

Inter-Spousal Mortality Effects Caregiver Burden Across the Spectrum of Disabling Disease

Nicholas A. Christakis and Paul D. Allison

The health of two people connected by a social tie may be interdependent. The impact of the *death* of one spouse on the risk of death of the other, known as the widow/er effect, is a classic example (Parkes and Fitzgerald 1969; Lillard and Waite 1995; Martikainen and Valkonen 1996a; and Schaefer, Quesenberry, and Soora 1995). The impact of *illness* in one spouse on the risk of ill health or death in the other spouse (the proband under study), is another example. This latter phenomenon, often termed caregiver burden, is typically studied as if it were unrelated to the widower effect (Clipp and George 1993; Dunkin and Anderson-Hanley 1998; Shaw et al. 1997; Schulz et al. 2003)—as if ill health in a spouse affects the morbidity, but not necessarily the mortality, of caregiving probands.

Indeed, most prior work on caregiver burden has focused on how spousal illness worsens the health of probands, but not on whether it increases their mortality, with the exception of one influential study that suggested that caregiving to dementia patients was a risk factor for death (Schulz and Beach 1999). Moreover, comparisons across different types of spousal diseases, in terms of how they may affect caregiver health, are lacking. Some studies have found that worse physical health in a spouse is

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linked to worse physical health in the proband, perhaps due to greater caregiving demand (Clipp and George 1993; Shaw et al. 1997; Pruchno and Resch 1989). Poor mental health in the spouse also appears to adversely influence the physical health of the caregiver (Zarit et al. 1986; Barusch and Spaid 1989; Pruchno and Resch 1989; Scholte op Reimer et al. 1998; Shaw et al. 1997). Indeed, it has been suggested that mental impairment in the patient may induce more caregiver burden than physical impairment. Very few studies, however, compare diseases in terms of the health consequences they impose on caregivers (Clipp and George 1993; Dura, Haywood-Niler, and Kiecolt-Glaser 1990).

Prior work on the widower and caregiver effects has suffered from a variety of further limitations that have complicated efforts to understand the effect on a proband's mortality risk of having a spouse fall ill or die. First, there is the challenge of separating the impact of spousal illness on proband death from the impact of spousal death on proband death; that is, we are interested in understanding how spousal illness itself, whether accompanied by subsequent spousal death or not, affects proband health.

Second, there is the problem of confounding. That is, if one spouse falls ill or dies, the next one may also fall ill or die, but not because the latter spouse is affected by caring for the first spouse. Rather, the second may fall ill because the two spouses share some traits that determined the health outcomes of both. Illness or death of one spouse could be associated with the death of the other because of (a) a common accident, (b) shared environmental exposures (such as environmental toxins, poor dietary practices, or poverty), or (c) selection because of assortative mating (e.g., the tendency of the unhealthy to marry the unhealthy). This problem, which is typically overlooked in studies of caregiver burden, requires special statistical methods and data to be addressed.

Third, prior work on the caregiver burden has typically focused on outcomes at a single point in time. But the effect of having a spouse fall ill might vary across time. The health consequences of being in the caregiving role might be demonstrably worse for probands at particular points in time after the occurrence of spousal illness.

Our work addresses the foregoing concerns, using data and methods that allow us to investigate caregiver mortality effects across the spectrum of disease and across time in the caregiving role. In addition, our study uses a reliable measure of caregiver burden (i.e., the risk of death) and a large, nationally representative sample with very long follow-up. We hypothesize that being in a caregiving role will: increase the mortality risk of probands; that this effect will be distinct from the effect of being widowed; that this effect will vary in patterned ways across different spousal illnesses; and that, moreover, this effect will depend upon the amount of time the proband is in the caregiving role.

15.1 Methods

15.1.1 Data

To assemble a suitably large, population-based inception cohort of elderly couples with sufficient temporal and diagnostic detail and with sufficient follow-up, we extracted and linked raw Medicare claims at an individual level (Lauderdale et al. 1993; Mitchell et al. 1994). In the first step of data development, all Medicare beneficiaries older than sixty-five as of January 1, 1993, as noted in the so-called Denominator File, were examined and subjected to a spousal identification algorithm (Iwashyna et al. 1998; Iwashyna et al. 2002). Notably, the Denominator File, which contains all Medicare beneficiaries, consequently captures 96 percent of all Americans older than sixty-five (Hatten 1980). We estimate that, among the 32,180,588 elderly people in this file, there are 6.6 million elderly couples where both partners are older than sixty-five, and we detected 5,496,444 (83 percent) of them. Of these, 4,874,817 were couples where both parties were sixty-five to ninety-eight years old and resided in the fifty states. From this group, we chose a simple random sample of 540,793 couples identified with one of two methods of detection (Iwashyna et al. 1998). The Denominator file provides demographic information (e.g., age, sex). A separate Vital Status file gives precise death dates, here censored at January 1, 2002. As a marker for coresidence, we observed whether both members of each couple had an address within the same zip code; 4.2 percent of the couples (N = 22,553) lived in different zip codes, and we excluded these couples from further analysis, leaving an analytic sample of 518,240.

Using so-called MEDPAR records for 1993–2002, we obtained the dates of all hospitalizations and also the reasons for hospital admission in the form of ICD-9 diagnostic codes. That is, we measured the occurrence of a serious disease in spouses during the follow-up period by using the principal diagnosis noted on inpatient claims, as categorized by using a 49-category indicator variable based on a Centers for Disease Control and Prevention (CDC) taxonomy of ICD-9 codes used in hospitalizations (Hall and DeFrances 2003). In the present analyses, for parsimony, the diagnoses were collapsed into sixteen categories, as shown in table 15.1. Other analyses (not shown here) using the 49-category system did not yield different results.

By using hospitalization claims, it is possible to detect the occurrence of serious diseases at least as accurately as asking people directly (Zhang, Iwashyna, and Christakis 1999). Given the seriousness of the diagnoses at hand (e.g., sepsis, stroke, Myocardial Infarction [MI], lung cancer, abdominal surgery, etc.), and given prior work on using hospitalizations to detect disease incidence, we used hospitalization as a marker for the occurrence of

Table 15.1 Percentage of spouses and probands dying within a year of spousal hospitalization, by condition, separately for husbands and wives

