Special Article

The Relationship of Mental and Behavioral Disorders to All-Cause Mortality in a 27-Year Follow-up of 4 Epidemiologic Catchment Area Samples

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Subjects from the Epidemiologic Catchment Area Program, interviewed during 1979–1983, were linked to data in the National Death Index through 2007 to estimate the association of mental and behavioral disorders with death. There were more than 25 years of follow-up for 15,440 individuals, with 6,924 deaths amounting to 307,881 person-years of observation. Data were analyzed by using age as the time scale and parametric approaches to quantify the years of life lost due to disorders. Alcohol, drug use, and antisocial personality disorders were associated with increased risk of death, but there was no strong association with mood and anxiety disorders. Results of high- and low-quality matches with the National Death Index were similar. The 3 behavioral disorders were associated with 5–15 years of life lost, estimated along the life course via the generalized gamma model. Regression tree analyses showed that risk of death was associated with alcohol use disorders in nonblacks and with drug disorders in blacks. Phobia interacted with alcohol use disorders in nonblack women, and obsessive-compulsive disorder interacted with drug use disorders in black men. Both of these anxiety disorders were associated with lower risk of death early in life and higher risk of death later in life.

anxiety disorders; generalized gamma distribution; mental disorder; mood disorders; mortality; personality disorders; proportional hazards model; substance-related disorders

The risk of death associated with mental disorders has been studied for more than a century (1, 2), mostly for severe disorders in institutionalized populations (3–7). The relationship to death is part of the basic descriptive epidemiologic information about mental and behavioral disorders, aiding clinicians and patients who desire information about natural history, informing estimates of disease burden, yielding potential insights into etiology, and prioritizing efforts at prevention. These relationships are less well-documented for common anxiety and mood disorders or disorders involving the use of alcohol or illegal drugs, because only a minority of individuals with these disorders receives treatment in residential settings (8, 9), where most of the research on mortality risk has been conducted. The enhanced specificity of criteria for diagnosis in the *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition (DSM-III) of the American Psychiatric Association, as well as improvements in survey technology, facilitated a shift in methodology to samples drawn probabilistically from household-residing populations by using interviews that generated diagnoses similar to those used in psychiatric practice and consistent with the DSM-III, in the National Institute of Mental Health's Epidemiologic Catchment Area (ECA) program (10, 11). Sampling and recruitment for the ECA surveys, conducted in 1979–1983, were combined with follow-up through 2007 to provide more than 300,000 person-years of observation.

In studies conducted so far, the common mental and behavioral disorders are associated with increased risk of death. A recent review of death linked to major depressive disorder

(12) included 14 prospective, population-based studies in which the median relative risk was 1.7. A study published after that review followed 78,282 women for 6 years and found a relative risk of 1.7 for depression (in women without diabetes) (13). There have been 7 studies of alcohol use disorders, with a median relative risk of 1.8. There have been no prior population-based studies of mortality risk and drug use disorders (DSM-III drug abuse and/or drug dependence) outside the ECA program. The research for other specific disorders includes 4 studies of panic disorder (3 were analyses of ECA data), 1 study of obsessive-compulsive disorder (from the ECA program), and no studies of social or simple phobic disorders. This knowledge gap promoted our collaboration to estimate the reduction of years of life associated with 11 categories of specific common mental and behavioral disorders by linking ECA data to the National Death Index (NDI).

MATERIALS AND METHODS

Sample

The methods of the ECA program have been described (14). This analysis combines 4 ECA sites (New Haven, Connecticut; Baltimore, Maryland; St. Louis, Missouri; and Durham, North Carolina), with a total sample size of 15,440 subjects drawn from the household-residing stratum of the population. There were 6,924 observed deaths during the follow-up period. A fifth site, in Los Angeles, California, was not included because the data permitting linkage to the NDI had been discarded. Sample weights are available that adjust the results to the population of the United States according to age, race, and sex in the 1980 US Census (15), but these weights are not used in this analysis because we have no information about vital status except for those actually interviewed.

Measures

Assessment of mental disorders was conducted by using the National Institute of Mental Health Diagnostic Interview Schedule (16, 17), which generates diagnoses according to the DSM-III (18). The Diagnostic Interview Schedule is designed for use by interviewers without clinical training, making population-based surveys such as the ECA feasible. We focused on lifetime prevalence of the 11 most common disorders. Demographic variables that may be important to the risk of death include age, race, and sex, as well as education, marital status, and a measure of socioeconomic position based on occupational prestige (19, 20).

Ascertaining vital status

The NDI provided linkage of individuals to vital statistics data from the 50 states. The following identifiers (where available) were linked to the NDI: last name, first name, sex, race, date of birth, social security number, father's surname, and last state of residence. The NDI provided up to 50 potential matches of deaths to each submitted person. Other sources of information about vital status included the Social Security Death Index and information obtained during the process of recruiting subjects for follow-up surveys.

From these sources we estimate that 6,924 of the 15,440 subjects who participated in baseline interviews were deceased by the end of 2007 (Table 1). Because there are many situations in which the matching is less than perfect, an ordinal scale ranking the quality of information about vital status from these various sources was created, allowing us to study the sensitivity of the results to the quality of the match (Table 1). For 1,771 subjects whose deaths were recorded in searches prior to this current project (21, 22), the scale could not be applied. The scale was applied to the remaining 5,153 subjects presumed to be dead (Table 1).

