Social Connections and Risk for Cancer: Prospective Evidence From the Alameda County Study

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The association between social connections and cancer incidence, mortality, and prognosis during 17 years of follow-up was examined in a population-based sample of 6,848 adults who lived in Alameda County, California, in 1965. Estimates of relative hazards were derived from Cox regression modeling, adjusting for age, smoking, physical health at baseline, alcohol consumption, and adjusted household income. Women who were socially isolated were at significantly elevated risk of dying of cancer of all sites and of smoking-related cancers. Social connections were not prospectively associated with cancer incidence or mortality among men, but men with few social connections showed significantly poorer cancer survival rates. These patterns of risk are consistent with the biology of different cancer outcomes. They also suggest a different role for social isolation in cancer among men and women.

The role of social connections in protecting against general disease morbidity and mortality has been of great interest in recent years, although the idea is far from new.[1] A number of community-based studies have demonstrated intriguing consistencies in the overall prospective association between limited social networks and all-cause mortality,[2-9] but there is conflicting evidence for the strength of association, the association within subgroups, and the association with disease incidence.

In 1979, Berkman and Syme[2] reported that a summary measure of social networks (including marital status, number of friends and relatives, church group membership, and membership in other groups) was significantly associated with subsequent all-cause mortality in a 9-year follow-up study of a population-based cohort of adults living in Alameda County, California. Somewhat consistent findings come from two other community-based samples—Tecumseh, Michigan, and Evans County, Georgia. The Tecumseh study[3] reported a protective social network relationship for men but not for women over 9 to 12 years of follow-up. Published data from the Evans County study indicate a similar significantly protective effect for 13-year survivorship among white men, but this association was reduced to nonsignificance when the authors controlled for potential confounders (age, smoking, relative weight, physical activity, and a variety of cardiovascular risk factors). The Evans County study[4] found only suggestive associations between social networks and all-cause mortality among black men and white and black women.

A community-based study of Japanese-American men living in Hawaii was designed to examine the influence of a variety of social network attributes on coronary heart disease incidence and prevalence.[5] In this special population, social networks tended to be significantly associated with coronary heart disease prevalence but not with coronary heart disease incidence between 1971 and 1979. Joseph[7] also found social connections to be negatively asso-

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ciated with coronary heart disease prevalence among men participating in the California portion of this study. Measures of family constellation (termed social networks) were not associated with the incidence of cancer among the men in the Hawaiian cohort.[8] These few community-based studies suggest some general consistency in the protective effects of social connections, but the inconsistencies in the studies highlight gaps in our understanding of the features of such connections that may contribute most to those effects. Also, little is known about the association between social connections and specific diseases such as cancer. In one of the few works addressing this association for cancer, an interesting study of Roswell Park cancer patients, Funch and Marshall[10] suggest an effect of social connections on survival, independent of age and stage of disease and also independent of stress. Suggestive evidence for an association between social networks and cancer mortality was reported by Berkman and Breslow.[11] Our study was designed to explore the prospective association between social connections and cancer incidence, mortality, and survival in the Alameda County sample during 17 years of follow-up, controlling for other risk factors for cancer.

METHODS

Study Population

The study sample consisted of 6,848 adults who lived in Alameda County, California, in 1965 and were not known to have a previous diagnosis of cancer. Aside from the exclusion for cancer, the sample was drawn from the same group as that for Berkman and Syme's study.[2] In 1965, the Human Population Laboratory of the California Department of Health Services selected a stratified sample, developed to be representative of the county population at the time, of all households in Alameda County. Identified residents were invited to participate in a survey designed to assess the prevalence of a variety of health behaviors, as well as the status of physical, social, and psychological health. The 6,928 respondents who participated in the survey were thought to be representative of the total selected sample. Details of the sampling strategy and sample characteristics are available elsewhere.[11]

