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Research Article

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Deaths of Despair: A Major and Increasing Contributor to United States Deaths

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Abstract

Objective: The International Classification of Disease (ICD) assumes that each disease entity is distinct. The hypothesis that each disease entity may have similar underlying and contributory factors have led to the emerging concept of "deaths of despair." Our objective was to explore temporal trends in the occurrence of United States (US) deaths of despair from 1999 to 2021.

Methods: We utilized the previously defined definition as a constellation of 19 underlying causes: chronic hepatitis; liver fibrosis/cirrhosis; suicide/sequelae of suicide; poisoning (accidental or undetermined intent) or exposure to nonopioid analgesics, antipyretics, rheumatic, antiepileptic's, sedative hypnotics, antiparkinson and psychotropic drugs; narcotics, psychodysleptics, drugs acting on the central nervous system, and alcohol. We used mortality data for those 25 to 74 years of age from 1999 to 2021 to calculate annual percent changes (APC) as measures of effect size and joinpoint regression to test for statistical significance. We used the US Centers for Disease Control and Prevention (CDC) Wide-Ranging Data for Epidemiologic Research (WONDER) and the Multiple Cause of Death files.

Results: Using this definition, deaths of despair were the fifth leading cause of US mortality in 2021. From1999 to 2021, the APC for deaths of despair increased 2.5-fold among people aged 25- to 74-years.

Conclusions: Using this definition, deaths of despair would have been the 5th leading cause of death in the US in 2021. Healthcare providers should have an increased awareness of deaths of despair. Public health practitioners may consider new initiatives to prevent deaths of despair locally, regionally, and nationally.

Keywords: International Classification of Diseases; Mortality; Cause of Death

Introduction

The International Classification of Diseases (ICD) is an extremely valuable medical classification used worldwide in epidemiology as well as for clinical and policy. The ICD is the global standard for health data, disease classification, and clinical documentation, and is universally adopted among World Health Organization (WHO) 132 Member States [1]. The ICD provides diagnostic codes that help classify and categorize the extent, causes, and consequences of human disease and death [1]. This system is designed to map health conditions to corresponding generic categories together with specific variations, assigning for these a designated code up to six characters long. Thus, major categories are designed to include a set of similar diseases.

The uses of the ICD include morbidity and mortality statistics, reimbursement systems, and in health care. This system promotes international comparability in collection, processing, classification, and presentation of statistics. As a comprehensive tool for the statistical classification of all health disorders, the ICD also provides essential diagnostic guidance.

Revised periodically to incorporate advances in medical knowledge, the ICD is now in its 11th revision [1,2]. The ICD has been utilized effectively for over a century to provide standardized codes for causes of death as well as the occurrence of diseases and related medical conditions. The ICD is based on the theory that maintains that each disease entity in its domain is distinct, defining outcomes based on anatomic and pathologic boundaries [1,2].

However, recent attention has shifted towards complex constellations of conditions crossing these boundaries, notably "deaths of despair" [3]. Deaths of despair are defined as a constellation of 19 underlying conditions including chronic hepatitis; liver fibrosis/cirrhosis; suicide or sequelae of suicide; poisoning (accidental or undetermined intent) or exposure to nonopioid analgesics, antipyretics, rheumatic, antiepileptic's, sedative hypnotics, antiparkinsonian and psychotropic drugs, narcotics, psychodysleptics, drugs acting on the central nervous system and alcohol [4]. Recent research has hypothesized economic stagnation, rising medical costs, and declining social cohesion as major contributors [3]. Public health initiatives emphasize expanding access to mental health care and substance use treatment, yet experts contend that these measures must be part of a broader strategy addressing structural issues like income inequality and weakened support systems [3].

In this rapid report, we explored temporal trends in the occurrence of United States (US) deaths of despair from 1999 to 2021 among those 25 to 74 years of age aiming to underscore the public health challenges they present and to advocate for comprehensive strategies that address both clinical and socio-economic risk factors.

Materials and Methods

We observed yearly mortality from deaths of despair from 1999 to 2021 among those 25 to 74 years of age. The US Centers for Disease Control and Prevention's (CDC) publicly available Wide-Ranging Online Data for Epidemiologic Research (WONDER) provided overall age-adjusted rates for mortality from deaths of despair (ICD-10 codes include K73-74, X60-84, Y87.0, X40-45, Y10-15, Y45, Y47, and Y49) [4] and corresponding data for the 15 leading Underlying Causes of Death (UCD) in 2021 [5]. Death certificates are estimated to be 99% complete for legal US residents [5]. We obtained annual percent changes (APC) as measures of effect size and used joinpoint regression analyses to test for statistical significance. This original research was considered to be exempt by the Florida Atlantic University Institutional Review Board.

Results

From 1999 to 2021, the APC for deaths of despair increased 2.5-fold among people aged 25- to 74-years (Figure 1). In 2021, using these aforementioned definitions, deaths of despair were the 5th leading cause of death in the US. The order of deaths was first disorders of the heart accounting for 695,547 deaths. Malignant neoplasms were in second place causing 605,213 deaths. COVID-19 was in third place accounting for 416,893. In fourth place were accidents (unintentional injuries) causing 224,835 deaths. Deaths of despair using the aforementioned definition accounted for 176,386 US deaths. This figure exceeds that of the sixth cause, cerebrovascular disease, which accounted for 162, 890 deaths [6].

