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Factors Influencing the First and Second Peak of COVID-19 Global Cases: A Survival Analysis

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Abstract

The first cases of coronavirus disease 2019 (COVID-19) were reported in December 2019, followed by a rapid global increase in confirmed cases. This study aimed to characterize the time patterns of reaching the first and second peaks of COVID-19 cases across different countries and identify potential determinants associated with the timing of these peaks using global COVID-19 data obtained from the Our World in Data dataset from January 22, 2020, to January 21, 2021. A semi parametric Cox proportional hazards (Cox-PH) model was applied to evaluate the effects of potential covariates on the time to reach the peaks. The results demonstrated significant differences in survival times across categories of several covariates for both the first and second peaks. For the first peak, continent, Human Development Index, population density, life expectancy, cardiovascular death rate, hospital beds per thousand people, and total number of deaths were identified as significant determinants. For the second peak, Human Development Index, population density, and diabetes prevalence were found to be significant factors. This study provides insights into the factors associated with the timing of COVID-19 waves and may assist public health organizations in improving preparedness and resource allocation strategies for future infectious disease outbreaks.

Keywords: COVID-19 disease; Cox-PH model; first peak; second peak.

I. Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a newly identified coronavirus. Most individuals infected with COVID-19 experience mild to moderate respiratory illness and recover without requiring specialized medical treatment. However, older adults and individuals with underlying medical conditions, including cardiovascular disease, diabetes, chronic respiratory diseases, and cancer, are at a higher risk of developing severe illness[1].

The first human cases of COVID-19, caused by the novel coronavirus later named SARS-CoV-2, were reported by health authorities in Wuhan City, China, in December 2019. Retrospective investigations by Chinese authorities identified human cases with symptom onset as early as December 2019[2].

The severity of the COVID-19 pandemic increased rapidly worldwide. By 18 February 2021, the total number of confirmed cases had reached approximately 110 million[3]. This pandemic had profound negative impacts on human life, while public health systems, food security, and the global economy faced immense challenges. The social and economic consequences triggered by the pandemic were devastating. According to the World Health Organization (WHO), approximately 150 million people were at risk of falling into extreme poverty by 2021.

Health care delivery organizations faced unprecedented challenges due to the rapid increase in COVID-19 cases. Hospitals struggled with limited capacity to manage the growing number of patients, and many patients died because of inadequate access to intensive care unit (ICU) beds and ventilators at critical times. In addition, ensuring adequate safety measures for healthcare workers remained a major concern.

Understanding the timing of COVID-19 peaks is essential for healthcare organizations to effectively plan and allocate resources. Accurate estimates of peak timing can help health care systems prepare appropriate strategies to manage the pandemic. Many countries experienced the first and second waves of COVID-19 transmission. By January 2021, the first peak had been observed in almost all countries, while the second peak had occurred in several countries.

Although numerous studies have investigated the clinical outcomes, mortality risk, and survival probability of COVID-19 patients, relatively less attention has been given to understanding the temporal pattern of COVID-19 transmission at the country level. The timing of epidemic peaks varies substantially among countries due to differences in demographic characteristics, healthcare capacity, public health interventions, environmental conditions, and socioeconomic factors. Identifying the factors associated with the time required to reach epidemic peaks can provide important insights into the progression of infectious disease outbreaks and support evidence-based decision-making.

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Traditional statistical approaches often focus on the magnitude of COVID-19 cases or deaths rather than the time dynamics of epidemic progression. However, the occurrence of a peak represents an event that happens after a certain period from the initial outbreak, making it suitable for analysis using survival methods. Survival analysis provides a flexible framework to evaluate time-to-event outcomes while accounting for censored observations and estimating the influence of multiple covariates on the timing of an event. Therefore, this approach can be useful for evaluating differences in peak occurrence times among countries.

In this study, we focused on the time required to reach the first and second peaks of COVID-19 cases. The time interval was defined as the duration between the date of the first confirmed COVID-19 case and the date when the corresponding peak occurred. This interval can be considered time-to-event data and analyzed using survival analysis methods. We aimed to investigate the underlying factors associated with the time required to reach the first and second peaks of COVID-19 cases.

