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Mortality From Drug Overdoses, Homicides, Unintentional Injuries, Motor Vehicle Crashes, and Suicides During the Pandemic, March-August 2020

The initial COVID-19 outbreak in the US caused disruptions in usual behavioral patterns.[1-3] To assess associated changes in external causes of death, we analyzed monthly trends from 2015 to 2020 in deaths resulting from drug overdoses, homicide, unintentional injuries, motor vehicle crashes, and suicide in the first 6 months of the pandemic.

Supplemental content

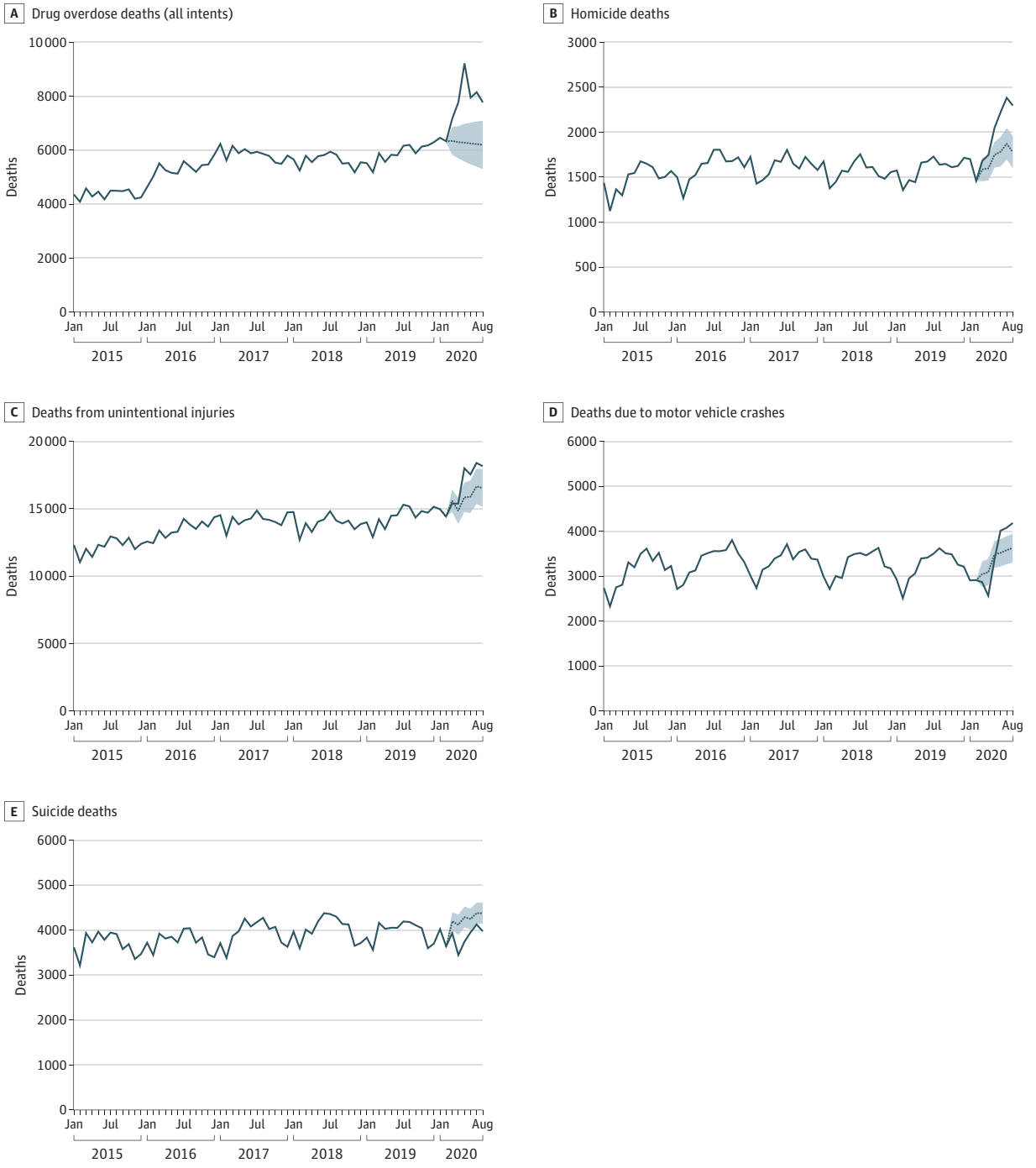
Table. Excess and External Causes of Death in the US, March 1 to August 31, 2020

