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Problem 1
For Chulalongkorn AI Academy candidate screening

Drug Allergy Prediction

Description

Problem introduction

- All doctors want to avoid prescribing drugs that maybe allergic to the patients
- Enzyme-linked immunospot (ELISpot) is a laboratory technique that tests whether the patient's immune cells will respond to particular drugs. This allows doctor to screen whether a drug is likely to be safe for the patient.
- As with any test, ELISpot is not perfect. Drugs that the patient is allergic to sometimes do not elicit any response in ELISpot test (False Negative) and vice versa.
- Hence, we want to develop a prediction model for drug allergy based on patient information, drug information, and ELISpot result.

The dataset

- Here, we have put together an anonymized dataset of ELISpot test results for ~800 patient and drug combinations.
- Ground truth drug allergy labels (last column) are available for only 14% of the dataset (115 patient and drug combinations). This is because the only way to obtain ground truth for drug allergy is to re-challenge the patients with the suspected drugs.
- There are also some missing feature values. This is because some information is not available for some patients.

Data dict

- ELISpot_Control is the ELISpot test result for the POSITIVE CONTROL (i.e., we expect to see strong response)
- ELISpot_Result is the ELISpot test result for SUSPECTED DRUG (i.e., this is the result that indicate whether the patient would be allergic to that drug)
- NARANJO_Category is ORDINAL.
- Exposure_Time is the amount of times since the patient has taken the drug until the ELISpot test date
- Suspicion_Score is the suspicion level of the drug (1 = suspected drug, 2 = similar to suspected drug, 3 = negative control). This is ORDINAL.
- Allergic_Reaction_Group is the severity of patient's allergic reaction. This is ORDINAL.

- Drug_Group is CATEGORICAL.
- Drug_Rechallenge_Result is the ground truth of this dataset that we want to predict.

The tasks

- Develop and present a prediction model for drug allergy.
- Address the issue of missing feature values in some way.
- Make use of data points with missing ground truth labels.

Acknowledgements

- We would like to thank Assoc. Prof. Jettanong Klaewsongkram and Dr. Yuda Chongpison for collecting and sharing the dataset.

License

Source

- https://www.kaggle.com/dataset/164839c70ca43c870151479e85f496daa3b68be24a93c44fa1cd153c (https://www.kaggle.com/dataset/164839c70ca43c870151479e85f496daa3b68be24a93c44fa1cd153c

In [ ]:

Methods

This study consists of 8 processes. The details are described follows;

1. **Data acquisition**
   The collection of data in this study is retrieved from kaggle following this Link (https://www.kaggle.com/dataset/164839c70ca43c870151479e85f496daa3b68be24a93c44fa1cd153c including an anonymized dataset of ELISpot test results for ~800 patient and drug combinations.

1. **Exploratory Data Analysis**
   The exploratory data analysis or “EDA” is a critical first step in analyzing the data from an experiment. Here are the main reasons we use EDA:

   - detection of mistakes and also missing value
   - checking of assumptions
   - preliminary selection of appropriate models
   - determining relationships among the explanatory variables, and
   - assessing the direction and rough size of relationships between explanatory and outcome variables.

1. **Data preparation and preprocessing.**

3.1 Missing-data Imputation

In statistics, imputation is the process of replacing missing data with substituted values. In this study we will try to impute category data with machine learning classifier and continuous data with linear regression.

3.2 Encoding Categorical Features

One hot encoding is a process by which categorical variables are converted into a form that could be provided to ML algorithms to do a better job in prediction.

3.3 Handling Imbalanced Data

Imbalanced classes are a common problem in machine learning classification where there is a disproportionate ratio of observations in each class. Class imbalance can be found in many different areas, including medical diagnosis, spam filtering, and fraud detection. In this study, due to we have a small dataset; thus, we will perform the oversampling technique for the minority class(Drug_Rechallenge_Result: Class 1.0).

1. **Transform Feature**

   After we get the list of selected feature, we have to eliminate feature value which is not relevant to outcome (e.g. PatientID). We will use this step to transform feature before we encode feature and split data to train and test.

1. **Split data**

   For developing machine learning classifier, we will split data into two sets, which are training set and testing set with balancing class. The new model is developed on the training set and test it on the holdout set.

1. **Developing model and Fine-tuning hyperparameter**

   In this study, we will develop a model from Logistic Classifier and Naive Bayes classifier. The model hyperparameters are tuned by using grid-search based on accuracy to get the best parameter.

1. **Semi-supervised learning: Pseudo-labeling**

   Due to we have many data with unlabeled which is useless for supervised learning. However, we can even use it to help train our model with semi-supervised learning – combining both unlabeled and labeled data for model training. In this technique, instead of manually labeling the unlabelled data, we give approximate labels on the basis of the labelled data.
2. **Evaluation**

   After the model is built, we will evaluates it with test set by using Sensitivity(Recall) and other metrics such as AUC, Specifivity, and Precision to estimate the performance. The model with the highest performance is chosen.

Let's conduct the experiment

Table of Contents

Install Neccessary Library

Top

- Install a pip package in the current Jupyter kernel

```
import sys
!{sys.executable} -m pip install --upgrade pip
!{sys.executable} -m pip install -r requirements.txt
```

Check Version of Library

Top

In [1]:
```
import sys
import numpy as np
import matplotlib
import seaborn as sns
import tqdm
import sklearn
import pandas
import scipy


print ( "Python", sys.version )
print ( "Numpy", np.__version__ )
print ( "Matplotlib", matplotlib.__version__ )
print ( "Seaborn", sns.__version__ )
print ( "tqdm", tqdm.__version__ )
print ( "scikit-learn", sklearn.__version__ )
print ( "pandas", pandas.__version__ )
print ( "scipy", scipy.__version__ )
```

```
Python 3.7.5 (default, Oct 25 2019, 10:52:18)
[Clang 4.0.1 (tags/RELEASE_401/final)]
Numpy 1.17.3
Matplotlib 3.0.3
Seaborn 0.9.0
tqdm 4.40.0
scikit-learn 0.22.1
pandas 0.25.3
scipy 1.4.1
```

Importing Required Libraries

Top

In [76]:
```
# Basic library
import os
import pandas as pd
import numpy as np
import matplotlib.pyplot as plt
import seaborn as sns
from time import time
from collections import Counter
import pickle

# Feature Selection
from scipy.stats import chi2_contingency

# Data preprocessing
from sklearn.model_selection import train_test_split

# Evaluation
from sklearn.model_selection import cross_val_score, cross_val_pred
ict
from sklearn.metrics import classification_report, confusion_matrix
from sklearn.metrics import average_precision_score, roc_auc_score
from sklearn.metrics import accuracy_score, f1_score, recall_score,
precision_score
```

Display and Parameter Setting

In [3]:
```
# Set dataframe display
pd.set_option('display.max_columns', None)  # default = 20
pd.set_option('display.expand_frame_repr', False) # default = True
pd.set_option('display.max_colwidth', -1) # default = 50
pd.set_option('display.float_format', lambda x: '%.3f' % x)

import warnings
warnings.filterwarnings("ignore",category=DeprecationWarning)
warnings.simplefilter(action='ignore', category=FutureWarning)
```

1. Define function

Top

from utils import percent_countplot, chi2_indtest, plot_feature_importances, cvt_type, makeOverSamplesADASYN, LogReg_HPTune, LogReg_HPTune_w_OverSam, NB_HPTune, Pseudo_labeling