Cancer Ascertainment

Cancer incidence for this study was ascertained using record linkage to the population-based tumor registry serving this geographic area. Incidence was defined as the first diagnosis of any invasive neoplasm (excluding basal and squamous cell carcinomas of the skin). The Cancer Prevention Section of the California Department of Health Services has maintained a population-based tumor registry in Alameda County continuously since 1960—first as the Alameda County Cancer Registry (1960–1968), expanded to the five Bay Area counties that make up the San Francisco-Oakland Metropolitan Statistical Area (MSA) for the Third National Cancer Survey (1969–1971), and subsequently as part of the National Cancer Institute's Surveillance, Epidemiology, and End Results Program. Thus, incidence was based on the study respondents who remained in one of the five counties included in the MSA during the period of follow-up.

Cancer mortality for the study was assessed by means of automated record linkage to statewide death files, supplemented by notification from other states to California, and active tracing. During the first 9 years of follow-up, vital status was determined for 96.1% of the cohort.[11] Cancer mortality was defined as any death with cancer coded as the underlying cause. This analysis utilized both cancer incidence and mortality follow-up information through 1982.

Review of the cancer mortality data (ascertained statewide) showed that 6.6% of the observed cancer deaths occurred among respondents living outside of the cancer incidence surveillance area. This may indicate a minor underascertainment of incidence for the cohort. In order to assess any potential bias that might result from this, we examined the association between social connections and residential mobility.

Respondents known to have moved outside of Alameda County or the adjacent communities in Contra Costa County (approximately 24%) between 1965 and a follow-up enumeration in 1974 did not significantly differ with respect to baseline social isolation status from those who had not moved outside of the two counties (9.7% of this group of movers were isolated, compared with 10.9% of those who did not move or moved locally). Those who had moved to San Francisco, San Mateo, or Marin counties were still within the cancer surveillance area. There is no reason to believe that those who had moved farther away would differ greatly enough to bias the observed risk relationship for cancer incidence.

Study Variables

A number of measures of social connections were used in our analysis, including the social network index reported by Berkman and Syme[2] in their 9-year mortality analysis of the Alameda data. The social network index is a composite measure of four sources of social contact: marital status (married *v* not married), sociability (frequency and number of contacts with friends and relatives, coded on a scale of 1 to 5, with high values associated with

many contacts and low values with few), church group membership (yes *v* no), and membership in other organizations (any *v* none). The social network index score takes on values from 0 to 12 but, in previously published work, has been reported by four levels (from I to IV), ranging from those with the fewest connections to those with the most. Preliminary analyses comparing the continuous score with the four-level version did not indicate any important inconsistencies between these two versions of the social network index. For consistency with earlier work, our analysis used the same categorical version as the four-level index.

In addition to the social network index, we also considered several other measures of social connections, including a measure of social isolation that has been used in a number of other Human Population Laboratory analyses.[12,13] This dichotomous variable is based on the same items in the questionnaire as the sociability measure (three questions relating to the number of friends and relatives to whom the respondent feels close, and how many of these the respondent reports seeing at least once a month). We coded a respondent who reported fewer than three contacts on two out of three of these questions as isolated; all others were coded as not isolated.

In the Berkman and Syme[2] index, the category of church membership reflects respondents' reports of belonging to "a church group." In addition, information is available on church attendance in response to the question: "About how often do you go to church services?" In our study, "regular" attendance was coded for respondents who went to church at least once a month.

Finally, a measure of "feeling isolated" was constructed from four psychological items on the questionnaire. One point was assigned for a response of *true* to each of the following statements:

1. It's hard for me to feel close to others.
2. Often when I'm with a group of people, I feel left out—even if they are friends of mine.
3. I tend to keep people at a distance.
4. I often feel lonely or remote from other people.

Respondents who agreed with two or more items (roughly 20% of the sample) were classified as "feeling isolated."

