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Yajni Warnapala
Roger Williams University
One Old Ferry Road Bristol,
RI 02809, United States

Danielle Vogt
Roger Williams University
One Old Ferry Road Bristol,
RI 02809, United States

Corresponding Author:
Yajni Warnapala
Roger Williams University
One Old Ferry Road Bristol,
RI 02809, United States

An integral equation approach for long COVID-19 (LC Model)

Yajni Warnapala and Danielle Vogt

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Abstract
This research was based on creating a Volterra-Fredholm integral Equation Model of the second kind for determining the variables associated with recovery R(T) of long COVID symptoms. Long COVID was determined to have post COVID symptoms longer than 3 months. It was deduced that long COVID symptoms were dependent on many independent variables, vaccination status β, race λ, gender δ (male), pre-existing conditions ε (heart disease), and death age impact factor ∝. Each of these variables was included in a multiple regression analysis in order to verify the significance of each variable and the significant variables were added to the Volterra-Fredholm Integral LC Model. The model was built using USA state data [1]. The model also included the infection rate γ and sample size N. It was our assumption that this predictive model would be able to predict future outcomes of similar pandemics and endemics.

Keywords: Volterra-Fredholm Integral, Gaussian quadrature method, Long COVID-19

1. Introduction

A Volterra-Fredholm Integral Equation Model of the second kind was created for determining the variables associated with recovery R(t) of long COVID symptoms. It was deduced that long COVID symptoms were dependent on many independent variables. Each of these variables was included in a multiple regression analysis to verify each variable's significance and the significant variables were added to the Volterra-Fredholm Integral LC Model. The LC (Long COVID) model was modified from the COVID-19 models previously built by one of the authors [2, 3]. The model also includes the infection rate γ.

2. Integral Methods

2.1 Volterra-Fredholm Integral Equation

The integral equation model was based on the Volterra Fredholm Integral equation of the second kind. We approximated the number of individuals with Long COVID symptoms (%), using a double integral with a weekly singular integrand. The constant, R_0, was the initial recovery rate that was available from [4]. The constant, γ, was found from [4], was the rate of recovery from Long COVID. Using available data, we created a logistic 4P model represented by R(T, t) function. The coefficient of determination of the logistic 4P model was 0.78. Within this model, gender, race, vaccination status, death and age impact factor, and heart disease were included as significant factors impacting recovery from Long COVID. In the Volterra Fredholm Integral model R_0 = 0.17, α = 0.0019, β = 0.17712, δ = 0.4936, λ = 0.1221, ε = 0.0442, γ = 0.11, t was the number of months since contracting COVID, and R(t) was the percent of recovered individuals after contracting COVID 19. Here T was the number of months since contracting COVID, R(T) was the % number of recovered individuals.
From known data it was deduced that 6%-8% adults who have contacted COVID are suffering from Long COVID [5].

R(t) was given by:

$$R(0.5,t) = 10.47599 + \frac{8.827277}{1+e^{-1.0273426(t-8.0127444)}}$$

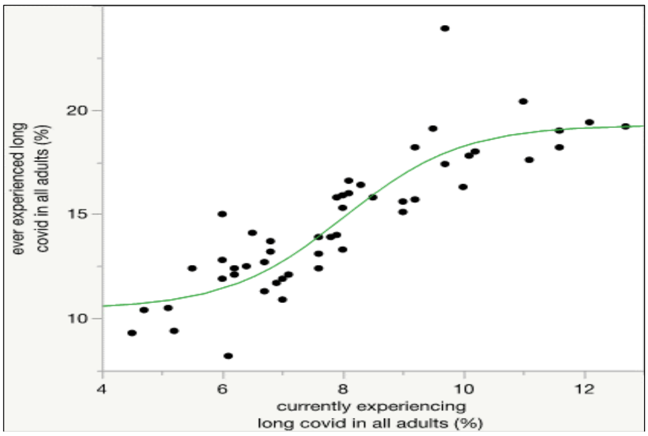

Fig 1: The figure shows the recovery function of ever experienced Long COVID in terms of currently experiencing Long COVID in all adults. The rate of change of ever experienced Long COVID in all adults in terms of currently experiencing Long COVID was 2.27% at 8%.

