RESEARCH LETTER

Change in Epidemiology of Creutzfeldt-Jakob Disease in the US, 2007-2020

Creutzfeldt-Jakob disease (CJD) is a rapidly progressive and universally fatal prion disease.[1] Research on CJD in the US showed stable incidence from 1979 to 2006, though recent trends are not as well described.[2] The incidence of sporadic CJD, the most common type, is higher among older patients.[1,2] Due to aging populations worldwide, the epidemiology of CJD is evolving.[3] We examined death certificate data from 2007 to 2020 to better understand recent US trends of CJD.

Supplemental content

Methods | This cross-sectional study used data from the Wide-Ranging Online Data for Epidemiologic Research multiple cause of death database.[4] Data were retrieved on September 7, 2023, and analyzed between September 7 and September 23, 2023. The Johns Hopkins Medicine institutional review board determined that this study did not constitute human participant research; thus, informed consent was not sought. We followed STROBE reporting guidelines.

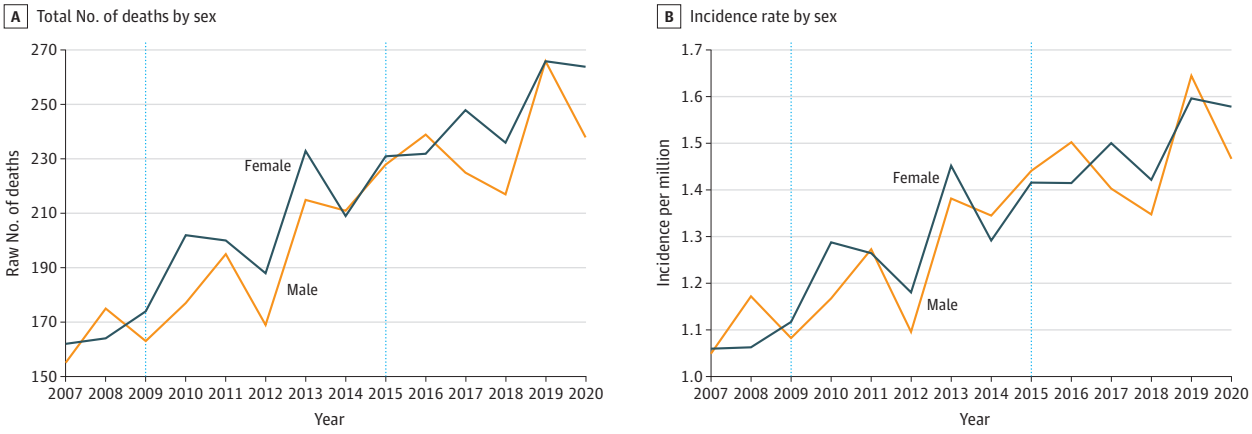
We examined death certificates with *ICD-10* code A81.0 from 2007 to 2020 for CJD incidence and age and sex distribution.[2] Patient-level demographic information could not be collected due to limitations of the mortality surveillance database. Joinpoint Regression Program, version 4.9.1.0 (National Cancer Institute) was used to characterize inflection points and average annual percent change (AAPC) (eMethods in Supplement 1). We used Stata, version 18.0 (StataCorp LLC) to conduct *t* tests for cohort changes across the study period, with a 2-sided $P < .05$ considered significant.

Results | Reported CJD incidence rose consistently in 2007-2020 (5882 total cases; 3009 female [51.2%] and 2873 male [48.8%]). Males saw an increase from 155 deaths and incidence of 1.05 (95% CI, 0.88-1.21) per million in 2007 to 238 deaths and incidence of 1.47 (95% CI, 1.28-1.65) per million ($P = .001$) in 2020. Females saw a greater increase from 162 deaths and incidence of 1.06 (95% CI, 0.89-1.22) per million to 264 deaths and incidence of 1.58 (95% CI, 1.39-1.77) per million ($P < .001$) across the same period (**Figure**). After age adjustment, the increase in incidence was not significant for males (1.06 [95% CI, 0.89-1.23] to 1.19 [95% CI, 1.04-1.35] per million; $P = .25$), but remained significant for females (0.92 [95% CI, 0.78-1.06] to 1.12 [95% CI, 0.99-1.26] per million; $P = .045$). In individual age groups, the largest increase in incidence was in those aged 75 to 84 years, though this finding was not significant in males (3.50 [95% CI, 2.65-4.55] to 7.48 [95% CI, 5.62-9.75] per million; $P = .18$) or females (3.38 [95% CI, 2.21-4.95] to 5.20 [95% CI, 3.84-6.90] per million; $P = .07$).

