Data Analysis for Epileptic Seizure Prediction

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Abstract

Terminal remission – also known as epileptic seizure freedom at the end of follow-up by a pediatrician – will be analyzed using data analysis tools such as generalized linear models with Binomial distribution, classification trees, and random forests due to the binary nature of the response variable. The status of terminal remission is a binary data with no missing values and two levels: in remission and not in remission. The above data analysis techniques will be used to determine which factors – patient's sex, age at first seizure, health condition, types of seizures, socio-economic status of their family, etc. – are important in predicting terminal remission status. While trying to identify the key factors that affect the outcome of epilepsy, the said techniques will be discussed in depth by looking at their similarities, differences, advantages, and disadvantages.

Introduction

Children who have epilepsy can outgrow the condition or can control the condition with medication; thus, the main purpose of the analysis is to identify the key factors that affect the outcome of epilepsy. The dataset that will be used to answer that scientific question of interest is a collection of records on 554 children diagnosed with epilepsy provided by two retired pediatricians from the IWK Health Centre in Halifax, Nova Scotia. When in it comes keeping clinical records, it is a common practice to record all observations made during a clinical encounter. Although there are 451 variables in the data, only few of them carry some explanatory value; thus, a careful variable exploration and selection are required when working with medical data. In this case, the Exploratory Data Analysis will be the first step in making "an educated guess" and selecting the variables that might potentially be correlated with the terminal remission status. Later, the preselected variables will be used to fit a logistic regression model, to build a classification tree, and to grow a random forest.

Methods

Exploratory Data Analysis

Exploratory Data Analysis (EDA) should always be the first step taken in any data analysis project. It involves using graphical and descriptive tools that help to better understand the data before beginning any analysis. It tells what kind of model to use and what kind of assumptions to make. Examining the variables helps to catch mistakes, find patterns, discover potential outliers, and determine whether any of the assumptions made have been violated.

Although the analysis will be mainly carried out in Python, Excel is an efficient tool that can be used for visual inspection of the data due to its substantial size. Once the process of variable selection is done, the data visualization tools, such as bar plots, histograms, and boxplots, will be used to visualize the data. Most of the explanatory variables are categorical, but there are some continuous measures as well. The variable 'aedend' which stores the status of terminal remission should be inspected for any missing values.

Generalized Logistic Regression

The logistic regression – more specifically a generalized linear model with Binomial distribution – will be used to make a suitable model for predicting the response variable and to test the significance of the preselected input variables. First, all of the variables will be used to fit a so called full or null model, and then all of the redundant variables will be removed – one at a time based on the largest p-value – in order to arrive to the simplest yet the most efficient model based on AIC criterion. It is crucial to note that AIC by itself does not tell anything about the quality/goodness of a single model. It becomes useful in comparing several models between each other to identify the most effective one. The lower the AIC, the better the fit. AIC is calculated using the following formula:

AIC = 2k - 2(log-likelihood), where k is the number of parameters used in the model

The AIC criterion is very similar to R-squared, which penalizes the use of too many explanatory variables to improve the fit. Similarly, AIC goes up in case the model is too complex.

The model assumptions, such as observation independence, absence of multicollinearity, and balanced sample, should be checked after the model is fit. Splitting the data into train and test sets will allow us to calculate the classification accuracy rate, which will later be used to compare the three data analysis techniques. The goal is essentially to use the train set to train a model, and then use the test set to test the previously trained model.

Classification Tree

Classification tree, also known as CART, is a data analysis technique used to classify observations into classes of a categorical response variable based on the values of the input variables. When one fits linear models and GLMs, they need to make sure that appropriate distributional assumptions are made. They need to check that the residuals are independent and identically distributed from a normal distribution with mean zero and constant standard deviation for linear models; and need to specify the distribution of the response variable for GLMs. The main advantage of the CARTs is that they do not require making any distributional assumptions such as the ones mentioned above. In addition, the CARTs are easier to interpret and visualize, and they have a way to use observations with missing values (using surrogate splits) instead of simply removing them. The first step will be using the train set to build a classification tree, and then test the performance of the classification tree on the test set.

Further, the said classification tree can be pruned in order to reduce overfitting. Pruning a decision tree reduces its size by removing branches that "contribute the least"; thus, making it less complex and increasing its (test) classification accuracy. Although, the pruned classification tree might not fit or predict the train set as well as before, it will be easer to interpret a simpler tree.

