Supervised Learning Project - Genetic Variant Classification

January 26, 2021

1 Summary

The dataset for this project was collected from kaggle and originates from ClinVar. ClinVar is a public resource containing annotations about human genetic variants. These variants are classified by clinical laboratories on a categorical spectrum ranging from benign, likely benign, uncertain significance, likely pathogenic, and pathogenic. Variants that have conflicting classifications (from laboratory to laboratory) can cause confusion when clinicians or researchers try to interpret whether the variant has an impact on the disease of a given patient.

The objective is to predict whether a ClinVar variant will have conflicting classifications. This is presented here as a binary classification problem, where each record in the dataset is a genetic variant.

Conflicting classifications are when two of any of the following three categories are present for one variant, two submissions of one category are not considered conflicting.

- Likely Benign or Benign
- VUS
- Likely Pathogenic or Pathogenic

Conflicting classification has been assigned to the CLASS column. It is a binary representation of whether or not a variant has conflicting classifications, where **0** represents **consistent classifications** and **1** represents **conflicting classifications**.

In this project, we will employ four different classifier models to find the best candidate algorithm that accurately predicts whether a ClinVar variant will have conflicting classifications.

2 Exploratory Data Analysis

```
from sklearn.metrics import confusion matrix, accuracy score, u
      →classification_report, precision_score, f1_score, roc_auc_score
     from sklearn.linear_model import LogisticRegression
     from sklearn.tree import DecisionTreeClassifier
     from sklearn.ensemble import RandomForestClassifier
     from sklearn.metrics import precision recall fscore support as score
     # Mute the sklearn and IPython warnings
     import warnings
     warnings.filterwarnings('ignore', module='sklearn')
     warnings.filterwarnings('ignore', module='IPython')
[2]: data = pd.read_csv('./clinvar_conflicting.csv', sep=',')
     data.head()
                                        AF_EXAC
       CHR.OM
                              AF ESP
[2]:
                  POS REF ALT
                                                AF_TGP
           1 1168180
                        G
                               0.0771
                                        0.10020
                                                 0.1066
           1 1470752
                             A 0.0000 0.00000 0.0000
     1
                        G
     2
                             G 0.0000
                                        0.00001 0.0000
           1 1737942
                         Α
     3
           1 2160305
                             A 0.0000 0.00000
                                                 0.0000
           1 2160305
                             T 0.0000 0.00000 0.0000
                                                  CLNDISDB CLNDISDBINCL
     0
                                           MedGen: CN169374
                                                                     NaN
     1 MedGen: C1843891, OMIM: 607454, Orphanet: ORPHA9877...
                                                                   NaN
     2 Human Phenotype Ontology: HP: 0000486, MedGen: C00...
                                                                   NaN
     3 MedGen: C1321551, OMIM: 182212, SNOMED_CT: 83092002...
                                                                   NaN
     4
           MedGen: C1321551, OMIM: 182212, SNOMED_CT: 83092002
                                                                     NaN
                                                      CLNDN ...
     0
                                             not_specified ...
     1
                   Spinocerebellar_ataxia_21|not_provided ...
     2
        Strabismus | Nystagmus | Hypothyroidism | Intellectu... ...
     3
                Shprintzen-Goldberg_syndrome|not_provided ...
     4
                              Shprintzen-Goldberg_syndrome ...
                               SIFT
                                              PolyPhen MOTIF_NAME MOTIF_POS
     0
                         tolerated
                                                 benign
                                                               NaN
                                                                          NaN
     1
        deleterious_low_confidence
                                                 benign
                                                               NaN
                                                                          NaN
     2
                                                               NaN
                       deleterious
                                     probably_damaging
                                                                          NaN
     3
                                NaN
                                                    NaN
                                                               NaN
                                                                         NaN
     4
                                NaN
                                                    NaN
                                                                         NaN
                                                               NaN
       HIGH_INF_POS MOTIF_SCORE_CHANGE LoFtool
                                                  CADD PHRED CADD RAW BLOSUM62
     0
                NaN
                                    NaN
                                             NaN
                                                        1.053 -0.208682
                                                                              2.0
     1
                NaN
                                    NaN
                                             NaN
                                                       31.000 6.517838
                                                                             -3.0
     2
                NaN
                                    NaN
                                             NaN
                                                       28.100 6.061752
                                                                             -1.0
```

```
3 NaN NaN NaN 22.500 3.114491 NaN 4 NaN NaN NaN NaN 24.700 4.766224 -3.0
```