Analysis

The analyses reported below used the Cox proportional hazards procedure to quantify the relative hazard of each mental disorder adjusted for 6 sociodemographic characteristics, as well as for the presence of 1 or more additional disorders (i.e., comorbidities). To quantify reductions in absolute years of life due to mental disorders, we used the generalized gamma (GG) distribution (23). The GG method fits a curve to the survival distribution and estimates 3 parameters, β, σ, and κ, corresponding to location (e.g., median), scale (e.g., ratio of third to first quartiles), and shape (e.g., form of the hazard), respectively. The pth percentile of the GG $t(p; \beta, \sigma, \kappa)$ can be expressed in terms of the 3 parameters by the equation $t(p; \beta, \sigma, \kappa) = e^{\beta}[t(p; 0, 1, \kappa)]^{\sigma}$, which determines the percentiles of the distribution (i.e., the pth percentile of the standard ($\beta = 0$ and $\sigma = 1$) GG with shape κ elevated to the power σ and multiplied by the antilog of β yields the pth percentile of GG(β, σ, κ)). Once the shape is fixed by a value for κ, the ratio of 2 percentiles (e.g., third to first quartiles) determines the value of the scale parameter σ, and the median determines the value of the location parameter β. The lognormal distribution corresponds to the case of $\kappa = 0$ and, in this case, the location parameter β corresponds to the logarithm of the median. It often occurs that results from proportional hazards models agree closely with those of Weibull regression, which is the case of a GG for $\kappa = 1$ (23). The analyses based on the GG distribution do not require the assumption of proportionality for the hazards and have the advantage of describing the nature of the hazard function, as well as measures of the extension or contraction of the survival times due to a beneficial or harmful exposure (23). Software to fit GG models is available (e.g., streg in Stata software (StataCorp LP, College Station, Texas), liferег in SAS software (SAS Institute, Inc., Cary, North Carolina), R (R Foundation for Statistical Computing, Vienna, Austria), and S-PLUS (Insightful Corporation, Seattle, Washington) as offered at www.statepi.jhsph.edu/software/general gamma). The goodness of fit of the GG models was assessed by comparing the nonparametric Kaplan-Meier curves to the curves estimated by the GG models.

The time scale for survival analysis was age, allowing control over this strong predictor of death. Because there were only 23 deaths (out of 6,924) in subjects under 30 years of age, we used years after age 30 as the time scale for the analysis, and these early deaths were excluded from the analysis, yielding an analytical sample of 15,417 individuals. The 23 excluded individuals were 74% male and 48% white and included 11 individuals who had any mental or behavioral

Table 1. Frequency and Percent of Rating Criteria for Matching Subjects From 4 Epidemiologic Catchment Area Program[a] Sites With the National Death Index, 1979–1983 Through 2007

Match Quality	New Haven, Connecticut		Baltimore, Maryland		St. Louis. Missouri		Durham, North Carolina		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Definite[b]	0	0.0	940	73.6	80	8.2	0	0.0	1,020	19.8
Near definite[c]	0	0.0	52	4.1	51	5.3	0	0.0	104	2.0
Very probable[d]	1,112	79.0	175	13.7	560	57.6	1,087	72.7	2,933	56.9
Probable[e]	138	9.8	63	4.9	85	8.7	162	10.8	448	8.7
Likely[f]	32	2.3	19	1.5	36	3.7	68	4.6	155	3.0
Possible[g]	45	3.2	3	0.2	21	2.2	55	3.7	124	2.4
Potential[h]	81	5.8	26	2.0	139	14.3	123	8.2	369	7.2
Total rated	1,408	100.0	1,278	100.0	972	100.0	1,495	100.0	5,153	100.0
Not rated	1,409		362		0		0		1,771	
Percent of total		50.0		22.1		0.0		0.0		25.6
Total deceased	2,817		1,640		972		1,495		6,924	

[a] National Institute of Mental Health's Epidemiologic Catchment Area Program (Eaton, et al. *Public Health Rep.* 1981;96(4):319–324).

[b] All submitted identifying characteristics, including the social security number, matched perfectly.

[c] All characteristics matched except 1 digit in the social security number.

[d] The social security number was not submitted, but all submitted fields matched.

[e] All submitted fields matched except race ($n = 53$), or race was not submitted ($n = 6$), or 1 or more letters after the first letter of the first name did not match ($n = 156$), or 1 field in the date of birth did not match.

[f] In the absence of a good National Death Index match, there was a strong match to the Social Security Death Index, including name, date of birth, and, often, state of death.

[g] The day of birth and the social security number were not submitted, but all other fields matched, and the name was not 1 of the 1,000 most common.

[h] Presumed to be deceased, but the match is less convincing.

disorder. Those who were younger than 30 years at baseline contributed to the analysis with years after age 30 entered into the analysis at time 0 (i.e., no late entry). Subjects alive on December 31, 2007, or whose apparent ages were greater than 105 years were censored.

The multivariable analysis included use of the GG model to construct regression trees to maximize the ability to detect interactions (especially comorbidities of mental and behavioral disorders). For each race- and sex-specific stratum, binary recursive partitioning methodology (24, 25) was used for the presence/absence of each of the 11 behavioral and mental disorders. At a given node, for each of the disorders eligible to determine a split, we fit 2 GG models (1 for those with and 1 for those without a given disorder) and determined the significance of the difference in survival between the 2 groups by the likelihood ratio test. The variable that yielded the highest likelihood ratio statistic was then used as the splitter to define subsequent child nodes. This process continued until the likelihood ratio statistic was no longer significant at the α level of 0.05 under a χ^2 distribution with 3 degrees of freedom, and/or a child node contained fewer than 25 individuals. Once the final nodes for each race- and sex-specific stratum were determined, we compared the percentiles of the GG model describing the survival of the reference group (i.e., free of behavioral and mental disorders) with those of each of the other nodes corresponding to a particular profile of disorders. Statistical significance was determined by using 1,000 bootstrap replica-tions to estimate 95% confidence intervals for the differences in the first and last deciles and the median age or life expectancy for each node relative to the reference node.

In this study, it was assumed that all individuals died by age 105 years (i.e., even if not matched in the NDI). To consider these as interval-censored observations (26) and to develop the regression trees, we programmed the maximum likelihood methods by using PROC NLMIXED in SAS software (SAS Institute, Inc.). The studies reported here were approved by the Johns Hopkins Bloomberg School of Public Health's institutional review board.

