```
# Install required libraries
!pip install pandas numpy matplotlib seaborn scikit-learn tensorflow keras imbalanced-learn xgboost

# Import libraries
import pandas as pd
import numpy as np
import matplotlib.pyplot as plt
import seaborn as sns
from sklearn.model_selection import train_test_split, cross_val_score, GridSearchCV
from sklearn.preprocessing import StandardScaler, OneHotEncoder
from sklearn.impute import SimpleImputer
from sklearn.compose import ColumnTransformer
from sklearn.pipeline import Pipeline
from sklearn.metrics import mean_absolute_error, mean_squared_error, r2_score, accuracy_score, precision_score, recall_score, f1_sc
from sklearn.linear_model import LinearRegression, Ridge, Lasso
from sklearn.ensemble import RandomForestRegressor, GradientBoostingRegressor, RandomForestClassifier
from sklearn.svm import SVR, SVC
from sklearn.tree import DecisionTreeRegressor, DecisionTreeClassifier
from imblearn.over_sampling import SMOTE
import warnings
warnings.filterwarnings('ignore')

```

```
Requirement already satisfied: numpy in /usr/local/lib/python3.11/dist-packages (2.0.2)
Requirement already satisfied: matplotlib in /usr/local/lib/python3.11/dist-packages (3.10.0)
Requirement already satisfied: seaborn in /usr/local/lib/python3.11/dist-packages (0.13.2)
Requirement already satisfied: scikit-learn in /usr/local/lib/python3.11/dist-packages (1.6.1)
Requirement already satisfied: tensorflow in /usr/local/lib/python3.11/dist-packages (2.18.0)
Requirement already satisfied: keras in /usr/local/lib/python3.11/dist-packages (3.8.0)
Requirement already satisfied: imbalanced-learn in /usr/local/lib/python3.11/dist-packages (0.13.0)
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Requirement already satisfied: python-dateutil>=2.8.2 in /usr/local/lib/python3.11/dist-packages (from pandas) (2.9.0.post0)
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Requirement already satisfied: fonttools>=4.22.0 in /usr/local/lib/python3.11/dist-packages (from matplotlib) (4.57.0)
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Requirement already satisfied: packaging>=20.0 in /usr/local/lib/python3.11/dist-packages (from matplotlib) (24.2)
Requirement already satisfied: pillow>=8 in /usr/local/lib/python3.11/dist-packages (from matplotlib) (11.2.1)
Requirement already satisfied: pyparsing>=2.3.1 in /usr/local/lib/python3.11/dist-packages (from matplotlib) (3.2.3)
Requirement already satisfied: scipy>=1.6.0 in /usr/local/lib/python3.11/dist-packages (from scikit-learn) (1.15.2)
Requirement already satisfied: joblib>=1.2.0 in /usr/local/lib/python3.11/dist-packages (from scikit-learn) (1.5.0)
Requirement already satisfied: threadpoolctl>=3.1.0 in /usr/local/lib/python3.11/dist-packages (from scikit-learn) (3.6.0)
Requirement already satisfied: absl-py>=1.0.0 in /usr/local/lib/python3.11/dist-packages (from tensorflow) (1.4.0)
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Requirement already satisfied: google-pasta>=0.1.1 in /usr/local/lib/python3.11/dist-packages (from tensorflow) (0.2.0)
Requirement already satisfied: libclang>=13.0.0 in /usr/local/lib/python3.11/dist-packages (from tensorflow) (18.1.1)
Requirement already satisfied: opt-einsum>=2.3.2 in /usr/local/lib/python3.11/dist-packages (from tensorflow) (3.4.0)
Requirement already satisfied: protobuf!=4.21.0,!=4.21.1,!=4.21.2,!=4.21.3,!=4.21.4,!=4.21.5,<6.0.0dev,>=3.20.3 in /usr/local/lib
Requirement already satisfied: requests<3,>=2.21.0 in /usr/local/lib/python3.11/dist-packages (from tensorflow) (2.32.3)
Requirement already satisfied: setuptools in /usr/local/lib/python3.11/dist-packages (from tensorflow) (75.2.0)
Requirement already satisfied: six>=1.12.0 in /usr/local/lib/python3.11/dist-packages (from tensorflow) (1.17.0)
Requirement already satisfied: termcolor>=1.1.0 in /usr/local/lib/python3.11/dist-packages (from tensorflow) (3.1.0)
Requirement already satisfied: typing-extensions>=3.6.6 in /usr/local/lib/python3.11/dist-packages (from tensorflow) (4.13.2)
Requirement already satisfied: wrapt>=1.11.0 in /usr/local/lib/python3.11/dist-packages (from tensorflow) (1.17.2)
Requirement already satisfied: grpcio<2.0,>=1.24.3 in /usr/local/lib/python3.11/dist-packages (from tensorflow) (1.71.0)
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Requirement already satisfied: h5py>=3.11.0 in /usr/local/lib/python3.11/dist-packages (from tensorflow) (3.13.0)
Requirement already satisfied: ml-dtypes<0.5.0,>=0.4.0 in /usr/local/lib/python3.11/dist-packages (from tensorflow) (0.4.1)
Requirement already satisfied: tensorflow-io-gcs-filesystem>=0.23.1 in /usr/local/lib/python3.11/dist-packages (from tensorflow)
Requirement already satisfied: rich in /usr/local/lib/python3.11/dist-packages (from keras) (13.9.4)
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Requirement already satisfied: optree in /usr/local/lib/python3.11/dist-packages (from keras) (0.15.0)
Requirement already satisfied: sklearn-compat<1,>=0.1 in /usr/local/lib/python3.11/dist-packages (from imbalanced-learn) (0.1.3)
Requirement already satisfied: nvidia-nccl-cu12 in /usr/local/lib/python3.11/dist-packages (from xgboost) (2.21.5)
Requirement already satisfied: wheel<1.0,>=0.23.0 in /usr/local/lib/python3.11/dist-packages (from astunparse>=1.6.0->tensorflow)
Requirement already satisfied: charset-normalizer<4,>=2 in /usr/local/lib/python3.11/dist-packages (from requests<3,>=2.21.0->ten
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Requirement already satisfied: markdown>=2.6.8 in /usr/local/lib/python3.11/dist-packages (from tensorboard<2.19,>=2.18->tensorfl
Requirement already satisfied: tensorboard-data-server<0.8.0,>=0.7.0 in /usr/local/lib/python3.11/dist-packages (from tensorboard
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Requirement already satisfied: MarkupSafe>=2.1.1 in /usr/local/lib/python3.11/dist-packages (from werkzeug>=1.0.1->tensorboard<2.
```

```
import pandas as pd  # Make sure to import pandas first

# Read the Excel file - specify sheet_name as a string or index
warfarin_data = pd.read_excel('PS206767-553247439.xls', sheet_name='Subject Data')  # Adjust sheet name as needed
```

```
5
6 # Display the first few rows
7 print(warfarin_data.head())
```

```
  PharmGKB Subject ID PharmGKB Sample ID  Project Site  Gender  \
0         PA135312261        PA135312629             1    male
1         PA135312262        PA135312630             1  female
2         PA135312263        PA135312631             1  female
3         PA135312264        PA135312632             1    male
4         PA135312265        PA135312633             1    male

  Race (Reported) Race (OMB)    Ethnicity (Reported)         Ethnicity (OMB)  \
0           White      White  not Hispanic or Latino  not Hispanic or Latino
1           White      White  not Hispanic or Latino  not Hispanic or Latino
2           White      White  not Hispanic or Latino  not Hispanic or Latino
3           White      White  not Hispanic or Latino  not Hispanic or Latino
4           White      White  not Hispanic or Latino  not Hispanic or Latino

       Age  Height (cm)  ...  \
0  60 - 69      193.040  ...
1  50 - 59      176.530  ...
2  40 - 49      162.560  ...
3  60 - 69      182.245  ...
4  50 - 59      167.640  ...

   VKORC1 QC genotype: -4451 C>A (861); Chr16:31018002; rs17880887; A/C  \
0                                                NaN
1                                                C/C
2                                                NaN
3                                                NaN
4                                                NaN

  CYP2C9 consensus VKORC1 -1639 consensus  VKORC1 497 consensus  \
0            *1/*1                    A/G                   G/T
1            *1/*1                    A/A                   G/T
2            *1/*1                    G/G                   T/T
3            *1/*1                    A/G                   G/T
4            *1/*3                    A/G                   T/T

   VKORC1 1173 consensus  VKORC1 1542 consensus VKORC1 3730 consensus  \
0                    NaN                    C/G                   A/G
1                    T/T                    C/C                   G/G
2                    NaN                    G/G                   A/G
3                    NaN                    C/G                   G/G
4                    NaN                    C/G                   A/G

   VKORC1 2255 consensus  VKORC1 -4451 consensus  \
0                    NaN                     NaN
1                    T/T                     C/C
2                    NaN                     NaN
3                    NaN                     NaN
4                    NaN                     NaN

             Comments regarding Project Site Dataset
0                                        Project 1:
1               Warfarin Therapeutic Dose Definition:
2  The dose (unchanged for 6 days) that yielded a...
3                                                NaN
4                                                NaN

[5 rows x 68 columns]
```

```
1 warfarin_data.head()
```

	PharmGKB Subject ID	PharmGKB Sample ID	Project Site	Gender	Race (Reported)	Race (OMB)	Ethnicity (Reported)	Ethnicity (OMB)	Age	Height (cm)	...	VKORC1 QC genotype: -4451 C>A (861); Chr16:31018002; rs17880887; A/C	CYP2C9 consensus
0	PA135312261	PA135312629	1	male	White	White	not Hispanic or Latino	not Hispanic or Latino	60 - 69	193.040	...	NaN	*1/*
1	PA135312262	PA135312630	1	female	White	White	not Hispanic or Latino	not Hispanic or Latino	50 - 59	176.530	...	C/C	*1/*
2	PA135312263	PA135312631	1	female	White	White	not Hispanic or Latino	not Hispanic or Latino	40 - 49	162.560	...	NaN	*1/*
3	PA135312264	PA135312632	1	male	White	White	not Hispanic or Latino	not Hispanic or Latino	60 - 69	182.245	...	NaN	*1/*
4	PA135312265	PA135312633	1	male	White	White	not Hispanic or Latino	not Hispanic or Latino	50 - 59	167.640	...	NaN	*1/*

