Empirical Article

Clinical Psychological Science
1–15

DOI: 10.1177/21677026261425570
www.psychologicalscience.org/CPS

Longer Residence in Disadvantaged Neighborhoods Predicts Both a Syndrome of Despair and Deaths of Despair: Complementary Evidence From Nationwide Register and Birth-Cohort Studies

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Abstract

Deaths of despair have been difficult to predict by focusing solely on individual-level factors. In two complementary studies, we tested whether individuals living in disadvantaged neighborhoods in a country with robust social safety nets (New Zealand) were at greater risk for a despair-related death (suicides, drug overdoses, alcohol poisonings, and liver disease, Study 1) or a "premorbid" midlife syndrome of despair-related maladies (suicidality, substance misuse, sleep problems, and chronic pain, Study 2). In 2 decades of observation, New Zealanders residing in disadvantaged neighborhoods across adulthood were at greater risk for a despair-related death (N = 2.4 million; analytic sample using nationwide administrative data, population risk ratio per quintile increase in cumulative disadvantage = 1.27, 95% confidence interval [CI] = 1.23, 1.30) and a more severe premorbid syndrome of despair-related maladies (N = 907; analytic sample using a population-representative birth cohort, β = 0.24, 95% CI = 0.17, 0.31). Findings held after adjustment for individual-level socioeconomic status and in Study 2, adjustment for childhood antecedents and adult difficulties that could provoke despair. Neighborhoods could be intervention targets to reduce despair-related deaths.

Keywords

deaths of despair, neighborhoods, factor analysis, longitudinal, suicide, overdose, alcohol

Received 1/28/25; Revision accepted 2/3/26

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Deaths of despair, involving deaths from suicides, accidental drug overdoses, alcohol poisonings, and alcohol-related liver disease, have been increasing among working-age adults in the United States and many wealthy, industrialized countries (Allik et al., 2020; Gold, 2020; Kim et al., 2011; Piñeiro et al., 2023; Richmond-Rakerd et al., 2024; Shiels et al., 2020; Walsh et al., 2021) for the past several decades. Since the phenomenon was first identified in the United States in 2015 (Case & Deaton, 2015), the trend has continued (with enhancement during the COVD-19 pandemic; Friedman & Hansen, 2024 Heuveline, 2022; Rahimi-Ardabili et al., 2022; Schöley et al., 2022) and contributed to recent declines in U.S. life expectancy (Gold, 2020; Harris et al., 2021). Better characterization of modifiable factors that might precipitate deaths of despair is urgently needed to advance public health and identify potential intervention targets (Dow et al., 2019; Rehder et al., 2021; Scutchfield & Keck, 2017).

Deaths of despair tend to involve a constellation of related maladies—chronic pain, substance misuse, sleep problems, and suicidality coinciding with hopelessness about the future, social isolation, and low-status, physically demanding jobs (Case & Deaton, 2017, 2022; Oquendo & Volkow, 2018; Rehder et al., 2021; Scutchfield & Keck, 2017). The co-occurrence and coexacerbation of these conditions by one another has led to the identification of a multifaceted "syndrome of despair" that more fully captures an individual's psychological and physiological distress (and therefore potential risk of premature mortality) than does consideration of individual despair-related maladies in isolation (Brennan et al., 2023; Dent et al., 2024; Gutin et al., 2023). The despair syndrome is a potentially powerful construct for identifying the risk and causal drivers of despair and developing targeted interventions to reduce deaths of despair.

Although deaths of despair have been most robustly associated with individual-level socioeconomic disadvantage (e.g., low relative income and educational attainment) in countries with both weak (Case & Deaton, 2022) and strong (Richmond-Rakerd et al., 2024) social safety nets, they also appear to follow poorly understood geographic gradients such that rates of individual diseases of despair (e.g., drug overdose, suicide) vary across small geographic areas over and above the individual sociodemographic characteristics of people living in those areas. For example, in the United States, drug and alcohol misuse and suicide deaths show marked variation across neighborhoods within a county, counties within a state, and states within a region (Karriker-Jaffe, 2013; Lee et al., 2023)—a finding echoed in geographic investigations of suicidality and self-harm in multiple European countries (Fountoulakis et al., 2016; Gunnell et al., 2012; Jakobsen & Lund, 2022; Kandrychyn, 2004; Middleton et al., 2006; Salmerón et al., 2013; Voracek & Marušič, 2008) and Australia and New Zealand (Collings et al., 2009; Hetrick et al., 2024; Hielscher et al., 2024). In general, these studies have produced mixed and fragmented findings, identifying, for example, that high rurality and urbanicity each may increase risk for suicidality depending on context (Lee et al., 2023; Middleton et al., 2006), as may colder weather (Fountoulakis et al., 2016) *and* hotter weather (Fountoulakis et al., 2016; Salmerón et al., 2013), and as may lower *and* higher levels of residents from minoritized racial and ethnic identities (e.g., owing to greater social cohesion or concentrated structural disadvantage, respectively; Lee et al., 2023; Voracek & Marušič, 2008).

In this context, the concept of neighborhood socioeconomic disadvantage may offer a useful framework for investigating the geographic patterning of despair. Disadvantaged neighborhoods are those with poorer physical, social, and economic conditions relative to other neighborhoods in a region or wider society. Disadvantaged neighborhoods could elevate risk for despair through selection effects (e.g., the concentration of people already at risk because of individual characteristics, such as low income or preexisting substance-use problems) or through causal effects (e.g., the concentration of social and environmental risks that may elevate despair-related maladies, such as higher crime rates, lower access to mental-health treatment, and greater density of alcohol outlets).

Although neighborhood disadvantage has been previously associated with greater prevalence of individual despair-related maladies (pain, Fuentes et al., 2007; substance misuse, Karriker-Jaffe, 2013; sleep problems, Fuller-Rowell et al., 2016; Nahmod et al., 2022; and suicidality, Jakobsen & Lund, 2022; Xi et al., 2023) over short time spans or in ecological studies, it has yet to be examined in relation to the full despair syndrome (reflecting comorbidity and symptom severity) or in a long-term (multidecade) longitudinal investigation with prospectively measured antecedents to despair. Such empirical investigation is necessary to rule out selection effects, approach causal inference and identify potential causal mechanisms, better characterize individuals and communities at high risk for despair, and support the potential development of novel neighborhood-based interventions that could complement individual-level health-care-based medical approaches (Rehder et al., 2021; Scutchfield & Keck, 2017).