RESULTS

Sixty percent of the baseline sample was women, and 27% was black. The nonblack subjects (73%) included a small proportion (3.5%) of Asians, Hispanics, and Native Americans. At the New Haven and Baltimore sites, more than one-third of the total sample (combined) was age 65 years or older because of oversampling in that age group. Table 2 provides the number of individuals, the total person-years, and the death rates per 1,000 person-years in 3 strata of age at enrollment (18–44, 45–64, and ≥65 years).

The death rates in the 3 age groups were radically different (3.6, 24.5, and 68.2 per 1,000 person-years for age groups 18–44, 45–64, and ≥65 years, respectively). This dictated the need to describe the death rates for the rest of the variables

Table 2.   Sociodemographic Characteristics, Person-years, and Mortality Rate Stratified by Age Group From 4 Epidemiologic Catchment Area Program[a] Sites, 1979–1983 Through 2007

	18–44 Years of Age			45–64 Years of Age			≥65 Years of Age		
	No.[b]	Person-years	Mortality Rate, %	No.[b]	Person-years	Mortality Rate, %	No.[b]	Person-years	Mortality Rate, %
Total	6,683	170,186	3.6	3,439	70,570	24.5	5,318	67,125	68.2
Site									
New Haven, Connecticut	1,655	43,692	2.7	803	17,436	22.1	2,576	31,602	73.2
Baltimore, Maryland	1,716	43,383	5.3	842	15,941	33.4	923	10,091	87.0
St. Louis, Missouri	1,705	43,580	3.5	721	15,222	22.2	578	7,413	64.8
Durham, North Carolina	1,607	39,531	2.9	1,073	21,971	21.4	1,241	18,019	50.6
Sex									
Male	2,794	70,587	4.2	1,355	26,007	31.3	1,988	22,398	79.0
Female	3,889	99,599	3.2	2,084	44,564	20.5	3,330	44,727	62.9
Race/ethnicity									
Nonblack	4,382	113,018	2.8	2,519	52,382	24.0	4,338	53,286	72.2
Black	2,294	56,986	5.3	915	18,069	26.1	957	13,608	52.6
Educational level									
Some/no elementary	40	988	7.1	162	2,929	33.8	539	6,312	69.2
Elementary graduate	50	1,184	10.1	216	3,864	32.1	512	6,185	69.4
Some high school	1,251	31,227	5.6	1,185	23,029	29.9	2,276	28,588	69.5
High school graduate	2,549	64,827	3.6	1,087	23,154	21.9	1,023	13,378	66.2
Some college	1,452	37,171	3.3	379	8,316	19.2	467	6,226	64.7
College graduate	1,319	34,245	1.9	391	8,887	15.9	439	5,806	66.8
Marital status									
Married	3,159	80,981	3.1	2,021	42,653	22.7	2,155	28,480	65.2
Widowed	70	1,726	6.4	566	10,859	28.8	2,428	29,375	71.4
Divorced/separated	1,187	29,675	5.3	608	12,386	24.5	369	4,759	64.7
Never married	2,261	57,667	3.4	241	4,620	30.3	354	4,451	69.2
Occupational status percentile[c]									
0.0%–25.0%	1,233	31,127	4.3	852	16,367	29.0	1,456	19,018	63.0
25.1%–50.0%	2,406	60,964	4.1	1,189	24,463	24.7	1,666	20,896	70.5
50.1%–75.0%	1,454	37,187	3.2	709	14,956	22.4	1,017	12,423	72.6
75.1%–100.0%	1,140	29,439	2.2	474	10,423	19.9	577	7,532	67.3
Missing	450	11,469	4.1	215	4,361	24.1	602	7,256	68.8

[a] National Institute of Mental Health's Epidemiologic Catchment Area Program (Eaton, et al. *Public Health Rep.* 1981;96(4):319–324).
[b] Because of missing data, the figures in some categories do not sum to the total for each age category.
[c] According to the Nam-Powers occupational status index described in Nam C, et al. *Soc Forces.* 1968;47(2):158–170.

in Table 2, stratifying by age, as well as providing logic for using age as the time scale in the analysis. Death rates among women were consistently lower than those among men in each age group (Table 2). In contrast, young blacks (18–44 years of age) had twice the risk of dying compared with non-blacks (i.e., 5.3 and 2.8, respectively), but the directionality reversed among those older than 65 years, when blacks had three-fourths the rate of nonblacks (i.e., 52.6 and 72.2, respectively). This change in relative risk over the lifespan would be masked by an analysis assuming proportional hazards, contributing to the logic of the GG approach. Education had a strong protective effect among those less than 44 years of

age, which attenuated among those between 45 and 64 years of age and essentially vanished among those older than 65 years. Widowed, divorced, or separated individuals younger than 45 years had close to double the risk of dying compared with those who were married, but otherwise there was no strong association with marital status. Those in the lower quartile of occupational prestige had a higher risk of death in the young and middle age groups, but not among those over age 65 years.