In [63]:
```
# Countplot Visualization
def percent_countplot(df, col_name, col_hue = None, order_by_value
= False, topn = 0, dropna = True,
                      orient = 'v', annot_percent = True, figsize =
(14,8)):

    import matplotlib
```

```
    import matplotlib.pyplot as plt
    import seaborn as sns

    # Fill Paramter
    fs = 16 # Font size
    x_data = df.copy()
    x_col = col_name # column to count
    x_hue = col_hue # For divide column
    tittle = 'Distribution by '+x_col

    matplotlib.rc('xtick', labelsize = fs-2)
    matplotlib.rc('ytick', labelsize = fs-2)
    fig = plt.figure(figsize= figsize)

    data_col = x_data

    # topn > 0 we will combine the rest as "Other"
    if topn:
        counts = data_col[x_col].value_counts()
        topn_name = counts.nlargest(topn).index
        data_col[x_col] = data_col[x_col].where(data_col[x_col].isi
n(topn_name), other = 'Other')
    elif topn == 0:
        topn = data_col[x_col].nunique()

    # arrange order by value or index?
    if order_by_value :
        counts = data_col[x_col].value_counts()
        max_count = max(counts) # for adjust text alignment
    else:
        if str in list(map(type,data_col[x_col])) or not dropna:
            data_col[x_col] = data_col[x_col].astype(str)
        counts = data_col[x_col].value_counts().sort_index()
        max_count = max(counts.iloc[:topn]) # for adjust text align
ment

    if orient == 'v':
        ax = sns.countplot(x = x_col, hue = x_hue, data= data_col,
order = counts.iloc[:topn+1].index)
        ax.set_xlabel(x_col, color = 'r', fontsize = fs, fontweight
='bold')
        ax.set_ylabel('Frequency', color = 'b', fontsize = fs, font
weight='bold')
        # Set rotation of xticks if name is too long
        data_col[x_col] = data_col[x_col].astype(str)
        xrot = 15 if max(list(map(len,data_col[x_col].unique()))) >
10 else 0
        ax.get_yaxis().set_major_formatter(plt.FuncFormatter(lambda
x, loc: "{:,}".format(int(x))))
    elif orient == 'h':
        ax = sns.countplot(y = x_col, hue = x_hue, data= data_col,
order = counts.iloc[:topn+1].index)
        ax.set_ylabel(x_col, color = 'b', fontsize = fs, fontweight
='bold')
        ax.set_xlabel('Frequency', color = 'r', fontsize = fs, font
weight='bold')
        xrot = 0
```

```
        ax.get_xaxis().set_major_formatter(plt.FuncFormatter(lambda
x, loc: "{:,}".format(int(x))))

    total_count = sum(counts) # for calculate percentage
    # print(counts)

    # fig.suptitle('test title', fontsize=12)
    ax.set_title(tittle, fontsize = fs, fontweight='bold' )

    plt.xticks(rotation=xrot, color='r', size=16)
    plt.yticks(rotation=0, color='b', size=16)

    if x_hue == None and orient == 'v':
        for i, v in enumerate(counts[:topn+1]):
            ax.text(x = i, y=v + max_count*0.01 , s='{:,}'.format(v
), horizontalalignment='center', color='black', fontweight='bold')
            if annot_percent:
                ax.text(x = i, y= v/2, s=str('{:.2f}'.format(v*100/
total_count))+'%',
                        color='yellow', fontweight='bold', size = 1
4,
                        horizontalalignment='center',
                        verticalalignment='center'
                        )
    elif x_hue == None and orient == 'h':
        for i, v in enumerate(counts[:topn+1]):
            ax.text(x = v + max_count*0.03, y=i , s='{:,}'.format(v
), horizontalalignment='center', color='black', fontweight='bold')
            if annot_percent:
                ax.text(x = v/2, y=i , s=str('{:.2f}'.format(v*100/
total_count))+'%',
                        color='yellow', fontweight='bold', size = 1
4,
                        horizontalalignment='center',
                        verticalalignment='center'
                        )
    return ax

def chi2_indtest(df_feature, df_target, pvalue = 0.05, verbose =0):
    import pandas as pd
    from scipy.stats import chi2_contingency

    feature_list_chi = []
    feature_list_chi_score = []
    for series in df_feature:
        nl = "\n"

        crosstab = pd.crosstab(df_feature[series], df_target.values
.ravel())
        if verbose: print(crosstab, nl)
        chi2, p, dof, expected = chi2_contingency(crosstab)
        if verbose: print(f"Chi2 value= {chi2}{nl}p-value= {p}{nl}D
egrees of freedom= {dof}{nl}")
        if p < pvalue:
            feature_list_chi.append(series)
            feature_list_chi_score.append(chi2)
    return feature_list_chi, feature_list_chi_score
```

```
def plot_feature_importances(df, threshold = 0.90, normalized = True):
    """
    Plots 15 most important features and the cumulative importance of features.
    Prints the number of features needed to reach threshold cumulative importance.

    Parameters
    --------
    df : dataframe
        Dataframe of feature importances. Columns must be feature and importance
    threshold : float, default = 0.9
        Threshold for prining information about cumulative importances

    Return
    --------
    df : dataframe
        Dataframe ordered by feature importances with a normalized column (sums to 1)
        and a cumulative importance column

    """

    plt.rcParams['font.size'] = 18

    # Sort features according to importance
    df = df.sort_values('importance', ascending = False).reset_index(drop=True)

    # Normalize the feature importances to add up to one
    df['importance_normalized'] = df['importance'] / df['importance'].sum()
    df['cumulative_importance'] = np.cumsum(df['importance_normalized'])

    # Make a horizontal bar chart of feature importances
    plt.figure(figsize = (10, 6))
    ax = plt.subplot()

    # Need to reverse the index to plot most important on top
    colors = ['b', 'g', 'r', 'c', 'm', 'y','#4ef7ae','#d96d09', '#2b9900','#f7184d', '#1b5c44','#f25e60','#e59400']

    if normalized:
        ax.barh(list(reversed(list(df.index[:15]))),
                df['importance_normalized'].head(15),
                align = 'center', edgecolor = 'k',color = colors)
        plt.xlabel('Normalized Importance')
    else:
        ax.barh(list(reversed(list(df.index[:15]))),
                df['importance'].head(15),
                align = 'center', edgecolor = 'k',color = colors)
        plt.xlabel('Importance')
```

```
        # Set the xticks format
        ax.get_xaxis().set_major_formatter(plt.FuncFormatter(lambda
x, loc: "{:.2f}".format(int(x))))

#     for i, v in enumerate(df['importance_normalized'].head(15)):
#         ax.text(v + 0.001, i , '{:.4f}'.format(v), color='blue',
fontweight='bold')

    # Set the yticks and labels
    ax.set_yticks(list(reversed(list(df.index[:15]))))
    ax.set_yticklabels(df['feature'].head(15))



    # Plot labeling
    plt.title('Feature Importances')
    plt.show()

    # Cumulative importance plot
    plt.figure(figsize = (10, 6))
    ax = plt.subplot()
    n_fea = len(df)
    ax.plot(np.arange(n_fea)+1, df['cumulative_importance'], 'r-')
    plt.xlabel('Number of Features'); plt.ylabel('Cumulative Import
ance');
    plt.title('Cumulative Feature Importance');

    if threshold:
        # Index of minimum number of features needed for cumulative
importance threshold
        # np.where returns the index so need to add 1 to have corre
ct number
        importance_index = np.min(np.where(df['cumulative_importanc
e'] > threshold))
        plt.vlines(x = importance_index + 1, ymin = 0, ymax = thres
hold,
                   linestyles='--', colors = 'blue' )
        plt.text(importance_index +0.02*n_fea, 0, str(importance_in
dex + 1), color='red', fontweight='bold')
        plt.text(importance_index +0.05*n_fea, threshold, str(thres
hold*100)+'%', color='orange', fontweight='bold')
        plt.show();

    print('%d features required for %0.2f of cumulative importance'
% (importance_index + 1, threshold))


    return df


# Before we use 'get_dummies' function we have to convert data type
of all feature to be 'category'
def cvt_type(df, col_list, dtype = 'category'):
    for col in col_list:
        df[col] = df[col].astype(int).astype('category')
    return df
```

```
# Oversampling
def makeOverSamplesADASYN(X,y):
    from imblearn.over_sampling import ADASYN
    """
    Purpose
    ----------
    Increasing the observation of minority class

    Parameters
    ----------
    X: Independent Variable in DataFrame
    y: Dependent Variable in Pandas DataFrame format
    Returns:
    ----------
    Returns Independent and Dependent variable with resampling mino
rity class
    """
    X_resampled, y_resampled = ADASYN(random_state=7).fit_sample(X,
y)
    return(X_resampled, y_resampled)


# Logistic Regression
def LogReg_HPTune(X, y, verbose = 0):
    """
    Purpose
    ----------
    Choosing a set of optimal hyperparameters for a Logistic Regres
sion Classifier

    Parameters
    ----------
    X: Data set with all feature or predictor
    y: Data set with Class
    verbose: 0 mean not show summary of tuning
             1 mean show summary of tuning
    Returns:
    ----------
    Returns grid search model of Logistic Regression Classifier wit
h tuned hyperparameter
    """
    from sklearn.linear_model import LogisticRegression
    from sklearn.model_selection import GridSearchCV, RandomizedSea
rchCV

    # Logistic Regression Classifier
    LogReg_clf = LogisticRegression(random_state = 7, fit_intercept
=False)

    # Create regularization hyperparameter space
    C = np.logspace(-5, 5, 100)

    # Create regularization penalty space
    penalty = ['none', 'l2']

    # Create class weight mode space
    class_weight = [None, 'balanced']
```

```
    # Create solver function space
    solver = ['saga', 'lbfgs', 'newton-cg']


    # Define Search Param
    param_dist = dict(C = C,
                      penalty = penalty,
                      class_weight = class_weight,
#                       solver = solver
                     )
    rs = RandomizedSearchCV(estimator=LogReg_clf,
                            param_distributions=param_dist,
                            refit=True,
                            scoring=score_param,
                            n_iter=n_iter_search,
                            cv=cv,
                            n_jobs=-1,
                            verbose =1,
                            random_state=7,
                            iid=True)
    if verbose == 1:
        start = time()
        rs.fit(X,y)
        print("RandomizedSearchCV took %.2f seconds for %d
candidate parameter settings."
              % (time() - start, len(rs.cv_results_['params'])))

    elif verbose == 0:
        rs.fit(X,y)

    # Best parameter from RandomizedSearchCV
    bs_C = rs.best_params_['C']
    bs_penalty = rs.best_params_['penalty']
    bs_class_weight = rs.best_params_['class_weight']
#     bs_solver = rs.best_params_['solver']
    d_C = np.log10(bs_C)

    param_grid = dict(C = np.append(bs_C,np.logspace(d_C-2,d_C+2,nu
m=100)),
                      penalty = [bs_penalty],
                      class_weight = [bs_class_weight],
#                       solver = [bs_solver]
                     )
    gs = GridSearchCV(estimator=LogReg_clf,
                      param_grid=param_grid,
                      refit=True,
                      scoring=score_param,
                      cv=cv,
                      n_jobs=-1,
                      verbose =1,
                      iid=True)

    if verbose == 1:
        start = time()
        gs.fit(X,y)
        print("GridSearchCV took %.2f seconds for %d candidate para
```

```
meter settings."
              % (time() - start, len(gs.cv_results_['params'])))

    elif verbose == 0:
        gs.fit(X,y)

    return rs, gs


# Logistic Regression with ovesampling
def LogReg_HPTune_w_OverSam(X, y, verbose = 0):
    """
    Purpose
    ----------
    Choosing a set of optimal hyperparameters for a Logistic Regres
sion Classifier with balancing data

    Parameters
    ----------
    X: Data set with all feature or predictor
    y: Data set with Class
    verbose: 0 mean not show summary of tuning
             1 mean show summary of tuning
    Returns:
    ----------
    Returns grid search model of Logistic Regression Classifier wit
h tuned hyperparameter
    """
    from sklearn.linear_model import LogisticRegression
    from sklearn.model_selection import GridSearchCV, RandomizedSea
rchCV

    # Oversampling
    X, y = makeOverSamplesADASYN(X,y)

    # Logistic Regression Classifier
    LogReg_clf = LogisticRegression(random_state = 7, max_iter=1000
, fit_intercept=False)

    # Create regularization hyperparameter space
    C = [0.1,1,10] #np.logspace(-1, 1, 50)

    # Create regularization penalty space
    penalty = ['none', 'l2']

    # Create class weight mode space
    class_weight = [None, 'balanced']

    # Create solver function space
    solver = ['saga', 'lbfgs', 'newton-cg']

    #
    fit_intercept = [True, False]


    # Define Search Param
    param_dist = dict(C = C,
```

```
#                       penalty = penalty,
#                       class_weight = class_weight,
#                       solver = solver,
#                       fit_intercept = fit_intercept,
                      )
    rs = RandomizedSearchCV(estimator=LogReg_clf,
                            param_distributions=param_dist,
                            refit=True,
                            scoring=score_param,
                            n_iter=n_iter_search,
                            cv=cv,
                            n_jobs=-1,
                            verbose =verbose,
                            random_state=7,
                            iid=True)
    if verbose == 1:
        start = time()
        rs.fit(X,y)
        print("RandomizedSearchCV took %.2f seconds for %d
candidate parameter settings."
              % (time() - start, len(rs.cv_results_['params'])))

    elif verbose == 0:
        rs.fit(X,y)

    # Best parameter from RandomizedSearchCV
    bs_C = rs.best_params_['C']
#     bs_penalty = rs.best_params_['penalty']
#     bs_class_weight = rs.best_params_['class_weight']
#     bs_solver = rs.best_params_['solver']
#     bs_fit_intercept = rs.best_params_['fit_intercept']
    d_C = np.log10(bs_C)

    param_grid = dict(C = np.append(bs_C,np.logspace(d_C-1,d_C+1,nu
m=50)),
#                       penalty = [bs_penalty],
#                       class_weight = [bs_class_weight],
#                       solver = [bs_solver],
#                       fit_intercept = [bs_fit_intercept],
                      )
    gs = GridSearchCV(estimator=LogReg_clf,
                      param_grid=param_grid,
                      refit=True,
                      scoring=score_param,
                      cv=cv,
                      n_jobs=-1,
                      verbose =verbose,
                      iid=True)

    if verbose == 1:
        start = time()
        gs.fit(X,y)
        print("GridSearchCV took %.2f seconds for %d candidate para
meter settings."
              % (time() - start, len(gs.cv_results_['params'])))

    elif verbose == 0:
```

```
        gs.fit(X,y)

    return rs, gs

# Naive Bayes
def NB_HPTune_w_OverSam(X, y, verbose = 0):
    """
    Purpose
    ----------
    Choosing a set of optimal hyperparameters for a Naive Bayes Cla
ssifier

    Parameters
    ----------
    X: Data set with all feature or predictor
    y: Data set with Class
    verbose: 0 mean not show summary of tuning
             1 mean show summary of tuning
    Returns:
    ----------
    Returns grid search model of Naive Bayes Classifier with tuned
hyperparameter
    """
    from sklearn.naive_bayes import GaussianNB
    from sklearn.model_selection import GridSearchCV, RandomizedSea
rchCV

    # Oversampling
    X, y = makeOverSamplesADASYN(X,y)

    gnb = GaussianNB(priors=None)
    param_dist = dict(var_smoothing = np.logspace(-16,0,200) ) # de
fault is 1e-9
    rs = RandomizedSearchCV(estimator=gnb,
                            param_distributions=param_dist,
                            scoring=score_param,
                            refit=True,
                            n_iter = n_iter_search,
                            cv=cv,
                            n_jobs=-1,
                            random_state=7,
                            iid=True)
    if verbose == 1:
        start = time()
        rs.fit(X, y)
        print("RandomizedSearchCV took %.2f seconds for %d
candidate parameter settings."
              % (time() - start, len(rs.cv_results_['params'])))
    elif verbose == 0:
        rs.fit(X, y)

    # Best parameter from RandomizedSearchCV
    bs_var_sm = rs.best_params_['var_smoothing']
    bs_var_sm_pw = np.log10(bs_var_sm)

    param_grid = dict(var_smoothing = np.logspace(bs_var_sm_pw*0.9,
bs_var_sm_pw*1.1,50))
```

```
    gs = GridSearchCV(estimator=gnb,
                      param_grid=param_grid,
                      scoring=score_param,
                      refit=True,
                      cv=cv,
                      n_jobs=-1,
                      iid=True)

    if verbose == 1:
        start = time()
        gs.fit(X, y)
        print("GridSearchCV took %.2f seconds for %d candidate para
meter settings."
              % (time() - start, len(gs.cv_results_['params'])))
    elif verbose == 0:
        gs.fit(X, y)

    return rs, gs

# Semi-supervised learning: Pseudo-labeling
def Pseudo_labeling(df_train, df_NaN, LogReg_HPTune_w_OverSam, n_sa
m = 100, verbose=0):

    print("Initiate base model from training set....")
    # Training set
    X_encoded = df_train.drop(['Drug_Rechallenge_Result','Patient_I
D'], axis=1)
    y_data = df_train[['Drug_Rechallenge_Result']]

    print(X_encoded.shape)
    print(y_data.shape)

    LogReg_rs, LogReg_gs = LogReg_HPTune_w_OverSam(X_encoded,y_data
.values.ravel(), verbose=0)

    # Make a copy of df_NaN
    df_NaN_temp = df_NaN.copy()

    n_sam = n_sam
    n_min = n_sam
    n_frac = n_sam
    if type(n_sam) != int:
        n_sam = n_frac * len(y_data)
        n_min = 100
    n_round = 0

    print("Start Pseudo-labeling Process")

    while len(df_NaN_temp) > n_min and len(df_NaN_temp) > n_sam:
        n_round += 1
        print("Round: ", n_round, "\nProcessing....")

        # Sampling n_sam sample to predict class and store idx with
high confidence
        df_NaN_train = df_NaN_temp.sample(n = int(n_sam), random_st
ate=7)
        df_NaN_temp = df_NaN_temp.drop(df_NaN_train.index)
```

```
        X_encoded_NaN = df_NaN_train.drop(['Drug_Rechallenge_Result
','Patient_ID'], axis=1)
#         y_data_NaN = df_NaN_train[['Drug_Rechallenge_Result']]

        # Search idx with high predict_proba
        high_confidence_idx = []
        predict_result = []
        threshold_pos = 0.8
        for idx in X_encoded_NaN.index:
            Pos_confidence = LogReg_gs.predict_proba(X_encoded_NaN.
loc[[idx]])[:,1]
            if Pos_confidence > threshold_pos:
                high_confidence_idx.append(idx)
                predict_class = LogReg_gs.predict(X_encoded_NaN.loc
[[idx]])
                predict_result.append(predict_class)
            elif Pos_confidence < (1-threshold_pos):
                high_confidence_idx.append(idx)
                predict_class = LogReg_gs.predict(X_encoded_NaN.loc
[[idx]])
                predict_result.append(predict_class)

        # Create dataframe to store high confidence result
        df_feature_NaN = X_encoded_NaN.loc[high_confidence_idx]
        df_predict_NaN = pd.DataFrame(predict_result, columns=['Dru
g_Rechallenge_Result'], index=high_confidence_idx)

        # Concat new predicted data to X_encoded and y_data
        X_encoded = pd.concat([X_encoded,df_feature_NaN])
        y_data = pd.concat([y_data,df_predict_NaN])

        print(X_encoded.shape)
        print(y_data.shape)

        # GridSearch CV - Retraining
        score_param = 'accuracy' # Score for tune model
        n_iter_search = 100 # Max candidate parameter for Randomize
dSearchCV
        cv = 5 # Number of k-fold cross validation
        LogReg_rs, LogReg_gs = LogReg_HPTune_w_OverSam(X_encoded,y_
data.values.ravel(), verbose=0)

        # Append row which has low confident to df_NaN_temp
        low_con_idx = df_NaN_train[~df_NaN_train.index.isin(high_co
nfidence_idx)].index
        df_NaN_temp = pd.concat([df_NaN_temp,df_NaN_train.loc[low_c
on_idx]])

        # Display performance of each round
        print('Training score: ', LogReg_rs.best_score_)
        print('Test score: ', accuracy_score(LogReg_rs.predict(X_en
coded_test),y_data_test))

        # Re-calculate n_sam
        if type(n_frac) != int:
            n_sam = n_frac * len(y_data)
```

```
    # If the rest NaN sample less than n_sam
    df_NaN_train = df_NaN_temp
    X_encoded_NaN = df_NaN_train.drop(['Drug_Rechallenge_Result','P
atient_ID'], axis=1)
    predict_class = LogReg_gs.predict(X_encoded_NaN)
    df_predict_NaN = pd.DataFrame(predict_class, columns=['Drug_Rec
hallenge_Result'], index=X_encoded_NaN.index)

    # Concat new predicted data to X_encoded and y_data
    X_encoded = pd.concat([X_encoded,X_encoded_NaN])
    y_data = pd.concat([y_data,df_predict_NaN])

    print("========== Finish ==========")
    print(X_encoded.shape)
    print(y_data.shape)

    return X_encoded, y_data, LogReg_gs


# Make a model summary report
def model_report(Feature_data,Target_data,model_name_List,model_fun
c, best_param_clf =None):

    import sklearn
    from sklearn.metrics import confusion_matrix
    from sklearn.metrics import average_precision_score, roc_auc_sc
ore
    from sklearn.metrics import accuracy_score, f1_score, recall_sc
ore, precision_score,balanced_accuracy_score

    model_list = []
    accuracy_list = []
    balanced_acc_list = []
    auc_list = []
    cm_list = []
    cm_nor_list = []
    recall_list = []
    precision_list = []
    precision_neg_list = []
    specificity_list = []
    ap_list = []
    f1_list = []
    best_params_list = []

    for i,(name, model, X_test, y_test) in enumerate(zip(model_name
_List, model_func, Feature_data, Target_data)):

        if isinstance(model,
                      (sklearn.model_selection._search.RandomizedSe
archCV,
                       sklearn.model_selection.GridSearchCV)):
            y_pred = model.best_estimator_.predict(X_test)
            P_true = model.predict_proba(X_test)[:, 1]
            best_params = model.best_params_
            best_params_list.append(best_params)
        else:
```

```
            y_pred = model.predict(X_test)
            P_true = model.predict_proba(X_test)[:, 1]
            best_param = dict( C = model.get_params(deep=False)['es
timator'].C,
                                    class_weight = model.get_params(d
eep=False)['estimator'].class_weight
                                    )
            best_params_list.append(best_param)

        model_name = name
        TP, FN, FP, TN = confusion_matrix(y_test, y_pred, labels=[1
, 0]).ravel()
        n_data = TP+FN+FP+TN


        Accuracy = round(accuracy_score(y_test, y_pred), 2)
        bal_acc = round(balanced_accuracy_score(y_test, y_pred),2)
        auc = round(roc_auc_score(y_test, P_true), 2)
        cm = dict(TP=TP, FP=FP, FN=FN, TN=TN)
        cm_nor = dict(TP=f'{TP/n_data:.2f}', FP=f'{FP/n_data:.2f}',
FN=f'{FN/n_data:.2f}', TN=f'{TN/n_data:.2f}')
        Recall = round(recall_score(y_test, y_pred, average='binary
'), 2)
        Precision = round(precision_score(y_test, y_pred, average='
binary'), 2)
        Precision_neg = round(precision_score(y_test, y_pred, pos_l
abel = 0, average='binary'), 2)
        Specificity = round(TN/float(TN+FP), 2)
        ap = round(average_precision_score(y_test, P_true, pos_labe
l=1), 2)
        F1_score = round(f1_score(y_test, y_pred,average='binary'),
2)


        model_list.append(model_name)
        accuracy_list.append(Accuracy)
        balanced_acc_list.append(bal_acc)
        auc_list.append(auc)
        cm_list.append(cm)
        cm_nor_list.append(cm_nor)
        recall_list.append(Recall)
        precision_list.append(Precision)
        precision_neg_list.append(Precision_neg)
        specificity_list.append(Specificity)
        ap_list.append(ap)
        f1_list.append(F1_score)



    report = dict(LogReg_Model = model_list,
                  Accuracy = accuracy_list,
                  Balanced_Accuracy = balanced_acc_list,
                  AUC = auc_list,
                  Confusion_Matrix = cm_list,
                  Confusion_Matrix_Normalized = cm_nor_list,
                  Recall = recall_list,
                  Precision = precision_list,
```

```
                    Precision_neg = precision_neg_list,
                    Specificity = specificity_list,
                    Average_Precision = ap_list,
                    F1_score = f1_list,
                    Best_Parameters = best_params_list
                   )

    df_report = pd.DataFrame.from_dict(report)
    pd.set_option('display.max_colwidth', -1)

    return df_report

def print_score(clf, X, y, cv=0):

    y_pred = clf.predict(X)
    acc_score = accuracy_score(y, y_pred)
    clf_report = classification_report(y, y_pred)
#     conf_matrix = confusion_matrix(y, y_pred)
    TP, FN, FP, TN = confusion_matrix(y, y_pred, labels=[1, 0]).rav
el()
    n_data = TP+FN+FP+TN
    cm = dict(TP=TP, FP=FP, FN=FN, TN=TN)
    cm_nor = dict(TP=f'{TP/n_data:.2f}', FP=f'{FP/n_data:.2f}', FN=
f'{FN/n_data:.2f}', TN=f'{TN/n_data:.2f}')

    print(f"Results:\n")
    print(f"accuracy score: {acc_score:.4f}\n")
    print(f"Classification Report: \n {clf_report}\n")
    print(f"Confusion Matrix: \n {cm}\n")
    print(f"Confusion Matrix Normalized: \n {cm_nor}\n")

    if cv > 1:
        res = cross_val_score(clf, X, y, cv=cv, scoring='accuracy')
        print(f"Average Accuracy: \t {np.mean(res):.4f}")
        print(f"Accuracy SD: \t\t {np.std(res):.4f}")
```

2. Importing Dataset

Top

In [5]:
```
df = pd.read_csv('DrugAllergyKaggle_v3_050720.csv')
df = df.sort_values(by = 'Patient_ID').reset_index(drop=True); df.h
ead()
```

Out[5]:

	Patient_ID	Gender	Age_Year	ELISpot_Control	ELISpot_Result	Naranjo_Score	Naranjo_
0	2	1	26	2504	0.000	nan	
1	7	0	75	1868	51.000	5.000	
2	13	0	81	1617	10.000	nan	
3	13	0	81	1617	10.000	nan	
4	18	1	60	3136	0.000	nan	

In [6]:
```
df.describe(include='all')
```

Out[6]:

	Patient_ID	Gender	Age_Year	ELISpot_Control	ELISpot_Result	Naranjo_Score	Nar
count	799.000	799.000	799.000	799.000	798.000	431.000	
mean	375.078	0.566	51.013	1698.603	11.974	3.237	
std	144.888	0.496	22.345	879.909	51.111	1.797	
min	2.000	0.000	0.000	60.000	0.000	-3.000	
25%	318.000	0.000	36.000	1120.000	0.000	2.000	
50%	403.000	1.000	53.000	1592.000	0.000	3.000	
75%	486.000	1.000	70.000	2166.000	0.000	4.000	
max	570.000	1.000	97.000	5290.000	554.000	9.000	