In addition, the data set included a number of other risk factors for cancer: age at entry, smoking (calculated as pack-years of exposure), physical health at baseline (categorically coded for the presence of disabilities, chronic conditions, and symptoms), adjusted household income (total income adjusted for the number of household members), and alcohol consumption (number of drinks per month based on report of usual amount and frequency of consumption of beer, wine, and liquor). The multivariate analyses presented here were adjusted for these covariables. All variables were as reported in the 1965 questionnaire.

Analysis

Cancer incidence and mortality rates were calculated for the time period 1966–1982, using the "density" method described by Kleinbaum, Kupper, and Morgenstern for cohort studies.[14] This method uses person-years of observation as the denominator for the rates. Rates were age-adjusted, using the direct method, to the 1970 adult (age 20+) population of the United States. Multivariate analyses used the Cox proportional hazards regression model[15] to allow for deaths from competing causes. The regression parameter of interest in these analyses was the (log) relative hazard associated with low levels of social connection, a measure that can be interpreted as the "instantaneous" relative risk of cancer death or incidence associated with few connections. For ease of interpretation, all relative logs are presented so that values greater than one indicate increased risk associated with lower levels of social connections.

RESULTS

During 17 years of follow-up, 476 newly diagnosed cases of cancer were recorded among members of the study group, and a total of 257 study respondents died with cancer coded as the underlying cause of death. Because the number of cancer events was insufficient to analyze risks for specific sites of cancer, we report associations for all sites of cancer combined and for the site groups representing common etiologies that occur most frequently (ie, smoking-related sites of cancer among men and hormone-related cancers among women). The distributions of incidence cases and of cancer deaths by sex and major etiologically homogeneous anatomical site groups are summarized in Table 1. The cancer experience of the study cohort was comparable to that among adults residing in the Bay Area during the same time period.

Average annual age-adjusted cancer incidence and mortality rates were computed by level of the social network index (Table 2). For male mortality and for female mortality and incidence, the highest rates were in those who were the least connected. Consistent gradients were evident only for women.

A similar pattern of results was seen when we adjusted for other risk factors for cancer (Table 3). Estimates of the relative hazards associated with the fewest social connections (as measured by lowest levels of the social net-

TABLE 1
Distribution of Cancers by Site Group, 1965–1982

Site group (ICD-O† codes)	Incidence‡		Mortality§	
	Men	Women	Men	Women
Total, all sites	215	261	123	134
Smoking-related sites	70	51	44	33
Lung (162)	38	27	31	19
Larynx (161)	2	1	0	0
Mouth (140–141, 143–145)	4	4	1	0
Esophagus (150)	2	3	3	3
Liver (155)	1	1	1	1
Pancreas (157)	5	8	4	5
Bladder (188)	12	5	2	3
Kidney (189)	6	2	2	2
Hormone-related sites		116		43
Breast (174)		71		30
Uterine corpus (182)		31		4
Ovary (183)		14		9
Other sites	145	94	79	58
Other digestive (151–159)	50	38	28	23
Hematopoietic & reticulo-endothelial (169)	13	9	16	10
Other genitourinary (179–180, 184–187)	47	17	12	7
Lymph nodes (196)	9	5	10	4
Other miscellaneous	23	18	12	6
Primary unknown (199)	3	7	1	8

†International Classification of Diseases for Oncology, World Health Organization, 1976.
‡Newly diagnosed invasive cancers occurring among respondents who continued to be residents of the San Francisco-Oakland Metropolitan Statistical Area.
§Deaths coded to cancer as underlying cause for all respondents for whom vital status was known.

work index) compared with the most connections were different at a statistically significant level only for cancer mortality among women: relative hazard (RH) = 2.2 for all sites combined, RH = 5.7 for smoking-related cancers. The data in Table 2 also show no evidence for an association between social networks and risk for cancer incidence or mortality among men, nor for cancer incidence among women.

