Prevalence of Chain-of-Event and Contributing Conditions Among Treated COVID-19 Patients in the United States: Identifying Risk Factors Associated with Deaths

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Background

- The Coronavirus disease 2019 (COVID-19) pandemic resulted in 184,341 confirmed deaths involving COVID-19 infection during the first 6 months in the United States (US), increasing to over a million deaths by the end of 2022.[1]
- Deaths attributed to COVID-19 have been under-reported due to missed COVID-19 diagnoses among deaths attributed to pneumonia.[2]
- Chronic health conditions such as diabetes, hypertension, and chronic obstructive pulmonary disease are significantly associated with death following COVID-19 infection.[3]
- Of the 357,133 US deaths attributed to COVID-19 in 2020, 97.3% had a diagnosis for a chain-of-event condition (COE) (e.g., pneumonia or respiratory failure), significant contributing condition (SCC) (e.g., hypertension or diabetes), or both.[4]

Objective

- This study assessed the burden of COE and/or SCC among all patients with a healthcare claim with COVID-19 diagnosis as well as those confirmed dead after COVID-19 diagnosis.

Methods: Study Design

- For this retrospective observational study, patients with any medical claim including COVID-19 diagnosis in IQVIA's Professional Fee claims database (Dx) from 01 April 2020 to 30 April 2022 (selection window) were identified (Figure 1).
- Among these patients, the presence of any claim with ICD-10 CM diagnosis code for COE within +/- 7 days of last COVID-19 diagnosis were assessed.
- The presence of any SCC were reported between 01 April 2019 and end of follow-up period (study period).[4]
- Patients with COE or SCC or both and no subsequent claims activity anytime during the follow-up period starting 30 days after the last COVID-19 diagnosis were classified as 'possibly dead'.
- Linkage to Veritas Data Research mortality database was performed using IQVIA's proprietary algorithm applying a deterministic approach.
- Patients who were 'confirmed dead' in Veritas Data Research database were identified.
- The proportion of patients identified as possibly dead and confirmed dead was assessed overall and by patient characteristics.

Figure 1. Illustration of study design
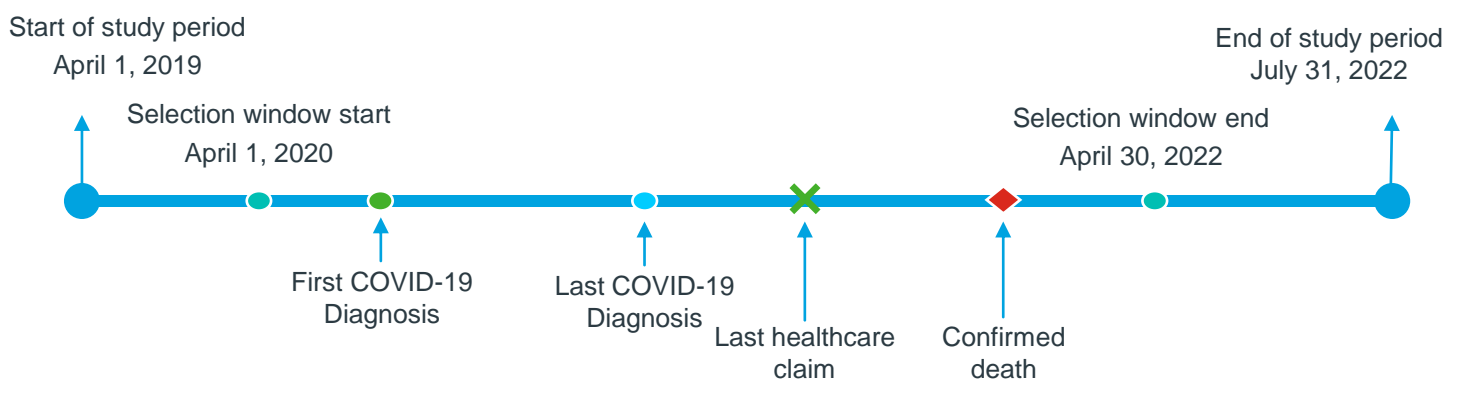
Data Sources