Wife's diagnosis	Number of couples with this disease occurring in the wife	Percentage of husbands dead within one year of the wife's diagnosis	Percentage of wives dead within one year of the wife's diagnosis	
Sepsis	3,971	7.38	27.73	
Pneumonia	15,884	7.17	17.92	
Colon cancer	5,056	6.39	19.44	
Pancreas cancer	641	6.86	80.97	
Lung cancer	2,416	5.55	55.09	
Leukemia or Lymphoma	1,538	7.54	52.93	
All Other Malignancies	18,158	5.06	27.57	
Stroke	24,674	6.90	18.59	
Dementia	2,642	8.55	21.23	
Psychiatric disease	4,893	7.50	7.26	
Ischemic heart disease	30,188	6.19	13.39	
Congestive heart failure	13,261	7.46	25.60	
COPD	8,335	6.37	13.95	
Abdominal surgical disease	27,042	6.29	8.02	
Hip and serious fractures	18,087	8.59	12.63	
All other diagnoses	170,483	5.91	9.76	
Total	347,269	6.33	13.76	
Husband's diagnosis	Number of couples with this disease occurring in the husband	Percentage of wives dead within one year of the husband's diagnosis	Percentage of husbands dead within one year of the husband's diagnosis	
Sepsis	5.022	4.04	24.05	
Pneumonia	5,022 23,594	4.04	34.87	
Colon cancer	6,559	4.51	30.23	
Pancreas cancer	6,339	2.99 3.54	23.65	
Lung cancer	: 4.220		82.01	
Leukemia or Lymphoma	ى 4,329 2,121	3.44 3.35	66.20	
All other malignancies	21,263	2.82	65.11	
Stroke	31,471		36.66	
Dementia	3,348	3.65	22.73	
Psychiatric disease	•	4.99	37.81	
Ischemic heart disease	2,666 50,596	5.74	19.50	
Congestive heart failure	18,644	2.94	15.89	
COPD	9,532	4.25 4.12	34.47	
Abdominal surgical disease	26,623	4.12 3.46	24.12	
Hip and serious fractures	9,800		12.81	
		5.09	28.10	
All other diagnoses	167 224			
All other diagnoses Total	167,234 383,480	3.39	17.22	

the diagnoses of interest. Of course, in some cases, the disease in question could have been noted prior to the time of hospitalization during the follow-up period (e.g., during outpatient visits), but we nevertheless regard hospitalization as a marker for a particularly burdensome stage of the diseases in question. We treated the date of first hospital admission during the time period after January 1, 1993 as the anchoring date of disease occurrence for the purpose of assessing impact of spousal illness on probands. Each person in each couple in our cohort could have multiple hospitalizations (though most, 60 percent, had zero, one, or two) over the nine-year follow-up, but we marked each spouse only upon the occurrence of their first hospitalization.

For each individual, we also looked back through three years (1990–1992) of prior inpatient claims in order to detect what illnesses, if any, they had at baseline and thus establish a morbidity burden as of January 1, 1993. The necessity of determining baseline morbidity at cohort inception is the reason for the criterion of greater than sixty-eight years of age for certain analyses (i.e., the Cox models in table 15.2), because patients who were less than sixty-eight in 1993 could not have had Medicare claims filed for a full antecedent three-year period. This three-year duration of retrospective ascertainment of health problems has been shown to be adequate for the detection of prevalent chronic conditions (Zhang, Iwashyna, and Christakis 1999; McBean, Warren, and Babish 1994). We used the Charlson score to summarize baseline morbidity (Zhang, Iwashyna, and Christakis 1999), and we trichotomized it as 0, 1, or ≥ 2. As a further measure of baseline health, we also counted the number of weeks each individual had spent in the hospital in the prior three years.

All of the variables used here have been previously validated or extensively exploited. Investigators have assessed, for example, the optimal use of Medicare data for measuring age (Kestenbaum 1992) and race (Lauderdale and Goldberg 1996). We determined whether the couple was below the state poverty line using previously described methods (Carpenter 1998; Clark and Hulbert 1998; Escarce et al. 1993; Pope et al. 1998). With respect to reliability of claims for detection of specific diseases, prior work has shown that claims have a sensitivity ranging from 89 percent to 93 percent for the detection of a wide variety of conditions in medical charts (e.g., cancers of various kinds, congestive heart failure, hip fracture, etc.) (Fisher et al. 1992; Romano and Mark 1994; Bergmann et al. 1998; Krumholz et al. 1998; Cooper et al. 1999; Benesch et al. 1997). Specificity for these conditions is also very high and ranges from 99 percent to 100 percent (Romano and Mark 1994). The properties of claims in the more global assessment of overall morbidity burden have also been validated (Zhang, Iwashyna, and Christakis 1999).

For certain results, there is one further proviso, namely, that neither member of the couple be a member of a staff-model HMO. This restriction

, and the second se	Hazard ratio o	of death (95% CI)
	Male probands	Female probands
Spousal de	eath	
Widowhood	1.205***	1.169***
	(1.189–1.221)	(1.151–1.187)
Spousal hospitalizati	on (diagnosis)	
Sepsis	1.089**	1.071
•	(1.012-1.172)	(0.979-1.171)
Pneumonia	1.062***	1.058***
	(1.025-1.100)	(1.015-1.103)
Colon cancer	1.016	1.012
	(0.949–1.087)	(0.933–1.096)
Pancreas cancer	0.863	1.18
	(0.536–1.388)	(0.654–2.132)
Lung cancer	0.939	1.135
Duilg Culled	(0.800–1.103)	(0.958–1.344)
Leukemia or Lymphoma	1.077	1.081
Leukenna of Lymphoma		
All other canages	(0.911–1.273)	(0.869–1.344)
All other cancers	0.988	0.956
C41	(0.950–1.028)	(0.908–1.007)
Stroke	1.061***	1.047**
D	(1.030–1.092)	(1.009–1.085)
Dementia	1.215***	1.279***
	(1.115-1.323)	(1.143–1.433)
Psychiatric disease	1.191***	1.315***
	(1.122-1.265)	(1.182-1.462)
Ischemic heart disease	1.045***	0.966**
	(1.018-1.072)	(0.938-0.995)
Congestive heart failure	1.115***	1.146***
	(1.071-1.162)	(1.092-1.204)
Chronic obstructive pulmonary disease	1.118***	1.131***
	(1.065-1.175)	(1.061-1.207)
Abdominal surgery	1.038***	1.026
•	(1.011-1.065)	(0.990-1.062)
Hip and other serious fractures	1.146***	1.106***
•	(1.112-1.182)	(1.043-1.173)
All other diagnoses	1.019***	1.008
	(1.006–1.032)	(0.990–1.026)
Covariate co	*	(51525 ;21525);
Age of husband (years)	1.093***	1.001
rigo or museuma (jours)	(1.091–1.094)	(0.999–1.003)
Age of wife (years)	1.001	1.096***
Age of whe (years)		
Wife older than husband	(1.000–1.003)	(1.094–1.098)
Wife older than husband	1.051***	1.042***
Counts halow november lin -	(1.037–1.065)	(1.025–1.059)
Couple below poverty line	1.341***	1.433***
	(1.318-1.364)	(1.404-1.462)