[5 rows x 46 columns]

```
[3]: data.shape
```

[3]: (65188, 46)

We have a lot more consistent than conflicting classifications.

```
[4]: data.CLASS.value_counts()
```

[4]: 0 48754 1 16434

Name: CLASS, dtype: int64

[5]: pd.DataFrame([[i, len(data[i].unique())] for i in data.columns], columns=['Variable', 'Unique Values']).set_index('Variable')

[5]: Unique Values Variable CHROM 38 POS 63115 REF 866 ALT 458 AF_ESP 2842 AF_EXAC 6667 AF_TGP 2087 CLNDISDB 9234 CLNDISDBINCL 94 CLNDN 9260 CLNDNINCL 102 CLNHGVS 65188 CLNSIGINCL 138 CLNVC 7 CLNVI 27655 MC 91 ORIGIN 31 SSR 3 2 CLASS Allele 374 Consequence 48 IMPACT 4 SYMBOL 2329 3 Feature_type Feature 2370 BIOTYPE 3

EXON	3265
INTRON	1930
cDNA_position	13971
CDS_position	13664
Protein_position	7340
Amino_acids	1263
Codons	2221
DISTANCE	97
STRAND	3
BAM_EDIT	3
SIFT	5
PolyPhen	5
MOTIF_NAME	3
MOTIF_POS	2
HIGH_INF_POS	2
MOTIF_SCORE_CHANGE	3
LoFtool	1196
CADD_PHRED	9325
CADD_RAW	63804
BLOSUM62	7

Dropping columns that have too many unique values and therefore they do not carry any information.

```
[7]: pd.DataFrame([[i, len(data[i].unique())] for i in data.columns], columns=['Variable', 'Unique Values']).set_index('Variable')
```

[7]:		Unique	Values
	Variable		
	CHROM		38
	REF		866
	ALT		458
	AF_ESP		2842
	AF_TGP		2087
	CLNDISDBINCL		94
	CLNDNINCL		102
	CLNSIGINCL		138
	CLNVC		7
	MC		91
	ORIGIN		31
	SSR		3

CLASS	2
Allele	374
Consequence	48
IMPACT	4
SYMBOL	2329
Feature_type	3
Feature	2370
BIOTYPE	3
INTRON	1930
Amino_acids	1263
Codons	2221
DISTANCE	97
STRAND	3
BAM_EDIT	3
SIFT	5
PolyPhen	5
MOTIF_NAME	3
MOTIF_POS	2
HIGH_INF_POS	2
MOTIF_SCORE_CHANGE	3
LoFtool	1196
BLOSUM62	7

2.1 Featureset Exploration

CHROM: Chromosome the variant is located on

 \mathbf{REF} : Reference Allele

ALT: Alternaete Allele

AF ESP: Allele frequencies from GO-ESP

AF_EXAC: Allele frequencies from ExAC

AF_TGP: Allele frequencies from the 1000 genomes project

CLNDISDB: Tag-value pairs of disease database name and identifier, e.g. OMIM:NNNNNN

 $\begin{tabular}{ll} \bf CLNDISDBINCL: For included Variant: Tag-value pairs of disease database name and identifier, e.g. OMIM:NN \end{tabular}$

CLNDN: ClinVar's preferred disease name for the concept specified by disease identifiers in CLNDISDB

More information on many of the features can be found at these two links:

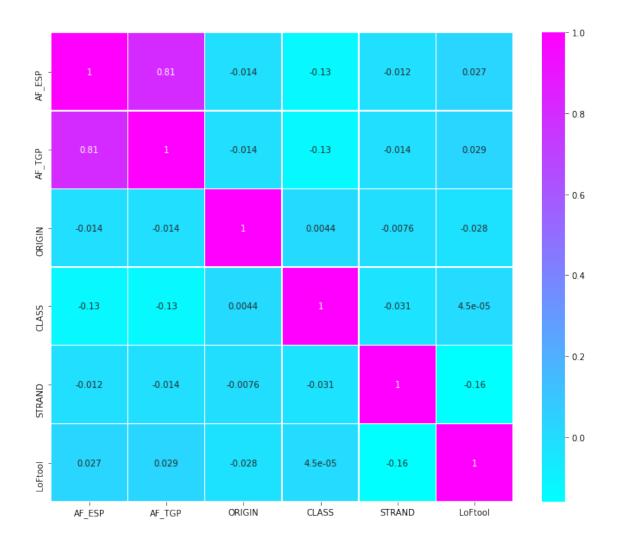
https://useast.ensembl.org/info/docs/tools/vep/vep_formats.html#output

https://useast.ensembl.org/info/genome/variation/prediction/predicted_data.html#consequences

```
[8]: num_missing = data.isnull().sum()
percentage_missing = data.isnull().sum().apply(lambda x: x/data.shape[0]*100)
```

```
[9]: missing_data = pd.DataFrame({'Number of Missing': num_missing,
                                    'Percentage of Missing': percentage_missing})
      missing_data['Percentage of Missing'].sort_values(ascending = False)
 [9]: MOTIF_SCORE_CHANGE
                             99.996932
      HIGH_INF_POS
                             99.996932
      MOTIF_POS
                             99.996932
      MOTIF_NAME
                             99.996932
      DISTANCE
                             99.834325
                             99.800577
      SSR
      CLNDISDBINCL
                             99.743818
      CLNSIGINCL
                             99.743818
      CLNDNINCL
                             99.743818
      INTRON
                             86.495981
      PolyPhen
                             61.962324
      SIFT
                             61.900963
      BLOSUM62
                             60.739707
      BAM_EDIT
                             50.958765
      Amino_acids
                             15.346383
      Codons
                             15.346383
      LoFtool
                              6.462846
      MC
                              1.297785
      SYMBOL
                              0.024544
      BIOTYPE
                              0.024544
                              0.021476
      Feature_type
      Feature
                              0.021476
      STRAND
                              0.021476
                              0.000000
      Consequence
      Allele
                              0.000000
      CLASS
                              0.000000
      IMPACT
                              0.000000
      ORIGIN
                              0.000000
      CLNVC
                              0.000000
      AF_TGP
                              0.000000
                              0.000000
      AF_ESP
      ALT
                              0.000000
      REF
                              0.000000
      CHROM
                              0.000000
      Name: Percentage of Missing, dtype: float64
     Drop the columns where more than 20% of the data is missing.
[10]: drop_list = list(missing_data[missing_data['Percentage of Missing'] >= 20].
       →index)
      data.drop(drop_list,axis = 1, inplace=True)
[11]: data.isnull().sum()
```

```
[11]: CHROM
                          0
      REF
                          0
      ALT
                          0
      AF_ESP
                          0
                          0
      AF_TGP
      CLNVC
                          0
      MC
                        846
      ORIGIN
                          0
      CLASS
                          0
      Allele
                          0
      Consequence
                          0
      IMPACT
                          0
      SYMBOL
                         16
      Feature_type
                         14
      Feature
                         14
      BIOTYPE
                         16
      Amino_acids
                      10004
      Codons
                      10004
      STRAND
                         14
      LoFtool
                       4213
      dtype: int64
[12]: plt.figure(figsize = (12, 10))
      sns.heatmap(data.corr(), annot = True, linewidths=.5, cmap = plt.cm.cool)
```



The correlation of **AF_ESP** with **AF_TGP** is above 0.8 hence dropping the **AF_TGP** column.

```
[13]: data.drop(['AF_TGP'],axis = 1, inplace=True)
[14]: # check the types
      df = pd.DataFrame(data.isnull().sum().astype(int), columns=['Null'])
      null_list = list(df[df['Null'] != 0].index)
      data[null_list].dtypes
[14]: MC
                       object
      SYMBOL
                       object
                       object
      Feature_type
      Feature
                       object
      BIOTYPE
                       object
      Amino_acids
                       object
      Codons
                       object
```

