RESEARCH LETTER

All-Cause Excess Mortality and COVID-19–Related Mortality Among US Adults Aged 25-44 Years, March-July 2020

Coronavirus disease 2019 (COVID-19) has caused a marked increase in all-cause deaths in the US, mostly among older adults.[1] Although the burden of COVID-19 among hospitalized younger adults has been described, fewer data focus on mortality in this demographic, owing to lower case-fatality rates.[2]

Excess mortality reflects the full burden of the pandemic that may go uncaptured due to uncoded COVID-19 and other pandemic-related deaths. Accordingly, we examined all-cause excess mortality and COVID-19–related mortality during the early pandemic period among adults aged 25 to 44 years. Because unintentional drug overdoses are the usual leading cause of death in this demographic, COVID-19 deaths were compared with unintentional opioid deaths.

Multimedia

Supplemental content

Methods | To determine excess mortality (the gap between observed and expected deaths), projected monthly expected deaths for 2020 were calculated by applying autoregressive integrated moving averages to US population and mortality counts (2015-2019).[3] We examined 2020 population and seasonal autoregressive integrated moving averages for each of the 10 US Department of Health and Human Services (HHS) regions, which comprise the entire US and are the smallest subdivisions for which 2020 age-stratified COVID-19 mortality data are currently available from the National Center for Health Statistics. Population covariates were used to calculate 95% CIs for expected deaths.

Observed all-cause mortality and COVID-19 mortality (coded as either "underlying cause" or "multiple cause" of death) for March 1, 2020, to July 31, 2020, were obtained from provisional National Center for Health Statistics data (released October 28, 2020).[4] Unintentional opioid overdose death counts (*International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* codes X41-X44, Y11-Y15, and T40.0-6) for the corresponding period of 2018 (the most recently available data) were assembled for each HHS region.[3] Incident rates per 100 000 person-months with 95% CIs were calculated for COVID-19 and unintentional opioid deaths using SAS, version 9.4. Statistical significance was defined as a 95% CI that excluded the null value.

This study used publicly available data and was not subject to institutional review approval.

Results | From March 1, 2020, to July 31, 2020, a total of 76 088 all-cause deaths occurred among US adults aged 25 to 44 years, which was 11 899 more than the expected 64 189 deaths (incident rate ratio, 1.19 [95% CI, 1.14-1.23]; **Table**). Nationally, excess mortality occurred in every month of the study period and overall in every HHS region (Table and eTable in the Supplement). Among adults aged 25 to 44 years, 4535 COVID-19 deaths were recorded, accounting for 38% (95% CI, 32%-48%) of the measured excess mortality.

During surges in HHS Region 2 (New York, New Jersey), the incident rate for all-cause mortality was 2.30 (95% CI, 2.03-2.66) and 80% of deaths were related to COVID-19; during surges in HHS Region 6 (Arkansas, Louisiana, New Mexico, Oklahoma, Texas), the incident rate was 1.46 (95% CI, 1.33-1.63) and 48% were related to COVID-19; and during surges in HHS Region 9 (Arizona, California, Hawaii, Nevada), the incident rate was 1.47 (95% CI, 1.36-1.59) and 40% were attributed to COVID-19.

In contrast, from March through July 2018, a total of 10 347 unintentional opioid deaths occurred among US adults aged 25 to 44 years. Deaths due to COVID-19 exceeded 2018 unintentional opioid deaths during 1 month in 2020 in HHS Region 2 (April), HHS Region 6 (July), and HHS Region 9 (July) and either exceeded (HHS Region 6) or were similar to (HHS Regions 2 and 9) unintentional opioid deaths during the entire study period (Table).

Discussion | The COVID-19 pandemic was associated with increases in all-cause mortality among US adults aged 25 to 44 years from March through July 2020. In 3 HHS regions, COVID-19 deaths were similar to or exceeded unintentional opioid overdoses that occurred during several corresponding months of 2018.