3. Data Exploration

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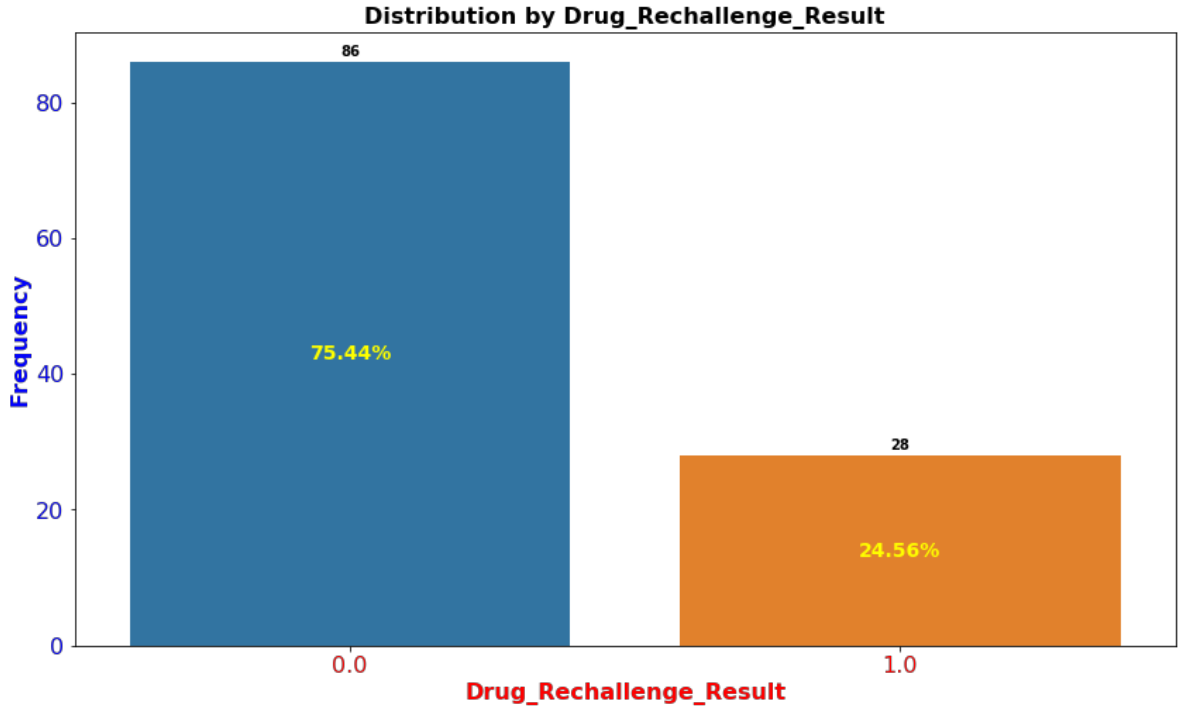
In [7]:
```
print ("Rows     : " ,df.shape[0])
print ("Columns  : " ,df.shape[1])
print ("\nFeatures : \n" ,df.columns.tolist())
print ("\nMissing values :  ", df.isnull().sum().values.sum())
n_uniq = df.nunique()
print ("\nUnique values :  \n",n_uniq)
print ("\nTotal Unique values :  {:,}".format(n_uniq.values.sum()))
```

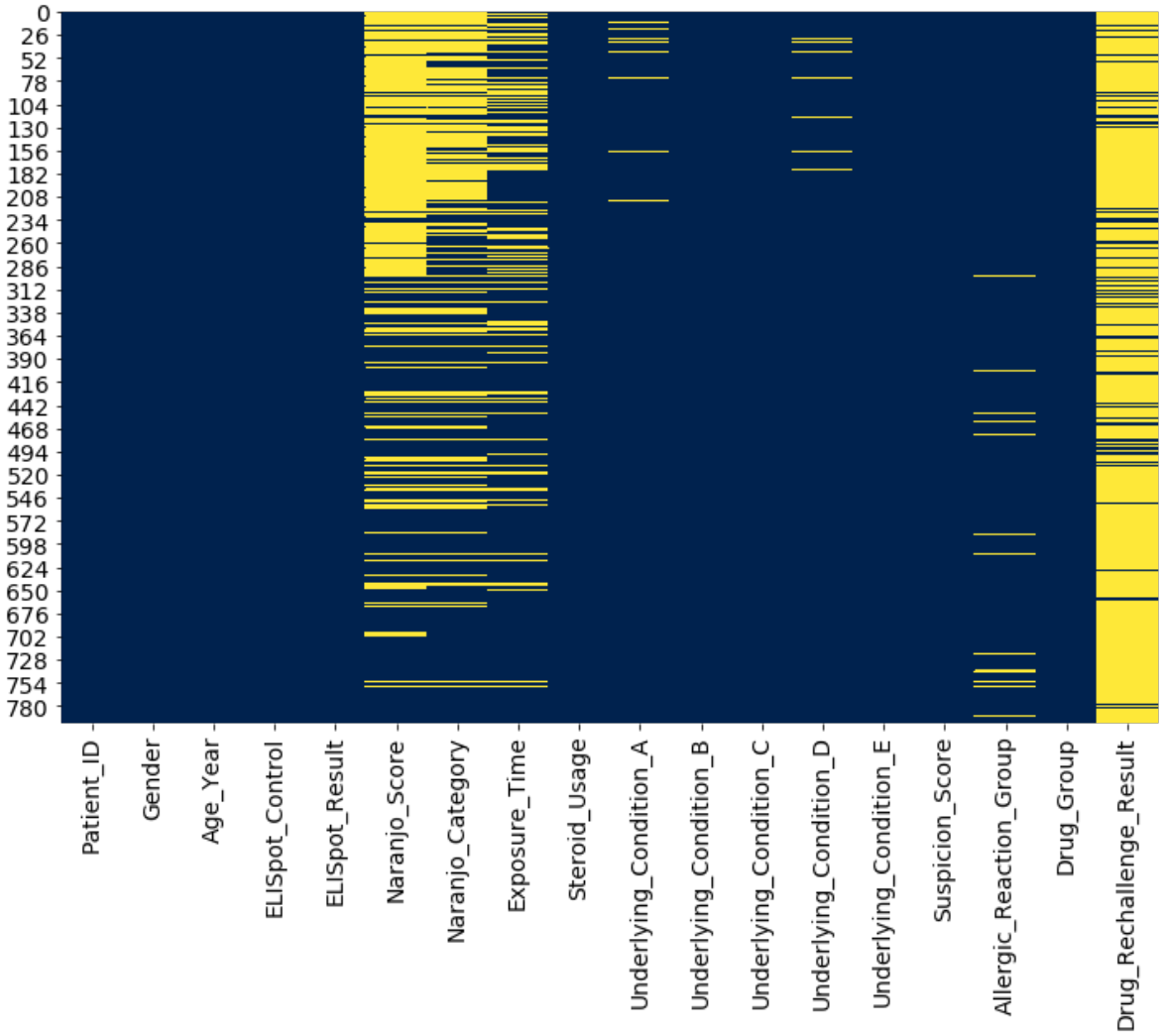
```
Rows     :  799
Columns  :  18

Features :
 ['Patient_ID', 'Gender', 'Age_Year', 'ELISpot_Control', 'ELISpot_
Result', 'Naranjo_Score', 'Naranjo_Category', 'Exposure_Time', 'St
eroid_Usage', 'Underlying_Condition_A', 'Underlying_Condition_B',
'Underlying_Condition_C', 'Underlying_Condition_D', 'Underlying_Co
ndition_E', 'Suspicion_Score', 'Allergic_Reaction_Group', 'Drug_Gr
oup', 'Drug_Rechallenge_Result']

Missing values :   1582

Unique values :
 Patient_ID                 298
Gender                      2
Age_Year                    94
ELISpot_Control             261
ELISpot_Result              77
Naranjo_Score               13
Naranjo_Category            4
Exposure_Time               77
Steroid_Usage               2
Underlying_Condition_A      2
Underlying_Condition_B      2
Underlying_Condition_C      2
Underlying_Condition_D      2
Underlying_Condition_E      2
Suspicion_Score             3
Allergic_Reaction_Group     8
Drug_Group                  8
Drug_Rechallenge_Result     2
dtype: int64

Total Unique values :  859
```

In [8]:
```
# See class distribution
percent_countplot(df, col_name='Drug_Rechallenge_Result',topn=0, dr
opna=True)
```

Out[8]: <matplotlib.axes._subplots.AxesSubplot at 0x1a2425b890>



In [9]:
```
plt.figure(figsize=(12,8))
sns.heatmap(df.isnull(), cbar=False, cmap = 'cividis');
```



There are so many missing value with 'Naranjo_Score', 'Naranjo_Category', 'Exposure_Time', and 'Drug_Rechallenge_Result' columns.

Univariate analysis

Feature(X)\Response(y)	Continuous	Categorical
Continuous	Pearson's Correlation	LDA
Categorical	ANOVA	Chi-Square

Pearson's correlation coefficient is the test statistics that measures the statistical relationship, or association, between two continuous variables. It is known as the best method of measuring the association between variables of interest because it is based on the method of covariance. It gives information about the magnitude of the association, or correlation, as well as the direction of the relationship. A Pearson correlation is a number between -1 and 1 that indicates the extent to which two variables are linearly related.

Chi-Square Test: In general term, this method is used to test the independence of two events. If a dataset is given for two events, we can get the observed count and the expected count and this test measures how much both the counts are derivate from each other.

H_0: Two categorical variables are independent.

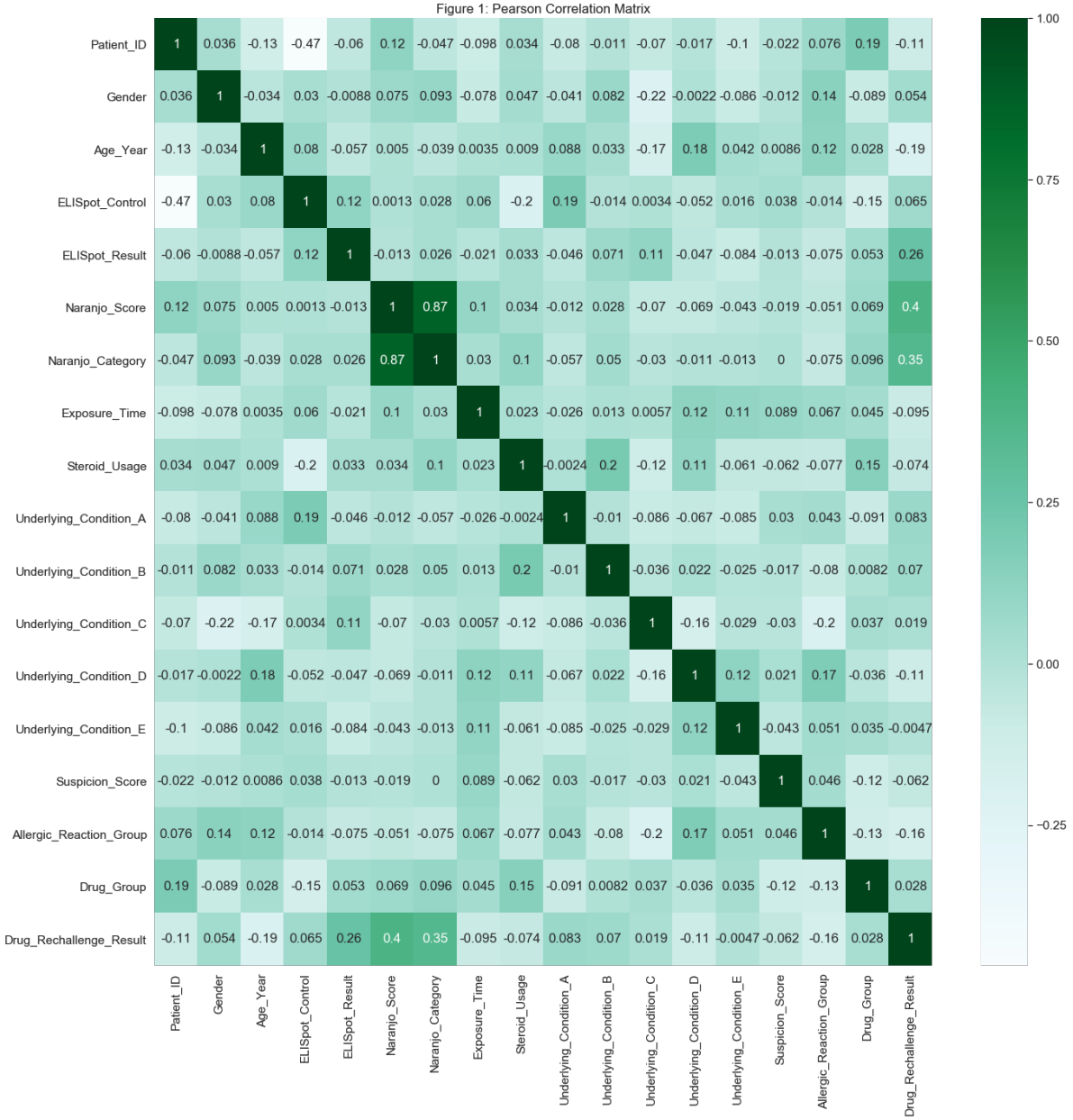
[or The proportions of interested event between two independent groups are not different.]

H_a: Twocategorical variables are dependent or associated.

In [10]:
```
# Pearson's correlation coefficient
plt.figure(figsize=(22,22))
sns.set(font_scale=1.4)
plt.title('Figure 1: Pearson Correlation Matrix')
sns.heatmap(df.corr(), annot=True, cmap='BuGn')
```

Out[10]:
```
<matplotlib.axes._subplots.AxesSubplot at 0x10ebd2f90>
```

Figure 1: Pearson Correlation Matrix



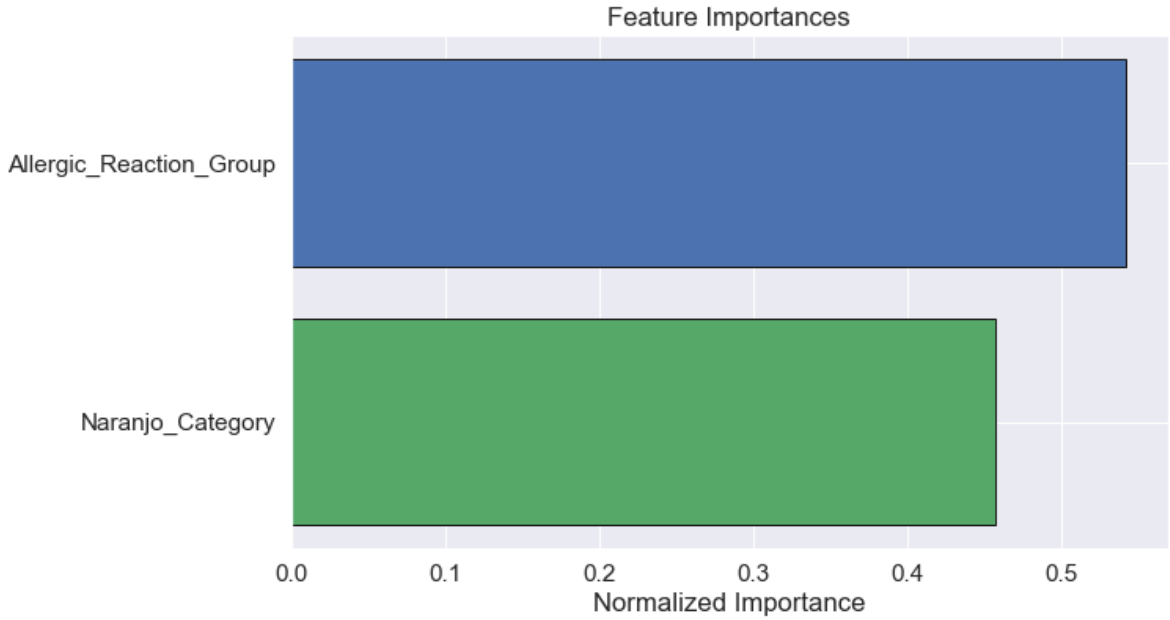
The the Naranjo_Score and Naranjo_Category have highest Pearson Correlation to target variable (Drug_Rechallenge_Result). And also between Naranjo_Score and Naranjo_Category themself have a very high Pearson Correlation. Therefore, we might remove one of them to prevent the colinearity issue.

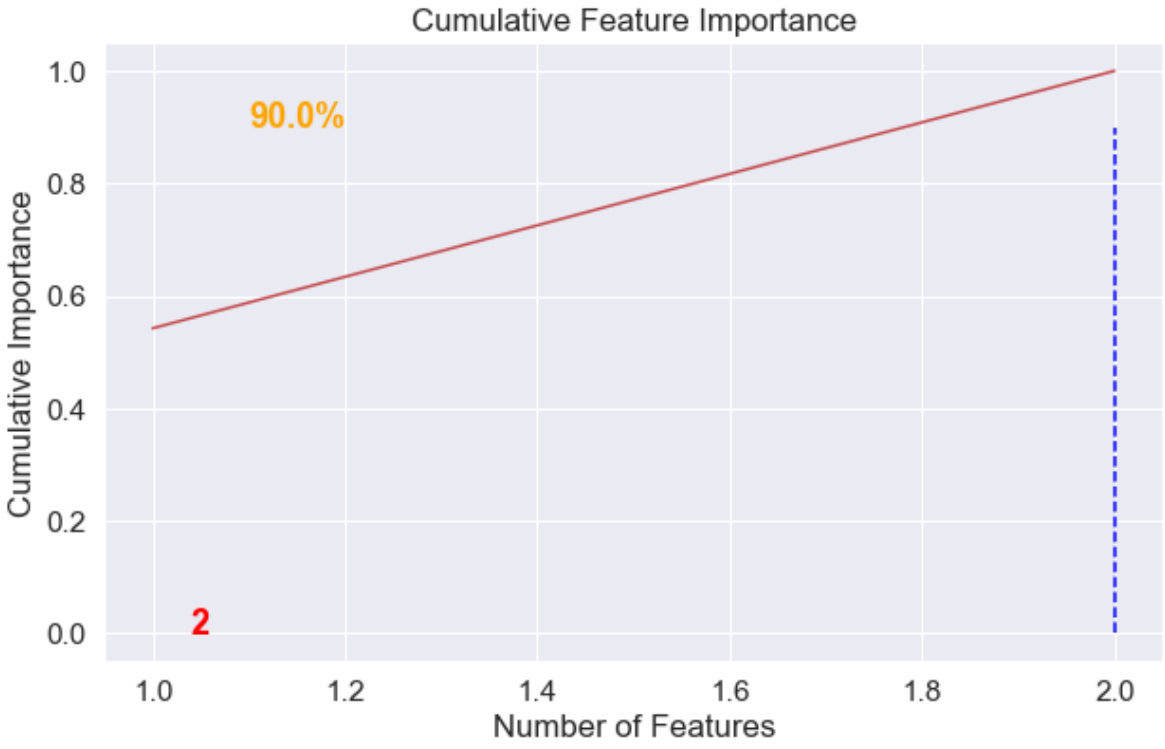
Although, the Pearson Correlation can see the relationship between continuous data, however, in our study the target variable is category data as well as many features. Then we should look at the Chi-Square Test to see the relation or dependency instead.