STRAND

float64

LoFtool float64 dtype: object

```
[15]: data[null_list].sample(5)
[15]:
                                        MC SYMBOL Feature_type
                                                                       Feature
      16552
            S0:0001819|synonymous_variant
                                                    Transcript
                                                               XM_005253733.1
                                             WNK1
              SO:0001583|missense_variant
      22550
                                           ESRRB
                                                    Transcript
                                                                XM_005267403.1
            S0:0001819|synonymous_variant
                                             JPH2
                                                    Transcript
      46034
                                                                   NM_020433.4
              S0:0001583|missense variant
                                             TTN
                                                    Transcript
                                                               NM 001267550.1
      42307
      60830
              S0:0001583|missense_variant
                                             PLEC
                                                    Transcript
                                                               XM_005250976.1
                   BIOTYPE Amino_acids
                                         Codons STRAND LoFtool
                                     Y taC/taT
      16552 protein coding
                                                     1.0 0.54000
            protein_coding
                                    P/L cCg/cTg
      22550
                                                     1.0 0.19300
      46034
            protein coding
                                     K aaG/aaA
                                                    -1.0
                                                              NaN
            protein_coding
                                    I/V Atc/Gtc
      42307
                                                    -1.0 0.97100
      60830 protein_coding
                                    A/T Gcc/Acc
                                                    -1.0 0.00999
```

3 Feature Transformation

- Replace nan in MC, SYMBOL, Feature_type, Feature, BIOTYPE, Amino_acids, Codons, STRAND with the most frequent value
- Replace nan in **LoFtool** with the mean

```
[16]: CHROM
                         0
      REF
                         0
      ALT
                         0
      AF_ESP
                         0
      CLNVC
                         0
      MC
                         0
      ORIGIN
                         0
      CLASS
                         0
      Allele
                         0
      Consequence
                         0
      IMPACT
                         0
      SYMBOL
                         0
      Feature_type
                         0
      Feature
                         0
```

```
BIOTYPE 0
Amino_acids 0
Codons 0
STRAND 0
LoFtool 0
dtype: int64
```

Now identify which variables are binary, categorical and ordinal by looking at the number of unique values each variable takes, then create list variables for categorical, numeric, binary, and ordinal variables.

```
[18]: #display the number of unique values for columns type object

df = data[object_columns_names]

df_uniques = pd.DataFrame([[i, len(df[i].unique())] for i in df.columns],

columns=['Variable', 'Unique Values']).

→set_index('Variable')
```

[19]: df_uniques

```
[19]:
                     Unique Values
      Variable
      CHROM
                                  38
      REF
                                866
      ALT
                                458
      CLNVC
                                   7
      MC
                                 90
      Allele
                                374
                                  48
      Consequence
      IMPACT
                                   4
      SYMBOL
                               2328
      Feature_type
                                   2
      Feature
                               2369
      BIOTYPE
                                   2
      Amino_acids
                               1262
      Codons
                               2220
```

```
[20]: binary_variables = list(df_uniques[df_uniques['Unique Values'] == 2].index) binary_variables
```

```
[20]: ['Feature_type', 'BIOTYPE']
```

```
[21]: categorical_variables = list(df_uniques[(df_uniques['Unique Values'] > 2)].

→index)

categorical_variables
```

```
[21]: ['CHROM',
       'REF',
       'ALT',
       'CLNVC',
       'MC',
       'Allele',
       'Consequence',
       'IMPACT',
       'SYMBOL',
       'Feature',
       'Amino_acids',
       'Codons']
[22]: for col in categorical_variables:
          data[col] = data[col].apply(lambda x: str(x))
      data[categorical_variables].dtypes
[22]: CHROM
                     object
      REF
                     object
      ALT
                     object
                     object
      CLNVC
     MC
                     object
      Allele
                     object
      Consequence
                     object
      IMPACT
                     object
      SYMBOL
                     object
      Feature
                     object
      Amino_acids
                     object
      Codons
                     object
      dtype: object
[23]: numeric_variables = list(set(data.columns) - set(categorical_variables) -___
      ⇒set(binary_variables))
      data[numeric_variables].dtypes
[23]: CLASS
                   int64
     LoFtool
                 float64
      STRAND
                 float64
      ORIGIN
                   int64
      AF ESP
                 float64
      dtype: object
[24]: lb, le = LabelBinarizer(), LabelEncoder()
      #encoding ordinary variables
      for col in categorical_variables:
```

```
data[col] = le.fit_transform(data[col])

# binary encoding binary variables
for col in binary_variables:
    data[col] = lb.fit_transform(data[col])
```

