Trends in cardiac conduction disorder–associated mortality among young adults in the United States, 2010–2020

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BACKGROUND Cardiac Conduction Disorders (CCDs) in young adults aged 25–44 years represent an important and poorly investigated condition associated with death.

OBJECTIVE We assessed trends in CCD-associated mortality in the United States (US) from 2010 to 2020 among young adults to determine differences by sex, ethno-racial groups, urbanization, census region, and underlying causes of death.

METHODS Mortality data were obtained from the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research database, covering the period from 2010 to 2020. Age-adjusted mortality rates (AAMRs) were analyzed using joinpoint regression modeling and presented as the estimated average annual percentage change (AAPC), along with corresponding 95% confidence intervals (95% CIs).

RESULTS In the US, between 2010 and 2020, 4312 US young adults aged between 25 and 44 years died from CCD, equating to a rate of 10.9 deaths per 1000 population. The relative AAMR increased with a seemingly exponential distribution (AAPC: +10.7%; 95% CI: 9.1–12.3; $P < .001$), without sex differences. Furthermore, the AAMR increase was more pronounced in white patients. The AAMR has similarly increased in both urban and rural areas. Higher absolute numbers of CCDs were clustered in the South (45.1%). The most common underlying causes of mortality in US young adults dying from CCD were cardiomyopathies (11.4%), sepsis (6.0%), myocardial infarction (5.9%), pulmonary embolism (4.7%), and poisoning by drugs, medicaments, and biological substances (4.5%).

CONCLUSION CCD-associated mortality among young adults has increased over the last decade in the US, with notable racial and regional disparities.

KEYWORDS Cardiac Conduction Disorders; Mortality; Race; Ethnicity; Trend

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Introduction

Cardiac conduction disorders (CCDs) represent a significant yet often underappreciated category of cardiovascular diseases (CVDs), potentially leading to severe morbidity and mortality, particularly among young adults.[1,2] Historically, most investigations have focused on the epidemiology and clinical impact of CCDs in older populations, frequently neglecting their implications for younger patients. However, emerging evidence suggests a shift in the epidemiology of CCDs among young adults, who are estimated to comprise about 13% of all conduction disorder cases.[3] Understanding the trend in CCD-associated mortality is crucial for better characterizing the disease's impact on young adults and informing potential preventive efforts to treat these subjects, which represent the "working force" of the country.[1]

This study aimed to analyze the trend in mortality associated with CCD among young adults in the United States (US) over the past decade, using data from the Centers for Disease Control and Prevention (CDC) Wide-ranging Online Data for Epidemiologic Research (WONDER) dataset.[4] Additionally, we examined the primary underlying causes of death in this demographic group during the same timeframe to provide potential explanations for these mortality trends.

Methods

For this analysis, data were sourced from the publicly accessible CDC WONDER dataset,[4] which is routinely updated to provide information from death certificates of all US residents based on the International Classification of Diseases, Tenth Revision (ICD-10). This database includes demographic

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KEY FINDINGS

- Cardiac conduction disorder (CCD)-associated mortality among young adults in US increased from 2010 to 2020, with no significant sex differences.
- The highest mortality rates were observed in the southern region, particularly among white, black, and Hispanic/Latinx individuals.
- Cardiomyopathies were the most frequent underlying cause of CCD-associated deaths.

and geographic information, such as age, sex, race, Hispanic/Latinx ethnicity, urbanization status, and census region.

CCD-associated mortality deaths occurring between January 2010 and December 2020 in young adults from US, defined as those aged between 25 and 44 years old,[5] were ascertained when the ICD-10 codes for CCDs I44 and I45 (Supplemental File 1) were listed in the first position of death certificate, defined as the disease or event that started the chain of events that led to death. Population estimates and mortality trends were stratified by sex, race, ethnicity, and urban-rural classification. Despite being introduced for billing and patient care in late 2015, the World Health Organization approved the publication of ICD-10 in 1999, which has been used for cause of death classification on US death certificates since then. The study did not require institutional review board approval since the analysis was based on de-identified and publicly available data, following the EQUATOR Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines (Supplemental File 2).[6]