Here, we report, to the best of our knowledge, the first test of the hypothesis that following cumulative-disadvantage theory (Dannefer, 1987; Rehder et al., 2021), longer residence in disadvantaged neighborhoods

across adulthood is associated with greater risk of despair-related mortality and before death, a syndrome of despair-related maladies. To perform this test, we turned to the country of New Zealand, which has a population-representative longitudinal birth cohort with prospectively measured antecedents to despair (the Dunedin Study, followed to age 45) embedded in a full-population administrative data architecture (the New Zealand Integrated Data Infrastructure [NZ-IDI]) that includes health records with nationwide coverage. As previously described in a recent investigation of the prevalence of deaths of despair in New Zealand (Richmond-Rakerd et al., 2024), the country has the additional benefit of nationwide health care, robust pharmaceutical regulations, and a strong social safety net, which together allow for tests of potential neighborhood effects in a setting in which despair-related health disparities should be relatively limited. ("Social safety net" in this context refers to the wider package of government programs and policies designed to support potentially vulnerable individuals and families to limit inequality and financial hardship, which in New Zealand includes significant public support for sole and young parents, the unemployed and disabled, and individuals seeking higher education, among other programs; Haigh, 2018). As that empirical study reported, however, deaths of despair are not uncommon in New Zealand. In concert with the United States and European countries over the past 3 decades, New Zealand has experienced uneven economic growth across sectors and regions. Slow nationwide recovery from an austerity-policy-initiated economic recession in the 1990s, aging transportation and communication infrastructure, and low investment in research and development have interacted to generate levels of social and economic disparity that match other Western, developed countries (OECD, 2013; Pearson et al., 2013). The death-of-despair rate in New Zealand across the 2000s and early 2010s was approximately 17 per 100,000 for working-age women and 42 per 100,000 for working-age men—approximately 25% to 50% lower than the reported rate for the United States across the same time period, with variation by year, type of death, and subpopulation (Richmond-Rakerd et al., 2024). Rates of opioid-related deaths have been much lower in New Zealand than the United States, for example (0.5 per 100,000 in New Zealand vs. 11.3 per 100,000 in the United States in 2015), and suicide rates have been only slightly lower (11.1 per 100,000 in New Zealand vs. 12.3 per 100,000 in the United States in 2015; Our World in Data, 2024, 2025).

We first tested whether deaths of despair follow neighborhood socioeconomic ("disadvantage") gradients in the full New Zealand population (NZ-IDI; N = 2.4 million; Study 1). We then tested whether this potential geographic patterning of despair deaths is preceded by geographic gradients in a syndrome of despair-related maladies by midlife in the New Zealand Dunedin Study birth cohort (full cohort: N = 1,037; Study 2). Through prespecified follow-up tests in the birth cohort, we (a) attempt to rule out confounding by individual social class or neighborhood urbanicity, (b) determine whether multidecade trajectories of neighborhood quality (increasing or decreasing disadvantage over time) are differentially predictive of despair, (c) evaluate selection effects (i.e., examine preexisting developmental risk factors for despair, such as poor childhood cognitive, physical, and mental health and low educational attainment by adulthood), and (d) evaluate potential mediating adult physical, social, or economic difficulties that individuals may be more likely to experience while living in disadvantaged neighborhoods.

Transparency and Openness

Preregistration

The Study 1 analysis plan was submitted to Stats New Zealand before data analysis. The Study 2 analysis plan was preregistered (in 2023; https://tinyurl.com/mr28n9wk).

Data, materials, code, and online resources

Whole-of-country results for New Zealand (Study 1) are not official statistics. They have been created for research purposes from the NZ-IDI, which is carefully managed by Statistics New Zealand. For more information about the NZ-IDI and to learn about data-set access, see https://www.stats.govt.nz/integrated-data/. Statistics New Zealand approved the use of the NZ-IDI for this project (Reference MAA2019-35). The Dunedin Study data (Study 2) are available on request by qualified scientists (https://dunedinstudy.otago.ac.nz/for-investigators). Requests require a concept paper describing the purpose of data access, ethical approval at the applicant's university, and provision for secure data access. Statistical code for the current report is available at https://github.com/aaronreuben/Neighborhood-Despair.

Reporting

The Supplemental Material available online includes additional supporting information about the study. We report how we determined our sample size, all data exclusions, and all study measures. Because the two

studies involve analysis of preexisting data, no experimental manipulations were introduced.

Ethical approval

For analyses in the NZ-IDI, informed consent was not obtained per rule 11(2)(c)(iii) of the NZ-Health Information Privacy Code, which allows for anonymized health-data research. Participants in the Dunedin Study birth cohort gave written informed consent, and Study protocols were approved by the NZ-Health and Disability Ethics Committee (UAHPEC023995). Additional ethical approval was obtained from the University of Auckland Human Participants Ethics Committee and the Duke University Campus and Medical School Institutional Review Boards. Research activities were carried out in accordance with the provisions of the World Medical Association Declaration of Helsinki.

Study 1: Deaths of Despair in the NZ-IDI

Method

The NZ-IDI is a whole-population collection of de-identified, individually linked, administrative data sources that combine government records with individual health data from hospital, clinic, pharmacy, and laboratory (Milne et al., 2019; Richmond-Rakerd et al., 2022; Stats New Zealand, n.d.). The study population included the 2,378,070 individuals who were born between 1955 and 1994 and were alive and resident in New Zealand at the start of the observation period (January 1, 2015). We divided the population into age bands (born between 1955–1974 and 1975–1994). Ethical approval was obtained from the University of Auckland Human Participants Ethics Committee (Reference UAHPEC023995). Output data underwent confidentiality review by Statistics New Zealand-Tatauranga Aotearoa. Informed consent was not obtained per rule 11(2)(c)(iii) of the New Zealand Health Information Privacy Code (Stats New Zealand, 2017a), which, under certain circumstances, allows for anonymized health data to be used for research without the authorization of the individual concerned.