	Hazard ratio of death (95% CI)			
	Male probands	Female probands		
Charlson score of husband = 1	1.520*** (1.500-1.540)	0.977** (0.960–0.994)		
Charlson score of husband = 2	2.205*** (2.181–2.230)	0.972*** (0.956–0.988)		
Charlson score of wife = 1	1.01	1.936***		
Charlson score of husband = 2	(0.995–1.026) 0.99	(1.904–1.968) 2.959***		
Number of weeks husband in hospital in 1990–1992	(0.975–1.007) 1.030***	(2.915–3.004) 0.995***		
Number of weeks wife in hospital in 1990–1992	(1.030–1.031) 0.998***	(0.993–0.997) 1.030***		
Race of husband: black	(0.996-0.999) 1.096***	(1.029–1.031) 1.120***		
Race of husband: Asian	(1.025–1.171) 0.818***	(1.032–1.216) 0.923		
	(0.757–0.883) 0.879***	(0.839–1.015) 1.01		
Race of husband: Hispanic	(0.852–0.906) 1.039	(0.973–1.048) 0.910		
Race of husband: other	(0.958–1.127)	(0.822–1.008) 0.837***		
Race of husband: unknown	2.028*** (1.953–2.105)	(0.795-0.882)		
Race of wife: black	0.953 (0.892–1.018)	0.96 (0.884-1.042)		
Race of wife: Asian	0.877*** (0.807–0.953)	0.720*** (0.646–0.802)		
Race of wife: Hispanic	0.954 (0.907–1.002)	0.735*** (0.689-0.785)		
Race of wife: other	0.99	1.210*** (1.125–1.302)		
Race of wife: unknown	(0.929–1.054) 0.819*** (0.783–0.855)	1.834*** (1.753–1.920)		

Notes: The table shows Cox regression models of survival, separately for husbands and wives, with hazard ratios and 95% confidence intervals. Subjects were followed from January 1, 1993 to January 1, 2002. Widowhood and spousal hospitalizations are treated as time-varying covariates during the follow-up period. Spousal hospitalizations were the principal diagnosis for the first hospitalization, if any, noted during follow-up. All covariates measured at baseline at January 1, 1993. The omitted category for Charlson score measures is zero and for race is white.

^{***} Significant at less than the 1 percent level.

^{**} Significant at less than the 5 percent level.

is required since such individuals cannot have their complete health histories ascertained in the claims. This exclusion accounts for less than 7.0 percent of the impaneled sample.

15.1.2 Statistical Methods

We employ both conventional survival models (Cox regression) and also fixed effects methods to analyze our data. The former offer the advantage of explicitly estimating the effects of measured attributes (e.g., age) on the outcomes of interest and, more importantly, permit a more flexible parameterization that allows us to separately estimate the effects of caregiving and widowhood. The latter offer the substantial advantage of controlling for time-invariant factors that might confound the effects of interest, whether they are measured or not.

In the Cox regression models, the dependent variable is the duration of survival of the proband, from January 1, 1993 until January 1, 2002. Pertinently, we treat spouse's diagnosis with a disease and spouse's death as *separate* time-varying covariates, with the result that the estimate of the impact of a spouse being hospitalized with one of the sixteen conditions upon a proband takes into account whether the spouse does or does not subsequently die. These models are restricted so that all subjects are a minimum of sixty-eight years old. We used a Wald test to evaluate the difference between the time-varying indicators of spousal hospitalization and spousal death in the same model. Tests for violations of the proportionality assumption for key variables revealed no problems.

Fixed effects models permit the estimation of the effect of factors such as the occurrence of a particular diagnosis in a spouse, which does change over the longitudinal follow-up, while accounting for any measured or unmeasured factors that do not change—whether these factors pertain to the spouse, the proband, or the couple. This is accomplished by using each couple as its own control, comparing the time at which a spousal diagnosis occurred with times at which it had not. While it is true that the measured and unmeasured variables we wish to control for (e.g., poverty, smoking, education, toxic exposure history, marital happiness) might indeed not be absolutely stable over time, their temporal variability (which we cannot control) is likely to be very small relative to their between-couple variability (which we can control).

Hence, taking a discrete-time approach with couple-days as the units of analysis, we performed a conditional logistic regression predicting whether or not a death occurs on a given day. Each couple is treated as a separate stratum, thereby controlling for all stable differences between couples. This approach has seen several methodological and applied articles in the epidemiology literature, where it is called the case-crossover design (Maclure 1991; Marshall and Jackson 1993; Redelmeier and Tibshirani 1997), and we used a modification called the case-time-control design (Suissa 1998).

Despite its salient advantages, this method has some limitations. For example, the covariates of interest cannot be monotonic functions of time. Consequently, our modeling approach uses dummy variables for spouse hospitalized for disease X within the last 30, 60, 90, 180, 360, and so on, days. This feature also offers the advantage of allowing us to explicitly investigate the shape of the effect of a spouse's illness (and/or death) on a proband's death across time (Allison and Christakis 2006). As implemented, these models estimate the effect of spousal diagnosis, with or without subsequent death, on proband death.

15.2 Results

15.2.1 Cohort Attributes

At cohort inception (N=518,240), the mean age of the husbands was 75.4 years and of the wives 72.9 years; in 79.1 percent of the couples, the husband was older than the wife; 90.1 percent of the husbands and 92.1 percent of the wives were white; 5.4 percent of the couples were below their state poverty line. The mean Charslon comorbidity score of the husbands at cohort inception was 0.50 and of the wives, 0.30. From January 1, 1993 to January 1, 2002, 383,480 (74.0 percent) of the husbands and 347,269 (67.0 percent) of the wives were hospitalized at least once. Over the same time period, 252,557 of the husbands (48.7 percent) died and 156,004 (30.1 percent) of the wives died; in 95,330 couples, both parties died.

15.2.2 Spousal Illness and Proband Death in the Elderly: Unadjusted Results

Table 15.1 shows the percentage of probands who die within one year of their spouse being hospitalized with one of sixteen disease categories at any time during the nine-year follow-up. For example, whereas 6.39 percent of husbands die within a year of their wife being hospitalized with colon cancer, 6.90 percent die within a year of their wife being hospitalized with a stroke, 8.55 percent die within a year of their wife being hospitalized with dementia, and 7.50 percent die within a year of their wife being hospitalized for psychiatric disease. Symmetrically, whereas 2.99 percent of wives die within a year of their husband being hospitalized with colon cancer, 3.65 percent with a stroke, 4.99 percent with dementia, and 5.74 percent with psychiatric disease.

The median number of days between a wife's hospitalization and a man's subsequent death, in those couples with both these events, was 1,103, and between a husband's hospitalization and a woman's death was 1,287.

Table 15.1 also reports the percentage of spouses who themselves die within a year of their own hospitalization; the disease categories show substantial and plausible variation in their lethality. For many diseases, the

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majority of patients themselves die within a year of hospitalization, further supporting the importance of separating the impact on probands of the occurrence of disease versus death in spouses.