In [11]:
```
# Chi-Square Test
category_feature = ['Gender','Naranjo_Category', 'Steroid_Usage', '
Underlying_Condition_A', 'Underlying_Condition_B', 'Underlying_Cond
ition_C', 'Underlying_Condition_D', 'Underlying_Condition_E', 'Susp
icion_Score', 'Allergic_Reaction_Group', 'Drug_Group']
target = ['Drug_Rechallenge_Result']
pvalue = 0.05
feature_list_chi, feature_list_chi_score = chi2_indtest(df[category
_feature],df[target], pvalue = pvalue)

print('Select only IMPORTANT feature which p-value less than', pval
ue)
print('Number of IMPORTANT feature for Prediction:', len(feature_li
st_chi), '\n',feature_list_chi)
```

```
Select only IMPORTANT feature which p-value less than 0.05
Number of IMPORTANT feature for Prediction: 2
 ['Naranjo_Category', 'Allergic_Reaction_Group']
```

In [12]:
```
df_Chi2_feaimp = pd.DataFrame({'feature': feature_list_chi,
                               'importance': feature_list_chi_score
})\
                                .sort_values('importance', ascendin
g = False)

df_Chi2_feaimp_norm = plot_feature_importances(df_Chi2_feaimp, thre
shold= 0.90, normalized=True)
```






```
2 features required for 0.90 of cumulative importance
```

The Allergic_Reaction_Group and Naranjo_Category have p-value of Chi-Square Test less than 0.05 which mean we reject the null hypothesis and conclude that Allergic_Reaction_Group and Naranjo_Category is significantly associated with the Drug_Rechallenge_Result.

4. Data preparation and preprocessing

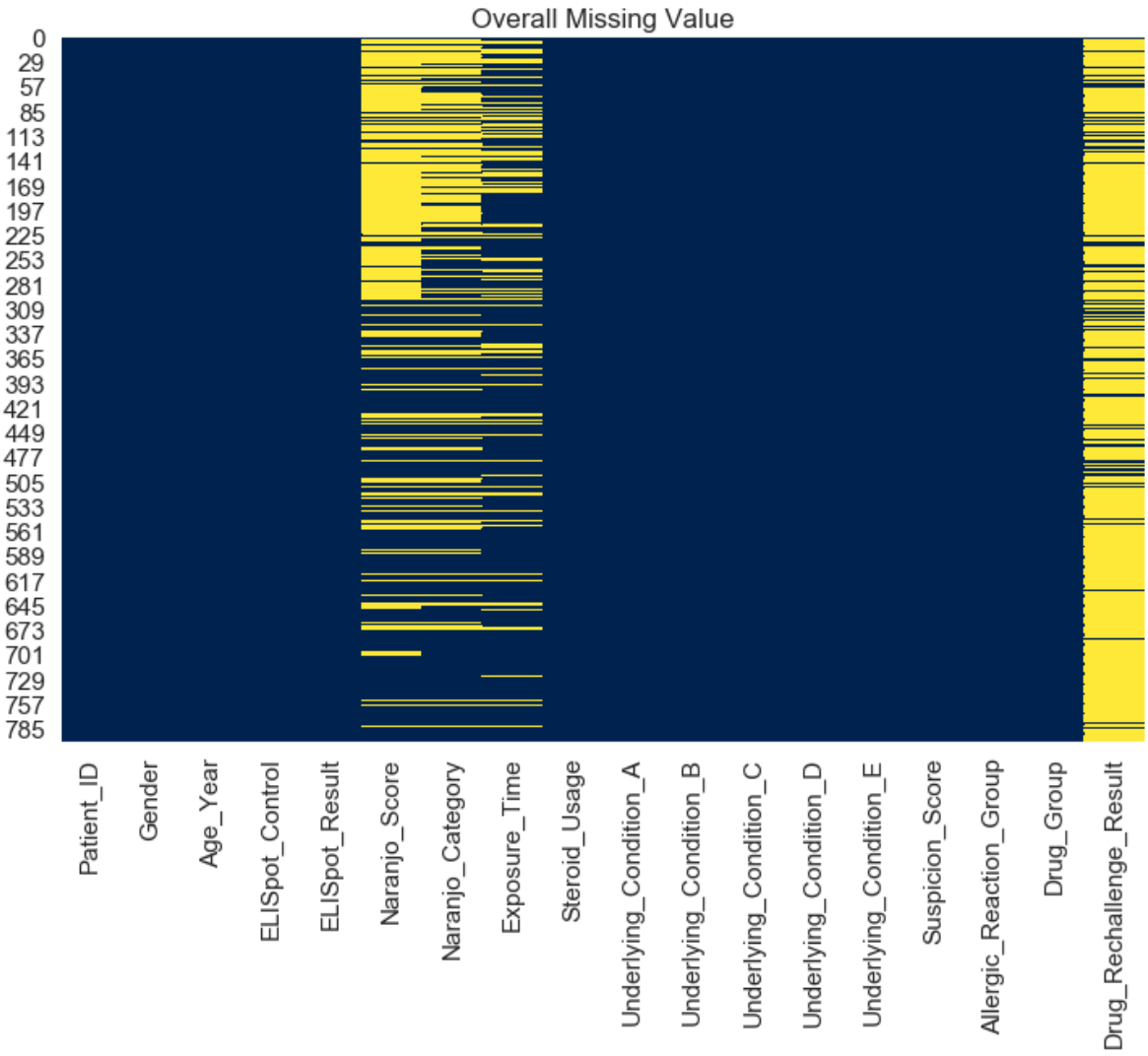
Top

Impute column which having few missing value

In [13]:
```
# Use statistical imputation technique
df.Underlying_Condition_A.fillna(df.Underlying_Condition_A.mode()[0
], inplace=True)
df.Underlying_Condition_D.fillna(df.Underlying_Condition_D.mode()[0
], inplace=True)
df.Underlying_Condition_E.fillna(df.Underlying_Condition_E.mode()[0
], inplace=True)
df.Allergic_Reaction_Group.fillna(df.Allergic_Reaction_Group.mode()
[0], inplace=True)

# Drop 1 row for null value in ELISpot_Result
df.dropna(subset=['ELISpot_Result'], inplace=True)
```

Due to these features have only a few missing values, so we decide to tackle it with a statistical imputation technique by using fill the most frequency occurrence (mode) to a missing value. And for ELISpot_Result, we decide to drop it because it has missed only one row.

In [14]:
```
plt.figure(figsize=(12,8)); plt.title('Overall Missing Value')
sns.heatmap(df.isnull(), cbar=False, cmap = 'cividis');
```



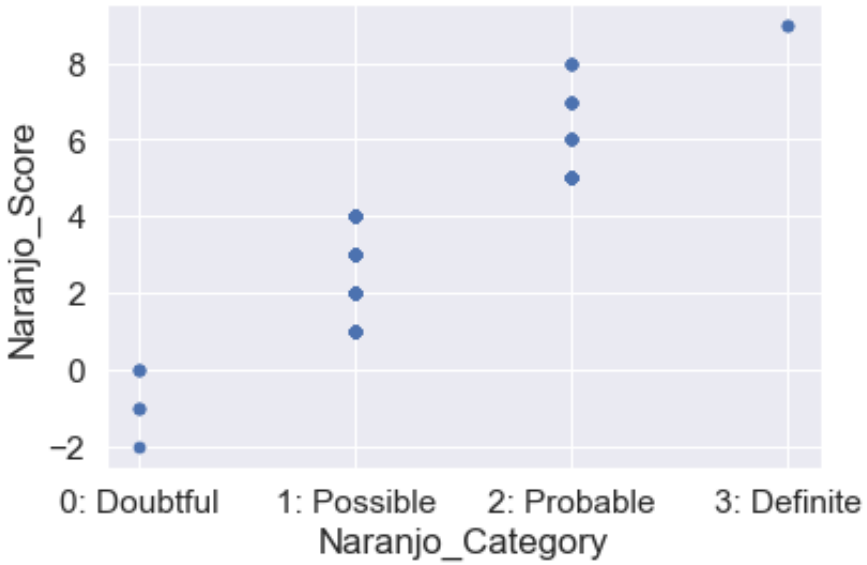
Explore Naranjo_Score and Naranjo_Category

In [15]:
```
labels = [str(i)+': ' + name for i,name in zip(range(4), ['Doubtful
', 'Possible', 'Probable', 'Definite'])]
labels
```

Out[15]:
```
['0: Doubtful', '1: Possible', '2: Probable', '3: Definite']
```

In [16]:
```
ax = df.plot(x='Naranjo_Category', y ='Naranjo_Score', kind='scatte
r')
ax.set_xticks(range(4));
ax.set_xticklabels(labels);
```

```
'c' argument looks like a single numeric RGB or RGBA sequence, whi
ch should be avoided as value-mapping will have precedence in case
its length matches with 'x' & 'y'.  Please use a 2-D array with a
single row if you really want to specify the same RGB or RGBA valu
e for all points.
```



According to above figure, Naranjo_Score and Naranjo_Category have high-correlation, which Naranjo Category is a grouping category of Naranjo Score. Hence, we can impute Naranjo_Category by using Naranjo_Score to Naranjo_Category and then remove Naranjo_Score.

In [17]:
```
df.iloc[493:494,:][['Naranjo_Score','Naranjo_Category']]
```

Out[17]:

	Naranjo_Score	Naranjo_Category
494	3.000	1.000

In [18]:
```
# Impute Naranjo_Category by Naranjo_Score

def Categorize_Naranjo_Score(score):
    if score <= 0:
        return 0
    elif score in range(1,5):
        return 1
    elif score in range(5,9):
        return 2
    elif score in range(9,11):
        return 3
    else:
        return score
```

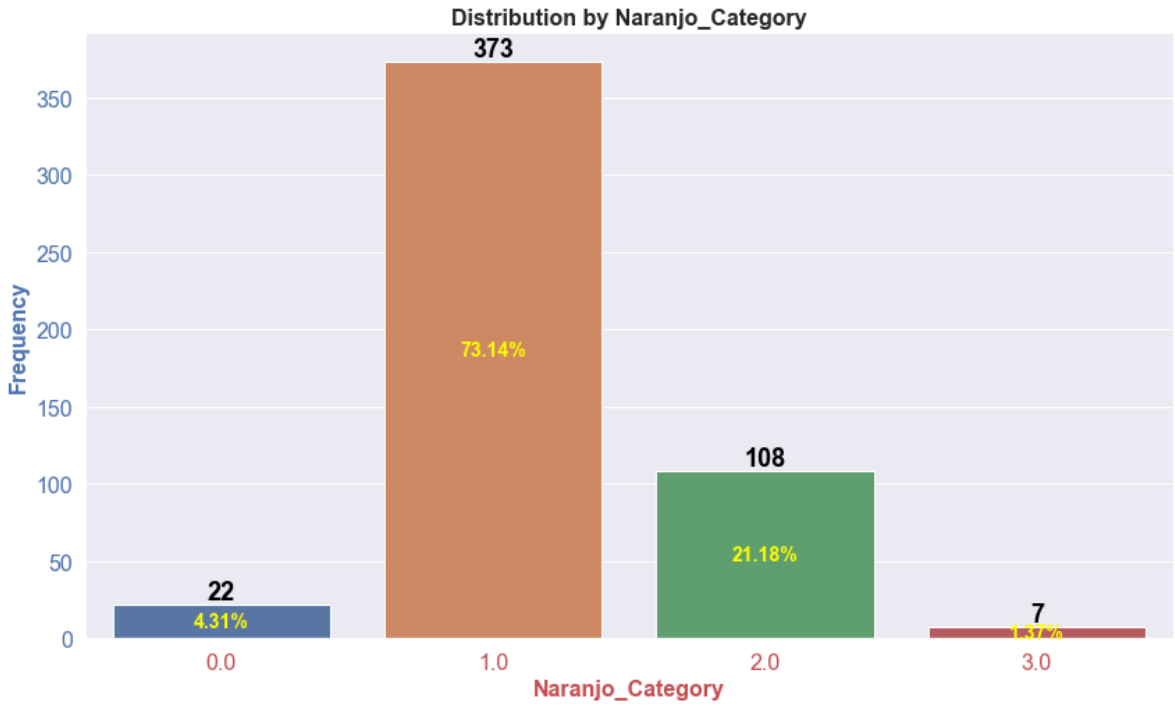
In [19]:
```
df.Naranjo_Category.fillna(value = df.Naranjo_Score.apply(Categoriz
e_Naranjo_Score), inplace =True)
df.iloc[493:494,:][['Naranjo_Score','Naranjo_Category']]
```

Out[19]:

	Naranjo_Score	Naranjo_Category
494	3.000	1.000

In [20]:
```
percent_countplot(df, col_name='Naranjo_Category',topn=0, dropna=Tr
ue)
```

Out[20]: <matplotlib.axes._subplots.AxesSubplot at 0x1a267fe750>



In [21]:
```
category_feature = ['Gender','Naranjo_Category', 'Steroid_Usage', '
Underlying_Condition_A', 'Underlying_Condition_B', 'Underlying_Cond
ition_C', 'Underlying_Condition_D', 'Underlying_Condition_E', 'Susp
icion_Score', 'Allergic_Reaction_Group', 'Drug_Group']
print(category_feature)
category_feature.remove('Naranjo_Category')
print(category_feature)
```

```
['Gender', 'Naranjo_Category', 'Steroid_Usage', 'Underlying_Condit
ion_A', 'Underlying_Condition_B', 'Underlying_Condition_C', 'Under
lying_Condition_D', 'Underlying_Condition_E', 'Suspicion_Score', '
Allergic_Reaction_Group', 'Drug_Group']
['Gender', 'Steroid_Usage', 'Underlying_Condition_A', 'Underlying_
Condition_B', 'Underlying_Condition_C', 'Underlying_Condition_D',
'Underlying_Condition_E', 'Suspicion_Score', 'Allergic_Reaction_Gr
oup', 'Drug_Group']
```

Imputation to Naranjo_Category

- One Hot Encoding & Oversampling
- Compare between result performance from Logistic Classifier and Naive Bayes classifier then choose the best classifier to impute Naranjo_Category.

> We found that Logistic Classifier has better performance than Naive Bayes classifier. Therfore, we impute missing value by Logistic Classifier.

In [22]:
```
pvalue = 0.05
feature_list_chi, feature_list_chi_score = chi2_indtest(df[category
_feature],df['Naranjo_Category'], pvalue = pvalue)
feature_list_chi
```

Out[22]:
```
['Underlying_Condition_A',
 'Underlying_Condition_B',
 'Underlying_Condition_D',
 'Allergic_Reaction_Group',
 'Drug_Group']
```

> Using only associated feature to Naranjo_Category to build the classifier to impute the missing value which is
>
> - 'Underlying_Condition_A',
> - 'Underlying_Condition_B',
> - 'Underlying_Condition_D',
> - 'Allergic_Reaction_Group',
> - 'Drug_Group'

In [23]:
```
# Define feature
print('Original data: ', df.shape)
df_temp_Naranjo_Category = df[feature_list_chi + ['Naranjo_Category
']].copy()
df_train = df_temp_Naranjo_Category.dropna(subset = ['Naranjo_Categ
ory'])

# Store unknown Naranjo_Category to df_unk
NaN_index = df_temp_Naranjo_Category[~df.index.isin(df_train.index)
].index
df_unk = df_temp_Naranjo_Category.loc[NaN_index] # Select index tha
t not in df_train


# Drop na row
df_train = df_temp_Naranjo_Category.dropna()
print('df_train dropna: ', df_train.shape)
print('Unknown Naranjo: ', df_unk.shape)

# Focus only Naranjo_Category class 1&2
df_train_w1_2 = df_train[df_train.Naranjo_Category.isin([1,2])]
print('Naranjo Cat1&2: ', df_train_w1_2.shape)

# Convert data type to category
df_train_cvt = cvt_type(df_train_w1_2, col_list=feature_list_chi)
X_data = df_train_cvt.drop('Naranjo_Category', axis= 1)
y_data = df_train_cvt[['Naranjo_Category']]

df_unk_cvt = cvt_type(df_unk, col_list=feature_list_chi)
X_unk_data = df_unk_cvt.drop('Naranjo_Category', axis= 1)

# Get dummies
X_encoded = pd.get_dummies(X_data, prefix_sep='_', drop_first=False
)
X_unk_encoded = pd.get_dummies(X_unk_data, prefix_sep='_', drop_fir
st=False)
print('Train encode: ', X_encoded.shape)
print('Class shape: ', y_data.shape)
print('Unknown encode: ', X_unk_encoded.shape)
```

```
Original data:  (798, 18)
df_train dropna:  (510, 6)
Unknown Naranjo:  (288, 6)
Naranjo Cat1&2:  (481, 6)
Train encode:  (481, 22)
Class shape:  (481, 1)
Unknown encode:  (288, 22)

/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/ipykernel_launcher.py:191: SettingWithCopyWarning:
A value is trying to be set on a copy of a slice from a DataFrame.
Try using .loc[row_indexer,col_indexer] = value instead

See the caveats in the documentation: http://pandas.pydata.org/pan
das-docs/stable/user_guide/indexing.html#returning-a-view-versus-a
-copy
```