Estimates of the lifetime prevalence of the mental disorders shown in Table 3 are consistent with early publications from the ECA program (27). Phobic disorder was the most common (15.2%), and alcohol use disorder was the second most common

Table 3. Lifetime Prevalence of 11 Mental Disorders at Baseline, Frequency of Death, Person-years, and Adjusted Proportional Hazards From 4 Epidemiologic Catchment Area Program[a] Sites, 1979–1983 Through 2007

Mental Disorder	Total		Deceased		Person-years	Adjusted Proportional HR[b]	95% CI
	No.	%	No.	%			
Panic disorder	205	1.3	49	23.9	4,742	1.01	0.76, 1.36
Any phobic disorder	2,348	15.2	912	38.8%	49,050	1.00	0.92, 1.08
Agoraphobia	969	6.3	390	40.3%	20,191	1.02	0.92, 1.14
Social phobia	324	2.1	105	32.4%	7,035	1.08	0.89, 1.32
Simple phobia	1,966	12.7	776	39.5%	40,810	1.02	0.94, 1.10
Obsessive-compulsive disorder	389	2.5	113	29.1%	8,548	0.78	0.63, 0.95
Major depressive disorder	731	4.7	164	22.4%	17,133	0.86	0.72, 1.03
Dysthymic disorder	465	3.0	162	34.8%	10,119	0.84	0.71, 1.00
Drug dependence/abuse	603	3.9	81	13.4%	15,100	1.44	1.13, 1.84
Alcohol dependence/abuse	1,590	10.3	642	40.4%	32,882	1.33	1.21, 1.47
Antisocial personality disorder	272	1.8	88	32.4%	6,037	2.03	1.61, 2.57
Cognitive impairment	380	2.5	269	70.8%	5,057	1.02	0.89, 1.16
Any of the above disorders	4,779	31.0	1,829	38.3%	99,351	1.09	1.03, 1.16

Abbreviations: CI, confidence interval; HR, hazard ratio.

[a] National Institute of Mental Health's Epidemiologic Catchment Area Program (Eaton, et al. *Public Health Rep.* 1981;96(4):319–324).

[b] Proportional hazards are adjusted for all variables in Table 2, as well as for comorbidity, indicated by a dichotomous variable taking the value of 0 for no other disorder and 1 for the presence of 1 or more additional disorders (data not shown). The model for any disorder was not adjusted for comorbidity. The time scale was years of age after 30. Data on diagnosis were missing for 579 individuals who were too ill or cognitively impaired to respond to questions or whose interviews were cut short for various reasons.

(10.3%). Nearly a third of the sample (31.0%) had at least 1 of the 11 specific disorders. Even the rarest specific disorder (panic, 1.3%) provided more than 4,700 person-years of risk.

The following 3 behavioral disorders were associated with a significantly higher risk of death: DSM-III drug use disorder (44% increased risk of death); alcohol use disorder (33% higher risk of death); and antisocial personality disorder (double the risk of death) (Table 3). Obsessive-compulsive disorder was associated with a 22% reduced risk of death. Risk of death was higher if the individual reported more than 1 disorder (not shown).

An analysis of the sensitivity of the results to the quality of the match was conducted by running the proportional hazards models again, eliminating observations in which the match was probable, likely, possible, and potential, changing the number of deaths from 6,924 to 5,828 (data not shown). Matches obtained in earlier submissions to the NDI were included in this analysis, assuming that the majority of these would be in the "very probable" category. The results were similar, not changing the significance levels of any of the mental and behavioral disorders and changing the proportional hazards only trivially (not shown).

The GG model is not constrained by the assumption of proportional hazards and is statistically more efficient, yielding significant differences at the 5% level in all but 3 of the 13 comparisons shown in Table 4. Only 3 disorders (panic disorder, major depressive disorder, and dysthymia) did not indicate differences at the level of $P < 0.05$. The median and 90th percentiles for persons meeting diagnostic criteria at baseline for panic, agoraphobic, simple phobic, obsessive-compulsive, major depressive, or dysthymic disorder were only slightly different than for persons without those disorders. As with the proportional hazards model, the 3 behavioral disorders (drugs, alcohol, and antisocial personality) were associated with the largest reduction in years of life. The 10th, 50th, and 90th percentiles were approximately 10 years earlier for those with antisocial personality disorder compared with those without this disorder and approximately 7 years earlier for those with alcohol or drug use disorder.

By starting with the full sample to develop the regression tree, we found that the most significant variable was sex (women living longer); within each category of sex, the most significant variable was race (prior to the 70th percentile, nonblacks living longer). Figure 1 depicts the Kaplan Meier and GG curves for the sex/race strata that defined the first 4 nodes of the regression tree. The fit of the GG model to the empirical survival data was good for all groups except black men, for whom there is a suggestion of bimodality with a small subset dying at a young age (~35 years). Nonblack women (curves in purple) had the best survival, and black men (curves in blue) had the worst, with the other 2 groups (nonblack men in red; black women in green) in the middle. The curves that cross in Figure 1 show that the assumption of proportional hazards was violated for both sex and race. In the GG model, the relative hazards of black to nonblack were substantially higher at younger ages with downward trends crossing the

Table 4.   Generalized Gamma Models of Mental and Behavioral Disorders Using Years of Age After 30 as the Time Scale, With Selected Percentiles From 4 Epidemiologic Catchment Area Program[a] Sites, 1979–1983 Through 2007