Random Forest

In theory, random forest does a better job than classification trees because it consists of 500 reasonably uncorrelated trees and it uses the most frequent classification (something like majority vote) out of these 500 trees to make predictions. Due to the fact that every tree is trained on a different sample of data, the random forest is good at the reduction of overfitting.

As mentioned previously, decision trees are quite prone to overfitting; therefore, we use random forests in order to reduce the risk of overfitting. Since every tree in a random forest is trained on a different/random subset of the data, the trees are relatively uncorrelated and altogether produce a higher classification accuracy than a single decision tree. At the same time, single decision trees are easier to interpret and plot; and they can be plotted rather quickly. Unlike single classification trees, random forests cannot handle missing values and simply removes them.

Results

Symptomatic epilepsy is a type of epilepsy that caused by an injury to the brain as a result of significant head injury, CNS infection, stroke, brain tumor, surgery, etc. The bar charts in Figure 1 demonstrate that a significant proportion of patients who were diagnosed with symptomatic epilepsy are in remission; thus, this suggests that there might be a significant relationship which should be investigated further. The following frequency table clearly illustrates that relationship as well:

	Non-symptomatic	Symptomatic
In remission	156	57
Not in remission	315	26



Bar Charts of aedend and symptomatic

Figure 1. The bar charts for terminal remission status and

symptomatic seizure status

Although most of the input variables are categorical, the 'agefirst' variable is a continuous variable which indicates the age of a patient at first seizure which can be a variable of interest. The sideby-side boxplots in Figure 2 suggest that, on average, the patients in remission experience their first seizures at a slightly younger age and the spread of the ages is much larger for them; this also suggests a potential relationship.



Figure 2. The side-by-side boxplots of age at first seizure (in months) for two levels of terminal remission status

The previously mentioned variables and six more were chosen to be included in the null logistic regression model and the model summary is displayed in Figure 3. As it was predicted, the variables 'symptomatic' and 'agefirst' are significant at the significance level of alpha = 0.01; in addition, the variables 'generalized' – indicator variable for a type of epilepsy that occurs throughout the whole brain – and 'fu' – total follow-up from first seizure to last contact in months – show some potential to be significant in a reduced model. The summary of the null model is illustrated in Figure 3.

Optimization termin Current fu Iterations	ated suc nction 5	ccessfully value: 114	.569145					
		Kesults: L	ogit 					
Model: Dependent Variable: Date: No. Observations: Df Model: Df Residuals: Converged: No. Iterations:	Logit y 2020-0 554 8 545 1.0000 5.0000	4-20 10:06	Pseudo AIC: BIC: Log-Lik LL-Null LLR p-v Scale:	R-square celihood: L: value:	ed: inf 12696 12699 -6347 0.000 1.000 1.000	inf 126960.6128 126999.4673 -63471. 0.0000 1.0000 1.0000		
Со	ef. S	td.Err.	Z	P> z	[0.025	0.975]		
intercept -0. agefirst 0. symptomatic 1. sex -0. focal -0. fu -0. poor -0. adequate 0. generalized 0.	8361 0066 7685 0287 0806 0014 0339 0458 2808	0.5116 - 0.0019 0.5168 0.1866 - 0.4769 - 0.0009 - 0.2283 - 0.2273 0.5271	1.6344 3.4623 3.4223 0.1538 0.1689 1.5571 0.1487 0.2014 0.5328	0.1022 0.0005 0.0006 0.8777 0.8659 0.1194 0.8818 0.8404 0.5942	-1.8388 0.0029 0.7557 -0.3944 -1.0153 -0.0031 -0.4813 -0.3998 -0.7522	0.1665 0.0103 2.7813 0.3370 0.8542 0.0004 0.4135 0.4914 1.3139		

Figure 3. The summary of the null GLM model

The said reduced model is obtained by manually removing the insignificant variables one at a time and its summary is displayed in Figure 4. Unfortunately, the variables 'fu' and 'generalized' did not prove to be significant and the reduced model only contain two variables: 'symptomatic' and 'agefirst', but it is the best model based on the AIC criterion. The AIC for two models is shown in the table below:

Model	AIC
Full	126960.6128
Reduced	122936.9132
Reduced	123637.9815
(with an interaction term)	

Results. Logit									
						====:			
Model:	I	Logit		Pseudo	o R-squa	red:	inf		
Dependent Vari	able: y	y		AIC:			1229	36.9132	
Date:	1	2020-04-20	10:05	BIC:			1229	49.8647	
No. Observations:		554		Log-Li	ikelihoo	d:	-61465.		
Df Model:		2		LL-Nu	11:		0.0000		
Df Residuals:		551	LLR p-value:			1.0000			
Converged:		1.0000	Scale:			1.0000			
No. Iterations	: !	5.0000							
	Coef	. Std.Er	r.	Z	P> z	[0	.025	0.975]	
intercept	-1.242	20 0.18	6 2 -6.	6686	0.0000	-1.	5070	-0.8770	
agefirst	0.000	65 0.00	18 3.	5375	0.0004	0.0	0029	0.0101	
symptomatic	1.883	0.28	34 6.	6384	0.0000	1.	3259	2.4369	
						====			

Results: Logit

Figure 4. The summary of the reduced GLM model

The side-by-side boxplots in Figure 5 demonstrate a potential relationship between the symptomatic epilepsy status and the age at first seize; therefore, the possibility of interaction between 'symptomatic' and 'agefirst' should not be ignored. An additional model with the interaction term was constructed; however, the interaction term has a huge p-value, shown in Figure 6, and almost no contribution to the model (increase in AIC), thus will not be included in the reduced model.



Figure 5. The side-by-side boxplots of age at first seizure (in months) for two levels of symptomatic epilepsy status

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==========		===:		=====			====:		======
Model:		Logi	it		Pseud	do R-squa	red:	inf	
Dependent Vari	able:	у			AIC:			1236	37.9815
Date:		2020	0-04-20	10:05	BIC:			1236	55.2502
No. Observatio	ns:	554			Log-L	ikelihoo	d:	-618	15.
Df Model:		3			LL-Nu	ull:		0.00	00
Df Residuals:		550			LLR p	o-value:		1.00	00
Converged:		1.00	000		Scale	2:		1.00	00
No. Iterations	:	5.00	000						
	Coef	•	Std.Err	•	Z	P> z	[0]	.025	0.975]
	4 27								
intercept	-1.2/	18	0.190	2 -6	.6883	0.0000	-1.0	5445	-0.8991
agefirst	0.00	68	0.001	9 3	.6345	0.0003	0.0	0032	0.0105
symptomatic	2.06	16	0.356	3 5	.7853	0.0000	1.	3631	2.7600
interaction	-0.00	70	0.008	1 -0	.8682	0.3853	-0.0	0230	0.0089
		====							

Figure 6. The summary of the GLM with an interaction term

Since the patients are independent of each other and the diagnostic plot (Residuals vs. Fitted) in Figure 7 shows no anomalies – the residuals are randomly scattered around the mean – the model assumptions are satisfied, so it is valid to proceed with predicting the remission status using the reduced model. The prediction accuracy will be displayed later in the analysis after the prediction accuracies for other techniques are obtained as well.



Figure 7. The residuals versus fitted plot

Unlike the logistic model which uses only two variables, the classification tree finds the two other variables to be important: 'fu', total follow-up from first seizure to last contact in months, and 'edum', the education level of mother.



Figure 8. The original classification tree

Although, the decision trees are prone to overfitting and perhaps that is the reason why these variables are included in the tree, but it is important to understand why 'fu' can be quite misleading: as it is usually the case with medical trials, some patients tend to withdraw from a study if they recover or instead if they did not, but stopped attending doctor's appointments because they do

not help anymore. For that reason, it is reasonable to use a pruned tree which also relies on 'symptomatic' in predicting the terminal remission which confirms the results of the logistic regression



Figure 9. The pruned classification tree

The last step will be to grow a random forest: unlike the decision trees, a random forest's implementation in Python is not able to handle missing values. For that reason, the size of the train set is slightly reduced by removing the 'fu' and 'generalized' variables which have lots of missing values and were previously proven to have no explanatory power. The classification accuracy rates are given in the following table:

Technique	Classification Accuracy Rate
Logistic Regression	68.345%
Classification Tree	61.871%
Classification Tree (Pruned)	67.625%
Random Forest	62.589%

It is important to note that the above techniques all provide similar results, and all agree on the important variables.