In [24]:
```
X_resampled, y_resampled = makeOverSamplesADASYN(X_encoded,y_data)
print(y_resampled['Naranjo_Category'].value_counts())

from sklearn.linear_model import LogisticRegression
LogReg_clf = LogisticRegression(random_state=7, fit_intercept=False
)
LogReg_clf.fit(X_resampled, y_resampled)
print(accuracy_score(LogReg_clf.predict(X_resampled),y_resampled))
print(classification_report(LogReg_clf.predict(X_resampled),y_resam
pled))
```

```
Using TensorFlow backend.

2.000    383
1.000    373
Name: Naranjo_Category, dtype: int64
0.6415343915343915
              precision    recall  f1-score   support

         1.0       0.71      0.62      0.66       430
         2.0       0.57      0.67      0.62       326

    accuracy                           0.64       756
   macro avg       0.64      0.65      0.64       756
weighted avg       0.65      0.64      0.64       756


/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/utils/validation.py:760: DataConversionWarning: A c
olumn-vector y was passed when a 1d array was expected. Please cha
nge the shape of y to (n_samples, ), for example using ravel().
  y = column_or_1d(y, warn=True)
```

In [25]:
```
df['Naranjo_Category'][NaN_index] = LogReg_clf.predict(X_unk_encode
d)
df.Naranjo_Category.isnull().sum()
```

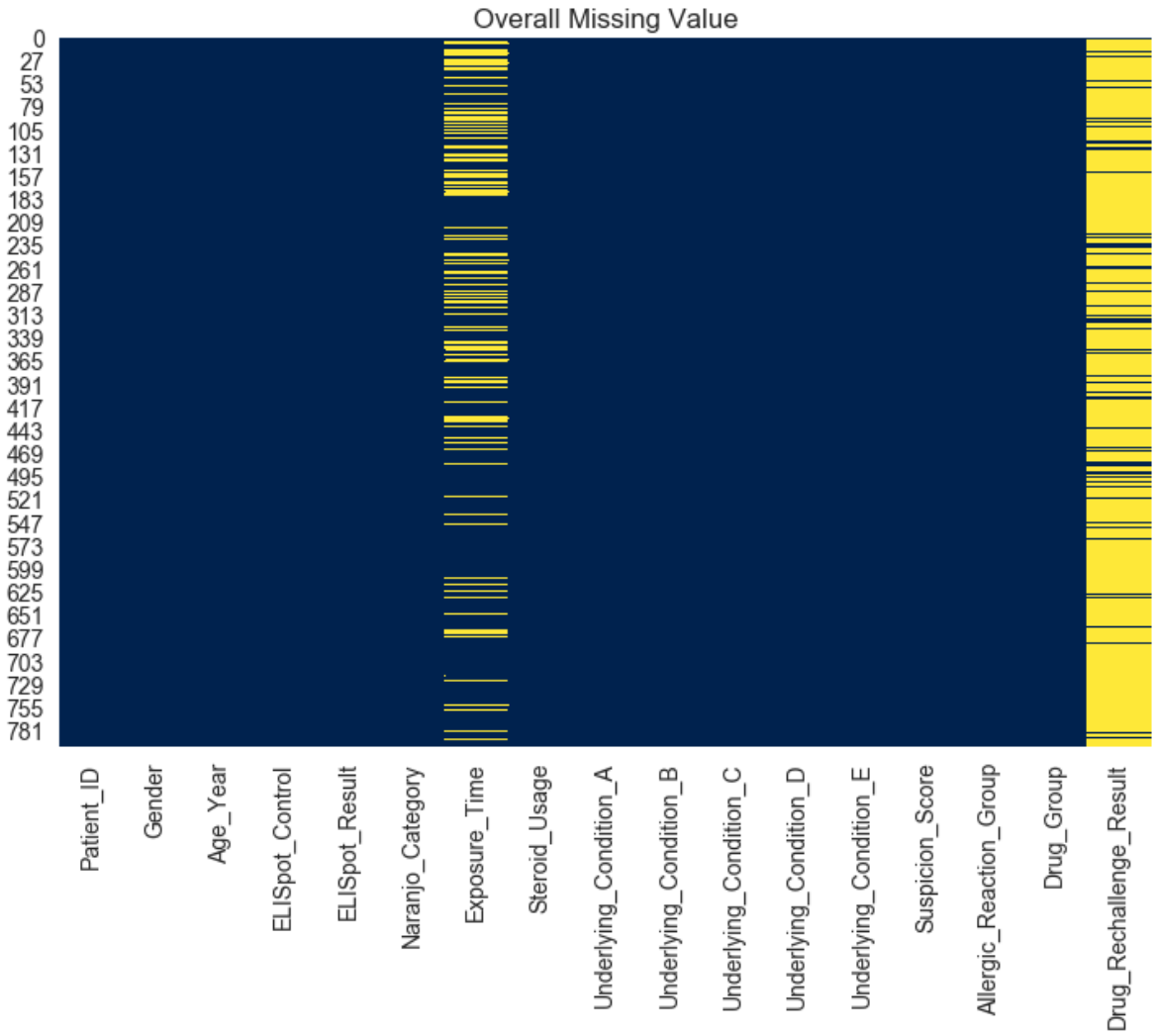
```
/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/ipykernel_launcher.py:1: SettingWithCopyWarning:
A value is trying to be set on a copy of a slice from a DataFrame

See the caveats in the documentation: http://pandas.pydata.org/pan
das-docs/stable/user_guide/indexing.html#returning-a-view-versus-a
-copy
  """Entry point for launching an IPython kernel.
```

Out[25]: 0

We will use only Naranjo_Category not Naranjo_Score. So, we can drop Naranjo_Score now

In [26]:
```
df.drop('Naranjo_Score', axis=1 ,inplace=True)
```

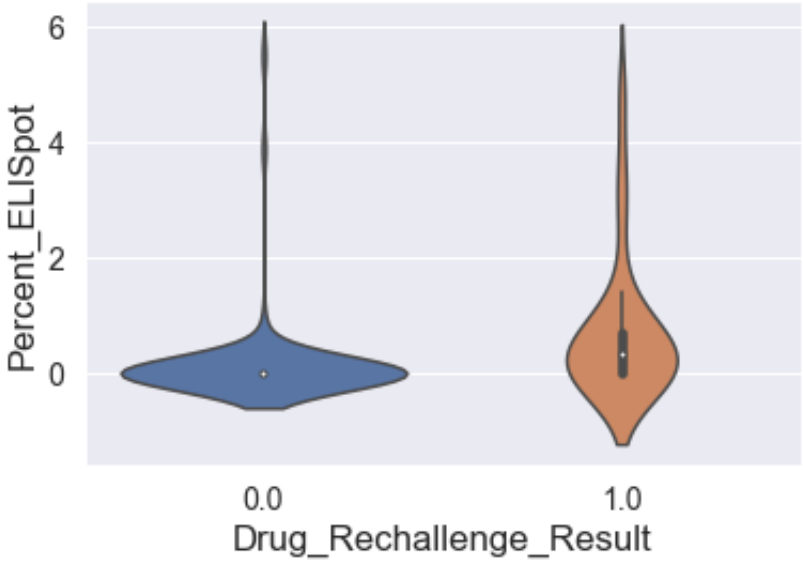
In [27]:
```
plt.figure(figsize=(12,8)); plt.title('Overall Missing Value')
sns.heatmap(df.isnull(), cbar=False, cmap = 'cividis');
```



Explore `ELISpot_Control` and `ELISpot_Result`

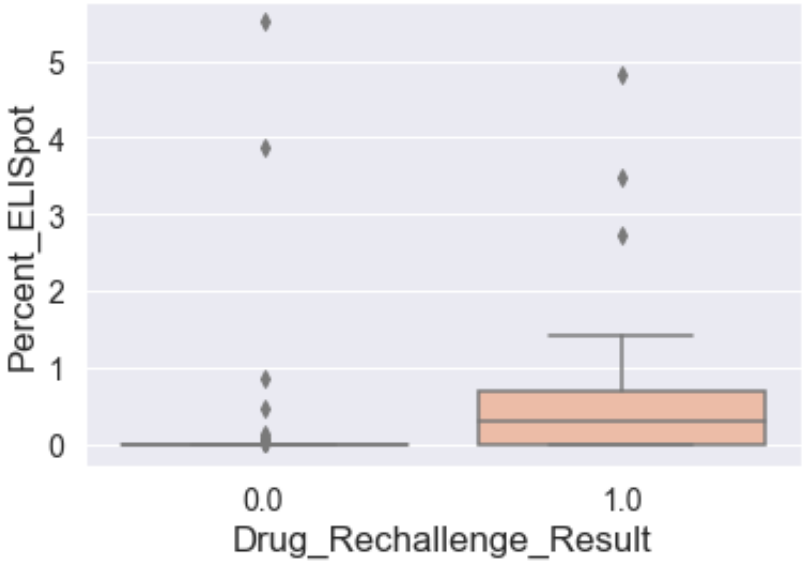
In [28]:
```
df_temp =df.copy()
df_temp['Percent_ELISpot'] = df_temp.ELISpot_Result / df_temp.ELISp
ot_Control *100

# remove outlier
df_temp = df_temp[df_temp['Percent_ELISpot']<10]

# Violinplot shows the kernel density estimation
# Bandwidth of the kernel shows the influence on theresulting estim
ate

sns.violinplot(x= "Drug_Rechallenge_Result", y ="Percent_ELISpot",
data=df_temp)
```

Out[28]: <matplotlib.axes._subplots.AxesSubplot at 0x1a37e7acd0>



In [29]:
```
sns.boxplot(x="Drug_Rechallenge_Result", y="Percent_ELISpot",data=d
f_temp, palette="coolwarm")
```

Out[29]: <matplotlib.axes._subplots.AxesSubplot at 0x1a37ed5e10>



In [30]:
```
from scipy import stats
data_0 = df_temp[df_temp.Drug_Rechallenge_Result == 0].Percent_ELIS
pot
data_1 = df_temp[df_temp.Drug_Rechallenge_Result == 1].Percent_ELIS
pot
stats.ttest_ind(data_0,data_1)
```

Out[30]:
```
Ttest_indResult(statistic=-2.9312655665515877, pvalue=0.0040999268
217664165)
```

Let calculate new feature is Percent_ELISpot which is the proportion of ELISpot_Result and ELISpot_Control. According to above figure, most patient with positive Drug_Rechallenge_Result has higher avearges of Percent_ELISpot than negative Drug_Rechallenge_Result significantly (p-value < 0.05) which mean we reject the null hypothesis of equal averages and conclude that the Percent_ELISpot of positive Drug_Rechallenge_Result has higher value than negative Drug_Rechallenge_Result.

Explore `Exposure_Time`

In [31]:
```
Exposure_Time_corr = df.corr()[['Exposure_Time']]
Exposure_Time_corr[np.abs(Exposure_Time_corr.Exposure_Time) > 0.1]
```

Out[31]:

	Exposure_Time
Exposure_Time	1.000
Underlying_Condition_D	0.123
Underlying_Condition_E	0.108

In [32]:
```
# Convert negative time to zero

ExT_neg_idx = df[df['Exposure_Time'] < 0][['Exposure_Time']].index

display(df.loc[ExT_neg_idx])

df.Exposure_Time = df.Exposure_Time.apply(lambda x: max(0,x))
df.loc[ExT_neg_idx]
```

	Patient_ID	Gender	Age_Year	ELISpot_Control	ELISpot_Result	Naranjo_Category	Ex
202	319	1	56	1664	0.000	1.000	
275	352	0	13	2060	0.000	0.000	

Out[32]:

	Patient_ID	Gender	Age_Year	ELISpot_Control	ELISpot_Result	Naranjo_Category	Ex
202	319	1	56	1664	0.000	1.000	
275	352	0	13	2060	0.000	0.000	

In [33]:
```
target = ['Drug_Rechallenge_Result']

selected_feature = df.columns.tolist()
selected_feature.remove('Patient_ID')
# selected_feature.remove('Percent_ELISpot')
selected_feature.remove('Drug_Rechallenge_Result')
print(selected_feature)
```

```
['Gender', 'Age_Year', 'ELISpot_Control', 'ELISpot_Result', 'Naran
jo_Category', 'Exposure_Time', 'Steroid_Usage', 'Underlying_Condit
ion_A', 'Underlying_Condition_B', 'Underlying_Condition_C', 'Under
lying_Condition_D', 'Underlying_Condition_E', 'Suspicion_Score', '
Allergic_Reaction_Group', 'Drug_Group']
```

In [34]:
```
df_Exposure_Time = df[selected_feature].copy()
df_Exposure_Time.head()
```

Out[34]:

	Gender	Age_Year	ELISpot_Control	ELISpot_Result	Naranjo_Category	Exposure_Time
0	1	26	2504	0.000	1.000	31.000
1	0	75	1868	51.000	2.000	1.000
2	0	81	1617	10.000	2.000	19.000
3	0	81	1617	10.000	2.000	19.000
4	1	60	3136	0.000	2.000	0.000

In [35]:
```
df_Exposure_Time = df[selected_feature].copy()
df_ExT_train = df_Exposure_Time.dropna(subset = ['Exposure_Time'])
df_ExT_unk = df_Exposure_Time.iloc[~df.index.isin(df_ExT_train.inde
x)] # Select index that not in df_train
print(df.shape)
print(df_ExT_train.shape)

# Drop na row
df_ExT_train = df_Exposure_Time.dropna()
print(df_ExT_train.shape)
print(df_ExT_unk.shape)
```

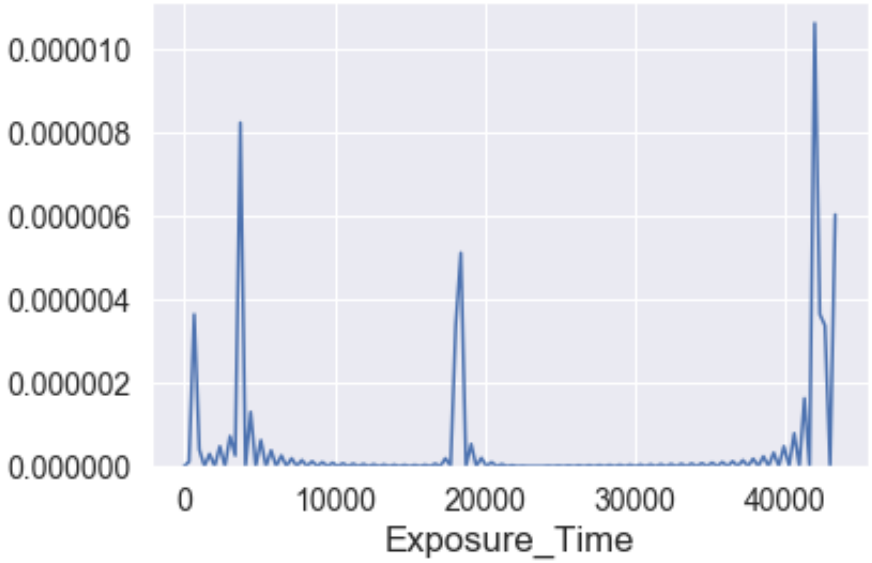
```
(798, 17)
(798, 15)
(798, 15)
(0, 15)
```

In [36]:
```
cat_col = ['Gender','Naranjo_Category', 'Steroid_Usage', 'Underlyin
g_Condition_A',
       'Underlying_Condition_B', 'Underlying_Condition_C',
       'Underlying_Condition_D', 'Underlying_Condition_E', 'Suspici
on_Score',
       'Allergic_Reaction_Group', 'Drug_Group']

df_train_cvt = cvt_type(df_ExT_train, col_list=cat_col)
X_ExT = df_train_cvt.drop('Exposure_Time',axis=1)
y_ExT = df_train_cvt[['Exposure_Time']]

# Get dummies
X_ExT_encoded = pd.get_dummies(X_ExT, prefix_sep='_', drop_first=Fa
lse)
print(X_ExT_encoded.shape)
```

```
(798, 40)
```

In [37]:
```
# understanding the data age distribution
sns.distplot(df_ExT_train["Exposure_Time"], bins=np.linspace(0,max(
df["Exposure_Time"]),1))
```

Out[37]: <matplotlib.axes._subplots.AxesSubplot at 0x1a37fe0210>



Regression imputation to Exposure_Time

In [38]:
```
from sklearn.linear_model import LinearRegression

lm = LinearRegression(fit_intercept = False)
lm.fit(X_ExT_encoded, y_ExT)

from sklearn import metrics
predictions = lm.predict(X_ExT_encoded)
y_test = y_ExT

print('MAE :'," ", metrics.mean_absolute_error(y_test,predictions))
print('MSE :'," ", metrics.mean_squared_error(y_test,predictions))
print('RMSE :'," ", np.sqrt(metrics.mean_squared_error(y_test,predi
ctions)))
print('R2 :'," ", metrics.r2_score(y_test,predictions))
```

```
MAE :   978.2083557385607
MSE :   10911643.984211002
RMSE :   3303.277763708496
R2 :   0.09118092740092809
```

Bad result from LinearRegression model

- Try to discretize Exposure_Time and impute value with classifier instead
- Discretize to 4 categories
  - < 1hr (60 min)
  - 1 - 6 hrs (60 - 360 mins)
  - 6 - 24 hrs (360 - 1440 mins)
  - > 24 hrs (1440 mins)