After data extraction and validation process (MZ), we gathered information on the number of CCD-associated deaths listed as the first cause of death, population sizes from 2010 to 2020, demographic data including age, sex, race, ethnicity, and census region for US young adults. Ethnicity was defined as Latinx/Hispanic or non-Latinx/non-Hispanic, whereas race was categorized as white, black, American Indian/Alaskan Native, and/or Asian/Pacific Islander. We did not perform a specific sub-analysis for Asian/Pacific Islanders and Alaskan Native/American Indian, because of their lower estimates, which do not allow us to analyze the relative trends; however, their estimates were considered in all the other analyses. The classification of counties into urban and rural categories was conducted according to the 2013 National Center for Health Statistics Urban-Rural Classification Scheme. Additionally, mortality trends were analyzed by US census regions, including the Northeast, Midwest, South, and West.[5] Moreover, using the same dataset, we also assess the most common underlying causes of mortality in US young adults aged 25 to 44 years dying from CCD.

Age-adjusted mortality rates (AAMRs) per 100,000 individuals, along with their 95% confidence intervals (CIs), were calculated using standardization based on data from the US Census Bureau and the 2000 US standard population. Nationwide annual trends were evaluated through the average percent change (APC) and average annual percent change (AAPC), both accompanied by relative 95% CIs, using joinpoint regression analyses. This statistical method was used since it offers several advantages over traditional linear regression as the detection of significant changes, or "joinpoints," in the trend of a time series dataset and the identification of acceleration or deceleration in the trend, which may be missed by linear trend analysis.[7] Paired comparison tests (P for parallelism) for subgroup trends were performed. Analyses were conducted using SPSS (SPSS, v 21.0, Chicago, IL) and joinpoint regression software (Joinpoint, version 4.6.0.0, National Cancer Institute, MD). Statistical significance was prespecified at $P < .05$ for findings in the entire population.

Results

Between 2010 and 2020, 393,989 young adults (249,516 men and 144,473 women) between 25 and 44 years old died in the US of CVD. Among these, 4312 deaths (2401 men and 1911 women) were associated with CCDs, equating to a rate of 10.9 deaths per 1000 population. The AAMR for CCD-associated mortality in young adults increased from 0.25 (95% CI: 0.21–0.29) per 100,000 population in 2010–0.72 (95% CI: 0.67–0.78) per 100,000 population in 2020 (AAPC: +2.5%, 95% CI: 1.4–3.6, $P < .001$) with a seemingly exponential distribution (AAPC: +10.7%, 95% CI: 9.1–12.3, $P < .001$) (Table 1). Men had higher CCD-associated mortality compared with women despite having a similar increase in AAMR (P for parallelism = .19). Specifically, in men, the AAMR increased from 0.25 (95% CI: 0.20–0.30) per 100,000 population in 2010 to 0.88 (95% CI: 0.79–0.97) per 100,000 population in 2020 (AAPC: +11.1, 95% CI: 8.8–13.5, $P < .001$). Similarly, in women, the AAMR increased from 0.20 (95% CI: 0.16–0.25) per 100,000 in 2010 to 0.61 (95% CI: 0.54–0.69) per 100,000 in 2020 (AAPC: +10.3%, 95% CI: 7.3–13.5, $P < .001$) (Table 1 and Figure 1A). In white individuals, the AAMR for CCD-associated mortality increased from 0.15 (95% CI: 0.12–0.18) per 100,000 population in 2010 to 0.67 (95% CI: 0.60–0.73) per 100,000 in 2020 (AAPC: +13.6%, 95% CI: 9.9–17.5, $P < .001$). Compared with white individuals, a smaller increase was also observed in non-Latinx/non-Hispanic black individuals (AAPC: +9.0%, 95% CI: 7.4–10.6, $P < .001$) (P for parallelism = .01). Similarly, Among Latinx/Hispanic individuals, the AAMR increased (AAPC: +13.2%, 95% CI: 9.2–17.3, $P < .001$), in a similar manner compared with white individuals (P for parallelism = .26) and to non-Latinx/non-Hispanic black individuals (P for parallelism = .52) (Figure 1B). Data discontinuity precluded the calculation of relative trends for Asian/Pacific Islanders and Alaskan Native/American Indian, although estimates for these demographic groups were included in the overall analysis and in those stratifying the population by sex, age, urbanicity, and census regions. A

