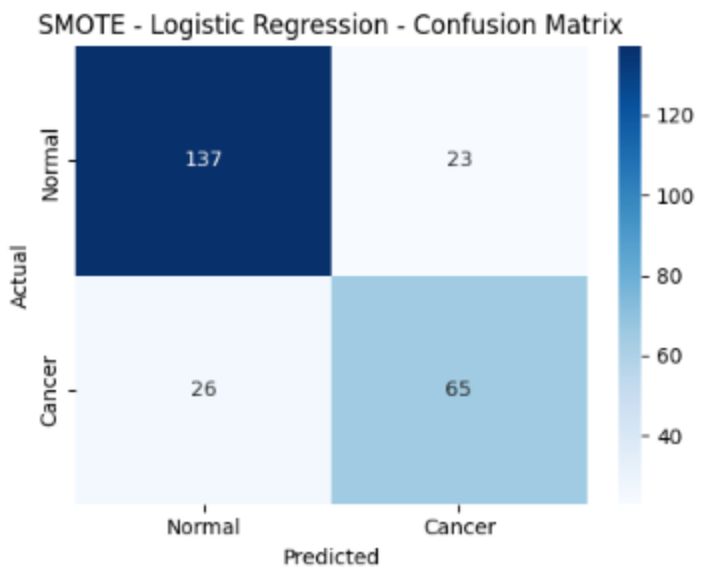
Bootstrapping - Logistic Regression

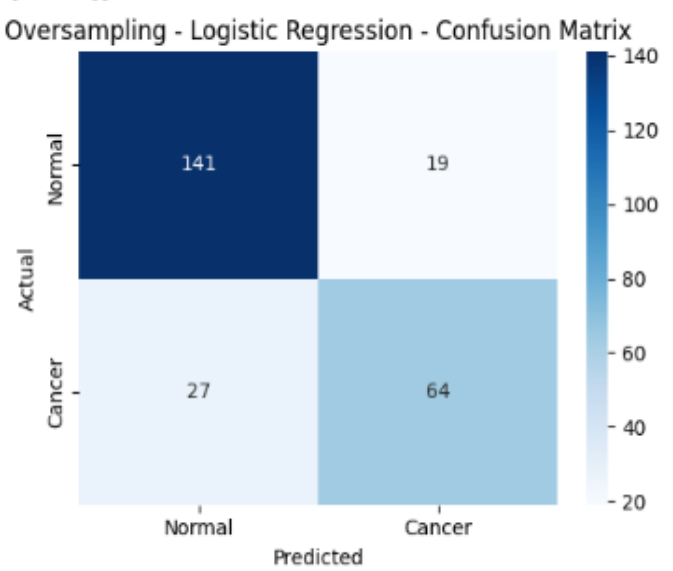
	precision	recall	f1-score	support
0	0.88	0.88	0.88	157
1	0.79	0.79	0.79	91
accuracy			0.85	248
macro avg	0.84	0.84	0.84	248
weighted avg	0.85	0.85	0.85	248

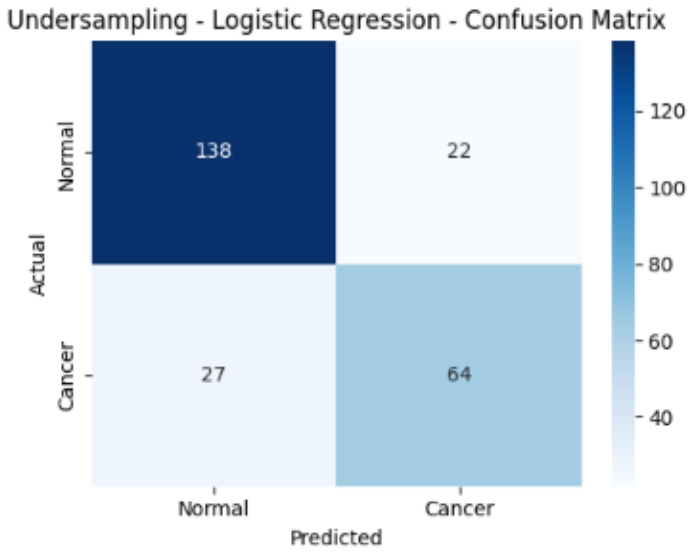


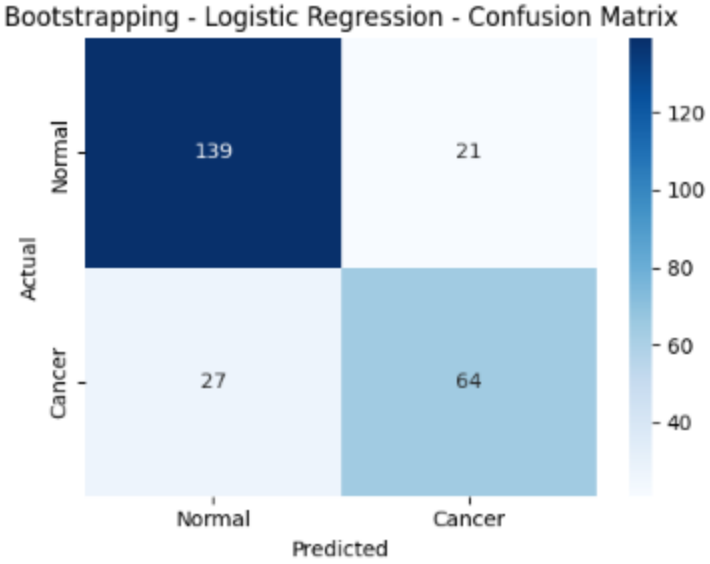
Logistic Regression overview and results:

- All sampling methods produced similar results with minor variations.
- **SMOTE** slightly outperformed others in detecting cancer cases (65 true positives).
- **Oversampling** and **Bootstrapping** showed consistent performance but had slightly more false negatives.
- Logistic Regression remained stable across all sampling strategies.









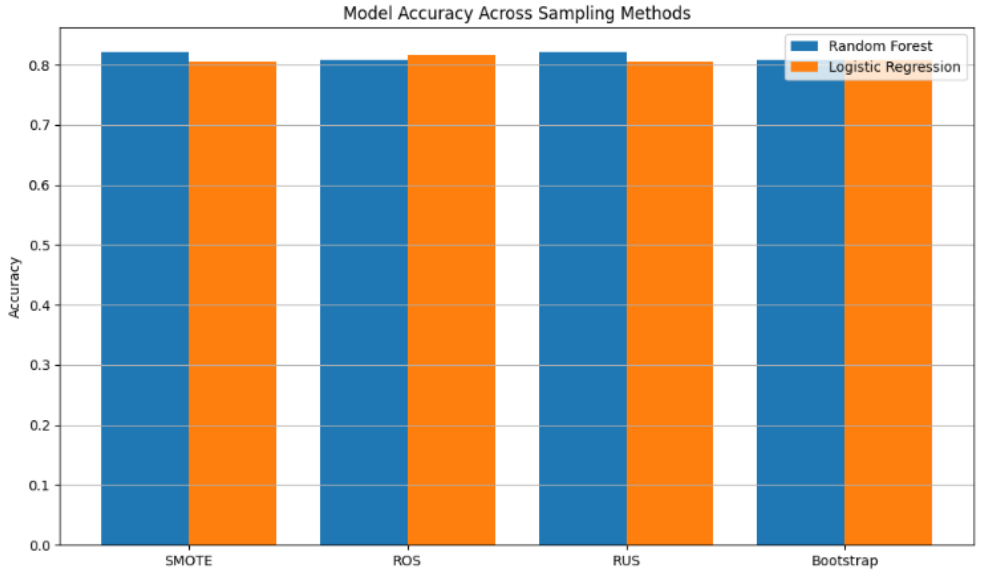
Evaluation Metrics Summary

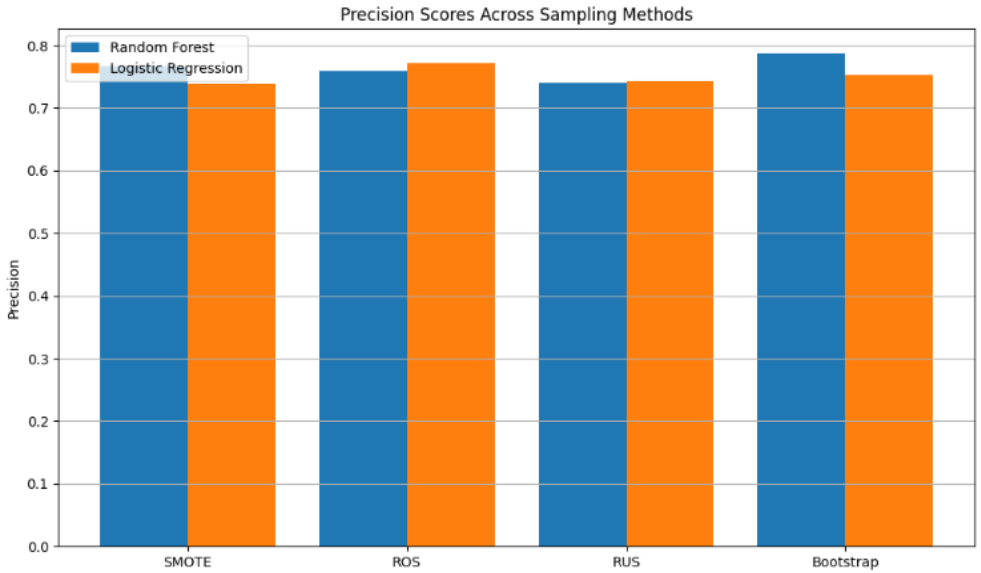
ACCURACY

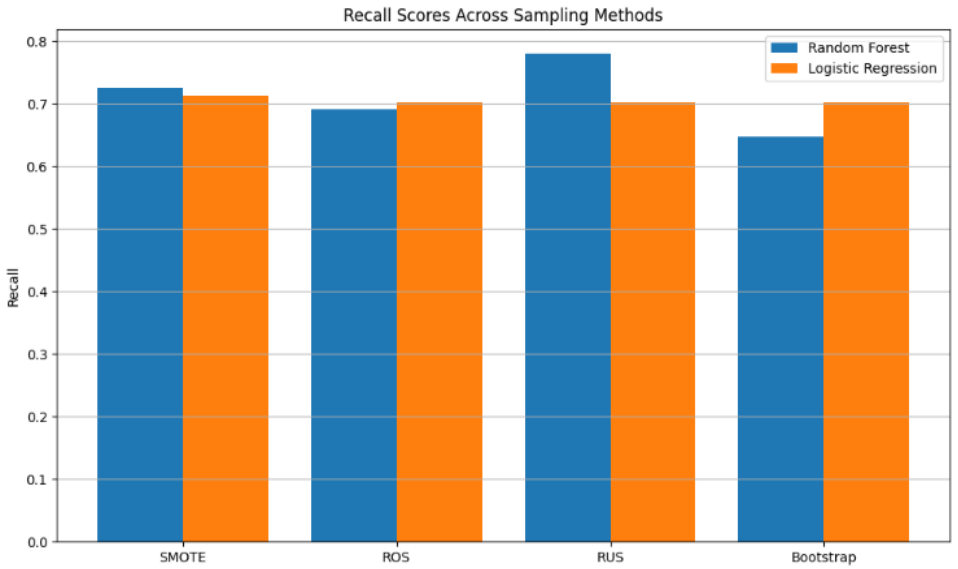
PRECISION

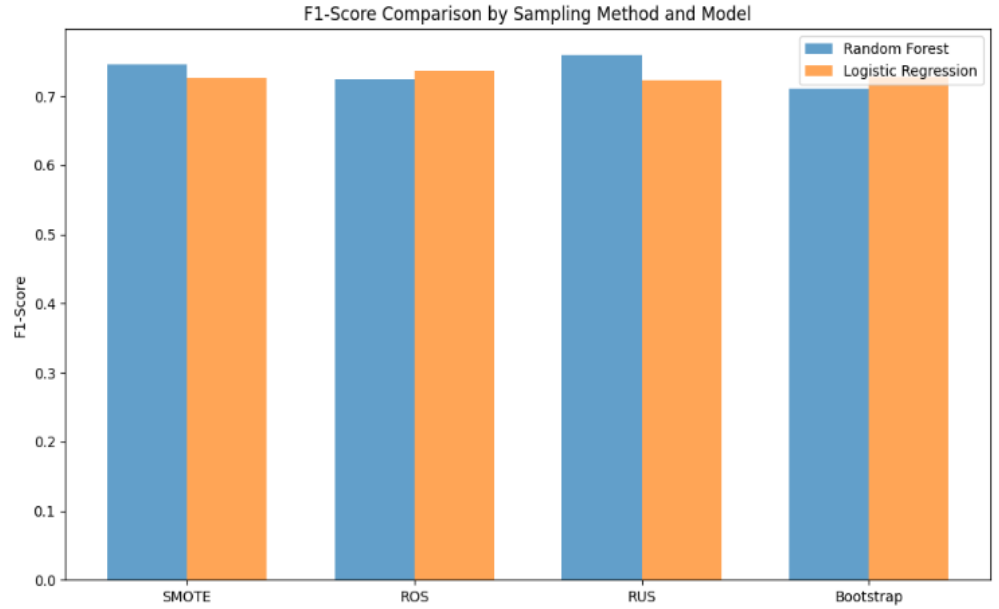
RECALL

F1-SCORE


Model Accuracy Across Sampling Methods
Random Forest
Logistic Regression
Accuracy
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
SMOTE
ROS
RUS
Bootstrap


Precision Scores Across Sampling Methods
Random Forest
Logistic Regression
Precision
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
SMOTE
ROS
RUS
Bootstrap


Recall Scores Across Sampling Methods
Random Forest
Logistic Regression
Recall
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
SMOTE
ROS
RUS
Bootstrap


F1-Score Comparison by Sampling Method and Model
Random Forest
Logistic Regression
F1-Score
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
SMOTE
ROS
RUS
Bootstrap

Model Comparison:

- The SMOTE AUC of 0.92 for Random forest classifier
- The SMOTE AUC of 0.89 for logistic regression
- The best model for predicting GI cancer is Random forest as it is evident that Random Forest consistently outperforms Logistic Regression across all sampling techniques.
- Undersampling + RF achieved the highest F1-score (0.82), showing strong class balance.
- SMOTE + RF provides balanced precision (0.76) and recall (0.83), making it a strong default choice.
- Logistic Regression performs reasonably but slightly lags behind Random Forest in all metrics.
- All sampling strategies helped mitigate class imbalance, with undersampling slightly outperforming others in final model performance.

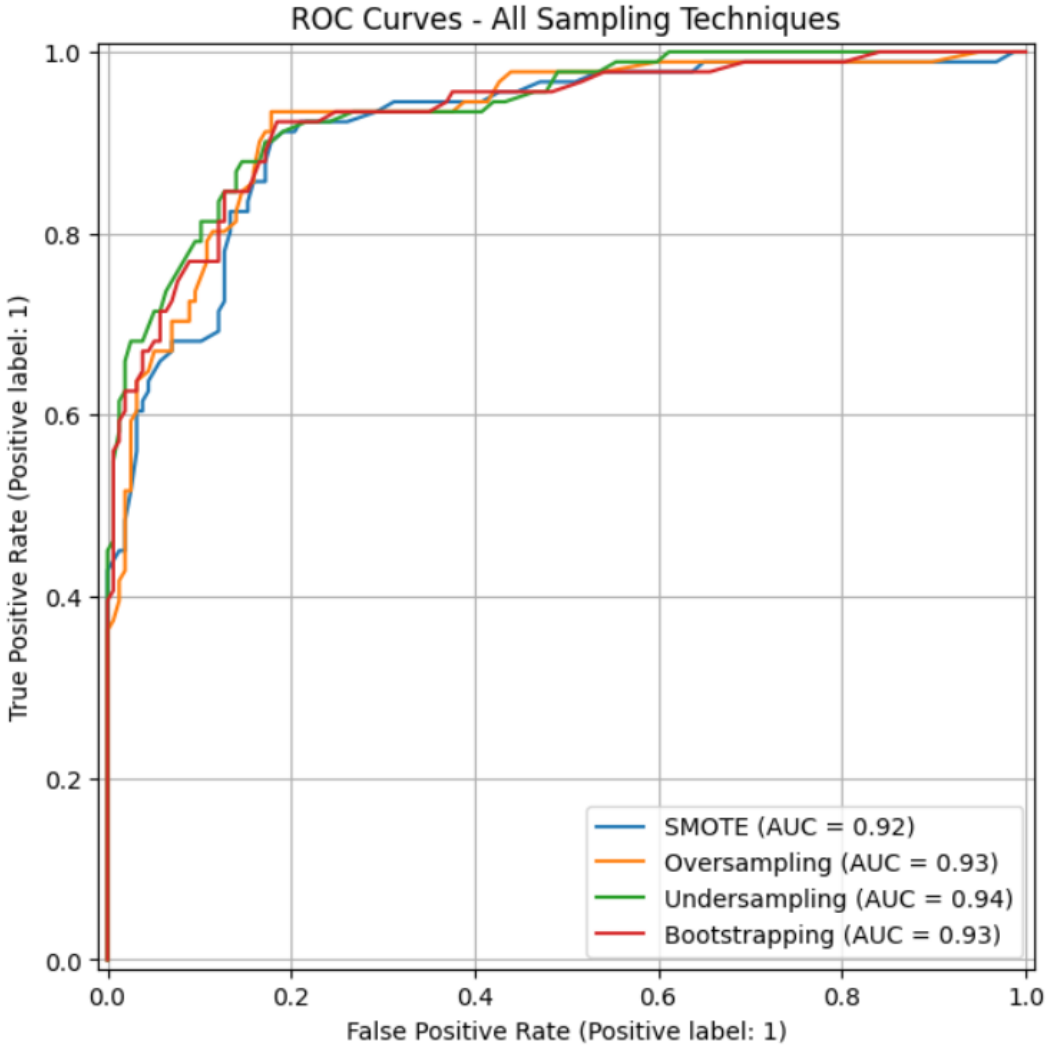
Performance summary table

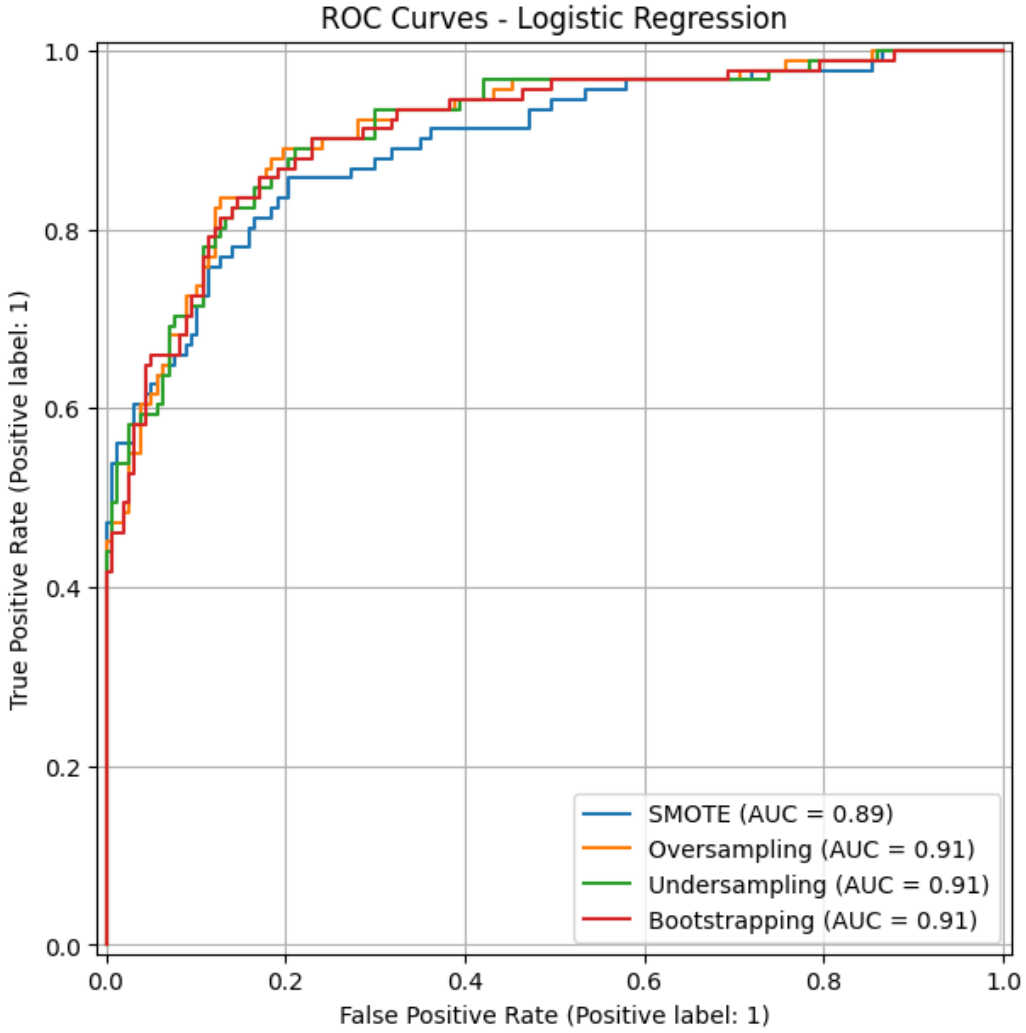
	Model	Accuracy	Precision	Recall	F1-Score
0	RF - SMOTE	0.843	0.760	0.835	0.796
1	RF - ROS	0.847	0.785	0.802	0.793
2	RF - RUS	0.863	0.782	0.868	0.823
3	RF - Bootstrapping	0.859	0.850	0.747	0.795
4	LR - SMOTE	0.823	0.742	0.791	0.766
5	LR - ROS	0.851	0.793	0.802	0.798
6	LR - RUS	0.843	0.765	0.824	0.794
7	LR - Bootstrapping	0.847	0.791	0.791	0.791

Model Comparison Summary

	Model	Sampling	Accuracy	Precision	Recall	F1-Score
0	Random Forest	SMOTE	0.84	0.76	0.83	0.79
1	Logistic Regression	SMOTE	0.82	0.74	0.79	0.76
2	Random Forest	Oversampling	0.84	0.78	0.80	0.79
3	Random Forest	Undersampling	0.84	0.78	0.86	0.82

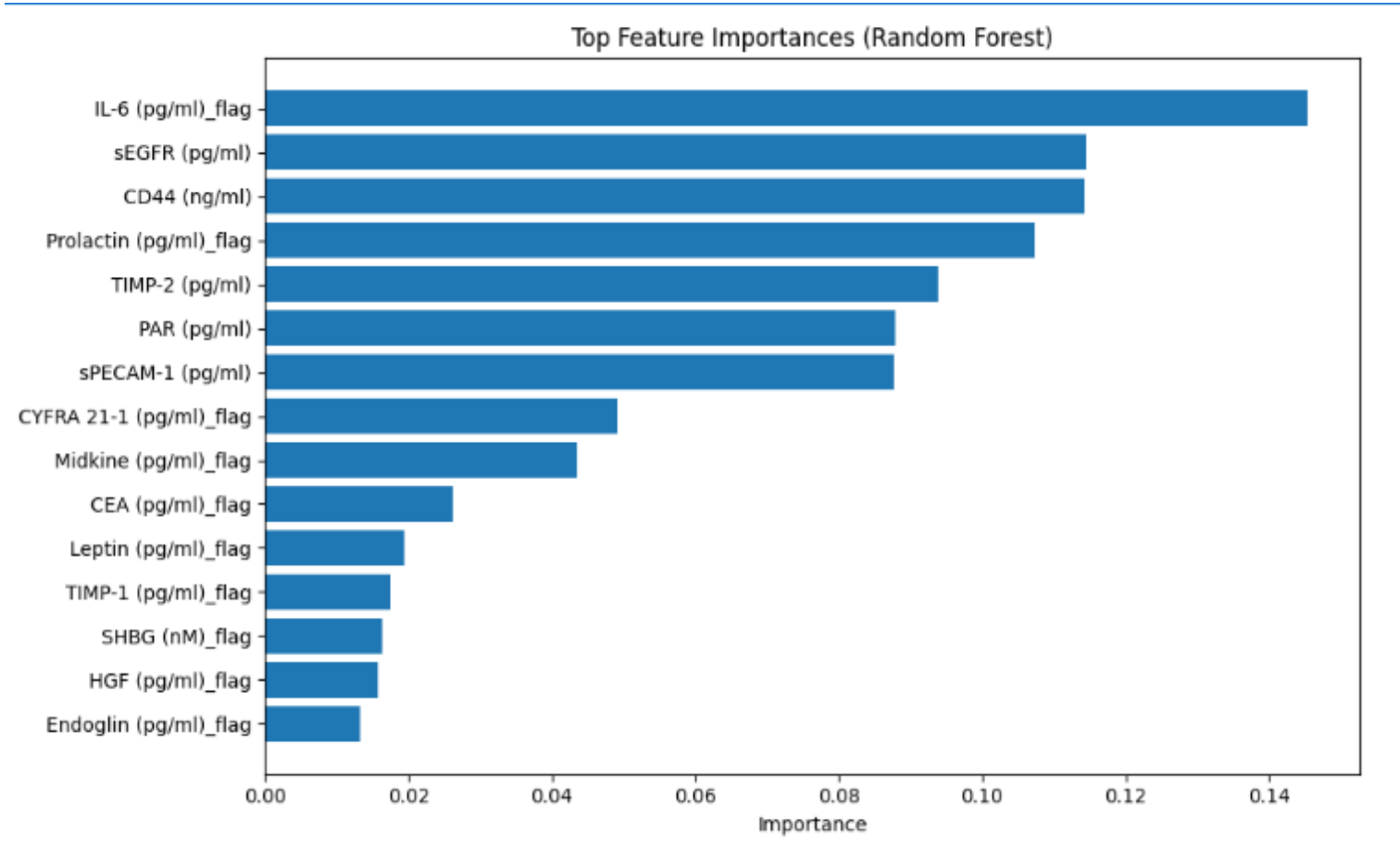
ROC Curves


ROC Curves - All Sampling Techniques
True Positive Rate (Positive label: 1)
False Positive Rate (Positive label: 1)
0.0
0.2
0.4
0.6
0.8
1.0
SMOTE (AUC = 0.92)
Oversampling (AUC = 0.93)
Undersampling (AUC = 0.94)
Bootstrapping (AUC = 0.93)


ROC Curves - Logistic Regression
True Positive Rate (Positive label: 1)
False Positive Rate (Positive label: 1)
0.0
0.2
0.4
0.6
0.8
1.0
SMOTE (AUC = 0.89)
Oversampling (AUC = 0.91)
Undersampling (AUC = 0.91)
Bootstrapping (AUC = 0.91)

Feature Importance

The Random Forest model revealed that a subset of biomarkers plays a major role in distinguishing GI cancer from normal cases. Features with higher importance scores contribute more to the model's decision-making, highlighting their potential relevance in diagnostic applications.



