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Antecedents of patients Covid-19 management outcomes

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Abstract

Background: Effective Covid-19 management calls for clear understanding of determinants of possible outcomes. The likelihood of mortality or extent of recovery are the only two eventual outcomes. Examining influences of exposure, effect multiplier, moderating, and confounding factors in Covid-19 management is key to safeguarding human life and protecting livelihoods.

Method: An assessment of covid-19 resurgence preparedness was conducted in Lake Region Economic Bloc Counties of Kenya. Data on cumulative cases, mortality, vaccination, oxygen flow per minute, and ages of infected was collected. Mortality is taken as the response variable where cumulative cases is exposure variable, vaccination as moderating variable, oxygen flow rate as effect multiplier, and age taken as a confounding factor. Age frequency is used as a categorical variable and divided in three groups: 0-19, 20-49, and 50 < years. A multiple logistic regression model is formulated, fitted, and estimated. Finally, an outcome predictive model is fitted.

Findings: Adjusting for all variables, the likelihood of mortality after being infected is 5.3%, (1.053:95% CI, 1.03 - 3.34). A patient is 27%, (95% CI, 7% -33%) more likely to succumb to Covid-19 because of insufficient oxygen compared to a patient without critical oxygen need. Unvaccinated patient is 1.27 times (95% CI, 1.14 -6.26) more likely to die of Covid-19 compared to the vaccinated. A patient aged (20-49) years is 21%, (95% CI, 2% -30.4%) more likely to succumb to Covid-19 compared to one aged (0-19) years. Lastly, a patient aged 50 years and older is 47%, (95% CI, 3% - 56%) more likely to succumb to Covid-19 compared to one in (0-19) years age bracket.

Keywords: oxygen, vaccination, age, Covid-19

Introduction

In May 2021, delta variant was reported in Lake Region Economic Bloc Kenya (LREB). Authorities commissioned an assessment exercise to appraise member counties on their level of preparedness to respond to the predicted surge without overrunning the fragile health infrastructure. The prediction was passed on a novel home-grown mathematical model. Based on the collected data, this manuscript examines statistical association between oxygen capacity, vaccination status, cumulative infections, and age with mortality in LREB counties. Statistically, the variables are considered together to eliminate the omitted variables bias in estimation. However, association of gender, and pregnancy with mortality is not considered. Co-morbidity is inadvertently partly covered as advance age is associated with underlying health conditions.

Previously, before covid-19, medical oxygen demand was limited to few critically ill patients and those undergoing operations in theater. That has now changed with advent and evolution of covid-19 infections (Lancet, 2021). Classification of infections as mild, moderate, and severe is done based on oxygen saturation in blood, Goud *et al.* (2021) [10]. All severe cases are on oxygen support in ICUs Wang *et al.* (2020) [20]. A study of risks associated with intensive care unit admissions found that oxygen saturation had the highest importance, (Alverez-Mon *et al.*., 2021).

In Africa, there is more demand than supply of medical oxygen (Lancet, 2021). In Kenya, the third and fourth waves resulted in increased demand for high flow oxygen in health facilities leading to more loss of life. An assessment report (LREB Counties Covid-19 Preparedness

Assessment Report, 2021) found overwhelming demand for medical supplementary oxygen among other gaps. For Instance, among 2363 health facilities in LREB, only 3 have sufficient supplementary medical oxygen. They are Kisumu County (JOOTRH), Kisii County Teaching and Referral Hospital, and Siaya County Referral Hospital. These facilities have both oxygen production plants and bulk tanks. In the model estimated, oxygen flow rate is an effect multiplier variable.

Best practice recommends that this combination ensures consistent supply of high flow oxygen to patients with acute and moderate needs. Unfortunately, the oxygen generating plants in the remaining 11 counties of LREB are mechanically dysfunctional. Biomechanically, the plants require consistent and timely maintenance to perform optimally. When they are not well maintained but patients need high flow oxygen, the plants' compressors get overwhelmed and break down. However, the oxygen concentrators with which they supplement generating plants are mechanically incapable of supplying high flow oxygen, even for moderate needs. These oxygen supply challenges are similar across Kenya and Africa.

Vaccination as a moderating determinant of Covid-19 patients' health outcome is considered. A study done in India by Muthukrishnan *et al.* (2021) found that fully vaccinated patients of varying ages have reduced risk of mortality compared to the unvaccinated. At the time of assessment in the region, only 45,292 adults had been fully vaccinated in the region and less than 2% nationally. There were challenges of hesitancy among essential workers and inadequate vaccine doses for the willing.

Where age being a confounding infleunce is considered as a co-determinant, it is divided mostly as cohorts of categorical variable: 0-19 years, 20-49 years, and 50< years. A study by Biswas *et al.* (2021) found that patients aged 50 years and above are associated with higher risk of mortality compared to those aged below 50 years. It has been established that the risk of severe covid-19 infection, due to underlying conditions, is more prevalent with increase in age, (Starke *et al.*, 2020).

Lastly, Covid-19 infections as exposure variable is viewed under lenses of case infection rate, case fatality, case fatality rates, case recovery, and case recovery rates. According to Shem (2020), case infection rates, fatality rates, and recovery rates in various regions as classified by WHO are not significantly different. In this study oxygen flow rate, cases, fatality, cumulative vaccination, and age are analyzed using multiple logistics regression.