The LC model was given by:

$$R(T) = R_0 + \frac{\propto\beta}{\delta\lambda\varepsilon}\int_3^T \int_{0.06}^{0.08} R(0.5,\, t)(1 + e^{-\gamma(T-t)})\, dt\, dT$$

The Recovery Rate was given by:

$$R'(T) = \frac{\propto\beta}{\delta\lambda\varepsilon}\int_{0.06}^{0.08} R(0.5,\, t)(1 + e^{-\gamma(T-t)})dt$$

Table 1: Recovery rate of long COVID

Months Since Contracting COVID (T)	**Rate of Recovery $R'(T)$**
4	0.04363810
8	0.03752443
12	0.03358701
16	0.03105117

Currently, 6-8% of the U.S. adult population is experiencing Long COVID. (AY 2023) The table gives the recovery rate from this population within one and a half years. Three percent of all individuals will never recover from Long COVID (see Table 1)

3 Additional Analysis

3.1 Shapiro Wilk Test-Normality

Normality was checked by using the Shapiro Wilk Test. For all distributions, we used a probability level of significance of p-value 0.1. The death/age Impact Factor did not follow a Cauchy or normal distribution at a significance p-value of 0.1.

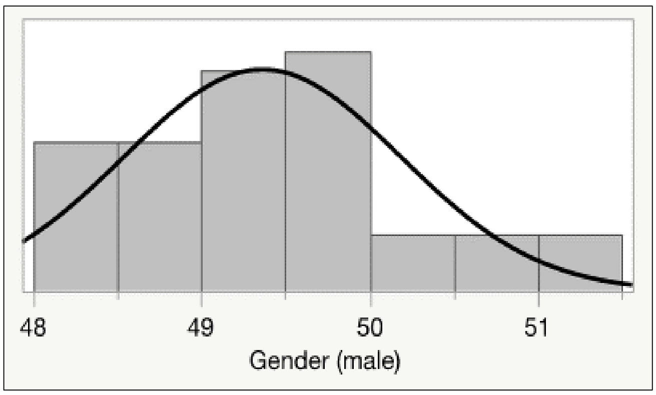

Fig 2: Male (% of all adults in the United States) have been recorded to be more likely to experience Long COVID [6]

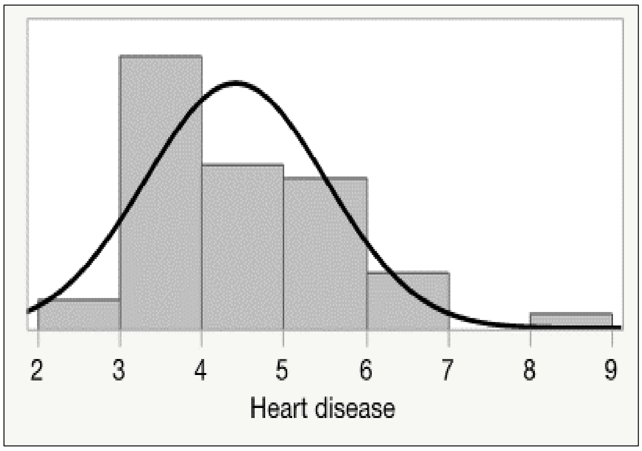

Fig 3: Heart Disease (% of all adults in the United States over the age of 18) was the most prevalent preexisting condition that had an impact on Long COVID 19 recovery [7]

Variable	**P-Value**
Gender	0.0758<0.1
Heart Disease	0.0131<0.05

3.2 Anderson-Darling-Cauchy

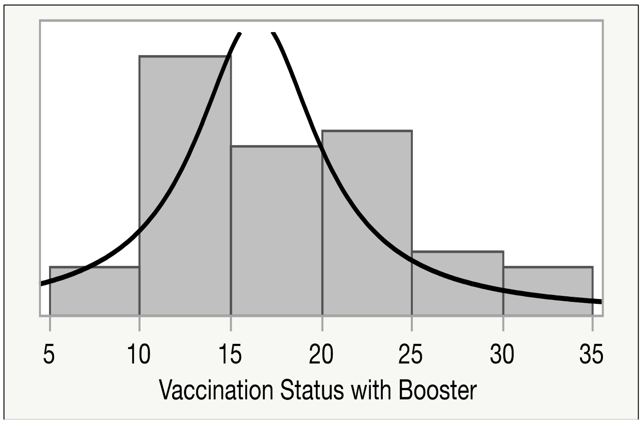

Fig 4: The number of vaccinated individuals (% of all adults in the United States) has impacted the recovery rate of Long COVID. The vaccination status included the booster. [8]