Demographic Analysis

Discussions and conclusion

NULL HYPOTHESIS (H_0): There is no statistically significant difference in biomarker values between GI cancer and normal patients.

- Statistical hypothesis testing was conducted to determine whether there are significant differences in biomarker levels between GI cancer and normal patients. Based on p-values from multiple tests (all $p < 0.05$), the **null hypothesis** – stating that there is no difference – was **rejected** for all listed features.

- Angiopoietin-2 p-value= 0.00001, reject null hypothesis (H_0)
- SHBG p-value= 0.00002, reject null hypothesis (H_0)
- CA-125 p-value= 0.00002, reject null hypothesis (H_0)
- AFP p-value= 0.00886 reject null hypothesis (H_0)
- Kalikrein-6 p-value= 0.02145 reject null hypothesis (H_0)
- PAR p-value= 0.00149, reject null hypothesis (H_0)
- TIMP2 p-value=0.00187 reject null hypothesis (H_0)
- CD4 p-value =0.03966, reject null hypothesis (H_0)

Conclusion: These features exhibit statistically significant differences between groups serve as important variables for cancer classification or prediction models.

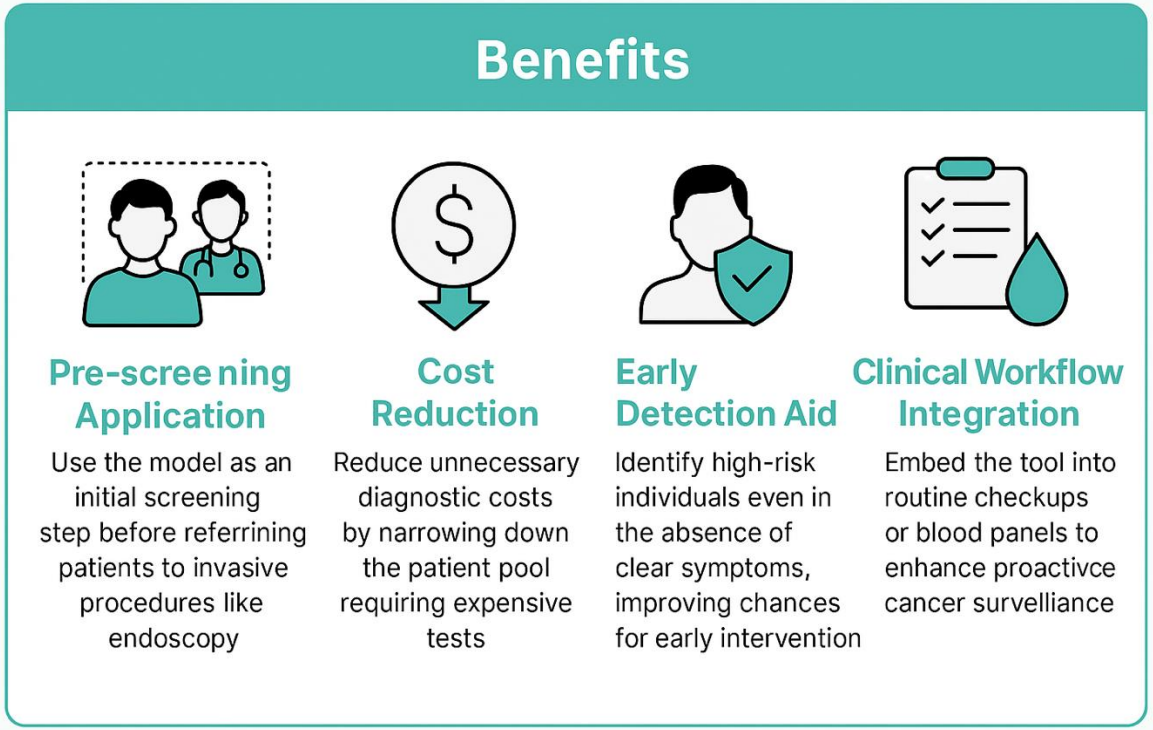
DISCUSSION:

- SMOTE improved model performance by addressing class imbalance, leading to higher AUC scores.
- Random Forest Classifier is the most effective model for predicting GI cancer in this dataset.
- Random Forest + SMOTE outperformed Logistic Regression with an AUC of 0.92, indicating better discrimination ability.
- Random Forest with undersampling achieved the highest F1-score (0.82) and strong recall (0.86), making it the most reliable model.
- Recall and AUC-ROC were prioritized, as minimizing false negatives is critical in cancer diagnosis
- Significant biomarkers ($p < 0.05$): IL-6, sEGFR, CD-44, Prolactin, TIMP-2, PAR, CEA , Leptin etc.. show strong potential for distinguishing GI cancer from normal cases, consistent with the findings and aided in rejection of null hypothesis (Sato et al., 2023; Tabari et al., 2022).
- **H_o Rejected:**
  Significant differences found in multiple biomarkers and demographics between cancer and normal patient records

Future scope:

- Future work: Include external validation or multi-class classification
- Evaluate model robustness using independent datasets from external sources to confirm generalizability.
- Extend to subtype classification (e.g., CRC vs gastric)
- Develop a web-based clinical tool for real-time GI cancer risk prediction
- Incorporate time-series or follow-up data to assess biomarker trends over disease progression or treatment response.

Clinical integration:



Challenges & Limitations

- Not all biomarkers have universal clinical cutoffs
- Black-box behavior of ensemble models
- **Class Imbalance**: The original dataset had a 64:36 imbalance (800 negative, 455) positive), which could bias the model toward the majority class
- **Synthetic Oversampling (SMOTE)**: While it helped balance the data, it may introduce artificial patterns not present in real-world data, risking overfitting
- **Small Sample Size**: Limits generalizability and may reduce model robustness across larger or more diverse populations.

Team Contributions:

Mahitha Gogu – Data cleaning and preprocessing

Geetanjali Karuturi – Data visualization and exploratory data analysis

Frederick Onyango – Statistical analysis and demographic insights

Rashmita Kudamala – Machine learning model training and evaluation

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THANK YOU

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Appendix: Code Snippets

```
myvars = {}
with open("rakuda-mysql-password") as myfile:
    for line in myfile:
        name, var = line.partition(":")[::2]
        myvars[name.strip()] = var.strip()
```

```
myvars.keys()
```

```
dict_keys(['DB username', 'DB databasename', 'DB password'])
```

```
import MySQLdb
conn = MySQLdb.connect(host="localhost", user=myvars['DB username'], passwd=myvars['DB password'], db=myvars['DB databasename'])
cursor = conn.cursor()
```

```
cursor.execute("USE I501_Spring2025_Sec27856_group04_db")
cursor.execute("SELECT DATABASE()")
print("Now using:", cursor.fetchone())
```

```
Now using: ('I501_Spring2025_Sec27856_group04_db',)
```

```
cursor.execute('select * FROM intro_project_dataset');

rows_table1 = cursor.fetchall()

cursor.execute('select * FROM intro_project_dataset_2');

rows_table2 = cursor.fetchall()
```

```
print("Rows in intro_project_dataset:", len(rows_table1))
print("Rows in intro_project_dataset_2:", len(rows_table2))
```

```
Rows in intro_project_dataset: 1822
Rows in intro_project_dataset_2: 1822
```

```
import pandas as pd

pd.set_option('display.max_rows', None)

cursor.execute('SELECT * FROM intro_project_dataset')
rows_table1 = cursor.fetchall()
columns_table1 = [desc[0] for desc in cursor.description]
df1 = pd.DataFrame(rows_table1, columns=columns_table1)

print("Full Dataset 1:")
display(df1.head())
```

```
Full Dataset 1:
```

	COL 1	COL 2	COL 3	COL 4	COL 5	COL 6	COL 7	COL 8	COL 9	COL 10	COL 11	COL 12	COL 13
0	Patient ID #	Plasma sample ID #	Primary tumor sample ID #	Age	Sex	Race	Tumor type	AJCC Stage	Histopathology	Plasma volume (mL)	Plasma DNA concentration (ng/mL)	CancerSEEK Logistic Regression Score	CancerSEEK Test Result
1	CRC 455	CRC 455 PLS 1	Not available	60	Male	Caucasian	Colorectum	I	Adenocarcinoma	5	6.08	0.938	Positive
2	CRC 456	CRC 456 PLS 1	CRC 456 PT1	59	Female	Caucasian	Colorectum	I	Adenocarcinoma	4	46.01	0.925	Positive
3	CRC 457	CRC 457 PLS 1	CRC 457 PT1	69	Female	Caucasian	Colorectum	II	Adenocarcinoma	4.5	6.94	0.852	Negative
4	CRC 458	CRC 458 PLS 1	CRC 458 PT1	70	Female	Caucasian	Colorectum	II	Adenocarcinoma	7.5	7.15	0.618	Negative

```
cursor.execute('SELECT * FROM intro_project_dataset_2')
rows_table2 = cursor.fetchall()
columns_table2 = [desc[0] for desc in cursor.description]
df2 = pd.DataFrame(rows_table2, columns=columns_table2)

print("Full Dataset 2:")
display(df2.head())
```

```
Full Dataset 2:
```

	COL 1	COL 2	COL 3	COL 4	COL 5	COL 6	COL 7	COL 8	COL 9	COL 10	COL 11	COL 12	COL 13	COL 14	COL 15	COL 16	COL 17	COL
0	Patient ID #	Sample ID #	Tumor type	AJCC Stage	AFP (pg/ml)	Angiopoietin-2 (pg/ml)	AXL (pg/ml)	CA-125 (U/ml)	CA 15-3 (U/ml)	CA19-9 (U/ml)	CD44 (ng/ml)	CEA (pg/ml)	CYFRA 21-1 (pg/ml)	DKK1 (ng/ml)	Endoglin (pg/ml)	FGF2 (pg/ml)	Follistatin (pg/ml)	Galec (ng/
1	CRC 455	CRC 455 PLS 1	Colorectum	I	1583.45	5598.5	3621.04	5.09	19.08	*16.452	9.81	540.1	*1938.654	0.78	2882.65	92.02	2144.33	1
2	CRC 456	CRC 456 PLS 1	Colorectum	I	*715.308	20936.35	2772.96	7.27	10.04	40.91	27.57	5,902.40	*1938.654	0.77	3921.77	164.06	1646.26	
		CRC																

```
cursor.execute("SELECT * FROM intro_project_dataset")
rows_table1 = cursor.fetchall()

cursor.execute("SELECT * FROM intro_project_dataset_2")
rows_table2 = cursor.fetchall()

# Using first row as column names
columns_table1 = rows_table1[0]
data_table1 = rows_table1[1:]

columns_table2 = rows_table2[0]
data_table2 = rows_table2[1:]

df1 = pd.DataFrame(data_table1, columns=columns_table1)
df2 = pd.DataFrame(data_table2, columns=columns_table2)

print("df1 columns:", df1.columns.tolist())
print("df2 columns:", df2.columns.tolist())
display(df1.head())
display(df2.head())
```

```
df1 columns: ['Patient ID #', 'Plasma sample ID #', 'Primary tumor sample ID #', 'Age', 'Sex', 'Race', 'Tumor type', 'AJCC Stage', 'Histopathology', '
lasma volume (mL)', 'Plasma DNA concentration (ng/mL)', 'CancerSEEK Logistic Regression Score', 'CancerSEEK Test Result']
df2 columns: ['Patient ID #', 'Sample ID #', 'Tumor type', 'AJCC Stage', 'AFP (pg/ml)', 'Angiopoietin-2 (pg/ml)', 'AXL (pg/ml)', 'CA-125 (U/ml)', 'CA
5-3 (U/ml)', 'CA19-9 (U/ml)', 'CD44 (ng/ml)', 'CEA (pg/ml)', 'CYFRA 21-1 (pg/ml)', 'DKK1 (ng/ml)', 'Endoglin (pg/ml)', 'FGF2 (pg/ml)', 'Follistatin (p
g/ml)', 'Galectin-3 (ng/ml)', 'G-CSF (pg/ml)', 'GDF15 (ng/ml)', 'HE4 (pg/ml)', 'HGF (pg/ml)', 'IL-6 (pg/ml)', 'IL-8 (pg/ml)', 'Kallikrein-6 (pg/ml)',
'Leptin (pg/ml)', 'Mesothelin (ng/ml)', 'Midkine (pg/ml)', 'Myeloperoxidase (ng/ml)', 'NSE (ng/ml)', 'OPG (ng/ml)', 'OPN (pg/ml)', 'PAR (pg/ml)', 'Pro
actin (pg/ml)', 'sEGFR (pg/ml)', 'sFas (pg/ml)', 'SHBG (nM)', 'sHER2/sEGFR2/sErbB2 (pg/ml)', 'sPECAM-1 (pg/ml)', 'TGFa (pg/ml)', 'Thrombospondin-2 (pg
ml)', 'TIMP-1 (pg/ml)', 'TIMP-2 (pg/ml)', 'CancerSEEK Logistic Regression Score', 'CancerSEEK Test Result']
```

```python
df1 = df1.rename(columns={"Plasma sample ID #": "Sample_ID"})
df2 = df2.rename(columns={"Sample ID #": "Sample_ID"})

# full outer join on Sample_ID
merged_df = pd.merge(df1, df2, on="Sample_ID", how="outer", suffixes=('_from_df1', '_from_df2'))

print("Merged DataFrame (with unmatched rows showing NaN):")
display(merged_df.head())
```

	Patient ID #_from_df1	Sample_ID	Primary tumor sample ID #	Age	Sex	Race	Tumor type_from_df1	AJCC Stage_from_df1	Histopathology	Plasma volume (mL)	Plasma DNA concentration (ng/mL)	CancerSEI Logist Regressi Score_from_d
0	CRC 455	CRC 455 PLS 1	Not available	60	Male	Caucasian	Colorectum	I	Adenocarcinoma	5	6.08	0.9
1	CRC 456	CRC 456 PLS 1	CRC 456 PT1	59	Female	Caucasian	Colorectum	I	Adenocarcinoma	4	46.01	0.9
2	CRC 457	CRC 457 PLS 1	CRC 457 PT1	69	Female	Caucasian	Colorectum	II	Adenocarcinoma	4.5	6.94	0.8
3	CRC 458	CRC 458 PLS 1	CRC 458 PT1	70	Female	Caucasian	Colorectum	II	Adenocarcinoma	7.5	7.15	0.6
4	CRC 459	CRC 459 PLS 1	CRC 459 PT1	43	Female	Caucasian	Colorectum	II	Adenocarcinoma	5	9.81	0.3
5	CRC 460	CRC 460 PLS 1	CRC 460 PT1	72	Male	Caucasian	Colorectum	II	Adenocarcinoma	5	16.33	0.9
6	CRC 461	CRC 461 PLS 1	CRC 461 PT1	70	Male	Caucasian	Colorectum	I	Adenocarcinoma	7.5	8.93	0.3

```
print("\nMissing values per column:")
print(merged_df.isna().sum())
```

```
Missing values per column:
Patient ID #_from_df1                              0
Sample_ID                                          0
Primary tumor sample ID #                          0
Age                                                0
Sex                                                0
Race                                               0
Tumor type_from_df1                                0
AJCC Stage_from_df1                                0
Histopathology                                     0
Plasma volume (mL)                                 0
Plasma DNA concentration (ng/mL)                   0
CancerSEEK Logistic Regression Score_from_df1      0
CancerSEEK Test Result_from_df1                    0
Patient ID #_from_df2                              0
Tumor type_from_df2                                0
AJCC Stage_from_df2                                0
AFP (pg/ml)                                        0
Angiopoietin-2 (pg/ml)                             0
AXL (pg/ml)                                        0
CA-125 (U/ml)                                      0
CA 15-3 (U/ml)                                     0
CA19-9 (U/ml)                                      0
CD44 (ng/ml)                                       0
CEA (pg/ml)                                        0
CYFRA 21-1 (pg/ml)                                 0
DKK1 (ng/ml)                                       0
Endoglin (pg/ml)                                   0
FGF2 (pg/ml)                                       0
Follistatin (pg/ml)                                0
```

```
has_null = merged_df.isnull().values.any()

if has_null:
    print("The dataset contains null values.")
    null_counts = merged_df.isnull().sum()
    print("\nNull value counts by column:")
    print(null_counts[null_counts > 0])
else:
    print("The dataset does not contain any null values.")

print("\nDataset info:")
merged_df.info()
```

```
The dataset does not contain any null values.
```

```
df = merged_df.applymap(lambda x: str(x).replace('*', '') if isinstance(x, str) else x)
df.head()
```

AJCC m_df1	Histopathology	Plasma volume (mL)	...	sFas (pg/ml)	SHBG (nM)	sHER2/sEGFR2/sErbB2 (pg/ml)	sPECAM-1 (pg/ml)	TGFa (pg/ml)	Thrombospondin-2 (pg/ml)	TIMP-1 (pg/ml)	TIMP-2 (pg/ml)	CancerSEEK Logistic Regression Score_from_df2	CancerSEEK Test Result_from_df2
I	Adenocarcinoma	5	...	204.792	55.06	6832.07	9368.53	16.086	21863.74	56428.71	39498.82	0.938	Positive
I	Adenocarcinoma	4	...	204.792	72.92	5549.47	6224.55	16.086	29669.66	73940.49	41277.09	0.925	Positive
II	Adenocarcinoma	4.5	...	204.792	173.78	3698.16	4046.48	179.03	6020.47	22797.28	28440.6	0.852	Negative
II	Adenocarcinoma	7.5	...	204.792	29.47	5856	6121.93	16.086	4331.02	20441.19	25896.73	0.618	Negative
II	Adenocarcinoma	5	...	204.792	78.07	5447.93	6982.32	16.086	2311.91	56288.51	49425.2	0.318	Negative

```
keywords = [
    'tumor type_from_df2', 'tumor type_from_df3',
    'patient id #_from_df1', 'patient id #_from_df2',
    'cancerseek logistic regression score_from_df1', 'cancerseek test result_from_df1',
    'cancerseek logistic regression score_from_df2', 'cancerseek test result_from_df2',
    'ajcc stage_from_df2', 'ajcc stage_from_df1', 'histopathology', 'primary tumor sample id #'
]

columns_to_drop = [col for col in merged_df.columns if any(key in col.lower() for key in keywords)]

print("Dropping columns:")
print(columns_to_drop)

df_cleaned = df.drop(columns=columns_to_drop)

df_cleaned.head()
```

```
Dropping columns:
['Patient ID #_from_df1', 'Primary tumor sample ID #', 'AJCC Stage_from_df1', 'Histopathology', 'CancerSEEK Logistic Regression Score_from_df1', 'Cancer
SEEK Test Result_from_df1', 'Patient ID #_from_df2', 'Tumor type_from_df2', 'AJCC Stage_from_df2', 'CancerSEEK Logistic Regression Score_from_df2', 'Can
cerSEEK Test Result_from_df2']
```

```
exclude_tumors = ['breast', 'esophagus', 'liver', 'lung', 'ovary', 'pancreas']

df_filtered = df_cleaned[~df_cleaned['Tumor type_from_df1'].str.lower().isin(exclude_tumors)]

print("Remaining tumor types:", df_filtered['Tumor type_from_df1'].unique())
print("Filtered dataset shape:", df_filtered.shape)
df_filtered
```

```
Remaining tumor types: ['Colorectum' 'Stomach' 'Normal']
Filtered dataset shape: (1255, 47)
```

```
# Data cleaning 3. Delete unwanted rows
df_cleaned = df_filtered.iloc[:1268]
df_cleaned.tail()
```

	Sample_ID	Age	Sex	Race	Tumor type_from_df1	Plasma volume (mL)	Plasma DNA concentration (ng/mL)	AFP (pg/ml)	Angiopoietin-2 (pg/ml)	AXL (pg/ml)	...	Prolactin (pg/ml)	sEGFR (pg/ml)	sFas (pg/ml)	SHBG (nM)
1698	NL PLSA 1850	58	Male	Unknown	Normal	7.5	1.36	740.016	1197.88	3780.3	...	9851.43	4677.93	1072.02	32.15
1699	NL PLSA 1851	51	Male	Unknown	Normal	7.5	2.2	740.016	1519.08	2893.79	...	7244.91	5158.71	192.948	22.91
1700	NL PLSA 1852	28	Male	Unknown	Normal	7.5	4.27	740.016	3916.14	3334.98	...	7783.77	2112.99	1016.67	147.48
1701	NL PLSA 1853	62	Male	Unknown	Normal	7.5	0.66	740.016	1142.66	1649.39	...	5271.87	2219.83	844.47	37.79
1702	NL PLSA 1854	64	Male	Unknown	Normal	7.5	0.59	740.016	2184.08	1492.69	...	5222.35	1732.68	1137.23	118.99

```
# Count missing values per column
missing_counts = df_cleaned.isna().sum()
missing_counts = missing_counts[missing_counts > 0]

if not missing_counts.empty:
    print("Columns with missing values:\n")
    for col in missing_counts.index:
        missing_rows = df_cleaned[df_cleaned[col].isna()].index.tolist()
        print(f"- {col}: {missing_counts[col]} missing (Rows: {missing_rows})")
else:
    print("No missing values found in the dataset!")
```

```
No missing values found in the dataset!
```

```python
import pandas as pd

df_cleaned = pd.read_csv("cleaned_dataset3.csv")

df_cleaned["Age"] = pd.to_numeric(df_cleaned["Age"], errors="coerce").fillna(0).astype(int)

for col in df_cleaned.columns:
    if col in ["Age", "Sample_ID", "Tumor type_from_df1"]:
        continue

    col_cleaned = df_cleaned[col].astype(str).str.replace(",", "")
    col_cleaned = col_cleaned.str.replace(r"[^0-9.\-]", "", regex=True)

    converted = pd.to_numeric(col_cleaned, errors="coerce")
    success_rate = converted.notna().mean()

    if success_rate > 0.5:
        df_cleaned[col] = converted
        print(f"Cleaned and converted '{col}' to float.")
    else:
        print(f"Skipped '{col}' — categorical")
```

```
Skipped 'Sex' — categorical
Skipped 'Race' — categorical
Cleaned and converted 'Plasma volume (mL)' to float.
Cleaned and converted 'Plasma DNA concentration (ng/mL)' to float.
Cleaned and converted 'AFP (pg/ml)' to float.
Cleaned and converted 'Angiopoietin-2 (pg/ml)' to float.
Cleaned and converted 'AXL (pg/ml)' to float.
Cleaned and converted 'CA-125 (U/ml)' to float.
Cleaned and converted 'CA 15-3 (U/ml)' to float.
Cleaned and converted 'CA19-9 (U/ml)' to float.
Cleaned and converted 'CD44 (ng/ml)' to float.
Cleaned and converted 'CEA (pg/ml)' to float.
Cleaned and converted 'CYFRA 21-1 (pg/ml)' to float.
Cleaned and converted 'DKK1 (ng/ml)' to float.
Cleaned and converted 'Endoglin (pg/ml)' to float.
Cleaned and converted 'FGF2 (pg/ml)' to float
```

```
df_cleaned['Label'] = df_cleaned['Tumor type_from_df1'].apply(lambda x: 0 if str(x).strip().lower() == 'normal' else 1)
df_cleaned.tail()
```

dase /ml)	NSE (ng/ml)	OPG (ng/ml)	OPN (pg/ml)	PAR (pg/ml)	Prolactin (pg/ml)	sEGFR (pg/ml)	sFas (pg/ml)	SHBG (nM)	sHER2/sEGFR2/sErbB2 (pg/ml)	sPECAM-1 (pg/ml)	TGFa (pg/ml)	Thrombospondin-2 (pg/ml)	TIMP-1 (pg/ml)	TIMP-2 (pg/ml)	Label
6.49	25.08	0.28	8913.64	11574.68	9851.43	4677.93	1072.020	32.15	6824.90	9314.25	15.258	4831.59	79549.74	42248.26	0
9.63	28.46	0.26	20352.33	4964.90	7244.91	5158.71	192.948	22.91	4776.64	3605.28	15.258	3678.90	59497.63	32619.49	0
7.56	22.30	0.29	31948.50	8118.53	7783.77	2112.99	1016.670	147.48	5327.25	4151.03	15.258	5595.27	59549.00	32305.11	0
6.83	12.74	0.25	21467.85	10695.84	5271.87	2219.83	844.470	37.79	5396.73	5784.36	15.258	835.00	51314.32	24498.68	0
9.69	22.90	0.28	15122.44	3341.92	5222.35	1732.68	1137.230	118.99	3535.00	3506.51	15.258	835.00	49214.66	31252.03	0

```python
import pandas as pd
df = pd.read_csv("draft_dataset4.csv")
missing_counts = df.isnull().sum()
missing_columns = missing_counts[missing_counts > 0]
if missing_columns.empty:
    print("No missing values in the dataset.")
else:
    print("Columns with missing values:")
    print(missing_columns.sort_values(ascending=False))
```

```
Columns with missing values:
AXL (pg/ml)                   6
CD44 (ng/ml)                  6
G-CSF (pg/ml)                 6
Kallikrein-6 (pg/ml)          6
Mesothelin (ng/ml)            6
Midkine (pg/ml)               6
PAR (pg/ml)                   6
sEGFR (pg/ml)                 6
sHER2/sEGFR2/sErbB2 (pg/ml)   6
sPECAM-1 (pg/ml)              6
Thrombospondin-2 (pg/ml)      6
sFas (pg/ml)                  1
dtype: int64
```

```python
# Drop missing value rows
df_cleaned = df.dropna()

print("Remaining rows:", df_cleaned.shape[0])
```

```
Remaining rows: 1255
```

```python
# Checking skewness for handling missing values
numeric_cols = df_cleaned.select_dtypes(include=['float64', 'int64']).columns
if 'Label' in numeric_cols:
    numeric_cols = numeric_cols.drop('Label')


skew_values = df_cleaned[numeric_cols].skew().sort_values(ascending=False)

print("Skewness of numeric columns:")
print(skew_values)
```

```
Skewness of numeric columns:
CA19-9 (U/ml)                  34.734604
CYFRA 21-1 (pg/ml)             32.489266
IL-8 (pg/ml)                   24.049594
AFP (pg/ml)                    22.573246
IL-6 (pg/ml)                   19.607046
HE4 (pg/ml)                    18.528075
G-CSF (pg/ml)                  18.114551
CA 15-3 (U/ml)                 12.075983
GDF15 (ng/ml)                  11.752472
CEA (pg/ml)                    11.449617
TGFa (pg/ml)                   11.370911
sFas (pg/ml)                    9.721895
Thrombospondin-2 (pg/ml)        9.677284
CA-125 (U/ml)                   9.000275
Midkine (pg/ml)                 8.451463
Angiopoietin-2 (pg/ml)          7.928636
Myeloperoxidase (ng/ml)         6.870869
HGF (pg/ml)                     6.777124
Galectin-3 (ng/ml)              6.141039
```

```
rows_with_na = df[df.isnull().any(axis=1)]
df_cleaned = df.dropna()

pd.set_option('display.max_columns', None)
rows_with_na.to_csv("Dropped_rows_table.csv", index=False)
```