Mental Disorder	Total No.	No. of Deaths	β (Location)	σ (Scale)	κ (Shape)	Age at Death, years			P Value
						10th Percentile	50th Percentile	90th Percentile	
Panic disorder									
No	14,701	6,474	4.051	0.202	1.808	57.2	79.2	94.8	
Yes	205	49	4.089	0.192	2.259	54.3	79.0	95.6	0.39
Phobic disorder									
No	12,573	5,620	4.056	0.197	1.848	57.4	79.5	94.8	
Yes	2,346	910	4.046	0.214	1.803	55.9	78.6	95.0	0.03
Agoraphobia									
No	13,969	6,150	4.051	0.201	1.800	57.4	79.3	94.8	
Yes	968	389	4.084	0.196	2.198	54.4	78.9	95.5	0.05
Social phobia									
No	9,687	3,714	4.061	0.201	1.888	56.7	79.3	95.2	
Yes	324	105	4.018	0.261	2.007	48.9	74.2	94.1	<0.0001
Simple phobia									
No	12,966	5,761	4.057	0.197	1.851	57.4	79.5	94.9	
Yes	1,965	775	4.039	0.219	1.779	55.6	78.2	94.8	0.01
Obsessive-compulsive									
No	14,473	6,385	4.051	0.201	1.806	57.3	79.3	94.8	
Yes	388	112	4.138	0.169	2.586	55.2	80.9	97.3	0.03
Major depressive									
No	14,179	6,359	4.050	0.203	1.809	57.0	79.2	94.8	
Yes	731	164	4.081	0.177	1.996	58.7	80.8	95.3	0.07
Dysthymia									
No	14,443	6,361	4.050	0.202	1.809	57.1	79.2	94.7	
Yes	464	161	4.119	0.167	2.350	57.3	81.3	96.5	0.17
Drug dependence/ abuse									
No	14,253	6,427	4.058	0.196	1.843	57.6	79.6	94.9	
Yes	598	76	3.946	0.266	1.725	50.2	72.7	91.0	<0.0001
Alcohol dependence/ abuse									
No	13,274	5,864	4.064	0.192	1.830	58.3	80.2	95.2	
Yes	1,584	636	3.923	0.263	1.571	51.6	72.8	90.1	<0.0001
Antisocial personality									
No	14,544	6,398	4.057	0.197	1.831	57.6	79.6	94.9	
Yes	270	86	3.818	0.284	1.554	48.4	68.1	85.0	<0.0001
Cognitive impairment									
No	14,682	6,385	4.051	0.200	1.814	57.3	79.3	94.7	
Yes	379	268	4.037	0.281	2.933	40.0	67.5	92.5	<0.0001
None of the above	10,333	4,851	4.066	0.187	1.835	58.9	80.4	95.1	
Any of the above	4,768	1,818	4.020	0.229	1.776	54.2	77.0	94.0	<0.0001

[a] National Institute of Mental Health's Epidemiologic Catchment Area Program (Eaton, et al. *Public Health Rep.* 1981;96(4):319–324).

null value of 1 at 79.5 years of age among women and 83.5 years of age among men. Thus, as in Table 2, the association of black race with death was prominent at low percentiles, but the top 20%–30% of each racial group died at similar old ages. The association of sex with death was prominent toward middle-level percentiles (40%–80%).
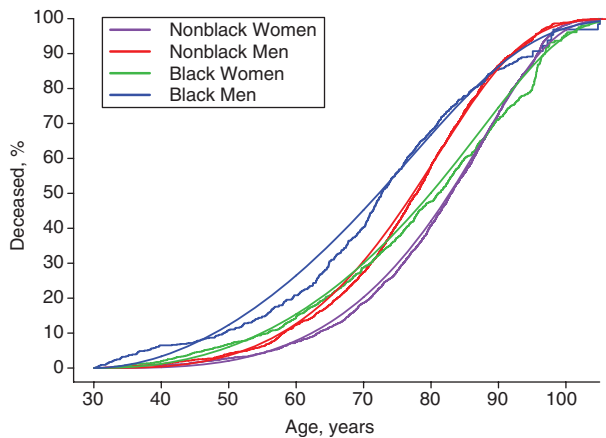
Figure 1. Survival curves for 4 sex/race strata in 4 sites of the Epidemiologic Catchment Area Study, 1979–1983 through 2007. Nonparametric Kaplan-Meier curves as step functions and smoothed curves for the generalized gamma (GG) distribution for cumulative proportion deceased in g groups according to nonblack/black race and female/male sex. The estimated parameters of GG models were: GG(4.10, 0.16, 1.86) for nonblack women, GG(3.99, 0.21, 1.53) for nonblack men, GG(4.11, 0.19, 2.23) for black women, and GG(3.97, 0.28, 1.87) for black men.

The regression tree identified 11 strata in final nodes with significantly distinct mortality trajectories (Table 5). Among nonblacks, alcohol use defined the first split of the regression trees for women and men. The second split among nonblack women was the protective effect of simple phobia, but only among alcohol users. In turn, the second split among nonblack men was the presence of antisocial personality, which elevated risk irrespective of alcohol use. Among blacks, drug use defined the first split of the regression trees for women and men. No other variable determined a second split among black women, but for black men, obsessive-compulsive disorder was protective for non–drug users.

Within each of the sex/race strata, the group with the lowest mortality risk served as the reference category (curves colored black in Figures 2A, 2C, 3A, and 3C). For nonblack women, the presence of an alcohol use disorder added risk, but simple phobia was protective for those with an alcohol use disorder (Figure 2A) until approximately age 70 years, at which point a history of simple phobia was associated with higher risk of death (dark purple curve; see also the 10th and 90th percentiles for simple phobia in Table 4). From Figure 2B, it can be seen that alcohol use in the absence of phobia (light purple curve) significantly reduced survival of the earliest 10% to die by 8 years (from age 63 years in the unexposed group), decreasing to 5 years for the median and 3.5 years for those dying in the latest 10%. In contrast, those with alcohol and simple phobia disorders (dark purple curve) were not different early, but the reduction in years of life for the top 10% was a dramatic and significant reduction of 14 years relative to age 96 years, when 90% of the unexposed were estimated to die.

For nonblack men, the presence of antisocial personality was so strongly associated with death that the distinction between those with and without alcohol disorders was trivial, yielding 3

important final nodes in the group of nonblack men (Figure 2C). Alcohol disorder was associated with a lower age at death by approximately 5 years, and this was slightly greater for the first 10% (6 years) relative to the top 10% (4 years), as depicted in the light red curve in Figure 2D. Among nonblack individuals, the associations of death with alcohol alone in both women and men were similar (compare the light purple curve in Figure 2B with the light red curve in Figure 2D). Antisocial personality disorder among nonblack men was associated with a lower age at death by approximately 12 years, and the effect was constant across the life course (dark red curve in Figure 2D).