Only 38% of all-cause excess deaths in adults aged 25 to 44 years recorded during the pandemic were attributed directly to COVID-19. Although the remaining excess deaths are unexplained, inadequate testing in this otherwise healthy demographic likely contributed. These results suggest that COVID-19–related mortality may have been underdetected in this population.

This study has limitations. The provisional data used represent lower-bound estimates due to reporting lags, necessitating future updates. Additionally, although COVID-19 deaths exceeded unintentional opioid deaths in 2018 in some areas, it is possible that simultaneous increases in opioid deaths may have occurred during the pandemic period, making it less clear which of these 2 diseases represents the current leading cause of death among younger adults in areas experiencing COVID-19 surges.

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Table. Excess, Coronavirus Disease 2019 (COVID-19)–Related, and Unintentional Opioid Overdose Deaths

HHS region	March-July 2020: Expected deaths, No. (95% CI)	Observed deaths, No.	Ratio of observed/expected deaths (95% CI)	Excess deaths, No. (95% CI)	COVID-19 deaths, No.	COVID-19 death rates per 100 000 person-months (95% CI)	Excess deaths attributed to COVID-19, %	March-July 2018: Unintentional opioid overdose deaths, No.	Unintentional opioid overdose death rates per 100 000 person-months (95% CI)
US total	64 189 (61 822-66 556)	76 088	1.19 (1.14-1.23)	11 899 (9373 to 14 266)	4535	1.02 (0.99-1.06)	38	10 347	2.38 (2.33-2.43)
March	12 881 (11 952-13 855)	13 531	1.05 (0.98-1.13)	650 (−333 to 1579)	332	0.38 (0.34-0.42)	51	2119	2.44 (2.33-2.54)
April	12 602 (11 611-13 620)	15 106	1.20 (1.11-1.30)	2504 (1476 to 3495)	1539	1.74 (1.65-1.83)	61	1994	2.29 (2.19-2.40)
May	12 848 (11 786-13 895)	15 792	1.23 (1.14-1.34)	2944 (1883 to 4006)	848	0.96 (0.89-1.03)	29	2068	2.38 (2.28-2.48)
June	12 761 (11 671-13 851)	15 078	1.18 (1.09-1.29)	2317 (1190 to 3407)	604	0.68 (0.63-0.74)	26	2062	2.37 (2.27-2.48)
July	13 098 (11 897-14 234)	16 581	1.27 (1.16-1.39)	3483 (2258 to 4684)	1212	1.37 (1.29-1.45)	35	2104	2.42 (2.32-2.52)
Region 2	4128 (3879-4377)	6305	1.53 (1.44-1.63)	2177 (1928 to 2426)	1310	3.56 (3.37-3.76)	60	1229	3.23 (3.05-3.42)
March	825 (721-929)	1120	1.36 (1.21-1.55)	295 (191 to 399)	172	2.34 (2.00-2.71)	58	238	3.13 (2.74-3.55)
April	810 (702-918)	1867	2.30 (2.03-2.66)	1057 (949 to 1165)	842	11.44 (10.68-12.24)	80	218	2.87 (2.50-3.27)
May	826 (715-937)	1286	1.56 (1.37-1.80)	460 (349 to 571)	221	3.00 (2.62-3.42)	48	260	3.42 (3.02-3.86)
June	824 (709-938)	1033	1.25 (1.10-1.46)	209 (95 to 324)	56	0.76 (0.57-0.99)	27	250	3.29 (2.89-3.72)
July	843 (725-961)	999	1.18 (1.04-1.38)	156 (38 to 274)	19	0.26 (0.16-0.40)	12	263	3.46 (3.05-3.90)
Region 6	8504 (8127-8882)	10 408	1.22 (1.17-1.28)	1904 (1526 to 2281)	725	1.21 (1.12-1.30)	38	539	0.92 (0.85-1.00)
March	1711 (1546-1875)	1774	1.04 (0.95-1.15)	63 (−101 to 228)	31	0.26 (0.18-0.37)	49	101	0.86 (0.70-1.05)
April	1688 (1521-1854)	1932	1.14 (1.04-1.27)	244 (78 to 411)	118	0.98 (0.81-1.18)	48	105	0.90 (0.73-1.09)
May	1712 (1543-1880)	2072	1.21 (1.10-1.34)	360 (192 to 529)	74	0.62 (0.48-0.77)	21	124	1.06 (0.88-1.26)
June	1689 (1517-1860)	2132	1.26 (1.15-1.41)	443 (272 to 615)	122	1.01 (0.84-1.21)	28	107	0.91 (0.75-1.10)
July	1706 (1533-1880)	2498	1.46 (1.33-1.63)	792 (618 to 965)	380	3.16 (2.85-3.50)	48	102	0.87 (0.71-1.06)
Region 9	8351 (8054-8648)	10 094	1.21 (1.17-1.25)	1743 (1446 to 2040)	668	0.91 (0.84-0.99)	38	677	0.94 (0.87-1.01)
March	1643 (1515-1772)	1698	1.03 (0.96-1.12)	55 (−74 to 183)	28	0.19 (0.13-0.28)	51	141	0.98 (0.82-1.15)
April	1656 (1525-1787)	1764	1.07 (0.99-1.16)	108 (−23 to 239)	90	0.62 (0.49-0.76)	83	117	0.81 (0.67-0.97)
May	1660 (1528-1793)	2015	1.21 (1.12-1.32)	355 (222 to 487)	99	0.68 (0.55-0.82)	28	122	0.85 (0.70-1.01)
June	1667 (1532-1802)	2086	1.25 (1.16-1.36)	419 (284 to 554)	129	0.88 (0.74-1.05)	31	155	1.08 (0.91-1.26)
July	1725 (1588-1861)	2531	1.47 (1.36-1.59)	806 (670 to 943)	322	2.20 (1.97-2.46)	40	142	0.99 (0.83-1.16)

