

# Letters

## 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.<sup>1</sup> 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.<sup>2</sup>

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.

**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).<sup>3</sup> 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).<sup>4</sup> Unintentional opioid overdose death counts (*International Classification of Diseases, Version 10* 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.<sup>3</sup> **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, ex-

cess 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 of 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 of 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.

Jeremy Samuel Faust, MD, MS  
Harlan M. Krumholz, MD, SM  
Chengan Du, PhD  
Katherine Dickerson Mayes, MD, PhD  
Zhenqiu Lin, PhD  
Cleavon Gilman, MD  
Rochelle P. Walensky, MD, MPH

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

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

**Author Affiliations:** Department of Emergency Medicine, Brigham and Women's Hospital, Boston, Massachusetts (Faust); Section of Cardiovascular Medicine, Yale School of Medicine, New Haven, Connecticut (Krumholz); Center for Outcomes Research and Evaluation, Yale School of Medicine, New Haven, Connecticut (Du, Lin); Harvard Affiliated Emergency Medicine Residency, Boston, Massachusetts (Mayes); Emergency Medicine Department, Yuma Regional Medical Center, Yuma, Arizona (Gilman); Division of Infectious Diseases, Massachusetts General Hospital, Boston (Walensky).

**Corresponding Author:** Jeremy Samuel Faust, MD, MS, Brigham and Women's Hospital Department of Emergency Medicine, 10 Vining St, Boston, MA 02115 ([jfaust@gmail.com](mailto:jfaust@gmail.com)).

**Accepted for Publication:** November 18, 2020.

**Published Online:** December 16, 2020. doi:[10.1001/jama.2020.24243](https://doi.org/10.1001/jama.2020.24243)

**Author Contributions:** Dr Faust had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

*Concept and design:* Faust, Lin, Mayes, Gilman, Walensky.

*Acquisition, analysis, or interpretation of data:* Faust, Krumholz, Du, Lin, Mayes, Walensky.

*Drafting of the manuscript:* Faust, Mayes, Gilman, Walensky.

*Critical revision of the manuscript for important intellectual content:* Faust, Krumholz, Du, Lin, Walensky.

*Statistical analysis:* Faust, Du, Lin, Mayes.

*Obtained funding:* Walensky.

*Administrative, technical, or material support:* Mayes, Walensky.

*Supervision:* Faust, Lin, Gilman.

**Conflict of Interest Disclosures:** Dr Krumholz reported receiving personal fees from UnitedHealth, IBM Watson Health, Element Science, Aetna, Facebook, Siegfried & Jensen Law Firm, Arnold & Porter Law Firm, Martin/Baughman Law Firm, F-Prime, and the National Center for Cardiovascular Diseases, Beijing;

being a co-founder of HugoHealth, a personal health information platform, and Refactor Health, an enterprise health care artificial intelligence-augmented data management company; receiving contracts from the Centers for Medicare & Medicaid Services, through Yale New Haven Hospital, to develop and maintain measures of hospital performance; and receiving grants from Medtronic, the US Food and Drug Administration, Johnson & Johnson, and Shenzhen Center for Health Information outside the submitted work. Dr Lin reported working under contract with the Centers for Medicare & Medicaid Services to develop quality measures. Dr Walensky reported receiving grants from the Mass General Research Institute as the Steven and Deborah Gorlin MGH Research Scholar during the conduct of the study. No other disclosures were reported.

**Additional Contributions:** We thank Lauren M. Rossen, PhD, MS (National Center for Health Statistics), for facilitating the public release of National Center for Health Statistics data used for this study and for providing expertise on excess death determination and Michael Colin Tasi, MD, MBA (Harvard Affiliated Emergency Medicine Residency), for assistance in supporting data preparation. Neither individual received compensation for their contributions.

1. Woolf SH, Chapman DA, Sabo RT, Weinberger DM, Hill L, Taylor DDH. Excess deaths from COVID-19 and other causes, March-July 2020. *JAMA*. 2020;324(15):1562-1564. doi:[10.1001/jama.2020.19545](https://doi.org/10.1001/jama.2020.19545)

2. Cunningham JW, Vaduganathan M, Claggett BL, et al. Clinical outcomes in young US adults hospitalized with COVID-19. *JAMA Intern Med*. Published online September 9, 2020. doi:[10.1001/jamainternmed.2020.5313](https://doi.org/10.1001/jamainternmed.2020.5313)

3. Underlying cause of death, 1999-2018. Centers for Disease Control and Prevention. Accessed October 28, 2020. <https://wonder.cdc.gov/ucd-icd10.html>

4. Monthly provisional counts of deaths by age group and HHS region for select causes of death Centers for Disease Control and Prevention. Accessed October 28, 2020. <https://data.cdc.gov/NCHS/Monthly-provisional-counts-of-deaths-by-age-group/-ezfr-g6hf>