Table 1 Age-adjusted mortality rate trends for cardiac conduction disorders-associated mortality in the United States, 2010 to 2020, stratified by sex, race, ethnicity, age, and urban density

Items	AAMR 2010 (95% CI)	AAMR 2020 (95% CI)	AAPC; (95% CI), p	Number of Joinpoints	*P* (for parallelism)
Overall	0.25 (0.21–0.29)	0.72 (0.67–0.78)	10.7; (9.1–12.3), $P < .001$	0	-
Men	0.25 (0.20–0.30)	0.88 (0.79–0.97)	11.1; (8.8–13.5), $P < .001$	0	.19
Women	0.20 (0.16–0.25)	0.61 (0.54–0.69)	10.3;(7.3–13.5), $P < .001$	0	
Race					
White	0.15 (0.12–0.18)	0.67 (0.60–0.73)	13.6; (9.9–17.5), $P < .001$	0	White vs black: $P = .01$
Black or African American	0.62 (0.48–0.79)	1.40 (1.19–1.62)	9.0; (7.4–10.6), $P < .001$	0	
Asian/Pacific Islander	NA	NA	NA	0	White vs Latinx/ Hispanic: $P = .26$
Alaskan Native/American Indian	NA	NA	NA	0	Black vs Latinx/ Hispanic: $P = .52$
Ethnicity					
Latinx/Hispanic	0.15 (0.09–0.23)	0.67 (0.55–0.79)	13.2; (9.2–17.3), $P < .001$	0	-
Urban density					
Urban areas	0.20 (0.17–0.24)	0.72 (0.66–0.79)	11.8; (8.9–14.7), $P < .001$	0	.32
Rural areas	0.20 (0.12–0.29)	0.93 (0.75–1.14)	9.8; (7.0–12.5), $P < .001$	0	

AAMR = age-adjusted mortality rate, expressed as deaths per 100.000 population; AAPC = average annual percent change; CI = confidence interval; NA = not applicable.

map showing the AAMR because of CCD, over the entire study period, stratified by states, is shown in Figure 2. CCD-associated mortality increased without statistical difference (P for parallelism = .32) both in urban (AAPC: +11.8%, 95% CI: 8.9–14.7, $P < .001$) and rural areas (AAPC: +9.8%, 95% CI: 7.0–12.5, $P < .001$) (Figure 1C). Higher percentages and absolute numbers of CCDs were clustered in the South (47.6%, n = 5011) compared with the rest of the country (Tables 1 and 2, Figure 1D, and Supplemental File 3). The most common underlying causes of mortality in young adults in the US aged 25–44 years dying from CCD were cardiomyopathies (11.4%), sepsis (6.0%), myocardial infarction (5.9%), pulmonary embolism (4.7%) and poisoning by drugs, medicaments, and biological substances (4.5%) (Figure 3).

Discussion

The present analysis, based on the CDC WONDER, showed that among US young adults aged between 25 and 44 years, AAMR for CCD-associated mortality increased with a seemingly exponential trend by approximately 220.0% between 2010 and 2020, with no differences between sexes. Relative increases in AAMR were observed among white, non-Hispanic/non-Latinx black, and Hispanic/Latinx individuals, and in individuals residing in the Southern region of the country. The highest prevalence of CCD-associated mortality was recorded in the South, with cardiomyopathies being the most frequent underlying cause of death (Central Illustration).

Overall, these observations suggest a concerning trend of increased CCD-associated mortality in the US among young adults. Indeed, as demonstrated by previous investigations, the underlying causes of CCD remain unknown in about half of patients aged < 50 years.[1,2] Several factors may explain these observed trends. First, the prevalence of cardiovascular risk factors such as systemic arterial hypertension, diabetes, obesity, tobacco use, alcohol consumption, unhealthy diets, and poor physical activity has increased among young adults in the US.[8] All these risk factors are well-established independent predictors of CCDs.[9] Additionally, the diagnosis of cardiomyopathies has increased over the past decade because of heightened recognition of these clinical conditions.[10] Alternatively, increased recognition of CCD as a potential cause of death, even in younger patients, may result in greater recognition and attribution of mortality to the diagnosis.