Cumulative neighborhood disadvantage exposure measure: The NZ-Index of Deprivation. Residential neighborhood socioeconomic status (disadvantage) was assessed via the NZ-Index of Deprivation (NZDep), an area-based measure of socioeconomic disadvantage derived from nine census variables capturing area-level rates of unemployment, education, homeownership, and other domains (see eAppendix 1 in the Supplemental Material; J. Atkinson et al., 2021). NZDep ranks all New Zealand neighborhoods from least to most socioeconomically disadvantaged for all New Zealand censuses from 1991 onward at the smallest geographic unit reported by Statistics New Zealand ("statistical area 1" in 2019, encompassing ≈100–200 residents). Neighborhood-disadvantage scores were available in the NZ-IDI beginning January 1, 2000, as decile scores, converted to quintiles for analysis, and neighborhoods were observed from January 1, 2000, to December 31, 2014 (a 15-year period). Mean neighborhood-disadvantage scores across up to 20 addresses during the 15-year period were considered the primary exposure variable to capture cumulative disadvantage, although sensitivity tests also examined disadvantage at the last registered home address (i.e., where individuals were living before they died from a despair-related cause). To maintain statistical power, disadvantage scores were kept as continuous variables without the use of cutoff scores or categorization (Royston et al., 2006).

Deaths of despair. We ascertained deaths of despair from January 1, 2015, to December 31, 2019 (a 5-year period) via mortality records maintained by the New Zealand Ministry of Health using primary cause-of-death codes (ICD-10 codes X60–X84 and Y87.0 [suicide]; X40–X45, Y10–Y15, Y45, Y47, and Y49 [poisonings]; and K70 and K73–K74 [alcoholic liver diseases and cirrhosis]; Case & Deaton, 2015). The 5-year observation window was chosen to encompass the most recent date for which full mortality data were available.

Statistical analyses. Multinomial logistic regressions with risk ratios (RRs) were used to (a) estimate the association of cumulative neighborhood disadvantage with deaths of despair per quintile increase in disadvantage (using a three-level outcome variable coded for "no death," "death of despair," and "other death" to take into account death from competing causes, such as accidents and illnesses, that could be more likely in disadvantaged neighborhoods) and (b) compare higher disadvantage quintiles against the lowest quintile. Following existing procedures (Richmond-Rakerd et al., 2021, 2022), data were weighted for logistic models based on time alive and in New Zealand to account for differences between individuals in observation time because of death from other causes or out-migration.

Associations were estimated within the total study population with present neighborhood data (analytic population) and by age band and sex. Baseline models controlled for ethnicity (European, Māori, Pacific, and Asian ethnicity), and adjusted models additionally controlled for immigration status and individual socioeconomic status (educational attainment and annual

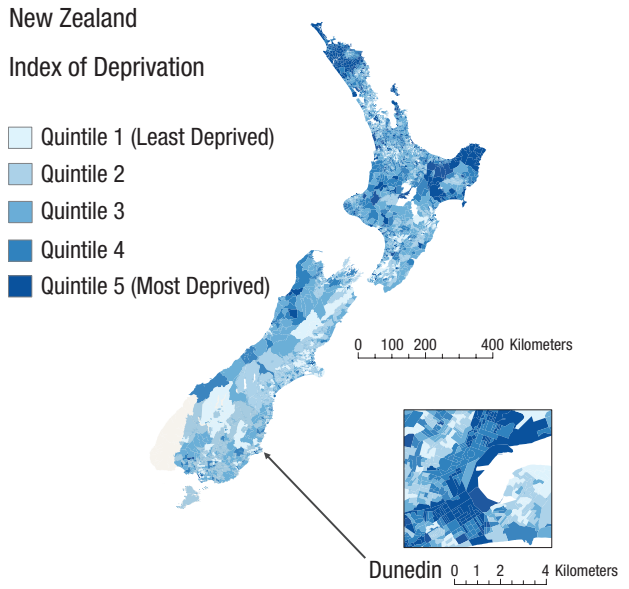

Fig. 1. Neighborhood disadvantage in New Zealand and in Dunedin. The New Zealand Index of Deprivation ranks all populated small areas (encompassing approximately 100–200 residents each on average) from least (Quintile 1) to most (Quintile 5) socioeconomically disadvantaged. Gray depicts the unpopulated area of Fiordland.

income). Models using the total population also controlled for sex and birth year. Per the confidentiality rules of Statistics New Zealand, reported frequencies/counts were randomly rounded to a base of 3. The threshold for statistical significance was two-tailed p value < .05. All reported analyses were conducted using Stata (Version 17.0). This report follows STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) reporting guidelines (von Elm et al., 2007).

Results

Is longer residence in disadvantaged neighborhoods predictive of deaths of despair in the New Zealand population? We observed 2,378,070 individuals (full study population; females: n = 1,195,812, 50.3%; age 5–44 years at baseline) who were born in New Zealand between 1955 and 1994 and resided in New Zealand for any period between January 2000 and December 2019; 589,704 (24.8%) were born between 1955 and 1964, 617,295 (26.0%) were born between 1965 and 1974, 550,884 (23.2%) were born between 1975 and 1984, and 617,295 (26.0%) were born between 1985 and 1994. During a 5-year observation, 2,934 individuals (0.13% of sample, 71.7% male) died from a despair-related cause: 1,890 from suicide (64.4% male), 585 from poisonings (74.8% male), and 522 from alcoholic liver diseases and cirrhosis (68.2% male). Māori residents experienced a higher rate of despair-related deaths (0.19%), and immigrant residents born overseas experienced a lower rate (0.07%). Men experienced a higher rate of despair-related deaths (0.18%) compared with women (0.07%). The death-of-despair rate was 21 of 100,000 in the first year of observation (2015) and 28 of 100,000 in the last year of observation (2019).