A classification modelling problem involves classifying observations into classes of a categorical response. At the same time, a model could predict the probability of assigning an observation to each of the possible classes. The logistic regression returns well calibrated predictions by default as it directly optimizes log-loss, shown in Figure 8.



Figure 10. The calibration plots

Conclusion

The three techniques used in the analysis – Logistic Regression, Classification Tree, and Random Forest – all agree on that the terminal remission status is highly affected by two major factors: the status of symptomatic epilepsy, whether epilepsy was caused by an injury to the brain or not; and the age at the first seizure, which is recorded in months. A patient is more likely to recover from epilepsy if they are diagnosed with symptomatic epilepsy, and if the first seizure occurs at a younger age. The three techniques all provided quite similar classification accuracy rates, meaning that the results are quite stable and reliable.

Data Analysis for Epileptic Seizure Prediction: Python code

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```
In [3]: #this is a package used to silence warnings
        import warnings
        warnings.filterwarnings('ignore')
In [4]: #importing packages
        import numpy as np
        import pandas as pd
        import matplotlib.pyplot as plt
        import matplotlib as mpl
        import seaborn as sns
        import statsmodels.api as sm
        from sklearn.linear model import LogisticRegression
        from sklearn.metrics import classification report, confusion matrix
        from patsy import dmatrices
        import sklearn
        from sklearn import datasets
        from sklearn.naive_bayes import GaussianNB
        from sklearn.linear model import LogisticRegression
        from sklearn.ensemble import RandomForestClassifier
        from sklearn.svm import LinearSVC
        from sklearn.calibration import calibration curve
        from sklearn.model selection import train test split
        from sklearn.tree import DecisionTreeClassifier
        from sklearn import metrics
        from sklearn import tree
        from sklearn.externals.six import StringIO
        from IPython.display import Image
        from sklearn.tree import export graphviz
        import pydotplus
```

Exploratory Data Analysis

```
In [5]: #reading in the data from a camfield.csv file
        data = pd.read_csv('camfield.csv', header = 0)
        #exploring the dataset
        data.head()
```

Out[5]:

	Column1	groupID	nogroup	dob	sex	ca
0	1	700.0	NaN	NaN	female	515
1	2	NaN	NaN	######################################	male	80
2	3	NaN	NaN	12421987200	female	250
3	4	NaN	NaN	######################################	female	6
4	5	777.0	NaN	NaN	female	478

5 rows × 462 columns

In [6]: #getting the dimensions data.shape #removing the first column data = data.drop(columns = "Column1") #checking data.shape

Out[6]: (554, 461)

```
In [7]: #some visualization tools
        %matplotlib inline
        table = pd.crosstab(data.symptomatic, data.aedend)
        table.div(table.sum(1).astype(float), axis=0).plot(kind='bar', stacked=True)
        plt.title('Bar Charts of aedend and symptomatic')
        plt.savefig('aedend_and_symptomatic')
```



Bar Charts of aedend and symptomatic

```
In [8]: #getting the needed columns
small_data = pd.concat([data.aedend, data.agefirst], axis = 1)
#making some boxplots
sns.boxplot(x = data.aedend, y = data.agefirst, palette = "Blues")
plt.show()
sns.boxplot(x = data.symptomatic, y = data.agefirst, palette = "Blues")
plt.show()
```



Generalized Logistic Regression

```
In [9]: #modifying the variables
    data.aedend = pd.get_dummies(data.aedend).yes
    data.sex = pd.get_dummies(data.sex).male
    data['intercept'] = 1
    data['interaction'] = data.agefirst*data.symptomatic
```