Open-source Medical Claims Database (Dx)
- Dx database has a wide coverage with approximately 1.2M health care practitioners represented (76% of the AMA coverage), 1.5B professional fee claims, 5.6B diagnostic claims services per year submitted, and over 150M active claims. Records are available from September 1999, with approximately 95% of claims available for analyses within 3 weeks of the service date. Over time, there is representation from approximately 236 physician specialties. The data includes details regarding patient demographics, physician demographics, diagnoses, procedures, and in-office administered drugs.

Veritas Data Research Database
- Veritas Data Research has sourced, collated, and indexed mortality data from over 40,000 sources to build the most complete and timely resource on the market. More than 30 million fact-of-death records are available over the last 10 years, representing 90% of the official CDC reporting, and 90% of the records are reported within a month of death.

Results

Study population
- Overall, 5.5% of the 17,682,111 patients with a medical claim for COVID-19 were flagged as possibly dead based on a concurrent COE/SCC as well as a cessation of claims activity at any point more than 30 days after the last COVID-19 diagnosis.
- Of the treated COVID-19 patients, 3.2% were confirmed dead using Veritas Data Research database (Figure 2).

Figure 2. Study population
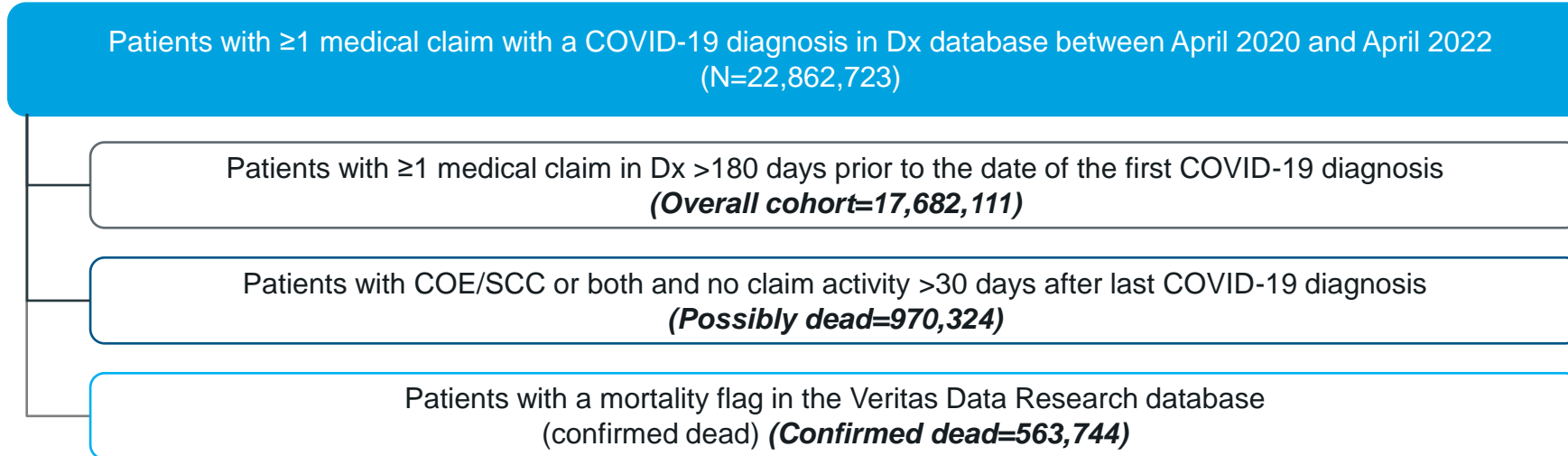
Demographic characteristics
- A large proportion of treated COVID-19 patients were <54 years of age; whereas large a proportion of the patients identified as possibly dead and confirmed dead were >65 years old (Table 1).
- While over 80% of treated COVID-19 patients and over 60% of those identified as possibly dead had commercial insurance coverage, about half of the confirmed dead patients had Medicare coverage.