To the best of our knowledge, few studies have applied survival analysis to investigate the determinants associated with the timing of the first and second peaks of COVID-19 cases using global country-level data.This study contributes to existing literature by examining the time required for countries to reach their first and second COVID-19 case peaks and identifying potential demographic, socioeconomic, and health-related factors associated with these timings.

Leulseged et al[4] applied survival analysis to estimate time to getting off supplemental oxygen therapy and identify predictors among COVID-19 patients admitted to Millennium COVID-19 Care Center in Addis Ababa, Ethiopia.This study revealed that average duration of supplemental oxygen therapy requirement among COVID-19 patients was 6 days and being 70 years and older having shortness of breath were found to be associated with prolonged duration of supplemental oxygen therapy requirement.

Oulhaj et al.[5] investigated through extensive simulations the bias in estimating the hazard ratio (HR) and the absolute risk reduction (ARR) of death when competing risks were ignored and suggested an alternative method and found that there were a substantial risk of misleading results in COVID-19 research if recovery and death due to COVID-19 were not considered as competing risk events.. Thai et al[6] used Cox-PH model to identify factors associated with the median duration of hospital stays of COVID-19 patients during the second COVID-19 wave that hit Vietnam from 5 March to 8 April 2020.

Atlametal.[7] developed Cox COVID-19 and Deep Cox COVID-19 systems based on Cox regression to perform survival analysis, assist hospitals in identifying patients with higher survival probabilities, and determine important predictors affecting survival out comes. Salinas-Escudero et al.[8] applied survival analysis to investigate the impact of COVID-19 on the Mexican population and found that the risk of dyingatany time during follow-up was clearly higher formen, individuals in older age groups, people with chronic kidney disease and people hospitalized in public health services. Implementing survival analysis, it was found that impaired renal function and advanced age were major predictors of in-hospital death in a large cohort of unselected patients with COVID-19, admitted to 30 different clinical centers all over Italy.[9]

Kundu and Mandal[10] carried out asurvival analysis to establish the variability in survivorshipamong age groups and sex at different levels that is national, state and district levelin India. Alietal.[11] implemented survival analysis to determine risk factors for death in patients with COVID-19 admitted to the main public sector hospital in Somalia and identify interventions contributing to improved clinical outcome in a low-resource and fragile setting. Implementing multivariate Cox-PH model it was found that preparation control measures of COVID-19 should involve the allocation of sufficient medical resources, especially in are as with older vulnerable populations and in areas that lack basic medical resources.[12]

II. Methods

Data and Variables

The COVID-19 dataset used in the analysis was collected from Our World in Data[3]from January 22, 2020 to21 January 2021.The dataset included country-level daily data on confirmed cases, deaths and testing, as well as other variables of potential interest. These data were compiled from multiple sources, including the European Centre for Disease Prevention and Control, the International Organization for Standardization (ISO), national government reports, the Department of Economic and Social Affairs of the United Nations(UN), UN Population Division, UN Statistics Division, Oxford COVID-19 Government Response Tracker, the World Bank, the Global Burden of Disease Collaborative Network, ion and Development.

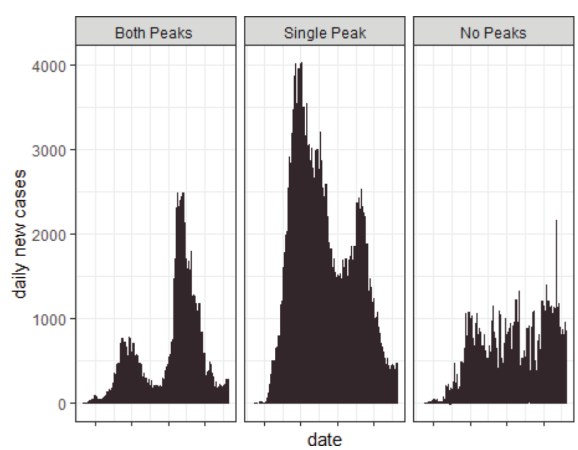

Fig.1. Defining and understanding Peak

For each country, we created a bar plot with the date on the x-axis and the number of daily COVID-19 cases on theyaxis. Based on these plots, we determined whether countries experienced the first peak, both first and secondpeak,or no peaks according to Figure 1.