Figures in Table 4 summarize the relative hazards associated with cancer incidence and mortality for each of the components of the social network index. These data suggest that the protective effect of social networks for women is not a function of marital status. In fact, it appears to be a function of social affiliations other than marital status, particularly contacts with friends and relatives. For men, we found no evidence that any of the components of the social network index were associated with subsequent cancer outcomes.

The data in Table 5 summarize the relative hazards associated with social variables not included in the social network index for incidence and mortality for all sites of cancer, for smoking-related sites, and for hormone-related sites. The most pronounced indicator of risk for women was social isolation, which appeared to be associated with both cancer incidence and mortality. Equally striking was the interesting suggestive association between feeling isolated and cancer mortality for women, which was accentuated for hormone-related cancers. None of these indicators of risk was associated with cancer outcomes among men, although men who attended church regular-

TABLE 2
Age-adjusted Rates of Cancer by Level of the Social Network Index, 1965–1982

Index level	Person-years	Incidence			Mortality		
		Cases	Rate	95% CI†	Cases	Rate	95% CI†
Women							
I (Least connected)	8,239	38	412.2	(273.4–551.0)	27	285.2	(170.3–400.1)
II	22,969	104	396.0	(318.7–473.4)	57	210.8	(154.3–266.5)
III	13,485	58	369.0	(272.9–465.1)	28	186.4	(116.6–256.2)
IV (Most connected)	16,629	61	293.0	(223.0–363.1)	22	109.8	(62.0–157.6)
Men							
I (Least connected)	4,431	14	359.0	(169.5–548.5)	13	327.1	(148.2–506.0)
II	15,491	52	332.0	(241.3–422.8)	32	201.6	(131.4–271.8)
III	15,211	68	451.2	(340.6–561.7)	35	233.8	(153.2–314.4)
IV (Most connected)	15,483	81	411.4	(318.0–504.8)	43	226.5	(155.5–297.5)

Note: Rates are per 100,000 person-years at risk; age-adjusted by the direct method to the 1970 US adult population.
†Confidence interval

TABLE 3
Relative Hazards for Cancer by Level of the Social Network Index

Social network index level	All sites		Smoking-related		Hormone-related	
	Incidence	Mortality	Incidence	Mortality	Incidence	Mortality
Women						
I (Least connected)	1.1	2.2*	2.5	5.7*	0.8	2.3
II	1.2	1.8*	2.0	2.9	1.1	1.5
III	1.1	1.5	2.4	2.5	0.8	1.0
IV (Most connected) reference level	1.0	1.0	1.0	1.0	1.0	1.0
Men†						
I (Least connected)	0.8	1.5	1.0	2.0		
II	0.8	0.9	0.8	0.7		
III	1.0	1.0	1.1	1.4		
IV (Most connected) reference level	1.0	1.0	1.0	1.0		

Note: Relative hazard compared to level IV (most connected) and adjusted for age, smoking (pack-years), physical health, household income, and alcohol consumption.
*$p < .05$.
†Hormone-related cancers in men were not covered in this study.

ly appeared to be at modestly, but not significantly, increased risk.

Data in Table 6 show, for men and women separately, the joint effects of *being isolated* (having few contacts with friends or relatives) and *feeling isolated.* Using those who reported neither being isolated nor feeling isolated as the comparison group, relative hazards were estimated for having many contacts but feeling isolated, having few

TABLE 4
Relative Hazards for Cancer by Component of the Social Network Index

Component	All sites		Smoking-related		Hormone-related	
	Incidence	Mortality	Incidence	Mortality	Incidence	Mortality
Women						
Marital status (0 = married, 1 = not)	0.8	1.0	0.8	0.9	0.7	1.1
Friend/relative contacts (1 = many, 5 = few)	1.1*	1.2*	1.0	1.2	1.1	1.3*
Church group member (0 = yes, 1 = no)	1.1	0.9	0.7	0.6	1.7*	1.9
Other group member (0 = many, 1 = few)	1.0	1.4	1.4	1.7	1.0	1.6
Men†						
Marital status (0 = married, 1 = not)	0.7	0.9	0.9	0.8		
Friend/relative contacts (1 = many, 5 = few)	1.0	1.0	1.0	1.0		
Church group member (0 = yes, 1 = no)	1.2	1.1	1.5	1.7		
Other group member (0 = many, 1 = few)	1.0	1.1	1.3	1.6		

Note: Adjusted for age, smoking (pack-years), physical health, household income, and alcohol consumption.
*$p < .05$.
†Hormone-related cancers in men were not covered in this study.