[25]: data.sample(3)

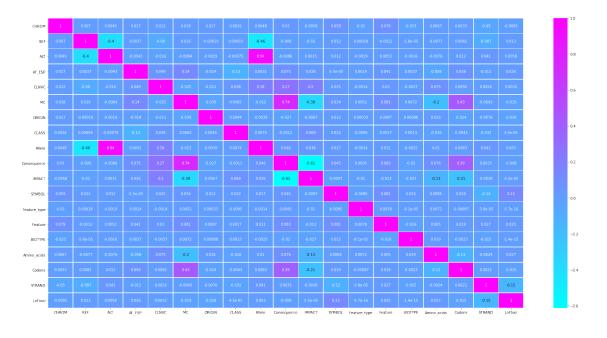
[25]:		CHROM	REF	ALT	AF_ESP	CLNVC	MC	ORIGIN	CLASS	Allele	Consequence	\
	29581	8	644	213	0.0	6	10	1	0	168	24	
	57695	19	644	106	0.0	6	81	1	0	88	31	
	21641	5	437	0	0.0	6	89	1	1	1	46	

	IMPACT	SYMBOL	${ t Feature_type}$	Feature	BIOTYPE	Amino_acids	Codons	
29581	0	1404	1	2104	1	78	1163	
57695	1	1430	1	1967	1	78	1163	
21641	1	1340	1	2251	1	201	1643	

STRAND LoFtool 29581 1.0 0.116000 57695 1.0 0.345058 21641 -1.0 0.068400

[26]: plt.figure(figsize = (30, 15))
sns.heatmap(data.corr(), annot = True, linewidths=.5, cmap = plt.cm.cool)

[26]: <AxesSubplot:>



The correlation of **ALT** with **Allele** and **MC** with **Consequence** are both above 0.8 hence dropping the **ALT** and **MC** columns.

```
[27]: data.drop(["ALT", "MC"],axis = 1, inplace=True)
    categorical_variables.remove('ALT')
    categorical_variables.remove("MC")
```

4 Apply Feature Scaling

```
[28]: mm = MinMaxScaler()
  for column in [categorical_variables + numeric_variables]:
          data[column] = mm.fit_transform(data[column])

[29]: # Save a copy of the processed data for later use
  outputfile = 'clinvar_conflicting_processed.csv'
     data.to_csv(outputfile, index=False)
```

5 Split the data

[32]: (19557, 45631)

Split the data into train and test data sets using **StratifiedShuffleSplit** to maintain the same ratio of predictor classes.

6 Train models

- Standard logistic regression, K-nearest neighbors algorithm, Decision Tree,mRandom Forest
- Plot the results using heatmaps
- Compare scores: precision, recall, accuracy, F1 score, auc

6.1 Logistic Regression

```
[33]: # create dataframe for metrics
      metrics = pd.DataFrame()
      # Standard logistic regression
      lr = LogisticRegression(solver='liblinear').fit(X_train, y_train)
      y_pred_lr = lr.predict(X_test)
      precision_lr, recall_lr = (round(float(x),2) for x in list(score(y_test,
                                                                           y_pred_lr,
      →average='weighted'))[:-2])
      # adding lr stats to metrics DataFrame
      lr_stats = pd.Series({'precision':precision_lr,
                            'recall':recall_lr,
                            'accuracy':round(accuracy_score(y_test, y_pred_lr), 2),
                            'flscore':round(fl_score(y_test, y_pred_lr), 2),
                            'auc': round(roc_auc_score(y_test, y_pred_lr),2)},
                           name='Logistic Regression')
      # Report outcomes
      pd.DataFrame(classification_report(y_test, y_pred_lr, output_dict=True)).iloc[:
       →3,:2]
```

```
[33]: 0.0 1.0 precision 0.747773 0.130435 recall 0.998633 0.000609 f1-score 0.855186 0.001211
```