Figure 1 displays the geographic distribution of neighborhood disadvantage in New Zealand. Neighborhood-disadvantage data were available for 2,369,934 individuals (the analytic sample, 99.7% of the study population). As hypothesized, after adjustment for covariates, including birth year, sex, and ethnicity, New Zealanders residing longer in disadvantaged neighborhoods across adulthood were more likely to die from a despair-related death across the 5-year observation period (RR per quintile increase in cumulative disadvantage = 1.27, 95% confidence interval [CI] = [1.23, 1.30]), reflecting greater risk of suicide (RR = 1.19, 95% CI = [1.15, 1.23]), drug overdose (RR = 1.53, 95% CI = [1.43, 1.64]), and alcohol-related death (RR = 1.29, 95% CI = [1.21, 1.38]). In general, neighborhood-despair associations tended to be moderately greater among men than women and among earlier born, older individuals than more recently born, younger individuals (Fig. 2). Associations remained with some attenuation after additional adjustment for immigration status and individual-level socioeconomic factors, including income and education (overall RR = 1.14, 95% CI = [1.11, 1.18]).

Pairwise comparisons of higher cumulative-disadvantage quintiles against the lowest quintile did not identify significant statistical-effect thresholds: Neighborhood-despair associations increased fairly linearly with increasing disadvantage (eTable 1 in the Supplemental Material), although the highest quintile of disadvantage demonstrated slightly lower risk than the fourth quintile. In sensitivity tests using disadvantage scores at individuals' last residential addresses (i.e., a neighborhood score for where they were living before they died from a despair-related cause rather than a cumulative mean of scores for up to 20 addresses across the previous 2 decades), despair associations were modestly lower but showed more clear linear dose-response associations (eTable 1 in the Supplemental Material).

Study 2: Midlife Syndrome of Despair and Its Antecedents in The Dunedin Study Birth Cohort

Method

Birth-cohort participants were members of the Dunedin Study. The full cohort comprises all individuals born between April 1972 and March 1973 in Dunedin, New

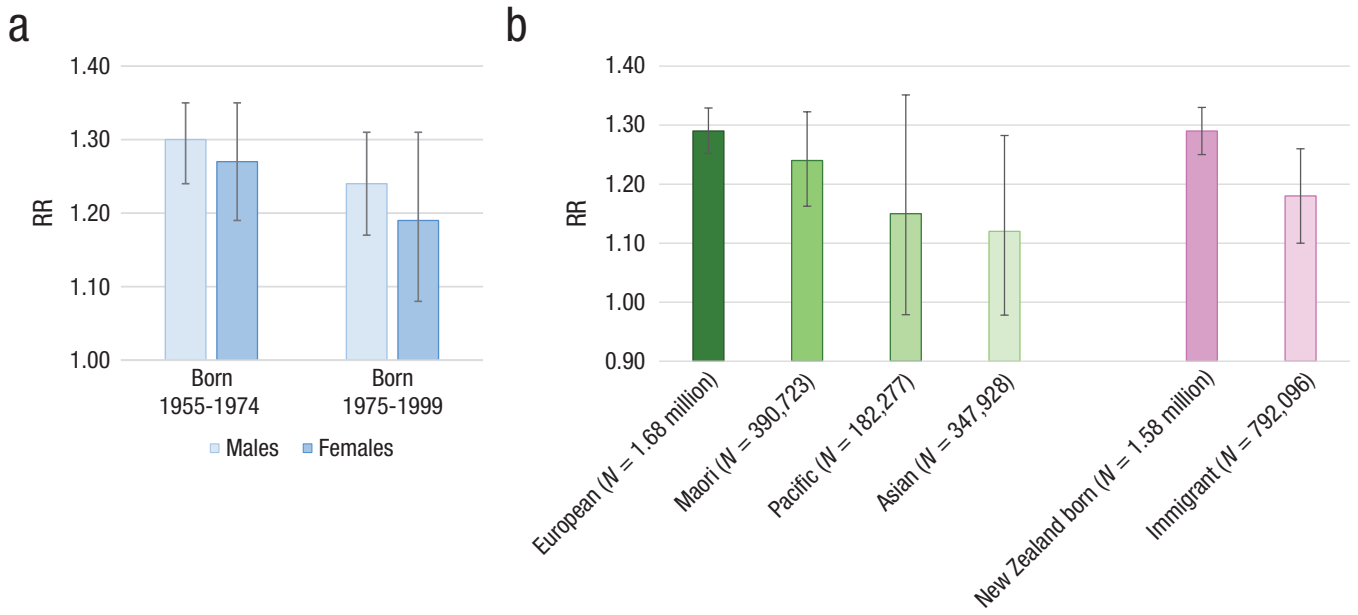

Fig. 2. Association of cumulative neighborhood disadvantage with despair-related deaths in the New Zealand study population. (a) Risk of despair-related death (risk ratio) per quintile increase in cumulative neighborhood disadvantage by sex and age cohort. (b) Risk of despair-related death (risk ratio) per quintile increase in cumulative neighborhood disadvantage by ethnicity. Ethnic categories are not exclusive. Individuals could belong to one or more of these ethnic groups, in line with the Statistical Standard for reporting ethnicity in New Zealand (Stats NZ, 2017b).

Zealand, who were eligible based on residence in the province and who participated in the first assessment at age 3. The cohort represents the full range of socioeconomic status in the general population of New Zealand's South Island (Poulton et al., 2015). On adult health, the cohort matches the New Zealand National Health and Nutrition Survey on key indicators (e.g., body mass index, smoking, physical activity, visits to a physician) and the New Zealand census of citizens of the same age on educational attainment (Richmond-Rakerd et al., 2020). Assessments were carried out at birth and ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, and 38, and the most recent data collection was completed in April 2019, at age 45 years. Study participants are primarily of New Zealand European ethnicity; 8.6% reported Māori ethnicity at age 45.