Method

Data from the fourteen counties of LREB Kenya is used in statistical analysis. A team of researchers in the study collected data from 12 to 30 June 2021 during resurgence preparedness assessment exercise. The data is cleaned and normalized since the values of response variable in multiple logistic models must be between zero (0) and one (1). The cleaned data is simulated during analysis to cover all 47 counties of Kenya. Variables considered in this paper are cumulative deaths (outcome) as response variable, cumulative infections per county (exposure), oxygen flow rate in litters per minute (effect multiplier), cumulative vaccination (moderating), and age (confounding) as explanatory variables. Age is further divided in three cohorts, that is, 0-19, 20-49, and 50 years and older. The analysis does not consider gender, and pregnancy but partially covers comorbidities in relation to age in literature review.

The data is used to formulate and estimate a multiple logistic model which establishes association between each variable and health outcomes, i.e., likelihood of succumbing to covid-19. The results of the estimated model are interpreted. Eventually, the likelihood of succumbing to covid-19 is predicted using the exponents of joint odds ratio. All test statistics, including deviance statistics, are done to establish validity and significance.

Finally, a predictive model is developed to estimate the possible outcome of patients infected with Covid-19 in the region. A hypothetical situation is used to predict the outcome based on the model formulated.

Theoretical Review

Menard (2000) examined coefficients of determination to evaluate predictive efficiency of logistic regressions and found that several outcomes are better predicted by specific models. The ease of probabilistic association of phenomena with causal factors give multiple logistic regression an advantage. In this regard, Choi *et al.* (2020) used the model to evaluate the impact of covid-19 on mental health of the residents of Hongkong and established that several people struggled with depression, anxiety, and other mental disorders to which home-based psychosocial support was recommended.

Logistic regression is robust enough to perform both estimation and prediction. As such Umana *et al.*., (2020) used multinomial logistic regression to estimate and predict perceptions of individuals and companies in Nube Chile in the advent of Covid-19.

Wibowo and Wahayati (2021) used logistic regression model to model the extent of Covid-19 outbreak in Indonesia. Based on appropriateness of associating causal factors to specific outcomes, Hills and Eraso (2021), used logistic model to evaluate the association between behaviours, demographics, housing situation, politics, psychology, and social support with non-adherence to social distancing.

If most importance variables are not jointly used to examine the association with mortality in LREB counties' facilities, there is high chance of omitted variable biases. The exposure, moderating, confounding, and effect multiplier variables must be included to estimate multiple regression model. In that regards, covid case fatality is used as the response variable while oxygen flow rate is an effect multiplier, cumulative cases is an exposure variable, vaccination is a moderating variable, and age as a confounding variable.

Empirical Review

A simple logistic model follows odds ratio (OR)

$$\mathrm{OR} = \frac{\text{Probability of event occuring}}{\text{Propability of event not occuring}}$$

that is, $\ln\left[\frac{p}{1-p}\right]$ (1)

For a simple binary model,

$$\ln \frac{P}{1-p} = \beta_0 + \beta_1 x_1 = \ln(\text{odds of event occuring}) \quad (2)$$

For multiple logistic model, $\ln\left[\frac{p}{1-p}\right] = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_k x_k$ (3)

where, $x_1, x_2 \cdots x_k$ are predictors

$\beta_1, \beta_2, \cdots \beta_k$ are partial regression coefficient
H_0: fitted model is the better fit.
H_1: Saturated model is the better fit
Test Statistic = Deviance Statistics
Degrees of Freedom = sample size − number of esimated parameters

Significance of predictors
$H_0: \beta_j = 0$

$H_1 \neq 0, j = 1,2, \ldots, k$

$$z_j = \frac{\beta_j}{s.e(\beta_j)} \sim N(0,1) \quad (4)$$

$p - \text{value} = 2 \times \Pr(z_c|z_c|)$

z_c is the computed value

The predictor is statistically significant if the $p - \text{vale} < \alpha$

Alternatively,

H_0: fitted model is the better fit.

H_0: Saturated model is the better fit.

The $100(1-\alpha)\%$ confidence interval is

$$\left[\hat{\beta}_j - z\alpha_{/2} s.e.\left(\hat{\beta}_j\right), \hat{\beta}_j + z\alpha_{/2} s.e\left(\hat{\beta}_j\right)\right] \quad (5)$$

The predictor is significant if value 1 is not included in the interval

Prediction
We predict the likelihood of event of interest using,

$$\hat{P} = \frac{e^{\beta_0 + \beta_1 x_1 + \cdots + \beta_k x_k}}{1 + e^{\beta_0 + \beta_1 x_1 + \cdots + \beta_k x_k}} \quad (6)$$

Results

Variable	Estimate	Std. Error	Z	P-value	Odds Ratio	OR Conf. Interval (2.5%)	OR Conf. Interval (97.5&)
Intercept	-0.86012	0.36406	-2.363	0.0202	0.4231112	0.1238567	0.7598534
Cases	0.05207	0.35511	1.47	0.0587	1.0534505	1.0291259	3.3897530
Oxygen flow rate	0.30887	0.42176	1.472	0.044	0.734274	0.6691902	0.92578152
Vaccination	0.8220	0.4302	2.297	0.0249	2.2750561	1.1553438	6.2624017
Age1	0.1608	0.5123	2.314	0.0319	1.1744	1.629893	4.9221917
Age 2	0.3515	0.4475	3. 786	0.0157	1.421198	1.5916352	3.427411
Age3 (50+)	0.5475	0.4826	2.135	0.0571	1.7289285	1.6726552	4.4726140