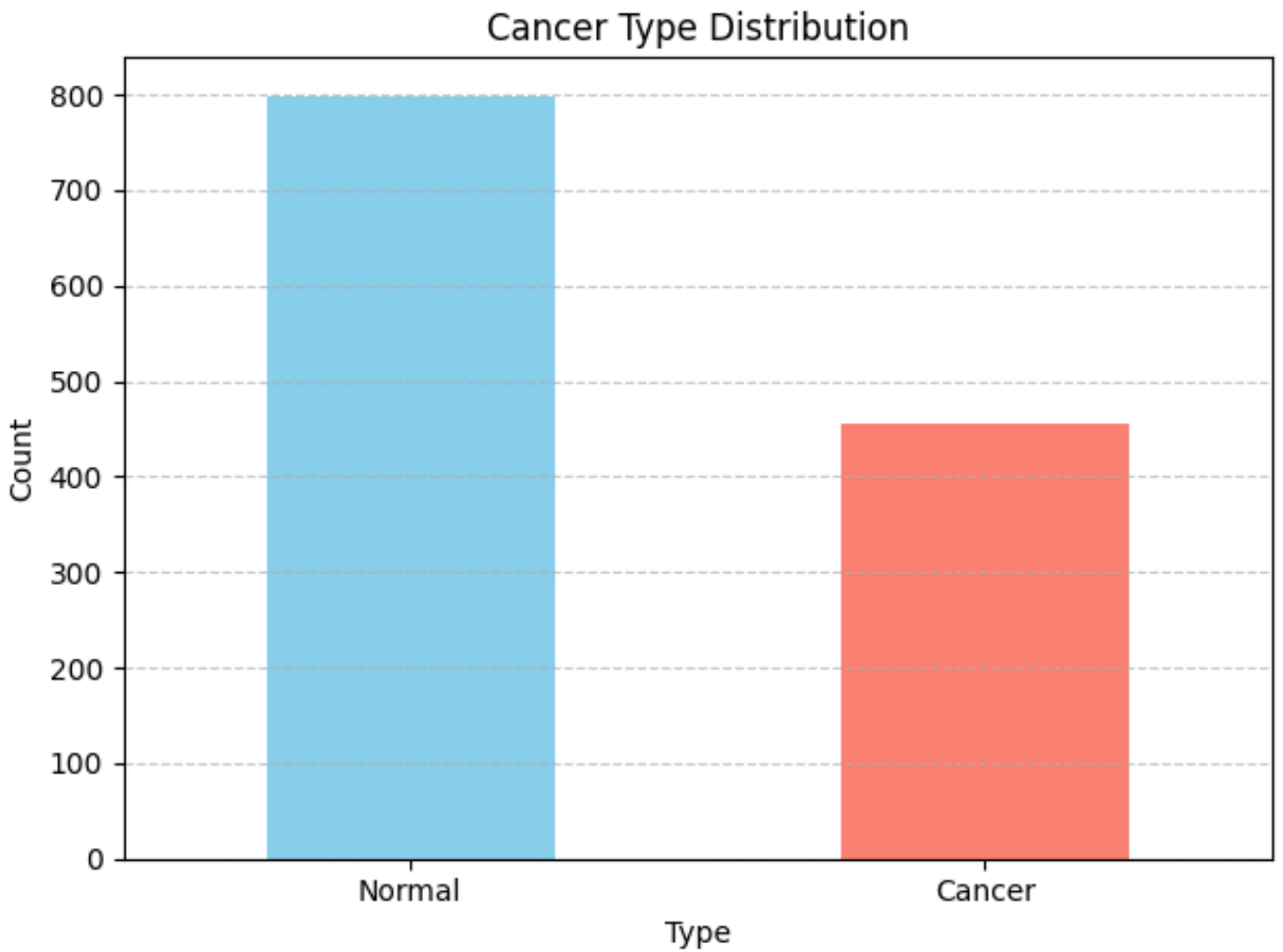
```
df_cleaned.tail()
```

	Sample_ID	Age	Sex	Race	Tumor type_from_df1	Plasma volume (mL)	Plasma DNA concentration (ng/mL)	AFP (pg/ml)	Angiopoietin-2 (pg/ml)	AXL (pg/ml)	...	sEGFR (pg/ml)	sFas (pg/ml)	SHBG (nM)
1263	NL PLSA 1866	55	Female	Unknown	Normal	7.5	2.17	740.016	1683.29	2151.58	...	2989.40	1237.140	60.85
1264	NL PLSA 1867	73	Female	Unknown	Normal	7.5	0.89	740.016	802.16	1069.51	...	1779.41	1237.140	24.30
1265	NL PLSA 1868	38	Male	Unknown	Normal	7.5	1.29	740.016	1112.37	1606.96	...	1823.73	623.750	14.60
1266	NL PLSA 1869	52	Female	Unknown	Normal	7.5	0.49	740.016	583.62	1708.47	...	2334.46	1142.230	28.83
1267	NL PLSA 1870	34	Female	Unknown	Normal	7.5	0.77	740.016	312.88	685.72	...	3263.91	192.948	109.81

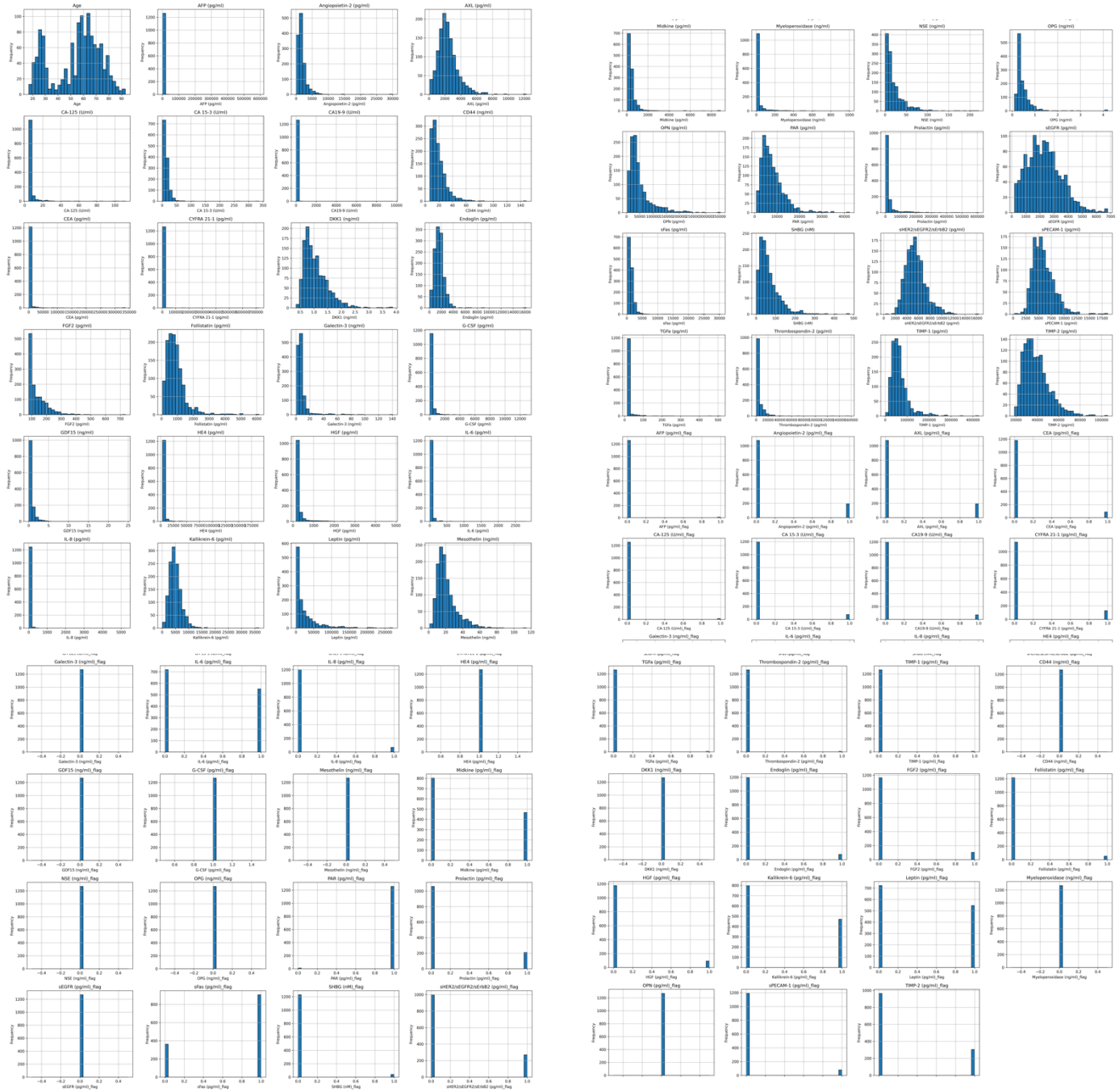
```
df_cleaned.describe().T
```

	count	mean	std	min	25%	50%	75%	max
Age	1255.0	54.697211	18.827110	17.000	39.000	59.000	68.000	93.000
Plasma volume (mL)	1255.0	7.439060	0.398912	2.000	7.500	7.500	7.500	7.500
Plasma DNA concentration (ng/mL)	1255.0	7.226183	12.575776	0.000	1.990	3.950	7.190	157.480
AFP (pg/ml)	1255.0	2744.607906	21275.864680	706.158	807.054	895.128	1603.800	592312.722
Angiopoietin-2 (pg/ml)	1255.0	1825.922755	1918.302916	38.391	925.125	1424.210	2125.260	30001.791
AXL (pg/ml)	1255.0	2378.595267	1254.514174	109.440	1567.680	2169.040	2960.785	12247.310
CA-125 (U/ml)	1255.0	6.628457	7.322471	4.608	4.854	4.980	5.355	111.490
CA 15-3 (U/ml)	1255.0	13.647175	14.988504	1.320	6.570	10.930	16.940	336.250
CA19-9 (U/ml)	1255.0	29.803707	272.517374	14.214	16.320	16.470	17.075	9615.690
CD44 (ng/ml)	1255.0	19.321235	11.187244	6.750	11.735	16.440	23.805	148.440
CEA (pg/ml)	1255.0	4333.668324	24266.226984	426.438	580.980	984.800	1752.435	336427.986
CYFRA 21-1 (pg/ml)	1255.0	3178.097793	20975.988332	1816.458	1946.196	1994.874	2035.440	722034.000
DKK1 (ng/ml)	1255.0	1.063578	0.447797	0.350	0.730	0.960	1.295	3.870

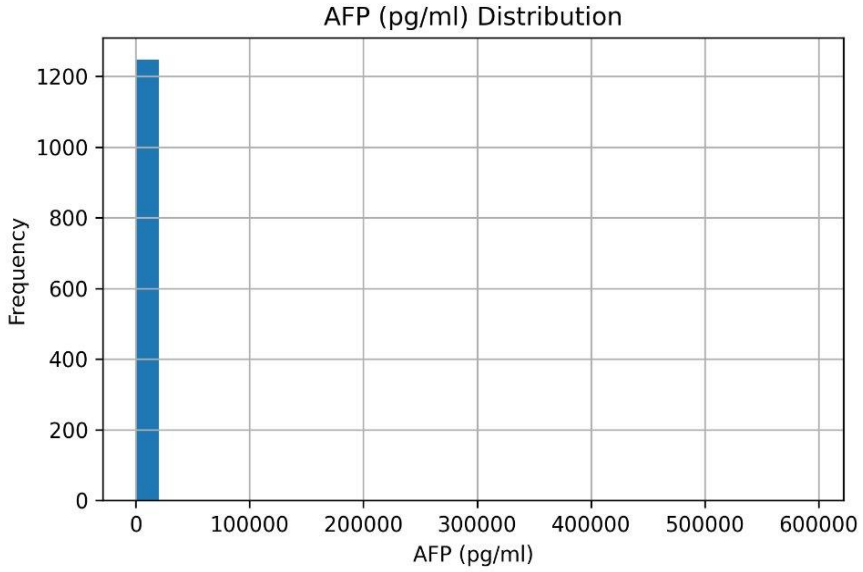
```python
#2. checking class distribution
import matplotlib.pyplot as plt

label_mapping = {0: 'Normal', 1: 'Cancer'}
label_counts = df_cleaned['Label'].map(label_mapping).value_counts()

label_counts.plot(kind='bar', title='Cancer Type Distribution', color=['skyblue', 'salmon'])
plt.xlabel('Type')
plt.ylabel('Count')
plt.xticks(rotation=0)
plt.grid(axis='y', linestyle='--', alpha=0.7)
plt.tight_layout()
plt.show()
```

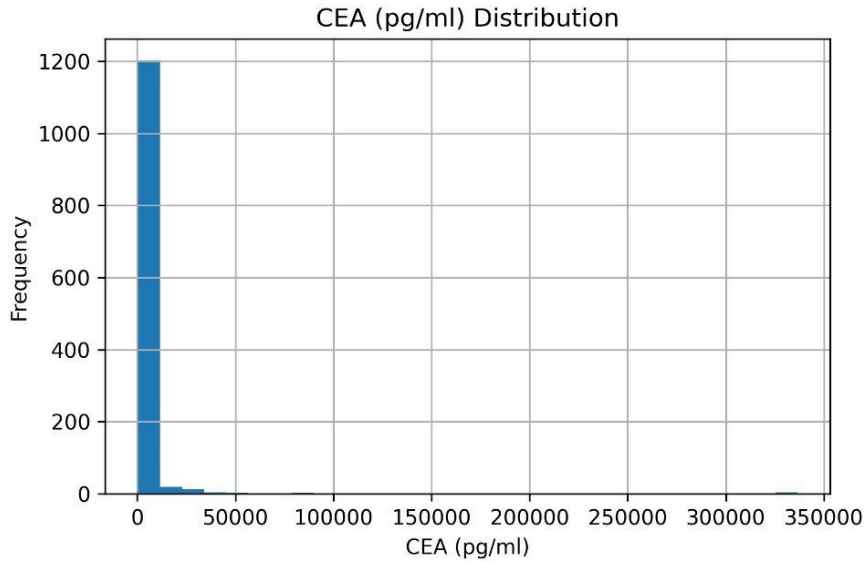


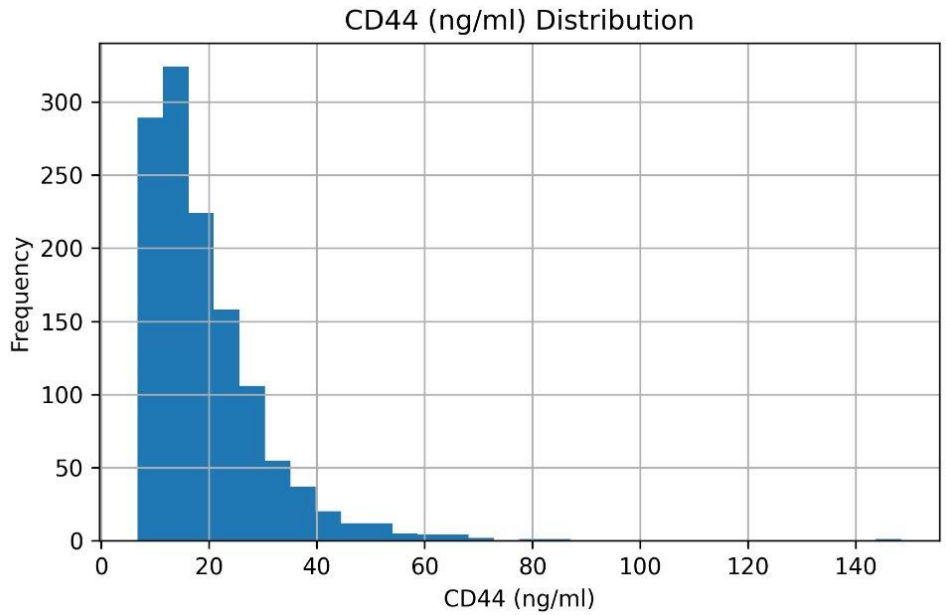
```python
import matplotlib.pyplot as plt
import numpy as np

numeric_cols = df_cleaned.select_dtypes(include=['float64', 'int64']).columns.drop('Label')
n_cols = 4
n_rows = int(np.ceil(len(numeric_cols) / n_cols))
fig, axes = plt.subplots(n_rows, n_cols, figsize=(20, n_rows * 4))
axes = axes.flatten()

for i, col in enumerate(numeric_cols):
    axes[i].hist(df_cleaned[col].dropna(), bins=30, edgecolor='black')
    axes[i].set_title(f'{col}')
    axes[i].set_xlabel(col)
    axes[i].set_ylabel('Frequency')
    axes[i].grid(True)

for j in range(i + 1, len(axes)):
    fig.delaxes(axes[j])

plt.tight_layout()
plt.show()
```



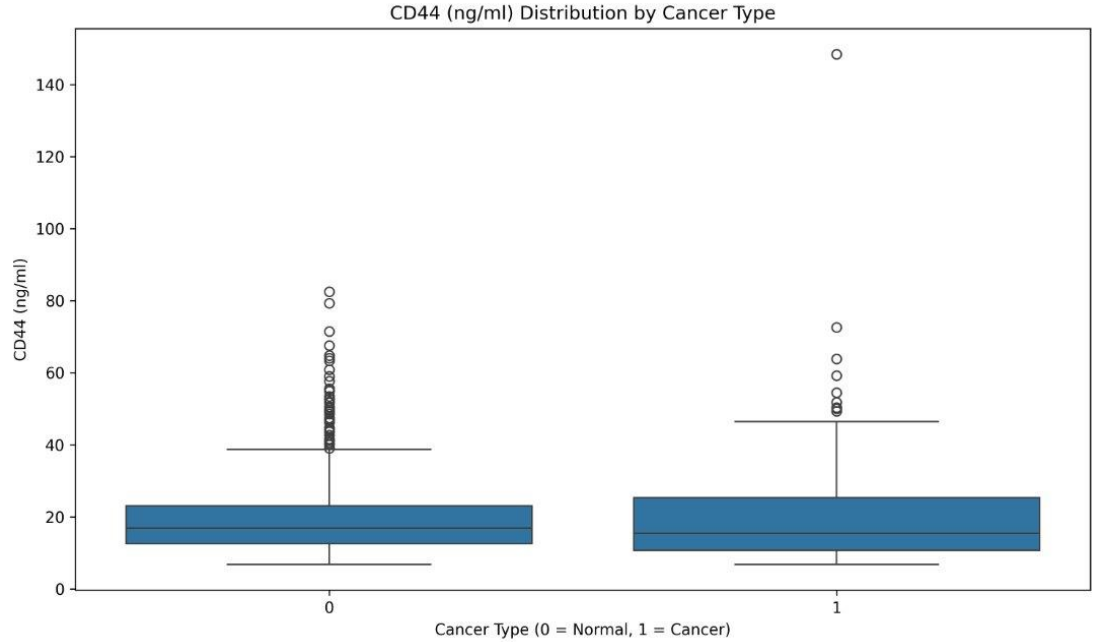
```python
# 3. Histogram for key biomarkers to visualize the distribution
import matplotlib.pyplot as plt

#key biomarkers
key_biomarkers = [
    'CEA (pg/ml)', 'AFP (pg/ml)', 'CA-125 (U/ml)', 'CD44 (ng/ml)',
    'GDF15 (ng/ml)', 'IL-6 (pg/ml)', 'CA 15-3 (U/ml)',
    'CYFRA 21-1 (pg/ml)', 'Thrombospondin-2 (pg/ml)'
]

for col in key_biomarkers:
    plt.figure(figsize=(6, 4))
    plt.hist(df_cleaned[col].dropna(), bins=30, edgecolor='black', color='skyblue')
    plt.title(f"Distribution of {col}")
    plt.xlabel(col)
    plt.ylabel("Frequency")
    plt.tight_layout()
    filename = f"{col.replace('/', '_').replace(' ', '_')}_histogram.png"
    plt.savefig(filename, dpi=300)
    plt.show()
```

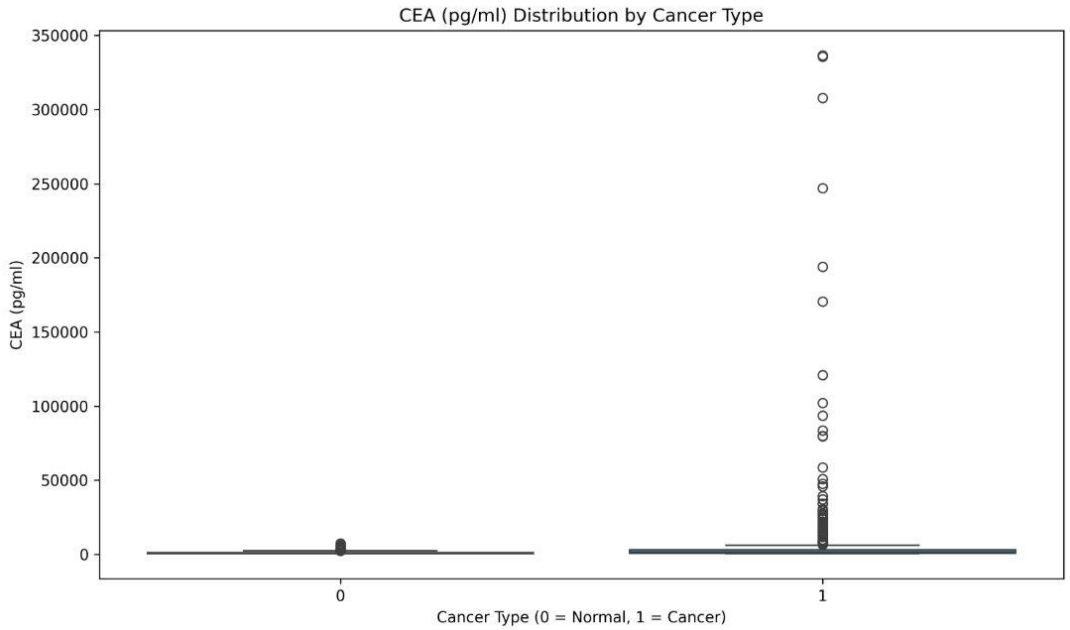


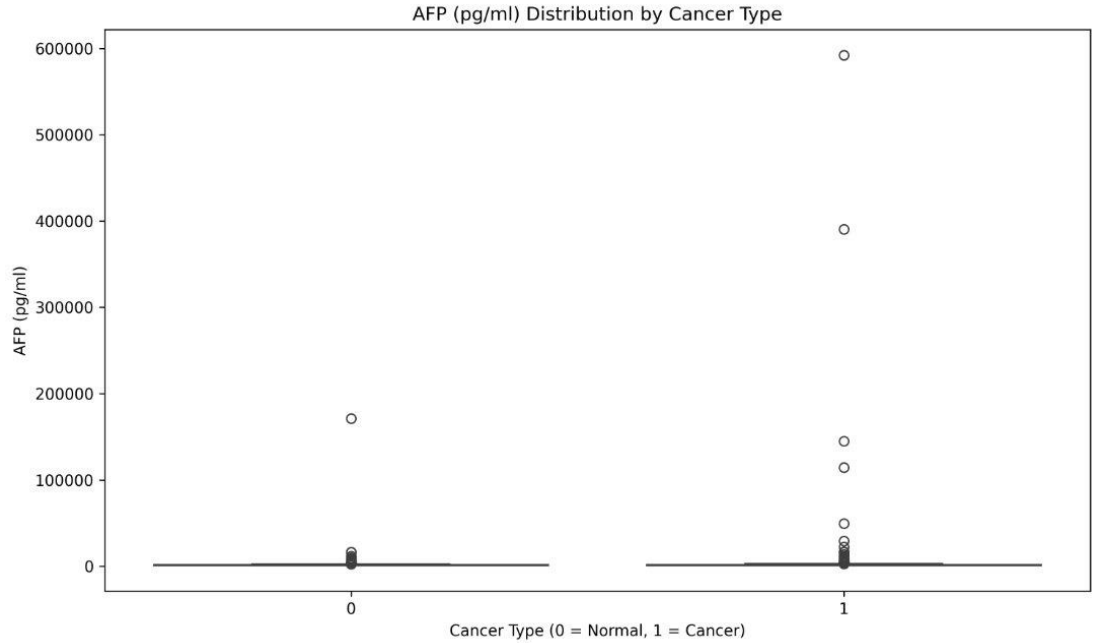




```python
# 4. Boxplots of biomarkers by cancer status
import matplotlib.pyplot as plt
import seaborn as sns

# Key biomarkers
key_biomarkers = [
    'CEA (pg/ml)', 'AFP (pg/ml)', 'CA-125 (U/ml)', 'CD44 (ng/ml)',
    'GDF15 (ng/ml)', 'IL-6 (pg/ml)', 'CA 15-3 (U/ml)',
    'CYFRA 21-1 (pg/ml)', 'Thrombospondin-2 (pg/ml)'
]

# boxplots grouped by Label
for col in key_biomarkers:
    plt.figure(figsize=(6, 4))
    sns.boxplot(x='Label', y=col, data=df_cleaned, hue='Label', palette='pastel', legend=False)
    plt.title(f"{col} by Cancer Status (0 = Normal, 1 = GI Cancer)")
    plt.xlabel("Label")
    plt.ylabel(col)
    plt.tight_layout()
    filename = f"{col.replace('/', '_').replace(' ', '_')}_boxplot.png"
    plt.savefig(filename, dpi=300)
    plt.show()
```