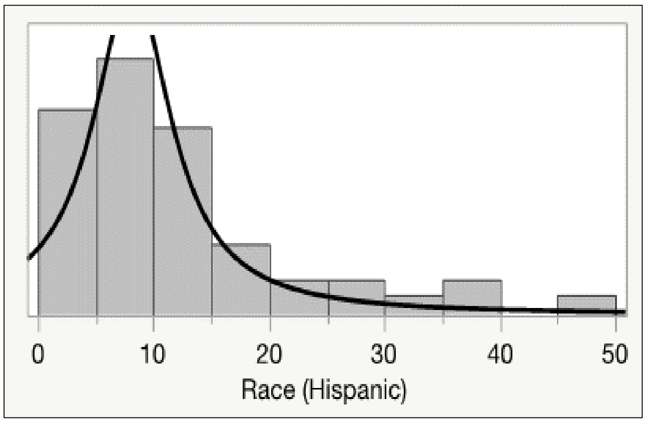

Fig 5: We chose to look at the Hispanic population (% of all adults in the United States) as multi-generation families living in the same household. This might have contributed more to the spread of COVID in Hispanic populations compared to other demographics. [9]

Variable	**P-Value**
Vaccination with Booster	0.0968<0.1
Race	0.0560<0.1

3.3 Multiple Linear Regression

Table 2: The Multiple Regression Coefficients

Term	Estimate	Prob>abs(t)
Intercept	-43.5006	0.0045
Gender (male)-δ	1.0125	0.0007
Vaccination status with booster-β	-0.1311	0.0013
Heart disease-ε	0.8026	0.0042
Race (Hispanic)-λ	0.02153	0.3367*

*significance level for Race (Hispanic) was 0.34 which was not ideal

The multiple regression equation was given by:

Y =-43.5006 + 1.0125δ.0.1311β + 0.8026ε+ 0.02153λ

Y is the percentage of all adults currently experiencing Long COVID. δ is gender (Male). β is the vaccination status with the booster. ε is heart disease. λ is race (Hispanic).

Table 3: Results based off the Multiple Regression Equation

Gender (male) (δ)	Race (Hispanic) (λ)	Heart disease (ε)	Vaccination status (with booster)(β)	Predicted percentage of all adults currently experiencing Long COVID
49.925	25.5	5.5	17.712	9.689306
50.555	25.5	5.5	17.712	10.32718
49.925	41.5	5.5	17.712	10.03380
49.925	25.5	7.53	17.712	8.288040
49.925	25.5	5.5	28.4	11.31859