5 rows × 68 columns

```
1 warfarin_data.columns
```

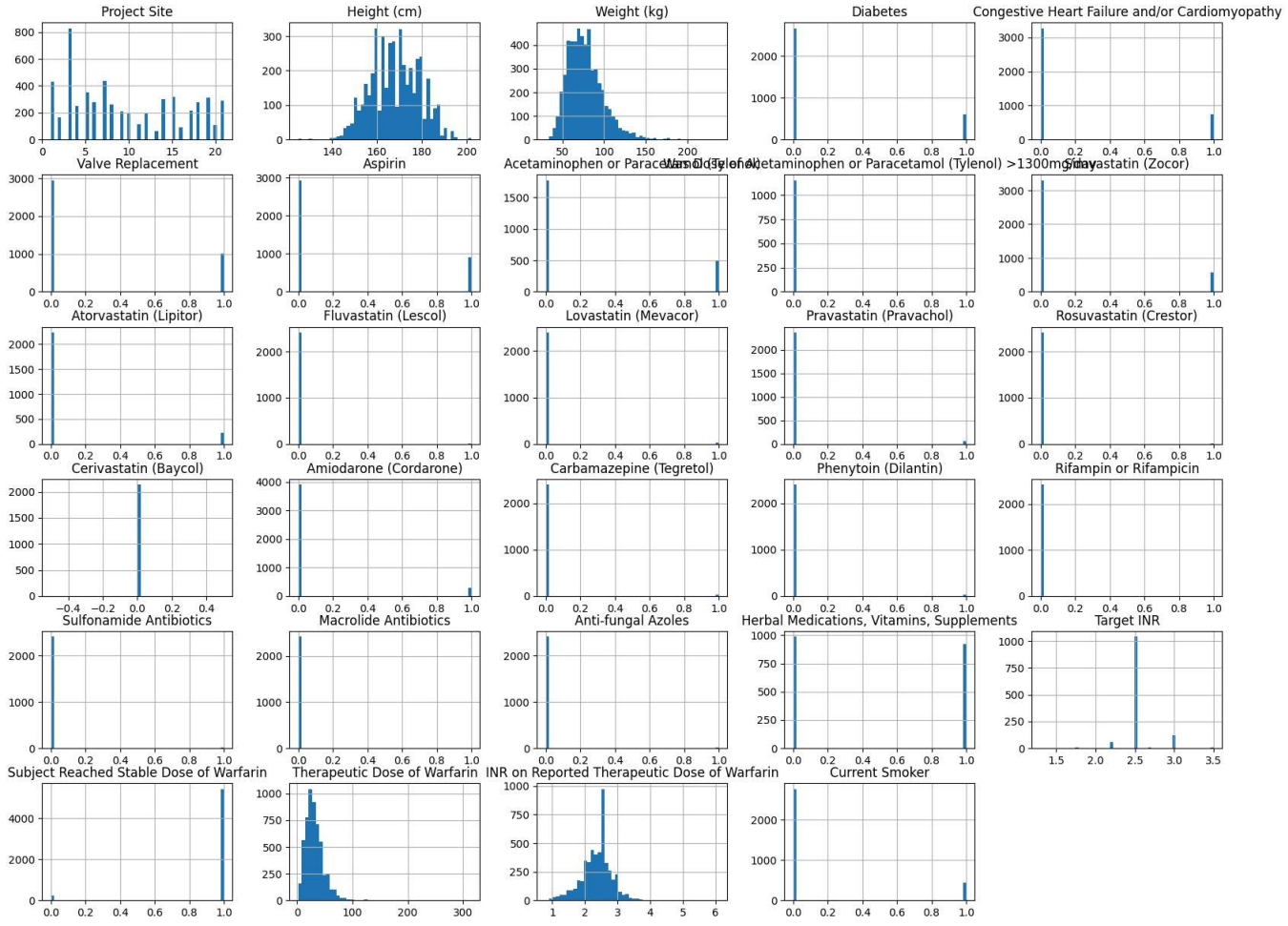
```
Index(['PharmGKB Subject ID', 'PharmGKB Sample ID', 'Project Site', 'Gender',
       'Race (Reported)', 'Race (OMB)', 'Ethnicity (Reported)',
       'Ethnicity (OMB)', 'Age', 'Height (cm)', 'Weight (kg)',
       'Indication for Warfarin Treatment', 'Comorbidities', 'Diabetes',
       'Congestive Heart Failure and/or Cardiomyopathy', 'Valve Replacement',
       'Medications', 'Aspirin', 'Acetaminophen or Paracetamol (Tylenol)',
       'Was Dose of Acetaminophen or Paracetamol (Tylenol) >1300mg/day',
       'Simvastatin (Zocor)', 'Atorvastatin (Lipitor)', 'Fluvastatin (Lescol)',
       'Lovastatin (Mevacor)', 'Pravastatin (Pravachol)',
       'Rosuvastatin (Crestor)', 'Cerivastatin (Baycol)',
       'Amiodarone (Cordarone)', 'Carbamazepine (Tegretol)',
       'Phenytoin (Dilantin)', 'Rifampin or Rifampicin',
       'Sulfonamide Antibiotics', 'Macrolide Antibiotics',
       'Anti-fungal Azoles', 'Herbal Medications, Vitamins, Supplements',
       'Target INR', 'Estimated Target INR Range Based on Indication',
       'Subject Reached Stable Dose of Warfarin',
       'Therapeutic Dose of Warfarin',
       'INR on Reported Therapeutic Dose of Warfarin', 'Current Smoker',
       'Cyp2C9 genotypes', 'Genotyped QC Cyp2C9*2', 'Genotyped QC Cyp2C9*3',
       'Combined QC CYP2C9',
       'VKORC1 genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T',
       'VKORC1 QC genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T',
       'VKORC1 genotype: 497T>G (5808); chr16:31013055; rs2884737; A/C',
       'VKORC1 QC genotype: 497T>G (5808); chr16:31013055; rs2884737; A/C',
       'VKORC1 genotype: 1173 C>T(6484); chr16:31012379; rs9934438; A/G',
       'VKORC1 QC genotype: 1173 C>T(6484); chr16:31012379; rs9934438; A/G',
       'VKORC1 genotype: 1542G>C (6853); chr16:31012010; rs8050894; C/G',
       'VKORC1 QC genotype: 1542G>C (6853); chr16:31012010; rs8050894; C/G',
       'VKORC1 genotype: 3730 G>A (9041); chr16:31009822; rs7294;  A/G',
       'VKORC1 QC genotype: 3730 G>A (9041); chr16:31009822; rs7294;  A/G',
       'VKORC1 genotype: 2255C>T (7566); chr16:31011297; rs2359612; A/G',
       'VKORC1 QC genotype: 2255C>T (7566); chr16:31011297; rs2359612; A/G',
       'VKORC1 genotype: -4451 C>A (861); Chr16:31018002; rs17880887; A/C',
       'VKORC1 QC genotype: -4451 C>A (861); Chr16:31018002; rs17880887; A/C',
       'CYP2C9 consensus', 'VKORC1 -1639 consensus', 'VKORC1 497 consensus',
       'VKORC1 1173 consensus', 'VKORC1 1542 consensus',
       'VKORC1 3730 consensus', 'VKORC1 2255 consensus',
       'VKORC1 -4451 consensus', 'Comments regarding Project Site Dataset'],
      dtype='object')
```

```
1 warfarin_data.describe()
```

	Project Site	Height (cm)	Weight (kg)	Diabetes	Congestive Heart Failure and/or Cardiomyopathy	Valve Replacement	Aspirin	Acetaminophen or Paracetamol (Tylenol)	Was Dose of Acetaminophen or Paracetamol (Tylenol) >1300mg/day	Sim
count	5700.000000	4554.000000	5413.000000	3283.000000	4012.000000	3958.000000	3840.000000	2274.000000	1159.000000	386
mean	9.555965	168.047778	77.852569	0.187024	0.183699	0.256443	0.238542	0.220317	0.006040	
std	6.340864	10.845992	21.859764	0.389990	0.387287	0.436724	0.426247	0.414551	0.077514	
min	1.000000	124.968000	30.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	
25%	4.000000	160.020000	62.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	
50%	8.000000	167.894000	75.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	
75%	15.000000	176.022000	90.000000	0.000000	0.000000	1.000000	0.000000	0.000000	0.000000	
max	21.000000	202.000000	237.700000	1.000000	1.000000	1.000000	1.000000	1.000000	1.000000	

8 rows × 29 columns

```
%matplotlib inline
import matplotlib.pyplot as plt
warfarin_data.hist(bins=50, figsize=(20,15))
plt.show()
```



```
np.random.seed(10)
```

```
# For illustration only. Sklearn has train_test_split()
def split_train_test(data, test_ratio):
    shuffled_indices = np.random.permutation(len(data))
    test_set_size = int(len(data) * test_ratio)
    test_indices = shuffled_indices[:test_set_size]
    train_indices = shuffled_indices[test_set_size:]
    return data.iloc[train_indices], data.iloc[test_indices]
```

```
# run the function to get the train & test set
train_set, test_set = split_train_test(warfarin_data, 0.2)
```

```
train_set.info()
```

```
 12  Comorbidities                                                    3028 non-null   object
 13  Diabetes                                                         2651 non-null   float64
 14  Congestive Heart Failure and/or Cardiomyopathy                   3218 non-null   float64
 15  Valve Replacement                                                3167 non-null   float64
 16  Medications                                                      3454 non-null   object
 17  Aspirin                                                          3094 non-null   float64
 18  Acetaminophen or Paracetamol (Tylenol)                           1826 non-null   float64
 19  Was Dose of Acetaminophen or Paracetamol (Tylenol) >1300mg/day   952 non-null    float64
 20  Simvastatin (Zocor)                                              3112 non-null   float64
 21  Atorvastatin (Lipitor)                                           1988 non-null   float64
 22  Fluvastatin (Lescol)                                             1957 non-null   float64
 23  Lovastatin (Mevacor)                                             1964 non-null   float64
 24  Pravastatin (Pravachol)                                          1965 non-null   float64
 25  Rosuvastatin (Crestor)                                           1957 non-null   float64
 26  Cerivastatin (Baycol)                                            1714 non-null   float64
 27  Amiodarone (Cordarone)                                           3359 non-null   float64
 28  Carbamazepine (Tegretol)                                         1963 non-null   float64
 29  Phenytoin (Dilantin)                                             1958 non-null   float64
 30  Rifampin or Rifampicin                                           1957 non-null   float64
 31  Sulfonamide Antibiotics                                          1955 non-null   float64
 32  Macrolide Antibiotics                                            1957 non-null   float64
 33  Anti-fungal Azoles                                               1960 non-null   float64
 34  Herbal Medications, Vitamins, Supplements                        1544 non-null   float64
 35  Target INR                                                       1005 non-null   float64
 36  Estimated Target INR Range Based on Indication                   3072 non-null   object
 37  Subject Reached Stable Dose of Warfarin                          4527 non-null   float64
 38  Therapeutic Dose of Warfarin                                     4425 non-null   float64
 39  INR on Reported Therapeutic Dose of Warfarin                     3971 non-null   float64
 40  Current Smoker                                                   2572 non-null   float64
 41  Cyp2C9 genotypes                                                 4449 non-null   object
 42  Genotyped QC Cyp2C9*2                                            388 non-null    object
 43  Genotyped QC Cyp2C9*3                                            388 non-null    object
 44  Combined QC CYP2C9                                               388 non-null    object
 45  VKORC1 genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T    3214 non-null   object
 46  VKORC1 QC genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T  388 non-null    object
 47  VKORC1 genotype: 497T>G (5808); chr16:31013055; rs2884737; A/C       1277 non-null   object
 48  VKORC1 QC genotype: 497T>G (5808); chr16:31013055; rs2884737; A/C    388 non-null    object
 49  VKORC1 genotype: 1173 C>T(6484); chr16:31012379; rs9934438; A/G      2687 non-null   object
 50  VKORC1 QC genotype: 1173 C>T(6484); chr16:31012379; rs9934438; A/G   388 non-null    object
 51  VKORC1 genotype: 1542G>C (6853); chr16:31012010; rs8050894; C/G      2661 non-null   object
 52  VKORC1 QC genotype: 1542G>C (6853); chr16:31012010; rs8050894; C/G   388 non-null    object
 53  VKORC1 genotype: 3730 G>A (9041); chr16:31009822; rs7294;  A/G       2476 non-null   object
 54  VKORC1 QC genotype: 3730 G>A (9041); chr16:31009822; rs7294;  A/G    388 non-null    object
 55  VKORC1 genotype: 2255C>T (7566); chr16:31011297; rs2359612; A/G      1755 non-null   object
 56  VKORC1 QC genotype: 2255C>T (7566); chr16:31011297; rs2359612; A/G   388 non-null    object
 57  VKORC1 genotype: -4451 C>A (861); Chr16:31018002; rs17880887; A/C    428 non-null    object
 58  VKORC1 QC genotype: -4451 C>A (861); Chr16:31018002; rs17880887; A/C  364 non-null    object
 59  CYP2C9 consensus                                                 4442 non-null   object
 60  VKORC1 -1639 consensus                                           3341 non-null   object
 61  VKORC1 497 consensus                                             1509 non-null   object
 62  VKORC1 1173 consensus                                            2873 non-null   object
 63  VKORC1 1542 consensus                                            2818 non-null   object
 64  VKORC1 3730 consensus                                            2661 non-null   object
 65  VKORC1 2255 consensus                                            2011 non-null   object
 66  VKORC1 -4451 consensus                                           727 non-null    object
 67  Comments regarding Project Site Dataset                          129 non-null    object
dtypes: float64(28), int64(1), object(39)
memory usage: 2.4+ MB
```

```
# After identifying the correct column names, let's define our features and target
# These need to be adjusted based on the actual column names from the dataset

# First check for the correct therapeutic dose column name
dose_columns = [col for col in warfarin_data.columns if 'dose' in col.lower() or 'therapeutic' in col.lower()]
print("Possible therapeutic dose columns:", dose_columns)

# Now check for other feature columns
demographic_columns = [col for col in warfarin_data.columns if any(term in col.lower() for term in ['gender', 'age', 'race', 'height
print("Demographic columns:", demographic_columns)