Cumulative neighborhood-disadvantage-exposure measure: the NZ-IDI. Residential neighborhood disadvantage was again assessed via the NZDep, described above. As previously reported (Reuben et al., 2024), neighborhood-disadvantage scores were available for study waves at ages 26, 32, 38, and 45 years (1998–2019). A cumulative adult neighborhood-disadvantage score was generated via confirmatory factor analysis (CFA), producing a single unitary factor from the four study waves via maximum likelihood estimation with robust standard errors in MPlus (Muthén & Muthén, 1998–2012; Version 7.11), with factor loadings set to 1 for each age to equalize disadvantage contributions across time (χ^2 = 95.607, p < .001, comparative fit index [CFI] = .834, Tucker-Lewis Index [TLI] = .815, root mean square error of approximation [RMSEA] = .096, standardized root mean squared residual [SRMR] = .092). This modeling approach was adopted to create a final composite score that would allow each study wave to contribute equally while maintaining the maximum analytic sample. A simple mean composite score taking the average of disadvantage scores across assessment waves while requiring study members to have present data for at least 50% of the waves correlated with the CFA-derived score r = .99 (p < .001) and fully reproduced the study results, albeit with a smaller analytic sample. Because it is common for New Zealand adults to spend portions of time living abroad, typically in Australia, NZDep data were supplemented by matched neighborhood-disadvantage scores for individuals living in Australia for at least 9 months in a given assessment year using the Australian Index of Relative Socioeconomic Advantage and Disadvantage, an area-based measure of socioeconomic disadvantage derived from 25 census variables (Australian Bureau of Statistics, 2018). For more information on the neighborhood indices and data-linkage process, see eAppendix 1 in the Supplemental Material.

Midlife syndrome of despair. We assessed 12 previously published (Brennan et al., 2023) indicators of

despair-related maladies at age 45 in four domains: suicidality, substance misuse, sleep problems, and musculoskeletal pain (eTable 2 in the Supplemental Material). Indicators of each domain were derived from at least three modalities, including self-report (e.g., sleep quality), informant-report (e.g., perceived misuse of alcohol and drugs), and national-register data (e.g., pain medication use). As previously reported (Brennan et al., 2023), CFA was used to investigate the structure of these midlife despair-related maladies. CFA indicated that a higher-order factor model, characterized by a general-despair superfactor and four subfactors (i.e., suicidality, substance misuse, sleep problems, and musculoskeletal pain) fit the data closely (eFig. 1 in the Supplemental Material; CFI = .96, TLI = .95, RMSEA = .04, SRMR = .07). Loadings for the suicidality, substance-misuse, sleep-problems, and pain subfactors on the general midlife-despair factor were all significant and positive, ranging from moderate (0.32 for pain) to strong (0.96 for suicidality). Factor scores for each of these five factors were then extracted for each participant (z-scored with $M = 0$, $SD = 1$ for interpretability), and higher scores indicate greater severity of despair-related conditions. Despair-syndrome scores were previously reported to have high construct validity in the cohort, correlating with low life satisfaction, loneliness, hopelessness, perceived stress, pessimism about aging, financial fears, depression symptoms, expectations of job loss because of physical disability, and low-status physically demanding jobs (Brennan et al., 2023).

Statistical analyses. We conducted a series of ordinary least squares (OLS) regression analyses using cumulative neighborhood disadvantage across adulthood as the predictor variable and the midlife-despair-syndrome scores as the outcome variables. First, baseline models predicted the general despair factor scores derived from CFA and constituent subfactors (suicidality, sleep problems, substance misuse, and pain) adjusting only for sex. Subsequent adjusted models attempted to rule out confounding by including individual midlife socioeconomic status and neighborhood urbanicity separately. Socioeconomic status at age 45 years was measured according to the occupation-based New Zealand Socioeconomic Index 2006 (eAppendix 2 in the Supplemental Material). Urbanicity was measured via the New Zealand government's urban-rural indicator for small areas (Stats New Zealand, 2004), which provides up to six urbanicity designations based on the area's total usual resident population (e.g., rural settlements = 200–999 residents, major urban areas = 100,000+ residents).

Second, because participants could move or neighborhoods can gentrify or decline, we tested the potential influence of different trajectories of changing neighborhood characteristics. We used Mplus to estimate longitudinal latent growth-curve models of neighborhood disadvantage using neighborhood residence at ages 26, 32, 38, and 45. Individual intercept (starting point) and linear slope (rate of change over time) were extracted for each study member and treated as predictors of midlife despair in OLS regressions.

Third, we tested whether selection effects could explain the association between neighborhoods and despair. We reran the primary analyses including a series of prespecified developmental risk factors (childhood antecedents) that could potentially account for the association of neighborhoods with despair, including low childhood socioeconomic status; a family history of mental illness; poor childhood physical, mental, and cognitive health; and low educational attainment by adulthood (all described in eAppendix 2 in the Supplemental Material).

Fourth, we tested whether adult difficulties that may be more common in disadvantaged neighborhoods could account for the associations of neighborhoods with despair. We reran the primary analyses including a series of prespecified adult difficulties: poor physical health; high levels of perceived stress, social isolation, and low social support; and indicators of economic hardship (unemployment and receiving government support; all described in eAppendix 2 in the Supplemental Material).

Reported results were checked for reproducibility by an independent data analyst, who recreated the code by working from the manuscript and applied it to a fresh copy of the data set. The threshold for statistical significance was two-tailed p value < .05. All reported analyses were conducted using Stata (Version 17.0), IBM SPSS (Version 28.0), and MPlus (Muthén & Muthén, 1998–2017; Version 8.7). This report follows STROBE reporting guidelines (von Elm et al., 2007).

Results

Are neighborhood gradients in deaths of despair preceded by a midlife syndrome of despair? The Dunedin Study sample included the 938 (49.5% female) study members who attended the age-45 assessment wave (94.1% of the original birth-cohort members alive at age 45; for Wave 45 attrition analysis, see eAppendix 3 in the Supplemental Material). Data on cumulative adult neighborhood disadvantage (ages 26–45) were available for 907 study members, who represented 96.7% of individuals who attended the age-45 assessment wave.

