Machine Learning-Based Identification of Long COVID Syndrome

Leveraging Encounter Notes Symptoms

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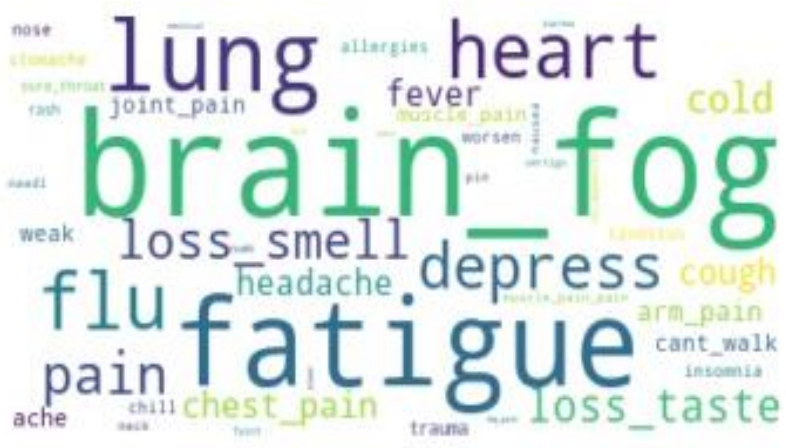
Introduction

- Long COVID Syndrome (LCS)
  - A condition in which individuals experience symptoms for weeks or months after recovering from COVID-19 [1].
  - Post-COVID symptoms 90 days after the COVID-19 index date.

- The need for consistent identification and treatment of Long COVID patients
  - 20-30% of COVID-19 survivors experience prolonged symptoms.
  - The condition can affect multiple organ systems [2,3].
  - Many are unaware of their condition.



[4]

Objective

- To develop a computational predictive model to identify LCS cases precisely.

- Importance:
  - Leveraging machine learning techniques offers a promising approach to accurately identifying and managing LCS cases.
  - Potential to revolutionize the identification process of LCS, making it a significant contribution to the medical field.
  - Improving patient care and management strategies.

Data Collection

Source of Data

- Manitoba Population Research Data Repository housed at the Manitoba Centre for Health Policy (MCHP)
- Electronic Medical Records (EMR) of COVID-19 patients pre- and post-COVID.
- Demographic information such as age, sex, and socioeconomic factor index.

Quantity and Quality

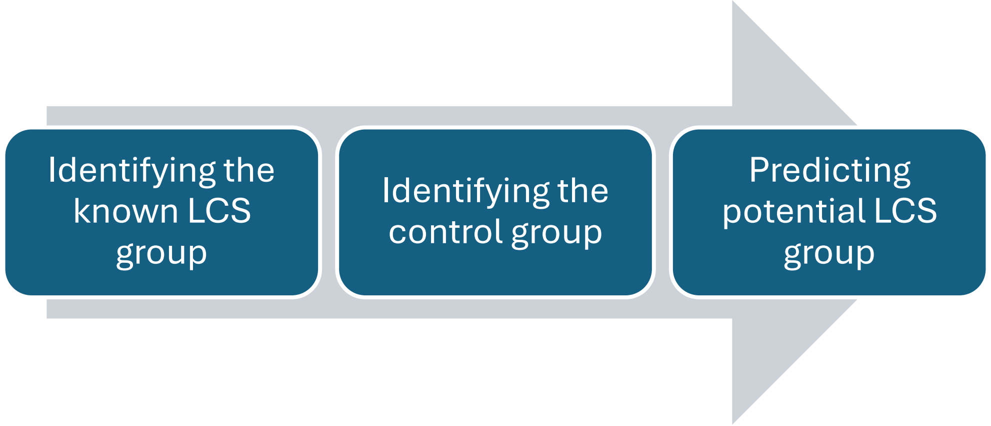
- A sample of the COVID-19 test-positive cohort was accessed.
- Patients who had received a COVID-19 index date from March 1, 2020, to December 31, 2021.
- The data set was narrowed to 4556 COVID-19-positive patients with written medical records.