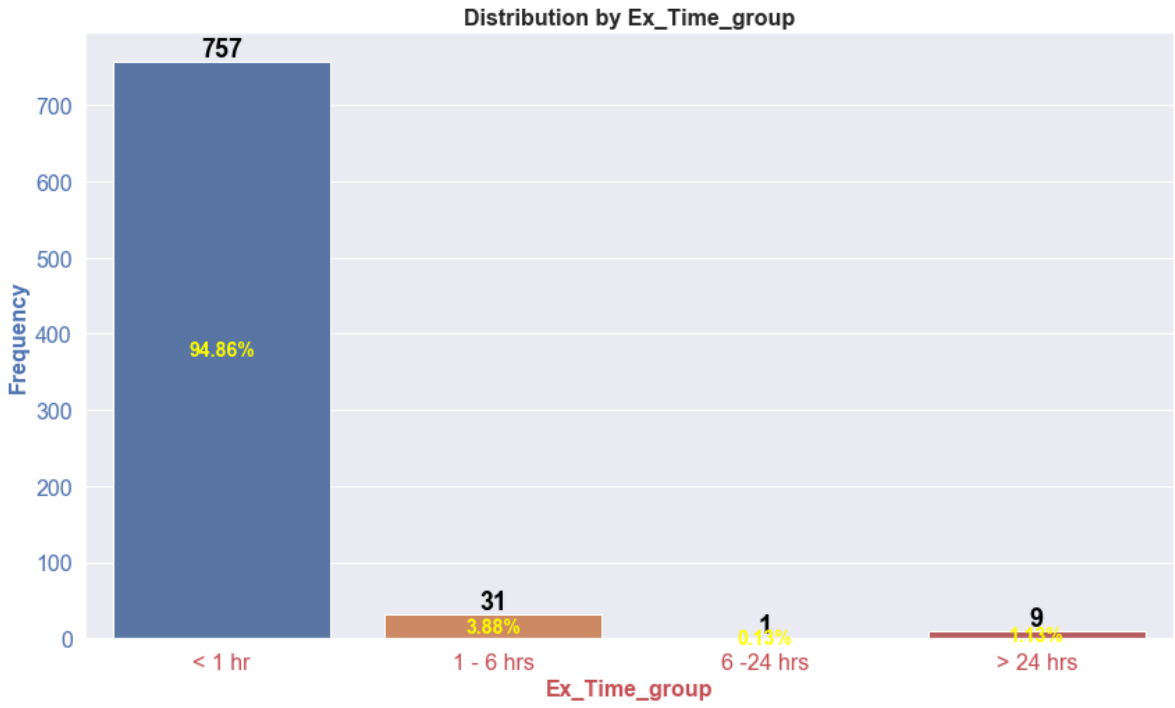
In [39]:
```
def discretize_time(time):
    if time < 60:
        return 0 #'less_1hr'
    elif 60 <= time < 360:
        return 1 #'1_6hrs'
    elif 360 <= time < 1440:
        return 2 #'6_24hrs'
    elif time >= 1440:
        return 3 #'over_24hrs'
    else:
        return time
```

In [40]:
```
df['Ex_Time_group'] = df.Exposure_Time.apply(discretize_time)
df.head()
```

Out[40]:

	Patient_ID	Gender	Age_Year	ELISpot_Control	ELISpot_Result	Naranjo_Category	Expo
0	2	1	26	2504	0.000	1.000	
1	7	0	75	1868	51.000	2.000	
2	13	0	81	1617	10.000	2.000	
3	13	0	81	1617	10.000	2.000	
4	18	1	60	3136	0.000	2.000	

In [41]:
```
# Exposure_Time in hour unit
ax = percent_countplot(df[["Ex_Time_group"]], col_name='Ex_Time_group', topn=0)

labels = ['< 1 hr', '1 - 6 hrs', '6 -24 hrs', '> 24 hrs']
# https://stackoverflow.com/questions/45056579/is-it-possible-to-format-the-labels-using-set-xticklabels-in-matplotlib
ax.set_xticklabels(labels);
```



Due to linear regression for predict Exposure_Time has low R-square (less than 0.10). I decide to drop Exposure_Time and use statistical imputation technique for Ex_Time_group instead.

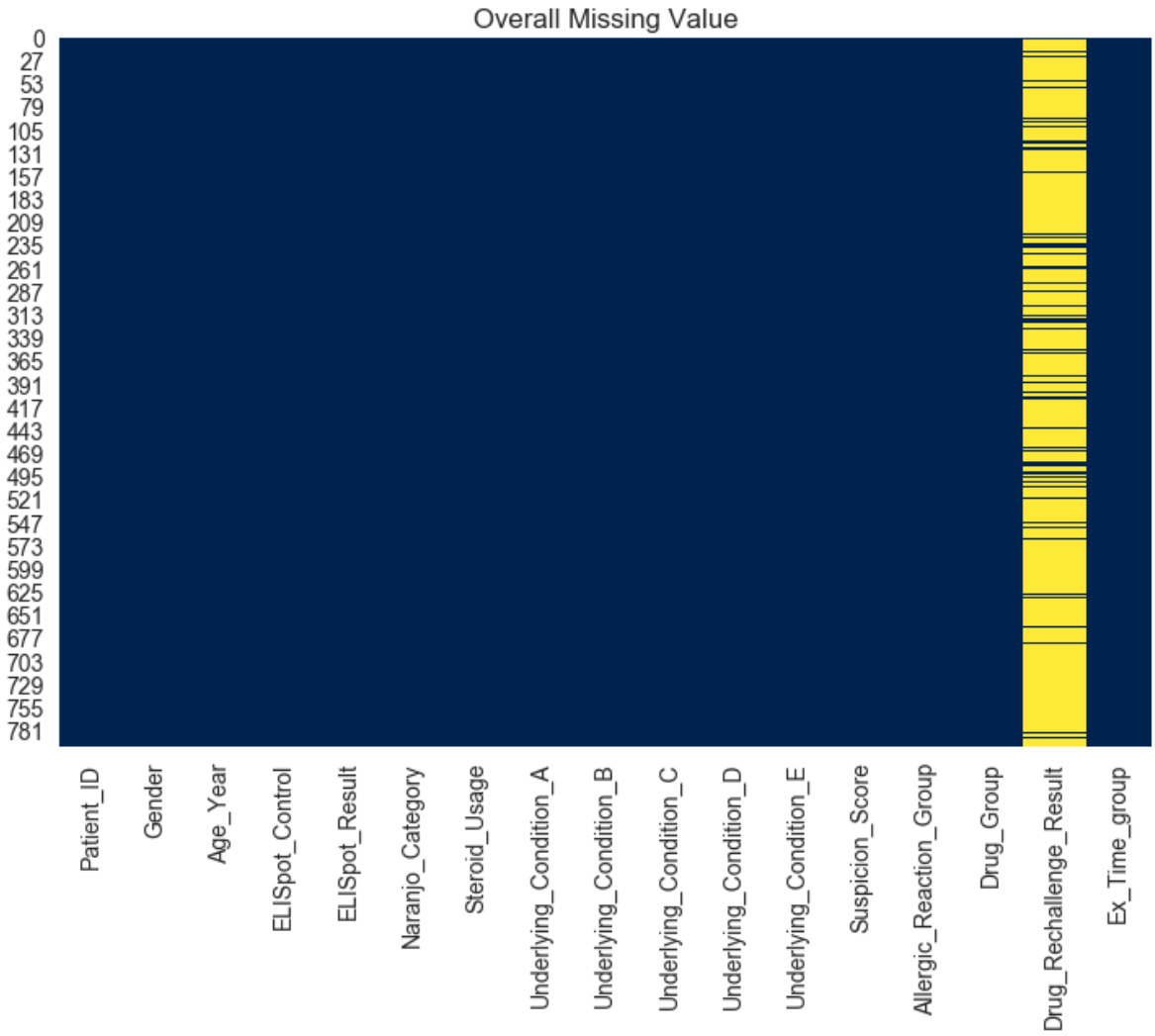
Imputation to Ex_Time_group

In [42]:
```
df.Ex_Time_group.fillna(df.Ex_Time_group.mode()[0], inplace=True)
```

We will use Ex_Time_group instead of Exposure_Time. So, we can drop Exposure_Time now

In [43]:
```
df.drop('Exposure_Time', axis=1 ,inplace=True)
```

In [44]:
```
plt.figure(figsize=(12,8)); plt.title('Overall Missing Value')
sns.heatmap(df.isnull(), cbar=False, cmap = 'cividis');
```



5. Developing model, Fine-tuning hyperparameters and Pseudo-labeling

Top

One Hot Encoding

In [45]:
```
cat_col = ['Gender', 'Naranjo_Category', 'Steroid_Usage', 'Underlyi
ng_Condition_A',
       'Underlying_Condition_B', 'Underlying_Condition_C',
       'Underlying_Condition_D', 'Underlying_Condition_E', 'Suspici
on_Score',
       'Allergic_Reaction_Group', 'Drug_Group','Ex_Time_group']

df_cat = cvt_type(df, col_list=cat_col)
df_cat.info()
```

```
<class 'pandas.core.frame.DataFrame'>
Int64Index: 798 entries, 0 to 798
Data columns (total 17 columns):
Patient_ID                  798 non-null int64
Gender                      798 non-null category
Age_Year                    798 non-null int64
ELISpot_Control             798 non-null int64
ELISpot_Result              798 non-null float64
Naranjo_Category            798 non-null category
Steroid_Usage               798 non-null category
Underlying_Condition_A      798 non-null category
Underlying_Condition_B      798 non-null category
Underlying_Condition_C      798 non-null category
Underlying_Condition_D      798 non-null category
Underlying_Condition_E      798 non-null category
Suspicion_Score             798 non-null category
Allergic_Reaction_Group     798 non-null category
Drug_Group                  798 non-null category
Drug_Rechallenge_Result     114 non-null float64
Ex_Time_group               798 non-null category
dtypes: category(12), float64(2), int64(3)
memory usage: 88.6 KB
```

In [46]:
```
print('Unique value')
for col in cat_col:
    print('{0:25}: {1:}'.format(col, df[col].unique().ravel()))
```

```
Unique value
Gender                    : [1 0]
Naranjo_Category          : [1 2 0 3]
Steroid_Usage             : [1 0]
Underlying_Condition_A    : [0 1]
Underlying_Condition_B    : [0 1]
Underlying_Condition_C    : [0 1]
Underlying_Condition_D    : [0 1]
Underlying_Condition_E    : [0 1]
Suspicion_Score           : [2 3 1]
Allergic_Reaction_Group   : [2 6 5 8 1 3 7 4]
Drug_Group                : [2 4 1 3 6 7 5 8]
Ex_Time_group             : [0 1 3 2]
```

In [47]:
```
# Get dummies
df_encoded = pd.get_dummies(df_cat, prefix_sep='_', drop_first=False)
print(df_encoded.shape)
df_encoded.head()
```

```
(798, 46)
```

Out[47]:

	Patient_ID	Age_Year	ELISpot_Control	ELISpot_Result	Drug_Rechallenge_Result	Gende
0	2	26	2504	0.000	nan	
1	7	75	1868	51.000	1.000	
2	13	81	1617	10.000	nan	
3	13	81	1617	10.000	nan	
4	18	60	3136	0.000	nan	

Split data to train and test set

In [48]:
```
df_data = df_encoded.dropna()
NaN_idx = ~df_encoded.index.isin(df_data.index) # Store [True, False] array
# NaN_index = df_encoded[~df_encoded.index.isin(df_data.index)].index # Store index
df_NaN = df_encoded[NaN_idx]
df_NaN.shape
```

Out[48]:
```
(684, 46)
```

In [49]:
```
# Split data to test set
df_test_pos = df_data[df_data.Drug_Rechallenge_Result == 1].sample(10,random_state=7)
df_test_neg = df_data[df_data.Drug_Rechallenge_Result == 0].sample(10,random_state=7)
df_test = pd.concat([df_test_pos,df_test_neg])
df_test_idx = df_test_pos.index.tolist() + df_test_neg.index.tolist()
print(df_test.shape)
df_test.Drug_Rechallenge_Result.value_counts()
```

```
(20, 46)
```

Out[49]:
```
0.000    10
1.000    10
Name: Drug_Rechallenge_Result, dtype: int64
```

In [50]:
```
# Split data to train set
df_train = df_data[~df_data.index.isin(df_test_idx)]
print(df_train.shape)
df_train.Drug_Rechallenge_Result.value_counts()
```

```
(94, 46)
```

Out[50]:
```
0.000    76
1.000    18
Name: Drug_Rechallenge_Result, dtype: int64
```

In [51]:
```
# Training set
X_encoded = df_train.drop(['Drug_Rechallenge_Result','Patient_ID'],
axis=1)
y_data = df_train[['Drug_Rechallenge_Result']]

# Test set
X_encoded_test = df_test.drop(['Drug_Rechallenge_Result','Patient_I
D'], axis=1)
y_data_test = df_test[['Drug_Rechallenge_Result']]
```

Develop and fine-tune model

- Logistic regression
- Naive Baye

In [52]:
```
score_param = 'accuracy' # Score for tune model
n_iter_search = 50 # Max candidate parameter for RandomizedSearchCV
cv = 5 # Number of k-fold cross validation
```

In [64]:

```
# Logistic regression
LogReg_rs, LogReg_gs = LogReg_HPTune_w_OverSam(X_encoded,y_data.values.ravel())

print(LogReg_gs.best_score_)
print(LogReg_gs.best_score_)
print(LogReg_gs.best_params_)
print(LogReg_gs.best_params_)

print('='*25)
print('Training set performance\n', y_data.Drug_Rechallenge_Result.value_counts())
print('='*25)
print(classification_report(LogReg_gs.predict(X_encoded),y_data))

print('='*25)
print('Test set performance\n', y_data_test.Drug_Rechallenge_Result.value_counts())
print('='*25)
print(classification_report(LogReg_gs.predict(X_encoded_test),y_data_test))

print(f"Average Accuracy: \t {LogReg_gs.best_score_:.4f}")
print(f"Accuracy SD: \t\t {LogReg_gs.cv_results_['std_test_score'][LogReg_gs.best_index_]:.4f}")
LogReg_gs.best_estimator_
```

```
/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/model_selection/_search.py:281: UserWarning: The to
tal space of parameters 3 is smaller than n_iter=50. Running 3 ite
rations. For exhaustive searches, use GridSearchCV.
  % (grid_size, self.n_iter, grid_size), UserWarning)

0.8609271523178808
0.8609271523178808
{'C': 2.442053094548651}
{'C': 2.442053094548651}
=========================
Training set performance
 0.000    76
1.000    18
Name: Drug_Rechallenge_Result, dtype: int64
=========================
              precision    recall  f1-score   support

         0.0       0.95      0.89      0.92        81
         1.0       0.50      0.69      0.58        13

    accuracy                           0.86        94
   macro avg       0.72      0.79      0.75        94
weighted avg       0.89      0.86      0.87        94

=========================
Test set performance
 0.000    10
1.000    10
Name: Drug_Rechallenge_Result, dtype: int64
=========================
              precision    recall  f1-score   support

         0.0       0.70      0.70      0.70        10
         1.0       0.70      0.70      0.70        10

    accuracy                           0.70        20
   macro avg       0.70      0.70      0.70        20
weighted avg       0.70      0.70      0.70        20

Average Accuracy:        0.8609
Accuracy SD:             0.0889
```

Out[64]:
```
LogisticRegression(C=2.442053094548651, class_weight=None, dual=Fa
lse,
                   fit_intercept=False, intercept_scaling=1, l1_ra
tio=None,
                   max_iter=1000, multi_class='auto', n_jobs=None,
penalty='l2',
                   random_state=7, solver='lbfgs', tol=0.0001, ver
bose=0,
                   warm_start=False)
```

In [65]:

```
# Naive Bayes
NB_rs, NB_gs = NB_HPTune_w_OverSam(X_encoded,y_data.values.ravel())

print(NB_gs.best_score_)
print(NB_gs.best_score_)
print(NB_gs.best_params_)
print(NB_gs.best_params_)

print('='*25)
print('Training set performance\n', y_data.Drug_Rechallenge_Result.
value_counts())
print('='*25)
print(classification_report(NB_gs.predict(X_encoded),y_data))

print('='*25)
print('Test set performance\n', y_data_test.Drug_Rechallenge_Result
.value_counts())
print('='*25)
print(classification_report(NB_gs.predict(X_encoded_test),y_data_te
st))

print(f"Average Accuracy: \t {NB_gs.best_score_:.4f}")
print(f"Accuracy SD: \t\t {NB_gs.cv_results_['std_test_score'][NB_g
s.best_index_]:.4f}")
NB_gs.best_estimator_
```

```
0.8211920529801324
0.8211920529801324
{'var_smoothing': 3.615414850916614e-07}
{'var_smoothing': 3.615414850916614e-07}
=========================
Training set performance
 0.000    76
1.000    18
Name: Drug_Rechallenge_Result, dtype: int64
=========================
              precision    recall  f1-score   support

         0.0       0.80      0.87      0.84        70
         1.0       0.50      0.38      0.43        24

    accuracy                           0.74        94
   macro avg       0.65      0.62      0.63        94
weighted avg       0.73      0.74      0.73        94

=========================
Test set performance
 0.000    10
1.000    10
Name: Drug_Rechallenge_Result, dtype: int64
=========================
              precision    recall  f1-score   support

         0.0       1.00      0.77      0.87        13
         1.0       0.70      1.00      0.82         7

    accuracy                           0.85        20
   macro avg       0.85      0.88      0.85        20
weighted avg       0.89      0.85      0.85        20

Average Accuracy:        0.8212
Accuracy SD:             0.1082
```

Out[65]:
```
GaussianNB(priors=None, var_smoothing=3.615414850916614e-07)
```

Although Naive Baye has higher accuracy than Logistic regression in the test set, however, it seems to overfit due to high standard deviation. Therefore, We decide to choose Logistic regression to be the base model for Pseudo-labeling.