After extracting the necessary variables for this study, we created two separate and independent datasets for the first and second peak. The dataset included information from a total of 188 countries. We identified the countries where the first peak of COVID-19 cases occurred and the countries where the first peak had not occurred by the data collection date. Countries where first peak was not found by the data collection date were considered as right censored. or 175 countries by data collection date. Then we created two variables called time and status as below.

$$\text{time} = \begin{cases} (1^{st}\text{ peak observed} \\ \text{date} - 1^{st}\text{ case} \\ \text{observed date}), & \textbf{if } 1^{st}\textbf{ peak found} \\ \text{data collection date} \\ \text{date} - 1^{st}\text{ case} \\ \text{observed date}), & \textbf{if } 1^{st}\textbf{ peak not found} \end{cases}$$

$$\text{status} = \begin{cases} 1, & \textbf{if } 1^{st}\textbf{ peak found} \\ 0, & \textbf{if } 1^{st}\textbf{ peak not found} \end{cases}$$

In the same way, we created a separate data set for the second peak. Among 188 Countries second peak occurredin 58 countries by data collection date. The time and statusvariable for second peak dataset were calculated as follows.

$$\text{time} = \begin{cases} (2^{nd}\text{ peak observed} \\ \text{date} - 1^{st}\text{ case} \\ \text{observed date}), & \textbf{if } 2^{nd}\textbf{ peak found} \\ \text{data collection date} \\ \text{date} - 1^{st}\text{ case} \\ \text{observed date}), & \textbf{if } 2^{nd}\textbf{ peak not found} \end{cases}$$

$$\text{status} = \begin{cases} 1, & \textbf{if } 2^{nd}\textbf{ peak found} \\ 0, & \textbf{if } 2^{nd}\textbf{ peak not found} \end{cases}$$

In this study, we focused primarily on the time (in days) required to reach the first and second peaks. We considered factors that may influence the time to hit the first peak and second peak. For the first peak dataset, the response variables were time (days) to reach the first peak and the censoring status for the first peak. Similarly, for the second peak dataset, the response variables were time (days) to reach the second peak and the corresponding censoring status.

All independent variables considered in this study were categorical. We considered the following independent variables in our analysis: continent, Human Development Index (HDI), population density, GDP per capita, life expectancy (in years), percentage of 70 years or above people, median age (in years), diabetes prevalence, cardiovascular death rate, hospital beds per thousand, total number of deaths (up to the data collection date).

Statistical Analysis

Frequencies and percentages were used to describe independent variables. Median time to reach the first and second peaks was also calculated across different categories of the covariates. Non-parametric Kaplan-Meier survival plots were used to explore the relationship between the time to reach the peaks and various explanatory variables. The log-rank test was applied to assess whether there was any significant difference in the time to reach the peaks among different groups.

The semi-parametric Cox proportional hazards model (Cox-PH) was applied to the survival data for finding out the potential risk factors that are associated with the first and the second peaks. The Cox-PH model[13] is essentially a regression model commonly used in statistics and medical research for investigating the association between the survival time of patients and one or more predictor variables.

The Cox-PH model is given by,

$$h(t/X_i)=h_0(t)\exp(\beta_1 X_{i1}+\cdots+\beta_k X_{ik}),$$

where t is survival time.$h_0(t)$ is called the baseline hazard function .$X_i=(X_{i1},X_{i2},\ldots, X_{ik})^t$ is the values of the vector of explanatory variables for a particular individual and $\beta=(\beta_1,\beta_2,\cdots,\beta_k)$ is a vector of regression coefficients.

All the statistical analyses were conducted with statistical software R.

III. Results

The first peak was observe dinalmost all the ountries, where as the second peak was observed in only for a few countries. 61 countries had a Human Development Index (HDI) below 0.65. Out of these 61 countries, the first peak was observed for 91.8% and the second peak was observed for 31.1% countries.The first peak was observed for all the countries with population density between 250 - 500. A similar pattern was observed for countries with GDP per capita above 30000 and countries with diabetes prevalence below 3 (See Table 1).