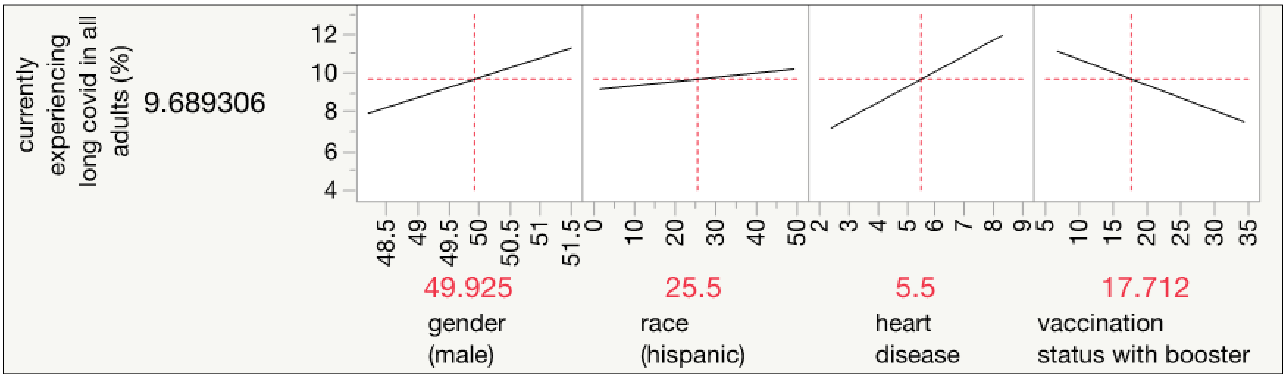

Fig 6: As the percentage of adults with the factors, male, Hispanic, and heart disease are increased, the number of all adults currently experiencing Long COVID is increased as well. These factors are directly proportional to each other. However, as the number of people vaccinated with the booster is increased, the number of all adults currently experiencing Long COVID decreased

3.4 Gaussian Quadrature Method

We used the Gaussian Quadrature Method to approximate the Volterra Fredholm integral equation. The Gaussian Quadrature method is a numerical approximation method for approximating integrals that are challenging to compute through analytical methods of integration. The original integral is converted to an integral defined in the closed interval [-1, 1], as the basis functions for this method are based on Legendre Polynomials.

The formulation is based on orthogonal polynomials, with the common domain of integration as indicated above from $[-1, 1]$, so the formulation is exact for polynomials of degree $2n-1$ or less. This exact rule is known as the Gauss-Legendre Quadrature rule. The Quadrature rule will only be an accurate approximation to the integral above if $f(x)$ is well-approximated by a polynomial of degree $2n-1$ or less on $[-1, 1]$. The Gauss-Legendre Quadrature rule is not typically used for integrable functions with endpoint singularities, as this does not apply to our integral we could use this method of approximation. The following formulation summarizes the process

$$\int_a^b f(x)dx = \int_{-1}^{1} P(x)dx = \sum_{i=1}^{n} c_i P(x_i)$$

Where c_i are the roots of the n^{th} Legendre polynomial $P_n(x)$ and $c_i = \prod_{j=1,\, j\neq i}^{n} \frac{x-x_j}{x_i-xj}$

The number of people recovered from Long COVID

$$R(T) = R_0 + \frac{\propto \beta}{\delta\lambda\varepsilon}\int_3^T \int_{0.06}^{0.08} \frac{\left(10.47599 + \frac{8.827277}{1+e^{(-1.0273426(t-8.0127444))}}\right)}{(1+e^{-\gamma(T-t)}}) dt\, dT$$

Table 4: Integration nodes 4 and 5

Number of months after contacting Long COVID	Recovered (%) 4 Nodes	Recovered (%) 5 Nodes
1	0.21461833	0.21461833
3	0.29837854	0.29837854
6	0.41298739	0.41298739
9	0.51769690	0.51769690
12	0.61528953	0.61528953
15	0.70776566	0.70776566
18	0.79656341	0.79656343
21	0.88271666	0.88271672
24	0.96696868	0.96696885

Table 4 shows the approximation of the number of months after contracting Long COVID at 5 nodes. It is evident from the table that 5 nodes were sufficient in the accuracy of results.

3.5 Neural Network Model

Table 5: Neural network linear function coefficients

Node	Intercept	Male(δ)	Hispanic (λ)	Heart Disease(ε)	Vaccination/ Booster(β)	Death/Age Impact Factor(∝)
N1	30.65	-0.65	-0.11	-0.44	0.15	800.85
N2	-4.38	0.02	0.13	-0.29	-0.004	349.07
N3	15.09	-0.22	-0.006	-0.21	-0.10	-620.89
N4	-31.79	0.41	0.10	1.40	0.23	-307.26