Null Deviance: 25.974, df=119
Residual Deviance: 24.514, df=113
The p-value for Residual Deviance=0.0000000035=0, there is not enough evidence to support null hypothesis. The saturated model is the better fit.
From the results the better model is given by,

$$\text{Fatal} = -0.86012_{(0.36406)} + 0.05207\text{CASE}_{(0.35511)} + 0.0308877\text{OXYGCA}_{(0.42167)} + 0.822\text{VAX}_{(0.4302)} + 0.1608\text{AGE1}_{C0.5123)} + 0.3515\text{AGE2}_{(0.4475)} + 0.5475\text{AGE3}_{(0.4826)} \quad (7)$$

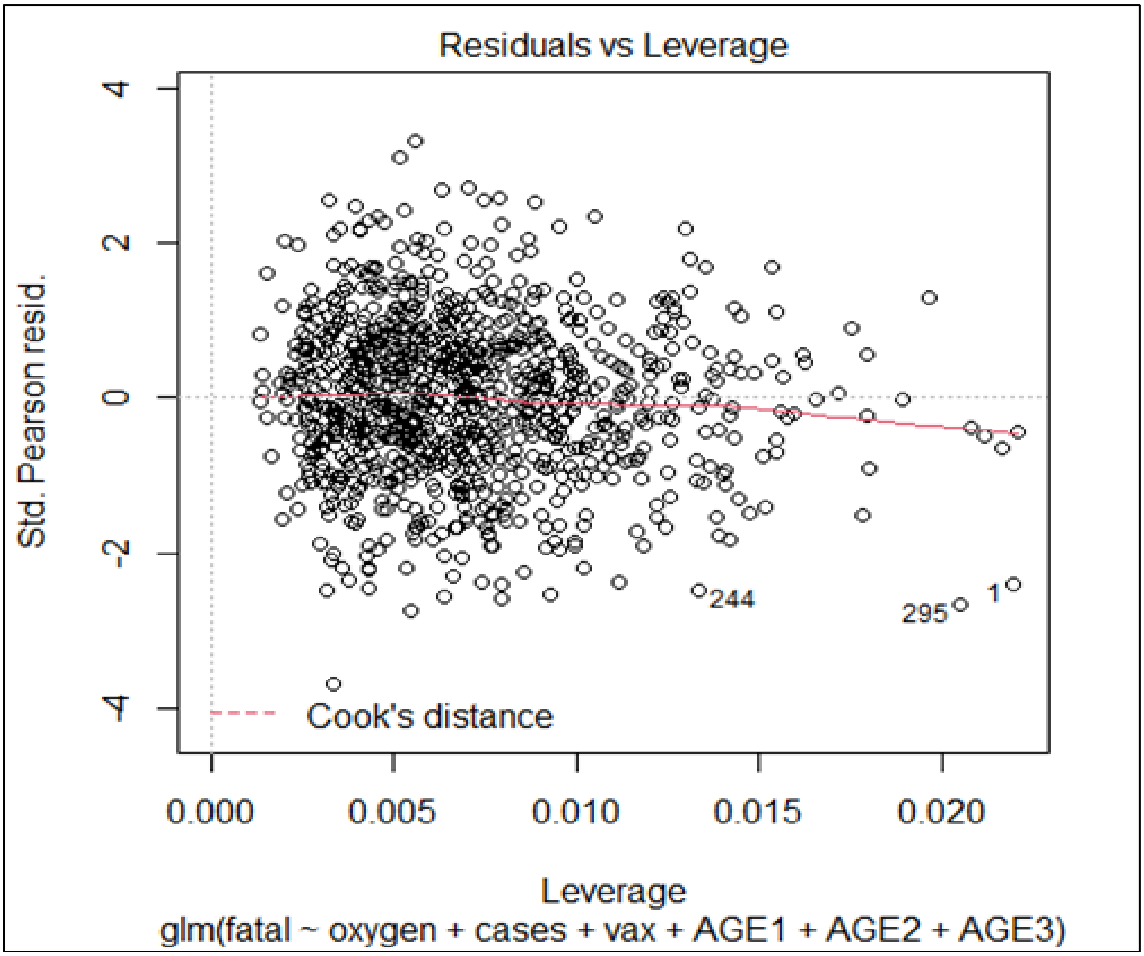

Fig 1: Residuals vs Leverage

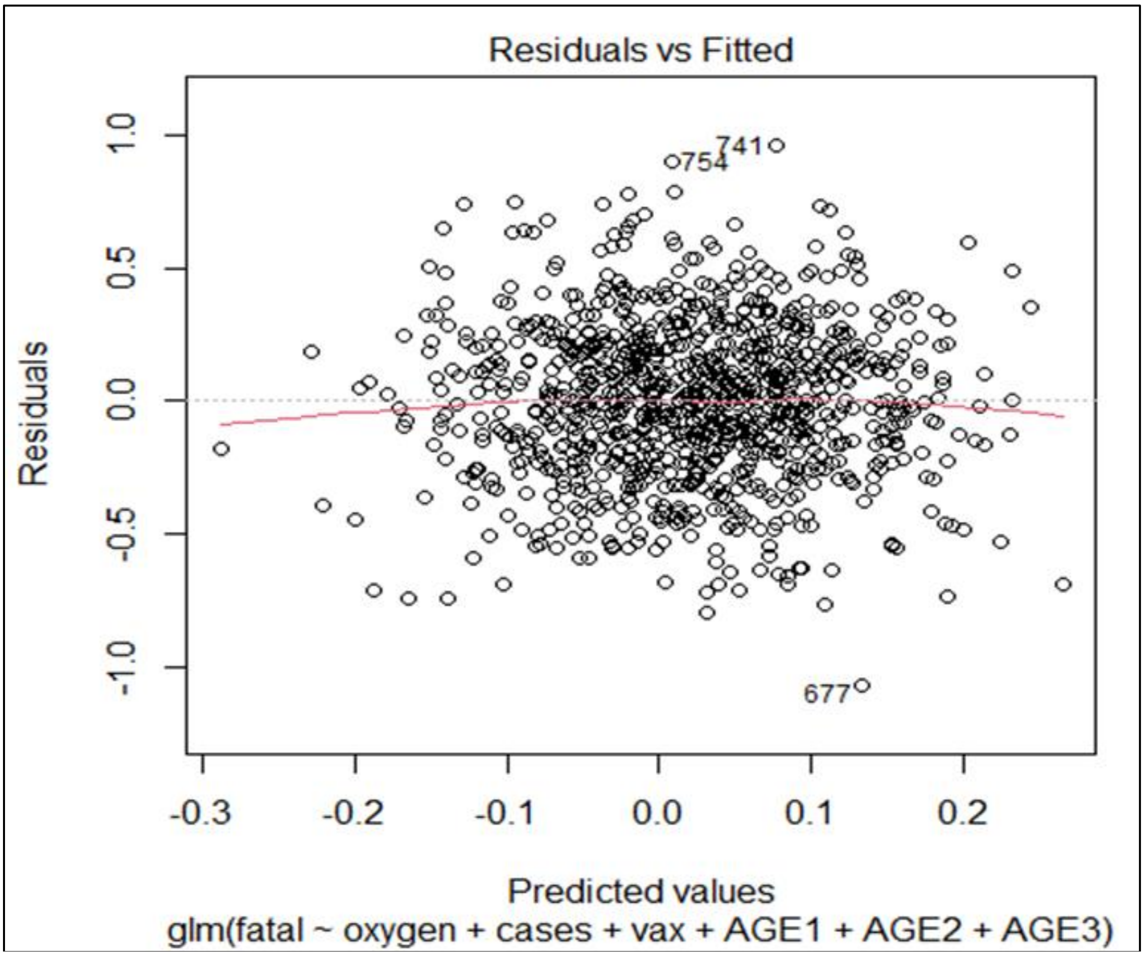

Fig 2: Residuals vs Fitted

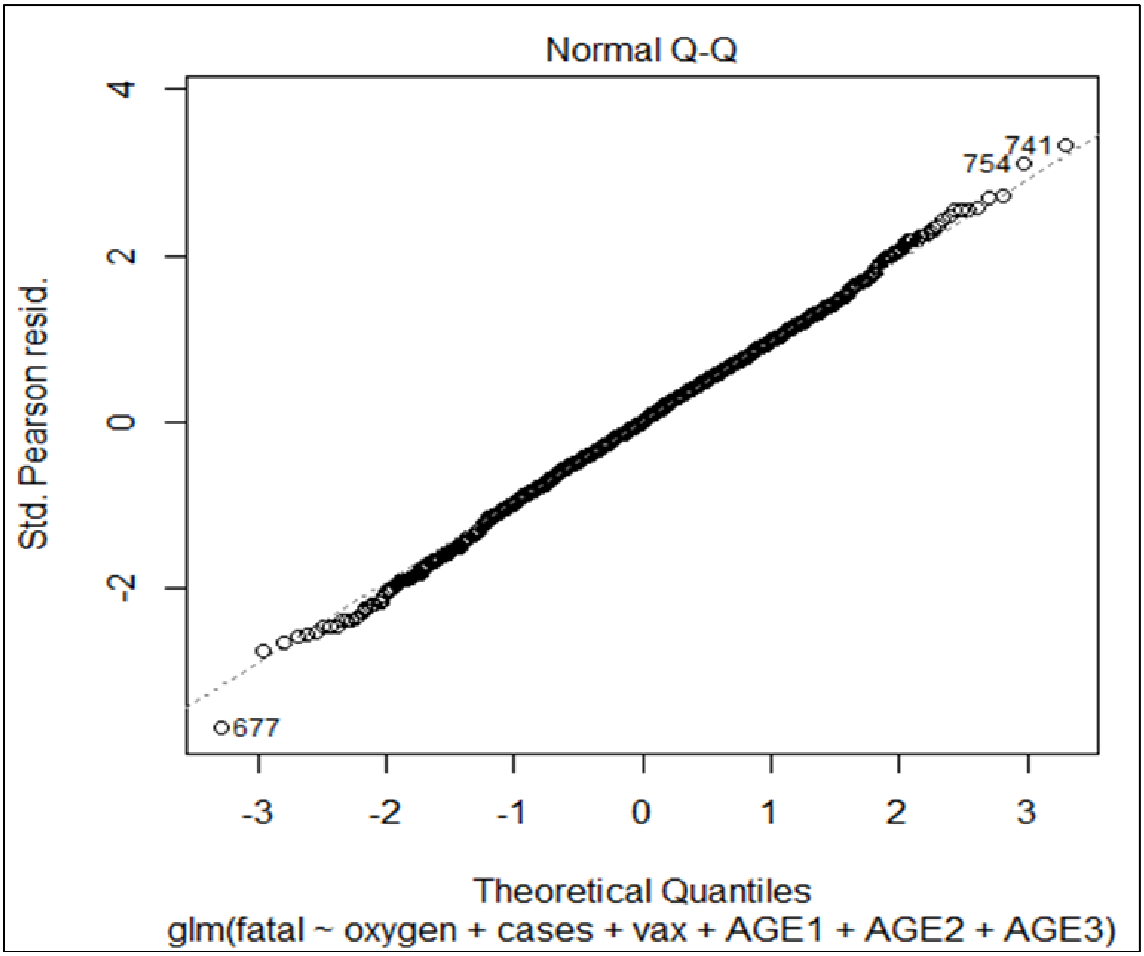

Fig 3: Normal Q-Q

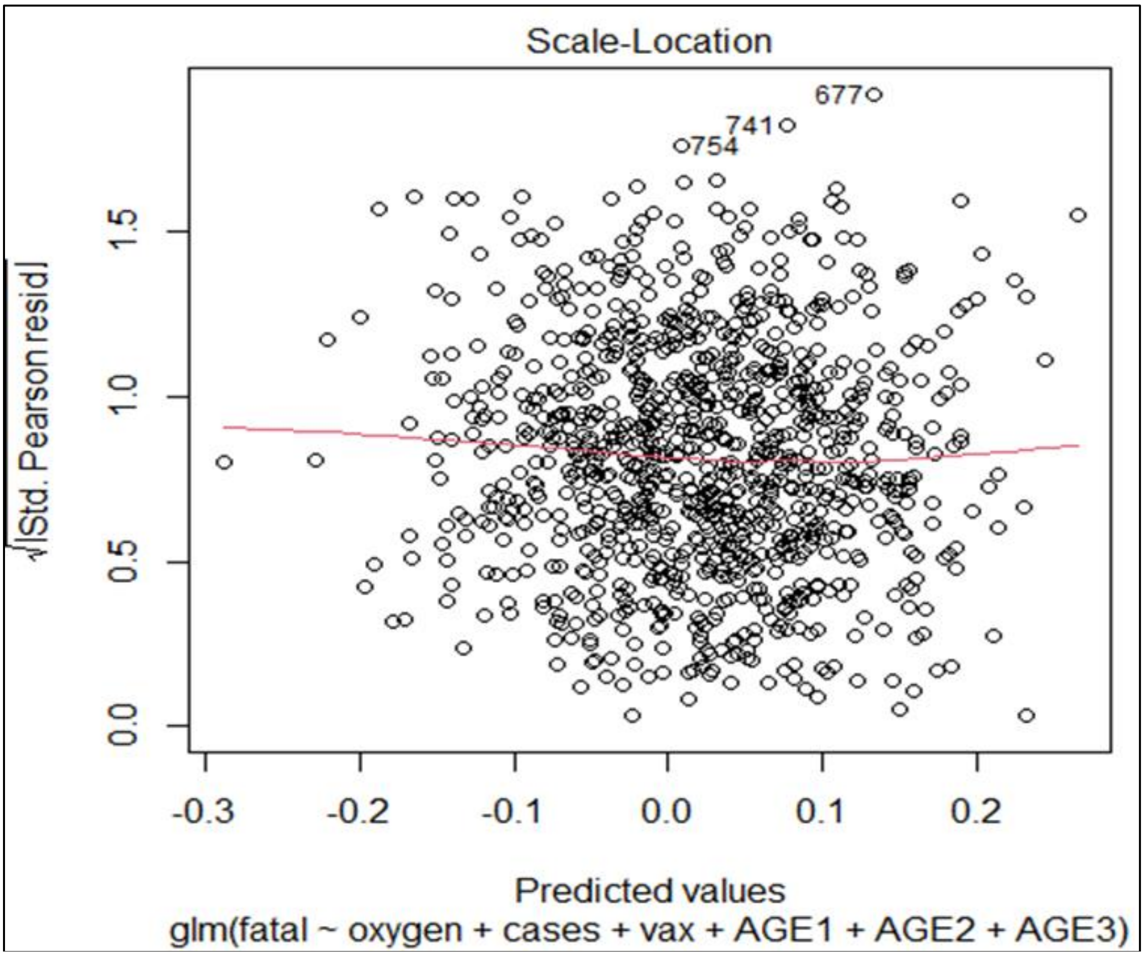

Fig 4: Scale-Location

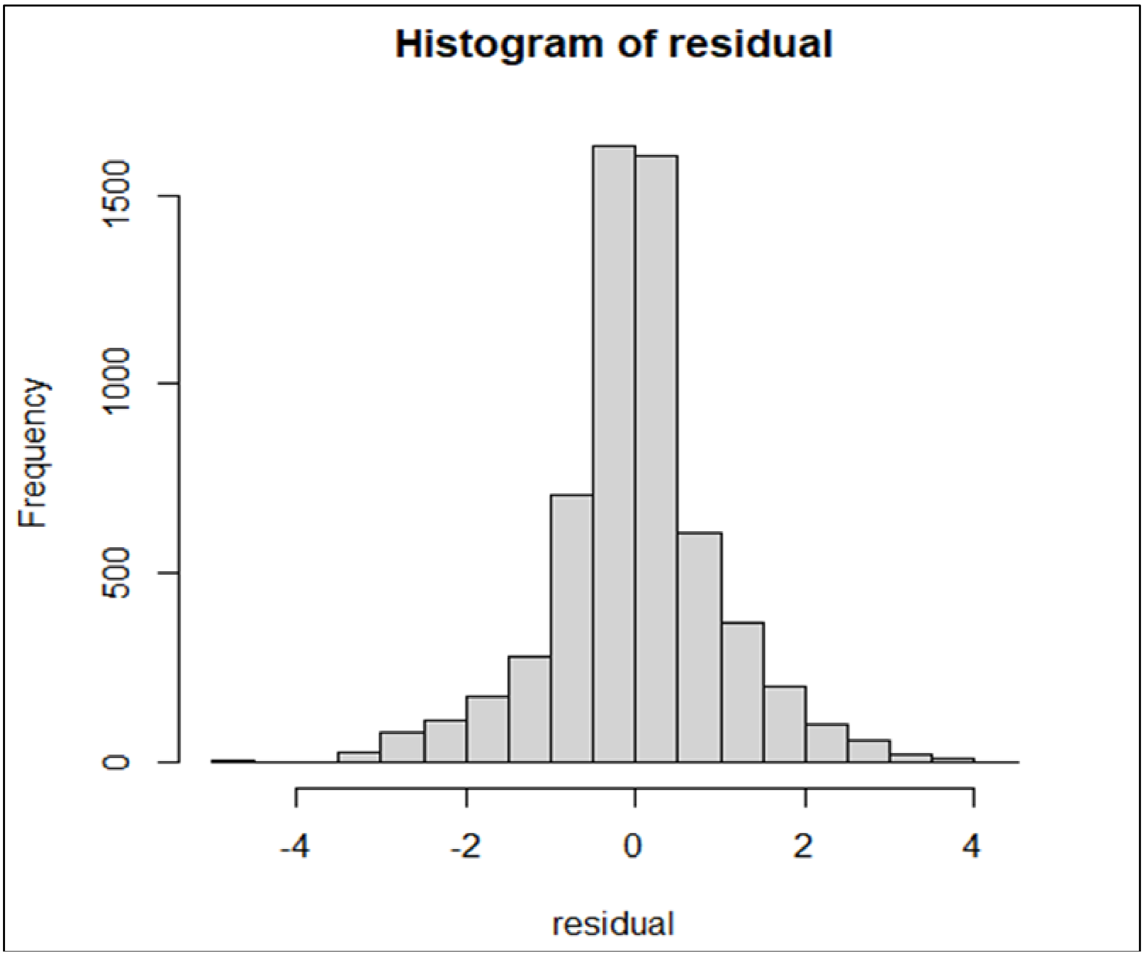

Fig 5: Histogram of residual

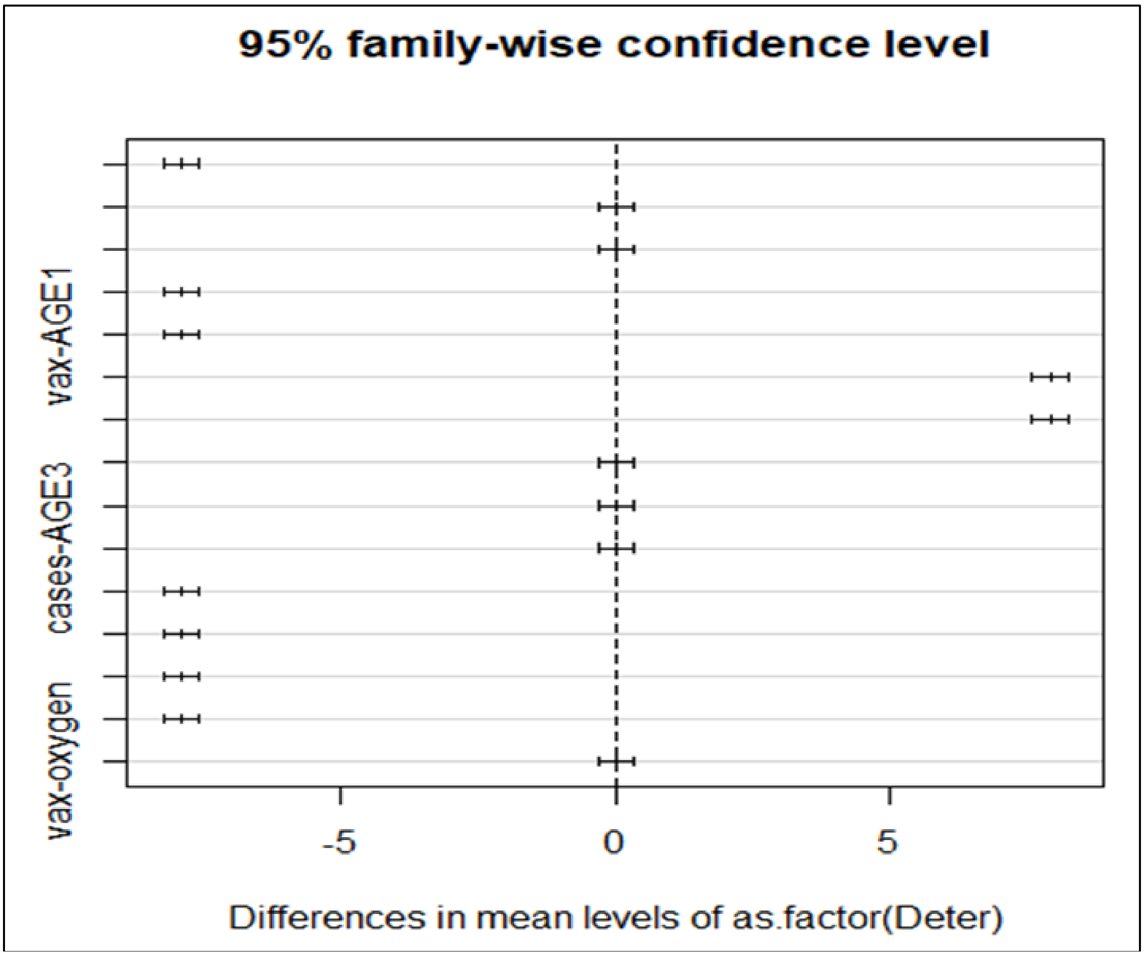