The median waiting time to reach the second peak was estimated for only a limited number of categories because the second peak was observed in only 58 countries. The median waiting time to reach the first peak was approximately 50 days for countries with HDI above 0.85. However, this value was only 109 days for countries with HDI below 0.65.

The median waiting time to reach the second peak was 267 days for countries with population density above 500. The median waiting time to reach the first peak was comparatively higher for countries from continents other than Asia and Europe compared with countries in Asia and Europe. The median waiting time was higher for countries with life expectancy above 75 years, percentage of 70 years plus population below 5, median age above 40, diabetes prevalence above12, hospitalbed per thousand is below 3 (See Table 1).

Results of the log- rank test indicated that there was no significant difference between the population survival times a cross different categories of variable continent for the first peak since p-value is greater than 0.05.Similar results were observed for population density, percentage of 70 years or above people, median age, diabetes prevalence, cardiovascular death rate & hospital beds per thousand. On the contrary, there was a significant difference among survival time sacross different categories of HD I,GDP percapita, life expectancy & total number of deaths at 5% level of significance. It was also observed that the time to reach the first peak was longer for countries with HDI between 0.65 and 0.85. Additionally, countries with lower life expectancy tended to reach the first peak later. Countries with a lower total number of deaths also had shorter waiting times to reach the first peak (See Figure 2).

According to Figure 3, there was no statistically significant difference in survival times among different categories of life expectancy for the second peak, as the p-value was greater than 0.05. Similar findings were observed for total number of deaths, percentage of the population aged 70 years or older, median age, diabetes prevalence, cardiovascular death rate, and hospital beds per thousand people. However, significant differences in survival times were found among categories of HDI, GDP per capita, continent, and population density at the 5% significance level. Figure 3 also showed that the time to reach the second peak was shorter for countries in Asia and Europe. Furthermore, countries with HDI between 0.65 and 0.85 also had a longer time to reach the second peak of COVID-19 cases.

Table 2 represents the results of multivariate Cox proportional hazards (Cox-PH) model for both peaks. The Cox-PH results indicated that continent, HDI, population density, GDP percapita, life expectancy, cardiovascular death rate, hospital beds per thousand & total number of deaths were the significant factor associated with the time to reach the first peak of COVID-19 cases. In addition, HDI, population density & diabetes prevalence were identified as significant factors associated with the time to hit the second peak.

Table 1. Characteristics of survival times by categorical covariates

Variable Category	No. of Countries	First Peak		Second Peak	
		No. of Events	Median Survival Time (days)	No. of Events	Median Survival Time (days)
Continent					
Asia & Europe	93	93.5%	84	40%	–
Others	95	92.6%	109	21%	–
Human Development Index					
Below 0.65	61	91.8%	109	31.1%	–
0.65 - 0.85	82	91.4%	122.5	21.9%	–
Above 0.85	39	97.4%	50	48.7%	338
Population density					
Below 25	39	89.7%	101	38.4%	–
25 - 100	66	93.9%	115.5	24.2%	–
100 - 250	46	91.3%	98	21.7%	–
250 - 500	20	100%	79	40%	–
Above 500	13	92.3%	43	61.5%	267
GDP per capita					
Below 3000	36	88.9%	80	27.8%	–
3000 - 8000	36	97.2%	122.5	25%	–
8000 - 16000	37	89.1%	143	29.7%	–
16000 - 30000	34	88.8%	102.5	14.7%	–
Above 30000	37	100%	53	56.75%	318
Life expectancy					
Below 75	101	93%	24.8	25%	–
75+	86	93%	69.5	38.4%	–
Percentage of 70 years or above people					
Below 5	106	93.4%	115	29.2%	–
5+	72	91.7%	69.5	33.4%	–
Median age					
Below 25	68	92.6%	110	27.9%	–
26 - 40	74	91.9%	112	32.4%	–
Above 40	37	94.6%	60	35.1%	–
Diabetes prevalence					
Below 3	18	100%	97.5	38.9%	–
3 - 12	141	92.1%	88	31.9%	–
Above 12	25	92%	104	24%	–
Cardiovascular death rate					
Below 350	145	91.7%	95	32.4%	–
350+	37	97.3%	85	24.3%	–
Hospital beds per thousand					
Below 3	107	94.4%	110	30.8%	–
3+	59	93.2%	62	32.25%	338
Total number of deaths					
Below 250	58	98.2%	75.5	25.8%	–
250 - 2500	56	87.5%	117.5	32.1%	–
2500 - 10000	34	97%	120	32.3%	–
Above 10000	30	90%	105	30%	–