```

```
medication_columns = [col for col in warfarin_data.columns if any(term in col.lower() for term in ['diabetes', 'simvastatin', 'amio
print("Medication and genetic columns:", medication_columns)

# Now define the features and target correctly
# Adjust these based on actual column names
target_regression = [col for col in dose_columns if 'therapeutic' in col.lower()][0]
print(f"Target regression column: {target_regression}")

# List of features - adjust based on your actual column names
features = demographic_columns + medication_columns
print(f"Features: {features}")

# Now display data types and missing values with correct column names
print("\nData types:")
warfarin_data[features + [target_regression]].info()

print("\nMissing values:")
print(warfarin_data[features + [target_regression]].isnull().sum())

# Descriptive statistics
print("\nDescriptive statistics:")
warfarin_data[features + [target_regression]].describe()
```

```
Possible therapeutic dose columns: ['Was Dose of Acetaminophen or Paracetamol (Tylenol) >1300mg/day', 'Subject Reached Stable Dos
Demographic columns: ['Gender', 'Race (Reported)', 'Race (OMB)', 'Age', 'Height (cm)', 'Weight (kg)', 'Acetaminophen or Paracetam
Medication and genetic columns: ['Diabetes', 'Simvastatin (Zocor)', 'Amiodarone (Cordarone)', 'Target INR', 'Estimated Target INR
Target regression column: Therapeutic Dose of Warfarin
Features: ['Gender', 'Race (Reported)', 'Race (OMB)', 'Age', 'Height (cm)', 'Weight (kg)', 'Acetaminophen or Paracetamol (Tylenol

Data types:
<class 'pandas.core.frame.DataFrame'>
RangeIndex: 5700 entries, 0 to 5699
Data columns (total 41 columns):
 #   Column                                                      Non-Null Count  Dtype
---  ------                                                      --------------  -----
 0   Gender                                                      5696 non-null   object
 1   Race (Reported)                                             5194 non-null   object
 2   Race (OMB)                                                  5700 non-null   object
 3   Age                                                         5658 non-null   object
 4   Height (cm)                                                 4554 non-null   float64
 5   Weight (kg)                                                 5413 non-null   float64
 6   Acetaminophen or Paracetamol (Tylenol)                      2274 non-null   float64
 7   Was Dose of Acetaminophen or Paracetamol (Tylenol) >1300mg/day  1159 non-null   float64
 8   Diabetes                                                    3283 non-null   float64
 9   Simvastatin (Zocor)                                         3861 non-null   float64
 10  Amiodarone (Cordarone)                                      4182 non-null   float64
 11  Target INR                                                  1259 non-null   float64
 12  Estimated Target INR Range Based on Indication              3818 non-null   object
 13  INR on Reported Therapeutic Dose of Warfarin                4968 non-null   float64
 14  Cyp2C9 genotypes                                            5567 non-null   object
 15  Genotyped QC Cyp2C9*2                                       478 non-null    object
 16  Genotyped QC Cyp2C9*3                                       478 non-null    object
 17  Combined QC CYP2C9                                          478 non-null    object
 18  VKORC1 genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T     4046 non-null   object
 19  VKORC1 QC genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T  478 non-null    object
 20  VKORC1 genotype: 497T>G (5808); chr16:31013055; rs2884737; A/C        1599 non-null   object
 21  VKORC1 QC genotype: 497T>G (5808); chr16:31013055; rs2884737; A/C     478 non-null    object
 22  VKORC1 genotype: 1173 C>T(6484); chr16:31012379; rs9934438; A/G       3363 non-null   object
 23  VKORC1 QC genotype: 1173 C>T(6484); chr16:31012379; rs9934438; A/G    478 non-null    object
 24  VKORC1 genotype: 1542G>C (6853); chr16:31012010; rs8050894; C/G       3330 non-null   object
 25  VKORC1 QC genotype: 1542G>C (6853); chr16:31012010; rs8050894; C/G    478 non-null    object
 26  VKORC1 genotype: 3730 G>A (9041); chr16:31009822; rs7294;  A/G        3124 non-null   object
 27  VKORC1 QC genotype: 3730 G>A (9041); chr16:31009822; rs7294;  A/G     478 non-null    object
 28  VKORC1 genotype: 2255C>T (7566); chr16:31011297; rs2359612; A/G       2223 non-null   object
 29  VKORC1 QC genotype: 2255C>T (7566); chr16:31011297; rs2359612; A/G    478 non-null    object
 30  VKORC1 genotype: -4451 C>A (861); Chr16:31018002; rs17880887; A/C     540 non-null    object
 31  VKORC1 QC genotype: -4451 C>A (861); Chr16:31018002; rs17880887; A/C  451 non-null    object
 32  CYP2C9 consensus                                            5556 non-null   object
 33  VKORC1 -1639 consensus                                      4201 non-null   object
 34  VKORC1 497 consensus                                        1883 non-null   object
 35  VKORC1 1173 consensus                                       3591 non-null   object
 36  VKORC1 1542 consensus                                       3521 non-null   object
 37  VKORC1 3730 consensus                                       3344 non-null   object
 38  VKORC1 2255 consensus                                       2536 non-null   object
 39  VKORC1 -4451 consensus                                      912 non-null    object
 40  Therapeutic Dose of Warfarin                                5528 non-null   float64
dtypes: float64(10), object(31)
memory usage: 1.8+ MB

Missing values:
Gender                                                        4
Race (Reported)                                             506
Race (OMB)                                                    0
Age                                                          42
Height (cm)                                                1146
Weight (kg)                                                 287
Acetaminophen or Paracetamol (Tylenol)                     3426
Was Dose of Acetaminophen or Paracetamol (Tylenol) >1300mg/day  4541
Diabetes                                                   2417
Simvastatin (Zocor)                                        1839
Amiodarone (Cordarone)                                     1518
Target INR                                                 4441
Estimated Target INR Range Based on Indication             1882
INR on Reported Therapeutic Dose of Warfarin                732
Cyp2C9 genotypes                                            133
Genotyped QC Cyp2C9*2                                      5222
Genotyped QC Cyp2C9*3                                      5222
Combined QC CYP2C9                                         5222
VKORC1 genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T      1654
VKORC1 QC genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T   5222
VKORC1 genotype: 497T>G (5808); chr16:31013055; rs2884737; A/C         4101
VKORC1 QC genotype: 497T>G (5808); chr16:31013055; rs2884737; A/C      5222
VKORC1 genotype: 1173 C>T(6484); chr16:31012379; rs9934438; A/G        2337
VKORC1 QC genotype: 1173 C>T(6484); chr16:31012379; rs9934438; A/G     5222
VKORC1 genotype: 1542G>C (6853); chr16:31012010; rs8050894; C/G        2370
VKORC1 QC genotype: 1542G>C (6853); chr16:31012010; rs8050894; C/G     5222
VKORC1 genotype: 3730 G>A (9041); chr16:31009822; rs7294;  A/G         2576
VKORC1 QC genotype: 3730 G>A (9041); chr16:31009822; rs7294;  A/G      5222
VKORC1 genotype: 2255C>T (7566); chr16:31011297; rs2359612; A/G        3477
VKORC1 QC genotype: 2255C>T (7566); chr16:31011297; rs2359612; A/G     5222
VKORC1 genotype: -4451 C>A (861); Chr16:31018002; rs17880887; A/C      5160
VKORC1 QC genotype: -4451 C>A (861); Chr16:31018002; rs17880887; A/C   5249
CYP2C9 consensus                                             144
```

```
VKORC1 -1639 consensus                                  1499
VKORC1 497 consensus                                    3817
VKORC1 1173 consensus                                   2109
VKORC1 1542 consensus                                   2179
VKORC1 3730 consensus                                   2356
VKORC1 2255 consensus                                   3164
VKORC1 -4451 consensus                                  4788
Therapeutic Dose of Warfarin                             172
dtype: int64

Descriptive statistics:
```