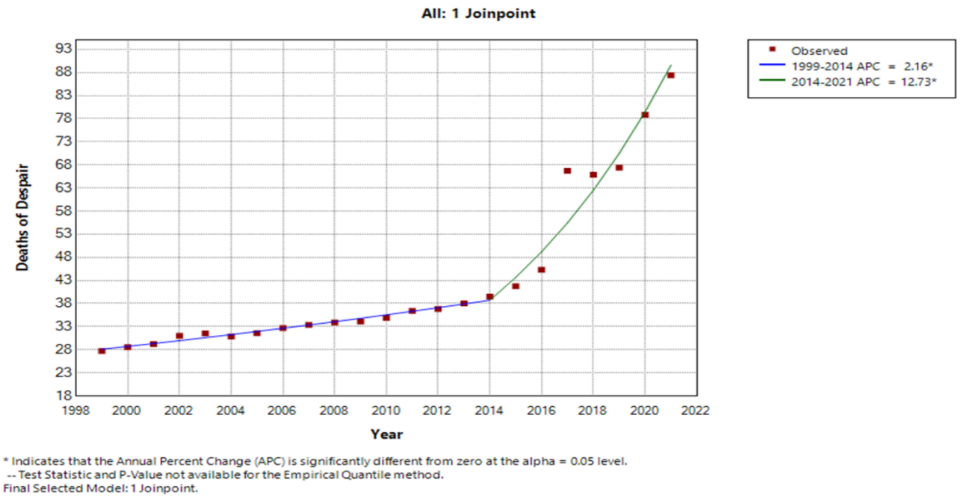

Figure 1: Age-adjusted Mortality from Deaths of Despair (25-74 Years of age). USA. 1999-2021.

Discussion

The findings of this study document an alarming 2.5 fold rise in deaths of despair in the US among individuals 25 to 74 years of age over the past two decades. Using a widely accepted definition of this concept, in 2021 in the US, deaths of despair would have constituted the 5th leading cause of death. A recently published research letter supports these findings, highlighting similar overall patterns. They also explored the findings by gender and reported that, as of 2022, rates among Blacks were higher than White individuals, and were highest among American Indian or Alaska Natives [7].

These data are descriptive and useful to formulate, not test hypotheses [8]. Nonetheless, they raise several clinical and public health challenges. We believe the challenges require attention from healthcare and public health providers as well as policymakers and public health officials who have the potential to exert a positive influence on medical care to reduce deaths of despair. These include preventive care, community health initiatives and improving education and awareness. These interventions may need to extend to address social determinants of health, such as income inequality, healthcare accessibility, and economic instability, all of which contribute to the despair that may underly these deaths. Policymakers should consider enhancing mental health and substance use services within primary care settings, integrating them as part of routine care to reduce stigma and improve access. Finally, they raise the question to policymakers about whether future iterations of the ICD should incorporate this classification.

Thus, addressing deaths of despair requires a multi-faceted approach, including improving both medical and social aspects of health. In addition, investing in research initiatives to improve our understanding of the causes of deaths of despair and evaluating the medical care provided to patients at risk are needed as well as evidence-based policies designed to reduce associated risk factors. Further, the classification of deaths of despair within the ICD codes could promote better tracking and allow healthcare providers to address these factors with targeted interventions. We believe that healthcare providers should increase their awareness of deaths of despair among their patients, while public health practitioners may consider implementing the aforementioned initiatives in the hope of preventing deaths of despair at local, regional, and national levels. By broadening the focus from individual risk factors to include structural issues—such as affordable housing, equitable economic policies, and social support systems—policymakers can foster resilience against despair-related condition. Finally, building collaborative networks among healthcare providers, community organizations, and policymakers is essential to sustaining a multi-faceted response to deaths of despair. This collaboration could support initiatives that promote mental health literacy, foster social connectedness, and address economic disparities. Such comprehensive strategies would not only improve individual outcomes but could also contribute to long-term reductions in deaths of despair on local, regional, and national scales.

The present data have several limitations to interpretability. For example, leading causes of death on the WONDER site are also based on the death certificates' underlying cause of death. Rates are likely lower than those that might have been obtained from occurrence based on whether conditions were considered

underlying or contributory. These considerations, however, are unlikely to have major impacts on the observed findings.

Conclusion

Addressing the rise in deaths of despair requires a comprehensive, multi-faceted approach that integrates medical, social, and economic interventions. Analytic research to better understand the causes and risk factors associated with these deaths is essential, as is the development of evidence-based policies aimed at reducing their occurrence. As we move forward, we believe that the medical community should continue to advocate for the inclusion of social determinants of health in disease classification systems like the ICD, ensuring that these factors are adequately captured and addressed in both clinical practice and public health policy.

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Ethical Guidelines: *This original research was considered to be exempt by the Florida Atlantic University Institutional Review Board.*

Conflict of Interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this manuscript. CH discloses that he serves as an independent scientist in an advisory role to investigators and sponsors as Chair of two Data Monitoring Committees for Amgen; to the United States Food and Drug Administration, and Up to Date; receives royalties for authorship or editorship of 3 textbooks; has an investment management relationship with the West-Bacon Group within Truist Investment Services, which has discretionary investment authority; does not own any common or preferred stock in any pharmaceutical or medical device If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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