Although all study members were born in the city of Dunedin, only 38.4% of the analytic sample were still living in Dunedin by age 45; 21.2% had moved to another large or midsized city in New Zealand, 21.9%

Table 1. Association of Cumulative Neighborhood Disadvantage With the Midlife Syndrome of Despair and Syndrome Components in the Dunedin Cohort After Adjusting for Sex, Individual-Level Social Class, and Urbanicity

Despair factor and subfactors	Model adjusting for sex only	Model adjusting for sex and individual-level social class	Model adjusting for sex, individual-level social class, and urbanicity
General despair syndrome	0.24*** [0.17, 0.31]	0.17*** [0.10, 0.24]	0.25* [0.18, 0.32]
Suicidality	0.25*** [0.18, 0.32]	0.18*** [0.11, 0.25]	0.25* [0.18, 0.32]
Substance misuse	0.20*** [0.13, 0.28]	0.14*** [0.06, 0.21]	0.20* [0.12, 0.27]
Sleep problems	0.20*** [0.13, 0.27]	0.14*** [0.07, 0.22]	0.21*** [0.14, 0.28]
Pain	0.17*** [0.09, 0.24]	0.13** [0.05, 0.20]	0.17*** [0.09, 0.24]

Note: Values presented are standardized effect sizes (β) and 95% confidence intervals.
*p < .05. **p < .01. ***p < .001.

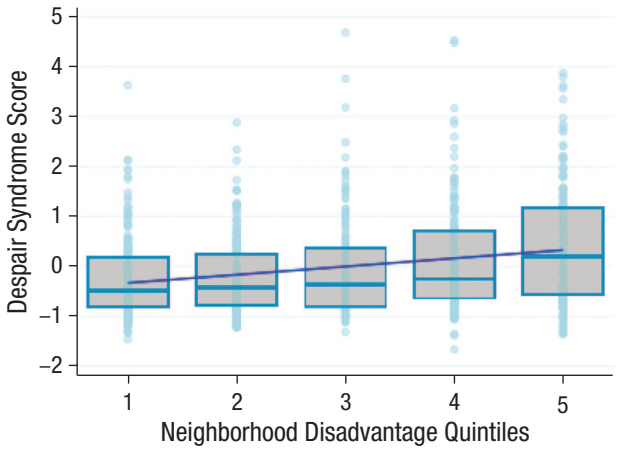

Fig. 3. Despair-syndrome scores in the Dunedin Study birth cohort were 0.64 *SD* higher among individuals residing in the most disadvantaged neighborhoods (Q5) compared with the least disadvantaged (Q1) across adulthood. (Despair-syndrome scores are scaled to $M = 0$, $SD = 1$.) Values presented are standardized effect sizes (β) and 95% confidence intervals.

were living elsewhere in New Zealand, and 18.5% had moved to Australia. (Study members who left the wider Australasia region, $N = 78$, were not included in the analysis.) Clustering of study members within neighborhoods was uncommon; at age 45, only 124 study members (14.6%) shared a neighborhood with another study member, most (71.0%) with just one other. Cumulative adult neighborhood disadvantage was normally distributed in the cohort (eFigure 2 in the Supplemental Material).

Study members who experienced more neighborhood disadvantage across adulthood (ages 26–45) had a more severe syndrome of despair-related maladies by age 45 (β = 0.24, 95% CI = [0.17, 0.31], p < .001; Table 1 and eTable 3 in the Supplemental Material). Despair-syndrome scores were 0.64 *SD* higher among participants residing in the most disadvantaged neighborhoods compared with participants from the least (Fig. 3). Individual components of despair were also higher among study members living in disadvantaged neighborhoods across adulthood (Table 1); these adults experienced higher rates of suicidality, sleep problems, substance misuse, and pain (βs = 0.17–0.25, p < .001). Associations held with modest attenuation after adjustment for individual-level socioeconomic status. There was no attenuation after adjustment for urbanicity; therefore, remaining models were adjusted for sex and socioeconomic status only.

Do trajectories of neighborhood disadvantage predict despair? In addition to testing whether cumulative neighborhood disadvantage was associated with a more severe syndrome of despair-related maladies by midlife, using growth-curve models, we tested whether study members' trajectories of neighborhood residence across adulthood (e.g., upward or downward neighborhood quality) were associated with midlife despair. In these models with both neighborhood intercept and slope entered simultaneously (slope and intercept were correlated $r = .21$, 95% CI = [.15, .27], p < .001), adults who lived in more disadvantaged neighborhoods at age 26 years experienced a more severe syndrome of despair-related maladies by age 45 years (β = 0.17, 95% CI = [0.10, 0.25], p < .001) regardless of their subsequent neighborhood trajectory. On average, cohort members tended to see improvement in neighborhood conditions over time. However, after controlling for where they lived at age 26 years, adults who experienced little or no improvement in neighborhood conditions from age 26 to 45 years demonstrated a more severe syndrome of despair-related maladies overall by midlife (β = 0.15, 95% CI = [0.08, 0.22], p < .001). These results indicated that both neighborhood starting point and multidecade change were uniquely predictive of midlife despair.

Model	β (95% CI)
Original sex- and individual SES-adjusted association	.17 (.11, .24)
Additionally adjusted for developmental risk factors	
Adjusted for family psychiatric history	.16 (.09, .23)
Adjusted for low family SES	.18 (.11, .25)
Adjusted for low childhood IQ	.17 (.11, .24)
Adjusted for poor childhood physical health	.18 (.10, .25)
Adjusted for adolescent psychopathology	.15 (.08, .21)
Adjusted for low educational attainment	.17 (.10, .24)
Adjusted for all developmental risks	.14 (.07, .21)
Additionally adjusted for adult difficulties	
Adjusted for poor physical health	.17 (.10, .24)
Adjusted for high perceived stress	.15 (.08, .21)
Adjusted for social isolation	.15 (.08, .22)
Adjusted for low social support	.15 (.09, .22)
Adjusted for unemployment	.16 (.09, .23)
Adjusted for receiving government support	.12 (.06, .19)
Adjusted for all adult difficulties	.11 (.04, .17)