	Height (cm)	Weight (kg)	Acetaminophen or Paracetamol (Tylenol)	Was Dose of Acetaminophen or Paracetamol (Tylenol) >1300mg/day	Diabetes	Simvastatin (Zocor)	Amiodarone (Cordarone)	Target INR	INR on Reported Therapeutic Dose of Warfarin	The
count	4554.000000	5413.000000	2274.000000	1159.000000	3283.000000	3861.000000	4182.000000	1259.000000	4968.000000	552
mean	168.047778	77.852569	0.220317	0.006040	0.187024	0.146335	0.066236	2.538324	2.364438	3
std	10.845992	21.859764	0.414551	0.077514	0.389990	0.353488	0.248724	0.198140	0.464644	1
min	124.968000	30.000000	0.000000	0.000000	0.000000	0.000000	0.000000	1.300000	0.800000	
25%	160.020000	62.000000	0.000000	0.000000	0.000000	0.000000	0.000000	2.500000	2.100000	1
50%	167.894000	75.000000	0.000000	0.000000	0.000000	0.000000	0.000000	2.500000	2.400000	2
75%	176.022000	90.000000	0.000000	0.000000	0.000000	0.000000	0.000000	2.500000	2.610000	3
max	202.000000	237.700000	1.000000	1.000000	1.000000	1.000000	1.000000	3.500000	6.100000	31

```python
# Step 3: Data Preprocessing

# 3.1 Handle Missing Values
print("\n--- Handling Missing Values ---")

# First, replace any non-standard missing values with NaN
warfarin_data.replace(['NA', 'N/A', '-99', -99], np.nan, inplace=True)

# Check updated missing values count
print("Missing values after standardization:")
print(warfarin_data[features + [target_regression]].isnull().sum())

# 3.2 Impute missing values
# For numeric features
numeric_features = warfarin_data[features].select_dtypes(include=['int64', 'float64']).columns
for col in numeric_features:
    median_value = warfarin_data[col].median()
    warfarin_data[col].fillna(median_value, inplace=True)
    print(f"Imputed {col} with median: {median_value}")

# For categorical features
categorical_features = warfarin_data[features].select_dtypes(include=['object']).columns
for col in categorical_features:
    mode_value = warfarin_data[col].mode()[0]
    warfarin_data[col].fillna(mode_value, inplace=True)
    print(f"Imputed {col} with mode: {mode_value}")

# 3.3 Create binary classification target
# Following the project description, create HRD (>30 mg/wk) and LRD (≤30 mg/wk) classes
print("\n--- Creating Classification Target ---")
dose_threshold = 30  # mg/wk
warfarin_data['dose_class'] = (warfarin_data[target_regression] > dose_threshold).astype(int)
warfarin_data['dose_class'] = warfarin_data['dose_class'].map({1: 'HRD', 0: 'LRD'})
print(f"Dose class distribution: {warfarin_data['dose_class'].value_counts()}")

# 3.4 Check for outliers in numeric features
print("\n--- Checking for Outliers ---")
for col in numeric_features:
    q1 = warfarin_data[col].quantile(0.25)
    q3 = warfarin_data[col].quantile(0.75)
    iqr = q3 - q1
    lower_bound = q1 - 1.5 * iqr
    upper_bound = q3 + 1.5 * iqr
    outliers = warfarin_data[(warfarin_data[col] < lower_bound) | (warfarin_data[col] > upper_bound)][col]
    if not outliers.empty:
```

```
        print(f"Outliers in {col}: {len(outliers)} values")
        # You can decide whether to cap outliers, remove them, or keep them based on domain knowledge
```

```
dtype: int64
Imputed Height (cm) with median: 167.89399999981867
Imputed Weight (kg) with median: 75.0
Imputed Acetaminophen or Paracetamol (Tylenol) with median: 0.0
Imputed Was Dose of Acetaminophen or Paracetamol (Tylenol) >1300mg/day with median: 0.0
Imputed Diabetes with median: 0.0
Imputed Simvastatin (Zocor) with median: 0.0
Imputed Amiodarone (Cordarone) with median: 0.0
Imputed Target INR with median: 2.5
Imputed INR on Reported Therapeutic Dose of Warfarin with median: 2.4
Imputed Gender with mode: male
Imputed Race (Reported) with mode: White
Imputed Race (OMB) with mode: White
Imputed Age with mode: 70 - 79
Imputed Estimated Target INR Range Based on Indication with mode: 2-3
Imputed Cyp2C9 genotypes with mode: *1/*1
Imputed Genotyped QC Cyp2C9*2 with mode: *1/*1
Imputed Genotyped QC Cyp2C9*3 with mode: *1/*1
Imputed Combined QC CYP2C9 with mode: *1/*1
Imputed VKORC1 genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T with mode: A/A
Imputed VKORC1 QC genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T with mode: G/G
Imputed VKORC1 genotype: 497T>G (5808); chr16:31013055; rs2884737; A/C with mode: T/T
Imputed VKORC1 QC genotype: 497T>G (5808); chr16:31013055; rs2884737; A/C with mode: T/T
Imputed VKORC1 genotype: 1173 C>T(6484); chr16:31012379; rs9934438; A/G with mode: T/T
Imputed VKORC1 QC genotype: 1173 C>T(6484); chr16:31012379; rs9934438; A/G with mode: C/C
Imputed VKORC1 genotype: 1542G>C (6853); chr16:31012010; rs8050894; C/G with mode: C/C
Imputed VKORC1 QC genotype: 1542G>C (6853); chr16:31012010; rs8050894; C/G with mode: C/G
Imputed VKORC1 genotype: 3730 G>A (9041); chr16:31009822; rs7294;  A/G with mode: G/G
Imputed VKORC1 QC genotype: 3730 G>A (9041); chr16:31009822; rs7294;  A/G with mode: G/G
Imputed VKORC1 genotype: 2255C>T (7566); chr16:31011297; rs2359612; A/G with mode: T/T
Imputed VKORC1 QC genotype: 2255C>T (7566); chr16:31011297; rs2359612; A/G with mode: C/C
Imputed VKORC1 genotype: -4451 C>A (861); Chr16:31018002; rs17880887; A/C with mode: C/C
Imputed VKORC1 QC genotype: -4451 C>A (861); Chr16:31018002; rs17880887; A/C with mode: C/C
Imputed CYP2C9 consensus with mode: *1/*1
Imputed VKORC1 -1639 consensus with mode: A/A
Imputed VKORC1 497 consensus with mode: T/T
Imputed VKORC1 1173 consensus with mode: T/T
Imputed VKORC1 1542 consensus with mode: C/C
Imputed VKORC1 3730 consensus with mode: G/G
Imputed VKORC1 2255 consensus with mode: T/T
Imputed VKORC1 -4451 consensus with mode: C/C

--- Creating Classification Target ---
Dose class distribution: dose_class
LRD    3296
HRD    2404
Name: count, dtype: int64

--- Checking for Outliers ---
Outliers in Height (cm): 69 values
Outliers in Weight (kg): 153 values
Outliers in Acetaminophen or Paracetamol (Tylenol): 501 values
Outliers in Was Dose of Acetaminophen or Paracetamol (Tylenol) >1300mg/day: 7 values
Outliers in Diabetes: 614 values
Outliers in Simvastatin (Zocor): 565 values
Outliers in Amiodarone (Cordarone): 277 values
Outliers in Target INR: 219 values
Outliers in INR on Reported Therapeutic Dose of Warfarin: 363 values
```

```
# Step 4: Data Visualization and Exploratory Analysis

# 4.1 Visualize the distribution of the target variable
plt.figure(figsize=(10, 6))
plt.hist(warfarin_data[target_regression], bins=30, color='skyblue', edgecolor='black')
plt.title('Distribution of Therapeutic Dose of Warfarin')
plt.xlabel('Dose (mg/week)')
plt.ylabel('Frequency')
plt.grid(True, alpha=0.3)
plt.savefig('dose_distribution.png')
plt.close()

# 4.2 Visualize the relationship between key features and the target
# Select a few important numeric features
key_numeric_features = numeric_features[:4]  # Adjust based on your data

plt.figure(figsize=(15, 10))
for i, feature in enumerate(key_numeric_features):
    plt.subplot(2, 2, i+1)
    plt.scatter(warfarin_data[feature], warfarin_data[target_regression], alpha=0.5)
    plt.title(f'{feature} vs Therapeutic Dose')
    plt.xlabel(feature)
    plt.ylabel('Therapeutic Dose (mg/week)')
    plt.grid(True, alpha=0.3)
plt.tight_layout()
```

```
plt.savefig('feature_vs_dose.png')
plt.close()

# 4.3 Visualize the class distribution
plt.figure(figsize=(8, 6))
warfarin_data['dose_class'].value_counts().plot(kind='bar', color=['skyblue', 'salmon'])
plt.title('Distribution of Dose Classes')
plt.xlabel('Dose Class')
plt.ylabel('Count')
plt.xticks(rotation=0)
plt.grid(True, alpha=0.3, axis='y')
plt.savefig('dose_class_distribution.png')
plt.close()

# 4.4 Correlation heatmap for numeric features
corr_matrix = warfarin_data[list(numeric_features) + [target_regression]].corr()
plt.figure(figsize=(12, 10))
sns.heatmap(corr_matrix, annot=True, cmap='coolwarm', fmt='.2f', linewidths=0.5)
plt.title('Correlation Matrix')
plt.tight_layout()
plt.savefig('correlation_heatmap.png')
plt.close()

print("Visualizations have been saved as PNG files.")
```

```
Visualizations have been saved as PNG files.
```

```
# 1. Start with cleaned features and proper target
X_filtered = warfarin_data.drop(columns=[target_regression, 'dose_class'] +
                                [col for col in warfarin_data.columns if
                                 'dose' in col.lower() or
                                 'therapeutic' in col.lower() or
                                 'warfarin' in col.lower() or
                                 'inr' in col.lower()])

# Keep only demographics and genetic features as mentioned in the project description
valid_features = ['Gender', 'Race (Reported)', 'Age', 'Height (cm)', 'Weight (kg)',
                  'Diabetes', 'Simvastatin (Zocor)', 'Amiodarone (Cordarone)',
                  'Cyp2C9 genotypes', 'VKORC1 genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T']

X_filtered = X_filtered[[col for col in X_filtered.columns if any(feat in col for feat in valid_features)]]

# 2. Handle missing values and preprocess
numeric_features = X_filtered.select_dtypes(include=['int64', 'float64']).columns.tolist()
categorical_features = X_filtered.select_dtypes(include=['object', 'category']).columns.tolist()

# Process numeric features
numeric_imputer = SimpleImputer(strategy='median')
X_numeric = X_filtered[numeric_features].copy() if numeric_features else pd.DataFrame()
if not X_numeric.empty:
    X_numeric_imputed = pd.DataFrame(
        numeric_imputer.fit_transform(X_numeric),
        columns=numeric_features,
        index=X_numeric.index
    )

# Process categorical features
if categorical_features:
    cat_imputer = SimpleImputer(strategy='most_frequent')
    X_cat = X_filtered[categorical_features].copy()
    X_cat_imputed = pd.DataFrame(
        cat_imputer.fit_transform(X_cat),
        columns=categorical_features,
        index=X_cat.index
    )

    # One-hot encode categorical features
    X_cat_encoded = pd.get_dummies(X_cat_imputed, drop_first=True)

    # Combine numeric and categorical features
    X_processed = pd.concat([X_numeric_imputed, X_cat_encoded], axis=1) if not X_numeric.empty else X_cat_encoded
else:
    X_processed = X_numeric_imputed

# 3. Define target variables
y_reg = warfarin_data[target_regression].copy()
y_cls = (y_reg > 30).astype(int)  # Binary classification (>30 mg/wk = high dose)

# 4. Split data
X_train_reg, X_test_reg, y_train_reg, y_test_reg = train_test_split(
    X_processed, y_reg, test_size=0.2, random_state=42)

```

```
X_train_cls, X_test_cls, y_train_cls, y_test_cls = train_test_split(
    X_processed, y_cls, test_size=0.2, random_state=42)
```

```
# Step 6: Split Data for Modeling

# 6.1 Prepare data for both regression and classification tasks using processed data
print("\n--- Splitting Data for Modeling ---")

# Define the regression target (Update this column name if needed)
# You can also use: warfarin_data.columns to confirm the exact name
y_reg_imputed = warfarin_data['Therapeutic Dose of Warfarin']  # <-- Replace with actual column if different

# For regression task
X_train_reg, X_test_reg, y_train_reg, y_test_reg = train_test_split(
    X_processed, y_reg_imputed, test_size=0.2, random_state=42
)

# For classification task - create the binary target first
dose_threshold = 30  # mg/week
y_cls = (y_reg_imputed > dose_threshold).astype(int)
print(f"Dose class distribution: {y_cls.value_counts()}")

# Split for classification
X_train_cls, X_test_cls, y_train_cls, y_test_cls = train_test_split(
    X_processed, y_cls, test_size=0.2, random_state=42
)

# Print shapes
print(f"Training set size: {X_train_reg.shape[0]} samples")
print(f"Testing set size: {X_test_reg.shape[0]} samples")
print(f"Number of features: {X_train_reg.shape[1]}")