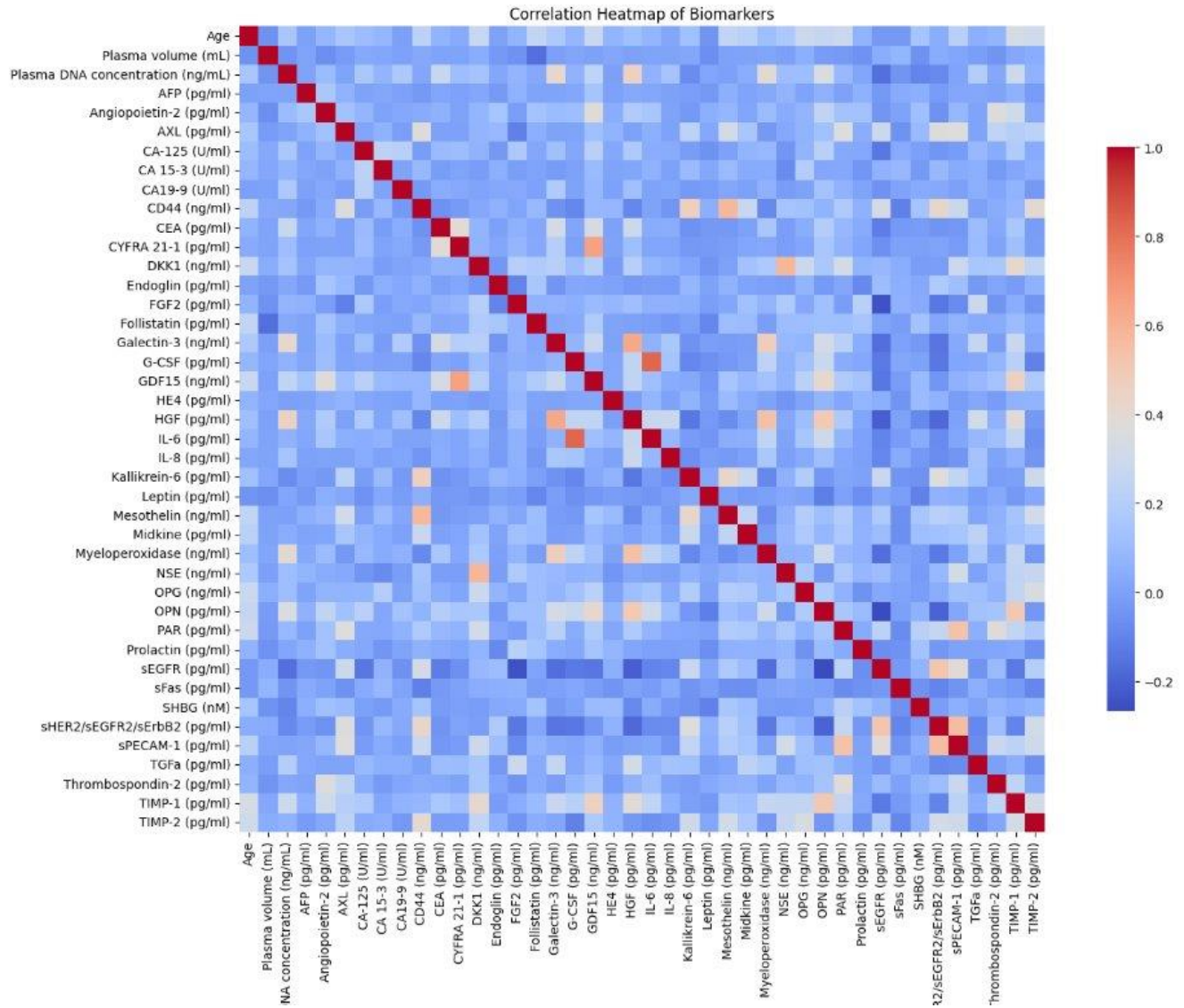
```python
# 5. Statistical comparison between Normal and Cancer
from scipy.stats import ttest_ind

stats_summary = []

for col in biomarkers:
    group0 = df_cleaned[df_cleaned['Label'] == 0][col].dropna()
    group1 = df_cleaned[df_cleaned['Label'] == 1][col].dropna()

    stat, p_value = ttest_ind(group0, group1, equal_var=False)
    stats_summary.append({
        'Biomarker': col,
        'Mean (Normal)': round(group0.mean(), 2),
        'Mean (Cancer)': round(group1.mean(), 2),
        'p-value': round(p_value, 5)
    })

# Display the summary table
import pandas as pd
stats_df = pd.DataFrame(stats_summary)
print(stats_df)
```

	Biomarker	Mean (Normal)	Mean (Cancer)	p-value
0	CEA (pg/ml)	1094.01	10010.17	0.00000
1	AFP (pg/ml)	1676.21	4616.65	0.07017
2	CA-125 (U/ml)	5.52	8.58	0.00000
3	CD44 (ng/ml)	19.46	19.08	0.57499
4	GDF15 (ng/ml)	0.44	1.02	0.00000
5	IL-6 (pg/ml)	8.05	47.93	0.00000
6	CA 15-3 (U/ml)	13.98	13.07	0.38371
7	CYFRA 21-1 (pg/ml)	2069.59	5120.42	0.06132
8	Thrombospondin-2 (pg/ml)	4179.51	5143.08	0.06015

```python
# 6. Detect outliers and summarize for key biomarkers
import numpy as np
import pandas as pd

#key biomarkers
key_biomarkers = [
    'CEA (pg/ml)', 'AFP (pg/ml)', 'CA-125 (U/ml)', 'CD44 (ng/ml)',
    'GDF15 (ng/ml)', 'IL-6 (pg/ml)', 'CA 15-3 (U/ml)',
    'CYFRA 21-1 (pg/ml)', 'Thrombospondin-2 (pg/ml)'
]

outlier_summary = []

for col in key_biomarkers:
    for label in [0, 1]:
        group = df_cleaned[df_cleaned['Label'] == label][col].dropna()
        Q1 = np.percentile(group, 25)
        Q3 = np.percentile(group, 75)
        IQR = Q3 - Q1
        lower = Q1 - 1.5 * IQR
        upper = Q3 + 1.5 * IQR
        outliers = group[(group < lower) | (group > upper)]

        outlier_summary.append({
            'Biomarker': col,
            'Label': 'Normal' if label == 0 else 'GI Cancer',
            'Num Outliers': len(outliers),
            'Outlier Min': round(outliers.min(), 2) if not outliers.empty else None,
            'Outlier Max': round(outliers.max(), 2) if not outliers.empty else None
        })

outlier_df = pd.DataFrame(outlier_summary)
print(outlier_df)
outlier_df.to_csv("outlier_summary.csv", index=False)
```

Biomarker	Label	Num Outliers	Outlier Min	Outlier Max
CEA (pg/ml)	Normal	39	2575.2	7377.64
CEA (pg/ml)	GI Cancer	69	6637.5	336427.99
AFP (pg/ml)	Normal	85	2811.58	171255.75
AFP (pg/ml)	GI Cancer	66	3066.13	592312.72
CA-125 (U/ml)	Normal	167	5.24	33.07
CA-125 (U/ml)	GI Cancer	70	9.88	111.49
CD44 (ng/ml)	Normal	45	38.62	82.53
CD44 (ng/ml)	GI Cancer	9	49.31	148.44
GDF15 (ng/ml)	Normal	56	1.08	8.56
GDF15 (ng/ml)	GI Cancer	39	2.27	24.29
IL-6 (pg/ml)	Normal	156	6.9	356.64
IL-6 (pg/ml)	GI Cancer	61	92.08	2818.46
CA 15-3 (U/ml)	Normal	32	36.17	102.98
CA 15-3 (U/ml)	GI Cancer	21	29.75	336.25
CYFRA 21-1 (pg/ml)	Normal	108	1816.46	13499.0
CYFRA 21-1 (pg/ml)	GI Cancer	66	4541.87	722034.0
rombospondin-2 (pg/ml)	Normal	76	10756.08	131014.81
rombospondin-2 (pg/ml)	GI Cancer	52	12973.51	157461.07

```python
# 7. Correlation heatmap of biomarkers
import matplotlib.pyplot as plt
import seaborn as sns

numeric_features = df_cleaned.select_dtypes(include=['float64', 'int64']).drop(columns=['Label'])

corr_matrix = numeric_features.corr()

#heatmap
plt.figure(figsize=(16, 12))
sns.heatmap(corr_matrix, cmap='coolwarm', annot=False, fmt=".2f", square=True, cbar_kws={"shrink": 0.7})
plt.title("Correlation Heatmap of Biomarkers")
plt.tight_layout()
plt.savefig("correlation_heatmap.png", dpi=300)
plt.show()
```



```python
# 8. Grouped key feature averages with demographic insights
# A.  Mean of Key Biomarkers by Sex
key_biomarkers = [
    'CEA (pg/ml)', 'AFP (pg/ml)', 'CA-125 (U/ml)', 'CD44 (ng/ml)',
    'GDF15 (ng/ml)', 'IL-6 (pg/ml)', 'CA 15-3 (U/ml)',
    'CYFRA 21-1 (pg/ml)', 'Thrombospondin-2 (pg/ml)'
]


mean_by_sex = df_cleaned.groupby("Sex")[key_biomarkers].mean().round(2)
print("Mean biomarker levels by Sex:")
print(mean_by_sex)
```

```
Mean biomarker levels by Sex:
        CEA (pg/ml)  AFP (pg/ml)  CA-125 (U/ml)  CD44 (ng/ml)  GDF15 (ng/ml)  \
Sex
Female      3708.55      2330.50           7.03         19.12           0.67
Male        4905.25      3113.07           6.36         19.41           0.64

        IL-6 (pg/ml)  CA 15-3 (U/ml)  CYFRA 21-1 (pg/ml)  \
Sex
Female         15.84           12.11             3944.94
Male           28.21           14.90             2603.49

        Thrombospondin-2 (pg/ml)
Sex
Female                   4668.85
Male                     4407.40
```

```python
# C. Correlation of Age with Biomarkers
age_corr = df_cleaned[["Age"] + key_biomarkers].corr().round(2)['Age'].drop('Age')
print("Correlation of Age with biomarkers:")
print(age_corr)
```

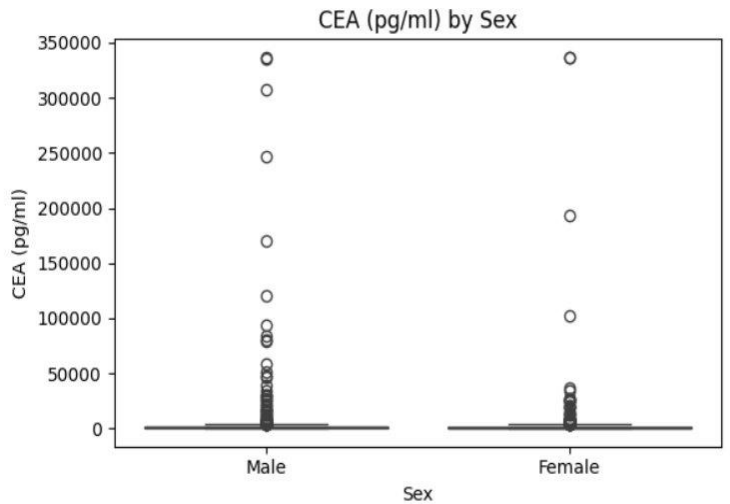
```
Correlation of Age with biomarkers:
CEA (pg/ml)                0.07
AFP (pg/ml)                0.00
CA-125 (U/ml)              0.11
CD44 (ng/ml)               0.23
GDF15 (ng/ml)              0.28
IL-6 (pg/ml)               0.08
CA 15-3 (U/ml)             0.08
CYFRA 21-1 (pg/ml)         0.03
Thrombospondin-2 (pg/ml)   0.07
Name: Age, dtype: float64
```

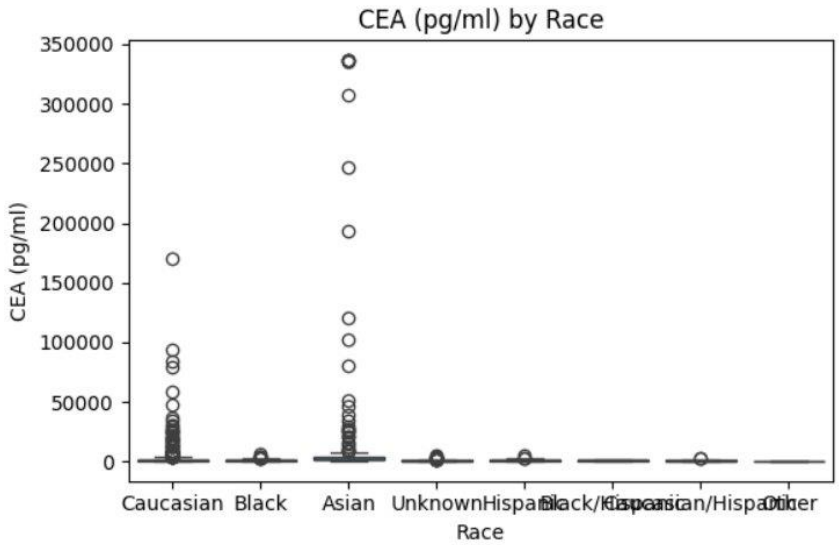
```python
#B. Mean of Key Biomarkers by Race
mean_by_race = df_cleaned.groupby("Race")[key_biomarkers].mean().round(2)
print("Mean biomarker levels by Race:")
print(mean_by_race)
```

```
Mean biomarker levels by Race:
                  CEA (pg/ml)  AFP (pg/ml)  CA-125 (U/ml)  CD44 (ng/ml)  \
Race
Asian                16812.84      5958.07           8.99         17.14
Black                 1232.25      1522.12           5.26         15.15
Black/Hispanic        1062.46      1250.15           5.20         14.84
Caucasian             2939.40      2561.94           6.90         21.50
Caucasian/Hispanic    1013.29      1180.23           5.44         14.42
Hispanic              1186.77      1000.16           5.48         18.08
Other                  504.11      1928.40           4.98         25.24
Unknown                931.86      2310.46           5.26         19.11

                  GDF15 (ng/ml)  IL-6 (pg/ml)  CA 15-3 (U/ml)  \
Race
Asian                      1.20         72.64           12.29
Black                      0.24          6.44           15.33
Black/Hispanic             0.18          3.99            9.02
Caucasian                  0.76         18.45           14.47
Caucasian/Hispanic         0.14          4.73           10.01
Hispanic                   0.17         11.83           12.19
Other                      0.35          3.84            9.40
Unknown                    0.41          7.43           12.46

                  CYFRA 21-1 (pg/ml)  Thrombospondin-2 (pg/ml)
Race
Asian                         7849.40                   4333.06
Black                         2056.87                   3599.83
Black/Hispanic                2008.97                   2406.38
Caucasian                     2624.14                   4546.46
Caucasian/Hispanic            2007.82                   3920.96
Hispanic                      1973.03                   2490.55
Other                         2035.44                   2245.65
Unknown                       1975.28                   6749.04
```

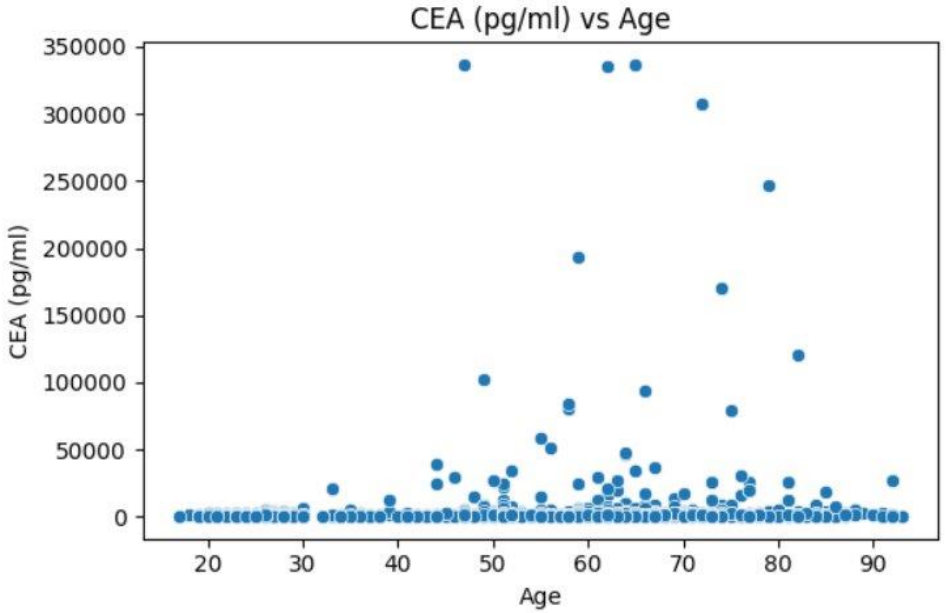
```python
# Visualizing demographic insights
# D. Box plot of key biomarkers by Sex and Race
import matplotlib.pyplot as plt
import seaborn as sns

key_biomarkers = [
    'CEA (pg/ml)', 'AFP (pg/ml)', 'CA-125 (U/ml)', 'CD44 (ng/ml)',
    'GDF15 (ng/ml)', 'IL-6 (pg/ml)', 'CA 15-3 (U/ml)',
    'CYFRA 21-1 (pg/ml)', 'Thrombospondin-2 (pg/ml)'
]

# Boxplots by Sex
for col in key_biomarkers:
    plt.figure(figsize=(6, 4))
    sns.boxplot(x="Sex", y=col, data=df_cleaned)
    plt.title(f"{col} by Sex")
    plt.xlabel("Sex")
    plt.ylabel(col)
    plt.tight_layout()
    plt.show()
```

```python
# Boxplots by Race
for col in key_biomarkers:
    plt.figure(figsize=(6, 4))
    sns.boxplot(x="Race", y=col, data=df_cleaned)
    plt.title(f"{col} by Race")
    plt.xlabel("Race")
    plt.ylabel(col)
    plt.tight_layout()
    plt.show()
```





```python
# E. Scatterplots with Age
for col in key_biomarkers:
    plt.figure(figsize=(6, 4))
    sns.scatterplot(x="Age", y=col, data=df_cleaned)
    plt.title(f"{col} vs Age")
    plt.xlabel("Age")
    plt.ylabel(col)
    plt.tight_layout()
```




```python
from scipy.stats import shapiro
import pandas as pd

normality_results = []

for col in key_biomarkers:
    stat, p_value = shapiro(df_cleaned[col].dropna())
    normality_results.append({
        'Biomarker': col,
        'Shapiro-Wilk p-value': round(p_value, 5),
        'Normality': 'Not Normal' if p_value < 0.05 else 'Normal'
    })

normality_df = pd.DataFrame(normality_results)
print(normality_df)
normality_df.to_csv("Normality_test_results.csv", index=False)
```

	Biomarker	Shapiro-Wilk p-value	Normality
0	CEA (pg/ml)	0.0	Not Normal
1	AFP (pg/ml)	0.0	Not Normal
2	CA-125 (U/ml)	0.0	Not Normal
3	CD44 (ng/ml)	0.0	Not Normal
4	GDF15 (ng/ml)	0.0	Not Normal
5	IL-6 (pg/ml)	0.0	Not Normal
6	CA 15-3 (U/ml)	0.0	Not Normal
7	CYFRA 21-1 (pg/ml)	0.0	Not Normal
8	Thrombospondin-2 (pg/ml)	0.0	Not Normal

```python
import pandas as pd

df_cleaned = pd.read_csv("Dropped_rows_dataset.csv")
clinical_thresholds = {
    'AFP (pg/ml)': 20000,
    'Angiopoietin-2 (pg/ml)': 4141,
    'AXL (pg/ml)': 1243,
    'CA-125 (U/ml)': 35,
    'CA 15-3 (U/ml)': 30,
    'CA19-9 (U/ml)': 37,
    'CYFRA 21-1 (pg/ml)': 3500,
    'CEA (pg/ml)': 5000,
    'DKK1 (ng/ml)': 2.03 * 1000,  # ng/ml to pg/ml
    'Endoglin (pg/ml)': 2000,
    'FGF2 (pg/ml)': 10,
    'Follistatin (pg/ml)': 4700,
    'Galectin-3 (ng/ml)': 22.1 * 1000,
    'G-CSF (pg/ml)': 15,
    'GDF15 (ng/ml)': 1200 * 1000,
    'HE4 (pg/ml)': 3500,
    'HGF (pg/ml)': 1000,
    'IL-6 (pg/ml)': 5,
    'IL-8 (pg/ml)': 57.7,
    'Kallikrein-6 (pg/ml)': 1000,
    'Mesothelin (ng/ml)': 2 * 1000,
    'Midkine (pg/ml)': 400,
    'Myeloperoxidase (ng/ml)': 220 * 1000,
    'NSE (ng/ml)': 16.3 * 1000,
    'OPG (ng/ml)': 0.2 * 1000,
    'OPN (pg/ml)': 200000,
    'sFas (pg/ml)': 150,
    'sHER2/sEGFR2/sErbB2 (pg/ml)': 15000,
    'TGFa (pg/ml)': 100,
    'Thrombospondin-2 (pg/ml)': 45000,
    'TIMP-1 (pg/ml)': 126000,
}
```

```python
#Sex-specific thresholds
sex_specific_thresholds = {
    'Leptin (pg/ml)': {'Male': 15200, 'Female': 12500},
    'Prolactin (pg/ml)': {'Male': 18000, 'Female': 25000},
    'SHBG (nM)': {'Male': 54, 'Female': 145},
}

#Convert biomarker columns to numeric
for col in df_cleaned.columns:
    df[col] = pd.to_numeric(df_cleaned[col], errors='coerce')

#clinical threshold flags
for biomarker, threshold in clinical_thresholds.items():
    if biomarker in df_cleaned.columns:
        df_cleaned[f"{biomarker}_flag"] = (df_cleaned[biomarker] > threshold).astype(int)

#sex-specific thresholds
for biomarker, thresholds in sex_specific_thresholds.items():
    if biomarker in df_cleaned.columns and 'Sex' in df_cleaned.columns:
        df_cleaned[f"{biomarker}_flag"] = df_cleaned.apply(
            lambda row: int(row[biomarker] > thresholds.get(row['Sex'], float('inf'))), axis=1
        )

#Remove any mistakenly flagged non-biomarker
non_biomarker_flags = ['Sex_flag', 'Sample_ID_flag']
df_cleaned.drop(columns=[col for col in non_biomarker_flags if col in df_cleaned.columns], inplace=True)

df_cleaned.to_csv("threshold_flagged_dataset_final.csv", index=False)
df_cleaned.head()
```

Label	AFP (pg/ml)_flag	ngiopoietin-2 (pg/ml)_flag	AXL (pg/ml)_flag	CA-125 (U/ml)_flag	CA 15-3 (U/ml)_flag	CA19-9 (U/ml)_flag	CYFRA 21-1 (pg/ml)_flag	CEA (pg/ml)_flag	DKK1 (ng/ml)_flag	Endoglin (pg/ml)_flag
1	0	1	1	0	0	0	0	0	0	1
1	0	1	1	0	0	1	0	1	0	1
1	0	0	1	0	0	0	0	0	0	1
1	0	0	1	0	0	0	0	0	0	0
1	0	0	1	0	0	0	0	0	0	1
1	0	0	1	0	0	1	0	0	0	1
1	0	0	1	0	0	0	0	0	0	0
1	0	0	1	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0
1	0	0	1	0	0	0	0	0	0	1
1	0	0	1	0	0	1	0	0	0	0
1	0	0	1	0	0	0	0	0	0	1
1	0	0	1	0	0	0	0	1	0	1
1	0	0	1	0	0	0	0	1	0	0
1	0	0	0	0	0	0	0	0	0	1
1	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0
1	0	0	1	0	0	1	0	1	0	0
1	0	0	1	0	0	0	0	0	0	0
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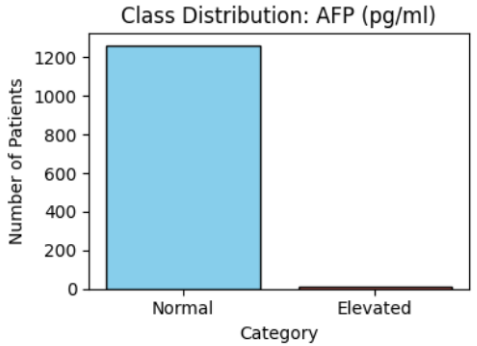
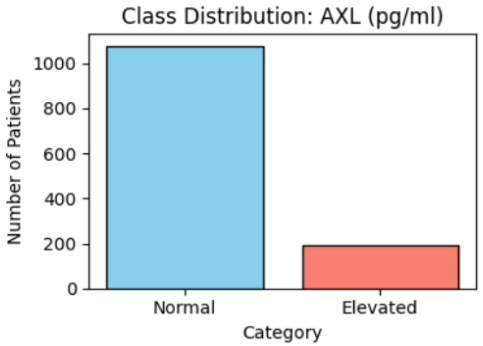
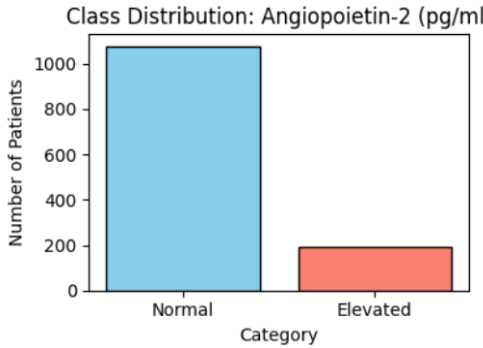
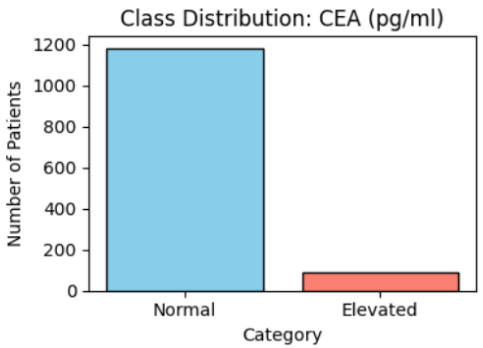
1	0	0	0	0	0	0	0	0	0	0
1	0	0	1	0	0	0	1	0	0	0
1	0	0	1	0	0	0	0	0	0	1
1	0	0	1	0	0	0	0	0	0	0
1	0	0	1	0	0	0	0	0	0	1