Fig 6: 95% family-wise confidence level

Tests of results

All tests of validity and significance show that the estimated model is valid and significant. However, residual-leverage, fitted-residual, normality Q-Q plots, scale-location tests all reveal only 3 outlying observations.

Interpretation of Results

1. Based on the odds ratios $Intercept$: $e^{\beta_0} = 0.42$, implies that controlling for all factors, an individual is $100(1-0.42)\% = 58\%$, $(95\%\ CI$, 24% - 88%) less likely to die of covid-19 infections.
2. Case infection: $e^{0.05207} = 1.053$, implying, controlling for other factors, an individual infected with covid-19 is $100(1.053 - 1)\% = 5.3\%$, $(1.053{:}\ 95\%\ \text{CI}, 1.03\ -\ 3.34)$ more likely to succumb compared to uninfected person.
3. Oxygen flow rate: $e^{0.30887} = 0.734274$, implies $100(1-0.73)\%$ =27%, (95% CI, 7% -33%) controlling for other factors, given the average oxygen flow rate in LREB, an individual admitted in ICU is 27% less likely to die of covid-19 complication compared to other patients in facilities that do not have supplementary oxygen.
4. Cumulative Vaccination: $e^{0.822} = 2.27$, implies $100(2.66-1)\% = 127\%\ or\ 1.27\ times$: Controlling for other factors, an unvaccinated individual is 1.27, (95% CI, 1.14 -6.26) times more likely to have severe covid-19 infection and die compared to a fully vaccinated individual.
5. The ages are made categorical variable: 0-19 years is chosen as the reference group. Theoretically, persons aged 0-19 years have less likelihood of getting severe Covid-19 and succumbing. So, we compare odds ratios of the two cohorts as shown below:

$$\text{OR} = \frac{\text{Odds of reference cohort}}{\text{Odds of specific cohort}} \tag{8}$$