TABLE 5
Relative Hazards for Cancer by Social Variables Not in the Social Network Index

Social variable	All sites		Smoking-related		Hormone-related	
	Incidence	Mortality	Incidence	Mortality	Incidence	Mortality
Women						
Social isolation (0 = no, 1 = yes)	1.5**	1.7*	1.0	1.6	1.5	1.9
Feeling isolated (0 = no, 1 = yes)	1.3	1.7**	1.2	1.1	1.5*	3.5***
Church attendance (0 = regular, 1 = seldom)	1.0	1.0	1.1	1.4	1.2	1.0
Men†						
Social isolation (0 = no, 1 = yes)	1.0	0.9	0.8	0.3		
Feeling isolated (0 = no, 1 = yes)	0.9	0.7	0.7	1.0		
Church attendance (0 = regular, 1 = seldom)	1.3	1.3	1.7	1.5		

Note: Adjusted for age, smoking (pack-years), physical health, household income, and alcohol consumption.
*$p < .05$; **$p < .01$; ***$p < .005$.
†Hormone-related cancers in men were not covered in this study.

TABLE 6
Relative Hazards for Cancer by Social Isolation Status

Social isolation status	All sites		Smoking-related		Hormone-related	
	Incidence	Mortality	Incidence	Mortality	Incidence	Mortality
Women						
Many contacts/but feel isolated	1.2	1.4	1.2	1.1	1.6	2.4*
Few contacts/don't feel isolated	1.6*	1.4	1.0	2.0	1.7	0.7
Few contacts/and feel isolated	1.7*	2.5**	1.2	1.5	1.8	4.8**
Men†						
Many contacts/but feel isolated	0.7	0.7	0.7	1.2		
Few contacts/don't feel isolated	0.9	1.0	0.9	0.4		
Few contacts/and feel isolated	1.3	0.9	0.6	0.3		

Note: Adjusted for age, smoking (pack-years), physical health, household income, and alcohol consumption.
*$p < .05$; **$p < .005$.
†Hormone-related cancers in men were not covered in this study.

contacts but not feeling isolated, and for having few contacts and also feeling isolated. There were no notable associations for men, either for all sites of cancer combined or for smoking-related sites of cancer (see Table 6). The elevated risk of cancer mortality from all sites for women who felt isolated (shown in Table 5) appeared to be a function of the dual risk of both feeling and being isolated. In addition, the observed increased risk for hormone-related cancer mortality associated with feeling isolated (in Table 5) appeared to be independent of the measure of social contacts. This pattern of results was unaffected by adjustment for additional risk factors or for further adjustment for parity (not shown). The same set of risk models was executed using lung cancer and breast cancer in women as the defined event outcomes. Because of the smaller number of events, the estimators of risk were less stable but in the same direction as those for the larger site groupings to which these sites contributed. The only substantial difference was that the lung cancer analyses showed an enhancement of the point estimates associated with the social network index over that associated with women's smoking-related cancers.

In order to examine the impact of social connections on survival from cancer, we examined the survival time of respondents diagnosed with a first cancer primary, adjusting for age at diagnosis and stage of disease at diagnosis (localized *v* regional or remote). These relative hazards are presented in Table 7. As would be expected, the single most powerful predictor of survival in these analyses was stage of disease. Although the number of observed cases was small, there was a strongly elevated independent risk of poorer prognosis among men with few social connections (as measured by the social network index). For women, however, none of the social variables independently predicted prognosis.

