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The role of ACE2 cause of death between COVID-19 and various complications

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ABSTRACT

The COVID-19 pandemic has affected millions of people worldwide. While the virus primarily targets the respiratory system, it also affects other organs in the body, leading to multiple organ dysfunction syndrome (MODS) and death. Recent studies have shown that angiotensin-converting enzyme 2 (ACE2) plays a crucial role in pathogenesis of COVID-19 and development of MODS.

Since its discovery in 2000, ACE2 has garnered widespread attention for its multiple physiological roles, leading to subsequent interest in the influence of the Renin-angiotensin system (RAS) on SARS-CoV-2 infection and COVID-19 during the pandemic.

ACE2 is both an enzyme and a functional receptor on cell surfaces through which SARS-CoV-2 enters the host cells. Recent research has highlighted the multifaceted impact of the virus on various organs, showcasing its ability to induce severe multi-organ injuries. Understanding the intricate interplay between ACE2, RAS, and the pathophysiological changes associated with COVID-19 is crucial for the development of effective treatment strategies and preventative measures.

This study investigates the differences in causes of death related to COVID-19 and its complications. Data from cumulative records for all age groups across the 50 states of the USA and the District of Columbia was retrospectively analyzed. The results revealed significant differences in the incidence of COVID-19 deaths associated with various medical conditions, with respiratory complications showing notably higher incidence compared to other medical conditions besides COVID-19, circulatory, and diabetes.

Keywords: COVID-19, multiple organ dysfunction syndrome, angiotensin-converting enzyme 2

INTRODUCTION

The COVID-19 pandemic has led to a significant number of deaths, with various medical complications contributing to mortality [1, 2]. Understanding the differences in causes of death related to COVID-19 and its complications is crucial for informing public health strategies and clinical management [3]. This study seeks to explore the distinct patterns of mortality rates associated with COVID-19 and its complications, shedding light on the impact of respiratory complications and potential factors influencing the relationship between COVID-19 and its associated mortality.

METHODS

The data for this analysis was obtained from cumulative records for all age groups across the 50 states of the USA and the District of Columbia between 2020-2023 [1]. The data was retrospectively analyzed and categorized based on the year and medical conditions.

Table 1 shows descriptive statistics of conditions.

Table 2 shows descriptive statistics of years.

In the first regression analysis there was no significant difference found between the years in incidence of COVID-19 deaths, thus a two-way ANOVA test was not possible due to no degrees of freedom being present between categories in each year. Thus, two one-way ANOVA tests were performed to compare the incidence of COVID-19 deaths across the years and different medical complications. The study's use of ANOVA tests to compare the incidence of COVID-19 deaths across different medical complications aligns with established statistical methods for analyzing categorical data. Prior literature on epidemiological analysis has emphasized the utility of ANOVA in comparing mortality rates across distinct medical conditions, supporting the robustness of the current study's statistical approach [4].

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Table 1. Descriptive statistics of conditions

Conditions	Mean	Standard deviation
Respiratory	426,191.00	220,928.862
Other conditions	238,760.50	137,080.770
Alzheimer	17,688.50	10,772.375
Vascular dementia	46,558.50	30,305.331
Renal failure	64,837.00	40,562.839
Obesity	26,660.50	22,689.835
Circulatory	410,580.50	224,503.616
COVID-19	573,121.00	361,168.792
Diabetes	84,415.00	56,723.633
Sepsis	59,500.00	36,970.770
Injury	15,550.50	8,806.083
Neoplasms	35,834.50	16,418.240
Total	166,641.46	228,682.227

Note. Dependent variable: COVID-19 death

Table 2. Descriptive statistics of years

Year	Mean	Standard deviation	n
2020	214,266.83	254,914.125	12
2021	260,365.17	309,923.936	12
2022	151,669.33	173,481.370	12
2023	40,264.50	50,893.633	12
Total	166,641.46	228,682.227	48

Note. Dependent variable: COVID-19 death

RESULTS

Table 3 shows a significant difference in the incidence of COVID-19 death due to various medical complications, with respiratory complications showing significantly higher incidence compared to other medical conditions.