Table 1. Baseline demographic characteristics of treated COVID-19 cohort, possibly dead and confirmed dead patients

Demographic Characteristics	Overall treated COVID-19 cohort		Possibly dead		Confirmed dead	
	N=17,682,111		N=970,324		N=563,744	
Age Group: (n, %)						
Missing/Unknown	43,972	0.25%	2929	0.30%	3	0.00%
0 - 17 y	2,544,842	14.39%	27137	2.80%	2,023	0.36%
18-34 y	3,657,848	20.69%	92728	9.56%	8,606	1.53%
35-44 y	2,309,158	13.06%	80187	8.26%	11,517	2.04%
45-54 y	2,404,011	13.60%	90393	9.32%	25,572	4.54%
55-64 y	2,522,787	14.27%	126133	13.00%	63,136	11.20%
65 -75 y	2,250,096	12.73%	191214	19.71%	133,157	23.62%
> 75 y	1,949,397	11.02%	359603	37.06%	319,730	56.72%
Gender (n,%)						
Male	7,498,820	42.41%	517825	53.37%	274,955	48.77%
Female	10,139,688	57.34%	449594	46.33%	288,789	51.23%
Missing/Unknown	43,603	0.25%	2905	0.30%	0	0.00%
Geographic Region						
Northeast	3,778,734	21.37%	178361	18.38%	92,967	16.49%
Midwest	3,484,577	19.71%	196537	20.25%	154,950	27.49%
South	7,444,318	42.10%	408141	42.06%	255,580	45.34%
West	2,961,029	16.75%	186623	19.23%	60,192	10.68%
Missing/unknown	13,453	0.08%	662	0.07%	55	0.01%
Insurance Type						
Cash/uninsured	26	0.00%	0	0.00%	0	0.00%
Commercial	14,680,364	83.02%	613789	63.26%	267,730	47.49%
Medicare	2,582,054	14.60%	335064	34.53%	286,249	50.78%
Medicaid	415,149	2.35%	21118	2.18%	9,577	1.70%
Other	4,518	0.03%	353	0.04%	188	0.03%

Figure 3. Proportion of confirmed dead COVID-19 patients identified based on comorbid COE/SCC and lack of subsequent claims activity stratified by age, sex, insurance coverage type and time period

Figure 3a: Confirmed deaths by age group	Figure 3b: Confirmed deaths by sex	Figure 3c: Confirmed deaths by insurance type	Figure 3d: Confirmed deaths by quarter
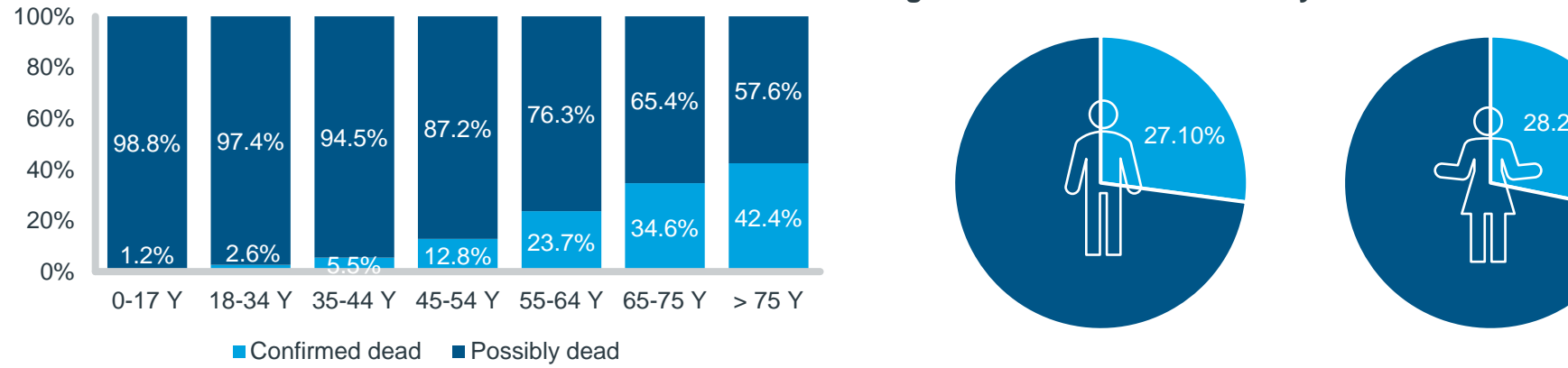
Clinical characteristics
- Among the 17,682,111 treated COVID-19 patients, acute respiratory failure (7.35%), pneumonia (5.10%) and asphyxia (4.73%) were the most common COE.
- Essential hypertension (36.50%) was the most common SCC, followed by hyperlipidemia (22.46%), obesity (19.66%) and type 2 diabetes (19.06%) among treated COVID-19 patients.
- The prevalence of each COE was three times or higher among possibly dead and confirmed dead than the overall treated COVID-19 patients.
- The proportion of patients with comorbid SCC like Alzheimer's disease or dementia was over six times higher among those confirmed dead compared to the overall treated COVID-19 cohort. (Table 2)