The increase in CCD-associated mortality across all ethno-racial and geographic subgroups warrants further consideration, particularly given the significant disparities in treatment and outcomes for CVD across the US population.[11] Limited access to healthcare in certain US regions and for specific demographic groups may impact the timely diagnosis and treatment of CCD, contributing to the observed increased mortality rate.[12] Data discontinuity precluded the calculation of relative trends for Asian/Pacific Islanders and Alaska Native/American Indians, although estimates for these groups were included in the overall analysis and stratified by sex. Further dedicated analyses are required to elucidate the trends of CCD-associated mortality trends in these ethno-racial groups.

Previous US reports have described higher arrhythmia-associated deaths among older adults over the last 2 decades, especially in rural areas.[13] In contrast, our analysis showed a similar AAMR increase in both urban and rural areas. However, a higher percentage and absolute number of CCDs were clustered in the south, likely reflecting a complex interplay of socioeconomic and environmental factors. Individuals in rural areas often face delays in diagnosis and access to advanced treatments, potentially contributing to elevated mortality rates.[14] Additionally, the south has historically exhibited a higher prevalence of cardiometabolic risk factors,

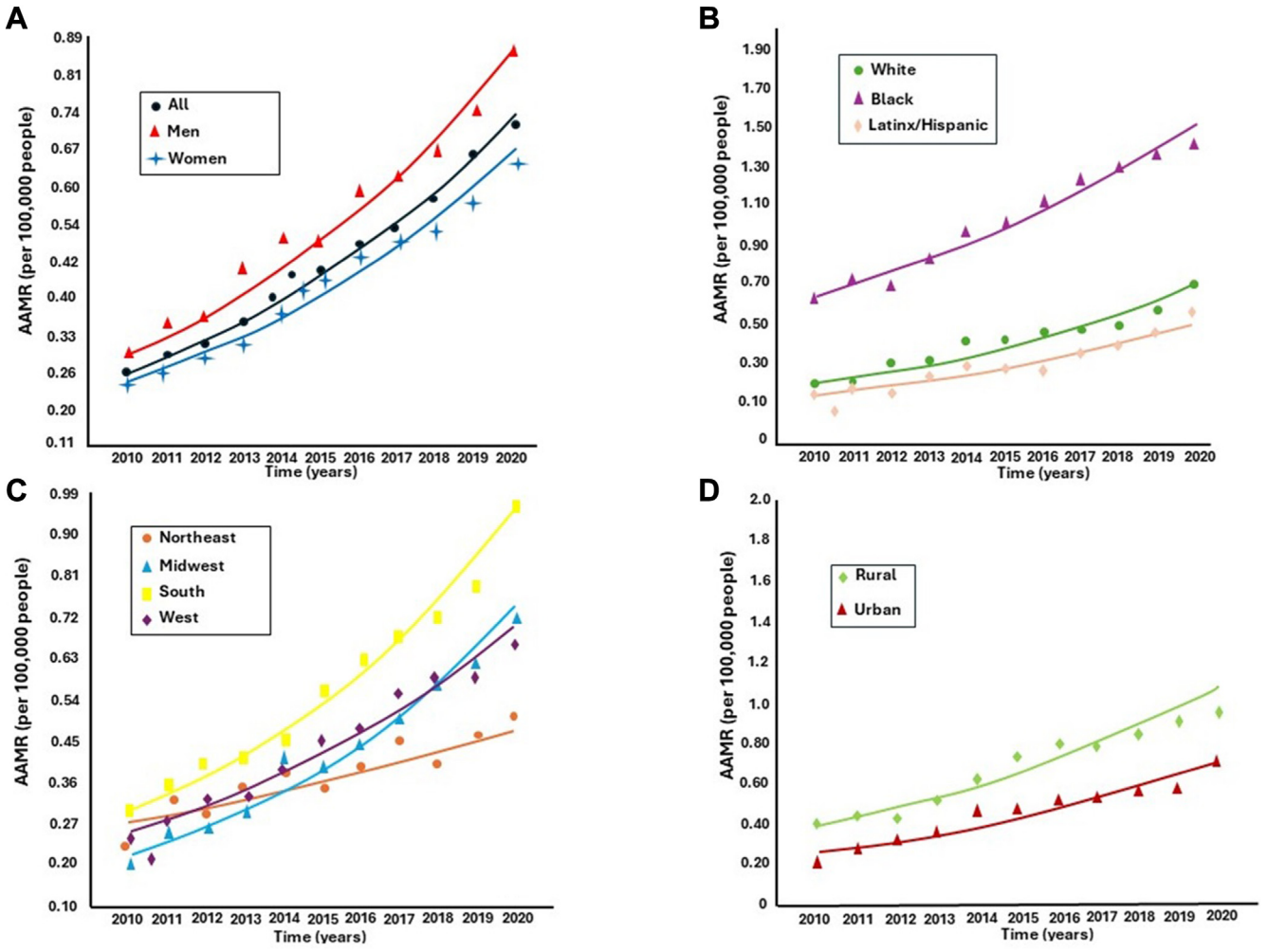