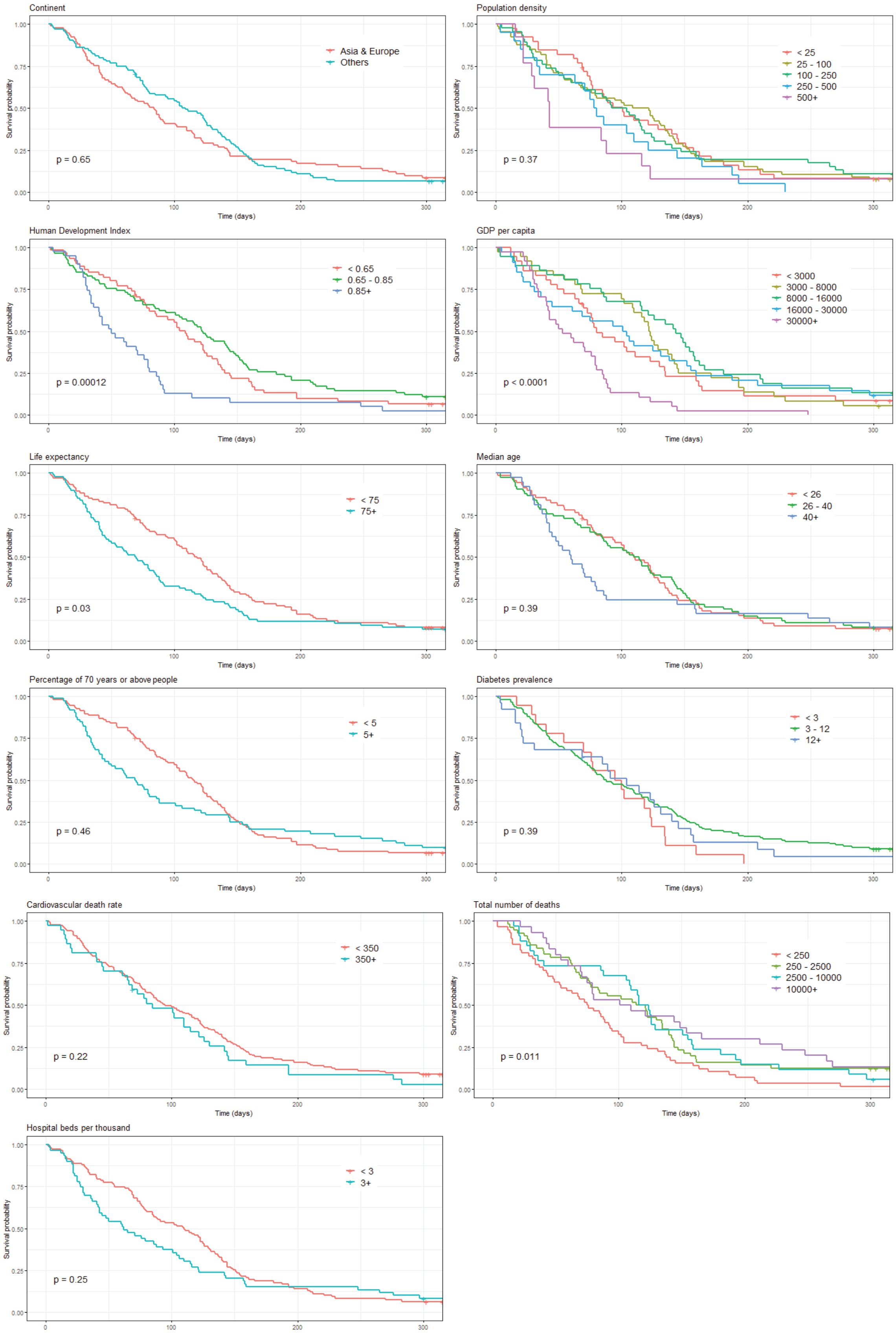

Fig. 2. Kaplan–Meier survival function estimates for the first peak against covariates