Joinpoint analysis revealed a significant increase in crude incidence for males (AAPC, 2.9; 95% CI, 2.3-3.6; $P < .001$) and females (AAPC, 3.5; 95% CI, 2.2-4.7; $P < .001$) overall. The crude incidence decreased after age adjustment but remained significant for both sexes (AAPC: males, 0.8 [95% CI, 0.1-1.5; $P = .02$]; females, 1.9 [95% CI, 0.6-3.2; $P = .005$]). Males aged 55 to 64 years were the only male age group with a significant increase, but females showed a significant increase in all age cohorts (**Table**).

Discussion | Our findings indicate the reported incidence of CJD has risen considerably, disproportionately affecting older and female individuals. These trends align with data from Japan[3] and could be influenced by changing demographics. However, our findings may also reflect improved detection of CJD

Figure. Trends in Creutzfeldt-Jakob Disease Deaths and Incidence by Sex, 2007-2020



The first dotted vertical line indicates the publication of magnetic resonance imaging diagnostic criteria in 2009, and the second indicates the introduction of real-time quaking-induced conversion testing in 2015.

Table. Joinpoint Analysis of Incidence Trends in Creutzfeldt-Jakob Disease by Age Group and Sex, 2007-2020

	Crude incidence rate,[a] AAPC (95% CI)	*P* value	Age-adjusted incidence rate,[a] AAPC (95% CI)	*P* value
Overall	3.0 (2.5 to 3.5)	<.001	1.2 (0.7 to 1.7)	<.001
Sex				
Male	2.9 (2.3 to 3.6)	<.001	0.8 (0.1 to 1.5)	.02
Female	3.5 (2.2 to 4.7)	<.001	1.9 (0.6 to 3.2)	.005
Age group, y				
55-64	1.6 (0.4 to 2.9)	.01	NA	NA
65-74	1.4 (0.6 to 2.2)	.002	NA	NA
75-84	1.3 (−0.2 to 2.7)	.08	NA	NA
Subgroup by sex and age				
Male				
55-64 y	1.7 (0.1 to 3.3)	.04	NA	NA
65-74 y	1.0 (−0.2 to 2.3)	.09	NA	NA
75-84 y	0.2 (−1.8 to 2.3)	.82	NA	NA
Female				
55-64 y	1.7 (0.1 to 3.4)	.04	NA	NA
65-74 y	1.8 (0.9 to 2.6)	.001	NA	NA
75-84 y	2.1 (0.6 to 3.7)	.01	NA	NA

Abbreviations: AAPC, average annual percent change; NA, not applicable.

[a] Crude and age-adjusted incidence were estimated from crude and age-adjusted mortality rates, respectively. The best-fit model for most analyses was calculated to be a single segment from 2007 to 2020 without inflection points. Two analyses exhibited multiple segments: crude incidence rate in the female group, with 2 segments from 2007 to 2010 (annual percent change [APC], 6.4; 95% CI, 2.8-16.7; *P* = .04) and 2010 to 2020 (APC, 2.6; 95% CI, −3.9 to 3.9; *P* < .001) and age-adjusted incidence rate in the female group, with 2 segments from 2007 to 2010 (APC, 5.6; 95% CI, −0.8 to 12.3; *P* = .08) and 2010 to 2020 (APC, 0.8; 95% CI, 0.2-1.43; *P* = .02).

with new diagnostic tools, such as magnetic resonance imaging and real-time quaking-induced conversion testing.

This study is limited by a reliance on death certificate data for estimating CJD incidence. While research supports this approach,[5] such data may be subject to miscoding or misdiagnosis. Results from both neuropathologic and genetic testing may complement death certificate data and enhance surveillance.[6] The findings underscore the changing landscape of CJD and suggest a need for monitoring among the aging US population.

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Accepted for Publication: October 9, 2023.

Published Online: December 11, 2023. doi:10.1001/jamaneurol.2023.4678

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Critical review of the manuscript for important intellectual content: All authors.
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Conflict of Interest Disclosures: None reported.

Disclaimer: This article reflects the views of the authors and should not be construed to represent the views or policies of the US Food and Drug Administration, the Department of Health and Human Services, or the US government.

Data Sharing Statement: See Supplement 2.

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