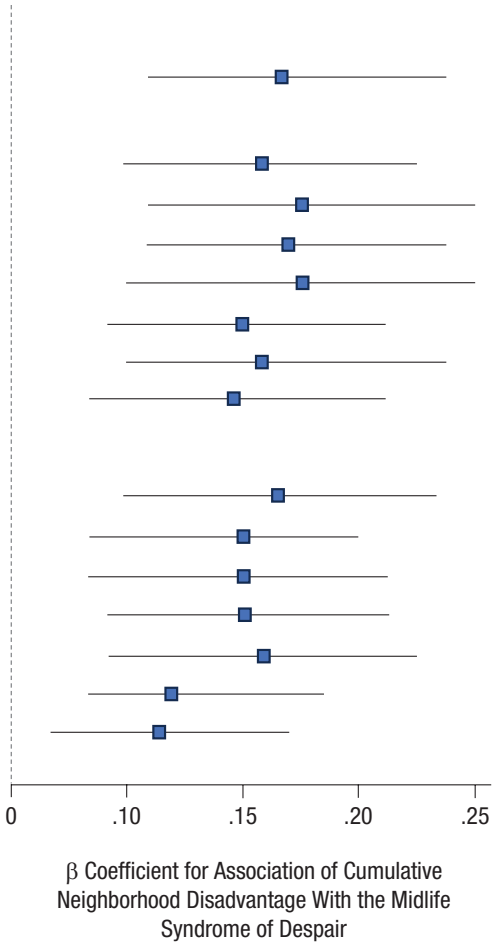

Fig. 4. The association of neighborhood disadvantage with midlife despair in the Dunedin cohort was not significantly altered by adjustment for preexisting developmental risk factors or adult physical, social, or financial difficulties. Values presented are standardized effect sizes (β) and 95% confidence intervals.

Evaluating potential selection effects. The next set of tests sought to evaluate whether study members in disadvantaged neighborhoods had elevated risk for despair because of preexisting individual characteristics that may have selected them into disadvantaged neighborhoods (e.g., led them to choose to live there, have fewer options regarding what neighborhoods they could live in). We reran the primary study models including additional adjustment, separately and altogether, for a wide range of potential childhood/developmental antecedents that could be related to both the quality of adult neighborhoods and risk of adult despair (Fig. 4 and eTable 4 in the Supplemental Material), such as poor childhood mental, physical, and cognitive health and low educational attainment by adulthood. Adjusting for these characteristics did not significantly alter the pattern of results when tested individually or in aggregate (fully adjusted $\beta = 0.14$, 95% CI = [0.07, 0.21], $p < .001$), suggesting that neighborhood-despair gradients cannot be fully explained by the selection of more vulnerable individuals into disadvantaged neighborhoods.

Evaluating potential mediating adult difficulties. Because disadvantaged neighborhoods have, by definition, a variety of disadvantageous characteristics, spanning physical, social, and economic inequities, in our final tests, we sought to determine whether physical, social, and financial difficulties that individuals may experience in adulthood could account for neighborhood-despair associations. We reran the primary study models including additional adjustment, separately and altogether, for a wide range of potential adult experiences that could mediate neighborhood-despair associations, such as poor physical health, low social support, and financial hardship. Adjusting for these difficulties did not significantly alter the pattern of results when tested individually (Fig. 4 and eTable 4 in the Supplemental Material) or in aggregate (fully adjusted $\beta = 0.11$, 95%

CI = [0.04, 0.17], $p < .01$), suggesting that living in disadvantaged neighborhoods across adulthood is associated with increased risk for a syndrome of despair by midlife regardless of one's own specific physical, social, or financial health.

Discussion

This multidecade nationwide analysis of neighborhood socioeconomic disadvantage and deaths of despair produced five findings. First, deaths of despair were found to follow neighborhood socioeconomic gradients in the full New Zealand population. Over 2 decades of observation, the odds of a despair-related death were nearly 60% greater for individuals living in the most disadvantaged neighborhoods across adulthood compared with the least even after taking into account individual sociodemographic characteristics, such as ethnicity, immigration, education, and income. This finding was true for suicides, drug overdoses, and alcohol-related deaths, and the largest effect sizes identified were for drug overdoses. This replicates past cross-sectional reports of geographic gradients in suicide and alcohol-related deaths in several high-income countries, including the United States, United Kingdom, and Denmark (Camacho et al., 2024; Jakobsen & Lund, 2022; Shiels et al., 2020), but is, to our knowledge, the first nationwide deaths-of-despair analysis to follow individuals across adulthood. Observed modest differences in despair risk by sex, age band, ethnicity, and immigration status suggest that neighborhood-despair associations may be slightly greater among men, older populations, individuals of European descent, and individuals born in New Zealand.

Second, neighborhood gradients in deaths of despair were found to be preceded, in a population-representative New Zealand birth cohort, by the geographic aggregation of a syndrome of despair-related maladies, including suicidality, substance misuse, sleep problems, and chronic pain. Cohort members who had spent more time living in disadvantaged neighborhoods across adulthood experienced a more severe syndrome of despair by age 45 years regardless of their own social-class position or their neighborhoods' level of urbanicity.

Third, longitudinal latent growth-curve modeling indicated that cohort members who entered adulthood residing in disadvantaged neighborhoods (at age 26) and/or saw little improvement in neighborhood quality over the subsequent 20 years were more likely to experience a more severe syndrome of despair-related maladies by midlife. Indeed, both neighborhood starting point and lack of improvement over time were significant, unique predictors of despair.

Fourth, inclusion of a wide range of preexisting individual characteristics that could have resulted in individuals at risk for despair migrating into disadvantaged neighborhoods over time (including a family history of mental illness; low family socioeconomic status; poor childhood cognitive, physical, and mental health; and low educational attainment by adulthood) did not significantly alter results, indicating that the neighborhood-despair association is unlikely to be due solely to the selection of at-risk individuals into disadvantaged neighborhoods.

Fifth, accounting for a wide range of contemporaneous physical, social, and financial difficulties that individuals may experience in adulthood (including poor physical health and high levels of perceived stress, high social isolation and low social support, and indicators of economic hardship) did not significantly alter results, indicating that the neighborhood-despair association cannot be attributed solely to a specific set of physical, social, and economic difficulties.