DISCUSSION

These data present evidence for a role for social connections in incidence, mortality, and prognosis for cancer. Ours is the only study to date that has addressed these risk relationships prospectively and in this kind of detail. Both consistencies and inconsistencies between these results and the limited evidence from previous research in this area, however, underscore the complexities of this risk relationship. In particular, they contribute to three of the many unanswered questions that have been raised in the literature regarding the direct effects of social connections and health.

TABLE 7
Relative Hazards for Cancer Survival Associated with Social Variables

Social variables	Men	Women
Number at risk †	154	185
Cancer decedents	70	79
Social network index level		
I (Least connected)	3.43*	1.54
II	0.92	1.23
III	1.12	0.87
IV (Most connected) reference level	1.00	1.00
Few contacts (isolated) (0 = no, 1 = yes)	0.84	1.06
Feel isolated (0 = no, 1 = yes)	0.94	1.26
Marital status (0 = married, 1 = not married)	1.25	1.46
Friend/relative contacts (1 = many, 5 = few)	1.12	1.06
Church group membership (0 = yes, 1 = no)	1.22	0.91
Other group memberships (0 = many, 1 = few)	0.95	1.30
Church attendance (0 = regular, 1 = seldom)	1.12	1.00

Note: Relative hazards associated with time from diagnosis to death from cancer, adjusting for age at diagnosis and stage of disease.
*$p < .01$
†Respondents with missing information on stage of disease are excluded.

The first of these questions concerns the issue of general versus specific disease susceptibility. Nearly all of the existing studies of social connections have focused on all-cause mortality as the outcome of interest. In a 9-year follow-up of the original Alameda County study, Berkman and Breslow[10] presented suggestive evidence that respondents with limited social connections experienced elevated rates of mortality from ischemic heart disease, cerebrovascular and other circulatory diseases, cancer, and other underlying causes of death. The same clear gradient of risk was not reported in the all-cause analysis,[2] nor were these data adjusted for other risk factors of interest. In a separate analysis of this sample, however, Kaplan[16] found social isolation to be significantly related to mortality from ischemic heart disease, even after adjustment for other risk factors. The Tecumseh study investigators,[3] although limited by a small number of deaths, explored the consistency in their findings for deaths specifically from coronary heart disease and cancer. They reported that the protective effects of social connections were consistent, although presumably not statistically significant, for these specific causes (with the exception of coronary heart disease mortality in women, which did have a significant association).

The current analysis, designed to examine the influence of social connections on cancer incidence, cancer mortality, and cancer patient survival, suggests that, even for cancer outcomes alone, the results are variable. This may be, in part, because cancer represents a different set of diseases in men than in women. The most common cancers in men are smoking-related (especially cancer of the lung), and the most common cancers in women are hormone-related (especially cancer of the breast). The fact that these are etiologically very different may help to explain why social connections predict so differently for men and for women.

A second common debate regarding social connections and health involves hypothesized pathways—in particular, whether the advantages associated with greater social connections are a consequence of higher levels of instrumental support and/or emotional support. Although our data set had no direct measures for these dimensions of support, the issue can be considered, in part, by examining the intimacy of social ties. That more "intimate" ties, other than spouse (eg, friends and relatives), seem to account for more of the overall network-disease association in the present analyses than do ties through church or organizational participation suggests that emotional sup-

port may play a pivotal role in this risk relationship. This is underscored by the accentuated risks for cancer among women in this analysis who "feel isolated" in addition to having few social contacts.