```
Optimization terminated successfully.
```

Current function value: 114.569145 Iterations 5

Results: Lo	ogit
-------------	------

=======================================	====	====	=====	====	===		=====	=====	======	======
Model:		Logi	t			Pseudo	R-squ	uared	: inf	
Dependent Variab	ole:	у				AIC:			12696	0.6128
Date:		2020	-04-20	10:	06	BIC:			12699	9.4673
No. Observations	5:	554				Log-Li	keliho	od:	-6347	1.
Df Model:		8				LL-Nul	1:		0.000	00
Df Residuals:		545				LLR p-	value	1	1.000	00
Converged:		1.00	00			Scale:			1.000	00
No. Iterations:		5.00	00							
	Coe	ef.	Std.E	rr.		Z	P> z		[0.025	0.975]
intercept	-0.8	 3361	0.5	5116	 -1		0.102	22 -:	 1.8388	0.1665
agefirst	0.0	9066	0.0	019	З	3.4623	0.000	95 (0.0029	0.0103
symptomatic	1.7	7685	0.5	168	З	3.4223	0.000	96 (0.7557	2.7813
sex	-0.6	9287	0.1	.866	-6	.1538	0.877	77 -(0.3944	0.3370
focal	-0.6	9806	0.4	769	-6	.1689	0.865	59 -:	1.0153	0.8542
fu	-0.6	014	0.0	009	- 1	.5571	0.119	94 -(0.0031	0.0004
poor	-0.6)339	0.2	283	-6).1487	0.881	L8 -(0.4813	0.4135
adequate	0.0	9458	0.2	273	e	.2014	0.840	94 -(0.3998	0.4914
generalized	0.2	2808	0.5	271	e	.5328	0.594	12 -0	0.7522	1.3139
	====	====	======	====	===	======	=====	=====	======	======

în [16]:	<pre>#The reduced model logit_model = sm.Logit(data.aedend.to_numpy(), data[['intercept','agefirst', 'symptomatic']].to_numpy()) result = logit_model.fit() print(result.summary2(xname = ['intercept','agefirst', 'symptomatic']))</pre>									
	Optimization terminated successfully. Current function value: 110.948478 Iterations 5 Results: Logit									
	Model: Dependent Varia Date: No. Observation Df Model: Df Residuals: Converged: No. Iterations	Log able: y 202 ns: 554 2 551 1.6 : 5.6	ze git 20-04-20 10 4 1 0000 0000	Pseudo R-squared: inf AIC: 122936.9132 0:05 BIC: 122949.8647 Log-Likelihood: -61465. LL-Null: 0.0000 LLR p-value: 1.0000 Scale: 1.0000						
		Coef.	Std.Err.	Z	P> z	[0.025	0.975]			
	intercept agefirst symptomatic	-1.2420 0.0065 1.8814	0.1862 0.0018 0.2834	-6.6686 3.5375 6.6384	0.0000 0.0004 0.0000	-1.6070 0.0029 1.3259	-0.8770 0.0101 2.4369			

```
In [15]: #The model with interaction
       logit_model = sm.Logit(data.aedend.to_numpy(), data[['intercept','agefirst',
       'symptomatic', 'interaction']].to_numpy())
       result = logit model.fit()
       print(result.summary2(xname = ['intercept','agefirst', 'symptomatic', 'interac
       tion']))
       Optimization terminated successfully.
              Current function value: 111.579406
              Iterations 5
                            Results: Logit
       _____
                       Logit
       Model:
                                    Pseudo R-squared: inf
                                   AIC:
5 BTC:
       Dependent Variable: y
                                                  123637.9815
                       2020-04-20 10:05 BIC:
       Date:
                                                 123655.2502
       No. Observations: 554
                                   Log-Likelihood: -61815.
                                 LL-Null: 0.0000
LLR p-value: 1.0000
Scale: 1.0000
       Df Model:
                     3
       Df Residuals: 550
Converged: 1.0000
       No. Iterations: 5.0000
       _____
                 Coef. Std.Err. z P>|z| [0.025 0.975]
       intercept -1.2718 0.1902 -6.6883 0.0000 -1.6445 -0.8991
                  0.0068 0.0019 3.6345 0.0003 0.0032 0.0105
       agefirst
                  2.0616 0.3563 5.7853 0.0000 1.3631 2.7600
       symptomatic
       interaction -0.0070 0.0081 -0.8682 0.3853 -0.0230 0.0089
       In [19]: #making predictions
       x_train, x_test, y_train, y_test = train_test_split(data[['intercept','agefirs
       t', 'symptomatic']].to_numpy(),
                                                data.aedend.to numpy(), te
       st_size = 0.25, random_state = 0)
       logisticRegr = LogisticRegression()
       logisticRegr.fit(x train, y train)
       predictions = logisticRegr.predict(x test)
       score = logisticRegr.score(x_test, y_test)
       print(score)
```