What can explain this pattern of findings? The despair syndrome evaluated here has been shown to reflect a pervasive lack of hope about one's own future that can be statistically detected when the many despair-related maladies are considered simultaneously (Brennan et al., 2023) and in other contexts, when diverse behavioral, cognitive, and emotional indicators of despair are modeled as giving rise to a latent despair factor that is itself an antecedent to premature mortality (Gutin et al., 2023). Consistent with the hypothesis that the despair syndrome reflects deep hopelessness, in past investigations of the syndrome in the Dunedin Study (Brennan et al., 2023), study members with greater despair scores were also more pessimistic about growing older, less likely to believe that they could continue physically to work their current jobs, less likely to believe they would live to age 75, and more likely to report feeling lonely, less socially supported, and more stressed (Brennan et al., 2023). The current study indicates that this underlying sense of despair is, at least in part, geographically patterned such that where people live contributes to despair over and above a vast array of childhood risk factors and adult difficulties. This could emerge from a real or perceived lack of opportunity—for jobs, education, or social enrichment—or from a community-level sense of alienation from more advantaged society. Some limited qualitative research supports this view; in-depth interviews of individuals who live and work in disadvantaged neighborhoods in the UK identified an underlying and pervasive "fatalism" that was not apparent in more socioeconomically "mixed areas" (R. Atkinson & Kintrea, 2004). Conversely, despair could also reflect a psychological or physiological response to life in some neighborhoods being harder than others because

disadvantaged neighborhoods tend to have less reliable transportation, more crime, fewer street trees, more air pollutants, and numerous vacant or derelict properties (Nutsford et al., 2013; Reuben et al., 2021)—disparities as prevalent in New Zealand as in other countries despite New Zealand's social-safety-net programs (e.g., Fleming et al., 2016; Pearce & Kingham, 2008; Richardson et al., 2010; Rose et al., 2009; Witten et al., 2012). Previous studies have reported neighborhood socioeconomic gradients in stress response (e.g., cortisol levels; Dulin-Keita et al., 2012) and epigenetic regulation (DNA methylation) of genes involved in inflammation (Reuben et al., 2020; Smith et al., 2017). Recent research using epigenetic markers of biological aging suggests that indeed, some individuals living in disadvantaged neighborhoods age or physically "weather" at faster rates than their peers (Lawrence et al., 2020), and efforts to improve neighborhood conditions, such as greening initiatives, can improve community mental health even when residents are unaware of the intervention (Pearson et al., 2013; South et al., 2018). Among other hypotheses, future research could test the extent to which changing neighborhood conditions (or general neighborhood socioeconomic rank) over time may result in greater or lower rates of despair-related maladies and deaths.

Collectively, the current results hold implications for research, clinical care, and public policy. First, results support the hypothesis that there is a geographic patterning to maladies of despair that, specifically, follows area-level socioeconomic gradients. Thus, if researchers wish to better understand, treat, and prevent diseases of despair, they should not ignore the wider context in which a person lives (i.e., their spatially constrained physical, social, and economic environment). Research on risk, protective, and treatment factors would benefit from including area-level-disadvantage information on study participants based on residential addresses, as would health-care providers seeking to better index patient prospective risk for future disease and ill health.

Second, interventions targeting despair epidemics or individual components of despair (e.g., substance misuse, suicidality) may benefit from considering neighborhood-based catchment programs (i.e., targeting resources to individuals living in specific areas) or neighborhood-based interventions (e.g., expanding access to transportation or recreation opportunities, decreasing alcohol availability; Hetrick et al., 2024). Critically, these need not exclude individual-level intervention (e.g., support groups, medication, psychotherapy) and could be tested as complementary or adjunctive to existing health-care approaches to despair-related maladies.

This study has limitations. First, it is observational and cannot establish causation. Second, it was conducted in only one country and should be replicated in other samples in other settings. Third, neighborhood disadvantage was assessed only across adulthood, leaving open the possibility that neighborhood-despair associations may take different forms across the life course.

Conclusion

Individuals residing in more disadvantaged neighborhoods across adulthood are at greater risk for experiencing a death of despair, including suicides, drug overdoses, and alcohol-related deaths, and before death, exhibit a more severe syndrome of midlife despair-related maladies, spanning suicidality, substance misuse, sleep problems, and chronic musculoskeletal pain. These patterns emerge irrespective of individual sociodemographic characteristics, childhood risk factors, or adult physical, social, and financial difficulties. Neighborhoods should be considered as potential intervention targets in research, policy, and clinical care targeting deaths of despair.

Transparency

Action Editor: Tamika C. Zapolski
Editor: Jennifer L. Tackett
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Declaration of Conflicting Interests

The authors declared that there were no conflicts of interest with respect to the authorship or the publication of this article.

Funding

This research was supported by National Institute on Aging (NIA) Grants R01AG032282 and R01AG069939 and UK Medical Research Council Grant MR/X021149/1. Additional support was provided by NIA P30 AG028716 and NIA P30 AG034424. The Dunedin Multidisciplinary Health and Development Research Unit was supported by the New Zealand Health Research Council (Project Grants 15-265 and 16-604), Brain Research New Zealand, and the New Zealand Ministry of Business, Innovation, and Employment. A. Reuben was supported by the U.S. National Institute of Environmental Health Sciences Grant F32ES34238 and a Duke/University of North Carolina Alzheimer's Disease Research Center (NIA Award No. P30 AG072958) Research Education Component scholarship. G. Brennan was supported by the Duke Aging Center Postdoctoral Research Training Grant (NIA T32 AG000029).

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Acknowledgments

The Dunedin Multidisciplinary Health and Development Research Unit at the University of Otago is within the Ngāi Tahu tribal area, who we acknowledge as first peoples, tangata whenua (translation: people of this land). We thank the Dunedin Study members, their parents, unit research staff, study founder Phil Silva, and previous study director, emeritus distinguished professor, the late Richie Poulton, for his leadership during the study's research transition from young adulthood to aging (2000–2023). We thank Statistics New Zealand and their staff for access to the Integrated Data Infrastructure data and review of output data. We thank the Public Policy Institute at the University of Auckland for access to their Statistics New Zealand data lab. The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Supplemental Material

Additional supporting information can be found at http://journals.sagepub.com/doi/suppl10.1177/21677026261425570.

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