The results indicate that there was no significant difference in the overall incidence of COVID-19 deaths across the four years (p=0.09), as illustrated in **Table 4**. **Table 5** shows the pertinent ANOVA analysis to this study. However, full ANOVA with all conditions is listed in **Table A1** in **Appendix A**. The conclusion drawn from the analysis supports studies citing that the incidence of COVID-19 death was highest due to COVID-19, and respiratory complications caused by COVID-19 while maintaining no significant difference between COVID-19 and the respiratory complication mortalities [5-10]. We include descriptive statistics, regression tables, and multiple comparisons, providing a comprehensive overview of the findings. Additionally, the analysis suggests the potential influence of angiotensin-converting enzyme 2 (ACE2) on the relationship between COVID-19 and its complications, which could be further explored to understand the differences in the causes of death related to COVID-19.

Table 3. Regression analysis of conditions: Tests of between-subjects effects-conditions

Source	Type III sum of squares	df	Mean square	F	Sig.
Corrected model	1,688,176,529,144.917[a]	11	153,470,593,558.629	7.178	<.001
Intercept	1,332,930,030,502.083	1	1,332,930,030,502.083	62.342	<.001
Conditions	1,688,176,529,144.918	11	153,470,593,558.629	7.178	<.001
Error	769,714,839,373.000	36	21,380,967,760.361		
Total	3,790,821,399,020.000	48			
Corrected total	2,457,891,368,517.917	47			

Note. [a]R-squared=.687 (adjusted R-squared=.591)

Table 4. Regression analysis of years: Tests of between-subjects effects-years

Source	Type III sum of squares	df	Mean square	F	Sig.
Corrected model	326,971,319,666.916[a]	3	108,990,439,888.972	2.250	.096
Intercept	1,332,930,030,502.083	1	1,332,930,030,502.083	27.523	<.001
Year	326,971,319,666.917	3	108,990,439,888.972	2.250	.096
Error	2,130,920,048,851.000	44	48,430,001,110.250		
Total	3,790,821,399,020.000	48			
Corrected total	2,457,891,368,517.917	47			

Note. [a]R-squared=.133 (adjusted R-squared=.074)

Table 5. Multiple comparisons (Tukey HSD)

(I) Conditions	(J) Conditions	Mean difference (I-J)	Standard error	Sig.	95% confidence interval	
					Lower bound	Upper bound
Respiratory	Other conditions	187,,430.50	103,394.796	.801	-173,450.58	548,311.58
	Alzheimer	408502.50*	103,394.796	.016	47,621.42	769,383.58
	Vascular dementia	379,632.50*	103,394.796	.032	18,751.42	740,513.58
	Renal failure	361,354.00*	103,394.796	.049	472.92	722,235.08
	Obesity	399,530.50*	103,394.796	.020	38,649.42	760,411.58
	Circulatory	15,610.50	103,394.796	1.000	-345,270.58	376,491.58
	COVID-19	-146,930.00	103,394.796	.951	-507,811.08	213,951.08
	Diabetes	341,776.00	103,394.796	.077	-19,105.08	702,657.08
	Sepsis	366,691.00*	103,394.796	.044	5,809.92	727,572.08
	Injury	410,640.50*	103,394.796	.015	49,759.42	771,521.58
	Neoplasms	390,356.50*	103,394.796	.025	29,475.42	751,237.58

Note. Dependent variable: COVID-19 death; *Mean difference is significant at .05 level; & Error term is mean square (error)=21,380,967,760.361

Table 5 (continued). Multiple comparisons (Tukey HSD)

(I) Conditions	(J) Conditions	Mean difference (I-J)	Standard error	Sig.	95% confidence interval	
					Lower bound	Upper bound
COVID-19	Respiratory	146,930.00	103,394.796	.951	-213,951.08	507,811.08
	Other conditions	334,360.50	103,394.796	.091	-26,520.58	695,241.58
	Alzheimer	555,432.50*	103,394.796	<.001	194,551.42	916,313.58
	Vascular dementia	526,562.50*	103,394.796	<.001	165,681.42	887,443.58
	Renal failure	508,284.00*	103,394.796	.001	147,402.92	869,165.08
	Obesity	546,460.50*	103,394.796	<.001	185,579.42	907,341.58
	Circulatory	162,540.50	103,394.796	.908	-198,340.58	523,421.58
	Diabetes	488,706.00*	103,394.796	.002	127,824.92	849,587.08
	Sepsis	513,621.00*	103,394.796	<.001	152,739.92	874,502.08
	Injury	557,570.50*	103,394.796	<.001	196,689.42	918,451.58
	Neoplasms	537,286.50*	103,394.796	<.001	176,405.42	898,167.58

Note. Dependent variable: COVID-19 death; *Mean difference is significant at .05 level; & Error term is mean square (error)=21,380,967,760.361

DISCUSSION

ACE2 is expressed in various tissues, including the respiratory tract, cardiovascular system, and gastrointestinal tract, which may contribute to the multi-organ involvement observed in severe COVID-19 cases 11.3, 12.4, 13.5.