Ethical Considerations

- Data collection adhered to ethical guidelines, with measures in place to ensure patient privacy and confidentiality.

Challenges in Predicting LCS Patients at Risk

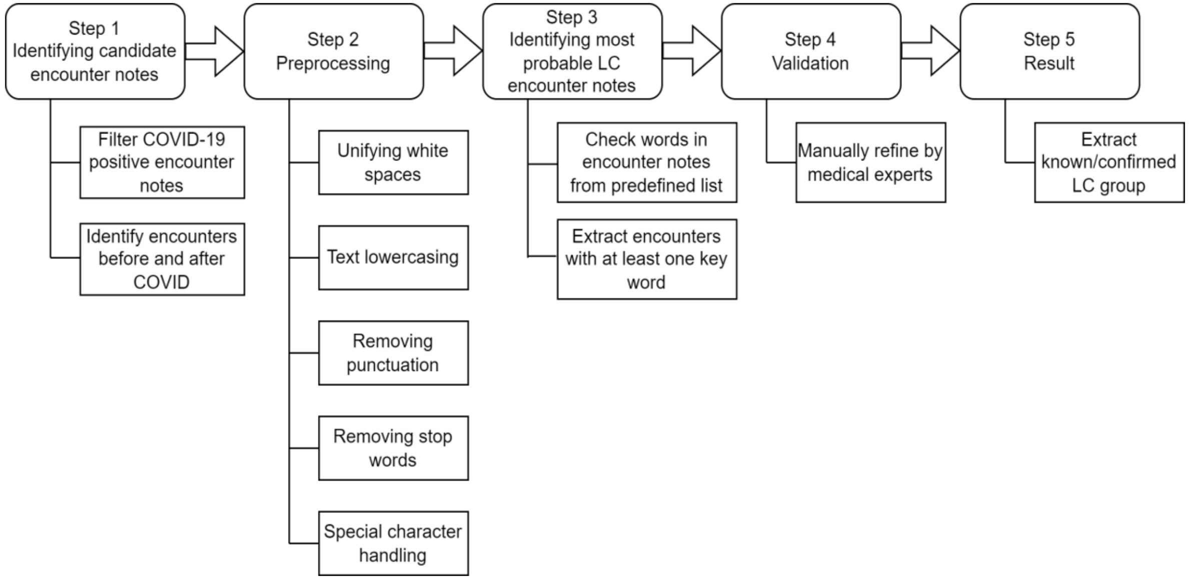
- The absence of a definitive diagnostic test for Long COVID Syndrome
  - Identifying the known LCS Group for classification
  - Defining the Control Group



- Class Imbalance Issue

Identifying the known LCS Group & Control Group

- Identifying the known LCS Group
  - Use Natural Language Processing (NLP) methodologies.
  - Conducted word extraction processes.
  - Out of 121 patients identified, **81** were confirmed LCS patients.



- Defining the Control Group
  - who remained within the dataset for at least 90 days with no documented medical records beyond 90 days from COVID-19 onset.
  - Identified **1945** patients.

Class Imbalance Issue

- One or more classes are underrepresented.
  - Class imbalance Ratio: 0.96:0.04

- Used resampling techniques
  - Random Over-Sampling
  - Random Under-Sampling

Symptom Extraction and Negation Identification

- Assessing post-COVID symptoms 90 days after the COVID-19 index date.

- Pre-COVID symptoms
  1. symptoms within 90 days before the COVID-19 index date.
  2. symptoms within one year before the COVID-19 index date.

- Extracted non-negated LCS-related symptoms by referring to a predetermined list [4].
  - Using ‘Negex’ allowed us to filter out all negated medical terms from the EMRs of patients.