$$\text{OR for } (20-49)\text{yrs} = \frac{\text{Odds}(20-49)}{\text{Odds }(0-19)} = \frac{1.421198}{1.1744} = 1.21 = 100(1.21-1)\% = 21\% \tag{9}$$

When infected, an individual aged between 20 and 49 years is 21%, (CI 95: 2%, 30.4%) more likely to succumb to Covid-19 as compared to one aged between 0 and 19 years old.

$$\text{OR for } (50+\text{ years}) = \frac{\text{Odds for}(50+)\text{years}}{\text{Odds for}(0-19)\text{years}} = \frac{1.728925}{1.1744} = 1.47 = 100(1.47-1)\% = 47\% \tag{10}$$

When infected, an individual aged 50 years and older is 47%, (95% CI: 3%,36%) more likely to succumb to Covid-19 compared to one aged between 0 and 19 years old.

Prediction

$$\widehat{\text{P}} = \frac{\text{e}^{(-0.86012+0.05207\text{CASE}+0.30887\text{OXYGCA}+0.822\text{VAX}+0.1608\text{AGE1}+0.3515\text{AGE2}+0.5475\text{AGE3})}}{(1+(\text{e}^{((-0.86012+0.05207\text{CASE}+0.30887\text{OXYGCA}*\frac{1}{2}+0.822\text{VAX}+0.1608\text{AGE1}+0.3515\text{AGE2}+0.5475\text{AGE3})}} \tag{11}$$

We can now predict the probability of an infected unvaccinated individual aged 65 years admitted in covid-19 management facility whose oxygen flow rate is 5.54 litres per minute succumbing to covid-19.
We set vaccinated=1, not vaccinated=0, infected (case)=1, uninfected=0) and run the model as shown below.

$$\widehat{\text{P}} = \frac{\text{e}^{(-0.86012+0.05207*1+0.30887*5.54+0.822*0+0.1608*0+0.3515*0+0.5475*65)}}{(1+(\text{e}^{\left(0.86012+0.05207*1+0.30887*\frac{1}{2}2.27+0.822*0+0.1608*0+0.3515*0+0.5475*65\right)})} = 0.9 \tag{12}$$

There is a 90% chance that the individual in question will die of covid-19 complication when admitted in ICU with conditions described above.