Table 2. Prevalence of COE and SCC among treated COVID-19 patients, those identified as possibly dead and those confirmed as dead

Comorbid conditions	Overall cohort		Possibly dead		Confirmed dead	
	N=17,682,111		N=970,324		N=563,744	
	N	%	N	%	N	%
Chain of event conditions[1]						
Pneumonia, unspecified	902,008	5.10%	179,606	18.51%	117,341	20.81%
Acute respiratory failure	1,299,699	7.35%	345,131	35.57%	202,655	35.95%
Respiratory failure, unspecified	237,023	1.34%	92,623	9.55%	52,086	9.24%
Cardiac arrest, unspecified	56,356	0.32%	40,355	4.16%	19,608	3.48%
Adult respiratory distress syndrome	144,919	0.82%	69,519	7.16%	35,391	6.28%
Sepsis, unspecified	394,375	2.23%	124,229	12.80%	75,212	13.34%
Viral pneumonia, unspecified	83,313	0.47%	15,401	1.59%	9,112	1.62%
Asphyxia	836,361	4.73%	171,868	17.71%	111,371	19.76%
Respiratory arrest	6,369	0.04%	3,118	0.32%	1,762	0.31%
Significant contributing conditions[2]						
Essential (primary) hypertension	6,453,254	36.50%	575,498	59.31%	426,581	75.67%
Unspecified diabetes mellitus without complications	54,377	0.31%	4,231	0.44%	3,884	0.69%
Unspecified dementia	617,863	3.49%	123,072	12.68%	133,609	23.70%
Chronic obstructive pulmonary disease, unspecified	1,298,901	7.35%	159,435	16.43%	158,276	28.08%
Atherosclerotic heart disease	1,751,310	9.90%	199,860	20.60%	191,764	34.02%
Type 2 diabetes mellitus without complications	3,370,452	19.06%	329,212	33.93%	251,498	44.61%
Atrial fibrillation and flutter	1,155,564	6.54%	181,681	18.72%	179,097	31.77%
Congestive heart failure	1,350,220	7.64%	207,489	21.38%	213,213	37.82%
Tobacco use	1,268,898	7.18%	104,907	10.81%	40,999	7.27%
Chronic kidney disease, unspecified	870,893	4.93%	137,089	14.13%	133,266	23.64%
Alzheimer disease, unspecified	269,817	1.53%	55,765	5.75%	63,145	11.20%
Hypertensive heart disease without (congestive) heart failure	379,199	2.14%	30,884	3.18%	28,192	5.00%
Hyperlipidemia, unspecified	3,970,804	22.46%	293,210	30.22%	224,836	39.88%
Other specified disorders of kidney and ureter	878,380	4.97%	84,377	8.70%	76,769	13.62%
Obesity, unspecified	3,476,655	19.66%	220,414	22.72%	95,685	16.97%
Stroke, not specified as hemorrhage or infarction	487,416	2.76%	63,123	6.51%	65,183	11.56%