Similarly, the lack of more intimate ties was found to be a better predictor of coronary heart disease prevalence in the Hawaiian Japanese-American study[4] and of cancer incidence in the California Japanese-American study[7] than were other social measures. The importance of emotional support was even more directly addressed in Dunkel-Schetter's[17] study of adjustment among cancer patients (primarily female patients with cancers of the breast and colon). In that study, emotional support was perceived to be the most important of several types of available support. In addition, other researchers have suggested that lack of social support may be associated with poorer prognosis in cancer patients.[18,19]

Contrary evidence for the importance of intimate ties was reported by the Tecumseh investigators,[3] who found social group participation to be a more important predictor for men than was affiliation with friends and relatives. They explained this difference as a possible reflection of the differences in social integration in a small community as opposed to a large urban community such as Alameda County. It should be noted, however, that the questions about friends and relatives asked in the Tecumseh and Alameda County studies were fundamentally different. In the Tecumseh study, respondents were asked about the frequency of "visiting" friends and relatives, whereas in the Alameda County study, respondents were asked to identify "close" friends and relatives—"People that you feel at ease with, can talk to about private matters, and can call on for help."

Another apparent inconsistency for the effect of "intimate" ties was the lack of a protective effect for marriage in our analysis. In fact, when adjusting only for age, women who were married in 1965 gave evidence of significantly higher risks for cancer incidence than did women never married, separated, divorced, or widowed in 1965 (RH = 1.5, $p < .05$). Although the evidence for a "protective" association with marriage has been demonstrated to be equivocal for a cross-section of incident cancers,[20] this apparent disparity may also reflect a methodological artifact of the current study. It is possible that marital status may be more likely to change over nearly 20 years than are patterns of relationships with friends and relatives. Furthermore, given that cancer is more prevalent in the aged, elderly respondents who were married in 1965 are those at highest risk to become widowed in the follow-up interval. In the same way, given the well-known differences in the life expectancy of men and women, this particular change in marital status is most likely to affect female respondents. Review of the marital status of respondents at the time of cancer diagnosis tends to confirm such a pattern of changes in marital status. Unfortunately, comparable information is not available for respondents who had no subsequent cancer diagnoses.

A third issue commonly debated in the social epidemiology literature is whether social connections influence mortality by way of pathways related to etiology or survival. Our study allowed us to examine the risk relationship to a variety of cancer outcomes. The strongest effects appeared to be on cancer mortality (but not necessarily incidence) in women and on cancer survival (but neither incidence nor overall cancer mortality) in men. The crux of the risk relationship for women appeared to be emotion-focused and most strongly apparent in the hormone-related cancers, which are also the most common cancers in women. The risk factor of major interest for women appeared to be social isolation, not only *being* isolated, but also of *feeling* isolated. The fact that this risk relationship worked so strongly for incidence and mortality, but not for cancer survival, suggests that social isolation may be associated with cancer risk for women. Given the effect of emotions on hormonal regulation,[21] it is not unlikely that isolation may have a direct promotional effect on the development of this set of cancers.

There is no really biologically equivalent group of cancers for men, so it is not possible to make a direct comparison of this risk relationship for men. The major etiologically homogeneous set of cancers for men are related to smoking. Our analysis suggests that social connections make no independent contribution to risk for these sites. Smoking has been estimated to have as much as a 90% attributable risk for cancer of the lung. It is unlikely that, in the presence of such a powerfully direct risk factor for cancer, social connections could make an additional etiologic contribution. That the prognosis (for all sites of cancer combined) is significantly worse in men with few social connections, even after adjustment for age at diagnosis and stage of disease, and that women with the fewest connections (as measured by the social network index) are at significantly increased risk of dying of, but not being diagnosed with, smoking-related cancers suggests that social connections may well play a direct role in survival differences for these sites.

Our study was designed to explore prospectively the direct association of social connections with a well-defined set of disease outcomes for which appropriate risk factors could be controlled. The results suggest that social isolation (variously measured) may be an independent risk factor for both cancer etiology and prognosis. This

strongly supports Cassel's[22] hypothesis regarding the additional health risks of the isolated or "marginal" members of society. The complex nature of this relationship, however, underscores the importance of considering it in the context of the biology of the disease.

INDEX TERMS

cancer incidence, cancer mortality, social isolation, social networks

NOTE

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