Figure 1 Cardiac conduction disorder-associated mortality trends in the United States, 2010 to 2020, and by subgroups. **A:** Age-adjusted mortality rates because of cardiac conduction disorder-associated mortality in United States, also stratified by sex. **B:** Age-adjusted mortality rates because of cardiac conduction disorders -associated mortality in United States stratified by race and ethnicity, 2010–2020. **C:** Trends in age-adjusted mortality rates because of cardiac conduction disorder-associated mortality in United States, 2010–2020, stratified by urban density. **D:** Trends in age-adjusted mortality rates because of cardiac conduction disorder-associated mortality in United States, 2010–2020, stratified by Census regions. Age-adjusted estimates were obtained through direct standardization to the 2000 US standard population, with joinpoint regression analysis used to assess trends. AAMR = Adjusted mortality rate.

such as obesity, diabetes, high blood pressure, high cholesterol, and smoking, and socioeconomic factors like poverty, unemployment, and limited educational opportunities, particularly in rural areas.[15] These factors may have amplified racial disparities and contributed to the higher CCD-associated mortality rate.

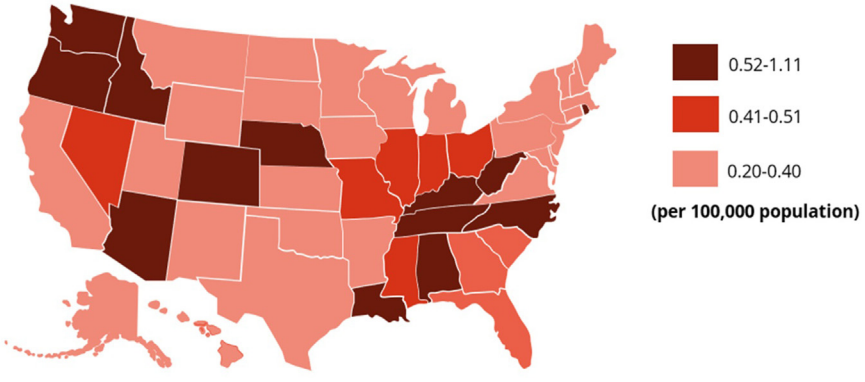

Figure 2 Map of the United States illustrating the distribution of age-adjusted cardiac conduction disorders-associated mortality from 2010 to 2020, across individual states.