Machine Learning Approach

- Supervised machine learning
- Train-test split
- Binary classification methods
  - Logistic Regression
  - Logistic Regression with Elastic Net Regularization for Classification
  - Random Forest Classification
- Cross-validation and hyperparameter optimization techniques

Logistic Regression with Elastic Net Regularization

- Based on a linear combination of L1 and L2 regularization penalties, which are applied to the coefficients of the linear classification model.
- Elastic net regularization seeks to find coefficients that can minimize,

$$\min_{(b,w)\in\mathbb{R}^{\{m+1\}}}\left(-\frac{l(b,w)}{n}+\lambda P_{\alpha}(w)\right),\ \text{where, } P_{\alpha}(w)=(1-\alpha)\frac{1}{2}\left|\left|w\right|\right|_2^2+\alpha\left|\left|w\right|\right|_1$$

Also,

$$\left|\left|w\right|\right|_1=\sum_{j=1}^{p}|w_j| \quad \text{and} \quad \left|\left|w\right|\right|_2=\left(\sum_{j=1}^{p}w_j^2\right)^{\frac{1}{2}},\quad \alpha\geq 0,\ \ \lambda\in[0,1]$$

Accuracy Measures

- Assessed the overall performance of LCS prediction models by striking a balance between sensitivity and specificity.
- Sensitivity:
  - model's ability to correctly detect individuals with the disease.

$$Sensitivity = \frac{TP}{(TP + FN)}$$

- Specificity:
  - model's ability to accurately classify individuals who do not have the disease as negative.

$$Specificity = \frac{TN}{(TN + FP)}$$

where,

TP – True Posotives, TN – True Negatives, FP – False Posotives, FN – False Negatives