```

```
--- Splitting Data for Modeling ---
Dose class distribution: Therapeutic Dose of Warfarin
0    3296
1    2404
Name: count, dtype: int64
Training set size: 4560 samples
Testing set size: 1140 samples
Number of features: 47
```

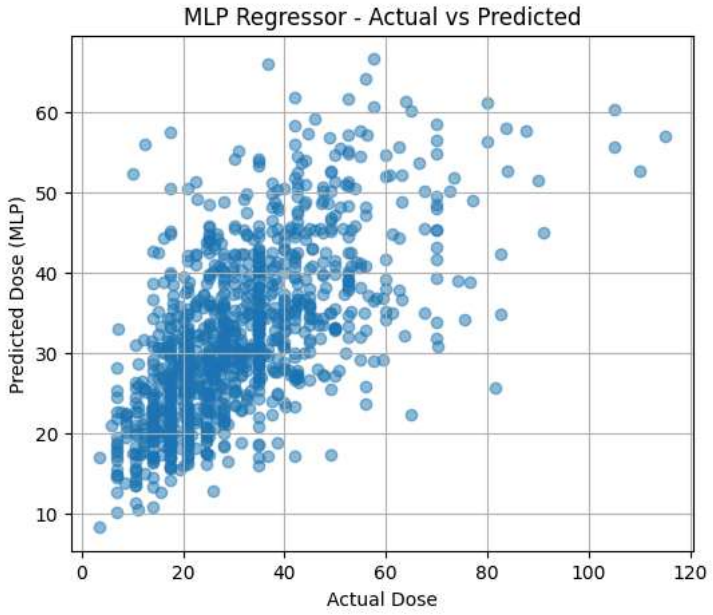
```
# Clean target variable before modeling
y_reg_imputed = warfarin_data['Therapeutic Dose of Warfarin']  # Replace with actual column if different
non_nan_mask = y_reg_imputed.notna()

# Filter both features and target
X_clean = X_processed[non_nan_mask]
y_clean = y_reg_imputed[non_nan_mask]

# Train-test split
from sklearn.model_selection import train_test_split
X_train_reg, X_test_reg, y_train_reg, y_test_reg = train_test_split(
    X_clean, y_clean, test_size=0.2, random_state=42
)


# Step 7: Build and Evaluate Regression Models

from sklearn.linear_model import LinearRegression, Ridge, Lasso
from sklearn.ensemble import RandomForestRegressor, GradientBoostingRegressor
from sklearn.svm import SVR
from sklearn.tree import DecisionTreeRegressor
from sklearn.metrics import mean_squared_error, mean_absolute_error, r2_score
from sklearn.model_selection import cross_val_score
import matplotlib.pyplot as plt
import numpy as np

print("\n--- Building Regression Models ---")

# 7.1 Define the regression models
regression_models = {
    'Linear Regression': LinearRegression(),
    'Ridge Regression': Ridge(alpha=1.0),
    'Lasso Regression': Lasso(alpha=0.1),
    'Decision Tree': DecisionTreeRegressor(random_state=42),
    'Random Forest': RandomForestRegressor(n_estimators=100, random_state=42),
    'Gradient Boosting': GradientBoostingRegressor(n_estimators=100, random_state=42),
    'SVR': SVR(kernel='rbf')
}

```

```python
# 7.2 Train and evaluate each model
results_reg = {}
best_model_reg = None
best_score_reg = float('inf')  # Lower RMSE is better

for name, model in regression_models.items():
    print(f"\nTraining {name}...")

    # Train the model
    model.fit(X_train_reg, y_train_reg)

    # Make predictions
    y_pred_train = model.predict(X_train_reg)
    y_pred_test = model.predict(X_test_reg)

    # Calculate metrics
    train_mse = mean_squared_error(y_train_reg, y_pred_train)
    test_mse = mean_squared_error(y_test_reg, y_pred_test)
    train_rmse = np.sqrt(train_mse)
    test_rmse = np.sqrt(test_mse)
    train_mae = mean_absolute_error(y_train_reg, y_pred_train)
    test_mae = mean_absolute_error(y_test_reg, y_pred_test)
    train_r2 = r2_score(y_train_reg, y_pred_train)
    test_r2 = r2_score(y_test_reg, y_pred_test)

    # Cross-validation score
    cv_scores = cross_val_score(model, X_train_reg, y_train_reg, cv=5, scoring='neg_mean_squared_error')
    cv_rmse = np.sqrt(-np.mean(cv_scores))

    # Store results
    results_reg[name] = {
        'Train MSE': train_mse,
        'Test MSE': test_mse,
        'Train RMSE': train_rmse,
        'Test RMSE': test_rmse,
        'Train MAE': train_mae,
        'Test MAE': test_mae,
        'Train R²': train_r2,
        'Test R²': test_r2,
        'CV RMSE': cv_rmse,
        'model': model
    }

    # Print results
    print(f"Results for {name}:")
    for metric, value in results_reg[name].items():
        if metric != 'model':
            print(f"  {metric}: {value:.4f}")

    # Track best model
    if test_rmse < best_score_reg:
        best_score_reg = test_rmse
        best_model_reg = model
        best_model_name_reg = name

print(f"\nBest regression model: {best_model_name_reg}")
print(f"Best RMSE: {best_score_reg:.4f}")

# Step 7.8: MLP Regressor (Deep Learning)
from sklearn.neural_network import MLPRegressor
from sklearn.metrics import mean_squared_error, mean_absolute_error, r2_score
import matplotlib.pyplot as plt
import numpy as np

print("\n--- Training MLP Regressor (Deep Learning) ---")

# Define the model
mlp_model = MLPRegressor(
    hidden_layer_sizes=(100, 50),
    activation='relu',
    solver='adam',
    max_iter=1000,
    random_state=42
)

# Fit the model
mlp_model.fit(X_train_reg, y_train_reg)

# Predictions
y_pred_train_mlp = mlp_model.predict(X_train_reg)
y_pred_test_mlp = mlp_model.predict(X_test_reg)

```

```
# Evaluation metrics
train_mse_mlp = mean_squared_error(y_train_reg, y_pred_train_mlp)
test_mse_mlp = mean_squared_error(y_test_reg, y_pred_test_mlp)
train_rmse_mlp = np.sqrt(train_mse_mlp)
test_rmse_mlp = np.sqrt(test_mse_mlp)
train_mae_mlp = mean_absolute_error(y_train_reg, y_pred_train_mlp)
test_mae_mlp = mean_absolute_error(y_test_reg, y_pred_test_mlp)
train_r2_mlp = r2_score(y_train_reg, y_pred_train_mlp)
test_r2_mlp = r2_score(y_test_reg, y_pred_test_mlp)

# Print results
print("MLP Regressor Results:")
print(f"  Train RMSE: {train_rmse_mlp:.4f}")
print(f"  Test RMSE: {test_rmse_mlp:.4f}")
print(f"  Train MAE: {train_mae_mlp:.4f}")
print(f"  Test MAE: {test_mae_mlp:.4f}")
print(f"  Train R²: {train_r2_mlp:.4f}")
print(f"  Test R²: {test_r2_mlp:.4f}")

# Plot predicted vs actual for test set
plt.figure(figsize=(6, 5))
plt.scatter(y_test_reg, y_pred_test_mlp, alpha=0.5)
plt.xlabel("Actual Dose")
plt.ylabel("Predicted Dose (MLP)")
plt.title("MLP Regressor - Actual vs Predicted")
plt.grid(True)
plt.show()
```

```
--- Building Regression Models ---

Training Linear Regression...
Results for Linear Regression:
  Train MSE: 181.9974
  Test MSE: 145.7731
  Train RMSE: 13.4906
  Test RMSE: 12.0737
  Train MAE: 9.2498
  Test MAE: 8.8517
  Train R²: 0.3759
  Test R²: 0.4043
  CV RMSE: 13.6324

Training Ridge Regression...
Results for Ridge Regression:
  Train MSE: 182.1058
  Test MSE: 146.0475
  Train RMSE: 13.4947
  Test RMSE: 12.0850
  Train MAE: 9.2565
  Test MAE: 8.8588
  Train R²: 0.3755
  Test R²: 0.4031
  CV RMSE: 13.6244

Training Lasso Regression...
Results for Lasso Regression:
  Train MSE: 191.7559
  Test MSE: 154.8631
  Train RMSE: 13.8476
  Test RMSE: 12.4444
  Train MAE: 9.5593
  Test MAE: 9.1486
  Train R²: 0.3424
  Test R²: 0.3671
  CV RMSE: 13.9295

Training Decision Tree...
Results for Decision Tree:
  Train MSE: 2.9176
  Test MSE: 421.7495
  Train RMSE: 1.7081
  Test RMSE: 20.5365
  Train MAE: 0.2692
  Test MAE: 13.7100
  Train R²: 0.9900
  Test R²: -0.7236
  CV RMSE: 19.4312

Training Random Forest...
Results for Random Forest:
  Train MSE: 31.0276
  Test MSE: 193.8273
  Train RMSE: 5.5702
  Test RMSE: 13.9222
  Train MAE: 3.8813
  Test MAE: 10.0460
  Train R²: 0.8936
  Test R²: 0.2079
  CV RMSE: 14.7079

Training Gradient Boosting...
Results for Gradient Boosting:
  Train MSE: 158.7664
  Test MSE: 153.9739
  Train RMSE: 12.6003
  Test RMSE: 12.4086
  Train MAE: 8.9534
  Test MAE: 9.0369
  Train R²: 0.4555
  Test R²: 0.3707
  CV RMSE: 13.9424

Training SVR...
Results for SVR:
  Train MSE: 254.4010
  Test MSE: 209.2221
  Train RMSE: 15.9500
  Test RMSE: 14.4645
  Train MAE: 11.0463
  Test MAE: 10.7077
  Train R²: 0.1276
  Test R²: 0.1449
  CV RMSE: 15.9813

Best regression model: Linear Regression
Best RMSE: 12.0737
```

```
--- Training MLP Regressor (Deep Learning) ---
MLP Regressor Results:
  Train RMSE: 13.4102
  Test RMSE: 12.1261
  Train MAE: 9.3065
  Test MAE: 9.0232
  Train R²: 0.3833
  Test R²: 0.3991
```




```python
# Step 8: Build and Evaluate Classification Models

from sklearn.linear_model import LogisticRegression
from sklearn.ensemble import RandomForestClassifier, GradientBoostingClassifier
from sklearn.svm import SVC
from sklearn.tree import DecisionTreeClassifier
from sklearn.metrics import accuracy_score, precision_score, recall_score, f1_score, roc_auc_score, confusion_matrix

# 8.1 Define the classification models
print("\n--- Building Classification Models ---")
classification_models = {
    'Logistic Regression': LogisticRegression(random_state=42, max_iter=1000),
    'Decision Tree': DecisionTreeClassifier(random_state=42),
    'Random Forest': RandomForestClassifier(n_estimators=100, random_state=42),
    'Gradient Boosting': GradientBoostingClassifier(n_estimators=100, random_state=42),
    'SVC': SVC(probability=True, random_state=42)
}

# 8.2 Train and evaluate each model
results_cls = {}
best_model_cls = None
best_score_cls = 0  # Higher accuracy is better

for name, model in classification_models.items():
    print(f"\nTraining {name}...")

    # Train the model
    model.fit(X_train_cls, y_train_cls)

    # Make predictions
    y_pred_train = model.predict(X_train_cls)
    y_pred_test = model.predict(X_test_cls)

    # Calculate metrics
    train_acc = accuracy_score(y_train_cls, y_pred_train)
    test_acc = accuracy_score(y_test_cls, y_pred_test)
    test_precision = precision_score(y_test_cls, y_pred_test, average='weighted')
    test_recall = recall_score(y_test_cls, y_pred_test, average='weighted')
    test_f1 = f1_score(y_test_cls, y_pred_test, average='weighted')

    # ROC AUC for binary classification
    if hasattr(model, 'predict_proba'):
        y_pred_proba = model.predict_proba(X_test_cls)[:, 1]
        test_roc_auc = roc_auc_score(y_test_cls, y_pred_proba)
```

```
    else:
        test_roc_auc = None

    # Cross-validation score
    cv_scores = cross_val_score(model, X_train_cls, y_train_cls, cv=5, scoring='accuracy')
    cv_acc = np.mean(cv_scores)

    # Store results
    results_cls[name] = {
        'Train Accuracy': train_acc,
        'Test Accuracy': test_acc,
        'Test Precision': test_precision,
        'Test Recall': test_recall,
        'Test F1': test_f1,
        'Test ROC AUC': test_roc_auc,
        'CV Accuracy': cv_acc,
        'model': model  # Store the model object
    }

    # Print results
    print(f"Results for {name}:")
    for metric, value in results_cls[name].items():
        if value is not None and metric != 'model':
            print(f"  {metric}: {value:.4f}")
        elif metric != 'model':
            print(f"  {metric}: N/A")

    # Confusion matrix
    cm = confusion_matrix(y_test_cls, y_pred_test)
    print(f"Confusion Matrix:\n{cm}")

    # Check if this is the best model
    if test_acc > best_score_cls:
        best_score_cls = test_acc
        best_model_cls = model
        best_model_name_cls = name

print(f"\nBest classification model: {best_model_name_cls}")
print(f"Best accuracy: {best_score_cls:.4f}")

# 8.3 Visualize model performance comparison
model_names = list(results_cls.keys())
test_acc_values = [results_cls[name]['Test Accuracy'] for name in model_names]
test_f1_values = [results_cls[name]['Test F1'] for name in model_names]

plt.figure(figsize=(12, 10))

# Plot Accuracy
plt.subplot(2, 1, 1)
bars = plt.bar(model_names, test_acc_values, color='lightgreen')
plt.title('Test Accuracy by Model (Higher is Better)')
plt.ylabel('Accuracy')
plt.xticks(rotation=45)
plt.grid(axis='y', alpha=0.3)
for bar in bars:
    plt.text(bar.get_x() + bar.get_width()/2, bar.get_height() + 0.02,
             f'{bar.get_height():.2f}', ha='center')

# Plot F1 Score
plt.subplot(2, 1, 2)
bars = plt.bar(model_names, test_f1_values, color='lightblue')
plt.title('Test F1 Score by Model (Higher is Better)')
plt.ylabel('F1 Score')
plt.xticks(rotation=45)
plt.grid(axis='y', alpha=0.3)
for bar in bars:
    plt.text(bar.get_x() + bar.get_width()/2, bar.get_height() + 0.02,
             f'{bar.get_height():.2f}', ha='center')

plt.tight_layout()
plt.savefig('classification_model_comparison.png')
plt.close()
print("Classification model comparison plot saved as 'classification_model_comparison.png'")
```