Drug use disorder raised the risk of death for black women (Figure 3A) and shortened life by approximately 9 years, consistently and significantly over the course of life (Figure 3B). For black men, the presence of drug use disorder at baseline had the most important association with risk of death, lowering the age at death by approximately 9 years for the first 10%–30% and decreasing to 6 years for the top 10% (light blue curves Figure 3C and 3D). Among black men who did not have a drug disorder at baseline, obsessive-compulsive disorder was associated with more than 10 years' reduction in years of life for the 50th–90th percentiles (Figure 3D). This association had wide confidence limits because of the small number of subjects ($n = 28$, with 11 deaths) in this category (confidence interval not shown).

DISCUSSION

Alcohol use and antisocial personality disorders were strongly associated with death in nonblacks and with drug use disorder in blacks. The risk of death associated with mood, anxiety, and other psychiatric disorders was low, and there was evidence that obsessive-compulsive disorder was protective, consistent with a prior study of the protective effect of trait anxiety (28). The association of death with the 3 behavioral disorders is consistent with those reported in the existing literature on alcohol use disorders and adds weight to the literature on personality disorders (for which there are only 2 existing population-based studies (29, 30)) and drug use disorders (for which there are 2 prior ECA studies (22, 31)).

The combination of the GG model with regression tree analyses yielded new results on simple phobia and obsessive-compulsive disorder. Simple phobia might be associated with lower risk of death in nonblack women who have a history of alcohol use disorders because greater levels of anxiety might contribute to avoidance of injury and enhanced health-protective behaviors. Likewise, obsessive-compulsive disorder might be protective in black men who have no history of drug use disorders. However, it is not clear why both of these disorders are associated with added risk after the age of 55 or 60 years. This result might be caused by sampling variation and the limited number of subjects in these groups, or it could be caused by comorbid physical disorders that develop during this part of the life course.

The results on major depressive disorder are not consistent with those in the literature. The inconsistency is puzzling because major depressive disorder has been associated with fatal self-directed violence (32), onset of type 2 diabetes (33), heart attack (34), stroke (35), and dementia (36). It could be

Table 5. Characteristics of 11 Categories of Respondents With Significant Relationships to Risk of Death, Proportion Deceased, and Percentile for Age at Death From 4 Epidemiologic Catchment Area Program[a] Sites, 1979–1983 Through 2007

Sex and Mental or Behavioral Disorder by Race	No. of Deaths	Total No.	Age at Death, years		
			10th Percentile	50th Percentile	90th Percentile
Nonblack					
Women	2,950	6,308			
No alcohol use disorder[b]	2,891	6,090	62.8	83.0	96.1
Alcohol use disorder	59	218			
No simple phobia disorder	44	166	54.5	78.0	92.5
Simple phobia disorder	15	52	62.9[c]	76.1	82.4
Men	2,127	4,476			
No alcohol use disorder	1,772	3,534			
No antisocial personality disorder[b]	1,761	3,546	60.4	78.7	92.5
Alcohol use disorder	355	892			
No antisocial personality disorder	312	771	54.4	73.7	89.5
Antisocial personality disorder[d]	54	159	47.8	67.9	81.0
Black					
Women	841	2,646			
No drug use disorder[b]	825	2,553	55.4	80.2	97.0
Drug use disorder	16	93	48.0	71.3	87.3
Men	556	1,373			
No drug use disorder	533	1,296			
No obsessive compulsive disorder[b]	522	1,268	49.1	73.0	92.5
Obsessive compulsive disorder	11	28	54.1[c]	60.7[c]	79.3[c]
Drug use disorder	23	77	40.5	64.8	86.6

[a] National Institute of Mental Health's Epidemiologic Catchment Area Program (Eaton, et al. *Public Health Rep.* 1981;96(4):319–324).

[b] Reference category.

[c] Not significantly different from the race-by-sex reference category (see Figures 2 and 3 for confidence intervals).

[d] The group diagnosed with antisocial personality disorder contains individuals from both the alcohol use disorder group and the no alcohol use disorder group.

that earlier studies revealed an association because they did not adjust for the sociodemographic characteristics included in Table 2. However, an unadjusted model with these data (not shown) also estimated no increased risk of death associated with major depressive disorder. It could be that the influence of depressive disorder on death has been exercised earlier in the life history of individuals not included in the sample because they have died. However, an analysis that included 305 individuals who had never met criteria for major depressive disorder at baseline and who experienced an episode meeting criteria for the first time in their lives during the first year of follow-up showed little difference in results (odds ratio = 1.15, 95% confidence interval: 1.02, 1.30). The age span of the follow-up may explain the discrepancy. In the systematic review noted above (12), 6 of the 14 studies were of samples with a minimum age of 60 years or older (37–42); in another study, the minimum