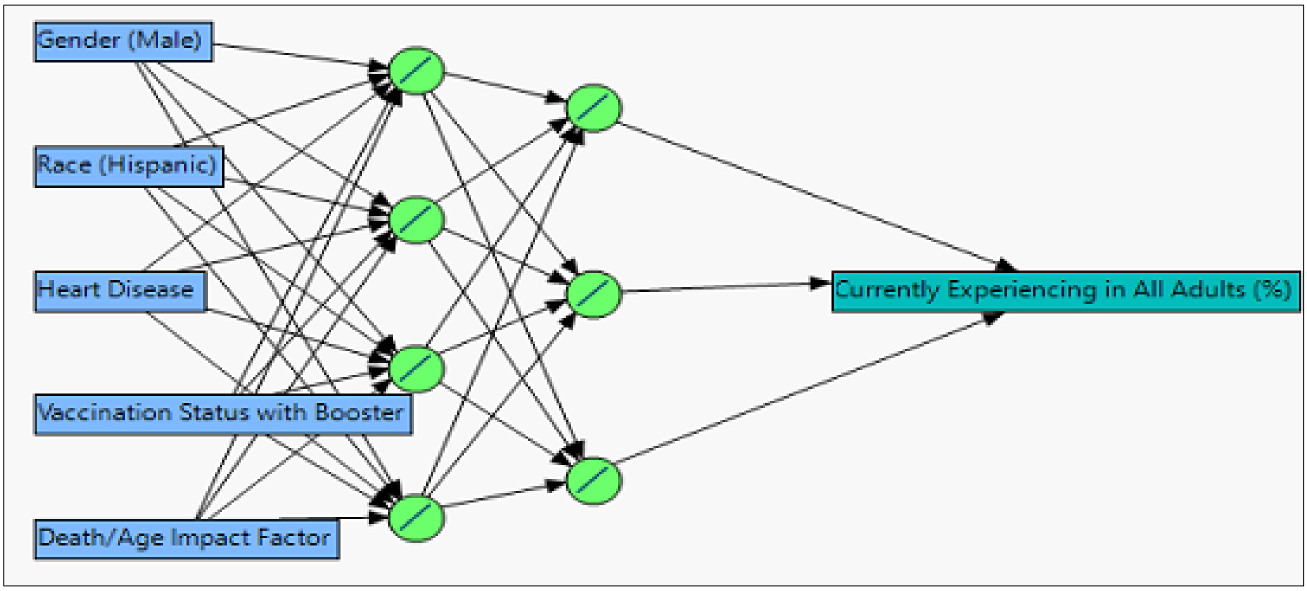

Fig 6: Neural Network Model: Each layer of the Network is a linear Function Shown below

The Neural Network Model depicts the fully connected multi-layer connection with one or two layers. The Neural Network Model was used to further predict one or more response variables of Long COVID-19 using a flexible function of the input variables. This Neural Network was very good in predicting the necessary description of the functional form of the response variables, and in describing the relationship between the input variables and the output response, recovery rate R′(T).

3.6 The combined result by using the nodes from Table 5

The final result of the Neural Network Model is given by the following

Currently Experiencing Long COVID (Y) = $6.26\text{-}0.83_{N1.1} + 0.81_{N2.1}\ 0.08_{N3.1}$

Table 5.1: Neural network second layer of linear coefficients

Node	Intercept	N1	N2	N3	N4
N1.1	-0.34	1.49	-0.59	-0.49	0.80
N2.1	0.73	0.74	-0.94	-0.16	0.55
N3.1	0.24	-0.77	0.28	-0.94	1.53

For the Neural Network Model, we imputed specific values for each variable and obtained the following results in Tables 6 and 6.1.

Table 6: Results of Internal Nodes (%)

Male(δ)	Hispanic(λ)	Heart Disease (ε)	Vaccination/ Booster(β)	Death/Age Impact Factor (∝)	N1	N2	N3	N4
50	15	5	15	0.002	-1.84830	-2.24186	0.20822	0.04548
49	16	4	16	0.001	-1.51915	-2.19493	1.15311	-1.12726
55	14	5	17	0.0015	-5.48915	-2.62893	-0.46489	2.76274
45	17	3	14	0.002	1.91170	-1.49786	1.81622	-4.83452
40	18	2	20	0.00175	6.1914875	-1.2891275	2.6754425	-6.7277050