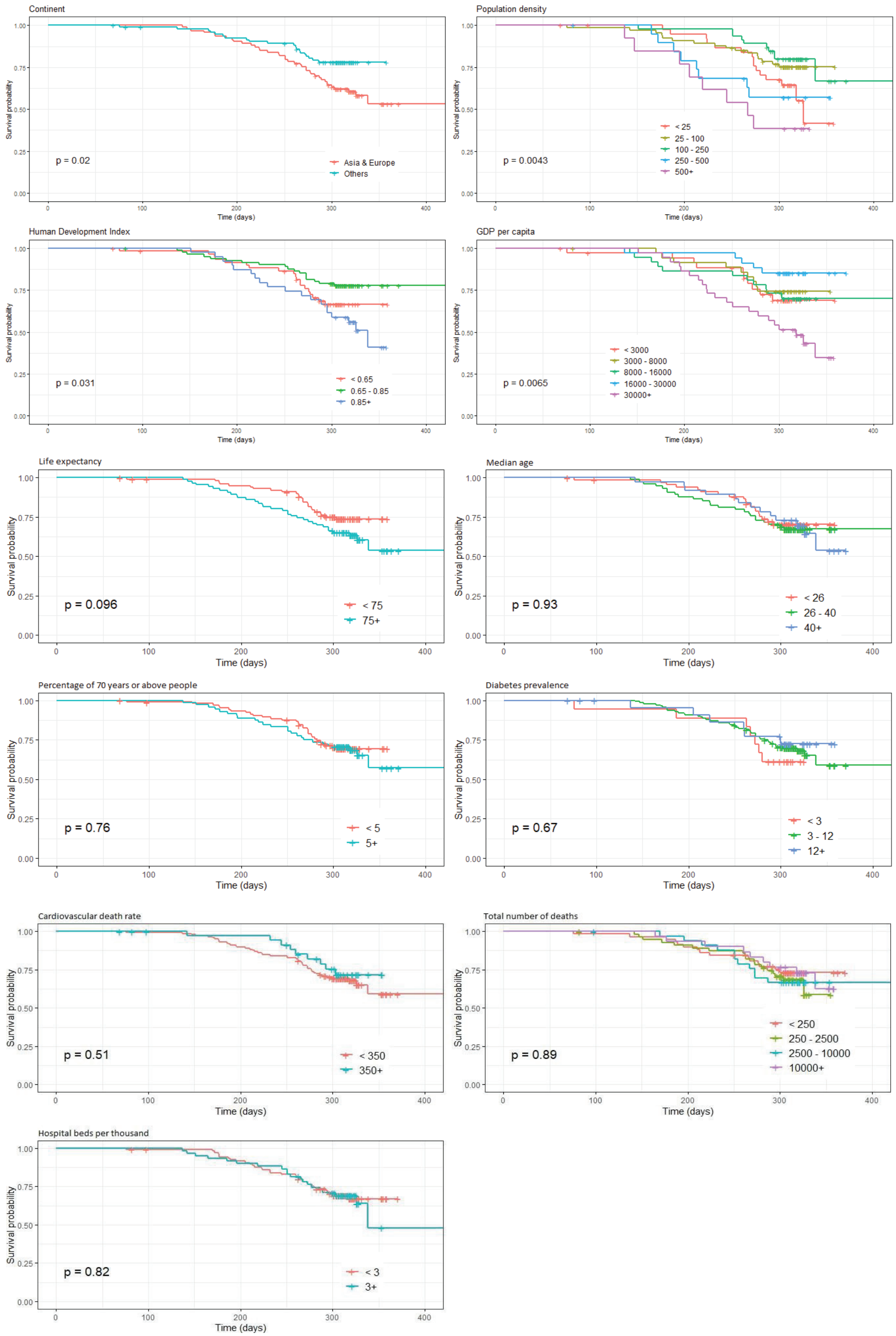

Fig. 3. Kaplan–Meier survival function estimates for the second peak against covariates

