# Epidemiology of Creutzfeldt-Jakob Disease in the United States, 2007-2020

Matthew A. Crane, BS 1,2,3

Sameer Nair-Desai, BS 4,5

John A. Romley, PhD 2,6,7

John C. Probasco, MD 8

1. Johns Hopkins University School of Medicine, Baltimore, MD, USA
2. Leonard D. Schaeffer Center for Health Policy and Economics, University of Southern California, Los Angeles, CA, USA
3. Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public

Health, Baltimore, MD, USA

1. Department of Economics, Stanford University
2. Meridian Collective
3. Price School of Public Policy, University of Southern California, Los Angeles, CA, USA 6 USC School of Pharmacy, University of Southern California, Los Angeles, CA, USA
4. Department of Neurology, Johns Hopkins School of Medicine, Baltimore, MD, USA.

**Corresponding Author:**

Matthew A. Crane, BS

Johns Hopkins University School of Medicine

Edward D. Miller Research Building

733 North Broadway, Suite 137

Baltimore, MD 21205-2196

Email: crane@jhu.edu

Phone: 410-955-3416

Word Count: 329

# INTRODUCTION

Creutzfeldt–Jakob disease (CJD) is a rapidly progressive and universally fatal neurologic condition characterized by cognitive and motor dysfunction.1 Prior research on CJD in the US demonstrated a stable incidence from 1979-2006, though recent trends are not well described.2 The incidence of sporadic CJD (sCJD), the most common variant of CJD, is higher among older patients.3 Due to demographic trends worldwide towards increasing aging populations, the epidemiology of CJD is evolving.4 In this study we examined extended death certificate data from 2007 - 2020 in order to better understand current trends of CJD in the US.

# METHODS

This study used data from the Centers for Disease Control and Prevention (CDC) WONDER database.5 ICD-10 codes on death certificates were used from 2007 - 2020. Given the clinical course of CJD, many studies suggest death certificates are an accurate measure of incidence.6

Joinpoint regression modeling (using the National Cancer Institute’s Joinpoint Regression Program, version 4.9.1.0)7, was used to identify and characterize inflection points in trends. A BIC3 analysis model with homoscedastic errors and estimates for first-order autocorrelation was fit to longitudinal data to pull crude and age-adjusted annual percentage changes across a range of demographic groups (see **Table 1**). Additional details on data collection and methodology are available in the **Supplemental Materials**.

This study was determined to not constitute human subjects research by the Johns Hopkins Medicine Institutional Review Board.

# RESULTS

**Figure a**: Crude Number of Deaths, Male, Female

****

**Figure b**: Age-Adjusted Mortality: Male, Female



**Figure c**: Age-Specific Mortality: Male

****

**Figure d**: Age-Specific Mortality: Female



**Table 1**: Joinpoint Analysis of Mortality Trends in Creutzfeldt–Jakob Disease, by Demographics

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Demographic Group** | **Time Interval** | **Joinpoint Location** | **Crude AAPC (95% CI)** | **Crude p-value** | **Age Adjusted AAPC (95% CI)** | **Age-Adjusted p-value** |
| **Age Groups** |  |  |  |  |  |  |
| 55 – 64 Years Old | 2007 - 2020 | . | 1.7 (0.6, 2.9) | 0.006 | . | . |
| 65 – 74 Years Old | 2007 - 2020 | . | 1.5 (0.6, 2.4) | 0.004 | . | . |
| 75+ Years Old | 2007 - 2020 | . | 1.4 (-0.2, 3.0) | 0.087 | . | . |
| **Gender** |  |  |  |  |  |  |
| Male | 2007 - 2020 | . | 3.0 (2.4, 3.7) | 0.000 | 1.0 (0.2, 1.8) | 0.023 |
| Female | 2007 - 2020 | 1: 2010 | 3.6 (2.4, 4.7) | 0.000 | 1.8 (1.3, 2.3) | 0.000 |
| **Race/Ethnicity** |  |  |  |  |  |  |
| Non-Hispanic Black | 2013 - 2020 | . | -0.1 (-1.4, 1.2) | 0.898 | -2.9 (-5.4, -0.3) | 0.035 |
| Non-Hispanic White | 2013 - 2020 | . | 3.2 (2.7, 3.8) | 0.000 | 1.2 (0.7, 1.7) | 0.000 |

# DISCUSSION

Our findings demonstrate that the incidence of CJD has risen considerably in recent years in the US, disproportionately affecting older patients and female patients. These results align closely with recent data from Japan and may be largely attributed to demographic changes in recent years.4 Our study’s main limitation is a reliance on death certificate data for estimating CJD incidence. This data may be subject to miscoding or misdiagnosis, though existing research supports the use of death certificates for understanding CJD epidemiology.6 This analysis underscores the changing landscape of CJD in the US in recent years and suggests a need for close surveillance among the aging US population.

# REFERENCES

1. Watson N, Brandel JP, Green A, et al. The importance of ongoing international surveillance for Creutzfeldt-Jakob disease. *Nat Rev Neurol.* 2021;17(6):362-379. doi:10.1038/s41582-021-00488-7
2. Holman RC, Belay ED, Christensen KY, et al. Human prion diseases in the United States. *PLoS One*. 2010;5(1):e8521. Published 2010 Jan 1. doi:10.1371/journal.pone.0008521
3. Stoeck K, Hess K, Amsler L, et al. Heightened incidence of sporadic Creutzfeldt-Jakob disease is associated with a shift in clinicopathological profiles. *J Neurol.*

2008;255(10):1464-1472. doi:10.1007/s00415-008-0900-0

1. Nishimura Y, Harada K, Koyama T, Hagiya H, Otsuka F. A nationwide trend analysis in the incidence and mortality of Creutzfeldt-Jakob disease in Japan between 2005 and 2014. *Sci Rep.* 2020;10(1):15509. Published 2020 Sep 23. doi:10.1038/s41598-02072519-0
2. Underlying cause of death 1999−2018 on CDC WONDER online. Centers for Disease Control and Prevention. [http://wonder.cdc.gov/ucd-icd10.html.](http://wonder.cdc.gov/ucd-icd10.html) Updated March 4, 2020. Accessed December 23, 2022.
3. Davanipour Z, Smoak C, Bohr T, Sobel E, Liwnicz B, Chang S. Death certificates: an efficient source for ascertainment of Creutzfeldt-Jakob disease cases. *Neuroepidemiology*. 1995;14(1):1-6. doi:10.1159/000109771
4. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med.* 2000;19(3):335-351. doi:10.1002/(sici)10970258(20000215)19:3<335::aid-sim336>3.0.co;2-z

# Supplemental Methods

* Provide specific ICD-10 for CJD
* Defend use of broad CJD code for what is estimating mostly sCJD

-