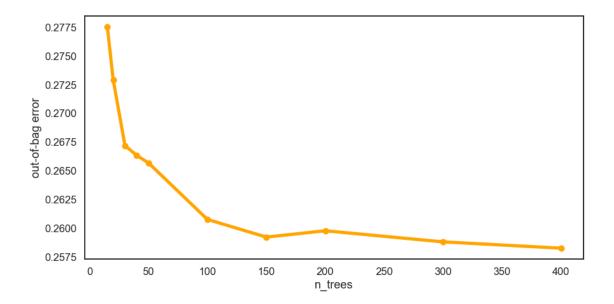
6.2 K-nearest Neighbors

```
# adding KNN stats to metrics DataFrame
      knn_stats = pd.Series({'precision':precision_knn,
                            'recall':recall_knn,
                            'accuracy':round(accuracy_score(y_test, y_pred_knn), 2),
                            'flscore':round(fl_score(y_test, y_pred_knn), 2),
                            'auc': round(roc_auc_score(y_test, y_pred_knn),2)},__
      →name='KNN')
      # Report outcomes
      pd.DataFrame(classification_report(y_test, y_pred_knn, output_dict=True)).iloc[:
       →3,:2]
[34]:
                      0.0
                                1.0
     precision 0.773786 0.349403
     recall
                0.817324 0.291075
      f1-score
                0.794960 0.317583
     6.3 Decision Tree
[35]: dt = DecisionTreeClassifier(random_state=42)
      dt = dt.fit(X_train, y_train)
      dt.tree_.node_count, dt.tree_.max_depth
[35]: (21179, 44)
[36]: y_train_pred = dt.predict(X_train)
      y_pred_dt = dt.predict(X_test)
      precision_dt, recall_dt = (round(float(x),2) for x in list(score(y_test,
                                                                      y_pred_dt,
      →average='weighted'))[:-2])
      # adding dt stats to metrics DataFrame
      dt_stats = pd.Series({'precision':precision_dt,
                            'recall':recall_dt,
                            'accuracy':round(accuracy_score(y_test, y_pred_dt), 2),
                            'flscore':round(fl_score(y_test, y_pred_dt), 2),
                            'auc': round(roc_auc_score(y_test, y_pred_dt),2)},__
      →name='Decision Tree')
      # Report outcomes
      pd.DataFrame(classification_report(y_test, y_pred_dt, output_dict=True)).iloc[:
       →3,:2]
[36]:
                      0.0
                                1.0
     precision 0.788235 0.381372
     recall
                0.803377 0.359635
      f1-score
                0.795734 0.370185
```

6.4 Random forest

ax.set(ylabel='out-of-bag error');

```
[37]: # Initialize the random forest estimator
      RF = RandomForestClassifier(oob_score=True,
                                  random_state=42,
                                  warm_start=True,
                                  n_jobs=-1
      # initialise list for out of bag error
      oob_list = list()
      # Iterate through all of the possibilities for number of trees
      for n_trees in [15, 20, 30, 40, 50, 100, 150, 200, 300, 400]:
          # Use this to set the number of trees
          RF.set_params(n_estimators=n_trees)
          # Fit the model
          RF.fit(X_train, y_train)
          # Get the out of bag error and store it
          oob_error = 1 - RF.oob_score_
          oob_list.append(pd.Series({'n_trees': n_trees, 'oob': oob_error}))
      rf_oob_df = pd.concat(oob_list, axis=1).T.set_index('n_trees')
[38]: sns.set context('talk')
      sns.set_style('white')
      ax = rf_oob_df.plot(legend=False, marker='o', color="orange", figsize=(14, 7),__
      →linewidth=5)
```