15.2.3 Cox Regression Models: Adjusting for Measured Covariates

The Cox models in table 15.2 provide estimates of the effect of spousal illness on proband risk of death after adjusting for whether the spouse dies and after adjusting for other measured attributes of both parties, including their age and baseline morbidity. For example, the occurrence of colon cancer in a wife does not itself affect the husband's risk of death (HR 1.02, 95 percent CI: 0.95-1.09), whereas the occurrence of a stroke in a wife raises the husband's risk by 6 percent (HR 1.06, 95 percent CI: 1.03–1.09), CHF by 12 percent (HR 1.12, 95 percent CI 1.07-1.16), dementia by 22 percent (HR 1.22, 95 percent CI: 1.12-1.32), and psychiatric disease by 19 percent (HR 1.19, 95 percent CI: 1.12-1.27). Similarly, the occurrence of colon cancer in a husband has no effect on a wife (HR 1.01, 95 percent CI: 0.93-1.10), whereas a husband's stroke raises a wife's risk of death by 5 percent (HR 1.05, 95 percent CI: 1.01-1.09), CHF by 15 percent (HR 1.15, 95 percent CI: 1.09-1.20), dementia by 28 percent (HR: 1.28, 95 percent CI: 1.14-1.43), and psychiatric disease by 32 percent (HR 1.32, 95 percent CI: 1.18-1.46).

The results in table 15.2 also reveal that in the case of both husbands and wives, the death of a spouse is associated with 20 percent and 17 percent increase, respectively, in the hazard of death net of the health burden imposed by the spouse's anteceding illness as marked by their hospitalization. Moreover, for men, their hazard of death (over the following nine years) is higher if they are older in age, their wife is older than they are, they are black, they have a higher baseline morbidity (measured either as a Charlson score or number of days spent in the hospital), or they are poor. For women, their hazard of death is higher for the same reasons.

A reduced form Cox model (not shown) with an indicator for the occurrence of any disease at all showed that the occurrence of any hospitalization in a wife increases a husband's risk of death by 4.2 percent and the occurrence in a husband increases a wife's risk of death by 2.3 percent, even after controlling for whether the hospitalized person subsequently dies. Moreover, comparison of the effect of any hospitalization to a death reveals that a spouse's (husband's or wife's) recent diagnosis (within the past thirty days) is about 75 percent as bad for a proband's mortality as a spouse's death within the past thirty days.

15.2.4 Fixed Effects Models: Adjusting for Measured and Unmeasured Attributes

Table 15.3 gives the relative odds of a proband dying on a particular day within six months of a spouse's hospitalization, depending on whether a

Table 15.3 Odds ratios for proband death within six months conditional on new spousal hospitalization, by spousal diagnosis

Disease category	Impact of wife's diagnosis on husband's odds of death within six months	95%	6 CI	Impact of husband's diagnosis on wife's odds of death within six months	95%	% CI
Sepsis	1.198	1.006	1.427	1.142	0.924	1.411
Pneumonia	1.325	1.213	1.448	1.232	1.122	1.353
Colon cancer	1.153	0.970	1.371	0.974	0.780	1.215
Pancreas cancer	1.310	0.818	2.098	1.658	0.936	2.937
Lung cancer	0.963	0.742	1.252	1.271	0.995	1.624
Leukemia/Lymphoma	1.605	1.231	2.093	1.101	0.768	1.579
All other cancers	1.033	0.934	1.143	1.060	0.933	1.205
Stroke	1.105	1.024	1.191	1.102	1.006	1.207
Dementia	1.472	1.217	1.780	1.381	1.105	1.725
Psychiatric disease	1.584	1.356	1.851	1.771	1.389	2.256
Ischemic heart disease	1.119	1.041	1.203	1.132	1.045	1.226
CHF	1.105	1.003	1.217	1.272	1.144	1.416
COPD	1.212	1.064	1.381	1.364	1.172	1.587
Abdominal surgery	1.124	1.042	1.213	1.189	1.075	1.315
Hip and other Serious fractures	1.352	1.253	1.460	1.178	1.026	1.352
All other diagnoses	1.140	1.105	1.175	1.178	1.131	1.226

spouse is hospitalized with one of the sixteen conditions at any time between 1993 and 2001, separately for male and female probands. Hospitalization for a variety of serious conditions in wives increases the risk of a husband's death within six months of the diagnosis: the diagnosis of acute events such as a stroke, heart attack, pneumonia, or hip fracture in a woman will increase a husband's odds of death within six months, net of all stable attributes of both partners, between 10 percent and 35 percent. The diagnosis of diseases such as dementia or psychiatric conditions increase the odds of a husband's death within six months by 47 percent and 58 percent, respectively. The diagnosis of most cancers in a wife does not appear to affect her husband's risk of death within six months.

Similarly, hospitalization for a variety of serious conditions in husbands increases the risk of wife's death within six months of the diagnosis: the diagnosis of acute events such as a stroke, heart attack, pneumonia, or hip fracture in a woman will increase a husband's odds of death within six months, net of all stable attributes of both partners, between 10 percent and 23 percent. The diagnosis of diseases such as dementia or psychiatric conditions increase the odds of a husband's death within six months at 38 percent and 77 percent, respectively. The diagnosis of any cancer in a husband does not appear to affect his wife's risk of death within six months.

Expanding to a broader time window than just six months, figure 15.1 shows the impact of the occurrence of a spousal hospitalization in general, without regard to spouse's particular diagnosis, upon a partner's risk of death. When one person is hospitalized with any disease, the other's risk of death shows a statistically significant increase above baseline and remains elevated for at least two years. This is the case even after accounting for all stable measured or unmeasured attributes of the couples, which are controlled for in this model, and without regard to whether the hospitalized spouse lives or dies. For both men and women, the effect of spousal diagnosis is greatest just after the hospitalization and lowest at roughly six months after the occurrence.

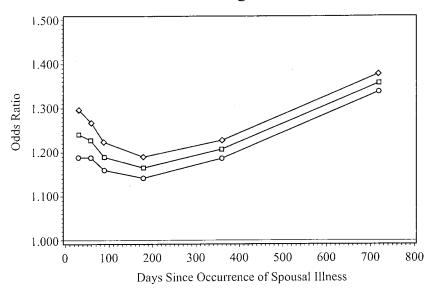
Figures 15.2 and 15.3 graphically show the impact of spousal diagnosis on proband risk of death across a two-year horizon for a selection of eight of the sixteen conditions, separately for male and female probands. In general, these graphs have a U shape with a nadir at 90–180 days.

15.3 Discussion

Prior work on the widower effect and caregiver burden may conflate the two phenomena. It is important, in studies of caregiver burden, to parse out the adverse health impact of widowhood itself and, in studies of the widower effect, to parse out the impact on a proband of a spouse's predeath illness or disability. Indeed, we find that it may be roughly as bad for a proband's health, relatively speaking, to have a partner be hospitalized with a serious disease as it is for that partner to die. Our diagnosis-specific results suggest that possibly a substantial part of the widower effect may be related not to the death of the spouse, but to the fact that they were ill with particular kinds of diseases before they died. Moreover, independent of the foregoing, the temporal pattern of the caregiver burden effect also suggests that the impact of caregiving may involve both the acute stress of the occurrence of the spouse's illness and a longer-term effect of losing the ongoing support of the spouse.