Table 6.1: Percentage of adults currently experiencing long COVID-19

N1.1	N2.1	N3.1	Currently experiencing symptoms
-1.8369134	1.4613052	0.9093278	9.041041558
-2.7753567	0.8645726	-2.0134661	9.102772579
-4.5297767	0.7331126	8.3945339	11.28509858
-1.3653934	0.6030652	-10.7554722	7.021321558
2.952770775	2.395172050	-17.69670568	4.333553163

In Node 1(N1), the Death/Age Impact Factor is most positively impactful. The highest negative value in Node 1(N1) is Male. In Node 2(N2), Death/Age Impact Factor is the highest positive. In Node 2(N2), Heart Disease is the highest negative value. In Node 3 (N3), the Death/Age Impact Factor is the highest negative value. In Node 4 (N4), Death/Age Impact Factor is the highest negative value while heart disease is the highest positive value.

Referring to Table 6.1 from Nodes N1.1, N2.1, and N3.1, the percentage of Adults Currently Experiencing Long COVID increases to 11% when the percentage of males are high. In table 6.1, the percentage of Adults Currently Experiencing Long COVID decreases to 4% when the vaccination percentage is high.

4. Assumptions

One of the drawbacks of our model was that we only considered the Hispanic population. The model that shows the data of currently experiencing long COVID by ever experienced long COVID, plotted into a logistic 4P model only had a significance of 0.78. We extrapolated our model results taken from a data set that had recorded data from Jan 4th-Jan 16th of 2023. When initially determining what factors had an impact on Long COVID, Age was determined to not be significant. The Death/Age Impact factor was created due to the idea that many individuals of old age passed away from Long COVID. This factor was created by dividing the percentage of deaths (based on 8 different age ranges) by the midpoint of age distribution, resulting in 8 different values. [10]

We took the mean of these values, resulting in our Death/Age Impact factor. The death age impact factor is not included in the multiple regression model because of the insufficient data points.

The efficiency of our Volterra Fredholm Integral Model was recorded in Table 7. There was a gradual increase in computation time due to the complicated nature of the outer integral.

Table 7: Efficiency of the Method

Number of Months experiencing Long COVID	Computation Time at 4 Nodes (minutes)	Computation Time at 5 Nodes (minutes)
1	5:30	10:01
3	4:59	5:10
6	4:30	4:30
9	4:10	4:15
12	3:51	4:35
15	3:16	4:55
18	3:14	5:00
21	3:03	4:45
24	3:18	4:50

Our model predicted the recovery rate of Long COVID given by:

$$R'(T) = \frac{\propto \beta}{\delta \lambda \varepsilon} \int_{0.06}^{0.08} R(0.5,\, t)(1 + e^{-\gamma(T-t)})dt$$

It is clear that the rate of recovery is higher one month after experiencing Long COVID, but that rate converges to a 3% as time goes on. The time in Table 8 is calculated by the time of 3 months after experiencing Long COVID symptoms.

Table 8: Recovery Rate for 5 Nodes

Number of Months experiencing Long COVID	5 Nodes
1	0.04363810
5	0.03752443
9	0.03358701
13	0.03105117

Table 9: Convergence results

Time in months after contracting long COVID	Approximated Recovery (%)
1	0.21461833
3	0.29837854
6	0.41298739
9	0.51769690
12	0.61528953
15	0.70776566
18	0.79656343
21	0.88271672
24	0.96696885

5. Conclusions

The vaccination status has the highest impact on the recovery rate of Long COVID. Race (Hispanic) had the least impact when it comes to the recovery rate of Long COVID. From our analysis, it was evident that most adults (96%) recovered after 2 years. We obtained 10^{-8} convergence result from our integral equation model by assuming that 6-8% of the U.S. adult population has suffered from Long COVID. Five Gaussian Quadrature nodes were used to obtain good convergence results for obtaining the percentage of recovery rate by Long COVID. The Volterra Fredholm integral equation approach is a viable method in predicting the recovery rate of long COVID given the following indicators are known, initial recovery rate R_0, infection rate γ, vaccination status with Booster β, race λ (Hispanic), gender (δ) (male), pre-existing conditions ε (heart disease), and death/age impact factor ∝.

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7. References

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