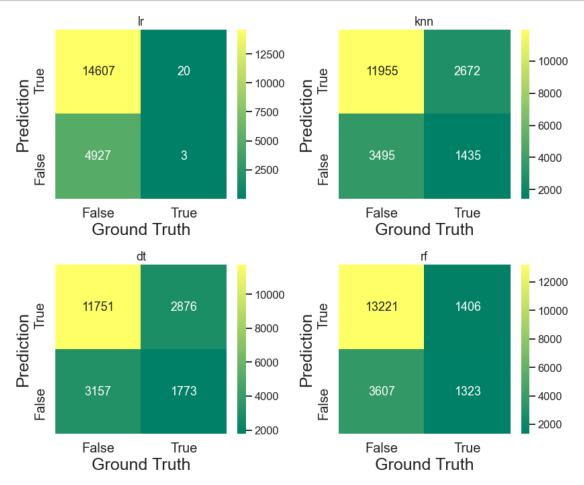


The error looks like it has stabilized around 100-150 trees.

```
[39]: rf = RF.set_params(n_estimators=100)
      y_pred_rf = rf.predict(X_test)
      precision rf, recall rf = (round(float(x),2) for x in list(score(y_test,
                                                                           y_pred_rf,
      →average='weighted'))[:-2])
      rf_stats = pd.Series({'precision':precision_rf,
                            'recall':recall_rf,
                            'accuracy':round(accuracy_score(y_test, y_pred_rf), 2),
                            'flscore':round(fl_score(y_test, y_pred_rf), 2),
                            'auc': round(roc_auc_score(y_test, y_pred_rf),2)},__
       →name='Random Forest')
      # Report outcomes
      pd.DataFrame(classification_report(y_test, y_pred_rf, output_dict=True)).iloc[:
       →3,:2]
[39]:
                      0.0
                                1.0
     precision 0.785655 0.484793
     recall
                 0.903876
                          0.268357
```

```
f1-score 0.840629 0.345476

[40]: fig, axList = plt.subplots(nrows=2, ncols=2)
axList = axList.flatten()
fig.set_size_inches(12, 10)
```



```
[41]: pd.DataFrame(classification_report(y_test, y_pred_lr, output_dict=True)).iloc[:
       →3,:2]
[41]:
                       0.0
                                  1.0
                 0.747773
                            0.130435
      precision
      recall
                  0.998633
                             0.000609
      f1-score
                  0.855186
                            0.001211
[42]: pd.DataFrame(classification_report(y_test, y_pred_knn, output_dict=True)).iloc[:
       \rightarrow3,:2]
[42]:
                       0.0
                                  1.0
                  0.773786
      precision
                             0.349403
      recall
                  0.817324
                             0.291075
      f1-score
                  0.794960
                            0.317583
[43]: pd.DataFrame(classification_report(y_test, y_pred_dt, output_dict=True)).iloc[:
       \hookrightarrow3,:2]
[43]:
                       0.0
                                  1.0
      precision
                  0.788235
                             0.381372
      recall
                  0.803377
                             0.359635
      f1-score
                  0.795734
                            0.370185
[44]: pd.DataFrame(classification_report(y_test, y_pred_rf, output_dict=True)).iloc[:
       →3,:2]
[44]:
                       0.0
                                  1.0
                 0.785655
      precision
                             0.484793
      recall
                  0.903876
                             0.268357
      f1-score
                  0.840629
                            0.345476
```

7 Results

Random Forest

The classification report of each classifier shows that I am able to predict consistent classification, with an F1 score of 0.855186 for **Logistic Regression** model. Similar result can be achieved using any of the model above. I predicted conflicting classification with F2 score 0.370185 with **Decision Tree** algorithm which is significantly better than the Logistic Regression with F1 score 0.001211.

There is a large amount of misclassification which can be seen on the average error report below.

```
[45]: metrics.append([lr_stats, knn_stats, dt_stats, rf_stats])
[45]:
                            precision recall
                                               accuracy
                                                          f1score
                                                                    auc
      Logistic Regression
                                 0.59
                                         0.75
                                                    0.75
                                                             0.00
                                                                   0.50
                                         0.68
      KNN
                                 0.67
                                                    0.68
                                                             0.32
                                                                   0.55
      Decision Tree
                                 0.69
                                         0.69
                                                    0.69
                                                             0.37
                                                                   0.58
```

0.74

0.71

0.74

0.59

0.35

8 Next Steps

We could further optimize these models by using **GridSearchCV** or **Boosting** algorithms. It took a significant amount of time when training AdaBoostClassifier so we might need to limit the amount of training data.