Patient characteristics and risk of death
- Overall, 970,324 patients were flagged with COE and/or SCC and no subsequent claims activity >30 days after the last COVID-19 diagnosis; of those, 34.6% of the patients aged 65-75 and 42.4% aged >75 years had a death flag in Veritas database (Figure 3a).
- A higher proportion of confirmed dead patients were identified using both comorbid COE and SCC in combination with a lack of subsequent claims activity among those in older age groups.
- The proportion of confirmed dead patients identified among 'possibly dead' men and women were similar (Figure 3b).
- Over 40% of the Medicare patients identified as possibly dead were confirmed dead (Figure 3c).
- The proportion of confirmed deaths identified among patients flagged as possibly dead decreased from 40.3% in fourth quarter of 2020 to 16.0% in first quarter of 2022 (Figure 3d).

Discussion

- The prevalence of metabolic SCC were high among patients treated for COVID-19 in the US.
- The presence of COE or SCC along with lack of claims activity after last COVID-19 infection was found among over one third of deaths among elderly patients. This is in keeping with past research that identifies age in combination with various comorbid conditions as a significant risk factor of death among COVID-19 patients.
- The decrease in proportion of treated COVID-19 patients with confirmed death among those with comorbid COE/SC over time indicates the decreasing role of comorbidities in the risk of death.
- The high proportion of confirmed deaths among patients with neurological SCC such as Alzheimer's disease and dementia indicate the need for further research in the pathogenesis and natural history of COVID-19 infection among these patients.

Conclusions

- Age continues to be a critical risk factor associated with mortality among treated COVID-19 patients
- Early on during the COVID-19 pandemic, elderly patients and those with comorbid SCC diagnosis for conditions such as diabetes mellitus received prioritization for vaccine administration. With the diminishing importance of SCC in mortality among COVID-19 patients, there is need for further assessment in the drivers of mortality risk among these patients.
- This study highlights the demographic and clinical risk factors prevalent among patients dying after being treated for COVID-19. There is need for evaluation of the cumulative role of demographic and clinical factors driving the risk of mortality among COVID-19 patients.

Limitations

- The Dx open-source claims database is subject to missing data hypothetically greater than closed claims; therefore, some diagnoses and medication use may be under reported.
- The linkage between the Veritas Data Research database and the claims data was not complete; therefore, some patients that died during the study period may not have been identified.
- Claims data is subject to incomplete or inaccurate coding, missing data, and the lack of specific billing codes for some conditions.

References

1. Centers for Disease Control and Prevention. Daily updates of totals by week and state: provisional death counts for coronavirus disease 2019 (COVID-19). Accessed on September 22 2020. https://www.cdc.gov/nchs/nvss/vsrr/COVID19/index.htm
2. Yan H, Fox M, Gunbrecht J. CDC official affirms coronavirus deaths really are coronavirus deaths. CNN. Accessed on September 25, 2020. https://www.cnn.com/2020/09/02/health/us-coronavirus/wednesday/index.html
3. Parohan M, Yaghoubi S, Seraji A, Javanbakht MH, Sarraf P, Djalali M. Risk factors for mortality in patients with Coronavirus disease 2019 (COVID-19) infection: a systematic review and meta-analysis of observational studies. Aging Male. 2020 Dec;23(5):1416-1424.
4. Gundlapalli AV, Lavery AM, Boehmer TK, Beach MJ, Walke HT, Sutton PD, Anderson RN. Death Certificate-Based ICD-10 Diagnosis Codes for COVID-19 Mortality Surveillance - United States, January-December 2020. MMWR Morb Mortal Wkly Rep. 2021 Apr 9;70(14):523-527.