Pseudo-labeling

In [66]:
```
# Logistic regression
start = time()

X_encoded_new, y_data_new, LogReg_gs_final = Pseudo_labeling(df_tra
in, df_NaN, LogReg_HPTune_w_OverSam, n_sam = 0.5)

t = time() - start
print('Execution time = ', t, ' seconds')
```

```
Initiate base model from training set....
(94, 44)
(94, 1)

/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/model_selection/_search.py:281: UserWarning: The to
tal space of parameters 3 is smaller than n_iter=50. Running 3 ite
rations. For exhaustive searches, use GridSearchCV.
  % (grid_size, self.n_iter, grid_size), UserWarning)

Start Pseudo-labeling Process
Round:  1
Processing....
(124, 44)
(124, 1)

/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/model_selection/_search.py:281: UserWarning: The to
tal space of parameters 3 is smaller than n_iter=50. Running 3 ite
rations. For exhaustive searches, use GridSearchCV.
  % (grid_size, self.n_iter, grid_size), UserWarning)
/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/linear_model/_logistic.py:940: ConvergenceWarning:
lbfgs failed to converge (status=1):
STOP: TOTAL NO. of ITERATIONS REACHED LIMIT.

Increase the number of iterations (max_iter) or scale the data as
shown in:
    https://scikit-learn.org/stable/modules/preprocessing.html
Please also refer to the documentation for alternative solver opti
ons:
    https://scikit-learn.org/stable/modules/linear_model.html#logi
stic-regression
  extra_warning_msg=_LOGISTIC_SOLVER_CONVERGENCE_MSG)
/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/linear_model/_logistic.py:940: ConvergenceWarning:
lbfgs failed to converge (status=1):
STOP: TOTAL NO. of ITERATIONS REACHED LIMIT.

Increase the number of iterations (max_iter) or scale the data as
shown in:
    https://scikit-learn.org/stable/modules/preprocessing.html
Please also refer to the documentation for alternative solver opti
ons:
    https://scikit-learn.org/stable/modules/linear_model.html#logi
stic-regression
  extra_warning_msg=_LOGISTIC_SOLVER_CONVERGENCE_MSG)
```

```
Training score:  0.8962264150943396
Test score:  0.7
Round:  2
Processing....
(169, 44)
(169, 1)

/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/model_selection/_search.py:281: UserWarning: The to
tal space of parameters 3 is smaller than n_iter=50. Running 3 ite
rations. For exhaustive searches, use GridSearchCV.
  % (grid_size, self.n_iter, grid_size), UserWarning)
/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/linear_model/_logistic.py:940: ConvergenceWarning:
lbfgs failed to converge (status=1):
STOP: TOTAL NO. of ITERATIONS REACHED LIMIT.

Increase the number of iterations (max_iter) or scale the data as
shown in:
    https://scikit-learn.org/stable/modules/preprocessing.html
Please also refer to the documentation for alternative solver opti
ons:
    https://scikit-learn.org/stable/modules/linear_model.html#logi
stic-regression
  extra_warning_msg=_LOGISTIC_SOLVER_CONVERGENCE_MSG)

Training score:  0.9178571428571428
Test score:  0.7
Round:  3
Processing....
(222, 44)
(222, 1)

/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/model_selection/_search.py:281: UserWarning: The to
tal space of parameters 3 is smaller than n_iter=50. Running 3 ite
rations. For exhaustive searches, use GridSearchCV.
  % (grid_size, self.n_iter, grid_size), UserWarning)

Training score:  0.9536784741144414
Test score:  0.7
Round:  4
Processing....
(300, 44)
(300, 1)
```

```
/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/model_selection/_search.py:281: UserWarning: The to
tal space of parameters 3 is smaller than n_iter=50. Running 3 ite
rations. For exhaustive searches, use GridSearchCV.
  % (grid_size, self.n_iter, grid_size), UserWarning)
/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/linear_model/_logistic.py:940: ConvergenceWarning:
lbfgs failed to converge (status=1):
STOP: TOTAL NO. of ITERATIONS REACHED LIMIT.

Increase the number of iterations (max_iter) or scale the data as
shown in:
    https://scikit-learn.org/stable/modules/preprocessing.html
Please also refer to the documentation for alternative solver opti
ons:
    https://scikit-learn.org/stable/modules/linear_model.html#logi
stic-regression
  extra_warning_msg=_LOGISTIC_SOLVER_CONVERGENCE_MSG)
/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/linear_model/_logistic.py:940: ConvergenceWarning:
lbfgs failed to converge (status=1):
STOP: TOTAL NO. of ITERATIONS REACHED LIMIT.

Increase the number of iterations (max_iter) or scale the data as
shown in:
    https://scikit-learn.org/stable/modules/preprocessing.html
Please also refer to the documentation for alternative solver opti
ons:
    https://scikit-learn.org/stable/modules/linear_model.html#logi
stic-regression
  extra_warning_msg=_LOGISTIC_SOLVER_CONVERGENCE_MSG)

Training score:  0.9715447154471545
Test score:  0.7
Round:  5
Processing....
(401, 44)
(401, 1)
```

```
/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/model_selection/_search.py:281: UserWarning: The to
tal space of parameters 3 is smaller than n_iter=50. Running 3 ite
rations. For exhaustive searches, use GridSearchCV.
  % (grid_size, self.n_iter, grid_size), UserWarning)
/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/linear_model/_logistic.py:940: ConvergenceWarning:
lbfgs failed to converge (status=1):
STOP: TOTAL NO. of ITERATIONS REACHED LIMIT.

Increase the number of iterations (max_iter) or scale the data as
shown in:
    https://scikit-learn.org/stable/modules/preprocessing.html
Please also refer to the documentation for alternative solver opti
ons:
    https://scikit-learn.org/stable/modules/linear_model.html#logi
stic-regression
  extra_warning_msg=_LOGISTIC_SOLVER_CONVERGENCE_MSG)
/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/linear_model/_logistic.py:940: ConvergenceWarning:
lbfgs failed to converge (status=1):
STOP: TOTAL NO. of ITERATIONS REACHED LIMIT.

Increase the number of iterations (max_iter) or scale the data as
shown in:
    https://scikit-learn.org/stable/modules/preprocessing.html
Please also refer to the documentation for alternative solver opti
ons:
    https://scikit-learn.org/stable/modules/linear_model.html#logi
stic-regression
  extra_warning_msg=_LOGISTIC_SOLVER_CONVERGENCE_MSG)

Training score:  0.9835796387520526
Test score:  0.7
Round:  6
Processing....
(539, 44)
(539, 1)

/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/model_selection/_search.py:281: UserWarning: The to
tal space of parameters 3 is smaller than n_iter=50. Running 3 ite
rations. For exhaustive searches, use GridSearchCV.
  % (grid_size, self.n_iter, grid_size), UserWarning)
/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/linear_model/_logistic.py:940: ConvergenceWarning:
lbfgs failed to converge (status=1):
STOP: TOTAL NO. of ITERATIONS REACHED LIMIT.

Increase the number of iterations (max_iter) or scale the data as
shown in:
    https://scikit-learn.org/stable/modules/preprocessing.html
Please also refer to the documentation for alternative solver opti
ons:
    https://scikit-learn.org/stable/modules/linear_model.html#logi
stic-regression
  extra_warning_msg=_LOGISTIC_SOLVER_CONVERGENCE_MSG)
```

```
Training score:  0.986335403726708
Test score:  0.7
=========== Finish ===========
(778, 44)
(778, 1)
Execution time =  248.56687903404236  seconds

/Users/PLoTAir/opt/anaconda3/envs/DS_project/lib/python3.7/site-pa
ckages/sklearn/linear_model/_logistic.py:940: ConvergenceWarning:
lbfgs failed to converge (status=1):
STOP: TOTAL NO. of ITERATIONS REACHED LIMIT.

Increase the number of iterations (max_iter) or scale the data as
shown in:
    https://scikit-learn.org/stable/modules/preprocessing.html
Please also refer to the documentation for alternative solver opti
ons:
    https://scikit-learn.org/stable/modules/linear_model.html#logi
stic-regression
  extra_warning_msg=_LOGISTIC_SOLVER_CONVERGENCE_MSG)
```

Final result

In [67]:
```
# Concat X_encoded_new and y_data_new
df_final = pd.concat([X_encoded_new, y_data_new],axis=1).sort_index
()
df_final_train = pd.concat([df['Patient_ID'],df_final],axis=1).drop
na()
df_final_train.head()
```

Out[67]:

	Patient_ID	Age_Year	ELISpot_Control	ELISpot_Result	Gender_0	Gender_1	Naranjo_Ca
0	2	26.000	2504.000	0.000	0.000	1.000	
1	7	75.000	1868.000	51.000	1.000	0.000	
2	13	81.000	1617.000	10.000	1.000	0.000	
3	13	81.000	1617.000	10.000	1.000	0.000	
4	18	60.000	3136.000	0.000	0.000	1.000	

In [68]:
```
# save the model to disk
filename = './Model/LogReg_gs_Pseudo_labeling.pkl'
pickle.dump(LogReg_gs_final, open(filename, 'wb'))

df_final_train.to_csv('./Model/df_final_train.csv', index=False)
```

In [69]:
```
# Load the model to disk
filename = './Model/LogReg_gs_Pseudo_labeling.pkl'
LogReg_gs_final = pickle.load(open(filename,"rb"))

df_final_train = pd.read_csv('./Model/df_final_train.csv')
```

In [70]:
```
X_encoded_new = df_final_train.drop(['Patient_ID', 'Drug_Rechalleng
e_Result'], axis =1)
y_data_new = df_final_train[['Drug_Rechallenge_Result']]
```

6. Evaluate Model Performance

Top

- Accuracy
- Balanced_Accuracy
- AUC
- Confusion Matrix
- Recall(Sensitivity)
- Precision
- Specifivity
- Average_Precision
- F1_score

In [74]:
```
print(LogReg_gs_final.best_score_)
print(LogReg_gs_final.best_score_)
print(LogReg_gs_final.best_params_)
print(LogReg_gs_final.best_params_)

print('='*25)
print('Training set performance\n', y_data_new.Drug_Rechallenge_Res
ult.value_counts())
print('='*25)
print(classification_report(LogReg_gs_final.predict(X_encoded_new),
y_data_new))

print('='*25)
print('Test set performance\n', y_data_test.Drug_Rechallenge_Result
.value_counts())
print('='*25)
print(classification_report(LogReg_gs_final.predict(X_encoded_test)
,y_data_test))

print(f"Average Accuracy: \t {LogReg_gs_final.best_score_:.4f}")
print(f"Accuracy SD: \t\t {LogReg_gs_final.cv_results_['std_test_sc
ore'][LogReg_gs.best_index_]:.4f}")

LogReg_gs_final.best_estimator_
```

```
0.9875776397515528
0.9875776397515528
{'C': 16.768329368110074}
{'C': 16.768329368110074}
==========================
Training set performance
 0.000    518
1.000    260
Name: Drug_Rechallenge_Result, dtype: int64
==========================
              precision    recall  f1-score   support

         0.0       1.00      0.99      0.99       524
         1.0       0.97      1.00      0.98       254

    accuracy                           0.99       778
   macro avg       0.99      0.99      0.99       778
weighted avg       0.99      0.99      0.99       778

==========================
Test set performance
 0.000    10
1.000    10
Name: Drug_Rechallenge_Result, dtype: int64
==========================
              precision    recall  f1-score   support

         0.0       0.70      0.70      0.70        10
         1.0       0.70      0.70      0.70        10

    accuracy                           0.70        20
   macro avg       0.70      0.70      0.70        20
weighted avg       0.70      0.70      0.70        20

Average Accuracy:        0.9876
Accuracy SD:             0.0273
```

Out[74]:
```
LogisticRegression(C=16.768329368110074, class_weight=None, dual=F
alse,
                   fit_intercept=False, intercept_scaling=1, l1_ra
tio=None,
                   max_iter=1000, multi_class='auto', n_jobs=None,
penalty='l2',
                   random_state=7, solver='lbfgs', tol=0.0001, ver
bose=0,
                   warm_start=False)
```

Model summary

In [72]:
```
model_List = ['Training set','Test set']
model_func = [LogReg_gs_final, LogReg_gs_final]
best_param_list = [LogReg_gs_final, LogReg_gs_final]
Feature_data = [X_encoded_new, X_encoded_test]
Target_data = [y_data_new, y_data_test]
model_report(Feature_data, Target_data, model_List, model_func, bes
t_param_clf = best_param_list)
```

Out[72]:

	LogReg_Model	Accuracy	Balanced_Accuracy	AUC	Confusion_Matrix	Confusion_Matri
0	Training set	0.990	0.990	1.000	{'TP': 253, 'FP': 1, 'FN': 7, 'TN': 517}	{'TP': '0.33', 'FI '0.0
1	Test set	0.700	0.700	0.590	{'TP': 7, 'FP': 3, 'FN': 3, 'TN': 7}	{'TP': '0.35', 'FI '0.1

Result

Top

According to model summary on testing data, the logistic regression with oversampling get the accuracy 99%. However, in test set, it get only 70%. For the coefficient rank , we found that Suspicion_Score_2 is the most important feature following by Drug_Group_2, Ex_Time_group_0, Allergic_Reaction_Group_2, Allergic_Reaction_Group_5, Drug_Group_5, and etc. respectively.

Coefficient rank

In [73]:
```
coef_dict = {}
coef_dict['intercept'] = LogReg_gs_final.best_estimator_.intercept_
.ravel()[0]
for coef, feat in zip(LogReg_gs_final.best_estimator_.coef_.ravel()
,X_encoded_new.columns):
    coef_dict[feat] = coef
display(sorted(coef_dict.items(), key= lambda kv:kv[1], reverse=Tru
e)[:15])
```

```
[('Suspicion_Score_2', 6.847875509119067),
 ('Drug_Group_2', 2.902104836335738),
 ('Ex_Time_group_0', 2.5667883692968676),
 ('Allergic_Reaction_Group_2', 2.550147601894827),
 ('Allergic_Reaction_Group_5', 2.541746124388258),
 ('Drug_Group_5', 1.4436977465612477),
 ('Underlying_Condition_A_1', 0.9503026508812268),
 ('Naranjo_Category_2', 0.8772092894911446),
 ('Allergic_Reaction_Group_4', 0.48948901248383875),
 ('Allergic_Reaction_Group_8', 0.4728632752284823),
 ('Drug_Group_4', 0.4536478815069558),
 ('Naranjo_Category_3', 0.2594754007767484),
 ('Underlying_Condition_B_0', 0.13496993642999955),
 ('ELISpot_Result', 0.04965579453736806),
 ('Age_Year', 0.008357656146612907)]
```

Analysis of Classification Error

Top

Due to limitation of time, then we did not perform for this task. However, in term of prediction error, as a result, the standard deviation of average accuracy in the logistic classifier is rather low. It means that the model has low variance and not has any overfitting issue. However, bias notwithstanding, value is rather high despite the low average accuracy in test set. It means that the model is underfitting; thus, we have a room for improving the performance which we mention in future direction section.

Conclusions, Limitations, and Discussion

Top

Conclusions

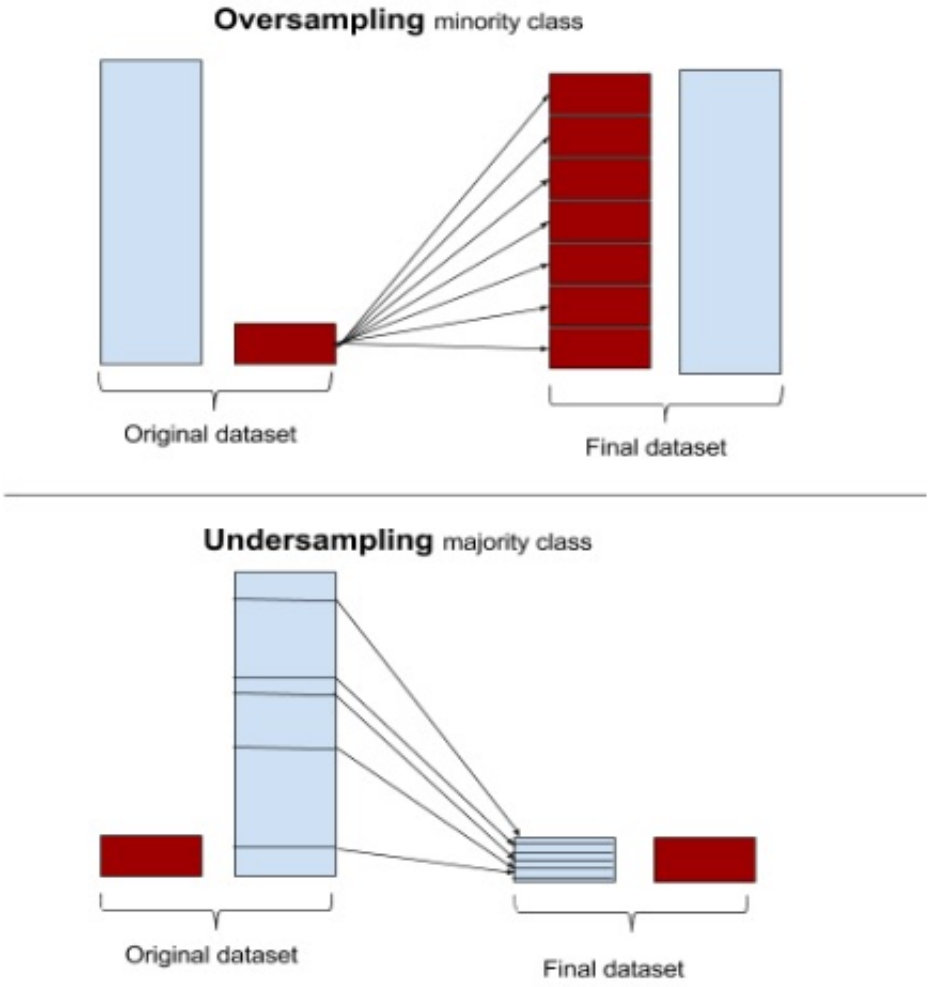
This study is a classification problem that focuses on the drug rechallenge result which all doctors want to avoid prescribing drugs that maybe allergic to the patients. Enzyme-linked immunospot (ELISpot) is a laboratory technique that tests whether the patient's immune cells will respond to particular drugs. This allows doctor to screen whether a drug is likely to be safe for the patient. However, as with any test, ELISpot is not perfect. Drugs that the patient is allergic to sometimes do not elicit any response in ELISpot test (False Negative) and vice versa. Due to point of concern is false negative which doctor try to avoid prescribing drugs that maybe allergic to the patients. Hence, the model evaluation should be based on positive class rather than negative class. The possible metrics to evaluate this model should mainly base on sensitivity. As the result from the model evaluation after developing the model, we found that logistic regression get the decent performance with sensitivity and specificity is 70% and 70% respectively.