	Observed	Expected (95% CI)	OER (95% CI)
US total (all cause)	1 661 271	1 404 634 (1 309 448-1 499 821)	1.18 (1.27-1.11)
Drug overdose			
March	7172	6341 (5819-6863)	1.13 (1.04-1.23)
April	7775	6297 (5699-6896)	1.23 (1.13-1.36)
May	9219	6277 (5574-6980)	1.47 (1.32-1.65)
June	7946	6249 (5476-7022)	1.27 (1.13-1.45)
July	8149	6225 (5386-7063)	1.31 (1.15-1.51)
August	7771	6200 (5306-7093)	1.25 (1.1-1.46)
Total	48 032	37 589 (33 261-41 917)	1.28 (1.15-1.44)
Homicide			
March	1681	1585 (1455-1716)	1.06 (0.98-1.16)
April	1747	1599 (1463-1736)	1.09 (1.01-1.19)
May	2049	1749 (1607-1891)	1.17 (1.08-1.28)
June	2223	1783 (1618-1948)	1.25 (1.14-1.37)
July	2383	1872 (1699-2045)	1.27 (1.17-1.40)
August	2296	1777 (1596-1959)	1.29 (1.17-1.44)
Total	12 379	10 365 (9437-11 293)	1.19 (1.1-1.31)
Unintentional injuries			
March	15 379	15 583 (14 749-16 417)	0.99 (0.94-1.04)
April	15 371	14 844 (13 871-15 817)	1.04 (0.97-1.11)
May	17 998	15 838 (14 744-16 932)	1.14 (1.06-1.22)
June	17 534	15 881 (14 678-17 084)	1.10 (1.03-1.19)
July	18 393	16 655 (15 352-17 958)	1.10 (1.02-1.20)
August	18 157	16 534 (15 138-17 930)	1.10 (1.01-1.20)
Total	102 832	95 335 (88 532-102 138)	1.08 (1.01-1.16)
Motor vehicle crashes			
March	2867	3044 (2759-3329)	0.94 (0.86-1.04)
April	2563	3086 (2794-3378)	0.83 (0.76-0.92)
May	3354	3479 (3180-3778)	0.96 (0.89-1.05)
June	4010	3517 (3211-3823)	1.14 (1.05-1.25)
July	4074	3576 (3263-3889)	1.14 (1.05-1.25)
August	4182	3624 (3304-3943)	1.15 (1.06-1.27)
Total	21 050	20 325 (18 510-22 140)	1.04 (0.95-1.14)
Suicide			
March	3933	4196 (3996-4396)	0.94 (0.89-0.98)
April	3447	4118 (3893-4344)	0.84 (0.79-0.89)
May	3742	4289 (4057-4521)	0.87 (0.83-0.92)
June	3951	4246 (4012-4480)	0.93 (0.88-0.98)
July	4126	4377 (4143-4611)	0.94 (0.89-1)
August	3973	4377 (4143-4612)	0.91 (0.86-0.96)
Total	23 172	25 604 (24 243-26 964)	0.91 (0.86-0.96)

Abbreviation: OER, observed-to-expected ratios.

Methods | We measured monthly excess mortality (the gap between observed and expected deaths) from 5 external causes using provisional national-level underlying cause death certificate data published by the National Center for Health Statistics (NCHS) through August 2020 (released March 2021). Data from March to August 2020 were aggregated by the NCHS into 5 groups: drug overdose (all intents), assault (homicide), unintentional injuries, motor vehicle

Figure. Cause-Specific Mortality Due to Select External Causes in the US, January 2015 to August 2020



The solid line indicates raw cause-specific death counts from January 2015 to August 2020; the dotted line and shading represent the point estimate and projected 95% CI for cause-specific expected deaths from March to August 2020 using the seasonal adjusted model. The y-axes are raw death counts.

crashes, and intentional self-harm (suicide) (see the Supplement for *ICD-10* codes).[4,5]

To forecast all-cause and cause-specific expected monthly deaths from March to August 2020, we used seasonal autoregressive integrated moving average (sARIMA) models developed with cause-specific monthly mortality counts and US population data from January 2015 to February 2020. We plotted observed and expected deaths monthly with 95% CIs estimated from sARIMA models.

We estimated the contribution of individual cause-specific mortality to all-cause non–COVID-19 excess mortality by dividing cause-specific mortality by total non–COVID-19

excess mortality from March to August 2020 (see the Supplement). Confidence intervals for the percent contribution to non–COVID-19 excess mortality were determined by subtracting the observed number of deaths from the upper and lower 95% thresholds for the expected number of deaths. For excess mortality counts, any figure not crossing 0 was considered statistically significant. For observed-to-expected ratios (OERs) of cause-specific mortality, statistical significance was defined as a 95% CI that excluded the null value of 1.00.

Analyses were conducted using R version 4.0.2. This study used publicly available data and was not subject to institutional review approval per HHS regulation 45 CFR 46.101(c).

Results | From March to August 2020, there were 256 635 (95% CI, 161 450-351 823) all-cause excess deaths (1 661 271 observed; 1 404 634 expected) and 174 334 COVID-19 deaths (underlying cause). For the study period, OERs for 3 external causes of death were significantly higher than expected (drug overdoses, homicides, unintentional injuries), 1 unchanged (motor vehicle crashes), and 1 lower (suicides) (**Table**).