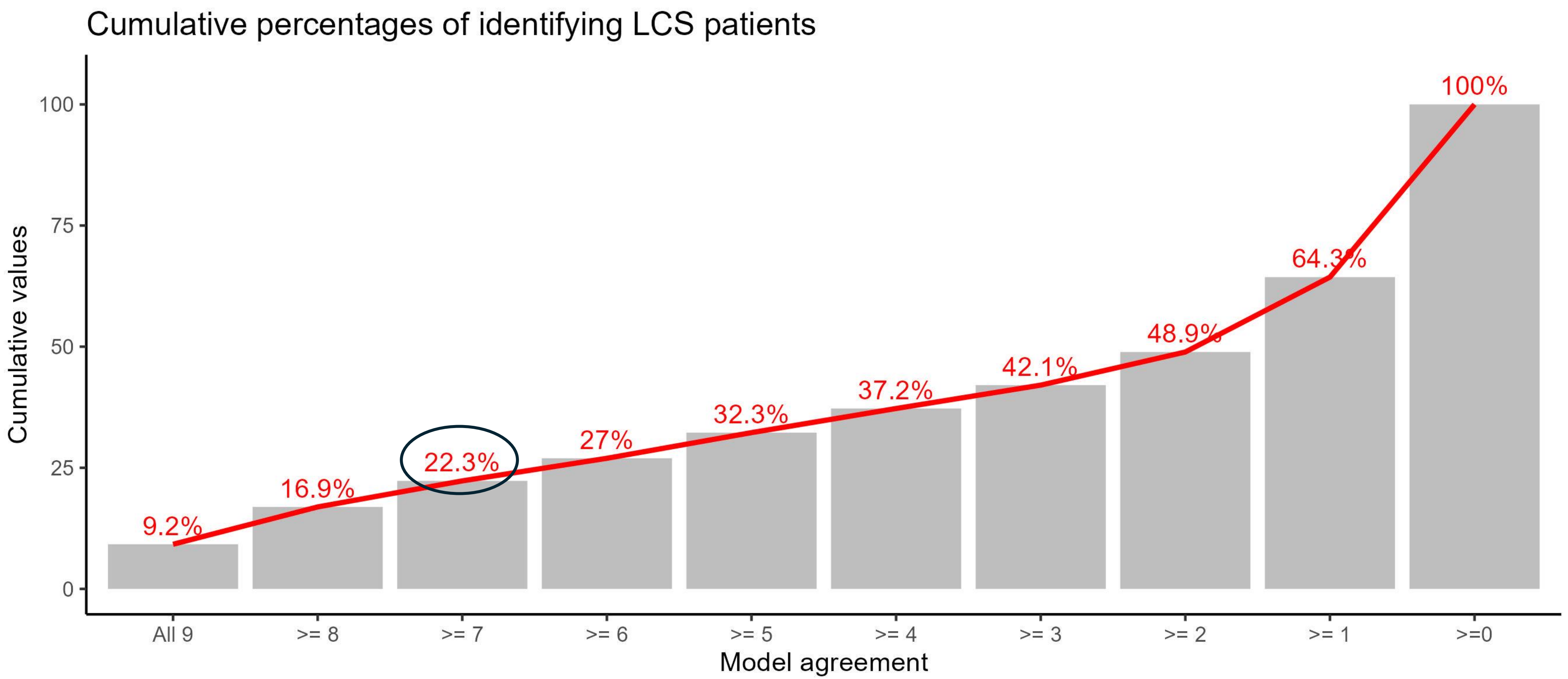
Model Results

Pre-COVID symptom scenario	Dataset	Re-sampling Technique	Classification Method	No LCS Counts (%)	LCS Counts (%)	Total LCS Counts (%) (Development + Application)	AUC	Sensitivity	Specificity
90 days	Development Dataset			1945 (96%)	81 (4%)				
	Application Dataset	Baseline (Without Re-sampling)	Logistic	1657 (65%)	873 (35%)	954 (20.9%)	0.87	0.85	0.82
			Elastic Net	1857 (73%)	673 (27%)	754 (16.5%)	0.93	0.85	0.91
			Random Forest	1656 (65%)	874 (35%)	955 (21%)	0.93	0.9	0.85
		Random Over-Sampling	Logistic	1912 (76%)	618 (24%)	699 (15.3%)	0.88	0.85	0.86
			Elastic Net	1689 (67%)	841 (33%)	922 (20.2%)	0.93	0.9	0.83
			Random Forest	1779 (70%)	751 (30%)	832 (18.3%)	0.9	0.85	0.84
		Random Under-Sampling	Logistic	1480 (58%)	1050 (42%)	1131 (24.8%)	0.66	0.7	0.71
			Elastic Net	**1487 (59%)**	**1043 (41%)**	**1124 (24.7%)**	**0.94**	**0.95**	**0.81**
			Random Forest	1659 (66%)	871 (34%)	952 (20.9%)	0.93	0.9	0.86
1 year	Development Dataset			1592 (95%)	81 (5%)				
	Application Dataset	Baseline (Without Re-sampling)	Logistic	1825 (72%)	705 (28%)	786 (18.7%)	0.69	0.69	0.88
			Elastic Net	1459 (58%)	1071 (42%)	1152 (27.4%)	0.86	0.85	0.84
			Random Forest	1225 (48%)	1305 (52%)	1386 (33%)	0.84	0.85	0.79
		Random Over-Sampling	Logistic	1626 (64%)	904 (36%)	985 (23.4%)	0.66	0.69	0.79
			Elastic Net	1753 (69%)	777 (31%)	858 (20.4%)	0.75	0.77	0.84
			Random Forest	1347 (53%)	1183 (47%)	1264 (30.1%)	0.87	0.85	0.79
		Random Under-Sampling	Logistic	1594 (63%)	936 (37%)	1017 (24.2%)	0.79	0.69	0.84
			Elastic Net	1621 (64%)	909 (36%)	990 (23.6%)	0.79	0.85	0.83
			Random Forest	1816 (72%)	714 (28%)	795 (18.9%)	0.89	0.85	0.9

Model Results

- Most Important Features
  - Breathing/lung issues
  - Fatigue
  - Chest pain
  - Brain fog
  - Dizziness
  - Cough
  - Age group 70-79
- Noticeable Groups
  - Female (59.7%)
  - aged between 50 and 59 years old (18.8%)

Agreement between Nine Models



Conclusion

- Using natural language processing to identify initial confirmed LCS patients.
- Applying machine learning models addresses a significant challenge within the healthcare sector.
- The outcomes of this approach underscore its potential to accurately identify individuals prone to LCS, with accuracy metrics: sensitivity of 0.95, specificity of 0.81, and AUC of 0.94.
- The LCS patient cohort created using this method is a valuable resource for conducting robust assessments of LCS clinical progression.

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