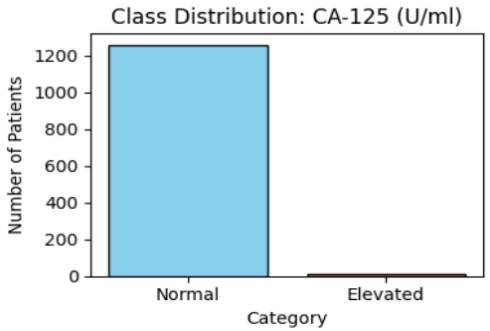
```python
import matplotlib.pyplot as plt

flag_columns = [col for col in df_cleaned.columns if col.endswith('_flag')]

for biomarker_flag in flag_columns:
    plt.figure(figsize=(4, 3))
    counts = df_cleaned[biomarker_flag].value_counts().sort_index()

    plt.bar(counts.index, counts.values, color=['skyblue', 'salmon'], edgecolor='black')
    plt.xticks([0, 1], labels=["Normal", "Elevated"])
    plt.xlabel("Category")
    plt.ylabel("Number of Patients")
    plt.title(f"Class Distribution: {biomarker_flag.replace('_flag', '')}")
    plt.tight_layout()
    plt.show()
```

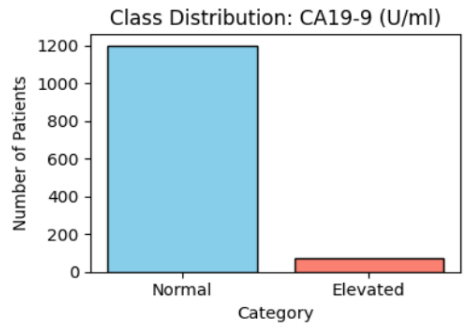


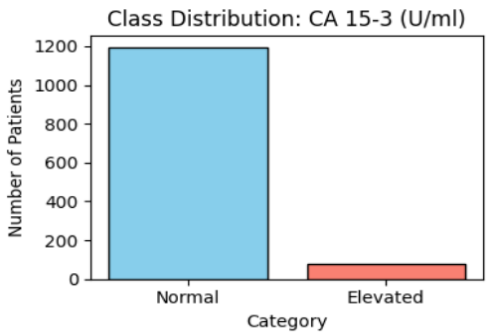


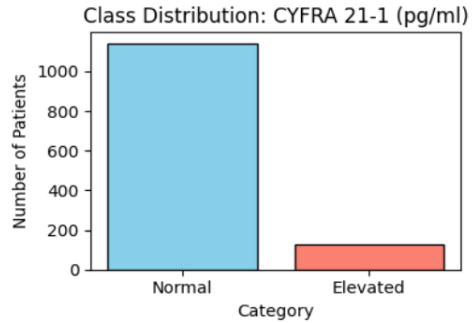












```python
from scipy.stats import chi2_contingency
import pandas as pd

flag_columns = [col for col in df_cleaned.columns if col.endswith('_flag') and col != 'Sex_flag']
chi2_results = []

for col in flag_columns:
    contingency_table = pd.crosstab(df_cleaned[col], df_cleaned['Label'])

    if contingency_table.shape == (2, 2):  # Ensure it's a valid 2x2 table
        chi2, p, dof, expected = chi2_contingency(contingency_table)
        chi2_results.append({
            'Biomarker': col,
            'p_value': round(p, 5),
            'Significant': 'Yes' if p < 0.05 else 'No'
        })

chi2_df = pd.DataFrame(chi2_results).sort_values(by='p_value')
chi2_df.to_csv("chi_square_results.csv", index=False)
print(chi2_df.head())
```

```
             Biomarker  p_value Significant
11    IL-6 (pg/ml)_flag      0.0         Yes
20  Leptin (pg/ml)_flag      0.0         Yes
19  TIMP-1 (pg/ml)_flag      0.0         Yes
15     OPN (pg/ml)_flag      0.0         Yes
5    CA19-9 (U/ml)_flag      0.0         Yes
```

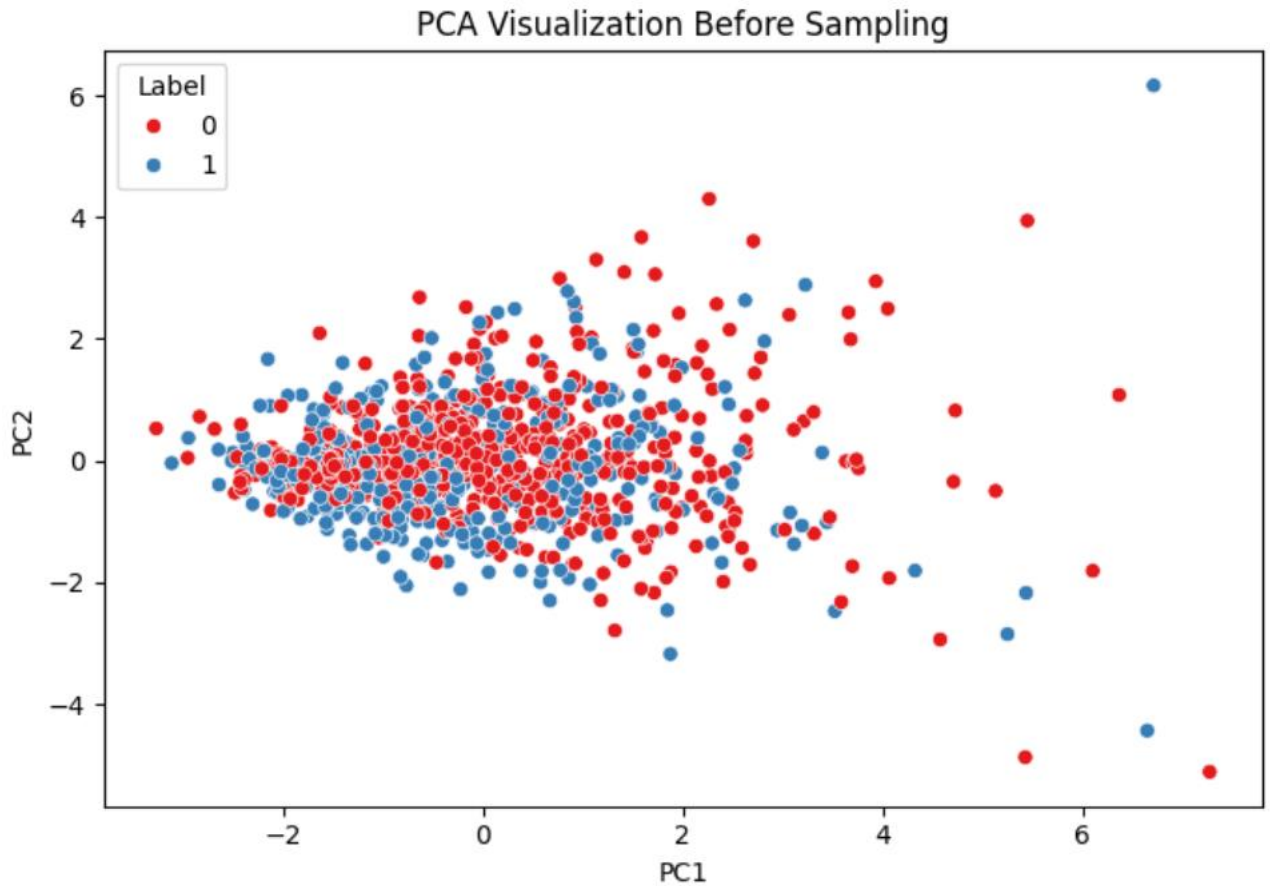
Biomarker	p_value	Significant
IL-6 (pg/ml)_flag	0.0	Yes
Leptin (pg/ml)_flag	0.0	Yes
TIMP-1 (pg/ml)_flag	0.0	Yes
OPN (pg/ml)_flag	0.0	Yes
CA19-9 (U/ml)_flag	0.0	Yes
CYFRA 21-1 (pg/ml)_flag	0.0	Yes
CEA (pg/ml)_flag	0.0	Yes
Midkine (pg/ml)_flag	0.0	Yes
IL-8 (pg/ml)_flag	0.0	Yes
HGF (pg/ml)_flag	0.0	Yes
Prolactin (pg/ml)_flag	0.0	Yes
ngiopoietin-2 (pg/ml)_flag	1e-05	Yes
SHBG (nM)_flag	2e-05	Yes
CA-125 (U/ml)_flag	2e-05	Yes
AFP (pg/ml)_flag	0.00886	Yes
Kallikrein-6 (pg/ml)_flag	0.02145	Yes
CA 15-3 (U/ml)_flag	0.05517	No
TGFa (pg/ml)_flag	0.09993	No
AXL (pg/ml)_flag	0.14044	No
Endoglin (pg/ml)_flag	0.8987	No
FR2/sErbB2 (pg/ml)_flag	1.0	No
bospondin-2 (pg/ml)_flag	1.0	No
Follistatin (pg/ml)_flag	1.0	No

```python
import pandas as pd
from scipy.stats import mannwhitneyu

df = pd.read_csv("threshold_flagged_dataset_final.csv")
continuous_biomarkers = [
    'CD44 (ng/ml)',
    'PAR (pg/ml)',
    'sEGFR (pg/ml)',
    'sPECAM-1 (pg/ml)',
    'TIMP-2 (pg/ml)'
]

mannwhitney_results = []

for biomarker in continuous_biomarkers:
    if biomarker in df.columns:
        group_0 = df[df['Label'] == 0][biomarker].dropna()
        group_1 = df[df['Label'] == 1][biomarker].dropna()

        stat, p = mannwhitneyu(group_0, group_1, alternative='two-sided')
        mannwhitney_results.append({
            'Biomarker': biomarker,
            'Mann-Whitney U': round(stat, 2),
            'p-value': round(p, 5),
            'Significant': 'Yes' if p < 0.05 else 'No'
        })

mannwhitney_df = pd.DataFrame(mannwhitney_results)
mannwhitney_df = mannwhitney_df.sort_values(by='p-value')
mannwhitney_df.to_csv("mannwhitney_results.csv", index=False)

print(mannwhitney_df)
```

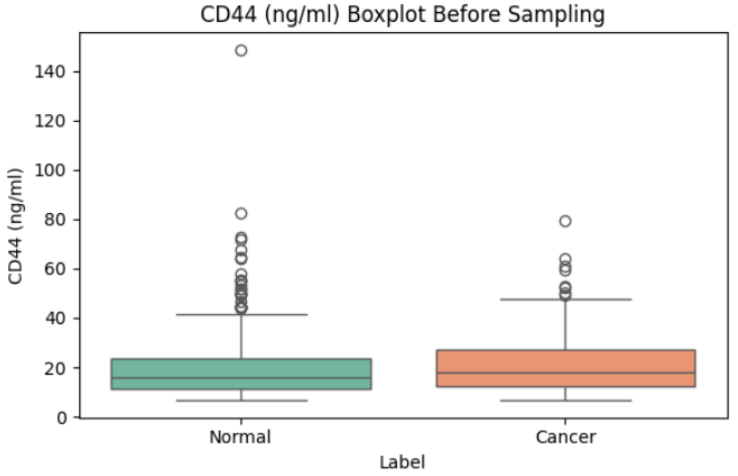
	Biomarker	Mann-Whitney U	p-value	Significant
2	sEGFR (pg/ml)	248907.0	0.00000	Yes
1	PAR (pg/ml)	159440.5	0.00149	Yes
4	TIMP-2 (pg/ml)	197661.0	0.00187	Yes
0	CD44 (ng/ml)	191261.5	0.03966	Yes
3	sPECAM-1 (pg/ml)	187833.5	0.13531	No

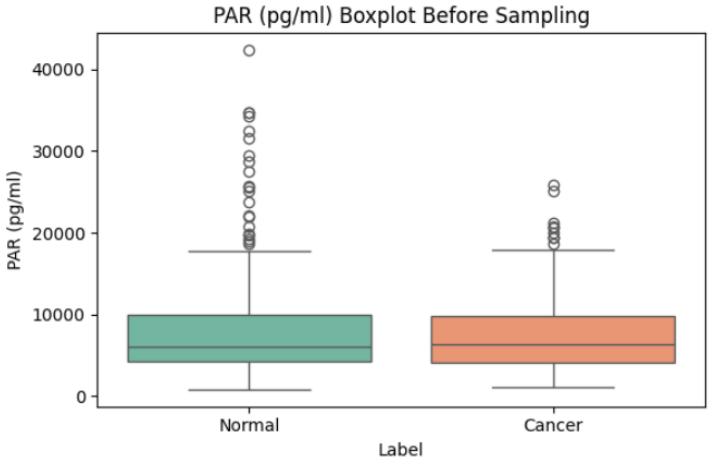
```python
import pandas as pd
from sklearn.model_selection import train_test_split
from sklearn.preprocessing import StandardScaler

df = pd.read_csv("threshold_flagged_dataset_final.csv")

y = df["Label"]

flagged_features = [col for col in df.columns if col.endswith('_flag')]
continuous_features = [
    "CD44 (ng/ml)", "PAR (pg/ml)", "sEGFR (pg/ml)",
    "sPECAM-1 (pg/ml)", "TIMP-2 (pg/ml)"
]

X_categorical = df[flagged_features]
X_continuous = df[continuous_features]
X_full = pd.concat([X_categorical, X_continuous], axis=1)

#Splitting before scaling to avoid data leakage
X_train, X_test, y_train, y_test = train_test_split(
    X_full, y, test_size=0.2, stratify=y, random_state=42
)

scaler = StandardScaler()
X_train_cont = scaler.fit_transform(X_train[continuous_features])
X_test_cont = scaler.transform(X_test[continuous_features])

X_train_scaled = X_train.copy()
X_test_scaled = X_test.copy()
X_train_scaled[continuous_features] = X_train_cont
X_test_scaled[continuous_features] = X_test_cont

X_train_scaled.to_csv("X_train_prepared.csv", index=False)
X_test_scaled.to_csv("X_test_prepared.csv", index=False)
y_train.to_csv("y_train.csv", index=False)
y_test.to_csv("y_test.csv", index=False)
```

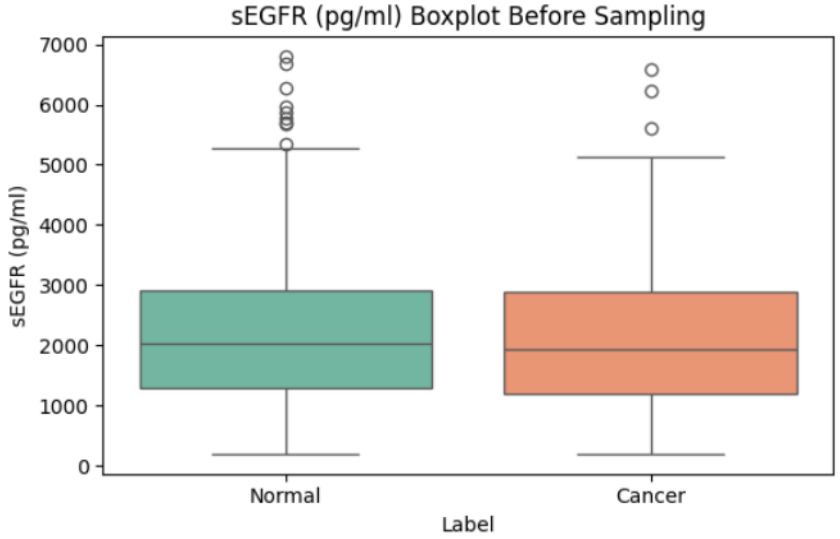
```python
import seaborn as sns
from sklearn.decomposition import PCA

X_pca_pre = PCA(n_components=2).fit_transform(X_train_scaled)

pca_pre_df = pd.DataFrame(X_pca_pre, columns=["PC1", "PC2"])
pca_pre_df["Label"] = y_train.reset_index(drop=True)

plt.figure(figsize=(7, 5))
sns.scatterplot(x="PC1", y="PC2", hue="Label", data=pca_pre_df, palette="Set1")
plt.title("PCA Visualization Before Sampling")
plt.tight_layout()
plt.show()
```

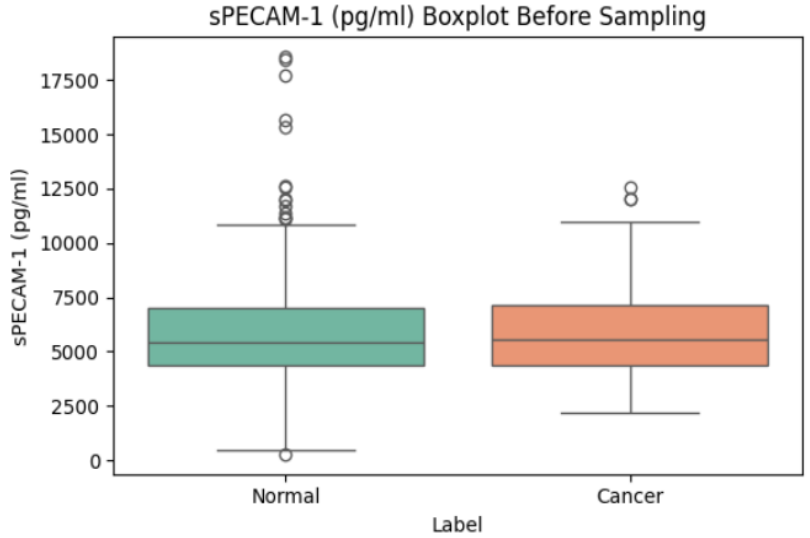


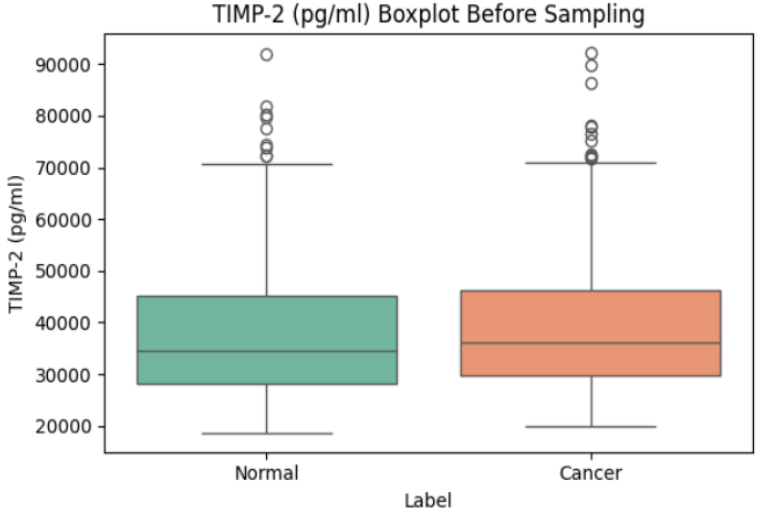
```python
boxplot_df = X_train[["CD44 (ng/ml)", "PAR (pg/ml)", "sEGFR (pg/ml)",
                      "sPECAM-1 (pg/ml)", "TIMP-2 (pg/ml)"]].copy()
boxplot_df["Label"] = y_train.reset_index(drop=True)

for col in boxplot_df.columns[:-1]:
    plt.figure(figsize=(6, 4))
    sns.boxplot(x='Label', y=col, data=boxplot_df, palette='Set2')
    plt.title(f"{col} Boxplot Before Sampling")
    plt.xlabel("Label")
    plt.xticks([0, 1], ['Normal', 'Cancer'])
    plt.tight_layout()
    plt.show()
```









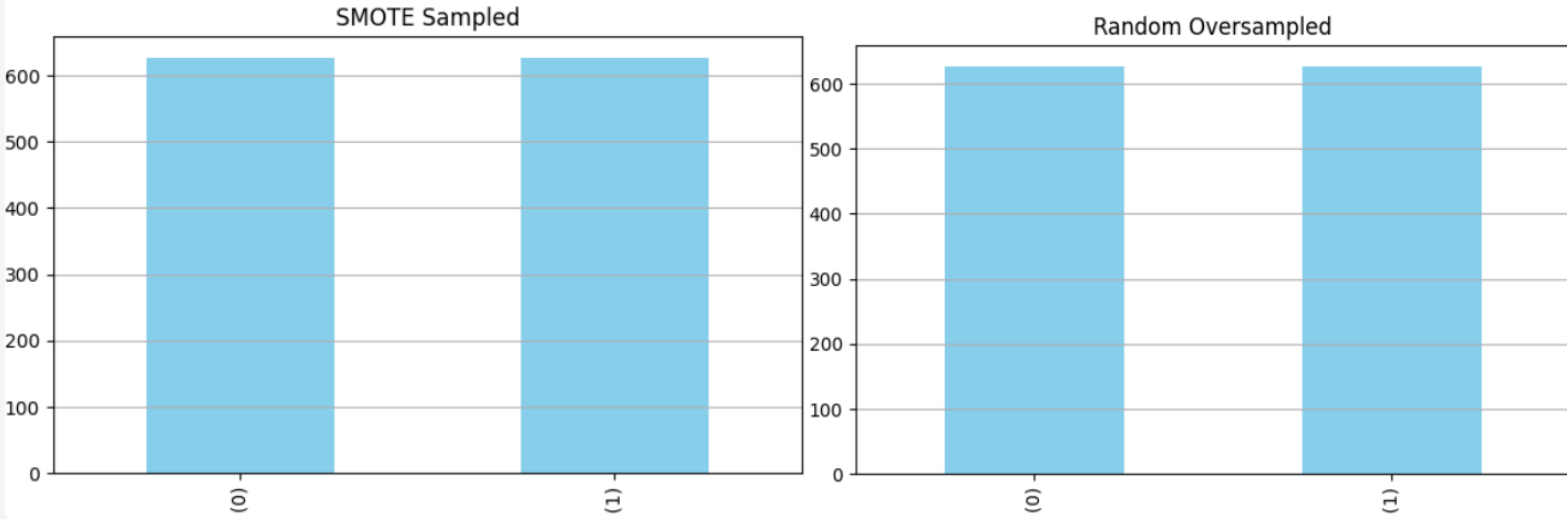


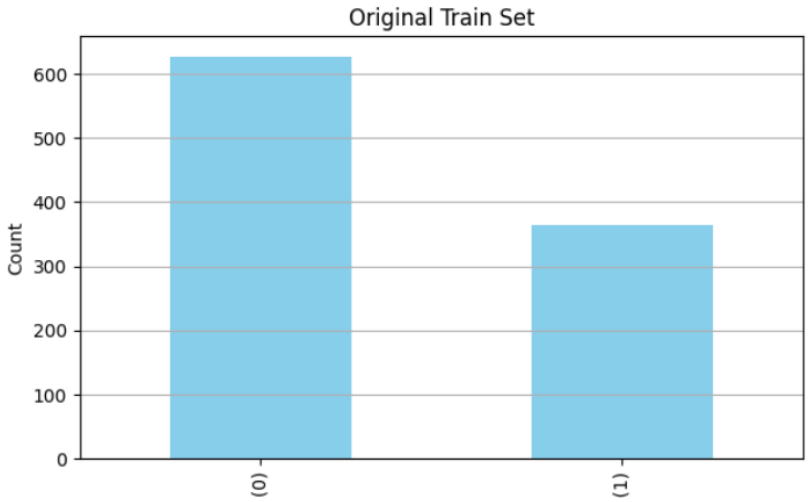
```python
from imblearn.over_sampling import SMOTE, RandomOverSampler
from imblearn.under_sampling import RandomUnderSampler
from sklearn.utils import resample
from collections import Counter
import pandas as pd

# 1. SMOTE
smote = SMOTE(random_state=42)
X_train_smote, y_train_smote = smote.fit_resample(X_train_scaled, y_train)

# 2. Random Oversampling
ros = RandomOverSampler(random_state=42)
X_train_ros, y_train_ros = ros.fit_resample(X_train_scaled, y_train)

# 3. Random Undersampling
rus = RandomUnderSampler(random_state=42)
X_train_rus, y_train_rus = rus.fit_resample(X_train_scaled, y_train)

# 4. Bootstrapping the minority class
df_train = X_train_scaled.copy()
df_train['Label'] = y_train.values

df_majority = df_train[df_train.Label == 0]
df_minority = df_train[df_train.Label == 1]

df_minority_boot = resample(
    df_minority,
    replace=True,
    n_samples=len(df_majority),
    random_state=42
)

df_bootstrap = pd.concat([df_majority, df_minority_boot])
X_train_bootstrap = df_bootstrap.drop(columns=['Label'])
y_train_bootstrap = df_bootstrap['Label']
```