Test F1: 0.6410

```
  Test F1: 0.6410
  Test ROC AUC: 0.6311
  CV Accuracy: 0.6397
Confusion Matrix:
[[440 213]
 [197 290]]

Training Random Forest...
Results for Random Forest:
  Train Accuracy: 0.9917
  Test Accuracy: 0.6982
  Test Precision: 0.6982
  Test Recall: 0.6982
  Test F1: 0.6982
  Test ROC AUC: 0.7592
  CV Accuracy: 0.6928
Confusion Matrix:
[[481 172]
 [172 315]]

Training Gradient Boosting...
Results for Gradient Boosting:
  Train Accuracy: 0.7520
  Test Accuracy: 0.7360
  Test Precision: 0.7344
  Test Recall: 0.7360
  Test F1: 0.7332
  Test ROC AUC: 0.8087
  CV Accuracy: 0.7274
Confusion Matrix:
[[532 121]
 [180 307]]

Training SVC...
Results for SVC:
  Train Accuracy: 0.6520
  Test Accuracy: 0.6561
  Test Precision: 0.6684
  Test Recall: 0.6561
  Test F1: 0.6244
  Test ROC AUC: 0.7032
  CV Accuracy: 0.6542
Confusion Matrix:
[[582  71]
 [321 166]]

Best classification model: Logistic Regression
Best accuracy: 0.7412
Classification model comparison plot saved as 'classification_model_comparison.png'
```

```python
# Step 9: Hyperparameter Tuning for Best Models

from sklearn.model_selection import GridSearchCV

# 9.1 Tune the best regression model
print("\n--- Hyperparameter Tuning for Regression Model ---")
print(f"Tuning {best_model_name_reg}...")

# Define parameter grid based on the best model type
if best_model_name_reg == 'Random Forest':
    param_grid = {
        'n_estimators': [50, 100, 200],
        'max_depth': [None, 10, 20, 30],
        'min_samples_split': [2, 5, 10],
        'min_samples_leaf': [1, 2, 4]
    }
elif best_model_name_reg == 'Gradient Boosting':
    param_grid = {
        'n_estimators': [50, 100, 200],
        'learning_rate': [0.01, 0.1, 0.2],
        'max_depth': [3, 5, 7],
        'min_samples_split': [2, 5]
    }
elif best_model_name_reg in ['Ridge Regression', 'Lasso Regression']:
    param_grid = {
        'alpha': [0.001, 0.01, 0.1, 1.0, 10.0, 100.0]
    }
elif best_model_name_reg == 'SVR':
    param_grid = {
        'C': [0.1, 1, 10, 100],
        'gamma': ['scale', 'auto', 0.01, 0.1],
        'kernel': ['linear', 'rbf']
    }
else:
    param_grid = {}  # Empty grid for models without tunable hyperparameters

# Only run grid search if there are parameters to tune
```

```
if param_grid:
    grid_search = GridSearchCV(best_model_reg, param_grid, cv=5,
                               scoring='neg_mean_squared_error', n_jobs=-1)
    grid_search.fit(X_train_reg, y_train_reg)

    print(f"Best parameters: {grid_search.best_params_}")
    print(f"Best CV score: {np.sqrt(-grid_search.best_score_):.4f} RMSE")

    # Update the best model
    best_model_reg_tuned = grid_search.best_estimator_

    # Evaluate the tuned model
    y_pred_test_tuned = best_model_reg_tuned.predict(X_test_reg)
    test_rmse_tuned = np.sqrt(mean_squared_error(y_test_reg, y_pred_test_tuned))
    test_r2_tuned = r2_score(y_test_reg, y_pred_test_tuned)

    print(f"Tuned model performance:")
    print(f"  Test RMSE: {test_rmse_tuned:.4f}")
    print(f"  Test R²: {test_r2_tuned:.4f}")

    # Compare with the untuned model
    print(f"Improvement over untuned model:")
    print(f"  RMSE improvement: {best_score_reg - test_rmse_tuned:.4f}")
    print(f"  R² improvement: {test_r2_tuned - results_reg[best_model_name_reg]['Test R²']:.4f}")

    # Update the best model
    best_model_reg = best_model_reg_tuned
    best_score_reg = test_rmse_tuned
else:
    print(f"No hyperparameter tuning needed for {best_model_name_reg}")

# 9.2 Tune the best classification model
print("\n--- Hyperparameter Tuning for Classification Model ---")
print(f"Tuning {best_model_name_cls}...")

# Define parameter grid based on the best model type
if best_model_name_cls == 'Random Forest':
    param_grid = {
        'n_estimators': [50, 100, 200],
        'max_depth': [None, 10, 20, 30],
        'min_samples_split': [2, 5, 10],
        'min_samples_leaf': [1, 2, 4]
    }
elif best_model_name_cls == 'Gradient Boosting':
    param_grid = {
        'n_estimators': [50, 100, 200],
        'learning_rate': [0.01, 0.1, 0.2],
        'max_depth': [3, 5, 7],
        'min_samples_split': [2, 5]
    }
elif best_model_name_cls == 'Logistic Regression':
    param_grid = {
        'C': [0.001, 0.01, 0.1, 1, 10, 100],
        'penalty': ['l2'],
        'solver': ['lbfgs', 'liblinear']
    }
elif best_model_name_cls == 'SVC':
    param_grid = {
        'C': [0.1, 1, 10, 100],
        'gamma': ['scale', 'auto', 0.01, 0.1],
        'kernel': ['linear', 'rbf']
    }
else:
    param_grid = {}

# Only run grid search if there are parameters to tune
if param_grid:
    grid_search = GridSearchCV(best_model_cls, param_grid, cv=5,
                               scoring='accuracy', n_jobs=-1)
    grid_search.fit(X_train_cls, y_train_cls)

    print(f"Best parameters: {grid_search.best_params_}")
    print(f"Best CV score: {grid_search.best_score_:.4f} accuracy")

    # Update the best model
    best_model_cls_tuned = grid_search.best_estimator_

    # Evaluate the tuned model
    y_pred_test_tuned = best_model_cls_tuned.predict(X_test_cls)
    test_acc_tuned = accuracy_score(y_test_cls, y_pred_test_tuned)
    test_f1_tuned = f1_score(y_test_cls, y_pred_test_tuned, average='weighted')

```

```
    print(f"Tuned model performance:")
    print(f"  Test Accuracy: {test_acc_tuned:.4f}")
    print(f"  Test F1 Score: {test_f1_tuned:.4f}")

    # Compare with the untuned model
    print(f"Improvement over untuned model:")
    print(f"  Accuracy improvement: {test_acc_tuned - best_score_cls:.4f}")
    print(f"  F1 Score improvement: {test_f1_tuned - results_cls[best_model_name_cls]['Test F1']:.4f}")

    # Update the best model
    best_model_cls = best_model_cls_tuned
    best_score_cls = test_acc_tuned
else:
    print(f"No hyperparameter tuning needed for {best_model_name_cls}")

    # 9.3 Tune the Deep Learning Model (MLP Regressor)
print("\n--- Hyperparameter Tuning for MLP Regressor (Deep Learning) ---")

from sklearn.neural_network import MLPRegressor

# Define parameter grid
mlp_param_grid = {
    'hidden_layer_sizes': [(50,), (100,), (100, 50), (128, 64)],
    'activation': ['relu', 'tanh'],
    'solver': ['adam'],
    'learning_rate_init': [0.001, 0.01],
    'max_iter': [500, 1000]
}

mlp_grid_search = GridSearchCV(
    estimator=MLPRegressor(random_state=42),
    param_grid=mlp_param_grid,
    cv=3,
    scoring='neg_mean_squared_error',
    n_jobs=-1
)

mlp_grid_search.fit(X_train_reg, y_train_reg)

print("Best MLP Parameters:", mlp_grid_search.best_params_)

# Evaluate tuned MLP
best_mlp_tuned = mlp_grid_search.best_estimator_
y_pred_mlp_tuned = best_mlp_tuned.predict(X_test_reg)

mlp_rmse_tuned = np.sqrt(mean_squared_error(y_test_reg, y_pred_mlp_tuned))
mlp_r2_tuned = r2_score(y_test_reg, y_pred_mlp_tuned)

print("Tuned MLP Performance:")
print(f"  Test RMSE: {mlp_rmse_tuned:.4f}")
print(f"  Test R²: {mlp_r2_tuned:.4f}")