We specifically hypothesized that particular spousal diagnoses could vary in how burdensome they are to probands and hence the extent to which they affect proband health and mortality. The more a disease interferes with a person's physical or mental ability, regardless of the extent to which it is deadly, the worse for the partner of the ill person. There are a number of possible ways that diseases might be assessed in terms of their impact on the afflicted person's health status and consequently their burdensomeness. For example, prior work has documented that diseases vary in their impact on the activities of daily living (ADL) score (Ferrucci et al. 1997; Rosen et al. 2000; Covinsky et al. 1997). Other studies have specifically examined disability rates in individuals at various time intervals after hospitalization with various diseases (Gill et al. 2004; Landrum and

All Diagnoses



All Diagnoses

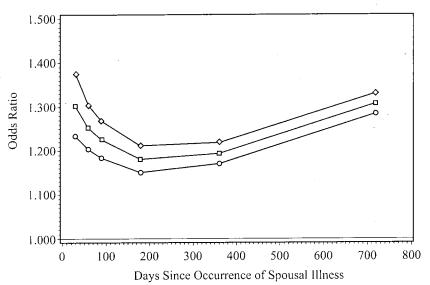


Fig. 15.1 Proband risk of death over various time intervals after spousal hospitalization with any condition (fixed effects estimates), for husbands and wives

Notes: The top panel shows the husband's risk of death (odds ratio and 95% time intervals) on days falling within certain time periods, depending on whether his wife has been hospitalized in the relevant time period, compared to days when his wife had not died within the relevant time period, as generated by fixed effects models. The bottom panel shows the wife's risk of death.

Steward 2004). One study found that stroke or hip fracture are more likely to cause new and serious disability than Congestive Heart Failure (CHF) or cancer (Ferrucci et al. 1997). Yet another way to rank diseases relies on SF-36 measures of physical or mental function, and one meta-analysis of over 15,000 patient reports ranked disease groups in the following order,

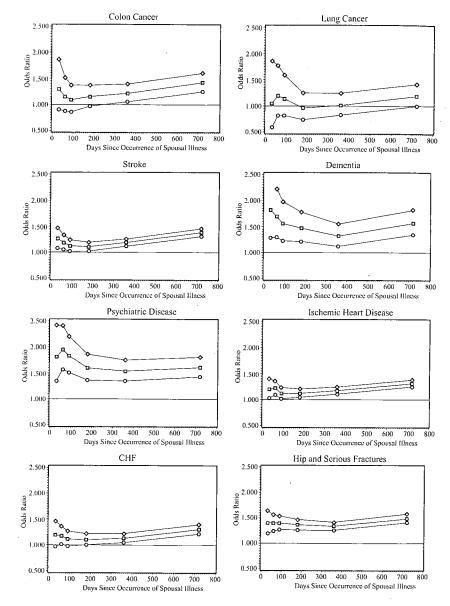


Fig. 15.2 Husband's risk of death over various time intervals depending on occurrence of illness in wife

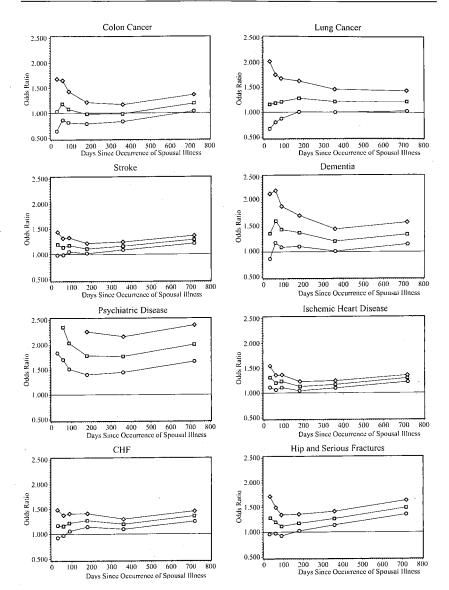


Fig. 15.3 Wife's risk of death over various time intervals depending on occurrence of illness in husband

from most to least impact: cerebrovascular conditions, cardiovascular conditions, respiratory conditions, and cancer (Sprangers et al. 2000).

The purpose of ranking diagnoses according to such measures is not to adjudicate among the various ways of ranking diseases, nor to directly estimate the effect of ADL or other decrements per se on a partner's health. For such a purpose, it would clearly be ideal (though impossible, given our

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sample size requirements) if we could have, for each patient regardless of their diagnosis, more detailed measures of their health or disability status or even the actual demands they make of their partner. Rather, the object in using this prior work is to provide support for the contention that diagnoses do indeed vary in their burdensomeness and therefore to assist in interpreting our results. In general, our results confirm that diseases do vary and that cancer diagnoses appear especially nonburdensome. While dementia, the most frequently studied diagnosis with respect to caregiving, is on the upper end of burdensomeness (at least as we have measured it here. in terms of risk to a proband's life), other diseases, such as chronic obstructive pulmonary disease (COPD) and psychiatric conditions appear to rival it even though they are less lethal.

Both the widow/er and caregiver effects conform to theories and findings regarding the role of stress and social support in health and mortality (House, Landis, and Umberson 1988; Berkman and Syme 1997; Thoits 1995; Berkman, Geo-Summers, and Horwitz 1992; Berkman and Glass 2000; Cohen et al. 1997; Esterling, Kiecolt-Glaser, and Glaser, 1996). As such, it is possible to postulate two broad mechanisms whereby illness in one spouse might affect the health and risk of death of the other: illness or death in a spouse may impose stress on the proband, and illness or death in a spouse may deprive a proband of social support previously offered by the spouse. These two effects, while both negative, may, however, operate over different time frames. For example, the stress effect might last for a few weeks or months and the support effect might last for several years. Moreover, the former might have immediate onset and decrease with time (as the proband recovers from the acute shock of the onset of serious illness in the spouse) and the latter might increase with time (as the absence of spousal support cumulates). Once a spouse falls seriously ill (or dies), probands might begin to exhibit harmful behaviors, ranging from drinking to bad dietary practices to accident-prone activities with an attendant increase, over the longer term, in the hazard of death (Umberson 1987, 1992; Iwashyna 2001). Stress and the lack of social support may also adversely affect biological parameters (Cohen et al. 1997).

Thus, we also hypothesized that the impact of being in a caregiving role might vary according to the duration in that role and we found, across a broad range of diagnoses, a U-shaped function with a nadir at 90–180 days. One interpretation of this shape is that early in the course of a spouse's illness, a proband experiences a stress effect, to which he or she eventually adapts such that the health risks of being a caregiver decline; eventually, however, the lack of social support from the newly seriously ill spouse becomes a problem, and health risks in the proband increase again. Interestingly, some prior work on the risk of death in probands depending on the duration of bereavement (i.e., time since the death of their spouse) has suggested a similar U-shaped function with a nadir between 0.5 and 1.0 years (Martikainen and Valkonen 1996b), and work on how duration of awareness of a husband's impending death affects a wife's long-term anxiety reveals a similar U-shape (Vadimarsdottir et al. 2004).