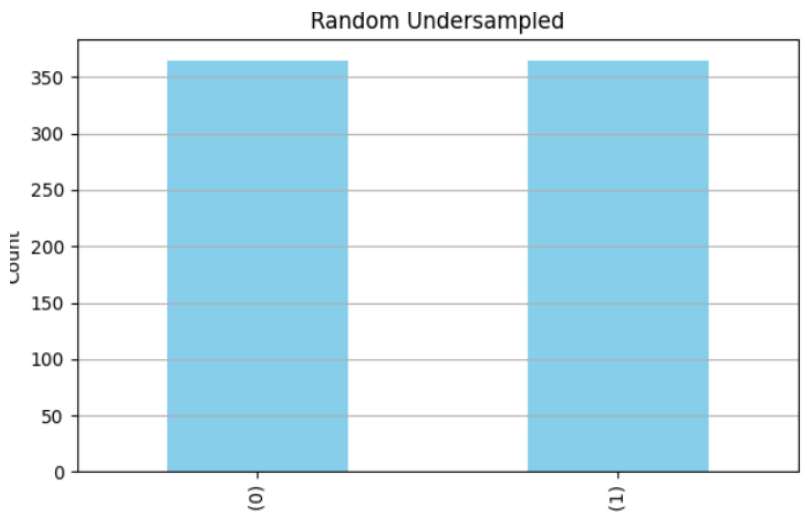
```python
# Summary of class balance
print("Original:", Counter(y_train))
print("SMOTE:", Counter(y_train_smote))
print("Random Oversampling:", Counter(y_train_ros))
print("Random Undersampling:", Counter(y_train_rus))
print("Bootstrapped:", Counter(y_train_bootstrap))
```

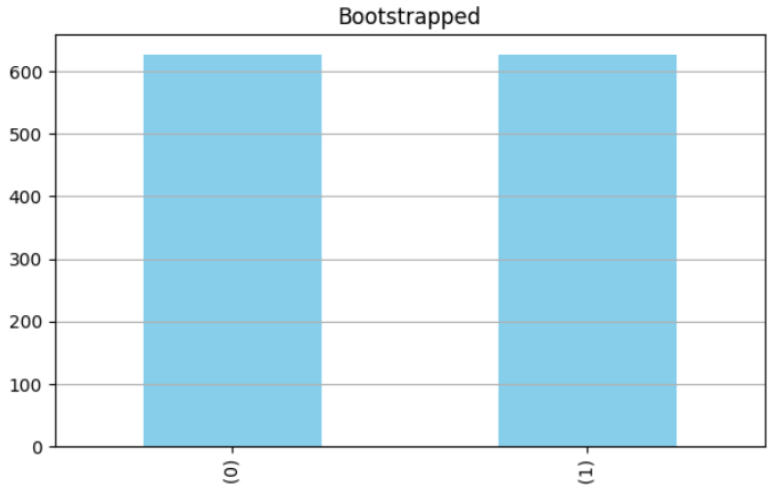
```
Original: Counter({0: 627, 1: 365})
SMOTE: Counter({0: 627, 1: 627})
Random Oversampling: Counter({0: 627, 1: 627})
Random Undersampling: Counter({0: 365, 1: 365})
Bootstrapped: Counter({0: 627, 1: 627})
```

```python
import matplotlib.pyplot as plt

def plot_class_distribution(labels, title):
    labels.value_counts().sort_index().plot(kind='bar', color='skyblue')
    plt.title(title)
    plt.xlabel('Class')
    plt.ylabel('Count')
    plt.xticks([0, 1], ['Normal (0)', 'Cancer (1)'])
    plt.grid(axis='y')
    plt.tight_layout()
    plt.show()

# Plots
plot_class_distribution(y_train, "Original Train Set")
plot_class_distribution(y_train_smote, "SMOTE Sampled")
plot_class_distribution(y_train_ros, "Random Oversampled")
plot_class_distribution(y_train_rus, "Random Undersampled")
plot_class_distribution(y_train_bootstrap, "Bootstrapped")
```

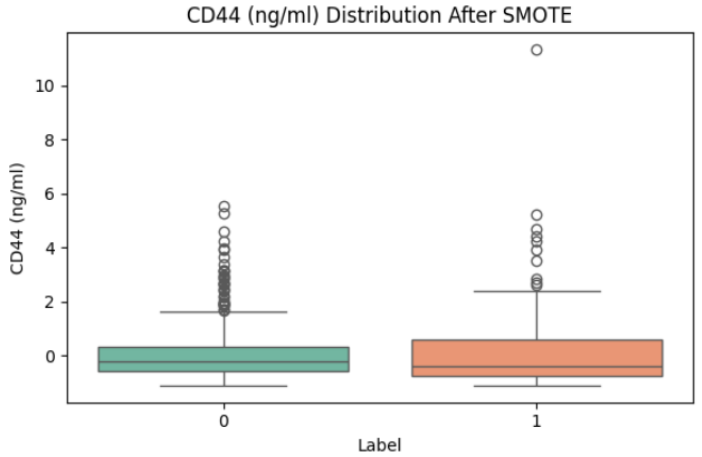


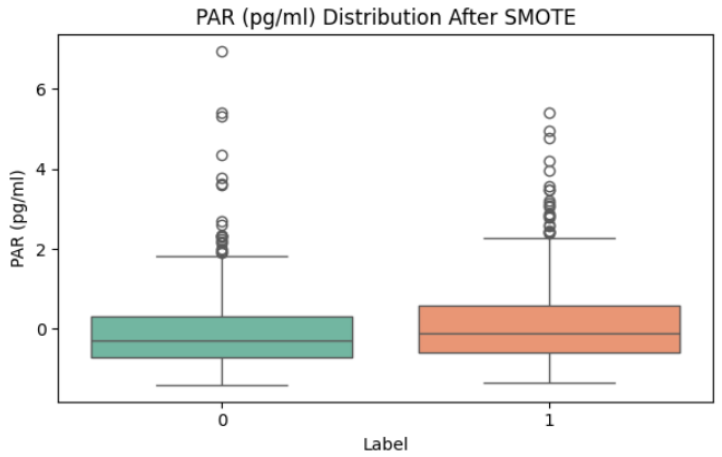


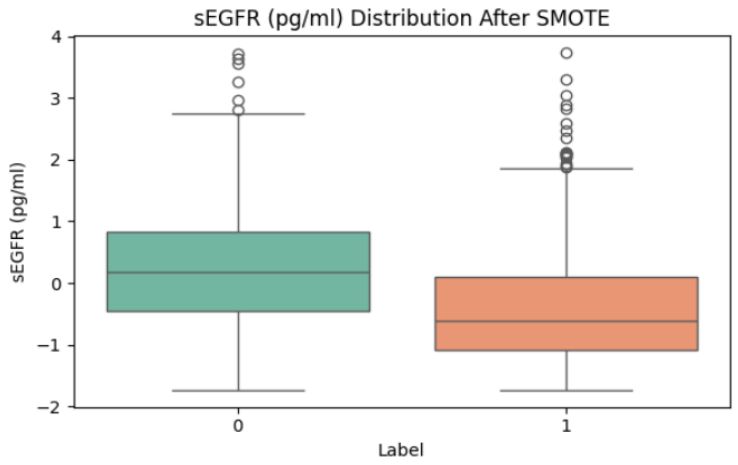


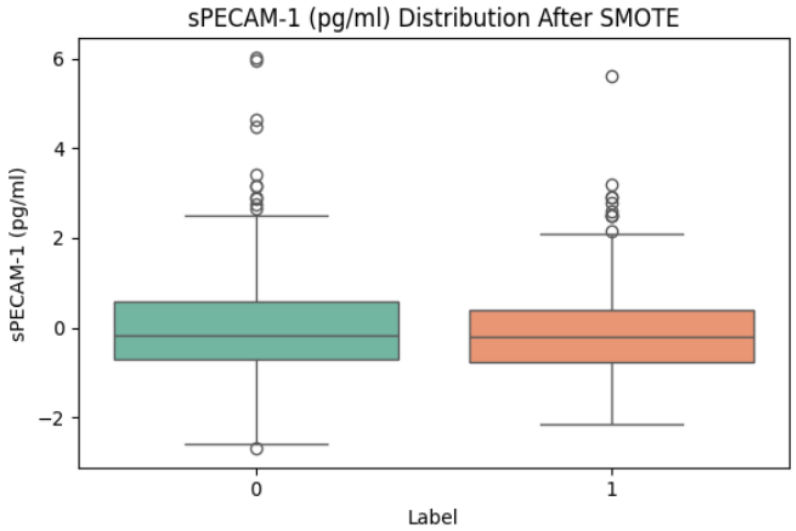


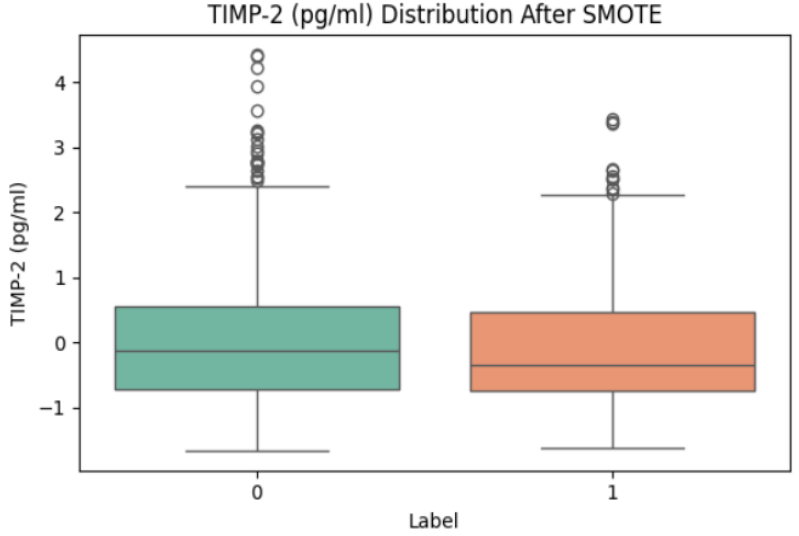
```python
smote_cont_df = pd.DataFrame(X_train_smote, columns=X_train_scaled.columns)
smote_cont_df['Label'] = y_train_smote.reset_index(drop=True)

continuous_features = ["CD44 (ng/ml)", "PAR (pg/ml)", "sEGFR (pg/ml)",
                       "sPECAM-1 (pg/ml)", "TIMP-2 (pg/ml)"]

import seaborn as sns
import matplotlib.pyplot as plt

for feature in continuous_features:
    plt.figure(figsize=(6, 4))
    sns.boxplot(x='Label', y=feature, data=smote_cont_df, palette="Set2")
    plt.title(f"{feature} Distribution After SMOTE")
    plt.tight_layout()
    plt.show()
```



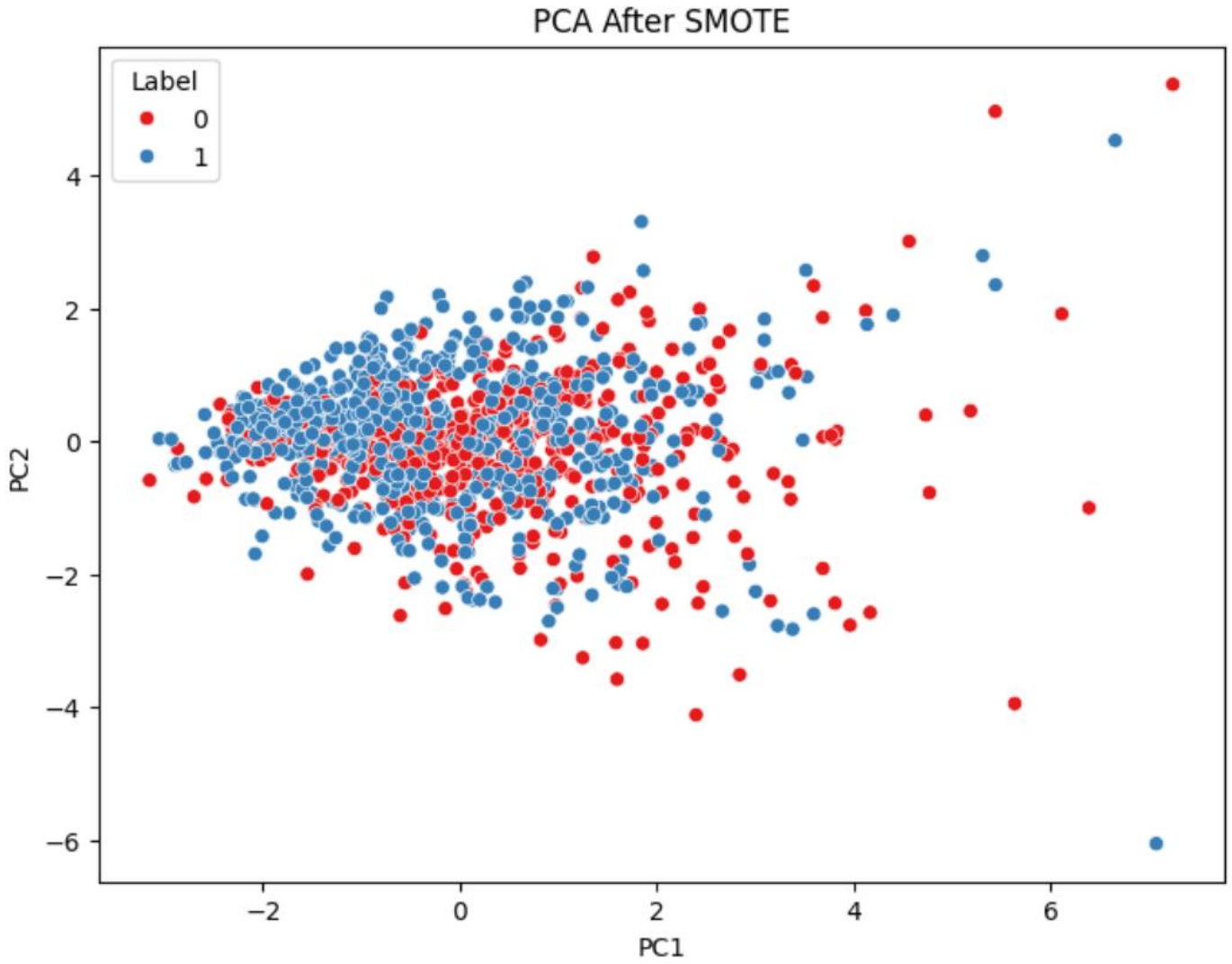








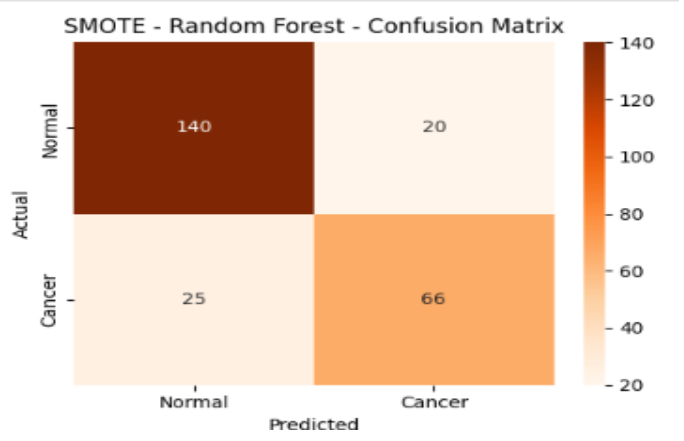
```python
from sklearn.decomposition import PCA

pca = PCA(n_components=2)
X_pca = pca.fit_transform(X_train_smote)

pca_df = pd.DataFrame(X_pca, columns=['PC1', 'PC2'])
pca_df['Label'] = y_train_smote.reset_index(drop=True)

plt.figure(figsize=(8, 6))
sns.scatterplot(x='PC1', y='PC2', hue='Label', data=pca_df, palette='Set1')
plt.title("PCA After SMOTE")
plt.show()
```

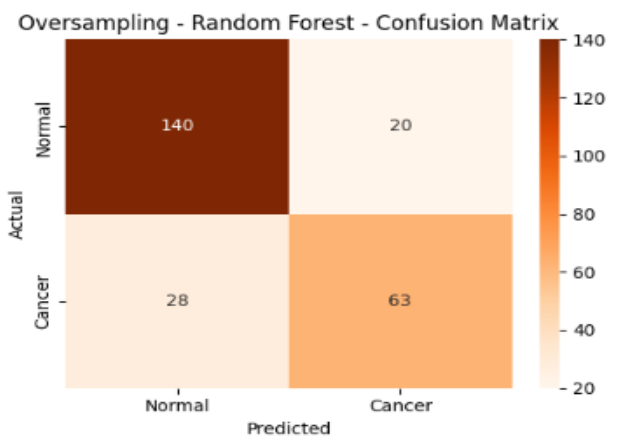


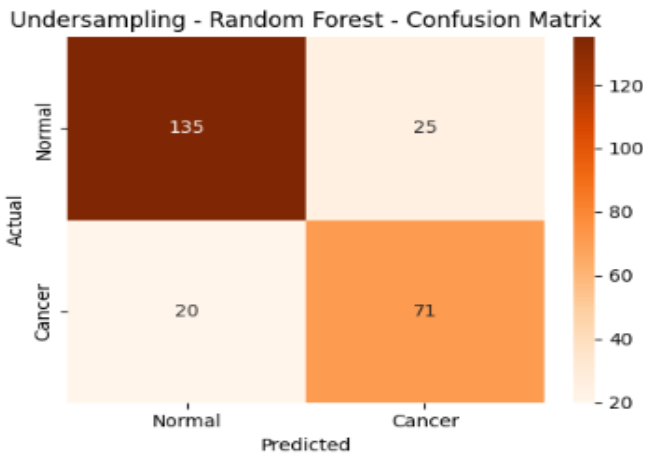
```python
from sklearn.ensemble import RandomForestClassifier
from sklearn.metrics import classification_report

rf_model = RandomForestClassifier(n_estimators=100, random_state=42)

#SMOTE
rf_model.fit(X_train_smote, y_train_smote)
y_pred_smote = rf_model.predict(X_test_scaled)
print("SMOTE")
print(classification_report(y_test, y_pred_smote))

#Random Oversampling
rf_model.fit(X_train_ros, y_train_ros)
y_pred_ros = rf_model.predict(X_test_scaled)
print("Random Oversampling")
print(classification_report(y_test, y_pred_ros))

#Random Undersampling
rf_model.fit(X_train_rus, y_train_rus)
y_pred_rus = rf_model.predict(X_test_scaled)
print("Random Undersampling")
print(classification_report(y_test, y_pred_rus))

#Bootstrapping
rf_model.fit(X_train_bootstrap, y_train_bootstrap)
y_pred_boot = rf_model.predict(X_test_scaled)
print("Bootstrapping")
print(classification_report(y_test, y_pred_boot))
```

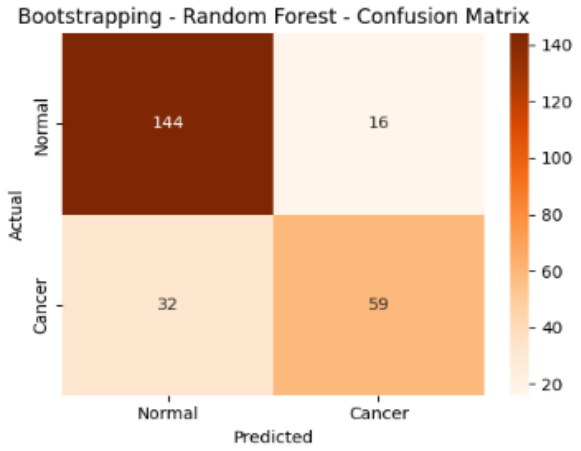
```
SMOTE
              precision    recall  f1-score   support

           0       0.90      0.85      0.87       157
           1       0.76      0.84      0.80        91

    accuracy                           0.84       248
   macro avg       0.83      0.84      0.83       248
weighted avg       0.85      0.84      0.84       248

Random Oversampling
              precision    recall  f1-score   support

           0       0.88      0.87      0.88       157
           1       0.78      0.80      0.79        91

    accuracy                           0.85       248
   macro avg       0.83      0.84      0.84       248
weighted avg       0.85      0.85      0.85       248

Random Undersampling
              precision    recall  f1-score   support

           0       0.92      0.86      0.89       157
           1       0.78      0.87      0.82        91

    accuracy                           0.86       248
   macro avg       0.85      0.86      0.86       248
weighted avg       0.87      0.86      0.86       248

Bootstrapping
              precision    recall  f1-score   support

           0       0.86      0.92      0.89       157
           1       0.85      0.75      0.80        91

    accuracy                           0.86       248
   macro avg       0.86      0.84      0.84       248
weighted avg       0.86      0.86      0.86       248
```

```python
import seaborn as sns
import matplotlib.pyplot as plt
from sklearn.metrics import confusion_matrix
def plot_conf_matrix(y_true, y_pred, title):
    cm = confusion_matrix(y_true, y_pred)
    plt.figure(figsize=(5, 4))
    sns.heatmap(cm, annot=True, fmt='d', cmap='Oranges', xticklabels=['Normal', 'Cancer'], yticklabels=['Normal', 'Cancer'])
    plt.title(f"{title} - Confusion Matrix")
    plt.xlabel('Predicted')
    plt.ylabel('Actual')
    plt.tight_layout()
    plt.show()

#SMOTE
plot_conf_matrix(y_test, y_pred_smote, "SMOTE - Random Forest")
print("SMOTE Confusion Matrix")
print(confusion_matrix(y_test, y_pred_smote))

# Oversampling
plot_conf_matrix(y_test, y_pred_ros, "Oversampling - Random Forest")
print("\nRandom Oversampling Confusion Matrix")
print(confusion_matrix(y_test, y_pred_ros))

#Undersampling
plot_conf_matrix(y_test, y_pred_rus, "Undersampling - Random Forest")
print("\nRandom Undersampling Confusion Matrix")
print(confusion_matrix(y_test, y_pred_rus))

#Bootstrapping
plot_conf_matrix(y_test, y_pred_boot, "Bootstrapping - Random Forest")
print("\nBootstrapping Confusion Matrix")
print(confusion_matrix(y_test, y_pred_boot))
```