age was 40 years, and the average age was 67 years (21); and in the recent analysis from the Nurses' Health Study, the minimum age was 54 years (13). Thus, depression in the elderly may take a different form (43) associated with physical decline. However, in an analysis of these data stratified by age at baseline, there was no increase in the risk of death associated with depressive disorder in those aged 65 years or older. It could be that the measure of depression in the ECA is not as sensitive as in earlier studies. To address this possibility, we conducted analyses that estimated the association of a diagnosis of depressive disorder with death at either the baseline wave *or* the 1-year follow-up wave, with no appreciable change in the pattern of results. It could be that the Diagnostic Interview Schedule taps a less severe form of depressive disorder than has been assessed in prior literature. To address this possibility, we created a measure of depressive disorder in which subjects reported that
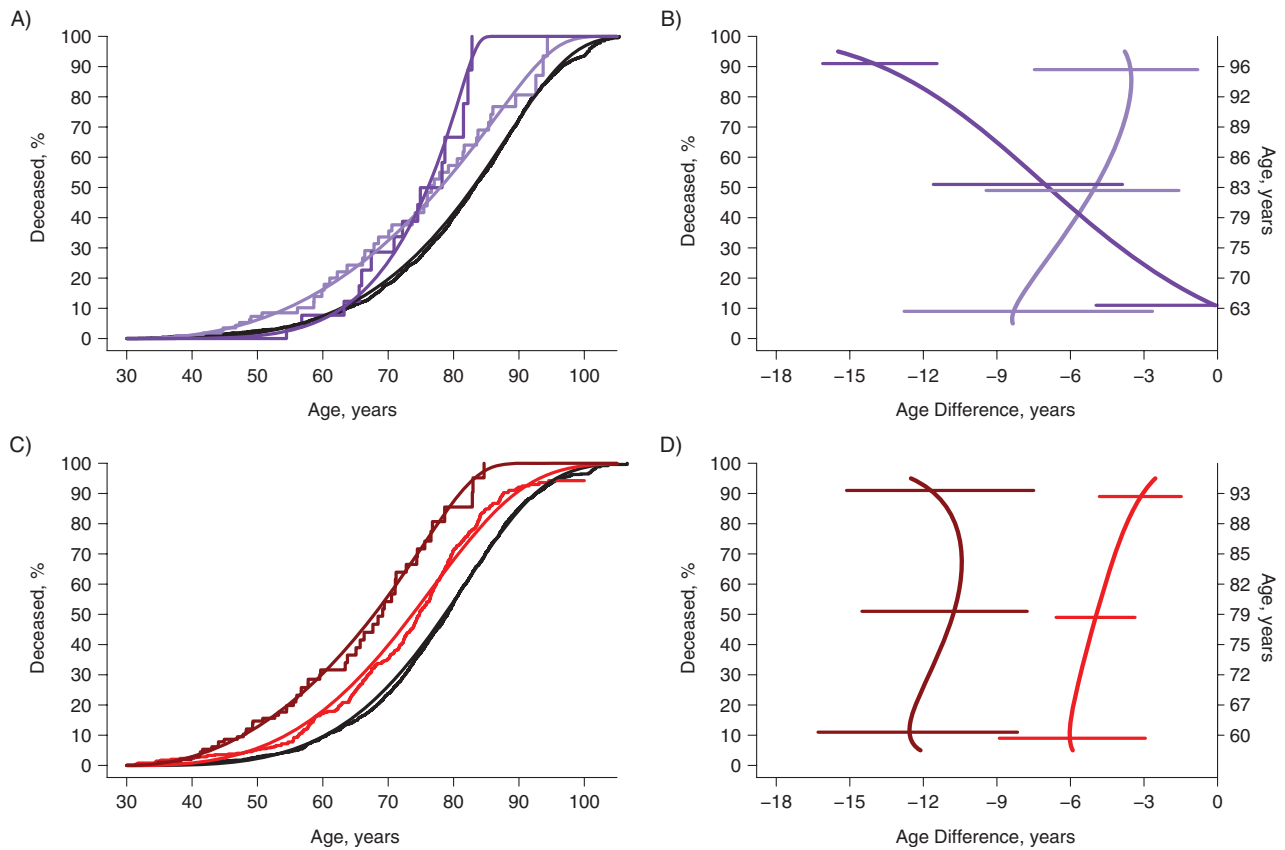
Figure 2. Survival curves and estimates of years of life lost due to alcohol, phobia, and antisocial personality disorders, among nonblack women and men in 4 sites of the Epidemiologic Catchment Area Study, 1979–1983 through 2007. Kaplan-Meier and generalized gamma survival curves for nonblack women and men, showing the estimated effects of alcohol use disorder and simple phobia and alcohol use disorder and antisocial personality disorder. B and D show the years of life lost compared with individuals in the general population who do not have a history of the disorders (age at death in those without disorders is displayed on right-hand axes) with 95% confidence intervals from bootstrapping procedures represented by horizontal bars. For women (A and B), black lines denote no alcohol use disorder (2,891 of 6,090), light purple lines denote alcohol use disorder and no simple phobia disorder (44 of 166), and dark purple lines denote alcohol use and simple phobia disorders (15 of 52). For men (C and D), black lines denote no antisocial personality and no alcohol use disorders (1,761 of 3,546), red lines denote alcohol use disorder and no antisocial personality disorder (312 of 771), and burgundy lines denote antisocial personality disorder (54 of 159).

they had told their doctors about the problem, with no appreciable change in results (not shown). It could be that the lifetime form of prevalence used in these analyses fails to include early episodes more distant in time from the interview, and that these forgotten episodes are more severe; or, perhaps the lifetime form includes early episodes that are mild and dilute the effect. But the pattern of results of analyses with the 1-year form of prevalence was no different than for lifetime prevalence (data not shown). It could be that the risk of death is more likely to appear in a study of the elderly in which the follow-up is not as long as in this study, because episodes more distant in time are less likely to be recalled by the elderly, and more recent episodes are of the form more highly associated with death (44, 45). Indeed, it could be that the somatic symptoms of chronic fatal diseases (e.g., problems with fatigue, sleep, appetite, movement, or concentration) overlap with those of depressive disorder, and that individuals who recognize themselves to be in physical decline are sad, anhedonic,

and/or thinking of death. Of the population-based studies reviewed (13, 39, 41, 42, 46–51), only the Stirling County Study (52) and the Nurses' Health Study (13) had follow-up periods longer than 10 years. When we analyzed these data by time since baseline assessment, we saw a slightly heightened risk for depression in the first 9 years of follow-up and a reduced risk in the next 15 years of follow-up (data not shown). Therefore, the most credible explanation for the entire sum of results is that depressive disorder itself is not strongly associated with high risk of death, but rather is concomitant with rapidly declining health and may even be protective in the long term. Future analyses of these data focused on specific causes of death may yield insight into this issue.