The virus binds to ACE2 on the surface of human cells and serves as the entry receptor for the SARS-CoV-2 virus, which is responsible for COVID-19. Despite many similarities to SARS coronavirus, SARS-CoV-2 exhibits a higher affinity to ACE2 and shows higher transmissibility, resulting in explosive increase of infected people and COVID-19 patients [2, 11].

The findings from the analysis suggest that the incidence of COVID-19 death was highest due to COVID-19, and respiratory complications caused by COVID-19. This is consistent with the known high expression of ACE2, the receptor for SARS-CoV-2, in the respiratory tract, and may contribute to the high incidence of COVID-19 death associated with respiratory complications.

The findings also indicate that the incidence of COVID-19 death was not significantly different from the incidence of COVID-19 death due to respiratory complications, suggesting that respiratory complications play a critical role in COVID-19 mortality. The expression of ACE2 in the respiratory tract may have paradoxical effects, aiding SARS-CoV-2 pathogenicity, yet conversely limiting viral infection. The high expression of ACE2 in the respiratory tract may facilitate viral entry and infection, contributing to the pathogenicity of SARS-CoV-2 [12].

However, the expression of ACE2 may also limit viral infection by sequestering the virus and preventing its spread to other tissues. This may explain the high incidence of COVID-19 death associated with respiratory complications, as the virus may be more likely to cause severe disease when it infects the respiratory tract.

It is thought that the expression of ACE2 in the respiratory and gastrointestinal tracts may help to regulate the immune response to the virus and prevent it from causing more severe disease. This may help to explain why some people experience only mild symptoms of COVID-19, while others develop more severe disease [5, 13-17].

The interaction between SARS-CoV-2 and ACE2 has implications for viral entry, replication, and the host immune response. Additionally, the downregulation of ACE2 expression due to viral infection may disrupt the balance of the renin-angiotensin system, potentially contributing to the pathophysiology of COVID-19 and potentially contributing to severe and multiple organ injury [17, 18].

Additionally, ACE2 is highly expressed in the heart, kidneys, and lungs, and its expression and its previously mentioned potential paradoxical effects could aid SARS-CoV-2 pathogenicity, yet conversely limiting viral infection, which is seen in findings [11, 19, 20].

The study's findings are consistent with prior research that has highlighted the significant impact of respiratory complications on COVID-19 mortality [16, 17]. Studies have suggested that found that ACE2 expression levels in the respiratory tract may influence the severity of COVID-19, with higher ACE2 expression potentially leading to more severe lung injury causing acute respiratory distress syndrome, pneumonia and other respiratory complications [5, 13, 15, 18, 21].

Research on ACE2 in the context of COVID-19 has focused on understanding its role in viral pathogenesis, disease severity, and potential therapeutic targets.

CONCLUSIONS

The significance of the findings from the analysis of COVID-19 deaths across different medical complications lies in the identification of the highest incidence of COVID-19 deaths due to COVID-19 and respiratory complications caused by COVID-19. These findings underscore the critical impact of respiratory complications in contributing to COVID-19 mortality.

The analysis revealed that the incidence of COVID-19 deaths associated with respiratory complications was significantly higher than those associated with other medical conditions, except for COVID-19, circulatory, and diabetes. Additionally, the incidence of death due to COVID-19 was found to be comparable to the incidence of COVID-19 deaths caused by respiratory complications.

The significance of these findings is multifaceted. Firstly, it highlights the need for targeted interventions and public health strategies to address respiratory complications in COVID-19 patients, potentially leading to improved clinical

management and outcomes. Secondly, the identification of ACE2 enzyme's potential influence on the relationship between COVID-19 and its complications suggests a novel avenue for further research. ACE2 enzyme has been implicated in mediating the entry of the SARS-CoV-2 virus into host cells, and its role in the pathogenesis of COVID-19 and its associated complications warrants further investigation.

The significance of these findings extends to public health policy, clinical practice, and ongoing research efforts aimed at understanding and mitigating the impact of COVID-19.

The identification of respiratory complications as a significant contributor to COVID-19 mortality underscores importance of targeted preventive measures and therapeutic interventions for this specific medical condition. Furthermore, the potential role of ACE2 enzyme opens avenues for exploring novel treatment modalities and understanding the mechanistic underpinnings of COVID-19 complications.