Table 2 Age-adjusted mortality rate trends for cardiac conduction disorder-associated mortality in the United States, 2010 to 2020, stratified by census region

Items	AAMR 1999 (95% CI)	AAMR 2020 (95% CI)	AAPC; (95% CI), *P*	Number of Joinpoints
Northeast	0.20 (0.13–0.28)	0.51 (0.40–0.51)	5.4; (0.7–10.3), $P = .02$	0
Midwest	0.15 (0.09–0.23)	0.67 (0.54–0.79)	13.4; (9.4–17.6), $P < .001$	0
South	0.31 (0.25–0.39)	0.99 (0.87–1.10)	11.9; (10.1–13.1), $P < .001$	0
West	0.25 (0.18–0.34)	0.64 (0.55–0.77)	10.4; (6.3–14.6), $P < .001$	0

AAMR = age-adjusted mortality rate, expressed as deaths per 100.000 population; AAPC = average annual percent change; CI = confidence interval.

Young adults represent a crucial subgroup of the population, forming a large part of the workforce and typically characterized by lower overall mortality rates. The unexpected rise in deaths associated with CCDs in this demographic raises critical questions about the adequacy of current medical practices, screening protocols, and public health initiatives aimed at early detection and intervention.

Our study has limitations stemming from its retrospective nature, reliance on ICD-10 codes data with potential inaccuracies, such as miscoding and misdiagnosis, and lack of procedural and baseline cardiovascular data. In this regard, no major nationwide interventions or systematic changes to the death certification process were implemented in the US between 2010 and 2020 that would specifically account for the trends observed in our analysis. Moreover, because no diagnostic studies have validated the accuracy of the ICD-10 code identifying CCDs, especially in young adults and in the US population, we cannot exclude potential intrinsic biases in the selection of patients. Additionally, death certificates can underestimate cardiovascular mortality in younger subjects, as with most administrative datasets.[16] However, retrospective assessments remain the predominant method used to estimate the incidence and trends of most CVDs. Additionally, we can explore only the major underlying causes of death because the remaining associated conditions were either individually reported in less than 1% of cases or categorized under broader or nonspecific diagnostic codes that did not allow for precise attribution to a single underlying cause. Moreover, data discontinuity in the reporting of several major underlying causes of death throughout the study period limited our ability to reliably assess their temporal variations. Finally, we were not able to estimate the CCD-associated mortality rate after 2020 since mortality data after that year are still provisional. Further analyses are needed to explore the trend in ACM-attributable mortality following the coronavirus disease 2019 pandemic to confirm our findings.

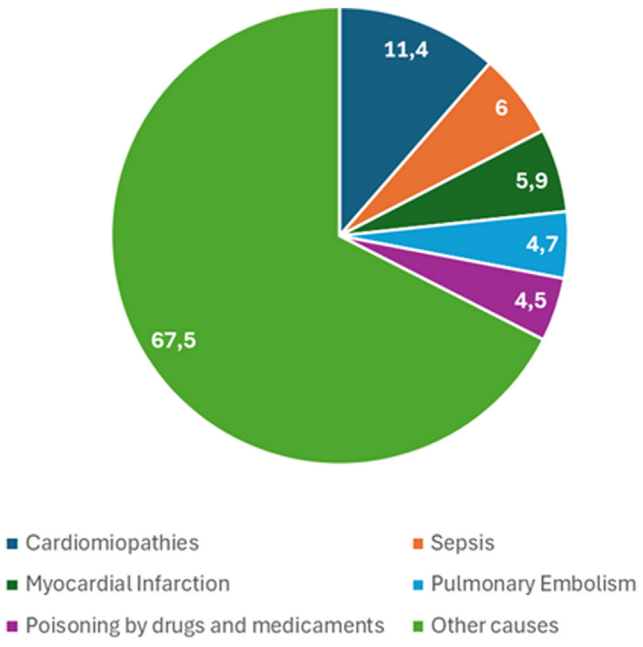

Figure 3 Most common underlying causes of mortality in US young adults aged 25–44 years dying from cardiac conduction disorders.

Conclusion

In conclusion, CCD-associated mortality is increasing among young US adults. Understanding the demographic and clinical characteristics of these cases can highlight potential risk factors, including lifestyle choices, genetic predispositions, and environmental influences that may contribute to the development of CCDs in this demographic group.

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Authorship: All authors attest they meet the current ICMJE criteria for authorship.

Ethics Statement: The study did not require institutional review board approval since the analysis was based on de-identified and publicly available data, following the EQUATOR Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hroo.2025.05.009.

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