Table 2. **Hazard ratios and their 95% confidence intervals**

Variable Category	First Peak		Second Peak	
	Hazard Ratio	95% Confidence Interval	Hazard Ratio	95% Confidence Interval
Continent				
Others	1		1	
Asia & Europe	1.753*	(1.046, 2.936)	0.649	(0.227, 1.855)
Human development index				
Below 0.65	1		1	
0.65 - 0.85	0.349*	(0.148, 0.820)	0.085*	(0.008, 0.915)
Above 0.85	0.572	(0.172, 0.920)	0.030*	(0.002, 0.584)
Population density				
Below 25	1		1	
25 - 100	1.182	(0.689, 2.027)	0.538	(0.210, 1.379)
100 - 250	0.965	(0.555, 1.680)	0.329*	(0.119, 0.908)
250 - 500	2.259*	(1.149, 4.444)	1.805	(0.617, 5.278)
Above 500	1.294	(0.488, 3.249)	1.795	(0.496, 6.497)
Life expectancy				
Below 75	1		1	
75+	1.871*	(1.003, 3.490)	3.1	(0.745, 12.899)
GDP per capita				
Below 3000	1		1	
3000−8000	1.422	(0.650, 3.108)	0.498	(0.082, 3.039)
8000−16000	2.303	(0.798, 6.643)	0.2.514	(0.161, 39.311)
16000−30000	2.416	(0.858, 6.797)	1.373	(0.084, 22.424)
Above 30000	9.579*	(2.436, 37.658)	15.085	(0.565, 400.830)
Percentage of 70 years or above people				
Below 5	1		1	
5+	0.742	(0.411, 1.339)	0.861	(0.246, 3.016)
Median age				
Below 26			1	
26 - 40	1.004	(0.498, 2.023)	2.281	(0.361, 14.434)
Above 40	0.600	(0.208, 1.729)	1.017	(0.113, 9.145)
Diabetes prevalence				
Below 3	1		1	
3 - 12	0.451	(0.201, 1.010)	0.155*	(0.036, 0.680)
Above 12	0.392	(0.138, 1.112)	0.113*	(0.014, 0.898)
Cardiovascular death rate				
Below 350	1		1	
350+	2.941***	(1.595, 5.426)	1.497	(0.430, 5.213)
Hospital beds Per thousand				
Below 3	1		1	
3+	1.902*	(1.099, 3.291)	1.680	(0.646, 4.371)
Total number of deaths				
Below 250	1		1	
250 - 2500	0.595*	(0.370, 0.958)	0.690	(0.286, 1.665)
2500 - 10000	0.654	(0.374, 1.143)	1.862	(0.716, 4.84)
Above 10000	0.402**	(0.223, 0.722)	0.860	(0.304, 2.428)

**p-value* < 0.05; ***p-value* < 0.01; ****p-value* < 0.001

IV. Discussion

Results from the Cox proportional hazards (Cox-PH) model showed that the hazard ratio for countries in Asia and Europe was 1.753 with a p-value < 0.05. Compared with countries from other continents, countries in Asia and Europe had approximately 75% higher likelihood of reaching the first peak of COVID-19 cases. In contrast, for the second peak, the hazard ratio for countries in Asia and Europe was 0.649 and was not statistically significant (p-value > 0.05), indicating that there was no significant difference in the likelihood of reaching the second peak across different continent categories.

For the variable Human Development Index (HDI), the reference category was "Below 0.65". For the first peak, the hazard ratios for countries with HDI categories "0.65 to 0.85" and "Above 0.85" were 0.349 (p-value < 0.05) and 0.572 (p-value > 0.05), respectively. This indicated that countries with HDI between 0.65 and 0.85 were approximately 65% less likely to reach the first peak of COVID-19 cases compared with countries with HDI below 0.65. However, there was no statistically significant difference between countries with HDI below 0.65 and above 0.85. For the second peak, countries with HDI between 0.65 and 0.85 and above 0.85 had hazard ratios of 0.085 and 0.030, respectively, compared with countries with HDI below 0.65.