Although wives are more likely than husbands to be caregivers (for numerous reasons, ranging from longer female life expectancy to the pressure to fill a social role), most studies have suggested that wives report higher levels of burden than husbands who are caregivers or than control populations (Barusch and Spaid 1989; Pruchno and Resch 1989; Russo and Vitaliano 1995; Dunkin and Anderson-Hanley 1998), with attendant psychological consequences. Our work shows that, over a broad range of diseases, and when burden is measured as the risk of death, husbands suffer as much, marginally speaking, as wives from having a seriously ill partner. However, some of these effects may be gendered in ways that warrant further exploration. Since husbands and wives bring different benefits to a marriage, husbands and wives may rely on each other for different kinds of assistance (Waite and Gallagher 2000); therefore, different health deficits in partners might affect husbands and wives differently. Thus, for example, mental deficits in husbands may be worse for wives than mental deficits in wives are for husbands; physical deficits in wives may be worse for husbands than physical deficits in husbands are for wives. We found some suggestive evidence of disease heterogeneity in this regard, but more work is needed to clarify any such gendered effects.

We used observational epidemiological methods to evaluate the effects of interest since a randomized controlled intervention trial—involving assigning spouses to different diseases—clearly would be impossible. In such circumstances, observational studies are our best source of clinical evidence (Abel and Koch 1999, Concato, Shah, and Horwitz 2000). Epidemiological studies, however, raise unavoidable concerns regarding confounding or selection. In order to get the large size and long follow-up needed to evaluate the phenomena of interest here, we had to forego other information about cohort members that would have been useful. Moreover, we lack information about time-varying traits of probands and couples other than the occurrence of spousal disease or death. Such a lack of information, and the non-random assignment of couples to different spousal illness conditions, is unavoidable.

However, the implementation of fixed effects models helps to partly mitigate this concern. This method also helps mitigate concerns regarding the possible endogeneity of the processes leading to a spouse's hospitalization and the proband's likelihood of dying. For example, there might be unmeasured traits that make a proband unable to care for a spouse, that therefore increase the spouses' probability of being hospitalized (given the onset of a particular condition), and that are correlated with the proband's own risk of death during the caregiving period. In addition to the fact that our fixed effects models can adjust for such (unmeasured) traits, it is also

worth noting that the probability of being hospitalized for most of the diseases we are considering here (e.g., MI, stroke, sepsis, hip fracture, abdominal surgery) is unlikely to depend much on attributes of a proband. Finally, such fixed effects models seem especially appropriate in the present setting because once people reach the age of sixty-five, their educational status, wealth, taste for health care, and health habits tend to be stable, and such attributes can be seen as having a fixed effect on individual's propensity to fall ill or die.

The supposition that being in a caregiver role is causally associated with subsequent harm to the health of a proband is supported by additional aspects of our findings, not limited to the magnitude of the effects we observe. For example, our data suggest a kind of dose/response relationship whereby different diseases, of different burdensomeness (as described by prior work), have different marginal risks of death. In addition, our findings comport with other customary criteria regarding the likelihood of causation based on epidemiological data, including the temporal order, consistency with past studies, and biological plausibility of the association. Nevertheless, further study will be needed.

Our work has a number of other limitations. We use "caregiver" to signify being in the caregiving role. But we cannot actually be sure that the proband provided any care to the spouse. The kind of data required for our study of mortality effects (e.g., the sample size) necessarily lacks detail on caregiving activities and on whether caregivers other than the spouses are also involved. Nevertheless, we do document an effect on the partners of ill persons. We also focus here on a single (hard) endpoint, namely, proband death. However, we see this as an advantage. That is, whereas in prior studies of widowhood both the exposure (death of a spouse) and the outcome (death of a proband) have been unambiguously and consistently defined, prior studies of caregiver burden—or the effect of illness of one party on the health of the other—have used variable outcomes that make comparisons across populations and diseases difficult and have typically been conducted with one disease or one type of couple. Our work avoids this problem by focusing on death as an outcome.

Though inter-individual health effects of the kind investigated here are frequently overlooked, they may have substantial clinical and policy significance. Most generally, illness and death in individuals who, being embedded in social networks, are connected to their spouses and to others, can impose health externalities on these other people (Christakis 2004; Christakis and Iwashyna 2003). Whatever the adverse health consequences to a person from falling ill, and whatever the mitigation of these consequences attributable to the receipt of medical care, there may be health consequences that also accrue to those to whom the sick person is connected. This in turn means that efforts to reduce disease, disability, and

death can be self-reinforcing as a decrease in the burden of these events in one individual can have cascading benefits for others. Therefore, health care might indeed be more socially efficient than an individual, patient-level perspective might suggest (Christakis and Iwashyna 2003). For example, there is evidence that disability rates among the elderly have been falling at 0.5 percent to 2.5 percent per year over the last decades (Freedman, Martin, and Schoeni 2002). It is conceivable that some fraction of the decline in disability may be related to positive health externalities or may be self-reinforcing. That is, if disability or death in one person can contribute to disability or death in others, then reductions in disability may have multiplicative effects because of social network ties.

Our findings therefore have implications for the assessment of costeffectiveness of medical interventions. There may be collateral benefits of
health care interventions upon the relatives of patients, and these benefits
may enhance the cost-effectiveness of the intervention. Thus, in the present
case, medical care delivered to patients that alleviates the burdensomeness
of their condition may benefit not only the patients, but also their spouses
or other loved ones, and this may increase the overall cost-effectiveness of
medical care.

Our findings can also inform the delivery of support services to caregivers. A recent randomized controlled trial of 300 stroke patients and their caregivers found that training the caregivers in caregiving lowered the costs of care for the patients and decreased their anxiety; moreover, trained caregivers experienced less caregiver burden, anxiety, and depression, and they had a superior quality of life (Kalra et al. 2004). Our work suggests that such interventions to assist caregivers are especially likely to be useful in diseases like stroke and selected others, but less so in cancer. Moreover, the timing of such interventions might be optimally matched to the time of greatest risk of caregivers: for example, just after the initial occurrence of the disease.

Finally, patients themselves care about how their illness affects others to whom they are connected (Steinhauser et al. 2000). The fact that illnesses can have palpable effects on the health of others to whom patients are connected will likely interest patients as they seek to maintain their social relations and seek to avoid imposing burdens on their loved ones throughout their own experience of their condition.

References

Abel, U., and A. Koch. 1999. The role of randomization in clinical studies: Myths and beliefs. *Journal of Clinical Epidemiology* 52:487–97.

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Allison, P. D., and N. A. Christakis. 2006. Fixed effects methods for the analysis of non-repeated events. Sociological Methodology 36 (1): 155-72.