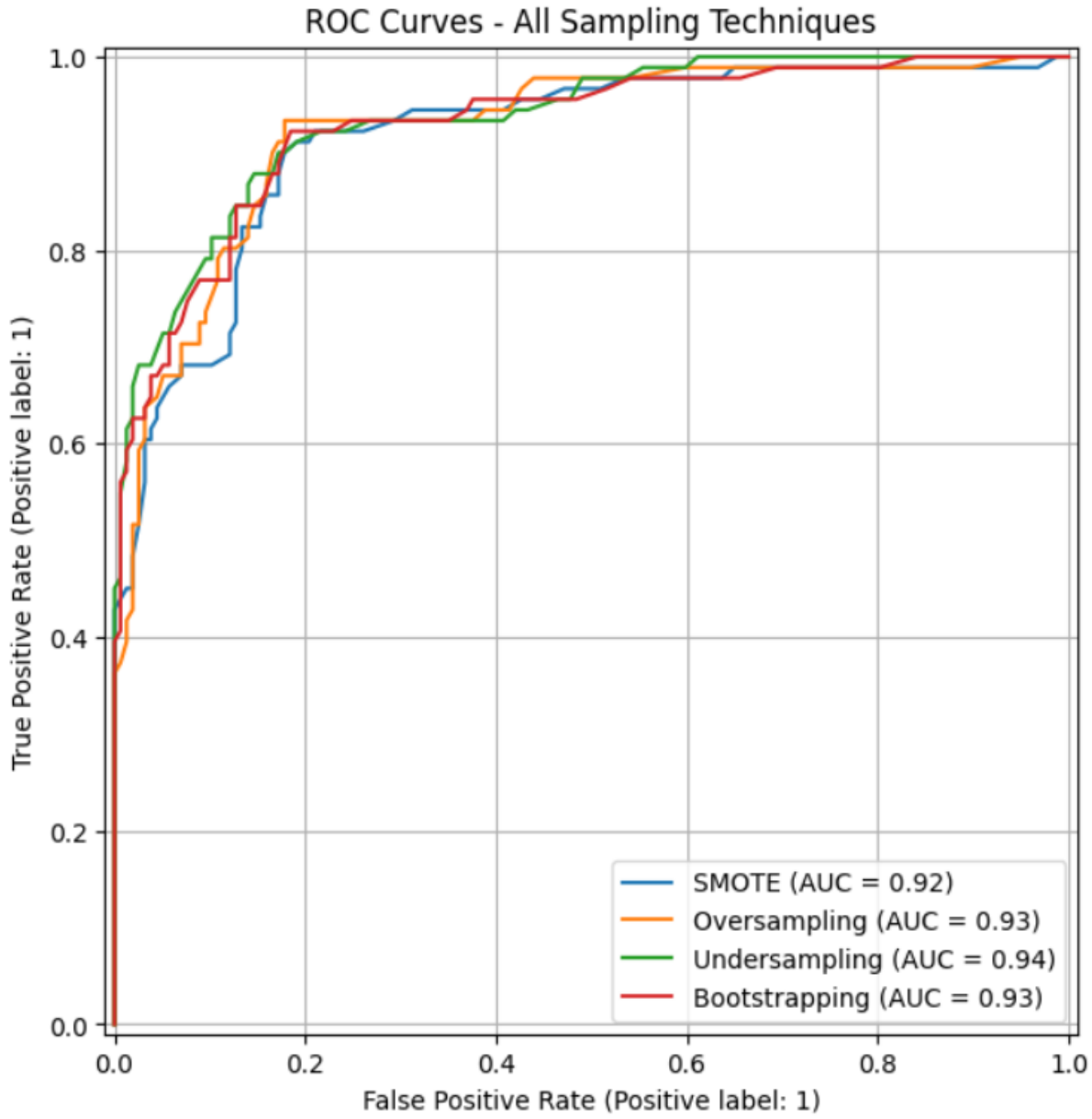




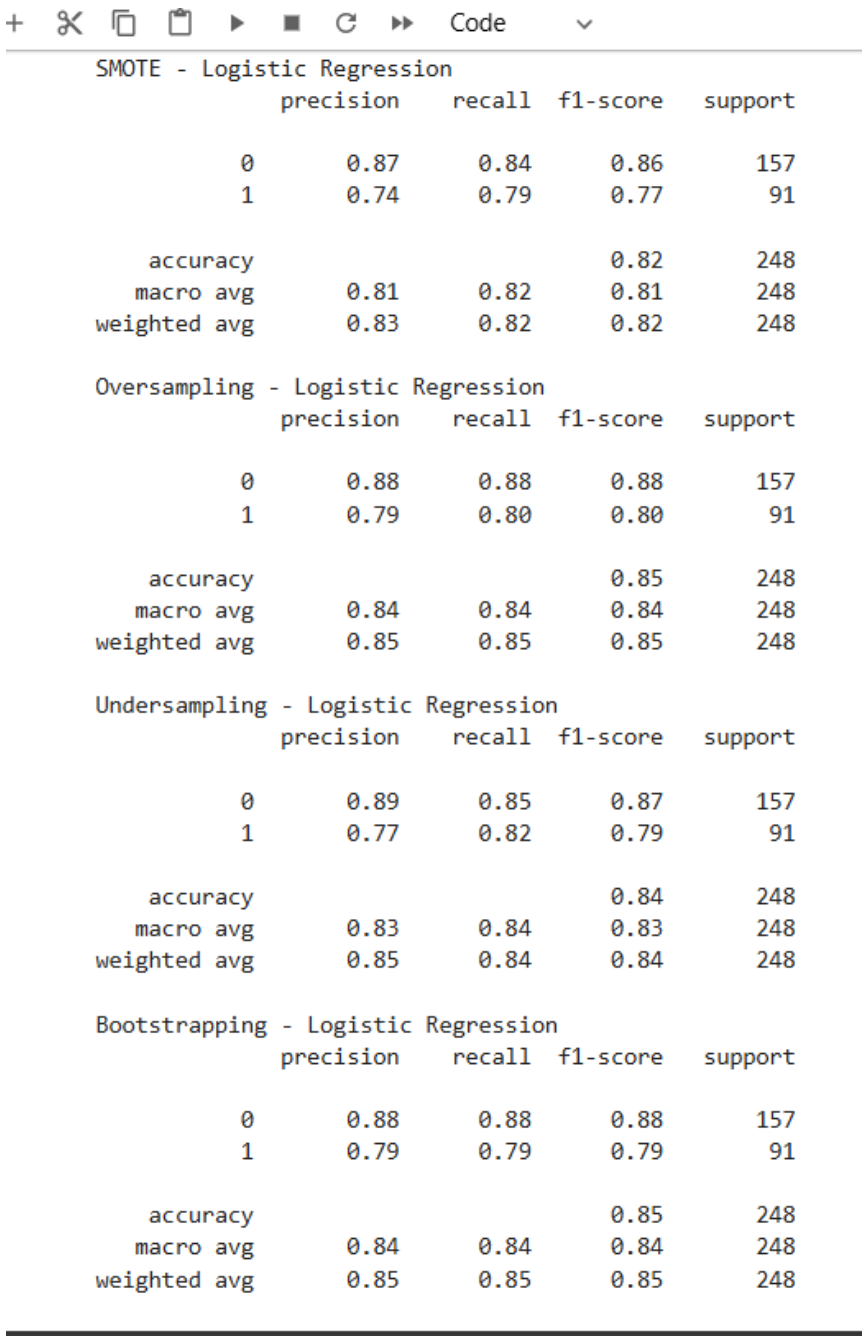


```python
from sklearn.metrics import roc_auc_score, RocCurveDisplay
import matplotlib.pyplot as plt

# Probabilities for ROC
y_proba_smote = rf_model.predict_proba(X_test_scaled)[:, 1]
rf_model.fit(X_train_smote, y_train_smote)
y_proba_smote = rf_model.predict_proba(X_test_scaled)[:, 1]

rf_model.fit(X_train_ros, y_train_ros)
y_proba_ros = rf_model.predict_proba(X_test_scaled)[:, 1]

rf_model.fit(X_train_rus, y_train_rus)
y_proba_rus = rf_model.predict_proba(X_test_scaled)[:, 1]

rf_model.fit(X_train_bootstrap, y_train_bootstrap)
y_proba_boot = rf_model.predict_proba(X_test_scaled)[:, 1]

# AUC Scores
print("SMOTE AUC:", roc_auc_score(y_test, y_proba_smote))
print("Random Oversampling AUC:", roc_auc_score(y_test, y_proba_ros))
print("Random Undersampling AUC:", roc_auc_score(y_test, y_proba_rus))
print("Bootstrapping AUC:", roc_auc_score(y_test, y_proba_boot))

# Plot ROC Curves
plt.figure(figsize=(10, 7))
RocCurveDisplay.from_predictions(y_test, y_proba_smote, name="SMOTE", ax=plt.gca())
RocCurveDisplay.from_predictions(y_test, y_proba_ros, name="Oversampling", ax=plt.gca())
RocCurveDisplay.from_predictions(y_test, y_proba_rus, name="Undersampling", ax=plt.gca())
RocCurveDisplay.from_predictions(y_test, y_proba_boot, name="Bootstrapping", ax=plt.gca())
plt.title("ROC Curves - All Sampling Techniques")
plt.grid(True)
plt.show()
```

```
SMOTE AUC: 0.9172324490795828
Random Oversampling AUC: 0.925211730944215
Random Undersampling AUC: 0.9357457828795408
Bootstrapping AUC: 0.9288864002239798
```

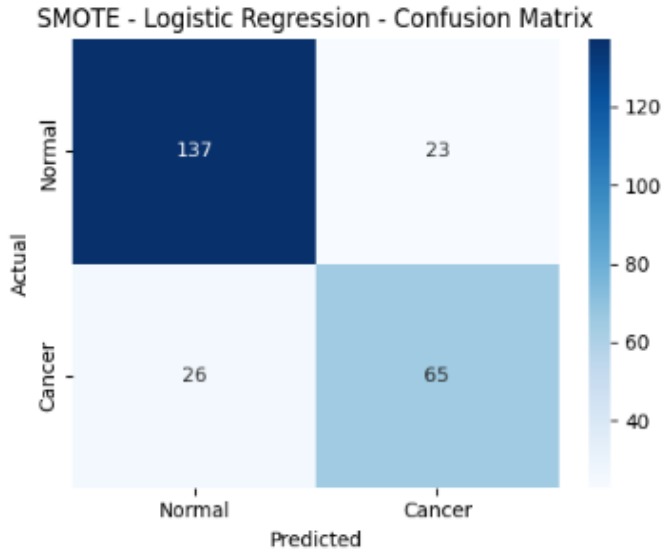


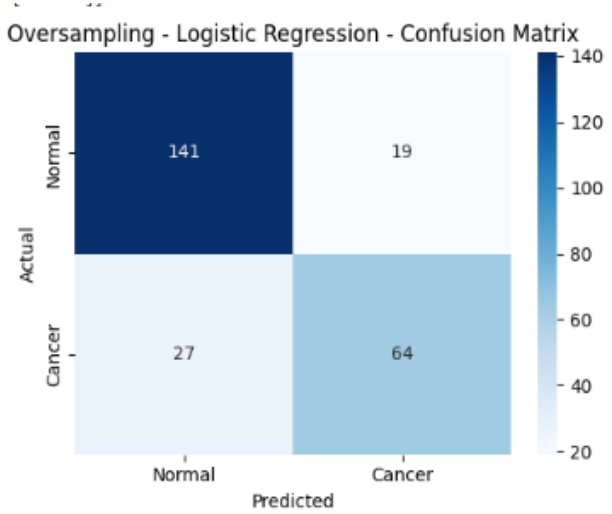
```python
from sklearn.linear_model import LogisticRegression
from sklearn.metrics import classification_report

lr_model = LogisticRegression(max_iter=1000, random_state=42)

#SMOTE
lr_model.fit(X_train_smote, y_train_smote)
y_pred_smote_lr = lr_model.predict(X_test_scaled)
print("SMOTE - Logistic Regression")
print(classification_report(y_test, y_pred_smote_lr))

#Random Oversampling
lr_model.fit(X_train_ros, y_train_ros)
y_pred_ros_lr = lr_model.predict(X_test_scaled)
print("Oversampling - Logistic Regression")
print(classification_report(y_test, y_pred_ros_lr))

#Random Undersampling
lr_model.fit(X_train_rus, y_train_rus)
y_pred_rus_lr = lr_model.predict(X_test_scaled)
print("Undersampling - Logistic Regression")
print(classification_report(y_test, y_pred_rus_lr))

#Bootstrapping
lr_model.fit(X_train_bootstrap, y_train_bootstrap)
y_pred_boot_lr = lr_model.predict(X_test_scaled)
print("Bootstrapping - Logistic Regression")
print(classification_report(y_test, y_pred_boot_lr))
```

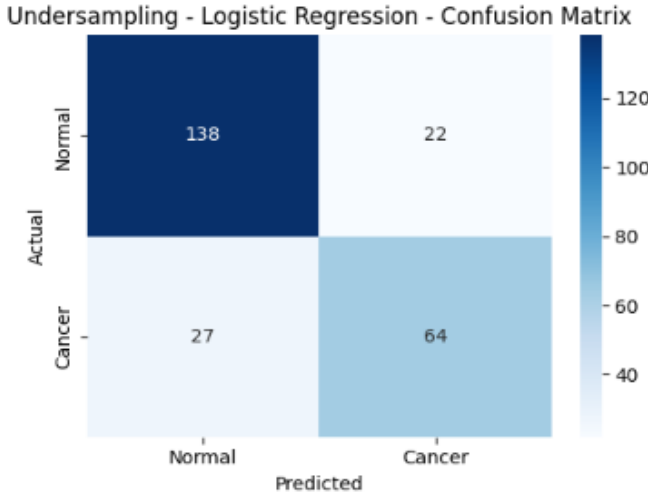


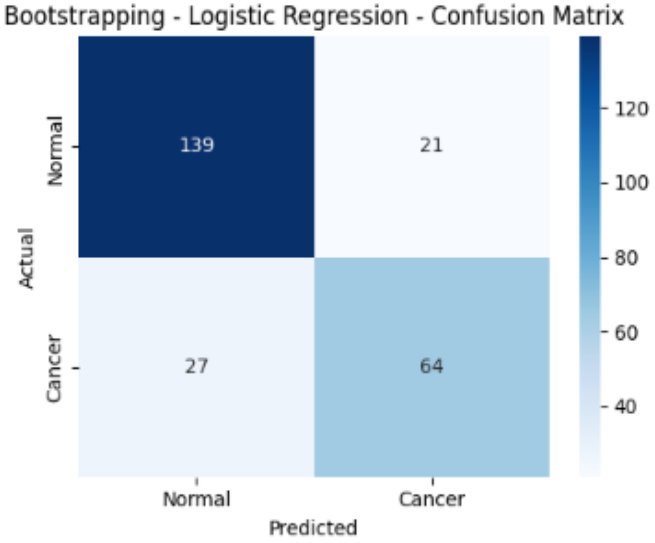
```
SMOTE - Logistic Regression
              precision    recall  f1-score   support

           0       0.87      0.84      0.86       157
           1       0.74      0.79      0.77        91

    accuracy                           0.82       248
   macro avg       0.81      0.82      0.81       248
weighted avg       0.83      0.82      0.82       248

Oversampling - Logistic Regression
              precision    recall  f1-score   support

           0       0.88      0.88      0.88       157
           1       0.79      0.80      0.80        91

    accuracy                           0.85       248
   macro avg       0.84      0.84      0.84       248
weighted avg       0.85      0.85      0.85       248

Undersampling - Logistic Regression
              precision    recall  f1-score   support

           0       0.89      0.85      0.87       157
           1       0.77      0.82      0.79        91

    accuracy                           0.84       248
   macro avg       0.83      0.84      0.83       248
weighted avg       0.85      0.84      0.84       248

Bootstrapping - Logistic Regression
              precision    recall  f1-score   support

           0       0.88      0.88      0.88       157
           1       0.79      0.79      0.79        91

    accuracy                           0.85       248
   macro avg       0.84      0.84      0.84       248
weighted avg       0.85      0.85      0.85       248
```

```python
import seaborn as sns
import matplotlib.pyplot as plt
from sklearn.metrics import confusion_matrix

def plot_conf_matrix(y_true, y_pred, title):
    cm = confusion_matrix(y_true, y_pred)
    plt.figure(figsize=(5, 4))
    sns.heatmap(cm, annot=True, fmt='d', cmap='Blues', xticklabels=['Normal', 'Cancer'], yticklabels=['Normal', 'Cancer'])
    plt.title(f"{title} - Confusion Matrix")
    plt.xlabel('Predicted')
    plt.ylabel('Actual')
    plt.tight_layout()
    plt.show()

#SMOTE
plot_conf_matrix(y_test, y_pred_smote_lr, "SMOTE - Logistic Regression")
print("SMOTE Confusion Matrix")
print(confusion_matrix(y_test, y_pred_smote_lr))

#Oversampling
plot_conf_matrix(y_test, y_pred_ros_lr, "Oversampling - Logistic Regression")
print("\nOversampling Confusion Matrix")
print(confusion_matrix(y_test, y_pred_ros_lr))

#Undersampling
plot_conf_matrix(y_test, y_pred_rus_lr, "Undersampling - Logistic Regression")
print("\nUndersampling Confusion Matrix")
print(confusion_matrix(y_test, y_pred_rus_lr))

#Bootstrapping
plot_conf_matrix(y_test, y_pred_boot_lr, "Bootstrapping - Logistic Regression")
print("\nBootstrapping Confusion Matrix")
print(confusion_matrix(y_test, y_pred_boot_lr))
```



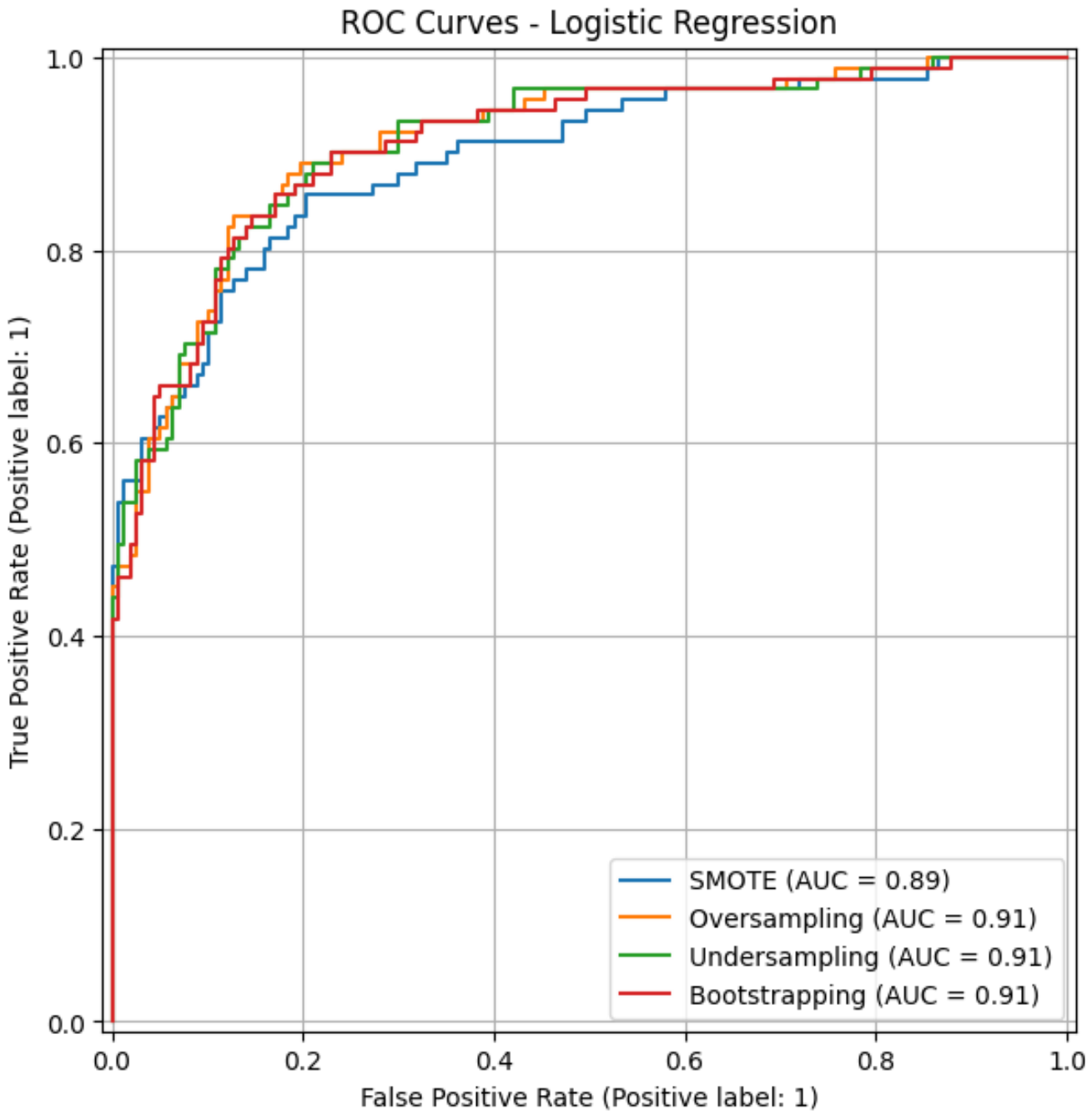






```python
from sklearn.metrics import roc_auc_score, RocCurveDisplay
import matplotlib.pyplot as plt

lr_model.fit(X_train_smote, y_train_smote)
y_proba_smote_lr = lr_model.predict_proba(X_test_scaled)[:, 1]

lr_model.fit(X_train_ros, y_train_ros)
y_proba_ros_lr = lr_model.predict_proba(X_test_scaled)[:, 1]

lr_model.fit(X_train_rus, y_train_rus)
y_proba_rus_lr = lr_model.predict_proba(X_test_scaled)[:, 1]

lr_model.fit(X_train_bootstrap, y_train_bootstrap)
y_proba_boot_lr = lr_model.predict_proba(X_test_scaled)[:, 1]

# AUC
print("SMOTE AUC (LogReg):", roc_auc_score(y_test, y_proba_smote_lr))
print("Oversampling AUC (LogReg):", roc_auc_score(y_test, y_proba_ros_lr))
print("Undersampling AUC (LogReg):", roc_auc_score(y_test, y_proba_rus_lr))
print("Bootstrapping AUC (LogReg):", roc_auc_score(y_test, y_proba_boot_lr))

# Plot
plt.figure(figsize=(10, 7))
RocCurveDisplay.from_predictions(y_test, y_proba_smote_lr, name="SMOTE", ax=plt.gca())
RocCurveDisplay.from_predictions(y_test, y_proba_ros_lr, name="Oversampling", ax=plt.gca())
RocCurveDisplay.from_predictions(y_test, y_proba_rus_lr, name="Undersampling", ax=plt.gca())
RocCurveDisplay.from_predictions(y_test, y_proba_boot_lr, name="Bootstrapping", ax=plt.gca())
plt.title("ROC Curves - Logistic Regression")
plt.grid(True)
plt.show()
```

```
SMOTE AUC (LogReg): 0.8949394554490097
Oversampling AUC (LogReg): 0.9125078742913137
Undersampling AUC (LogReg): 0.9117379435850773
Bootstrapping AUC (LogReg): 0.9097081262686358
```



```python
from sklearn.metrics import accuracy_score, precision_score, recall_score, f1_score, roc_auc_score
import pandas as pd
def summarize_model_performance(y_true, y_pred, model_name):
    return {
        "Model": model_name,
        "Accuracy": accuracy_score(y_true, y_pred),
        "Precision": precision_score(y_true, y_pred),
        "Recall": recall_score(y_true, y_pred),
        "F1-Score": f1_score(y_true, y_pred)
    }

# Random Forest
rf_results = [
    summarize_model_performance(y_test, y_pred_smote, "RF - SMOTE"),
    summarize_model_performance(y_test, y_pred_ros, "RF - ROS"),
    summarize_model_performance(y_test, y_pred_rus, "RF - RUS"),
    summarize_model_performance(y_test, y_pred_boot, "RF - Bootstrapping")
]

# Logistic Regression
lr_results = [
    summarize_model_performance(y_test, y_pred_smote_lr, "LR - SMOTE"),
    summarize_model_performance(y_test, y_pred_ros_lr, "LR - ROS"),
    summarize_model_performance(y_test, y_pred_rus_lr, "LR - RUS"),
    summarize_model_performance(y_test, y_pred_boot_lr, "LR - Bootstrapping")
]
performance_table = pd.DataFrame(rf_results + lr_results)
performance_table = performance_table.round(3)
performance_table.to_csv("model_performance_summary.csv", index=False)

print(performance_table)
```

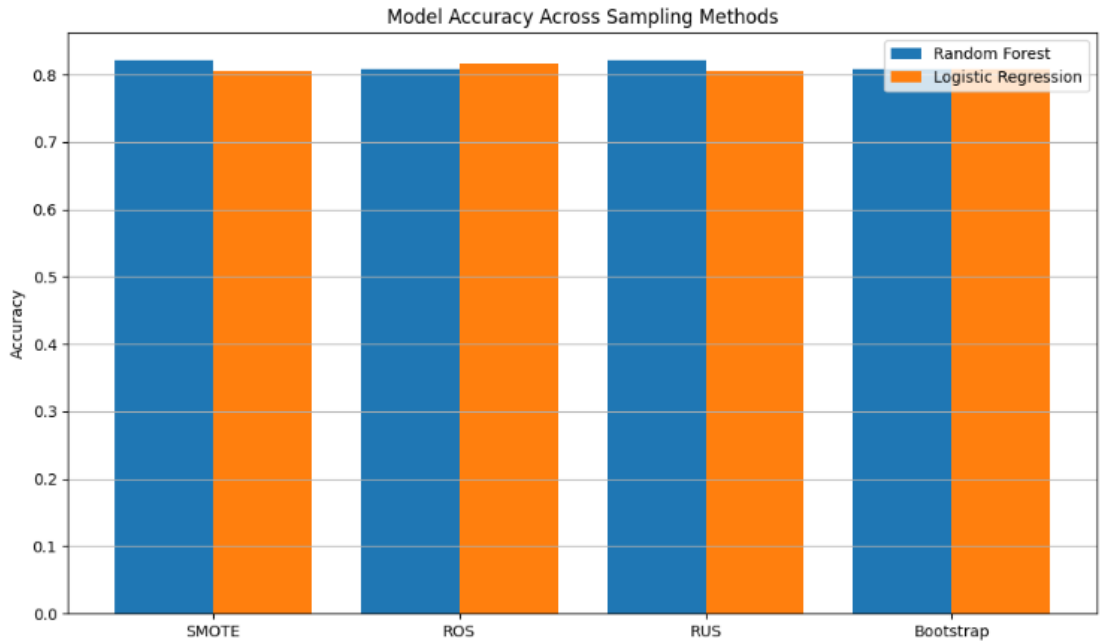
	Model	Accuracy	Precision	Recall	F1-Score
0	RF - SMOTE	0.843	0.760	0.835	0.796
1	RF - ROS	0.847	0.785	0.802	0.793
2	RF - RUS	0.863	0.782	0.868	0.823
3	RF - Bootstrapping	0.859	0.850	0.747	0.795
4	LR - SMOTE	0.823	0.742	0.791	0.766
5	LR - ROS	0.851	0.793	0.802	0.798
6	LR - RUS	0.843	0.765	0.824	0.794
7	LR - Bootstrapping	0.847	0.791	0.791	0.791

```python
import pandas as pd

# Model performance summary
performance_data = [
    ['Random Forest', 'SMOTE', 0.84, 0.76, 0.83, 0.79],
    ['Logistic Regression', 'SMOTE', 0.82, 0.74, 0.79, 0.76],
    ['Random Forest', 'Oversampling', 0.84, 0.78, 0.80, 0.79],
    ['Random Forest', 'Undersampling', 0.84, 0.78, 0.86, 0.82]
]

columns = ['Model', 'Sampling', 'Accuracy', 'Precision', 'Recall', 'F1-Score']
summary_df = pd.DataFrame(performance_data, columns=columns)
styled_table = summary_df.style \
    .highlight_max(subset=['F1-Score'], color='lightgreen') \
    .set_caption("Model Comparison Summary") \
    .format({'Accuracy': '{:.2f}', 'Precision': '{:.2f}', 'Recall': '{:.2f}', 'F1-Score': '{:.2f}'})

styled_table
```