```
0.6834532374100719
```

Classification Tree

Accuracy: 0.6187050359712231

In [23]: #pruning the above tree
dt = DecisionTreeClassifier(max_leaf_nodes=5)
dt.fit(x_train, y_train)
y_pred = dt.predict(x_test)
print("Accuracy:", metrics.accuracy_score(y_test, y_pred))

Accuracy: 0.6762589928057554

```
In [24]: tree.plot tree(dt.fit(x train, y train))
Out[24]: [Text(223.2000000000002, 195.696, 'X[1] <= 0.5\ngini = 0.472\nsamples = 415
         \nvalue = [257, 158]'),
          Text(167.4, 152.208, 'X[0] <= 115.0\ngini = 0.442\nsamples = 349\nvalue = [2
         34, 115]'),
          Text(111.600000000001, 108.72, 'X[4] <= 38.5\ngini = 0.374\nsamples = 245
         \nvalue = [184, 61]'),
          Text(55.8000000000004, 65.232, 'gini = 0.0\nsamples = 5\nvalue = [0, 5]'),
          Text(167.4, 65.232, 'X[4] <= 357.0\ngini = 0.358\nsamples = 240\nvalue = [18
         4, 56]'),
          Text(111.600000000001, 21.744, 'gini = 0.401\nsamples = 180\nvalue = [130,
         50]'),
          Text(223.200000000002, 21.744, 'gini = 0.18\nsamples = 60\nvalue = [54,
         6]'),
          Text(223.2000000000002, 108.72, 'gini = 0.499\nsamples = 104\nvalue = [50,
         54]'),
          Text(279.0, 152.208, 'gini = 0.454\nsamples = 66\nvalue = [23, 43]')]
```



Random Forest

```
In [26]: # Instantiate model with 500 decision trees
rf = RandomForestClassifier(n_estimators=1000)
# Train the model on training data
rf.fit(x_train, y_train)
y_pred = rf.predict(x_test)
print("Accuracy:", metrics.accuracy_score(y_test, y_pred))
```

Accuracy: 0.6258992805755396

Probability Calibration

```
In [40]: X_train = data[['intercept', 'agefirst', 'symptomatic']].to_numpy()[:400]
         X_test = data[['intercept', 'agefirst', 'symptomatic']].to_numpy()[400:]
         y train = data.aedend.to numpy()[:400]
         y test = data.aedend.to numpy()[400:]
         # Create classifiers
         lr = LogisticRegression()
         gnb = GaussianNB()
         svc = LinearSVC(C=1.0)
         rfc = RandomForestClassifier()
         #
         # Plot calibration plots
         plt.figure(figsize=(10, 10))
         ax1 = plt.subplot2grid((3, 1), (0, 0), rowspan=2)
         ax2 = plt.subplot2grid((3, 1), (2, 0))
         ax1.plot([0, 1], [0, 1], "k:", label="Perfectly calibrated")
         for clf, name in [(lr, 'Logistic'),
                          (gnb, 'Naive Bayes'),
                          (svc, 'Support Vector Classification'),
                          (rfc, 'Random Forest')]:
             clf.fit(X_train, y_train)
             if hasattr(clf, "predict proba"):
                 prob_pos = clf.predict_proba(X_test)[:, 1]
             else: # use decision function
                prob_pos = clf.decision_function(X_test)
                 prob_pos = \setminus
                    (prob_pos - prob_pos.min()) / (prob_pos.max() - prob_pos.min())
             fraction of positives, mean predicted value = \
                 calibration_curve(y_test, prob_pos, n_bins=10)
             ax1.plot(mean predicted value, fraction of positives, "s-",
                      label="%s" % (name, ))
             ax2.hist(prob pos, range=(0, 1), bins=10, label=name,
                     histtype="step", lw=2)
         ax1.set ylabel("Fraction of positives")
         ax1.set ylim([-0.05, 1.05])
         ax1.legend(loc="lower right")
         ax1.set title('Calibration plots (reliability curve)')
         ax2.set_xlabel("Mean predicted value")
         ax2.set ylabel("Count")
         ax2.legend(loc="upper center", ncol=2)
         plt.tight layout()
         plt.show()
```