```

```
--- Hyperparameter Tuning for Regression Model ---
Tuning Linear Regression...
No hyperparameter tuning needed for Linear Regression

--- Hyperparameter Tuning for Classification Model ---
Tuning Logistic Regression...
Best parameters: {'C': 1, 'penalty': 'l2', 'solver': 'lbfgs'}
Best CV score: 0.7357 accuracy
Tuned model performance:
  Test Accuracy: 0.7412
  Test F1 Score: 0.7381
Improvement over untuned model:
  Accuracy improvement: 0.0000
  F1 Score improvement: 0.0000

--- Hyperparameter Tuning for MLP Regressor (Deep Learning) ---
Best MLP Parameters: {'activation': 'relu', 'hidden_layer_sizes': (100,), 'learning_rate_init': 0.01, 'max_iter': 500, 'solver': 'ad
Tuned MLP Performance:
  Test RMSE: 12.1317
  Test R²: 0.3985
```

```
# Step 10: Feature Importance Analysis

# 10.1 Analyze feature importance for regression model
print("\n--- Feature Importance for Regression Model ---")

if hasattr(best_model_reg, 'feature_importances_'):
    # For tree-based models
```

```
    importances = best_model_reg.feature_importances_
    indices = np.argsort(importances)[::-1]

    # Print feature ranking
    print("Feature ranking for regression model:")
    for i, idx in enumerate(indices[:15]):  # Print top 15 features
        if i < len(X_processed.columns):
            print(f"{i+1}. {X_processed.columns[idx]} ({importances[idx]:.4f})")

    # Plot feature importances
    plt.figure(figsize=(12, 8))
    plt.title(f"Feature Importances for {best_model_name_reg}")
    plt.bar(range(min(15, len(indices))), importances[indices[:15]], align="center")
    plt.xticks(range(min(15, len(indices))), [X_processed.columns[i] for i in indices[:15]], rotation=90)
    plt.tight_layout()
    plt.savefig('regression_feature_importance.png')
    plt.close()
    print("Feature importance plot saved as 'regression_feature_importance.png'")

elif hasattr(best_model_reg, 'coef_'):
    # For linear models
    coefficients = best_model_reg.coef_
    importance = np.abs(coefficients)
    indices = np.argsort(importance)[::-1]

    # Print feature ranking
    print("Feature ranking for regression model:")
    for i, idx in enumerate(indices[:15]):  # Print top 15 features
        if i < len(X_processed.columns):
            print(f"{i+1}. {X_processed.columns[idx]} ({coefficients[idx]:.4f})")

    # Plot feature coefficients
    plt.figure(figsize=(12, 8))
    plt.title(f"Feature Coefficients for {best_model_name_reg}")
    plt.bar(range(min(15, len(indices))), coefficients[indices[:15]], align="center")
    plt.xticks(range(min(15, len(indices))), [X_processed.columns[i] for i in indices[:15]], rotation=90)
    plt.tight_layout()
    plt.savefig('regression_feature_coefficients.png')
    plt.close()
    print("Feature coefficients plot saved as 'regression_feature_coefficients.png'")

# 10.2 Analyze feature importance for classification model
print("\n--- Feature Importance for Classification Model ---")

if hasattr(best_model_cls, 'feature_importances_'):
    # For tree-based models
    importances = best_model_cls.feature_importances_
    indices = np.argsort(importances)[::-1]

    # Print feature ranking
    print("Feature ranking for classification model:")
    for i, idx in enumerate(indices[:15]):  # Print top 15 features
        if i < len(X_processed.columns):
            print(f"{i+1}. {X_processed.columns[idx]} ({importances[idx]:.4f})")

    # Plot feature importances
    plt.figure(figsize=(12, 8))
    plt.title(f"Feature Importances for {best_model_name_cls}")
    plt.bar(range(min(15, len(indices))), importances[indices[:15]], align="center")
    plt.xticks(range(min(15, len(indices))), [X_processed.columns[i] for i in indices[:15]], rotation=90)
    plt.tight_layout()
    plt.savefig('classification_feature_importance.png')
    plt.close()
    print("Feature importance plot saved as 'classification_feature_importance.png'")

elif hasattr(best_model_cls, 'coef_'):
    # For linear models
    coefficients = best_model_cls.coef_[0] if best_model_cls.coef_.ndim > 1 else best_model_cls.coef_
    importance = np.abs(coefficients)
    indices = np.argsort(importance)[::-1]

    # Print feature ranking
    print("Feature ranking for classification model:")
    for i, idx in enumerate(indices[:15]):  # Print top 15 features
        if i < len(X_processed.columns):
            print(f"{i+1}. {X_processed.columns[idx]} ({coefficients[idx]:.4f})")

    # Plot feature coefficients
    plt.figure(figsize=(12, 8))
    plt.title(f"Feature Coefficients for {best_model_name_cls}")
    plt.bar(range(min(15, len(indices))), coefficients[indices[:15]], align="center")
    plt.xticks(range(min(15, len(indices))), [X_processed.columns[i] for i in indices[:15]], rotation=90)
```

```
    plt.tight_layout()
    plt.savefig('classification_feature_coefficients.png')
    plt.close()
    print("Feature coefficients plot saved as 'classification_feature_coefficients.png'")

    # 10.3 Analyze feature importance for MLP Regressor (Deep Learning)

from sklearn.inspection import permutation_importance

print("\n--- Feature Importance for MLP Regressor (Deep Learning) ---")

# Run permutation importance
perm_importance = permutation_importance(
    estimator=best_mlp_tuned,         # this is the tuned MLP from Step 9.3
    X=X_test_reg,
    y=y_test_reg,
    scoring='neg_mean_squared_error',
    n_repeats=10,
    random_state=42,
    n_jobs=-1
)

# Get importances and sort
importances = perm_importance.importances_mean
indices = np.argsort(importances)[::-1]

# Print top 15 features
print("Feature ranking for MLP Regressor:")
for i, idx in enumerate(indices[:15]):
    print(f"{i+1}. {X_processed.columns[idx]} ({importances[idx]:.4f})")

# Plot
plt.figure(figsize=(12, 8))
plt.title("Permutation Importance for MLP Regressor")
plt.bar(range(15), importances[indices[:15]], align="center")
plt.xticks(range(15), [X_processed.columns[i] for i in indices[:15]], rotation=90)
plt.tight_layout()
plt.savefig("mlp_regressor_feature_importance.png")
plt.close()
print("Permutation importance plot saved as 'mlp_regressor_feature_importance.png'")