In summary, the findings from the analysis of COVID-19 deaths across different medical complications provide critical insights into the impact of respiratory complications on COVID-19 mortality and suggest a potential role for ACE2 enzyme in mediating the relationship between COVID-19 and its complications, thereby informing public health strategies, clinical management, and future research directions.

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Data sharing statement: Data supporting the findings and conclusions are available upon request from the author.

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APPENDIX A

Table A1. Full AVOVA (Tukey HSD)

(I) Conditions	(J) Conditions	Mean difference (I-J)	Standard error	Sig.	95% confidence interval	
					Lower bound	Upper bound
Respiratory	Other conditions	187,430.50	103,394.796	.801	-173,450.58	548,311.58
	Alzheimer	408,502.50*	103,394.796	.016	47,621.42	769,383.58
	Vascular dementia	379,632.50*	103,394.796	.032	18,751.42	740,513.58
	Renal failure	361,354.00*	103,394.796	.049	472.92	722,235.08
	Obesity	399,530.50*	103,394.796	.020	38,649.42	760,411.58
	Circulatory	15,610.50	103,394.796	1.000	-345,270.58	376,491.58
	COVID-19	-146,930.00	103,394.796	.951	-507,811.08	213,951.08
	Diabetes	341,776.00	103,394.796	.077	-19,105.08	702,657.08
	Sepsis	366,691.00*	103,394.796	.044	5,809.92	727,572.08
	Injury	410,640.50*	103,394.796	.015	49,759.42	771,521.58
	Neoplasms	390,356.50*	103,394.796	.025	29,475.42	751,237.58
Other conditions	Respiratory	-187,430.50	103,394.796	.801	-548,311.58	173,450.58
	Alzheimer	221,072.00	103,394.796	.601	-139,809.08	581,953.08
	Vascular dementia	192,202.00	103,394.796	.775	-168,679.08	553,083.08
	Renal failure	173,923.50	103,394.796	.865	-186,957.58	534,804.58
	Obesity	212,100.00	103,394.796	.658	-148,781.08	572,981.08
	Circulatory	-171,820.00	103,394.796	.873	-532,701.08	189,061.08
	COVID-19	-334,360.50	103,394.796	.091	-695,241.58	26,520.58
	Diabetes	154,345.50	103,394.796	.933	-206,535.58	515,226.58
	Sepsis	179,260.50	103,394.796	.841	-181,620.58	540,141.58
	Injury	223,210.00	103,394.796	.587	-137,671.08	584,091.08
	Neoplasms	202,926.00	103,394.796	.714	-157,955.08	563,807.08
Alzheimer	Respiratory	-408,502.50*	103,394.796	.016	-769,383.58	-47,621.42
	Other conditions	-221,072.00	103,394.796	.601	-581,953.08	139,809.08
	Vascular dementia	-28,870.00	103,394.796	1.000	-389,751.08	332,011.08
	Renal failure	-47,148.50	103,394.796	1.000	-408,029.58	313,732.58
	Obesity	-8,972.00	103,394.796	1.000	-369,853.08	351,909.08
	Circulatory	-392,892.00*	103,394.796	.023	-753,773.08	-32,010.92
	COVID-19	-555,432.50*	103,394.796	<.001	-916,313.58	-194,551.42
	Diabetes	-66,726.50	103,394.796	1.000	-427,607.58	294,154.58
	Sepsis	-41,811.50	103,394.796	1.000	-402,692.58	319,069.58
	Injury	2,138.00	103,394.796	1.000	-358,743.08	363,019.08
	Neoplasms	-18,146.00	103,394.796	1.000	-379,027.08	342,735.08
Vascular dementia	Respiratory	-379,632.50*	103,394.796	.032	-740,513.58	-18,751.42
	Other conditions	-192,202.00	103,394.796	.775	-553,083.08	168,679.08
	Alzheimer	28,870.00	103,394.796	1.000	-332,011.08	389,751.08
	Renal failure	-18,278.50	103,394.796	1.000	-379,159.58	342,602.58
	Obesity	19,898.00	103,394.796	1.000	-340,983.08	380,779.08
	Circulatory	-364,022.00*	103,394.796	.046	-724,903.08	-3,140.92
	COVID-19	-526,562.50*	103,394.796	<.001	-887,443.58	-165,681.42
	Diabetes	-37,856.50	103,394.796	1.000	-398,737.58	323,024.58
	Sepsis	-12,941.50	103,394.796	1.000	-373,822.58	347,939.58
	Injury	31,008.00	103,394.796	1.000	-329,873.08	391,889.08
	Neoplasms	10,724.00	103,394.796	1.000	-350,157.08	371,605.08
Renal failure	Respiratory	-361,354.00*	103,394.796	.049	-722,235.08	-472.92
	Other conditions	-173,923.50	103,394.796	.865	-534,804.58	186,957.58
	Alzheimer	47,148.50	103,394.796	1.000	-313,732.58	408,029.58
	Vascular dementia	18,278.50	103,394.796	1.000	-342,602.58	379,159.58
	Obesity	38,176.50	103,394.796	1.000	-322,704.58	399,057.58
	Circulatory	-345,743.50	103,394.796	.071	-706,624.58	15,137.58
	COVID-19	-508,284.00*	103,394.796	.001	-869,165.08	-147,402.92
	Diabetes	-19,578.00	103,394.796	1.000	-380,459.08	341,303.08
	Sepsis	5,337.00	103,394.796	1.000	-355,544.08	366,218.08
	Injury	49,286.50	103,394.796	1.000	-311,594.58	410,167.58
	Neoplasms	29,002.50	103,394.796	1.000	-331,878.58	389,883.58