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- Barusch, A. S., W. M. Spaid. 1989. Gender differences in caregiving: Why do wives report greater burden? The Gerontologist 29 (5): 667–76.
- Benesch, C., D. M. Witter, Jr., A. L. Wilder, P. W. Duncan, G. P. Samsa, and D. B. Matchar. 1997. Inaccuracy of the International Classification of Disease (ICD-9-CM) in identifying the diagnosis of ischemic cerebrovascular disease. Neurology 49:660-64.
- Berkman, L., and T. Glass. 2000. Social integration, social networks, and health. In Social epidemiology, eds. L. F. Berkman and I. Kawachi, 174-90. Oxford: Oxford University Press.
- Berkman, L., R. Horwitz, and L. Leo-Summers. 1992. Emotional support and survival after myocardial infarction: A prospective, population-based study of the elderly. Annals of Internal Medicine 117:1003-9.
- Berkman, L., and L. Syme. 1997. Social networks, host resistance, and mortality: A nine-year follow-up study of Alameda County residents. American Journal of Epidemiology 109:186-204.
- Bergmann, M. M., T. Byers, D. S. Freedman, and A. Mokdad. 1998. Validity of self-reported diagnoses leading to hospitalization: A comparison of self-reports with hospital records in a prospective study of American adults. American Journal of Epidemiology 147:969-77.
- Carpenter, L. 1998. Evolution of Medicaid Coverage of Medicare Cost Sharing. Health Care Financing Review 20:11–18.
- Christakis, N. A. 2004. Social networks and collateral health effects. British Medical Journal 329:184-85.
- Christakis, N. A., and T. J. Iwashyna. 2003. The health impact on families of health care: A matched cohort study of hospice use by decedents and mortality outcomes in surviving, widowed spouses. Social Science and Medicine 57:465–75.
- Clark, W. D., and M. M. Hulbert. 1998. Research issues: Dually eligible Medicare and Medicaid beneficiaries, challenges and opportunities. Health Care Financing Review 20:1–10.
- Clipp, E. C., and L. K. George. 1993. Dementia and cancer: A comparison of spouse caregivers. The Geronotologist 33 (4): 534–41.
- Cohen, S., W. J. Doyle, D. P. Skoner, B. S. Rabin, J. Gwaltney, and M. Jack. 1997. Social ties and susceptibility to the common cold. Journal of the American Medical Association 277:1940-44.
- Collins, C., and R. Jones. 1997. Emotional distress and morbidity in dementia carers: A matched comparison of husbands and wives. International Journal of Geriatric Psychiatry 12:1168-73.
- Concato, J., N. Shah, and R. I. Horwitz. 2000. Randomized, controlled trials, observational studies, and the hierarchy of research designs. New England Journal of Medicine 342:1887-92.
- Cooper, G. S., Z. Yuan, K. C. Stange, L. K. Dennis, S. B. Amini, and A. A. Rimm. 1999. The sensitivity of Medicare claims data for case ascertainment of six common cancers. Medical Care 37:436–44.
- Covinsky, K. E., A. C. Justice, G. E. Rosenthal, R. M. Palmer, and C. S. Ladnefeld. 1997. Measuring prognosis and case mix in hospitalized elders: The importance of functional status. Journal of General Internal Medicine 12:203-8.
- Dunkin, J. J., and C. Anderson-Hanley. 1998. Dementia caregiver burden: A review of the literature and guidelines for assessment and intervention. Neurology 51 (Suppl. no. 1): S53-S60.
- Dura, J. R., E. Haywood-Niler, and J. K. Kiecolt-Glaser. 1990. Spousal caregivers

- of persons with Alzheimer's and Parkinson's Disease dementia: A preliminary comparison. The Gerontologist 30 (3): 332-36.
- Escarce, J. J., K. R. Epstein, D. C. Colby, and J. S. Schwartz. 1993. Racial differences in the elderly's use of medical procedures and diagnostic tests. American Journal of Public Health 83:948-54.
- Esterling, B. A., J. K. Kiecolt-Glaser, and R. Glaser. 1996. Psychosocial modulation of cytokine-induced natural killer cell activity in older adults. Psychosomatic Medicine 58:264-72.
- Ferrucci, L., J. M. Furalnik, M. Pahor, M. C. Corti, and R. J. Havlik. 1997. Hospital diagnoses, Medicare Charges, and nursing home admissions in the year when older persons become severely disabled. Journal of the American Medical Association 277:728-34.
- Fisher, E. S., F. S. Whaley, M. Krushat, D. J. Malenka, C. Fleming, J. A. Baron, and D. C. Hsia. 1992. The accuracy of Medicare's hospital claims data: Progress has been made, but problems remain. American Journal of Public Health 82:243-48.
- Fitting, M., P. Rabins, M. J. Lucas, and J. Eastham. 1986. Caregivers for dementia patients: A comparison of husbands and wives. The Gerontologist 26 (3): 248-52.
- Freedman, V. A., L. G. Martin, and R. F. Schoeni. 2002. Recent trends in disability and functioning among older adults in the United States: A systematic review. Journal of the American Medical Association 288:3137–46.
- Gill, T. M., H. G. Allore, T. R. Holford, and Z. Guo. 2004. Hospitalization, restricted activity, and the development of disability among older persons. Journal of the American Medical Association 292:2115-24.
- Hall, M. J., and C. J. DeFrances. 2003. 2001 National Hospital Discharge Survey. Advance Data from Vital and Health Statistics, no. 332. Hyattsville, MD: National Center for Health Statistics.
- Hatten, J. 1980. Medicare's common denominator: The covered population. Health Care Financing Review Fall: 53-64.
- House, J. S., K. R. Landis, and D. Umberson. 1988. Social relationships and health. Science 241:540-45.
- Iwashyna, T. J. 2001. In sickness and in health: Understanding the effects of marriage on health. Chicago: University of Chicago, Dissertation Library.
- Iwashyna, T. J., G. Brennan, J. X. Zhang, and N. A. Christakis. 2002. Finding married couples in Medicare claims data. Health Services and Outcomes Research Methodology 3:75-86.
- Iwashyna, T. J., J. Zhang, D. Lauderdale, and N. A. Christakis. 1998. A methodology for identifying married couples in Medicare data: Mortality, morbidity, and health care use among the married elderly. Demography 35:413-19.
- Kalra, L., A. Evans, L. Perez, A. Melbourne, A. Patel, M. Knapp, and N. Donaldson. 2004. Training caregivers of stroke patients: Randomised controlled trial. British Medical Journal 328:1099-1101.
- Kestenbaum, B. 1992. A description of the extreme aged population based on improved Medicare enrollment data. Demography 29:565-80.
- Kiecolt-Glaser, J. K., J. R. Dura, C. E. Speicher, O. J. Trask, and R. Glaser. 1991. Spousal caregivers of dementia victims: Longitudinal changes in immunity and health. Psychosomatic Medicine 53:345-62.
- Krumholz, H. M., M. J. Radford, Y. Wang, J. Chen, A. Heiat, and T. A. Marciniak. 1998. National use and effectiveness of the beta-blockers for treatment of elderly patients after acute Myocardial Infarction. Journal of the American Medical Association 280:623-29.
- Landrum, M. B., and K. Steward. 2004. Pathways to disability. NBER Working Paper no. 13304. Cambridge, MA: National Bureau of Economic Research.

Lauderdale, D., S. E. Furner, T. P. Miles, and J. Goldberg. 1993. Epidemiological uses of Medicare data. American Journal of Epidemiology 15:319–27.