```

```
--- Feature Importance for Regression Model ---
Feature ranking for regression model:
1. Cyp2C9 genotypes_*3/*3 (-23.1252)
2. Cyp2C9 genotypes_*2/*3 (-18.4668)
3. Cyp2C9 genotypes_*1/*14 (-17.8902)
4. Race (Reported)_Black African (-15.9044)
5. Cyp2C9 genotypes_*1/*13 (-15.6725)
6. Age_90+ (-15.2158)
7. Age_80 - 89 (-12.1793)
8. Race (Reported)_Hispanic (-11.0533)
9. Race (Reported)_other (-11.0229)
10. Cyp2C9 genotypes_*2/*2 (-11.0174)
11. Race (Reported)_Japanese (-10.7450)
12. Age_70 - 79 (-10.6297)
13. Race (Reported)_Han Chinese (-10.3989)
14. VKORC1 genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T_G/G (10.3562)
15. Cyp2C9 genotypes_*1/*3 (-9.7862)
Feature coefficients plot saved as 'regression_feature_coefficients.png'

--- Feature Importance for Classification Model ---
Feature ranking for classification model:
1. Cyp2C9 genotypes_*3/*3 (-2.4757)
2. Cyp2C9 genotypes_*2/*3 (-2.4307)
3. Race (Reported)_Black other (-1.4596)
4. Age_90+ (-1.4376)
5. Cyp2C9 genotypes_*1/*3 (-1.3811)
6. Cyp2C9 genotypes_*2/*2 (-1.3441)
7. Race (Reported)_Japanese (-1.3007)
8. Race (Reported)_Indian (1.2518)
9. Race (Reported)_Han Chinese (-1.2369)
10. VKORC1 genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T_G/G (1.1361)
11. Race (Reported)_Asian (-1.1242)
12. Age_80 - 89 (-1.0865)
13. Age_70 - 79 (-1.0039)
14. Cyp2C9 genotypes_*1/*5 (-0.9940)
15. Amiodarone (Cordarone) (-0.9700)
Feature coefficients plot saved as 'classification_feature_coefficients.png'

--- Feature Importance for MLP Regressor (Deep Learning) ---
Feature ranking for MLP Regressor:
1. VKORC1 genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T_G/G (33.7822)
2. Weight (kg) (26.9051)
3. Cyp2C9 genotypes_*1/*3 (16.6198)
```

```
    4. Race (Reported)_Japanese (14.3420)
    5. Age_70 - 79 (10.5568)
    6. Cyp2C9 genotypes_*2/*3 (10.3220)
    7. Cyp2C9 genotypes_*1/*2 (6.5104)
    8. Age_80 - 89 (6.2551)
    9. Race (Reported)_Han Chinese (5.9399)
    10. Amiodarone (Cordarone) (4.1803)
    11. Race (Reported)_Caucasian (3.6003)
    12. Cyp2C9 genotypes_*3/*3 (3.5078)
    13. Age_40 - 49 (3.2009)
    14. Race (Reported)_Indian (2.3737)
    15. Cyp2C9 genotypes_*2/*2 (2.3593)
    Permutation importance plot saved as 'mlp_regressor_feature_importance.png'
```

```
# Step 11: Model Visualization and Interpretation

# 11.1 Visualize regression model predictions
print("\n--- Visualizing Regression Model Predictions ---")

# Predict values using the best regression model
y_pred_reg = best_model_reg.predict(X_test_reg)

# Plot predicted vs actual values
plt.figure(figsize=(10, 6))
plt.scatter(y_test_reg, y_pred_reg, alpha=0.5)
plt.plot([y_test_reg.min(), y_test_reg.max()], [y_test_reg.min(), y_test_reg.max()], 'k--', lw=2)
plt.xlabel('Actual Therapeutic Dose')
plt.ylabel('Predicted Therapeutic Dose')
plt.title(f'Actual vs. Predicted Therapeutic Dose: {best_model_name_reg}')
plt.grid(True, alpha=0.3)
plt.savefig('regression_predictions.png')
plt.close()
print("Regression predictions plot saved as 'regression_predictions.png'")

# Plot residuals
plt.figure(figsize=(10, 6))
residuals = y_test_reg - y_pred_reg
plt.scatter(y_pred_reg, residuals, alpha=0.5)
plt.axhline(y=0, color='r', linestyle='-')
plt.xlabel('Predicted Therapeutic Dose')
plt.ylabel('Residuals')
plt.title(f'Residual Plot: {best_model_name_reg}')
plt.grid(True, alpha=0.3)
plt.savefig('regression_residuals.png')
plt.close()
print("Regression residuals plot saved as 'regression_residuals.png'")

# Residual histogram
plt.figure(figsize=(10, 6))
plt.hist(residuals, bins=30, alpha=0.7, color='skyblue', edgecolor='black')
plt.axvline(x=0, color='r', linestyle='-')
plt.xlabel('Residual Value')
plt.ylabel('Frequency')
plt.title('Histogram of Residuals')
plt.grid(True, alpha=0.3)
plt.savefig('regression_residuals_histogram.png')
plt.close()
print("Residuals histogram saved as 'regression_residuals_histogram.png'")

# 11.2 Visualize classification model predictions
print("\n--- Visualizing Classification Model Predictions ---")

# Predict values using the best classification model
y_pred_cls = best_model_cls.predict(X_test_cls)

# Create confusion matrix
cm = confusion_matrix(y_test_cls, y_pred_cls)

# Plot confusion matrix
plt.figure(figsize=(8, 6))
sns.heatmap(cm, annot=True, fmt='d', cmap='Blues', cbar=False)
plt.xlabel('Predicted Label')
plt.ylabel('True Label')
plt.title(f'Confusion Matrix: {best_model_name_cls}')
plt.savefig('classification_confusion_matrix.png')
plt.close()
print("Classification confusion matrix saved as 'classification_confusion_matrix.png'")

# Plot ROC curve for binary classification
if hasattr(best_model_cls, 'predict_proba'):
    y_pred_proba = best_model_cls.predict_proba(X_test_cls)[:, 1]
    fpr, tpr, thresholds = roc_curve(y_test_cls, y_pred_proba)
    roc_auc = roc_auc_score(y_test_cls, y_pred_proba)
```

```
    plt.figure(figsize=(8, 6))
    plt.plot(fpr, tpr, color='darkorange', lw=2, label=f'ROC curve (area = {roc_auc:.2f})')
    plt.plot([0, 1], [0, 1], color='navy', lw=2, linestyle='--')
    plt.xlim([0.0, 1.0])
    plt.ylim([0.0, 1.05])
    plt.xlabel('False Positive Rate')
    plt.ylabel('True Positive Rate')
    plt.title(f'ROC Curve: {best_model_name_cls}')
    plt.legend(loc="lower right")
    plt.grid(True, alpha=0.3)
    plt.savefig('classification_roc_curve.png')
    plt.close()
    print("ROC curve saved as 'classification_roc_curve.png'")
```

```
--- Visualizing Regression Model Predictions ---
Regression predictions plot saved as 'regression_predictions.png'
Regression residuals plot saved as 'regression_residuals.png'
Residuals histogram saved as 'regression_residuals_histogram.png'

--- Visualizing Classification Model Predictions ---
Classification confusion matrix saved as 'classification_confusion_matrix.png'
ROC curve saved as 'classification_roc_curve.png'
```

```
# Step 12: Save Final Models

import pickle
import joblib

# 12.1 Create folder for saving models
import os
os.makedirs('models', exist_ok=True)

# 12.2 Save the best regression model
print("\n--- Saving Best Models ---")
joblib.dump(best_model_reg, 'models/best_regression_model.pkl')
print(f"Best regression model ({best_model_name_reg}) saved as 'models/best_regression_model.pkl'")

# 12.3 Save the best classification model
joblib.dump(best_model_cls, 'models/best_classification_model.pkl')
print(f"Best classification model ({best_model_name_cls}) saved as 'models/best_classification_model.pkl'")

# 12.4 Save preprocessing objects
joblib.dump(numeric_imputer, 'models/numeric_imputer.pkl')
print(f"Numeric imputer saved as 'models/numeric_imputer.pkl'")

if 'cat_imputer' in locals():
    joblib.dump(cat_imputer, 'models/categorical_imputer.pkl')
    print(f"Categorical imputer saved as 'models/categorical_imputer.pkl'")

# 12.5 Save feature names
with open('models/feature_names.pkl', 'wb') as f:
    pickle.dump(X_processed.columns.tolist(), f)
print("Feature names saved as 'models/feature_names.pkl'")
```

```
--- Saving Best Models ---
Best regression model (Linear Regression) saved as 'models/best_regression_model.pkl'
Best classification model (Logistic Regression) saved as 'models/best_classification_model.pkl'
Numeric imputer saved as 'models/numeric_imputer.pkl'
Categorical imputer saved as 'models/categorical_imputer.pkl'
Feature names saved as 'models/feature_names.pkl'
```

```
# Step 13: Create Web Application with Gradio

# 13.1 Generate Gradio application code
print("\n--- Creating Gradio Web Application ---")

gradio_code = """
import gradio as gr
import pandas as pd
import numpy as np
import joblib
import pickle

# Load the trained models and preprocessing components
best_reg_model = joblib.load('models/best_regression_model.pkl')
best_cls_model = joblib.load('models/best_classification_model.pkl')
numeric_imputer = joblib.load('models/numeric_imputer.pkl')

# Load feature names
```

```
with open('models/feature_names.pkl', 'rb') as f:
    feature_names = pickle.load(f)

def predict_warfarin_dose(gender, race, age, height, weight, diabetes,
                          simvastatin, amiodarone, cyp2c9, vkorc1):
    # Create input data dictionary
    input_data = {
        'Gender': [gender],
        'Race (Reported)': [race],
        'Age': [age],
        'Height (cm)': [height],
        'Weight (kg)': [weight],
        'Diabetes': [1 if diabetes else 0],
        'Simvastatin (Zocor)': [1 if simvastatin else 0],
        'Amiodarone (Cordarone)': [1 if amiodarone else 0],
        'Cyp2C9 genotypes': [cyp2c9],
        'VKORC1 genotype: -1639 G>A (3673); chr16:31015190; rs9923231; C/T': [vkorc1]
    }

    # Convert to DataFrame
    input_df = pd.DataFrame(input_data)

    # Preprocess input
    # One-hot encode categorical variables
    cat_cols = [col for col in input_df.columns if input_df[col].dtype == 'object']
    num_cols = [col for col in input_df.columns if col not in cat_cols]

    # Handle numeric columns
    if num_cols:
        input_df[num_cols] = numeric_imputer.transform(input_df[num_cols])

    # Handle categorical columns
    if cat_cols:
        input_df_encoded = pd.get_dummies(input_df, columns=cat_cols)
    else:
        input_df_encoded = input_df.copy()

    # Align columns with training data
    final_df = pd.DataFrame(0, index=[0], columns=feature_names)
    for col in input_df_encoded.columns:
        if col in feature_names:
            final_df[col] = input_df_encoded[col].values

    # Make predictions
    dose_prediction = best_reg_model.predict(final_df)[0]
    class_prediction = best_cls_model.predict(final_df)[0]

    # Get probability for classification
    class_proba = best_cls_model.predict_proba(final_df)[0]
    high_dose_prob = class_proba[1] if len(class_proba) > 1 else 0

    # Format results
    class_label = "High Dose (>30 mg/week)" if class_prediction == 1 else "Low Dose (≤30 mg/week)"

    # Create detailed results
    results = f"## Warfarin Dosing Prediction Results\n\n"
    results += f"### Predicted Weekly Dose\n"
    results += f"**{dose_prediction:.1f} mg/week**\n\n"
    results += f"### Dose Classification\n"
    results += f"**{class_label}** (Confidence: {high_dose_prob*100:.1f}%)\n\n"
    results += f"### Patient Information\n"
    results += f"- Gender: {gender}\n"
    results += f"- Race: {race}\n"
    results += f"- Age: {age} years\n"
    results += f"- Height: {height} cm\n"
    results += f"- Weight: {weight} kg\n"
    results += f"- Diabetes: {'Yes' if diabetes else 'No'}\n"
    results += f"- Taking Simvastatin: {'Yes' if simvastatin else 'No'}\n"
    results += f"- Taking Amiodarone: {'Yes' if amiodarone else 'No'}\n"
    results += f"- CYP2C9 Genotype: {cyp2c9}\n"
    results += f"- VKORC1 Genotype: {vkorc1}\n\n"
    results += f"### Clinical Considerations\n"
    results += f"- This prediction is based on a machine learning model and should be used as a decision support tool only.\n"
    results += f"- Regular INR monitoring is still necessary regardless of the predicted dose.\n"
    results += f"- Clinical judgment should always prevail when determining the appropriate warfarin dose.\n"

    return results

# Create Gradio interface
with gr.Blocks(title="Warfarin Dosing Prediction Tool") as demo:
    gr.Markdown("# Warfarin Dosing Prediction Tool")
    gr.Markdown("Enter patient information to predict the optimal warfarin dosage")
```

```
101
102     with gr.Row():
103         with gr.Column():
104             # Demographics
105             gr.Markdown("### Patient Demographics")
106             gender = gr.Dropdown(
107                 ["Male", "Female"],
108                 label="Gender"
109             )
110             race = gr.Dropdown(
111                 ["White", "Asian", "Black or African American", "Unknown"],
112                 label="Race"
113             )
114             age = gr.Slider(
115                 minimum=0, maximum=100, step=1, value=60,
116                 label="Age (years)"
117             )
118             height = gr.Number(
119                 value=170,
120                 label="Height (cm)"
121             )
122             weight = gr.Number(
123                 value=70,
124                 label="Weight (kg)"
125             )
126
127             # Medical information
128             gr.Markdown("### Medical Information")
129             diabetes = gr.Checkbox(
130                 label="Diabetes"
131             )
132             simvastatin = gr.Checkbox(
133                 label="Taking Simvastatin (Zocor)"
134             )
135             amiodarone = gr.Checkbox(
136                 label="Taking Amiodarone (Cordarone)"
137             )
138
139             # Genetic information
140             gr.Markdown("### Genetic Information")
141             cyp2c9 = gr.Dropdown(
142                 ["*1/*1", "*1/*2", "*1/*3", "*2/*2", "*2/*3", "*3/*3"],
143                 label="CYP2C9 Genotype"
144             )
145             vkorc1 = gr.Dropdown(
146                 ["G/G", "A/G", "A/A"],
147                 label="VKORC1 Genotype"
148             )
149
150             # Submit button
151             submit_btn = gr.Button("Predict Warfarin Dose", variant="primary")
152
153         with gr.Column():
154             # Output
155             output = gr.Markdown()
156
157     # Set default values
158     gender.value = "Male"
159     race.value = "White"
160     cyp2c9.value = "*1/*1"
161     vkorc1.value = "G/G"
162
163     # Connect the function
164     submit_btn.click(
165         predict_warfarin_dose,
166         inputs=[gender, race, age, height, weight, diabetes, simvastatin, amiodarone, cyp2c9, vkorc1],
167         outputs=output
168     )
169
170     gr.Markdown("### About This Model")
171     gr.Markdown('''
172     This tool uses a machine learning model trained on data from the International Warfarin Pharmacogenetics Consortium.
173     The model considers patient demographics, medical conditions, and genetic factors to predict the optimal warfarin dose.
174
175     **Important Disclaimer**: This prediction tool is for educational and research purposes only.
176     It should not replace professional medical advice, diagnosis, or treatment. Always consult with a healthcare provider
177     for medical decisions regarding warfarin dosing.
178     ''')
179
180 # For running the app locally
181 if __name__ == "__main__":
182     demo.launch()
```