There were 10 443 excess drug overdoses (95% CI, 6115 to 14 771; **Figure**, A), accounting for 12.7% of non–COVID-19 excess mortality (95% CI, 7.4% to 17.9%); 2014 excess homicide deaths (95% CI, 1086 to 2942) (Figure, B), accounting for 2.4% of non–COVID-19 excess mortality (95% CI, 1.3% to 3.6%); and 7497 excess deaths due to unintentional injuries (95% CI, 694 to 14 300) (Figure, C), accounting for 9.1% of non–COVID-19 excess mortality (95% CI, 0.8% to 17.4%). There was no significant change in motor vehicle crash deaths overall (725; 95% CI, −1090 to 2540) but fewer than expected motor vehicle crash deaths occurred in April (−523; 95% CI, −815 to −231), and significant increases were recorded monthly from June to August (1550; 95% CI, 611 to 2489) (Figure, D). Suicide deaths were statistically significantly lower than projected by 2432 deaths (95% CI, 1071 to 3792 fewer deaths) (Figure, E).

Discussion | Provisional mortality data showed that deaths from some but not all external causes increased during the pandemic, representing thousands of lives lost and exceeding prepandemic trends.

Explanations for these changes are unknown. Drug overdoses and homicides may have been related to economic stress. Pandemic-associated changes in access to substance use disorder treatments may have exacerbated mortality from overdoses.[6] Decreases in motor vehicle crash deaths in April coincided with less traffic, despite increases in drivers testing positive for drugs and alcohol and lower seatbelt use.[3] Increases in motor vehicle crash deaths in June to August occurred as traffic increased (though still below 2019 levels), likely reflecting higher-risk behaviors.[3] Lower than projected suicide deaths are paradoxical with reported increases in depressive and other mental health symptoms during the pandemic. Additional data are needed to understand the mechanism behind this finding.

This study has limitations, including death certificate accuracy and that 2020 data published by NCHS are considered preliminary. However, substantial changes to March to August 2020 data are unlikely. Also, the true number of non–COVID-19 medical deaths may have been lower than projected during the pandemic period, as evidenced by the observation that in May, the total excess deaths due to drug overdoses, assaults, and unintentional injuries exceeded the apparent number of all non–COVID-19 excess deaths.

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COMMENT & RESPONSE

Immune Checkpoint Inhibitor Therapy Toxicities

To the Editor A recent JAMA Clinical Guidelines Synopsis discussed the management of immunotherapy-related toxicities in patients treated with immune checkpoint inhibitors, summarizing guidelines issued by the National Comprehensive Cancer Network (NCCN) in December 2019. However, the synopsis by Dr Reid and colleagues[1] failed to address fatigue, one of the most common adverse effects of immune checkpoint inhibitors. Fatigue, which has been reported as an adverse event in up to 42% of patients being treated in a therapeutic clinical trial,[2] can also present as a symptom of other immune-related adverse events such as endocrine dysfunction. A recent collaboration with the GO2 Foundation for Lung Cancer found that among participants in their registry treated with an immune checkpoint inhibitor, 85% retrospectively reported fatigue, with 41% experiencing moderate to severe fatigue.[3]

The NCCN guidelines on immune checkpoint inhibitors summarized by Reid and colleagues indicate that patients experiencing fatigue should be first evaluated for an underlying immune-related adverse event, such as hypothyroidism. If no treatable underlying immune-related adverse event is found, clinicians may consider adding low-dose steroids for treatment of moderate fatigue. If fatigue is severe, however, withholding or discontinuing immune checkpoint inhibitor treatment should be considered.

Although fatigue in patients treated with immune checkpoint inhibitors is understudied, cancer-related fatigue in patients treated with other forms of therapy has been extensively characterized. Fatigue is associated with reduced likelihood of returning to work following cancer treatment, which can result in negative financial and insurance consequences. Thus, effective treatment of cancer-related fatigue is a high priority.

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In Reply In our article[1] about immune checkpoint inhibitors, we focused on immunotherapy-related toxicities that were life threatening or had important treatment implications. Because of space limitations, we were unable to address every adverse event of immune checkpoint inhibitors. We do not disagree that fatigue has been widely reported as one of the most prevalent symptoms after immune checkpoint inhibitor therapy.[2] However, as Dr Jim and colleagues point out, fatigue is not specific to immune checkpoint inhibitor therapy and can be patient, malignancy, or treatment associated.[3] Fatigue is a well-recognized symptom among patients with cancer, with an aggregate prevalence of almost 50% as noted in a large meta-analysis of studies published between 1993 and 2000.[4] Placebo-controlled clinical trials have additionally identified a high incidence of fatigue in placebo groups, demonstrating the significance of fatigue as a disease-related rather than treatment-related phenomenon.[5,6]

The development of fatigue after immune checkpoint inhibitor use is poorly understood and does not necessarily portend an immune-mediated mechanism of action.[2] Its presence should first prompt evaluation for immune-related adverse events, such as but not limited to immune checkpoint inhibitor–induced endocrinopathies.

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