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Concept and design: Faust, Lin, Mayes, Gilman, Walensky.
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COMMENT & RESPONSE

Risk of Spinal Hematoma After Lumbar Puncture

To the Editor The recently published article by Dr Bodilsen and colleagues reported the association between lumbar puncture and spinal hematoma in patients with coagulopathy.[1] When interpreting their results, some issues should be considered. First, this study defined spinal hematoma based on diagnosis codes regarding spinal hematoma–related symptoms or treatments. The diagnosis of spinal hematoma should be based on neuroimaging data, including magnetic resonance imaging and computed tomographic scan results[2] since diagnosis codes without regard to neuroimaging data may cause a misdiagnosis of spinal hematoma. Second, the location of lumbar puncture–related spinal hematoma was not mentioned in this article. The location of spinal hematoma (eg, lumbar, cervical, thoracic, epidural, intradural, subarachnoid) may affect the outcome of spinal hematoma[2] so should have be included in this study. Third, because differentiating traumatic spinal tap from subarachnoid hemorrhage can be difficult in clinical practice,[3] the authors should have more clearly stated how these conditions were distinguished. Fourth, this article did not include cases with failed attempts of lumbar puncture. Among patients with successful lumbar puncture, some may have to undergo multiple attempts, which can be associated with higher risk of lumbar puncture–related injury. Fifth, although not mentioned in this study, in clinical practice, some patients may have more than 1 coagulation disorder, such as thrombocytopenia and an increased international normalized ratio, which may increase their risk of spinal hematoma.

In summary, while this study can aid in decision-making, the safety of lumbar puncture in patients with coagulopathy deserves further investigation via prospective studies and clinical trials.

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To the Editor Dr Bodilsen and colleagues showed very low rates of spinal hematoma in patients both with and without coagulopathy in their large patient cohort.[1] In a subgroup analysis of 1694 lumbar punctures among 1237 patients, the authors reported that the median needle size was 22 gauge (interquartile range, 22-22), and listed the number of procedures performed with traumatic vs atraumatic needles. Needle size and the use of atraumatic pencil-point needles have been previously shown to modulate the risk of other post–lumbar puncture complications; the use of smaller, atraumatic needles reduces the risk of complications such as postdural puncture