Table A1 (Continued). Full AVOVA (Tukey HSD)

(I) Conditions	(J) Conditions	Mean difference (I-J)	Standard error	Sig.	95% confidence interval	
					Lower bound	Upper bound
Obesity	Respiratory	-15,610.50	103,394.796	1.000	-376,491.58	345,270.58
	Other conditions	171,820.00	103,394.796	.873	-189,061.08	532,701.08
	Alzheimer	392,892.00*	103,394.796	.023	32,010.92	753,773.08
	Vascular dementia	364,022.00*	103,394.796	.046	3,140.92	724,903.08
	Renal failure	345,743.50	103,394.796	.071	-15,137.58	706,624.58
	Obesity	383,920.00*	103,394.796	.029	23,038.92	744,801.08
	COVID-19	-162,540.50	103,394.796	.908	-523,421.58	198,340.58
	Diabetes	326,165.50	103,394.796	.108	-34,715.58	687,046.58
	Sepsis	351,080.50	103,394.796	.063	-9,800.58	711,961.58
	Injury	395,030.00*	103,394.796	.022	34,148.92	755,911.08
	Neoplasms	374,746.00*	103,394.796	.036	13,864.92	735,627.08
Circulatory	Respiratory	146,930.00	103,394.796	.951	-213,951.08	507,811.08
	Other conditions	334,360.50	103,394.796	.091	-26,520.58	695,241.58
	Alzheimer	555,432.50*	103,394.796	<.001	194,551.42	916,313.58
	Vascular dementia	526,562.50*	103,394.796	<.001	165,681.42	887,443.58
	Renal failure	508,284.00*	103,394.796	.001	147,402.92	869,165.08
	Obesity	546,460.50*	103,394.796	<.001	185,579.42	907,341.58
	COVID-19	162,540.50	103,394.796	.908	-198,340.58	523,421.58
	Diabetes	488,706.00*	103,394.796	.002	127,824.92	849,587.08
	Sepsis	513,621.00*	103,394.796	<.001	152,739.92	874,502.08
	Injury	557,570.50*	103,394.796	<.001	196,689.42	918,451.58
	Neoplasms	537,286.50*	103,394.796	<.001	176,405.42	898,167.58
COVID-19	Respiratory	-341,776.00	103,394.796	.077	-702,657.08	19,105.08
	Other conditions	-154,345.50	103,394.796	.933	-515,226.58	206,535.58
	Alzheimer	66,726.50	103,394.796	1.000	-294,154.58	427,607.58
	Vascular dementia	37,856.50	103,394.796	1.000	-323,024.58	398,737.58
	Renal failure	19,578.00	103,394.796	1.000	-341,303.08	380,459.08
	Obesity	57,754.50	103,394.796	1.000	-303,126.58	418,635.58
	Circulatory	-326,165.50	103,394.796	.108	-687,046.58	34,715.58
	COVID-19	-488,706.00*	103,394.796	.002	-849,587.08	-127,824.92
	Sepsis	24,915.00	103,394.796	1.000	-335,966.08	385,796.08
	Injury	68,864.50	103,394.796	1.000	-292,016.58	429,745.58
	Neoplasms	48,580.50	103,394.796	1.000	-312,300.58	409,461.58
Diabetes	Respiratory	-366,691.00*	103,394.796	.044	-727,572.08	-5,809.92
	Other conditions	-179,260.50	103,394.796	.841	-540,141.58	181,620.58
	Alzheimer	41,811.50	103,394.796	1.000	-319,069.58	402,692.58
	Vascular dementia	12,941.50	103,394.796	1.000	-347,939.58	373,822.58
	Renal failure	-5,337.00	103,394.796	1.000	-366,218.08	355,544.08
	Obesity	32,839.50	103,394.796	1.000	-328,041.58	393,720.58
	Circulatory	-351,080.50	103,394.796	.063	-711,961.58	9,800.58
	COVID-19	-513,621.00*	103,394.796	<.001	-874,502.08	-152,739.92
	Diabetes	-24,915.00	103,394.796	1.000	-385,796.08	335,966.08
	Injury	43,949.50	103,394.796	1.000	-316,931.58	404,830.58
	Neoplasms	23,665.50	103,394.796	1.000	-337,215.58	384,546.58
Sepsis	Respiratory	-15,610.50	103,394.796	1.000	-376,491.58	345,270.58
	Other conditions	171,820.00	103,394.796	.873	-189,061.08	532,701.08
	Alzheimer	392,892.00*	103,394.796	.023	32,010.92	753,773.08
	Vascular dementia	364,022.00*	103,394.796	.046	3,140.92	724,903.08
	Renal failure	345,743.50	103,394.796	.071	-15,137.58	706,624.58
	Obesity	383,920.00*	103,394.796	.029	23,038.92	744,801.08
	COVID-19	-162,540.50	103,394.796	.908	-523,421.58	198,340.58
	Diabetes	326,165.50	103,394.796	.108	-34,715.58	687,046.58
	Sepsis	351,080.50	103,394.796	.063	-9,800.58	711,961.58
	Injury	395,030.00*	103,394.796	.022	34,148.92	755,911.08
	Neoplasms	374,746.00*	103,394.796	.036	13,864.92	735,627.08