The strengths of this analysis include the large number of person-years of observation, the population-based sample, the sensitivity analyses that suggest that imprecise matching has not threatened the results, and the use of GG and regression tree models that generate enhanced precision, as well as informative
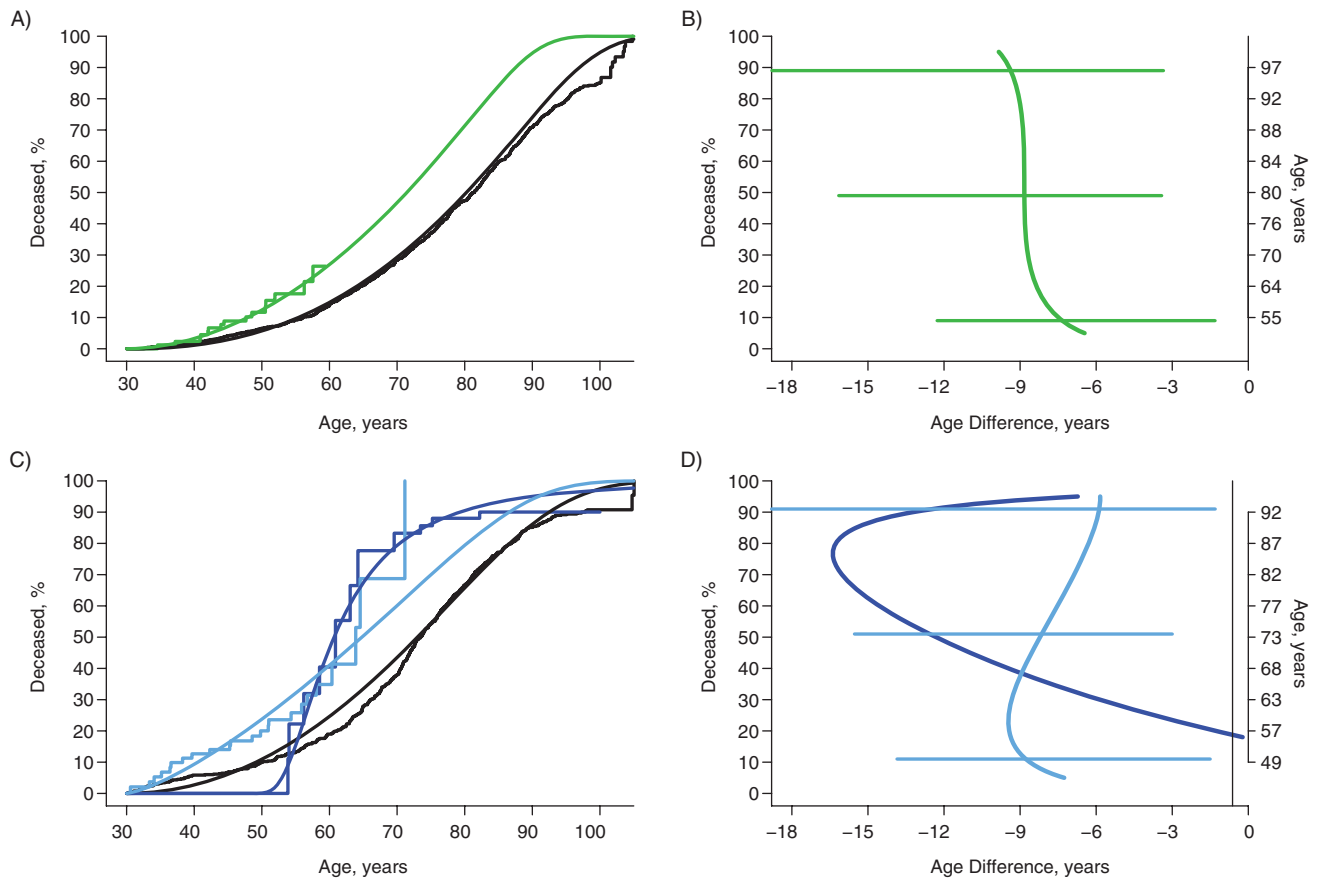
Figure 3. Survival curves and estimates of years of life lost due to drug use disorder and obsessive-compulsive disorder in black women and men in 4 sites of the Epidemiologic Catchment Area Study, 1979–1983 through 2007. Kaplan-Meier and generalized gamma survival curves for black women and men, showing the estimated effects of drug use disorder in black women and the combination of drug use disorder and obsessive-compulsive disorder in black men. B and D show the years of life lost compared with individuals in the general population who do not have a history of the disorders (age at death in those without disorders displayed on right-hand axes), with the 95% confidence intervals from bootstrapping procedures represented by horizontal bars. The confidence intervals for the 28 individuals with no drug use disorder or obsessive-compulsive disorder (D) were so large as to be uninformative and are not shown. For women (A and B), black lines denote no drug use disorder (825 of 2,553) and green lines denote drug use disorder (16 of 93). For men (C and D), black lines denote no obsessive-compulsive disorder and no drug use disorder (522 of 1,268), dark blue lines denote obsessive-compulsive disorder and no drug use disorder (11 of 28), and light blue lines denote drug use disorder (23 of 77).

analysis of comorbidity. The parametric approach based on the GG model provided excellent goodness of fit, did not restrict the analysis to proportional hazards, and facilitated quantification of reduction of life expectancies due to deleterious exposures at all percentiles of the distribution of ages at death for different groups (Figures 2B, 2D, 3B, and 3D). Weaknesses include the relatively small number of subjects in some of the groups defined by the regression tree procedure and the limitation to common mental and behavioral disorders, excluding important disorders with documented effects on mortality risk, such as schizophrenia and bipolar disorder. The regression tree analysis has the advantage of being flexible and directly incorporating effect modification (e.g., among nonblack individuals, alcohol is a primary risk factor for death, but among blacks, it is drug use); however, to arrive at the final tree, many comparisons are estimated. As a result, the nominal significance level may be higher than 5%, and it is important to describe the magnitude of the differences in years of life lost as indicated in the tables and figures herein, as well as the level of statistical significance.

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