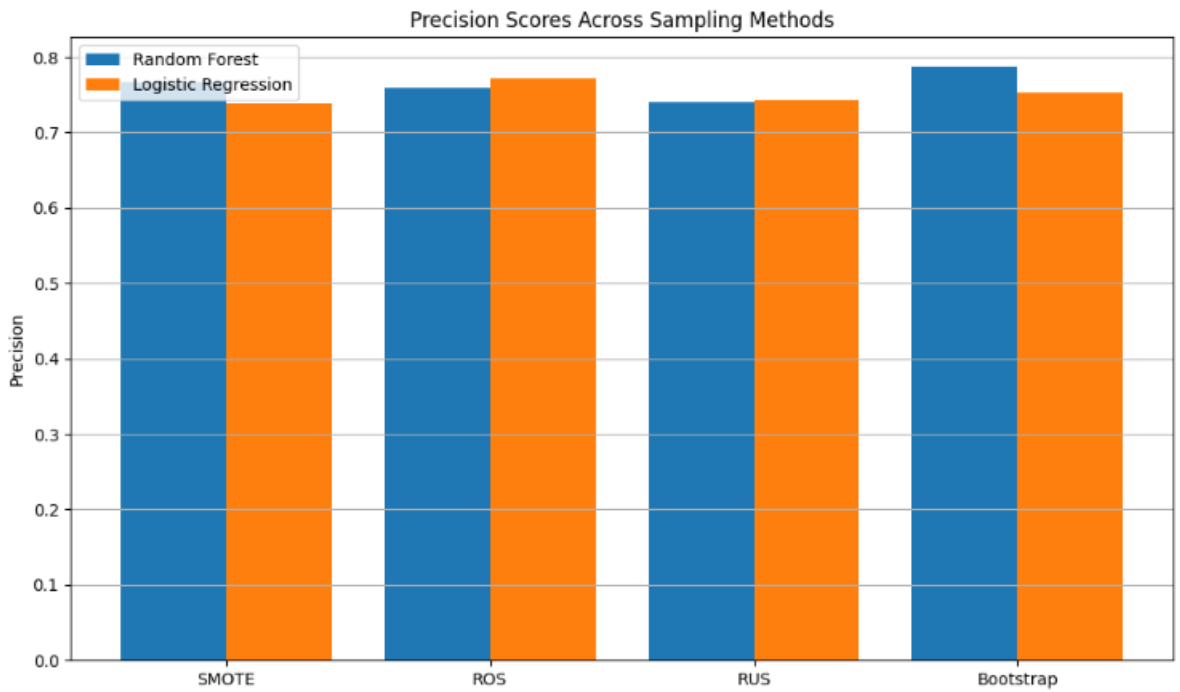
Model Comparison Summary

	Model	Sampling	Accuracy	Precision	Recall	F1-Score
0	Random Forest	SMOTE	0.84	0.76	0.83	0.79
1	Logistic Regression	SMOTE	0.82	0.74	0.79	0.76
2	Random Forest	Oversampling	0.84	0.78	0.80	0.79
3	Random Forest	Undersampling	0.84	0.78	0.86	0.82

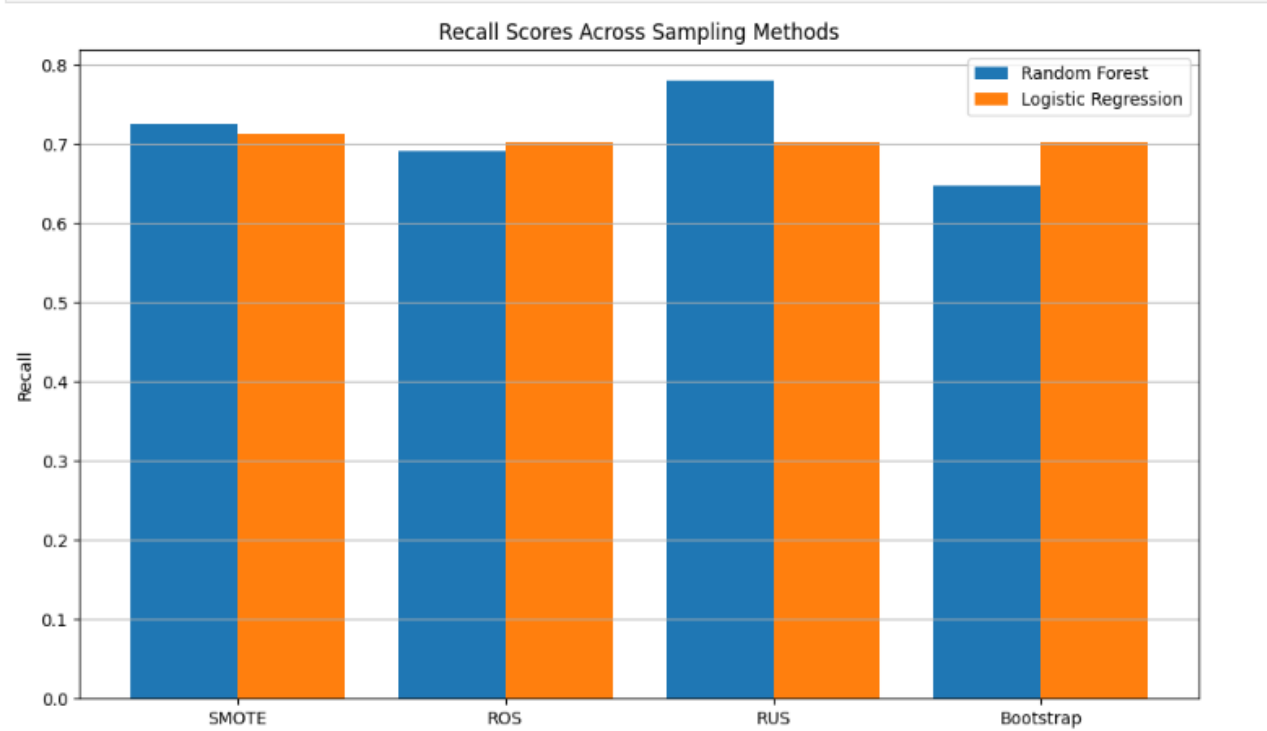
```python
import matplotlib.pyplot as plt
accuracy_rf = {
    'SMOTE': performance_table[performance_table['Model'] == 'RF - SMOTE']['Accuracy'].values[0],
    'ROS': performance_table[performance_table['Model'] == 'RF - ROS']['Accuracy'].values[0],
    'RUS': performance_table[performance_table['Model'] == 'RF - RUS']['Accuracy'].values[0],
    'Bootstrap': performance_table[performance_table['Model'] == 'RF - Bootstrapping']['Accuracy'].values[0]
}

accuracy_lr = {
    'SMOTE': performance_table[performance_table['Model'] == 'LR - SMOTE']['Accuracy'].values[0],
    'ROS': performance_table[performance_table['Model'] == 'LR - ROS']['Accuracy'].values[0],
    'RUS': performance_table[performance_table['Model'] == 'LR - RUS']['Accuracy'].values[0],
    'Bootstrap': performance_table[performance_table['Model'] == 'LR - Bootstrapping']['Accuracy'].values[0]
}

sampling_methods = list(accuracy_rf.keys())
x = range(len(sampling_methods))
rf_scores = list(accuracy_rf.values())
lr_scores = list(accuracy_lr.values())

plt.figure(figsize=(10, 6))
plt.bar([i - 0.2 for i in x], rf_scores, width=0.4, label='Random Forest')
plt.bar([i + 0.2 for i in x], lr_scores, width=0.4, label='Logistic Regression')
plt.xticks(ticks=x, labels=sampling_methods)
plt.ylabel("Accuracy")
plt.title("Model Accuracy Across Sampling Methods")
plt.legend()
plt.grid(axis='y')
plt.tight_layout()
plt.show()
```



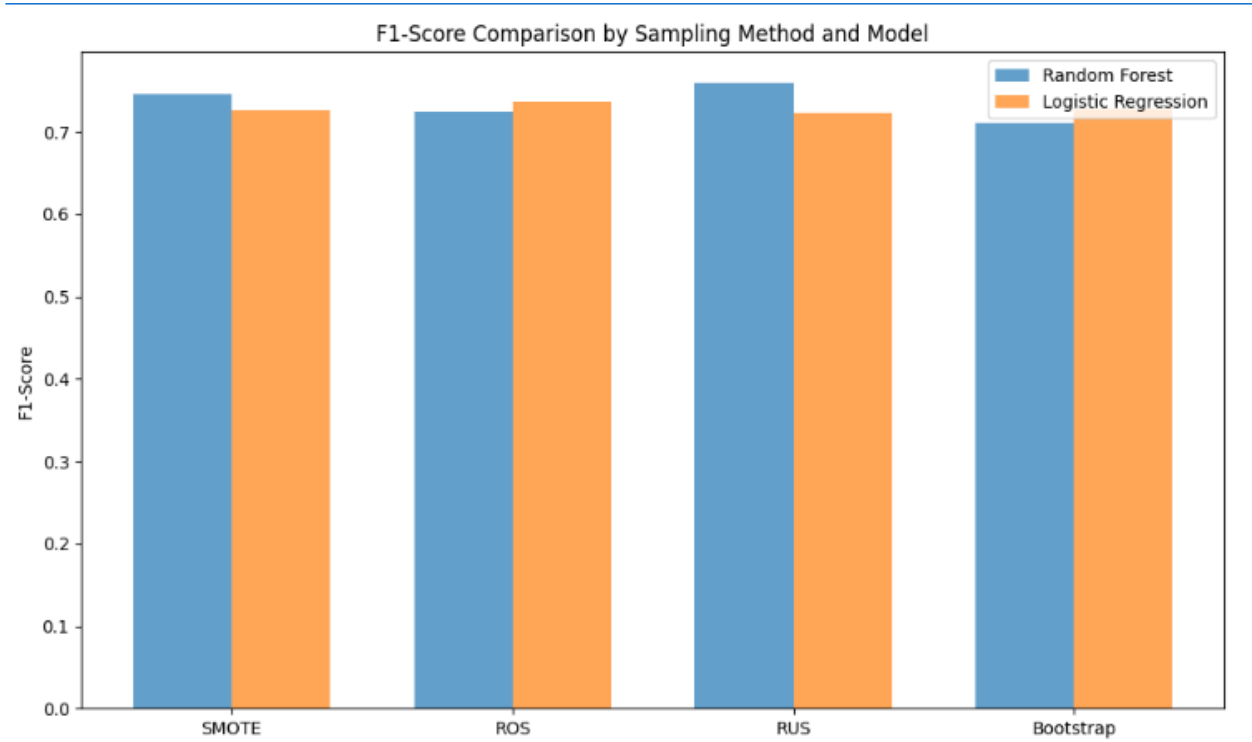
```
precision_rf = {
    'SMOTE': performance_table[performance_table['Model'] == 'RF - SMOTE']['Precision'].values[0],
    'ROS': performance_table[performance_table['Model'] == 'RF - ROS']['Precision'].values[0],
    'RUS': performance_table[performance_table['Model'] == 'RF - RUS']['Precision'].values[0],
    'Bootstrap': performance_table[performance_table['Model'] == 'RF - Bootstrapping']['Precision'].values[0]
}

precision_lr = {
    'SMOTE': performance_table[performance_table['Model'] == 'LR - SMOTE']['Precision'].values[0],
    'ROS': performance_table[performance_table['Model'] == 'LR - ROS']['Precision'].values[0],
    'RUS': performance_table[performance_table['Model'] == 'LR - RUS']['Precision'].values[0],
    'Bootstrap': performance_table[performance_table['Model'] == 'LR - Bootstrapping']['Precision'].values[0]
}

plt.figure(figsize=(10, 6))
plt.bar([i - 0.2 for i in x], list(precision_rf.values()), width=0.4, label='Random Forest')
plt.bar([i + 0.2 for i in x], list(precision_lr.values()), width=0.4, label='Logistic Regression')
plt.xticks(ticks=x, labels=sampling_methods)
plt.ylabel("Precision")
plt.title("Precision Scores Across Sampling Methods")
plt.legend()
plt.grid(axis='y')
plt.tight_layout()
plt.show()
```



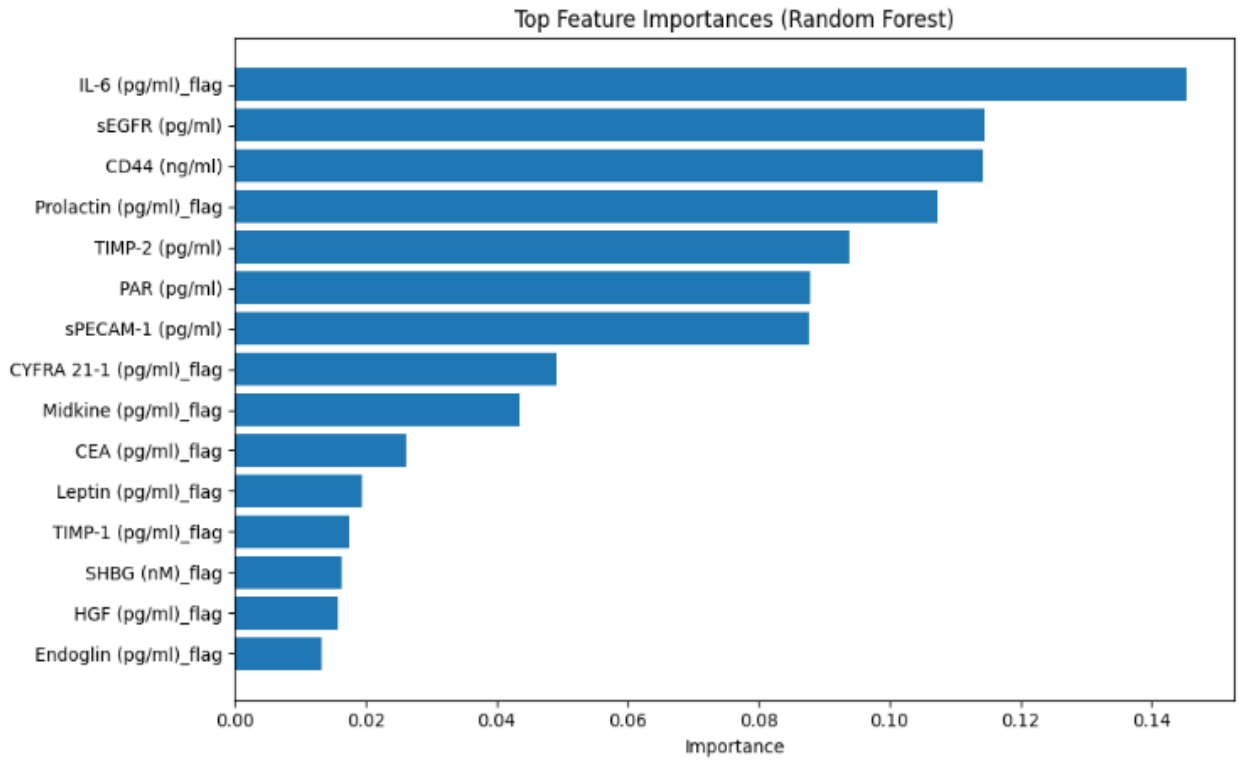
```python
# Recall values
recall_rf = {
    'SMOTE': performance_table[performance_table['Model'] == 'RF - SMOTE']['Recall'].values[0],
    'ROS': performance_table[performance_table['Model'] == 'RF - ROS']['Recall'].values[0],
    'RUS': performance_table[performance_table['Model'] == 'RF - RUS']['Recall'].values[0],
    'Bootstrap': performance_table[performance_table['Model'] == 'RF - Bootstrapping']['Recall'].values[0]
}

recall_lr = {
    'SMOTE': performance_table[performance_table['Model'] == 'LR - SMOTE']['Recall'].values[0],
    'ROS': performance_table[performance_table['Model'] == 'LR - ROS']['Recall'].values[0],
    'RUS': performance_table[performance_table['Model'] == 'LR - RUS']['Recall'].values[0],
    'Bootstrap': performance_table[performance_table['Model'] == 'LR - Bootstrapping']['Recall'].values[0]
}

plt.figure(figsize=(10, 6))
plt.bar([i - 0.2 for i in x], list(recall_rf.values()), width=0.4, label='Random Forest')
plt.bar([i + 0.2 for i in x], list(recall_lr.values()), width=0.4, label='Logistic Regression')
plt.xticks(ticks=x, labels=sampling_methods)
plt.ylabel("Recall")
plt.title("Recall Scores Across Sampling Methods")
plt.legend()
plt.grid(axis='y')
plt.tight_layout()
plt.show()
```



```python
import matplotlib.pyplot as plt

f1_rf = {
    'SMOTE': performance_table[performance_table['Model'] == 'RF - SMOTE']['F1-Score'].values[0],
    'ROS': performance_table[performance_table['Model'] == 'RF - ROS']['F1-Score'].values[0],
    'RUS': performance_table[performance_table['Model'] == 'RF - RUS']['F1-Score'].values[0],
    'Bootstrap': performance_table[performance_table['Model'] == 'RF - Bootstrapping']['F1-Score'].values[0]
}

f1_lr = {
    'SMOTE': performance_table[performance_table['Model'] == 'LR - SMOTE']['F1-Score'].values[0],
    'ROS': performance_table[performance_table['Model'] == 'LR - ROS']['F1-Score'].values[0],
    'RUS': performance_table[performance_table['Model'] == 'LR - RUS']['F1-Score'].values[0],
    'Bootstrap': performance_table[performance_table['Model'] == 'LR - Bootstrapping']['F1-Score'].values[0]
}

bar_width = 0.35
methods = list(f1_rf.keys())
x = range(len(methods))

plt.figure(figsize=(10, 6))
plt.bar(x, f1_rf.values(), width=bar_width, label='Random Forest', alpha=0.7)
plt.bar([i + bar_width for i in x], f1_lr.values(), width=bar_width, label='Logistic Regression', alpha=0.7)

plt.xticks([i + bar_width / 2 for i in x], methods)
plt.ylabel('F1-Score')
plt.title('F1-Score Comparison by Sampling Method and Model')
plt.legend()
plt.tight_layout()
plt.show()
```



```python
importances = rf_model.feature_importances_
features = X_train_scaled.columns

importance_df = pd.DataFrame({
    'Feature': features,
    'Importance': importances
}).sort_values(by='Importance', ascending=False)

#Top features
top_n = 15
plt.figure(figsize=(10, 6))
plt.barh(importance_df['Feature'][:top_n][::-1], importance_df['Importance'][:top_n][::-1])
plt.xlabel('Importance')
plt.title('Top Feature Importances (Random Forest)')
plt.tight_layout()
plt.show()
```



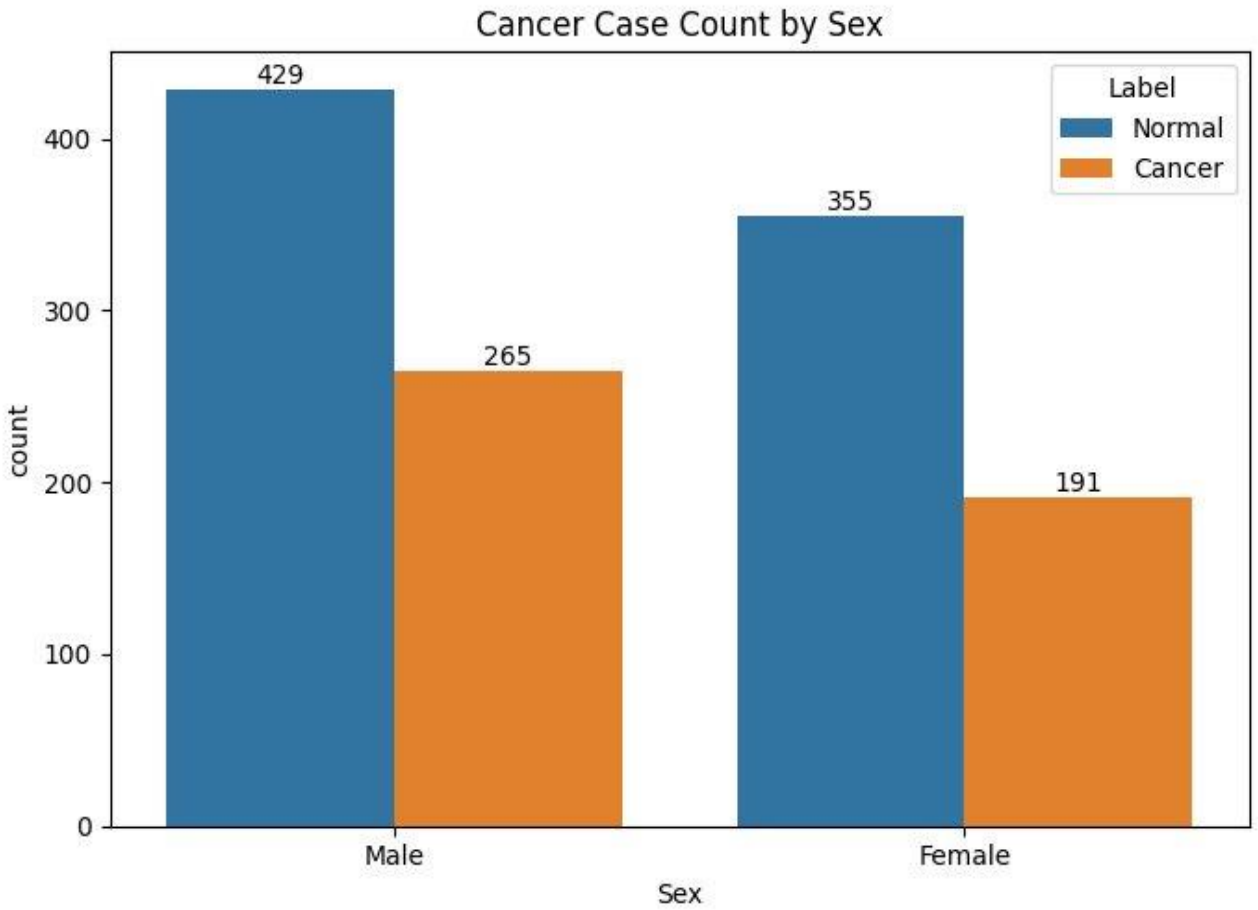
```python
from scipy.stats import chi2_contingency

sex = df['Sex']
label = df['Label']
contingency = pd.crosstab(sex, label)
chi2, p, _, _ = chi2_contingency(contingency)
print(f"Chi2: {chi2:.2f}, p-value: {p:.4f}")
```

```
Chi2: 1.21, p-value: 0.2706
```

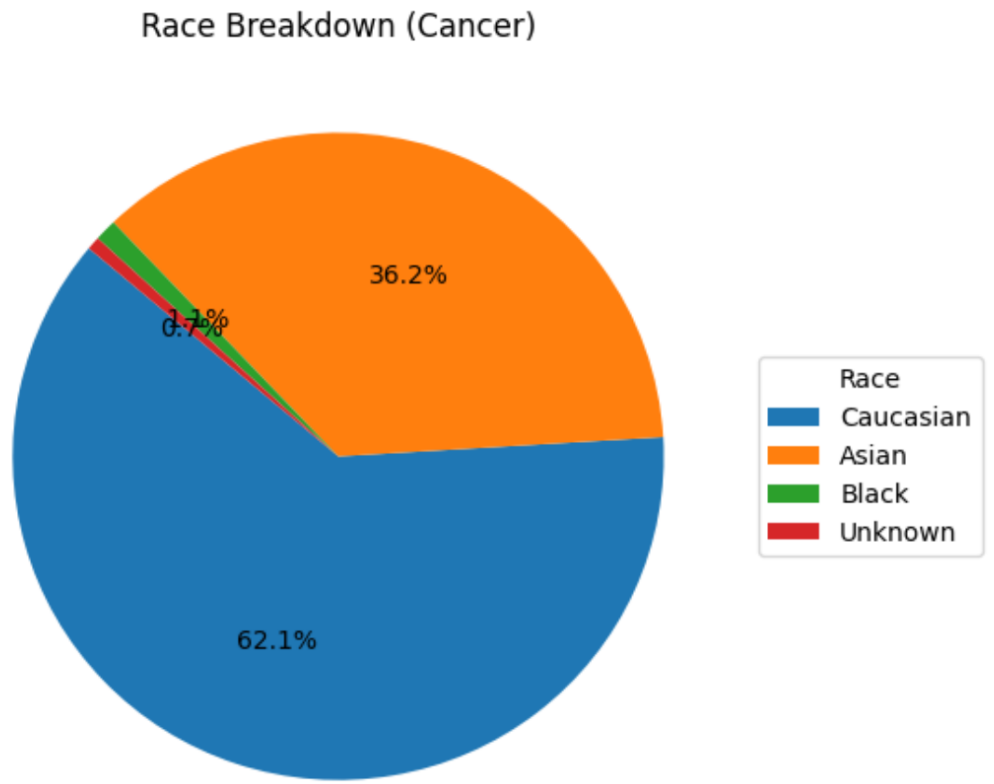
```python
from scipy.stats import mannwhitneyu

group0 = df[df['Label'] == 0]['Age']
group1 = df[df['Label'] == 1]['Age']
stat, p_age = mannwhitneyu(group0, group1)
print(f"Mann-Whitney U test for Age: p-value = {p_age:.4f}")
```

```
Mann-Whitney U test for Age: p-value = 0.0000
```

```
plt.figure(figsize=(7, 5))
sns.countplot(data=df, x='Sex', hue='Label')
plt.title("Cancer Case Count by Sex")
plt.legend(title='Label', labels=['Normal', 'Cancer'])
for container in plt.gca().containers:
    plt.bar_label(container, label_type='edge', fontsize=10)
plt.tight_layout()
plt.show()
```




```
race_counts = df[df['Label'] == 1]['Race'].value_counts()

plt.figure(figsize=(6, 6))
wedges, texts, autotexts = plt.pie(
    race_counts,
    labels=None,
    autopct='%1.1f%%',
    startangle=140
)

plt.title("Race Breakdown (Cancer)")
plt.legend(wedges, race_counts.index, title="Race", loc="center left", bbox_to_anchor=(1, 0.5))
plt.tight_layout()
plt.show()
```



```
plt.figure(figsize=(7, 5))
sns.boxplot(x='Label', y='Age', data=df, palette='Set2')
plt.title("Age Distribution by Cancer Status")
medians = df.groupby('Label')['Age'].median()
for i, median in enumerate(medians):
    plt.text(i, median + 1, f"Median: {median:.1f}", ha='center', color='black')
plt.axhline(df[df['Label'] == 1]['Age'].median(), linestyle='--', color='orange', label='Median (Cancer)')
plt.axhline(df[df['Label'] == 0]['Age'].median(), linestyle='--', color='blue', label='Median (Normal)')
plt.legend()
plt.tight_layout()
plt.show()
```