Limitations

The limitation of this study is the data which is very highly missing value as well as the limitation of time and resource which can perform just a few classifier, few technique, and few candidate for develop and fine-tuning hyperparameter. These lead to the model performance is not as good as it could be and we might miss the better performance from the other classifier.

Discussion

Undersampling/Oversampling



source (https://towardsdatascience.com/breaking-the-curse-of-small-datasets-in-machine-learning-part-1-36f28b0c044d)

- In this experiment, the data has imbalanced classes issue, which can affect the model performance if we do not handle this issue before we develop the model. However, we should not interrupt the testing data distribution. On the other hand, we should do undersampling/oversampling on only the training data. By undersampling/oversampling only on the training data, none of the information in the validation data is being used to create synthetic observations. So these results should be generalizable.
- For this dataset we will perform overampling(uppersampling) because we have small dataset.

Evaluation

		Condition Phase (Worst Case)		
		Condition Positive/ Shaded	Condition Negative/ Unshaded	
Testing Phase (Best Case)	Test Positive/ Shaded	True positive shaded T_p (*Correct*)	False positive shaded F_p (*Incorrect*)	Precision/Positive Predictive Value (PPV) $\frac{T_p}{T_p + F_p}$ x 100%
	Test Negative/ Unshaded	False negative unshaded F_n (*Incorrect*)	True negative unshaded T_n (*Correct*)	Negative Predictive Value (NPV) $\frac{T_n}{T_n + F_n}$ x 100
		Sensitivity/Recall Rate (RR) $\frac{T_p}{T_p + F_n}$ x 100%	Specificity Rate (SR) $\frac{T_n}{T_n + F_p}$ x 100%	

$$\textbf{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN}$$

- When making a prediction for a two-class classification problem, the following types of errors can be made by a classifier:
  - False Positive (FP): predict an event when there was no event.
  - False Negative (FN): predict no event when in fact there was an event.
  - True Positive (TP): predict an event when there was an event.
  - True Negative (TN): predict no event when in fact there was no event.

- **Accuracy:** Accuracy tell us about the overall performance of the model.
- **Recall:** Recall gives us an idea about when it's actually yes, how often does it predict yes.
- **Precision:** Precision tells us about when it predicts yes, how often is it correct.
- **ROC Curves:** summarise the trade-off between the true positive rate and false positive rate for a predictive model using different probability thresholds.
- **Precision-Recall curves:** summarise the trade-off between the true positive rate and the positive predictive value for a predictive model using different probability thresholds.

Note that in computing precision and recall there is never use of the true negatives, these measures only consider correct predictions

- With imbalanced classes, it's easy to get a high accuracy without actually making useful predictions. So, accuracy as an evaluation metrics makes sense only if the class labels are uniformly distributed as well as ROC curves are appropriate when the observations are balanced between each class, whereas precision-recall curves are appropriate for imbalanced datasets. In both cases, the area under the curve (AUC) can be used as a summary of the model performance.
- As shown before when one has imbalanced classes, precision and recall are better metrics than accuracy, in the same way, for imbalanced datasets a Precision-Recall curve is more suitable than a ROC curve.

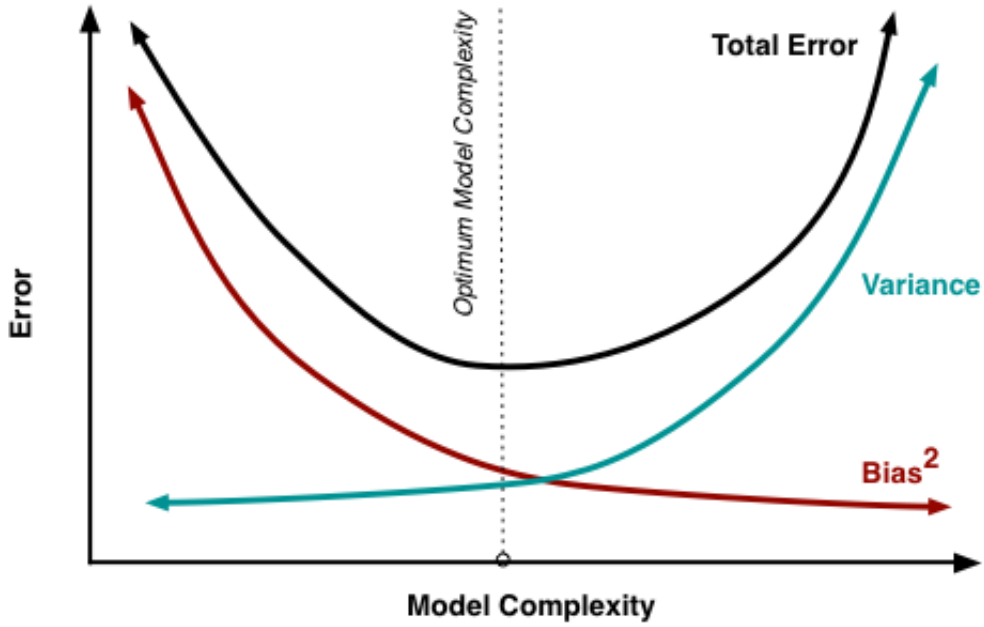
- However, for this Drug Allergy Prediction dataset, we tackle these issues by balancing the data in the test set. Therefore, we can use any metric to evaluate this ML experiment depend on the objective of the problem or point of concern from the result. For example, if false negative is point of concern from user, we should focus on Recall(Sensitivity). On the other hand if false positive is point of concern from user, we should focus on Specificity instead.

Prediction Error

Bias is the difference between the average prediction of our model and the correct value which we are trying to predict. Model with high bias pays very little attention to the training data and oversimplifies the model. It always leads to high error on training and test data.

Variance is the variability of model prediction for a given data point or a value which tells us spread of our data. Model with high variance pays a lot of attention to training data and does not generalize on the data which it hasn't seen before. As a result, such models perform very well on training data but has high error rates on test data.

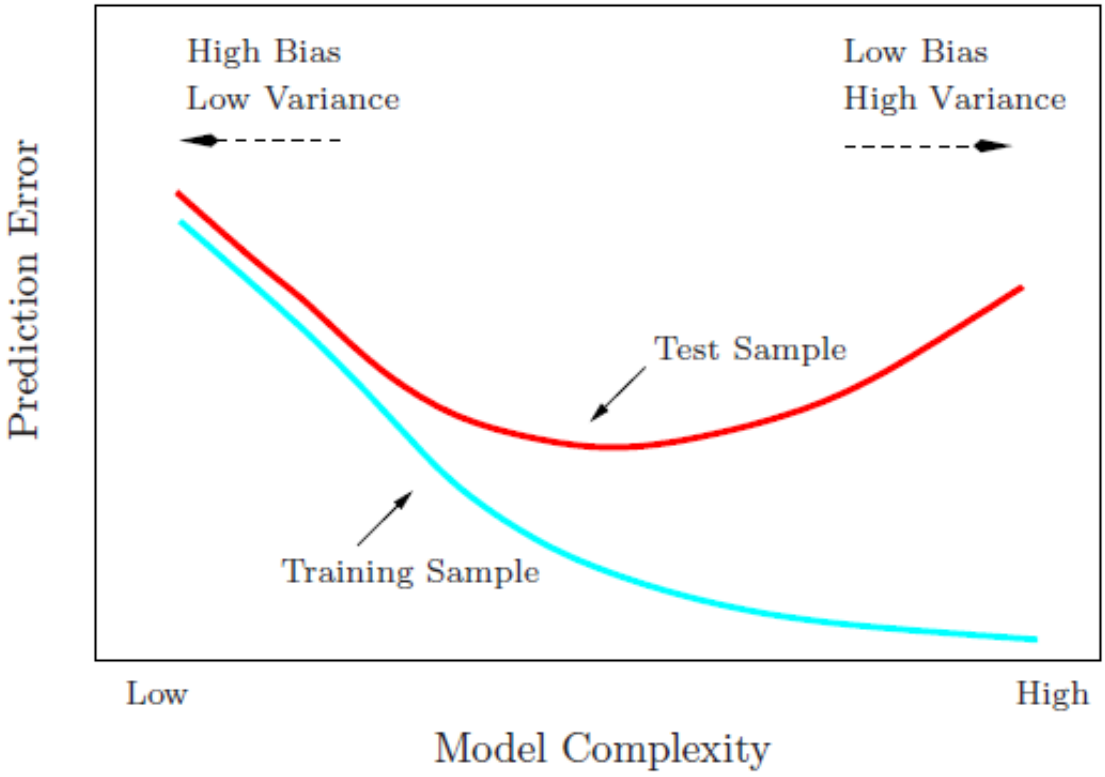
$$Err(x_i) = Bias^2 + Variance + IrreducibleError$$



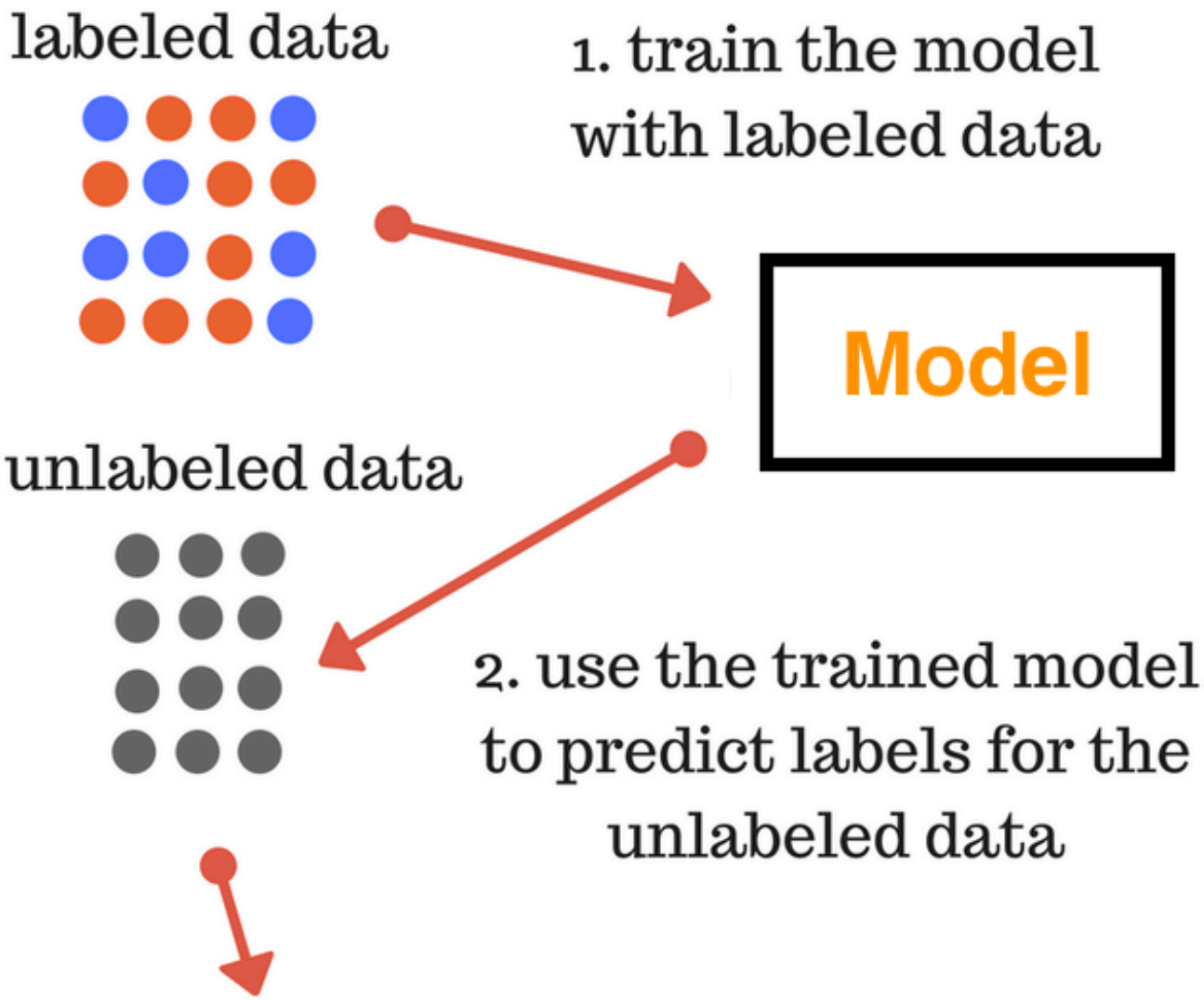
There is no escaping the relationship between bias and variance in machine learning.

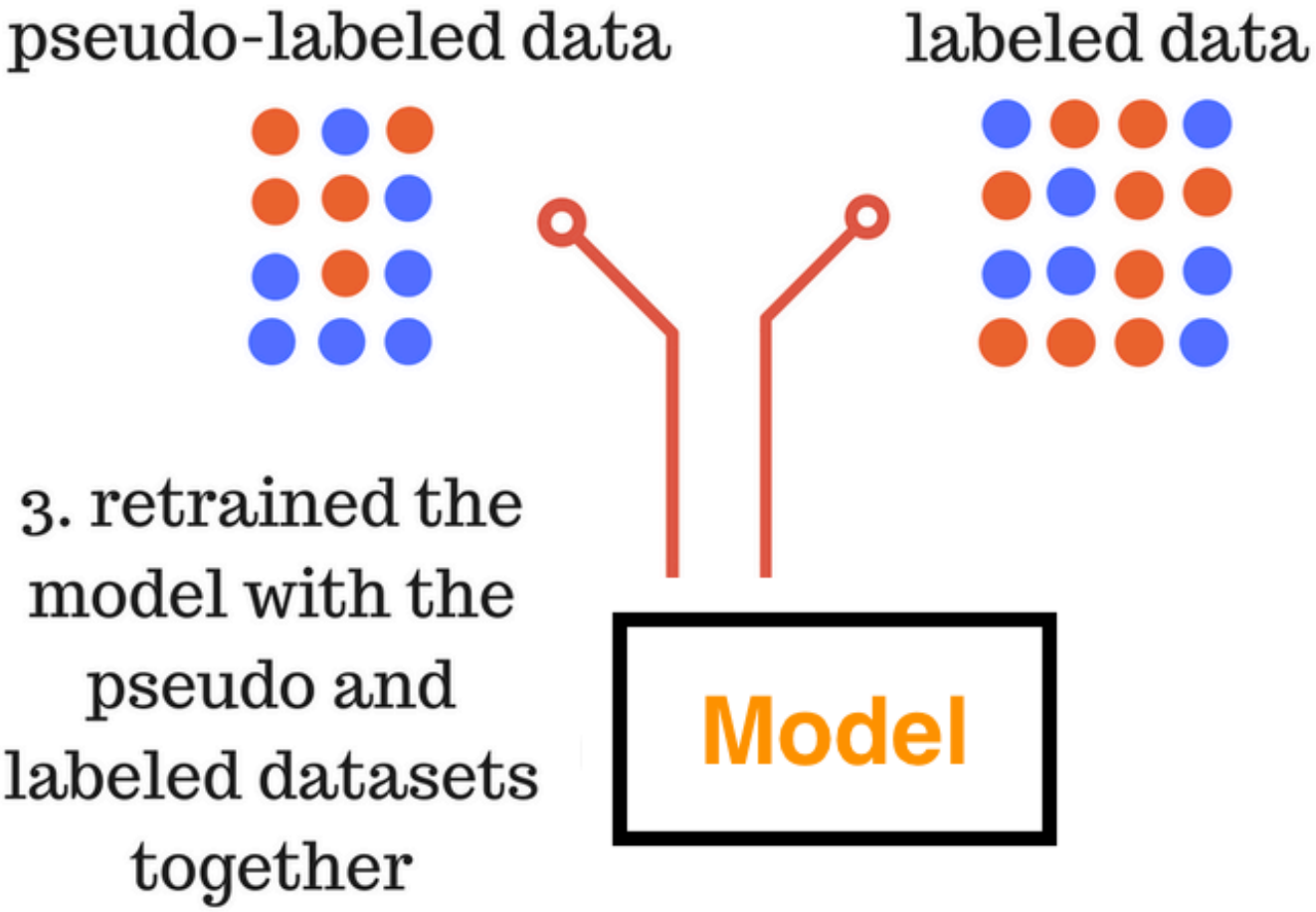
- Increasing the bias will decrease the variance.
- Increasing the variance will decrease the bias.

There is a trade-off at play between these two concerns and the algorithms you choose and the way you choose to configure them are finding different balances in this trade-off for your problem.



Pseudo-labeling





source (https://datawhatnow.com/pseudo-labeling-semi-supervised-learning/)

Future Direction

Top

- Feature engineering by perform standardize scaling, dimension reduction(PCA), and using polyfeature to see the interaction between variable.
- Add extra column with `An Extension To Imputation` Ref (https://www.kaggle.com/alexisbcook/missing-values). Due to the rows with missing values may be unique in some other way. In that case, our model would make better predictions by considering which values were originally missing.
- Splitting data by patient to make sure that a patient data only occur in one of the sets. This can prevent model memorizes the information of same patient or data leakage which refers to a mistake make by the creator of a machine learning model in which they accidentally share information between the test and training data-sets.
- Try more variety of classifiers to compare the performance.

Reference

Top

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