Note. Dependent variable: COVID-19 death; *Mean difference is significant at .05 level; & Error term is mean square (error)=21,380,967,760.361

Table A1 (Continued). Full AVOVA (Tukey HSD)

(I) Conditions	(J) Conditions	Mean difference (I-J)	Standard error	Sig.	95% confidence interval	
					Lower bound	Upper bound
Injury	Respiratory	-410,640.50*	103,394.796	.015	-771,521.58	-49,759.42
	Other conditions	-223,210.00	103,394.796	.587	-584,091.08	137,671.08
	Alzheimer	-2,138.00	103,394.796	1.000	-363,019.08	358,743.08
	Vascular fementia	-31,008.00	103,394.796	1.000	-391,889.08	329,873.08
	Renal failure	-49,286.50	103,394.796	1.000	-410,167.58	311,594.58
	Obesity	-11,110.00	103,394.796	1.000	-371,991.08	349,771.08
	Circulatory	-395,030.00*	103,394.796	.022	-755,911.08	-34,148.92
	COVID-19	-557,570.50*	103,394.796	<.001	-918,451.58	-196,689.42
	Diabetes	-68,864.50	103,394.796	1.000	-429,745.58	292,016.58
	Sepsis	-43,949.50	103,394.796	1.000	-404,830.58	316,931.58
	Neoplasms	-20,284.00	103,394.796	1.000	-381,165.08	340,597.08
Neoplasms	Respiratory	-390,356.50*	103,394.796	.025	-751,237.58	-29,475.42
	Other conditions	-202,926.00	103,394.796	.714	-563,807.08	157,955.08
	Alzheimer	18,146.00	103,394.796	1.000	-342,735.08	379,027.08
	Vascular dementia	-10,724.00	103,394.796	1.000	-371,605.08	350,157.08
	Renal failure	-29,002.50	103,394.796	1.000	-389,883.58	331,878.58
	Obesity	9,174.00	103,394.796	1.000	-351,707.08	370,055.08
	Circulatory	-374,746.00*	103,394.796	.036	-735,627.08	-13,864.92
	COVID-19	-537,286.50*	103,394.796	<.001	-898,167.58	-176,405.42
	Diabetes	-48,580.50	103,394.796	1.000	-409,461.58	312,300.58
	Sepsis	-23,665.50	103,394.796	1.000	-384,546.58	337,215.58
	Injury	20,284.00	103,394.796	1.000	-340,597.08	381,165.08

Note. Dependent variable: COVID-19 death; *Mean difference is significant at .05 level; & Error term is mean square (error)=21,380,967,760.361