Nicholas A. Christakis and Paul D. Allison

- Lauderdale, D. S., and J. Goldberg. 1996. The expanded racial and ethnic codes in the Medicare data files: Their completeness of coverage and accuracy. American Journal of Public Health 86:712–16.
- Lillard, L. A., and L. J. Waite. 1995. 'Til death do us part: Marital disruption and mortality. American Journal of Sociology 100:113–56.
- Maclure, M. 1991. The case-crossover design: A method for studying transient effects on the risk of acute events. American Journal of Epidemiology 133:144-53.
- Marshall, R. J., and R. J. Jackson. 1993. Analysis of case-crossover designs. Statistics in Medicine 12:2333-41.
- Martikainen, P., and T. Valkonen. 1996a. Mortality after the death of a spouse: Rates and causes of death in a large Finnish cohort. American Journal of Public Health 8:1087-93.
- . 1996b. Mortality after death of spouse in relation to duration of bereavement in Finland. Journal of Epidemiology and Community Health 50:264-68.
- McBean, A. M., J. L. Warren, and J. D. Babish. 1994. Measuring the incidence of cancer in elderly Americans using Medicare claims data. Cancer 73:2417–25.
- Mitchell, J. B., T. Bubolz, J. E. Paul, C. L. Pashos, J. J. Escarce, L. H. Muhlbaier, J. M. Wiesman, W. W. Young, R. S. Epstein, and J. C. Javitt. 1994. Using Medicare claims for outcomes research. Medical Care 32: JS38-JS51.
- Mittelman, M. S., S. H. Ferris, E. Shulman, G. Steinberg, A. Ambinder, J. A. Mackell, and J. Cohen. 1995. A comprehensive support program: Effect on depression in spouse-caregivers of AD patients. The Gerontologist 35 (6): 792–802.
- Parkes, C. M., B. Benjamin, and R. G. Fitzgerald. 1969. Broken heart: A statistical study of increased mortality among widowers. British Medical Journal 1:740-43.
- Pope, G. C., K. W. Adamache, E. G. Walsh, and R. K. Khandker. 1998. Evaluating Alternative Risk Adjusters for Medicare. Health Care Financing Review 20:109-
- Pruchno, R. A., M. H. Kleban, E. Michaels, and N. P. Dempsey, 1990. Mental and physical health of caregiving spouses: Development of a causal model. Journal of Gerontology 45 (5): P192-99.
- Pruchno, R. A., and S. L. Potashnik. 1989. Caregiving spouses: Physical and mental health in perspective. Journal of the American Geriatrics Society 37:697–705.
- Pruchno, R. A., and N. L. Resch. 1989a. Abberrant behaviors and Alzheimer's Disease: Mental health effects on spouse caregivers. Journal of Gerontology 44 (5): S177-82.
- -. 1989b. Husbands and wives as caregivers: Antecedents of depression and burden. The Gerontologist 29 (2): 159-65.
- Redelmeier, D. A., and R. J. Tibshirani. 1997. Association between cellulartelephone calls and motor vehicle collisions. New England Journal of Medicine 336:453-58.
- Romano, P. S., and D. H. Mark. 1994. Bias in the coding of hospital discharge data and its implications for quality assessment. Medical Care 32 (1): 81-90.
- Rosen, A., J. Wu, B. Chang, D. Berlowitz, A. Ash, and M. Moskowitz. 2000. Does diagnostic information contribute to predicting functional decline in long-term care? Medical Care 38:647-59.
- Russo, J., and P. P. Vitaliano. 1995. Life events as correlates of burden in spouse caregivers of persons with Alzheimer's Disease. Experimental Aging Research
- Russo, J., P. P. Vitaliano, D. D. Brewer, W. Katon, and J. Becker. 1995. Psychiatric disorders in spouse caregivers of care recipients with Alzheimer's Disease and

- matched controls: A diathesis-stress model of psychopathology. Journal of Abnormal Psychology 104 (1): 197-204.
- Schaefer, C., C. P. Quesenberry, and W. Soora. 1995. Mortality following conjugal bereavement and the effects of a shared environment. American Journal of Epidemiology 141:1142-52.
- Scholte op Reimer, W. J. M., R. J. de Haan, P. T. Rijnders, M. Limburg, and G. A. van den Bos. 1998. The burden of caregiving in partners of long-term stroke survivors. Stroke 29 (8): 1605-11.
- Schulz, R., and S. R. Beach. 1999. Caregiving as a risk factor for mortality: The caregiver health effects study. Journal of the American Medical Association 282 (23): 2215-19.
- Schulz, R., A. B. Mendelsohn, W. E. Haley, D. Mahoney, R. S. Allen, S. Zhang, L. Thompson, and S. H. Belle. 2003. End-of-life care and the effects of bereavement on family caregivers of persons with dementia. New England Journal of Medicine 349:1936-42.
- Shaw, W. S., T. L. Patterson, S. J. Semple, S. Ho, M. R. Irwin, R. L. Hauger, and I. Grant. 1997. Longitudinal analysis of multiple indicators of health decline among spousal caregivers. Annals of Behavioral Medicine 19 (2): 101-9.
- Siegel, K., V. H. Raveis, V. Mor, and P. Houts. 1991. The relationship of spousal caregiver burden to patient disease and treatment-related conditions. Annals of Oncology 2:511-16.
- Sprangers, M. A. G., E. B. De Regt, F. Andries, H. M. E. Van Agt, R. V. Bijl, J. B. De Boer, M. Foets, et al. 2000. Which chronic conditions are associated with better or poorer quality of life? Journal of Clinical Epidemiology 53:895-907.
- Steinhauser, K. E., N. A. Christakis, E. C. Clipp, M. McNeilly, L. McIntyre, and J. A. Tulsky. 2000. Factors considered important at the end of life by patients, family, physicians, and other care providers. Journal of the American Medical Association 284:2476-82.
- Suissa, S. 1998. The Case-Time-Control Design: Further assumptions and conditions. Epidemiology 9:441-45.
- Thoits, P. A. 1995. Stress, coping, and social support processes: Where are we? What next? Journal of Health and Social Behavior (Extra Issue): 53-79.
- Umberson, D. 1987. Family status and health behaviors: Social control as a dimension of social integration. Journal of Health and Social Behavior 28:306-19. -. 1992. Gender, marital status and the social control of health behavior. So-
- cial Science and Medicine 34:907-17.
- Vadimarsdottir, U., A. R. Helgason, C. J. Furst, J. Adolfsson, and G. Steineck. 2004. Awareness of husband's impending death from cancer and long-term anxiety in widowhood: A nationwide follow-up. Palliative Medicine 18:432-43.
- Waite, L., and M. Gallagher. 2000. The case for marriage. New York: Doubleday. Zarit, S. H., P. T. Todd, and J. M. Zarit. 1986. Subjective burden of husbands and wives as caregivers: A longitudinal study. The Gerontologist 26 (3): 260-66.
- Zhang, J., T. J. Iwashyna, and N. A. Christakis. 1999. The performance of different lookback periods and sources of information for Charlson comorbidity adjustment in Medicare claims. Medical Care 37:1128-39.