For population density, only the category "250–500" had a significant hazard ratio for the first peak (p-value < 0.05). The reference category was "Below 25". Countries with population density between 250 and 500 were approximately 2.25 times more likely to reach the first peak of COVID-19 cases compared with countries with population density below 25. Similarly, only the category "100–250" was significant for the second peak. Countries with population density between 100 and 250 were approximately 67% less likely to experience the second peak compared with the reference category.

Life expectancy was identified as a significant factor associated with reaching the first peak but not the second peak. The reference category was "Below 75 years". The hazard ratio for countries with life expectancy above 75 years was 1.871, indicating that these countries were approximately 87% more likely to reach the first peak compared with countries with life expectancy below 75 years.

For GDP per capita, only the category "Above 30,000" showed a significant hazard ratio for the first peak. No category of GDP per capita was significantly associated with the second peak. Countries with GDP per capita above 30,000 were approximately 9.5 times more likely to reach the first peak compared with countries with GDP per capita below 3,000.There was no statistically significant difference in the likelihood of reaching either the first or second peak across categories of the percentage of the population aged 70 years or older and median age. Compared with countries with diabetes prevalence below 3, countries with diabetes prevalence between 3 and 12 and above 12 had hazard ratios of 0.16 and 0.11, respectively, for reaching the second peak.

For the first peak, the hazard ratio for countries with cardiovascular death rates above 350 per 100,000 people was 2.941. This indicated that countries with cardiovascular death rates above 350 per 100,000 people were approximately 2.94 times more likely to reach the first peak compared with other countries. There was no significant difference in the likelihood of reaching the second peak across categories of hospital beds per thousand people. However, for the first peak, countries with more than 3 hospital beds per thousand people were approximately 1.9 times more likely to reach the first peak compared with countries with fewer than 3 hospital beds per thousand people.

For total number of deaths, the reference category was below 250". The hazard ratios for countries with total deaths between 250 and 2,500 and above 10,000 were 0.595 and 0.402, respectively. This indicated that countries with total deaths between 250 and 2,500 and above 10,000 were approximately 0.59 and 0.40 times as likely to reach the first peak compared with countries with total deaths below 250. However, there was no significant difference between countries with total deaths between 2,500 and 10,000 and those below 250. For the second peak, all categories of total number of deaths had insignificant hazard ratios (p-value > 0.05), indicating no statistically significant difference in the likelihood of reaching the second peak across death categories.

V. Limitations & Further Scope

Our study had several limitations. The data used here contained several missing values which were omitted while performing Cox regression. Here missing values could be replaced with any imputed values. We had skipped some important variables due to data deficiency such as hand-washing facilities, smokers' prevalence, hospital patients per million, poverty rate etc. Adjustment of those variables could yield better results.

VI. Conclusion

Through this analysis, we identified the time patterns for different countries to reach the first and second peaks of COVID-19 cases. We also identified several potential covariates that had significant effects on the time required to reach these peaks. The number of days to reach the first peak was shorter for countries in Asia and Europe compared with countries from other continents. Life expectancy was also found to be a significant factor associated with the timing of the first peak. Countries with lower life expectancy tended to take longer to reach the first peak. Similar patterns were observed for cardiovascular death rate and hospital beds per thousand people. The number of days required to reach the second peak was significantly longer in countries with higher diabetes prevalence. A similar pattern was observed for the Human Development Index. Additionally, the occurrence of the second peak was more likely in densely populated countries.

Author's Contributions

YAO contributed to designing, analyzing and drafting the manuscript, both BZ and DB contributed to analyzing and finalizing the drafting, MHRK contributed to designing methodds and manuscript, arranging data, and drafting.

Availability of Data and Materials

The dataset used in this study is publicly available and can be accessed from the corresponding data source.

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