Discussion

In this study, statuses of determinants of desirable health outcome are discussed based on data collected during the assessment exercise. The determinants of successful prevention of Covid-19 infections which focus on exposure and social distancing are not considered. Alternatively, the focus is on conditions that influence covid-19 patients management outcomes. These include oxygen capacity in terms of flow rate per minute, cumulative vaccination, age as associated with underlying conditions, and actual number of covid-19 cases. The likelihood of fatality is an outcome of covid-19 management.

Theoretically, vaccination is a moderating factor; cumulative cases is an exposure variable; age is a confounding factor; and oxygen need is an effect multiplier. These determinants cannot be considered in isolation for the risk of running into omitted variable biases.

To arrive at the desired objective, cumulative fatalities are treated as response variable while oxygen capacity, vaccination, cases, and age are independent variables. The multiple logistic regression model is chosen because of the sensitivity of odds ratio to likelihood of events occurring and ease of association of joint causal variables. All the variables are individually normalized before estimating the model. For likelihood function, the dependent variable must have values between zero (0) and One (1). A predictive model is then formulated from the exponentiated estimated coefficients of used variables. A hypothetical case is then considered to test the suitability of the model.

Findings indicate that controlling for other factors, given the average oxygen flow rate in LREB health facilities, an individual admitted in ICU is 27%, (95% CI, 7% -33%) more likely to succumb to Covid-19 because of insufficient oxygen compared to a patient without critical oxygen needs. From the assessment, it was found that all fourteen (14) counties of LREB have access to oxygen, however, only Siaya, Kisumu, and Kisii counties have sufficient capacity. The remaining counties had oxygen production plants that do not operate optimally because compressors got overwhelmed and broke down. The explanation offered by biomechanical teams suggested that oxygen generation plants require regular maintenance, without which they breakdown. Also, when pants run continually for hours because of increased high oxygen flow demand, the compressors stall. The best practice supplements production plants with bulk storage tanks. However, oxygen concentrators which are mostly relied on do not supply sufficient oxygen for even patients with moderate needs. These findings agree with (Lancet, 2021).

In the model vaccination is considered as a moderating influence. Adjusting for other factors, unvaccinated patient is 1.27 times (95% CI, 1.14 -6.26) more likely to die of Covid-19 compared to the fully vaccinated. At the time of assessment, out of a targeted adult population of 8,003,755 only 45,292 people had been fully vaccinated, accounting for 0.56%. At the time of assessment two issues were at play; inadequate vaccine doses available; and vaccine hesitancy. There was a third, not widely spread, delay in entering the vaccinated people data into the COVAX platform. Sometimes the system took too long to upload resulting in under reporting. Whereas Alverez-Mon *et al*. (2021) in Spain found basal oxygen saturation to have the highest importance in association with covid-19 management outcome, the study found vaccination to be having higher influence on whether a patient will recover or succumb. The findings are in line with Xiang, *et al.* (2021) [17] which concluded that vaccination of at least on dose of (BioNTech BNT162 or AstraZeneca ChAdOX1 nCoV-19) is associated with decrease in hospitalization and mortalities of cardiovascular and other diseases (preprint).

Age is a confounding factor. Studies have associated age with prevalence of underlying medical conditions Alveraz-Mon *et al.* (2021). Susceptibility increases with advancement in ages. In this study, age is divided into three groups: Age1 (0-19) years, Age2 (20-49) years, and Age3 (50 years and older) cohorts. For analysis, (0-19) years cohort is taken as the reference group. The other two cohorts are then compared to it. Adjusting for other factors, a patient aged (20-49) years is 21%, (95% CI, 2% -30.4%) more likely to succumb to Covid-19 compared to one aged (0-19) years. Also, a patient aged 50 years and older is 47%, (95% CI, 3% - 56%) more likely to succumb to Covid-19 compared to one in (0-19) years age bracket. The finding on association of age with covid-19 fatalities concurs with *Biswas et al.* (2021) which found increased risk of fatality for patients aged 50 years and older compared to younger patients.

Adjusting for all variables, the likelihood of mortality after being infected is 5.3% or (1.053:95% CI, 1.03 - 3.34). With this information a predictive model is formulated, and a hypothetical situation is simulated: an infected unvaccinated individual aged 65 years admitted in covid-19 management facility whose oxygen flow rate is 5.54 litres per minute has the probability of 0.9 chances of succumbing to covid-19.

Recommendations

1. Vaccination, according to this study, has the highest importance. As such, vaccination efforts must be accelerated to cover the eligible adult population quickly to safeguard life and livelihoods.
2. Oxygen production plants should be maintained regularly and supplemented with bulk storage tanks.
3. Persons aged 50 years and older have higher risk of death and severe covid-19 upon exposure and infection. There are equally have low digital literacy to register for vaccination online. They need digital literacy support to access online platforms and get vaccinated.
4. Most rural populations have lower digital literacy levels compared to urban dwellers. The also have fewer smartphones to enable registration on online vaccination platform. They need support to register and get vaccinated to avoid severe covid-19 and death.
5. People aged 50 years and older must be protected from exposure by having reduced movement, avoiding all indoor gatherings and other super spreader events, social distancing notwithstanding.
6. A study should investigate association of co-morbidities, gender, and pregnancy with covid-19 fatalities.

Conclusion

Lake Region Economic Region has gaps in vaccination, oxygen production, testing, boarder surveillance, resources coordination, and research to accelerate sustainable clinical and socioeconomic recovery

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